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Epicardial Conductors Can Lower the Defibrillation Threshold in Rabbit Hearts

Jared A. Sims and **Stephen B. Knisley**[*] **[Member, IEEE]**

Jared A. Sims: jsims@email.unc.edu; Stephen B. Knisley: sknisley@email.unc.edu

Department of Biomedical Engineering of the School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599 USA

[*]Department of Biomedical Engineering of the School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599 USA (phone: 919-966-6653; fax: 919-966-2963

Abstract

During a defibrillation shock, epicardial conductors can introduce anti-stimulatory effects due to lowering of the voltage gradient in myocardial tissue under the conductor and stimulatory effects due to membrane polarization near edges. We hypothesized that increasing the area of conductors increases the defibrillation threshold (DFT), while increasing the amount of stimulatory edge of conductors decreases the DFT. To test this, we measured the DFT in excised rabbit hearts with and without sets of rectangular conductors having 250 or 500 mm2 area and 100, 200 or 400 mm length of edges perpendicular to the line intersecting the shock electrodes. Unlike previous reports in which conductors increased or did not change DFT, present results indicate a conductor geometry having area of 250 mm2 and edge of 200 mm decreases the DFT. This result is consistent with the hypothesis that stimulatory effects of the edge of a conductor can enhance defibrillation shock efficacy.

Index Terms

activating function; antiarrhythmic therapy; defibrillation; edge effects; electro-stimulation; electric field; inactive conductor

I. Introduction

The presence of an inactive epicardial conductor has been shown to either have no effect or decrease efficacy of defibrillation in animal models by shocks delivered externally or endocardially [1–4]. The described mechanism for decreased efficacy was that an epicardial conductor acts as current shunt and lowers the voltage gradient in the region under the conductor [1]. By the upper limit of vulnerability theory a minimum gradient must be reached in all tissue for defibrillation to succeed. A stronger shock is then needed to overcome the lowering of voltage gradient [5]. Otherwise the heart is vulnerable to postshock reentry in areas of low gradient [5]. Also it was shown in dogs that defibrillation occurs when a critical amount of the myocardium becomes depolarized, but that it is not necessary to depolarize every cell in both ventricles [6]. If a conductor prevents depolarization of cells in a sufficiently large area, then defibrillation may fail because the critical amount of depolarized myocardium is not achieved.

In addition to lowering the voltage gradient in some regions, conductors produce membrane polarization in tissue near edges perpendicular to the line intersecting the shock electrodes due to current redistribution between intracellular and extracellular spaces [7]. The sign of the polarization depends on whether conductor/heart interfacial current flows from the conductor to the heart or vice-versa. Depolarization occurs near the edge that is facing toward the shock anode, while hyperpolarization occurs near the edge toward the shock cathode [8].

Given that defibrillation was shown to depend on the voltage gradient and membrane polarization, [9,10] lowering of the voltage gradient in areas under the conductor may increase the defibrillation threshold (DFT) as described, while polarization near edges perpendicular to the line intersecting the shock electrodes may decrease the DFT. Thus, we hypothesized that increasing the area of conductors increases the DFT while increasing the amount of stimulatory edge of conductors decreases the DFT, and hence a certain geometry of conductors having sufficient edge can lower the DFT.

Knowledge of whether areas and edges influence defibrillation would be important for patients who have devices or abandoned electrodes in contact with heart tissue. Also it may impact on the design of future antiarrhythmic devices, and on hypotheses in which cardiac mapping electrodes or conductors such as blood vessels influence defibrillation [8].

In the present experiments, effects on the DFT were measured for five different sets of conductors having various amounts of area and edge. To investigate whether the area influences the efficacy, conductor-induced changes in the DFT were compared for sets having the same amount of edge perpendicular to the line intersecting the shock electrodes but different areas. To investigate whether the edge influences the efficacy, the changes in DFT were compared for sets having identical area but different amounts of edge.

II. Methods

A. Heart preparation

Hearts were removed from 30 heparinized and anesthetized New Zealand White Rabbits. The hearts were arterially perfused with Tyrodes solution containing (in mM) 129 NaCl, 4.5 KCl, 1.8 $CaCl_2$, 1.1 $MgCl_2$, 26 $NaHCO_3$, 1 Na_2HPO_4, 11 glucose, 0.04 g/L bovine serum albumin. The solution was warmed to 37° C and equilibrated with 95% O_2 and 5% CO_2. The heart was not placed in a bath.

B. Fibrillation-defibrillation procedure

Ventricular fibrillation (VF) was induced by rapid bipolar pacing of the left ventricle at 2 times the pacing threshold. The initial pacing interval was 220 ms. The interval was decreased in 10 ms steps until VF was observed upon turning off the pacing. VF was maintained for at least 10 seconds before defibrillation was attempted.

A stainless steel mesh shock electrode was placed on the surface of the right atrium. A 10 mm coil shock electrode was inserted through the Superior Vena Cava into the apex of the right ventricle. The atrial mesh was the anode and the ventricular coil was the cathode for 5 ms monophasic defibrillation shocks. The DFT was determined using an up-down procedure. The initial defibrillation shock in each heart had a leading edge voltage of 200 volts. If a defibrillation shock failed, the voltage of the next shock was increased 20 volts. After successful defibrillation the voltage was lowered 20 volts. The up-down step was approximately 10% of the baseline DFT. Defibrillation was considered successful when sinus rhythm was observed within 5 seconds after the shock. This procedure was continued until 3 changes in behavior were observed, either success to failure or failure to success. The six voltages at the change points were averaged to determine the DFT.

C. Conductors

Rectangular conductors having various aspect ratios were cut from 99.95 % silver sheets with a thickness of 0.076 mm. There were 5 sets of conductors (Table I). Each set consisted of 2, 4, or 8 electrically isolated conductors, of which half of the conductors were placed on the anterior epicardial surface and the other half on the posterior surface. The set was held with an insulated flexible arm attached to a stationary post. Conductors were slightly bent to conform to the contour of the heart surface.

The size of conductors in the horizontal direction (direction perpendicular to the line intersecting the shock electrodes) was 25 mm in all cases. The size of conductors and spaces between adjacent conductors in the vertical direction (parallel to the line intersecting the shock electrodes) was constant within a set, and was 2.5, 5 or 10 mm for different sets.

The conductor sets are identified by the names given in the first column of Table I. The number following the A gives the total area in mm2 of all conductors in the set. The number following the E gives the total length in mm of the edges oriented in the horizontal direction for all conductors in the set.

DFTs were measured with no conductors on the heart and with a set of conductors on the same heart. The order of measurements with and without conductors was varied. In the first 10 hearts, set A500E200 was tested. In the next 10 hearts sets A500E400 and A500E100 were tested. In the final 10 hearts sets A250E100 and A250E200 were tested.

D. Statistical analysis

Results were analyzed using SAS statistical software (Cary, North Carolina). Paired two-tailed t-tests were used to compare results from the same hearts. Unpaired tests were used when results from different hearts were compared. Two-way ANOVA with repeated measures was used to compare the effects of edge, area and the interaction between these two factors on the DFT. Significance was determined when $p < 0.05$.

III. Results

In all measurements with no conductors on the heart, the DFT was 212±11 V (mean ± SEM, n=50). Fig. 1A shows the changes in DFT in volts for each set of conductors (value with conductors on the heart minus the value with no conductors). None of the sets of conductors significantly increased the DFT. Four of the sets resulted in no significant change in the DFT. The A250E200 set produced a significant decrease in the DFT by 62±16 V ($p = 0.005$).

Two-way ANOVA with repeated measures showed a significant effect of edge ($p = 0.033$), which suggests the edge may influence the DFT. The ANOVA did not show a significant effect of area ($p = 0.34$). The interaction factor, which indicates whether an effect of either of these variables on the DFT is altered by a change in the other variable, nearly reached significance with $p = 0.052$.

The results in Fig. 1A for sets with equal areas but differing edge were compared. For an area of 250 mm^2, the change in DFT was significantly different for A250E100 vs A250E200 ($p = 0.018$). None of the three comparisons with an area of 500 mm^2 (A500E200 vs A500E100, A500E200 vs A500E400 or A500E100 vs A500E400) produced a significantly different change in DFT ($p = 0.099$, $p = 0.75$ and $p = 0.29$).

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The results in Fig. 1A for sets with equal edge but differing areas (A250E100 vs A500E100 and A250E200 vs A500E200) were also compared. These did not produce a significantly different change in DFT ($p = 0.17$ and $p = 0.084$).

The changes in DFT were also examined as a percent of the DFT with no conductors on the heart (Fig. 1B). The t tests applied to the percent changes agreed with the results described for the DFTs in volts.

IV. Discussion

To our knowledge there are no published reports that conductors decrease the DFT. Previous studies have shown increases or no effect, however those studies only investigated single large patch conductors [1–4]. Large patches are thought to decrease the voltage gradient in the tissue under the conductor [1]. This effect could increase the DFT according to either the upper limit of vulnerability theory or critical mass theory [6,11]. However a decrease in the voltage gradient does not explain the decrease in DFT.

The statistically significant results are that 1) the A250E200 set produced a decrease in the DFT, 2) this decrease was significantly different from the effect of the A250E100 set, and 3) ANOVA indicated a significant effect of edge on DFT, consistent with the hypothesis that increasing edge length decreased the DFT. Edges or ends of inactive conductors can produce stimulatory effects during a shock. Girouard and Ideker showed that an inactive wire can produce current that is sufficient to excite the left ventricle when a shock is delivered from electrodes in the right ventricle and superior vena cava [12]. Also heterogeneity of conductance produced by artificial conductors or a bath affect virtual electrode formation and produce membrane polarization near edges of the conductor [7,8,13–15]. The polarization may excite voltage-dependent membrane ion channels that are available during fibrillation [16].

A. Hypothesized role of stimulation near the edge

If we assume edges will stimulate tissue under the conductors within one space constant (0.5 mm) from the edge, we can compare hypothetical amounts of tissue stimulated by the edges for different conductor geometries [17]. Fig. 2 illustrates the areas under the conductors stimulated by the top and bottom edges and the area of low voltage gradient under the conductors away from the edges. When the vertical size of the conductor is made smaller, a larger fraction of the tissue under the conductor is stimulated by the edges. For example, the 10 mm conductor has only 10% of the tissue under the conductor stimulated by edges. This percentage is larger for the 5 mm and 2.5 mm conductors, becoming 20% and 40 %, respectively.

An increase in edge-stimulated tissue is consistent with the decreased DFT found for the A250E200 set compared with A250E100, which had the same amount of area and half as much edge. However, A500E200 and A500E400 did not decrease DFT significantly even though they had the same or more edge compared with A250E200.

B. Hypothesized role of area of reduced voltage gradient

A reduction in voltage gradient under a conductor will lessen the ability to achieve a certain voltage gradient or critical mass of depolarized tissue needed for defibrillation [1]. Hypothetical low-gradient tissue areas (total area of the conductors on the heart from Table I × percentage of area with low gradient from Fig. 2) are 300 mm^2 for A500E400, 150 mm^2 for A250E200, 400 mm^2 for A500E200, 200 mm^2 for A250E100 and 450 mm^2 for A500E100. The set that decreased the DFT in our experiments, A250E200, had the smallest low gradient area. We speculate that edge-stimulation by A500E400 or A500E200 might be unimportant when the conductors also introduce a large area of low gradient that prevents depolarization of a critical mass of tissue [1,6].

C. Clinical implications

Artificial conductors that contact myocardium in patients include stimulation electrodes for pacemakers and for cardiac resynchronization therapy, bystander or abandoned electrodes and some cardiac assist devices. Results suggest the geometry of the conductors will influence whether they enhance effectiveness of defibrillation. Novel devices may use conductors to enhance the direct depolarization of tissue where it is impractical to position a venous shock electrode. This may be useful on the left ventricle where defibrillation failure with transvenous lead systems has been associated with postshock excitation fronts [18]. Use of lower shock strengths, enabled by a lower DFT, would lessen cellular electroporation and allow design of smaller implantable defibrillators or defibrillators with increased battery life. Results support the hypothesis that electrodes used during cardiac mapping can influence defibrillation [8]. Also results do not exclude a role of natural conductors in the heart such as blood vessels in the process of defibrillation.

D. Limitations of the study

The distance of tissue that is stimulated by an edge probably depends on factors in addition to the length constant such as the shock strength and tissue thickness in which current redistribution between the conductor and tissue occurs. A mechanistic explanation for the change in DFT is beyond the scope of this study.

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Biographies

Jared A. Sims received the Bachelor's of Engineering in biomedical engineering from Vanderbilt University, Nashville, Tennessee USA in 2002. He worked in the Department of Surgery at Vanderbilt University Medical Center from May 2002 to August 2004. He is currently working toward the Ph.D degree in biomedical engineering at the University of North Carolina at Chapel Hill.

Stephen B. Knisley received the BS degree in biomedical bngineering at Duke University, Durham, NC. He received the PhD in biomedical bngineering at The University of North Carolina at Chapel Hill in 1988

He joined Duke University as a research faculty member. He was in the departments of Biomedical Engineering and Medicine at The University of Alabama at Birmingham from 1994 to 2000. He is currently on the faculty in Biomedical Engineering, Medicine, and The Curriculum in Applied Engineering at The University of North Carolina at Chapel Hill. He serves as the Director of the Joint Graduate Program in Biomedical Engineering at The University of North Carolina at Chapel Hill and North Carolina State University, and is an AIMBE Fellow. He teaches and directs student projects in electrophysiology and instrumentation

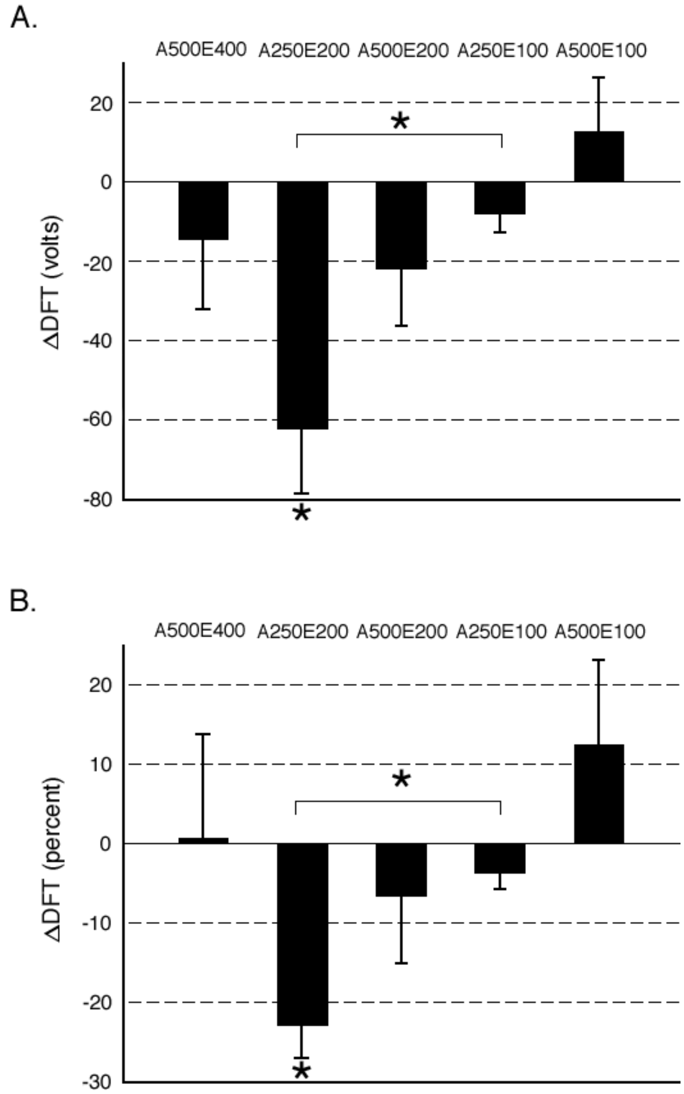

Fig 1.

Summary of the changes in defibrillation threshold (ΔDFT) produced by placing conductors on the heart. Panel A: Bars show ΔDFT in volts (mean ± SEM, n=10) for each of the conductor geometries in Table I. Panel B: Same data is shown as a percent of the DFT with no conductors on the heart. Asterisks indicate $p < 0.05$

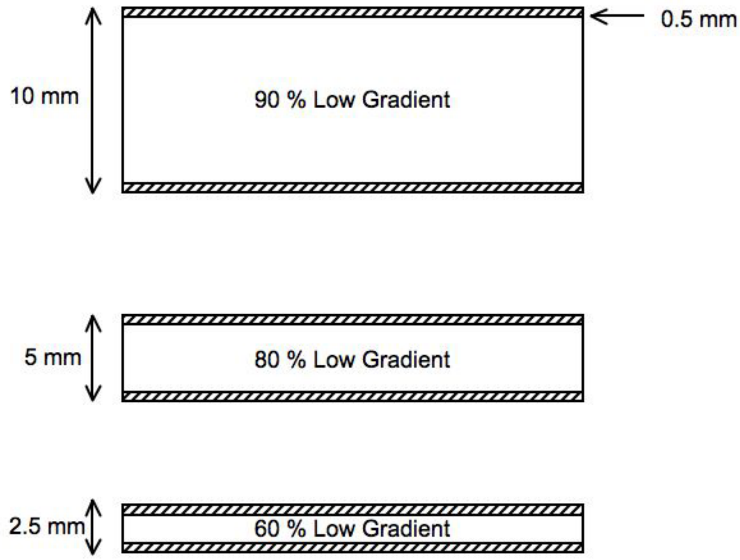

Fig. 2.
Hypothetical regions that may undergo stimulation by the edge of the conductor and low voltage gradient under the conductor away from the edge. The 10, 5 and 2.5 mm correspond to various sizes of conductors in experiments. Cross-hatch regions represent tissue within one length constant from the edge where stimulation may occur. Percentages indicate remaining areas under conductors that undergo low voltage gradient.

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TABLE I

Conductor Geometries

		Horizontal Size	Vertical Size	Total Area	Total Horizontal Edge
A500E100		25 mm	10 mm	500 mm^2	100 mm
A250E100		25 mm	5 mm	250 mm^2	100 mm
A500E200		25 mm	5 mm	500 mm^2	200 mm
A250E200		25 mm	2.5 mm	250 mm^2	200 mm
A500E400		25 mm	2.5 mm	500 mm^2	400 mm