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Reentry in Cardioversion: ‘We can see it from here...’:

An Editorial Comment on: Ripplinger CM, Lou Q, Li W, Hadley J, Efimov IR: Panoramic Imaging Reveals Basic Mechanisms of Induction and Termination of Ventricular Tachycardia in Rabbit Heart with Chronic Infarction: Implications for Low Voltage Cardioversion. *Heart Rhythm*. In Press

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Successful cardioversion by electrical shock is a cornerstone in the treatment of life-threatening cardiac arrhythmias. As such, improving cardioversion efficiency is a matter of great medical relevance. Fundamental to this goal is the design of shock waveforms that achieve a positive outcome while reducing the energy that needs to be delivered to the heart. In this effort, the early use of monophasic waveforms has given way to biphasic, or multi-component waveforms, including truncated exponential decay functions that seek to match the charge and discharge of the membrane capacitor. In spite of significant advances, a high energy shock is still needed, and anesthesia during elective cardioversion remains a necessity due to the fact that the strong transthoracic currents resulting from the shock can produce a painful contraction of the thoracic wall.¹

Understanding the dynamics of the interaction between the shockwave and the arrhythmic tissue remains a fundamental area of investigation. It is paradoxical that important early clues about defibrillation were the result of studies on how to induce VF. In 1988, Shibata et al² showed that applying a shock through patch electrodes on the canine ventricular epicardium can induce VF, but it can also halt it; yet, the power required for defibrillation was 1000-fold higher than that used to induce it. Efforts to optimize the biphasic shock waveforms needed for minimal defibrillation thresholds (DFT) proceeded through the years, though insight into the physiological bases of defibrillation remained rather limited (see Ideker, 2007 for review³). The early studies of Efimov et al⁴ represented a major step forward in this area. These authors applied high-resolution cardiac fluorescence mapping to show that the first phase of a biphasic wave created virtual electrodes in the tissue, which halted the activation present at the time of shock; yet, those virtual electrodes were removed by the second phase of the shock, thus preventing new activation fronts that could potentially reinitiate VF.

The study cited above serves as an example of what constitutes a fundamental avenue for investigation: To better map and understand the organization of the arrhythmogenic sources that maintain VF in an effort to advance our knowledge of cardioversion shock design. It is generally accepted that reentrant activity is a major underlying mechanism for ventricular

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tachycardia and ventricular fibrillation, and that the mechanistic boundary between these two rests on the rotational frequency of the reentry, and/or its stability in time and space. In this issue of *Heart Rhythm*, Ripplinger et al⁵ seek a better understanding of the spatiotemporal organization of the reentrant source that maintains the arrhythmia, and apply this knowledge to the mechanisms of low-voltage defibrillation. The rationale for this study is based on the hypothesis, originally put forward by Pumir and Krinsky,⁶ that anatomically anchored reentries can be transformed into functional reentries by application of a weak external electrical field that depolarizes the tissue at the pivoting point near the obstacle, at the appropriate time within the cycle. Those functional reentries, in turn, would be unstable and terminate, thus ceasing the arrhythmia. In their study, Ripplinger et al used a model of post-myocardial infarction (MI) in the rabbit to show that a low voltage shock can interrupt VT if appropriately timed within the cycle.⁵ The authors used an elegant panoramic mapping system to give thorough information on epicardial propagation during the VT, during the application of the shock, and during the time that follows the shock. The panoramic approach unequivocally shows examples of VT driven by a single reentry at the border zone (BZ), which is destabilized by the external electric shock, then drifts and eventually disappears. This example represents, as the authors put it, “the culmination of [an] idea” and a confirmation of the original hypothesis. This is an important contribution that greatly advances this field of research. It also provokes (as any important contribution should), some new and interesting questions. First to come to mind is the extent to which these results can be generalized to other systems, or even to the analysis of all phases within the very same system under study. Indeed, a low voltage shock applied at a given phase (or phases) would destabilize the reentry and cause delayed termination, in agreement with the hypothesis originally proposed by Pumir and Krinsky.⁶ Yet, one may envision the possibility that at the same or different phase (or phases), the low-voltage input could cause immediate termination of the reentry by a full resetting of the tissue, without detectable delay. A separate question relates to the identity of the relevant time-marker used to define the phase of the low-threshold voltage input. Is the panoramic view provided by the ECG too “global” to be used as a reliable marker? Additional experiments exploring the optimal phase for cardioversion, and how this parameter is affected by the relative location and orientation of the reentry in relation to the site of recording may be a further step forward towards a clinically-relevant application. Finally, it will be interesting to bring these hypotheses into the next level of complexity, that is, to assess whether low-voltage, properly timed shocks can be used in cases where multiple rotors co-exist. Establishing the boundaries that frame the applicability of this approach may be important for further development. In summary, this elegant and thought-provoking study of Ripplinger et al⁵ supports important principles and encourages additional basic research that may, in the future, open a viable door in the direction of novel clinical applications.

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