Strength–Duration and Probability of Success Curves for Defibrillation With Biphasic Waveforms

Scott A. Feeser, MD, Anthony S.L. Tang, MD, Katherine M. Kavanagh, MD, Dennis L. Rollins, MS, William M. Smith, PhD, Patrick D. Wolf, MS, and Raymond E. Ideker, MD, PhD

Certain biphasic waveforms require less energy to defibrillate than do monophasic pulses of equal duration, although the mechanisms of this increased effectiveness remain unclear. This study used strength–duration and percent success curves for defibrillation with monophasic and biphasic truncated exponential waveforms to explore these mechanisms. In part 1, defibrillation thresholds were determined for both high- and low-tilt waveforms. The monophasic pulses tested ranged in duration from 1.0 to 20.0 msec, and the biphasic waveforms had first phases of either 3.5 or 7.0 msec and second phases ranging from 1.0 to 20.0 msec. In part 2, defibrillation percent success curves were constructed for 6.0 msec/6.0 msec biphasic waveforms with a constant phase-one amplitude and with phase-two amplitudes of approximately 21%, 62%, 94%, and 141% of phase one. This study shows that if the first phase of a biphasic waveform is held constant and the second phase is increased in either duration or amplitude, defibrillation efficacy first improves, then declines, and then again improves. For pulse durations of at least 14 msec, the second-phase defibrillation threshold voltage of a high-tilt biphasic waveform is higher than that of a monophasic pulse equal in duration to the biphasic second phase (p<0.05), indicating that the previously proposed hypothesis of stimulation by the second phase is not the sole mechanism of biphasic defibrillation. These facts indicate the importance of the degree of tilt for the defibrillation efficacy of biphasic waveforms and suggest at least two mechanisms exist for defibrillation with these waveforms, one that is more effective for smaller second phases and another that becomes more effective as the second phase is increased. (Circulation 1990;82:2128–2141)

Certain biphasic waveforms require less energy to defibrillate or produce less cardiac dysfunction than do monophasic pulses of equal duration.1–4 The lower defibrillation threshold (DFT) for certain biphasic waveforms has important implications for the effectiveness and lifespan of automated, implantable cardioverter/defibrillators with power supplies that are constrained by space considerations.5–7

Research seeks to answer the following two closely related questions. First, what is the mechanism that makes biphasic shocks so effective? Several explanations have been offered. Jones et al8 suggested that the first phase acts as a hyperpolarizing “conditioning prepulse” that activates sodium channels, and the second phase acts as a depolarizing “excitation pulse.” Other possible reasons are 1) that the first phase may shorten cardiac cell refractoriness, enabling more cells to be excited by the second phase, 2) that reduced cardiac impedance during the second phase permits greater current delivery during that phase, and 3) that the biphasic waveform is less able to stimulate myocardium to reinitiate fibrillation after the shock.9

Information regarding the first question may help answer the second question. Which are the optimum biphasic waveforms for defibrillating, based on energy requirements,1,3,4,9–13 postshock cardiac function2,14,15 or other criteria?8,16 For exponential decay waveforms, several authors have shown that the second-phase duration must be less than or equal to the first-phase...
duration to achieve a minimum DFT. Others have shown the importance of the relative amplitudes of the two phases, the pulse separation, or the electrode orientations.

This study uses strength–duration curves and percent success curves for defibrillation with monophasic and biphasic truncated exponential waveforms to explore further the mechanism of defibrillation by biphasic waveforms while also providing information on which waveforms require minimum energy for defibrillation. The study shows that two separate mechanisms of defibrillation must exist to explain the behavior of biphasic waveforms with lower energy second phases versus those with higher energy second phases.

**Methods**

This study comprised five similar but distinct protocols, described subsequently as part 1a–d and part 2. Part 1 protocols determined defibrillation strength–duration curves, and the part 2 protocol measured percent success curves. The common portions of each protocol are described first.

**Surgical Preparation**

Fifty-two mongrel dogs (22.3±3.3 kg body wt) were anesthetized with pentobarbital (30–35 mg/kg). The dose of pentobarbital was adjusted according to the depth of anesthesia assessed by signs such as shivering, eyelid reflexes, and pedal reflexes. Each dog was intubated with a cuffed endotracheal tube and ventilated with 30–60% oxygen through a Harvard respirator (Harvard Apparatus, South Natick, Mass.). Succinylcholine was initially given at a dose of 1 mg/kg and later at 0.25–0.5 mg/kg no more than once per hour to decrease muscle contraction induced by the electric shocks. This dose is much less than that required to alter cardiac excitability. A femoral arterial line was inserted to continuously monitor systemic blood pressure. Lactated Ringer’s was continuously infused. Normal metabolic status was maintained throughout the study by taking blood every 30–60 minutes, determining the pH, PO2, PCO2, base excess, CO2 and HCO3 concentration, and correcting any abnormal values.

The chest was opened by median sternotomy, and the pericardial sac opened to expose the heart. A 33-cm2 contoured mesh electrode sutured onto the right ventricular epicardium served as the anode and a 39-cm2 electrode sutured onto the left ventricle was the cathode, as previously described.

**Protocol**

Each dog underwent up to 90 fibrillation/defibrillation sequences performed at 5-minute intervals. For each sequence, fibrillation was induced by using a 35 V, 60-Hz pulse for 1–2 seconds delivered between pacing wires inserted into the right ventricle. Defibrillation was attempted after 10 seconds by applying to the epicardial electrodes one of the truncated exponential waveforms described herein (Figures 1–3). If this initial attempt failed, a rescue shock with the minimum reliable defibrillation energy was applied between these same electrodes. A Ventritex HVS 150 μF defibrillator (Ventritex, Sunnyvale, Calif.) delivered all shocks in parts 1a, 1b, and 2. A custom 750-μF defibrillator was used during parts 1c and 1d to achieve a longer decay time constant. In part 1d, the time constant was further lengthened by wiring the defibrillator in series with a 200-Ω resistor. During each attempted defibrillation, the applied current and voltage across the heart were sampled at 20 kHz by a DATA 6000 waveform analyzer (Data Precision, Danvers, Mass.), and the impedance between the electrodes and the total delivered energy of each phase of the pulse were computed. To ensure proper equipment functioning and to stabilize the ionic and hormonal milieu of the heart, each study was begun by conducting three conditioning fibrillation/defibrillation sequences.

![Figure 1](https://example.com/figure1.png)

**FIGURE 1.** Waveforms tested in parts 1a and 1b. Tilts ranged from 10% to 90% based on phase duration. Panel A: Six monophasic waveforms used in both parts 1a and 1b. Panel B: Eight one-capacitor biphasic waveforms used in part 1a, with the phase-two leading edge voltage (V2) equal to the phase-one trailing edge voltage (V1). Panel C: Eight one-capacitor biphasic waveforms used in part 1b. Panel D: Eight two-capacitor biphasic waveforms used in part 1b, with V2 equal to the phase-one leading edge voltage (V1).
FIGURE 2. Waveforms tested in parts 1c and 1d. Panel A: Five low-tilt biphasic waveforms tested in part 1c. Tilts ranged from 1% to 17% depending on pulse duration. Panel B: Voltage profile of 11 monophasic and 11 biphasic low-tilt waveforms tested in part 1d. The tilts ranged from 1% to 14%. The rounding of the leading edge of each phase resulted from connecting the nonconstant impedance of the heart in series with a 200-Ω resistor to achieve long decay times. The current profiles did not show this pronounced rounding.

Part 1

In parts 1a and 1b, strength–duration curves for high-tilt waveforms (exponential decay time constant, \(\tau\), of 7–9 msec) were determined, and in parts 1c and 1d these curves were determined for low-tilt waveforms (\(\tau=40–180\) msec). For the biphasic waveforms studied, the first-phase duration was held constant, whereas the second-phase duration was varied. The goal of these protocols was to compare the defibrillation thresholds of monophasic shocks with those of biphasic shocks, paying particular attention to the regions of the strength–duration curves where the biphasic DFTs change from being lower to being higher than the monophasic DFTs.

The DFT for each waveform was determined by a modified Bourland protocol. Each trial consisted of first attempting defibrillation at a voltage that was our best estimate of the DFT for that waveform. The phase-one leading edge voltage (\(V_{\text{nl}}\)) was increased in increments of approximately 20% after a failed attempt or was decremented by the same percentage after a success. When the transition from failure to success or success to failure was found, a final shock was tested with \(V_{\text{nl}}\) midway between the successful and unsuccessful voltages. The minimum successful voltage as measured across the heart was considered the DFT for that waveform. This value was thereby established within \(\pm 10\%\). Because the Ventritex HVS defibrillator is limited to 10-V increments, however, when \(V_{\text{nl}}\) at the DFT is less than 100 V in parts 1a, 1b, and 2, the potential error of the DFT determination is greater than 10%. To avoid damaging the heart, \(V_{\text{nl}}\) above 560 V was not given. In the seven of 66 DFT determinations that did not defibrillate with this maximum voltage, the DFT was assumed to be 10% higher than the highest delivered shock. Had the DFT determination been completed in these cases, the resulting DFT would have been at least as high as the assumed value. If the “true” DFT were higher than the assumed value, it would only have strengthened the statistical significance of the results reported for these data points. All DFTs were determined in random order. Eight dogs were used in parts 1a, eight were used in part 1b, 14 were used in part 1c, and 14 were used in part 1d.

Part 1a. In part 1a, the following waveforms were tested: 1) six monophasic truncated exponential monophasic waveforms of durations of 3.5, 7.0, 10.5, 14.0, 17.5, and 20.0 msec and 2) eight biphasic truncated exponential waveforms with phase-one durations of 3.5 msec and phase-two durations of 1.0, 2.0, 3.5, 7.0, 10.5, 14.0, 17.5, and 20.0 msec. These biphasic waveforms were “one-capacitor” pulses with
the phase-two leading edge voltage ($V_{21}$) equal to the phase-one trailing edge voltage ($V_{11}$) (Figure 1, panels A, B). Subsequently, biphasic waveforms are referred to by the notation “phase-one duration/phase-two duration,” as in, for example, a 3.5/10.5 one-capacitor waveform.

**Part 1b.** In part 1b, the waveforms used were 1) six monophasic waveforms identical to those in part 1a, 2) eight biphasic waveforms that differed from the part 1a biphasic shocks only in that the phase-one duration was 7.0 msec, and 3) eight “two-capacitor” biphasic waveforms ($V_{21}=V_{11}$) with 7.0-msec first phases and the same duration second phases as the other biphasic shocks (Figure 1, panels A, C, D).

**Part 1c.** In part 1c, low-tilt truncated exponential biphasic waveforms were studied. These pulses had 3.5-msec first phases and 1.0-, 2.0-, 3.5-, 6.0-, and 8.5-msec second phases. With $\tau=40$ msec, the tilts varied between 1% and 17% depending on pulse duration (Figure 2, panel A).

**Part 1d.** The part 1d waveforms were 1) 11 very-low-tilt truncated exponential monophasic pulses with durations of 1.0, 2.0, 3.0, 3.5, 4.0, 5.0, 6.0, 7.0, 8.5, 10.5, and 14.0 msec and 2) 11 very-low-tilt biphasic stimuli with 3.5-msec first phases and second phases of 1.0, 2.0, 3.0, 3.5, 4.0, 5.0, 6.0, 7.0, 8.5, 10.5, and 14.0 msec. Average tilt ranged from 1% to 14% with $\tau=180$ msec (Figure 2, panel B). This long time constant was achieved by connecting a 200 $\Omega$ resistor in series with the nonconstant impedance of the heart, which varies with both shock voltage and duration. Thus, the actual voltage pulse seen by the heart was not a pure exponential decay waveform, particularly during the first several milliseconds of each phase. The 200 $\Omega$ resistor acted as a voltage divider such that the defibrillator could deliver a maximum of about 200 V to the heart, which was not always enough to defibrillate. In these cases, most often involving the 1.0- and 2.0-msec monophasic pulses, the series resistance was reduced to 100 $\Omega$ or 50 $\Omega$. The tilts remained below 14% even with these changes.

**Part 2**

Kavanagh et al.\(^{13}\) have shown that a 6.0/6.0 one-capacitor pulse defibrillates with a lower $V_{11}$ than does a comparable two-capacitor form. This result suggests that if the first-phase amplitude is held constant for this 6.0/6.0 waveform, the probability of success curve will decrease as $V_{21}$ is raised from approximately 50% of $V_{11}$ to 100% of $V_{11}$. This possibility was tested in part 2.

First, to establish the voltage range at which both defibrillation successes and failures could be expected, the DFT was determined for a 6.0/6.0 biphasic truncated exponential waveform with $V_{21}$ about 50% of $V_{11}$. The DFT was determined twice by using the protocol previously described, and the average of the two $V_{11}$ values was computed.

Next, to search for the two waveforms that would most dramatically demonstrate a decrease in defibrillation efficacy with increasing phase-two amplitude, the defibrillation success or failure of four sets of four shocks was tested. The four waveforms in each set were 6.0/6.0 biphasic truncated exponentials with $V_{11}$ as just established and $V_{21}$ levels that were approximately 50%, 67%, 83%, and 100% of $V_{11}$ (Figure 3).
Figure 5. Scatterplots of leading edge voltage (panel A), leading edge current (panel B), and total delivered energy (panel C) versus total pulse duration for parts 1a and 1b waveforms at threshold. The monophasic thresholds from parts 1a and 1b are combined. On at least one occasion for each of the one-capacitor biphasic waveforms with second phases of 17.5 or 20.0 msec (*), defibrillation was not achieved with the maximum shock of $V_{10}=560$ V. Thus, defibrillation thresholds for these waveforms may be low estimates. For biphasic waveforms with a 7.0-msec first phase, the leading edge voltage and current are lower for the two-capacitor waveform than for the one-capacitor waveform at all total durations except 14.0 and 17.5 msec ($\$p<0.05$, $\uparrow p<0.02$). The total energy is lower for the two-capacitor waveform only when the total duration is at least 24.5 msec, whereas the one-capacitor waveform performs better in terms of energy at 10.5, 14.0, and 17.5 msec.
The shocks within each set were given in random order. Based on the results of these 16 shocks and the algorithm outlined in Figure 4, two waveforms (subsequently called waveforms B and C) were selected for further study. This complex method for choosing waveforms was devised because pilot studies revealed the pronounced impact on defibrillation success of just a 10-V change in \( V_1 \) or a 10% variation in \( V_2 / V_1 \). The process resulted in using the 67% and 100% waveforms in five dogs, the 50% and 83% waveforms in two dogs, and the 67% and 83% waveforms in one dog. Having selected waveforms B and C, these two waveforms and two more 6.0/6.0 biphasic pulses with the same \( V_1 \) and with \( V_2 \) 20% and 140% of \( V_1 \) (waveforms A and D, respectively) were tested for defibrillation success 12 times each. Again, each set of four shocks was randomly ordered. Only these final 12 trials of each waveform were used in determining the defibrillation percent success.

After completing one of the protocols just described, the dog was euthanized by electrically induced fibrillation. The electrodes were removed, and the heart was excised and weighed.

**Statistical Analysis**

In part 1, all comparisons between defibrillation threshold values of leading edge voltage, leading edge current, and total energy were made with paired \( t \) tests. In part 2, paired \( t \) tests were applied to compare the percent success of waveforms A versus B, B versus C, and C versus D. Statistically significant comparisons discussed subsequently imply \( p < 0.05 \) unless stated otherwise.
TABLE 1. Leading Edge Voltage, Leading Edge Current, and Total Delivered Energy for Parts 1a and 1b Waveforms at the Defibrillation Threshold

<table>
<thead>
<tr>
<th>Leading edge voltage for</th>
<th>Phase-two duration for biphasic waveforms and total duration for monophasic waveforms (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Part 1a monophasic</td>
<td>...</td>
</tr>
<tr>
<td>Phase 1=3.5 msec, 1-cap</td>
<td>111.1±16.3</td>
</tr>
<tr>
<td>Part 1b monophasic</td>
<td>...</td>
</tr>
<tr>
<td>Phase 1=7.0 msec, 1-cap</td>
<td>134.6±33.6§</td>
</tr>
<tr>
<td>Phase 1=7.0 msec, 2-cap</td>
<td>103.4±23.3</td>
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Leading edge current for

<table>
<thead>
<tr>
<th>Total energy for</th>
<th>1.0</th>
<th>2.0</th>
<th>3.5</th>
<th>7.0</th>
<th>10.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part 1a monophasic</td>
<td>...</td>
<td>...</td>
<td>3.76±0.87</td>
<td>3.37±1.01</td>
<td>3.56±0.64</td>
</tr>
<tr>
<td>Phase 1=3.5 msec, 1-cap</td>
<td>2.68±0.50</td>
<td>2.25±0.41</td>
<td>2.39±0.47†</td>
<td>5.56±1.71†</td>
<td>6.44±2.06†</td>
</tr>
<tr>
<td>Part 1b monophasic</td>
<td>...</td>
<td>...</td>
<td>4.31±1.31</td>
<td>3.89±1.12</td>
<td>4.25±1.19</td>
</tr>
<tr>
<td>Phase 1=7.0 msec, 1-cap</td>
<td>3.33±0.98†§</td>
<td>2.78±0.56§</td>
<td>2.82±0.63†§</td>
<td>3.00±0.77†</td>
<td>3.99±1.63</td>
</tr>
<tr>
<td>Phase 1=7.0 msec, 2-cap</td>
<td>2.59±0.67</td>
<td>2.25±0.67</td>
<td>2.42±0.57†</td>
<td>2.84±0.77†</td>
<td>4.51±1.80</td>
</tr>
</tbody>
</table>

Total energy for

| Part 1a monophasic       | ...      | ...      | 1.22±0.44 | 1.43±0.78 | 1.83±0.65 |
| Phase 1=3.5 msec, 1-cap   | 0.71±0.20 | 0.56±0.18 | 0.75±0.28* | 4.61±2.33† | 6.30±3.69† |
| Part 1b monophasic       | ...      | ...      | 1.52±0.76 | 1.83±0.93 | 2.36±1.26 |
| Phase 1=7.0 msec, 1-cap   | 1.43±0.77 | 0.98±0.32 | 0.98±0.45† || 1.19±0.40† || 2.37±1.67§ |
| Phase 1=7.0 msec, 2-cap   | 0.99±0.43 | 0.92±0.47 | 1.29±0.57 | 1.99±1.01* | 4.82±2.89* |

cap, capacitor; DFT, defibrillation threshold.

*p<0.05, ‡p<0.02 for difference between indicated biphasic waveform and corresponding monophasic waveform of equal total duration.

†p<0.05, §p<0.02 for difference between corresponding one and two-capacitor waveforms with phase-one duration=7.0 msec.

‡DFT not reached at 560 V in at least one dog for these waveforms.

There has been some debate about the use of DFTs as a means of comparing waveforms, with some authors preferring the use of percent success curves\(^\text{23,24}\) and others finding the DFT to be a practical measure when comparing numerous waveforms.\(^\text{25}\) In this study, DFTs were used in part 1 because of the many waveforms being compared, and percent success curves were used in part 2 where just four waveforms were compared.

**Results**

**Parts 1a and 1b**

The mean DFT leading edge voltages (V\(_L\)) and V\(_3\)), leading edge current (I\(_L\)), and total and phase-two energies (J\(_L\) and J\(_2\)) for all waveforms are shown in Figures 5 and 6. The monophasic DFTs from parts 1a and 1b have been combined to give 16 measurements per data point, and the biphasic DFTs each represent eight dogs per point.

Whether examining voltage, energy, or current (Figure 5), the mean DFT for monophasic waveforms is greater than for one-capacitor biphasic waveforms of equal total duration when the biphasic second phase is equal to or shorter than the first phase, but the monophasic DFT is lower when the biphasic second phase is longer. For the biphasic waveforms with a 7.0-msec first phase, V\(_L\) at threshold for two-capacitor waveforms is significantly lower than for one-capacitor waveforms for all second-phase durations except 7.0 and 10.5 msec. Because the second phase of the two-capacitor waveform is larger than the second phase of a one-capacitor waveform with the same V\(_L\) these results are not also true for shock energy; the total delivered energy is significantly lower for the two-capacitor form only when the second phase is at least 17.5 msec. With increase in the second-phase duration, the defibrillation effectiveness of the one-capacitor waveforms degrade much more dramatically than either the monophasic

**FIGURE 7.** Scatterplot of trailing edge voltage versus total waveform duration for parts 1a and 1b stimuli. For the biphasic waveforms, the open datum points represent the phase-one voltages and the solid points denote the phase-two voltages.
or two-capacitor biphasic waveforms. Table 1 displays the means, standard deviations, and significance levels for these data.

Figure 6 compares the defibrillation effectiveness of the second phase of biphasic waveforms to that of monophasic waveforms. Interestingly, a one-capacitor waveform with a 3.5-msec first phase and a second phase at least 14.0 msec long requires more voltage and energy to defibrillate than does a monophasic pulse equal in duration to the biphasic second phase. For example, for the 3.5/20.0 one-capacitor waveform, the presence of a first phase makes defibrillation by the second phase more difficult than had the first phase been absent. Also, for the biphasic waveform with a 7.0-msec first phase and a long second phase, V21 and J2 approach the corresponding monophasic values.

Figure 7 shows the phase-one and phase-two trailing edge voltages (V1t and V2t) at threshold for the part 1a and 1b waveforms. The shapes of the V1t curves are similar to the leading edge voltage curves in Figures 5 (panel A) and 6 (panel A). The V2t curves appear to be determined at longer durations primarily by the rapid decay time constant. That is, the phase-two trailing edge voltage does not determine the DFT in any simple manner. The trailing edge voltages for the subsequent low-tilt waveforms are not shown because, as expected, the trailing edge curves are nearly identical to the leading edge curves for those waveforms.

**Part 1c**

Figure 8 shows the leading edge voltage and current and total energy at threshold versus phase-two duration for the five low-tilt waveforms of part 1c illustrated in Figure 2 (panel A). A hump in each curve is evident when the second-phase duration is 6.0 msec. The 3.5/6.0 waveform has a significantly higher leading edge voltage and current than the neighboring 3.5/3.5 or 3.5/8.5 forms, and a higher total energy than the 3.5/3.5 form. Thus, the strength–duration curves in terms of voltage and current increase and then, surprisingly, decrease as the second-phase duration is increased.

**Part 1d**

Part 1d expands the information provided in part 1c about low-tilt waveforms by including the strength–duration curves for monophasic waveforms and by determining the DFTs for a wider range of pulse durations (Figure 2, panel B). For the four total pulse durations at which both monophasic and biphasic waveforms were tested (7.0, 8.5, 10.5, and 14.0 msec), the voltage, current, and energy thresholds for biphasic waveforms were significantly lower (p<0.02) than for monophasic pulses, except at 8.5 msec (Figure 9). The peak seen at 8.5 msec in the biphasic curves of Figure 9 (top panel) is greater than the neighboring portions of the curve for durations of 7.5 msec and 10.5 msec (p<0.03). The apparent hump at 7.0 msec is not significantly different from neighboring values for current thresholds. For voltage thresholds, it is greater than the DFT at 7.5 msec (p=0.04) but not greater than the DFT at 6.5 msec. Given this weak and inconsistent statistical support for the presence of a second hump at 7.0 msec separate from the peak at 8.5 msec, this second hump will not be considered further. The presence of at least one hump reaffirms the findings of part 1c and again shows that the strength-duration curve for biphasic waveforms does not follow a simple hyperbolic curve.

Figure 10 for part 1d, like figure 6 for parts 1a and 1b, compares the DFT values of the biphasic second phase with that of comparable monophasic waveforms. The phase-two leading edge voltage at threshold is lower than the threshold voltage of an equi-duration monophasic pulse for all durations tested (p<0.005). The current is lower for the biphasic second phase at all durations (p<0.04) except 5.0 and 8.5 msec, where there is merely a trend (p=0.06 and 0.19, respectively). These results contrast with those shown in Figure 6 (panel A) for high-tilt waveforms, where for longer durations, V2t of biphasic waveforms is as great or greater than the leading edge voltage for monophasic pulses.

**Part 2**

Figure 11 plots the defibrillation percent success for waveforms A–D shown in Figure 3. Phase-two defibrillation success does not follow a sigmoidal dose–response curve for these waveforms. Thus, increasing the total energy of a pulse does not always assure a more probable defibrillation. As V2t is raised from 0.61 V1t to 0.94V1t and then to 1.41V1t, the

<table>
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</table>
percent success first decreases \((p<0.005)\) and then increases \((p<0.02)\). The wide range of percent success for a given waveform results from sensitivity of success to \(V_{1f}\). For example, in dog 3 no waveform was more than 20% successful. Had \(V_{1f}\) been increased 10 V and \(V_{2f}\) adjusted proportionately, however, all four waveforms may have succeeded a majority of the time. Also, because the average difference in percent success between waveforms B and C was only about 20%, the effectiveness of using just 16 preliminary shocks to choose the optimal \(V_{2f}\) for these waveforms may be questioned. In other words, the protocol for choosing waveforms B and C, even though complex due to the sensitivity of success to slight changes in \(V_{1f}\) and \(V_{2f}\), probably did not consistently select the optimal waveforms. The decline in efficacy between waveforms B and C was significant despite this limitation.

**Discussion**

**Mechanisms of Defibrillation With Biphasic Waveforms**

The most striking findings of this study are that for the second phase of certain biphasic waveforms, the defibrillation strength–duration curve is not a simple hyperbola or parabola and the defibrillation percent success curve is not sigmoidal. Thus, the response to the second phase is not the same as the response to monophasic defibrillation waveforms.\(^{23,26,27}\) Instead, as the second-phase charge is increased, either by lengthening the phase (Figures 8–10) or increasing its amplitude (Figure 11), defibrillation efficacy first improves, then declines, and then again improves. Another major finding is that under certain conditions, the presence of the first phase of a biphasic waveform makes defibrillation less effective than had only the second phase been delivered. For a high-tilt one-
capacitor biphasic waveform with a 3.5-msec first phase and a second phase at least 14 msec long, the phase-two voltage and energy at threshold are higher than the threshold values for a monophasic pulse equal in duration to that second phase (Figure 6). Interestingly, this relation does not hold for low-tilt waveforms (Figure 10).

These results suggest current theories about the mechanism of biphasic waveform effectiveness must be altered or expanded. Jones and coworkers\(^8\) have suggested that the first phase acts as a "conditioning prepulse" and the second phase as an "excitation pulse." Because the resting membrane potential has been reported to be about \(-60\) mV during fibrillation,\(^{28}\) Jones et al\(^8\) posit that the first phase may serve to hasten recovery of sodium channels so the second phase can more easily open channels to excite the tissue. A similar theory, based on the observation of Cranefield and Hoffman\(^{29}\) that a hyperpolarizing pulse given during phase two of the action potential can shorten the refractory period, postulates that the first phase of a biphasic waveform may act to shorten refractoriness so the second phase can excite more cells.\(^9\)

These ideas are strengthened by the observation that in rabbit hearts, the ratio of the monophasic waveform DFT to the biphasic waveform DFT increases when the heart fibrillates for 30 seconds before shock delivery versus fibrillating for 5 seconds.\(^{30}\) If the myocytes become progressively more depolarized during the 30 seconds of fibrillation, the ability to hasten recovery of sodium channels and shorten refractoriness would make the biphasic waveform especially advantageous for longer fibrillation times.

This study suggests more is involved in lowering the DFT of biphasic waveforms than just reactivating

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**Figure 9.** Scatterplots of maximum voltage and maximum current (top panel), and total delivered energy (bottom panel) versus total pulse duration for part 1d waveforms at threshold. Biphasic curves have been extended by dotted lines to include the defibrillation threshold for the "biphasic" waveform with a zero-amplitude second phase (3.5/0.0). Hump seen in the biphasic curves at 8.5 msec (top panel) is greater than the neighboring portions of the curve for durations of 7.5 msec and 10.5 msec (p<0.03).
sodium channels. If the first phase simply speeds recovery of sodium channels so the second phase can more easily excite tissue, increasing the second phase amplitude for high-tilt waveforms (part 2) or duration for low-tilt waveforms (part 1c and part 1d) should continually improve defibrillation efficacy, as is true for monophasic waveforms. A decline in efficacy should occur only when the second phase begins to damage tissue. Once that occurs, further increasing phase two should not improve its efficacy. Contrary to this expectation, we found that increasing the second phase of some biphasic waveforms causes a decrease in defibrillation efficacy followed by an increase in efficacy as the second phase is increased still further. Because the decline in defibrillation efficacy occurs with either increases in the duration or amplitude of the second phase, the decline is not likely just due to time limitations of the sodium channel recovery.

If the second phase is indeed the excitatory phase, it must be able to depolarize previously hyperpolarized membranes. For each of the waveform types tested, adding a 1.0-msec second phase to a monophasic stimulus reduces the DFT. For example, a 3.5/1.0 biphasic stimulus is more effective than a 3.5-msec monophasic pulse. It is not clear if a 1.0-msec pulse can depolarize previously hyperpolarized membranes. Estimates of myocyte membrane time constants range from 0.2 to 4.9 msec. If the membrane behaves linearly, the second phase of a 3.5/1.0 square biphasic stimulus can depolarize a membrane hyperpolarized by the first phase only if the membrane time constant is shorter than 1.6 msec (see "Appendix"). For longer time constants, there is not enough energy in the second phase to overcome the hyperpolarizing effects of the first phase. Thus, depending on the membrane properties during fibrillation, depolarization may or may not be achieved by a 1.0-msec second phase. Even if depolarization is achieved, it is small in magnitude and lasts less than a millisecond.

Some models of a discrete cardiac strand yield different results, suggesting a 1.0-msec second phase can depolarize the myocyte membrane. These models indicate that the transmembrane potential...
induced by an applied field consists of an aperiodic term and a periodic term. The aperiodic term changes from depolarizing close to the cathode to hyperpolarizing close to the anode and arises with a time constant of about 20 msec. The periodic term varies from hyperpolarization to depolarization across each cell and achieves its maximum value within 1 msec after applying the stimulus. The aperiodic term has a significant effect only near the defibrillation electrodes, whereas the periodic term is responsible for the effects of the defibrillation shock throughout most of the myocardium. Thus, the fast response of the periodic term could explain how very short second phases can excite tissue and reduce DFTs. The gradation from depolarization to hyperpolarization induced within each cell has also been predicted by Chernysh and coworkers\(^35\) based on a different mathematical model.

The results discussed thus far suggest at least two mechanisms exist for defibrillation with biphasic waveforms, one that is more effective for smaller second phases and another that becomes more effective as the second phase is increased. The concept that each phase of a stimulus induces a gradation from hyperpolarization to depolarization along each myocyte provides a starting point for hypothesizing one possible physical interpretation for the dual mechanisms. If the first phase of a biphasic waveform opens sodium channels on one half of each myocyte and the second phase opens channels on the other half without closing all of those on the first half, the biphasic pulse might be more likely to defibrillate than if only the first phase were given. If the total charge of the second phase were increased by either lengthening that phase (part 1c and part 1d) or increasing its amplitude (part 2), however, the second phase might completely close channels on the half of the membrane initially depolarized by phase one. This would undo the positive interaction between the phases, and could explain the poor performance of the 3.5/6.0 waveform in part 1c, the 3.5/5.0 and 3.5/6.0 waveforms in part 1d, and waveform C in part 2. The ability to halt myocyte excitation even after sodium channels have opened and the threshold has been reached has been demonstrated by Weidmann.\(^36\) He showed that delivering a hyperpolarizing pulse of sufficient amplitude to a cell that has been depolarized above threshold can halt excitation during phase 0 of the action potential. This mechanism could offer a reason for the decline in efficacy as the second-phase amplitude or duration is increased. As the second phase is further increased, it should gain sufficient energy to excite cells by itself, opening channels on half of the membrane just as a monophasic pulse would. This could explain the increase in efficacy with waveform D in part 2 and with those waveforms in part 1c and 1d having second phases at least 7.0 msec long.

The idea that the first phase hastens recovery of sodium channels can be incorporated to help explain the part 1d data. If sodium channel activation occurs within the portion of each cell hyperpolarized by the first phase, the second phase of a biphasic waveform should defibrillate by using less energy than a comparable monophasic pulse equal in duration to that second phase. This fact is demonstrated in part 1d (Figure 10).

High-tilt biphasic waveforms, however, perform quite poorly as the second phase is extended (Figures 5 and 6). Recall that a long second phase of a truncated exponential biphasic waveform requires a greater voltage and current to defibrillate than a comparable monophasic pulse (Figure 6), whereas a long square second phase performs better than the comparable monophasic stimulus (Figure 10). The poor performance of truncated exponential waveforms with long tails, reported previously,\(^37,38\) has been suggested to result from reinducing fibrillation\(^38\) and has been reproduced with a mathematical model based on linear dynamic system theory.\(^39\) If the poor performance of exponential waveforms is indeed due to reinducing fibrillation, this implies that not only can some biphasic waveforms defibrillate more effectively than monophasic pulses, but certain biphasic waveforms can also reinduce fibrillation more easily. If each of these processes are forms of activating tissue, it is not contradictory to suggest biphasic waveforms both defibrillate and reinduce effectively. Wharton et al.,\(^40\) however, found that the peak voltage that will induce fibrillation when delivered during the vulnerable period is lower for a 3.5/2.0 biphasic stimulus than for a 5.5-msec monophasic shock. And, certain biphasic waveforms are less able than monophasic pulses to excite tissue during the relative refractory period,\(^41,42\) suggesting that defibrillation efficacy might be enhanced for biphasic waveforms because they are less able to reinduce fibrillation in partially refractory tissue.\(^43\) Thus, although no unifying explanation is yet apparent for these seemingly contradictory findings, it may be inferred that more may be involved in defibrillating myocardium than simply exciting tissue.

**Most Effective Waveforms**

This study confirms that biphasic waveforms defibrillate with less voltage, current, and energy than equiduration monophasic pulses when the biphasic second phase is equal to or shorter than the first phase.\(^1,3,4,9,12,13\) As the second phase is lengthened, the performance of high-tilt one-capacitor waveforms deteriorates dramatically, whereas the efficacy of comparable two-capacitor waveforms degrades less dramatically (Figures 5 and 6) and that of low-tilt waveforms improves in terms of voltage and current (Figure 9). Thus, these results illustrate the pronounced effect of the amount of tilt on defibrillation efficacy with biphasic waveforms.

Apart from the broad guideline that smaller second phases are preferable to larger ones, specific recommendations about optimal waveforms are difficult to establish because of the remarkable sensitivity of the defibrillation threshold to phase durations. For example, in part 1b, the defibrillation threshold voltage for two-capacitor waveforms was lower than
for comparable one-capacitor waveforms in all cases except for the 7.0/7.0 and 7.0/10.5 shocks, in which case the one-capacitor and two-capacitor waveforms were not significantly different. The work by Kavanagh et al, however, further substantiated by part 2 of this study, showed that when each phase was only 1 msec shorter, that is, 6.0/6.0, the one-capacitor waveform defibrillated more effectively than the two-capacitor form. Because canine hearts do not provide an exact model of human hearts, this sensitivity of defibrillation to phase-duration changes means bi-phasic waveforms that are optimal for defibrillating canine hearts require testing before clinical implementation in humans. With this qualification in mind, the lowest defibrillation energy found in this study for a high-tilt one-capacitor biphasic waveform is lower when the first phase is 3.5 msec than when it is 7.0 msec (3.5/2.0 versus 7.0/2.0, p<0.01).

Conclusion

This study has shown that more than one mechanism must operate to explain the strength–duration and probability of success curves for defibrillating with monophasic and biphasic stimuli. Possible mechanisms have been hypothesized. Further experimentation will be required to verify these theories.

Appendix

Assume that a myocyte membrane behaves like a simple resistance-capactitance circuit with a time constant \( \tau \). The value of \( \tau \) at which the second phase of a 3.5/1.0 square biphasic waveform has delivered enough charge to reverse the polarity imposed on the membrane by the first phase is computed herein. Given a unity driving voltage, the transmembrane voltage after the first phase is

\[ v_1 = 1 - e^{-3.5 \text{ msec}/\tau} \]

The total driving voltage of the second phase is then the \( v_1 \) already on the membrane plus the unity voltage applied by the waveform (i.e., \( v_1 + 1 \)). Thus, the change in transmembrane voltage effected by the second phase is

\[ v_2 = (v_1 + 1)(1 - e^{-1.0 \text{ msec}/\tau}) \]

Setting \( v_1 \) plus \( v_2 \) equal to zero and solving for \( \tau \) by iteration gives \( \tau = 1.6 \) msec. Only if \( \tau \) is less than 1.6 msec would the second phase reverse the transmembrane polarity.

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References


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