Effects of Postshock Atrial Pacing on Atrial Defibrillation Outcome in the Isolated Sheep Heart

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Background—Failed atrial defibrillation shocks are associated with organization of postshock activity and a substantial postshock electrical quiescence. We investigated the ability of a train of pacing stimuli to capture or locally entrain atrial myocardium during the quiescent period after low-energy shocks and to alter defibrillation outcome.

Methods and Results—High-resolution video imaging of near-defibrillation-threshold atrial shocks was performed in 12 Langendorff-perfused sheep hearts. A train of 10 pacing stimuli (10-ms pulse width, 200-ms cycle length) was coupled to the shock at various delays in 7 hearts. Coupling intervals of 40 to 130 ms were investigated for feasibility of capture of the first pacing stimulus. The success rate of capture was 0.08 ± 0.08, 0.43 ± 0.13, 0.73 ± 0.13, and 0.11 ± 0.1 for 40-, 60-, 80-, 100-, and 120-ms coupling intervals, respectively (P < 0.001). In 5 experiments, the coupling interval was fixed at 100 ms (highest success, see above), and the pacing stimulus amplitude was varied between 1.0, 2.0, and 4.0 V. Successful capture rates were 0.38 ± 0.08, 0.75 ± 0.08, and 0.64 ± 0.08, respectively (P < 0.003 for 1.0 versus 2.0 V, P = 0.2 for 2.0 versus 4.0 V). Rates of successful defibrillation for the groups without and with pacing were 0.56 ± 0.07 and 0.64 ± 0.04, respectively (P = 0.3). With capture of the first pacing stimulus, the rate of successful defibrillation rose to 0.75 ± 0.05 (P < 0.01); it remained unchanged without capture (0.48 ± 0.07 versus 0.56 ± 0.07 for no pacing).

Conclusions—Pacing during the quiescent period that follows defibrillation shocks is feasible. A pacing train whose first pacing stimulus successfully captures during the quiescent period of near-defibrillation-threshold shocks appears to alter the outcome. (Circulation. 1998;98:64-72.)

Key Words: pacing ■ electrophysiology ■ defibrillation ■ atrium

Both animal studies1–4 and human studies5–12 have demonstrated the safety and efficacy of an automated implanted atrial defibrillator. However, transvenous catheter cardioversion of AF has been limited by patient discomfort at energies well below defibrillation threshold.13 Furthermore, the long-term effects of repeated atrial shocks at intensities near defibrillation threshold are unknown. It therefore becomes advantageous to reduce atrial defibrillation energy requirements as much as possible. “Hybrid” or combination therapy in the form of pharmacotherapy, atrial pacing, or radiofrequency ablative techniques used in conjunction with defibrillation shocks may serve to reduce energy requirements.

In our laboratory,14 we have recently studied the effect of atrial defibrillation shocks on the dynamics of wave-front propagation using high-resolution optical mapping in the Langendorff-perfused sheep heart. We found that defibrillation shocks resulted in 1 of 4 outcomes: (1) immediate cessation of all atrial activity, (2) a single PSA, (3) organized activation for 0.8 to 1.5 seconds followed by termination, or (4) organized activity followed by degeneration into AF. For the defibrillation attempts that were unsuccessful or resulted in delayed termination, the cycle length of the first atrial activation was significantly longer than the AF cycle length (~170 versus ~140 ms). Furthermore, the activation sequences immediately after the shock were more synchronized than during AF, as measured by a reduction in a dispersion of activation index (see Methods section and Reference 14).

On the basis of these observations, we used a video imaging technique to study the role of pacing during this quiescent period as an adjunct to low-energy atrial defibrillation shocks. The specific objective of this study was to investigate the ability of a train of pacing stimuli to capture or locally entrain atrial myocardium during the quiescent period after low-energy (near-defibrillation-threshold) shocks. Our hypothesis was that a train of pacing stimuli whose first stimulus was able to capture during the quiescent period immediately after a shock would progressively entrain large
areas of the atria. Hence, large areas of atrial myocardium could come under local control. We further hypothesized that should this occur, the outcome of near-threshold but unsuccessful shocks could be altered and result in a successful outcome. In essence, a low-energy shock would serve to organize the atrial activity for a pacing train to progressively entrain the atria. Some of the results of this study have been reported elsewhere in abstract form.\textsuperscript{15}

**Methods**

**Langendorff-Perfused Sheep Heart Preparation**

Young sheep of either sex (18 to 25 kg) were anesthetized with sodium pentobarbital (35 mg/kg). The heart was rapidly removed through a midline sternotomy, then connected to a Langendorff apparatus. This method has been described elsewhere in detail.\textsuperscript{14,16} Briefly, the coronary arteries were continuously perfused via a cannula in the aortic root with warm (36°C to 38°C) Tyrode’s solution buffered to a pH of 7.4, under a constant flow of 115 to 140 mL/min, and bubbled with 95% O\textsubscript{2}/5% CO\textsubscript{2}. We ensured that the heart was in sinus rhythm and contracting forcefully and rhythmically at the initiation of the experiment. Two defibrillation catheters with 6-cm	extsuperscript{2} area coil electrodes (InControl Inc) were inserted via the venae cavae to the right atrial appendage and the coronary sinus. A custom-made programmable defibrillator (InControl Inc) was used to deliver a biphasic shock (duration of each phase was 3 ms). AF was induced by burst rapid atrial pacing from the epicardial surface of the right atrium adjacent to the sulcus terminalis at its intercaval region. Successful capture of the first paced beat was assessed on the basis of the following 3 criteria via optical mapping recordings: (1) earliest activation occurring at the site of the pacing stimulus, (2) propagation of the wave front away from the pacing site to rule out the possibility of a breakthrough near or adjacent to the pacing site, and (3) timing of the propagating wave in relation to the pacing stimulus. Preliminary experiments demonstrated that the latency of successful capture pacing stimuli could be as long as 40 ms (5 frames at 8.3 ms per frame). Timing of the pacing stimulus was marked during the optical recordings by use of a red LED timed to the pacing stimulus. Those pacing stimuli that did not capture were divided into 2 types based on the mechanism of failure to capture. Type I NC occurred when the impulse did not capture secondary to postshock refractoriness. Type II NC was designated as such if external wave fronts invaded the region of the pacing stimulus before the timing of the stimulus; ie, the local tissue was refractory as a result of immediately preceding activation.

**Pacing Amplitude**

After the results of the initial experiments, which tested timing of the pacing stimulus to the ability to capture, pacing amplitude of the pacing stimuli was varied to study its effect on the ability to capture after the shock in 5 more experiments. These studies were performed at 100-ms delay, the optimal delay as determined in the initial experiments (see Figure 2). Pacing amplitude was randomly varied between 0 (ie, no pacing), 1.0, 2.0, and 4.0 V in a balanced approach.

**Assessment of Outcome**

To examine the effect of pacing on shock outcome, the success rate of shocks with and without pacing were compared. Protocols included a defibrillation trial with no pacing for each series of defibrillation trials. This allowed direct comparison of outcomes for the pacing and no-pacing groups. Because the video imaging technique is immune to shock artifact, we were able to determine whether the first pacing stimulus successfully captured. Therefore, the pacing group was further stratified into those trials in which the first pacing stimulus successfully captured and those in which it did not capture; the success rates of these groups were also compared. Whether the first pacing stimulus successfully captured was compared.

**Statistical Analyses**

Continuous variables are reported as mean±SD and probabilities as proportion±SD. Continuous variables were compared by use of Student’s t-tests, and probabilities were compared by χ\textsuperscript{2} analysis.
Results

Mapping PSA

In their original optical mapping study of the effects of atrial defibrillation on wave propagation, Gray et al. described a period of approximately 110 ms after the shock during which no atrial activity was manifest. Thereafter, a short run of PSA waves could appear in succession and be followed either by quiescence and then sinus rhythm or by immediate resumption of AF. Similar results were obtained in our experiments.

The data illustrated in Figure 1 were taken from an episode of AF immediately before and after an unsuccessful defibrillation shock. Panel A shows the atrial electrogram obtained as the difference between the 2 epicardial leads, 1 located on the right atrium and the other on the left atrium. In Panel B, we present 3 isochrone maps obtained from the anterior surface of the right atrial free wall, as shown by the gray region in the top left diagram. The map on the top right corresponds to activity before the shock. Notice the complex sequence of activation, with multiple activation wave fronts and epicardial breakthroughs emerging, colliding, and mutually annihilating. The other 2 maps show the activation sequence during the first (middle) and second (right) PSAs, which appeared on the right atrial free wall at $t=75$ ms and $t=175$ ms, respectively, after the shock. During the first PSA, the mapped area was activated by a broad and homogeneous wave front that emerged near the lower portion of the sulcus terminalis (see diagram of preparation) and activated the entire right atrial anterior wall within 40 ms. The second PSA also emerged from the lower portion of the sulcus terminalis but moved somewhat more slowly, following a more tortuous route. In subsequent beats, activation became increasingly disorganized, and AF was reinitiated.

Figure 1. Electrogram and 8-ms isochrone map of failed defibrillation shock. A, Difference electrogram recorded for this shock. AF is seen before shock. First 2 PSAs are labeled 1 and 2, respectively. Postshock artifact is seen. After these 2 activations, disorganized electrical activity resumes. B shows 8-ms isochrone maps of segment of AF before shock and first 2 PSAs. Top left diagram in B shows area of optical recording in gray. After quiescent period of 75 ms, right atrial free wall is activated by a broad wave front that propagates homogeneously and activates entire surface in 41 ms. No activity is seen for a further 66 ms until a second wave front propagates from lower left of mapping region. It collides with another wave front at left. Right atrial surface is now activated by 2 wave fronts over 66 ms in a more heterogeneous pattern. Activity becomes increasingly complex until AF resumes. SVC indicates superior vena cava; IVC, inferior vena cava; ST, sulcus terminalis; and RAA, right atrial appendage.

Feasibility of Pacing After the Shock

Mapping the Pacing-Induced Wave Fronts

In Figure 3A, we present an electrogram obtained from an experiment during the application of a defibrillating shock that was followed by pacing at the lower left border of the tissue, near the sulcus terminalis (see asterisks in maps of panel B). Clearly, the first as well as all subsequent pacing stimuli (10 total) captured the atrium. This resulted in...
successful defibrillation. As in Figure 2, VF was seen after successful atrial defibrillation. Eight-millisecond isochrone maps of the first 2 paced beats after the shock are shown in Figure 3B. The asterisks designate the site of pacing. These stimuli resulted in broad wave fronts that activated the entire right atrial free wall in 66 and 58 ms, respectively. Pacing was not followed by resumption of fibrillation, and none of the stimuli gave rise to unidirectional block or initiated reentry over the right atrial free wall even though the first paced beat occurred 100 ms after an 80-V (0.25-J) shock and subsequent ones occurred at relatively brief cycle lengths (200 ms). In fact, in all experiments, despite successful capture of pacing stimuli of various amplitudes between 60 and 130 ms after shocks that ranged from 0.03 to 3.17 J (see below), in no case did the wave front propagating from a successfully captured pacing stimulus result in reentry within the imaging area.

Although it is difficult to ensure that propagation of these beats did not induce reentry elsewhere in the atria, beyond our field of view, it seems unlikely, because successful capture of the first paced beat was associated with successful outcome and therefore was unlikely to have been proarrhythmic in nature.

**Figure 3.** Successful defibrillation with successful capture of first and all pacing stimuli. A, After shock, pacing train is seen to successfully capture all 10 stimuli. B, Isochrone maps of first and second successfully captured stimuli 100 and 300 ms after shock. Activation propagates from broad, nonfragmented elliptical front. Although slowing of wave front is seen as crowding of isochrones, no reentry is induced.

**Success of Capture for Each Coupling Interval**

<table>
<thead>
<tr>
<th>Delay, ms</th>
<th>V</th>
<th>n</th>
<th>Capture</th>
<th>% Capture ±SD</th>
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<tbody>
<tr>
<td>40 and 50</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>0</td>
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<td>2</td>
<td>14</td>
<td>0</td>
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<td></td>
<td>1 and 2</td>
<td>22</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>60 and 70</td>
<td>1</td>
<td>9</td>
<td>2</td>
<td>0.22±0.14</td>
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<td></td>
<td>2</td>
<td>12</td>
<td>1</td>
<td>0.08±0.08</td>
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<tr>
<td></td>
<td>1 and 2</td>
<td>21</td>
<td>3</td>
<td>0.14±0.08</td>
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<tr>
<td>80</td>
<td>1</td>
<td>13</td>
<td>3</td>
<td>0.23±0.12</td>
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<td></td>
<td>2</td>
<td>14</td>
<td>6</td>
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<td>1 and 2</td>
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<tr>
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<td>10</td>
<td>4</td>
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<td></td>
<td>2</td>
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<tr>
<td></td>
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<td>12</td>
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<tr>
<td></td>
<td>2</td>
<td>9</td>
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<td>0.11±0.10</td>
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<tr>
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<td>1 and 2</td>
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<td>1</td>
<td>0.06±0.06</td>
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</table>

**Figure 4.** Percentage capture of first paced beats as a function of coupling interval from shock. A, At each coupling interval, rate of successful capture calculated as percent (%C) is presented for 1.0- and 2.0-V pacing amplitude and for combined data (1.0 and 2.0 V). Capture rate increases with coupling interval and is maximal at 160-ms coupling interval. Capture rate then drops abruptly at 120 ms. At each coupling interval, capture rate is higher for 2.0 than for 1.0 V and combined data (except for 60-ms coupling interval). Capture rate at 100-ms coupling interval and 2.0-V pacing amplitude was 0.73±0.13. B, Distribution of types of NC as a function of coupling interval. Percentage of each type of NC (type I vs type II) is plotted for each coupling interval. At short coupling intervals (40 to 80 ms), type I NCs predominated. Type II NCs increased in frequency with increasing coupling interval. At 100-ms coupling interval, predominant type of NC changed to type II.

**Coupling Interval**

In the first group of 5 experiments, we analyzed the ability of the first paced beat to capture after the shock as a function of the coupling interval. The first stimulus of the pacing train was coupled to the shock at intervals of 40, 50, 60, 70, 80, 100, 120, and 130 ms. Success of capture for each coupling interval is tabulated in the Table and represented graphically in Figure 4A. From these data, it is evident that as the coupling interval of the first pacing stimulus increased, the ability to successfully capture increased, until the success rate peaked at 100 ms. The success rate subsequently decreased dramatically at 120 ms. At these pacing amplitudes, the maximal capture rate was 0.73±0.13 at a delay of 100 ms and
pacing amplitude of 2.0 V. The data suggested 2 different mechanisms by which pacing stimuli at each coupling interval failed to capture, depending on the coupling interval. We labeled these mechanisms “type I” and “type II.” In type I, the first pacing stimulus failed to capture at short coupling intervals because its occurrence was too early after the shock. In type II, at long coupling intervals, interference by post-shock activity reduced the ability of the first pacing stimulus to capture. We compared the rate of type I versus type II NC at each coupling interval. This is represented in Figure 4B, in which we have plotted the number of each type of NC as a percentage of the total number. The percentages at each coupling interval therefore add to 100%. At short coupling intervals, the pacing stimulus was unable to capture because of postshock refractoriness; at 40 ms, 94.9±3.5% of the failures to capture were type I. As the coupling interval was increased, the mechanism of NC shifted to a greater proportion of type II; ie, at 100 ms, 64±6.6% of the failures to capture were due to encroachment by a postshock wave front. At longer coupling intervals, the relative frequencies of these phenomena did not appear to change. The crossover point of these curves (see Figure 4B) occurred between 80 and 100 ms.

**Pacing Amplitude**

In these initial experiments, at a pacing amplitude of 2.0 V and a coupling interval of 100 ms, ≈73% of the pacing stimuli captured. Therefore, in 5 additional experiments, we attempted to increase this probability by increasing the pacing stimulus amplitude. At a fixed coupling interval of 100 ms, we compared 1.0-, 2.0-, and 4.0-V pacing amplitudes (n=34, 32, and 33, respectively). These data are represented graphically in Figure 5A. The ability of the first pacing stimulus to capture increased sharply when the pacing amplitude was increased from 1.0 to 2.0 V (0.38±0.08 to 0.75±0.08, P<0.003). However, no incremental improvement in successful capture rate occurred with a subsequent increase in pacing amplitude to 4.0 V compared with 2.0 V (0.75±0.08 versus 0.64±0.08, P=0.2). The decrease in capture rate from 2.0 to 4.0 V was not statistically different. To further analyze this difference, we compared the types of NC in both groups. The 4.0-V pacing group had a larger rate of type II NC (9 of 12, versus 5 of 8 for 2.0 V). This difference presumably occurred by chance alone. When the rate of successful capture was compared after these events were removed (see Figure 5B), the successful capture rates were similar (0.89±0.06 at 2.0 V versus 0.88±0.07 for 4.0 V, P=NS). Furthermore, we compared the rate of type I NCs in the 3 groups. We felt this to be appropriate because the optimal pacing strategy would limit the number of type I NCs; type II NCs presumably could not be altered by the pacing stimuli. The rates of type I NCs for pacing amplitudes of 1.0, 2.0, and 4.0 V were 0.43±0.11, 0.38±0.17, and 0.25±0.13, respectively (Figure 5C).

**Outcome**

To determine whether pacing as an adjunct to defibrillation shocks could alter outcome, we compared the rate of successful defibrillation for the no-pacing and pacing groups (see Figure 6). The rate of successful defibrillation in the no-pacing group was 0.56±0.07 (n=54), reflecting our desire to be near defibrillation threshold. In comparison, the rate of success for shocks with pacing immediately after the shock was 0.64±0.04 (n=119, P=0.3). This difference was not statistically significant. However, the optical mapping technique allowed us to further group the shocks with pacing into those whose first pacing stimulus did or did not capture. The success rate of defibrillation associated with successful capture of the first paced beat was 0.75±0.05 (n=69, P<0.01 compared with no pacing). The success rate associated with NC of the first paced beat, 0.48±0.07, was not different from the no-pacing rate (n=50, P=0.3). The defibrillation energies for the corresponding groups in Figure 6A are represented graphically in Figure 6B. No statistical differences were present between the energies.

**Dynamics of Interaction of Aftershocks With Captured Pacing Stimuli**

Figures 7 and 8 demonstrate the dynamics of postshock activity and the interaction of PSA with successfully captured pacing stimuli. In Figure 7, successful capture by the first pacing stimulus resulted in collision and mutual annihilation of a PSA that appeared on the right atrial surface at t=108 ms.
after the shock. Note that the electrogram of the first PSA was different from the remainder of the recorded pacing electrograms. All subsequent pacing stimuli captured, and the result was successful defibrillation. An 8-ms isochrone map of the collision is shown in Figure 7B. In Figure 8, we demonstrate that a complex interplay can occur between the pacing-induced wave fronts and postshock wave fronts. Immediately after the shock, the first pacing stimulus captures and the resulting wave front collides with and results in the annihilation of the first PSA wave front. A second PSA wave propagated from the superior edge of the preparation to invade the pacing region before the second pacing stimulus. Hence, the second pacing stimulus was unable to capture. However, the third pacing stimulus and all subsequent pacing stimuli did capture.

Discussion
Feasibility of Pacing Immediately After the Shock
The most important result of this study is the demonstration that successful capture of the atria during pacing after a shock increases the effectiveness of atrial defibrillation. The video imaging approach used in this study allowed us to record the transmembrane potentials simultaneously from >20 000 sites from the epicardial surface of the right atrium during AF and defibrillation as well as during subsequent pacing. In contrast to multiple-electrode mapping, video imaging is immune to shock-induced signal distortion and is able to distinguish propagating fronts that are initiated by pacing stimuli from wave fronts that result from postshock activity. Indeed, our results show that it is possible to successfully capture atrial myocardium by pacing as early as 60 ms after a defibrillation shock.

The success rate of capture was dependent on the amplitude of the pacing stimulus and the coupling interval of the pacing stimulus to the shock. The optimal coupling interval appeared to be between 80 and 100 ms. At coupling intervals shorter than this window, postshock refractoriness limited the ability to capture. At longer coupling intervals, the encroachment of postshock activity into the vicinity of the pacing site limited the success rate. With 1.0- and 2.0-V stimuli, success rates were limited to \(\approx 75\%\). Even though the pacing stimuli were increased to 4.0 V specifically at the optimized coupling interval, 100 ms, rates of successful capture remained unchanged. Therefore, these data suggest a limitation of rates of successful capture of \(\approx 75\%\) despite optimization of both coupling interval and pacing amplitude.

Outcome
We tested the hypothesis that successful capture of a significant portion of the atrium with a pacing train might alter the outcome of near-threshold shocks. During the course of investigation of the feasibility of successful capture after the shock, we compared the outcome of shocks in the no-pacing and pacing groups. Although overall, the success rate of

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**Figure 6.** Defibrillation shock outcome for different pacing strategies. A, Percentage of successful defibrillation shocks is plotted for no-pacing strategy, pacing strategy, with successful capture of first paced stimulus (C), and failure to successfully capture (NC). Success rate was 0.55 ± 0.07 for no-pacing group, which demonstrates that near-threshold shocks were delivered as per protocol. With pacing, success rate rose to 0.64 ± 0.04 (\(P<0.01\) vs no-pacing). When pacing strategy was stratified according to successful capture of first paced stimulus, success rate increased to 0.75 ± 0.05 (\(P<0.01\) vs no-pacing strategy). When first pacing stimulus did not capture, successful defibrillation occurred, 0.48 ± 0.07. B, Energies in joules for each group in A. No difference was found.

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**Figure 7.** Successful defibrillation with collision of aftershock with first paced wave front. A, Electrogram as in Figures 1 to 3, which corresponds to electrical signal for isochrone maps as seen in B. Notice that first electrogram complex after shock is different from subsequent complexes as a result of collision of postshock activity and pacing-induced wave front. B, Isochrone map of collision of first paced wave front with PSAs over surface of right atrial free wall. Collision results in mutual annihilation of both waves. All subsequent paced stimuli resulted in homogeneously propagating waves, as in Figure 3B.
Postshock Atrial Pacing

The current limitations of our experimental design, it is impossible to confirm or disprove this hypothesis.

It is also possible that the source of the postshock activity is focal in origin from an automatic source induced by the shock. Studies of ventricular defibrillation have suggested that shocks may induce ectopic activity.22,23 In the atria, where interval should result in progressively enlarging areas of entrainment and possible pacing-mediated termination of AF. However, in the above-mentioned studies, the area of entrainment was limited by the block of pacing-induced wave fronts as they propagated away from the pacing site or by collision of the pacing-induced wave fronts with fibrillation wave fronts. Regional control was lost by pacing either too slowly, in which case fibrillatory wave fronts invaded the pacing region, or too rapidly, in which case local reentry circuits were induced that reentered the pacing region before the next pacing stimulus. The window of cycle lengths during which entrainment occurred was 16±5 ms. Pacing termination of AF did not occur in any of those experiments. Although never demonstrated, it is at least theoretically possible that AF could be pacing-terminated if a sufficiently large area of the atria was entrained by increasing either the number of pacing sites or the area of entrainment for each pacing site. Previous work in our laboratory has shown that failed defibrillation shocks are followed by a 110-ms quiescent period and by organized activity on the right atrial free wall.14 The results from this study suggest that a pacing train whose first pacing stimulus successfully captures during the quiescent period has the ability to alter outcome. The wave front induced by capture of the first pacing stimulus propagated in a homogeneous, broad front over the entire mapped surface. As such, the right atrial free wall was effectively “entrained” in an organized manner for the 2-second duration of the pacing train. It is therefore possible that the remaining atrial tissue was insufficient to allow the reinitiation of AF.

Impact on Postshock Activity

The source of the postshock activity remains unclear. There are 3 likely possibilities: (1) The shock induces reentrant activity in an area of critical potential gradient in a manner similar to the critical-point hypothesis for ventricular shocks15; (2) the shock triggers focal activity from areas in the atria with pacemaker activity, either from the right atrium or elsewhere; and (3) the shock fails to completely terminate AF, and a remaining wavelet lingers at some distant point from the recording area. In the first and third cases, it is possible that the paced wave fronts propagate toward and collide with postshock activity, resulting in the mutual annihilation of both wave fronts. This phenomenon has been documented to occur at least over the right atrial free wall (see Figure 8). Continued pacing would potentially result in the progressive invasion of the source of activity and its possible termination either directly or by driving the source of rotating activity to a boundary. It has been demonstrated that externally induced wave fronts can collide with and terminate rotating sources of activity (spirals) in both isolated atrial and ventricular preparations.20,21 This can occur through collision and mutual annihilation of activity or by shifting the spiral core close to a boundary, which results in termination. Given the current limitations of our experimental design, it is impossible to confirm or disprove this hypothesis.

Possible Mechanisms for Alteration in Outcome: Entrainment

Recently, it was shown that AF has a partially if not fully excitable gap by the demonstration that rapid pacing could locally entrain a portion of the atrium during AF.17,18 In an open-chest canine model of AF, pacing at cycle lengths slightly shorter or longer than the median AF interval and at pacing amplitudes 6 times diastolic threshold could repeatedly capture and thus entrain an area of ~4-cm diameter in the left atrium. Theoretically, regional entrainment of AF at a pacing cycle length slightly shorter than the median AF interval should result in progressively enlarging areas of entrainment and possible pacing-mediated termination of AF. However, in the above-mentioned studies, the area of entrainment was limited by the block of pacing-induced wave fronts as they propagated away from the pacing site or by collision of the pacing-induced wave fronts with fibrillation wave fronts. Regional control was lost by pacing either too slowly, in which case fibrillatory wave fronts invaded the pacing region, or too rapidly, in which case local reentry circuits were induced that reentered the pacing region before the next pacing stimulus. The window of cycle lengths during which entrainment occurred was 16±5 ms. Pacing termination of AF did not occur in any of those experiments. Although never demonstrated, it is at least theoretically possible that AF could be pacing-terminated if a sufficiently large area of the atria was entrained by increasing either the number of pacing sites or the area of entrainment for each pacing site. Previous work in our laboratory has shown that failed defibrillation shocks are followed by a 110-ms quiescent period and by organized activity on the right atrial free wall.14 The results from this study suggest that a pacing train whose first pacing stimulus successfully captures during the quiescent period has the ability to alter outcome. The wave front induced by capture of the first pacing stimulus propagated in a homogeneous, broad front over the entire mapped surface. As such, the right atrial free wall was effectively “entrained” in an organized manner for the 2-second duration of the pacing train. It is therefore possible that the remaining atrial tissue was insufficient to allow the reinitiation of AF.

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It is also possible that the source of the postshock activity is focal in origin from an automatic source induced by the shock. Studies of ventricular defibrillation have suggested that shocks may induce ectopic activity.22,23 In the atria, where
a greater abundance of "pacemaker"-type tissue resides, this mechanism may be even more tenable. If, indeed, the postshock activity is automatic in nature and induced by the shock, it is reasonable to believe that paced wave fronts could invade and suppress these sources. The present study does not address the nature of induction of postshock activity or its relation to failed defibrillation. However, regardless of the mechanism, it is theoretically possible that externally induced wave fronts have the potential to result in annihilation or suppression of this activity.

**Advantages of Video Imaging**

The video imaging technique used in these studies offered several unique advantages. First, video imaging allowed the recording of transmembrane signals during high-voltage defibrillation shocks because there was no contamination by electrical artifact. In addition, methoxyverapamil removed the mechanical contraction associated with shocks, such that recordings were not corrupted by motion artifact. Second, video imaging provides high spatial resolution with simultaneous recordings from 10,000 to 30,000 sites. This is 2 orders of magnitude greater than other cardiac mapping systems and allowed us to determine with a high degree of accuracy whether the wave fronts that appeared on the epicardium immediately after the shock were indeed from the pacing site or spontaneous activity from elsewhere. Moreover, the interaction of pacing-induced wave fronts with postshock activity could be studied with high spatial resolution.

**Limitations of the Approach**

The experiments in which optical recordings were used to study the feasibility of pacing were performed in the presence of ACh (10^-6 mol/L) to facilitate the induction of AF. The absolute values of the coupling intervals for pacing after the shock and pacing amplitudes may not be applicable to experiments without ACh. It is likely that pacing after the shock without ACh is feasible; however, this will need documentation.

Our model is that of AF induced by burst pacing in the Langendorff-perfused isolated sheep heart after infusion of ACh. As such, ours is a model of acute AF in a normal heart. Hence, extrapolation of these data to the human condition in which atrial disease causes dilatation and/or patchy fibrosis is made with caution. We limited our pacing site to the optical field of view on the right atrial free wall to investigate the ability to capture. Hence, other pacing sites were not investigated. Other pacing sites, especially on the left atrium, may be more or less successful in altering outcome. The effects of pacing at other sites, especially those in the left atrium, after defibrillation shocks warrants further study, ideally studies in which the effects of pacing can be recorded simultaneously from both atria.

The optical recordings were made exclusively from the epicardial surface of the right atrium. There is considerable evidence that transmural propagation occurs during AF. It is unlikely that transmural propagation continued during the quiescent period for 95 ms without propagation to the epicardium. Furthermore, when epicardial activity did reappear after the shock, it did not occur as an epicardial breakthrough but rather from the edges of the field of view. However, video imaging was performed exclusively from the right atrial free wall. Therefore, the dynamics of wave propagation and interaction of paced wave fronts with other postshock wave fronts could only be studied in the field of view of the video camera. In an attempt to understand our results, we extrapolated our observations of the dynamics of wave propagation of paced stimuli and the interaction of pacing-induced wave fronts with postshock wave fronts to the entire surface of the atria. This obviously is less than ideal. Currently, however, no cardiac mapping systems exist that can record atrial defibrillation simultaneously from all surfaces of the atria with sufficient resolution and without shock artifact.

**Clinical Implications**

The impact of adjuvant approaches to atrial defibrillation shocks is currently under investigation. This study provides evidence that it is feasible to deliver a pacing train immediately after an atrial defibrillation shock with a reasonable expectation that the first pacing stimulus will capture. Furthermore, we have presented evidence that pacing during the quiescent period that follows atrial defibrillation shocks alters outcome of near-defibrillation threshold shocks. We introduce a new method by which pacing may be used in conjunction with defibrillation shocks. However, further studies are required to determine whether this "hybrid" therapy is a reasonable approach in conjunction with implanted atrial defibrillators to alter outcomes in humans.

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Effects of Postshock Atrial Pacing on Atrial Defibrillation Outcome in the Isolated Sheep Heart
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