Marked Reduction in Internal Atrial Defibrillation Thresholds With Dual-Current Pathways and Sequential Shocks in Humans

Randolph A.S. Cooper, MD; Vance J. Plumb, MD; Andrew E. Epstein, MD; G. Neal Kay, MD; Raymond E. Ideker, MD, PhD

**Background**—This study tested the ability of sequential shocks delivered through dual-current pathways to lower the atrial defibrillation threshold (ADFT) compared with a biphasic shock through a standard single-current pathway.

**Methods and Results**—Electrodes were positioned in the right atrial appendage (RA), left subclavian vein (LSV), proximal coronary sinus (CSos), and distal coronary sinus (DCS) in 14 patients with chronic atrial fibrillation (170±185 days). Using a step-up protocol, we compared ADFTs for a single-current pathway (RA→DCS) that used a single 7.5/2.5-ms biphasic shock from a 150-μF capacitor with those for a dual-current pathway system (RA→DCS followed by CSos→LSV) using sequential 7.5/2.5-ms biphasic shocks with capacitor discharge waveforms for 150-μF and 600-μF capacitors. Both dual-current pathway configurations (2.0±0.4 J for 150-μF capacitance, 2.4±0.5 J for 600-μF capacitance) had a significantly lower ADFT than the single-current pathway (5.1±1.8 J). Whereas the dual-current pathway with 150-μF capacitor shocks had a significantly lower energy threshold, there was no statistical difference in terms of leading-edge voltage compared with the dual-current pathway with 600-μF capacitance shocks. There were no ventricular arrhythmias induced with appropriately synchronized shocks.

**Conclusions**—For internal atrial defibrillation in humans, sequential biphasic waveforms delivered over dual-current pathways resulted in a markedly reduced (50% reduction) ADFT compared with a single shock over a single-current pathway. (Circulation. 1998;97:2527-2535.)

**Key Words:** defibrillation ▪ atrium ▪ fibrillation

Atrial fibrillation is the most common arrhythmia encountered in clinical medicine and often requires pharmacological and/or electrical therapy to restore sinus rhythm.1–3 Recently, biphasic waveform shocks delivered via transvenous defibrillation electrodes have been shown to be an effective and feasible technique in animals4 and humans5–9 for the termination of atrial fibrillation. Clinical evaluation of an implantable atrial defibrillator is currently in progress.10 This device delivers biphasic shocks through a single-current pathway with electrodes in the lateral coronary sinus and right atrium.11 However, the present energy requirements for successful atrial defibrillation with this lead configuration remain sufficiently high that they are usually painful to the patient.5,9,12–15 Some clinical studies have demonstrated that the pain associated with internal atrial defibrillation shocks is related to the intensity of the shock.5,9,12,13,15,16 Current research efforts focus on methods to lower the defibrillation threshold in hope of lowering the shock intensity and decreasing the pain associated with internal atrial defibrillation. In both human17–20 and animal21–25 studies, sequential shocks delivered over dual-current pathways have been shown to reduce the ventricular defibrillation threshold. We26 have recently shown that sequential shocks delivered over dual-current pathways with transvenous electrodes can markedly reduce the atrial defibrillation threshold (ADFT) in a sheep model of acutely induced atrial fibrillation. The effect of dual-current defibrillation pathways with sequential shocks on ADFTs in humans is unknown. The purpose of the present study was to investigate the effect of sequential shocks delivered through single- and dual-current pathways on internal ADFTs in humans with atrial fibrillation who are candidates for cardioversion. In addition, the effect of defibrillator capacitance on the dual-current configuration threshold was investigated.

**Methods**

**Patients**

Fourteen patients who were referred to the University of Alabama Medical Center or Birmingham Veterans Administration Medical Center Electrophysiological Services were originally screened and enrolled. All patients were seen in consult or referred for cardioversion of atrial fibrillation. Informed consent was obtained in all cases, and the study protocol was approved by the Institutional Review Board of the University of Alabama Medical Center and Birmingham Veterans Administration Medical Center. The patients were...
brought to the clinical electrophysiology laboratory in a fasting, non-sedated state. All patients were in atrial fibrillation on arrival at the electrophysiology laboratory. The patients were given intravenous sedation/analgesia, and local anesthesia was used at the sites of catheter insertion. Synchronization of the shocks to ventricular activation was accomplished with the use of the filtered and amplified signal of the surface ECG lead II or aVF from a standard electrophysiological mapping system (Cardiolab, Prucka Engineering Inc.). External pacing and defibrillation patches (PD2200, Zoll Medical Corp) were positioned in the anterior-posterior position for back-up external defibrillation and postshock external bradycardia pacing if necessary via a standard external defibrillator/external pacemaker (PD 2000 Zoll Medical Corp).

Defibrillation Electrodes
Two 6F catheters with 10 rings and one 6F catheter with 30 rings (Electro-Catheter Corp) were used as the defibrillation electrodes. Each ring consisted of a 5-mm electrode with 2-mm interelectrode spacing. One 10-pole catheter was used as the anode and was advanced from the right femoral jugular vein until the body of the electrodes was positioned at the junction of the innominate and left subclavian vein (Figure 1). All 10 poles were combined to make the defibrillation electrode. Of the 14 patients, 12 were receiving oral warfarin therapy for at least 3 weeks before the procedure, and oral anticoagulation was withheld the night before the procedure. Venous access was not attempted unless the international normalized ratio was <1.7 the morning of the procedure. The other 2 patients were receiving oral warfarin therapy until admission to the hospital, at which time warfarin was discontinued and intravenous heparin therapy was started. The intravenous heparin was discontinued 4 hours before the procedure. Oral anticoagulation with warfarin was resumed for all patients before discharge from the hospital.

Defibrillator and Waveforms
The defibrillation waveforms were delivered from a Ventritex HVS-02 programmable cardioverter/defibrillator (Ventritex Inc.), which has a capacitance of 150 μF. For the single-current pathway configuration, two defibrillators were used. Each device has two programmable outputs, each capable of delivering a truncated exponential monophasic waveform. The pulse widths and polarities of both outputs are programmable. The shocks were synchronized to the QRS by use of an electrophysiological stimulator (DTU 201, Bloom Associates, Ltd). The analog output from the electrophysiological mapping system (surface limb lead II or aVF) was sensed by the stimulator as an external S1, which then stimulated the dual-electrode isolation units for the trigger pulse inputs for each defibrillator. For the single-current pathway system, a biphasic shock from a single-capacitor defibrillator was emulated, with the leading-edge voltage ($V_{(L)}$) of the second phase set equal to the trailing-edge voltage ($V_{(T)}$) of the first phase (Figure 2A). For the dual-current pathway system, a single-capacitor system was also emulated (Fig-
The leading-edge voltage of the first phase of the second current pathway shock ($V_{LPh1}$) was set equal to the trailing-edge voltage of the second phase of the first current pathway shock ($V_{TPh2}$). Trailing-edge voltages for each phase $V_T$ were calculated by use of the following equation:

$$V_T = V_L e^{-t/RC}$$

where $V_L$ is the leading-edge voltage of the previous phase, $t$ is the duration of the previous phase, $R$ is the resistance estimated by the resistance from the previous shock, and $C$ is the capacitance. The polarity of each phase was opposite to the preceding phase, with an interphase delay of 0.2 ms.

The ADFT for one single-current pathway with a single 7.5/2.5-ms biphasic waveform (Figure 2A) was compared with that for the dual-current pathways with two sequential 7.5/2.5-ms biphasic waveforms (Figure 2B). All four phases of the two biphasic waveforms emulated a single 150-μF capacitor discharge in that the trailing-edge voltage of phase 1 ($V_{TPh1}$) was equal ($\pm 10$ V) to the leading-edge voltage of phase 2 ($V_{LPh2}$). Also, phase 2 of the biphasic waveform was opposite in polarity to phase 1. B, Two biphasic waveforms delivered sequentially through dual-current pathways (DP). All four phases of the two biphasic waveforms emulated a single 150-μF capacitor discharge in that the trailing-edge voltage of phase 1 ($V_{TPh1}$) was equal ($\pm 10$ V) to the leading-edge voltage of phase 2 ($V_{LPh2}$), the trailing-edge voltage of phase 2 ($V_{TPh2}$) was equal ($\pm 10$ V) to the leading-edge voltage of phase 3 ($V_{LPh3}$), and the trailing-edge voltage of phase 3 ($V_{TPh3}$) was equal ($\pm 10$ V) to the leading-edge voltage of phase 4 ($V_{LPh4}$). Also, each phase was opposite in polarity to its preceding phase. C, Two biphasic waveforms delivered sequentially through dual-current pathways. All four phases of the two biphasic waveforms emulated a single 600-μF capacitor discharge.

Defibrillation Protocol

On arrival at the electrophysiological laboratory, all patients were in sustained atrial fibrillation. We determined the order of testing the configurations by drawing chits. The chits were not replaced until after 3 patients had been studied successfully, so that each configuration was tested as the first configuration four times, second four times, and third four times in 12 of the 14 patients successfully studied. This was to help control for the effect of duration of atrial fibrillation before each shock. After a successful defibrillation, atrial fibrillation was reinduced with rapid atrial pacing from the right atrial appendage or coronary sinus and allowed to persist for $\sim$1 minute.
TABLE 1. Patient Clinical Characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Cardiac History</th>
<th>Age, y</th>
<th>Weight, kg</th>
<th>Height, cm</th>
<th>Estimated EF by Echo, %</th>
<th>Echo Left Atrial Size, cm</th>
<th>Echocardiographic Valvular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>AF, HTN</td>
<td>42</td>
<td>91</td>
<td>160</td>
<td>60</td>
<td>4.3</td>
<td>Mild TR</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>AF, HTN, CAD</td>
<td>45</td>
<td>79</td>
<td>164</td>
<td>63</td>
<td>4.2</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>AF</td>
<td>48</td>
<td>100</td>
<td>155</td>
<td>65</td>
<td>4.9</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>AF, CAD, CABG, DM</td>
<td>69</td>
<td>84</td>
<td>153</td>
<td>58</td>
<td>4.1</td>
<td>Mild TR</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>AF, VT, CAD, MI, CABG, CHF, DM</td>
<td>76</td>
<td>98</td>
<td>151</td>
<td>30</td>
<td>4.4</td>
<td>Moderate MR, mild TR</td>
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<td>6</td>
<td>M</td>
<td>AF, CAD</td>
<td>49</td>
<td>118</td>
<td>158</td>
<td>50</td>
<td>4.1</td>
<td>Mild MR, TR, and PR</td>
</tr>
<tr>
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<td>F</td>
<td>AF, HTN, CAD, MVP</td>
<td>68</td>
<td>79</td>
<td>144</td>
<td>50</td>
<td>4.8</td>
<td>Moderate MR and TR, MVP</td>
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<td>8</td>
<td>M</td>
<td>AF, HTN, DM</td>
<td>71</td>
<td>96</td>
<td>167</td>
<td>58</td>
<td>4.3</td>
<td>Moderate MR</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>AF, HTN</td>
<td>42</td>
<td>91</td>
<td>159</td>
<td>60</td>
<td>4.3</td>
<td>Mild TR</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>AF, HTN, HOCM</td>
<td>73</td>
<td>83</td>
<td>144</td>
<td>55</td>
<td>4.6</td>
<td>Mild MR and TR</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>AF, HTN</td>
<td>69</td>
<td>115</td>
<td>155</td>
<td>55</td>
<td>3.7</td>
<td>Mild MR</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>AF, VT, HTN, DCM, CHF, DM</td>
<td>74</td>
<td>92</td>
<td>164</td>
<td>25</td>
<td>5.1</td>
<td>Moderate MR and TR</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>AF, HTN, CAD, CHF</td>
<td>63</td>
<td>79</td>
<td>149</td>
<td>35</td>
<td>5.0</td>
<td>Moderate MR, mild TR</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>AF, DCM, CHF</td>
<td>64</td>
<td>59</td>
<td>142</td>
<td>15</td>
<td>4.3</td>
<td>Moderate MR, severe TR</td>
</tr>
<tr>
<td>Mean</td>
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<td></td>
<td>61</td>
<td>90</td>
<td>155</td>
<td>48.5</td>
<td>4.4</td>
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<td></td>
<td>13</td>
<td>15</td>
<td>8.0</td>
<td>15.7</td>
<td>0.4</td>
<td></td>
</tr>
</tbody>
</table>

EF indicates ejection fraction; Echo, echocardiogram; AF, atrial fibrillation; HTN, hypertension; TR, tricuspid regurgitation; CAD, coronary artery disease; CABG, coronary artery bypass grafting; DM, diabetes mellitus; VT, ventricular tachycardia; MI, myocardial infarction; CHF, congestive heart failure; MR, mitral regurgitation; PR, pulmonic regurgitation; MVP, mitral valve prolapse; HOCM, hypertrophic obstructive cardiomyopathy; and DCM, dilated cardiomyopathy.

For the single-current pathway, a step-up protocol was used starting with a shock strength of 150 V and increasing or decreasing by 50-V steps up to a maximum of 500 V. If a shock failed, the next shock strength was increased by 50 V; if the shock succeeded, the next shock was decreased by 50 V. For dual-current shocks, a step-up protocol was used starting with a shock strength of 150 V and increasing by 50-V steps until a successful result was achieved. The lowest step was 150 V because of the minimal 50-V output of the Ventritex defibrillator. With a tissue/electrode interface impedance of 50 Ω, setting the leading trailing-edge of the first phase to 150 V allowed for adequate programming of the other phases of the two biphasic waveforms. The ADFT for each configuration was defined as the lowest-strength shock that successfully defibrillated the atria.

For each delivered shock or shocks, the leading-edge voltage and the shock waveform phase durations were programmed in the HVS-02 defibrillator or defibrillators. The actual current waveform delivered to each pair of electrodes was recorded across a 0.25-Ω resistor in series with the electrodes, and the actual voltage waveform was recorded with a 200:1, 100-MΩ resistor divider in parallel with the electrodes. These data were digitized at 20 000 Hz and recorded on a waveform analyzer (DATA6100, Data Precision). The impedance between the electrodes and the total delivered energy of each phase of the two biphasic waveforms were computed from the current and voltage waveforms.

Statistical Methods

Results are expressed as mean ± SD unless otherwise specified. For all statistical tests, a P value ≤ 0.05 was considered significant. Student's t test was used to compare the ADFT leading-edge voltages, leading-edge currents, and total delivered energies for different shock configurations. Individual differences in ADFT for different pathways were tested, controlling for multiple comparisons, with the Student-Newman-Keuls test. The overall effect of current-pathway configuration was tested by use of repeated-measures ANOVA. The correlation between duration of atrial fibrillation and ADFT was measured by standard parametric coefficient methods and by Spearman's rank nonparametric correlation coefficient methods.

Results

Patient Characteristics

Clinical characteristics of the study population are summarized in Table 1. Left atrial size and ejection fraction were estimated by transthoracic echocardiography. Echocardiographic data were obtained within the 2- to 3-month period before performance of the defibrillation protocol. Table 2 shows the duration of atrial fibrillation for each patient and the antiarrhythmic medications that the patients were taking at the time of the protocol. Also, patients who had undergone transthoracic cardioversion within the 3 months preceding the protocol are shown in Table 2 along with the electrode location, number of attempted shocks, maximum transthoracic energy delivered, and internal cardioversion outcome.

All patients were in atrial fibrillation at the time of the protocol, with a mean duration of 165 ± 187 days (range, 34 to 740 days). The duration of atrial fibrillation was determined from the time of the first ECG evidence of atrial fibrillation without any intercurrent therapy to restore sinus rhythm to the day of the protocol. Six patients were receiving antiarrhythmic therapy at the time of the internal procedure. Nine patients had undergone recent transthoracic cardioversion, which failed to convert seven of them to sinus rhythm. The other two patients had short-term successes with transthoracic cardioversion.

Internal cardioversion was successful in 12 of the 14 patients (Table 2). In 2 patients, internal cardioversion was unsuccessful. In 1 patient (patient 6), cardioversion could not be achieved by any of the three configurations despite a maximum voltage of 500 V. This patient was successfully cardioverted with a 360-J transthoracic countershock at the time of the protocol and maintained in sinus rhythm for 15 hours. In the other unsuccessfully treated patient (patient 7),
the coronary sinus could not be engaged, and thus the coronary sinus catheter could not be positioned. Internal cardioversion was not attempted, and the patient was successfully cardioverted with a 200-J transthoracic countershock and maintained sinus rhythm for at least 24 hours, when the patient was discharged from the hospital.

**Atrial Defibrillation Threshold**

Table 3 shows the ADFT data for leading-edge voltage, leading-edge current, mean impedance for the first current pathway, mean impedance for the second current pathway, and total delivered energy for each electrode configuration. The single-current pathway had a significantly higher ADFT in terms of delivered energy than the 150-μF dual-current pathway configuration. There was no significant difference in mean impedance among the three electrode configurations for each current pathway.

The effect of randomization on the mean leading-edge voltage at ADFT is shown in Figure 4. These data are from the 12 patients who could be successfully defibrillated with an internal method. Although there appeared to be a trend toward a higher ADFT for the single-current pathway when it was given first, it was not statistically significant. Thus, randomization so that each configuration was the first one given on four separate occasions controlled for the effect of first shock and for the duration of atrial fibrillation before the shock. There was no relationship between ADFT and duration of atrial fibrillation with the randomization scheme used for these 12 patients. If we used an estimated ADFT of 15 J and included data for patient 6, who could not be successfully defibrillated and who had been in atrial fibrillation for >2 years, standard correlation coefficients comparing the duration of atrial fibrillation and ADFT total energy were 0.862

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**TABLE 2. Patient Electrophysiological and Cardioversion Characteristics**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Duration of AF, <em>d</em></th>
<th>Current Antiarrhythmic</th>
<th>Recent Transvenous Electrode Location</th>
<th>Transthoracic Electrode Location</th>
<th>Number of Transvenous Shock Energy, J</th>
<th>Maximum Transthoracic Shock Energy, J</th>
<th>Outcome of Transthoracic Cardioversion</th>
<th>Outcome of Internal Cardioversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>342</td>
<td>None</td>
<td>Yes</td>
<td>AP</td>
<td>3</td>
<td>300</td>
<td>Failed</td>
<td>Successful</td>
</tr>
<tr>
<td>2</td>
<td>49</td>
<td>None</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>300</td>
<td>Failed</td>
<td>Successful</td>
</tr>
<tr>
<td>3</td>
<td>132</td>
<td>Procaainamide</td>
<td>Yes</td>
<td>AP</td>
<td>3</td>
<td>300</td>
<td>Failed</td>
<td>Successful</td>
</tr>
<tr>
<td>4</td>
<td>87</td>
<td>None</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>300</td>
<td>Failed</td>
<td>Successful</td>
</tr>
<tr>
<td>5</td>
<td>67</td>
<td>Quinidine</td>
<td>Yes</td>
<td>AP</td>
<td>4</td>
<td>360</td>
<td>Failed</td>
<td>Successful</td>
</tr>
<tr>
<td>6</td>
<td>740</td>
<td>Amiodarone</td>
<td>Yes</td>
<td>AP</td>
<td>4</td>
<td>360</td>
<td>Failed</td>
<td>Failed</td>
</tr>
<tr>
<td>7</td>
<td>168</td>
<td>None</td>
<td>No</td>
<td>No</td>
<td>4</td>
<td>360</td>
<td>Failed</td>
<td>Failed</td>
</tr>
<tr>
<td>8</td>
<td>58</td>
<td>Procaainamide</td>
<td>No</td>
<td>No</td>
<td>4</td>
<td>360</td>
<td>Successful for 14 days</td>
<td>Successful</td>
</tr>
<tr>
<td>9</td>
<td>95</td>
<td>Amiodarone</td>
<td>No</td>
<td>No</td>
<td>5</td>
<td>360</td>
<td>Successful for 14 days</td>
<td>Successful</td>
</tr>
<tr>
<td>10</td>
<td>34</td>
<td>None</td>
<td>Yes</td>
<td>AP</td>
<td>6</td>
<td>360</td>
<td>Successful for 14 days</td>
<td>Successful</td>
</tr>
<tr>
<td>11</td>
<td>195</td>
<td>None</td>
<td>Yes</td>
<td>AP</td>
<td>6</td>
<td>360</td>
<td>Successful for 14 days</td>
<td>Successful</td>
</tr>
<tr>
<td>12</td>
<td>232</td>
<td>Sotalol</td>
<td>Yes</td>
<td>AP</td>
<td>3</td>
<td>360</td>
<td>Failed</td>
<td>Successful</td>
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<tr>
<td>13</td>
<td>75</td>
<td>None</td>
<td>Yes</td>
<td>AP</td>
<td>2</td>
<td>360</td>
<td>Failed</td>
<td>Successful</td>
</tr>
<tr>
<td>14</td>
<td>38</td>
<td>None</td>
<td>Yes</td>
<td>AP</td>
<td>2</td>
<td>200</td>
<td>Successful for 5 days</td>
<td>Successful</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; AP, anterior-posterior; and CS, coronary sinus.

*Mean, 165 ± 187 days; range, 34–740 days.

**TABLE 3. Atrial Defibrillation Threshold Data**

<table>
<thead>
<tr>
<th>Electrode Configuration</th>
<th>Leading Edge Voltage, V</th>
<th>Leading Edge Current, A</th>
<th>First Pathway Mean Impedance, Ω</th>
<th>Second Pathway Mean Impedance, Ω</th>
<th>Total Delivered Energy, J</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single 150-μF biphasic shock, single-current pathway (SP 150)</td>
<td>297±58*</td>
<td>6.1±1.1*</td>
<td>47±5</td>
<td>NA</td>
<td>5.1±1.8*</td>
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<tr>
<td>Dual 150-μF biphasic shocks, dual-current pathways (DP 150)</td>
<td>176±35</td>
<td>3.8±0.5</td>
<td>47±4</td>
<td>2.0±0.4</td>
<td></td>
</tr>
<tr>
<td>Dual 600-μF biphasic shocks, dual-current pathways (DP 600)</td>
<td>176±26</td>
<td>3.7±0.5</td>
<td>47±6</td>
<td>61±7</td>
<td>2.4±0.5†</td>
</tr>
</tbody>
</table>

*P<.05 compared with both dual-current pathways (DP 150 and DP 600); †P<.05 compared with dual 150-μF biphasic shocks dual-current pathways (DP 150).
for the 150-μF single pathway, 0.863 for the 150-μF dual-current pathway, and 0.0869 for the 600-μF dual-current pathway, which were all statistically significant. However, Spearman’s rank correlation coefficients were 0.55 for the 150-μF single pathway, 0.066 for the 150-μF dual-current pathway, and 0.033 for the 600-μF dual-current pathway, which were not statistically significant.

Discussion

Background

In this study, we compared the cardioversion efficacies of a single biphasic shock delivered via a single-current defibrillation pathway with that of sequential shocks delivered via a dual-current electrode system in humans with atrial fibrillation. We also studied the effect of capacitance on the sequential-shock, dual-pathway electrode system with the hope that an electrode and waveform configuration could be found that halted atrial fibrillation with shock strengths of low voltage and current. We chose to study these configurations for several reasons. First, internal ADFTs when a single-current pathway is used in humans have been shown to be in the 1- to 5-J range for patients with a history of paroxysmal atrial fibrillation5–9; however, these shock strengths are still in a range that is associated with significant discomfort.6,12–15 Second, studies in animals with acutely induced atrial fibrillation have shown a significant decrease in defibrillation threshold requirements when dual-current pathways with sequential shocks are used compared with single-current pathways with single shocks. Third, some clinical studies have demonstrated that the pain associated with internal atrial defibrillation shocks is related to the intensity of the shock,6,9,12,13,15 and it is hypothesized that pain is more closely related to the leading-edge voltage and current of the shock than to the shock energy.15,25 By increasing the capacitance of the sequential shocks, we hypothesized that the leading-edge voltage and current of the shock would be reduced, possibly decreasing the pain associated with internal atrial defibrillation shocks.

Comparison With Previous Defibrillation Studies

Animal studies28–33 have demonstrated a close relationship between the extracellular potential gradient distribution produced throughout the ventricles by a shock and whether or not the shock successfully terminates 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.31–33 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-gradient areas farther away from the electrodes.31,33 These areas of low gradient are the regions in which earliest activation originates after unsuccessful defibrillation shocks.31,33 Furthermore, high-potential gradients can have detrimental effects on the heart, including postshock arrhythmias,34 conduction disturbances,35,36 myocardial dysfunction,37 and myocardial necrosis.38 The potential gradient distribution created by a shock in the heart depends on several factors, including electrode size and location.39 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 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.39 These findings and theories have been used to develop more efficient lead systems for implantable ventricular defibrillators.40 One way to potentially increase the minimum gradient throughout the heart and to minimize the gradient near the electrodes is by giving two smaller shocks separated spatially and temporally instead of one large shock.24,41,42

We previously demonstrated in a sheep model of atrial fibrillation that certain biphasic waveforms were superior to monophasic waveforms with a single defibrillation current pathway. Also, we showed that the optimal single-current...
pathway used electrodes that encompassed both atria (right atrial appendage and distal coronary sinus). Furthermore, we have shown in this same sheep model that the use of a dual-current defibrillation pathway and sequential biphasic shocks, with the first shock delivered between the right atrial appendage and the distal coronary sinus and the second shock delivered between the proximal coronary sinus and the left pulmonary artery, demonstrated >70% reduction in energy requirements compared with the optimum single-current pathway of the right atrial appendage to distal coronary sinus. In this sheep study, selection of the electrode configurations was guided by a mapping study in sheep with acutely induced atrial fibrillation. That mapping study demonstrated that the earliest sites of atrial activation after unsuccessful single-current pathway shocks were dependent on electrode configuration and appeared to occur in regions in which the potential gradient field produced by the shock would be predicted to be low. The dual-electrode configurations used in this animal study were designed to use a second shock and current pathway that encompassed the areas in which the previous mapping study had shown the earliest activations to occur.

Several clinical studies have demonstrated the efficacy and safety of internal atrial defibrillation that uses a single shock with a single-current pathway. Cooper et al compared multiple monophasic and biphasic waveforms for internal atrial defibrillation in patients with induced atrial fibrillation. They demonstrated that certain biphasic waveforms (7.5/2.5 ms) were more efficacious than symmetrical biphasic waveforms (5/5 ms) with a single-pathway right atrial appendage to distal coronary sinus electrode configuration. The ADFT for the best biphasic waveform (7.5/2.5 ms) was 1 to 2 J, which is still in the range that is considered painful to most patients.

The present study represents the first published data for the use of sequential shocks and dual-current pathways for atrial defibrillation in humans. The 7.5/2.5-ms biphasic waveforms used in the present study were chosen on the basis of previous work by Cooper and coworkers. In that clinical study, the use of a dual-current defibrillation pathway and sequential biphasic shocks, with the first shock delivered between the right atrial appendage and the distal coronary sinus and the second shock delivered between the proximal coronary sinus and the left subclavian vein, demonstrated >50% reduction in energy requirements compared with the single-current pathway of the right atrial appendage to distal coronary sinus. The dual-electrode configurations used in the present clinical study were designed to use a second shock and current pathway that encompassed areas of the atria in which the potential gradient field was predicted to be low after a single-current shock delivered from the right atrial appendage to distal coronary sinus. Thus, these findings in humans are similar to the animal models of internal atrial defibrillation that used dual-current pathways and sequential biphasic shocks. In both the animal and human studies, the dual-current sequential-shock configurations demonstrated a significant reduction in ADFT compared with a single-current, single-shock configuration. The differences in actual threshold values between animals and humans can be explained by differences in species as well as by type of atrial fibrillation (induced versus chronic). Furthermore, the ADFT for the single-current pathway configuration was at least one step above the minimal output of the cardioverter/defibrillator used. The ADFTs for several patients with both dual-current systems were at the minimal output of the cardioverter/defibrillator used, and therefore the real ADFTs could have been even lower. Thus, the actual difference between the single- and dual-current systems might have been underestimated by the defibrillation protocol used in the present study.

Effect of Capacitance
Animal and human studies have demonstrated that ventricular defibrillation energy requirements are significantly lower for capacitances of <120 μF than for higher capacitances. Peak voltage and current are greater for the lower-capacitor waveforms; however, some clinical studies but not others have demonstrated that the pain associated with internal atrial defibrillation shocks is related to the intensity of the shock. It has been hypothesized that the pain associated with an internal shock is in part related to the leading-edge voltage and/or current instead of the energy. Therefore, defibrillation energy might be minimized with a lower capacitance, but the pain associated with the shock might be minimized with a higher capacitance. In the present study, increasing the capacitance of the delivered sequential biphasic waveforms by a factor of four did not result in a difference in defibrillation threshold in terms of leading-edge voltage or leading-edge current. Because of their higher tilt, the lower-capacitance sequential biphasic shocks defibrillated with a lower total delivered energy than the higher-capacitance sequential biphasic shocks.

Safety
The safety of internal atrial defibrillation has been addressed in several previous animal and human studies. All of those studies demonstrated that as long as the shocks were synchronized to the ventricular activation, almost no ventricular arrhythmias were seen. In the present study, when the shocks were appropriately synchronized to the R wave, no ventricular arrhythmias were observed in >100 single- and dual-current pathway shocks. The only serious complication was induction of ventricular fibrillation due to inappropriate synchronization from equipment error and delivery of the shock during the ventricular vulnerable period. This emphasizes the critical importance of ensuring accurate synchronization of the shock to the R wave to avoid potentially lethal postshock ventricular arrhythmias in implantable devices; if this is not done, back-up ventricular defibrillation will be needed. There were no long-term complications and temporary pacing was not required in any of the patients for postshock conduction delays. No permanent sinus or AV nodal dysfunction occurred as a complication of the defibrillation protocol.

Tolerability and Clinical Implications
Several clinical studies have shown the efficacy of biphasic waveforms through a single-current pathway for internal atrial fibrillation. ADFTs, in terms of mean en-
nergy, have varied between these studies from as low as 1.9±1.6 J to as high as 9.6±6.6 J. 47

Murgatroyd and coworkers, using a right atrial appendage to coronary sinus single-current vector and a 3/3-ms biphasic waveform, evaluated the tolerability of transvenous atrial defibrillation shocks in 19 patients. Shock strengths were increased until defibrillation was achieved, and shocks that required sedation were scored as causing “severe discomfort.” They found that the range of tolerable shock strengths not requiring sedation was 0.1 to 1.2 J; however, the mean defibrillation threshold was 2.16±1.02 J (range, 0.7 to 4.4 J). Thus, the majority of the patients required sedation to achieve successful atrial defibrillation, with only 2 of the 19 patients being successfully defibrillated without sedation.

Another study46 evaluated the discomfort of internal single-current pathway biphasic shocks for atrial defibrillation in 11 nonsedated patients with a history of paroxysmal or chronic atrial fibrillation. Shocks were delivered in 0.5-J increments between right atrial and coronary sinus electrodes. The majority (73%) of the patients indicated that shock strengths ≤1 J were painful, and all patients required sedation for shock strengths >2 J. The mean ADFT was 9.6±6.6 J (range, 0.5 to 20 J).

Tomassoni et al16 compared the effect of different capacitances on ADFT and pain perception in humans. They found that a higher-capacitance waveform (120 µF) was associated with a higher ADFT energy requirement but a decreased perception of pain in 6 of 10 patients compared with a lower-capacitance waveform (50 µF). They found that the ADFT for 120-µF shocks was 2.0±1.0 J and that even shocks of <0.5 J were considered painful by most patients.

Ammer and coworkers15 evaluated the differences in pain threshold between different defibrillation waveforms in humans undergoing internal atrial cardioversion. They compared two biphasic waveforms and found that a 6/6-ms biphasic waveform had significantly lower leading-edge voltage requirements at ADFT and was associated with a decrease in pain perception, with patients requiring less sedation than for a 3/3-ms biphasic waveform. The mean ADFT energy requirement for the 6/6-ms biphasic waveform was 6.8±2.8 J. From these studies, it appears that discomfort caused by the shock is related to the strength of the shock and that even with optimization of electrode and waveform configurations, the mean ADFTs determined in previous clinical studies were still >1 J, which level has been shown to cause severe discomfort in most patients.6,9,12–15

The present study did not measure discomfort of the shocks because deep analgesia/sedation was used in all patients. For the two dual-current defibrillation pathways, there was at least a slight decrease in ADFT for each individual patient compared with the single-current pathway configuration. However, the mean ADFT of 2.0±0.4 J for the best configuration (150-µF dual current) was still in a range that other studies would predict to be painful to most patients. The dual-current pathways did result in a markedly reduced ADFT; however, it remains to be determined if this reduction in defibrillation voltage and energy decreases discomfort sufficiently to justify the added complexity of additional electrodes. Use of an active left pectoral can electrode to replace the left subclavian vein electrode used in the present study would mean that three internal electrodes would be needed with a dual-current pathway system. However, the proximal and distal coronary sinus electrodes could be on the same catheter. This configuration may be desirable in patients with a high ADFT and may enable more patients to be candidates for an implantable device.

**Summary**

Sequential shocks delivered through dual-current pathways resulted in a marked reduction in ADFT energy requirements. Increased-capacitance/lower-tilt sequential biphasic shocks did not result in a significantly lower leading-edge voltage or current than lower-capacitance/higher-tilt sequential biphasic shocks. Although the sequential-shock configurations evaluated in the present study were more efficient for internal atrial defibrillation, threshold levels were still in the range in which most patients probably feel significant discomfort without sedation. It is hoped that continued research into this area will result in even more efficient defibrillation waveforms and lead systems to help further minimize discomfort to the patient. A dual-current defibrillation system could make more patients eligible for an implantable device.

**References**


Marked Reduction in Internal Atrial Defibrillation Thresholds With Dual-Current Pathways and Sequential Shocks in Humans

Randolph A. S. Cooper, Vance J. Plumb, Andrew E. Epstein, G. Neal Kay and Raymond E. Ideker

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