ENHANCING CLINICAL OUTCOMES IN ATRIAL FIBRILLATION ABLATION: EVALUATION OF HIGH- AND VERY HIGH-POWER SHORT-DURATION TECHNIQUES AND THE ROLE OF LOCAL IMPEDANCE DROP IN GUIDING EFFECTIVE PULMONARY VEIN ISOLATION

PhD thesis

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Budapest

2026

1. INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia encountered in contemporary clinical practice and one of the most important challenges of modern electrophysiology. Its significance extends far beyond rhythm disturbance alone: AF is associated with stroke, heart failure, impaired quality of life, increased mortality, and substantial healthcare utilization. Because of the progressive nature of the disease, patients often move from short and self-terminating episodes (paroxysmal AF) toward a persistent form as structural and electrical atrial remodeling advances. This clinical course has made effective rhythm control a central component of AF management in selected symptomatic patients.

Catheter ablation has become a cornerstone of rhythm control therapy in AF. Pulmonary vein isolation (PVI) remains the fundamental lesion set, because ectopic activity originating from the pulmonary veins plays a decisive role in arrhythmia initiation in a large proportion of patients. Nevertheless, the long-term success of PVI depends not only on achieving acute isolation but also on creating durable, contiguous, and transmural lesions. In everyday practice, arrhythmia recurrence after AF ablation is still frequently related to incomplete lesion sets and pulmonary vein reconnection. For this reason, improving lesion durability without compromising safety is a major objective of current ablation research.

Radiofrequency (RF) point-by-point ablation remains the most widely used energy source for AF ablation. Over the last decade, technological progress has markedly improved our ability to deliver RF energy in a more controlled and reproducible manner. Contact force-sensing catheters, electroanatomical mapping systems, lesion-quality indices, and refined workflow strategies have all contributed to better outcomes. Among these developments, increasing

interest has focused on high-power short-duration (HPSD) and very high-power short-duration (vHPSD) RF applications. These approaches aim to shorten individual RF delivery times, improve catheter stability during lesion deployment, reduce left atrial dwell time, and accelerate the overall procedure.

The rationale for high-power ablation is based on lesion biophysics. Higher power leads to faster resistive heating of tissue near the catheter tip, while shorter application times may prevent excessive conductive heating of deeper and surrounding tissues. In atrial ablation, this approach can create effective lesions with less catheter instability compared to traditional low-power, long-duration (LPLD) methods. However, faster energy delivery alone isn't enough. The operator still needs reliable information to determine whether the lesion is truly effective and whether the circumferential line will remain durable.

In addition to long-term efficacy, procedural efficiency has become increasingly important as the number of AF ablations continues to rise. Shorter procedures may reduce anesthesia exposure, left atrial dwell time, fluid load, and the overall burden on electrophysiology laboratories. Within this framework, first-pass isolation (FPI) has emerged as a particularly valuable procedural endpoint. It reflects whether the initial circumferential lesion set is sufficiently continuous to isolate the veins without further touch-up applications. Because FPI is closely linked to lesion quality and long-term durability, it provides an important bridge between intraprocedural performance and long-term clinical outcome.

Ablation index-guided workflows have improved standardization, but composite indices do not directly reflect the tissue's immediate physiological response to RF delivery. In contrast, local impedance (LI) monitoring offers real-time information on tissue heating at the catheter-tissue interface. A fall in LI reflects biophysical changes associated with lesion formation and may therefore serve as a direct marker of lesion efficacy. Although experimental

work suggested that LI monitoring could guide both effective and safe energy delivery, clinical validation, especially with newer contact force-sensing technologies, is still pending.

The present doctoral work addressed these two closely connected aspects of AF ablation. First, it evaluated whether increasing RF power from a conventional LPLD workflow toward HPSD and vHPSD settings improves procedural efficiency and acute procedural efficacy during PVI, and whether these changes translate into better rhythm outcomes during follow-up. Second, it examined whether LI drop can be used as a clinically meaningful real-time marker of effective lesion formation during high-power RF ablation and sought to define practical cut-off values for lesion guidance. Together, these investigations were designed to support a shift from empiric lesion delivery toward a more efficient and physiology-guided ablation strategy.

2. OBJECTIVES

The primary objective of this doctoral thesis was to investigate technologies that may improve the efficacy, safety, and reproducibility of RF catheter ablation for AF.

In the first part, to compare conventional LPLD, HPSD, and vHPSD ablation techniques during PVI with regard to total procedure time, left atrial dwell time, total RF application time, delivered energy, and the number of lesions required. Further, to determine whether increasing RF power improves the acute efficacy of PVI, particularly the rate of FPI, and to assess the relation between FPI and mid-term arrhythmia-free survival.

In the second part, the aim was to clinically validate LI monitoring during high-power PVI using a novel contact force-sensing ablation catheter and to

identify wall-specific LI drop thresholds that predict effective lesion formation and may support real-time ablation guidance in clinical practice.

3. METHODS

3.1. Study design and ethical background

This doctoral research was conducted at the Heart and Vascular Center of Semmelweis University and focused on patients with symptomatic, drug-refractory AF undergoing their first PVI procedure. The investigations were performed in accordance with the Declaration of Helsinki and were approved by the Regional and Institutional Committee of Science and Research Ethics of Semmelweis University (approval numbers 134/2020 and 280/2020). All participants provided written informed consent before enrollment and pre-procedural imaging.

3.2. Periprocedural management

Periprocedural management was standardized across the study population. Patients receiving vitamin K antagonists continued therapy uninterrupted, while those treated with direct oral anticoagulants omitted the morning dose on the day of the procedure and resumed therapy after the intervention if no major bleeding occurred. Before ablation, transoesophageal echocardiography or computed tomography was performed to exclude left atrial appendage thrombus. Procedures were carried out under local anesthesia with conscious sedation. After transseptal puncture, systemic anticoagulation with heparin was used to maintain an activated clotting time >300 seconds. Patients were observed overnight after the procedure, antiarrhythmic medication was generally continued during the blanking period, and proton-pump inhibitor therapy was prescribed for four weeks.

3.3. Power-delivery comparison study

The first clinical study compared three RF power-delivery strategies during point-by-point PVI. Altogether, 156 consecutive patients were prospectively enrolled between January 2019 and June 2021. The ablation strategies were introduced sequentially: LPLD ablation at 30 W in 53 patients, HPSD ablation at 50 W in 50 patients, and vHPSD ablation at 90 W for 4 seconds in 53 patients. In the LPLD and HPSD groups, procedures were performed with the CARTO 3 mapping system and a contact force-sensing irrigated catheter, using an ablation index-guided CLOSE workflow with anterior and posterior target values of 500 and 400, respectively, and an interlesion distance below 6 mm. In the vHPSD group, a QDot Micro catheter was used in QMODE+ with temperature-controlled settings, a target contact force of 10-20 g, and an interlesion distance below 5 mm.

3.4. Definition of procedural endpoints and follow-up

In the power-comparison study, a circular mapping catheter was positioned in the contralateral pulmonary veins during lesion deployment in order to blind the operator to immediate FPI. After completion of the circumferential lesion set, the circular catheter was advanced into the ablated veins and both entrance and exit block were assessed. FPI was defined as a complete entrance and exit block after the first initial circumferential lesion set without the need for any touch-up applications. When conduction persisted, additional RF lesions were delivered until durable acute isolation was achieved. A 20-minute waiting period was used in every case. Follow-up visits were scheduled at 3, 6, and 9 months and included clinical evaluation, 12-lead electrocardiography, and 24-hour Holter monitoring. Recurrence was defined as any atrial tachyarrhythmia lasting at least 30 seconds after the 2-month blanking period.

3.5. LI pilot study

The second investigation was a pilot clinical study evaluating LI as a marker of acute lesion efficacy during high-power PVI. Eight patients with symptomatic, drug-refractory paroxysmal AF were included, and 645 RF applications were analyzed in detail. High-density electroanatomical mapping of the left atrium was performed with the Rhythmia system and a 64-electrode basket catheter. Ablation was carried out with the StablePoint irrigated contact force-sensing catheter at 40-50 W with a maximum temperature of 43 °C. Lesions were intentionally overlapped, with an interlesion distance of less than 6 mm. The contralateral veins were used to position the mapping catheter during energy delivery, so that catheter contact would not distort contact force or LI measurements.

3.6. Lesion assessment

In the LI study, lesion efficacy was assessed with the loss-of-local-capture method. After completion of the circumferential line, bipolar pacing was performed along the lesion set. Lesions were considered successful when local tissue capture was absent and unsuccessful when capture persisted. Additional applications were delivered at unsuccessful sites until unexcitability was achieved. For every first-pass lesion, offline analysis included baseline LI, LI drop, application duration, mean/minimum/maximum contact force, contact force range, and force-time integral. Receiver operating characteristic analysis was used to determine optimal LI drop cut-off values separately for the anterior and posterior pulmonary vein walls.

3.7. Statistical analysis

Most variables showed a non-parametric distribution. Continuous variables were expressed as medians with interquartile ranges, and categorical variables

as counts and percentages. Depending on the comparison, Mann-Whitney U, Kruskal-Wallis, chi-square, and Fisher's exact tests were applied. Univariate logistic regression was used to examine associations between ablation strategy, FPI, long-term procedural success, and LI cut-off values. A two-sided p value below 0.05 was considered statistically significant.

4. CONCLUSIONS

The results of this doctoral work demonstrate that procedural efficiency and lesion durability are not opposing goals in AF ablation. When RF delivery is embedded in a controlled workflow that preserves catheter stability and lesion contiguity, the use of higher power can shorten the intervention while maintaining or improving acute and mid-term efficacy. At the same time, real-time physiological feedback from LI can refine lesion delivery at the point of contact and help define whether the applied lesion is likely to be effective.

Higher RF power substantially improved procedural efficiency during PVI. Median procedure time decreased from 85 minutes in the LPLD group to 79 minutes with HPSD and to 70 minutes with vHPSD. Left atrial dwell time showed a parallel reduction from 61 to 53 and 45 minutes, respectively, while total RF delivery time fell from 1,567 seconds to 1,398 seconds and then to 336 seconds. High-power strategies improved acute procedural efficacy as well. Bilateral FPI was achieved in 57% of patients treated with LPLD, compared with 78% in the HPSD group and 80% in the vHPSD group. HPSD significantly outperformed LPLD, whereas vHPSD did not produce an additional statistically significant gain over HPSD in FPI despite the marked reduction in RF time. Mid-term arrhythmia free survival was superior with high-power workflows. At 9 months, atrial arrhythmia recurrence was documented in 36% of patients in the LPLD group, compared with 10% in the HPSD group and 8% in the vHPSD

group. FPI proved to be a strong marker of procedural quality, because its achievement was closely associated with a lower likelihood of recurrence during follow-up.

LI drop was validated as a clinically useful real-time marker of acute lesion efficacy. Successful lesions were characterized by a significantly larger LI drop than unsuccessful lesions (median 23.1 vs. 16.7 Ohms) despite the absence of significant differences in mean contact force, minimum contact force, maximum contact force, or force-time integral. These findings indicate that the immediate local tissue response to RF delivery carries information beyond conventional force-based metrics alone. Wall-specific LI thresholds could be defined for this catheter-platform combination. On the anterior pulmonary vein wall, an LI drop above 21.80 Ohms predicted effective lesion formation; on the posterior wall, the corresponding threshold was above 18.30 Ohms. These cut-off values were associated with markedly higher odds of successful lesion creation and provide clinically practical targets for real-time lesion guidance.

The combined interpretation of both studies supports a physiology-guided ablation concept. HPSD ablation offers a balanced solution by accelerating the procedure and improving FPI, while LI monitoring helps individualize lesion duration and prevents both under-treatment and unnecessary prolongation of energy delivery. Wider clinical adoption should be supported by larger prospective studies with longer follow-up and multicenter validation of LI-guided thresholds.

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