Catheter Ablation of Atrial Fibrillation Using Pulsed Field Ablation

Pulsed field ablation (PFA) has rapidly emerged as a leading ablation modality for the interventional treatment of atrial fibrillation (AF) and is increasingly used in contemporary clinical practice. PFA offers high procedural efficiency and reduces the risk of thermal collateral damage. However, this shift introduces novel complications, including intravascular haemolysis and proximity-related coronary vasospasm. This review explores the contemporary technological landscape, the shifting safety profile, and strategies for optimal patient selection.

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ABSTRACT

Background: Over the past three decades, thermal ablation modalities defined atrial fibrillation (AF) treatment. By 2026, pulsed field ablation (PFA) has gained widespread adoption and is becoming an increasingly important modality for AF ablation.

Aim: To provide an up-to-date overview of AF ablation in 2026, focusing on efficacy, the integration of PFA with 3D mapping, procedural efficiency, evolving complication profiles, and contemporary approaches to individualized patient selection and shared decision-making.

Summary: Data from recent pivotal trials and large-scale registries demonstrate that PFA is at least as effective and more efficient compared to thermal ablation of AF. The safety profile has shifted, with previously recognized thermal complications, such as atrio-oesophageal fistulae and persistent phrenic nerve palsy, now being extremely rare with PFA. However, non-thermal tissue electroporation introduces modality-specific adverse events. A key safety consideration in PFA is the management of proximity-related coronary vasospasm, especially during cavotricuspid isthmus ablation, alongside intravascular haemolysis that may rarely lead to acute kidney injury.

Conclusion: PFA provides high workflow efficiency and minimizes thermal collateral damage compared to thermal ablation platforms. While efficacy and efficiency are favourable, active management of potential PFA-specific risks is necessary, and definitive long-term arrhythmia-free survival data compared to thermal modalities remain subject to ongoing evaluation.

Keywords: Pulsed field ablation, atrial fibrillation, 3D mapping, complications, patient selection

Introduction

Catheter ablation for atrial fibrillation (AF) has steadily evolved into the cornerstone of interventional rhythm control, relying historically on thermal energy sources. Building on the seminal discovery by Haïssaguerre and colleagues in 1998 that AF is primarily triggered by ectopic beats originating in the pulmonary veins (1), the field progressed from point-by-point radiofrequency ablation (RFA) to single-shot cryoballoon technologies. During this era, ablation has proven superior to antiarrhythmic drugs for maintaining sinus rhythm, as established by landmark trials such as A4 and RAAFT-2 (2,3). Furthermore, the clinical paradigm has shifted toward early rhythm control (EAST-AFNET 4) (4) and first-line ablation strategies (EARLY-AF, STOP AF First) (5,6), continuously expanding procedural volumes.

While clinically effective, all the different thermal modalities achieve pulmonary vein isolation (PVI) through conductive heating or freezing. This propagates energy contiguously through tissues, carrying an inherent risk of thermal collateral damage to adjacent anatomical structures. The necessity to avoid these complications previously limited the speed and extent of ablation procedures.

Evolving Role in AF Ablation

Following early proof-of-concept studies such as IMPULSE and PEFCAT (7), pulsed field ablation (PFA) has emerged as a non-thermal alternative utilizing irreversible electroporation (IRE). The biophysical mechanism differs fundamentally from the immediate coagulative necrosis caused by thermal methods such as radiofrequency ablation (RFA) or cryoablation. PFA delivers ultra-short, high-voltage electrical pulses that destabilize cell membranes, creating nanoscale pores. If this disruption of homeostasis is of sufficient magnitude, the cell cannot restore normal function and undergoes programmed cell death, predominantly via apoptosis (8,9).

A hallmark of PFA is its tissue selectivity. Myocardial tissue has a low threshold for electroporation, whereas adjacent tissues, including oesophageal smooth muscle, vascular endothelium, and nerve fibres, are considerably more resist-

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ant. This allows for effective lesion creation while sparing critical contiguous structures (9). The 2023 ACC/AHA/ACCP/HRS and 2024 ESC guidelines gave Class I recommendations for catheter ablation, including PVI as the primary lesion set in selected patients with symptomatic paroxysmal AF, but they did not make energy-source-specific recommendations for PFA (10,11,). Subsequent randomized trials and the 2026 EHRA/HRS/APHRS/LAHRS/CHRS scientific statement support PFA as an effective alternative to radiofrequency and cryoballoon ablation, with potential safety and procedural-efficiency advantages (9,12,13). Whether it should be considered the universal primary standard of care remains to be determined in future studies.

The Evolution of 3D Mapping

The rapid clinical adoption of PFA has been accelerated by its integration with 3D electroanatomical mapping (EAM) systems. While pre-procedural imaging with computed tomography (CT) or magnetic resonance imaging (MRI) may be obtained to characterize pulmonary vein anatomy, intra-procedural guidance has evolved significantly. During early PFA development, platforms lacked mapping capabilities, necessitating fluoroscopy-guided workflows or pre- and post-procedural mapping using multipolar catheters in conjunction with available EAM systems. This required additional sheath exchanges, increasing procedural complexity and the risk of cerebral embolic events (9).

Routine integration with 3D mapping is now widely available for different PFA platforms. It allows for precise lesion-tagging and ensures contiguous ablation lines with the goal to achieve transmural lesions. Whereas no randomized trial has been shown to increase freedom from AF using an EAM system, its use is associated with reduced fluoroscopy exposure. While the rapidly expanding commercial landscape offers a multitude of PFA catheter geometries, two fundamental conceptual approaches dominate contemporary practice. The following two distinct catheter designs serve as representative examples:

- **Anatomical Mapping using a multi-spline catheter (e.g., FARAWAVE NAV, Boston Scientific):** This system employs an over-the-wire, multi-electrode pentaspline catheter designed for PVI using PFA. The FARAVIEW software specifically integrates the catheter with its proprietary EAM system (OPAL), facilitating fast anatomical reconstruction of the left atrium and real-time lesion tagging. Energy is delivered in a basket or flower configuration for PVI and lesions beyond PVI (Figure 1) (14).
- **High-Density Focal Mapping using a large-footprint catheter (e.g., Affera Sphere-9, Medtronic):** Multi-electrode large-footprint catheters combine high-density mapping with ablation (PFA and RFA) within a lattice-tip. The flexible mesh-like tip equipped with microelectrodes allows for detailed substrate mapping to identify specific electrophysiological targets and delivery of dual-energy ablation (toggling between RFA and PFA). This is relevant for persistent and long-standing persistent AF, where tailored contiguous ablation lesions beyond PVI (e.g., posterior wall isolation or mitral isthmus line) may be required (Figure 2) (15).

Data from pivotal randomized trials, such as ADVENT (13), and large-scale real-world registries, such as EU-PORIA (16), consistently demonstrate that these integrated PFA workflows yield substantially shorter skin-to-skin procedure times compared to thermal modalities (13,14,16).

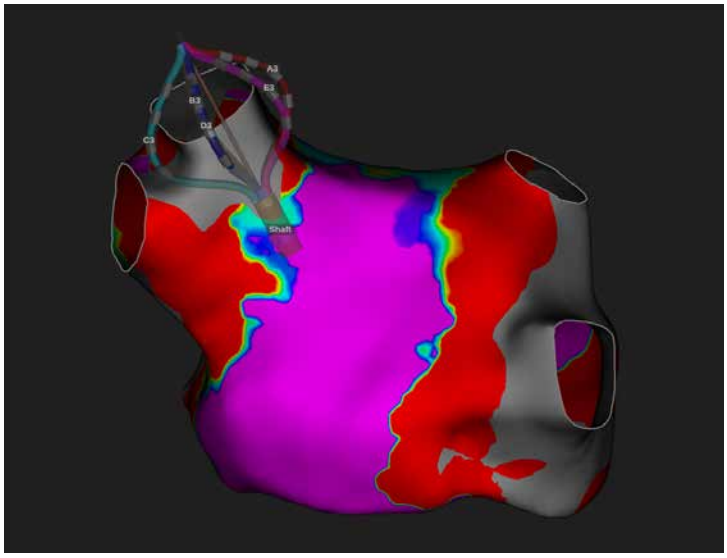


Figure 1: 3D Electroanatomical ***Mapping using a multi-spline catheter (FARAWAVE NAV, Boston Scientific).*** *The pentaspline system (FARAPULSE), initially reliant on a fluoroscopy-guided workflow, demonstrates contemporary integration with 3D mapping in the OPAL system for real-time catheter visualization. A postero-anterior view of the left atrium with the pentaspline catheter in a basket configuration at the ostium of the left superior pulmonary vein. All 4 pulmonary veins are isolated in a patient after PVI (ablated areas with low voltage shown in red). (Image provided by the University Hospital Basel)*

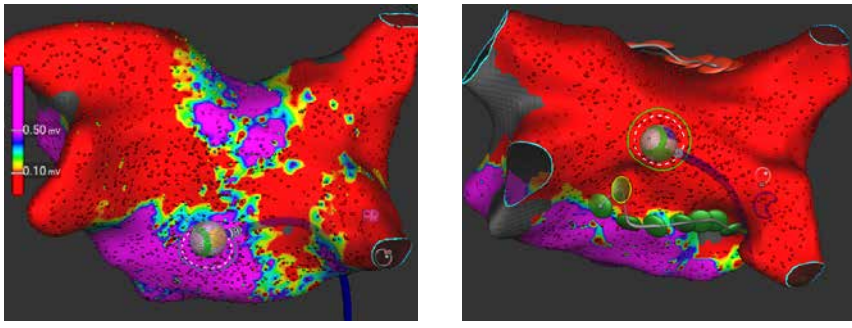


Figure 2: High-Density Focal Mapping using a large-footprint catheter (Affera Sphere-9, Medtronic). The platform operates exclusively with mapping integration, providing high-density voltage maps to delineate prior ablation lesions and low voltage areas. Left: A postero-anterior view of the left atrium in a patient with recurrence of AF after a previous PVI. Mapping shows residual signals at the right inferior pulmonary vein and low voltage areas at the posterior wall. Right: Isolation of the posterior wall using the Affera Sphere-9 dual-energy large-footprint catheter (Anterior roof line using RFA (red dots) and posterior line using PFA (green dots). (Images provided by the University Hospital Basel)

Complication Profiles: Thermal vs. Electroporation

The transition to PFA has fundamentally altered the procedural risk profile. Real-world data and comparative randomized and non-randomized analyses demonstrate that PFA is associated with both a similar overall incidence of adverse events, however the types of complications are significantly different (14,17,18). While generic catheterization risks (e. g., vascular access site complications, cardiac tamponade, stroke, or transient ischaemic attack) remain comparable across all modalities, the mechanism of tissue injury has shifted from thermal contiguity to electrical field effects. This requires a distinctly different approach to complication management (Figure 3).

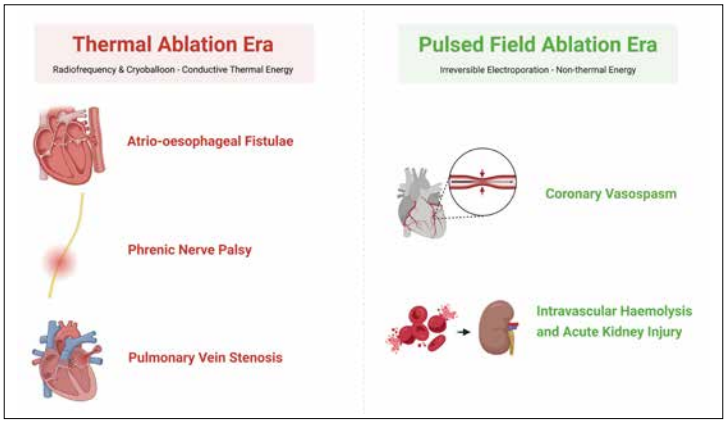


Figure 3: The Shifting Safety Paradigm in Atrial Fibrillation Ablation. A comprehensive side-by-side comparison of complication profiles between thermal ablation (radiofrequency and cryoballoon) and non-thermal pulsed field ablation (PFA). While PFA's tissue selectivity mitigates classical risks such as atrio-oesophageal fistulae, pulmonary vein stenosis, and phrenic nerve palsy, it introduces specific adverse events, notably proximity-related coronary vasospasm and dose-dependent intravascular haemolysis. (Created with BioRender.com)

The Mechanism of Thermal Injury

Thermal ablation modalities (RFA and cryoablation) relied on conductive energy transfer, which inherently affects any tissue in direct contact with or in close proximity to the ablation site. This non-selective mechanism led to several specific procedural risks (17,19):

- **Atrio-oesophageal Fistulae (AEF):** During ablation of the posterior left atrial wall, thermal energy could conduct through the thin myocardial wall into the adjacent anterior oesophagus, causing ischaemic necrosis. Despite the use of oesophageal temperature probes, this rare but life-threatening complication remained a clinical limitation of thermal ablation.
- **Phrenic Nerve Palsy (PNP):** The right phrenic nerve descends in close anatomical proximity to the right superior pulmonary vein. Contiguous freezing from a cryoballoon or less frequently heat from an RFA catheter could result in direct thermal injury to the nerve fibres. While continuous phrenic nerve pacing was used as a monitoring tool during cryoablation to prematurely halt energy delivery, transient and persistent phrenic nerve palsy remained a recognized complication.
- **Pulmonary Vein Stenosis:** Direct thermal injury inside the tubular structure of the vein ostium could cause fibrotic remodelling and subsequent narrowing of the vessel.

Registry data, including the comprehensive MANIFEST-17K cohort, demonstrate that the tissue-selective properties of electroporation have substantially reduced the incidence of these thermal injuries, reporting near-zero rates of phrenic nerve palsy and pulmonary vein stenosis, and no atrio-oesophageal fistulae (14,20). Of note, the incidence of pericarditis has also been reported to be very low (approximately 0.1 – 0.2%) with PFA (20–22).

Modality-Specific PFA Adverse Events

While thermal risks are mitigated, the application of high-voltage electrical fields introduces modality-specific risks that operators must actively manage (9,14):

- **Proximity-related Coronary Vasospasm:** Proximity-related coronary vasospasm has been documented during PFA, particularly during ablation of the cavotricuspid isthmus (CTI) or mitral isthmus (23). In the MANIFEST-17K registry, coronary spasm occurred in 0.14% of patients (14). Pathophysiologically, this relates to transient functional electroporation of vascular smooth muscle cells or local autonomic effects. Current clinical consensus recommends the prophylactic or therapeutic administration of intracoronary or intravenous nitroglycerin prior to ablating in close proximity to coronary arteries (9,23,24).
- **Intravascular Haemolysis and Acute Kidney Injury (AKI):** The electrical fields generated during PFA cause pore formation in erythrocytes passing near the active electrode, leading to intravascular haemolysis (25). This phenomenon is dose-dependent, correlating directly with the number of PFA applications. While subclinical haemolysis is common, severe cases resulting in haptoglobin depletion and AKI requiring temporary haemodialysis occur in rare instances (0.03% in MANIFEST-17K) (14). Pre- and intra-procedural intravenous hydration may be used to maintain renal perfusion and minimize tubular toxicity (9,25). Interestingly, in a non-randomized comparison of 2570 patients undergoing AF ablation, PFA was associated with a 1% incidence of AKI, which was lower compared with thermal ablation (26).
- **Myocardial Injury (Troponin Elevation):** PFA procedures are associated with a significantly higher post-procedural release of cardiac biomarkers (high-sensitivity troponin) compared to thermal ablation (27). It is an expected physiological response to ablation and has not been associated with adverse clinical outcomes. Interestingly, there are marked differences in myocardial injury across different PFA platforms (28).

Efficacy Profile

While the procedural efficiency and specific safety profile of PFA are well documented, its long-term efficacy remains the

subject of ongoing evaluation. Initial pivotal trials, including ADVENT and PULSED AF, demonstrated that PFA is non-inferior to conventional RFA and cryoballoon ablation regarding 1-year arrhythmia-free survival for paroxysmal AF (12,13). Recent randomized trials, including BEAT PAROX AF and SINGLE SHOT CHAMPION, demonstrated that PFA is at least as effective as thermal ablation for paroxysmal AF. Notably, SINGLE SHOT CHAMPION, using continuous rhythm monitoring with implantable loop recorders, showed non inferiority and a borderline superiority of PFA over cryoballoon for 1 year arrhythmia free survival (P = 0.046 for superiority) (18,19).

In persistent AF, where the substrate is often characterized by advanced left atrial cardiomyopathy and fibrosis, PFA's ability to create extensive lesion sets (e.g., posterior wall isolation) without the risk of thermal oesophageal injury provides a potential procedural advantage (15). A recent randomized trial (PIFPAF-PFA) analysing the potential incremental value of posterior wall ablation in addition to PVI in patients with persistent AF was negative regarding the primary endpoint of atrial arrhythmia recurrence lasting > 30 seconds after 1 year, but there was a significant difference favouring additional posterior wall ablation regarding recurrences with longer duration (> 1 hour). However, these findings are hypothesis generating and merit further investigation (30).

Finally, whereas re-mapping studies with PFA indicate high rates of durable PVI, more randomized data beyond 1 to 5 years are required to determine whether PFA suppresses arrhythmia progression more effectively than thermal technologies in the long term (31).

Patient Selection & Management

Guided by the 2024 ESC Guidelines and international expert consensus, patient selection strategies are evolving to leverage the specific safety and efficiency profiles of modern PFA systems (9,11,32). Rather than a niche technology, PFA has rapidly become a preferred modality across a broad spectrum of AF phenotypes. Crucially, modern management emphasizes robust shared decision-making, ensuring that patient values, bleeding risks, and individual symptom burden are thoroughly integrated into the procedural roadmap.

De Novo Atrial Fibrillation

For de novo paroxysmal AF, PFA has demonstrated substantial clinical advantages, establishing it as an optimal first-line strategy (9). High-quality randomized data confirm the robust safety and acute efficacy of PFA in this setting (18). Furthermore, PFA mitigates acute and long-term complications, with evidence indicating that phrenic nerve palsy, atrio-oesophageal fistula, and pulmonary vein stenosis are largely absent following PFA compared to thermal modalities (9,33).

In persistent AF, where ablation beyond PVI may be performed, PFA's tissue selectivity enables extensive substrate modification without the risks historically associated with thermal energy, especially with ablation at the posterior wall (15,34,35). However, more robust randomized trials are needed in this patient population.

Repeat Ablation (Redo Procedures)

Patient selection for redo procedures may favour PFA platforms with integrated high-density 3D mapping. Large-scale registry data have reported on the safety and effectiveness of PFA in repeat interventions, but randomized trials using PFA for repeat ablation are lacking (36). In redo settings after prior failed thermal ablation, high-density mapping delineates PV reconnections prior to PFA delivery (37,38). However, the optimal lesion set in redo procedures especially in case of persistent isolation of all pulmonary veins is still unclear.

Specific Vulnerable Populations

The procedural characteristics of PFA require specific considerations for several clinical subgroups:

- **Heart Failure with Reduced Ejection Fraction (HFrEF):** Specific patient populations with AF and heart failure may benefit from AF ablation (39,40). With PFA, shorter procedure times reduce the duration of sedation or anaesthesia, and the fluid-neutral profile avoids the volume overload seen with irrigated radiofrequency ablation, thereby lowering the risk of peri-procedural acute decompensated heart failure.
- **Elderly and Frail Patients:** Because modern PFA workflows enable shorter procedures that can often be performed under deep sedation rather than general anaesthesia, the risks of postoperative delirium and prolonged recovery may be reduced. This makes PFA an appealing option for octogenarians and frail patients (41). However, this potential advantage has not been tested in a randomized setting.
- **Left Atrial Appendage Occlusion (LAAO) and Cardiac Implantable Electronic Devices (CIEDs):** While PFA simplifies many procedural aspects, specific aspects require caution. In patients with pre-existing lobe-and-disk LAA occluders or those with CIEDs (e.g., pacemakers and implantable cardioverter-defibrillators), operators must carefully navigate to avoid energy delivery in direct contact with device leads or metallic occluder components (9,32,42,43).

Conclusion

The current landscape of AF ablation includes the widespread adoption of PFA integrated with mapping systems. This combination provides procedural efficiency and mitigates the risk of thermal collateral injuries previously associated with radiofrequency and cryoballoon ablation. While the short- to medium-term safety and efficacy profiles are comparable to thermal methods, the shift to non-thermal energy requires clinicians to actively manage modality-specific risks, particularly proximity-related coronary vasospasm and intravascular haemolysis. Ultimately, although PFA is becoming the contemporary standard of care for pulmonary vein isolation, long-term arrhythmia-free survival will require further longitudinal evaluation. □

KEY MASSAGES

- **Technological Shift:** Pulsed field ablation (PFA) has replaced thermal modalities as the standard of care, utilizing tissue-selective irreversible electroporation.
- **Workflow Efficiency:** The integration of PFA with 3D electroanatomical mapping (EAM) is transforming procedures, enabling rapid procedures with low radiation exposure.
- **Shifting Safety Paradigm:** The incidence of thermal collateral damage (e. g., atrio-oesophageal fistulae, phrenic nerve palsy, pulmonary vein stenosis) is substantially reduced compared to thermal ablation. The clinical focus has shifted to managing PFA-specific adverse events, including proximity-related coronary vasospasm and intravascular haemolysis-induced acute kidney injury.
- **Individualized Selection:** Patient management relies on targeted phenotypic stratification, supported by comprehensive shared decision-making.
- **Clinical Outlook:** While currently available trial data show that PFA is at least as effective as thermal ablation, long-term arrhythmia-free survival data in different AF phenotypes and patient populations are still the subject of ongoing clinical investigation.

SUGGESTED READING

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