Vilnius University

Faculty of Medicine

Medicine

Clinic of Cardiac and Vascular Diseases

Ville-Heikki Matias Ahlholm 2025, group 2

Integrated Study Master´s Thesis

Pulsed Field Energy in the Treatment of Atrial Arrhythmias

Supervisor — Assoc. Prof. Gediminas Rackauskas

Head of the Department — Prof. dr. Sigita Glaveckaitė

Vilnius, 2025

matias.ahlholm(a)mf.stud.vu.lt

Table of Contents

Abstract

Background: Pulsed Field Ablation (PFA) is the latest commercially available energy modality for arrhythmia treatment. Initially used in cancer therapy, PFA has now emerged as a promising approach for atrial fibrillation (AF) ablation. Alongside radiofrequency (RF) and cryoablation, PFA is widely used in clinical practice. Comparative studies with small patient cohorts, such as the ADVENT trial have employed a noninferiority design, showing no statistically significant differences between these ablation modalities.

Methods: A systematic review of recent studies, including randomized clinical trials, meta-analyses, and registry-based investigations, was conducted. Key findings from studies such as PULSED AF, MANIFEST-17K and ECLIPSE AF were analyzed to determine acute and long-term success rates, procedural efficiency, and complication rates.

Results: Findings indicate that PFA achieves high acute success rates (95–98%) with durable pulmonary vein isolation in 85–95% of cases after one year. Registry data suggest that PFA may offer superior safety compared to RF and cryoablation, as it has not been associated with energy-specific complications such as phrenic nerve palsy, pulmonary vein stenosis, or atrioesophageal fistula. Additionally, procedural efficiency is improved, as PFA enables faster ablations with potentially lower procedural risks. Clinical experience also suggests that post-procedural symptoms, such as chest discomfort, are less frequent following PFA compared to RF or cryoablation.

Conclusion: PFA represents a safe and efficient alternative to traditional ablation techniques for AF treatment. Tissue selectivity is among its key advantages. The reviewed studies highlight its superior safety profile, procedural efficiency, and long-term effectiveness. However, data on repeat ablations remain inconclusive, and further large-scale comparative trials are necessary to assess the long-term advantages of PFA over conventional energy sources.

Background

Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia, contributing to increased morbidity, stroke risk, and healthcare burden [1][2]. The global prevalence of AF has risen significantly due to an aging population and the increasing incidence of cardiovascular comorbidities such as hypertension, obesity, and diabetes [1][2]. AF management strategies primarily aim to alleviate symptoms, prevent thromboembolic events, and maintain sinus rhythm through pharmacological and interventional approaches [1].

Catheter ablation has emerged as a key interventional therapy for rhythm control in AF, particularly in patients who are refractory to antiarrhythmic drug therapy [2]. Traditional catheter ablation techniques include radiofrequency (RF) ablation, which utilizes thermal energy to create controlled lesions, and cryoablation, which employs extreme cold to achieve tissue necrosis [3]. While effective, these thermal-based ablation methods carry risks of collateral damage to surrounding structures, including the esophagus, pulmonary veins, and phrenic nerve [4][5]. Consequently, there has been a growing interest in non-thermal ablation technologies, with pulsed field ablation (PFA) emerging as a promising alternative [6][7][8].

PFA relay in the principle of electroporation, selectively targeting cardiomyocytes while sparing adjacent non-cardiac tissues. [6][7][9][10] This tissue selectivity reduces the risk of complications, such as pulmonary vein stenosis and esophageal injury [4][6][7][9][10][11][13], which are associated with traditional thermal ablation. Recent clinical trials, including ADVENT, have demonstrated that PFA offers comparable efficacy to RF and cryoablation, [14], while studies such as PULSED AF and MANIFEST-17K have supported its favorable safety profile and procedural efficiency. [15][16] This makes PFA an attractive first-line strategy for AF ablation in contemporary electrophysiology practice.

As PFA continues to be evaluated in large-scale studies and real-world clinical settings, it is essential to assess its mechanism of action, efficacy, durability, safety, and catheter technologies to determine its role in the evolving landscape of AF management.

Methods

A comprehensive literature search was conducted using PubMed, Google Scholar, Scopus and Embase to identify relevant studies on pulsed field ablation (PFA) in atrial fibrillation. The search included studies published up to February 2025, without restrictions on language or study design. A combination of controlled vocabulary (MeSH terms) and free-text keywords was used, including terms such as "pulsed field ablation," "electroporation," "atrial fibrillation," "catheter ablation," and "pulmonary vein isolation." Boolean operators were applied to refine the search, using "OR" within keyword groups and "AND" to combine them.

Selection of Studies

Single author screened the search results, first by title and abstract and then by full-text review. Duplicate records were removed before screening. Studies were included if they reported clinical outcomes, safety profiles, efficacy, different catheter type data on PFA for atrial fibrillation. One of the goals for article search screening also was to find most recently published articles.

Eligibility

Studies were included if they were published and investigated PFA in human subjects with atrial fibrillation, reported on safety, efficacy, lesion durability, or procedural outcomes, and utilized randomized controlled trials, cohort studies, or large-scale observational studies.

Exclusion criteria included studies focusing solely on preclinical animal models, case reports or small case series with fewer than ten patients, and studies using PFA for non-cardiac applications. Also articles published later 10 years were excluded.

Quality Assessment

The quality of included studies was assessed using the Downs and Black checklist, which evaluates study reporting, external and internal validity, and statistical power. Two reviewers independently scored each study, with discrepancies resolved by consensus.

Mechanism of pulsed field ablation

Pulsed field ablation (PFA) is a non-thermal technique that induces electroporation, forming nanopores in cell membranes and resulting in irreversible cardiomyocyte death. Because cardiomyocytes have lower electroporation thresholds than adjacent tissues, PFA selectively ablates myocardial tissue while minimizing injury to nearby structures such as the esophagus, phrenic nerve, and pulmonary veins [7][8][9][17].

Electroporation occurs in two forms: reversible, commonly used for intracellular drug delivery, and irreversible, which enables tissue ablation through high-voltage pulses that destroy targeted myocardial cells with minimal collateral damage [8][9].

The mechanism of action of PFA involves delivering ultra-short, high-voltage electrical pulses to myocardial tissue, triggering irreversible electroporation. High-voltage pulsed electric fields (PEF) create hydrophilic pore channels in the lipid bilayer of the cytomembrane, disrupting cellular homeostasis and leading to programmed cell death. The stepwise transition from RE to IRE depends on the amplitude, duration, and frequency of the applied PEF. Notably, IRE is the core mechanism by which PFA achieves necrosis of targeted cardiac cells, ensuring effective lesion formation without excessive thermal injury. [18]

This process selectively disrupts cardiomyocytes while preserving adjacent tissues, which have higher electroporation thresholds. Preclinical studies suggest that PFA produces well-demarcated lesions with uniform tissue necrosis and reduced inflammation compared to thermal ablation methods. Additionally, histological analyses indicate that PFA spares nerve fibers more effectively than radiofrequency ablation, potentially lowering the risk of autonomic dysfunction [18].

Unlike traditional thermal ablation methods, PFA avoids excessive heating, reducing risks such as fibrosis, char formation, and collateral damage [23]. However, while PFA is considered non-thermal, studies suggest that mild hyperthermia (40–50°C) can occur in approximately 30% of IRE-treated regions, with temperatures exceeding 50°C in about 5% of cases. This remains significantly lower than the temperatures seen in conventional thermal ablation but highlights the importance of optimizing energy parameters to avoid unintended thermal effects. [18]

Another distinct feature of PFA is its role in cardiac autonomic modulation. By selectively targeting abnormal pacemaker and conduction cells, PFA not only isolates pulmonary veins but also disrupts ectopic pacing sites and autonomic nerve inputs involved in atrial fibrillation (AF) pathophysiology. This is particularly relevant for persistent AF (PsAF), where additional ablation targets beyond pulmonary vein isolation (PVI) are often required for improved clinical outcomes. [18] Compared to thermal ablation, PFA was noted to have minimal effect on cardiac ANS. [19]

Advancements in pulsed field ablation (PFA) technology have focused on optimizing catheter designs and energy delivery protocols to improve procedural efficiency and lesion durability. For instance, the FARAPULSE™ PFA System has been engineered to provide a non-thermal, tissue-selective ablation method, enhancing both safety and efficacy in the treatment of atrial fibrillation (AF) [20][21]. Early clinical studies and device evaluations suggest that newer catheter models improve energy distribution and procedural consistency, potentially contributing to better long-term arrhythmia control [30]. Moreover, real-world registries such as MANIFEST-PF and MANIFEST-17K continue to assess PFA's large-scale safety and effectiveness outcomes, reinforcing its potential as a future standard of care in AF ablation [16][22].

In summary, PFA represents a promising advancement in atrial fibrillation treatment, offering precise myocardial ablation with a reduced risk of collateral damage. While early studies demonstrate its safety and efficacy, continued research is essential to establish its long-term clinical benefits and position it as a preferred alternative to thermal ablation techniques.

Comparison of PFA with Conventional Ablation Techniques

Traditional catheter ablation techniques rely primarily on thermal energy to create lesions that interrupt aberrant electrical circuits responsible for AF. Radiofrequency ablation (RFA) utilizes resistive heating to produce transmural lesions, effectively isolating the pulmonary veins. However, the application of heat carries risks such as collateral damage to adjacent structures, including the esophagus and phrenic nerve, leading to complications such as atrioesophageal fistula and pulmonary vein stenosis [14].

Cryoablation, in contrast, relies on extreme cold to achieve tissue necrosis. This method generally results in more homogeneous lesion formation and a lower risk of charring compared to RFA, but it requires longer procedural times and carries a risk of pulmonary vein reconnection due to incomplete lesion durability [14]. Laser ablation is a more specialized technique that delivers concentrated light energy to ablate tissue, often used in pulmonary vein isolation. While it allows for precise lesion creation, its high cost and limited availability restrict widespread adoption [14].

The study by Reddy, V. Y. et al. [14] conducted a comprehensive analysis (2023) in ADVENT Trial, comparing trial compared pulsed field ablation (PFA to traditional) with conventional thermal ablation methods.(radiofrequency or cryoballoon) for treating paroxysmal atrial fibrillation (AF). Their study emphasized that PFA's primary advantage lies in its tissue selectivity, enabling myocardial ablation with minimal impact on surrounding structures. [4][11][12][13][14]

Unlike radiofrequency and cryoablation, which rely on thermal energy, PFA utilizes irreversible electroporation to disrupt cardiomyocyte membranes without excessive heat-induced injury, reducing the likelihood of complications such as esophageal injury, phrenic nerve damage, and pulmonary vein stenosis. [14].

Furthermore, Reddy, V. Y. et al. (2023) found that PFA ensures consistent lesion formation while maintaining procedural safety, reducing complications commonly associated with thermal ablation. However, the study also noted that the durability of PFA lesions requires further long-term evaluation to confirm its superiority over traditional ablation methods. [14]

Clinical trials, including ADVENT, have demonstrated that PFA is non-inferior to RFA and cryoablation in terms of both efficacy and safety, while offering the additional advantage of faster procedural times due to its single-shot pulmonary vein isolation capability [14]. Also Li R. et all (2024) reported noninferiority to thermal ablation. [23]

Despite these advantages, certain challenges remain in the widespread adoption of PFA over medical therapy. While the safety profile is improved and procedural success rates are high, access to catheter ablation remains limited in some healthcare settings due to cost, resource availability, and expertise. [24] Furthermore, not all patients with AF are ideal candidates for ablation, as underlying comorbidities, AF duration, and left atrial size play significant roles in determining the effectiveness of the procedure. [22]

Maccioni et al. (2024) compared the safety of pulsed field ablation (PFA) and cryoballoon ablation (CBA) for treating paroxysmal atrial fibrillation (PAF). Their study reviewed data from 497 PFA patients and 1,113 CBA patients to assess the risk of complications. Data showed that pulsed field energy had fewer major complications compared to cryoballoon ablation. [24]

Types of electrodes used in clinical practice of PFA

Different electrode designs impact lesion formation, efficiency, and safety in PFA. Various catheter types are currently in use:

Multi-Electrode Pentaspline Catheter- Multipolar electrode catheter, VARIPULSE™

The multi-electrode pentaspline catheter is one of the most extensively studied PFA technologies, evaluated in trials such as IMPULSE, PEFCAT, and PersAFOne [3]. It features five splines with multiple electrodes, allowing for circumferential pulmonary vein isolation with a single application. This catheter design enables consistent lesion formation, reducing the risk of pulmonary vein reconnection and AF recurrence [25][26].

Reddy et al. (2021) [25] conducted a study demonstrating that the pentaspline catheter achieved durable pulmonary vein isolation in the majority of cases, with a high success rate at a one-year follow-up. The catheter's ability to deliver pulsed field energy across multiple electrodes simultaneously allows for shorter procedure times and higher procedural efficiency compared to conventional point-by-point ablation strategies [25].

Additionally, the pentaspline catheter's single-shot approach contributes to improved patient outcomes by minimizing the need for repositioning and repeat ablation applications. [26] Studies also suggest that the pentaspline structure reduces the risk of collateral damage, as the uniform electric field distribution enhances myocardial selectivity while preserving adjacent tissues, such as the esophagus and phrenic nerve [25][26].

The EU-PORIA registry, a multicenter European study, analyzed the real-world safety, efficacy, and learning curve characteristics of the pentaspline, multielectrode PFA catheter across seven high-volume AF ablation centers. A total of 1,233 patients were treated by 42 operators with varying levels of AF ablation experience and different primary ablation modality backgrounds. [27]

The findings demonstrated a favorable single-procedure success rate along with short procedural times, highlighting the feasibility and efficiency of PFA in a real-world, all-comer AF patient population. Additionally, the median procedure time was notably short average of 58 minutes. [27]

Findings from a comparative study by Chaumont et al. (2024) [3] indicate that pentaspline PFA catheters demonstrated superior acute pulmonary vein isolation rates compared to cryoballoon ablation. PFA also exhibited shorter procedural times and a lower rate of phrenic nerve injury, reinforcing its role as an efficient and safer alternative for atrial fibrillation ablation. The study further highlighted the consistent lesion durability with PFA, which may contribute to lower AF recurrence rates over time [3]. Additional studies are needed to confirm its impact on AF recurrence

These findings reinforce the pentaspline catheter's effectiveness in real-world clinical settings, confirming its safety and efficiency in diverse AF populations.

Lattice Mesh Electrode Catheter, FAPULSE ™

The lattice electrode catheter is designed for focal PFA applications and allows precise lesion formation in non-pulmonary vein sites. Unlike conventional ablation catheters, the lattice design enables a more even distribution of pulsed field energy, minimizing energy loss while improving lesion predictability [28].

Yavin et al. (2020) [28] conducted a study evaluating the biophysical characteristics, lesion durability, and safety of the lattice electrode catheter. Their findings demonstrated that this catheter design produced uniform and deeper lesions, making it particularly effective for targeting areas outside the pulmonary veins. The study also showed that the lattice electrode catheter minimized thermal damage while enhancing tissue selectivity, reducing the risk of complications such as esophageal injury and phrenic nerve damage. Another advantage of the lattice electrode catheter is its ability to maintain lesion consistency across different tissue types, which is crucial for effective ablation of persistent AF cases where arrhythmogenic substrates extend beyond the pulmonary veins [28].

Additionally, studies suggest that the lattice catheter improves procedure efficiency by delivering energy in a broader field with fewer applications, reducing overall ablation time and increasing procedural success rates [28].

In the study by Reddy et al. (2020), a novel 7.5F lattice-tip ablation catheter was evaluated in a first-in-human trial across three centers, involving 76 patients with paroxysmal or persistent atrial fibrillation (AF). This catheter is uniquely designed to toggle between delivering radiofrequency (RF) and pulsed field ablation (PFA) energies, allowing for flexible lesion sets beyond pulmonary vein isolation (PVI). [29]

The trial demonstrated that the catheter could safely and rapidly achieve PVI and create linear lesions, such as mitral isthmus and left atrial roof lines, with all lesion sets being acutely successful. Notably, the procedure involved minimal fluoroscopy time (mean of 4.7±3.5 minutes) and reported no device-related complications, including strokes. [29]

Focal Ablation Catheter (Toggling PFA/RF)

The focal ablation catheter, which integrates both PFA and RF energy, is designed to offer customizable lesion depth, making it particularly useful for treating complex arrhythmias requiring variable ablation strategies. Reddy et al. (2023) [20] investigated this hybrid approach and found that PFA produced uniform lesions with significantly less collateral damage compared to RF alone. The ability to toggle between energy types provided greater precision, particularly in areas where variable lesion depth is needed. In thinner regions, such as the posterior left atrium, pulsed field energy offers a safer alternative, while in thicker myocardial regions, radiofrequency energy may be utilized to ensure effective lesion formation. Their findings suggest that this hybrid technology can optimize lesion formation while reducing procedural risks [20].

Additionally, the ECLIPSE AF study (Anić et al., 2024) evaluated the use of PFA with contact force–sensing focal catheters for the treatment of atrial fibrillation (AF). The study used the CENTAURI system with three commercially available catheters: TactiCath SE, StablePoint, and ThermoCool ST. A total of 82 patients underwent pulmonary vein isolation (PVI) using PFA, and the results demonstrated a 100% acute success rate, with first-pass isolation achieved in 92.2% of cases. At the one-year follow-up, 80.2% of patients remained free from atrial arrhythmia recurrence. These findings support PFA as a safe and effective method for AF ablation, particularly when using contact force–sensing focal catheters [30].

Different PFA systems have shown high success rates in the short term, few complications, and quick procedures, regardless of the type of catheter used, whether a single-shot catheter (which delivers energy in one go) or a focal catheter (which targets specific areas). [14][21][27]

Balloon-Based PFA Catheter

The balloon-based PFA catheter is designed to integrate a spherical electrode array that delivers pulsed fields in a controlled manner. It allows for a single-shot approach to pulmonary vein isolation, significantly reducing procedural time compared to point-by-point ablation methods. The ability to deliver consistent, circumferential lesions in a single application makes it an attractive option for AF ablation. [15][27]

Verma et al. (2023) [15] studied the efficacy and safety of balloon-based PFA catheters in the PULSED AF trial. This study demonstrated that balloon-based PFA was highly effective for pulmonary vein isolation in both paroxysmal and persistent AF patients. The findings indicated that over 90% of pulmonary veins were successfully isolated with a single application, reducing the need for repositioning and repeat energy delivery. The study also reported that procedure times were significantly shorter compared to RF and cryoablation techniques. [15]

Belalcazar et al. (2024) [31] conducted a computational modeling study comparing the efficiency of different PFA catheter designs, including balloon-based catheters. Their analysis found that balloon-based PFA catheters provided a more uniform electric field distribution around the pulmonary veins, leading to more consistent lesion formation. This uniformity is crucial for ensuring durable pulmonary vein isolation and reducing the likelihood of arrhythmia recurrence. [31]

Another advantage of balloon-based PFA catheters is their favorable safety profile. In the PULSED AF trial, no serious complications such as phrenic nerve injury, esophageal damage, or pulmonary vein stenosis were reported, supporting the safety of balloon-based PFA in clinical use [15]. Moreover, computational modeling has shown that balloon-based catheters provide a uniform electric field around the pulmonary veins, which may help minimize energy delivery to adjacent structures and reduce the risk of collateral injury [31].

Results- Effectiveness of PFA

Effectiveness of PFA is measured by arrhythmia- free survival long term- success, acute pulmonary vein isolation (PVI) success rate, durability of lesion and need for repeated ablation.

PFA has demonstrated comparable or superior efficacy to traditional ablation methods. A meta-analysis of clinical trials comparing PFA and RF ablation reported that PFA achieved acute pulmonary vein isolation success rates comparable to RF ablation and with a potentially lower incidence of specific complications. [14]

By EU-PORIA Registry one of the key findings was the high arrhythmia-free survival rate, with 74% of patients remaining free of atrial arrhythmia recurrence at one year. When stratified by AF subtype, 80% of paroxysmal AF (PAF) patients and 66% of persistent AF patients, maintained sinus rhythm, demonstrating that PFA offers strong efficacy across both patient groups [27].

A study by Verma et al. (2023) in the PULSED AF Trial reported 12-month effectiveness rates of 66.2% for paroxysmal AF and 55.1% for persistent AF, indicating that approximately 66.2% of paroxysmal AF patients and 55.1% of persistent AF patients remained free from arrhythmia recurrence at one year. [15] These numbers are slightly lower than those reported in the EU-PORIA Registry. Pulsed AF Trial demonstrated 100% of acute isolation of all pulmonary veins. Pulsed field ablation showed a clinically meaningful improvements in quality of life in study population. [15]

Durability studies suggest that PFA lesions maintain their structural integrity over time, unlike RF ablation lesions, which may regress due to thermal injury-related tissue remodelling. The PULSED AF trial reported that over 90% of PFA-treated pulmonary veins remained electrically isolated at a one-year follow-up [15].

Reddy VY et al. (2021) [25] provides a comprehensive review of initial trials assessing the efficacy of pulsed field ablation (PFA) for atrial fibrillation (AF). The authors report that initial trials demonstrated) include the IMPULSE, PEFCAT, and PEFCAT II studies. Collectively, these trials reported a 78.5% arrhythmia-free survival rate at one-year post-PFA. [25] However, subsequent studies, such as the PULSED AF trial, indicated lower success rates, with 66.2% in paroxysmal AF and 55.1% in persistent AF. [25]

Real-world data appear more encouraging, showing an 80% event-free estimate at one year. [22] The review also highlights that PFA achieves 100% acute success in pulmonary vein isolation, with durable isolation observed in 84–96% of cases at 75 to 90 days post-procedure. [32]

The authors discuss potential mechanisms for recurrences, including pulmonary vein reconnection and the role of the autonomic nervous system, noting that PFA may spare ganglionated plexi, which could influence late arrhythmia recurrences. [19]

Additionally, the AdmIRE Trial confirmed that PFA was non-inferior to thermal ablation methods and demonstrated a shorter procedure duration, leading to increased efficiency [33].

Kueffer Maurhofer et al. (2024) reported repeat ablation rates of 16% for PFA, 20% for cryoballoon ablation (CBA), and 30% for RF ablation (RFA) within the first year. This suggests that PFA may have a lower repeat ablation rate compared to RFA. [34] It also reported freedom from arrhythmia recurrence rates at one year for patients with persistent atrial fibrillation (AF) undergoing pulmonary vein isolation (PVI) for Pulsed-Field Ablation PFA 80.3%, CBA 83.1%, RFA 66.2%. [34]

While PFA has proven to be an effective treatment for atrial fibrillation, recurrences still occur, making repeat ablations necessary. However, the efficacy and safety of these repeat ablations using PFA remain largely unexplored.

The inspIRE trial evaluated the effectiveness of a fully integrated biphasic pulsed field ablation (PFA) system with a variable-loop circular catheter for treating drug-refractory paroxysmal atrial fibrillation (AF). The patient cohort included 186 patients. It was conducted across 13 centers in Europe and Canada. The primary effectiveness endpoint was an acute pulmonary vein isolation (PVI) plus freedom from any atrial arrhythmia at 12 months. It was achieved in 75.6% of patients. Notably, among those who received an optimal number of PFA applications (≥12 per vein), the success rate increased to approximately 80%. [35]

MANIFEST-REDO STUDY focused on patients who needed a second ablation after initial PFA, analyzing durability of lesions and recurrence mechanisms. It analyzed data from 427 patients across 22 European centers. It included patients who underwent repeat ablation due to recurrent AF or atrial tachycardia (AT) after an initial PFA procedure using the pentaspline catheter. The median interval between the initial PFA and the repeat procedure was nine months. [36]

At the time of the repeat ablation, 55% of patients exhibited reconnection in at least one pulmonary vein (PV), indicating that 45% maintained durable isolation from the initial procedure. After undergoing a repeat ablation, 65% of patients remained free from atrial fibrillation (AF) or atrial tachycardia (AT) episodes lasting 30 seconds or longer. This was measured after a 3-month blanking period, and these patients did not require additional class I or III antiarrhythmic medications. Success rates varied based on the type of recurrent arrhythmia. For paroxysmal atrial fibrillation population, it was 65% and population suffering from persistent atrial fibrillation 56%. [36]

In a sub-study of PULSED AF trial analysed post-procedural AF burden. Researchers collected 12,264 hours of Holter recordings from 300 patients, ensuring comprehensive arrhythmia monitoring.

The findings showed that 87% of paroxysmal AF patients and 82% of persistent AF patients had an AF burden of less than 10%, reflecting a high procedural success rate and effective rhythm control. Furthermore, 83% of paroxysmal AF patients and 75% of persistent AF patients experienced no more than one week of atrial arrhythmia recurrence, suggesting durable suppression of AF episodes when monitored via trans-telephonic ECG recordings. These findings underscore PFA's effectiveness in significantly reducing AF burden, contributing to long-term rhythm stability and improved patient outcomes. [37]

In a subset analysis focusing on the durability of pulmonary vein isolation (PVI), 144 patients who experienced arrhythmia recurrence underwent repeat ablation procedures. During these procedures, it was observed that 71% of the pulmonary veins remained durably isolated, indicating a substantial rate of sustained PVI post-initial ablation. [26]

AdmIRE Pivotal Trial also suppoted efficacy profile of PFA. In study it achieved a 74.6% freedom from atrial arrhythmias at 12 months, demonstrating strong efficacy for treating paroxysmal atrial fibrillation (AF). [33]

Factors such as pulse intensity, waveform shape, number of pulses, and electrode configuration significantly influence PEF's efficacy and safety. Careful optimization of these parameters is essential for successful outcomes. [38]

Safety Profile of PFA

The MANIFEST-PF Survey [39], MANIFEST-PF Registry [22], and MANIFEST-17K Study [16] form a progressive continuum of clinical evaluations, each expanding upon the previous findings to provide a comprehensive real-world assessment of PFA's safety and efficacy.

One of the most significant advantages of PFA is its improved safety profile. The MANIFEST-17K study, which evaluated over 17,000 PFA-treated patients, reported a major complication rate of only 1.0%. [16]. This number is significantly lower than what has been reported in most studies on conventional ablation techniques.

Minor events were reported to be 3.21%. Adverse events were sorted based on PF energy specific and non-energy specific adverse events. What was important, of 17 000 participants there was no esophageal events reported. Same percentage for 0% of PV stenosis and phrenic paralysis. That is supporting the fact that PFA is an extremely preferential to ablation of myocardial tissue. [16] In contrast, RF ablation is associated with higher rates of esophageal injury (2-5%) and pulmonary vein stenosis (1-3%) due to excessive thermal injury [16]. Hemolysis related kidney failure was reported in 0.03% of patients. Transient hemodialysis was utilized and renal function normalized in all in follow-up. [16]

It is worth noting that a key limitation of this study is that it exclusively investigated ablation using the pentaspline catheter. Therefore, the safety outcomes observed in this study may not necessarily be applicable to other catheter designs, which could exhibit different risk profiles and procedural characteristics.

Comparing same numbers from initial MANIFEST-PF study, tamponade and stroke rates, which initially reported from first 1700 patients, we see substantial improvements. [16] In MANIFEST-PF pericardial tamponade rate was 0.97% and for stroke 0.39% and later in 17 k study only 0.36% and for stroke 0.12%. That is evidence of learning what has been translated in the field. [16][39]

A key limitation of this study is that it exclusively investigated ablation using the pentaspline catheter. [16] As a result, the safety outcomes observed may not be directly applicable to other catheter designs, which may differ in risk profiles and procedural characteristics. Further studies comparing various PFA catheter technologies are necessary to determine whether these findings hold true across different systems.

When comparing the initial findings from the MANIFEST-PF study, which analyzed the first 1,700 patients, with the later MANIFEST-17K study, we observe substantial improvements in safety outcomes. In the MANIFEST-PF study, the pericardial tamponade rate was 0.97%, and the stroke rate was 0.39%. However, in the MANIFEST-17K study, these rates were reduced to 0.36% for tamponade and 0.12% for stroke [16][39]. These findings demonstrate a clear learning curve and procedural refinement, which have been effectively translated into clinical practice, leading to enhanced safety of pulsed field ablation.

The PULSED AF trial evaluated the safety of pulsed field ablation (PFA) in treating atrial fibrillation (AF). The study reported a low primary safety event rate of 0.7%, indicating a favorable safety profile for PFA. There was no evidence of phrenic, esophageal, pulmonary vein injury or coronary artery spasm in the 300-patient study population. [15] The safety profile was favorable, with a primary adverse event rate of 0% in inspIRE study as well. [35]

However, some reports have highlighted potential complications such as coronary artery spasm and transient ST-segment elevations during PFA procedures [40][41][42][43]. Other rare complications include atrioventricular block and ventricular fibrillation [48]. A systematic review by Hasegawa et al. (2025) suggests close monitoring for coronary artery-related complications [44]. PFA did not cause thermal lesions or ulcers in the bronchial system, indicating its safety concerning bronchial thermal injury. [45]

Vivek Y et al. (2022) reported coronary artery spasm, which were transient and resolved without long-term effects. Importantly, this vasospasm was attenuated by administering nitroglycerin, either post op to treat the spasm or as prophylaxis. PFA did not induce vasospasm in areas remote areas from coronary arteries. ST- segment elevation was not observed. [40].

Recent findings by Kurita [46] indicate that coronary artery spasms during PFA may result in transient ST-segment elevations, mimicking myocardial infarction. This phenomenon is likely due to autonomic nervous system stimulation or microvascular dysfunction induced by the pulsed electric fields. Proper patient monitoring and vasodilator administration during procedures may reduce these risks and improve procedural safety [46].

Esophageal safety is a major concern with thermal ablation techniques. PFA has demonstrated a significantly reduced incidence of esophageal injury due to the myocardial selectivity of electroporation [15][18]. Additionally, phrenic nerve injury, common in RFA and cryoablation, is minimized with PFA due to lower energy penetration beyond cardiac tissue [16][24][29][40].

However, some reports have highlighted potential complications such as coronary artery spasm and transient ST-segment elevations during PFA procedures [40][41][42]. Other rare complications include atrioventricular block and ventricular fibrillation [48]. A systematic review by Hasegawa et al. (2025) suggests close monitoring for coronary artery-related complications [44].

Results from the EU-PORIA registry, the major complication rate was 1.7%, which included pericardial tamponade (1.1%) and transient ischemic attack or stroke (0.6%). These results suggest that PFA is an effective and safe ablation modality, even in a diverse, real-world AF population. These rates are lower than or comparable to those observed in traditional thermal ablation methods, suggesting a favourable safety profile. [27][49]

A cohort study by Zhang et al. 2024 [50] investigated the incidence of coronary artery spasm during pulsed field ablation (PFA) compared to radiofrequency ablation (RFA) of the mitral isthmus in patients undergoing atrial fibrillation ablation. Coronary vasospasm occurred more frequently during PFA than RFA when ablating the mitral isthmus, a region anatomically close to the circumflex coronary artery. Despite the higher incidence of vasospasm with PFA, these events were often subclinical. The vasospasms observed were transient and resolved without significant clinical intervention. RFA caused no observed spasms in the study, but when they occur, they can be clinically more significant and may require monitoring or treatment. [50] These findings highlight the importance of being vigilant for potential coronary vasospasm during PFA of the mitral isthmus. Although these spasms are often subclinical and self-resolving, awareness and appropriate intra-procedural monitoring are crucial to ensure patient safety during ablation procedures near coronary arteries.

Maccioni et al. (2024) compared the safety of pulsed field ablation (PFA) and cryoballoon ablation (CBA) for treating paroxysmal atrial fibrillation (PAF). Their study reviewed data from 497 PFA patients and 1,113 CBA patients to assess the risk of complications. Data showed that pulsed field energy had fewer major complications compared to cryoballoon ablation. [24]

The overall risk of serious side effects was about 4.3% lower with PFA. Also, less adverse events were reported with PFA, with a risk reduction of 2.5% compared to CBA. In PFA-treated patients, major complications occurred in 0.4% of cases, compared to 5.6% in CBA-treated patients and minor complications were also lower with PFA (2.7% vs. 5.8% for CBA). While PFA demonstrates promising safety advantages, the smaller study population highlights the need for larger, long-term trials to confirm its superiority over cryoballoon ablation (CBA) [24]. As PFA technology continues to evolve, further studies comparing different systems are necessary to establish standardized safety and effectiveness profiles across various PFA platforms.

As PFA technology continues to evolve, further studies comparing different systems are necessary to establish standardized safety and effectiveness profiles across various PFA platforms.

Catheter Ablation compared to Medical Therapy

The CABANA trial was a pivotal study that assessed catheter ablation (PFA) against conventional medical therapy in patients with AF, particularly those with heart failure. The results demonstrated that ablation significantly reduced the AF burden and improved overall symptom control compared to medical therapy alone. Patients who underwent ablation experienced fewer symptomatic episodes and exhibited a greater likelihood of maintaining sinus rhythm during follow-up [2].

Beyond symptom control, catheter ablation has been shown to have positive impacts on long-term cardiovascular outcomes, specifically in HF population. Evidence suggests that ablation therapy may contribute to a reduction in heart failure hospitalizations and an improvement in left ventricular ejection fraction (LVEF) among patients with AF-related cardiomyopathy. Medical therapy, on the other hand, relies on rate and rhythm control strategies that, while effective in symptom management, may not provide the same level of long-term structural and functional cardiac benefits as catheter ablation, especially in patients with AF-related cardiomyopathy or reduced LVEF. [2].

Discussion

Recent reviews have emphasized the increasing role of pulsed field ablation (PFA) in modern atrial fibrillation management, highlighting its favorable safety profile and growing clinical adoption across Europe. [47] Trials such as PULSED AF, ADVENT, and MANIFEST-17K have demonstrated that PFA achieves comparable or superior procedural efficacy compared to RF and cryoablation, with a lower complication profile [15][16][14]. These studies not only reinforce PFA's favorable safety profile but also raise important questions regarding its long-term applicability across diverse patient populations. The consistently low complication rates point to a change in thinking in how we evaluate ablation-related risk.

Studies conducted in Europe and North America show a consistent success rate of >90% for acute pulmonary vein isolation, supporting PFA as a viable option for ablation [15][25][27]. Large-scale studies conducted across Europe and North America consistently report acute pulmonary vein isolation (PVI) success rates exceeding 90%, supporting PFA as a viable and effective ablation strategy. However, despite these promising results, some important considerations remain, particularly regarding lesion durability, recurrence mechanisms, and real-world applicability [26][36].

Strengths

PFA has been extensively studied in multiple large-scale randomized controlled trials (RCTs) and observational studies, providing a strong foundation for assessing its clinical efficacy and safety [14] [15][16][33]. These trials, including ADVENT, PULSED AF, and AdmIRE, have confirmed that PFA offers comparable or superior outcomes to conventional thermal ablation techniques while significantly reducing collateral damage [14][15][33]. The growing evidence suggests that PFA may be particularly beneficial for patients at high risk of esophageal or phrenic nerve injury, as the selective nature of electroporation preserves adjacent tissues [15][16][18][40]. Additionally, the procedural efficiency of PFA, which requires shorter energy application times and fewer catheter repositioning maneuvers, enhances workflow in the electrophysiology lab, leading to improved patient throughput and potentially reducing overall healthcare costs [15][33][35].

One of the most promising aspects of PFA is the durability of its lesions, which appear to remain stable over time with lower rates of lesion regression compared to RF ablation [15][26][36]. Clinical studies have demonstrated that PFA-treated pulmonary veins exhibit persistent electrical isolation at long-term follow-up, reducing the likelihood of arrhythmia recurrence and minimizing the need for repeat procedures [26][36].

This durability is likely attributed to the unique mechanism of irreversible electroporation, which targets cardiomyocytes without inducing excessive fibrosis or thermal injury [18][28]. The preservation of extracellular matrix integrity may contribute to the long-term stability of ablation lesions, making PFA a more sustainable treatment option for AF [18][28].

Limitations

Despite its promising advantages, PFA remains a relatively new technology, and long-term follow-up data beyond five years is still lacking. While initial results indicate strong lesion durability, further longitudinal studies are needed to confirm the sustained efficacy of PFA and determine whether late pulmonary vein reconnection occurs at rates similar to or lower than those observed with RF ablation [32][36].

Additionally, although large-scale trials have validated the safety of PFA, rare but notable complications such as coronary artery spasm and transient ST-segment elevation have been reported [40][41][42][43][44][46][50]. The mechanisms behind these occurrences are not yet fully understood, and ongoing research is necessary to establish protocols for minimizing and managing these potential risks [44][46].

Another challenge to widespread adoption is the limited real-world experience and availability of PFA technology. Unlike RF ablation, which has been refined over decades and is widely accessible in electrophysiology labs worldwide, PFA requires specialized equipment and training. The adoption curve may be slower in certain regions, particularly in centers with limited access to advanced electrophysiology technologies [16][27][39]. Furthermore, the cost of PFA systems and disposables is an important consideration for healthcare institutions, as it may impact reimbursement policies and procedural accessibility. Comparative cost-effectiveness analyses are needed to evaluate the long-term economic benefits of PFA relative to conventional ablation techniques [1][2].

While PFA has proven to be an effective treatment for atrial fibrillation, recurrences still occur, making repeat ablations necessary. However, the efficacy and safety of these repeat ablations using PFA remain largely unknown [36]. Another key reason for further investigation is the durability of pulmonary vein isolation (PVI), which is essential for maintaining sinus rhythm in atrial fibrillation patients. PVI durability has not been thoroughly studied in the context of PFA, particularly in patients undergoing repeat ablations [26] [36].

The variability in catheter designs used for PFA is another factor that require further investigation. While multiple electrode configurations, such as pentaspline, balloon-based, and lattice electrode catheters, have been studied, it remains unclear which design provides the optimal balance of lesion effectiveness, procedural efficiency, and safety [15][25][29][31][35]. Future comparative studies are essential to determine whether certain catheters yield superior clinical outcomes in different patient subgroups, such as those with paroxysmal versus persistent AF. As more catheter technologies enter the market, standardization of PFA delivery parameters will be crucial to ensuring consistent and reproducible results across different centers and operators [38].

While the clinical benefits of PFA are well-documented, its long-term impact on atrial remodeling and fibrosis remains an open question. Traditional thermal ablation methods have been associated with progressive atrial scarring, which may contribute to substrate modification and long-term rhythm stability. However, PFA's ability to preserve surrounding connective tissue and avoid excessive scarring raises questions about its role in modifying the arrhythmogenic substrate over time [18][28]. Further histopathological studies are needed to elucidate whether PFA can provide comparable or superior substrate modification effects compared to thermal ablation.

While PFA has proven to be an effective treatment for atrial fibrillation, recurrences still occur, making repeat ablations necessary. However, the efficacy and safety of these repeat ablations using PFA remain largely unknown [36].

Another key reason for further investigation is the durability of pulmonary vein isolation (PVI), which is essential for maintaining sinus rhythm in atrial fibrillation patients. PVI durability has not been thoroughly studied in the context of PFA, particularly in patients undergoing repeat ablations [26].

Conclusion

This study highlights pulsed field ablation (PFA) as an effective and safe modality for atrial fibrillation (AF) treatment, demonstrating procedural efficiency, high success rates, and a favorable safety profile.

PFA's primary advantages include its tissue selectivity, reducing damage to surrounding structures, and its high acute pulmonary vein isolation (PVI) success rates, consistently reported across multiple clinical studies. Long-term efficacy is promising, with real-world data showing that a substantial proportion of patients remain arrhythmia-free at one year. Additionally, early evidence suggests that PFA lesions are more durable than RF-induced lesions, reducing the likelihood of pulmonary vein reconnection.

While repeat ablations remain necessary in some patients, PFA appears to have lower reintervention rates than RF and cryoablation. However, the impact of lesion durability on long-term arrhythmia recurrence requires further investigation. Additionally, the variability in catheter designs and procedural approaches may influence outcomes, emphasizing the need for standardization.

Furthermore, an important area for future research is the effectiveness of PFA in patients with recurrent AF, particularly those requiring repeat ablations. While early data suggest that PFA may offer advantages in lesion durability, recurrence mechanisms such as pulmonary vein reconnection and autonomic remodeling remain incompletely understood. More research is needed to determine the optimal approach for repeat PFA procedures and whether specific procedural modifications can improve outcomes in persistent and long-standing AF patients.

When treating patients with pulsed field ablation (PFA) using the pentaspline catheter, the use of imaging and electroanatomical mapping systems is recommended. These tools help ensure precise catheter positioning, optimize lesion formation, and reduce the risk of procedural complications.

For patients presenting with recurrent arrhythmia after initial PFA with a pentaspline catheter, a repeat ablation should be encouraged. Evidence from recent studies suggests that outcomes after a second procedure are generally favorable, contributing to improved long-term arrhythmia-free survival and symptom control.

Furthermore, the development of second-generation catheters, integration of 3D mapping technologies, and refinements in energy delivery protocols are expected to enhance the durability of pulmonary vein isolation (PVI). These advances may lead to more uniform lesion formation, reduce conduction gaps, and improve the overall efficacy and safety profile of the ablation procedure.

In conclusion, PFA represents a significant advancement in AF ablation, offering high procedural success rates, a strong safety profile, and potential long-term advantages. Further research should focus on lesion durability, optimal catheter technologies, effectiveness in recurrent AF cases, and cost-effectiveness to guide its widespread clinical adoption.

Ablation Method	Mechanism	Advantages	Disadvantages
Radiofrequency ablation	Uses heat to create lesions	Effective for AF, widely available	Risk of collateral damage, esophageal injury
Cryoablation	Freezes tissue	Lower risk of collateral damage than RFA	Longer freeze time, potential for pulmonary vein stenosis
Laser ablation	Uses light energy for ablation	Precise lesion formation	Limited availability, costly
Pulsed field ablation (PFA)	Electroporation (non-thermal)	Selective for cardiomyocytes, minimal collateral damage	Newer technology, long-term data still emerging

Figure 1. Traditional ablation method relies on thermal energy.

Reddy VY, Anic A, Koruth J, Petru J, Funasako M, Minami K, et al. Pulsed field or conventional thermal ablation for paroxysmal atrial fibrillation. N Engl J Med. 2023;389(18):1660-71. doi:10.1056/NEJMoa2307291. [14]

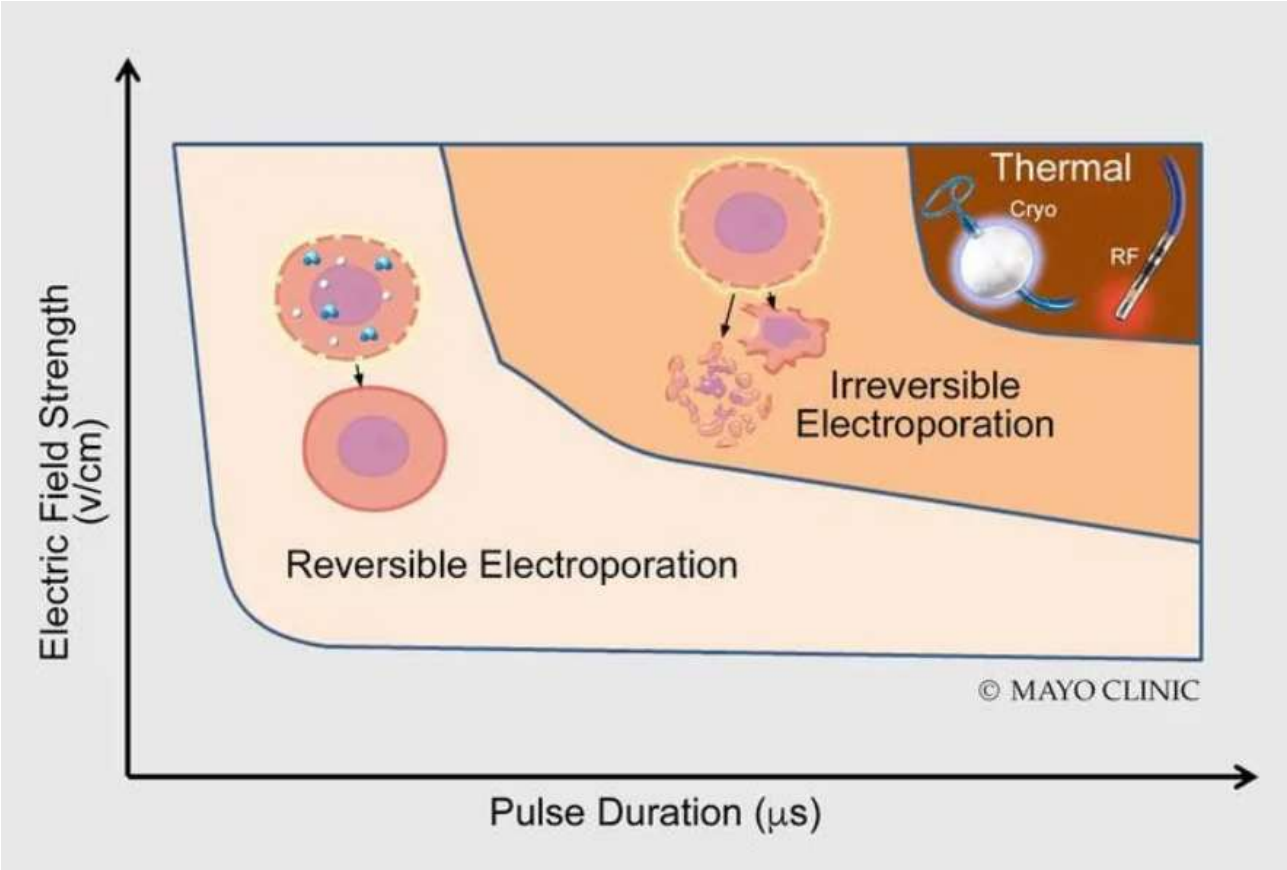


Figure 2. Mayo Clinic. Figure 1, Pulsed field ablation procedure [Internet]. Rochester, MN: Mayo Clinic; 2023 [cited 2025 Feb 16]. Available from: https://www.mayoclinic.org/medical-professionals/cardiovascular-diseases/news/novel-pulsed-field-ablation-offers-patients-safer-and-faster-atrial-fibrillation-ablation/mac-20567834

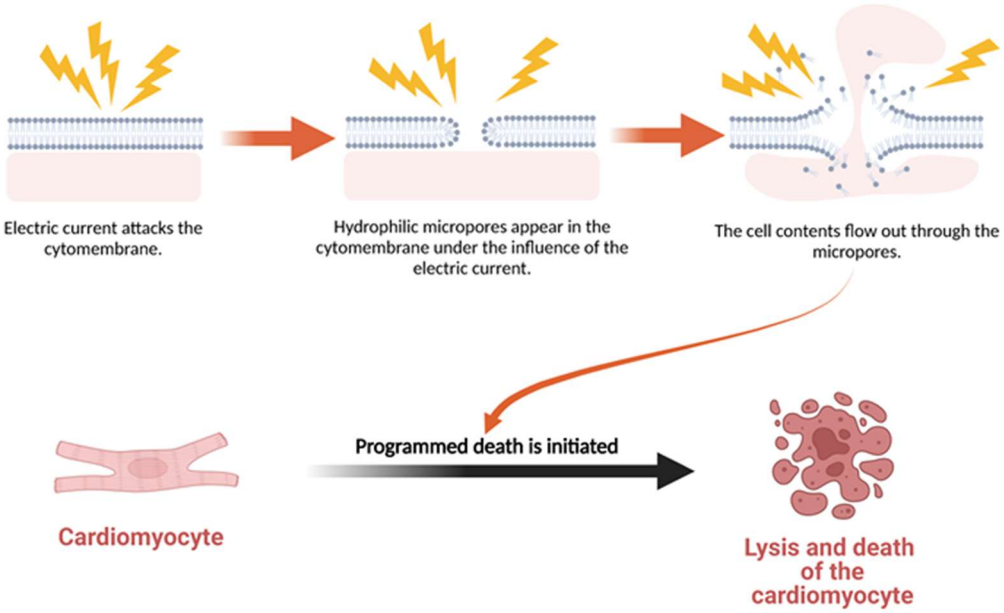


Fig. 1. Mechanism of Cardiomyocyte Death Induced by Electroporation. Electroporation consists of three stages over time: cell membrane charging, pore generation, and pore radius evolution. When the radius of the hydrophilic pore is large enough, the cellular contents will flow out through the pore, which will disrupt intracellular homeostasis and induce programmed cell death.

Figure 3. Jiang S, Qian F, Ji S, Li L, Liu Q, Zhou S, Xiao Y. Pulsed Field Ablation for Atrial Fibrillation: Mechanisms, Advantages, and Limitations. Figure 1. Rev Cardiovasc Med. 2024;25(4):138. doi:10.31083/j.rcm2504138. [18]

Figure 4. Summary of results.

Study	Population/Approach	Key Findings
ADVENT Trial [14]	PFA vs RF/cryo	Non-inferior efficacy; shorter procedure time
EU-PORIA Registry [27]	Real-world PFA	74% arrhythmia-free at 1 year (PAF: 80%, PsAF: 66%)
PULSED AF Trial [15]	Balloon-based PFA	12-mo success: PAF 66.2%, PsAF 55.1%; 100% acute PVI; QoL improved
IMPULSE/PEFCAT [25]	PFA trials	78.5% arrhythmia-free at 1 year
MANIFEST-PF [22]	Real-world registry	~80% event-free survival at 1 year
Meta-analysis [32]	Systematic review	100% acute PVI; 84–96% durable PVI (75–90 days)
MANIFEST-REDO [36]	Repeat ablation after PFA	55% PV reconnection; 65% arrhythmia-free after redo
inspIRE Trial [35]	Variable-loop PFA catheter	75.6% success at 12 mo; ~80% with ≥12 applications/vein
PULSED AF Burden [37]	Holter monitoring	AF burden <10%: PAF 87%, PsAF 82%; Low recurrence
AdmIRE Trial [33]	Focal PFA system	74.6% arrhythmia-free at 12 months; shorter procedures
Maurhofer et al. [34]	PFA vs CBA vs RFA	Repeat ablation: PFA 16%, CBA 20%, RFA 30%; PsAF freedom: PFA 80.3%, CBA 83.1%, RFA 66.2%

Figure 5. PFA Safety Summary

Study	Population	Key Safety Findings
MANIFEST-17K [16]	>17,000 PFA patients	1.0% major complications; 0% esophageal injury, PV stenosis, or phrenic nerve palsy; 0.03% renal injury
MANIFEST-PF [39]	First 1,700 PFA patients	0.97% tamponade, 0.39% stroke; compared to 0.36% and 0.12% in MANIFEST-17K
PULSED AF [15]	300 patients	0.7% primary safety event rate; no esophageal, phrenic, PV injury, or coronary spasm
inspIRE [35]	186 patients	0% primary adverse events
EU-PORIA [27]	Real-world registry	1.7% major complication rate (1.1% tamponade, 0.6% TIA/stroke)
Zhang et al. [50]	Mitral isthmus ablation	Higher coronary vasospasm incidence with PFA vs RFA; events transient and subclinical
Maccioni et al. [24]	PFA vs CBA (497 vs 1,113 pts)	Major events: 0.4% PFA vs 5.6% CBA; Minor: 2.7% PFA vs 5.8% CBA
Vivek Y et al. [40]	Case series	Coronary vasospasm observed; nitroglycerin effective; no long-term effects
Kurita [46]	Review	ST elevation due to vasospasm/autonomic trigger; monitoring and vasodilators recommended
Hasegawa et al. [44]	Systematic review	Coronary complications rare but important to monitor
Füting et al. [45]	Bronchial safety	No bronchial thermal lesions or ulcers observed in PFA
Various case reports [41,42,43,48]	Case-based	Transient ST elevations, AV block, VF during PFA reported

Graphical Abstract

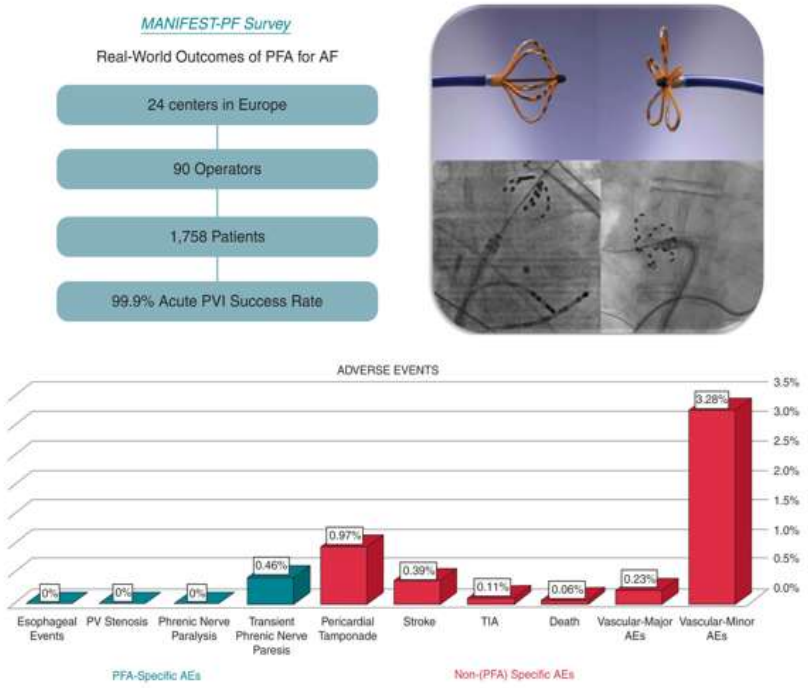


Figure 6. Graphical summary of the MANIFEST-PF Survey evaluating real-world clinical outcomes of pulsed field ablation (PFA) for atrial fibrillation (AF). The study included 1,758 patients across 24 centers in Europe and involved 90 operators. It demonstrated a high acute pulmonary vein isolation (PVI) success rate of 99.9% using the pulsed field ablation technique.

The bar chart presents the observed adverse events (AEs). Importantly, no esophageal injury, pulmonary vein stenosis, or phrenic nerve paralysis was reported-supporting the tissue selectivity and safety of PFA. The most notable PFA-specific AE was pericardial tamponade (0.97%), while other complications such as stroke (0.39%), transient ischemic attack (0.11%), and vascular complications (minor: 3.28%, major: 0.23%) were infrequent and not specific to the ablation modality.

This figure supports the favorable safety profile of PFA in real-world practice and demonstrates its effectiveness and consistency across diverse European electrophysiology centers.

Ekanem E, Reddy VY, Schmidt B, Reichlin T, Neven K, Metzner A, et al. Multi-national survey on the methods, efficacy, and safety on the post-approval clinical use of pulsed field ablation (MANIFEST-PF). Europace. 2022;24(8):1256-1266. doi: 10.1093/europace/euac050. [39]

Procedural Characteristics:

Parameter	PFA	CBA	RFA
Procedure Time (min)	94	75	182
Fluoroscopy Dose (Gy·cm²)	5.0	5.7	1.6

1-Year Clinical Outcomes:

Outcome	PFA	CBA	RFA
Arrhythmia-Free Survival at 1-Year Follow-Up (%)	85.0	66.2	73.8

Figure 7. This table summarizes key procedural characteristics and one-year clinical outcomes from a matched comparison of pulsed field ablation (PFA), cryoballoon ablation (CBA), and radiofrequency ablation (RFA). PFA demonstrated the highest arrhythmia-free survival at 12 months (85%), with moderate procedure time and fluoroscopy exposure. While RFA had the longest procedure time, it resulted in the lowest radiation dose. These results underline the growing role of PFA as a balanced and effective ablation strategy.

Maurhofer J, Kueffer T, Madaffari A, Stettler R, Stefanova A, Seiler J, et al. Pulsed-field vs. cryoballoon vs. radiofrequency ablation: a propensity score matched comparison of one-year outcomes after pulmonary vein isolation in patients with paroxysmal atrial fibrillation. J Interv Card Electrophysiol. 2024;67(2):389-397. doi:10.1007/s10840-023-01651-4. [34]

MANIFEST-17K Study [16]	MANIFEST-REDO Study [36]
Safety outcomes in 17,000+ PFA-treated patients	Repeat ablation procedures after PFA failure
Evaluate complication rates and procedural safety of PFA in a large cohort	Analyze causes of AF recurrence and lesion durability in patients requiring redo procedures
17,000+ patients who underwent PFA for AF	427 patients who underwent a second ablation (redo) after initial PFA
Not the main focus, but shows low major complication rates (~1%)	Found that 45% of patients had durable PVI, while 55% showed pulmonary vein reconnection
Confirmed PFA has fewer major complications than RF ablation (~1% vs. ~3–5%)	Reported a 2.8% complication rate for redo procedures
Shows PFA is safe in large-scale real-world use	Helps understand why PFA may fail and what happens in repeat procedures

Figure 8. Comparison MANIFEST 17k Study vs MANIFEST-REDO Studies

Category	Findings
Study Population	121 patients with paroxysmal atrial fibrillation (AF) underwent PFA
Acute Efficacy	100% acute pulmonary vein isolation (PVI) success rate
Arrhythmia-Free Survival (12 months)	87.4% of patients remained free from AF recurrence at one-year follow-up
Lesion Durability (Follow-up PVI assessment)	84%–96% of pulmonary veins remained durably isolated at 75–90 days post-procedure
Procedure Time	Shorter than RF ablation (but exact median time not reported in this study)
Complications	Low complication rates; No pulmonary vein stenosis, phrenic nerve injury, or esophageal injury
Major Complications	1% incidence of pericardial effusion requiring intervention
Minor Complications	Transient chest discomfort and mild pericarditis, self-resolving within days
Overall Safety Profile	Favorable, with lower risk of thermal injury-related complications compared to RF ablation

Figure 9. Key findings from IMPULSE, PEFCAT, and PEFCAT II Trials.

Reddy VY, Dukkipati SR, Neuzil P, Anic A, Petru J, Funasako M, Cochet H, Minami K, Breskovic T, Sikiric I, Sediva L, Chovanec M, Koruth J, Jais P. Pulsed Field Ablation of Paroxysmal Atrial Fibrillation: 1-Year Outcomes of IMPULSE, PEFCAT, and PEFCAT II. JACC Clin Electrophysiol. 2021 May;7(5):614-627. [25]

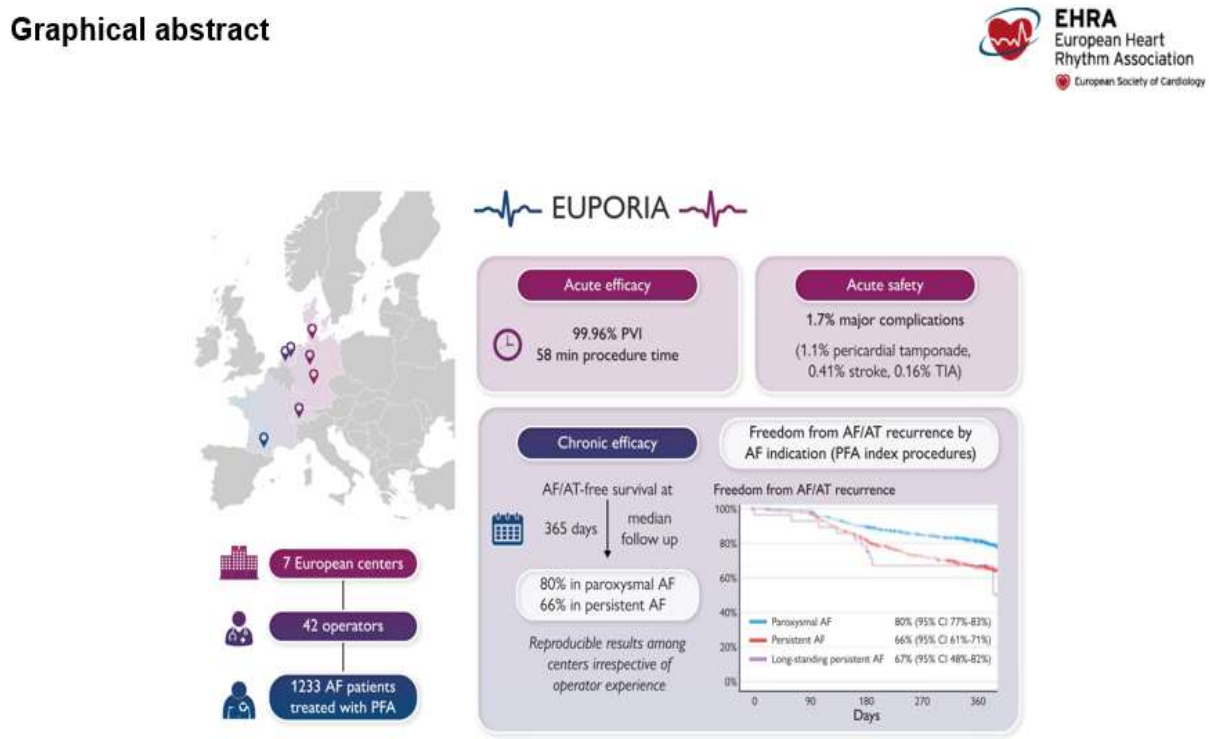


Figure 10. Summary of procedural and clinical outcomes from the EUPORIA registry evaluating pulsed field ablation (PFA) for atrial fibrillation (AF).

Schmidt B, Bordignon S, Neven K, Tondo C, Graziosi M, Halbfass P, et al. European real-world outcomes with pulsed field ablation in patients with symptomatic atrial fibrillation: lessons from the

multi-centre EU-PORIA registry. Europace. 2023;25(7): euad185. doi: 10.1093/europace/euad185. [27]

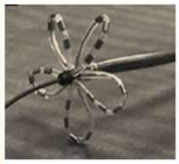
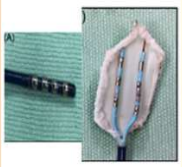
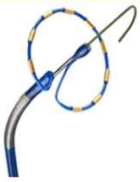
Organization	University of Utrecht	Farapulse	AtriAN	Medtronic PFA	Affera	Galaxy
Primary Catheter Style	Circular: 10 electrodes	Basket/Flower: 5 splines with 4 electrodes each	Focal catheter & glove	Circular: 9 electrodes	Large focal basket	Focal
Catheter Image						
Electrode Configuration	Monopolar	Bipolar	Monopolar	Bipolar	Monopolar	Monopolar
Waveform Style	Long Monophasic (Exponential Decay)	Biphasic	Monophasic	Biphasic	Biphasic	Biphasic
Target Applications	Endocardial atrial ablation	Endocardial atrial ablation	Neuronal ganglionated plexus	Endocardial atrial ablation	Endocardial atrial ablation	Endocardial atrial ablation
Guidance	Fluoroscopy	Fluoroscopy	Epicardial Access	Fluoroscopy	Proprietary 3D electroanatomical mapping	Existing 3D electroanatomical mapping systems

Figure 11. Summary of clinical pulsed electrical field systems currently under evaluation or approved for human cardiac ablation. 3D indicates 3-dimensional; and PFA, pulsed field ablation.

Verma A, Asivatham SJ, Deneke T, Castellvi Q, Neal RE 2nd. Primer on pulsed electrical field ablation: understanding the benefits and limitations. Circ Arrhythm Electrophysiol. 2021;14(9):e010086. Figure 8. doi: 10.1161/CIRCEP.121.010086. [38]

References

[1] Mark DB, et al. Effect of catheter ablation vs medical therapy on quality of life among patients with atrial fibrillation. JAMA. 2019;321(13):1275–85. doi:10.1001/jama.2019.0692

[2] Packer, D.L, et al. Ablation versus drug therapy for atrial fibrillation in heart failure: results from the CABANA trial. Circulation. 2021;143(14):1377-1390. doi:10.1161/CIRCULATIONAHA.120.050463.

[3] Chaumont C, Hayoun C, Savoure A, Al Hamoud R, Auquier N, McDonnell E, et al. Pentaspline pulsed field ablation catheter versus cryoballoon for atrial fibrillation ablation: results from a prospective comparative study. J Am Heart Assoc. 2024;13. doi: 10.1161/JAHA.123.03 46

[4] Koruth JS, Kuroki K, Kawamura I, Brose R, Viswanathan R, Buck ED, et al. Pulsed field ablation versus radiofrequency ablation: esophageal injury in a novel porcine model. Circ Arrhythm Electrophysiol. 2020;13(3):e008303. doi:10.1161/CIRCEP.119.008303.

[5] Cochet H, Nakatani Y, Sridi-Cheniti S, Cheniti G, Ramirez FD, Nakashima Tet al. Pulsed field ablation selectively spares the oesophagus during pulmonary vein isolation for atrial fibrillation. Europace 2021;23:1391–9.

[6] Carta-Bergaz A, Ríos-Muñoz GR, Ávila P, Atienza F, González-Torrecilla E, Arenal Á. Pulsed Field Ablation of Atrial Fibrillation: A Novel Technology for Safer and Faster Ablation. Biomedicines. 2024 Sep 30;12(10):2232. DOI: 10.3390/biomedicines12102232.

[7] Di Biase L, Diaz JC, Zhang X-D, Romero J. Pulsed field catheter ablation in atrial fibrillation. Trends Cardiovasc Med. 2022;32(6):378-387. doi:10.1016/j.tcm.2021.07.006.

[8] Pierucci N, Mariani MV, Laviola D, Silvetti G, Cipollone P, Vernile A, et al. Pulsed field energy in atrial fibrillation ablation: from physical principles to clinical applications. J Clin Med. 2024;13(10):2980. doi:10.3390/jcm13102980.

[9] Kotnik T, Rems L, Tarek M, Miklavčič D. Membrane electroporation and electropermeabilization: mechanisms and models. Annu Rev Biophys. 2019;48:63–91. doi: 10.1146/annurev-biophys-052118-115451.

[10] Reddy VY, Anic A, Koruth J, Petru J, Funasako M, Minami K, et al. Pulsed field ablation in patients with persistent atrial fibrillation. J Am Coll Cardiol. 2020;76(9):1068–1080. doi: 10.1016/j.jacc.2020.07.007.

[11] Reddy VY, Neuzil P, Koruth JS, et al. Pulsed field ablation for pulmonary vein isolation in atrial fibrillation. J Am Coll Cardiol. 2019;74(3): 315-326. DOI: 10.1016/j.jacc.2019.04.021

[12] Reddy VY, Koruth J, Jais P, Petru J, Timko F, Skalsky I, et al. Ablation of atrial fibrillation with pulsed electric fields: an ultra-rapid, tissue-selective modality for cardiac ablation. JACC Clin Electrophysiol. 2018;4(8):987-995. doi: 10.1016/j.jacep.2018.04.005.

[13] Koruth JS, Kuroki K, Iwasawa J, Enomoto Y, Viswanathan R, Brose R, et al. Preclinical evaluation of pulsed field ablation: electrophysiological and histological assessment of thoracic vein isolation. Circ Arrhythm Electrophysiol. 2019;12(5):e007781. doi: 10.1161/CIRCEP.119.007781.

[14] Reddy VY, Anic A, Koruth J, Petru J, Funasako M, Minami K, et al. Pulsed field or conventional thermal ablation for paroxysmal atrial fibrillation. N Engl J Med. 2023;389(18):1660-71. doi:10.1056/NEJMoa2307291.

[15] Verma A, Haines DE, Boersma LV, Sood N, Natale A, Marchlinski FE, Calkins H, Sanders P, Packer DL, Kuck KH, Hindricks G, Onal B, Cerkvenik J, Tada H, DeLurgio DB; PULSED AF Investigators. Pulsed Field Ablation for the Treatment of Atrial Fibrillation: PULSED AF Pivotal Trial. Circulation. 2023 May 9;147(19):1422-1432. doi:10.1161/CIRCULATIONAHA.123.063988.

[16] Ekanem E, Neuzil P, Reichlin T, Kautzner J, van der Voort P, Jais P, et al. Safety of pulsed field ablation in more than 17,000 patients with atrial fibrillation in the MANIFEST-17K study. Nat Med. 2024;30(7):2020-2029. doi:10.1038/s41591-024-03114-3.

[17] 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(9):euad244. doi:10.1093/europace/euad244.

[18] Jiang S, Qian F, Ji S, Li L, Liu Q, Zhou S, Xiao Y. Pulsed Field Ablation for Atrial Fibrillation: Mechanisms, Advantages, and Limitations. Rev Cardiovasc Med. 2024;25(4):138. 138. doi: 10.31083/j.rcm2504138.ins

[19] Musikantow DR, Neuzil P, Petru J, Koruth JS, Kralovec S, Miller MA, et al. Pulsed field ablation to treat atrial fibrillation: autonomic nervous system effects. JACC Clin Electrophysiol. 2023;9(4):481-493. doi:10.1016/j.jacep.2022.10.028.

[20] Reddy VY, Peichl P, Anter E, Rackauskas G, Petru J, Funasako M, Minami K, Koruth JS, Natale A, Jais P, Marinskis G, Aidietis A, Kautzner J, Neuzil P. A Focal Ablation Catheter Toggling Between Radiofrequency and Pulsed Field Energy to Treat Atrial Fibrillation. JACC Clin Electrophysiol. 2023 Aug;9(8 Pt 3):1786-1801. DOI: 10.1016/j.jacep.2023.04.002

[21] Kawamura I, Koruth J. Novel Ablation Catheters for Atrial Fibrillation. Rev Cardiovasc Med. 2024 May 23;25(5):187. doi:10.31083/j.rcm2505187. DOI: 10.31083/j.rcm2505187

[22] Turagam MK, Neuzil P, Schmidt B, Reichlin T, Neven K, Metzner A, et al. Safety and effectiveness of pulsed field ablation to treat atrial fibrillation: one-year outcomes from the MANIFEST-PF registry. Circulation. 2023;148(1):35-46. DOI: 10.1161/CIRCULATIONAHA.123.064959

[23] Li R, Zhang X, Liu X, Gu Z, He J, Dong Y, et al. Effectiveness and safety of pulsed field ablation in patients with atrial fibrillation. JACC Asia. 2024;5(1):143-157. doi:10.1016/j.jacasi.2024.09.014.

[24] Maccioni S, Sharma R, Lee DD, et al. Comparative safety of pulsed field ablation and cryoballoon ablation technologies for pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a critical literature review and indirect treatment comparison. Adv Ther. 2024;41(3): 932-944. DOI: 10.1007/s12325-023-02765-x

[25] Reddy VY, Dukkipati SR, Neuzil P, Anic A, Petru J, Funasako M, Cochet H, Minami K, Breskovic T, Sikiric I, Sediva L, Chovanec M, Koruth J, Jais P. Pulsed Field Ablation of Paroxysmal Atrial Fibrillation: 1-Year Outcomes of IMPULSE, PEFCAT, and PEFCAT II. JACC Clin Electrophysiol. 2021 May;7(5):614-627. DOI: 10.1016/j.jacep.2021.02.014

[26] Kueffer T, Bordignon S, Neven K, Blaauw Y, Hansen J, Adelino R, et al. Durability of pulmonary vein isolation using pulsed-field ablation: results from the multicenter EU-PORIA registry. JACC Clin Electrophysiol. 2024;10(4):698-708. doi:10.1016/j.jacep.2023.11.026.

[27] Schmidt B et al. European real-world outcomes with pulsed field ablation in patients with symptomatic atrial fibrillation: lessons from the multi-centre EU-PORIA registry. Europace. 2023;25(7):euad185. doi: 10.1093/europace/euad185re

[28] Yavin, H. et al. Pulsed field ablation using a lattice electrode for focal energy delivery: biophysical characterization, lesion durability, and safety evaluation. Circ. Arrhythm. Electrophysiol. 2020;13: e008580. doi:10.1161/CIRCEP.120.008580.

[29] Reddy VY, Anter E, Rackauskas G, et al. Lattice-tip focal ablation catheter that toggles between radiofrequency and pulsed field energy to treat atrial fibrillation: a first-in-human trial. Circ Arrhythm Electrophysiol. 2020;13(9):e008718. doi: 10.1161/CIRCEP.120.008718.

[30] Anić A, Debruyne P, Pavlović N, de Asmundis C, Mugnai G, Ströker E, et al. Pulsed field ablation using focal contact force–sensing catheters for treatment of atrial fibrillation: 1-year outcomes of the ECLIPSE AF study. Circ Arrhythm Electrophysiol. 2024;17(2):e012794. doi:10.1161/CIRCEP.124.012794.

[31] Belalcazar A, Heist EK. Comparison of efficiency of PFA catheter designs by computer modelling. J Am Coll Cardiol. 2024;35:2382–2393. doi: 10.1111/jce.16459.

[32] Serban T, Mannhart D, Abid QUA, Höchli A, Lazar S, Krisai P, et al. Durability of pulmonary vein isolation for atrial fibrillation: a meta-analysis and systematic review. Europace. 2023;25(11):euad335. doi:10.1093/europace/etissue uad335.

[33] Reddy VY, Calkins H, Mansour M, Wazni O, Di Biase L, Bahu M, Newton D, Liu CF, Sauer WH, Goyal S, Iyer V, Nair D, Athill C, Hussein A, Whalen P, Melby D, Natale A; AdmIRE Trial Investigators. Pulsed Field Ablation to Treat Paroxysmal Atrial Fibrillation: Safety and Effectiveness in the AdmIRE Pivotal Trial. Circulation. 2024 Oct 8;150(15):1174-1186. doi:10.1161/CIRCULATIONAHA.124.070333.

[34] Maurhofer J, Kueffer T, Madaffari A, Stettler R, Stefanova A, Seiler J, et al. Pulsed-field vs. cryoballoon vs. radiofrequency ablation: a propensity score matched comparison of one-year outcomes after pulmonary vein isolation in patients with paroxysmal atrial fibrillation. J Interv Card Electrophysiol. 2024;67(2):389-397. doi:10.1007/s10840-023-01651-4.

[35] Tom De Potter T, Grimaldi M, Duytschaever M, Anic A, Vijgen J, Neuzil P, et al. Predictors of success for pulmonary vein isolation with pulsed-field ablation using a variable-loop catheter with 3D mapping integration: complete 12-month outcomes from inspIRE. Circ Arrhythm Electrophysiol. 2024;17(5):e012667. doi:10.1161/CIRCEP.123.012667.

[36] Scherr D, Turagam MK, Maury P, Blaauw Y, van der Voort P, Neuzil P, et al. Repeat procedures after pulsed field ablation for atrial fibrillation: MANIFEST-REDO study. Europace. 2025 Jan 17;euaf012. doi:10.1093/europace/euaf012.

[37] Verma A, Haines DE, Boersma LV, Sood N, Natale A, Marchlinski FE, et al. Influence of atrial arrhythmia burden on quality of life in patients undergoing pulsed field ablation: a sub-study of the PULSED AF trial. Heart Rhythm. 2023;20(7):1080-1081. doi:10.1016/j.hrthm.2023.04.056.

[38] Verma A, Asivatham SJ, Deneke T, Castellvi Q, Neal RE 2nd. Primer on pulsed electrical field ablation: understanding the benefits and limitations. Circ Arrhythm Electrophysiol. 2021;14(9):e010086. doi:10.1161/CIRCEP.121.010086.

[39] Ekanem E, Reddy VY, Schmidt B, Reichlin T, Neven K, Metzner A, et al. Multi-national survey on the methods, efficacy, and safety on the post-approval clinical use of pulsed field ablation (MANIFEST-PF). Europace. 2022;24(8):1256-1266. doi: 10.1093/europace/euac050.

[40] Vivek Y. Reddy, Jan Petru, Moritoshi Funasako, et al. Coronary Arterial Spasm During Pulsed Field Ablation to Treat Atrial Fibrillation. Circulation. 2022, Vol.146, No.24, p.1808. doi:10.1161/CIRCULATIONAHA.122.061497.

[41] Farina J, Clò S, Vitali F, Azzolini G. ST-segment elevation in pulsed field ablation for atrial fibrillation. Heart Rhythm. 2024;21(5):698. doi:10.1016/j.hrthm.2023.12.001.

[42] Schaack D, Plank K, Bordignon S, et al. Severe ST-segment elevation and AV block during pulsed-field ablation due to vasospastic angina- a novel observation. J Interv Card Electrophysiol. 2024;67(4):675. doi:10.1007/s10840-024-01813-y.

[43] Ramirez DA, Garrott K, Garlitski A, Koop B. Coronary spasm due to pulsed field ablation: a state-of-the-art review. Pacing Clin Electrophysiol. 2024 Nov 4. doi: 10.1111/pace.15101.

[44] Hasegawa K, Tada H. Coronary artery injury related to catheter ablation for cardiac arrhythmias: a systematic review. *Circ J*. 2025;Adv Pub. doi:10.1253/circj.CJ-24-0859

[45] Füting A, Reinsch N, Höwel D, Brokkaar L, Hartl S, Essling A, et al. Bronchial safety after pulsed field ablation for paroxysmal atrial fibrillation. Circ Arrhythm Electrophysiol. 2023;16(4):e011547. doi:10.1161/CIRCEP.122.011547.

[46] Kurita T. Coronary artery spasms and ST-segment elevation during catheter ablation of pulmonary vein isolation: cause, mechanism, and management. Circ J. 2021;85(3):272-274. doi: 10.1253/circj.CJ-20-1238.

[47] Boriani G, Proietti M. A year in review: atrial fibrillation 2024. Eur Heart J Suppl. 2024;26(Suppl B):B1–B10. doi:10.1093/eurheartj/suaa045.

[48] Della Rocca DG, Del Monte A, Bala G, Pannone L, Ströker E, Monaco C, et al. Transient inferior ST-segment elevation and ventricular fibrillation after cavotricuspid isthmus pulsed-field ablation. JACC Clin Electrophysiol. 2023;9(6):704-706. doi:10.1016/j.jacep.2022.11.027

[49] Vio R, Forlin E, China P. Recurrences after pulsed field ablation of atrial fibrillation: incidence, mechanisms, predictors, and comparison with thermal energy. Medicina. 2024;60(5):817. doi: 10.3390/medicina60050817.

[50] Zhang C, Neuzil P, Petru J, Funasako M, Hala P, Kopriva K, et al. Coronary artery spasm during pulsed field vs radiofrequency catheter ablation of the mitral isthmus. JAMA Cardiol. 2024;9(1):72-77. doi:10.1001/jamacardio.2023.4405.