Electroporation-based Platform for Trans-catheter Cardiac Interventions – summary

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Study objective: To evaluate the effect of a novel modified irreversible electroporation (IRE) protocol of high-frequency high-voltage (HF-EP) pulses on a beating heart in terms of muscle contractions and myocardial damage, in order to potentially develop in the future an alternative non-thermal heart ablation method.

Methods: Project was composed of two parts. First, designing and assembly of a custom-made high frequency high voltage pulse generator capable of producing up to 150kHz and 1.1kV pulses. This was followed by calibrating the system and pretesting with different protocols using in-vivo rodent model. We used high frequency 2-channel oscilloscope to measure frequencies and voltages delivered from the pulse generator to the rodent myocardium. The second part was the animal experiment. 30 Sprague-Dawley rats were divided into 4 different electroporation groups. Groups 1-3 used high frequencies (100kHz and 150kHz) and different number of pulses (20 and 60). Group 4 used as a control group and was composed of 10 monopolar pulses. This protocol was already proved in previous studies to create a substantial damage to the myocardium. All protocols used amplitude 550V (1.1kVp-p) and 2-needle configuration. Full study protocols are shown in **table 1**. During IRE application degree of muscle contractions was evaluated qualitatively and documented with video. Animals were euthanized after 14 days and evaluation of myocardial damage was made using histological morphometric and computer-assisted analysis of the degree of fibrosis.

Preliminary Results: In contrast to the standard IRE protocol, all three HF-EP protocols were not associated with collateral muscle contractions. Standard IRE protocol was associated with significant damage as was predicted, based on previous studies. Compared to standard 10 monopolar electroporation pulses, 20 pulses of HF-EP of 100 and 150 kHz were associated with lesser extent of myocardial damage (infarct to healthy tissue fibrosis ratio of 27.5 ± 11.2 vs. 12.8 ± 9.4 and 7.44 ± 2.1; p=.03 and <.01 respectively). In contrast, increasing the number of pulses from 20 to 60 in the 150kHz group was associated with significant damage that was comparable in all parameters (fibrosis, diameter and thickness - infarct to healthy tissue ratio) to standard IRE pulses (27.5 ± 11.2 vs. 19.44 ± 4.23, p=.17; 25.10 ± 12.6 vs. 19.42 ± 8.18, p=.34; 23.38 ± 8.3 vs. 32.90 ± 19.33, p=.26, respectively).

Conclusion: A novel high frequency IRE protocol can cause comparable myocardial damage without causing collateral muscle contractions. HF-EP holds the potential of becoming an alternative non-thermal method for heart ablation. Abstract of this work was submitted to the International Dead Sea Symposium (2020) and to the Kellerman young investigator competition (Israeli Heart Society meeting 2020)

Protocol #	Frequency	# of pulses	Pulse amplitude	Pulse Duration
1	100kHz	20	550V	100uS
2	150kHz	20	550V	100uS
3	150kHz	60	550V	100uS
4	DC	10	550V	100uS

Table 1. Electroporation study protocols. Protocols 1-3 are high frequency protocols differ in either frequency or number of pulses. Protocol 4 is a monopolar protocol using as a positive control group

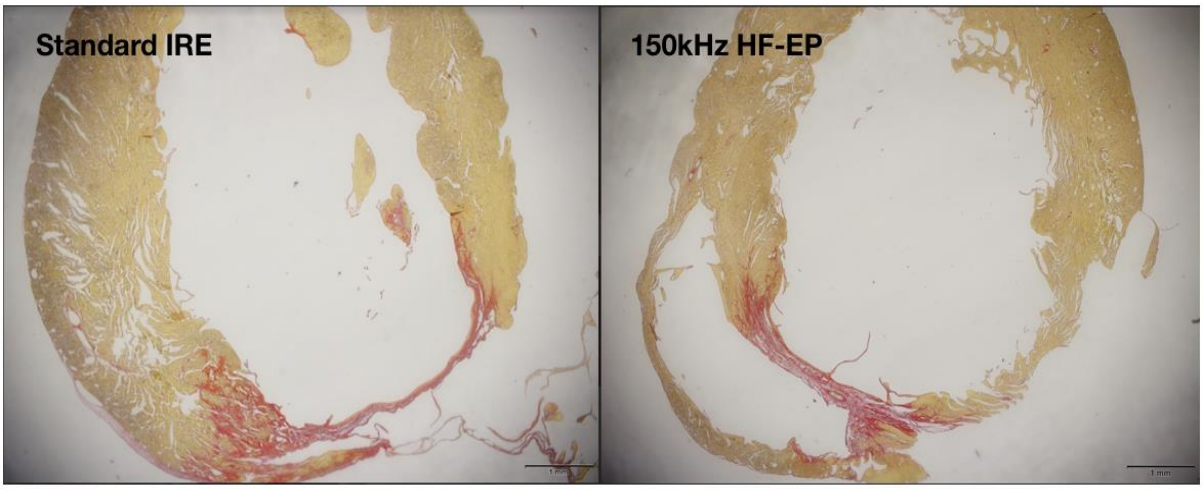

Fig.1 Histology of myocardial tissue after standard IRE protocol (left) and 150kHz HF-EP (right) demonstrating comparable damage. Red area - fibrin, indicating tissue damage. Yellow area - normal myocardial tissue