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Efficacy and safety of the reciprocal pulse defibrillator current waveform

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ABSTRACT

The efficacy and safety of a new defibrillating current waveform, consisting of a low-tilt 5 ms trapezoidal pulse followed closely by a second identical pulse of opposite polarity, was tested m seven isolated, perfused, working canine hearts suspended in an isoresistive, isosmotic shock bath at 37 ^{o}C. The efficacy and safety of the reciprocal pulse was compared with a single 5 ms pulse, a single 10 ms pulse, and a dual (unidirectional) 5 ms pulse waveform. The mean threshold average current densities for the 5 ms single pulse, 10 ms single pulse, dual 5 ms pulse, and reciprocal pulse (absolute values) were 50, 38, 36, and 37 mA/cm^2, respectively. The corresponding mean threshold energy densities in the shock bath were 2.8, 2.9, 2.9, and 3.1 mJ/cm^3. Despite the differences in threshold current density among the waveforms, no differences in safety factor (shock strength for 50 per cent post-shock depression, divided by threshold shock strength) were found among the waveforms. The current safety factors were 5.4, 5.4, 5.6, and 5.5 for the 5 ms single pulse, 10 ms single pulse, dual unidirectional pulse and reciprocal pulse, respectively. The corresponding energy density safety factors were 25, 27, 29, and 27. Thus the use of this reciprocal pulse waveform provides no advantage in efficacy or safety over waveforms of the same total duration.

Key words: Biphasic, Canine, Contractility, Defibrillation, Electric shock, Isolated heart

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INTRODUCTION

In a short communication JUDE *et al.* (1962a) reported that a reciprocal current waveform consisting of an upward 4 ms pulse followed in 6 ms by a downward 4 ms pulse offered some advantage for defibrillating animal and human hearts. More recently SCHUDER (1981) reported that the reciprocal pulse is more effective for defibrillating very large animal hearts. Dual, unidirectional pulses have been advocated for defibrillation as well. KUKELBERG (1965; 1967) reported that two upright rectangular pulses of 20 ms duration separated by 100 ms required less energy for defibrillation than the damped sine wave. However, SCHUDER (1970) compared the energy required for defibrillating animals with single and twin rectangular pulses and found that more energy was required with the latter. GEDDES *et al.* (1973) found that slightly less peak current but more energy was required for defibrillation when two half-sinusoidal pulses were compared with a single pulse. Because there appears to be some controversy over the efficacy of reciprocal and twin pulses, the present study was undertaken using the isolated, perfused, working canine heart, which provides the opportunity of obtaining highly accurate and reproducible defibrillation threshold values.

An important figure of merit for any therapeutic agent is the safety factor, which is defined as the ratio of the harmful dose to the effective dose. In the case of defibrillator shocks, the dose can be measured in terms of delivered current or energy. These values have been determined for defibrillation waveforms using different measures of toxicity and effectiveness (BABBS, 1980; JONES, 1981). Obviously, the waveform with the highest safety factor would be most desirable for clinical use. Previously, we (NIEBAUER *et al.,* 1983) reported that longer duration, rectangular waveforms were safer than short-duration waveforms that exhibit high peak currents.

Accordingly, we elected to determine if a higher safety factor exists for a reciprocal pulse waveform of short separation (0.2 ms) using a convenient criterion of toxicity: 50 per cent depression in the left ventricular post-defibrillation systolic pressure of the isolated heart preparation.

METHODS

The isolated, perfused heart preparation (Fig. 1) was used because it eliminates the effects of tissue hypoxia and automatic reflexes. The preparation consists of a canine heart removed from a donor dog and suspended in a fluid-filled bath through which the defibrillator shocks are delivered. The fluid is isoresistive and isotonic with the myocardium and maintained at 37 ^{o}C. Arterial blood from a support dog perfuses the coronary arteries of the isolated heart, which continues to beat vigorously. The venous outflow is returned to the femoral vein of the support dog.

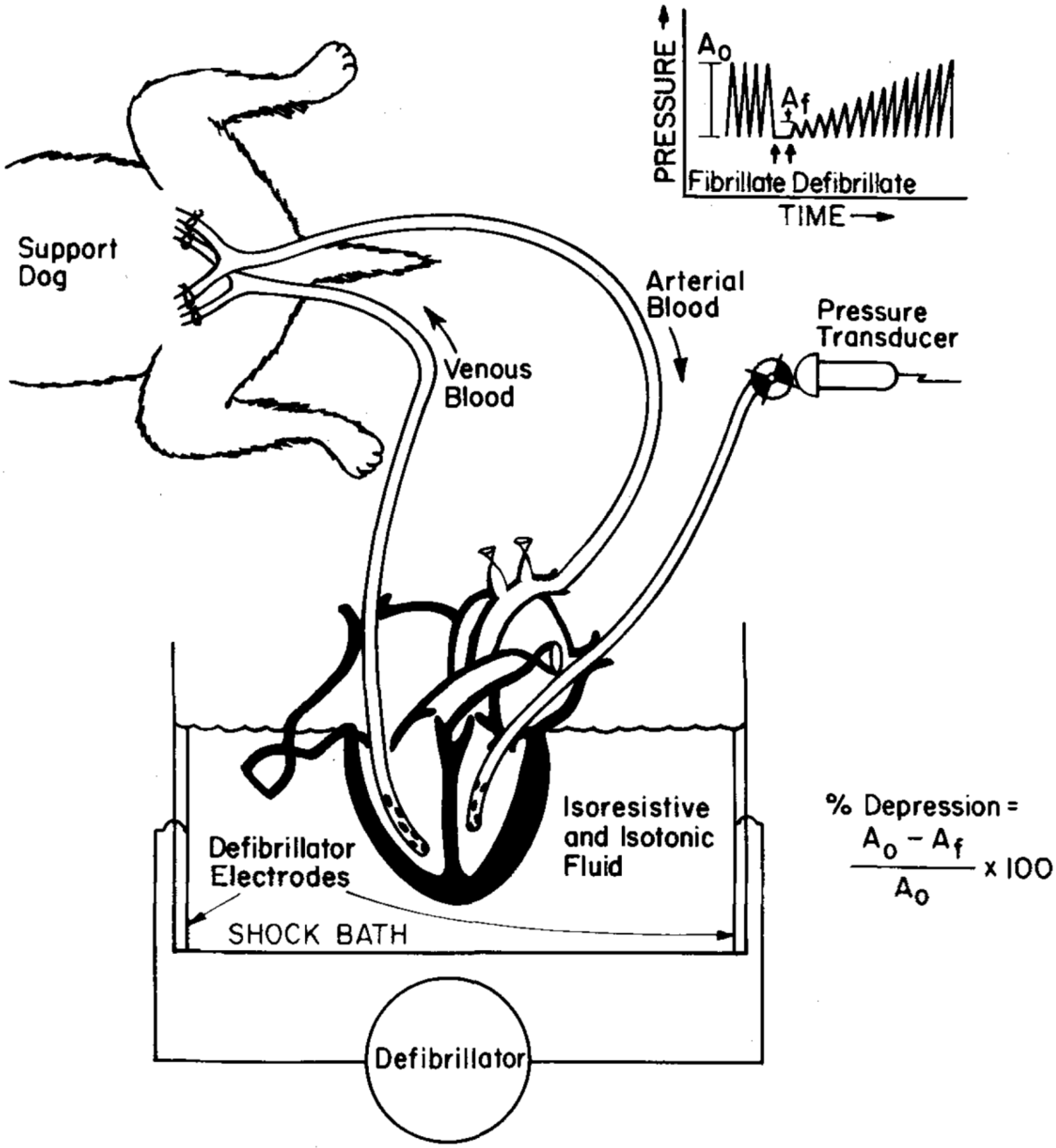

Fig.1. Experimental model utilizing a modified Langendorff isolated heart preparation. The heart is suspended in an isoresistive, isotonic, and temperature regulated (37 ^{o}C) bath through which the defibrillator shocks are delivered. The heart is constantly perfused with oxygenated blood throughout the experiment. Cardiac function is evaluated by comparing postshock left ventricular pressure A_f with the preshock control value A_o.

The decreased contractility following a defibrillating shock is assessed by comparing the systolic left ventricular pressure, A_f , in the isovolumic left ventricle immediately following the shock to the immediate prefibrillation value, A_o. Thus a change in cardiac function can be attributed to defibrillator shock, since left ventricular end-diastolic volume and coronary perfusion are constant. The inset of Fig. 1 illustrates the method of computing the percentage myocardial depression, which is equal to $100(A_o – A_f)/A_o$.

An experimental defibrillator delivered single or double truncated exponential (trapezoidal) waveform pulses of controllable tilt, duration, polarity, and pulse separation. Fig. 2 illustrates the four waveforms studied. The double pulse waveforms consisted of two 5 ms pulses separated by 0.2 ms, with less than 20 per cent tilt, so that the total duration of the waveforms was 10 ms (tilt is the percentage decrease in current amplitude during the pulse). Preliminary studies indicated that a separation ranging from 0.1 to 1.0 ms provided the lowest defibrillation threshold for reciprocal and unidirectional dual-pulse waveforms as compared with single pulses of the same total duration. The single-pulse trapezoidal waves were 5 and 10 ms duration, respectively. Defibrillator shocks were delivered to the isolated heart via two plate electrodes placed at each end of the shock bath. Delivered voltage and current were recorded on a dual-trace storage oscilloscope (Model D55 Tektronix, Portland OR).

The average current and delivered energy were calculated from the initial and final values of each pulse (BOURLAND *et al.*, 1978b). Average current is defined as the total charge delivered in a pulse divided by the duration of the pulse. The average current I_{av} for the single trapezoidal wave was calculated from the peak current I as follows:

$$I_{av} = TI/1\text{n}\left(\frac{1}{1-T}\right)$$

where T is the fractional tilt (per cent tilt/100) of the current waveform. For the reciprocal pulse and dual-pulse waveforms, the absolute values of charge of both pulses (either positive or negative) were divided by the total duration to yield the average current. Delivered energy was calculated from the product of the square of the average current, the resistance of the bath and the total duration of the waveform. Average current density was calculated by dividing the average current by the cross-sectional area of the shock bath. The delivered energy density was calculated by dividing the delivered energy by the volume of the bath between the plate electrodes.

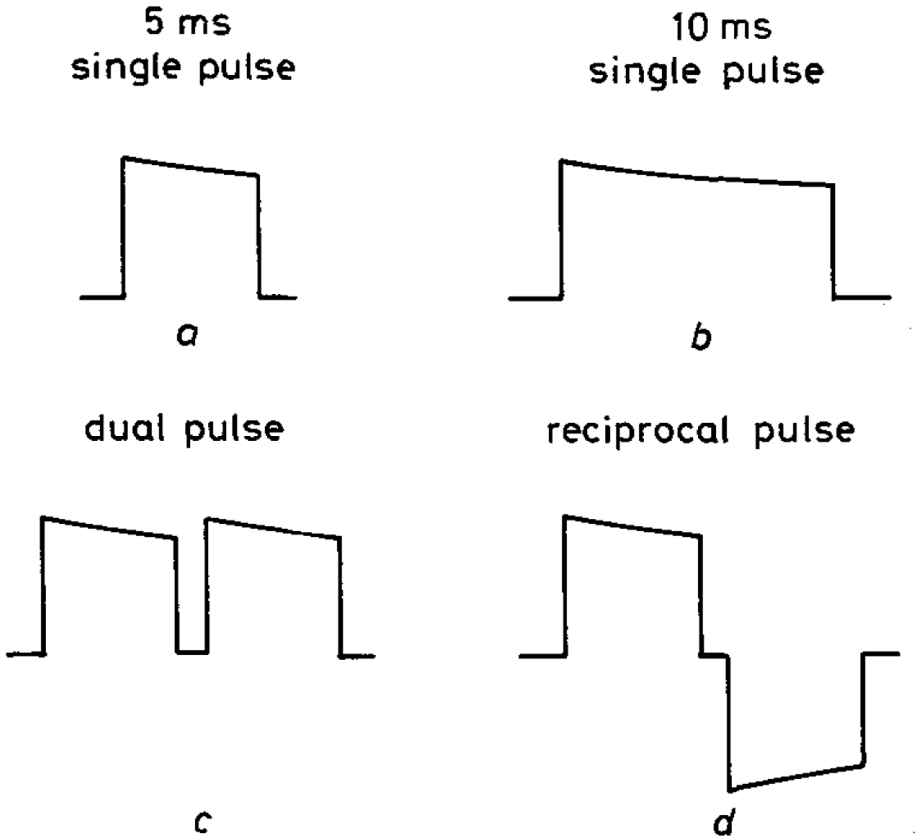

Fig. 2 The four waveforms evaluated in this study: (a) a 5 ms low tilt trapezoidal pulse (b) a 10 ms, low-tilt trapezoidal pulse (c) a dual-pulse waveform consisting of two 5 ms low-tilt trapezoidal pulses of the same polarity (d) a reciprocal pulse waveform consisting of two 5 ms low-tilt trapezoidal pulses of opposite polarity.

Defibrillation threshold current and energy were first determined for each waveform so that the overdose shocks could be scaled from these values. Defibrillation threshold was determined by first inducing ventricular fibrillation, using a hand-held bipolar electrode on the epicardium and delivering 60 Hz, 2 ms rectangular pulses to the ventricles. Then defibrillator shocks were delivered via the plate electrodes in the bath at increasing strengths until defibrillation was achieved. When a successful shock intensity exceeded an unsuccessful shock by no more than 10 per cent, that value was recorded as threshold.

Overdose shocks of 3, 4.5, 6 and 9 times the threshold current density were then delivered. Myocardial depression was defined as the percentage decrease in postshock left ventricular systolic pressure from the stable immediate prefibrillation value (Fig. 1 inset). The various waveforms were tested in a randomized order in each of seven preparations.

The safety factor was defined as the shock overdose ratio required to produce a 50 per cent decrease in the postshock isovolumic systolic pressure. Any level of depression can be used to define a standardized safety factor. We chose to define the toxic dose as the current overdose ratio required to produce 50 per cent depression in postshock systolic pressure. This point on the dose/response curve was selected on the basis of the linearity of this portion of the curve. The safety factors for the four waveforms were interpolated from the percentage depression against overdose curves.

Waveform and shock intensity effects were initially evaluated by a multifactor analysis of variance. The percentage depression produced by the four waveforms was compared at each overdose shock strength using the Neuman-Keuls sequential range test. Defibrillation thresholds and safety factors were compared in the same manner. We selected a level of significance of $p = 0.05$.

RESULTS

The mean average current densities at threshold for the 5 ms single pulse, 10 ms single pulse, dual pulse, and reciprocal pulse were 50, 38, 36 and 37 mA cm^{-2}, respectively. The corresponding threshold energy densities were 2.8, 2.9, 2.9 and 3.1 $mJcm^{-3}$. Table 1 summarizes the data. No statistically significant differences ($p = 0.05$) in current threshold were found between the 10 ms waveforms (single pulse, dual 5 ms pulses and the reciprocal 5 ms pulses). The 5 ms single-pulse current threshold was significantly higher ($p = 0.05$) than the current thresholds of the other three waveforms of longer total duration, as would be expected from the strength/duration concept for defibrillation (GEDDES *et al.*, 1970).

Table 1. Threshold defibrillation values

Waveform	Current density mA cm^{-2}	Threshold energy density mJ cm^{-3}
5 ms low-tilt trapezoid	50	2·8
10 ms low-tilt trapezoid	38	2·9
Twin 5 ms low-tilt trapezoids	36	2·9
Reciprocal 5 ms low-tilt trapezoids	37	3·1

Fig. 3 shows the cardiac depression in the seven isolated hearts for the four waveforms at the four current overdose shock intensities. For the waveforms no significant differences (p = 0.05) in depression were found for the same overdose ratios. Fig. 4 shows the dose/response curves constructed from the experimental results and fitted to a sigmoid dose/response curve using the probit transformation.

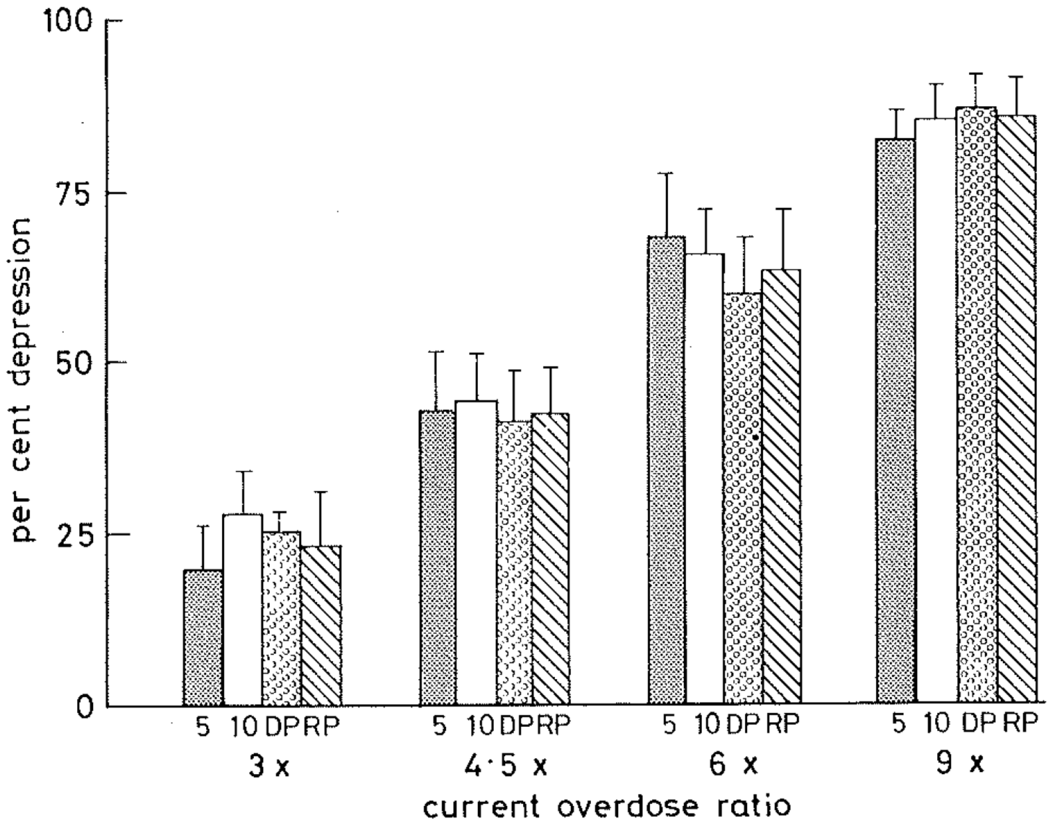

Fig. 3 Histogram showing the mean percentage depression produced by the four waveforms studied at each shock strength (overdose ratio). Bars represent the standard error of the mean. No statistically significant differences (p = 0.05) were found between waveforms at the different shock strengths.

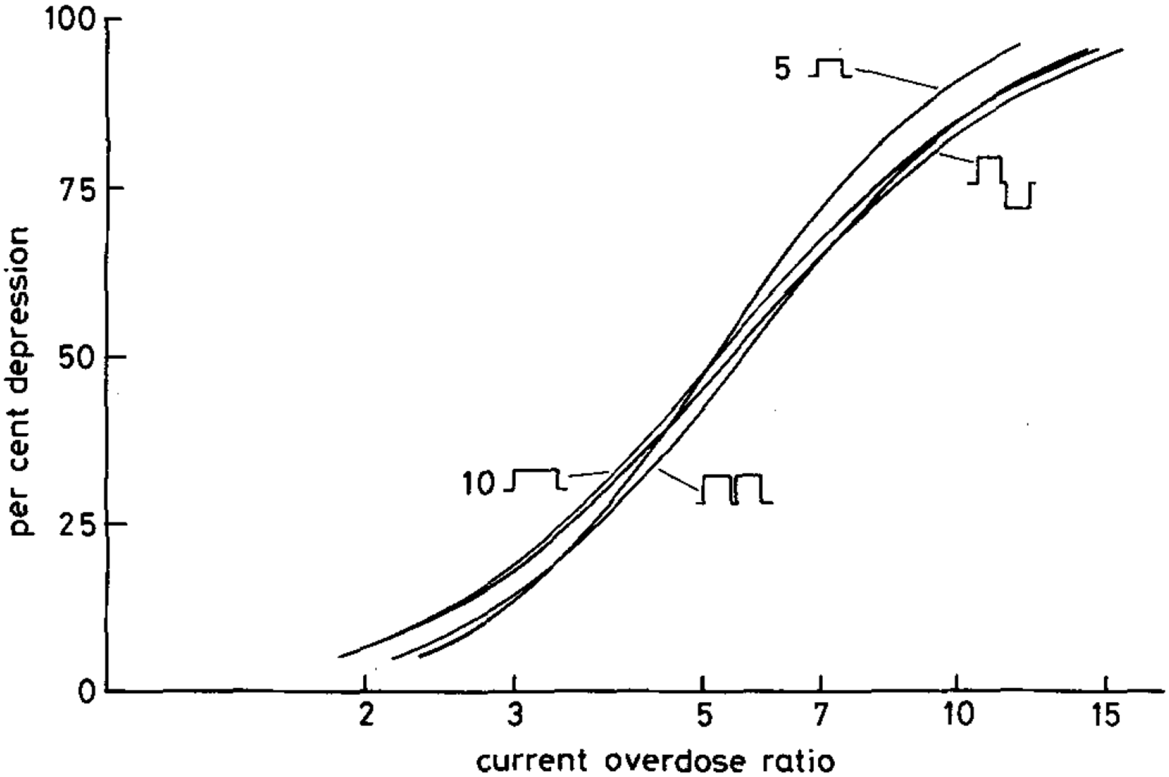

Fig. 4 Plot of functional depression (percentage decrease in left ventricular isovolumic pressure) produced by a suprathreshold defibrillator shock as a function of the shock strength. Shock strength is normalized for the four test waveforms as the ratio of the delivered current to the threshold current (overdose ratio).

Since the shock is expressed as the overdose ratio (delivered shock strength/threshold shock strength), the overdose ratio required to produce a defined depression (50 per cent) is the safety factor (toxic dose/threshold dose). Thus the current and energy safety factors were determined directly by interpolation of the dose/response curves. The current safety factors were 5.4, 5.4, 5.6 and 5.5 for the 5 ms single pulse, 10 ms single pulse, unidirectional dual pulse, and reciprocal pulse, respectively. The corresponding energy safety factors were 25, 27, 29 and 27. Table 2 summarizes these data.

Table 2 Safety factors

Waveform	Current	Energy
5 ms low-tilt trapezoid	5·4	25
10 ms low-tilt trapezoid	5·4	27
Twin 5 ms low-tilt trapezoids	5·6	29
Reciprocal 5 ms low-tilt trapezoids	5·5	27

DISCUSSION

For effectiveness of defibrillation, dual and reciprocal current waveforms of 10 ms total duration were found to be no more or less effective than a single 10 ms monophasic waveform. Also, the safety factors of these three 10 ms waveforms are not significantly different ($p = 0.05$) than the 5 ms single pulse. The higher defibrillation threshold current density for the 5 ms single pulse is expected because of the well known strength/duration relationship for tissue stimulation and defibrillation (GEDDES *et al.*, 1970; KONING *et al.*, 1975; BOURLAND *et al.*, 1978a). Hence, if the total pulse duration is held constant, there is no physiological advantage to the reciprocal pulse waveform.

Earlier studies on non-fibrillating cultured chick myocardial cells by JONES and JONES (1981) did indicate a higher safety factor for biphasic (reciprocal) waveforms than monophasic waveforms. Jones' safety factor refers to the ratio of shock strengths which produce a 4 s arrest of spontaneous contraction to that necessary to elicit an extrasystole. Using a basic damped sinusoidal current waveform of 4 or 16 ms duration, they compared the safety factors obtained when the pulse was truncated after the first zero crossing (monophasic) and when the pulse was allowed to undershoot to a negative value (biphasic). The safety factors of the biphasic waveforms were 12-14 per cent greater than those of the corresponding truncated monophasic waveforms. These investigators also have found small but statistically significant safety differences between rectangular and exponential waveforms of similar duration in non-fibrillating myocardial cells (JONES and JONES, 1981).

The differences in results obtained with the two model systems are not unreasonable, since quite different definitions of effective and toxic shock strength were employed. If one believes that the fibrillating isolated heart model more closely simulates the situation *in vivo,* then the reciprocal and dual pulses are as effective as the 10 ms single pulse and equally safe. The use of such waveforms neither enhances nor reduces the safety of defibrillation.

On the basis of these studies, there appears to be no significant efficacy or safety advantage to dual-pulse or reciprocal pulse defibrillating current waveforms. However, the fact that the true average current is zero for the reciprocal pulse waveform may make it useful when it is desirable to minimize corrosion of the defibrillating electrodes.

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