Low-energy, single-pulse surface stimulation defibrillates large mammalian ventricles

Angel Moreno, PhD,*† Richard D. Walton, PhD,*‡§ Olivier Bernus, PhD,*‡§ Edward J. Vigmond, PhD,*† Jason D. Bayer, PhD*†

From the *IHU-LIRYC, Electrophysiology and Heart Modeling Institute, Fondation Bordeaux Université, Pessac, Bordeaux, France, †Centre National De La Recherche Scientifique, Institut de Mathématiques de Bordeaux, UMR5251, Bordeaux, France, ‡Centre de Recherche Cardio-Thoracique de Bordeaux, Université de Bordeaux, U1045, Bordeaux, France, and §INSERM, Centre de Recherche Cardio-Thoracique de Bordeaux, U1045, Bordeaux, France.

BACKGROUND Strong electric shocks are the gold standard for ventricular defibrillation but are associated with pain and tissue damage. We hypothesized that targeting the excitable gap (EG) of reentry with low-energy surface stimulation is a less damaging and painless alternative for ventricular defibrillation.

OBJECTIVE The purpose of this study was to determine the conditions under which low-energy surface stimulation defibrillates large mammalian ventricles.

METHODS Low-energy surface stimulation was delivered with five electrodes that were 7 cm long and placed 1–2 cm apart on the endocardial and epicardial surfaces of perfused pig left ventricle (LV). Rapid pacing (≥4 Hz) was used to induce reentry from a single electrode. A 2 ms defibrillation pulse ≤0.5 A was delivered from all electrodes with a varied time delay from the end of the induction protocol (0.1–5 seconds). Optical mapping was performed and arrhythmia dynamics analyzed. For mechanistic insight, simulations of the VF induction and defibrillation protocols were performed in silico with an LV model emulating the experimental conditions and electrodes placed 0.25–2 cm apart.

RESULTS In living LV, reentry was induced with varying complexity and dominant frequencies ranging between 3.5 to 6.2 Hz over 8 seconds postinitiation. Low-energy defibrillation was achieved with energy <60 mJ and electrode separations up to 2 cm for less complex arrhythmia. In simulations, defibrillation consistently occurred when stimulation captured >75% of the EG, which blocked reentry <2.9 mm in front of the leading reentrant wavefront.

CONCLUSION Defibrillation with low-energy, single-pulse surface stimulation is feasible with energies below the human pain threshold (100 mJ). Optimal defibrillation occurs when arrhythmia complexity is minimal and electrodes capture >75% of the EG.

KEYWORDS Defibrillation; Low energy; Reentry; Surface stimulation; Ventricular fibrillation

Introduction

Sudden cardiac death from ventricular fibrillation (VF) accounts for >15% of deaths worldwide. The most effective therapy for ventricular defibrillation is a strong electric shock that rapidly depolarizes cardiac tissue. In high-risk patients with VF, defibrillation is accomplished with an implantable cardioverter-defibrillator (ICD). However, the discharge of several joules per shock is associated with adverse effects, including severe pain and anxiety disorders from misfires and myocardial damage from repeated shocks, which lead to increased mortality. To mitigate the risks of strong electric shocks, high-voltage nanosecond shocks, antifibrillation pacing, and light-induced stimulation of genetically modified cardiomyocytes were proposed to decrease defibrillation energy requirements. Nonetheless, animal studies demonstrating defibrillation using these approaches have mostly been performed in small mammalian hearts with tissue properties and dimensions substantially different from those of humans, or they achieved defibrillation at energies above the pain threshold (>100 mJ). Recently, low-energy surface stimulation has been shown to rapidly activate wide areas of porcine myocardium without tissue damage, which may safely defibrillate large mammalian ventricles by targeting the excitable gap (EG) of reentry. However, the precise electrode...
placement and surface stimulation timing for optimal EG capture to achieve ventricular defibrillation remain unknown.

The main objective of this study was to determine the optimal conditions under which ventricular defibrillation with low-energy, single-pulse surface stimulation is feasible. Specifically, this study sought to investigate (1) how VF complexity changes over time between its initiation/detection and when an ICD is charged to deliver shocks (~5 seconds); (2) the optimal electrode placement and timing of low-energy, single-pulse surface stimulation with respect to VF complexity in order to capture maximal EG for defibrillation; and (3) the mechanisms of defibrillation with low-energy, single-pulse surface stimulation. Ex vivo experiments and in silico computer simulations in porcine left ventricular (LV) wedges were performed to reach these objectives.

Methods
Animal model
Animal research adhered to ARRIVE, the Guide for Care and Use of Laboratory Animals, and the European Parliament Directive 2010/63/EU. All protocols were approved by the local ethics committee (CEEA50) at the University of Bordeaux. Age-matched (3 months, weight 35 kg) white pig hearts (n = 6) were coronary perfused via the left anterior descending and circumflex arteries with a bicarbonate-buffered solution at 37°C and a constant flow of 30 mL/min. LV preparations were extracted and perfused for experimentation according to previous studies, and on average were 10 cm (left to right) × 7 cm (apex to base) × 1 cm (transmural). A 2-lead pseudo-electrocardiogram (ECG) was used to assess electrical activity during the experiments.

Optical mapping
For the LV preparations, blebbistatin (10 μM) was administered to minimize motion artifacts from cardiac contractions and the voltage-sensitive dye di-4-ANEPPS (5 μM) was administered to detect changes in transmembrane potential. The epicardium and endocardium were illuminated simultaneously by 4 high-power LED lights (530 nm, Cairn Research, Kent, United Kingdom). The emitted signal was bandpass filtered (650 ± 40 nm) and recorded using 2 high-speed CMOS cameras (MiCAM Ultima, SciMedia, Costa Mesa, CA). Images were captured at fine temporal and spatial resolutions (1000 frames/s, 100 × 100 pixels).

Cardiac electrical stimulation
Five line electrodes, each 7 cm long and 1 mm in diameter, were placed on the epicardium and endocardium (Figure 1A) to capture EG. Lines were spaced 1–2 cm apart with optimal contact on the myocardial surfaces. To ensure a relatively uniform effect on all electrodes, the ground electrode was placed at the bottom of the perfusion chamber 1.5–2 cm away from the tissue and between the epicardial and endocardial surfaces. Electrodes were stimulated in unipolar mode using a 10-channel constant current stimulator (D343, Digitimer, Hertfordshire, United Kingdom) to deliver 2 ms wide (t) pulses at currents (I) 8 × capture threshold to ensure homogeneous activation across all electrodes. Output voltage (V) was measured using the stimulator’s built-in meter module (D335, Digitimer). Energy (E) per pulse was calculated as E (joules) = I (amperes) * V (volts) * t (seconds).

Ex vivo VF induction and defibrillation protocol
S1 pacing was established at 2.5 Hz for 4 seconds from a single line electrode located at the center of the
epicardium (Figure 1B). This frequency was set above the normal sinus rate of a pig (60–120 bpm) to ensure capture and a stable pacing baseline. To induce VF, the frequency was increased to 4 Hz for 2.5 seconds from the same line electrode (S2 pacing). If VF was not induced, the protocol was repeated with the maximum frequency increased by 0.5 Hz until induction. A single low-energy defibrillation pulse (S3) was then delivered from all surface line electrodes with a delay of 0.1–5 seconds from the end of the VF induction protocol. The time of VF onset during the induction protocol was detected when unstable stimulus capture and disorganized activity were observed. The maximum delay of 5 seconds was set to the average time required to detect VF and charge an ICD. Successful defibrillation was defined when the arrhythmia terminated in the ECG within 2 seconds after S3 delivery. When S3 failed, defibrillation was achieved with a strong far-field electric shock (15–30 J). If electrophysiological changes from baseline recordings were observed during these protocols, the experiment was stopped.

**Computer simulations**

A 10 cm × 7 cm × 1 cm LV model with membrane kinetics and tissue properties emulating the experimental conditions was used to study the initiation, maintenance, and termination of reentrant ventricular arrhythmia (Figure 2A). Monodomain simulations were performed using the cardiac electrophysiology simulator openCARP (opencarp.org) with a time step of 20 μs (for details, see the Supplemental Methods).

**In silico VF induction and defibrillation protocol**

To load and equilibrate all model parameters, 1 s of simulation was performed without stimulation, followed by pacing from every apical mesh node at twice stimulus capture threshold for 10 beats (2 ms pulse width) at 1.33 Hz.
(Figure 2B). Following the animal protocol, the LV model was preconditioned with 10 S1 stimuli (2 ms pulse width) at 2.5 Hz from a single line 1 mm in diameter placed in the middle of the model with an epicubosal orientation. The 10 S2 stimuli at 4.25 Hz were delivered from different line combinations to induce a variety of reentrant arrhythmias resembling VF. Reentry persisting more than 2 seconds was classified as VF. For defibrillation, a single low-energy (136 \mu\text{A/cm}^2) S3 pulse, 2 ms in width, was delivered from lines oriented from apex to base and evenly spaced 0.25–2 cm along the width of the model. As in the \textit{ex vivo} studies, all lines were stimulated at 8× capture threshold.

To determine the dependency of defibrillation on stimulus timing, defibrillation was attempted at different times by delaying S3 delivery by 25 ms increments from 0 to 5 seconds after VF initiation. Defibrillation was deemed successful if reentry ceased within 1500 ms (95% of all defibrillations) after S3 delivery, that is, all mesh nodes had Vm less than –75 mV.

**Data analysis**

Optical action potentials (OAPs) were processed and analyzed with PV-WAVE (Rogue Wave Software, Minneapolis, MN). OAPs were low-pass, first-order Butterworth filtered with a 120 Hz cutoff frequency and 3 × 3 pixel spatial filter. OAP maps were visualized with ParaView-5.4.1 (Kitware, Clifton Park, NY). \textit{In silico}, activation was determined when the derivative of the membrane potential during the action potential upstroke was maximal, and action potential duration as the time interval between activation and when membrane potential fell below 80% repolarization. Simulation data were visualized using Meshalyzer (git.open-carp.org/openCARP/meshalyzer).

\textit{Ex vivo} and \textit{in silico}, VF complexity was determined by calculating the dominant frequency (DF) and manually tracking reentrant circuits (rotors = scroll waves) and wavebreak. DF was computed by a fast Fourier transform with a 1–75 Hz band around the DF and total spectrum area from a 0 to 12 Hz frequency window. At any timepoint, EG was defined as the percentage of nonrefractory surface nodes (epicardial + endocardial) with respect to the entire OAP map, and the percentage of mesh nodes with membrane potential less than –75 mV in simulations. \textit{In silico}, phase singularities (PSs) of rotors were located by identifying the intersection points of activation and recovery, and the distances of PSs to adjacent line electrodes were calculated along the model’s x-axis (Supplemental Figure 1). To compute the defibrillation window of the line electrode position with respect to PSs, a single electrode stimulated at 8× capture threshold was moved from left to right at increments of 475 \mu\text{m} over a single reentrant circuit (Supplemental Figure 1). EG capture was defined as (1.0 – EG\textsubscript{after}/EG\textsubscript{before}) * 100%. EG\textsubscript{after} was determined 5 ms after S3 delivery (EG\textsubscript{before}), which is the duration for surface stimulation to transverse myocardium ~1 cm thick. EG line occupancy was defined as the percentage of EG surface nodes occupied by electrodes.

**Statistical analysis**

Statistical analysis was performed using GraphPad Prism 7.04 (GraphPad Software, La Jolla, CA). Data for all defibrillation attempts over all samples are given as mean ± SEM. Data normality was determined by a D’Agostino-Pearson test. An unpaired t test was performed to compare between groups. Significance was established for P < .05.

**Results**

\textit{Ex vivo} VF induction and dynamics

VF resulted from reentry during the rapid pacing protocol in pig LV (Figure 1). Pacing at 4 Hz induced fibrillation in all experiments (n = 6). After 5 to 10 induction cycles in the same preparation, 4.5 Hz pacing was required half of the time. The average induction time was 1.55 ± 0.44 seconds and 1.73 ± 0.47 seconds from the start of pacing at 4 and 4.5 Hz, respectively.

VF complexity increased over time (Figures 3 and 4). When induced with 4 Hz pacing, DF was significantly higher (P < .0001) in the epicardium (3.79 ± 0.58 Hz to 6.22 ± 0.91 Hz) than in the endocardium (3.56 ± 0.51 Hz to 5.47 ± 0.99 Hz). The same trend was observed when paced at 4.5 Hz (P < .0001), where DF ranged from 4.59 ± 0.50 Hz to 6.45 ± 0.84 Hz in the epicardium, and from 4.24 ± 0.79 Hz to 5.30 ± 1.19 Hz in the endocardium (Supplemental Figure 2). No significant difference was noticed in DF between VF induced with 4 and 4.5 Hz pacing (P > .10 and P > .59 in the epicardium and endocardium, respectively). Likewise, the CL of reentry was significantly longer (P < .001) within 1 second from VF detection compared to after 3–5 seconds (203 ± 5.30 ms vs 161 ± 5.86 ms, respectively). Furthermore, 73.3% of all cases showed a single stationary rotor within 1–1.5 seconds after VF detection in contrast to 2 or more rotors, which evolved into more complex VF after 3 seconds from its onset since wavebreak occurred more frequently in the rotor’s periphery (Figure 3D). A higher dispersion in both DF and regularity index (Figure 4) were observed in the entire tissue as arrhythmia evolved, which is consistent with more conduction heterogeneity and wavebreak over time.

\textit{Ex vivo} defibrillation

A single defibrillation pulse (8× capture threshold 52.1 ± 2.92 mJ) was delivered to the LV preparation at different time intervals from VF detection. Low-energy defibrillation was achieved following an S3 pulse when ≥26.8% of the total OAP map area was EG and a single rotor was present (2/6...
hearts), which occurred <3 seconds from VF detection (Figures 5A and 5B). As VF complexity increased, the amount of EG available for line stimulation was reduced, oscillating rapidly between 2.54% and 21.4%, resulting in defibrillation failure (Figure 5C) (see Supplemental Videos 1–3 for Figures 5A–5C).

Figure 3  Arrhythmia complexity over time in the ex vivo studies. A: Without a defibrillation pulse, dominant frequency (DF) gradually increased over time as the arrhythmia became more complex. B: The electrocardiogram revealed organization in the form of ventricular tachycardia postinduction that quickly degenerated into ventricular fibrillation (VF). As the arrhythmia progressed, more complex conduction heterogeneities were observed, which was consistent with increased DF (C) with multiple wavebreaks that resulted in new rotor formations (D). Arrows indicate wavefront propagation in epicardial optical action potential maps. CL = cycle length of reentry.
A

![Figure 4](image)

**Figure 4**  Heterogeneous activation over time in the *ex vivo* studies. A: Histograms revealed more spatial organization in regularity index (RI) and dominant frequency (DF) during early ventricular fibrillation (VF) compared to late VF (>5 seconds), which is consistent with progressive increases in arrhythmia complexity and heterogeneity. B: This was also observed for progressive increases in RI and DF standard deviation from arrhythmia induction. Arrows indicate wavefront propagation in epicardial optical action potential maps.

**In silico VF induction and dynamics**

A figure-of-eight reentrant pattern with DF = 4.17 ± 0.001 Hz and reentry CL = 240 ± 0.02 ms was induced during S2 pacing (Figure 2B). When pacing from different or multiple lines, reentry complexity either increased, forming a dual figure-of-eight reentrant pattern with DF = 4.17 ± 0.02 Hz and reentry CL = 240 ± 0.95 ms, or decreased, forming a single rotor with DF = 4.17 ± 0.001 Hz and reentry CL = 240 ± 0.01 ms. These 3 cases (single, figure-of-eight, dual figure-of-eight) in Figure 2B served as the arrhythmia states for low-energy defibrillation testing (see Supplemental Videos 4–6 for Figure 2B).

In *silico* defibrillation

For the 3 arrhythmia test cases, the average EG available at the time of a successful defibrillation pulse was 23.0% ± 0.38% for single, 23.1% ± 0.53% for figure-of-eight, and 26.7% ± 0.19% for dual figure-of-eight reentry. Defibrillation success with zero failures was observed when EG capture by the electrode configurations was ≥75% for all cases, which in turn rendered ≥94.5% of the entire tissue refractory. A linear relationship was observed between defibrillation success and line electrode spacing (R² = 0.98), where defibrillation success, EG capture, and EG line occupancy all declined as electrode spacing increased from 0.25 to 2 cm (Table 1 and Figures 6B–6E). Defibrillation attempted with line electrodes spaced 0.25 cm apart yielded the highest efficacy, with 100% S3 attempts being successful while capturing 100% of the EG with only an average of 41% of the EG being covered by line electrodes (Table 1) (see Supplemental Results and Supplemental Figures 3–5 for additional analysis, and Supplemental Videos 7–10 for Figures 6B–6E).

In *silico* defibrillation mechanisms

To understand the relationship between line stimulation and defibrillation success, the defibrillation window was computed and analyzed with respect to line spacing (see Supplemental Methods for more details). Defibrillation occurred for lines placed from 7.6 to 10.5 mm (defibrillation window = 2.9 mm) in front of the PS for the leading wavefront of the single rotor case (Supplemental Figure 1B), which blocked and terminated the reentrant wavefront. If <7.6 mm, line stimulation did not alter the trajectory of the propagating wavefront. If >10.5 mm, the wavefront would collide with the line of block from the stimulation and would then quickly travel around this barrier to form similar or new reentrant patterns. Importantly, this <2.9-mm defibrillation window is consistent with the 100% defibrillation success rate for the electrodes spaced 0.25 cm apart vs the rapid decrease in defibrillation success as spacing increased (Table 1). It also helps explain why it was challenging to achieve defibrillation in *ex vivo* experiments with electrodes spacings >1 cm (for detailed descriptions of defibrillation failures and successes, see the Supplemental Results).

**Discussion**

In large animal and computational models, low-energy, single-pulse surface stimulation safely terminated VF at energies below the human pain threshold (100 mJ). Defibrillation *ex vivo* was most successful when surface stimulation was applied <3 seconds from VF detection when arrhythmia complexity was lowest. In *silico*, finer electrode spacings increased defibrillation efficacy by maximizing EG capture. Adjusting stimulation timing and electrode placement with respect to the reentrant wavefront was crucial for defibrillation success when electrode spacings were sparse. These findings provide new evidence that painless ventricular defibrillation is feasible in human-sized hearts by targeting ventricular surfaces for low-energy, single-pulse stimulation. However, a highly sophisticated delivery system with fine temporal and spatial resolutions is required to maximize defibrillation success for *ex vivo* and *in vivo* applications.
Defibrillation with low-energy surface stimulation is painless

To the best of our knowledge, this study shows for the first time in large mammalian hearts that surface stimulation, which activates wide areas of ventricular tissue within milliseconds,\(^9\) was able to successfully terminate VF with a single pulse at energies below the perceptive human pain threshold (100 mJ).\(^2\) This demonstration of low-energy defibrillation could have a direct impact on the development of novel electrotherapies, in which lower pulse energy in the range of 400–1600 times less than conventional ICD designs\(^{12}\) could result in devices with higher autonomy, battery life, and endurance while also diminishing the pain and suffering associated with ICD.

**Figure 5** Defibrillation with a single low-energy pulse in the *ex vivo* studies. A: An S3 pulse was delivered <1 second after arrhythmia initiation/detection that terminated reentry when arrhythmia complexity was minimal. B: Even with partial excitable gap (EG) capture, it was possible to defibrillate several seconds after arrhythmia detection (<3 seconds). C: As time progressed, arrhythmia patterns became more complex and achieving tissue stimulation that blocked and terminated reentrant circuits was more difficult. Arrows indicate wavefront propagation in epicardial optical action potential maps.

### Table 1 Defibrillation success, EG capture, and EG line occupancy as a function of line electrode spacing in the LV computer model

<table>
<thead>
<tr>
<th>Line (cm)</th>
<th>Success (%)</th>
<th>EG capture (%)</th>
<th>EG line occupancy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S F8 dF8</td>
<td>S F8 dF8</td>
<td>S F8 dF8</td>
</tr>
<tr>
<td>0.25</td>
<td>100 100 100</td>
<td>100.0 ± 0.0</td>
<td>100.0 ± 0.0</td>
</tr>
<tr>
<td>0.5</td>
<td>62.5 56.5 67.5</td>
<td>59.4 ± 1.93 59.6 ± 1.63</td>
<td>60.6 ± 5.10</td>
</tr>
<tr>
<td>1</td>
<td>35.5 40.5 47.5</td>
<td>27.4 ± 3.18 29.3 ± 3.89</td>
<td>29.3 ± 12.5</td>
</tr>
<tr>
<td>2</td>
<td>20.5 24.5 19.5</td>
<td>16.1 ± 4.43 16.7 ± 4.50</td>
<td>10.3 ± 5.78</td>
</tr>
</tbody>
</table>

EG = excitable gap; LV = left ventricle.

Reentry types: dF8 = double figure-of-eight; F8 = figure-of-eight; S = single.
misfires. Further investigation is needed to quantify its effectiveness in intact hearts and whether it can be simplified to a single surface as suggested by computer simulations (Supplemental Table 1). Furthermore, because the in silico study was performed after the ex vivo study, repeating the animal experiments with electrode spacings 0.5 cm and a pulse delivery focused at 3 seconds after VF detection are expected to significantly increase defibrillation success.

Low-energy defibrillation success depends on arrhythmia complexity
The majority of reentrant patterns <3 seconds from VF detection were in the form of a single rotor resembling polymorphic VT with peripheral wavebreak. Similar to animal and clinical studies, arrhythmia complexity rapidly increased within seconds thereafter, possibly from impaired calcium cycling or structural/electrical heterogeneity. At this point, reentrant patterns contained multiple wavebreaks that led to new rotors and wavelet formation known to hinder defibrillation success. Accordingly, we found higher defibrillation success for early VF (<3 seconds from VF detection) when more abundant and stable EG was available to target for stimulation, which also is advantageous to other promising approaches targeting EG to defibrillate or convert VF to VT. Furthermore, lower numbers of preshock PSs and rotors are associated with a higher probability of rapid defibrillation.

Clinical and experimental significance
Whereas some electrotherapies require delivering pulse(s) at specific times to synchronize or generate antidromic
electronic devices for defibrillation, our configuration relies on optimally placing electrodes to maximize EG capture that blocks and terminates reentry. Although the correct timing for defibrillation pulse(s) may be less predictable and infinite, determining a minimal spacing for electrodes to terminate all forms of reentry is not. Importantly, we found a linear relationship between line electrodes and defibrillation success that suggests a high resolution of electrodes is needed to guarantee defibrillation for any timing of the surface stimulation (Table 1). This was confirmed by the simulation studies that determined the relatively short defibrillation window of 2.9 mm.

To extinguish all focal sources of reentry while also preventing the generation of new rotors, that is, the critical mass hypothesis, this new approach requires a very dense pattern of electrodes to be placed on the surface of large mammalian hearts. In defibrillation studies using field shocks,23 defibrillation success is highest when a voltage gradient of 5 V/cm is generated throughout 95% of the myocardium. Importantly, we achieved >95% refractory myocardium when capturing >75% of the EG with surface stimulation at only a fraction of the energy, which could be reduced even further with a more efficient means to target EG than line electrodes. For example, when the EG is small, only a few localized electrodes would be needed to reach the critical mass for defibrillation, and vice versa for larger EG.

Developing such a device would be challenging but feasible given modern technological advancements. Ideally, it would be integrated into state-of-the-art conformable bi-electronic devices24 to precisely target EG for ventricular defibrillation. This approach has the capability to fully adapt to the morphology of the heart while providing continuous electrophysiological sensing and, when needed, stimulation without restraining cardiac electromechanics. The idea would be that this new technology would not entirely eliminate the need for ICDs, but rather be a complementary pretherapy while the ICD charges to try to first defibrillate the heart, or convert VF to VT, with painless and damage-free surface stimulation. If it fails, then the ICD would deliver its more brute-force defibrillating shocks.

Study limitations

Ex vivo
The animals were healthy without prior cardiomyopathy, so arrhythmia dynamics were relatively similar across all experiments. In patients with diseased hearts, reentrant circuits may show an even more complex pattern in the presence of fibrosis and scar, or from intramural 3D reentry,25,26 which the authors plan to investigate in future studies. VF performance was not analyzed in real time, thus limiting our ability to target and tailor the defibrillation protocol to every individual case. Due to hardware constraints, the number of independent channels for line electrode stimulation during the ex vivo studies was 10, thereby limiting the number and spacing of electrodes able to be placed on each cardiac surface to capture EG.

In silico
VF complexity did not significantly increase over 5 seconds, akin to the ex vivo studies, so we could not test cases similar to late VF observed in the ex vivo study. The simpler arrhythmia dynamics may be explained by the absence of a Purkinje network providing alternative transmural pathways for reentrant circuits,27 differences in fiber orientation influencing reentry stability,28 and missing complex ventricular structures (papillary muscles, trabeculae, blood vessels) that could provide substrates for wavebreak and/or anchoring sites for drifting rotors.29 However, the simplicity of the model worked in our favor in that it provided a clear understanding of arrhythmia dynamics and defibrillation via surface stimulation.

Conclusion
Defibrillating large mammalian hearts is feasible with low-energy, single-pulse surface stimulation. Defibrillation approaches should not focus solely on the timing of lifesaving pulses but also on the arrhythmia state with respect to the electrode configuration so that EG capture is maximized. The low defibrillation energies achieved during this study (<60 mJ per pulse) could help improve the endurance and autonomy of defibrillation electrotherapies, as well as enhance quality of life by painlessly terminating lethal ventricular arrhythmias in patients.

Appendix
Supplementary data
Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.hrthm.2021.10.006.

References


