Reduction of Atrial Defibrillation Threshold With an Interatrial Septal Electrode

Xiangsheng Zheng, MD; Michael E. Benser, PhD; Gregory P. Walcott, MD; Steven D. Girouard, PhD; Dennis L. Rollins, MS; William M. Smith, PhD; Raymond E. Ideker, MD, PhD

Background—The standard lead configuration for internal atrial defibrillation consists of a shock between electrodes in the right atrial appendage (RAA) and coronary sinus (CS). We tested the hypothesis that the atrial defibrillation threshold (ADFT) of this RAA→CS configuration would be lowered with use of an additional electrode at the atrial septum (SP).

Methods and Results—Sustained atrial fibrillation was induced in 8 closed-chest sheep with burst pacing and continuous pericardial infusion of acetyl-β-methylcholine. Defibrillation electrodes were situated in the RAA, CS, pulmonary artery (PA), low right atrium (LRA), and across the SP. ADFTs of RAA→CS and 4 other lead configurations were determined in random order by use of a multiple-reversal protocol. Biphasic waveforms of 3/1-ms duration were used for all single and sequential shocks. The ADFT delivered energies for the single-shock configurations were 1.27±0.67 J for RAA→CS and 0.86±0.59 J for RAA+CS→SP; the ADFTs for the sequential-shock configurations were 0.39±0.18 J for RAA→SP/CS→SP, 1.16±0.72 J for CS→SP/RAA→SP, and 0.68±0.46 J for RAA→CS/LRA→PA. Except for CS→SP/RAA→SP versus RAA→CS and RAA→CS/LRA→PA versus RAA+CS→SP, the ADFT delivered energies of all of the configurations were significantly different from each other (P<0.05).

Conclusions—The ADFT of the standard RAA→CS configuration is markedly reduced with an additional electrode at the atrial SP. (Circulation. 2000;102:2659-2664.)

Key Words: defibrillation ■ atrium ■ electrophysiology

Electrical cardioversion remains a first-line therapy for atrial fibrillation (AF).1,2 Antiarrhythmic drugs and curative surgical and ablative therapies are still of limited efficacy, and their incidence of adverse effects is not insignificant.3–5 Because cardioversion with intrathoracic electrodes is more efficacious than transthoracic defibrillation6 and the implantable atrial defibrillator has been shown to be feasible,7 many recent investigations have focused on minimizing the energy requirements of internal cardioversion through novel waveforms or electrode configurations.8–12 Still, the most efficient cardioversion strategy clinically used, with biphasic waveforms and lead systems in which shock fields encompass both atria, requires shock strengths that are not sufficiently low to be tolerated by most patients without sedation.1,2,13–15

Atrial defibrillation may require a minimum potential gradient to be generated by the shock throughout the atrial myocardium, as does ventricular defibrillation throughout the ventricles. The lowest-gradient areas, usually distant from the defibrillation electrodes, are the areas from which earliest activations arise after unsuccessful shocks.16,17 The region of earliest activation, and presumably lowest gradient, with a right atrial appendage–to–coronary sinus defibrillation configuration (RAA→CS) is in the posterior left atrium.18 An electrode configuration with an interatrial septal (SP) electrode approximately midway between the RAA and CS electrodes should increase the potential gradient in this region. The purpose of this study was to determine whether the atrial defibrillation threshold (ADFT) could be reduced by use of configurations with an atrial SP electrode.

Methods
The use of experimental animals in this study was approved by the Institutional Animal Care and Use Committee at the University of Alabama at Birmingham. All studies were performed in accordance with the guidelines established in the “Position of the American Heart Association on Research Animal Use” adopted by the American Heart Association on November 11, 1984 (Circulation. April 1985).

Of 11 adult sheep, 8 completed the experimental protocol (body mass 41±6 kg, heart mass 217±8 g). Only the data from these 8 animals are reported.

Animal Preparation
As a preanesthetic agent, a 1-to-1 mixture of tiletamine and zolazepam (8 to 10 mg/kg) was given intramuscularly. Approximately 10 minutes later, thiopental (2 to 6 mg/kg) was administered as a slow intravenous bolus. The animal was laid on its back on a fluoroscopy table, intubated, and placed on a volume-cycled ventilator (tidal volume 15 to 20 mL/kg) with a 4% isoflurane/oxygen mixture at a rate of 8 to 12 breaths per minute. The isoflurane concentration was later decreased to 1.5% to 3.5% to maintain a deep surgical plane of anesthesia. Ventilator settings were adjusted to maintain blood gases.
A catheter (Endotak DSP, Guidant Corp) was inserted through the other jugular vein with its defibrillation electrodes in the right ventricle and superior vena cava, and a tip electrode in the right ventricle for ventricular pacing. A 3-wire subcutaneous array was inserted over the left side of the heart. In the event of ventricular tachyarrhythmias, these electrodes were used to rescue the animal.

**Figure 2.** Fluoroscopic images of positions of defibrillation electrodes. Left anterior oblique $\sim 30^\circ$ (A) and right anterior oblique $\sim 30^\circ$ (B) projections show electrodes in RAA, CS, right ventricle, and across atrial SP.

### Induction of Atrial Fibrillation

To allow AF to be maintained, acetyl-$\beta$-methylcholine chloride (Sigma Chemical Co) was continuously infused into the pericardial space. The pericardial space was approached percutaneously under fluoroscopic guidance with a 3-in-long 16-gauge needle from just inferior to the right subxiphoid position with the animal turned $\sim 20^\circ$ toward the right side. When the needle was confirmed by contrast injection to be within the pericardial space, a guidewire was gently inserted through it into the pericardial space. The pericardial location for the guidewire was confirmed by inability to move it outside the fluoroscopic image of the heart silhouette. After removal of the needle, a 6F sheath was advanced into the pericardial space over the wire. After flushing with acetyl-$\beta$-methylcholine chloride, a 4F pigtail catheter was inserted through the sheath. Typically, the catheter tip was advanced near the left atrium and the sheath was removed.

Acetyl-$\beta$-methylcholine chloride solution (1 g/250 mL saline) was infused at a rate of 20 $\mu$L/min with a microinfuser. Burst pacing...
TABLE 1. Test Configurations

<table>
<thead>
<tr>
<th>First Shock</th>
<th>Second Shock</th>
<th>Biphasic Waveform</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anode*</td>
<td>Cathode*</td>
<td>Anode*</td>
</tr>
<tr>
<td>A1</td>
<td>RAA + CS</td>
<td>SP</td>
</tr>
<tr>
<td>A2</td>
<td>RAA</td>
<td>CS</td>
</tr>
<tr>
<td>A3</td>
<td>CS</td>
<td>SP</td>
</tr>
<tr>
<td>B</td>
<td>RAA</td>
<td>CS</td>
</tr>
<tr>
<td>C</td>
<td>RAA</td>
<td>CS</td>
</tr>
</tbody>
</table>

*First-phase anode and cathode.

Defibrillation Waveforms and Lead Configurations

Once AF was maintained for >10 minutes, the defibrillation protocol was begun. Briefly, a monophasic, truncated-exponential waveform was produced by a programmable defibrillator (HVS-02, Ventritex, Inc) with a discharge capacitance of 150 μF. This monophasic waveform was divided into a biphasic waveform by a set of high-voltage, cross-point switches; for sequential shocks, 2 biphasic, truncated-exponential waveforms were created with the use of an additional set of cross-point switches. Each biphasic waveform had a first-phase duration of 3 ms and a second-phase duration of 1 ms. The interval between each phase of the biphasic waveforms and between the 2 biphasic waveforms of sequential shocks was 0.02 ms. All phases of the waveforms exhibited decaying voltage from a form had a first-phase duration of 3 ms and a second-phase duration of 1 ms. The interval between each phase of the biphasic waveforms and between the 2 biphasic waveforms of sequential shocks was 0.02 ms. All phases of the waveforms exhibited decaying voltage from a single capacitor, in which the trailing-edge voltage of each preceding phase was equal to the leading-edge voltage of the succeeding phase.

For each test shock, the leading-edge voltage and current were recorded, and the impedance and delivered energy were computed by a waveform analyzer (DATA 6100, Data Precision). The stored energy for each shock was calculated as \( CV^2/2 \), in which \( C \) is the discharge capacitance (150×10^-6 F) and \( V \) is the commended peak voltage of the shock. The ADFT leading-edge voltage, current, impedance, and delivered and stored energies were derived from the ADFT shock.

Data Acquisition

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Figure 3. ADFT leading-edge voltages. Bars give mean and SD voltages. Percentages are mean ± SD by which A2 is lower than other configurations. Leading-edge voltage of configuration A2 is significantly lower than each of others.

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In each animal, the ADFTs of 5 test configurations (Table 1) were determined. Three configurations that used the SP electrode were named A1, A2, and A3. The 2 others were named B and C. The order of determining the ADFTs was randomized as follows. The order among A, B, and C was initially randomized, and then the order of A1, A2, and A3 (within A) was randomized. ADFTs of the SP electrode configurations were measured consecutively to obviate the need for repositioning this electrode. During ADFT testing, passive electrodes not delivering any shock for that configuration were removed. Shock delivery was synchronized to right ventricular pacing at a cycle length of 250 to 400 ms, depending on the intrinsic ventricular rate during AF. Shocks were delivered 20 ms after the eighth pacing pulse.

Each ADFT was determined by a multiple-reversal method with an initial commended peak voltage of 100 V and step sizes of 40/20/10 V. If the initial shock failed, the next and subsequent shock voltages were increased by 40 V until a shock succeeded. After the first shock that successfully terminated AF, voltages of subsequent shocks were decreased by 20 V until a shock failed. Then shock voltages were increased by 10 V until a shock succeeded again. Conversely, if the initial shock succeeded, subsequent shock voltages were decreased by 40 V until a shock failed. Then shock voltages were increased by 20 V until a shock succeeded, after which shock voltages were decreased by 10 V until a shock failed again. The last successful shock of the third reversal was deemed the ADFT shock for that configuration. The ADFT characteristics for each configuration were derived from this ADFT shock. All test shocks were applied after AF was sustained for 1 minute. When a test shock failed, a rescue shock of 200 to 300 V was given. A 1- to 2-minute period of sinus rhythm was allowed before the next AF induction.

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Results are expressed as mean ± SD. The overall effects of the 5 test configurations on each ADFT characteristic and the impedance differences of current pathways were tested by repeated-measures ANOVA. Differences between the 5 configurations were tested by Duncan’s multiple range test. A value of \( P<0.05 \) was considered significant.

Results

Reproducible, sustained AF was induced in all animals. The ventricular rates in sinus rhythm before and 20 minutes after administration of acetyl-β-methylcholine chloride were similar (112±8 versus 109±11 bpm, respectively, \( P=NS \)). The drug significantly lowered the sinus-rhythm systolic and diastolic blood pressure, however (107±8 versus 84±7 and 83±4 versus 62±5 mm Hg, respectively). During AF, the ventricular rate was 131±36 (range 80 to 178) bpm. In 1 sheep with an unusually long sinus recovery time, temporary postshock atrial pacing was performed.

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ADFT Leading-Edge Voltages

The ADFT leading-edge voltage of configuration A2 was significantly lower than each of the other 4 configurations (Figure 3). The ADFT leading-edge voltage of configuration A1 was significantly lower than that of configurations A3 and B, but not C. The ADFT leading-edge voltage of configuration B was significantly higher than each of the other 4 configurations.

ADFT Leading-Edge Currents

The ADFT leading-edge current of configuration A2 was significantly lower than that of A1, A3, and B and trended lower than that of C (Figure 4). The ADFT leading-edge current of configuration C was significantly lower than that of
configurations A1, A3, and B. The ADFT leading-edge current of configuration A1 was significantly higher than each of the other configurations.

Configuration Impedances
Impedances of the same current pathway in different test configurations were not significantly different. The impedance of the RAA₁-CS₃-SP current pathway was lower than that of all of the other pathways tested (Table 2). The impedance of CS₃-SP was significantly lower than that of RAA₃-CS, and the impedances of CS₃-SP and RAA₃-SP were both significantly lower than that of RAA₁-CS. The impedance of LRA₃-PA was significantly lower than that of RAA₁-CS.

ADFT Shock Energy
Configuration A2 had a significantly lower ADFT delivered energy than each of the other 4 test configurations (Figure 5). Configuration C had significantly lower ADFT energy than that of configurations A3 and B and trended lower than that of A1. The ADFT delivered energy of configuration C was 50±6% lower than that of configuration B. Configuration A1 had significantly lower ADFT energy than configurations A3 and B (by 18±52% and 37±15%, respectively). The differences in ADFT delivered energy between configurations A3 and B was not significant. The ADFT delivered energies for each animal are shown in Figure 5B. On each animal, the ADFT delivered energy of configuration A2 was lower than that of configuration B. The configuration A2 ADFT delivered energies of all 8 animals were lower than the configuration B mean ADFT delivered energy, as well.

The ADFT stored energies of configurations A1, A2, A3, B, and C were 1.32±0.88, 0.55±0.24, 1.66±0.94, 2.42±1.18, and 0.98±0.61 J, respectively. Except for A1 versus A3, A1 versus C, and A2 versus C, the ADFT stored energies for all of the test configurations were significantly different for each other.

Discussion
This study demonstrates that, in a sheep model of sustained AF, atrial defibrillation configurations that used an additional electrode at the interatrial SP required significantly lower energy than the standard RAA₁-CS configuration. The ADFT delivered energy of RAA₁-CS was 0.86±0.59 J, 37±15% lower than that of RAA₁-CS (1.27±0.67 J), and the ADFT delivered energy of the sequential-shock configuration RAA₁-CS/SP-CS was 0.39±0.18 J, 68±8% lower than that of RAA₁-CS.

Previous experimental and clinical studies found the most efficient simple single-shock configuration to be RAA₁-CS. 22,23 This is the most common configuration for in-hospital internal cardioversion and is the standard config-

### TABLE 2. Impedances of the Current Pathways

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Current Pathways</th>
<th>Impedance, Ω</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Single RAA₁-CS₃-SP</td>
<td>25±3</td>
</tr>
<tr>
<td>A2</td>
<td>First RAA₁-SP</td>
<td>46±3</td>
</tr>
<tr>
<td></td>
<td>Second CS₃-SP</td>
<td>34±4</td>
</tr>
<tr>
<td>A3</td>
<td>First CS₃-SP</td>
<td>35±4</td>
</tr>
<tr>
<td></td>
<td>Second RAA₁-SP</td>
<td>45±4</td>
</tr>
<tr>
<td>B</td>
<td>Single RAA₁-CS</td>
<td>54±6</td>
</tr>
<tr>
<td>C</td>
<td>First RAA₁-CS</td>
<td>54±7</td>
</tr>
<tr>
<td></td>
<td>Second LRA₃-PA</td>
<td>49±4</td>
</tr>
</tbody>
</table>
vation used by the first stand-alone implantable atrial defibrillator. With this RAA→CS configuration, ADFTs in humans without a significant history of AF are 1.5 to 2.5 J and are significantly greater in patients with chronic AF.1,2,4–27 Unfortunately, shocks of this magnitude are uncomfortable to unsedated patients; although a “discomfort threshold” has not been clearly defined with this or any other shock configuration, it appears that shocks need to be well below 1 J to be well tolerated in most patients.1,2,13–15

Cooper and colleagues have reported ADFTs < 1 J in a sheep model using a sequential, 2-current-pathway configuration. In this study, the RAA→distal CS/PA→proximal CS ADFT (0.36 ± 0.13 J) was significantly lower than that of the standard single-shock RAA→distal CS configuration (1.29 ± 0.26 J). In humans, a related sequential-shock configuration, RAA→distal CS/left subclavian vein→proximal CS, was tested and found to have lower ADFTs than RAA→distal CS (2.0 ± 0.4 versus 5.1 ± 1.8 J), as well.27

In the present study, the ADFT of RAA→CS/LRA→PA is similar to the RAA→distal CS/PA→proximal CS configuration studied by Cooper and colleagues. We used an electrode in the LRA near the ostium of the CS instead of one in the proximal CS because our CS catheter lacked an electrode at the CS ostium. In the present study, the RAA→CS/LRA→PA ADFT (0.68 ± 0.46 J) was 50 ± 9% lower than that of the RAA→CS configuration (1.27 ± 0.67 J). In the study by Cooper et al, the RAA→distal CS/PA→proximal CS configuration exhibited an ADFT energy 74% lower than that of RAA→distal CS. Thus, the RAA→CS/LRA→PA configuration did not exhibit quite the relative reduction in ADFT compared with the control RAA→CS configuration as the analogous configuration tested in the study by Cooper et al. Still, the RAA→SP/CS→SP ADFT, the most efficacious sequential configuration tested with the SP electrode in this study, was not only 68 ± 8% lower than the standard RAA→CS configuration but also 36 ± 15% lower than the RAA→CS/LRA→PA configuration.

In our model, reversing the order of the sequential shocks from RAA→SP/CS→SP to CS→SP/RAA→SP greatly increased the ADFT. The impedance of the RAA→SP pathway was 46 Ω, whereas that of the CS→SP pathway was 35 Ω (Table 2), which might be attributed to the facts that (1) the RAA electrode (4 cm) was shorter than the CS electrode (6 cm) and (2) the distance between the SP and CS electrodes was shorter than that between the SP and RAA electrodes. When the larger first shock of the sequential stimulus was delivered to the pathway with higher impedance, probably encompassing a larger mass of atrial tissue, and the smaller second shock was delivered to the pathway with lower impedance, the ADFT was lower. This is consistent with the concept that defibrillation requires a minimum potential gradient throughout the entire atrial myocardium.

In the present study, the atrial SP electrode was placed through a transseptal procedure with most of the electrode situated near the high left atrial SP and the smaller portion near the low right atrial SP. This electrode was between the RAA and CS electrodes near the posterior left atrial wall, where the earliest activations after unsuccessful RAA→CS shocks have been reported to appear. This SP electrode was far from the sinus and atroventricular nodes and remained firmly fixed in location throughout each study.

Study Limitations
The study was performed in sheep with acute AF maintained with acetyl-β-methylcholine chloride. Therefore, the results cannot be extrapolated directly to patients with AF. Furthermore, the SP electrode used in this study is not currently clinically acceptable, because it carries the risk of thrombus and embolism and may be problematic to extract.

Clinical Implications
As the population ages and the incidence of AF concomitantly rises, the clinical application of atrial cardioversion becomes broader. One of the prime deterrents to internal atrial defibrillation is the fact that the intensity of shocks required to successfully cardiovert patients is uncomfortable. If a wholly right-sided SP electrode can be developed that does not damage the sinus and atroventricular nodes, these data suggest a means for reducing atrial defibrillation energy requirements.

Acknowledgments
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References
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