Huge reduction of defibrillation thresholds using four electrode defibrillators

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Abstract

In the absence of a better solution, ventricular fibrillation is treated by applying one or several large electrical shocks to the patient. The question of how to lower the energy required for a successful shock is still a current issue in both fundamental research and clinical practice. In the study presented here we will compare defibrillation applied through a four electrode device with the standard procedure using two electrodes. The method is tested through intensive numerical simulations. Here we have used a one dimensional geometry. At the level of the cardiac tissue, the bidomain and the modified Beeler-Reuter models were used. Three different shock waveforms are tested: monophasic and two types of biphasic shocks. The results are compared with those obtained with standard two electrode device. A significant reduction in defibrillation thresholds is achieved for all the three tested waveforms when we use a four electrode device.

1. Introduction

Defibrillation is the only existing treatment for life-threatening arrhythmias. The therapy consists in applying an electrical shock via two electrodes applied externally on the chest or internally with an implanted device. One of the main drawback of this approach is the high energy associated with successful outcomes, typically in the range of 150 Joule in the case of transthoracic defibrillation. The design of the defibrillator devices is mainly based on experimental evidences. There are two main approaches in optimizing the delivered energy required for defibrillation: optimizing parameters of the waveform (typically generated with a capacitor discharge) or optimizing the timing of the polarity reversal of the electrodes. The first defibrillatory shocks were monophasic, i.e. the polarity of the electrodes was not changed during the shock. Later it was found empirically that biphasic shocks, where polarity of the electrodes is reversed during the shock, were more efficient. The delivered energy is approximately 25% less with respect to monophasic shocks.

Numerical simulations of the cardiac dynamics on a one-dimensional geometry have been used extensively to study arrhythmic behavior. A seminal work is the one by Glass and Josephson [1] where they studied the interaction of external shocks with the reentrant dynamics. Recently, by using the same strategy, we have used one-dimensional models to assess the efficiency of the defibrillation shocks [2]. In the latter work, three commonly used defibrillation protocols have been tested and their resulting relative efficiencies were found. In the present study, we will test the defibrillation efficiency of four electrode devices as opposed to the standard approach with two electrodes. The basis for such approach comes from the previous analysis of the defibrillation mechanisms on the 1D ring [2]. We have observed that for low to medium percentage of success (10 to 50%), the successful outcomes are achieved mainly by front to front or front to refractory tissue interactions. Therefore one suspects that these mechanisms of successful outcomes could be further enhanced by placing additional electrodes. The results presented here confirm that defibrillation thresholds are indeed greatly reduced when using four-electrode devices.

2. Model and methods

A schematic representation of the numerical experiments is depicted in Fig.1. Initially, the reentrant wave representing the arrhythmic dynamics is circulating on a ring or cardiac tissue. Subsequently, a shock of 8ms is applied by injecting current into the extracellular space through the four electrodes on the ring. Then, the shock is classified as successful if all the reentrant dynamics is removed in the lapse of time of 1000ms, and unsuccessful if a wave is still observed. Three well known shock protocols are tested: monophasic (M) in which the polarity of the electrodes is unchanged during the shock (8ms), symmetric biphasic or biphasic I (BI) in which the polarity of the electrodes is reversed at the middle of the shock (4ms–4ms) and asymmetric biphasic or biphasic II (BII) for which the duration of the second phase is shorter than the duration of the first phase (6ms–2ms). We have previously [2] compared these three protocols using the one-dimensional model and found that biphasic protocols will defibrillate with 20% (BI) and 26% (BII) less energy when compared with monophasic shocks [2]. These values are close to the experimentally found values [3,4]. Let us emphasize one important difference with respect to the aforementioned results. In the article by Bragard *et al.* [2], the dynamics prior to the shock is quasi-periodic and exhibits discordant–alternans [5].

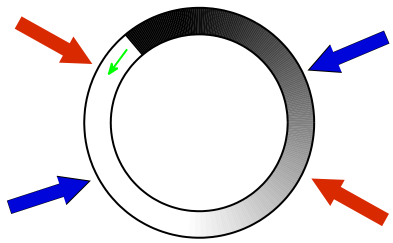

Figure 1. Schematic representation of the numerical experiment performed in this study. A defibrillatory shock is applied through four electrodes. Prior to the shock, the dynamics on the ring is chaotic in order to mimic the arrhythmic behavior of the cardiac tissue. The two anodes and cathodes are facing each other.

While here, the dynamics on the ring prior to the shock is chaotic. This was done following the work by Qu *et al.* [6] by modifying the outward potassium current.

Let us present the governing equations used in this numerical study. The propagation of the electrical wave in the cardiac tissue is modeled with the bidomain formulation:

$$\frac{\partial V_m}{\partial t} = -\frac{I_{ion}}{C_m} + \nabla\cdot(\mathbf{D_i}\cdot\nabla\mathbf{V_m}) + \nabla\cdot(\mathbf{D_i}\cdot\nabla\mathbf{\Phi_e}) \quad (1)$$

$$\nabla\cdot[(\mathbf{D_i}+\mathbf{D_e})\cdot\nabla\mathbf{\Phi_e}] = -\nabla\cdot(\mathbf{D_i}\cdot\nabla\mathbf{V_m}) - \frac{i_e}{\chi C_m} \quad (2)$$

where $V_m = \Phi_i - \Phi_e$ is the transmembrane potential, Φ_e is the extracellular electrical potential, Φ_i is the intracellular electrical potential, C_m is the membrane capacitance ($\approx 1\mu F/cm^2$), χ is the myocyte surface to volume ratio (1400 cm^{-1}) and $\mathbf{D_i}$ and $\mathbf{D_e}$ are the intracellular and extracellular diffusion tensors, respectively. It is important to mention that we have modified the intracellular diffusion constant (proportional to the intracellular conductance) by adding small scale spatial heterogeneities in the following way:

$$D_i(x) = \bar{D}(1 + \tilde{s}\,\delta_i(x)) \quad (3)$$

where $\bar{D}$ is the average value of internal diffusion and it is set to $1.5\cdot10^{-3}$$cm^2$/ms, $\delta_i(x)$ is a random variable drawn from a Gaussian distribution with zero mean and unit variance and $\tilde{s}$ is a parameter that controls the strength of the heterogeneities and is set here to 0.15. This modification of the conductivity follows the work by Fishler [7].

The membrane current denoted here by I_{ion} in Eq.(1) is composed of the currents of the Beeler-Reuter model [8] (I_{BR}) and two additional contributions intended to account for phenomena caused by high extracellular fields, namely, electroporation (I_{ep}) and anode break phenomena (I_{fu}):

$$I_{ion} = I_{BR} + I_{ep} + I_{fu} \quad (4)$$

The electroporation phenomenon denotes the opening of reversible pores in the cell membrane as a response to strong applied extracellular fields. As a result, the membrane potential V_m will saturate [9] rather than grow over the lysis point of the myocyte.

Here, we have incorporated the description of the electroporation current as modeled by DeBruin and Krassowska [10]. The anode break phenomenon refers to the unexpected onset of an action potential upon the termination of the anodal stimulation. In a model developed by Ranjan *et al.* [11] that we have followed here, the anodal excitation is brought by an hyperpolarization induced current I_{fu} in combination with time dependent blocking and subsequent unblocking of the potassium current. The classical Beeler-Reuter model is composed of four currents: fast sodium inward current I_{Na}, slow calcium inward current I_s, time independent potassium (I_K) and time-dependent delayed rectifier potassium outward current I_x. The latter, I_x is modified here according to [6] to induce a chaotic dynamics on the ring. The parameter a regulating the transition from quasiperiodicity to chaos is set here to 0.9. We have built return maps for the action potential (not shown here) for various values of the a parameter to check the agreement of the present model with the results reported in [6].

Let us comment briefly on the numerical methods used in the simulations. The ring size is set to L=6.7cm throughout the paper and the spatial discretization is set to dx = 0.025cm. The shock duration is fixed to 8ms. The time discretization step is set to dt = 0.001ms during and 10ms after the shock application, while for the rest of the simulation, the time step is increased to 0.01ms. The time integration of the membrane potential V_m in the Eq.(1) is performed using a forward Euler method. The integration of the Eq.(2), the most time-consuming part of the simulations, is performed using the generalized minimal residual method (GMRES). We have used the freely available PETSC library [12] to implement the GMRES method in our codes. The convergence of the iterative method was controlled by the residual norm relative to the norm of the right hand side. Let us mention that all the expressions for the currents are computed by using lookup tables. By doing so, we avoid the repeated computation of the costly exponential and similar functions.

3. Results

Figure 2 shows the dose-response curves for both two- and four-electrode systems. The percentage of success at each energy level is evaluated with 100,000 defibrillation trials. We have 50 different conductivity realizations (see Eq.(3)) $\times$ 2,000 different initial conditions. In Fig. 2 the spread shown by the boxplots is due to the conductivity heterogeneity of the ring. The fit of the data is performed using the generalized additive model (GAM) for which the log of odds can be written as:

$$\log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 \cdot s(E) \tag{5}$$

where $s(E)$ is a smooth function of the predictor which can take different forms. The results are obtained by using the R software for statistical computing [13] with the added *mgcv* package [14]. In a previous paper, the analysis of the two-electrode system [2], was done using a fit to the logistic function, a common approach for modeling defibrillation dose-response curves. In the case of the four-electrode system, we have observed a difference. The numerical data for the four-electrode protocol exhibit two plateaus. The first plateau- is the expected saturation at high shock strengths, while the second plateau is observed around medium shock strengths of approximately 3V/cm. The second plateau could not be fitted with a simple logistic regression, while this is easily achieved with the semi-parametric approach (GAM) that we have used here. Fig.2 also clearly shows that for E$\leq$7V/cm, the four-electrode device defibrillate with significantly higher percentage of success than the two-electrode system for all the protocols (monophasic and biphasics). The comparison of the two systems (two- and four- electrodes) can be better quantified by comparing the E_{50} and E_{90} thresholds, i.e. the extracellular electric field needed to achieve 50% and 90% of successful defibrillation. The results are summarized in Table 1. It is obvious that all values are smaller when shocks are applied with the four-electrode system rather than the two-electrode system. The most striking difference is achieved with the BII shock protocol. For the BII protocol we have found that the energy decrease between the two- and the four-electrode device is approximately 88%. This means close to one order of magnitude less energy for getting the same probability of defibrillation when using the four-electrode device. The analysis of Table 1 brings also, quite surprisingly, that the monophasic shock protocol is more efficient than the B1 protocol when applied with four-electrodes. When comparing the two- and the four-electrode device, we have found a decrease of energy of approximately 52% and 42% for the monophasic and biphasic I shock protocol, respectively.

It is known that the phase-duration ratio can have a significant effect on the defibrillation thresholds [15]. The large difference in the efficiency between the biphasic protocols (BI and BII) prompted a question of how does the percentage of success change as we vary the duration of the second phase. Fig. 3 shows the dependence of the percentage of success when we vary the duration of the second phase. We have varied the duration of the second phase for two shock strengths: E=3V/cm and E=6V/cm. The total shock duration is fixed to 8ms, while the second phase increases from 0ms (monophasic) to 8ms (again monophasic, but with reversed positions of the electrodes). In Fig. 3, one observes that the two tested energies will exhibit a maximum of defibrillation when the second phase duration is in between 1.5ms and 2ms. The maximum is much more pronounced for the four electrode system (lower graph) than for the two electrode system (upper graph in Fig. 3).

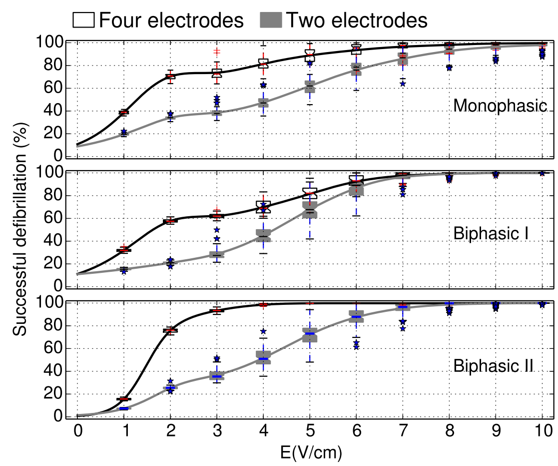

Figure 2. Fitted dose-response curves for monophasic (top), biphasic 1 (middle) and biphasic 2 (bottom) shock protocols. The gain in effectivity between the FE and TE devices are remarkable in all cases.

Table 1. Dose-response curves shown in Fig. 2 are used to evaluate E_{50} and E_{90}, i.e., the shock strength necessary to achieve 50% and 90% of successful defibrillation, respectively. The E_{50} and E_{90} are given with confidence intervals (with α=0.01) for both the two-electrode (TE) and four-electrode (FE) system.

	E_{50}(V/cm)		E_{90}(V/cm)	
	TE	FE	TE	FE
M	4.17–4.21	1.27–1.29	7.51–7.56	5.16–5.25
BI	4.22–4.24	1.61–1.64	6.23–6.25	5.71–5.76
BII	3.89–3.93	1.54–1.56	6.23–6.26	2.63–2.67

4. Conclusions

In this study we have compared the efficiency of defibrillatory shocks applied through four-electrodes with respect to the standard two-electrode approach. The comparison is done using a simple, but fast one-dimensional

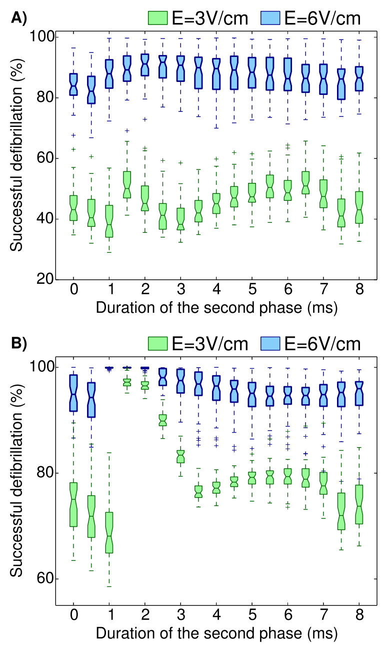

Figure 3. Defibrillation percentages for shock strength E = 3V/cm and E = 6V/cm vs duration of the second phase. Upper graph (A) corresponds to TE device and lower graph (B) corresponds to the FE device.

model developed previously [2]. Three defibrillation shock protocols are compared: monophasic (8ms), symmetric biphasic (4ms–4ms) and asymmetric biphasic (6ms–2ms). The reduction in defibrillation threshold is observed when using the FE rather than the TE system. The highest reduction is obtained with biphasic asymmetric protocol. The best phase duration ratios are obtained for a second phase duration of approximately 1.5ms to 2ms. Our next goal is to analyze in more detail the mechanisms behind the huge advantage of the BII protocol with respect to the BI and M protocols. One strong limitation of the present study is that we have used a one-dimensional model. An extension of this study will use a more realistic 3D geometry for simulating the vortices and rotors present in arrhythmic behavior. We hope that the results obtained here will still be valid in these more realistic simulations and confirm the huge advantage of the four-electrode defibrillator.

5. Acknowledgments

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