Letters to the Editor

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Kinetics of defibrillation shock-induced response: design implications for the optimal defibrillation waveform

Mowrey and colleagues[1] investigated the response of the myocardium with respect to defibrillation ‘shocks’. However, their trials are concerned with effective (Fig. 10) or partially ineffective (Fig. 6) voltage pulses within or outside the absolute refractory period. This is remarkable as they assume an equal mechanism for defibrillation and stimulation without expressing it, a thesis which we presented in 1990[2]. If the cell response is equal for stimulation and defibrillation, one has a simple opportunity to test the defibrillation hypotheses, for instance concerning efficient waveforms, by electrostimulation of the heart with higher accuracy and less physiological damage to the heart as must always be expected with defibrillation. Under this assumption we can ascertain that several statements of the authors contradict the stimulation theory or stimulation results:

1. Pacing with 10 μs pulse duration is possible without excessive voltage. The cell membrane integrates the applied voltage so that a sharp rise is especially suited to raise the membrane voltage. The membrane response would best be investigated with a step function.

2. Regardless of waveform, the pulse is effective if the voltage averaged during pulse duration (mean value) is equal to that of a square wave at threshold level (Weiss’ Law[3]). Following the Weiss Law, ascending and descending pulses are of equal effectiveness if their mean value is equal.

3. The above threshold definition is valid as long as parts of a pulse are not below rheobase as they do not contribute. Sinusoidal pulses are, therefore, less effective as they possess voltages below rheobase. These findings, which were surely experienced by others too, were published by us as early as 1976[4].

4. If the measured membrane time constants vary between 1.6 and 14.2 ms, the message is not clear as to what defibrillator time constant RC should best be chosen. Theoretical considerations suggest that lowest stored energy is reached with an RC of 0.8 times chronaxie, whereas lowest delivered energy is gained with RC = 1.19 times chronaxie for exponentially decaying pulses[5].

5. With 50 Ω assumed and an output capacitance of 150 μF (the 80 μF of the legend of Fig. 2 is not correct for the HVS02) the time constant is 7.5 ms. Theoretically[6] the corresponding pulse duration should be 4.9 ms, the tail of the exponential discharge beyond is below rheobase in the far field, which in other words, no longer contributes to the charging of the membrane capacitance. Its voltage starts to decrease again. It would be interesting to learn how within this limitation in pulse duration would influence the measured membrane time constants.

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Reply

We are happy to answer the letter of Professor Irnich regarding our recent report[1] in Europace on myocardial response to electric shocks of defibrillation strength. This response presents an opportunity to discuss our understanding of mechanisms of stimulation and defibrillation, which seems to differ significantly from that of Professor Irnich.

First, we would like to thank Professor Irnich for pointing out a mistake in the caption of Fig. 2. The HVS02 output capacitor is not 80 μF, but 150 μF as stated in the text. However, we respectfully disagree with Professor Irnich’s view that mechanisms of defibrillation and stimulation are essentially the same[7]. Furthermore, we cannot confirm his supposition that our paper suggested that equivalence exists in any form. On the contrary, our data presented in this paper[1] and earlier publications[3–8] clearly demonstrate that these two phenomena are governed by fundamentally different mechanisms. Therefore, we believe that the laws of stimulation, which Professor Irnich investigated for many years, are not applicable to defibrillation. This is why our data contradict the theoretical considerations of mechanisms of stimulation, as he elegantly presented in the letter.

Discussion of the fundamental differences of mechanisms of stimulation and mechanisms of defibrillation deserves a much wider format[9] than a letter to editor. Nevertheless, we would like briefly to summarize our experimental data, which provide a basis for our point of view and contradict that of Professor Irnich.

The factors responsible for these differences are the state of the myocardium and the magnitude of the stimulus necessary to produce the desired results. The expected outcome of stimulation and defibrillation significantly differ. Stimulation induces a propagated action potential in excitable myocardium. Thus, stimulation in most cases deals with the myocardium in the same electrophysiological state — resting potential. In contrast, defibrillation must satisfy two requirements, which are governed by different mechanisms: it must extinguish ongoing ventricular fibrillation and it must not induce new fibrillation. In both cases defibrillation shock deals with myocardium at all possible electrophysiological states, ranging from excitable to refractory states. There are numerous differences in the results of stimulation and defibrillation. For example,
defibrillation shock can produce de-excitation\textsuperscript{10}, while stimulation cannot. Because of the profound electrophysiological differences in the myocardium, the amplitudes necessary for success are drastically different. In our rabbit model, stimulation is achieved with a 1–5 V pulse. In contrast, the defibrillation threshold in this model is 160 V, nearly two orders of magnitude larger than a successful stimulation pulse. Thus, our protocol for this study investigated defibrillation shocks with amplitudes between 60 and 260 V. And because of the complete range of electrophysiological states seen during fibrillation, shocks of defibrillation strength were applied at different phases of the action potential in order to quantify the entire range of responses to defibrillation shocks.

Progress in the investigation of the fundamental mechanisms of stimulation and defibrillation achieved during the last two decades was primarily due to development of two novel methodologies, which were not available to previous generations of investigators. These two methodologies are: (1) fast fluorescent imaging\textsuperscript{9} with voltage-sensitive dyes, which for the first time permitted visualization of the spatial-temporal patterns of the stimulus-induced response of the myocardium, and (2) the computing power to solve the bidomain\textsuperscript{11} mathematical model in three dimensions with high spatial and temporal resolution. Lack of these technologies did not permit previous studies to determine the actual cellular response to a stimulus, allowing only a black-box approach, which assesses the input and output without experimental evidence relating the two. In contrast, direct measurements of transmembrane potential during stimulation and defibrillation have revealed quite remarkable spatial patterns of polarization induced by electrical stimulation\textsuperscript{12} and defibrillation\textsuperscript{5}, known as virtual electrodes\textsuperscript{13}.

These fluorescent imaging studies not only confirmed previous clinical observations, which Professor Irnich disagrees with, if we understood him correctly, but also formed the basis of a plausible mechanistic explanation. These observations are: (1) significant difference in anodal versus cathodal monophasic shock defibrillation and monophasic stimulation, (2) significant difference in efficacy of monophasic shocks with different waveforms, (3) significant superiority of biphasic defibrillation shocks over monophasic shocks. Basic and clinical evidence of these phenomena is so overwhelming\textsuperscript{14} that we do not quite understand how Professor Irnich can presume otherwise: “The shape of the defibrillation pulse and its polarity plays no role”\textsuperscript{2} (p. 1433, line 21–22). Our fluorescent imaging studies\textsuperscript{3} have clearly shown that the second phase of the shock can completely reverse response to the first phase of the shock, which is the cause of superiority of biphasic shocks over monophasic.

Many theories of stimulation and defibrillation have been developed over a century of research. However, majority of them had no direct experimental verification due to lack of experimental techniques allowing direct measurements of transmembrane response during stimulus or shock. This left significant room for speculation regarding the fundamental laws of stimulation and defibrillation, expressed as a simple mathematical formula. We do not believe that such a formula exists, due to the profound complexity of the heart. Now we have a significant body of experimental evidence regarding the electrophysiological response to an electrical field, which provides the foundation for testing these sometimes contradictory theories. We welcome this letter of Professor Irnich as the first step to compare existing theories with experimental data.

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