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Cardiac Ablation with Irreversible Electroporation: Insights from preclinical and clinical application

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Cardiac ablation has undergone a remarkable evolution over the last 50 years and today is a central pillar in the treatment of cardiac arrhythmias. At present the most commonly used energy source for ablation is radiofrequency (RF) followed by cryoablation. While largely efficacious, these energy modalities have noteworthy shortcomings and limitations largely due to their thermal means of tissue destruction. Specifically, there is a risk of; 1) char/coagulum formation which is associated with strokes and cognitive decline 2) collateral tissue damage, especially the esophagus, phrenic and vagus nerve all which lie or travel close to the heart and 3) coronary artery damage from collateral or direct energy application. In the context of these limitations, Irreversible electroporation (IRE) has emerged as a novel, and potentially revolutionary means to treat cardiac arrhythmias with its tissue-selective nature and non-thermal mechanism of ablation. Since the first publication on cardiac IRE by Lavee in 2007[1] there has been considerable growth in pre-clinical animal publications and this year we saw the publication of the first in human application of IRE for the treatment of atrial fibrillation (AF)[2].

The mounting preclinical animal work has provided some key takeaway messages on cardiac ablation with IRE:

1. IRE can directly ablate the Pulmonary Vein (PV) without stenosis[3,4]; AF is initiated by arrhythmogenic tissue (myocardial sleeves) inside the PVs. The cornerstone of current AF ablation is isolation of the PV from the surrounding cardiac tissue by performing circumferential ablation around these veins. Historically, ablation was performed inside the PV to directly target the tissue. However, this caused PV stenosis and significant morbidity in patients. Therefore we avoid energy delivery directly into the PVs. IRE, however, can be performed inside the PVs without any major adverse events or the development of stenosis. This potentially provides a means to directly ablate the PV tissue.

2. Perseveration of Collateral tissue[5,6]; One of the key potential advantages of IRE is the preservation of collateral tissue – a major concern with thermal based approaches. IRE (delivered at energy to cause myocardial lesions) does not affect the esophagus, the phrenic nerve or cause damage when applied directly to a coronary artery. This provides a remarkable advantage over current energies modalities, where tissue selectivity does not exist.

See verso for continuation…

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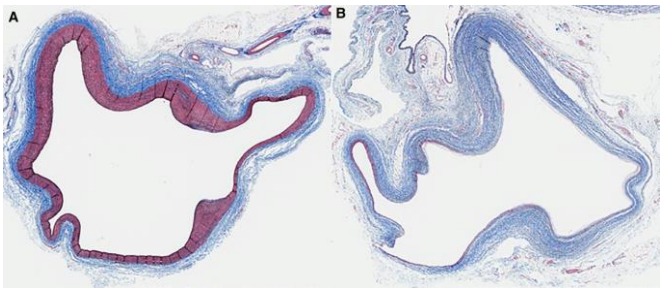
3. Non-Contact Ablation[7]; The need for contact to effectively ablate tissue is a major limitation of radiofrequency and cryoablation. Preliminary cardiac data suggests that IRE does not require direct contact to ablate and can be delivered from a distance.

4. Safety; IRE has been reported to cause both lethal and non-lethal cardiac arrhythmias. However, pre-clinical studies to date show that direct cardiac IRE delivery is safe, with no reported lethal arrhythmias when the pulse delivery is synchronized with the R wave of the surface electrocardiogram.

5. Efficiency; Current thermal ablation methods can be time-consuming, particular RF, requiring point by point ablation. IRE, on the other hand, can be delivered quickly (within secs to minutes) without compromising safety and cover a large area.

In addition to the extensive and ongoing preclinical studies, this year, we also saw the publication of the first in human experience using IRE to ablate the PVs in patients with AF[2]. In this study of 22 patients, IRE was able to acutely ablate PV tissue without any observed collateral damage or adverse safety concerns. Although further human data is needed on the durability of IRE lesions and its effect on AF long term, the successful translation to humans represents a real stepping stone and impetus for future studies (both clinical and preclinical). As we continue to develop our knowledge and understanding of cardiac ablation with IRE, its many attractive features create the potential for it to become the dominant modality for cardiac ablation in the future.



Slide sections with elastic Masson's trichrome stain demonstrating: (A) a control canine pulmonary vein without ablation; (B) a canine pulmonary vein after treatment with IRE showing near-complete absence of cardiomyocytes with preserved structural collagen and no stenosis[3].

[1] J Lavee et al., Heart Surg Forum, 2007. 10(2): p. E162-7
[2] VY Reddy et al., JACC: Clinical Electrophysiology, 2018: p. 674
[3] CM Witt et al., Journal of the American Heart Association, 2018. 7(14)
[4] FH Wittkampf et al., Journal of cardiovascular electrophysiology, 2011. 22(3): p. 302-309
[5] K Neven et al., Circulation: Arrhythmia and Electrophysiology, 2017. 10(5): p. e004672
[6] BC du Pre et al., Europace, 2013. 15(1): p. 144-9
[7] C Livia et al., Journal of the American Heart Association, 2018. 7(15): p. e009070

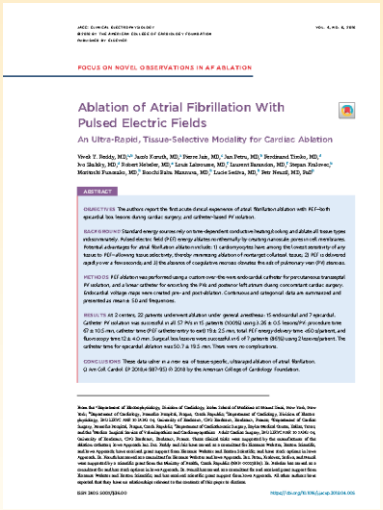
Forthcoming events

International Nonthermal Processing Workshop and Short Course

Sorrento, September 25 – 26, 2018
http://nonthermal.prodalricerche.com

Electroporation-Based Technologies and Treatments

Ljubljana, November 11 – 17, 2018
http://2018.ebtt.org



Ablation of Atrial Fibrillation With Pulsed Electric Fields: An Ultra-Rapid, Tissue-Selective Modality for Cardiac Ablation, doi.org/10.1016/j.jacep.2018.04.005

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