Internal Cardioversion of Atrial Fibrillation in Sheep

Randolph A.S. Cooper, MD; Clif A. Alferness, BSEE; William M. Smith, PhD; and Raymond E. Ideker, MD, PhD

Background. The cardioversion efficacy of multiple defibrillation waveforms and electrode systems was compared in a sheep model of atrial fibrillation.

Methods and Results. Sustained atrial fibrillation could be induced with rapid atrial pacing in 23 (55%) of the animals. This study was performed in four parts. Six sheep with sustained atrial fibrillation were used for data analysis for each part, except in part 4 where five sheep without sustained atrial fibrillation were used. In part 1, four lead systems and four single capacitor truncated exponential defibrillation waveforms (two monophasic and two biphasic) were tested. In part 2, two transvenous lead systems were compared; one was a right-to-left system with one electrode located in the right side of the heart and the other electrode located in the left side of the heart, and the other was a totally right-sided system with both electrodes located in the right side of the heart. Eight (four monophasic and four biphasic) waveforms were tested with each lead system. In part 3, eight transvenous lead systems were compared, and two waveforms (one monophasic and one biphasic) were tested with each lead system. For parts 1–3, probability of success curves were determined for each waveform/lead system configuration using an up-down technique with 15 shocks per configuration. In part 4, shocks were synchronized to the QRS and given through two lead configurations during sinus rhythm in 20-V steps starting with 40 and ending with 500 V, and two waveforms were tested with each lead system (one monophasic and one biphasic). Ventricular fibrillation thresholds were determined by giving shocks during the T wave of sinus rhythm. For part 1, the three lead systems that used only intravenous catheter electrodes had significantly lower defibrillation requirements than the catheter-to-chest wall patch system. A 3/3-msec biphasic waveform had significantly lower defibrillation requirements than any of the other three waveforms in part 1. In part 2, the 3/3-msec biphasic waveform with a right-to-left lead system configuration had significantly lower defibrillation requirements than any other waveform lead system combination tested, and for each waveform tested, the right-to-left configuration had significantly lower requirements than the totally right-sided configuration. In part 3, for each waveform the right-to-left configuration had significantly lower voltage and energy requirements than the corresponding totally right-sided configuration. Furthermore, in part 3, waveform/lead configurations that probably generated high potential gradients near the sinoatrial node and near the atrioventricular node resulted in more postshock conduction disturbances. In part 4, there were no episodes of ventricular arrhythmias with shocks synchronized to the QRS. However, with synchronization to the T wave, ventricular fibrillation was induced in all five animals with the minimum tested voltage, which was 40 V.

Conclusions. This acute model yielded sustained atrial fibrillation in approximately 55% of the animals. Cardioversion of atrial fibrillation in sheep is possible with very low energy requirements using transvenous electrode systems (50% successful energy of 1.3±0.4 J for the 3/3-msec biphasic waveform with a right-to-left lead system). The biphasic waveform had the lowest defibrillation requirements of any waveforms tested, and right-to-left lead systems resulted in lower defibrillation requirements than totally right-sided lead systems. Also, lead systems that probably generated high potential gradients near the sinoatrial and atrioventricular node areas resulted in more frequent episodes of postshock conduction disturbances. Furthermore, synchronization of the shock to the QRS was vital to avoid potentially lethal postshock ventricular arrhythmias. Internal cardioversion capabilities of atrial fibrillation with a right-to-left lead system and biphasic waveforms should be considered for use in electrophysiology laboratories, implantable cardioverters, and implantable defibrillator systems. (Circulation 1993;87:1673–1686)

Key Words • defibrillation • waveforms • atrial defibrillation

Atrial fibrillation remains one of the most common arrhythmias encountered in clinical medicine and often requires pharmacological and/or electrical therapy to restore sinus rhythm. Transthoracic electrical cardioversion has been shown to be an effec-

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From the Departments of Medicine (R.A.S.C., C.A.A., W.M.S., R.E.I.) and Pathology (R.E.I.), Duke University Medical Center, Durham; and the Engineering Research Center for Emerging Cardiovascular Technologies of the School of Engineering (W.M.S., R.E.I.), Duke University, Durham, N.C.

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Address for reprints: Randolph A.S. Cooper, MD, P.O. Box 3140, Duke University, Medical Center, Durham, NC 27710.

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tive treatment for atrial fibrillation. However, the high energy shocks required, in the range of 25–400 J, can be detrimental to the heart. They also are painful to the patient. Thus, transthoracic cardioversion of atrial fibrillation usually requires general anesthesia. If energy requirements for cardioversion of atrial fibrillation could be reduced, the possibility of myocardial damage from the shock would be reduced and the pain associated with energy delivery might be minimized so that general anesthesia might not be required.

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Several groups have investigated alternatives to transthoracic cardioversion of atrial tachyarrhythmias. These studies have been in animals and humans. Internal catheter techniques have been attempted using electrodes in the right atrium, superior vena cava, inferior vena cava, and right ventricle. Also, electrode configurations of internal or transesophageal to chest wall have been tested. Studies in dogs have demonstrated lower cardioversion energy requirements for two internal electrodes as well as internal transesophageal to chest wall electrode configurations compared with transthoracic cardioversion energy requirements.

Electrical cardioversion of atrial fibrillation has changed little over the past 30 years. One reason is the lack of a reproducible model of sustained atrial fibrillation. Many animal studies dealing with cardioversion of atrial tachyarrhythmias group all atrial tachyarrhythmias together and do not separate atrial fibrillation from the other primary atrial tachyarrhythmias such as atrial flutter. Experimental models of atrial fibrillation have been reported in dogs; however, the duration of the induced arrhythmia usually is transient unless some type of pharmacological or autonomic nervous system manipulation is used. Recently, a sheep model of reproducible sustained atrial fibrillation induced by temporary rapid atrial pacing was reported. This model does not require pharmacological or autonomic manipulation. Furthermore, the animal is put under general anesthesia, allowing cardioversion shock testing without causing pain to the animal.

Experimental studies of shocks to halt ventricular fibrillation have generated information about the optimal waveform and about the optimal location of the defibrillating electrodes to maximize the chance for successful defibrillation while minimizing the likelihood of adverse effects to the heart. In animals and humans, certain biphasic waveforms have been shown to be more efficacious for ventricular defibrillation than certain monophasic waveforms. It is hypothesized that one of the requirements of an efficient ventricular defibrillation electrode configuration is to encompass most of the ventricular tissue between the electrodes.

In this study, we used this knowledge from ventricular defibrillation research to develop more efficient methods for cardioversion in a sheep model of atrial fibrillation. The cardioversion efficacy of several different waveforms and electrode systems was compared. This study was performed in four separate parts. Part 1 compared three completely internal electrode configurations with each other and with an electrode configuration consisting of an internal electrode and a chest wall patch electrode configuration. The internal electrode systems were right-to-left systems characterized by one electrode fixed in the right atrial appendage and the other electrode in three different locations on the left side of the heart. Also, two biphasic defibrillation waveforms were compared with two monophasic waveforms. Part 2 compared a totally right-sided internal electrode system with a right-to-left internal electrode system. With each of these electrode configurations, four biphasic waveforms were compared with four monophasic waveforms. Part 3 evaluated the defibrillation efficacy of several internal right-to-left electrode configurations with four different locations of the right-sided electrode and with the left electrode fixed on the left side of the heart in the distal coronary sinus. Furthermore, in parts 3 and 4, certain safety factors involved with internal cardioversion shocks were evaluated. Finally, the overall yield of atrial fibrillation in this sheep model was characterized.

Methods

This study of experimental animals was approved by the Institutional Animal Care and Use Committee at Duke University. It conforms to the positions of the American Heart Association on Research Animal Use adopted November 11, 1984.

Animal Preparation

A total of 42 adult sheep of both sexes (weight, approximately 50–65 kg) were studied acutely. In parts 1–3, six sheep with sustained atrial fibrillation were used for data analysis for each part. More than six sheep had sustained atrial fibrillation in each part. However, due to the early deaths of some of the animals before completion of each experiment, each protocol was continued until six sheep completed the entire experiment. The five sheep without sustained atrial fibrillation in part 3 were used for data analysis in part 4. After initial sedation of the sheep with xylazine (0.1 mg/kg), two peripheral intravenous lines were established in the hind legs. Anesthesia was induced by intravenous pentobarbital as a 30–35 mg/kg slow intravenous bolus over 10–15 minutes and followed by a constant intravenous drip of approximately 0.05 mg · kg⁻¹ · min⁻¹. Once anesthesia was induced, the animal was endotracheally intubated and placed on a Harvard respirator (Harvard Apparatus Co., South Natick, Mass.) with supplemental oxygen. Neumomuscular blockade was achieved with succinylcholine (1 mg/kg i.v.) followed by supplemental doses of 0.5 mg/kg as needed depending on muscular tone. A femoral artery cut-down was performed, and a catheter (Quik Cath, Baxter Corp., Deerfield, Ill.) was placed in the femoral artery for continuous blood pressure monitoring (VSM, Physio-Control Corp., Redmond, Wash.), frequent arterial blood gas sampling, and frequent arterial electrolyte sampling. Surface ECG lead II was displayed continually on a Life-Pak 9 defibrillator (Physio-Control Corp.). Maintenance intravenous fluids were infused continuously. Electrolytes, oxygen delivery, and ventilator settings were adjusted to maintain normal physiological levels as indicated by blood sampling every 30–60 minutes.

At the end of each study for all 42 animals, euthanasia was induced with an intravenous bolus of potassium chloride. The location of each internal electrode was verified, and the heart was removed surgically. The great vessels were trimmed to the point of insertion into each cardiac chamber, and the pericardium was re-
moved. The heart was weighed and then preserved in formalin.

**Electrode Placement**

For parts 1–3, the animals were positioned supine, and cut-downs were performed to expose and isolate both external jugular veins. Defibrillation catheters along with a quadrapolar pacing catheter (Bard Critical Care, Billerica, Mass.) were placed via jugular veins. Either a median sternotomy or a right lateral thoracotomy in the fourth or fifth intercostal space was performed. Epicardial pacing wires were sutured to both atrial appendages. The defibrillation electrodes were placed with manual palpation. For each animal, a quadrapolar pacing catheter was placed in the right ventricular apex for sensing and endocardial electrogram recordings.

For part 1, a median sternotomy was performed, and the heart was suspended in a pericardial cradle. Defibrillation electrodes were placed in the following positions (Figure 1A). One type A (Figure 2) electrode was positioned in the left pulmonary artery just behind the left atrium, and an additional type A (Figure 2) electrode was positioned in the right atrial appendage. One type B (Figure 2) electrode was placed in the distal coronary sinus so that the distal two electrodes rested in the proximal portion of the great cardiac vein with the proximal four electrodes resting under the left atrial appendage. Chest tubes were placed in both pleural cavities, and the chest was closed in layers with externalization of the two atrial appendage pacing wires. The chest tubes were maintained at a continuous negative pressure of −20 cm H₂O. A 133-cm² adult R2 patch (Darox Corp., Niles, Ill.) was placed subcutaneously and centered in the left midaxillary line in the fourth or fifth intercostal space. The animals remained supine for the rest of the study.

For part 2, the animals were placed on their left sides, and a right lateral thoracotomy was performed. The heart was exposed and suspended in a pericardial cradle. Defibrillation electrodes were placed in the following positions (Figure 1B). One type A (Figure 2) electrode was placed in the superior vena cava so that the middle of the electrode was positioned at the superior vena cava–right atrial junction. One type C (Figure 2) electrode was positioned in the distal coronary sinus so that the distal two electrodes rested in the proximal portion of the great cardiac vein with the coiled electrode resting under the left atrial appendage. One type D (Figure 2) electrode was placed so that the coil rested in the right atrial appendage. The chest cavity was approximated but not closed, and the animal was left on its left side.

For part 3, the animals were placed on their left sides, and a right lateral thoracotomy was performed. The heart was exposed and suspended in a pericardial cradle. Defibrillation electrodes were placed in the following positions (Figure 1C). Three type A (Figure 2) electrodes were placed: one in the superior vena cava so that the middle of the electrode was positioned at the superior vena cava–right atrial junction, one in the middle right atrium along the lateral free wall, and one in the right atrium so the distal tip of the coil rested just above the tricuspid valve. One type C (Figure 2) electrode was positioned in the distal coronary sinus so

**FIGURE 1.** Schematic showing defibrillation electrode locations. Panel A: Electrode locations for part 1. Panel B: Electrode locations for parts 2 and 4. Panel C: Electrode locations for part 3. PA, main pulmonary artery; LPA, left pulmonary artery; RAap, right atrial appendage; LA, left atrium; RV, right ventricle; LV, left ventricle; CS, distal coronary sinus; SVC, superior vena cava; IVC, inferior vena cava; LRA, low right atrium; MRA, middle right atrium; SubQ Patch, subcutaneous patch.
that the distal two electrodes rested in the proximal portion of the great cardiac vein with the coiled electrode resting under the left atrial appendage. One type D (Figure 2) electrode was placed so that the coil rested in the right atrial appendage. The chest cavity was approximated but not closed, and the animal was left on its left side.

For part 4, the animals were placed on their left sides, and a right lateral thoracotomy was performed. The heart was exposed and suspended in a pericardial cradle. The same coronary sinus, superior vena cava, and right atrial appendage defibrillation catheters and locations from part 2 (Figure 1B) were used. The chest cavity was approximated but not closed, and the animal was left on its left side.

Defibrillators

For part 1, a Ventritex HVS-02 programmable defibrillator (Ventritex Inc., Sunnyvale, Calif.) with a capacitance of 150 μF was used to deliver the test shocks. For parts 2–4, a custom-designed programmable defibrillator (InControl Inc., Redmond, Wash.) with a capacitance of 80 μF was used to deliver single capacitor monophasic and biphasic shocks. The leading edge voltage as well as the duration of each phase were controlled by interfacing the defibrillator with a National Instruments (Austin, Tex.) MIO-16 board and using Labview (Austin, Tex.) software with a Macintosh computer (Apple Computer, Cupertino, Calif.). The leading edge voltage was adjustable over a range of 0–500 V. The pulse width of each phase was adjustable from 0 to 20 msec in 0.1-msec steps. There was a 100-μsec gap between the positive and negative phases of each biphasic waveform. Synchronization of the shocks was accomplished by an endocardial R wave detector (InControl Inc.) that had an output that was able to trigger both types of defibrillators used.

Atrial Fibrillation Induction and Definitions

Atrial fibrillation was induced by rapid atrial pacing with a 1-msec square-wave pulse (4–8 mA, 40–60 Hz) between the two atrial appendage pacing wires. Electrogram data during normal sinus rhythm (Figure 3A) and atrial fibrillation (Figure 3B) were recorded from the internal cardiac electrodes at 0, 1, 2, and 4 hours into each experiment as well as at the end of each experiment. Atrial electrograms were obtained by using the second and third electrodes from the end of the coronary sinus catheter as a bipole, and atrial/ventricular electrograms were obtained by using a bipole that consisted of the distal tip of the coronary sinus catheter and the tip of the pacing catheter in the right ventricular apex. Data were displayed on a three-channel ECG machine (model 34000-200A, Mortara Instruments, Milwaukee, Wisc.) at a paper speed of 50 mm/sec. Atrial and ventricular cycle lengths were determined by averaging over a 20-second period. Atrial fibrillation was defined as irregular atrial activity seen on atrial electrograms (Figure 3B) with an approximate cycle length of less than 150 msec and with an irregularly irregular ventricular response. Atrial fibrillation was defined as sustained if it lasted for at least 5 minutes after the rapid pacing was discontinued. Atrial flutter (Figure 3C) was defined as regular atrial activity seen on atrial electrograms with an approximate cycle length of less than 250 msec. Atrial flutter episodes were not shocked. Episodes of flutter were allowed to either degenerate spontaneously into atrial fibrillation or convert back to sinus rhythm. If sustained atrial fibrillation was inducible, then shocks were given approximately every 1–2 minutes until cardioversion was successful. Successful cardioversion was defined as the return of normal sinus rhythm 1–2 seconds after a shock or the return of normal sinus rhythm after any postshock conduction problem such as sinus arrest or atrioventricular block resolved. After successful cardioversion shocks, atrial fibrillation was induced again with rapid atrial pacing and was allowed to continue for 2–3 minutes after discontinuation of the pacing. If hemodynamic deterioration was noted or ventricular defibrillation was necessary, the animal was allowed to rest for at least 10 minutes or until normal hemodynamic status was established before reinucing atrial fibrillation.

FIGURE 2. Schematic showing types of defibrillation electrodes used. Type A was a 0.4-cm-diameter transvenous catheter with a distal pacing/sensing electrode and a proximal titanium coiled defibrillation electrode 3.7 cm long with a surface area of approximately 2.95 cm². Type B was a 0.2-cm-diameter transvenous hexapolar coronary sinus mapping catheter (Elecath®, Electro-Catheter Corp., Rahway, N.J.). Each ring electrode was 0.2 cm in diameter and 0.3 cm in length. Inter electrode spacing was 0.5 cm, except for the two distal rings, which were separated by 0.2 cm. The four proximal electrodes were tied together as a common defibrilla tion electrode with a surface area of approximately 0.03 cm². The three distal electrodes were used for sensing and endocardial electrogram recording. Type C was the same electrode as type B except that stainless-steel wire was soldered to the fourth electrode from the distal tip and wrapped toward the proximal end of the catheter for 6 cm. This defibrillation electrode had a surface area of approximately 3.5 cm². The three distal electrodes were used for sensing and endocardial electrogram recording. Type D was the same electrode as type B except that stainless-steel wire was soldered to the second electrode from the distal tip and wrapped toward the proximal end of the catheter for 6 cm. This defibrillation electrode had a surface area of approximately 3.5 cm². The distal electrode was used for sensing and endocardial electrogram recording.
Waveforms

Exponentially truncated monophasic and biphasic waveforms were tested (Figure 4). All biphasic waveforms were produced to emulate a single capacitor discharge so that the leading edge voltage of the second phase was equal to the trailing edge of the first phase within ±5 V. Each set of waveforms was tested with each set of lead systems in each part of the study. In part 1, four waveforms were tested: a 3/3-msec biphasic waveform where the polarity of the second phase was opposite to the polarity of the first phase with each phase being 3 msec in duration, a 6-msec monophasic waveform with a single phase 6 msec in duration, a 6/6-msec biphasic waveform, and a 12-msec monophasic waveform. In part 2, eight different waveforms were tested: 1.5-, 3-, 4.5-, and 6-msec monophasic waveforms and 1.5/1.5-, 3/3-, 4.5/4.5-, and 6/6-msec biphasic waveforms. In part 3 and 4, two waveforms were tested: a 3-msec monophasic waveform and a 3/3-msec biphasic waveform.

Lead Systems

For all four parts, the cardioversion shocks are listed below using the convention cathode→anode for the monophasic and the first phase of the biphasic waveform. In part 1, four lead configurations were tested (Table 1): right atrial appendage→coronary sinus, right atrial appendage→coronary sinus plus left pulmonary artery, right atrial appendage→left pulmonary artery, and right atrial appendage→patch. In part 2, two lead configurations were tested (Table 1): a right-to-left configuration, right atrial appendage→coronary sinus, and a totally right-sided configuration, right atrial appendage→superior vena cava. In part 3, eight lead configurations were tested (Table 1): four right-to-left configurations, right atrial appendage→coronary sinus, low right atrium→coronary sinus, middle right atrium→coronary sinus.

![Figure 3](image1.png)

**Figure 3.** Tracings of types of atrial rhythms. Panel A: Electrograms recorded during normal sinus rhythm before induction of atrial fibrillation. The atrial electrogram was recorded by a bipolar pair of electrodes in the distal coronary sinus (CS Bipole). The atroventricular electrogram (CS→RV) was recorded from electrodes in the distal coronary sinus (CS) and the right ventricular apex (RV). Panel B: Same electrodes as in panel A after induction of atrial fibrillation by rapid atrial pacing. Note the chaotic atrial electrogram with no discernible organized atrial electrical activity. Also, note the irregular ventricular response during atrial fibrillation. Panel C: Same electrodes as in panels A and B after induction of rapid atrial flutter with rapid atrial pacing. Note the more organized atrial activity. This rhythm might be classified as atrial fibrillation; however, we classified it as atrial flutter due to the more organized atrial activity seen on the atrial electrogram. This rhythm rapidly deteriorated into atrial fibrillation similar to that seen in panel B.

![Figure 4](image2.png)

**Figure 4.** Monophasic and biphasic waveforms used in all four parts. The biphasic waveforms emulated a single capacitor discharge in that the trailing edge voltage of phase 1 (V1T) was equal to the leading edge voltage of phase 2 (V2L). Also, phase 2 of the biphasic waveform was opposite in polarity to phase 1. In part 1, two monophasic waveforms with phase 1 durations equal to 6 and 12 msec were tested. In part 1, two biphasic waveforms were tested—one with phase 1 and phase 2 duration of 3 msec and the other with both phases equal to 6 msec. In part 2, four monophasic were tested with phase 1 durations of 1.5, 3, 4.5, and 6 msec. Four biphasic waveforms were tested in part 2 with equal phase 1 and phase 2 durations of 1.5, 3, 4.5, and 6 msec. In parts 3 and 4, one monophasic waveform with a phase 1 duration of 3 msec and one biphasic waveform with both phase durations of 3 msec were tested.

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RAap, right atrial appendage; CS, distal coronary sinus; LPA, left pulmonary artery; P, chest wall patch; SVC, superior vena cava; LRA, low right atrium; MRA, middle right atrium.

Arrows point from cathode to anode.
coronary sinus, and superior vena cava → coronary sinus; and four totally right-sided configurations, right atrial appendage → middle right atrium, low right atrium → right atrial appendage, middle right atrium → right atrial appendage, and superior vena cava → right atrial appendage. In part 4, two lead configurations were tested (Table 1): a right-to-left configuration, right atrial appendage → coronary sinus, and a totally right-sided configuration, right atrial appendage → superior vena cava.

Data Acquisition and Defibrillation Protocol
The actual current and voltage waveforms delivered to the electrodes were initially isolated and recorded across a 0.25-Ω resistor in series with the electrodes and a 200:1, 100-MΩ resistor divider in parallel with the electrodes. The voltage and current waveforms were digitized at 20 kHz using the National Instruments MIO-16 board. From these digitized waveforms, a custom-designed program using Labview software determined the leading and trailing edge voltages and currents of both the positive and negative pulses as well as the energies of each pulse and the resistances of the load. Energy was calculated by integration of the product of the voltage and current for the duration of each pulse. Resistance was calculated by dividing the root-mean-square voltage during the shock by the root-mean-square current during the shock. All data were recorded on disc in spreadsheet format using a Macintosh computer.

For parts 1–3, the defibrillation threshold was determined first for each waveform/lead combination in each animal. The defibrillation threshold was determined using a modified Purdue method.41 For the first animal, the voltage was estimated from other studies13-15 with similar experimental designs. Subsequent starting voltages were the mean values from the previous animals studied. If the initial shock failed, then the next and subsequent shock voltages were increased by 20 V until a shock succeeded. Then, the voltage was decreased by 10 V, and another shock was given. If the initial shock succeeded, the next and subsequent shock voltages were decreased by 20 V until a shock failed. The next shock after the failure was increased by 10 V and tested. The defibrillation threshold was defined as the lowest voltage and current that achieved defibrillation. The order in which each defibrillation threshold was determined was randomized for each animal by drawing chits.

After all defibrillation thresholds were determined, probability of success curves were determined for each waveform/lead system combination in each animal for parts 1–3. Starting with the previously measured defibrillation threshold value, a total of 15 shocks was given using an up-down technique with 20-V steps for each waveform/lead system combination. After each shock, the success or failure was noted. If a shock succeeded, the next shock was decreased by 20 V; if a shock failed, the next shock was increased by 20 V. Randomization was achieved by drawing chits for each waveform/lead system combination and giving three shocks for the particular waveform/lead system chosen. Once all chits were drawn and all combinations had been tested, the chits were replaced and selected again. This was repeated five times until a total of 15 shocks was given for each waveform/lead system combination.

Any postshock conduction disturbances noted on the surface lead II ECG were recorded by the single strip-chart recorder of the Life-Pak 9. Sinus arrest (sinoatrial block) was defined as the absence of atrial electrical activity for at least 2 seconds after a shock was given. Atrioventricular block was defined as the presence of coordinated atrial activity (P waves) without one-to-one atrial to ventricular conduction for at least 2 seconds after a shock was given.

For part 4, shocks synchronized to the QRS were given to determine the ventricular fibrillation threshold. The shock voltage initially was 40 V and then increased by 20-V steps to a maximum of 500 V. The order in which each waveform/lead system combination was tested in each animal was determined by drawing chits. After completion of the QRS synchronized shocks, a delay was set between the time of the sensed QRS and the time to shock delivery. This was accomplished by the Labview software that controlled the defibrillator. The interval from the Q wave to the peak of the T wave on surface lead II was determined during normal sinus rhythm. Then, starting with an interval 100 msec greater than the interval of the measured Q wave to peak of the T wave, shocks were delivered and the QRS-to-shock interval was decremented by 5-msec steps until ventricular fibrillation was induced. The starting shock voltage was 40 V. Due to difficulties in achieving ventricular defibrillation in sheep, usually only two or three ventricular fibrillation thresholds could be determined for each animal. Thus, randomization could not be done, and all waveform/lead system combinations were tested in as many sheep as necessary before any combination was repeated.

Statistical Analysis
Results are expressed as mean±SDs unless otherwise specified. For all statistical tests performed, a value of p=0.05 was considered significant. The heart weight data, atrial fibrillation cycle length, and ventricular rate during atrial fibrillation were compared between parts using unpaired t test analysis.42

The data obtained in parts 1–3 for each waveform/lead system combination were fit to a probit curve using standard SAS procedures.44 The 20%, 50%, and 80% success points in terms of leading edge voltage and total energy were derived from these curves for each animal. ANOVA multivariate analysis with repeated measures42 was used to compare the mean values of the 20%, 50%, and 80% success points among waveforms, lead systems, and sheep. Also, multiple comparisons were made among waveforms and lead systems using a Student-Newman-Keuls test.42

For part 3, unpaired t test analysis was used to compare the leading edge voltages and total energies associated with conduction block. For part 4, the ventricular fibrillation threshold values in terms of leading edge voltage and total energy were compared using unpaired t test analysis.42

Results
Sheep Model Data
Table 2 shows the mean values and standard deviations of the atrial fibrillation cycle length, the ventricular rate during atrial fibrillation, and the heart weights for
animals with and without sustained atrial fibrillation. This includes the animals with sustained atrial fibrillation that died before completion of the experiment. Also shown are the number of sheep in each group as well as the total for each category. There was no significant difference among parts 1–3 in terms of atrial fibrillation cycle length or the ventricular response rates during atrial fibrillation. For parts 1 and 3 the totals from all three parts, there was a significant difference in mean heart weights between the groups of sheep with sustained atrial fibrillation and the groups without sustained atrial fibrillation. There was not a significant difference between the heart weights of the two groups in part 2.

Part 1

Figure 5 shows the mean values and standard deviations for the 50% success points for defibrillation in terms of leading edge voltage for each waveform/lead system combination for the six animals that completed the entire experiment in part 1. For each waveform, there was no significant difference among the three totally internal lead systems (right atrial appendage→coronary sinus, right atrial appendage→coronary sinus plus left pulmonary artery, and right atrial appendage→left pulmonary artery). However, these three lead systems had significantly lower voltage requirements than the catheter-to-patch system (right atrial appendage→patch). For each lead system, the 3/3-msec biphasic waveform had significantly lower requirements than any of the other three waveforms. These findings were consistent for the mean values of the 20% and 80% successful leading edge voltage values. These findings also were consistent for the mean values of the 50% successful total energy requirements. However, for the 20% successful energy values, there was no significant difference between the 3/3-msec biphasic and the 6-msec monophasic with the right atrial appendage→coronary sinus lead system. Furthermore, for the 80% successful energy values, there was no significant difference between the 3/3-msec biphasic and the 6-msec monophasic with the right atrial appendage→patch lead system.

Part 2

Figure 6 shows the mean values and standard deviations for the 50% success points for defibrillation in terms of leading edge voltage for each waveform/lead system combination for the six animals that completed the entire experiment in part 2. For each waveform, the right-to-left lead system (right atrial appendage→coronary sinus) had significantly lower requirements than the totally right-sided lead system (right atrial appendage→superior vena cava). Furthermore the 3/3-msec biphasic waveform with
the right atrial appendage → coronary sinus lead system had significantly lower requirements than any other waveform/lead system combination with a 50% successful energy requirement of 1.4±0.3 J. These findings were consistent for the mean values of the 20% and 80% successful leading edge voltages as well as the mean values of the 20%, 50%, and 80% successful total energies.

Part 3 (Defibrillation Data)

Figure 7 shows the mean values and standard deviations for the 50% success points for defibrillation in terms of leading edge voltage for each waveform/lead system combination for the six animals that completed the entire experiment in part 3. For each lead system, the 3/3-msec biphasic waveform had significantly lower voltage requirements than the 3-msec monophasic waveform. This finding was consistent for the 20% and 80% values except for the 80% success value for the right atrial appendage → middle right atrium lead configuration, where there was not a significant difference between the two waveforms. For each waveform, there was no significant difference between the four right-to-left lead systems in terms of the mean values of the 20%, 50%, and 80% successful leading edge voltages. Also, for each waveform, there was no significant difference between the four totally right-sided lead systems in terms of the mean values of the 20%, 50%, and 80% successful leading edge voltage requirements. Furthermore, for each waveform group, each right-to-left lead system had significantly lower 20%, 50%, and 80% successful leading edge voltage requirements than the corresponding totally right-sided lead system. In terms of total energy requirements, each right-to-left lead system with the 3/3-msec biphasic waveform had significantly lower 20%, 50%, and 80% successful total energy requirements than with the 3-msec monophasic waveform. Within each waveform group, each right-to-left lead system had significantly lower 20%, 50%, and 80% successful total energy requirements than the corresponding totally right-sided lead system. Also, within each waveform group, there was no statistical difference between the first three right-to-left lead systems (superior vena cava → coronary sinus, left right atrium → coronary sinus, and middle right atrium → coronary sinus) in terms of the mean values of the 20%, 50%, and 80% successful total energy requirements; however, the fourth right-to-left lead system (right atrial appendage → coronary sinus) had significantly lower 20%, 50%, and 80% successful total energy requirements than the first three right-to-left lead systems. Furthermore, within each waveform group, there was no statistical difference between the four totally right-sided lead systems in terms of the mean values of the 20%, 50%, and 80% successful total energy requirements.

**Part 3 (Conduction Block Data)**

Table 3 shows the number of episodes of sinus arrest (sinoatrial block), the number of episodes of atrioventricular block, the mean leading edge voltage associated with the type of block, and the mean duration of the block with each waveform/lead system combination. Also shown are the total number of shocks given to the six sheep that completed the entire experiment in part 3 and the total number of shocks with each waveform/lead combination that resulted in conduction block.

Sinoatrial block occurred with both the 3/3-msec biphasic and the 3-msec monophasic waveform but only with the superior vena cava → right atrial appendage lead system. There were twice as many episodes of sinoatrial block associated with the 3-msec monophasic than the 3/3-msec biphasic waveform. The leading edge

<table>
<thead>
<tr>
<th>Lead system</th>
<th>Waveform</th>
<th>Type of block</th>
<th>No. of episodes</th>
<th>Total shocks</th>
<th>Voltage (V)</th>
<th>Duration (seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVC → RAap</td>
<td>3/3 Bi</td>
<td>SA</td>
<td>18</td>
<td>119</td>
<td>310±27*</td>
<td>3.4±1.2</td>
</tr>
<tr>
<td>SVC → RAap</td>
<td>3 Mo</td>
<td>SA</td>
<td>36</td>
<td>118</td>
<td>375±25*</td>
<td>3.6±1.2</td>
</tr>
<tr>
<td>LRA → CS</td>
<td>3 Mo</td>
<td>AV</td>
<td>42</td>
<td>120</td>
<td>301±27</td>
<td>3.2±0.8</td>
</tr>
<tr>
<td>MRA → CS</td>
<td>3 Mo</td>
<td>AV</td>
<td>39</td>
<td>122</td>
<td>307±20</td>
<td>3.1±0.7</td>
</tr>
</tbody>
</table>

SVC, superior vena cava; RAap, right atrial appendage; LRA, low right atrium; MRA, middle right atrium; CS, distal coronary sinus; 3/3 Bi, 3/3-msec biphasic waveform; 3 Mo, 3-msec monophasic waveform; SA, sinus arrest (sinus node block); AV, atrioventricular node block.

*p ≤ 0.05.
voltages that were associated with sinoatrial block were significantly lower for the 3/3-msec biphasic waveform compared with the 3-msec monophasic waveform. There was no difference in the total energy associated with sinoatrial block or the mean duration of sinoatrial block associated with each waveform.

Atrioventricular block occurred only with the 3-msec monophasic waveform and either the right atrium→coronary sinus or the middle right atrium→coronary sinus lead system. There was no statistical difference between the leading edge voltages, total energies, or duration of atrioventricular block with either lead system that was associated with atrioventricular block.

Part 4

Table 4 shows the mean values and standard deviations for the maximum and minimum leading edge voltages and total energies delivered during the QRS for each waveform/lead system combination. There were no episodes of sustained ventricular tachycardia or ventricular fibrillation with synchronization to the QRS. There were episodes of nonsustained ventricular tachycardia with the longest run being less than 5 beats.

Table 5 shows the mean leading edge voltages, mean total energies, and the times between the QRS and shock delivery for the ventricular fibrillation threshold determinations for each waveform/lead system combination. There was no significant difference between the four different waveform/lead system combinations in terms of ventricular fibrillation threshold leading edge voltage or total energy.

**Table 4. Shock Strengths for QRS Synchronized Shocks**

<table>
<thead>
<tr>
<th>Lead system</th>
<th>Waveform</th>
<th>Voltage (V)</th>
<th>Energy (J)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Minimum</td>
<td>Maximum</td>
</tr>
<tr>
<td>RAp→CS</td>
<td>3/3 Biph</td>
<td>42±2.0</td>
<td>409±22</td>
</tr>
<tr>
<td>RAp→SVC</td>
<td>3/3 Biph</td>
<td>40±1.4</td>
<td>433±15</td>
</tr>
<tr>
<td>RAp→CS</td>
<td>3 Mono</td>
<td>41±2.6</td>
<td>413±24</td>
</tr>
<tr>
<td>RAp→SVC</td>
<td>3 Mono</td>
<td>42±3.2</td>
<td>444±19</td>
</tr>
</tbody>
</table>

RAp, right atrial appendage; CS, distal coronary sinus; SVC, superior vena cava; 3/3 ms Biph, 3/3-msec biphasic waveform; 3 ms Mono, 3-msec monophasic waveform.

Discussion

**Model of Atrial Fibrillation**

In this set of experiments, we have examined the cardioversion requirements of several different defibrillation waveforms and lead systems in a sheep model of atrial fibrillation.15 We found this model of atrial fibrillation induced by rapid pacing to be easily reproduced. With general anesthesia, multiple shock testing can be performed without causing pain to the animal. Furthermore, several shock configurations can be tested without significantly changing the characteristics of the atrial fibrillation as shown by the stability of the atrial fibrillation cycle length and ventricular response throughout the duration of the experiments. This model does not require any type of pharmacological, autonomic nervous system, or surgical manipulation to induce atrial fibrillation. A limitation to this model is that only a little more than 50% of the animals will have inducible sustained atrial fibrillation. Larger animals or at least larger heart sizes were more likely to have inducible atrial fibrillation (Table 2). This finding supports the findings of Moore and Spear43 that there is a critical mass of tissue necessary to sustain atrial fibrillation.

We chose to study different defibrillation electrode systems and waveforms with atrial fibrillation for several reasons. First, little is known about different types of defibrillation lead systems and waveforms for the treatment of atrial fibrillation. Second, recent animal studies with "pure" atrial fibrillation and intracardiac electrode techniques have reported low cardioversion requirements in the range of 1–5 J in dogs14 as well as sheep.15 The third reason is that previous human trials with only right-sided intracardiac catheter systems and monophasic waveforms have reported low success rates44,45 unless

**Table 5. Ventricular Fibrillation Threshold Shock Data**

<table>
<thead>
<tr>
<th>Lead system</th>
<th>Waveform</th>
<th>QRS to shock delay (msec)</th>
<th>Voltage (V)</th>
<th>Energy (J)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAp→SVC</td>
<td>3/3 Biph</td>
<td>315±7</td>
<td>43±0.4</td>
<td>0.08±0.01</td>
</tr>
<tr>
<td>RAp→SVC</td>
<td>3 Mono</td>
<td>335±7</td>
<td>38±0.4</td>
<td>0.07±0.01</td>
</tr>
<tr>
<td>RAp→CS</td>
<td>3/3 Biph</td>
<td>325±15</td>
<td>41±0.3</td>
<td>0.07±0.01</td>
</tr>
<tr>
<td>RAp→CS</td>
<td>3 Mono</td>
<td>315±10</td>
<td>42±0.3</td>
<td>0.08±0.01</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>324±10</td>
<td>41±2.0</td>
<td>0.07±0.01</td>
</tr>
</tbody>
</table>

RAp, right atrial appendage; SVC, superior vena cava; CS, distal coronary sinus; 3/3 Biph, 3/3-msec biphasic waveform; 3 Mono, 3-msec monophasic waveform.
Table 6. Average Resistances

<table>
<thead>
<tr>
<th>Lead system</th>
<th>Resistance (Ω)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1</td>
<td></td>
</tr>
<tr>
<td>RAap→CS</td>
<td>69±11</td>
</tr>
<tr>
<td>RAap→LPA</td>
<td>50±10</td>
</tr>
<tr>
<td>RAap→LPA+CS</td>
<td>44±9</td>
</tr>
<tr>
<td>RAap→P</td>
<td>56±11</td>
</tr>
<tr>
<td>Parts 2 and 4</td>
<td></td>
</tr>
<tr>
<td>RAap→CS</td>
<td>57±7</td>
</tr>
<tr>
<td>RAap→SVC</td>
<td>45±12</td>
</tr>
<tr>
<td>Part 3</td>
<td></td>
</tr>
<tr>
<td>RAap→CS</td>
<td>55±9</td>
</tr>
<tr>
<td>SVC→CS</td>
<td>61±8</td>
</tr>
<tr>
<td>MRA→CS</td>
<td>52±7</td>
</tr>
<tr>
<td>LRA→CS</td>
<td>38±5</td>
</tr>
<tr>
<td>SVC→RAap</td>
<td>59±8</td>
</tr>
<tr>
<td>MRA→RAap</td>
<td>53±9</td>
</tr>
<tr>
<td>LRA→RAap</td>
<td>50±6</td>
</tr>
</tbody>
</table>

RAap, right atrial appendage; CS, distal coronary sinus; LRA, low right atrium; P, chest wall patch; SVC, superior vena cava; MRA, middle right atrium.

very high energies are used. The reasons for the disparity between animals and humans may be due to the use of biphasic waveforms and larger electrodes in the animal studies. Furthermore, these clinical studies involved patients with chronic atrial fibrillation that was refractory to medical and/or external cardioversion. We hoped that an electrode and waveform combination could be found that halted atrial fibrillation with low voltage.

Previous studies have dealt with the ability to treat the general category of atrial tachyarrhythmias with a certain type of cardioversion system. Kumagai et al. found that both completely internal electrode systems and internal electrode-to-chest wall electrode systems did not differ in cardioversion requirements of atrial tachyarrhythmias in a dog model. They showed low cardioversion energy requirements with a 70% successful energy requirement of ≤1 J. There are several important differences between these results and our findings. First, they used a sterile talc-induced pericarditis model in small dogs (9–20 kg), and we used large adult sheep (50–65 kg). The dog pericarditis model has been shown to produce a wide range of atrial tachyarrhythmias. It has been proposed that transthoracic cardioversion energy requirements are inversely related to the level of organization of atrial electrical activity. Thus, atrial fibrillation is the least organized, so it should have the highest energy requirements. Therefore, if atrial fibrillation can be effectively treated with a certain cardioversion method, then other more organized atrial tachyarrhythmias such as atrial flutter should be treatable with the same method. We studied atrial fibrillation separately from the other types of atrial tachyarrhythmias because if we had treated all atrial tachyarrhythmias similar to the study by Kumagai et al., animals mainly exhibiting atrial flutter probably would have had lower cardioversion thresholds than the ones that mainly went into atrial fibrillation.

Comparisons With Ventricular Defibrillation

Animal studies with ventricular fibrillation have demonstrated a close relation between the extracellular potential gradient produced by a shock and whether the shock will successfully terminate ventricular fibrillation. For defibrillation to occur, it is thought that a minimal potential gradient must be generated by the shock throughout most or all of the ventricular myocardium. The distribution of potential gradients in the heart after a shock is very uneven for electrodes located on or in the heart. There are high gradient areas near the electrodes and low areas far away from the electrodes. These areas of low gradient are sites for earliest activation after unsuccessful defibrillation shocks. Furthermore, the high gradient areas can have detrimental effects on the heart including post-shock arrhythmias, conduction disturbances, myocardial dysfunction, and myocardial necrosis. The potential gradient distribution created by a shock in the heart depends on the electrode size and location used to deliver the shock. The optimal electrode system for ventricular defibrillation minimizes the high gradient areas near the electrodes and raises the critical amount of ventricular tissue above the minimum gradient to achieve defibrillation. It has been argued that the electrodes for ventricular defibrillation should encompass as much of the fibrillating tissue as possible so that the current pathway for the shock traverses both ventricles as well as the intraventricular septum. These findings and theories have been used to develop more efficient lead systems for implantable ventricular defibrillators.

Certain biphasic waveforms have been shown to be more effective for ventricular defibrillation than certain monophasic waveforms in animals and humans. Biphasic waveforms also have been shown to be efficacious for internal atrial defibrillation in sheep and dogs as well as in an epicardial electrode system in humans. However, it has been suggested that the relative efficacy of biphasic versus monophasic waveforms may depend on the electrode configuration. Therefore, we tested both monophasic and biphasic waveforms of various durations to see which was most efficacious for atrial defibrillation.

Part 1

In part 1, we demonstrated that three different lead systems using only intracardiac electrodes were more effective for atrial defibrillation than a catheter-to-patch lead system (Figure 5). These intracardiac electrode systems all had one catheter on the right side of the heart and one or two electrodes on the left side of the heart. Also, we found no advantage to having an electrode in the left pulmonary artery compared with the distal coronary sinus. Furthermore, the 3/3-msec biphasic waveform was more effective than the other three waveforms used. As total pulse duration increased from 6 to 12 msec, cardioversion requirements increased. Part 1 demonstrated that atrial fibrillation in sheep could be halted with transvenous electrode techniques and low energy requirements with a 50% successful energy requirement of 1.5±0.4 J for the
3/3-msec biphasic waveform with the right atrial appendage→coronary sinus electrode system.

Part 2

In part 2, we showed that a right-to-left lead system (right atrial appendage→coronary sinus) was more effective than a totally right-sided lead system (right atrial appendage→superior vena cava) for eight different waveforms (Figure 6). We also found that shorter total duration biphasic and monophasic waveforms were less efficacious than the 3/3-msec biphasic waveform, and the 3/3-msec biphasic waveform with the right atrial appendage→coronary sinus electrode system had the lowest cardioversion requirements of the waveform/lead system combinations tested. The right-to-left lead system may be more effective because the minimum potential gradient created in the atrial muscle for a given shock strength is higher than that for a totally right-sided system. Thus, as with ventricular defibrillation, it appears that the most effective electrode system is the one that has the most fibrillating tissue between the electrodes.

Part 3

In part 3, we looked at different locations of electrodes in the right atrium and superior vena cava for two reasons. One purpose was to compare the cardioversion efficacy of different electrode locations in the right atrium. It would be much easier to place an electrode in the right atrial cavity or superior vena cava than in the right atrial appendage. Furthermore, in part 2, it appeared that the totally right-sided electrode system (right atrial appendage→superior vena cava) was associated with more frequent episodes of sinus arrest than the right-to-left lead system. Therefore, the second purpose for part 3 was to see if certain electrode locations were more likely to result in postshock conduction disturbances.

As in part 2, all right-to-left lead configurations were more effective than the corresponding totally right-sided system for each waveform (Figure 7). For all right-to-left lead configurations, the 3/3-msec biphasic again was more effective than the 3-msec monophasic waveform. In terms of voltage, there was no difference between the four right-to-left lead configurations with the 3/3-msec biphasic waveform. However, the 3/3-msec biphasic with the right atrial appendage→coronary sinus configuration had significantly lower energy requirements than the other three right-to-left lead configurations with the 3/3-msec biphasic waveform. Thus, there was a slight advantage in energy requirements to have the right electrode in the right atrial appendage.

The right atrial appendage→superior vena cava lead system with both the biphasic and monophasic waveforms was the only lead system of the eight tested that was associated with postshock sinus arrest. This probably is due to the high potential gradients produced near the superior vena cava electrode, which is close to the sinus node region, as well as to the fact that much of the current passing between the two electrodes probably traverses the sinus node region. The lack of sinus block when the superior vena cava catheter is replaced by the coronary sinus catheter probably is caused by at least two factors. First, for shocks of the same strength, the potential gradients within the sinus node region probably are lower for the right-to-left system (right atrial appendage→coronary sinus) than for the totally right-sided system (right atrial appendage→superior vena cava). Second, the shock strength required for atrial defibrillation is less with the right-to-left system (right atrial appendage→coronary sinus) than for the totally right-sided system, also decreasing the intensity of the potential gradient field throughout the sinus node region.

The low right atrium→coronary sinus and middle right atrium→coronary sinus lead systems were the only two systems associated with atrioventricular block. Atrioventricular block arose only with the 3-msec monophasic waveform. This also probably was due to at least two factors. First, the electrodes are located near the atrioventricular node, and most of the current pathway is directed through the atrioventricular node. Thus, the atrioventricular node region is exposed to high potential gradients, which can result in conduction block. Second, the 3-msec monophasic waveform has higher cardioversion requirements than the 3/3-msec biphasic waveform and results in higher potential gradient fields near the atrioventricular node region.

Part 4

In part 4, we showed that a right-to-left (right atrial appendage→coronary sinus) and a totally right-sided (right atrial appendage→superior vena cava) lead system with a 3/3-msec biphasic or a 3-msec monophasic waveform does not induce sustained postshock ventricular tachyarrhythmias as long as the shock is synchronized to the QRS during sinus rhythm. However, if the shock is not synchronized to the QRS and falls on the vulnerable period of the ventricles, very-low-strength shocks can result in ventricular fibrillation. Thus, even though most of the current is traversing the atria, the ventricles are not isolated from the effects of the shock.

Waveforms and Mechanisms of Atrial Defibrillation

Chapman et al showed with monophasic waveforms and ventricular defibrillation in dogs that shorter (2.5 msec) and longer (20 msec) pulse durations were associated with higher threshold voltages than pulse durations in the middle of this spectrum. They reported that the optimal pulse duration for the electrode/waveform configuration tested was 5–15 msec. Although we did not find this to be the case for atrial defibrillation with monophasic waveforms, we did find this relation to occur for biphasic waveforms with the right atrial appendage→coronary sinus electrode system but not for the right atrial appendage→superior vena cava electrode system. Furthermore, these findings suggest a waveform electrode system interaction for atrial defibrillation as has been suggested for ventricular defibrillation. Our research shows that a 3/3-msec biphasic waveform with a right atrial appendage→coronary sinus electrode system was the optimal configuration tested in sheep.

The mechanisms of atrial defibrillation are not clear. Several groups have demonstrated with ventricular defibrillation in animals that the defibrillation efficacy of a biphasic waveform is dependent on the duration as well as the amplitude of both of the phases. Biphasic waveforms with a second phase either shorter or equal to in duration and less than or equal to in amplitude of...
the first phase are more efficacious than biphasic waveforms with a second phase longer or larger in amplitude than the first phase. Also, to a point, the longer the total duration of the biphasic waveform, the more effective it is for defibrillation. Tang et al found that a 6/6-msec biphasic waveform was more efficacious for ventricular defibrillation in dogs than a 3.5/3.5-msec or 8.5/8.5-msec biphasic waveform. We found that the 3/3-msec biphasic waveform was more efficacious for atrial defibrillation in sheep in comparison with all of the other waveforms tested, including a 6/6-msec biphasic waveform. These differences between atrial defibrillation and ventricular defibrillation may be explained at least in part by differences in species, by differences in duration of waveform tested, by differences in type of capacitors used, and by differences in atrial and ventricular fibrillation.

Internal electrode systems may have lower energy requirements because more of the current is available to traverse the heart than the thorax as with external defibrillation electrode systems. Thus, less of the current is wasted. Furthermore, air in the lungs may act as an insulator. This would help current traverse the heart with internally applied current but would insulate the heart from externally applied current.

Levy et al postulated that barotrauma may play a role in endocardial defibrillation by the shock increasing endocardial pressure. Their research was done in humans with atrial fibrillation using shock strengths of 200–300 J, which probably resulted in higher increases in endocardial pressures than our shocks of 1–15 J. However, this pressure increase still may be an important factor for defibrillation success.

Resistances

Dunbar et al demonstrated that larger surface areas of defibrillation electrodes were associated with lower defibrillation thresholds in a dog model of atrial tachyarrhythmias. In the first part of our study, we showed that a coronary sinus defibrillation electrode with a surface area of only 0.03 cm² was associated with low cardioversion energy requirements of atrial fibrillation in sheep. We hypothesized that by using larger surface area electrodes, cardioversion energy requirements would be even lower. This is why we used the modified electrodes (types C and D, Figure 2) for parts 2–4. The larger surface area electrodes did result in lower average resistances; however, this did not appear to significantly affect the cardioversion threshold requirements. Future studies with lower resistance materials may show that larger electrodes with lower resistances have lower cardioversion thresholds than smaller electrodes with low resistances; however, we cannot conclude this from our study.

Summary of Parts 1–4

The optimal lead systems for internal cardioversion of atrial fibrillation are those that have electrodes that encompass as much of the fibrillating atrial tissue as possible and that do not create high potential gradients near the sinus or atrioventricular nodes. Thus, both the cardioversion threshold and the risk of postshock conduction disturbances are minimized. Waveforms with a low cardioversion threshold help decrease the potential gradients near the sinus or atrioventricular nodes. In the first three parts of this study, we found that the combination of a right-to-left lead system, using the distal coronary sinus as the left electrode, and a 3/3-msec biphasic waveform results in low energy requirements for cardioversion of atrial fibrillation in sheep. In part 4, we showed that with this waveform/lead system shocks up to approximately 430 V are safe in normal sheep hearts with electrically induced atrial fibrillation as long as the shock is synchronized to the QRS. Furthermore, this synchronization is crucial to avoid possible post-shock ventricular tachyarrhythmias.

Comparisons With Previous Animal Studies

Previous studies with “pure” atrial fibrillation are limited. Scott et al reported that atrial fibrillation could be cardioverted with approximately 180–190 V in vagally stimulated dogs with intracardiac electrodes and biphasic waveforms. It is difficult to compare our results with their results due to marked differences in experimental models; however, their results demonstrate the ability of intracardiac electrodes and biphasic waveforms to halt atrial fibrillation in another species. Powell et al reported a 70% successful cardioversion energy requirement of 5 J in adult sheep for a right atrial catheter-to-left chest wall patch lead system and a biphasic waveform. This cardioversion threshold for the catheter-to-patch system and biphasic waveform is slightly lower than ours for both the 3/3-msec (with our estimated 70% success of approximately 8 J) and the 6/6-msec biphasic (with our estimated 70% success of approximately 11 J) waveforms. Their study is very similar to part 1 of our study. However, the size of the electrodes they used and the duration as well as capacitance of the biphasic waveform they used were different from those of our study. They also opened the chest cavity before administering shocks. We made every attempt to remove all air from the chest cavity when a chest wall electrode was used (part 1) by using chest tubes that were maintained to constant negative suction. For the other parts of our study (parts 2–4), only internal electrodes were used, and most of the current probably traversed the heart and atria instead of the rest of the thorax. Thus, differences in experimental methods and equipment between our study and those of Powell and coworkers may explain the differences in the cardioversion thresholds.

Comparisons With Previous Clinical Studies

In humans, internal cardioversion of atrial fibrillation has had low success rates unless very high energies (200–300 J) are used. These studies have used either totally right-sided intracardiac electrode systems or right atrial catheter–to–chest wall electrode systems. There are no reports of using a right-to-left intracardiac electrode system in humans or animals. Keane et al reported the improved efficacy of a biphasic waveform compared with a monophasic waveform for epicardial defibrillation in humans with electrically induced atrial fibrillation during bypass surgery. They reported a mean 50% successful energy of 0.3±0.1 J. Yee et al reported the use of a distal coronary sinus catheter electrode in conjunction with a newer-generation implantable ventricular defibrillator in humans. In 14 patients, a distal coronary sinus catheter was placed without complications. Eleven of these patients were
followed for 2–13 months with no reports of complications due to the coronary sinus catheter. One patient who had received 16 shocks died of complications unrelated to the implant 3 months after implantation. Postmortem examination of the heart showed minimal changes associated with the coronary sinus catheter. Another study in humans using a temporary coronary sinus defibrillation electrode in the electrophysiology laboratory reported no incidence of coronary sinus rupture, occlusion, or other complications. The risk of perforation of the coronary sinus, as seen with direct current ablation shocks, is probably much less with defibrillation electrodes due to the lower-strength shocks given for atrial defibrillation compared with ablation shock strengths. Also, the lower current densities associated with the larger surface areas of the defibrillation electrodes should reduce the risk of perforation or damage to the coronary sinus compared with the ablation electrodes. Thus, although the experimental and clinical evidence is limited, a coronary sinus defibrillation electrode is feasible in humans and appears to be safe for at least the short term.

Study Limitations
The main limitation of this study is that atrial fibrillation was induced in normal sheep hearts. It remains to be seen if the diseased hearts with atrial fibrillation seen in the clinical setting will respond as the sheep hearts did. Many patients with atrial fibrillation are taking drugs, can develop ischemia, and can experience frequent ventricular ectopic beats. Although we found that shocks of more than 400 V synchronized to the QRS during sinus rhythm did not induce sustained ventricular tachyarrhythmias in normal sheep hearts, it remains to be seen if this is true in the presence of cardioactive drugs, ischemia, or ectopy.

Clinical Implications
There are several potential clinical applications for this type of cardioversion system. Atrial fibrillation remains a common postshock arrhythmia with implantable ventricular defibrillators and may result in inappropriate ventricular shocks. Adding an atrial cardioversion system to the ventricular system would allow for better arrhythmia detection and discrimination as well as provide more complete arrhythmia treatment coverage. Also, many patients with recurrent symptomatic atrial fibrillation that is resistant to pharmacological treatment and requires multiple cardioversions may be candidates for an implantable atrial cardioverter. This type of cardioversion system may be useful in the electrophysiology laboratory during various types of studies that may induce atrial fibrillation, such as accessory pathway mapping. This system would provide a quick method for termination of atrial fibrillation without having to resort to a large external cardioversion shock or to the use of antiarrhythmic drugs, which may delay the completion of the study. Furthermore, this system may be useful in post–cardiac surgery patients who develop atrial fibrillation. Instead of external cardioversion requiring a general anesthetic, which often causes cardiac depression in patients with already diminished cardiac output and decreased coronary blood flow, light sedation and analgesia could be given, and internal cardioversion could be used to attempt to restore normal sinus rhythm. Furthermore, antiarrhythmic drugs could be avoided.

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