EUropean Real World Outcomes with **P**ulsed Field Ablati**O**n in Patients with Symptomatic At**RIA**l Fibrillation - Lessons from the multicenter EU-PORIA Registry

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Short Title: Real world outcomes with pulsed field ablation

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ABSTRACT

Background and Aims: Pulsed field ablation (PFA) is a new, non-thermal ablation modality for pulmonary vein isolation (PVI) in patients with atrial fibrillation (AF). The multi-center EU-PORIA (EUropean Real World Outcomes with Pulsed Field AblatiOn in Patients with Symptomatic AtRIAl Fibrillation) registry sought to determine the safety, efficacy, and learning curve characteristics for the pentaspline, multielectrode PFA catheter.

Methods: All-comer AF patients from seven high-volume centers were consecutively enrolled. Procedural and follow-up data were collected. Learning curve effects were analyzed by operator ablation experience and primary ablation modality.

Results: In total, 1,233 patients (61% male, mean age 66±11years, 60% paroxysmal AF) were treated by 42 operators. In 169 patients (14%), additional lesions outside the PVs were performed, most commonly at the posterior wall (n=127). Median procedure and fluoroscopy times were 58 [IQR: 40-87] and 14 [9-21] min, respectively, with no differences due to operator experience. Major complications occurred in 21/1233 procedures (1.7%) including pericardial tamponade (14; 1.1%) and transient ischemic attack or stroke (n=7; 0.6%), of which one was fatal. Prior cryo-balloon users had less complications. At a median follow-up of 365 [323-386] days, the Kaplan-Meier estimate of arrhythmia-free survival was 74% (80% for paroxysmal and 66% for persistent AF). Freedom from arrhythmia was not influenced by operator experience. In 149 (12%) patients a repeat procedure was performed due to AF recurrence and 418/584 (72%) PVs were durably isolated.

Conclusion: The EU-PORIA registry demonstrates a high single-procedure success rate with an excellent safety profile and short procedure times in a real-world, all-comer AF patient population.

KEYWORDS: ablation, atrial fibrillation, pulsed field ablation, electroporation

Introduction

Atrial fibrillation (AF) is a growing global epidemic with substantial health economic burden. Increased awareness, advanced detection, and life expectancy contribute to the growing number of AF patients. An estimated 14-17 million Europeans will suffer from AF by 2030, and the expected number of new cases of AF per year will be 120,000-215,000.[1] Patients with AF have an increased risk of stroke, morbidity, and hospitalization, which places significant strain on an already overburdened healthcare system,[2] demonstrating the need for effective, safe, and readily available therapies.

Recent pivotal studies demonstrated catheter ablation as an effective first-line therapy in AF treatment[3-5] and as a means to slow AF progression.[6] With growing AF prevalence, the increased demand on electrophysiology labs necessitates continuous advancements in safe, effective, and efficient AF treatment strategies that allow for seamless adoption in clinical practice.[7]

Pulsed field ablation (PFA) is a new ablation modality for cardiac arrhythmias. Myocardium is characterized by a high susceptibility towards PFA in comparison to surrounding tissue.[8-10] This opens a broad therapeutic window composed of high efficacy (myocardial damage) with little to no collateral damage. PFA "tissue selectivity" was confirmed in pre-clinical and clinical studies showing low vulnerability of nerves, vasculature, and esophageal tissue to PFA.[11-16]

A dedicated "single shot" PVI device that obtained CE mark in Europe in January 2021 was the Farapulse™ PFA ablation system (Boston Scientific, Menlo Park, CA, USA). Since its commercial release, the pentaspline, multielectrode PFA catheter has shown encouraging acute efficacy and safety profiles.[13, 17-22] Feasibility studies and early single-center experiences have demonstrated lesion durability, safety, and initial long-term outcomes.[13,

[17, 19-25] However, real-world outcomes in large patient populations are still scarce.[18] Chronic data is needed to further evaluate the use of this novel technology in a real-world setting and understand the learning curve. The aim of this registry is to describe real-world adoption, workflow, and acute and long-term outcomes after PFA in AF patients in high-volume European centers.

Methods

The study was approved by the Frankfurt ethics committee (2023-3251-evBO) and complies with the declaration of Helsinki. It was registered at clinical trials.gov (NCT05823818). The study device is CE marked.

Centers

All centers involved in this study are high-volume AF ablation centers in Europe (400-1400 AF ablations per year) that participated in the early market release for the Farapulse PFA technology in Europe. This ensures a high number of patients per center as well as adequate follow-up time. All cases, including the initial use of the PFA catheter for each operator, were included in this study. Individual data on AF ablation experience was also collected. Operators were divided into three groups with <2 years, 2-5 years and >5 years of AF ablation experience. Moreover, operators were classified as primarily single shot cryoballoon operators, primarily point-by-point ablation radiofrequency (RF) operators, or both.

Patients

All patients who underwent a catheter ablation procedure for symptomatic AF using the Farapulse PFA system from March 25, 2021 until May 31, 2022 were consecutively included in the analysis. No specific inclusion and exclusion criteria were defined.

Data collection

An electronic database was designed to retrospectively collect patient data in a pseudo-anonymized fashion at each participating center. Data were then transferred to the leading investigational center for data assembly, data cleaning, and statistical analysis. In the case of missing data, queries were sent to the study centers.

Ablation procedure

The ablation procedures were carried out per each center's standard of care. Procedures were performed either under general anesthesia or deep sedation using a continuous propofol infusion. Procedural guidance varied between centers, with some using 3D electroanatomical mapping (EAM) while others used the pentaspline catheter with only fluoroscopic guidance.

The Farawave™ ablation catheter was introduced into the left atrium (LA) via a steerable sheath (13.0 F inner diameter; Faradrive™) and was navigated over-the-wire to the desired ablation area. For ablation, PFA applications were delivered using the generator (Farastar™) with a voltage output of 1.8-2.0 kV. Energy applications were delivered as a biphasic waveform on a microsecond scale, unsynchronized to cardiac rhythm.[26] A group of five consecutive pulse trains was delivered, accounting for a total of 2.5 seconds ablation time per PFA application. PFA lesion sets were performed based on institution standard of care. During conduct of this study, the use of the Farapulse PFA System for the treatment of

non-paroxysmal atrial fibrillation and for extra-PVI ablation is outside of the labeled indication.

Follow-up

Follow-up for subjects was based on each institution's standard practice, generally outpatient visits including 24-120h Holter monitoring were performed at 3-, 6-, and 12-months follow-up. Data on individual patient follow-up schedule was not recorded. Any episode of atrial tachycardia (AT) or AF lasting more than 30 seconds was considered an arrhythmia recurrence.

Major adverse clinical events including tamponade, air embolism, stroke, transient ischemic attack, atrioesophageal fistula, and death were captured. The relevance of each adverse event to the device and/or procedure was determined by the participating center. Moreover, information on antiarrhythmic drugs (AADs) and oral anticoagulation status were collected.

Repeat ablation

Patients with symptomatic AT/AF recurrences underwent a repeat mapping and ablation procedure. Procedures were performed using a 3D EAM system, and PVI durability was assessed using multipolar mapping catheters. Moreover, the durability of extra-PV ablation lesion sets was investigated (i.e., conduction block of linear lesions or durable posterior wall isolation). Subsequently, the AT mechanism was analyzed and categorized as either lesion-associated AT (e.g., the critical AT isthmus or AT focus was adjacent to the PFA lesion set) or substrate-associated AT (e.g., the critical AT isthmus or AT focus was located

within pre-existing low-voltage areas). Repeat ablation was carried out using commercially-available irrigated RF ablation catheters.

Statistical analysis

All categorical variables, such as patient and procedural characteristics, are reported as absolute and relative frequencies and were compared using Fisher's exact test. The continuous variables were tested for normal distribution using the Shapiro-Wilk test. They were reported as mean ± standard deviation in case of normal distribution and as median and interquartile range [first quartile, third quartile] otherwise. The continuous variables were compared using the non-paired Student's t test when normally distributed and the corresponding nonparametric test (Mann-Whitney U test) otherwise. The procedure time comparisons were performed using a Kruskal-Wallis test.

The association between variables and arrhythmia recurrence was assessed using binary logistic regression and is reported as odds ratio and 95% confidence intervals. The variables with a $p<0.05$ in the univariable model were included in a multivariable binary logistic regression model. Parameters with perfect collinearity were excluded from the logistic regression analysis and are reported descriptively.

Multivariate analysis modelled on the probability of a recurrence was performed using a Cox regression model.

All p-values are two sided. A p-value of <0.05 was considered significant. All statistical analyses were performed using SPSS version 28.0 (IBM SPSS Statistics).

Results

At seven participating centers, 1,233 patients were treated by 42 operators. The number of patients treated ranged from 78 to 347 per center and from 1 to 158 per operator (**Figure 1A & 1B**). The median number of ablation procedures per operator was 23 [6-35]. Of the 42 operators, three (7%), 13 (31%) and 26 (62%) reported <2, 2-5 and >5 years of experience in AF ablation, respectively. The primary ablation modality of the operators was point-by-point RF ablation in 11 (26%) operators, cryoballoon in 13 (31%) operators, and both in 18 (43%) operators.

Details of the patient characteristics are given in **Table 1**. In brief, mean age was 66 ± 11 years and 478/1233 (39%) patients were female. The mean CHA_2DS_2-VASc score was 2.3±1.6. Patients presented with paroxysmal, persistent and long-standing persistent AF in 60%, 37% and 3% of cases, respectively. For 65 patients, information on prior AAD use was unavailable, but in 647/1168 (55%) patients, ablations were carried out without current or previous use of membrane active AADs. Of the 1,233 PFA ablation procedures performed, 1184 (96%) were index procedures and 49 (4%) were repeat procedures after an initial thermal ablation.

Procedural Metrics and Ablation Results

Procedural characteristics are summarized in **Table 2**. The ablation procedure was carried out under deep sedation or general anesthesia in 983 (80%) and 250 (20%) of cases, respectively. In 412/1233 (33%) cases, complimentary 3D EAM was used. For ablation, the 31mm and the 35mm device were selected in 947 (77%) and 286 (23%) procedures. A total of 4870/4872 PVs (99.96%) were successfully isolated exclusively using the PFA catheter. In only 2 PVs (0.04%), irrigated RF touch-up ablation at residual conduction gaps was performed.

In 169 patients (14%), additional lesions were performed, most commonly at the LA posterior wall (n=127). During the index PFA procedure, ablation beyond PVI was performed in 41/723 (5.7%), 82/433 (18.9%) and 5/28 (17.9%) patients with paroxysmal, persistent, and long-standing persistent AF, respectively. In cases, where PFA was used for the repeat ablation after a prior thermal ablation, lesion sets beyond PVI were used in 12/19 (63.2%), 23/24 (95.8%) and 6/6 (100%) patients with paroxysmal, persistent, and long-standing persistent AF, respectively. The median skin-to-skin procedure time was 58 [40-87] min including a fluoroscopy time of 14 [9-21] min. In uncomplicated PVI-only cases, the median procedure and fluoroscopy times were 52 [38-78] min and 13 [8-19] min, respectively. Use of 3D mapping significantly prolonged the median procedure time from 45 [35-60] min to 94 [74-120] min ($p<0.0001$) and the fluoroscopy time from 11 [7-17] min to 20 [15-27] min ($p<0.0001$).

Procedural Safety

In total, 45 peri-procedural complications were noted (3.6%; **Table 3**). This included 21 major and 24 minor complications. Pericardial tamponade occurred in 14 cases (1.1%). Of the 14 reported cases, two patients (0.16%) underwent cardiac surgery. All remaining pericardial effusions were drained percutaneously. Root cause analysis of all pericardial tamponade events was performed, and the perforation was attributed to the straight tip guidewire (n=7; 50%), the diagnostic catheter (n=3; 21%), the transseptal puncture (n=3; 21%) and the sheath (n=1;7%), respectively. During surgery in one patient, right ventricular perforation by the diagnostic pacing catheter was confirmed, and in one patient a laceration at the junction of the right superior PV with the LA roof caused by the unprotected sheath was found. Pericardial tamponade occurred in cases performed by 6/42 (14.3%) operators (5

with >5 years AF ablation experience) after a median of 28 [17-78] PFA cases (Table 4). The rate of pericardial tamponade was significantly different between operators based on previous ablation modality. In 9/14 (64%) pericardial tamponades, the operator's primary ablation modality was point-by-point RF ablation (Table 5).

In addition, TIA and stroke were noted in 2 (0.16%) and 5 (0.41%) patients, respectively. Of the latter, one patient died 4 days after the ablation procedure despite successful thrombectomy.

Minor complications included access site complications in 12 (0.97%) patients. Phrenic nerve palsy, defined as an absent or weakening of the diaphragmatic contraction, was observed in 4 (0.3%) patients, only one of which had not resolved by the end of the follow-up. In a single patient, a coronary spasm with ST segment elevation was noted after ablation at the right superior PV, that completely resolved after intracoronary nitroglycerin injection.

PFA for repeat ablation procedures

In three centers, the pentaspline PFA catheter was used for repeat ablation of patients with recurrent tachyarrhythmias after an index thermal ablation. Data on 49 repeat procedures (4% of total cohort) were collected and analyzed. This included 19, 24 and 6 patients with paroxysmal, persistent, and long-standing persistent AF, respectively. In 8/49 (16%) patients, a PVI-only ablation strategy was performed. Extra-PV ablation was carried out in the majority of patients (41/49; 84%). Peri-procedural complications occurred in 2 (4%) patients, including TIA (n=1) and vascular access site complication (n=1), respectively.

Follow-up

At a median follow-up time of 365 [323-386] days, the Kaplan-Meier estimate of AF/AT-free survival was 74% for the total cohort (Figure 2A). At 12 months follow-up, 70 patients were still on class I or III AADs, including 54 because of a documented AF/AT recurrence (e.g., a primary endpoint event). The Kaplan-Meier estimate for AF-free survival for patients with an index PFA procedure for paroxysmal, persistent, and long-standing persistent AF was 80%, 66% and 67%, respectively (Figure 2B).

Twenty-seven patients were lost to follow-up. During follow-up, 13 (1.1%) patients died. Three patients (0.2%) experienced a stroke, and one patient (0.08%) experienced a myocardial infarction. No further procedure-related or device-related events occurred, in particular no atrial esophageal fistulas were noted.

Predictors of arrhythmia recurrence

Multivariate analysis identified CHA_2DS_2-VaSc score (Odds ratio (OR) 1.034; CI 1.008-1061; p=0.01) and body mass index (BMI; OR 1.154, CI 1.062-1.255; p=0.0008) as independent predictors for arrhythmia recurrence (TableS1 Supplement). As expected, the presence of paroxysmal AF was associated with a favorable outcome (OR 0.573; CI 0.44-0.746; p<0.001).

Findings during repeat procedures after an index PFA ablation

In 149 (12%) patients, a repeat ablation was performed a median of 226 [157-292] days after the index PFA procedure. The mean age of the patients was 67 ± 10 years and 57 (38%) were female. The index arrhythmia was paroxysmal AF in 78 (52%) patients, persistent AF in 66 (44%) patients, and long-standing persistent AF in 5 (3%) patients. Of the 149 patients undergoing repeat ablation, 52 (35%) had EAM performed during the index

procedure. The 31mm or the 35mm Farawave catheter had been used in 102 (68%) and 47 (32%) procedures, respectively. The ablation strategy was PVI-only in 121 (81%) and PVI plus extra-PV ablation in 28 (19%) patients. In the latter group, the LA posterior wall had been ablated in 22/28 (79%) patients.

The indication for the repeat procedure was AT in 50 (34%) patients and recurrent AF in the remaining 99 (66%) patients. Of the latter, 60 were in sinus rhythm during the repeat ablation procedure. During remapping, 418/584 (72%) of PVs (in 1 patient PVs were not mapped due to right sided AT) were found to be durably isolated. Complete durable PVI (i.e., all PVs in an individual patient) was found in 54/148 (36%) patients. In patients with reconnected PVs, a median of one PV demonstrated a gap in the lesion set. For patients with paroxysmal, persistent, and long-standing persistent AF, PV durability per PV was 232/305 (76%), 174/258 (67%) and 10/20 (50%), respectively. Complete durable PVI was observed in 34/78, 22/66 (33%) and 0/5 patients, respectively.

Of the 50 patients with recurrent AT, 14 (28%) had posterior wall-associated AT, peri-mitral AT occurred in 17 (34%) patients, the others were right AT (n=2; 4%), left focal AT (n=7; 14%) or remained unclassified (n=10; 20%).

Effects of Operator Experience

Procedural and outcome data were analyzed according to the operator experience with AF ablation. No significant differences were found for procedural metrics or procedural complications (**Table 4**). When stratifying for the primary ablation modality previously used by each operator, prior cryoballoon users had shorter procedure times and fewer cardiac perforations (**Table 5**). Neither ablation center, operator's AF ablation experience nor the

operator's previous primary ablation modality had an influence on the AF/AT free survival during follow-up for patients undergoing an index PFA procedure (**Figure 3**).

Discussion

The EU-PORIA registry provided real-world outcomes from seven high-volume European AF ablation centers on the early adoption of the novel Farapulse PFA technology. The results demonstrated consistent, short procedure times despite a large number of operators with varied experience. In EU-PORIA, the pentaspline PFA catheter was shown to be a safe and effective treatment strategy in a large spectrum of patients, including paroxysmal and non-paroxysmal AF patients with an overall atrial arrhythmia recurrence free rate of 74% and a safety event rate of 3.6%. A subset of 149 patients (12%), returned for repeat ablation during follow-up. In these patients, EAM revealed a high rate of PVI with 72% of PVs durably isolated.

Workflow & Procedural Efficiency

The median procedure time for all PFA cases, inclusive of varied indications and institutional workflow, included in this registry was 58 [40-87] min. This procedure time falls within the range of previously published procedure times in a real-world setting for the pentaspline PFA catheter.[18, 19, 22] These procedure times are considerably shorter than typically reported for thermal ablation, which averages 82-128 min for cryoballoon [27-29] and 140-162 min point-by-point RF ablation.[27, 28, 30] A most recent single-center comparison between CB and PFA ablation confirmed a 30% reduction in procedure times with PFA.[31] Further, procedure times in the present study were independent of operator's prior AF ablation experience. This may increase the availability of ablation to symptomatic AF

patients outside highly specialized ablation centers, thereby reducing waiting times. However, future randomized studies will have to investigate the noninferiority of PFA in comparison to established thermal ablation modalities.

Current ESC Guidelines for the diagnosis and management of AF provide a Class IA recommendation for first-line ablation therapy only to select patients with heart failure.[32] EU-PORIA data suggests that current clinical practice has already changed with 55% of patients with paroxysmal and persistent AF receiving interventional treatment without prior AAD use (specifically Class I or III AAD). This progressive approach to symptomatic AF patients is also reflected by current European surveys, where 42% of operators would favor first-line ablation in PAF patients.[33] Scientifically, this is supported by the findings of several randomized studies favoring ablation outcomes over medical therapy.[3-5, 34] Future growing demand may even prolong the already existing, extensive waiting times for an AF ablation in some geographies.[35] Nonetheless, during decision making with a symptomatic AF patient the merits and demerits of all treatment options should be carefully considered for an optimal individual counseling. Further studies are needed to answer questions with regards to ablation timing, lesion sets, and workflow to ensure patient safety.

Safety

In this registry, the overall safety event rate was 3.6% with 45 events reported in 1233 subjects. This event rate is similar to those previously reported for real-world experiences with thermal ablation modalities.[28-30] In EU-PORIA, the rate of cardiac tamponade was 1.1%. Most of the events were attributable to the learning curve and were mitigated by workflow changes (no pacing catheter in the right ventricle, introduction of J-tip guidewire) during the course of the study. Overall, one patient died from a peri-

procedural stroke in the early phase of the study. Aside from uninterrupted anticoagulation strategies, careful sheath management to avoid air embolism is critical. In this context, repeated catheter exchanges through the steerable sheath should be avoided, in particular since 3D mapping did not translate to improved procedural outcomes. Several ongoing studies will directly compare PFA to thermal ablation and will provide further insights into the safety profiles.

Efficacy

Although this registry reflects the very early European experience, including learning curves for all operators, the observed arrhythmia free survival rates may be comparable to thermal ablation technologies.[28-30] The reported observations from this registry are preliminary and PFA needs to prove noninferiority towards standard of care, thermal ablation. Randomized studies are key to further investigate its role in the landscape of ablation technologies. This holds also true for studies on different ablation strategies including PVI versus PVI plus extra-PV ablation. Most recently, a pilot study investigating a new multipolar circular PFA catheter demonstrated similar effectiveness rates and most importantly a very low adverse event rate of 0.7%.[36]

Lesion Durability

In EU-PORIA, 149 repeat ablation procedures were performed and subject to analysis. One key performance parameter of an ablation modality is durable PV isolation. For the Farapulse PFA system, PVI durability rates of 96% were reported in patients with planned re-mapping regardless of arrhythmia recurrences.[13] In a recent single center study, patients who were re-mapped due to clinical arrhythmia recurrences had a PVI durability

rate of 91%.[37] In EU-PORIA, 72% of all re-mapped PVs remained durably isolated. In comparison, a recently published pilot study using a variable loop circular PFA catheter had 13 patients returning for repeat ablation procedures and had a PV durability rate of 27% (13/49 PVs).[38] With thermal ablation in the CIRCA-DOSE trial, 112/201 (56%) of PVs exhibited durable PV isolation.[39] This real-world dataset provides additional evidence supporting the PVI ablation workflow with the pentaspline PFA catheter. Future studies systematically evaluating the lesion durability will be needed to directly compare across modalities.

In this clinical experience, the use of 3D mapping with the pentaspline catheter did not improve lesion durability. However, future full integration allowing for simulation of the electrical field within the acquired 3D map, may be beneficial.

Learning Curve

Several studies have shown a close relationship between center volume and safety. An annual procedural volume of <74 ablation procedures per year was significantly associated with an increase in adverse outcomes.[40] In the present registry, no difference in complication rate between experienced (>5 years) and less experienced (<5 years) operators was found. Similarly, operator experience had no influence on efficacy in terms of arrhythmia free survival. This may partly be explained by a technically less demanding procedure without the need for PV occlusion as during cryoballoon ablation or achieving pre-defined contact force values for longer periods of time at several locations during a point-by-point RF ablation.

In contrast, the primary ablation modality seems to exert an influence on the adoption speed of the PFA pentaspline catheter. No cardiac tamponade was observed in previous primary cryoballoon operators who may be more used to navigating an over-the-

wire device through a large bore steerable sheath. PVI durability was also improved which may be a result of better single-shot device positioning at the respective PV ostium.

Limitations

EU-PORIA was designed to evaluate the real-world use and adoption of a novel PFA technology for an all-comer AF patient population. No specified inclusion or exclusion criteria were considered. This was a retrospective, observational study, where AF ablation and patient management were all performed according to standard-of-care at each center. In particular, follow-up and arrhythmia recurrence monitoring were performed based on each center's standard practice and was not recorded for each patient. No data monitoring was applied. Several operators utilized 3D mapping for lesion visualization, but at this time, the current PFA system is not fully integrated into a 3D mapping system. Comparison to prospective studies with rigorous monitoring strategies in regard to effectiveness should therefore be carried out with caution since monitoring strategies may differ substantially. In contrast, most recently, the standard AF recurrence definition of 30 seconds episode duration has been challenged since clinically relevant increases in healthcare utilization occur only with episodes > 1 hour and AF burden > 0.1%.[6] Therefore, healthcare utilization parameters like the number of electrical cardioversions, repeat ablations, or hospitalizations should also be taken into account to assess the effectiveness of an ablation modality.

It needs to be highlighted, that operators used the PFA device for extra PV ablation I a subset of patients. This is 1) currently outside of the labeled indication for the pentaspline PFA catheter and 2) current guidelines recommend to reserve extra-PV ablation to select patients only (class II b).

Following commercialization of a medical device, systematic data collection on safety and efficacy as well as clinical adoption provide important insights into real-world outcomes

and may enhance our understanding of its value in everyday clinical practice. In this clinical experience, the observed characteristics of PFA-guided AF ablation, including short operator learning curves, fast procedure times, and favorable one-year outcomes may form a solid base for future prospective randomized trials.

Conclusion

The EU-PORIA registry demonstrates a favorable single procedure success rate along with short procedure times in a real-world, all-comer AF patient population. Future randomized, multi-center trials will compare PFA-guided ablation to thermal ablation modalities to assess its true value for patients with AF.

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Conflict of Interest

BS is a consultant for and has received honoraria as well as research funding from Abbott, Medtronic, Boston Scientific, Biosense Webster.

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Data Availability Statement

The data underlying this article will be shared on reasonable request to the corresponding author.

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Figure Legends

Figure 1. Overview of EU-PORIA patients and distribution per center and per operator. A) Enrollment per center. B) Catheter ablation procedures per operator. C) Operator experience and primary ablation modality.

Figure 2. Kaplan-Meier curve of AF/AT-free survival for (A) all patients and (B) patients who underwent an index PFA procedure.

Figure 3. Kaplan-Meier curves of AF/AT-free survival in patients who underwent an index PFA procedure by (A) operator experience and (B) operator ablation primary modality.

Table 1. Patient demographics
Table 2. Procedural characteristics
Table 3. Procedural complications
Table 4. Outcomes by operator experience
Table 5. Outcomes by operator primary ablation modality
Table S1. Univariate and multivariate Cox regression analysis

Table 1. Patient Demographics.

	N=1233
Female sex, n (%)	478 (39%)
Age (years)	66 ± 11
Hypertension, n (%)	668 (54%)
Diabetes, n (%)	138 (11%)
History of stroke / TIA, n (%)	80 (6%)
Heart failure, n (%)	204 (17%)
Coronary artery disease, n (%)	154 (12%)
CHA_2DS_2-VASc score	2.3 ± 1.6
BMI (kg/m^2)	28 ± 5
Type of AF	
Paroxysmal AF	742 (60%)
Persistent AF	457 (37%)
Long-standing persistent AF	34 (3%)
Prior use of Class I or III AAD	521/1168 (45%)
Left ventricular ejection fraction (%)	57 ±10%[a]

Data are given as absolute number and frequencies in parenthesis. Mean ± standard deviation are reported. AAD: Antiarrhythmic drug. AF: atrial fibrillation; BMI: Body mass index; LA: Left atrium; TIA: Transient ischemic attack.
[a]Left ventricular ejection fraction reported in 886 subjects.

Table 2. Procedural Characteristics

	N=1233
First AF ablation, n (%)	1184 (96%)
Sedation technique	
General anaesthesia, n (%)	250 (20%)
Deep sedation, n (%)	983 (80%)
Use of 3D mapping, n (%)	412 (33%)
No. of PVs isolated / attempted, n (%)	4870 / 4872 (99.96%)
Skin-to-skin procedure time (min)	58 [40-87]
Fluoroscopy time (min)	14 [9-21]
Ablation device used[a]	
31 mm, n (%)	947 (77%)
35 mm, n (%)	285 (23%)
PVI only ablation, n (%)	1064 (86%)
Extra-PV ablation	169 (14%)
Posterior wall isolation, n (%)	127 (10%)
LA isthmus ablation, n (%)	62 (5%)
Cavo-tricuspid isthmus ablation, n (%)	6 (0.5%)

Data are given as number of patients and frequencies in parenthesis. Times are given as median and [interquartile range]. LA: Left atrium; PV: Pulmonary Vein. PVI: Pulmonary Vein Isolation.
[a]Ablation device size recorded in 1230 subjects

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Table 3. Procedural Complications

Complications	N=1233
Major Complications, n (%)	**21 (1.7%)**
Pericardial tamponade, n (%)	14 (1.1%)
Stroke, n (%)	5 (0.41%)[a]
TIA, n (%)	2 (0.16%)
Minor Complications, n (%)	**24 (1.9%)**
Vascular access site complication	12 (0.97%)
Phrenic nerve dysfunction	4 (0.32%)[b]
Air embolism	3 (0.24%)
Coronary spasm	1 (0.08%)
Hemoptysis	1 (0.08%)
Pericarditis	2 (0.16%)
Pneumonia	1 (0.08%)

Data are given as absolute number of events and frequency. TIA: Transient ischemic attack.
[a] Including 1 fatal stroke.
[b] Phrenic nerve function did not recover in one patient by the end of the follow-up.

1

Table 4. Outcomes based on operator expereince

Year of Experience	<2 years 3 Operators 11 Procedures	2-5 years 13 Operators 281 Procedures	> 5 years 26 Operators 941 Procedures	P-value
Procedural Characteristics				
PVI only, n (%)	8 (72.7%)	262 (93.2%)	794 (84.3%)	<.0001
3D mapping, n (%)	1 (9.1%)	78 (27.8%)	333 (35.4%)	0.0114
General anaesthesia, n (%)	0	33 (11.7%)	217 (23.1%)	<.0001
Index PFA procedure	10 (90.9%)	276 (98.2%)	898 (95.4%)	0.0400
Type of AF				
Paroxysmal AF, n (%)	7 (63.6%)	175 (62.3%)	560 (59.5%)	n.s.
Persistent AF, n (%)	4 (36.3%)	100 (35.6%)	353 (37.5%)	n.s.
Long-standing persistent AF, n (%)	0	6 (2.1%)	28 (3.0%)	n.s.
Procedure Times				
Skin-to-skin procedure time, min	51 [46-77]	50 [38-78]	60 [40-88]	0.0878
Fluoroscopy time, min	19 [14-20]	12 [7-19]	15 [9-21]	0.0011
Safety				
Complications, n (%)	0	6 (2.1%)	39 (4.1%)	0.2566
Stroke / TIA, n (%)	0	1 (0.4%)	6 (0.6%)	1.0000
Pericardial tamponade, n (%)	0	2 (0.7%)	12 (1.3%)	0.7786
Efficacy				
PV reconnection rate, n (%)	0 / 8 (0%)	38 / 128 (29.7%)	128 / 448 (28.6%)	0.2056
Freedom from AF/AT at 12-months, n (%)	8 / 11 (72.7%)	200 / 281 (71.2%)	698 / 941 (74.2%)	

Data are given as absolute number of events and frequency. Times are given as median and interquartile range. AF: Atrial fibrillation; PFA: Pulsed field ablation PV: Pulmonary vein; TIA: Transient ischemic attack.

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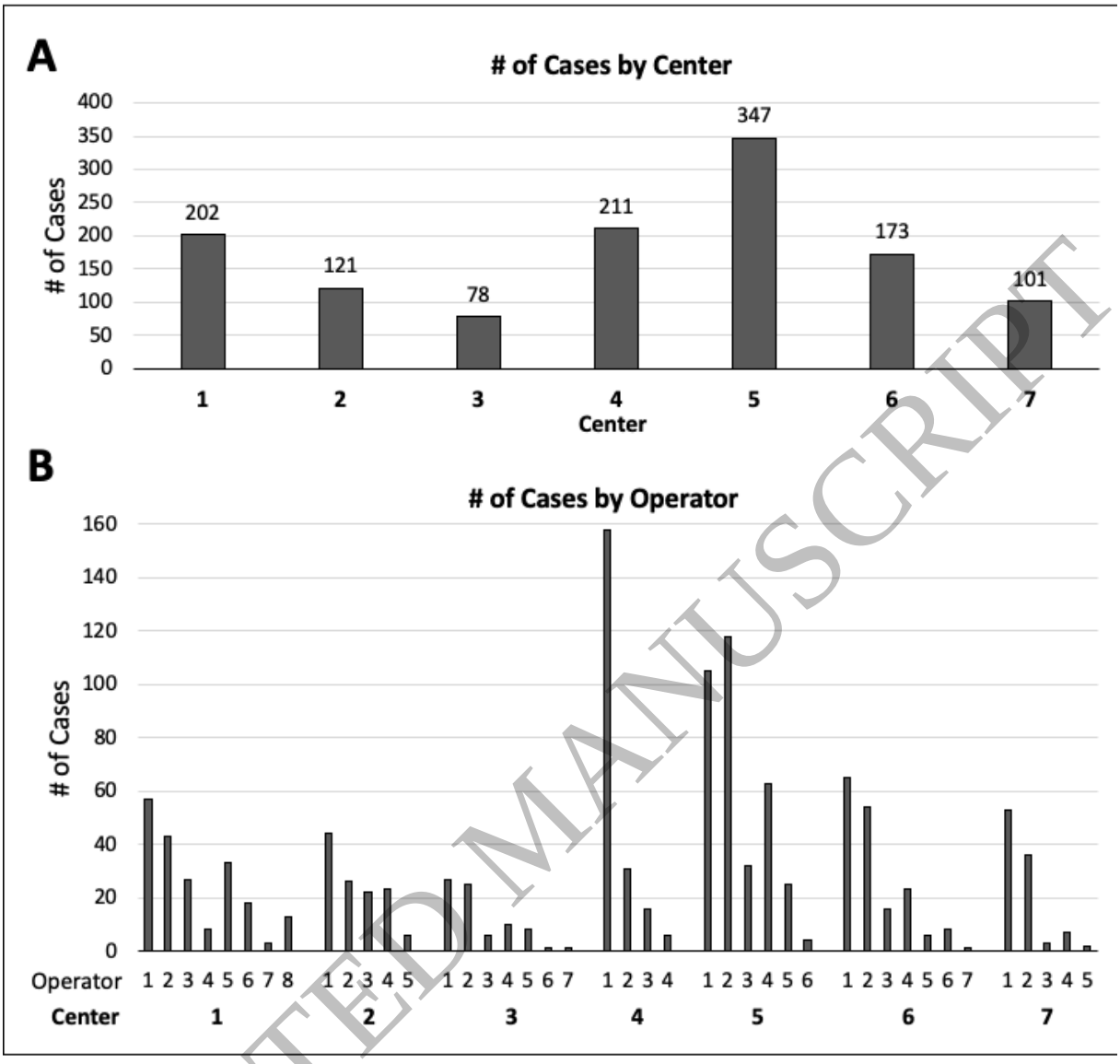


Figure 1
190x275 mm (x DPI)

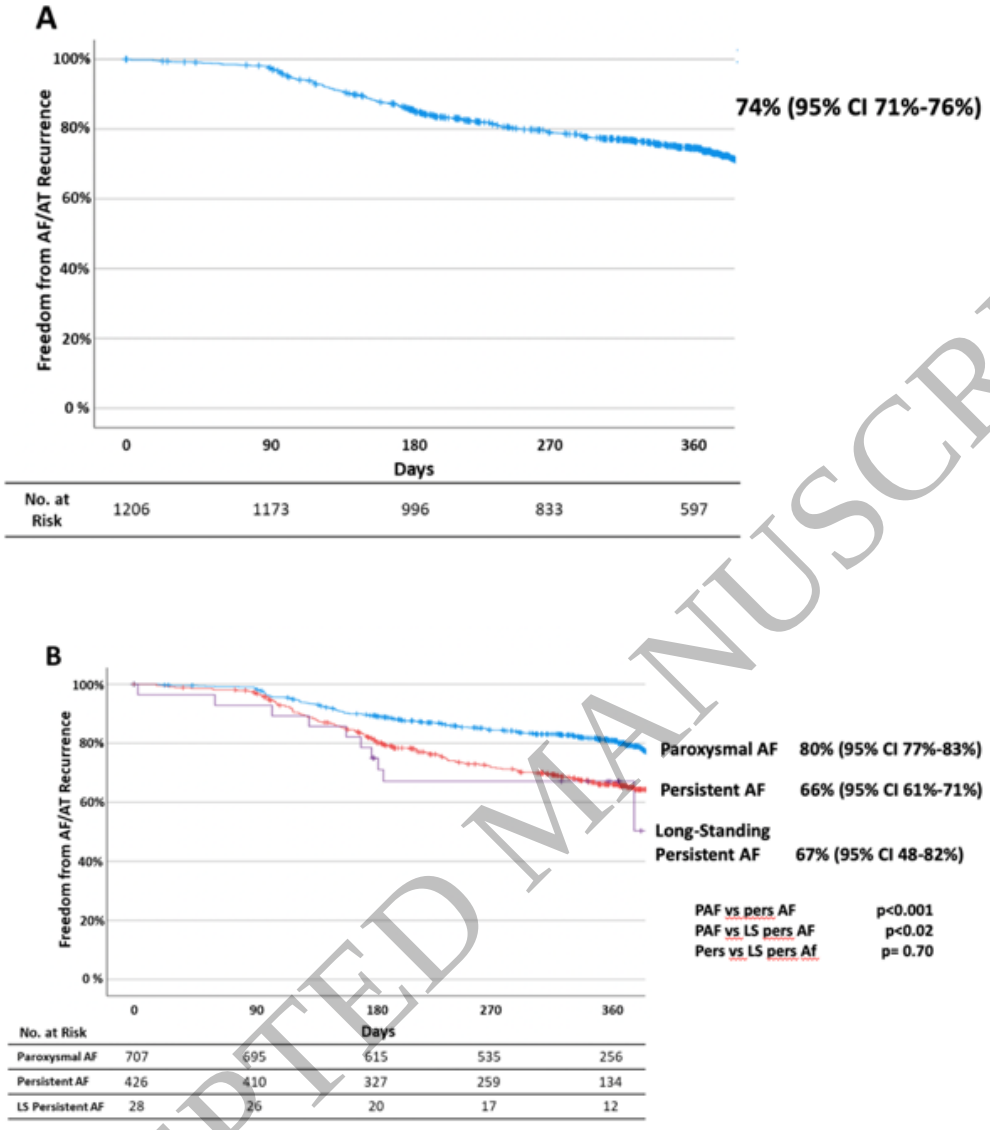
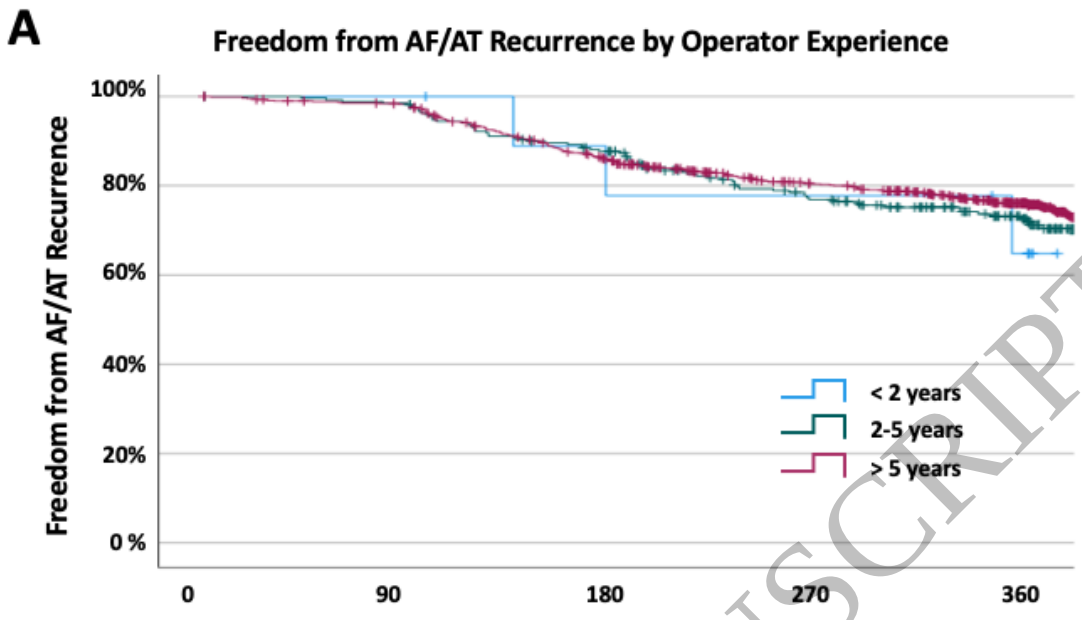
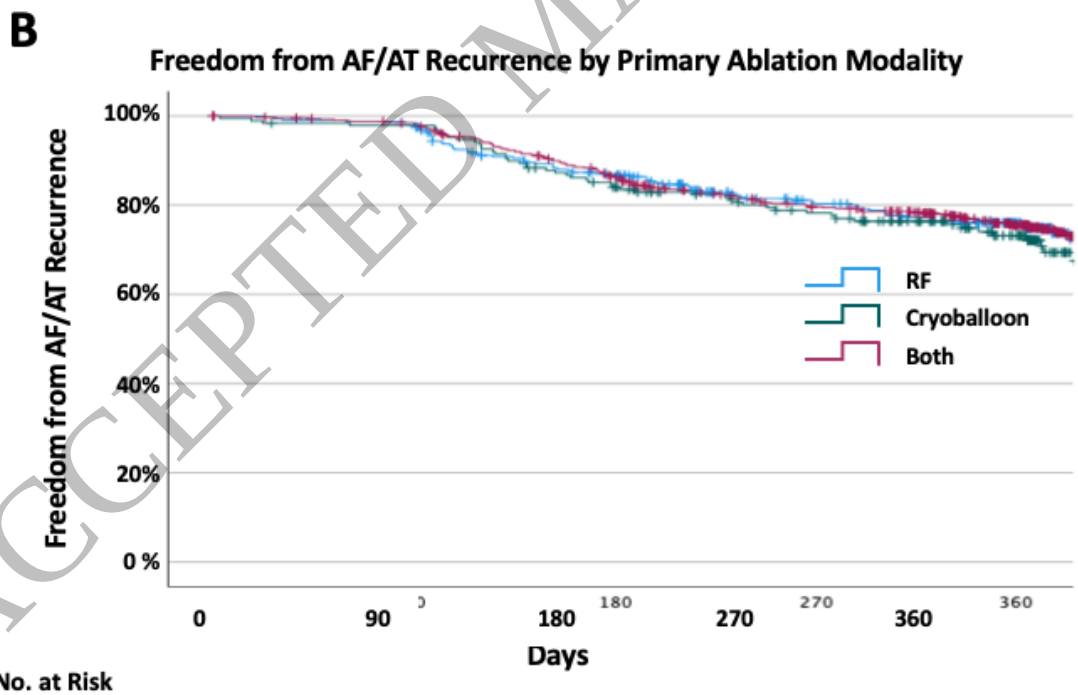


Figure 2
190x275 mm (x DPI)

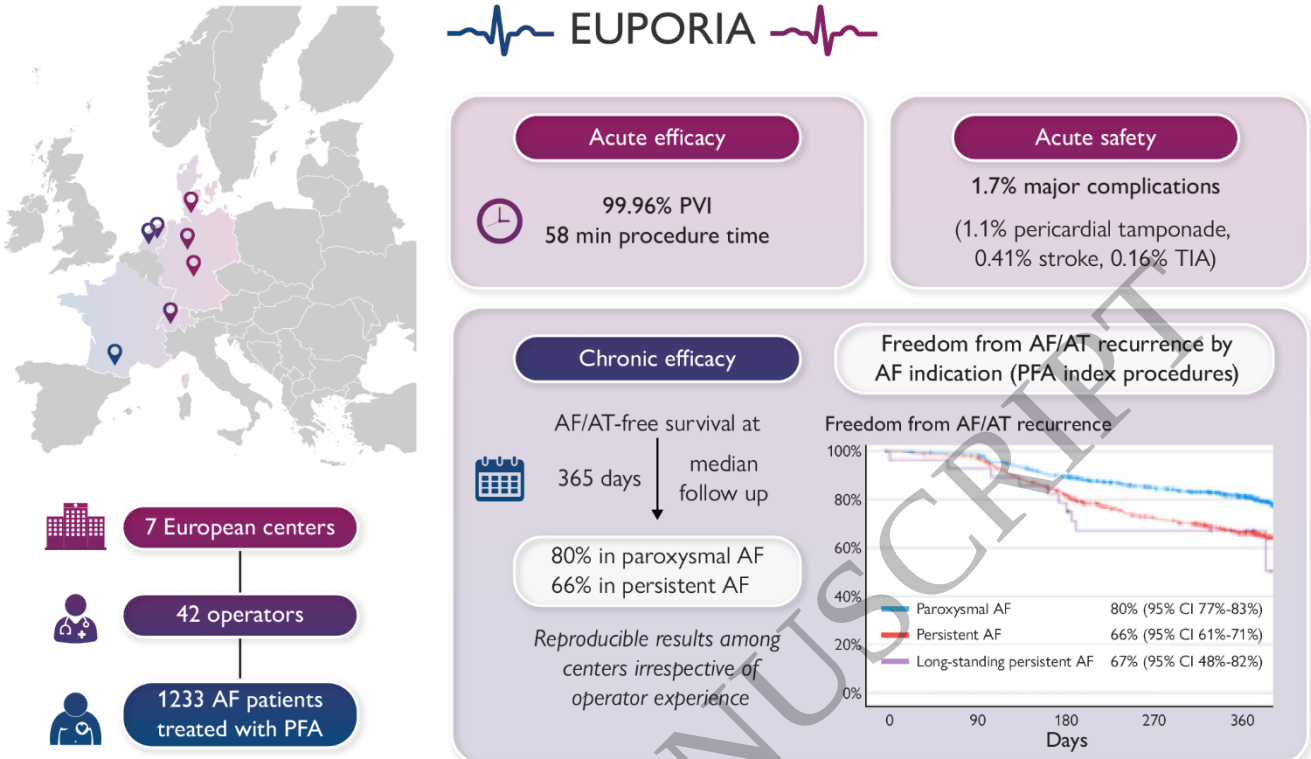


No. at Risk					
< 2 years	10	9	7	7	4
2-5 years	272	266	230	188	120
> 5 years	879	856	728	618	416



No. at Risk					
RF	322	317	268	211	131
Cryoballoon	190	185	155	129	72
Both	649	631	543	471	342

Figure 3
190x275 mm (x DPI)



Graphical Abstract