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ALTERED VASCULAR CONTRACTILITIES ASSOCIATED WITH THE APPLICATIONS OF IRREVERSIBLE ELECTROPORATION

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ABSTRACT

As electroporation therapies become more widely used in the cardiac ablation space, there is a critical need to study the potential effects on surrounding tissues: collateral damage. Here we explored methods to study the effects applying electroporative energies on vascular smooth muscle: i.e., loss of vascular function when exposed to energies needed to induce irreversibly electroporative therapy to the myocardium.

1. INTRODUCTION

In recent years irreversible electroporation (IRE) has returned as is gaining momentum as a cardiovascular ablation modality. It has been reported that there are many advantages of utilizing IRE over other ablative approaches[1], but there is little information associated with effects on induced collateral damage or specifically on arterial contractilities; i.e., when contrasted to the most widely utilized modality of RF ablation[2]. In previous studies the effect of IRE on vasculature has mainly focused on patency and not on active contractile function. Thus, the aim of this study was to elucidate the effects of IRE on the functional aspects of the arterial vasculature.

2. MATERIALS AND METHODS

Immediately post-mortem, swine carotid arteries (n=48) were extracted, dissected and sectioned into vascular rings preparations that were approximately 5mm thick. Each ring was then hung between a stationary rod and a force transducer and submerged in a temperature-controlled (37ºC) bath of modified Krebs-Heinseleit buffer, aerated with carbogen. Platinum electrodes were positioned on either side of each sample and used to supramaximally stimulate each every 10 minutes; this allowing for each contraction to achieve its peak level and also return to baseline.

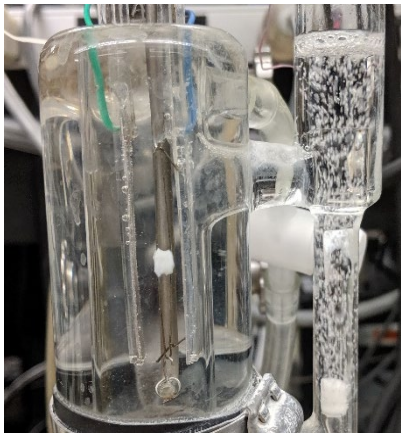

Figure 1: Carotid ring hung in muscle bath

After 1 hour of baseline data collection, the electrodes were temporarily replaced by 1cm long NanoKnife (Angiodynamics, Latham, NY) needles and electroporation therapies were applied (500, 700, and 900V all 90µs pulse width at 240ppm). The vascular rings were then allowed to recover for 3 hours while utilizing the same stimulus protocol as noted above.

To further elucidate IRE vascular effects, electroporation therapies were delivered across the left anterior descending arteries (LADs) of reanimated swine hearts on the Visible Heart® apparatus. In these studies, coronary flow rates were monitored prior to and post-delivery of a given IRE therapy. In order to place the ultrasonic flow probe (Transonic Systems, NY) a portion of the LAD surrounding tissues were carefully dissected, but otherwise the myocardium and coronary were left intact, so to allow continuous perfusion of the heart (see Figure 2). The exposed portion then gave access to place a cuff ultrasonic probe. The signal from the probe was then collected in a dedicated data acquisition system (EMKA Technologies, Paris, France).

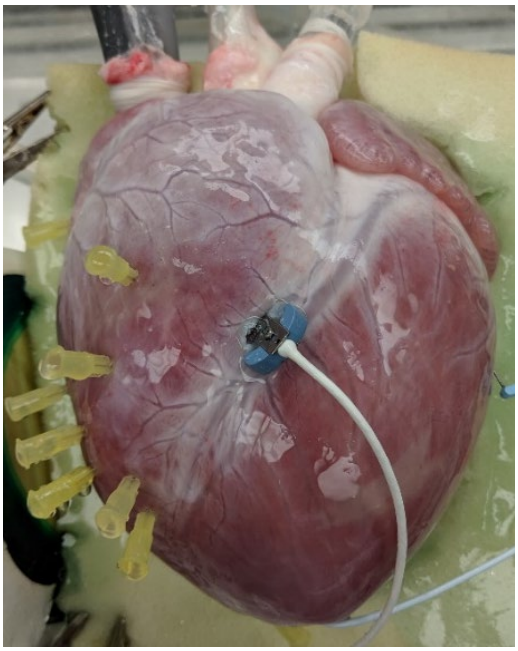

Figure 2: Reanimated swine heart with ultrasonic flow probe in LAD

3. RESULTS AND DISCUSSION

Carotid vascular rings exposed to electroporation therapies elicited an initial vasoconstrictive response. At the lowest energy field applied, 500V, the isolated vascular rings demonstrated abilities to recover up to 80% of their baseline stimulated contractile forces and achieve the same level of relaxation as that of the control group. Yet, as the administered IRE energies increased, the vascular rings were unable to relax and remained in a contracture state during the recording period. At 700V the stimulated contractile forces, calculated between relaxed state and peak of contraction, was 30% compared to controls. At the highest energy of 900V, it was not possible to elicit stimulated contractions; only sustained vasoconstrictive responses were observed.

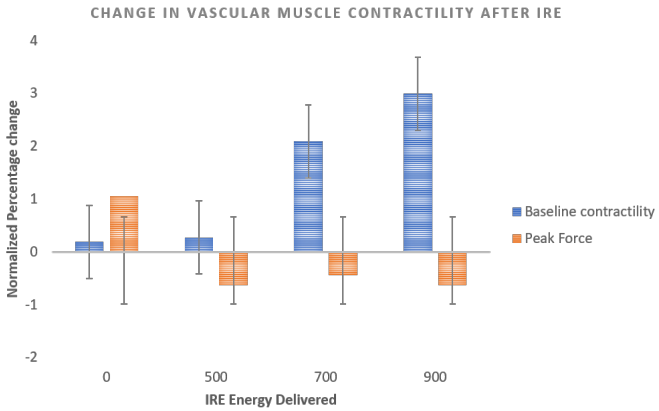

Figure 3: Peak force and contractility of carotid rings after recovery ffrom IRE delivery

In the ex-vivo beating hearts, coronary flows were significantly decreased following the applications high energy IRE. However, after some time, perhaps due to mechanical stresses of the arterial afterload pressures, coronary flows were observed to return to baseline values.

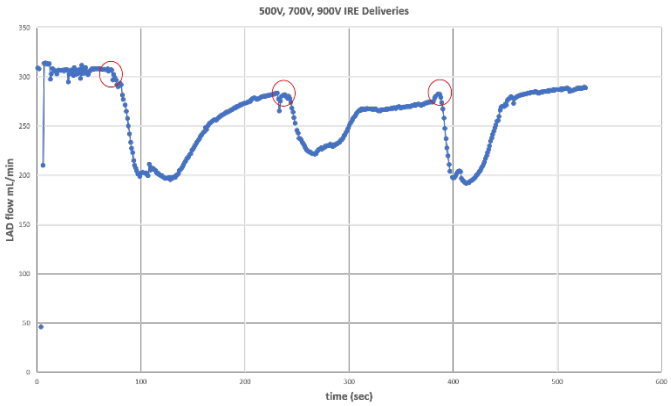

Figure 4: LAD flow during deliveries of 500, 700, and 900V IRE energies. Circles denote time of delivery

CONCLUSION

Contractilities of porcine vasculature were observed to be directly affected by the delivery of IRE therapies. This suggests that while the structures of the vessels remained intact, associated smooth muscle elicited partial or complete losses of function. These findings could aid in optimizing the applications of appropriate electroporation therapies within the cardiac space and/or within or near other vascular sensitive tissues.

ACKNOWLEDGMENTS

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