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Pulsed Field Ablation: The Future of AF Treatment

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Introduction

Catheter-based pulmonary vein isolation (PVI) is an established and effective treatment for symptomatic atrial fibrillation (AF), demonstrating superiority over antiarrhythmic drug therapy in maintaining sinus rhythm and improving symptoms (1–2).

Despite three decades of progress since the advent of PVI, two principal concerns remain. First, approximately one in three patients experience recurrence of atrial arrhythmias within one year of the procedure (3). Second, current ablation techniques employ radiofrequency or cryothermal energy, which may cause indiscriminate tissue injury to surrounding structures such as the oesophagus and phrenic nerve. Although infrequent, this can result in serious complications – in some cases leading to death (4–7).

Pulsed field ablation (PFA) promises to address both concerns. It utilises the delivery of rapid pulses of high voltage energy, increasing cell membrane permeability, disrupting cellular function, and leading to death - a process known as irreversible electroporation (Figure 1). Cardiomyocytes are preferentially affected as they have a lower

Take Home Messages

- Pulsed field ablation (PFA) is a promising alternative to conventional radiofrequency and cryoballoon ablation, causing selective myocardial electroporation.
- Clinical trial evidence demonstrates comparable efficacy to existing ablation modalities and a favourable short-term safety profile.
- PFA enables faster procedures, but the requirement for general anesthesia and higher procedural costs may limit widespread adoption.
- There is need for caution as longer term safety data and previously unreported complications emerge.

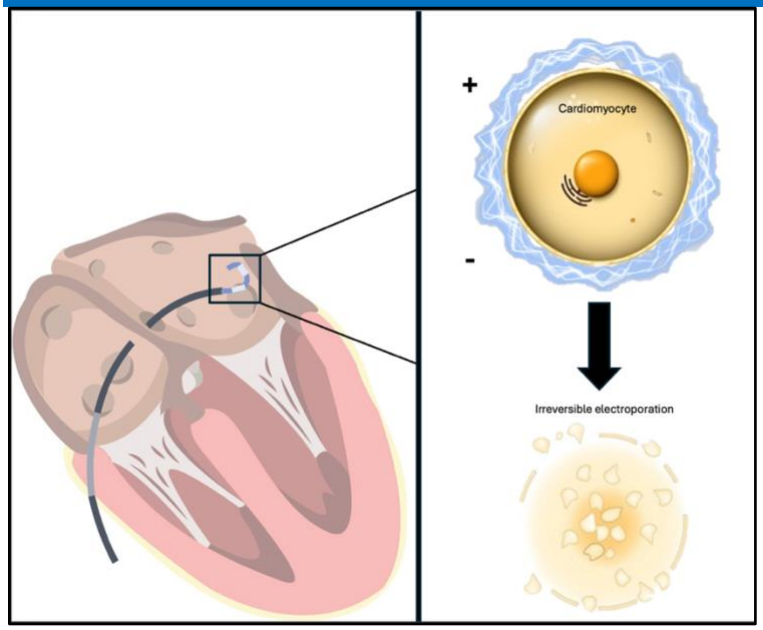

Figure 1: A visual schematic of pulsed field ablation. (Left) a PFA delivery catheter sits within the left atrium of the heart, at the ostium of the left upper pulmonary vein. (Right) an illustration of irreversible electroporation, the electrical field increases cell membrane permeability, resulting in cell function disruption and eventually cell death.

electrical threshold for electroporation – thus sparing surrounding structures (8–9). Preclinical studies show that PFA produces deep transmural lesions with effective electrical isolation (10–11).

Efficacy from Randomised Controlled Trials

ADVENT was a noninferiority randomised controlled trial (RCT) enrolling 706 patients with symptomatic paroxysmal AF to receive to either PFA or conventional (radiofrequency or cryoballoon) ablation (Figure 2)(12). The composite primary endpoint (freedom from initial procedural failure, recurrent atrial tachyarrhythmia, antiarrhythmic drug use, cardioversion or repeat ablation) was assessed over one year using weekly ECG recordings and 6-monthly 72-hour Holter monitoring.

- At one year, treatment success was achieved in 73.1% of patients in the PFA arm and 71.3% in the thermal ablation arm, meeting prespecified noninferiority criteria (>0.999 posterior probability; 95% BCI –1.5 to 1.5).
- There were no cases of atrioesophageal fistula or pulmonary vein stenosis in either group. Two phrenic nerve palsies occurred, both in the thermal ablation arm.

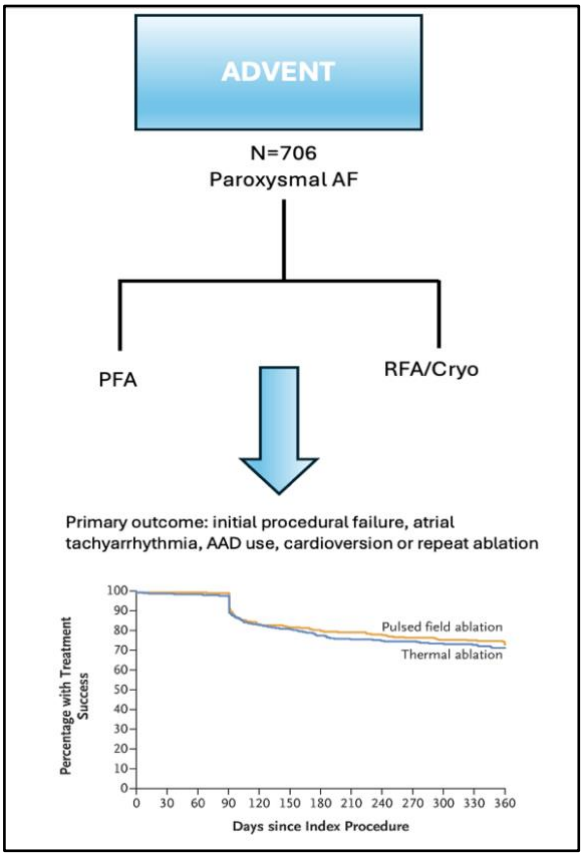

Figure 2: A Kaplan-Meier survival curve for freedom from the composite primary endpoint, comparing pulsed field ablation to thermal ablation in the ADVENT trial. Adapted from Reddy et. al[12]

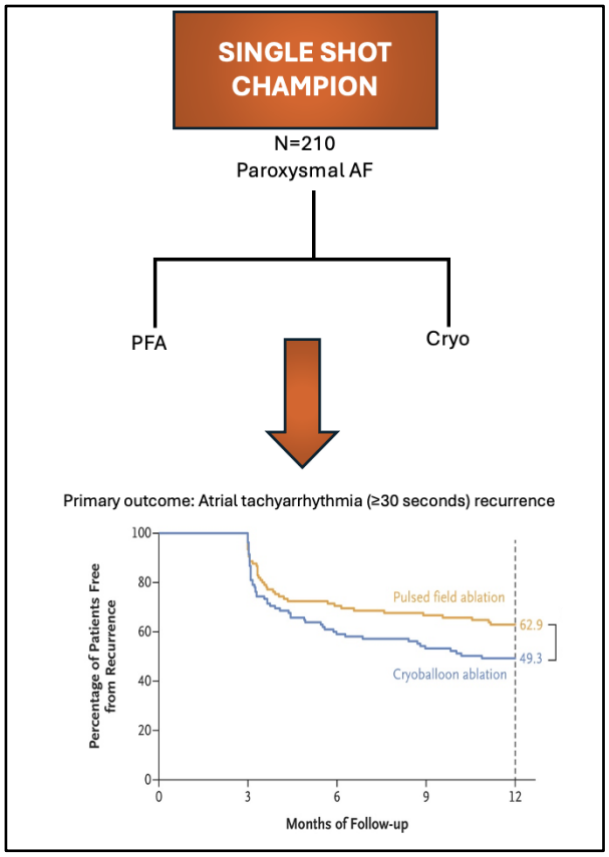

Figure 3: a Kaplan-Meier survival curve for freedom from the primary endpoint, comparing pulsed field ablation to thermal ablation in the SINGLE-SHOT CHAMPION trial. Adapted from Reichlin et. al[13]

SINGLE SHOT CHAMPION randomised 210 patients with paroxysmal AF to PFA or cryoballoon ablation. The primary endpoint was recurrence of atrial tachyarrhythmia (≥30 seconds), monitored by implantable loop recorder at one year (Figure 3)(13).

- Recurrence occurred in 37.1% of the PFA group and 50.7% of the cryoballoon group, meeting statistical thresholds for both noninferiority ($p<0.001$) and superiority ($p=0.046$).
- One stroke occurred in the PFA arm, and two cardiac tamponades requiring drainage were reported in the cryoballoon arm. No thermal-related complications were observed.

Practical Considerations

Time

PFA is known to have significantly shorter procedural times, compared to thermal ablation strategies due to faster lesion delivery. In a study by Calvert et. al (Table 1)(14) 707 consecutive patients underwent first time AF ablation. Median skin-to-skin duration for PFA was 68 minutes compared to 91 minutes for cryoballoon and 88 minutes for radiofrequency ($P<0.001$) whilst maintaining excellent procedural efficacy (98.6% acute procedural success) and safety (0.5% major complication).

Availability

Another consideration is the need for PFA to be performed under general anaesthesia. High-voltage electrical pulses cause involuntary skeletal muscle contractions, resulting in significant patient discomfort which cannot be adequately managed with conscious sedation alone. The mandatory requirement for general anaesthesia necessitates the presence of an anaesthetist, adding to both direct costs and scheduling complexity. In many UK centres, access to anaesthetic support is limited by competing demands from other surgical services, restricting PFA to dedicated lists rather than routine catheter laboratory slots. This constraint significantly impacts service flexibility and may prevent implementation across hospitals where anaesthetic resources are prioritised for emergency and surgical cases.

Cost

In cost-effectiveness analyses, PFA appears to be more expensive at £10,010 per procedure. This is 23% more than cryoballoon (£8,106) and 12% more than radiofrequency ablation (£8,949) (14). This is driven in the main by higher equipment prices and mandatory anaesthetic support costs. Early adoption requires consideration of the capital investment, though these must be weighed against greater procedural efficiency and shorter catheterisation laboratory occupancy.

	PFA	Cryoballoon	Radiofrequency
Skin-to-skin Time	68 min	91 min	88 min
General Anaesthesia	100%	10.2%	61.5%
Acute success	98.6%	95.1%	99.4%
Major complications	0.5%	1.5%	0.6%
Fluoroscopy time	19 min	18 min	4 min
Total Costs	£10,010	£8,106	£8949

Table 1: Real-world practical procedural data of 3 atrial fibrillation ablation modalities. Adapted from Calvert et. al (14)

Safety Profile and Emerging Concerns

In both RCTs, PFA demonstrated an excellent safety profile. MANIFEST-17K is the largest published registry of PFA safety outcomes (15). It contains observational data for 17,642 patients undergoing PFA over a 2 year period. Whilst PFA seems to avoid complications associated with thermal ablation, all studies to date have only evaluated short-medium term safety outcomes. In MANIFEST-17K, there were 25 (0.15%) reported instances of coronary artery spasm. Although these were related to proximity during ablation near coronary arteries, there has since been newer reports of remote and delayed severe coronary spasm following PFA, leading to cardiogenic shock and cardiac arrest (16). Other complications such as haemolysis and acute kidney injury have also been noted and warrant further investigation. There is need for caution as longer term safety data and previously unreported complications continue to emerge.

Conclusions

In summary, PFA's promise of rapid lesion delivery with myocardial selectivity and excellent short-term safety profile is cause for optimism for the future treatment of AF. However, the incidence of complications such as coronary spasm, and overall longer term cost-effectiveness of PFA remain to be established. As with all innovations in ablation technology, sustained benefit should be determined through continued longitudinal evaluation of real world-outcome data. Thus, we must move beyond short-term procedural success and invest in long-term, multicentre outcome studies that capture durability, safety, and meaningful patient benefit.

Disclosures

None

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