Complexity and perplexity of Pulsed Field Ablation – an engineering perspective

Supplementary data

A simplified anatomical model of the left atrium (LA) of a pig was created from CT images of a healthy 4-month-old female pig. Segmentation of cardiac structures was performed in Materialise Mimics to distinguish between myocardial tissue and blood volume. The geometry was processed in 3-matic (Materialise, Leuven, Belgium) and imported into COMSOL Multiphysics (COMSOL AB, Stockholm, Sweden). A 2D profile of the LA wall near the ostium of the pulmonary vein (PV) was revolved to create a symmetric 3D geometry. Additional layers representing a 3 mm thick myocardium and a 2 mm thick epicardium were added, and the surrounding thoracic tissue was modelled as a rectangular box (200 × 300 × 150 mm) to simulate monopolar configurations. Tissue properties used in the simulations are shown in Supplementary Table 1.

The three catheters are generic decapolar loop catheter[1] 8 mm spherical tip catheter[2], and custom bipolar balloon catheter [3]. Each catheter was tested with three pulse protocols: a single 6 ms monophasic exponentially decaying defibrillator pulse[4], 90 × 100 μs monophasic pulses delivered at 1 Hz[3] –IRE for short– and ten trains of a single burst of 333 biphasic pulses with 3 μs positive pulse width, 0 μs intraphase delay, 3 μs negative pulse width and 0 μs interpulse delay[5] –HFIRE for short. Pulse amplitudes were adjusted for each configuration to achieve transmural lesion depth (3 mm in the schematic atrium). These pulses are described in detail in Supplementary table 2.

A multiphysics simulation was implemented in COMSOL Multiphysics, including electric field calculation (with conductivity changes due to electroporation), fluid flow modelling (simulation of laminar blood flow from the PV to the mitral valve), and heat transfer simulation (with time-dependent heat sources corresponding to pulse duration and frequency). Blood cooling was explicitly modelled with pulsatile blood flow determined by the outflow boundary condition through the mitral valve.

The electric field thresholds for tissue damage were set as follows: 400 V/cm for the 6 ms pulse, 500 V/cm for 9x100 μs monophasic pulses and 650 V/cm for HFIRE to account for different expected required threshold [6,7]. These values represent a conservative estimation of thresholds, and are higher than experimentally defined thresholds reported in recent publications.[8,9]

Supplementary Table 1: Physical parameters used in the model

	Blood	Myocardium	Pericardium	Thorax
Initial conductivity [S/m]	0.7	0.12	0.06	0.1
Maximum conductivity [S/m]	1.05	0.36	0.18	/

Start of conductivity increase [V/cm]	400	300	300	/
End of conductivity increase [V/cm]	1100	700	700	/
Density [kg/m^3]	1060	1081	1081	1081
Heat capacity [J/kg]	3617	3686	3686	3686
Thermal conductivity [W/mK]	0.58	0.56	0.56	0.56

Supplementary Table 2: electrical pulse parameters for all investigated treatment combinations

	Parameter	6 ms defibrillator	90 × 100 µs IRE	3 µs biphasic HFIRE
Decapolar circular	Applied voltage [V]	2000	2000	3200
	Max current [A]	38	35	56.7
	Total energy [J]	269	607	3497
	Delivery type	Monopolar	Monopolar	Monopolar
PVAC	Applied voltage [V]	2000	1200	1500
	Max current [A]	41	35.5	45.4
	Total energy [J]	221	348	1230
	Delivery type	Monopolar	Bipolar	Bipolar
Balloon	Applied voltage [V]	2000	2000	2400
	Max current [A]	10.9	10.8	10.3
	Total energy [J]	69	214	488
	Delivery type	Bipolar	Bipolar	Bipolar

References:

1. Wijffels MCEF, Van Oosterhout M, Boersma LVA, et al. Characterization of *In Vitro* and *In Vivo* Lesions Made by a Novel Multichannel Ablation Generator and a Circumlinear Decapolar Ablation Catheter. *Journal of Cardiovascular Electrophysiology*. 2009;20:1142–1148. https://doi.org/10.1111/j.1540-8167.2009.01502.x.

2. Livia C, Sugrue A, Witt T, et al. Elimination of Purkinje Fibers by Electroporation Reduces Ventricular Fibrillation Vulnerability. *JAHA*. 2018;7:e009070. https://doi.org/10.1161/JAHA.118.009070.

3. Witt CM, Sugrue A, Padmanabhan D, et al. Intrapulmonary Vein Ablation Without Stenosis: A Novel Balloon-Based Direct Current Electroporation Approach. *J Am Heart Assoc*. 2018;7:1–8. https://doi.org/10.1161/JAHA.118.009575.

4. Wittkampf FH, Driel VJV, Wessel HV, et al. Feasibility of Electroporation for the Creation of Pulmonary Vein Ostial Lesions. *Journal of Cardiovascular Electrophysiology*. 2011;22:302–309. https://doi.org/10.1111/j.1540-8167.2010.01863.x.

5. Van Es R, Groen MHA, Stehouwer M, et al. In vitro analysis of the origin and characteristics of gaseous microemboli during catheter electroporation ablation. *Cardiovasc Electrophysiol*. 2019;30:2071–2079. https://doi.org/10.1111/jce.14091.

6. Pucihar G, Krmelj J, Reberšek M, et al. Equivalent pulse parameters for electroporation. *IEEE Trans Biomed Eng*. 2011;58:3279–3288. https://doi.org/10.1109/TBME.2011.2167232; PMID: 21900067.

7. Mercadal B, Beitel-White N, Aycock KN, et al. Dynamics of Cell Death After Conventional IRE and H-FIRE Treatments. *Annals of Biomedical Engineering*. 2020;48:1451–1462. https://doi.org/10.1007/s10439-020-02462-8.

8. Kos B, Mattison L, Ramirez D, et al. Determination of lethal electric field threshold for pulsed field ablation in ex vivo perfused porcine and human hearts. *Front Cardiovasc Med* [Internet]. 2023 [cited 2023 Jul 18];10:1160231. https://doi.org/10.3389/fcvm.2023.1160231.

9. Miklavčič D, Verma A, Krahn PRP, et al. Biophysics and electrophysiology of pulsed field ablation in normal and infarcted porcine cardiac ventricular tissue. *Sci Rep*. 2024;14:32063. https://doi.org/10.1038/s41598-024-83683-y.