Guaranteed Defibrillation on a Cardiomyocyte Model

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***Abstract*—On the model of cardiomyocyte under the influence of simulated fibrillation, the dependences of the threshold energy of guaranteed defibrillation on the duration of the defibrillation pulse of a half-sine and rectangular waveform are studied. Guaranteed defibrillation is achieved when a defibrillation pulse causes an extension of the current refractory period of cardiomyocytes to a pulse repetition period of fibrillation or more. In this case, the propagation of the fibrillation wave through the myocardium becomes impossible. The obtained dependences of the threshold energy of guaranteed defibrillation on the duration of the defibrillation pulse correspond to the Hoorweg–Weiss–Lapicque law on a limited range of relative values of the pulse duration. For a rectangular pulse, this range is much wider than for a half-sine pulse. The obtained dependence of the threshold energy of guaranteed defibrillation on the duration of a half-sine defibrillation pulse is close to the results of animal experiments. Therefore, the guaranteed defibrillation mechanism can be used to compare the energy efficiency of external defibrillation pulses.**

Keywords—cardiomyocyte model, excitation, simulated fibrillation, guaranteed defibrillation

I. INTRODUCTION

The works carried out by the Soviet scientist N.L. Gurvich since 1939 [1] led to the beginning of the release in 1952 of the first-ever serial pulsed defibrillator, later called ID-1-VEI [2]. The next serial defibrillator PREMA, developed under the direction of B. Peleška, was released in Czechoslovakia in 1957 [3]. It should be noted that in the USA the first pulse defibrillator Cardioverter, developed under the guidance of B. Laun, was released 10 years later than the ID-1-VEI defibrillator, in 1962 [4].

Despite the significant period of experimental and clinical use of pulsed defibrillators, there is still no complete clarity with the mechanisms of heart defibrillation. The hypothesis that a defibrillating impulse causes the simultaneous excitation of myocardial myocytes [5] - [7] is widespread. But with fibrillation, most myocardial myocytes are already in different phases of the refractory period. An alternative hypothesis based on experimental data was formed in 1990-1997 [7] - [11]. It was found that under the influence of a defibrillation pulse in cardiomyocytes, the refractory period is prolonged for a long time, which violates their susceptibility to fibrillation waves. Similar results were obtained on a two-dimensional myocardial model in 1997 [12].

In a previous study, based on the simulation data on the response of a cardiomyocyte in a state of simulated fibrillation to rectangular defibrillation pulses, diagrams of the dependence on the energy of the defibrillation pulse of the fraction of the fibrillation cycle were constructed, on which the defibrillation pulse causes a long-term extension of the refractory period of cardiomyocytes (defibrillation completeness index) [13]. In addition, the term "guaranteed defibrillation" was introduced, which is achieved when the refractory period of the cardiomyocyte becomes equal to the duration of the simulated fibrillation cycle under the influence of a defibrillation pulse. In this case, the propagation of the fibrillation wave through the myocardium becomes impossible. The aim of this work is a more detailed study of the defibrillation mechanism based on previously obtained results, and comparison with the available experimental data to confirm the assumption that the guaranteed defibrillation mechanism is an external defibrillation mechanism.

II. MATERIALS AND METHODS

The study was carried out in a BeatBox simulation environment [14] on a ten Tusscher-Panfilov 2006 model of human heart ventricular myocytes [15] for two pulse waveform: half-sine and rectangular. Materials and methods are described in [16]. In addition, in this study, the pulse energy was calculated during the simulation. The response of a cardiomyocyte in a state of simulated fibrillation to the effect of a depolarizing current pulse was evaluated. Simulation of fibrillation was caused by excitation impulses of 0.5ms duration with a frequency of 240 min^{-1} (the limiting frequency, perceived by the model of a cardiomyocyte). In determining the threshold of guaranteed defibrillation, the defibrillation pulse acted on the cardiomyocyte model immediately after exposure to the excitation impulse. The threshold amplitude of the defibrillation pulse was fixed when the excitation of the cardiomyocyte model was suppressed at the action of the next excitation impulse (Fig. 1).

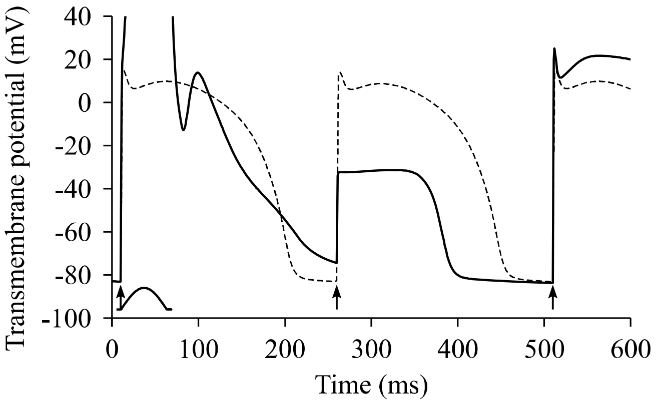

Fig. 1. Time chart of the transmembrane potential under the action of a half-sine depolarizing defibrillation pulse with duration of 53ms with a delay from the excitation impulse of 0.5ms and an amplitude of 73.213μA/cm^2 (dashed line shows the response of the cardiomyocyte model to the effects of impulses of simulated fibrillation, the arrows indicate the moments of action of these impulses)

The results were checked for compliance with the law of Hoorweg–Weiss–Lapicque [17]. The ratio of the threshold energy of a pulse to the threshold energy of an energy-optimal pulse according to the Hoorweg–Weiss–Lapicque law was calculated by the formula:

$$K_E = (1 - Topt / T)^2 \cdot T / (4 \cdot Topt), \quad (1)$$

where T – excitation impulse (defibrillation pulse) duration, K_E – the ratio of the threshold energy of an excitation impulse (defibrillation pulse) to the threshold energy of an energy-optimal excitation impulse (defibrillation pulse), $Topt$ – excitation impulse (defibrillation pulse) duration with a minimum of threshold energy ratio ($K_E = 1$).

All the materials and data in the article are presented in the online resource ResearchGate.[1]

III. Results and Discussions

A. Dependence of the threshold excitation energy of a cardiomyocyte on the duration of the acting impulse

For a half-sine and rectangular excitation impulses, dependences of the threshold excitation energy of the cardiomyocyte model on the excitation impulse duration were constructed. Since these dependencies have slight differences, Fig. 2 shows only the dependence graph for a half-sine pulse. For a rectangular excitation pulse, the minimum threshold energy ratio was E_{min}=116μA^2·ms/cm^4 for a pulse duration of 15.7ms (8% more than for a half-sine pulse). The values of the pulse duration relative to the duration of the energy-optimal pulse depending on the threshold values of the excitation energy of 1,2E_{min} и 1,5E_{min} are presented in Table I.

From Fig. 2 and Table I, it follows that for a cardiomyocyte model:

- the curves of the dependence of the threshold excitation energy on the duration of the excitation impulse correspond to the Hoorweg–Weiss–Lapicque law only in a first approximation,
- the deviation of the curve of the dependence of the threshold excitation energy on the Hoorweg–Weiss–Lapicque law depends on the waveform of the impulse.

A similar result for a rectangular impulse was obtained

[1] B. B. Gorbunov, V. A. Vostrikov, A. A. Galyastov, I. V. Nesterenko, D. V. Telyshev and M. V. Denisov, "Guaranteed defibrillation on a cardiomyocyte model," Supplementary resources, January 2020. http://doi.org/10.13140/RG.2.2.25051.52006

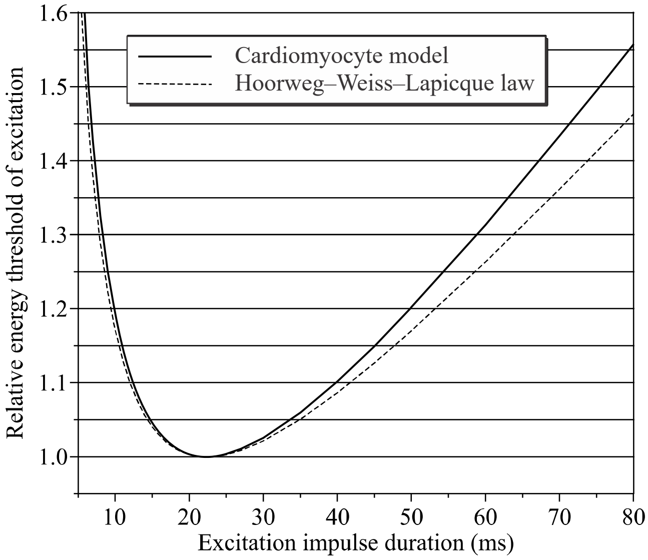

Fig. 2. Relatuve energy threshold of excitation depending on the half-sine impulse duration (minimum threshold energy ratio E_{min}=107μA^2·ms/cm^4 at impulse duration 22.4ms)

TABLE I COMPARISON OF EXCITATION IMPULSES WITH HALF-SINE AND RECTANGULAR WAVEFORM

Excitation impulse waveform	The impulse duration relative to the duration of the energy-optimal impulse depending on the threshold values of the excitation energy			
	***1.5E**$_{min}$*	***1.2E**$_{min}$*	***1.2E**$_{min}$*	***1.5E**$_{min}$*
Half-sine waveform	0.29	0.44	2.23	3.37
Rectangular waveform	0.30	0.46	2.12	3.11
Hoorweg–Weiss–Lapicque law	0.27	0.42	2.38	3.73

on the Luo-Rudy model on guinea pig cardiomyocyte [18]. In addition, it was found that the Hoorweg–Weiss–Lapicque law more accurately describes the behavior of a cardiomyocyte than the Blair model.

B. Dependence of the threshold energy of guaranteed defibrillation on the duration of the acting pulse

The dependences of the threshold energy of guaranteed defibrillation on the duration of the acting half-sine and rectangular pulses are presented in Fig. 3 and Fig. 4, respectively. For a rectangular pulse, the minimum energy coefficient of guaranteed defibrillation is 23% higher than for a half-sine pulse. The ratio of the duration of the energy-optimal pulse of guaranteed defibrillation to the duration of the energy-optimal excitation impulse for half-sine waveform was 2.37, and for a rectangular waveform – 2.42.

The values of the pulse duration relative to the duration of the energy-optimal pulse depending on the threshold energy values of guaranteed defibrillation of 1.2E_{min} and 1.5E_{min} are presented in Table II.

From Fig. 3, 4 and Table II it follows that for a cardiomyocyte model:

- in a first approximation, the curves of the dependence of the threshold energy of guaranteed defibrillation on the duration of the defibrillation pulse correspond to the Hoorweg–Weiss–Lapicque law on a limited range of relative values of the pulse duration,
- for a rectangular pulse, this range is much wider than for a half-sine pulse.

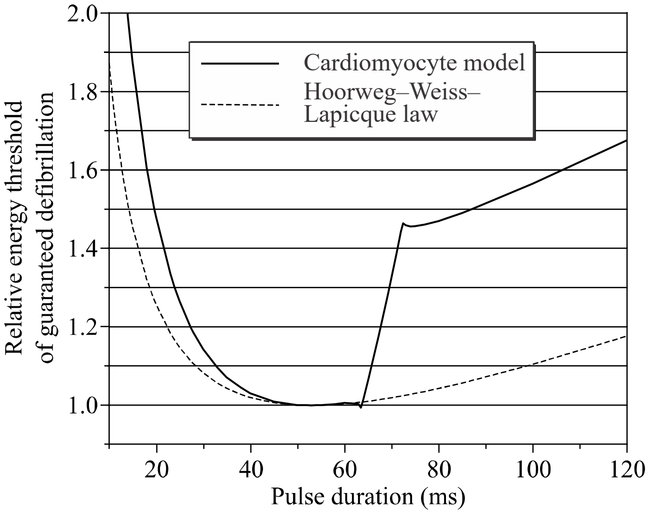

Fig. 3. Relative energy threshold of guaranted defibrillation depending on the half-sine pulse duration (minimum threshold energy ratio E_{min}=149910μA^2·ms/cm^4 at pulse duration 53ms)

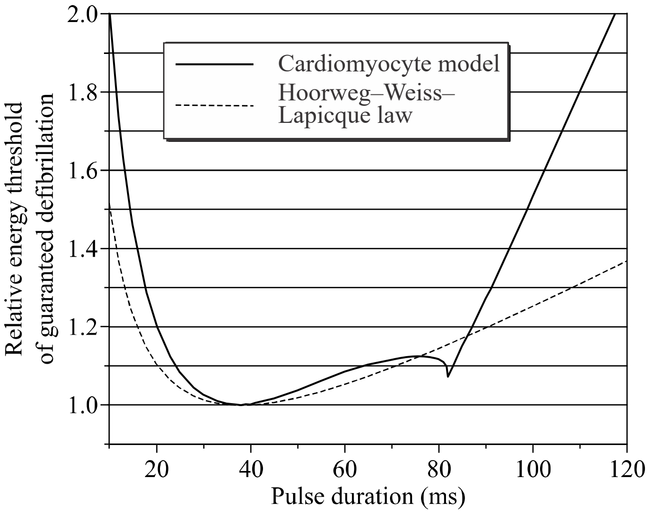

Fig. 4. Relative energy threshold of guaranted defibrillation depending on the rectangular pulse duration (minimum threshold energy ratio E_{min}=184632μA^2·ms/cm^4 at pulse duration 38ms)

TABLE II COMPARISON OF DEFIBRILLATION PULSES WITH HALF-SINE AND RECTANGULAR WAVEFORM

Defibrillation pulse waveform	**The pulse duration relative to the duration of the energy-optimal pulse, depending on the threshold energy values of guaranteed defibrillation**			
	1.5E$1.5E_{min}$	$1.2E_{min}$	$1.2E_{min}$	$1.5E_{min}$
Half-sine waveform	0.37	0.52	1.28	1.64
Rectangular waveform	0.30	0.46	2.12	3.11
Hoorweg–Weiss–Lapicque law	0.27	0.42	2.38	3.73

C. Comparison of the obtained results with the results of experimental studies

At first glance, the results obtained on a half-sine pulse seem paradoxical. However, they can be compared with the results of animal experiments performed by V.-K. K. Gasiunas [19]. The results of experiments on defibrillation with monophasic half-sine and biphasic quasi-sinusoidal pulses from [19] are presented in Table III.

Unfortunately, models of cardiomyocytes are imperfect. For a half-sine pulse in the cardiomyocyte model, the energy-optimal duration was 53ms, as indicated above, and according to the results of experiments [19] it was 5ms. Therefore, to compare the data, dimensionless values of the duration relative to the duration of the energy-optimal pulse were used. In addition, for a monopolar pulse, the average values of the relative threshold energy are divided by the value at the optimal duration (1.22). Fig. 5 presents the comparison result, where the dots represent the average values of the results from [19]. As can be seen from Fig. 5, the results obtained on the cardiomyocyte model are close to the results obtained in animal experiments.

IV. CONCLUSIONS

The obtained dependences of the threshold energy of guaranteed defibrillation on the duration of the defibrillation pulse correspond to the Hoorweg–Weiss–Lapicque law on a limited range of relative values of the pulse duration. This is consistent with the results of animal experiments. For a rectangular pulse, this range is much wider than for a half-sine wave. The obtained dependence of the threshold energy of guaranteed defibrillation on the duration of a half-sine defibrillation pulse is close to the results of animal experiments. Therefore, the guaranteed defibrillation mechanism can be used to compare the energy efficiency of external defibrillation pulses. It was also found that the energy-optimal duration of a half-sine and rectangular pulses

TABLE III RELATIVE VALUES OF THE THRESHOLD DEFIBRILLATION ENERGY OBTAINED BY V.-K. K. GASIUNAS IN ANIMAL EXPERIMENTS

Duration of a monophasic pulse (the first phase of a biphasic pulse), ms	**The ratio of the threshold energy of defibrillation to the threshold energy of a biphasic pulse with a duration of the first phase of 5 ms**	
	Monophasic pulse	***Biphasic pulse***
1.6	1.56±0.14	1.18±0.12
2.0	1.77±0.19	1.37±0.09
5.0	1.22±0.11	1.00
6.4	1.37±0.13	1.21±0.12
9.4	1.65±0.19	1.51±0.12

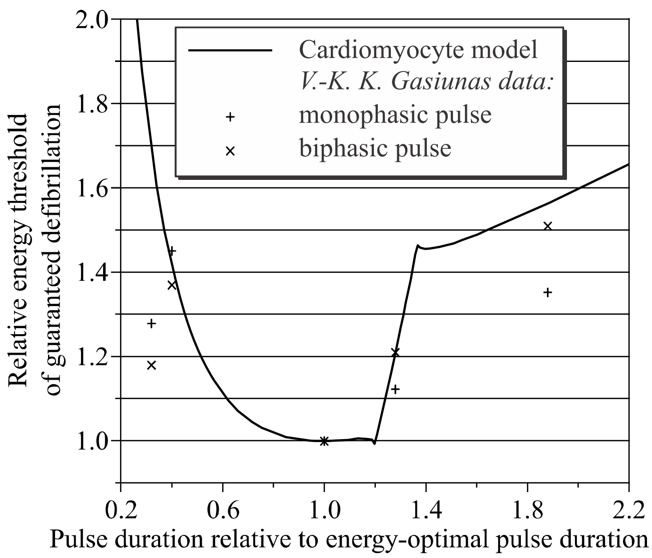

Fig. 5. Relative energy threshold of guaranted defibrillation depending on pulse duration relative to energy-optimal pulse duration in comparison with the data of V.-K. K. Gasiunas

of guaranteed defibrillation is approximately 2.4 times higher than the energy-optimal excitation impulses duration.

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