Thermal side effects during pulsed field ablation: An analysis using computer modeling

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1. Introduction

Pulsed field ablation (PFA) is the result of an impressive evolution in the technology of ablation, beginning with the first use as direct current (DC) ablation in the 1980's.[1, 2] PFA has been described as non-thermal, but abundant data exist in oncology applications [3, 4], and growing data are emerging in cardiology [5, 6], highlighting that thermal effects are in fact present with PFA. These thermal effects have been shown to result in luminal esophageal temperatures above the thresholds typically considered to increase the risk for atrioesophageal fistula (AEF) formation.[5] Although the predominant mechanism of cell destruction with PFA may rely on non-thermal electroporation, the fact that thermal effects are present has prompted experts to recommend that electroporation should in fact not be called "non-thermal".[3] Preclinical studies have shown that supratherapeutic PFA can induce acute esophageal lesions, and preclinical healing patterns may not be replicated in patients, so that it may take upwards of several thousands of patients (including those who undergo ablation of persistent AF, where multiple repeat applications may be performed) to truly conclude that fistula formation is not possible.[7] Finally, in the field of oncology, where PFA (also referred to as irreversible electroporation) has been used to treat solid tumors for well over a decade, thermal effects are well-documented, with fistulas occurring in up to 10.6% to 20% of patients.[4, 8] As such, we sought to evaluate the thermal effects arising from pulsed field ablation of myocardial and esophageal tissue using in-silico models examining a range of typical peak voltage operating conditions.

2. Methods

A three-dimensional computer model of the left atrium and esophagus was created to quantify the thermal effects from PFA applications. Specific details of the model are described in the work by Montoya et al.[8], and are similar to other published work.[9] Broadly, a 3D model representing the PFA procedure served as the computational framework, which encompassed a catheter featuring two cylindrical electrodes (representing momentary anode and cathode) separated by plastic. The model accounts for the myocardium, pericardium (fat layer), and esophagus, each with specific thicknesses (1.5 mm, 0.75 mm, and 2 mm, respectively). The catheter is assumed to have full contact with the myocardium.

3. Results

Minimal temperature rise in the esophagus was seen with 1 kV pulses (corresponding to 13.4 J input). With 1.5 kV and 2 kV peak voltages (corresponding to 32.3 J and 66.2 J), temperature elevations reaching 46.3 °C and > 62 °C were seen, respectively. These elevations occurred after only a single pulse train of 50 pulses, implying that further elevations in temperature would be seen with subsequent applications. Total energy for 1 kV, 1.5 kV, and 2 kV pulse peak voltages, are 214 J, 570 J, and 1282 J, respectively. Average energy per pulse for 1kV, 1.5kV, and 2kV pulse peak voltages, are 4.28 J, 11.4 J, and 26.7 J, respectively. Figure 1 presents the evolution with time of the maximum temperature in the esophagus, showing both the rising and falling temperature curves between pulses, as well as the accumulated thermal effect. This effect is most pronounced at 1500 V and 2000 V, with an apparent non-linearly increasing behaviour on the thermal damage by increasing the pulse peak voltages. This behaviour has been also seen by other authors in Aycock et al.[10], Faroja et al.[4], and van Gemert et al.[3], supporting the reliability of the numerical results.

4. Discussion

These results align well with recent data published in the electrophysiology literature, as well as abundant data in the field of oncology.[3, 4] For example, Faroja et al. measured tissue temperatures in a porcine model using a commercially available system (Nanoknife Tissue Ablation System, Angiodynamics).[4] Using voltage settings of up to 3kV and pulse durations of 100 microseconds, they found post ablation temperatures ranging between 34 °C for low-voltage 1500 V applications and 90 pulses to 84 °C for high-voltage 2900V applications and 360 pulses. All combinations of voltage greater than 2500 V for 90 or more pulses produced temperatures greater than 50° C, which were associated with gross and histopathologic findings of thermal coagulation.[4] [3, 8]

These data further reinforce the point that thermal effects occur with PFA, and although much less than with thermal ablation technologies, thermal effects from PFA can result in temperature rises sufficient to raise concern.[5, 9] Clinical validation through extensive patient studies is essential to better understand and confirm safety margins and potentially refine procedural guidelines. Kirstein et al. measured intraluminal esophageal temperatures in consecutive symptomatic patients undergoing first-time PFA, where 8 pulse trains (2 kV/2.5 s, bipolar, biphasic, x4 basket/flower configuration each) were delivered to each pulmonary vein, and two extra pulse trains per pulmonary vein in flower configuration were added for wide antral circumferential ablation. Continuous intraluminal esophageal temperature was monitored with a 12-pole temperature probe. The authors found that (1) median esophageal temperature change was statistically significant and increased by 0.8 ± 0.6°C, $p < .001$, (2) an esophageal temperature increase ≥ 1°C was observed in 10/43 (23%) patients, and (3) the highest esophageal temperature measured was 40.3°C.[5] Verma et al. measured the temperature profile of focal point, monopolar biphasic PFA on perfused thigh muscle of swine.[6] PFA lesions were performed with 3 compatible ablation catheters, and temperature changes in the tissue were measured using fluoroptic temperature probes inserted at the muscle surface and at 3 mm and 7 mm below the surface. Temperatures were recorded continuously at baseline, during delivery, and after ablation. The maximum average temperature rise for PFA was 7.6 °C, 2.8 °C, and 0.9 °C at the surface, 3-mm depth, and 7-mm depth, respectively. The temperature rise was dose dependent, with lower energy settings yielding less temperature rise.[6] Notably, in these studies, the thermal effects resulted in luminal esophageal temperatures above the thresholds typically used to cease radiofrequency energy delivery to avoid development of esophageal injury.

5. Conclusions

Thermal effects induced by PFA depend on total energy deposited, of which peak voltage is an important component, suggesting that current commercially available systems appear to have the potential to induce collateral thermal injury, particularly with peak voltages higher than 1.5 kV and repeated applications of pulsed field energy. Although real-world clinical outcomes suggest lower risks of esophageal injury compared to radiofrequency ablation, the potential for thermal injury with PFA remains.

6. References

[1] Scheinman MM, Morady F, Hess DS, Gonzalez R. Catheter-induced ablation of the atrioventricular junction to control refractory supraventricular arrhythmias. *Jama* 1982; **248**: 851-855.

[2] Boersma L, Andrade JG, Betts T, Duytschaever M, Pürerfellner H, Santoro F, et al. Progress in atrial fibrillation ablation during 25 years of Europace journal. *Europace* 2023; **25**.

[3] van Gemert MJ, Wagstaff PG, de Bruin DM, van Leeuwen TG, van der Wal AC, Heger M, et al. Irreversible electroporation: just another form of thermal therapy? *Prostate* 2015; **75**: 332-335.

[4] Faroja M, Ahmed M, Appelbaum L, Ben-David E, Moussa M, Sosna J, et al. Irreversible Electroporation Ablation: Is All the Damage Nonthermal? *Radiology* 2013; **266**: 462-470.

[5] Kirstein B, Heeger CH, Vogler J, Eitel C, Feher M, Phan HL, et al. Impact of pulsed field ablation on intraluminal esophageal temperature. *J Cardiovasc Electrophysiol* 2024; **35**: 78-85.

[6] Verma A, Zhong P, Castellvi Q, Girouard S, Mediratta V, Neal RE. Thermal Profiles for Focal Pulsed Electric Field Ablation. *JACC: Clinical Electrophysiology* 2023.

[7] Nies M, Watanabe K, Kawamura I, Koruth JS. Endocardial Pulsed Field Ablation and the Oesophagus: Are Atrio-oesophageal Fistulas Now History? *Arrhythmia & Electrophysiology Review 2024;13:e02* 2024.

[8] Mercado-Montoya M, Gomez-Bustamante T, Mickelsen SR, Kulstad E, González-Suárez A, Overzet LJ. Quantification of thermal side effects during pulsed field ablation. *bioRxiv* 2024: 2024.2011.2002.621664.

[9] Estevez-Laborí F, O'Brien B, González-Suárez A. Difference between endocardial and epicardial application of pulsed fields for targeting Epicardial Ganglia: An in-silico modelling study. *Comput Biol Med* 2024; **174**: 108490.

[10] Aycock KN, Campelo SN, Davalos RV. A Comparative Modeling Study of Thermal Mitigation Strategies in Irreversible Electroporation Treatments. *Journal of heat transfer* 2022; **144**: 031206.

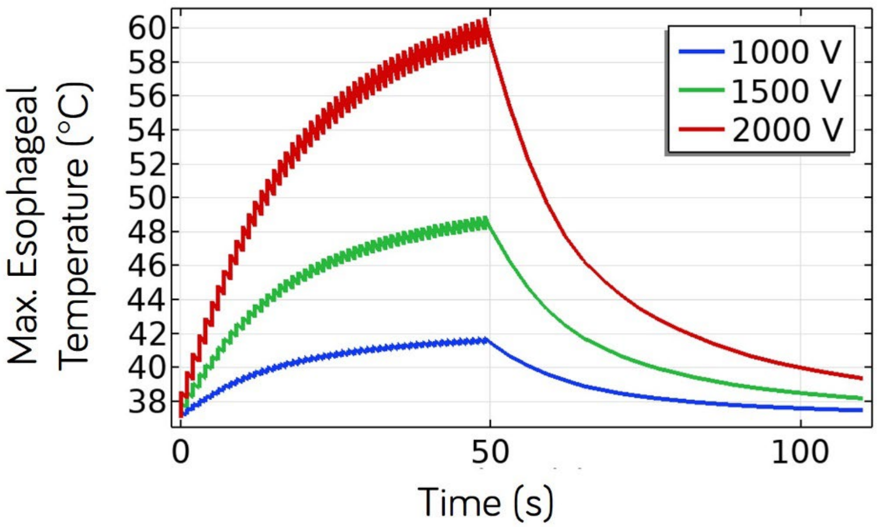

Figure 1. The evolution with time of the maximum temperature in the esophagus as a function of applied pulse peak voltage.