

Evaluation Of the Influence of The Second Phase Duration of The Depolarizing Biphasic Half-Sinusoidal Defibrillation Pulse on Its Energy Efficiency

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ABSTRACT

Diagrams of the dependence of the fibrillation cycle fraction on which the defibrillation pulse causes a long-term extension of the cardiomyocyte refractory period (defibrillation completeness index) on the defibrillation pulse relative energy have been constructed based on the simulation of the reaction of a cardiomyocyte in a state of fibrillation imitation on biphasic depolarizing half-sinusoidal defibrillation pulses with different values of the second phase duration. The constructed diagrams have shown that a reduction in the biphasic defibrillation pulse's second phase duration below the optimal value leads to a decrease in its energy efficiency in a wide range of energy values. An increase in the second phase duration above the optimal value leads to an increase in energy efficiency at low energy values.

Keywords: Defibrillation, biphasic defibrillation pulse, simulation, cardiomyocyte model, long-term extension of the refractory period, pulse's second phase duration, energy efficiency

Introduction

The study performed on ten Tusscher-Panfilov 2006 human ventricular cardiomyocyte model (Ten Tusscher & Panfilov, 2006) in BeatBox simulation environment (Antonioletti et al., 2017), has found that defibrillation pulses cause a long-term extension of the cardiomyocyte refractory period, which prevents the fibrillation wave propagation (Gorbunov, 2017). This effect was previously detected in experimental studies (Sweeney et al., 1990; Sweeney et al., 1991; Dillon, 1991; Tovar & Jones, 1997). Study (Gorbunov et al., 2018) has found that on the fibrillation cycle energy/phase diagram there are depolarizing monophasic defibrillation pulse areas of effectiveness, in which a long-term extension of the cardiomyocyte refractory period is achieved. Study (Gorbunov et al., 2021) has compared areas of effectiveness of half-sinusoidal monophasic and biphasic depolarizing half-sinusoidal defibrillation pulses. Study (Gorbunov et al., 2020) has investigated the dependence of the fibrillation cycle fraction on the monophasic defibrillation pulse energy coefficient, at which the defibrillation pulse causes a long-term extension of the cardiomyocyte refractory period (defibrillation

completeness index) for a number of pulse duration values. Study (Gorbunov et al., 2023) has investigated the dependence of the defibrillation completeness index on the relative energy of the biphasic half-sinusoidal depolarizing defibrillation pulse with phase durations equal to the optimal duration of a monophasic half-sinusoidal pulse established based on the guaranteed defibrillation hypothesis (Gorbunov et al., 2020), at different values of the pulse's second phase relative amplitude.

The purpose of this study is to compare the dependences of the defibrillation completeness index on the relative energy of the biphasic half-sinusoidal depolarizing defibrillation pulse with the optimal duration of the first phase established based on the guaranteed defibrillation hypothesis at different values of the pulse's second phase duration.

Materials and Methods

Cardiomyocyte model

The studies were carried out on ten Tusscher-Panfilov 2006 human ventricular myocyte model (Ten Tusscher & Panfilov, 2006), which is under the influence of fibrillation imitation,

in BeatBox simulation environment (Antonioletti et al., 2017) under Fedora operating system. The fibrillation was simulated by applying depolarizing excitation stimuli with an amplitude of $80 \mu\text{A}/\text{cm}^2$ and a duration of $0,5 \text{ ms}$ with a frequency 240 min^{-1} (the maximum excitation frequency perceived by the cardiomyocyte model (Gorbunov, 2017)).

Construction of defibrillation pulse effectiveness areas

On the fibrillation cycle energy/phase diagrams, areas were constructed in which, under the influence of a defibrillation pulse, a long-term extension of the refractory period was observed in the cardiomyocyte model (defibrillation pulse effectiveness areas). The fibrillation cycle phase was defined as the ratio of the delay in the defibrillation pulse onset from the excitation pulse to the fibrillation cycle duration. Each value of the phase of the fibrillation cycle in the areas of effectiveness corresponded to only one pair of values of the lower and upper boundaries. This is necessary for the subsequent calculation of the defibrillation completeness index.

When determining the boundary values, the value of the amplitude of the current density of the first phase of the pulse was set. The pulse energy was calculated during the simulation. Since the pulse current density expressed in $\mu\text{A}/\text{cm}^2$, is used as an external action parameter in the model, the energy coefficient represented by the time integral of the square of the current density expressed in $\mu\text{A}^2 \cdot \text{ms}/\text{cm}^4$ was used as a criterion of pulse energy. Energy values relative to the threshold coefficient of the energy of the cardiomyocyte model excitation by a monophasic half-sinusoidal pulse with duration of 53 ms were used when constructing the defibrillation pulse efficiency areas. At this monophasic pulse duration value, the threshold excitation energy coefficient is $132.1 \mu\text{A}^2 \cdot \text{ms}/\text{cm}^4$.

The long-term extension of the refractory period was observed visually on the time diagram formed during modeling when the reaction to every second excitation pulse was missed. **Fig. 1** shows an example of a timing chart of the transmembrane potential obtained for a defibrillation pulse with the duration of the first and second phase equal to 5 ms , a delay from the excitation pulse of 0.74 of the fibrillation cycle duration and a relative energy of 1.678 , which is the lower boundary value at which a long-term extension of the refractory period is achieved.

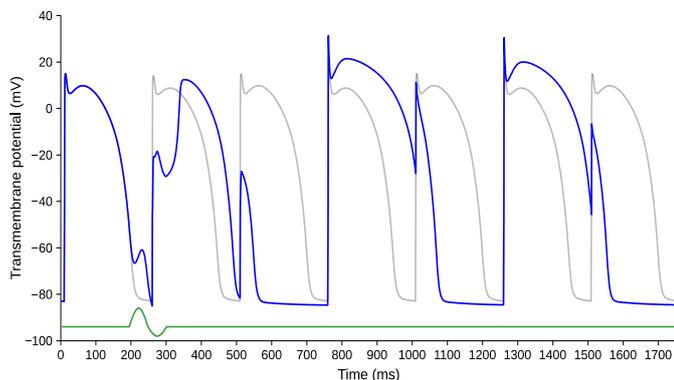


Figure 1: The timing chart of the transmembrane potential of the cardiomyocyte model under the influence of simulated fibrillation (gray dashed line) and under the influence of a defibrillation pulse (blue solid line). The moment of exposure to the defibrillation pulse is conventionally presented below (green solid line).

The diagrams were constructed for depolarizing half-sinusoidal monophasic pulse with a duration of 5 ms and biphasic defibrillation pulses with the first phase duration of 5 ms and a number of the second phase duration values in ms:

3; 4; 5; 6; 7. The second phase relative amplitude was -0.5 (the energetically optimal value obtained in (Gorbunov et al., 2023)). Coefficient 10.6 justified in (Gorbunov et al., 2020) was used to reduce the duration of the pulse phases in the cardiomyocyte model to the values obtained in biological experiments. Thus, in the cardiomyocyte model, the defibrillation pulse's first phase duration was 53 ms , and a number of the second phase duration values in ms was: 31.8 ; 42.4 ; 53.0 ; 63.6 ; 74.2 .

Construction of dependencies of the defibrillation completeness index on the defibrillation pulse energy

The dependences of the defibrillation completeness index on the defibrillation pulse energy were constructed according to the data obtained during the construction of the areas of effectiveness. The defibrillation completeness index was defined as the ratio of the sum of the intervals at which, at a given energy value, the pulse was effective (caused a long-term extension of the refractory period) to the fibrillation period duration. GNU Octave freeware system for mathematical calculations using a high-level language compatible with MATLAB (GNU Octave, 2023) was used to construct the dependencies of the defibrillation completeness index on the relative pulse energy. The script written for GNU Octave calculated the defibrillation completeness index on relative energy levels represented by the list in the text file. Relative levels of the pulse energy were set from 0.1 to 100 in the E192 series. The data of the lower and upper boundaries of the defibrillation areas of effectiveness were prepared in separate text files for each value of the second phase duration. The calculation results were recorded in a separate file for each value of the second phase duration. The results were calculated by linear interpolation from the values of the two nearest data points of the lower and upper boundaries of the defibrillation pulse areas of effectiveness.

Results

Defibrillation pulse areas of effectiveness

As an example, **Fig. 2** shows the lower and upper boundaries of the defibrillation biphasic depolarizing half-sinusoidal pulse's efficiency areas with duration of the first and second phases of 5 ms , **Fig. 3** - with the first phase duration of 5 ms , the second phase duration of 4 ms .

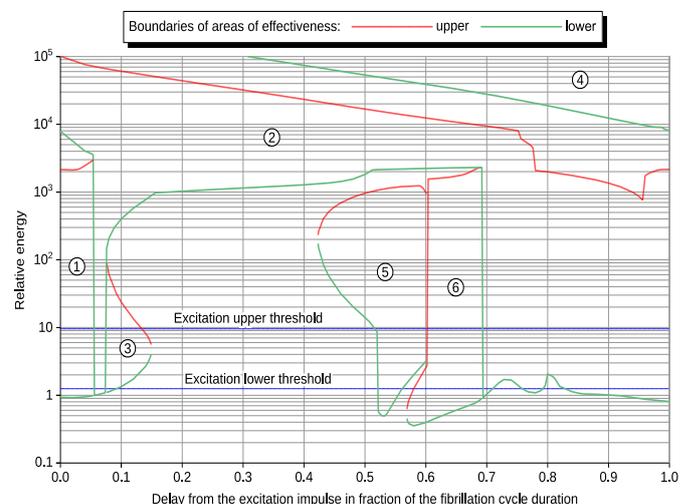


Figure 2: The lower and upper boundaries of the half-sinusoidal biphasic depolarizing defibrillation pulse's areas of effectiveness with duration of the first and second phases of 5 ms (the numbers of the areas of effectiveness are indicated).

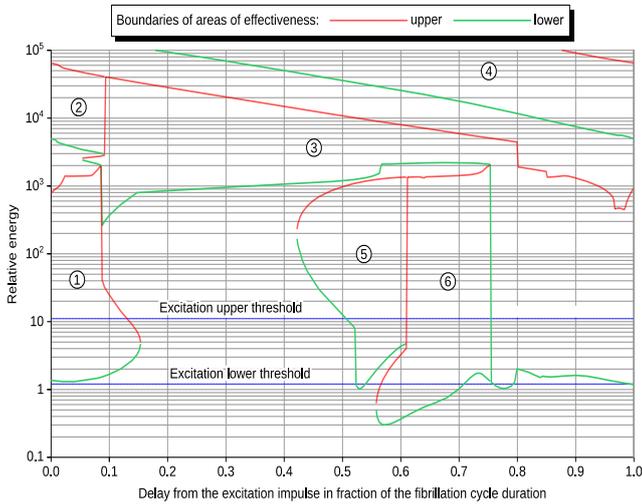


Figure 3: The lower and upper boundaries of the half-sinusoidal biphasic depolarizing defibrillation pulse’s areas of effectiveness with the first phase duration of 5 ms, the second phase duration of 4 ms (the numbers of the areas of effectiveness are indicated).

Fig. 2 and Fig. 3 also show the lower and upper thresholds of cardiomyocyte excitation by the corresponding defibrillation pulse. The lower threshold corresponds to the minimum pulse energy at which the action potential is formed by a cardiomyocyte at resting state. The upper threshold corresponds to the pulse energy at which the action potential has a maximum duration measured at -50 mV. When the pulse energy increases above this threshold, there is a sharp decrease in the duration of the action potential associated with its suppression by the hyperpolarizing second phase of the pulse. Presumably, the development of the fibrillation induced by the defibrillation pulse is most likely in the energy range between these thresholds.

Dependences of the defibrillation completeness index on the defibrillation pulse energy

Fig. 4 shows the dependence of the defibrillation completeness index on the relative energy of depolarizing half-sinusoidal biphasic defibrillation pulses with a duration of the first phase of 5 ms and a number of the second phase duration values and the monophasic pulse (the second phase duration is 0).

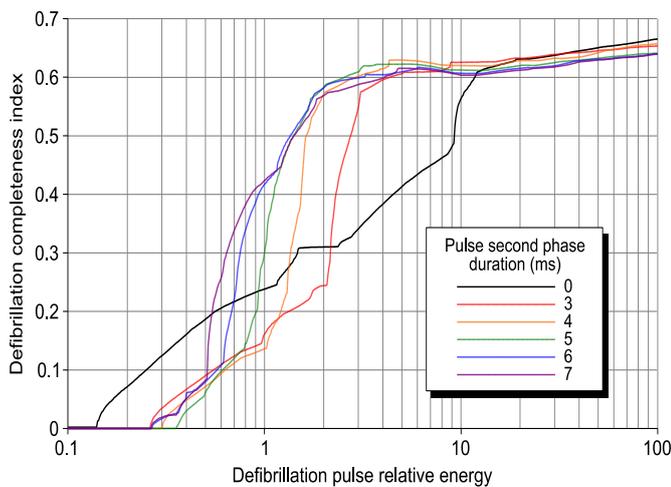


Figure 4: The dependence of the defibrillation completeness index on the relative energy of depolarizing half-sinusoidal biphasic defibrillation pulses with a duration of the first phase of 5 ms and a number of the second phase duration values and the monophasic pulse (the second phase duration is 0).

Fig. 4 shows that a reduction in the biphasic defibrillation pulse’s second phase duration below the optimal value of ρ ms leads to a decrease in its energy efficiency in a wide range of energy

values. It is possible that the energy efficiency with a decrease in the pulse’s second phase duration will increase with an increase in the absolute value of its relative amplitude, but this requires a separate study. An increase in the second phase duration above the optimal value leads to an increase in energy efficiency at low energy values. However, presumably a condition for a positive result of classical defibrillation is large values of the defibrillation completeness index.

Discussion

The study uses an empirical coefficient of 10.6 to link the results obtained on the cardiomyocyte model to the real time parameters of the defibrillation pulse. This coefficient was obtained based on the guaranteed defibrillation hypothesis (Gorbunov et al., 2020). At the same time, by the duration and form of the action potential, the model corresponds quite accurately to the parameters of cardiomyocytes in the human heart ventricles.

Another difference in the parameters of the cardiomyocyte model response to the impact of electric current is the energetically optimal duration of the excitation pulse. The energetically optimal duration of a rectangular excitation pulse for the model is about 15 ms (Gorbunov, 2017), while in animal experiments the energetically optimal duration of rectangular electrical stimulation pulses was determined to be 1,3 ms (Angelakos & Torres, 1964). Thus, the energetically optimal duration of the rectangular excitation pulse of the cardiomyocyte model is 11.5 times longer than that perceived by cardiomyocytes in the human heart ventricles. This value is close to the empirical coefficient 10.6 used in the study.

At the same time, differences in the cardiomyocyte excitation and defibrillation mechanisms are confirmed both in animal experiments and in the cardiomyocyte model. The energetically optimal duration of the half-sinusoidal excitation impulse of the cardiomyocyte model is about 22 ms, while the energetically optimal duration of the half-sinusoidal monophasic defibrillation pulse obtained in accordance with the guaranteed defibrillation hypothesis is 53 ms (Gorbunov, et al., 2020). Thus, in the model, the energetically optimal duration of the half-sinusoidal defibrillation pulse is 2.2 times longer than the energetically optimal duration of the excitation pulse. In animal experiments, the energetically optimal value of the duration of rectangular monophasic defibrillation pulses of 4 ms was determined (Koning et al., 1975). Thus, in animal experiments, the energetically optimal duration of rectangular defibrillation pulses is 3.1 times longer than the energy duration of excitation impulses.

Despite the imperfection of the cardiomyocyte model, the results obtained in this study clearly demonstrate the advantage of a biphasic defibrillation pulse over a monophasic one.

Conclusion

Based on the simulation results, it can be assumed that a reduction in the biphasic defibrillation pulse’s second phase duration below the optimal value leads to a decrease in its energy efficiency in a wide range of energy values. An increase in the second phase duration above the optimal value leads to an increase in energy efficiency at low energy values.

Conflict of Interest

The authors declare no conflicts of interest with any companies or commercial organizations per the definition of Japanese Society for Medical and Biological Engineering.

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Availability of Data and Materials

The simulation data and other materials related to the study are available at ResearchGate (Gorbunov et al., 2023).

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