



Pulsed-Field Ablation for Atrial Fibrillation: Tissue Selectivity, Learning Curves and Unanswered Durability Questions

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Introduction

Catheter ablation for atrial fibrillation has relied for two decades on thermal energy -- radiofrequency heating or cryoballoon freezing -- to destroy the cardiac tissue responsible for triggering or sustaining the arrhythmia, with esophageal injury, phrenic nerve palsy, and pulmonary vein stenosis as recognized, if uncommon, costs of that thermal indiscriminateness. Pulsed-field ablation uses very short high-voltage electric pulses instead, a mechanism its proponents argue is preferentially toxic to myocardial tissue and largely spares the structures thermal energy can injure. Four studies published in close succession now let this claim, and the technology's broader adoption, be assessed with real data rather than mechanism alone.

This review sets out what the pivotal randomized trial, its extended follow-up, a large real-world safety registry, and a dedicated learning-curve study together show about pulsed-field ablation's tissue selectivity, adoption trajectory, and durability.

The clinical stakes of getting this assessment right are not trivial. Catheter ablation for atrial fibrillation is now performed in large and growing numbers worldwide, and a technology change of this scale -- effectively a new default energy source for an already common procedure -- deserves scrutiny proportionate to how quickly it has been adopted. Esophageal injury, though uncommon with thermal energy, can be catastrophic when it occurs, and phrenic nerve palsy and

pulmonary vein stenosis, while rarely life-threatening, carry real morbidity and reintervention burden. A genuine reduction in these specific harms would be clinically meaningful even before any question of comparative efficacy is settled.

Material and Methods

This is a narrative review drawing on the ADVENT randomized trial, its 4-year extended follow-up (ADVENT-LTO), the MANIFEST-17K real-world safety registry, and a national learning-curve study, identified through the sources cited above and citation tracking between them, without a pre-registered protocol or systematic search string. All percentages, p-values, and confidence intervals reported here are taken directly from the cited sources; none has been invented, estimated, or extrapolated.

Where a source's full author list could not be independently confirmed beyond its indexed abstract, that limitation is stated explicitly alongside the corresponding finding, and no finding from any source has been reanalyzed, recalculated, or extrapolated beyond what the source itself reports.

Results

The pivotal trial: noninferior efficacy and safety, superior vein preservation

ADVENT randomized 305 patients with paroxysmal atrial fibrillation to pulsed-field ablation and 302 to conventional thermal ablation [1]. At one year, the primary efficacy outcome was 73.3% with PFA versus 71.3% with thermal ablation, and the primary safety outcome was 2.1% versus 1.5%, both meeting prespecified noninferiority criteria [1]. Figure 1 sets both primary outcomes out together. A secondary, superiority-tested measure told a different story: pulmonary vein cross-sectional area was reduced by only 3.3% with PFA versus 19.5% with thermal ablation, meeting the prespecified criterion for superiority of PFA [1]. Figure 2 sets this tissue-selectivity finding out directly -- the clearest trial-level evidence that PFA's mechanism translates into measurably less collateral structural injury.

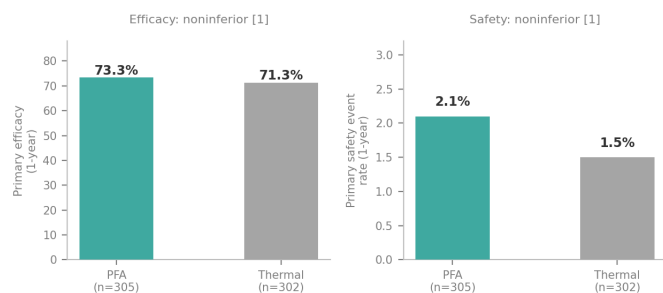


Figure 1: Primary efficacy and primary safety outcomes at 1 year, PFA versus thermal ablation, ADVENT trial [1].

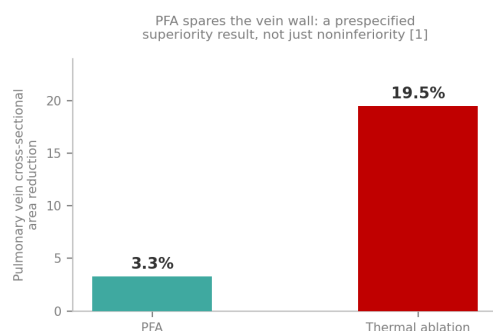


Figure 2: Pulmonary vein cross-sectional-area reduction, PFA versus thermal ablation, ADVENT trial (secondary, superiority-tested endpoint) [1].

Four-year follow-up narrows the efficacy gap while repeat ablation stays lower

ADVENT-LTO followed the same cohort to 4 years. Freedom from atrial fibrillation, atrial tachycardia, atrial flutter, cardioversion, or repeat ablation was 72.8% with PFA versus 64.3% with thermal ablation, a difference that was no longer statistically significant ($P=0.12$) [2]. Figure 3 sets this alongside repeat-ablation rates, which did remain significantly lower with PFA (10.4% vs 17.7%, $P=0.04$) [2]. Notably, only about 9% of patients free of recurrence in the first year after PFA went on to recur by 4 years, suggesting that durability, once achieved early, tends to hold [2].

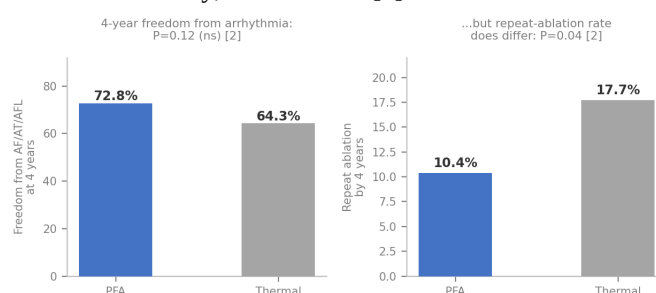


Figure 3: Freedom from atrial arrhythmia and repeat-ablation rate at 4 years, PFA versus thermal ablation, ADVENT-LTO [2].

Real-world safety at scale: fewer complications overall, but two new ones

MANIFEST-17K pooled 17,642 real-world PFA procedures across 106 centers in 20 countries [3]. Major complications occurred in about 0.98% of patients overall, with pericardial complications (0.36%), stroke (0.12%), and mortality (0.03%) all well below rates reported in a historical thermal-ablation registry (1.52%, 1.02%, and 0.42% respectively) [3]. Figure 4 sets this comparison out directly. Strikingly, this large series recorded zero esophageal complications, zero pulmonary vein stenosis, and zero persistent phrenic nerve palsy -- the three complications thermal energy is most associated with [3]. Figure 5 sets these zero counts alongside two complications this registry identified as apparently specific to pulsed-field energy: coronary arterial spasm (0.14%) and hemolysis-related acute renal failure (0.03%) [3]. Tissue selectivity, in other words, appears real for the thermal-injury pattern PFA was designed to avoid, but it has introduced a distinct, low-frequency complication profile of its own.

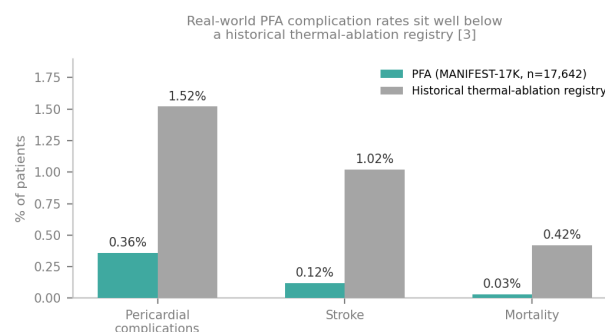


Figure 4: Major complication rates, PFA (MANIFEST-17K) versus a historical thermal-ablation registry [3].

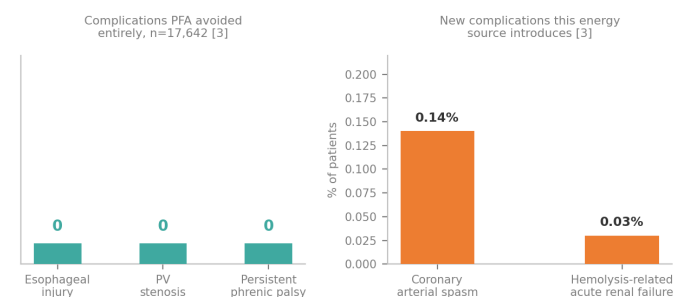


Figure 5: Complications PFA avoided entirely versus complications specific to this energy source, MANIFEST-17K [3].

The learning curve is real but resolves quickly

A national workflow study of 752 patients found time to pulmonary vein isolation fell from 25.6 minutes in an operator's first 10 procedures to 16.5 minutes beyond that ($p < 0.0001$), with fluoroscopy time falling similarly (19.8 to 15.9 minutes, $p = 0.0045$) [4]. Figure 6 sets both trends out together. The authors described a rapid, consistent linear improvement, with most of the procedural gain realized after only a handful of cases [4].

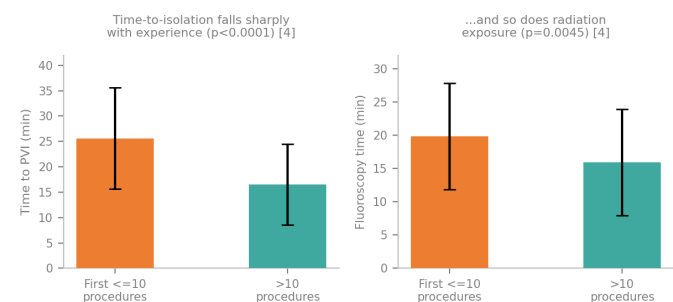


Figure 6: Time to pulmonary vein isolation and fluoroscopy time, first 10 procedures versus beyond, national workflow study [4].

Discussion

Taken together, these four sources support a specific and more nuanced claim than either 'PFA is simply better' or 'PFA is simply different': its tissue selectivity for the classic thermal-injury complications (esophageal, pulmonary vein, phrenic) appears genuinely substantiated, both in a randomized trial's structural imaging endpoint and in a 17,642-patient real-world registry recording zero events of each. Its overall real-world safety profile, at a system level, compares favorably to historical thermal-ablation rates. Its learning curve is short enough that most operators appear to reach steady-state procedural efficiency within about ten cases. What is not yet established is a durable efficacy advantage: the 4-year follow-up found the raw freedom-from-arrhythmia rates converging, even as the repeat-ablation rate stayed meaningfully lower with PFA. And the new, if rare, complications this registry identified -- coronary spasm and hemolysis-driven renal injury -- are a reminder that trading one injury mechanism for another is not the same as eliminating risk altogether.

For a clinician choosing between energy sources today, the evidence supports PFA's safety and structural-sparing claims with real confidence, while treating its long-term efficacy advantage, if any exists, as still an open empirical question.

Study limitations

This is a narrative review, not a systematic review with a pre-registered protocol, and it draws on a single pivotal randomized trial (restricted to paroxysmal, not persistent, atrial fibrillation), its own extended follow-up, one large but nonrandomized real-world registry, and one learning-curve study whose full author list could not be independently confirmed beyond its indexed abstract (reference 4). MANIFEST-17K's comparison to a historical thermal-ablation registry is not a concurrent randomized comparison, so temporal improvements in operator technique, patient selection, or periprocedural care more broadly could account for some of the apparent safety advantage, independent of the energy source itself. ADVENT-LTO's loss of statistical significance at 4 years could reflect a true narrowing of effect, reduced statistical power from patient dropout, or both, and this review cannot distinguish between those explanations. Finally, none of these sources addresses persistent atrial fibrillation, where ablation strategies and outcomes commonly differ from the paroxysmal population studied here.

Conclusion

Pulsed-field ablation's tissue-selectivity claim is now well supported by both randomized structural-imaging data and a large real-world safety registry recording zero cases of the classic thermal-injury complications, and its procedural learning curve resolves quickly. Its long-term efficacy advantage over thermal ablation, however, remains genuinely unresolved at 4 years, and its real-world safety profile, while favorable overall, includes a small set of complications specific to this energy source that clinicians adopting the technology should recognize rather than assume away.

None of the four sources reviewed here directly compares PFA against thermal ablation in persistent atrial fibrillation, in patients with prior failed ablation, or across the several distinct PFA catheter geometries now in clinical use (pentaspline, basket, and focal designs each create a different lesion set), so this review's conclusions should be read as applying most directly to first-time paroxysmal-AF ablation with the pentaspline catheter studied in ADVENT. As pulsed-field platforms diversify and accumulate their own longer-term registries, the specific balance of tissue selectivity, procedural efficiency, and durability described here will need to be re-examined catheter by catheter rather than assumed to generalize across the technology as a whole.

A further practical implication concerns training and credentialing. If most of the procedural-efficiency gain is

realized within an operator's first ten cases, as the national workflow study suggests, then structured proctoring during that early window -- rather than an open-ended apprenticeship model -- may be the more efficient way to bring new operators to competence, and could plausibly be tested directly in a future prospective study. Centers adopting pulsed-field ablation for the first time might also reasonably expect their own early procedural metrics to resemble the first-ten-case figures reported here rather than the steady-state figures, which has implications for how newly adopting programs schedule procedure time and counsel patients on expected case duration during a program's first months. Whether the same rapid learning curve holds for persistent, rather than paroxysmal, atrial fibrillation ablation -- a generally longer and more complex procedure -- has not yet been reported and should not be assumed to follow the same trajectory documented here.

1. Reddy VY, Gerstenfeld EP, Natale A, et al. "Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation" (ADVENT). *N Engl J Med* 389(2023):1660-1671.
2. Reddy VY, et al. "Pulsed field ablation versus conventional thermal ablation for paroxysmal atrial fibrillation: 4-year outcomes in the ADVENT-LTO study". *Nat Med* 32(2026):1444-1453.
3. Ekanem E, Reddy VY, et al. "Safety of pulsed field ablation in more than 17,000 patients with atrial fibrillation in the MANIFEST-17K study". *Nat Med* 30(2024):2020-2029.

Source	N	Design	Key finding
ADVENT [1]	607	RCT, 1-year	Noninferior efficacy/safety; superior PV preservation
ADVENT-LTO [2]	607	RCT, 4-year	Efficacy gap narrowed ($P=0.12$); repeat-ablation lower
MANIFEST-17K [3]	17,642	Real-world registry	Zero thermal-injury events; 2 new PFA-specific ones
National workflow [4]	752	Retrospective, single-arm	Learning curve resolves within ~10 cases

Table 1: Design and key finding of the four sources synthesized in this review [1-4].

It is worth restating the specific magnitude of MANIFEST-17K's major-complication comparison, since it is easy to read '0.98% versus a historical 1.52-2%' as a modest difference rather than the substantial relative reduction it represents: at the scale of tens of thousands of annual procedures nationally, a difference of this size translates into a meaningful number of avoided pericardial complications, strokes, and deaths, even before crediting PFA with zero esophageal, pulmonary-vein, or phrenic-nerve injury across the entire cohort [3]. Whether that registry-level advantage will persist as adoption broadens beyond the highest-volume early-adopting centers captured in MANIFEST-17K, and as operators further down each center's own learning curve

contribute an increasing share of procedures, is a question this review's sources cannot yet answer and that later registries with broader case-mix will need to address.

The two PFA-specific complications MANIFEST-17K identified also deserve a word on plausible mechanism, even though the registry itself was not designed to establish one: coronary arterial spasm has been attributed by others to direct electrical stimulation of vascular smooth muscle or coronary autonomic nerves near the ablation catheter, while hemolysis-related renal injury is consistent with the mechanical shear pulsed electric fields can place on circulating red cells in the immediate field region. Neither explanation is tested directly in any of the four sources reviewed here, and both remain proposed mechanisms rather than established ones [3].

4. [Authors not independently confirmed beyond the indexed abstract]. Bisignani A, et al. "National workflow experience with pulsed field ablation for atrial fibrillation: learning curve, efficiency, and safety". *J Interv Card Electrophysiol* 67(2024):2127-2136.

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