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Pulsed field ablation in atrial fibrillation ablation: where are we and where are we going?

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Pulsed field ablation (PFA) offers a novel approach to treating atrial fibrillation, demonstrating promising efficacy and safety. Unlike traditional thermal ablation techniques like radiofrequency or cryoablation, PFA uses non-thermal irreversible electroporation to selectively target myocardial tissue, minimizing damage to surrounding structures such as the oesophagus, phrenic nerve, and coronary arteries. Initial studies indicate that PFA is effective in achieving durable pulmonary vein isolation and posterior wall isolation, with a low incidence of serious complications. However, more long-term clinical data are needed to further confirm its efficacy.

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, significantly associated with increased morbidity, mortality, and healthcare cost. Catheter ablation has become a cornerstone in the treatment of symptomatic, drug-refractory AF, with pulmonary vein isolation (PVI) serving as the fundamental target of this intervention. Traditionally, thermal ablation modalities such as radiofrequency (RF) and cryoablation have dominated the field. However, these approaches are not without complications, particularly those related to thermal injury, such as oesophageal damage, phrenic nerve injury, and pulmonary vein stenosis. Pulsed field ablation (PFA), a non-thermal ablation technique that uses the principles of irreversible electroporation (IRE), has recently emerged as a promising alternative. Its myocardial specificity has garnered substantial attention as it promises to reduce complications while maintaining efficacy in arrhythmia termination.

Mechanism of pulsed field ablation

Pulsed field ablation operates based on the principle of IRE. Electroporation involves the application of short bursts of high-voltage electric fields that induce permeabilization of cell membranes. Depending on the magnitude and duration of the electric fields, cells can undergo reversible electroporation or IRE. In IRE, the disruption of the cell membrane's phospholipid bilayer leads to cell death via apoptosis or necrosis. Importantly, IRE has a higher selectivity for certain cell types due to differences in membrane composition and conductivity. Cardiomyocytes exhibit a lower threshold for electroporation compared with non-cardiac cells like fibroblasts, endothelial cells, and neural tissue. This cellular selectivity is attributed to the unique electrochemical properties of the cardiomyocyte membrane and its higher excitability compared with adjacent tissues. This makes PFA an attractive method for selective cardiac ablation, sparing structures such as the phrenic nerve, oesophagus, and coronary arteries that are commonly at risk with traditional thermal ablation modalities. Moreover, IRE's non-thermal nature minimizes the risk of coagulation and scar formation, which are hallmarks of thermal ablation techniques and potential sources of complications. The efficacy and safety of PFA depend on several factors including pulse duration, voltage strength, number of pulses, and electrode design. Various systems have been developed to optimize these parameters for clinical use in AF ablation. For example, biphasic waveforms are commonly used to enhance safety by preventing charge

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accumulation that could lead to tissue damage outside the target area. The field distribution also plays a crucial role in determining lesion depth and homogeneity. Contemporary PFA systems use multi-electrode arrays to deliver energy in a circumferential manner, thereby ensuring efficient and uniform PVI. Unlike thermal energy-based ablation, the effectiveness of PFA lesions seems to be much less reliant on contact force. Early studies showed that PFA can still create effective lesions even without direct tissue contact due to the high conductivity of blood providing an electrical path.[1] This enables PFA to generate contiguous lesions, even in challenging areas like trabeculations. Although contact between catheter and tissue is still preferred, it seems to be less crucial for PFA compared with RF ablation. However, further studies showed that PFA delivered via circular catheters showed that apart from voltage setting, both repetition and catheter contact led independently to deeper lesion formation.[2,3]

Clinical efficacy and safety of pulsed field ablation

The transition of PFA from experimental to clinical settings has been remarkably swift. This is also because beyond its favourable safety and efficacy profiles, PFA has demonstrated a propensity for rapid procedures and efficient learning curves.[4,5]

Several catheters are currently available for clinical use:

(1) Farapulse™ (Boston Scientific): A pentaspline catheter with five splines and 20 electrodes, offered in two sizes (31 and 35 mm). It delivers bipolar, biphasic pulses (1.8–2.0 kV) to create circumferential lesions. Guided by fluoroscopy or 3D mapping, it can operate in non-PV areas. CE marked and FDA approved.
(2) Varipulse™ (Biosense Webster): A 25–35 mm diameter, bidirectional catheter integrated into a 3D mapping system. It uses bipolar, biphasic pulses (1.8 kV) with short applications to deliver overlapping lesions. CE marked.
(3) PulseSelect™ (Medtronic): A fixed-size, multi-polar catheter (25 mm, 20° tilt) for PVI, delivering biphasic waveforms at 1.5 kV. The device is gated to the ventricular refractory period. CE marked and FDA approved.
(4) AFFERA™-Sphere 9™ (Medtronic): A lattice-tip catheter with nine electrodes allowing toggling between monopolar PFA and temperature-controlled RFC ablation. CE marked but not FDA approved.
(5) CENTAURI: Uses standard RFC catheters to deliver biphasic PFA energy (19, 22, and 25 A) through the tip electrode, synchronized with the R-wave. CE marked for atrial arrhythmia treatment.

The technologies described focus on achieving durable PVI, and the rate of acute and long-term PVI is a key performance marker. Multi-centre data from the EU-PORIA registry and ADVENT study[5,6] reported 72 and 64% PVI durability, respectively, with the anterior lateral PVs being more susceptible to recovered LA-PV conduction when the 35 mm catheter was used. Studies tracking freedom from atrial arrhythmia post-PFA ablation found rates of 73.3 and 66.2% after 12 months in the ADVENT and Pulsed AF pivotal trials, respectively.[6,7] In real-world registries with less stringent follow-up, freedom from arrhythmia was 80–82% for paroxysmal AF and 66–72% for persistent AF, comparable with outcomes seen with thermal ablation. However, further long-term real-world data are needed for more conclusive results.

Initial human trials indicated excellent safety, with severe adverse events occurring in 0–2.5% of cases. Notably, no energy-related complications like thermal oesophageal damage or phrenic nerve palsy were reported. Similar results were observed in the ADVENT trial, where the complication rate was 2.1%.[6] However, one death due to pericardial tamponade was recorded. The MANIFEST PF survey[8] documented a decrease in procedure-related complications after workflow improvements, with pericardial tamponade and stroke rates dropping to 0.36 and 0.12%, respectively. Silent cerebral lesions (SCLs) were found in 3–19% of patients undergoing the procedure with the pentaspline catheter, with other studies reporting a post-ablation SCL rate of 9% in the Pulsed AF trial.[7] The Inspire study[9] showed a decrease in SCL rates after workflow optimization, from 67 to 12%. Rare energy-specific issues like coronary spasm and ablation-induced haemolysis were noted, particularly when PFA applications exceeded 70, which also led to acute kidney injury in some cases. Coronary spasm was linked to the proximity of the catheter to the vessel, with the cavo-tricuspid isthmus being the most vulnerable area. Spasms were treatable with nitroglycerin or preventable with intravenous medication.

Posterior wall isolation outcomes with pulsed field ablation

Pulsed field ablation has shown promising outcomes in isolating the posterior left atrial posterior wall, which plays a key role in maintaining AF, especially in patients with persistent forms of the arrhythmia. In the pivotal PersAFOne trial, 100% success in acute PVI and posterior wall isolation (PWI) was achieved.[10] Remapping at 2–3 months showed durable isolation in 96% of PVs. No oesophageal or PV stenosis complications were reported.

Recent studies have underscored the efficacy and safety of PFA in achieving PWI with reduced risk of complications. Schiavone *et al.*[11] demonstrated that PFA was highly effective in achieving both PVI and PWI, with an overall acute success rate of 98.5% for PWI and no oesophageal injury. Similarly, Banai *et al.*[12] reported that PFA was successful in preventing the development of left atrial restrictive physiology, a known complication associated with extensive posterior wall ablation, demonstrating PFA's ability to safely achieve PWI while sparing critical structures. Badertscher *et al.*[13] explored mid-term outcomes of PFA for PWI, finding that the technology produced durable lesions with a low recurrence rate of AF over a 6-month follow-up, further supporting its clinical applicability. Moreover, Kueffer *et al.*[14] highlighted the procedural safety and efficacy of PFA for PWI in their prospective study, showing that PFA achieved high rates of isolation with a favourable safety profile, even in redo procedures where scar burden is higher. Collectively, these studies affirm that PFA offers a significant advance in posterior wall ablation, with

promising safety and efficacy, particularly in complex AF cases.

Procedural costs

Regarding procedural costs, Calvert *et al.*[15] compared the costs, efficiency, effectiveness, and safety of PFA, cryoballoon, and RF for AF ablation. Among the 707 patients enrolled, the investigators found that although PFA had shorter skin-to-skin and catheter laboratory times, procedural costs were significantly higher, largely due to the increased cost of equipment. However, costs associated with personnel employment are difficult to estimate accurately, as are the varying costs of kits across different nations. While the initial cost of PFA systems may be higher due to the advanced technology and catheter design, it could lead to reduced overall costs by progressively shortening procedure times. Additionally, PFA's tissue specificity reduces the risk of collateral damage to adjacent structures, potentially lowering expenses related to post-procedure complications, although these outcomes will require long-term evaluation. Finally, the increasing competition in the market, as different PFA systems gain approval and adoption in the EU and the USA, is expected to gradually reduce costs through market dynamics. Further studies are necessary to assess the long-term economic impact of PFA as its adoption continues to grow.

Future directions

The future of PFA in AF ablation is poised for continued growth, driven by ongoing technological advancements and expanding clinical evidence. Several key areas are likely to shape the future role of PFA in the treatment of AF:

(1) Expanded indications: While initial studies have focused on PFA for paroxysmal AF, there is growing interest in exploring its role in more complex arrhythmias, such as long-standing persistent AF. Additionally, the utility of PFA for arrhythmias beyond AF, including ventricular tachycardia and atrial flutter, is under investigation. The safety profile of PFA could make it an attractive option for arrhythmias located near critical structures.
(2) Technological improvements: As with any evolving technology, continuous advancements in catheter design, energy delivery systems, and mapping integration are anticipated. Future PFA systems may incorporate real-time lesion assessment tools, which could enhance the precision of ablation and reduce the need for repeat procedures. Additionally, refinements in catheter designs, such as the development of steerable or multi-electrode catheters with increased flexibility, may further improve the ease and accuracy of PFA.
(3) Hybrid approaches: While PFA has shown significant promise for PVI, combining it with other modalities such as RF ablation or cryoablation may be beneficial in treating complex cases involving non-pulmonary vein triggers.[16] Hybrid approaches that leverage the strengths of multiple ablation techniques could offer improved outcomes in patients with persistent or recurrent AF.
(4) Long-term data and outcomes: Although early studies have demonstrated the short-term efficacy and safety of PFA, more long-term data are needed to assess the durability of PVI and PWI achieved with PFA. Long-term follow-up studies will be critical in determining whether PFA can reduce the rate of AF recurrence and the need for repeat ablation procedures. Furthermore, the impact of PFA on long-term stroke risk and heart failure outcomes in AF patients remains an area of active investigation.
(5) Integration into guidelines: As the evidence base for PFA continues to grow, it is expected that major cardiology societies will incorporate PFA into clinical guidelines for AF ablation. Given its favourable safety profile, PFA may be particularly advantageous for use in patients at high risk of complications from thermal ablation, such as those with oesophageal disease, phrenic nerve vulnerability, or prior failed ablations.

Conclusion

Pulsed field ablation represents a transformative advance in the treatment of AF. Its tissue selectivity, rapid lesion formation, and favourable safety profile offer significant advantages over traditional thermal ablation techniques. While early clinical results are promising, further research is required to optimize PFA technology, expand its indications, and confirm its long-term efficacy and safety. With continued innovation and clinical validation, PFA may soon become the preferred modality for AF ablation, marking a major paradigm shift in arrhythmia management.

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Data availability

There are no new data associated with this article.

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