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Construction of Energy-Optimal Smooth Monophasic Defibrillation Pulse Waveforms Using Cardiomyocyte Membrane Model

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Abstract

The goal is to help create smooth energy-optimal monophasic pulse waveforms for defibrillation using the Luo-Rudy cardiomyocyte membrane computer model. The waveforms were described with the help of the piecewise linear function. Each line segment provides a transition from one present level of the transmembrane potential to the next with a minimal energy value. The duration of the last segment was defined as a minimum duration at which an action potential occurs. Monophasic waveforms of segments 3, 10 and 29 were built using different increments of the transmembrane potential. The pulse energy efficiency was evaluated according to their threshold energy ratios in $mA^2 \cdot ms/cm^4$. There was virtually no difference between the threshold energy ratios of the three waveforms constructed and those of the previously studied energy-optimal half-sine waveform: 241 - 242 and 243 $mA^2 \cdot ms/cm^4$. The pulse waveform constructed is characterized by a low rise and fall as the duration of the rise is ~1.5 times longer than that of the fall. Conclusion: Energy-optimal smooth monophasic pulse waveforms have the same threshold energy ratio as the optimal half-sine one which was studied before. The latter is equivalent to the first phase of biphasic quasi-sinusoidal Gurvich-Venin pulse which has been used in Russia since 1972. Thus, the use of the Luo-Rudy cardiomyocyte membrane model appears to offer no possibilities for a substantial increase in the energy efficiency (threshold energy ratio reduction) of the classical monophasic defibrillation pulse waveforms.

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Keywords

Energy-Optimal Defibrillation Pulse Waveform, Monophasic Defibrillation Pulse Waveforms, Modeling, Energy Ratio, Cardiomyocyte, Transmembrane Potential, Action Potential

1. Introduction

The world's first monophasic pulse defibrillators (ID-1-VEI) began to be produced in the USSR in 1952 [1] [2]. These defibrillators provided external defibrillation at maximum discharge energy of 360 - 400 J. The next stage of defibrillator development also began in the USSR when in 1972 it launched the world's first biphasic pulse defibrillators (DI-03) which generated a classic biphasic quasi-sinusoidal Gurvich-Venin pulse waveform [3]. This pulse waveform ensured up to 95% - 100% success of external defibrillation and cardioversion with maximum discharge energy of 200 J. In 1991, the Soviet Union became the world's first country to launch defibrillators with a biphasic truncated exponential pulse waveform (DKI-N-04) [4]. It should be noted that current practical medicine makes much use of biphasic defibrillators with the maximum discharge energy of 360 J. This energy indicates that the waveform and duration of the biphasic pulse are not optimal.

Thus, over the past 40 years, it has been possible to reduce the maximum energy defibrillator discharge which ensures a 95% - 100% success rate in the defibrillation/cardioversion of atrial and ventricular tachyarrhythmias, to as little as ~1.6 - 2 times (from 360 - 400 to about 200 joules). At the same time a significant decrease in the maximum discharge energy and current amplitude would be conducive to the solution of the following tasks:

- To minimize/avoid myocardial damage/dysfunction, and tissue damage beneath the electrodes and related inflammatory processes, especially when applying repeated maximum energy discharges;
- To alleviate painful sensations to enable external cardioversion without anesthetics by using only sedation in patients who are conscious;
- To reduce defibrillator size and cost.

2. Materials and Methods

2.1. The Energy Ratio Is an Indicator for Comparing the Energy Efficiency of Defibrillation Pulses

In physics, instantaneous electrical power of defibrillation pulse $P_{df}(t)$ is determined by the given defibrillation current value $I_{df}(t)$ and transthoracic impedance R_{TTI} (Equation (1)).

$$P_{df}(t) = I_{df}^2(t) R_{TTI} \tag{1}$$

Defibrillation pulse energy E_{df} is determined by the integral of the instantaneous power of the pulse during its operation T_{pulse} (Equation (2)).

$$E_{df} = \int_0^{T_{pulse}} P_{df}(t)\,\mathrm{d}t = \int_0^{T_{pulse}} I_{df}^2(t) R_{TTI}\,\mathrm{d}t \tag{2}$$

Typical for adult transthoracic defibrillation are energy E_{df} from 50 J to 200 - 360 J, transthoracic impedance R_{TTI} from 25 - 175 Ω (an average of about 100 Ω), the pulse duration T_{pulse} of 3 - 20 ms, the amplitude of the current I_{df} up to 50 A.

Let us tentatively accept the value of transthoracic impedance as a constant value, so that it can be taken out of the integral (Equation (3)).

$$E_{df} = R_{TTI} \int_0^{T_{pulse}} I_{df}^2(t)\,\mathrm{d}t \tag{3}$$

The integral of the square of the given current value of the defibrillation pulse will be called an energy pulse ratio K_E, with the dimension of A^2·s or W·s/Ω (Equation (4)).

$$K_E = \int_0^{T_{pulse}} I_{df}^2(t)\,\mathrm{d}t = \frac{E_{df}}{R_{TTI}} \tag{4}$$

Since comparison of the energy efficiency of different defibrillation pulses should be made using the same value of transthoracic impedance, pulse energy efficiency may be indicated by its energy ratio K_E.

2.2. Cardiomyocytes Are Objects Which Receive the Impact of a Defibrillation Impulse

During an electric shock current extends in the chest in such a manner that a mere ~4% of its total quantity flows directly through the heart affecting its cardiomyocytes [5]. According to the existing theory, for defibrillation to be successful most of the cardiomyocytes (probably, 75%, "a critical mass of the myocardium") [6] must be depolarized by an electric pulse [7]. To compare the energy efficacy of the pulse, we therefore evaluated (measured) the threshold energy ratio $K_{E_{thr}}$ which causes a cardiomyocyte to develop an action potential (Equation (5)). The lower this ratio is, the greater energy efficacy the pulse has.

$$K_{E_{thr}} = \int_0^{T_{pulse}} I_{df_{thr}}^2 (t) \mathrm{d}t = \frac{E_{df_{thr}}}{R_{TTI}} \tag{5}$$

For the purposes of the study we used the guinea pig cardiomyocyte membrane model—1994-2000 *Luo-Rudy mammalian ventricular model* II (*dynamic*) which is part of the open source *Cell Electrophysiology Simulation Environment* (*CESE*) *OSS* 1.4.7 [8]. The impact of electric pulses on the cardiomyocyte membrane model was made by replacing/clamping "the stimulus amplitude" parameter (st)—the amplitude of the current density of the acting pulse is expressed in $\mu A/cm^2$. The segments of the piecewise linear function describing the energy-optimal pulse waveforms were constructed by using energy-optimal trapezoidal segments (ramp), during which the transmembrane potential increases from the present level to the next, with the initial signal level of a subsequent segment being equal to the final signal level of the previous one. These segments are checked to determine the time required for the energy ratio to have a minimum value during the transition of the transmembrane potential from one predetermined level to another. Since exposure value in the model is not the current value, and its density, the dimension expressed in the energy ratio in the $\mu A^2 \cdot ms/cm^4$. The last segment showed the minimum duration during which the action potential occurs. The threshold pulse energy ratio was defined as the sum of the energy ratios of its segments.

3 pulse were constructed using different numbers of segments:
- 3-segment pulse (resting potential → 76 mV → 66 mV → action potential).
- 10-segment pulse (resting potential → from 83 to 59 mV with a 3 mV increment → action potential).
- 29-segment pulse (resting potential → from 85 to 58 mV with a 1 mV increment → action potential).

In constructing the pulse was convenient that their segments increased the transmembrane potential to an integer value of millivolts. Also note that during the pulse transmembrane potential changes from the resting potential of ~−86 mV to close to the threshold potential of ~−57 mV. Starting from this for construction have been chosen the pulse waveforms with segments altering the transmembrane potential at 10 mV (3 segments), 3 mV (10 segments) and 1 mV (29 segments). Selection was caused by a desire to assess the energy-effectiveness of pulses with different number of segments.

The threshold energy ratios of the three constructed waveforms were compared to that of the previously studied half-sine waveform which had been built using one segment of the sinusoidal function (sine) [9].

An example illustrating the impact of the 10-segment pulse on the cardiomyocyte model is given in **Figure 1**.

3. Results

The energy-optimal pulse waveforms and that of the energy-optimal half-sine pulse obtained in the simulation process are shown in **Figure 2**. The energy-optimal half-sine pulse [9] is a control (baseline) pulse compared with the 3 newly formed pulses.

It should be noted that the duration of the energy-optimal rectangular pulse in the threshold excitation energy pattern is 11 ms for a Luo-Rudy cardiomyocyte membrane [10], and about 4 ms for a human cardiomyocyte membrane [11]. In this regard, the duration of the pulses studied is 2.75 times higher than that of actual pulses generated by a defibrillator.

The parameters of the energy-optimal pulse waveforms are shown in **Table 1**.

Interestingly enough, all of the new energy-optimal pulse waveforms tend to share the same features-a shallow rise and fall, with the duration of the rise being about 1.5 times longer than that of the fall (asymmetric pulses). The half-sine pulse also has a shallow rise and fall, but their duration is the same. As can be seen from
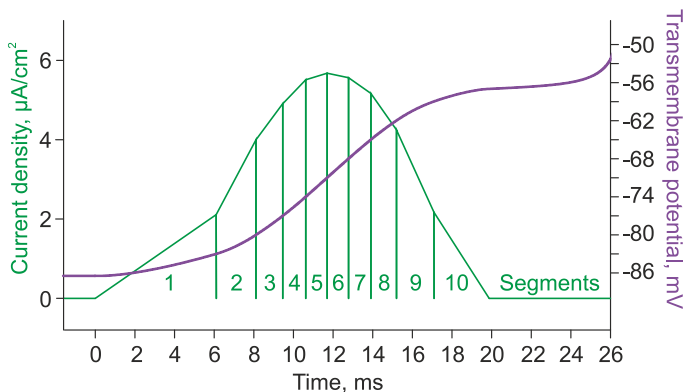
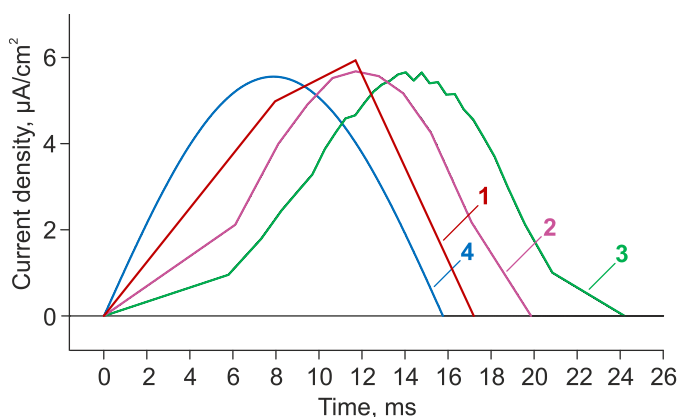**Figure 1.** Impact of 10-segment pulse on cardiomyocyte model.

Figure 2. Energy-optimal defibrillation pulse waveforms (1 - 3 segment pulse, 2 - 10 segment pulse, 3 - 29 segment pulse, 4-single-segment half-sine pulse).

Table 1. Parameters of the energy-optimal pulse waveforms.

Pulse	Threshold Current Density Amplitude in $\mu A/cm^2$	Threshold Energy Ratio in $\mu A^2 \cdot ms/cm^4$	Relative Threshold Energy
3 segment	5.93	241.7	1.00
10 segment	5.69	240.8	1.00
29 segment	5.66	240.9	1.00
Half-sine	5.55	242.9	1.01

Table 1, the threshold energy ratios of all the four pulses are virtually indistinguishable. At the same time, the first phase of the uneven (stepped) quasi-sinusoidal biphasic pulse (**Figure 3**) that we studied earlier, has the lowest threshold energy ratio $-229.6 \, \mu A^2 \cdot ms/cm^4$ (the relative threshold energy being 0.95) [12].

Noteworthy is the fact that during external defibrillation the threshold sloped pulse energy is decreased through reduced resistance of the chest, which was recorded during the pulse current surge [13].

4. Discussion

The present and previous our papers have focused on monophasic and first phase biphasic pulses of different waveforms (morphology) and duration which releases at least 70% - 80% of the pulse energy on the heart region during defibrillation [12] [14]. The results of this study suggest that it is impossible to achieve significant increase in the energy efficiency of monophasic defibrillation pulses by using the Luo-Rudy cardiomyocyte membrane model.
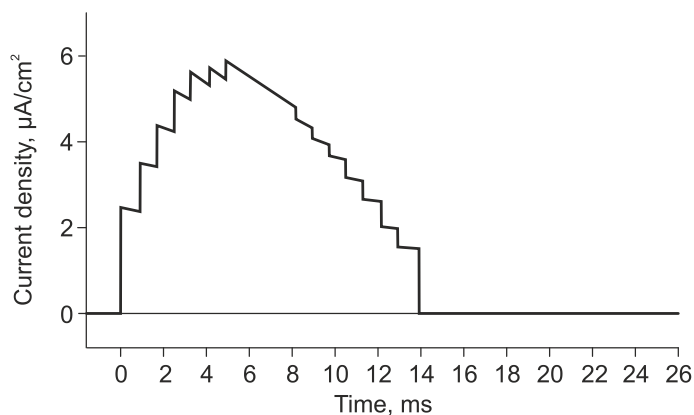
Figure 3. First phase of the quasi-sinusoidal stepped biphasic defibrillation pulse.

According to the results of the computer simulation, the Gurvich-Venin quasi-sinusoidal biphasic pulse (1972) proves to be close to the optimal as the previously studied first phase of which has a threshold energy factor equal to 249.2 $\mu A^2 \cdot ms/cm^4$ (relative threshold energy being 1.03) [12]. The Gurvich monophasic pulse defibrillator ID-1-VEI (1952) [1] [2] and the Lown cardioverter (1962) [15] [16] also have a pulse waveform which is very close to that of the previously studied half-sine pulse. Good results were shown by the previously studied first phase of the rectilinear pulse: 273.5 $\mu A^2 \cdot ms/cm^4$ (relative energy threshold being 1.14) [12]. Notwithstanding this, one of the important tasks for all type of biphasic pulse is to stabilize its duration (close to its optimal length of about 10 ms) irrespective of transthoracic impedance [17]. Along with this, the experimental results have shown pulse modulation to lower rather than enhance its efficacy [12] [18].

Does all of the above imply that there exists a possibility for a significant reduction of defibrillation pulse energy? There are objective prerequisites for this. During the experiments on animals [13] [19] [20], ventricular fibrillation was caused by using alternating current with a frequency of 50 Hz (the voltage being ~40 V), which was passed through the external defibrillator electrodes for 2 seconds. Thus, the amplitude of the current passing through the chest and equal to several tens of milliamps, caused excitation of some cardiomyocytes and occurrence of a parasitic self-oscillating wave in ventricular fibrillation. However, the fibrillation caused by the above method was removed by using a defibrillation discharge equal to 80 - 100 J (current amplitude being ~17 - 20 A). What is the reason behind this big current amplitude difference? During fibrillation the cardiomyocytes located in different parts of the myocardium are in different states, some being in the resting position, others in the state of refractoriness when they are insusceptible to an external impact by electric current. When they are in a transition period from the refractory state to the resting position the cardiomyocytes are susceptible to an impact by electric current only in case when the latter has much greater amplitude. To stop the propagation of the self-oscillating wave through the myocardium it is necessary to simultaneously put a significant (critical) part of the cardiomyocytes into the refractory state. But to do this, it is necessary to have the impact of current with much greater amplitude than that required for cells in the resting state. This requires an alternative method to be used to provide a defibrillation impact: to put different parts of the myocardium in the refractory state it is necessary to apply several low amplitude current pulses during the circulation of a fibrillation wave (~200 - 300 мs). The efficacy of the new method of cardioversion/defibrillation has been proved experimentally [21].

5. Conclusion

Constructed energy-optimal monophasic defibrillation pulse waveforms do not substantially differ in their threshold energy ratio from an energy-optimal half-sine pulse. A characteristic feature of all the above pulses is their shallow rise and fall. The above data obtained using the Luo-Rudy cardiomyocyte membrane model suggest that it is not possible to significantly increase energy efficiency for classic monophasic and, most likely, biphasic defibrillation pulses. On the other hand, the data obtained in the experimental studies [21] made it possible to develop a new alternative method for applying electrical stimulation, which can provide a significant reduction in energy and current amplitude during defibrillation/cardioversion.

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