

Pulsed Field Ablation for the Interventional Treatment of Atrial Fibrillation. A Scientific Statement of the European Heart Rhythm Association (EHRA) of the ESC, the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS) and the Canadian Heart Rhythm Society (CHRS)

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1 **Abstract**

2 Pulsed field ablation has emerged as a novel non-thermal treatment modality with a distinct
3 safety profile for the interventional treatment of atrial fibrillation. By inducing irreversible
4 electroporation, pulsed field ablation achieves myocardial ablation while preserving
5 surrounding structures such as nerves, vasculature, and the esophagus. This European
6 Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC) scientific
7 statement, endorsed by major international societies, reviews the biophysics, technology,
8 clinical evidence, workflow, safety, and training aspects of pulsed field ablation.
9 Randomized trials demonstrate comparable efficacy to radiofrequency and cryoballoon
10 ablation, with advantages in safety and efficiency. The statement provides practical advice
11 for clinical implementation, operator training, and identifies key gaps in evidence and
12 priorities for future research and innovation.

13

14 **Keywords:**

15 Pulsed field ablation, atrial fibrillation, electroporation

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1 Introduction

2 Catheter ablation has become a cornerstone in the treatment of atrial fibrillation (AF), aiming to
3 achieve durable pulmonary vein isolation (PVI) and thereby eliminate arrhythmogenic triggers
4 within the pulmonary veins (PV). For over two decades, radiofrequency (RF) and then cryothermal
5 ablation have been the predominant energy sources used for AF ablation. While effective, these
6 thermal modalities rely on tissue heating or freezing, potentially resulting in collateral injury to
7 surrounding structures such as the oesophagus and the phrenic nerve. Despite continuous
8 refinements in technology and workflow, major complications such as atrio-oesophageal fistula
9 and pulmonary vein stenosis remain rare but potentially fatal, whereas phrenic nerve palsy,
10 although generally non-fatal, is associated with significant morbidity. These limitations have driven
11 the search for alternative, safer, and more selective energy sources.

12 Pulsed field ablation (PFA) has emerged as a novel ablation modality based on the principle
13 of irreversible electroporation. PFA disrupts cell membrane integrity through the delivery of
14 high-voltage, short-duration electrical pulses. These pulses create nanoscale pores, alter
15 transmembrane potential, and disturb cellular homeostasis, ultimately leading to cell
16 death. Because myocardial tissue has a lower electroporation threshold than surrounding
17 structures, PFA may allow relatively selective myocardial injury.¹ The myocardial sensitivity
18 and short energy application duration of PFA translate into an improved safety profile and
19 the potential to simplify ablation workflows. In preclinical and clinical studies, PFA has
20 demonstrated durable lesion formation, minimal thermal effect, and preservation of
21 extracardiac structures.

1 Since its first clinical applications, PFA has progressed from early feasibility to widespread
2 adoption. Multiple catheter platforms and generators are now available, including multi-spline
3 catheters, circular catheters, large-footprint lattice-tip catheters, balloon systems, focal solid-tip
4 catheters, and dual-energy designs that combine both PFA and RF delivery. Randomized
5 controlled trials and large registries have confirmed the clinical efficacy of PFA to be at least
6 equivalent to that of thermal ablation, while procedure times are generally shorter and
7 complication rates - particularly oesophageal and phrenic nerve injury - are lower. Whether PFA
8 fundamentally alters ablation strategies beyond PVI, improves durability at non-pulmonary vein
9 targets, or safely expands the range of atrial substrate that can be treated by ablation remains an
10 area of active investigation.²

11 Given the rapid clinical uptake of PFA, comprehensive practical guidance on its principles,
12 procedural application, safety considerations, and associated training requirements is needed.
13 This scientific statement by the European Heart Rhythm Association (EHRA) of the ESC and
14 collaborating partner societies worldwide, summarizes current evidence, provides practical
15 guidance for clinical use and training, and outlines priorities for future research to ensure safe and
16 standardized global implementation of PFA in the interventional treatment of AF.

17 Biophysics of pulsed field ablation

18 Background and development

19 The year 2007 marked an important milestone in the development of Pulsed Field Ablation
20 (PFA), which gained significant interest due to two independent publications.^{3,4} The first PFA
21 systems were using DC/monophasic pulses, either exponentially decaying or monophasic
22 100 μ s pulses (**Figure 1**). The first PFA systems were developed for pulmonary vein isolation,

1 creating lesion depths of 2-5 mm. Currently, most of the systems can achieve these depths
2 easily but when tested in ventricles with thicker tissue they can only achieve lesion depths
3 of 6-8 mm, irrespective of different waveforms and catheter designs.⁵ In general, the
4 waveform parameters remain mostly undisclosed as proprietary information, which makes
5 comparison of PFA systems and collective learning difficult.

6 Mechanism of action

7 When high voltage pulses are delivered between two or more electrodes, an electric field and
8 current (density) are established in the tissue. The electric field is the highest close to the
9 electrode and decreases rapidly with distance. Similarly, current density is the highest around the
10 electrodes, in particular at sharp edges and between neighbouring electrodes on the catheter.
11 Current flow through the tissue causes tissue heating, albeit significantly less in magnitude and
12 duration than the resistive heating associated with radiofrequency energy. At low frequencies,
13 current mainly flows through the extracellular milieu. The lipid bilayer of the cell membrane is
14 poorly conductive and acts as a barrier to electrical current. As a result, a potential difference is
15 built across the membrane (e.g. 0,5 V), amplifying the electric field. This leads to a high field within
16 the membrane (0,5 V over 5 nm distance, 10^8 MV/m). This field causes pore formation, allowing
17 water and reactive oxidative species (ROS) to reach into the hydrophobic domain of the lipid
18 bilayer. This causes lipid oxidation and damages transmembrane proteins – all together
19 contributing to sustained increased membrane permeability.⁶ Increased membrane permeability
20 for molecules otherwise deprived of transmembrane transport mechanisms also results in often
21 only transient increased conductivity to ions (e.g. Na, K, Ca) and can affect a significantly larger
22 area, rendering cells in this area unexcitable and unable to propagate action potentials. This
23 phenomenon is also reflected by a rapid and significant decrease of bipolar EGM signals with
24 PFA.⁷ Membrane resealing and cell recovery, however, render some of these cells excitable

1 within minutes.⁸ Repair of the membrane and recovery of cells may require up to several minutes,
2 depending on the extent of electroporation and damage inflicted to the cell membrane but can be
3 quite unpredictable.⁹ Since sufficiently high electric fields can electroporate any cell, this may
4 result in stunning and damage of nerves and conduction system.^{10–14} If the cell does not recover,
5 cell death due to loss of homeostasis occurs (irreversible electroporation) which does not
6 necessarily occur instantaneously. Cell death pathway and its dynamics may depend on the
7 waveform and amplitude (**Figure 2**).¹⁵

8 In addition to membrane effects, electroporation induces transient microvascular changes,
9 including temporary capillary flow reduction and increased endothelial permeability.^{16–18}
10 These effects represent functional and largely reversible alterations in vascular tone and
11 endothelial integrity rather than structural damage to the extracellular matrix, which remains
12 preserved. Increased permeability may lead to transient oedema formation.¹⁹ The resulting
13 transient disruption of oxygen and nutrient supply to the tissue may further contribute to
14 lesion formation. Since electroporation is a membrane phenomenon, it does not affect
15 extracellular matrix (ECM), provided there is no significant increase in temperature. Factors
16 such as the availability of blood supply (preservation of microcirculation) and the
17 extracellular matrix facilitate tissue repair. Notably, lesion development and maturation in
18 PFA appear to occur more quickly compared to RF and cryoablation (**Table 1**).²⁰

19 During the delivery of high-voltage pulses (mostly ≤ 3000 V, 10-30 A), significant
20 instantaneous power is delivered. In areas where the electric field and current density are
21 highest, catheter and tissue can heat up. Depending on the duty cycle (i.e. how much energy
22 is delivered per unit of time) significant temperature increases can be achieved with varying
23 degrees of thermal damage to the tissue.^{19,21} The damage of tissue in the immediate vicinity

1 of the catheter is therefore likely to be thermal in nature indicating that during PFA the
2 endothelium may be damaged thermally,²² as may the phrenic nerve in case of epicardial
3 ablation.²¹ Lesion shape and size can differ, depending on the mode of PFA delivery
4 (monopolar vs bipolar) and characteristics of the catheter (solid tip, large focal vs
5 multipolar).²³ The characteristics of the delivery catheter also affect the required contact
6 with the tissue, enabling the formation of contiguous lesions even in trabeculated areas.^{24–26}
7 Furthermore, as blood is a better conductor than tissue, the electric field extends into the
8 blood pool causing electroporation of blood cells. With an increasing number of
9 applications, significant hemolysis has been observed (see chapter 6.2.1.1). Finally,
10 electroporation has been demonstrated in vitro to induce platelet activation and modulate
11 neutrophil activation.^{27,28}

12 Comparison with other ablation technologies

13 PFA destroys cells within the tissue by overwhelming their capacity to recover from
14 membrane damage and disruption of cell homeostasis (**Table 1**). Electroporation transiently
15 increases membrane permeability, allowing molecules and ions to cross the plasma
16 membrane, which consequently leads to cell death. Although the exact dynamics and
17 mechanisms of cell death are not entirely clear, a massive influx of Ca and ATP depletion are
18 contributing factors or are at least hallmarks of cell death. In contrast, RF creates irreversible
19 tissue injury when resistive or conductive heating results in tissue temperatures greater than
20 50°C leading to protein denaturation and coagulative necrosis, while cryoenergy leads to

1 irreversible cell death via freeze-thaw cycling, disrupting cell membranes and inducing
2 ischemia.

3 Biomarker release

4 Due to the different mechanism of action of PFA, but also probably because of a greater
5 extent of ablation, biomarkers exhibit different temporal dynamics and levels compared to
6 RF and Cryoablation. Recent studies have shown significant differences in the dynamics and
7 elevated levels of biomarkers indicative of myocardial injury (i.e. hs-cTnT, Myoglobin, CK-MB)
8 after PFA compared to RF ablation.²⁹ Furthermore, differences seem to exist between
9 different PFA systems, which may in part relate to variations in catheter design, including
10 electrode surface area, geometry, and energy delivery characteristics that influence blood-
11 electrode interaction and field distribution. Importantly, reduced glomerular filtration can
12 amplify these effects.³⁰ A recent systematic review of available studies suggested that the
13 severity of hemolysis correlates with procedural factors and catheter design.³¹ The increase
14 of inflammation biomarkers (i.e. CRP), following PFA and RF was found to be similar.
15 However, it was observed that CRP normalization occurred more rapidly after PFA than after
16 RF. Markers of renal function and electrolyte balance exhibited only minor fluctuations over
17 time, remaining within the expected physiological range for PFA and RF.³²

1 Technological considerations

2 Available PFA platforms

3 Contemporary PFA catheter technology can be categorized into three main groups.

4 Circumferential PVI tools are large-area or balloon-based systems designed for rapid and
5 efficient pulmonary vein isolation (**Table 2**). Their strengths lie in procedural simplicity, short
6 ablation times, and robust safety data.

7 The second group comprises large-footprint catheters that integrate with 3D
8 electroanatomical mapping systems (**Table 3**). These devices can be used both for PVI and
9 linear ablation, and potentially individualized lesion sets guided by 3D mapping. Their
10 principal advantage is adaptability and the ability to create broad lesion sets in both atrial
11 and ventricular tissue, while limitations include the need for advanced mapping, limited
12 clinical experience to date, and the ongoing development of reliable contact and lesion
13 assessment tools.

14 The third group includes systems that use conventional small-tip RF catheters to deliver PFA
15 through established contact-force mapping and ablation catheters (**Table 4**). This approach
16 combines the flexibility of point-by-point lesion creation with the familiarity of standard
17 workflows and is suitable for both atrial and ventricular arrhythmia ablation. Advantages
18 include versatility, individualized lesion sets, and integration into existing electrophysiology
19 labs. Limitations are that these systems require “point by point” operator skills, which may
20 translate into longer or workflow-dependent procedures for PVI, while PFA energy delivery

1 parameters still require optimization for some systems that are in early clinical evaluation.
2 Of note, multiple novel devices are currently under development; therefore, no complete list
3 can be obtained. Details of current catheter technologies are summarized in **tables 2-4**.
4 Given the substantial heterogeneity in PFA catheter design and terminology, harmonization
5 is needed to facilitate comparison across studies and platforms; current PFA catheters can
6 be grouped accordingly, and a recent consensus proposal suggests classifying systems
7 based on the largest dimension in contact with tissue as regional (>12 mm), large-tip focal
8 (>4 – ≤ 12 mm), or focal (≤ 4 mm, **Table 5**).

9 Energy delivery and dosing

10 Energy delivery in PFA is defined by pulse amplitude (typically 500–3000 V), pulse duration
11 (nanosecond to microsecond range), pulse number, repetition frequency, and waveform
12 (monophasic vs biphasic, monopolar vs bipolar, square vs sine wave). These parameters
13 determine the biological effect at the cellular level and drive lesion size and shape. Bipolar
14 delivery and biphasic waveforms can reduce charge buildup and muscle stimulation, while
15 monopolar delivery and monophasic waveforms typically produces deeper lesions.
16 Catheter design — including electrode geometry, interelectrode spacing, and
17 multielectrode arrays — shapes and affects the electric field distribution, lesion morphology
18 and its consistency. Irrigated versus non-irrigated designs influence thermal management
19 rather than primary lesion mechanism. Synchronized delivery with the cardiac cycle (ECG-
20 gating) is abandoned in most of the platforms currently in clinical use for atrial ablations due
21 to low arrhythmogenicity of biphasic pulses as demonstrated in large clinical studies.³³

1 Delivery strategies vary: focal or large-focal point-by-point PFA with steerable catheters for
2 linear or focal lesions, and multielectrode systems with diverse geometries for rapid PVI.
3 Safety considerations include preventing unintended arcing, monitoring for conduction
4 system capture, avoiding excessive overlap of high-intensity fields near critical structures,
5 and adherence to device-specific dosing protocols derived from preclinical and clinical
6 data.

7 Dual energy (PFA/RFA) ablation systems

8 Dual-energy ablation systems combine RF and PF technologies within a single device. RFA
9 and PFA delivery is integrated through unified power management and control architecture.
10 The electrode array of the catheter is connected to a generator capable of switching between
11 RF output and biphasic or monophasic high-voltage PF trains. Internal solid-state switching
12 circuits or H-bridge inverters reconfigure the output stage to match the impedance and
13 waveform requirements of each mode. During operation, impedance, temperature, and
14 voltage sensors embedded in the catheter provide continuous feedback to the generator's
15 microcontroller. This feedback loop governs energy delivery, preventing excessive tissue
16 heating during RF mode and provides over-current protection and reliable pulse delivery.
17 One dual-energy system (Affera Sphere 9, Medtronic) comprises a 9 mm tip sphere catheter,
18 formed by an expandable nitinol lattice³⁴. Another system (ThermoCool SmartTouch SF Dual
19 Energy Catheter and TRUPULSE Generator, Johnson & Johnson) uses an existing contact-
20 force RF catheter (SmartTouch SF) modified to deliver both RFA and PFA energy using a single

1 catheter/generator combination and integrates with the CARTO-3 mapping system. Other
2 systems are under investigation.

3 Dual-energy ablation platforms are designed to harness the complementary advantages of
4 PFA and RFA to maximise procedural safety, versatility, and efficacy. A dual-energy system
5 allows operators to tailor energy delivery based on anatomy, where PFA may be used for thin-
6 walled structures, while RFA is suitable for thicker myocardium and in locations where
7 coronary artery spasm may be a concern. A combination of PF and RF lesions may be
8 employed to create a deeper lesion.^{35,36} The ability to switch between PFA and RFA modes
9 within the same catheter and generator may reduce the need for multiple catheters, catheter
10 exchanges and may streamline procedures. For some ablations, this flexibility might
11 potentially reduce procedure times, increase first-pass success, and reduce complications,
12 but comparative outcome data is awaited.

13 Patient selection and procedural considerations

14 Primary uses of PFA

15 Clinical context of de novo AF ablation

16 Pulsed field ablation (PFA) for de novo paroxysmal atrial fibrillation (AF) has demonstrated
17 clinical advantages, particularly in terms of safety, efficiency, and procedural consistency.
18 To date, more than 500,000 procedures with the pentaspline PFA catheter have been
19 performed worldwide without a single reported case of atrio-esophageal fistula (AEF).^{37,38} In

1 addition, pulmonary vein narrowing remains exceedingly rare with PFA and has not been
2 linked to clinical symptoms to date (also see chapter 6).^{39,40}

3 Despite being a first-generation technology, PFA for ablation of paroxysmal AF already at
4 least matches the efficacy of established thermal energy sources.^{41,42} In cases of early
5 persistent AF with minimal atrial remodelling, PVI alone using PFA represents an appropriate
6 strategy and can be employed using an approach analogous to that used for paroxysmal AF.
7 In more advanced forms, a PVI-only strategy may still be acceptable but typically yields
8 lower success rates, and additional lesion sets may be required. In persistent AF, evidence
9 is emerging but remains less mature than in paroxysmal AF. The multicentre single-arm
10 ADVANTAGE AF program evaluated pentaspline PFA with PVI plus posterior wall ablation⁴³,
11 and Phase 2 uniquely used continuous insertable cardiac monitor follow-up, reporting 1-
12 year effectiveness rates of 65–75% and low adverse event rates⁴⁴. Similarly, the SPHERE Per-
13 AF study demonstrated non-inferior efficacy and safety and increased efficiency of PFA over
14 RF in patients with persistent AF.^{45,46} Based on the latest EHRA/HRS/APHRS/LAHR Expert
15 Consensus Document on Catheter and Surgical Ablation of Atrial Fibrillation⁴⁷, the role of
16 additional lesion sets beyond PVI in patients with persistent AF remains an area of
17 uncertainty. Ongoing randomized studies, such as PIFPAF-PFA (NCT05986526), are currently
18 evaluating whether posterior wall ablation using PFA improves outcomes in this population.

19 Repeat AF ablation procedures

20 Remapping series after index PFA ranged from very high PVI durability rates to comparable
21 results as achieved by thermal ablation.^{48–50} In remapping studies higher reconnection rates

1 were observed at the LSPV and RIPV with potential differences between different PFA
2 systems.⁵¹⁻⁵³ Posterior wall isolation (PWI) using PFA has emerged as an adjunctive therapy,
3 especially in the treatment of persistent AF. First data show high durability of PWI using
4 PFA.⁵⁴

5 The integration of 3D mapping into current PFA platforms has improved visualization of
6 catheter position, tissue contact, and lesion sets, enabling a “mapping-on-the-fly” workflow
7 in which mapping occurs before, during and after energy delivery. In redo procedures,
8 however, the approach often differs, with many operators preferring an additional high-
9 density mapping catheter to better delineate residual substrate. Redo ablation strategies
10 may include repeat PVI alone, posterior wall isolation, or adjunctive linear lesions such as a
11 left-atrial anterior line, mitral isthmus line, and/or cavo-tricuspid isthmus line (see chapter
12 6.2.1.3 for risks and mitigation strategies).⁵⁵⁻⁵⁷ Despite some favourable data outcome data
13 in redo procedures using PFA in the setting of persAF, larger prospective randomized data
14 are still lacking, and the ideal ablation approach remains to be determined.^{58,59}

15 Clinical considerations limiting PFA use

16 To our knowledge, no PFA specific contraindications have been identified beyond the general
17 contraindications to undergo catheter ablation. The use of PFA in specific subgroups, e.g.
18 patients with CIEDs and patients with LAO is described in chapters 5.1.5 and 5.1.6.

1 Procedural workflow

2 Pre-procedural preparation

3 Role of general anesthesia and sedation protocols

4 The choice between general anesthesia (GA) and deep sedation has been a subject of discussion
5 since the first-in-human electroporation studies. Early monophasic systems required GA because
6 of strong skeletal muscle capture.^{60,61} With the introduction of biphasic waveforms, muscular
7 contractions are significantly reduced, enabling most procedures to be performed under deep
8 sedation^{62,63} ⁶⁴. It should be noted that there remain differences between different systems in terms
9 of muscular contractions.^{63,65} For clarity, GA is generally defined as anesthesia requiring airway
10 control and often neuromuscular blockade, whereas deep sedation refers to the administration of
11 hypnotic and analgesic agents without neuromuscular blockade and typically without
12 endotracheal intubation, while maintaining spontaneous ventilation. However, terminology across
13 published studies has not always been used consistently. Large-scale registry data, such as the
14 MANIFEST-PF survey⁶⁶ (>17,000 patients), indicate that more than 80% of procedures are
15 conducted with deep sedation alone, with favorable safety and efficacy outcomes.⁵³ Sedation
16 regimens typically combine propofol, benzodiazepines, and short-acting opioids, supporting
17 streamlined early or same-day discharge workflows.^{67,68} An overview of common sedation
18 protocols used for PFA is provided in **Table 6**. Administration of agents such as propofol and
19 dexmedetomidine, has traditionally required the presence of an anesthesiologist, whereas in
20 some jurisdictions, deep sedation (also using propofol and dexmedetomidine), can be
21 administered by trained non-anesthesiologists.

1 Additional real-world evidence comes from the EU-PORIA registry, which enrolled 1,233
2 consecutive patients across seven European centers. In this cohort, 20% of procedures were
3 performed under GA and 80% under deep sedation. Deep sedation was associated with
4 significantly shorter skin-to-skin and fluoroscopy times, and there were no differences in serious
5 adverse events between groups. At 1-year follow-up, freedom from recurrent AF/AT was virtually
6 identical (approximately 74%)., supporting the clinical equivalence of both strategies when using
7 the pentaspline PFA catheter.⁶⁹

8 GA may be appropriate in patients with poor tolerance of deep sedation or with airway
9 management concerns due to obstructive sleep apnea or obesity. It also facilitates immobility and
10 catheter stability, particularly early in the learning curve. However, no randomized evidence
11 demonstrated superiority of GA over sedation for PFA. Both approaches are used, and the choice
12 should be individualized based on institutional practice, availability of GA, choice of PFA
13 technology, operator preference, and patient comorbidity profile. Standardized monitoring,
14 including continuous capnography, is advised according to local protocols when sedation is
15 used.⁷⁰ Of note, terminology regarding anesthesia and sedation in prior studies has often been
16 used inconsistently. Many procedures described as “deep sedation” employ the same hypnotic
17 and analgesic agents as general anesthesia, with the key distinction being the absence of
18 neuromuscular blockade. Therefore, clearer reporting of anesthetic strategies, including the
19 sedative agents used and the application of neuromuscular blockade, would improve
20 comparability across studies.

21 Role of imaging

22 Pre-procedural imaging of the left atrium with computed tomography (CT) or magnetic
23 resonance imaging (MRI) is frequently obtained before PVI. Such imaging permits
24 characterization of pulmonary vein anatomy and may be fused with electroanatomical

1 mapping (EAM) or fluoroscopy to guide ablation.⁷¹ Since some catheters are available in
2 more than one size, imaging may support device selection, although evidence for this
3 approach is lacking.⁷² The impact of pre-procedural imaging on efficacy and safety in PFA
4 remains uncertain. CT or MRI may be particularly useful in the early learning phase and in
5 patients with complex anatomy. With growing operator experience, fluoroscopy-only
6 workflows are safely used in high-volume centers. Of note, many centers still rely on intra-
7 procedural pulmonary venous angiography for anatomical delineation.

8 Intracardiac echocardiography (ICE) offers real-time visualization of pulmonary vein
9 anatomy, rules out left atrial appendage thrombus, guides safe trans-septal puncture,
10 confirms tissue contact of ablation catheters, and enables rapid detection of acute
11 complications such as pericardial effusion.

12 Fluoroscopy-only standardized workflow

13 Fluoroscopy-only workflows are attractive because they simplify logistics, shorten pre-
14 procedural planning, and reduce costs. The trade-off involves potentially increased
15 dependence on radiation exposure, underscoring the importance of operator experience
16 and adherence to radiation-sparing techniques. Recent evidence shows that fluoroscopy-
17 only PFA shortens procedure times without affecting safety or outcomes.^{73,74} Catheter-
18 tissue contact can be inferred by fluoroscopic spline indentation or change in circular shape.
19 Catheter positioning may be further optimized by pacing from the PFA catheter prior to the
20 first application and adjusting contact according to atrial capture.⁷⁵

1 Role of 3D-electroanatomical mapping

2 In the early development of PFA systems, no mapping capacities were available, and a
3 multipolar catheter had to be used for pre- and post-procedural mapping. This approach
4 required sheath exchange, increased procedural complexity, and costs, while the PFA
5 catheter itself could not be visualized. Later, PFA catheters became displayable within 3D
6 mapping systems via impedance-based localization, but only as simplified representations,
7 limiting positioning accuracy. Today, PFA is increasingly integrated into electroanatomical
8 mapping (EAM) systems. An overview of current EAM integration across available systems is
9 provided in **Table 7**. EAM is particularly useful in redo procedures or in patients with atypical
10 anatomy. It enhances lesion visualization and importantly, can be used to assess lesion
11 overlap which is essential for durability of lesion sets.

12 PFA in patients with CIED

13 Growing clinical experience indicates that PFA can be safely performed in patients with
14 pacemakers and ICDs. Larger series have no reported clinically significant interference, lead
15 dislodgement, or device malfunction.⁷⁶ Nonetheless, ablation in immediate proximity to
16 device leads should be avoided, and routine pre- and post-procedural device interrogation
17 is advised. Recent case reports illustrate rare but important exceptions: Nair et al. reported
18 permanent failure of a CRT-D and transient software reset with apparent battery depletion
19 of a leadless atrial pacemaker when monopolar PFA was delivered in presumed contact with
20 the SVC coil.⁷⁷ Furthermore, PFA-induced ventricular fibrillation has been described in a
21 patient with a dual-coil ICD, likely mediated by unintended myocardial capture via

1 electromagnetic induction in close proximity to the RV lead.⁷⁸ These observations
2 underscore that while PFA is generally safe in patients with intracardiac devices, lead
3 proximity and asynchronous PFA delivery may pose a pro-arrhythmic risk. Further data is
4 needed.

5 PFA in patients with LAAO

6 The combination of PFA and left atrial appendage occlusion is becoming increasingly relevant.
7 Endocardial plug-type occlusion systems and surgical clip-based closure techniques appear
8 compatible with PFA, whereas lobe-and-disk occluders may interfere with effective energy
9 delivery (**Figure 3**).⁷⁹

10 In a multicenter series, evaluating PFA performed after prior LAAO, one-third of patients with a
11 lobe-and-disk-occluder (such as Amplatzer Amulet, Abbott) experienced aborted applications at
12 left-sided veins due to device proximity, while plug-type occlusion system patients (such as
13 Watchman, Boston Scientific) showed no interference.⁷⁹ The mechanism is geometric, related to
14 disk protrusion into the pulmonary vein antrum, leading to distortion of the local electric field and
15 triggering system safety interruption, which may require catheter repositioning or in rare
16 circumstances even supplemental radiofrequency ablation. Whenever possible, PFA should
17 precede device implantation; if performed after LAAO, device type and anatomy should be
18 carefully evaluated.

19 Concomitant PFA and LAAO

20 Combined procedures of PFA and LAAO are feasible. However, whether they should be done
21 routinely is controversial. The OPTION trial demonstrated that LAAO after AF ablation was
22 associated with a significantly lower risk of non-procedure-related major or clinically

1 relevant non-major bleeding compared with oral anticoagulation, but was not superior for
2 major bleeding, which was not a prespecified superiority endpoint. The OPTION trial met its
3 prespecified non-inferiority endpoint for the composite of stroke, systemic embolism, or
4 death. Importantly, it was not designed to assess superiority for individual thromboembolic
5 endpoints.^{79 80} RThe limited currently available evidence supports an individualized
6 approach, and combined procedures of AF ablation using PFA and LAO could be evaluated
7 in experienced centers for carefully selected patients, even though guideline-level
8 recommendations are not yet established.

9

10 PFA in Patients with other intracardiac devices

11 Case reports and newer series show safe outcomes of PFA in patients with ASD/PFO
12 occluders, surgical LAA exclusion systems (AtriClip), and prosthetic heart valves.⁸¹ While no
13 major device dysfunctions have been reported, risks include arcing, electromagnetic
14 interference, and difficulty delivering energy adjacent to metallic valve components.
15 Therefore, PFA if considered in such patients should be performed with careful catheter
16 positioning, avoiding close proximity and direct contact, and being prepared to use alternate
17 lesion strategies where needed.

1 Step-by-Step procedure

2 Vascular access

3 Vascular access is via standard femoral venous puncture. Ultrasound guidance reduces
4 vascular complications.⁸² Anticoagulation is usually initiated pre-transseptal-puncture, with
5 ACT maintained ≥ 300 – 350 s during the procedure, however, for some systems, an ACT ≥ 350
6 s is required before catheter manipulation in the left atrium. Use of ultrasound-guided
7 femoral access and uninterrupted anticoagulation is advised.⁴⁷

8 Choice of guidewire

9 A standard J-tipped guidewire is generally sufficient for over-the-wire devices to advance
10 sheaths into the left atrium and is associated with a favorable safety profile. Extra-stiff wires
11 can provide additional support in patients with tortuous anatomy but increase the risk of
12 perforation. Recent evidence suggests that straight-tip guidewires may cause asymptomatic
13 bronchial bleeding,⁸³ whereas J-tip wires do not show this complication.

14 Transseptal puncture

15 Transseptal puncture remains a key step. Although a posterior puncture is commonly
16 performed, in cases without left atrial enlargement an anterior puncture may facilitate
17 access to the right inferior pulmonary vein, particularly with certain systems. TSP is often
18 performed using a standard transseptal sheath that is then exchanged over the wire for a
19 dedicated PFA sheath. An over-the-needle TSP directly with the dedicated PFA delivery

1 sheath has been described in a retrospective single-center experience of 100 patients
2 (“zero-exchange”).⁸⁴ Dedicated integrated systems with radiofrequency wires or short
3 deployable needles which fit into the larger sheath, also allow puncture in a “zero-exchange”
4 workflow. Advanced imaging with ICE or TEE can further enhance safety, particularly in
5 patients with thick septa or prior closure devices. In practice, TSP should be tailored to the
6 platform and patient anatomy, with ICE advised in challenging cases. Simple measures such
7 as marking the His bundle with a standard diagnostic electrophysiology catheter, marking
8 the aortic root with a guidewire via a retrograde aortic approach, registration of needle
9 pressure or contrast dye injection may assist in TSP in some cases.

10 Sheath/catheter exchanges & air embolism prevention

11 Air embolism is an uncommon but potentially serious complication during PFA. Preventive
12 measures include meticulous de-airing of sheaths and continuous saline flushing. Modern
13 “zero-exchange” approaches, available with different platforms further reduce the risk of air
14 ingress. In addition, “zero-exchange” designs streamline the procedure, shorten
15 fluoroscopy, and left atrial dwell time, and may lower embolic risk. The impact of sedation
16 type on air embolism is unknown and requires further research; limited data suggest that
17 negative left atrial pressures, more commonly encountered during deep or conscious
18 sedation than during positive-pressure ventilation under general anesthesia, may facilitate
19 air ingress through open hemostasis valves, although the clinical relevance remains to be
20 defined.

1 Vagal response during ablation

2 Vagal reflexes, including bradycardia, atrioventricular block, or transient asystole, are
3 common during PFA, particularly at the left superior pulmonary vein. Reported incidence
4 ranges from 30–70%, depending on the definition and patient cohort.⁸⁵ Most events are self-
5 limited; atropine (1.0 mg) or, rarely, temporary pacing may be required. Although
6 prophylactic parasympatholytics (e.g. atropine or glycopyrrolate) may reduce the need for
7 backup pacing, their use is contraindicated in patients with glaucoma or benign prostatic
8 hyperplasia owing to the risk of post-procedural urinary retention. In these patients, right
9 ventricular backup pacing may represent a safer alternative. Recently, a RSPV-first ablation
10 strategy has been proposed to mitigate vagal reactions, reducing their occurrence from 78%
11 to 13% compared with an LSPV-first approach.⁸⁶ These autonomic effects are likely due to
12 transient stimulation of the ganglionated plexi. In summary, vagal responses are frequent
13 and benign; atropine, glycopyrrolate, or pacing may be appropriate if clinically significant.

14 Assessment of catheter-tissue contact 5

15 Effective PFA requires stable catheter positioning at the PV antrum.⁶⁰ With pentaspline catheters,
16 coaxial alignment and avoidance of deep catheter positioning within the PV are critical, as
17 inadequate contact may predispose to reconnection. Surrogates for assessing contact include
18 tactile feedback, fluoroscopic spline or circular indentation (Supplementary video) or intracardiac
19 echocardiography (ICE), which provides real-time confirmation of ostial positioning. Impedance-
20 based markers integrated into electroanatomical mapping (EAM) can enable objective contact
21 assessment and have been proven to be useful in an in vivo study resulting in significantly larger
22 and more durable lesions, with 100% transmuralities when good contact was achieved.⁸⁷ These

1 findings underscore that, despite PFA's field-based mechanism, adequate catheter–tissue
2 proximity remains crucial for durable circumferential lesion formation. In contrast to RFA, PFA is
3 less forgiving with respect to intermittent or suboptimal contact, as its ultra-short pulse delivery
4 lacks thermal latency; consequently, adequate catheter–tissue proximity must be present at the
5 exact moment of energy application to achieve irreversible lesion formation. Moreover, field-
6 induced myocardial or phrenic nerve capture may cause transient catheter instability and could
7 contribute to reversible lesion formation and reconnection. In summary, PFA contact assessment
8 relies on coaxial antral positioning using fluoroscopy, ICE imaging, and increasingly EAM-based
9 tools based on real-time impedance measurements. Future and newly developed integrated
10 contact feedback may further improve durability and workflow standardization.

11 Pulsed-field ablation dosing strategies

12 Pulsed-field ablation dosing strategies are currently based largely on manufacturer
13 recommendations, typically defining a minimum number of applications per pulmonary vein
14 or vein pair. However, the scientific evidence supporting these dosing thresholds is limited,
15 and available clinical studies have not demonstrated a clear association between
16 application number and long-term lesion durability.⁸⁸ It remains unclear whether adjunctive
17 imaging or mapping tools improve durability beyond what could be achieved with additional
18 applications alone. Any escalation in dosing must be balanced against safety
19 considerations. The randomized DOPPIO trial (NCT07021313) is specifically designed to
20 evaluate whether a higher and more targeted number of PFA applications can improve
21 arrhythmia-free survival without compromising procedural safety.

1 Angiographic projections

2 Standard angiographic projections are typically left anterior oblique (LAO) for the left pulmonary
3 veins and right anterior oblique (RAO) for the right pulmonary veins, with both views aiding
4 catheter orientation and minimizing the risk of advancing the catheter too deeply into the PV. The
5 use of biplane imaging may be helpful.

6 Role of intracardiac echocardiography / zero-fluoroscopy workflow

7 Intracardiac echocardiography (ICE) offers real-time visualization of cardiac anatomy. ICE
8 has been proven to be not inferior to transesophageal echocardiography (TEE) in excluding
9 left atrial appendage thrombus.⁸⁹ ICE allows for a safe trans-septal puncture, including in
10 challenging anatomic variants as lipomatous hypertrophy of the interatrial septum, atrial
11 septal aneurysm, or in patients with prior surgical or PFO or ASD repair.⁹⁰ In atrial fibrillation
12 ablation using radiofrequency energy, ICE has been shown to reduce radiation exposure,
13 shorten the overall procedure duration, and enhance safety by facilitating early recognition
14 of acute complications, such as pericardial effusion.⁹⁰⁻⁹² ICE enables confirmation of tissue
15 contact and real-time monitoring of the PFA catheter position relative to the pulmonary veins
16 ostium (**Figure 4**). In some reports, the use of ICE has been shown to improve pulmonary
17 vein isolation durability, achieve better success rates, and significantly reduce reconnection
18 rates with the Pentaspline catheter.^{61,93} On the other hand, ICE remains an invasive
19 procedure that requires additional skills, venous access, and catheter manipulation, and it
20 carries potential risks such as vascular injury and cardiac perforation.

1 ICE can assist transseptal puncture, verify catheter positioning, contact, and detect
2 complications such as effusion. Although not mandatory, it may enhance safety in high-risk
3 patients. In centers pursuing a zero-fluoroscopy workflow, ICE also facilitates real-time
4 anatomical guidance that obviates the need for radiographic imaging.

5 **Troubleshooting (energy interruption, electrical arcing)**

6 Automatic interruption of energy delivery may occur across PFA platforms if the system detects
7 unsafe geometry, abnormal impedance behaviour or potential interaction with metallic implants.
8 Electrical arcing remains rare but has been described particularly when electrodes are in direct
9 contact with each other or adjacent metal. Prevention strategies should focus on optimized
10 catheter contact, flushing, and avoiding proximity and contact with metallic devices like occluders
11 and artificial valves. In most cases, energy delivery resumes after correction of catheter geometry
12 and stable antral alignment. **Table 8** summarises typical triggering conditions across different
13 catheter concepts.

14 **Procedural endpoint definition**

15 PFA leads to rapid attenuation of near-field signals, sometimes complicating their
16 distinction from far-field activity. Accurate electrogram interpretation remains essential,
17 although more challenging after PFA, to confirm PV isolation.⁹⁴ Differences in electrode size
18 and inter-electrode spacing across PFA catheter designs affect near-field vs. far-field
19 discrimination. Smaller electrodes with tighter spacing improve local resolution but may be
20 more susceptible to signal suppression after PFA, whereas larger electrodes with wider

1 spacing increase far-field content and may mask residual conduction. Thus, catheter-
2 specific behaviour needs to be accounted for when interpreting signals after PFA.

3 Durable entrance and exit block remain universal endpoints, however strategies vary by
4 platform. While fully mapping integrated systems rely on multipolar mapping after ablation,
5 others may be combined with dedicated 3D-EAM systems⁷³ or use pacing maneuvers.
6 Comparative studies assessing different strategies are lacking. The prognostic role of pacing
7 for PV isolation validation for long-term durability after PFA is less established than after RF
8 ablation.⁷⁵

9 In thermal ablation, adenosine identifies dormant conduction. With PFA, the yield is low,
10 since even stunned veins with incomplete isolation may not demonstrate dormant
11 conduction.⁵⁰ Similarly, the value of a standardized waiting time is low. Pharmacological
12 testing may be appropriate but is not required in routine PFA. Given the wide variation in
13 lesion delivery strategies across platforms, it is advisable to adhere to manufacturer-
14 recommended energy delivery protocols and to apply only a limited number of additional
15 applications in the presence of residual signals, to avoid unnecessary overtreatment.

16 Post-procedural care / same-day discharge protocols

17 Postprocedural management after PFA differs somewhat from thermal ablation⁹⁵ given its
18 lower incidence of pulmonary vein stenosis, pericarditis,⁹⁶ phrenic nerve injury, and
19 atrioesophageal fistula^{97,98}. PFA-specific complications such as hemolysis leading to acute
20 kidney injury (AKI)⁹⁹⁻¹⁰¹ or coronary vasospasm have been reported and are discussed

1 separately in Chapter 6.2.1.¹⁰² In line with current AF ablation practice, therapeutic
2 anticoagulation should be continued uninterrupted for at least 2 months post-ablation, with
3 subsequent continuation based on CHA₂DS₂-VA risk.⁴⁷ Most centers abandoned a standard
4 proton-pump inhibitor therapy after PFA. Venous vascular closure systems are increasingly
5 used after AF ablation, but data in the pulsed-field ablation era remain limited.¹⁰³ Same-day
6 discharge has been evaluated in prospective registries and shown to be safe in selected
7 patients.^{104,105} Recent data, including an admIRE trial sub-analysis¹⁰⁵ and an EHRA meta-
8 analysis¹⁰⁶, support the safety of same-day discharge after AF ablation when appropriate
9 patient selection and standardized protocols are applied. However, same-day discharge
10 may not be appropriate in patients with procedural complications, significant comorbidities,
11 or those requiring extended monitoring. Further practical advice will be provided in a
12 separate EHRA consensus document. Practical advice regarding procedural workflow in PFA
13 is summarized in **Table 9**.

14 **Efficacy and safety**

15 Clinical outcomes

16 Randomized controlled trials

17 To date there have been five randomized controlled trials comparing PFA to thermal ablation:
18 The Pulsed Field or Conventional Thermal Ablation for Paroxysmal AF trial (ADVENT), the
19 Pulsed Field or Cryoballoon Ablation for Paroxysmal AF trial (SINGLE SHOT CHAMPION) trial,
20 the PFA versus RFA for the treatment of paroxysmal AF trial (BEAT PAROX-AF), and the PFA

1 using a novel nanosecond biphasic catheter vs conventional thermal ablation for
2 paroxysmal AF trial (INSIGHT PFA) were performed in patients with paroxysmal AF.^{41,42,107} The
3 Dual-energy lattice-tip ablation system for persistent atrial fibrillation trial (SPHERE Per-AF)
4 was performed in patients with persistent AF.⁴⁵

5 The key findings of these five trials are summarized in **Table 10**. In aggregate, freedom from
6 atrial tachyarrhythmia recurrence following index ablation after a blanking period was
7 similar between randomized technologies, meeting non-inferiority but not superiority
8 (except for SINGLE SHOT CHAMPION¹⁰⁸). Similarly, there was no difference in time spent in
9 AF (AF burden), quality of life, or healthcare utilisation. Complications were low and not
10 significantly different between randomised technologies, but the use of PFA resulted in
11 shorter procedure times across all studies.

12 Single-arm registries

13 Several pivotal trials for regulatory approval of the different PFA devices have been
14 performed. Across these pivotal regulatory studies, efficacy outcomes were assessed using
15 protocol-defined rhythm monitoring in accordance with CE mark and FDA requirements,
16 including scheduled follow-up visits with systematic ECG and ambulatory monitoring
17 beyond symptom-driven assessment. The admIRE and inspire studies evaluated an irrigated
18 variable loop circular PFA catheter, the PULSED-AF study evaluated an over-the-wire loop
19 PFA catheter, the SmartfIRE study a dual-energy focal catheter and the Omny-IRE a large-tip
20 focal, multielectrode PFA catheter, the IMPULSE, PEFCAT, PEFCAT II and ADVANTAGE
21 studies evaluated the pentaspline catheter and the VOLT CE mark study³⁶ reported on a

1 basket-in-balloon PFA catheter (**Table 11**).^{53,61,98,109–114} Furthermore, large single-arm
2 registries and studies have reported on safety and efficacy outcomes with the pentaspline
3 catheter (EU-PORIA, MANIFEST, MANIFEST 17k, FARADISE) (**Table 12**).^{115,97,116,117} And finally,
4 several non-randomized trials compared PVI outcomes after PFA and thermal energies. In
5 aggregate, these studies reported a 1-year freedom from recurrent atrial tachyarrhythmia
6 ranging from 55-80% [paroxysmal 66–82%, vs. persistent 55–71%], with no statistically
7 significant difference in the rate of recurrence (RR 0.85; 95% CI 0.64–1.14; $p = 0.29$).¹¹⁸

8 Blanking period

9 For thermal ablation modalities, the duration of the post-procedure “blanking period” was
10 recently shortened from 3 months to 8 weeks.⁴⁷ PFA has a different inflammatory profile, and
11 there is emerging evidence that acute periprocedural changes are less profound than with
12 thermal ablation. In the SINGLE SHOT CHAMPION trial, a significantly lower rate of
13 recurrence was observed for PFA in the blanking period using continuous rhythm monitoring
14 (38.1% vs. 58.1%).⁴² A secondary analysis of the PULSED AF trial showed that early
15 recurrence of atrial tachyarrhythmia within the first 3 months after ablation was significantly
16 associated with an increased risk of late recurrence.¹¹⁹ This is consistent with two other
17 studies indicating that recurrences occurring in post-procedure months 2 and 3 were
18 universally associated with later treatment failure.^{120,121} As such, a blanking period of just 1
19 month after PFA may be reasonable for clinical decision-making, whereas the use of a
20 blanking period in clinical trials involving PFA should be reconsidered moving forward.²

1 Occurrence and management of adverse events

2 After the recent introduction of pulsed-field ablation (PFA) into clinical practice, an overall
3 favourable safety profile with some occasional but unexpected adverse events have been
4 reported (**Figure 5**).¹²² Although PFA was initially considered cardioselective and largely
5 contact-force independent, accumulating evidence indicates that PFA is tissue-selective,
6 contact-dependent, minimally thermal, and voltage-dependent, with safety profiles that
7 may vary across different PFA platforms and clinical applications.. Appropriate specialized
8 EP training remains key to maintain the quality and safety of PFA procedures (see also
9 chapter 7 “Training and Education”).

10 PFA related adverse events

11 *Hemolysis/acute kidney injury*

12 Post-PFA haemolysis and occasional acute kidney injury (AKI) has been observed,
13 correlated with high number of applications, particularly with higher-voltage systems.^{123,124}
14 The incidence appears to vary across PFA platforms, likely reflecting differences in waveform
15 characteristics, voltage amplitude, and catheter design. The risk of AKI may be reduced with
16 optimal pre-ablation hydration.^{100,112–114,116} Based on available evidence, the number of PFA
17 applications should be chosen mindfully and pre-ablation hydration may be appropriate,
18 especially in patients with pre-existing chronic kidney disease.^{100,125}

19 *Phrenic nerve injury*

20 Phrenic nerve injury (PNI), a known complication of thermal AF ablation, was reported to be
21 transient in 0.006% and permanent in none (0%) in the MANIFEST-17K study.¹¹⁶ Importantly,

1 phrenic nerve capture during PFA pulse delivery should be distinguished from nerve injury,
2 as these represent different electrophysiological mechanisms.

3 *Coronary injury/drug protocols for prevention of vasospasm*

4 Proximity-related coronary vasospasm was widely documented during PFA for cavo-
5 tricuspid and mitral isthmus ablation, initially when using the pentaspline PFA catheter,¹⁰²
6 but later similarly with several other PFA devices, most likely indicating a voltage/field
7 strength dependence. The likelihood and severity of vasospasm may therefore vary across
8 PFA systems, reflecting differences in energy delivery and electric field distribution. Spasm
9 typically develops within seconds to a few minutes after PFA, although delayed onset has
10 also been reported.¹²⁶ These observations are clinically relevant, particularly in the context
11 of streamlined procedural workflows and increasing use of same-day discharge strategies
12 after AF ablation. It can be largely attenuated by administration of nitroglycerin either for
13 treatment (1-2 mg intracoronary) or as prophylaxis (intracoronary 1 mg or intravenous 1-2
14 mg).¹⁰² Coronary vasospasm observed after PFA may relate to transient functional effects on
15 the coronary vasculature, including endothelial or smooth muscle electroporation,
16 autonomic influences, or circulating vasoactive factors, although the underlying
17 mechanisms remain incompletely understood.¹⁰² Given the potential for both acute and
18 delayed vasospasm, careful intraprocedural management and early post-procedural
19 monitoring may be warranted in selected patients. Also, the long-term effect of PFA on
20 coronary arteries is currently unknown.¹²⁷ Further systematic investigation will be important
21 to better define the incidence, mechanisms, and clinical implications of coronary
22 vasospasm across different PFA platforms.

1 *Pulmonary vein stenosis*

2 Although severe PV stenosis is rare, mild to moderate narrowing of pulmonary veins (PV) has
3 been observed frequently in patients undergoing thermal ablations but was not observed
4 with PFA-only devices.^{40,107} However, systematic assessment for subclinical pulmonary vein
5 narrowing is not routinely performed in real-world practice.

6 *Esophageal events*

7 Esophageal injury is a rare but often fatal complication of thermal ablation, occurring with
8 an incidence of 0.025% and a mortality of 66%. To date, not a single case of esophageal
9 fistula has been reported despite the use of PFA in >500'000 patients worldwide^{38,116,128}.

10 *Conduction system disturbances*

11 Collateral injury to the AV node or sinus node can occur using thermal energy. While cases
12 of occasional and often transient AV block or sinus node dysfunction have been reported
13 after ablation of atrial flutter or isolation of the superior vena cava using PFA, this scenario
14 is rare.^{56,129} The full impact of PFA on the conduction system however is yet to be explored.

15 *Pericarditis*

16 The incidence of acute pericarditis following pulsed-field AF ablation ranges from 0% to 0.3%
17 in recent multinational registries and prospective studies.^{41,98,115,116} Studies specifically
18 investigating pericarditis rates report a broader range (0%–4.4%), depending on the
19 definition used (e.g., with or without ESC criteria).⁹⁶ Similar variability is observed when
20 compared to thermal AF ablation procedures, where reported incidences range from 0% to
21 10.2%.^{41,130,131}

1 *Effect on left atrial function*

2 During the acute phase following PFA-PVI, most studies report a reduction in markers of left
3 atrial (LA) compliance and contractile function.¹³²⁻¹³⁴ This is observed both after PVI alone
4 and following more extensive LA ablation, likely reflecting transient LA-stunning.¹³²⁻¹³⁴ In the
5 long-term (chronic phase), markers of LA-compliance typically return to baseline,¹³²⁻¹³⁵
6 although persistent impairment of LA contractile function at 3 months after PFA-PVI despite
7 recovery of reservoir function has been described¹¹⁷. In contrast, RF-PVI with extensive LA
8 ablation leads to a long-term decline in LA-compliance markers.¹³⁶

9 *Non-PFA related events*

10 *Pericardial tamponade*

11 The incidence of pericardial tamponade during pulsed-field ablation for PVI ranges from 0%
12 to 1.1% in prospective randomized studies and large registries, which is similar compared to
13 thermal ablation.^{42,41,115,98,116 45,117,137,138}

14 *Stroke/TIA/cerebral emboli*

15 The incidence of stroke and transient ischemic attacks (TIA) during PFA for PVI has been
16 reported at 0-1% and 0-0.3%, respectively, in recent trials.^{41,115,98,42,116} Large registries of
17 thermal PVI procedures report similar combined stroke/TIA rates ranging from 0.1% to 1%.
18 Notably, post-market evaluation of a variable-loop circular PFA catheter (Varipulse,
19 Biosense Webster) led to updated use instructions following a numerically higher early
20 stroke/TIA rate. A recent meta-analysis reported silent cerebral event (SCE) rates of 14% for
21 PFA, 18% for RF, and 21% for cryoballoon ablation procedures.¹³⁹ Importantly, SCE observed

1 after PFA should not be attributed solely to the electroporation mechanism. Available
2 evidence suggests a multifactorial process that may involve air embolism during catheter
3 exchanges, thrombus formation on sheaths or electrodes, transient hypotension, and peri-
4 procedural anticoagulation management. Moreover, emerging data indicate substantial
5 variability between PFA platforms, suggesting that catheter design, waveform
6 characteristics, and energy delivery may influence cerebral embolic risk¹⁴⁰.

7 *Vascular access complications*

8 Vascular access complications in PFA procedures occurred in 0-2.2% of cases.^{41,98,115,116} The
9 use of ultrasound guidance in patients of the Manifest-17K cohort was associated with a two
10 thirds reduction in access site complications.¹¹⁶

11 *Death*

12 Reported mortality rates for PFA-based interventions range from 0 to 0.3% and are most
13 commonly attributable to cardiac tamponade or stroke.^{41,98,115,116} By comparison, registries
14 of thermal AF ablation report mortality rates between 0.02 and 0.46%.^{138,141} Rare cases of
15 delayed malignant arrhythmias, myocardial ischemia, and sudden cardiac death after PFA
16 have been reported, particularly following ablation beyond PVI. Although causality remains
17 unproven and incidence appears very low, these observations highlight the need for
18 vigilance and further mechanistic study¹⁴².

19 **Autonomic nervous system effects**

20 Pulsed-field (PF) energy interacts with the cardiac autonomic nervous system – specifically
21 the ganglionated plexi (GPs) – in ways that differ from thermal ablation. Acutely, the

1 application of PF-impulses during PVI often triggers vagal responses, likely due to intense
2 stimulation of nearby GPs, particularly during LSPV ablation.¹⁴³ Initiating PFA-PVI at the RSPV
3 – possibly “suppressing” the anterior right GP – can reduce vagal response during
4 subsequent ablation, e.g. of the LSPV.⁸⁶ Chronically, durable neural injury however appears
5 minimal. Unlike RF or cryo-PVI, PFA-PVI does not lead to a significant postprocedural
6 increase in heart rate or neuronal injury markers (e.g. SF100B).^{143–145}

7 Long-term follow-up data

8 Outcome data beyond one year after AF ablation using PFA is currently lacking. Data on the
9 durable effect on arrhythmia suppression after PFA-PVI and the prevention of progression
10 from paroxysmal AF to persistent AF will be important.

11 Training and education

12 PFA offers efficiency, and improved safety when compared with thermal ablation. These
13 features have generated enthusiasm across specialties. Specialized education in EP brings
14 essential expertise in arrhythmia mechanisms, mapping, and intracardiac signal
15 interpretation, competencies that allow comprehensive AF care. In line with these
16 principles, PFA procedures should be performed under the responsibility of physicians
17 holding recognized electrophysiology certification, such as the EHRA EP certification,
18 which delineates the requisite expertise for independent practice (**Figure 6**). In addition,
19 centers adopting PFA should ensure structured, center-specific education of the entire
20 electrophysiology team and actively encourage participation in nationwide procedural

1 registries to enable continuous quality assurance, benchmarking, and transparent
2 outcome monitoring.

3 **Structured training pathway**

4 Effective PFA training should integrate both theoretical and practical competencies.
5 Didactic instruction should include the biophysical principles of electroporation, tissue
6 specificity, safety margins, and device-dependent characteristics.¹⁴⁶ Equally important is
7 the acquisition of procedural knowledge such as patient selection, pre-procedural planning,
8 and peri-procedural management. Hands-on training should ideally begin with simulators or
9 animal models before progressing to supervised clinical practice under the guidance of
10 experienced PFA operators. Mentorship and proctoring during the early learning phase
11 prevent unsafe extrapolation from radiofrequency or cryoballoon ablation.¹⁴⁶ What
12 distinguishes PFA from prior innovations is not only its promise of efficiency but also the
13 depth of electrophysiological understanding required to harness it safely. Competence in
14 mapping, interpretation of intracardiac signals, and the management of complex atrial
15 arrhythmias remain fundamental.

16 **Learning curve and competency milestones**

17 Early experiences with PFA suggest that acute PVI can be achieved with high reproducibility
18 after relatively few procedures.¹⁴⁷⁻¹⁴⁹ Registry data indicate similar outcomes between junior
19 and senior electrophysiologists.¹¹⁵ These findings make PFA appear more accessible than
20 point-by-point radiofrequency ablation. Yet lessons from cryoballoon adoption caution
21 against oversimplification: inappropriate case selection, incomplete understanding of atrial

1 anatomy, and neglecting electrophysiological endpoints may compromise results despite
2 apparently straightforward workflows.¹⁵⁰

3 Thus, the real learning curve is broader—achieving competence not only in PVI but also in
4 ablation beyond the veins, repeat procedures, and non-PV arrhythmias (**Table 13, Figure 7**).

5 A structured pathway with exposure to different catheter designs and system platforms
6 (balloon-based and point-by-point)⁵³ and to anatomically challenging cases is essential (see
7 Chapter 5).^{151,152} Structured case numbers, milestone-based assessments, and continuous
8 procedural feedback should be incorporated into training.¹⁵³

9 The training requirements and skills of the latter are detailed in the EHRA Core Curriculum
10 document.¹⁵³

11 Integration into electrophysiology fellowship programs

12 Training in PFA should occur within established centres of excellence in cardiac
13 electrophysiology. High procedural volume, access to advanced imaging and mapping tools,
14 and a culture of mentorship create the optimal environment for structured learning.

15 Embedding PFA into electrophysiology fellowship curricula ensures early exposure and
16 integration into a comprehensive procedural repertoire. In this context, the EHRA
17 Educational Pathway provides a structured framework for competency-based training in AF
18 ablation, with AF-specific courses embedded at Level II and formal knowledge assessment
19 through the EHRA electrophysiology examination, which is strongly advised as part of
20 professional development.

1 Non-technical skills and professional standards

2 Alongside procedural competence, modern training must address non-technical skills.
3 These include clinical judgment for patient selection, recognition of contraindications,
4 interdisciplinary communication, and the capacity for patient-centered decision-making.
5 The recent consensus document on catheter and surgical ablation⁴⁷ emphasizes the
6 importance of institutional readiness, team-based training, and longitudinal follow-up.
7 Similarly, the atrial tachycardia consensus document (SMART-AT roadmap) highlights the
8 importance of structured pathways and standardization (PMID pending – in press).

9 Registries and collaborative learning networks play a critical role in training. They provide a
10 mechanism for monitoring procedural safety and outcomes while also documenting the
11 progression of operator competence.¹¹⁵

12 In conclusion, the emergence of PFA marks a pivotal moment in AF therapy. Its clinical
13 promise is clear, but its long-term success depends on how it is taught and practiced.
14 Structured training pathways, competency milestones, institutional responsibility, and
15 fellowship integration are indispensable for its safe adoption. By embedding PFA training
16 within the broader framework of electrophysiology education and professional standards,
17 the technology can be adopted responsibly, safeguarding both patient outcomes and the
18 integrity of the field.

1 Future directions

2 Innovations in PFA technology

3 Continuous efforts are being made to develop and validate new waveforms, as well as to
4 define the adequate PFA dose to obtain effective lesions while preserving safety.^{154,155}

5 Focal vs. large footprint innovations and dual energy ablation

6 Large footprint PFA platforms (e.g., lattice tip, multielectrode) enable rapid creation of
7 contiguous lesion sets. Dual energy systems that toggle between pulsed field and
8 radiofrequency leverage complementary biophysics to enhance lesion continuity and
9 transmural while preserving maneuverability.^{45,156,157} In this context, lesion stacking
10 (repeat applications along identical trajectories or sequential PF→RF dosing) has shown high
11 acute efficacy with encouraging durability.^{45,156,157,35}

12 3D mapping integration, real time signal analysis, lesion-effect markers

13 The integration of PFA catheters within three-dimensional electroanatomical mapping
14 systems with sufficient resolution may enable the identification of residual pulmonary vein
15 connections and confirmation of effective ablation in non-pulmonary vein regions, while
16 also reducing fluoroscopy exposure.^{158 159} Furthermore, electroanatomical mapping
17 integration may allow for the evaluation of lesion-effect parameters which are associated
18 with transmural and effective ablation lesion formation.¹⁶⁰ **(Figure 8)**

1 Ongoing research and clinical trials

2 Randomized trials such as REPEAT-AF (NCT06199180) will provide important head-to-head
3 comparisons between PFA and thermal ablation in patients with recurrence of AF after initial
4 ablation, a field where data on PFA is currently scarce; however, this represents only a small
5 fraction of a rapidly expanding research landscape, with more than 140 registered PFA
6 studies in patients with AF alone. . Beyond AF, early focal PFA series for typical flutter and
7 first clinical experiences in ventricular arrhythmias suggest procedural efficiency with
8 encouraging short-PFA series for typical flutter and first clinical experiences in ventricular
9 arrhythmias suggest procedural efficiency with encouraging short-term outcomes, though
10 standardized endpoints and longer follow-term outcomes, though standardized endpoints
11 and longer follow-up remain priorities.^{161,162}

12 Emerging Applications for PFA

13 Posterior Wall Isolation

14 RF ablation of the posterior wall (PW) is limited by concerns of thermal injury to the
15 esophagus and suboptimal lesion transmuralty,^{163,164} limitations that may be addressed by
16 PFA.

17 In a proof-of-principle study, lesion transmuralty following endocardial posterior wall PFA
18 with a pentaspline catheter was verified via direct epicardial mapping.¹⁶⁵ Several clinical
19 studies have subsequently demonstrated that posterior wall ablation is feasible with several
20 PFA systems, including a pentaspline catheter (**Figure 9**),^{46,117,166} a large-footprint lattice-tip

1 catheter,^{157,167} and a spherical array catheter.¹⁶⁸ Notably, no evidence of esophageal injury
2 has been reported across these studies, and procedure times have remained short.

3 Retrospective, observational data from the MANIFEST-PF registry suggested that adjunctive
4 posterior wall ablation was not associated with improved 12-month freedom from recurrent
5 AF compared to pulmonary vein isolation.¹⁶⁹ Future investigations will be necessary to
6 assess the impact of posterior wall ablation on AF burden, such as the PIFPAF-PFA study
7 (NCT05986526).

8 Superior vena cava isolation

9 Initial clinical data suggest that superior vena cava isolation can be effectively achieved
10 using either the pentaspline PFA catheter⁵⁵ or a circular multielectrode array PFA catheter.¹⁷⁰
11 Future studies are warranted to evaluate the clinical role of both empirical and targeted
12 (when superior vena cava triggers are identified during the procedure) vena cava isolation in
13 terms of rhythm outcomes, particularly given that safety profiles may differ between PFA
14 platforms.

15 Mitral isthmus line

16 Perimitral macroreentrant flutter usually follows prior AF ablation or, less commonly,
17 presents de novo.¹⁷¹ It is often associated with low-voltage zones, especially at the anterior
18 wall,¹⁷² which facilitate localized or macroreentrant circuits.¹⁷¹ Both anterior and posterior
19 mitral isthmus ablation lines present distinct challenges.^{173,174} Incomplete block
20 predisposes to recurrent perimitral or biatrial flutter.¹⁷¹⁻¹⁷⁵ Linear PFA may overcome these
21 limitations by achieving deeper, more uniform lesions with reduced fat or scar attenuation

1 and preserved microvasculature, although periannular coronary spasm remains a concern
2 **(Figure 10).**

3 Several single-arm studies have evaluated lateral mitral isthmus ablation using the
4 pentaspline catheter (Farapulse, Boston Scientific). Early small studies reported high acute
5 bidirectional block rates, but with 4–10% clinical and up to 40% subclinical coronary artery
6 spasm.^{176–178} A larger study showed that clinical spasm could be prevented with 1–2 mg IV
7 isosorbide dinitrate.¹⁷⁸ However, in a recent large study, despite 100% acute block, dormant
8 conduction was observed in 14.8% of patients after adenosine,¹⁷⁹ and remapping at the time
9 of left atrial appendage (LAA) occlusion showed durable block in only 5.5%. Consistently, a
10 prospective registry analysis comparing anterior mitral isthmus line ablation using
11 pentaspline PFA versus RFA demonstrated greater procedural efficiency with PFA but
12 similarly high rates of line reconnection and comparable mid-term arrhythmia recurrence.
13 These findings suggest that PFA using the pentaspline catheter does not ensure persistent
14 anterior or lateral mitral isthmus block¹⁸⁰.

15 The large-footprint dual energy lattice-tip catheter was evaluated in a dose-finding study
16 combining RF and PFA for lateral mitral isthmus ablation, achieving 100% acute success ,
17 with only one adverse event.¹⁵⁶ Remapping in 69% of patients showed 68% durability. Similar
18 outcomes were reported in the randomized Sphere Per-AF trial with 100% acute success and
19 a 1.4% adverse event rate.⁴⁵ Two recent real-world studies also reported high acute success
20 using this catheter for anterior and lateral mitral lines with short transpired ablation times
21 and low complications rates.¹⁵⁷ Similar outcomes were confirmed under deep sedation.¹⁸¹

1 Currently, clinical data on acute and long-term outcomes for focal small-tip or other large-
2 tip regional PFA catheters remain limited. Further studies are needed to define optimal
3 catheter design, energy settings, prevent subclinical coronary spasm, and assess long-term
4 durability

5 LAA isolation

6 Early clinical data suggest that acute isolation of left atrial appendage is feasible using the
7 pentaspline PFA catheter, requiring an average of 16 applications in both the flower and
8 basket configurations, with a low risk of complications.¹⁷⁹ However, systematic remapping
9 at 3 months demonstrated a 95% rate of left atrial appendage reconnection, indicating that
10 lesion durability remains a significant limitation.

11 Scar homogenization

12 A tailored substrate-based approach in patients with AF and advanced atrial substrate
13 including scar homogenization may improve outcomes, as shown in the ERASE-AF trial. A
14 recent single center study showed this approach to be safe and effective with a focal PFA
15 system.¹⁸² Acute procedural success was 100% with 64% freedom from arrhythmias after 6
16 months. However, larger randomized trials on this matter are still missing.

18 Use in typical atrial flutter

19 Cavotricuspid isthmus (CTI) ablation is advised for the management of CTI-dependent atrial
20 flutter (AFL), whether clinically documented or encountered during AF ablation.

1 The pentaspline catheter was initially used off-label for CTI ablation due to ease of use and
2 reported high acute success, although long-term efficacy was not systematically assessed.
3 In a large single-center experience using predominantly a pentaspline PFA catheter, CTI-
4 dependent flutter ablation achieved high acute success (99.5%) with low short-term
5 recurrence ($\approx 1.5\%$ after blanking)¹⁸³. However, PF-induced right coronary artery spasm—
6 occasionally with malignant ventricular arrhythmias—has been reported.^{102,184} High-dose IV
7 nitroglycerin prevented spasm in most but not all cases.^{102,185} As such, CTI ablation with the
8 pentaspline catheter is advised only with IV nitroglycerin, and its long-term efficacy remains
9 uncertain.¹⁶¹

10 The large-footprint lattice-tip catheter (Sphere-9, Affera) showed 100% acute success in a
11 dose-finding study, mainly using RF energy.¹⁵⁶ Similar outcomes were confirmed in the
12 randomized Sphere Per-AF trial.⁴⁵ In a real-world study CTI ablation was performed using RF
13 alone (71%), RF+PF (13%), or PF alone (16%), with 100% acute success and no
14 complications. Although acutely effective and safe, most procedures relied on RF, and
15 further data are needed regarding PF-only safety and coronary spasm risk.

16 A focal PFA catheter (Farapoint, Farapulse—Boston Scientific) has been evaluated for CTI
17 ablation. Initial studies showed consistent right coronary vasospasm, largely prevented by
18 IV nitroglycerin.¹⁸⁵ In the ADVANTAGE-AF Phase 2 study,¹¹¹ 141 patients underwent PVI and
19 posterior wall ablation with the pentaspline catheter, followed by CTI ablation using the focal
20 PFA catheter with 4 ± 2 mg IV nitroglycerin. Acute bidirectional block was achieved in almost
21 all patients without complications and flutter recurrence rate was low. These results support
22 the safety and efficacy of focal PFA CTI ablation with nitroglycerin prophylaxis.

1 Another focal PFA system (CardioFocus, Marlborough, MA) was recently compared to RF in
2 CTI ablation. First-pass block was more frequent and procedure time shorter with PFA, but
3 5% developed transient ST elevation and 2% transient complete AV block in spite of IV
4 nitroglycerin prophylaxis.¹⁵²

5 In summary, CTI ablation with PFA currently seems to be limited by proximity-induced right
6 coronary artery spasm, and should only be performed under high dose of IV nitroglycerin
7 prophylaxis.

8

9 Use in ventricular arrhythmias

10 Catheter ablation of ventricular arrhythmias is often limited by insufficient RF energy
11 penetration in scarred or fatty tissue and the presence of extensive substrate. Preclinical
12 data suggest that PFA lesion formation is not attenuated in these conditions and is rapid,
13 making it particularly promising for ventricular arrhythmia ablation.

14 Early feasibility studies using using focal contact force-sensing catheters with the
15 CENTAURI™ PFA generator (CardioFocus, Marlborough, MA) demonstrated reasonable acute
16 and mid-term success in PVC ablation (initial cohort of 20 patients).¹⁸⁶ A second 44 patient
17 cohort reproduced the PVC ablation results, but 3-month VT-free survival was only 52% in
18 those with scar-related VT and transient conduction system block occurred in 3 patients
19 (7%), likely due to current leakage.¹⁸⁷

20 The large-footprint lattice-tip catheter (Sphere-9™; Affera™) was evaluated in two early small
21 studies for VT ablation using combined RF and PF energy, demonstrating feasibility and

1 safety with acceptable acute and short-term outcomes.^{188,189} In the large multicenter
2 European AVAAR registry acute and mid-term success rates were reasonable and major peri-
3 procedural complications occurred in only 6%.¹⁹⁰

4 Recent prospective data further evaluated focal PFA for PVC and VT ablation in 35 patients.
5 Acute success was high (91%), despite nearly one-third having failed prior RF ablation. PVCs
6 mainly originated from the outflow tracts, and most VTs were ischemic. Over ~9 months of
7 follow-up, clinical success was 75% for PVCs but only 45% for VTs, with five patients
8 requiring repeat ablation. Complications included two transient conduction system blocks
9 and two cerebrovascular events (overall major complication rate 6%). These findings
10 suggest good acute efficacy for PVCs but continued uncertainty regarding durability and
11 safety in scar-related VT.¹⁹¹

12 Preclinical data³⁵ show that sequential, colocalized radiofrequency and pulsed-field
13 ablation significantly increases ventricular lesion depth and width compared with either
14 modality alone, supporting hybrid energy or lesion-stacking strategies for thick or fibrotic
15 myocardium. Consistently, the first-in-human VCAS trial¹⁹² demonstrated that focal high-
16 voltage PFA can achieve transmural ventricular substrate modification with high acute
17 success and VT burden reduction, although safety events and uncertain durability highlight
18 the need for further controlled studies.

19 In summary, these findings support the feasibility of the Sphere-9™ ablation system for
20 ventricular arrhythmia ablation, with a reasonable acute and short-term efficacy and safety

1 profile. Larger, controlled studies will be essential to determine lesion durability, procedural
2 safety, and the appropriate clinical role of PFA in ventricular arrhythmias.

3 Use in supraventricular tachycardia

4 Traditional RF ablation is highly effective and safe for the treatment of paroxysmal
5 supraventricular tachycardia (PSVT). PFA may offer shorter procedure times, provided
6 efficacy and safety are at least equivalent.

7 To date, focal PF systems have been studied for PSVT ablation in China. In the largest
8 multicenter cohort, initial PFA followed by PF or RF ablation using a focal contact force-
9 sensing catheter (PulsedFA FocalPoint™, JJET) and a 3D cardiac PFA system with magnetic
10 navigation (JJET, China) demonstrated high acute and mid-term success with infrequent
11 reversible AV block.¹⁹³ In a separate study using the same PulsedFA FocalPoint™ catheter,
12 100% acute and 6-month success with no complications was reported in patients with
13 AVNRT.¹⁹⁴ A more recent study with a different focal bipolar PFA catheter with contact force-
14 sensing (Pulse Magic™ TrueForce™, MicroPort, China) reported also 100% acute and 6-month
15 success but also transient AV block in 17.5% of patients¹⁹⁵

16 In summary, clinical data on PF ablation for PSVT remain limited, and further studies are
17 needed to establish its safety and efficacy.

18 Gaps in evidence

19 Evidence for PFA is most mature for -field ablation (PFA) is most mature for pulmonaryPVI,
20 while substantial uncertainties remain for non-vein isolation, while key uncertainties persist

1 across non-PV targets. Importantly, PFA does not represent a uniform class effect, as
2 substantial heterogeneity exists across technologies with respect to waveform design,
3 voltage, pulse duration, catheter geometry, and application strategies, potentially exceeding
4 the variability observed between RFA approaches. Lesion durability outside the PV, including
5 cavotricuspid isthmus and left atrial linear lesion, has been characterized mainly in small
6 series and repeat atrial linear lesion, has been characterized mainly in small series and
7 redoprocurement cohorts. More data from prospective systematic remapping studies with
8 standardized endpoints are needed to better define long-procedure cohorts. Prospective
9 remapping with standardized endpoints is needed to define long-term effectiveness.^{48,97}
10 Safety signals are generally favorable, but rare risks remain insufficiently quantified over
11 extended follow-up, particularly with respect to coronary vasculature, autonomic
12 structures, renal sequelae, and interactions with intracardiac leads or left-up, particularly
13 with respect to coronary vasculature, autonomic structures, renal sequelae, and
14 interactions with intracardiac leads or left atrial appendage occluders-atrial appendage
15 occluders.^{48,97} Whether specific patient subgroups, such as those with obesity or
16 inflammatory heart disease, derive differential benefit or risk from PFA remains unknown.
17 Moreover, the clinical benefit and durability of posterior wall ablation using PFA have not yet
18 been established. Methodological gaps include dose-response (field strength, pulse
19 number, catheter-tissue coupling), waveform definition and cross-tissue coupling),
20 waveform definition and cross-vendor standardization, and inter-vendor standardization,
21 and inter-system comparability given heterogeneous waveforms and catheter geometries.¹⁹⁶
22 In contrast to RFA, where surrogates such as contact force, impedance drop, temperature,

1 and stability are established, PFA-specific procedural variables predictive of irreversible
2 lesion formation remain to be defined and validated. Although tissue selectivity underpins
3 the rationale for PFA, quantitative profiles across myocardium, nerve, esophagus, and
4 vascular tissue require harmonized preclinical and clinical frameworks; biomarkers and
5 imaging markers of damage (e.g., troponin, late gadolinium enhancement on MRI-clinical
6 and clinical frameworks; biomarkers of damage (e.g., troponin, MRI LGE) and of effect (e.g.,
7 durable conduction block metrics) should be anchored to adjudicated outcomes.^{196,197}
8 Additional priorities span mapping integration and validation of linear lesions (and whether
9 criteria derived from RFA translate), blanking-derived criteria translate), blanking period
10 optimization, characterization of silent cerebral events-period optimization,
11 characterization of silent cerebral events and air, effects on coronary perfusion, autonomic
12 tone, and renal function, health-related quality of life relative to thermal ablation, radiation
13 exposure in real-related quality of life relative to thermal ablation, radiation exposure in
14 realworld workflows, cost-world workflows, cost-effectiveness, and global access.^{41,48,97,196}
15 Health economic data for PFA remain limited¹⁹⁸. While potential efficiency gains related to
16 shorter procedures, and lower complication rates may offset higher upfront device costs,
17 robust cost-effectiveness analyses comparing PFA with established thermal modalities
18 across different healthcare systems are lacking. Prospective studies incorporating
19 procedural costs, repeat interventions, resource utilization, and long-term outcomes are
20 required to define the economic value of PFA. While PFA appears easier to use and safer in
21 most hands, current evidence does not yet demonstrate superior effectiveness compared
22 with thermal energy sources. Addressing these questions will require head-to-head platform

1 trials, standardized lesion-head platform trials, standardized lesion
2 assessment-assessment protocols, and especially longer follow-up-up to align efficacy,
3 safety, and value across indications.^{41,48,97,161,162,196,197}

4 Writing committee position

5 The writing committee of this joint EHRA scientific statement recognizes PFA as a substantial
6 technological evolution in the interventional treatment of patients with AF. The non-thermal
7 mechanism of PFA, based on cell membrane electroporation, results in efficient myocardial
8 ablation while minimizing collateral damage to critical extracardiac structures. This
9 represents a transformation, a departure from thermal ablation, and a significant advance
10 in the management of patients with AF undergoing catheter ablation.

11 Based on the available preclinical and clinical evidence, the committee concludes that PFA
12 achieves at least comparable outcomes with a reduced risk of esophageal injury, pulmonary
13 vein stenosis, and phrenic nerve damage. Randomized trials and real-world registries
14 consistently demonstrate procedural efficiency, short learning curves, and reproducible
15 lesion durability. However, the committee underscores that the variability in catheter design,
16 waveforms, and dosing variables across platforms warrants cautious, evidence-driven
17 adoption of different systems. The writing committee advocates for the integration of PFA
18 into standard electrophysiology practice within structured, competency-based training
19 programs. Operators should have a comprehensive understanding of electroporation
20 principles, device-specific workflows, and the management of PFA-related complications

1 such as coronary vasospasm and hemolysis. Institutions implementing PFA should
2 maintain infrastructure that supports procedural monitoring, ensures device compatibility,
3 and enables participation in registries to foster continuous data collection and quality
4 improvement.

5 The committee highlights that PFA is an adjunct to, not a substitute for, comprehensive
6 electrophysiological expertise within an integrated arrhythmia management platform.
7 Future research should focus on long-term lesion durability, outcomes in patients with
8 persistent AF and patients undergoing repeat procedures, optimization of energy
9 parameters, and the role of PFA in treating non-pulmonary vein targets and ventricular
10 arrhythmias.

11

12 Summary of key points

- 13 • **Mechanism of action:** PFA represents a technological paradigm shift in AF
14 ablation, utilizing irreversible electroporation to achieve myocardial ablation while
15 preserving adjacent structures such as the esophagus, phrenic nerve, and
16 vasculature.
- 17 ▪ **Technology:** Multiple PFA platforms are available, and differences in waveform,
18 energy dosing, and catheter design necessitate platform-specific procedural
19 standardization.
- 20 ▪ **Efficacy:** Randomized trials and large registries demonstrate that PFA provides
21 freedom from AF recurrence at least comparable to radiofrequency or cryoballoon

1 ablation, with faster procedure times and a short learning curve. Nonetheless,
2 durable lesion formation beyond the pulmonary veins, long-term effectiveness, and
3 performance in complex substrates remain incompletely defined.

- 4 ▪ **Safety:** PFA has shown an improved safety profile, with no reported cases of atrio-
5 esophageal fistula or significant pulmonary vein stenosis among >500'000
6 procedures performed globally. However, the true event rate cannot yet be
7 considered zero, and continued vigilance is warranted. Rates of tamponade, stroke,
8 and vascular access complications are low and comparable to thermal ablation.
9 Rare but serious complications, including coronary vasospasm, hemolysis,
10 autonomic effects, and delayed malignant arrhythmias, have been reported, and true
11 event rates require continued surveillance and longer follow-up.
- 12 ▪ **Clinical indication:** PFA is established for de novo paroxysmal AF ablation. In
13 persistent AF and repeat procedures, where PFA is also increasingly used, more data
14 including randomized trials is needed.
- 15 ▪ **Procedural workflow:** Both general anesthesia and deep sedation are feasible and
16 can be integrated into an efficient and safe PFA workflow. Fluoroscopy-only, 3D
17 mapping, and ICE-integrated workflows are all viable options and dependent on case
18 complexity, and availability.
- 19 ▪ **Training:** Dedicated PFA education should be integrated into electrophysiological
20 curricula, emphasizing the theoretical understanding, procedural competence, and
21 awareness of PFA-related complications.

- 1 ▪ **Future directions:** Priorities include long-term outcome data in different patient
2 strata including health-related quality of life relative to thermal ablation, optimized
3 dosing strategies, standardized training and reporting, cost-effectiveness, sex-
4 specific research, and global access-related quality of life relative to thermal
5 ablation-effectiveness,

6 Conclusion

7 In summary, the joint EHRA writing committee supports the responsible clinical adoption of
8 PFA as first-line technology for patients with AF undergoing pulmonary vein isolation.
9 Continued global collaboration, multi-center research, transparent data reporting, and
10 harmonized training standards will be essential to ensure the safe, effective and equitable
11 implementation of this transformative technology. Understanding PFA biophysics and tissue
12 biological responses, its limitations and appreciation of the differences between PFA and
13 thermal energy-based ablations are essential. The writing committee also calls for
14 disclosure of waveforms and technical details by different manufacturers to enable greater
15 and faster progress and maximizing safe implementation of PFA into clinical practice.

16 Data availability

17 This scientific statement is based on published literature, registry data, and expert
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1

2

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6 **Section 2**

7 **Table 1. Comparison of various ablation energies and their effects on**
 8 **cells and tissue.**

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Ablation method	Energy delivery and propagation	Cell damage	(Micro) vasculature	Extracellular matrix	Healing
Radiofrequency ablation (thermal/heating)	Volumetric heating and thermal diffusion	Indiscriminate denaturation of proteins	Highly thrombogenic, indiscriminate thermal damage	Coagulation	Delayed, from periphery
Cryoablation (freeze-thaw)	Thermal diffusion	Crystal formation; cell membrane damage; osmotic imbalance	Clogging, and damage of microvasculature	Preserved	Delayed, from periphery
Pulsed Field Ablation (electroporation)	Electric field effect and volumetric heating	Membrane lipid oxidation and protein damage	Preserved with transient reduction of blood perfusion and increase microvascular permeability	Preserved	Enabled/facilitated, lesion accessible by preserved microcirculation

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Section 3

Table 2.1: Representative pulsed-field ablation (PFA) catheter platforms. Devices are categorized by catheter architecture and ablation strategy. Multielectrode “single-shot” systems are primarily designed for pulmonary vein isolation, whereas focal catheters allow point-by-point ablation similar to conventional RF technology. Differences in energy delivery (monopolar vs bipolar) and waveform characteristics contribute to variability between platforms.



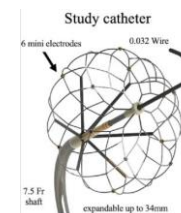
	Farapulse™	PulseSelect™	Varipulse™
	Boston Sci	Medtronic	Biosense Webster
Diameter	31/35 mm	25 mm	25-35 mm
Size	12 F	9 F shaft/9.8 F at array/shaft bond	8.5 F
Over the wire	Yes	Yes	No
Pulse amplitude / duration	1.8-2.0 kV/μs	1.5 kV/μs	1.8 kV/μs
Ablation mode	bipolar	bipolar	bipolar
Wave description	biphasic	biphasic	biphasic
PFA impulse duration	micro- to sub-millisecond	microseconds	microseconds

PFA application duration	2.5 s for a single application 8 minimum per PV advised	4-5 s per application 8 minimum per PV advised	~22 s per ablation (1 ablation = 3 applications) 4 ablation per PV advised
Contact sensing/type	No	No	No
Dedicated 3D Mapping	Yes	Yes	Yes
Approval	EU/USA/Japan/Australia	EU/USA/Japan/Australia	US/EU/APAC/LATAM

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3 Table 2.2

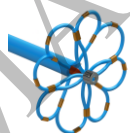


	Volt™	Globe PF™	Sphere 360™
	Abbott	Kardium	Medtronic
Diameter	28 mm	30 mm	34 mm
Size	13 F	16 F	8 F
Over the wire	Yes	No	Yes
Pulse amplitude / duration	1.5-1.8 kV/μs	1.7 kV/μs	1.3-2.0 kV/μs
Ablation mode	bipolar	bipolar	monopolar
Wave description	biphasic	biphasic	biphasic
PFA impulse duration	microseconds	microseconds	microseconds
PFA application duration	~20 s (10 bursts R wave gated)	2 s per train single application per vein/target area 2-6 trains per application	5-6 s per application 4 minimum per PV advised
Contact sensing / type	Yes / Impedance	Yes / Thermal	No
Dedicated 3D Mapping	Yes	Yes	Yes
Approval	EU/USA	USA	EU

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3 Table 2.3

**Adagio™****Lotos™****nsPFA™****Optishot™****SineBurst™****Adagio****Lifetech****Pulse Bioscience****Cardiofocus****Arga Medtech**

	Adagio™	Lotos™	nsPFA™	Optishot™	SineBurst™
	Adagio	Lifetech	Pulse Bioscience	Cardiofocus	Arga Medtech
Diameter	25 mm variable	28/31 mm	30 mm	Up to 40 mm	25 mm
Size	8.5 F	12 F	11 F	12 F	7 F
Over the wire	No	No	No	No	No
Pulse amplitude / duration	1.1 kV/ μ s	1.85-2.1 kV/ μ s	? kV/ns	2.0 kV/ μ s	2.25-3.25 kV/ μ s
Ablation mode	bipolar	bipolar	bipolar	bipolar	bipolar, monopolar, combination
Wave description	biphasic	biphasic	monophasic	biphasic	biphasic, coherent sine-wave
PFA impulse duration	micro- to sub-millisecond	nanosecond	nanosecond	microseconds	microseconds
PFA application duration	single set of 15 pulse trains between sequential electrodes, preceded by 30s ultra-low temperature ablation	5-11 s, 5 trains per site	5 s	25 s (1-2 app/PV)	13 s for nominal dose delivered through all 8 electrodes; phase shifting or maximum output prolongs application
Contact sensing/type	No	No	No		
Dedicated 3D Mapping	No	No	No	No (not required)	No
Approval	No	No	No	No	No

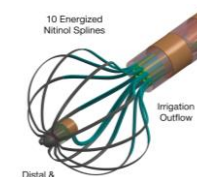
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1 Table 3

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	Sphere 9™ Medtronic	Omnipulse™ Biosense Webster	Faraflex™ Boston Scientific	QuickShot™ Cardiofocus
Diameter	9 mm	12 mm	9 mm	10 mm
Size	8 F	7.5 F	8 F	8.5 F
Steerability	bidirectional	bidirectional	bidirectional	bidirectional
Pulse amplitude / duration	2 kV/μs (P _{frev} : 32 A / <10 μs, EU only)	1.2-1.5 kV/μs	2 kV/μs	3.5 kV/μs
PFA mode	monopolar	bipolar	monopolar / bipolar	monopolar
Wave description	biphasic	biphasic	biphasic	biphasic
PFA impulse duration	microseconds	microseconds	microseconds	microseconds
PFA application duration	4 s	Up to 12 applications max (14.5 s for 12 apps), but duration varies according to PF index target value	2.5 s	QS: 3 s QS+: 6.8 s
RFC / PFA	Yes / Yes	No / Yes	No / Yes	No / Yes
Dedicated 3D Mapping	Yes	Yes	Yes	Open Platform
Approval	EU / USA	No	No	No

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1 Table 4



	Centauri™ Cardiofocus	STSF DualEnergy™ Biosense Webster	Tactiflex dual energy™ Abbott	Farapoint™ Boston Scientific
Electrode spacing	3,5-4 mm	3,5 mm	4 mm	3.5-4 mm
Size	8 F	8 F	8 F	8 F
Steerability	uni- /bidirectional	bidirectional	bidirectional	bidirectional
Contact force sensing	Yes	Yes	Yes	No, local impedance (future)
Amplitude / duration	19-25 A/ μ s	(pulse amplitude) 1.0-1.5 kV/ μ s	1.9-2.2 kV/ μ s	1.4-2.0 kV/ μ s
RFC / PFA	No / Yes	Yes / Yes	Yes / Yes	No / Yes
PFA impulse duration	microseconds	microseconds	microseconds	microseconds
PFA application duration	19 A: 3 s 22 A: 5 s 25 A: 7 s	up to 24 applications (max 28s for 24 apps), but duration varies according to PF index target value	2.2 kv: ~5 s 1.9 kv: ~10 s	2.5 s
Ablation mode	monopolar	monopolar	monopolar	bipolar
Wave description	biphasic	biphasic	biphasic	biphasic
Dedicated 3D Mapping	Open Platform	Yes	Yes	Yes
Approval	EU	EU	EU, Dec 2025	EU (and US approval CTI indication)

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Table 5: Suggested framework for harmonized classification of PFA catheters

Catheter classification	Proposed definition	Previous terms used
Regional catheter	Catheter with the largest dimension in contact with tissue > 12 mm	Circumferential PVI catheter; Single-shot catheter
Large-tip focal catheter	Catheter with the largest dimension in contact with tissue > 4 mm and ≤ 12 mm	Wide-area focal catheter; Large-tip or lattice-tip catheter (e.g. Affera); Large-tip focal catheter (e.g. Omnipulse)
Focal catheter	Catheter with the largest dimension in contact with tissue ≤ 4 mm	Conventional focal catheter; Large/intermediate footprint catheter; Focal catheter

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Section 5

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Table 6: Sedation and anaesthesia approaches for PFA (illustrative dosing)

Protocol	Drug(s)	Typical dosing	Notes
Local anaesthesia (adjunct only)	Local anaesthetic at access sites	Per institutional practice	Insufficient as sole strategy for PFA owing to discomfort and skeletal muscle contractions; used only as adjunct.
Conscious (moderate) sedation¹	Midazolam + short-acting opioid; multimodal adjuncts (e.g., lidocaine for coughing), optional bolus etomidate if required	Midazolam 0.01–0.03 mg/kg IV + fentanyl 0.5–1 µg/kg IV; lidocaine 1–1.5 mg/kg IV; optional etomidate bolus (e.g. 0.05–0.1 mg/kg)	Feasible for certain PFA systems in selected patients; without routine involvement of anaesthesiology personnel; preserves spontaneous respiration but may provide less immobility and comfort than deep sedation
Deep sedation²	Midazolam + short-acting opioid ± ketamine or dexmedetomidine	Midazolam 0.01–0.03 mg/kg IV; fentanyl 0.5–1.5 µg/kg IV; ketamine 0.5–1 mg/kg IV before first PFA, top-ups 0.1–0.2 mg/kg as needed	Increasingly preferred for PFA; preserves spontaneous respiration; high safety and short recovery when delivered by trained staff with structured monitoring.
Propofol-based deep sedation³	Propofol + short-acting opioid ± small benzodiazepine	Propofol 0.5–1 mg/kg IV bolus, then 0.25–0.5 mg/kg boluses or 25–75 µg/kg/min infusion; fentanyl 0.5–1 µg/kg IV; optional midazolam 0.01–0.03 mg/kg IV at start or minimal-propofol strategy ⁴ : Midazolam 0.01–0.03 mg/kg + fentanyl 0.5–1 µg/kg IV; propofol only in 0.25–0.5 mg/kg rescue boluses	Most commonly used in clinical routine; rapid onset; stable and predictable if titrated slowly; requires continuous monitoring and airway-trained personnel.
General anaesthesia	Per anaesthesiology practice	Per institutional standards	Provides full airway control and immobility; suitable for complex or high-risk cases or patients with obesity/anticipated difficult airway;

Protocol	Drug(s)	Typical dosing	Notes
			associated with longer lab occupancy and higher resource demand.

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Table 7. EAM integration across PFA systems (alphabetical order)

System	Mapping Integration	Limitations
Affera Sphere-9	Proprietary Affera mapping platform with combined mapping/ablation	Interoperability with external 3D systems (CARTO/EnSite) not available at present
Farapulse	Proprietary OPAL HDx mapping platform with catheter orientation and lesion tagging	Simplified visualization; positional accuracy lower than full EAM systems
PulseSelect	Compatible with CARTO, EnSite systems and Affera mapping platform	No native integration; Impedance based tracking only, no sensor-based tracking.
Varipulse	Fully integrated EAM with lesion tagging	Restricted to CARTO system
Volt	Fully integrated EAM with contact sensing and lesion tagging	At present limited to investigational clinical experience

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1 **Table 8. Examples of conditions associated with interruption of PFA energy delivery**

2

Catheter concept (generic)	Typical triggering condition	Practical implication
Multi-spline loop catheters (incl. pentaspline)	excessive proximity of individual splines / loss of stable antral alignment / electromagnetic interaction with adjacent metallic implants	if splines are touching or excessively close, energy delivery is inhibited
Variable-loop catheters	loop diameter reduced below the validated geometric range (electrode–electrode spacing too small)	generators will typically refuse to deliver energy until the loop diameter is increased
Focal PFA tip / lattice-tip catheters	abrupt temperature overshoot or impedance rise when the tip is wedged in a tight angle or excessive forward force is applied	gentle retraction or slight rotation to a less constrained angle often restores safe energy delivery
Balloon-based multi-electrode systems	partial loss of wall contact, or artefact from air/saline/blood mixing around the electrodes	correction of balloon position and elimination of air typically restores energy delivery

3 **Note:** only interference with a lobe-and-disk LAA occluder has been formally described as a cause of interrupted delivery;⁵ all other
4 scenarios reflect generic safety logic of contemporary PFA platforms.

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1 **Table 9: Practical advice: procedural workflow in pulsed field ablation**

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Step	Practical advice
Pre-procedure	Use either general anesthesia or deep sedation, or in selected platforms/centers conscious sedation, CT/MRI can support planning but is not mandatory.
Electroanatomical mapping	EAM use routinely for first-time PVI is not mandatory; could be employed in redo procedures, atypical anatomy, or when additional lesion sets are planned.
CIED patients	PFA can usually be performed safely in CIED patients using standard precautions: avoid close proximity and direct ablation near leads, and interrogate the device before and after the procedure. However, device–PFA interactions may be platform-dependent and cases of clinically relevant CIED malfunction have been reported; heightened caution and manufacturer-specific guidance are advised, particularly for hybrid RF/PFA systems.
LAAO patients	Be aware of potential arcing with metallic devices. Prefer performing PFA before LAAO implantation; if done after LAAO, proceed with caution. Reserve concomitant PFA+LAAO procedures for selected patients and expert centers.
Vascular access & anticoagulation	Use ultrasound-guided femoral access to reduce complications. Maintain ACT ≥ 300 –350 s and continue oral anticoagulation uninterrupted where possible.
Transseptal puncture	Use a posterior puncture as standard, use ICE in difficult cases. Tailor puncture site to system and patient anatomy.
Sheath handling	Apply strict flushing protocols where needed with continuous saline to minimize thromboembolism. “Zero-exchange” workflows can be employed where feasible.
Vagal responses	Anticipate vagal reflexes, especially at LSPV/LIPV. They are usually self-limited; treat clinically relevant episodes with atropine, and use pacing only rarely if needed.

Step

Practical advice

Catheter–tissue contact	Catheter–tissue contact is often inferred rather than directly measured: tactile feedback, fluoroscopic spline indentation, pacing response, ICE, or EAM/impedance-based feedback to confirm antral positioning and adequate proximity.
Validation	Always validate acute entrance (and when appropriate exit) block as the procedural endpoint. Be meticulous with near- vs far-field discrimination. Pacing and pharmacological testing may be used selectively, acknowledging that evidence for improved prediction of long-term durability is limited.
Post-procedure	Post-procedural management (including anticoagulation duration and rhythm monitoring) should follow contemporary AF ablation guidelines. Monitor for vascular complications, pericardial effusion, and coronary spasm. Same-day discharge is feasible in stable, low-risk patients.

1 **Section 6**

2 **Table 10: Randomized Controlled Trials comparing PFA to thermal ablation**

3

Registries	PF Catheter & Comparator	PF Catheter Manufacturer	Patients	Sites & Enrolment Period	AF Type	Endpoint Definition	Monitoring strategy	Efficacy Endpoint	Safety Endpoint	Procedure Time
ADVENT⁶	Pentaspine catheter Thermal ablation	Boston Scientific	607	30 (03/2021 – 06/2022)	PAF – 100.0%	Freedom from treatment failure, AT/AF recurrence, cardioversion, reinitiation of AAD, or reablation	Intermittent (72hr Holter after 6 & 12 months plus weekly TTM)	PFA – 73.3% Thermal -71.3%	PFA - 2.1% Thermal – 1.5%	PFA – 106 min Thermal – 123 min
SINGLE SHOT CHAMPION⁷	Pentaspine catheter Cryoballoon ablation	Boston Scientific	210	2 (09/2022 – 11/2023)	PAF – 100.0%	Freedom from AT/AF recurrence	Continuous (ICM)	PFA – 62.9% CBA – 49.3%	PFA – 1.0% CBA – 1.9%	PFA – 55 min CBA – 73 min

BEAT-AF	Pentaspine catheter	Boston Scientific	289	9 (04/2021 – 01/2024)	PAF – 100.0%	Freedom from AT/AF recurrence, reinitiation of AAD, or reablation	Intermittent (24hr Holter after 2, 6 & 12 months plus weekly TTM)	PFA – 77.2%	PFA – 4.8%	PFA – 56 min
	Radiofrequency ablation							RFA – 77.6%	RFA – 7.6%	RFA – 95 min
INSIGHT PFA	Lotos catheter	Insight Lifetech	287	9 (09/2023 – 06/2024)	PAF – 100.0%	Freedom from AT/AF recurrence, reinitiation of AAD	Intermittent (24hr Holter after 6 & 12 months)	PFA – 66.7%	PFA – 18.3%	PFA – 99 min
	Radiofrequency ablation							RFA – 67.4%	RFA – 17.9%	RFA – 113 min
Sphere persAF[®]	Lattice Tip dual energy catheter	Medtronic	420	23 (12/2021 – 12/2022)	PsAF – 100.0%	Freedom from treatment failure, AT/AF recurrence, cardioversion, reinitiation of AAD, or reablation	Intermittent (24hr Holter after 6 & 12 months)	Lattice Tip – 73.8%	Lattice Tip – 1.4%	Lattice Tip – 101 min
	Radiofrequency ablation							RFA – 65.8%	RFA – 1.0%	RFA – 126 min

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2 **AF**, atrial fibrillation. **AT**, atrial tachyarrhythmia. **PAF**, paroxysmal atrial fibrillation. **PFA**, pulsed-field ablation. **CBA**, cryoballoon ablation. **RBA**, radiofrequency ablation. **PersAF**,
3 persistent atrial fibrillation. **ICM**, implantable cardiac monitor. **AAD**, antiarrhythmic drugs.

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1 **Table 11: Pivotal trials for regulatory approval**

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Studies	PF Catheter	Manufacturer	Patients	Sites & Enrolment Period	AF Type	Acute Post-procedural Success	Follow-up	Freedom from AF/AT	Major Adverse Events ^a n (%)	PF-specific Adverse Events n (%)
inspire⁹	Variable-loop circular catheter	Biosense Webster	272 ⁹	13 (08/2020 – 05/2022)	PAF – 100.0%	97.1%	12 months	70.9%	Total: 0 •Tamponade – 0 •Death – 0 •Stroke – 0 •Major Vascular – 0	•Coronary spasm – NR •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR
AdmIRE¹⁰	Variable-loop circular catheter	Biosense Webster	277	30 (04/ 2022 – 11/2022)	PAF – 100.0%	100.0%	12 months	75.4%	Total: 8 (2.9%) •Tamponade – 3 (1.1%) •Death – 0 •Stroke – 2 (0.7%) •Major Vascular – 2 (0.7%)	•Coronary spasm – 0 •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – 0
PULSED AF¹¹	Circular array catheter	Medtronic	300	41 (03/ 2021 – 11/2021)	PAF – 50.0% PsAF – 50.0%	100.0%	12 months	PAF – 66.2% PsAF – 55.1%	Total: 2 (0.7%) •Tamponade – 1 (0.3%) •Death – 0 •Stroke – 1 (0.3%) •Major Vascular – 0	•Coronary spasm – NR •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR
Sphere-360 European Study¹⁵	Large-lattice circumferential catheter	Medtronic	100	3 (NR – NR)	PAF – 100.0%	100.0%	12 months	82.0%	Total: 0 •Tamponade – 0 •Death – 0 •Stroke/TIA – NA •Major vascular – 0	•Coronary spasm – NR •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR

IMPULSE, PEFCAT & PEFCATII ¹²	Pentaspine catheter Focal catheter for CTI	Boston Scientific	121	3 (NR – NR)	PAF – 100.0%	100.0%	12 months	79.3% ^b	Total: 2 (1.6%) •Tamponade – 1 (0.8%) •Death – 0 •Stroke – 1 (0.8%) •Major Vascular – 1 (0.8%)	•Coronary spasm – NR •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR
VOLT CE MARK Study ¹⁴	Balloon-in-basket Catheter	Abbott	150	11 (11/2023 – 03/2024)	PAF – 70.5% PsAF – 29.5%	98.1%	6 months	PAF – 88.2% PsAF – 76.7%	Total: 4 (2.7%) •Tamponade – 1 (0.7%) •Death – 0 •Stroke – 1 (0.7%) •Major Vascular – 2 (1.4%)	•Coronary spasm – 0 •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR
SPHERE Per-AF ⁸	Lattice-tip catheter	Medtronic	420	20 (12/2021 – 12/2022)	PsAF – 100.0%	NR	12 months	73.5%	Total: 0 (0.0%) •Tamponade – 0 (0.0%) •Death – 0 (0.0%) •Stroke/TIA – 0 •Major vascular – 0	•Coronary spasm – NR •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR
ADVANTAGE AF ¹³	Focal-linear catheter	Medtronic	255	29 (10/2023 – 03/2024)	PsAF – 100.0%	99.6%	12 months	77.8% ^c	Total: 6 (2.4%) •Tamponade – 1 (0.4%) •Death – 1 (0.4%) •Stroke/TIA – 3 (1.2%) •Major Vascular – 1 (0.4%)	•Coronary spasm – NR •Esophageal fistula – NR •PV Stenosis – NR •Persistent PNI – NR •Haemolysis – NR

1

2 **AF**, atrial fibrillation. **AT**, atrial tachyarrhythmia. **CTI**, cavotricuspid isthmus. **PAF**, paroxysmal atrial fibrillation. **PF**, pulsed-field. **PNI**, phrenic nerve injury. **PsAF**, persistent atrial
3 fibrillation. **PV**, pulmonary vein. **NR**, not reported. **TIA**, transient ischaemic attack.

4 ^a Major adverse events as defined in each individual study. Not all subcategories of major adverse events are described.

5 ^b Refers to single procedure (i.e. with no ablation during remapping or otherwise).

6 ^c Pulmonary vein and posterior wall isolation (100%) and 55.3% had concomitant cavotricuspid isthmus ablation.

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1 **Table 12: Large multicentre post-approval PFA registries**

Registries	PF Catheter	Manufacturer	Patients	Sites & Enrolment Period	AF Type	Acute Post-procedural Success	Follow-up	Freedom from AF/AT ^a	Major Adverse Events ^b n (%)	PF-specific Adverse Events n (%)
MANIFEST-PF¹⁶	Pentaspine catheter	Boston Scientific	1,568	24 (03/2021 – 05/2022)	PAF – 65.0% PsAF – 32.0%	99.2%	12 months	PAF – 81.6% PsAF – 71.5%	Total: 30 (1.9%) •Tamponade – 18 (1.1%) •Death – 1 (0.06%) •Stroke – 6 (0.4%) •Major vascular – 2 (0.1%)	•Coronary spasm – 2 (0.1%) •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR
MANIFEST-17k¹⁷	Pentaspine catheter	Boston Scientific	17,642	106 (01-03/2022 – 06/2023)	PAF – 57.8% PsAF – 35.2%	NR	Peri-procedural Only	N/A	Total: 173 (0.9%) •Tamponade – 63 (0.36%) •Death – 5 (0.03%) •Stroke – 22 (0.12%) •Major vascular – 53 (0.3%)	•Coronary spasm – 25 (0.14%) •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – 6 (0.03%)
EU-PORIA¹⁸	Pentaspine catheter	Boston Scientific	1,233	7 (03/2021 – 05/2022)	PAF – 60.2% PsAF – 39.8%	99.96%	12 months	PAF – 80.0% PsAF – 66.0%	Total: 21 (1.7%) •Tamponade – 14 (1.1%) •Death – 0 •Stroke – 5 (0.41%)	Coronary spasm – 1 (0.1%) •Esophageal fistula – 0 •PV Stenosis – 0 •Persistent PNI – 0 •Haemolysis – NR

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4 **AF**, atrial fibrillation. **AT**, atrial tachyarrhythmia. **PAF**, paroxysmal atrial fibrillation. **PF**, pulsed-field. **PsAF**, persistent atrial fibrillation. **PNI**, phrenic nerve injury. **PV**, pulmonary vein. **NA**,
5 not available. **NR**, not reported.

6 ^a Defined as AF/AT > 30 seconds. Typically follow-up at 3, 6, and 12 months and additional Holter monitors after 90 days of blanking period.

7 ^b Major adverse events as defined in each individual study. Not all subcategories of major adverse events are described.

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1 Section 7

2 **Table 13: Objective structured assessment of technical skills for AF ablation using PFA**
3 **(modified from EHRA core curriculum).**¹⁹
4

1. Safe use of EP laboratory equipment relevant to PFA, including fluoroscopy and/or electroanatomical mapping as required by the specific platform; understanding of PFA-specific biophysics (irreversible electroporation, tissue selectivity, pulse characteristics) and how these differ from thermal energy.
2. Venous access, transseptal puncture, anticoagulation management, and imaging guidance (fluoroscopy, ICE where indicated) tailored to PFA system requirements.
3. System-specific catheter handling (single-shot, balloon-based, lattice, or focal PFA), correct antral positioning, avoidance of deep or ostial deployment, and recognition of suboptimal positioning requiring repositioning or repeat applications.
4. Perform PVI using PFA, including anatomical understanding of the PV antra, appropriate application strategies, management of system-specific phenomena (e.g. phrenic nerve capture, extracardiac muscle stimulation), and recognition and management of acute complications.
5. Verification of <i>acute</i> pulmonary vein entrance (and when appropriate exit) block, with correct near- vs far-field signal interpretation; understanding the limitations of acute assessment in predicting long-term durability.
6. Recognition and management of vagal responses, transient conduction disturbances, coronary spasm, phrenic nerve capture, cough or diaphragmatic contraction, and platform-specific interactions with intracardiac devices or metallic implants.
7. System- and indication-specific use of PFA for additional lesion sets (e.g. posterior wall, superior vena cava, linear lesions), including appropriate patient selection, anatomical considerations, and safety limitations specific to PFA.

5

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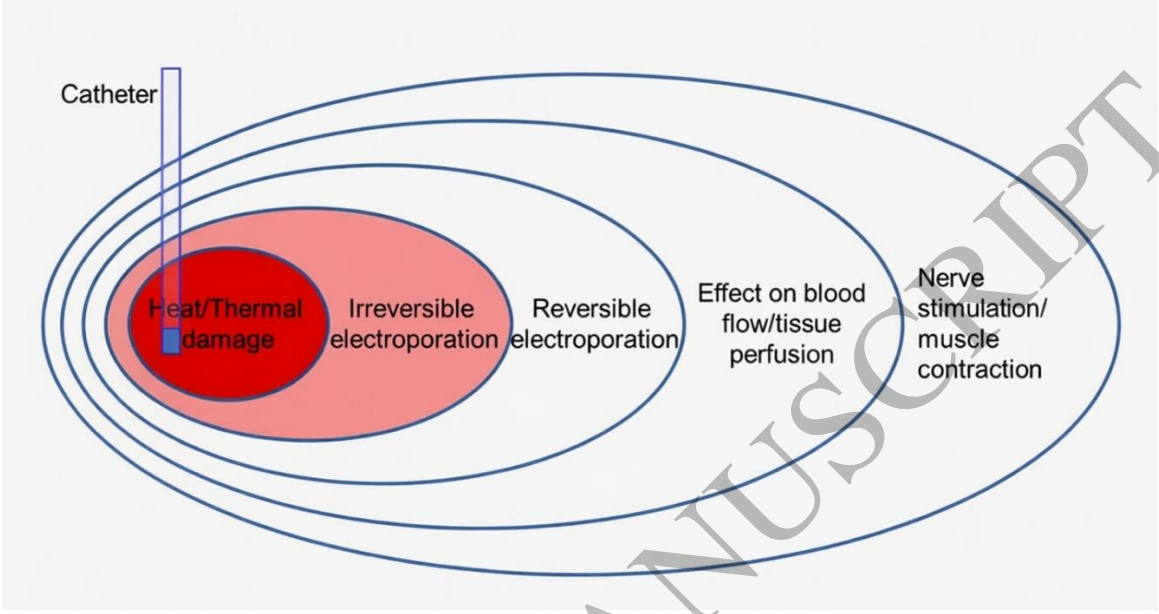
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32 **Figure 1:**

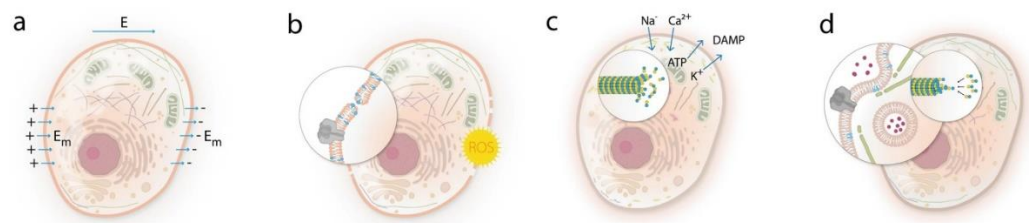
33 Each waveform produces distinct tissue responses in the region surrounding the catheter.
34 In the immediate vicinity, the highest electric field strength and current density result in
35 thermal injury, specifically coagulative necrosis. This is followed by zones of irreversible
36 electroporation, then reversible electroporation at greater distances, which leads to
37 cellular stunning and transient effects on vasculature and perfusion. At the greatest

- 1 distances from the catheter, nerve stimulation is expected, involving both autonomic
- 2 nerves and neuromuscular capture.



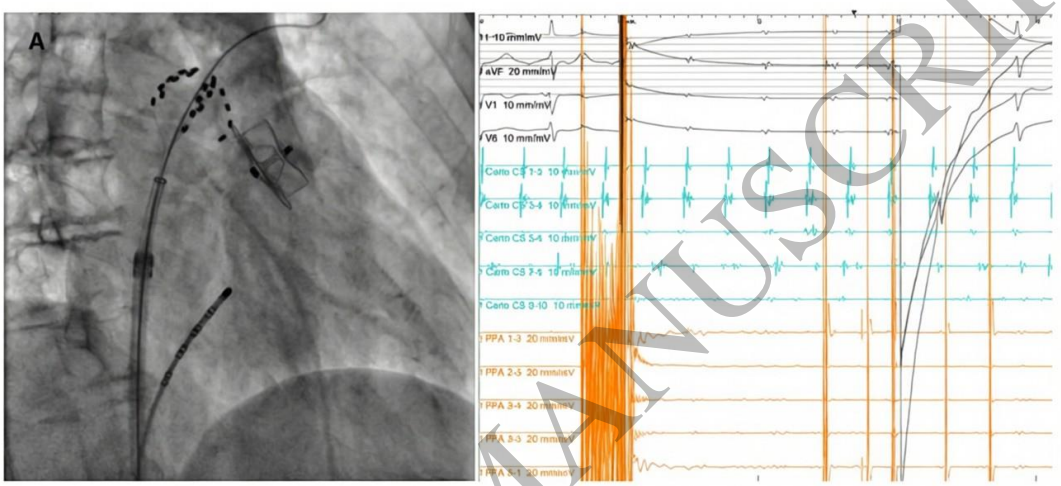
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Figure 2: Electroporation can be achieved using a variety of pulse shapes and parameter settings: duration (ns, μ s, ms), number of pulses or trains, and shape (e.g. mono-, biphasic, exponentially decaying, sinusoidal). Despite these differences, all electroporation modalities share common hallmarks: induced transmembrane voltage (comparable to that responsible for action potentials) leading to transient transmembrane protein damage and lipid oxidation. This process permits the transport of ions and molecules across the membrane, including calcium influx (causing calcium overload and disruption of the cytoskeleton), sodium influx, and potassium efflux. The resulting membrane depolarization produces cellular non-excitability and stunning, while the release of damage-associated molecular patterns (DAMPs) triggers an immune response. The outcome ultimately depends on membrane repair, leading either to cell recovery or to cell death. ROS: Reactive Oxygen Species.

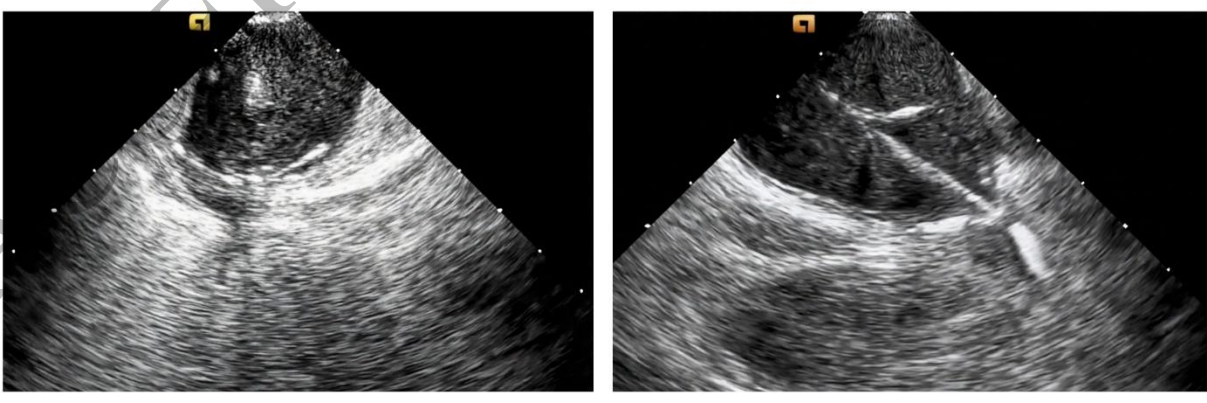


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1 **Figure 3:** Shown is in RAO the pentaspline PFA catheter and a left atrial appendage closure
2 device (Amplatzer Amulet device) with lobe-and-disc design. Real-time EGMs showed
3 artifacts recorded from the PFA catheter electrodes in contact with the adjacent LAA
4 occlusion device (A). Multiple attempts to deliver PFA were immediately stopped by the
5 system due to overlapping among the electrodes of the PFA catheter and the disk of the
6 Amulet. Repositioning of the PFA catheter allowed antral PFA and applications were
7 ultimately possible (B).

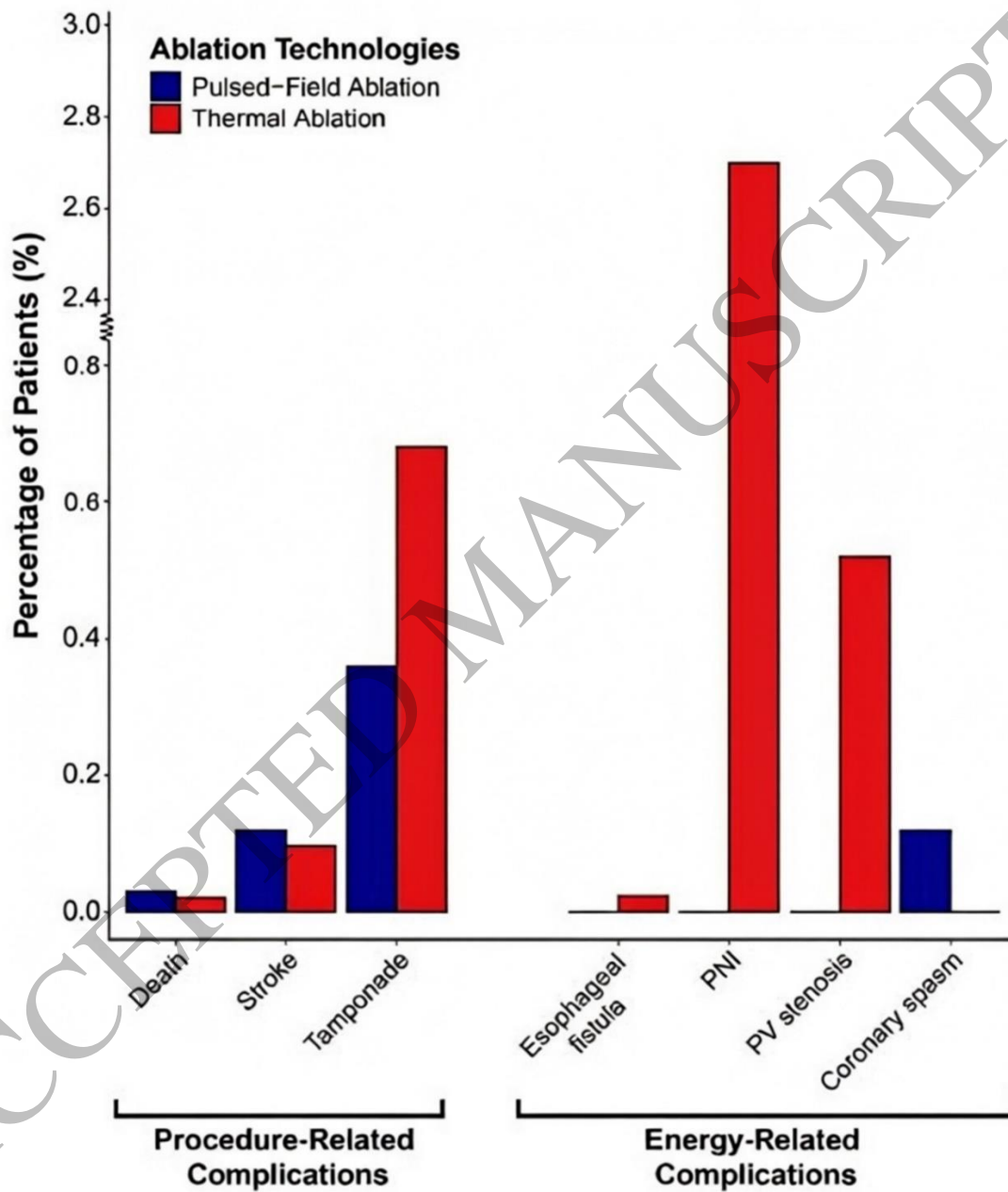


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9 **Figure 4:** Visualization of the pentaspline pulsed field ablation (PFA) catheter by
10 intracardiac echocardiography (ICE). The pentaspline PFA catheter is deployed in the
11 flower configuration in the right inferior pulmonary vein (left) and in the basket
12 configuration in the left inferior pulmonary vein (right). ICE allows visualization of catheter-
13 tissue contact. This also ensures that the PFA catheter remains at the ostium and not
14 inside the pulmonary vein.



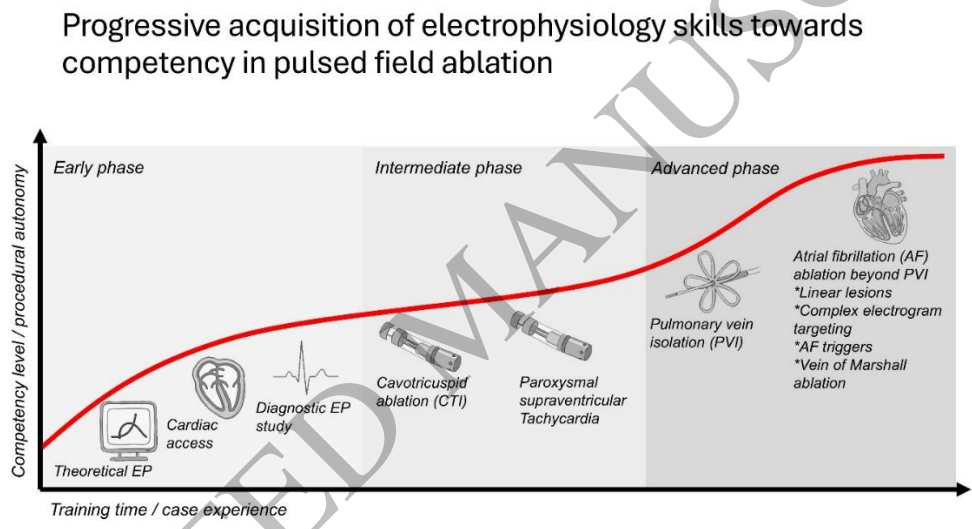
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1 **Figure 5:** Summary of procedure-related and energy-related complications associated with
2 thermal and pulsed-field ablation.

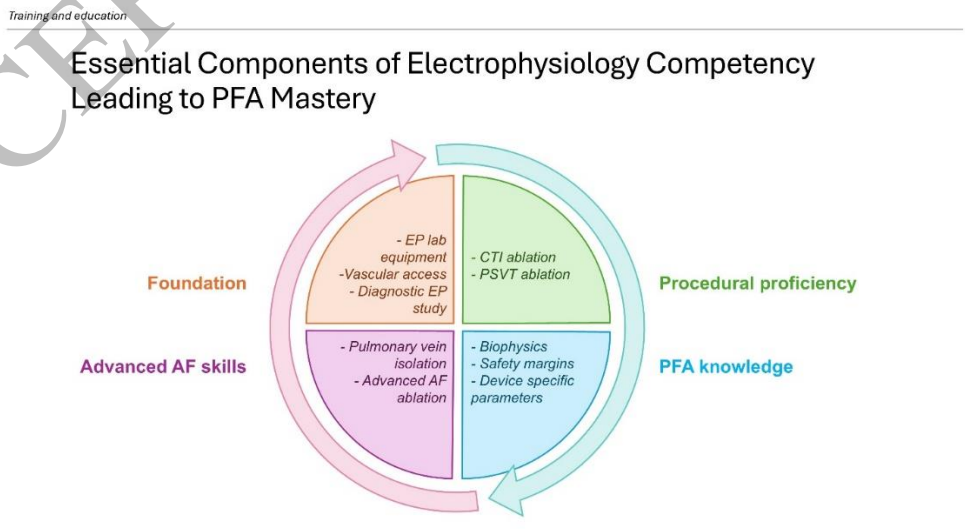


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1 **Figure 6:** Progressive acquisition of electrophysiology competencies toward pulsed field
 2 ablation (PFA) proficiency.
 3 The learning curve illustrates the sequential development of key procedural skills required
 4 to achieve competency in PFA. Foundational competencies include use of EP laboratory
 5 equipment, vascular and cardiac access, and performance of diagnostic EP studies.
 6 Intermediate competencies encompass cavotricuspid isthmus (CTI) and non-CTI atrial
 7 tachycardia ablations. Advanced competencies involve pulmonary vein isolation (PVI) and
 8 atrial fibrillation ablation beyond PVI, including linear lesions, complex electrogram
 9 targeting, and Vein of Marshall ablation. Mastery of these domains culminates in
 10 independent, safe, and efficient performance of PFA procedures



11
 12 **Figure 7:** Essential Components of Electrophysiology Competency Leading to PFA Mastery



1 **Figure 8:** Examples of electroanatomical integration of different pulsed field ablation
2 systems.

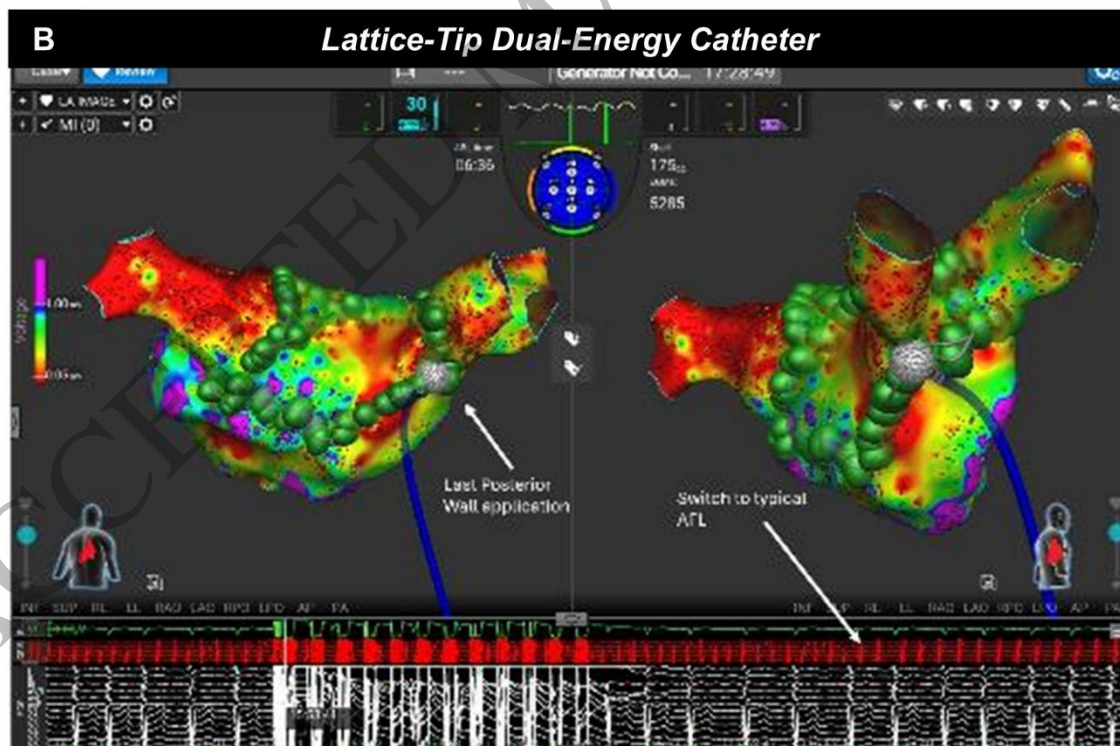
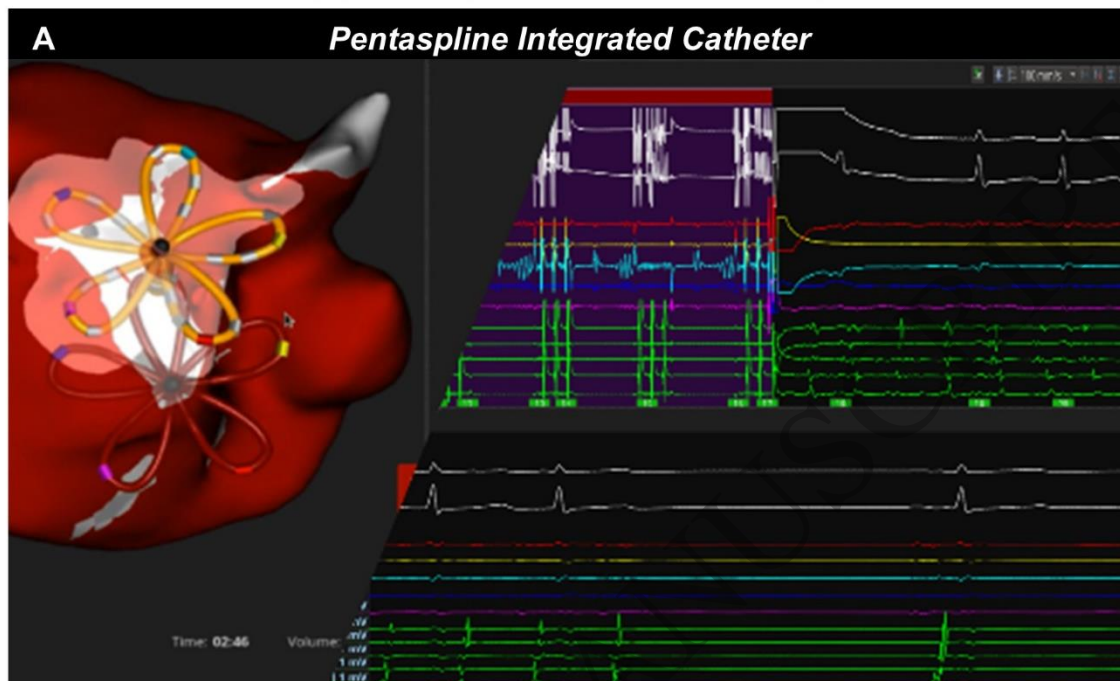
3 Panel A. Left and central images: 3D anatomical volume reconstruction using sequential
4 intracardiac echocardiography projections. The image on left side shows ablated zones
5 using the variable loop circular catheter in purple. Right image: spheres give accurate
6 indication of electrode contact (Tissue proximity indicator): sphere dimension is
7 proportional to amount of contact. Small dots predicts where energy will be delivered; red
8 indicates lesions overlapping, green unablated tissue.

9 Panel B: pulmonary vein signals were detected in a redo case using a large footprint lattice-
10 tip catheter. The lattice tip enables high-resolution recording of near-field signals while
11 effectively filtering out noise and far-field activity. Moreover, ablation can be performed
12 directly with the same catheter. The figure also shows the proximity indicator for the single
13 electrode, which helps ensure both accurate signal acquisition and effective lesion
14 formation during ablation.

15 Panel C: Balloon in basket PFA system with electroanatomical mapping integration
16 (LivePoint™ Display Algorithm), which allows for the evaluation of impedance-based lesion-
17 effect parameters through AutoMark lesions (that follow the Livepoint software color
18 legend) and eField integration. Energy Field (eField) displays projection of the electric field
19 of therapy delivery on the map.

20 Abbreviations: ICE, intracardiac echocardiography; PFA, pulsed field ablation.

POSTERIOR WALL ABLATION



1

2

1 **Figure 10:** Examples of linear left atrial ablation using different electroanatomical
2 integrated PFA systems.

3 *Panel A.* The large focal tip catheter also creates broader lesions, thereby facilitating the
4 formation of continuous linear lesions in the left atrium.

5 *Panel B:* Example of Atypical Flutter mapped with Farawave 2.0 and Faraview software. On
6 the left, the LAT map that shows a mitral isthmus-dependent atypical flutter; on the right,
7 energy delivered on the anterior mitral isthmus results in flutter termination.

8 *Panel C:* Successful Pulsed field ablation performed on the critical isthmus located in the
9 anterior roof, as identified by LAT map using the Coherent software module. PF index 500,
10 ITD \leq 6mm to ensure contiguity and lesion durability.

LINEAR LEFT ATRIAL ABLATIONS

