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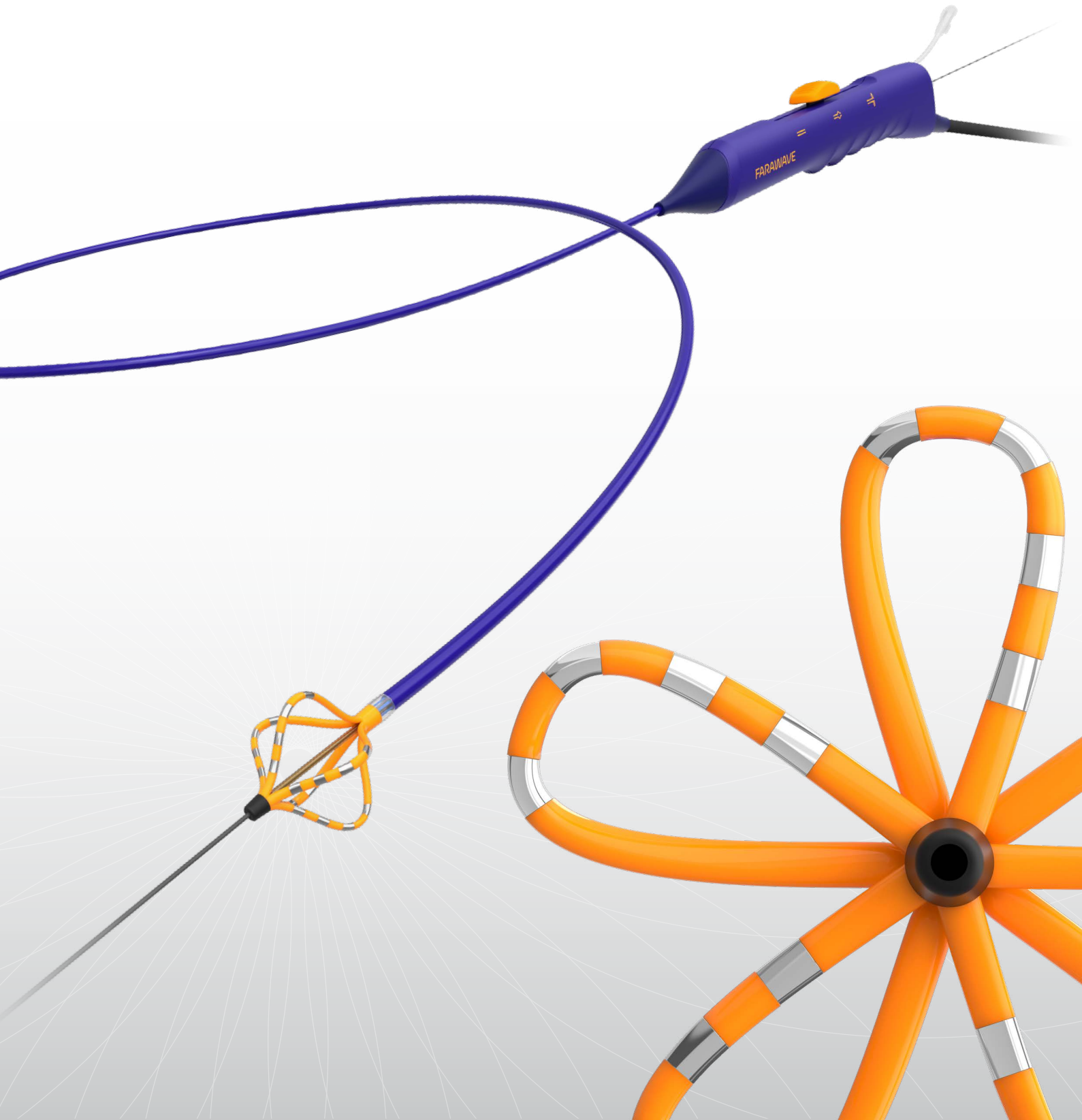
FARAPULSE™
Pulsed Field Ablation System
Clinical Compendium



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*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE™ PFA Catheter with the FARAPULSE PFA System

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2024 CLINICAL PUBLICATIONS

Procedural Performance and Outcome after PFA for Pulmonary Vein Isolation: Comparison with a Reference RF Database

De Becker B, El Haddad M, De Smet M, et al.

European Heart Journal (March, 2024), available here

- Patients were propensity matched, 161 CLOSE protocol guided RFA patients from the PowerPlus study and 161 PFA guided PAF or PersAF patients with FARAPULSE.
- Procedure time was significantly shorter in the FARAPULSE group (47 min vs 71 min for RFA) with the fluoroscopy time being significantly longer in the FARAPULSE group (15 min PFA vs 11 min RFA).
- One serious adverse event occurred (TIA) in a patient with thrombocytosis in the FAFAPULSE group.
- During a 6-month follow-up period, 24 (15%) FARAPULSE and 27 (17%) RFA patients experienced recurrence with 20 (12%) FARAPULSE repeat procedures and 11 (7%) RFA.
- HDM revealed that 7/20 (35%) patients in the FARAPULSE and 2/11 (18%) patients in the RFA group had all 4 PVs durably isolated.

Durability of Pulmonary Vein Isolation Using Pulsed-Field Ablation: Results from the Multicenter EU-PORIA Registry

Kueffer T, Bordignon S, Neven K, et al.

JACC: Clinical Electrophysiology (February, 2024), available here

- 1,184 patients (62% PAF) had a PVI procedure using FARAPULSE. 272 (23%) patients had an arrhythmia recurrence.
- Of these, 144 (53%) underwent a left atrial redo procedure a median of 7 months post-ablation.
- 3D electro-anatomical maps identified 404 of 567 pulmonary veins (71%) with durable isolation.
- Physicians with experience with CBA had a significantly higher PVI durability rate compared to operators with only RFA experience (76% vs 60%).
- The operators' experience in AF ablation (≤5 vs >5 years) or the size of the PFA device used (31 mm vs 35 mm) did not have an impact on lesion durability in redo patients.

Does Acute Coronary Spasm from Pulsed Field Ablation Translate into Chronic Coronary Arterial Lesions?

Malyshev Y, Neuzil P, Petru J, et al.

JACC: Clinical Electrophysiology (February, 2024), available here

- Single-center study where patients had coronary angiography performed in patients who previously had vasospasm during FARAPULSE ablation to determine long-term effects of PFA on coronary arteries.
- Coronary vasospasm occurred during FARAPULSE ablation in 30 patients.
- The spasm was localized as follows:
  - Adjacent to the RCA in 21 pts during CTI ablation with either FARAWAVE (38%) or FARAPOINT (62%) catheters.
  - Adjacent to the left circumflex artery in 8 pts.
- Intracoronary nitroglycerin helped resolve the vasospasm in 18 patients, whereas it spontaneously resolved in the remaining 12 patients with one patient (3.3%) having transient ST-segment depression.
- Coronary angiography was performed after a median of 11 months post-ablation.
- No patients (0 of 30) had new coronary irregularities or stenosis at the site of previous vasospasm, whether the initial PFA procedure had been performed with FARAWAVE or FARAPOINT.
- This was an initial description of favorable long-term safety of FARAPULSE PFA when performed in close proximity to coronary vessels.

2024 CLINICAL PUBLICATIONS

Pulmonary Vein Narrowing after Pulsed Field Versus Thermal Ablation
Mansour M, Gerstenfeld E, Patel C, et al.

Europace (February, 2024), available here

- ADVENT was a randomized, single-blind study comparing FARAPULSE with thermal ablation (RFA and CBA) to treat PAF. Pulmonary vein diameter and aggregate cross-sectional area were measured at baseline and 3 months with imaging.
- The pre-specified, formally tested, secondary safety endpoint found significantly less PV narrowing after PFA (-0.9%) vs. thermal ablation (-12%). No subject had significant (≥70%) PV stenosis.
- The aggregate PV cross-sectional area change was primarily driven by the RFA sub-cohort (–19.5%) vs. CBA sub-cohort (–3.3%).
- Almost half of all PFA PV diameters did not decrease, but the majority (80%) of RF PVs decreased, regardless of PV anatomic location.

Long-Term Outcomes of the Pentaspline Pulsed-Field Ablation Catheter for the Treatment of Paroxysmal Atrial Fibrillation: Results of the Prospective, Multicentre FARA-Freedom Study
Metzner A, Fiala M, Vijgen J, et al.

Europace (February, 2024), available here

- FARA Freedom (NCT05072964) was a prospective, non-randomized, single-arm, multicenter study of 179 PAF patients at 13 centers across 6 European countries.
- FARA-Freedom procedures were efficient (71.9 ± 17.6 min) with a left atrial dwell time of 41 minutes (inclusive of the 20-minute waiting period) and 11.5 minutes of fluoroscopy.
- The freedom from the primary safety event rate in FARA-Freedom was 98.9%. There were no reports of coronary spasm, persistent phrenic nerve palsy, PV stenosis, or AE fistula.
- The freedom from the primary effectiveness event rate was 66.6%. The monitoring compliance was high with an 88.4% compliance with weekly event monitoring and 90.3% with 72-hour Holter monitoring.
- In this study, FARAPULSE was found to be effective and safe with rigorous endpoint definitions and high monitoring compliance.

Acute Kidney Injury Resulting from Hemoglobinuria after Pulsed-Field Ablation in Atrial Fibrillation: Is It Preventable?
Mohanty S, Casella M, Compagnucci P, et al.

JACC: Clinical Electrophysiology (February, 2024), available here

- Patients were split into two groups, group 1 was patients who did not receive post-ablation hydration immediately after the procedure (n = 28), the remainder of study patients received planned fluid infusion (0.9% sodium chloride ≥2 L) after the procedure (n = 75).
- Of the 28 patients in group 1, 21 (75%) experienced hemoglobinuria during the 24 hours after catheter ablation and their post-ablation serum creatinine (S-Cr) was significantly higher than the baseline value in those 21 patients.
- Of those 21 patients, 4 (19%) had S-Cr >2.5 mg/dL. The mean number of PF applications was significantly higher in those 4 patients than in the other 17 patients experiencing hemoglobinuria.
- In the second group of patients who received fluid infusion, no significant changes in S-Cr were noted.
- In multivariable analysis, both hydration and number of PFA applications were independent predictors of post-procedure acute kidney injury.

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Peri-Procedural Intravascular Hemolysis during Atrial Fibrillation Ablation: A Comparison of Pulsed-Field with Radiofrequency Ablation

Osmancik P, Bacova B, Herman D, et al.

medRxiv (February, 2024), available here

- 70 PAF patients were enrolled, 47 patients in the PFA group (22 PVI only, 36.4±5.5 PFA applications vs. 25 PVI plus additional ablations, 67.3±12.4 PFA applications). 23 patients underwent RFA.
- Compared to baseline, the RBCμ concentration increased ~ 12-fold post-PFA and returned to baseline by 24 h. This increase was significantly greater in PVI-plus compared to PVI-only patients.
- There was also a significant peri-procedural increase in RBCμ after RFA.
- At 24 h with PFA, the concentration of LDH and indirect bilirubin increased, and haptoglobin significantly decreased.
- At 24 h with RFA, there were smaller significant changes in LDH and haptoglobin with no change in bilirubin.

Impact of Left Atrial Posterior Wall Ablation during Pulsed Field Ablation for Persistent Atrial Fibrillation: A MANIFEST-PF Registry Sub-Study

Turagam M, Neuzil P, Schmidt B, et al.

AF Symposium (February, 2024), available here

- 131/547 PersAF (24%) patients in MANIFEST-PF received adjunctive left atrial posterior wall (LAPW) ablation.
- Compared to PVI-alone, patients receiving adjunctive LAPW ablation were younger, had a lower CHA^2DS^2-VASc score, and were more likely to receive mapping and ICE imaging.
- The 1-year Kaplan-Meier estimate for freedom from atrial arrhythmias was similar between groups (PVI+LAPW: 66.4% vs PVI: 73.1%).
- After propensity matching, the 1-year effectiveness remained similar between groups (PVI+LAPW: 71.7% vs. PVI: 68.5%).
- There was no significant difference in major adverse events between the groups (2.2% vs. 1.4%).

A Zero-Exchange Approach for Left Atrial Access in Pulmonary Vein Isolation with Pulsed Field Ablation

Bejinariu A, Spieker M, Makimoto H, et al.

Journal of Cardiovascular Electrophysiology (February, 2024), available here

- Transeptal puncture (TSP) was performed with transesophageal echocardiography guidance in 166 patients, using the FARADRIVE sheath and a 98 cm matched Brockenbrough needle.
- The median duration of the procedure was 60 min, median time to TSP was 15 min.
- In one patient a non-TSP related pericardial tamponade occurred which was managed with pericardial puncture.
- Direct TSP with skipping sheath exchange using the large diameter FARADRIVE sheath was safe, feasible, and reduced costs.

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Left Atrial Posterior Wall Isolation Using Pulsed-Field Ablation: Procedural Characteristics, Safety, and Mid-Term Outcomes

Badertscher P, Mannhart D, Weidlich S, et al.

*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the FARAPULSE PFA System

Journal of Interventional Cardiac Electrophysiology (January, 2024), available here

- 100 patients underwent PFA-PVI with PWI with FARAWAVE.
- Median procedure time was 66 min, and fluoroscopy time was 11 (8–14) min.
- PWI using PFA was achieved in 100% of patients with a median of 19 applications with no reported major complications.
- Recurrent AF/AT was noted in 15 patients (15%) during a median follow-up of 144 days.

Pulsed-Field Ablation of Atrial Fibrillation: Kinetics of Release of Multiple Cardiac Biomarkers

Casella J, Compagnucci P, Malacrida M, et al.

Journal of Interventional Cardiac Electrophysiology (January, 2024), available here

- 72 patients were treated with FARAPULSE. Blood samples were evaluated for 14 cardiac biomarkers for stress, myocardial fibrosis, inflammation and coagulation activity 3, 24, and 48 hours after ablation.
- CK-MB, hs-cTnI, myoglobin, and WBC levels displayed an increase at 3-h post-ablation, followed by a decline towards lower values within 24 h. C-reactive protein peaked at 48 hours, exhibiting a gradual increase over time.
- Markers of hemolysis and potential end organ damage exhibited fluctuations within the normal range for this population.
- Following the procedure, markers indicating coagulation activity, such as hemoglobin, hematocrit, and platelet count, exhibited a decline which was similar to other ablation energies.
- There appeared to be no correlation between cardiac enzyme elevations and extension of PFA beyond the PVs.

Pulsed Field Ablation of the Right Superior Pulmonary Vein Prevents Vagal Responses Via Anterior Right Ganglionated Plexus Modulation

Del Monte, M, Della Rocca D, Pannone, L, et al.

Heart Rhythm (January, 2024), available here

- In 40 patients, PVI was performed first ablating the left superior pulmonary vein (LSPV-first group). In 40 patients the RSPV was targeted first, followed by left PVs and right inferior PV (RSPV-first group). Heart rate (HR) and extracardiac vagal stimulation (ECVS) were evaluated at baseline, during PVI, and post-ablation to assess GP modulation.
- Significantly more vagal responses occurred in the LSPV-first group, 31 (78%) patients and 5 (13%) occurred in the RSPV-first group.
- Temporary pacing was needed in 14 (35%) patients in the LSPV-first group and 3 (8%) in the RSPV-first group. RSPV isolation was associated with similar acute HR increase in the two groups.
- No significant residual changes in HR or ECVS response were documented in both groups at the end of the procedure.

2024 CLINICAL PUBLICATIONS

Pulsed Electric Field, Cryoballoon, and Radiofrequency for Paroxysmal Atrial Fibrillation Ablation: A Propensity Score-Matched Comparison

Della Rocca D, Marcon L, Magnocavallo M, et al.

Europace (January, 2024), available here

- PVI-only ablation outcomes via FARAPULSE, CBA and RFA were propensity score matched yielding 174 PFA, 348 CRYO, and 348 RF patients.
- There were significant differences in first-pass isolation; 98.8% of pulmonary veins (PVs) with PFA, 81.5% with CBA, and 73.1% with RFA.
- Procedure and dwell times were significantly shorter with PFA, and 3D mapping system usage led to a significant reduction in fluoroscopy exposure with RFA.
- Overall complication rates were 3.4% (n = 6) with PFA, 8.6% (n = 30) with CBA, and 5.5% (n = 19) with RFA.
- The one-year Kaplan–Meier estimated freedom from any atrial tachyarrhythmia was 79.3% with PFA, 74.7% with CBA, and 72.4% with RFA. Freedom from AF was 85.5% with PFA, 78.5% with CBA, and 77.4% with RF.
- Among 145 repeat ablation procedures, PV reconnection rate was significantly different: 19.1% after PFA, 27.5% after CBA, and 34.8% after RFA.
- The most common site of PFA reconnection was the left superior PV (27.3%) consistently involving the anterior aspect and the carina of the vein.

Impact of Pulsed Field Ablation on Intraluminal Esophageal Temperature

Kirstein B, Heeger C, Vogler J, et al.

Journal of Cardiovascular Electrophysiology (January, 2024), available here

- Median intraluminal esophageal temperature change was statistically significant and increased by 0.8 ± 0.6°C.
- A TESO increase ≥1°C was observed in 10/43 (23%) patients. The highest TESO measured was 40.3°C.
- All patients remained asymptomatic, and no atrio-esophageal fistula was reported on follow-up.

Posterior Wall Ablation by Pulsed-Field Ablation – Procedural Safety, Efficacy and Findings on Redo Procedures

Kueffer T, Tanner H, Madaffari A, et al.

Europace (January, 2024), available here

- Posterior wall ablation was performed in 215 patients (67% redo procedures) and was successful in all patients by applying a median of 36 PFA lesions.
- The rate of severe adverse events was 0.9%, one cardiac tamponade, and one vascular access complication.
- Median follow-up was 7.3 months. The one-year arrhythmia-free Kaplan–Meier analysis was 53%.
- A redo procedure was performed in 26 patients (12%) after a median of 6.9 months and showed durable PWA in 22 patients (85%) with minor lesion regression.
- There was posterior wall reconnection in four patients with three (75%) having roof-dependent AT.

2024 CLINICAL PUBLICATIONS

Pulsed Field Ablation and Cryoballoon Ablation for Pulmonary Vein Isolation: Insights on Efficacy, Safety and Cardiac Function

Rattka M, Mavrakis E, Vlachopoulou D, et al.

Journal of Interventional Cardiac Electrophysiology (January, 2024), available here

- 141 consecutive AF patients were treated with PFA (n=94) or CBA (n=47).
- At 1 year, 70% of the PFA patients and 61% of the CBA patients were free from AF/AT.
- After PFA, there was a significant improvement in left atrial volume index.
- PFA and CBA had similar efficacy outcomes, but PFA might induce left atrial reverse remodeling and contribute to left ventricular systolic function.

Pulsed Field versus Cryoballoon Ablation for Atrial Fibrillation: A Real-World Observational Study on Procedural Outcomes and Efficacy

van de Kar M, Slingerland S, Steenbergen G, et al.

Netherland Heart Journal (January, 2024), available here

- Retrospective cohort study conducted at a high-volume center comparing CBA and PFA in the real-world setting.
- 1714 procedures were analyzed: 1241 in the CBA group and 473 in the PFA group.
- The CBA group had a significantly higher incidence of phrenic nerve palsy compared with the PFA group (15 vs 0).
- The procedure duration was significantly shorter in the PFA group (95.0 vs 74.0 min).

Severe Acute Kidney Injury Related to Hemolysis After Pulsed Field Ablation for Atrial Fibrillation

Venier S, Vaxelaire N, Jacon P, et al.

Europace (January, 2024), available here

- Acute kidney injury (AKI) occurred in 2 patients which was secondary to acute and severe hemolysis after a PFA procedure.
- 68 consecutive patients had a blood sample the day after the procedure for the assessment of hemolysis indicators.
- FARAPULSE was used with a total number of median applications of 64.
- Nineteen patients (28%) showed significantly depleted haptoglobin levels with a significant inverse correlation between the plasma level of haptoglobin and the total number of applications.
- Two groups were compared:
  - The hemolysis+ group (haptoglobin < 0.04 g/L) vs. the hemolysis– group.
  - The number of applications was significantly higher in the hemolysis+ group (75) vs the hemolysis– group (62).
  - More than 70 applications seem to have better sensitivity and specificity to predict hemolysis.

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Efficacy and Safety of Pulmonary Vein Isolation with Pulsed Field Ablation versus Novel Cryoballoon Ablation System for Atrial Fibrillation
Badertscher P, Weidlich S, Knecht S, et al.

Europace (December, 2023), available here

- 181 AF patients underwent PVI (PFA = 106) and (CBA = 75).
- The median procedure, left atrial dwell, and fluoroscopic times were similar between the PFA and the CB group; 55 min vs. 58 min, 38 min vs. 37 min, and 11 min vs. 11 min, respectively.
- Three procedural complications were observed in the PFA group (two tamponades, one temporary ST elevation) and 3 complications in the CB group (3 reversible phrenic nerve palsies).
- During the median follow-up of 404 days, AF recurrence was similar in the PFA (24%) group and the CB (30%) group.

Pulsed Field Ablation of Atrial Fibrillation: An Initial Australian Single-Centre Experience
Lee X, Freeman B, Gunthorpe N, et al.

Heart, Lung and Circulation (December, 2023), available here

- 100 FARAPULSE procedures were performed in 97 patients under GA with a median procedure time of 74 minutes.
- At median follow-up of 218 days, the Kaplan-Meier estimate for freedom from atrial arrhythmias at 180 days was 87%.
- Two (2%) pseudoaneurysm vascular access complications occurred. There were no reported thromboembolic complications, stroke, phrenic nerve palsy, pulmonary vein stenosis, atrio-esophageal fistula, or pericardial tamponade.

Myocardial Injury and Inflammation Following Pulsed-Field Ablation and Very High-Power Short-Duration Ablation for Atrial Fibrillation
Popa M, Bahlke F, Kottmaier M, et al.

Journal of Cardiovascular Electrophysiology (December, 2023), available here

- 179 patients with paroxysmal AF received de novo PVI with standard power RFA (30–40 W/20–30 s, n = 52), power-controlled HPSD (70 W/5–7 s, n = 60), temperature-controlled HPSD (90 W/4 s, n = 32), and FARAPULSE PFA (n = 35).
- High-sensitivity cardiac troponin T (hs--cTnT), creatine kinase (CK), CK MB isoform (CK-MB), and white blood cell (WBC) count were determined before and after ablation.
- Post-ablation hs--cTnT release was significantly higher with PFA, HPSD-70W, and HPSD-90W than with standard RFA.
- CK and CK-MB release was increased with PFA by 3.4-fold and 5.8-fold, respectively, as compared to standard RFA.
- PFA was associated with the lowest elevation in WBC compared to standard RFA, HPSD-70W, and HPSD-90W.
- PFA was associated with the highest myocardial injury and the lowest inflammatory reaction compared to the other energies tested.

2023 CLINICAL PUBLICATIONS

Intracardiac Echocardiography–Guided Pulsed-Field Ablation for Successful Ablation of Atrial Fibrillation: A Propensity-Matched Analysis from a Large Nationwide Multicenter Experience
Dello Russo A, Tondo C, Schillaci V, et al.

Journal of Interventional Cardiac Electrophysiology (November, 2023), available here

- 556 patients were analyzed: 357 (66%) with paroxysmal AF, 499 (89.7%) undergoing de novo PVI.
- ICE-guided procedures (n = 138) were propensity matched with patients with a standard approach (n = 138).
- There were no differences in procedural metrics and no major procedure-related adverse events were reported.
- ICE guidance of PFA was not associated with an improvement in procedural metrics.

Pulsed-Field Ablation Does Not Induce Esophageal and Periesophageal Injury—A New Esophageal Safety Paradigm in Catheter Ablation of Atrial Fibrillation
Grosse Meininghaus D, Freund R, Koerber B, et al.

Journal of Cardiovascular Electrophysiology (November, 2023), available here

- 20 FARPULSE patients were compared to a previous cohort of 57 patients who underwent thermal ablation (33 CBA, 24 RFA).
- Following PFA, there were no mucosal lesions, food retention, or ablation induced vagal nerve injury; 4 patients showed periesophageal edema.
- After thermal ablation, 33/57 (58%) showed esophageal or periesophageal injury; 4/57 mucosal lesion, 18/57 food retention, 17/57 vagal nerve injury and 20/52 edema.
- In contrast to thermal methods, PFA was not associated with the same amount of esophageal injury.

Pulsed-Field Ablation Does Not Worsen Baseline Pulmonary Hypertension Following Prior Radiofrequency Ablations
Mohanty S, Della Rocca D, Torlapati P, et al.

JACC: Clinical Electrophysiology (November, 2023), available here

- 28 non-PAF patients with pulmonary hypertension (PH) that failed >1 RFA were treated with FARAPULSE and propensity matched to 28 AF patients treated with a repeat RFA after a failed procedure.
- The groups had comparable baseline mean pulmonary artery pressures (mPAP).
- After adjustment for baseline mPAP, the least-squares means change at 3 months after ablation was –1.71 ± 1.03 mm Hg and 19.67 ± 1.03 mm Hg in PFA and RFA.
- The RFA group had significantly higher mPAP than in the PFA group with the post ablation mPAP values increased in all (100%) of the RFA patients, and it either remained unchanged or was reduced in most (89.3%) of the PFA patients.
- In this propensity-matched population, no worsening of mPAP was detected following PFA in patients with PH undergoing a repeat procedure for recurrence.

2023 CLINICAL PUBLICATIONS

Myocardial Damage, Inflammation, Coagulation, and Platelet Activity During Catheter Ablation Using Radiofrequency and Pulsed-Field Energy
Osmancik P, Bacova B, Hozman M, et al.

JACC Clinical Electrophysiology (November, 2023), available here

- 65 AF patients were treated (PFA = 33) and (RFA= 32) with both groups being similar in baseline characteristics.
- Procedure and LA dwell times were substantially shorter in the PFA group (55 min vs 151 min and 36 min vs 116 min).
- Peak troponin release was substantially higher in the PFA group and both PFA and RFA were associated with similar extents (>50%) of platelet and coagulation activation.
- Despite 10 times more myocardial damage, pulsed-field ablation was associated with a similar degree of platelet/coagulation activation, and slightly lower inflammatory response.

Durability of Pulmonary Vein Isolation for Atrial Fibrillation. A Meta-Analysis and Systematic Review
Serban T, Mannhart D, Abid Q, et al.

Europace (November, 2023), available here

- Metanalysis of 19 studies investigating 1050 patients (mean age 60 years, 31% women, time to remap 2–7 months) were included.
- In a pooled analysis, 99.7% of the PVs and 99.4% of patients were successfully ablated at baseline and 75.5% of the PVs remained isolated and 51% of the patients had all PVs persistently isolated at follow-up across all energy sources.
- In a pooled analysis of the percentages of PVs durably isolated during follow-up, the estimates of RFA were the lowest at 71%, but comparable with CBA (79%).
- Higher durability percentages were reported in PVs ablated with laser-balloon (84%) and PFA (87%)).

Clinical Outcomes by Sex After Pulsed Field Ablation of Atrial Fibrillation
Turagam M, Neuzil P, Schmidt B, et al.

JAMA Cardiology (November, 2023), available here

- Of 1568 patients with AF who underwent PFA, female patients, as compared with male patients, were older, had more paroxysmal AF and fewer comorbidities such as coronary disease, heart failure, and sleep apnea.
- The 1-year Kaplan-Meier estimate for freedom from atrial arrhythmia was similar in male (79.9%) and female (76.3%) patients with no significant difference in acute major adverse events between groups.

Pulsed-Field Versus Cryoballoon Ablation for Atrial Fibrillation—Impact of Energy Source on Sedation and Analgesia Requirement
Wahedi R, Willems S, Feldhege J, et al.

Journal of Cardiovascular Electrophysiology (November, 2023), available here

- 100 PVI patients (PFA (n = 50), CBA (n = 50)) underwent PVI ablation.
- Requirement of propofol, midazolam, and sufentanyl was significantly higher in the PFA group compared to CBA.
- Sedation-associated complications did not differ between both groups.
- Non-sedation-associated complications procedure times did not differ between groups.

2023 CLINICAL PUBLICATIONS

A Real-World Case–Control Study on the Efficacy and Safety of Pulsed Field Ablation for Atrial Fibrillation

Yang M, Wang P, Hao Y, et al.

European Journal of Medical Research (November, 2023), available here

- 36 AF patients were treated with PFA and 36 patients with RFA.
- There were no significant differences in patient baseline demographics or AAD usage.
- The ablation time in the PFA group was markedly shorter than RFA.
- At 6 months, there was no statistically significant difference in efficacy.
- In this study, PFA was safe, efficient, and had a short learning curve.

Coronary Artery Spasm During Pulsed Field vs Radiofrequency Catheter Ablation of the Mitral Isthmus

Zhang C, Neuzil P, Petru J, et al.

JAMA Cardiology (November, 2023), available here

- 26 patients underwent PVI with either PFA (n = 17) or RFA (n = 9) along the mitral isthmus ablation.
- Coronary spasm was observed in 7 of 17 patients (41.2%) undergoing PFA: in 7 of 9 (77.8%) when the mitral isthmus ablation line was situated superiorly and in 0 of 8 when placed inferior.
- Coronary spasm did not occur in any of the 9 patients undergoing RFA.
- 5 patients received crossover PFA after RFA failed to achieve conduction block, coronary spasm occurred in 3 (60%).
- Most instances of spasm (9/10, 90%) were subclinical, with 2 (20%) requiring nitroglycerin administration. The median time to resolution of spasm was 5 minutes.

Versatility of the Novel Single-Shot Devices: A Multicenter Analysis

Cespón-Fernandez, M, Della Rocca D, Almorad A, et al.

Heart Rhythm (October, 2023), available here

- Procedural data from 12 electrophysiologists experienced with balloon technologies was analyzed for a total of 480 procedures (240 balloons, 120 FARAPULSE and 120 HELIOSTAR).
- During the follow-up period of 6.86 ± 3.82 months, there were 11 atrial tachyarrhythmia recurrences (9.17%) in the HELIOSTAR group and 8 (6.67%) in the FARAPULSE group after the 3-month blanking period.
- The number of cases needed to become confident with the new technology, we found a mean number of 10 and 17 procedures for FARAPULSE and HELIOSTAR.

Investigating Deep Sedation with Intravenous Ketamine in Spontaneous Respiration during Pulsed-Field Ablation

Iacopino S, Filannino P, Artale P, et al.

Journal of Cardiothoracic and Vascular Anesthesia (October, 2023), available here

- The sedation protocol was the intravenous administration of fentanyl (1.5 mg/kg) and midazolam (2 mg) at low doses before local anesthesia with lidocaine.
- A ketamine adjunct (1mg/kg) in 5-minute boluses was injected about 5 minutes before the first PFA delivery.
- 117 patients underwent ablation with a PFA LA dwell time of 24 ± 7 minutes.
- The mean time under sedation was 54.9 ±6 minutes, with 92 patients (79%) being sedated for <1 hour.
- The satisfaction level was found acceptable by both the patient and the primary operator in all procedures.

2023 CLINICAL PUBLICATIONS

Comparison of Pulsed-Field Ablation versus Very High-Power Short Duration-Ablation for Pulmonary Vein Isolation

Wörmann J, Schipper J, Lüker J, et al.

Journal of Cardiovascular Electrophysiology (October, 2023), available here

- Study that compared the procedural outcome data for PVI between FARAWAVE and very high-power short duration (vHPSD) defined as 70W/7 sec lesions or 70W/5 sec for posterior wall.
- There were 57 patients in each group.
- The FARAWAVE group had significantly shorter procedure duration (65 ± 17 min) versus the vHPSD (95 ± 23 min) with longer fluoroscopy times (15 ± 5 min) vs 12 ± 3 min for vHPSD.
- The freedom from arrhythmia recurrence at a median of 125 days was 80.7% in the FARAWAVE arm versus 77.2% in the vHPSD group.
- Safety event rates were low with 2 tamponades occurring in the FARAWAVE group and 2 groin bleeds in the vHPSD group. One clinically non-significant PV stenosis occurred in the vHPSD group.

Pulsed-Field Ablation Versus Single Catheter High-Power Short-Duration Radiofrequency Ablation for Atrial Fibrillation: Procedural Characteristics, Myocardial Injury and Midterm Outcomes

Badertscher P, Weidlich S, Serban T, et al.

Heart Rhythm (September, 2023), available here

- Compared FARAPULSE to high-power short-duration (HPSD) RF looking at efficiency, safety, myocardial injury and midterm outcomes.
- 115 patients (56% paroxysmal) underwent ablation, 52 patients had FARAPULSE ablation and 63 had HPSD RF ablation.
- PFA procedures were significantly shorter (PFA, 58 [53-71] minutes vs HPSD, 83 [71-99] minutes with significantly longer fluoroscopy times (PFA 13 [10-16] minutes vs HPSD 2.2 [1.3-3.6].
- The postoperative troponin levels were significantly higher in the PFA group (1540 ng/l [1010-1980]) vs HPSD (897 ng/l [725-1240]).
- The AF recurrence free rate at 6 months was 85% for the PFA group and 65% for the HPSD group.
- PFA procedures were shorter, there were higher cardiac troponin levels, and the AF-free survival during mid-term follow-up was similar.

Quantitative Assessment of Transient Autonomic Modulation after Single-Shot Pulmonary Vein Isolation with Pulsed-Field Ablation

Del Monte A, Cespon Fenandez M, Vetta G, et al.

Journal of Cardiovascular Electrophysiology (September, 2023), available here

- Assessed the effects of FARAPULSE ablation on the ganglionated plexi and autonomic nervous system (ANS) by looking at the degree of acute vagal modulation induced immediately following FARAPULSE ablation.
- De novo PVI patients treated with FARAPULSE (n=40) or cryoballoon (n=36) were assessed with extracardiac vagal simulation (ECVS) to capture the effects of ablation. To capture any transient effects, the subgroup was assessed before PVI, immediately after PVI and 10 minutes after the last ablation application.
- Baseline values were similar, but the vagal response induced by ECVS almost disappeared in the thermal group but persisted in the FARAPULSE group. Intraprocedural vagal reactions occurred more frequently with FARAPULSE than thermal. The heart rate 24-hour post ablation increased more with thermal than PFA ablation.

- In the subgroup with repeated ANS modulation assessment, PFA had a significant acute suppression of vagal response immediately after ablation which recovered almost completely within a few mins after ablation.
- FARAPULSE was found to be associated with only transitory, short vagal effects on the ANS.

Left Atrial Posterior Wall Isolation with Pulsed Field Ablation in Persistent Atrial Fibrillation

Gunawardene M, Frommeyer G, Ellermann C, et al.

*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the FARAPULSE PFA System

Journal of Clinical Medicine (September, 2023), available here

- Persistent AF patients were treated with PVI + (n=16) or PVI ++ posterior wall isolation (n=59) with FARAWAVE with 32 patients being de novo and 43 patients were repeat ablation patients.
- In the redo cohort, 67% of all PVs were isolated.
- PVI + PWI had an average procedure time of 91 ± 30 min and two minor complications occurred.
- The 354 ± 197-day freedom from atrial arrhythmias (allowing AADs) in the PVI + PWI cohort was 79.3%.
- PWI guided by FARAPULSE had favorable outcomes with a low number of complications.

Pulsed-Field vs. Cryoballoon vs. Radiofrequency Ablation: A Propensity Score Matched Comparison of One-Year Outcomes after Pulmonary Vein Isolation in Patients with Paroxysmal Atrial Fibrillation

Maurhofer J, Kueffer T, Madaffari A, et al.

Journal of Interventional Cardiac Electrophysiology (September, 2023), available here

- CBA and RFA AF patients were propensity matched to PFA, (PFA, n=40), (CBA, n=80) and (RFA, n=80).
- Median procedure times were the shortest with CBA (75 min), followed by PFA (94 min) and RFA (182 min), with RFA having the lowest fluoroscopy dose.
- After 1-year of follow-up, freedom from any atrial arrhythmia was 85% for PFA, 66.2% for CBA, and 73.8% for RFA.
- With propensity matched patients, the results were favorable for the initial use of PFA versus CBA and RFA.

Long-Term Clinical Outcomes of Pulsed Field Ablation in the Treatment of Paroxysmal Atrial Fibrillation

Musikantow D, Neuzil P, Anic A, et al.

JACC: Clinical Electrophysiology (September, 2023), available here

- The first long-term safety and recurrence outcomes for the FARAPULSE PFA system in clinical trial patients.
- 121 PAF patients were treated during these feasibility studies (IMPULSE, PEFCAT, PEFCAT II), of which 49 patients were treated with the optimized waveform ("Biphasic II"). DOI: 10.1016/j.jacep.2021.02.014
- 116 patients were included in long term follow-up with a mean follow-up duration of ~4 years [49 +/- 7 months].
- No new adverse events were reported.

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- All Follow-Up Results (Years 1-5) - With the optimized biphasic waveform, there was an 81% (38/47) freedom from AF/AFL recurrence.
- Late Recurrence Follow-Up Analysis (Years 2-5) - 95% freedom from AF/AFL/AT (optimized biphasic waveform).

Early Recurrences Predict Late Therapy Failure after Pulsed Field Ablation of Atrial Fibrillation
Plank K, Bordignon S, Urbanek L, et al.

Journal of Cardiovascular Electrophysiology (September, 2023), available here

- 231 AF patients (55% paroxysmal) were analyzed for a medial follow-up of 367 days.
- 46 (21%) experienced early recurrence of atrial tachyarrhythmia (ERAT) after a median of 23 days post-ablation.
- The KM estimated freedom from AF/AT was 74.2% at 1 year, 81.8% for paroxysmal and 64.8% for persistent AF.
  Multivariate analysis found that ERAT and female sex were independent predictors of late recurrence.

Characterization of Durability and Reconnection Patterns at Time of Repeat Ablation after Single-Shot Pulsed Field Pulmonary Vein Isolation
Ruwald M, Haugdal M, Worck R, et al.

Journal of Interventional Cardiac Electrophysiology (September, 2023), available here

- The pulmonary vein durability rate was 69% in repeat ablation patients (n=26) that had a FARAPULSE procedure an average of 292 ± 119 days after the de novo ablation.
- Patients who underwent posterior wall isolation had a durable PW isolation rate of 80% (4/5).
- Reconnection was observed in the LSPV (27%), LIPV (19%), RSPV (35%), RIPV (42%) with the gaps significantly clustered in the right sided anterior carina compared to other regions.

Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation
Reddy VY, Gerstenfeld EP, Natale A, et al.

New England Journal of Medicine (August, 2023), available here, supplement available here

- The ADVENT Pivotal Trial was the first randomized clinical trial that directly compared FARAPULSE™ PFA to standard-of-care thermal ablation devices (force-sensing radiofrequency (RFA) or cryoballoon ablation (CBA)), for the treatment of paroxysmal atrial fibrillation (PAF).
- It included an experienced group of thermal ablators with limited clinical experience with the novel FARAPULSE technology.
- In this RCT, FARAPULSE demonstrated:
  - Non-inferiority for both the primary safety and effectiveness outcomes compared to thermal ablation technology (posterior probability > .999).
  - Significantly less pulmonary vein cross-sectional narrowing compared to thermal ablation (posterior probability > .999).
  - Significantly shorter procedure times, reduced LA dwell time and total ablation time versus thermal ablation. Lower standard deviations across these characteristics also indicate less variability within the PFA procedures.

2023 CLINICAL PUBLICATIONS

Comparison of Pulsed Field Ablation and Cryoballoon Ablation for Pulmonary Vein Isolation
Schipper H, Steven D, Lüker J, et al.

Journal of Cardiac Electrophysiology (August, 2023), available here

- Retrospective analysis of de novo paroxysmal or persistent AF PVI with FARAWAVE (PFA) (n=54) and the POLARx Cryoballoon (CBA) (n=54).
- The total procedure times excluding the LA mapping were significantly shorter for the PFA group (58.0 ± 12.5 min) vs CBA (73.0 ± 24.8 min). Fluoroscopy time was significantly longer in the PFA arm. Subgroup analysis showed a significant reduction in procedure time with continued use of FARAPULSE.
- At 273 ± 129 days, the arrhythmia recurrence free rate was similar for both devices, 74% for PFA and 72% for CBA.
- HR changes between baseline and 3 month follow up did not differ between both groups (PFA: 4 ± 8 beats/min, CBA: 4 ± 11 beats/min).

Pulsed Field Ablation-Based Pulmonary Vein Isolation Using a Simplified Single-Access Single-Catheter Approach — The Fast and Furious PFA Study
Tilz R, Vogler J, Kirstei B, et al.

Circulation Journal (August, 2023), available here

- 50 paroxysmal (56%) and persistent AF patients underwent wide area circumferential ablation (WACA) with FARAPULSE.
- The mean procedure time was 27.4 ± 6.6 min with a mean LA dwell time of 14.4 ± 5.5 min.
- The mean time to ambulation was 3.3 ± 3.1 hours with a low rate of periprocedural complications.
- At a mean follow-up of 6.5 ± 2.1 months, 82% (41/50) patients remained in sinus rhythm.

Pulsed-Field Ablation on Mitral Isthmus in Persistent Atrial Fibrillation - Preliminary Data on Efficacy and Safety
Davong B, Adeliño R, Delasnerie H, et al.

*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the F ARAPULSE PFA System

JACC: Clinical Electrophysiology (July, 2023), available here

- PVI, posterior wall (PW) and mitrial isthmus (MI) ablation were performed in 45 patients with persistent AF.
- The acute success of PVI, PW isolation, and MI block was 100%.
- There were 2 (4.4%) coronary artery spasms which were reversible after intravenous nitrate infusion.
- During a mean follow-up of 107 ± 59.5 days, there was a 20% rate of arrhythmia recurrence.

2023 CLINICAL PUBLICATIONS

Pulmonary Vein Isolation Durability and Lesion Regression in Patients with Recurrent Arrhythmia after Pulsed Field Ablation

Kueffer T, Stefanova A, Madaffari A, et al.

Journal of Interventional Cardiac Electrophysiology (July, 2023), available here

- Redo ablation was performed on 29/341 (8.5%) of patients for arrhythmia recurrence.
- At 6-months post index ablation, mapping identified 69/110 (63%) durable PV isolation. In 6 (21%) all PVs were durability isolated.
- PV reconnections were often found on the right sided veins and on the anterior aspects of the upper veins.
- Importantly, only minor regression was observed between the index and redo procedures (median of 3 mm).

Acute Lesion Extension Following Pulmonary Vein Isolation with Two Novel Single Shot Devices: Pulsed Field Ablation versus Multielectrode Radiofrequency Balloon

My I, Lemoine M, Butt M, et al.

Journal of Cardiovascular Electrophysiology (July, 2023), available here

- Compared lesion formation and lesion extent (measured with mapping and biomarkers) between FARAPULSE and HELIOSTAR (multi-electrode RF balloon).
- 60 paroxysmal patients (28 PFA, 32, RF balloon) underwent PVI, high density mapping and Troponin I was quantified.
- The posterior wall ablation area was significantly larger in the PFA group.
- In a subset of 38 patients, the serum Troponin was significantly higher in the PFA group, likely due to it creating larger lesions.

Pulsed Field Versus Cryoballoon Pulmonary Vein Isolation for Atrial Fibrillation: Efficacy, Safety, and Long-Term Follow-Up in a 400-Patient Cohort

Urbanek L, Bordignon S, Schaack D, et al.

Circulation: Arrhythmia and Electrophysiology (July, 2023), available here

- 400 patients were treated with FARAPULSE (n=200) or cryoballoon ablation (CBA) (n=200).
- The mean procedure times were significantly shorter in the FARAPULSE group (34.5 [29-40] mins) vs CBA (50 [45-60] mins) with similar fluoroscopy times.
- The overall procedural complication rates were 6.5% in the CBA and 3.0% in the FARAPULSE group driven by a higher rate of phrenic nerve palsy in the CBA group.
- The 1-year freedom from arrhythmia recurrence rates in paroxysmal AF were similar with 83.1% in the CBA group and 80.3% in the FARAPULSE group.

2023 CLINICAL PUBLICATIONS

European Real-World Outcomes with Pulsed Field Ablation in Patients with Symptomatic Atrial Fibrillation - Lessons from the Multicenter EU-PORIA Registry

Schmidt B, Bordignon S, Neven K, et al.

EURPOACE (July, 2023), available here

- Registry to study the real-world adoption, workflow, acute and long-term outcomes after pulsed field ablation (PFA) in an all-comer atrial fibrillation (AF) patient population in high-volume European centers, inclusive of learning curve.
- This registry demonstrated consistent, short procedure times with a median of 58 minutes despite a large number of operators with varied experience and workflow.
- There was a low rate of safety events (3.6%) and promising one-year efficacy rate (74%) in a large spectrum of AF patients.
- Operator experience and previous primary ablation modality did not have an effect on the one-year AF/AT recurrence rates showing a rapid adoption of the technology by new operators and prior RF and cryo users.
- A small 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 pulmonary veins being durably isolated.

Electrophysiological Findings during Re-Do Procedures after Single-Shot Pulmonary Vein Isolation for Atrial Fibrillation with Pulsed Field Ablation

Magni F, Scherr D, Manninger M, et al.

Journal of Interventional Cardiac Electrophysiology (May, 2023), available here

- Patients who had a de novo procedure with FARAWAVE that had recurrence and subsequent repeat ablation (14/447) procedures were analyzed. The mean time to recurrence was 4.9 ± 1.9 months.
- PV reconnection was found in zero (35.7%), one (21.4%), two (14.3%) or three (28.6%) of patients.
- Durable PVI was observed in over 1/3 of redo patients. The most common arrhythmia recurrence following PVI only was AF. Concomitant (35.7%) or isolated AFL/AT (14.3%) recurrence was observed in 50% of patients.

Lesion Formation Following Pulsed Field Ablation for Pulmonary Vein and Posterior Wall Isolation

Sohns C, Fink T, Braun M, et al.

*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the FARAPULSE PFA System

PACE (May, 2023), available here

- Lesion formation was assessed with late gadolinium enhancement CMR (LGE-CMR) 3-months after FARAPULSE ablation.
- In 10 patients, PVI and posterior wall isolation (PWI) was performed with FARAWAVE. The mean procedure duration was 62 ± 7 min with a mean LA dwell time of 13 ± 2 min.
- The mean LA scar burden was 8.1 ± 2.1% with a mean scar width of 12.8 ± 2.1 mm. At 7 months, 9/10 (90%) of patients were recurrence free.
- LGE CMR analysis found homogenous and continuous lesion patterns with no evidence of PV stenosis or collateral damage to adjacent structures.

2023 CLINICAL PUBLICATIONS

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Safety and Effectiveness of Pulsed Field Ablation to Treat Atrial Fibrillation: One-Year Outcomes From the MANIFEST-PF Registry

Turagam MK, Neuzil P, Schmidt B, et al.

Circulation (May, 2023), available here

- Multi-national retrospective survey of all patients treated with FARAPULSE from 24 EU centers (77 operators), 1,568 patients.
- Low complication rates; 1.9% major complication rate and 4.0% minor complication rate with no reported esophageal damage or PV stenosis.
- There was an 81.6% 1-year freedom from AF/AFL/AT for paroxysmal AF patients with no difference in recurrence free outcomes based on the procedural volume (PFA procedure numbers).

2023 CLINICAL PUBLICATIONS

Bronchial Safety After Pulsed-Field Ablation for Paroxysmal Atrial Fibrillation
Füting A, Reinsch N, Brokkaar L, et al.

Circulation: Arrhythmia and Electrophysiology (April, 2023), available here

- Respiratory tract CT scans were performed on 60 patients post FARAPULSE ablation to look for bronchial damage with either straight-tip (n=30) or J-tip (n=30) guidewires.
- In 12/30 patients with the straight-tip, extra-stiff guidewire, small amounts of old blood without active bleeding were detected with no evidence of thermal lesions. There was no clinical relevance at 30 days post-procedure.
- Use of the straight-tip guidewire may lead to asymptomatic bronchial damage which was not detected when the J-tip guidewire was used.

Pulsed Field Ablation to Treat Atrial Fibrillation: Autonomic Nervous System Effects
Musikantow DR, Neuzil P, Petru J, et al.

JACC: Clinical Electrophysiology (April, 2023), available here

- Heart rate was assessed pre and post PVI using FARAPULSE (n=40), Cryoablation (n=40) and radiofrequency (n=40) PVI ablation to understand the impact of pulsed field ablation on the ganglionated plexi (GP).
- Between baseline and 3 months, heart rates increased by 8.9 ± 11.4 (RF), 11.1 ± 9.4 (CB), and -0.1 ± 9.2 (PFA) beats/min.
- Unlike thermal ablation, FARAPULSE PFA had minimal effects on the GPs.

PFA for Treatment of AF in Patients with Congenital Anomalies of Cardiac Veins
Castiglione A, Küffer T, Gräni C, et al.

*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the FARAPULSE PFA System

Journal of Cardiovascular Electrophysiology (March, 2023), available

- Five patients with congenital anomalies were treated with FARAPULSE.
- PVs were isolated with no phrenic nerve palsy or other complications.
- Pre-procedural imaging and 3D mapping was found to be well suited, efficient, and versatile in AF patients with anomalous cardiac veins.

Effects of Pulsed Field Ablation on Autonomic Nervous System in Paroxysmal Atrial Fibrillation: A Pilot Study
Guo F, Wang J, Deng Q, et al.

Heart Rhythm (March, 2023), available here

- Nerve injury biomarkers and DW-MRI were conducted on 18 patients in a pilot study.
- Serum nerve injury biomarkers did not differ between pre- and post--ablation. Heart rate variability did not differ and there were no acute cerebral microemboli events.
- FARAPULSE PVI did not induce nerve injury in this study.

2023 CLINICAL PUBLICATIONS

Visualization of Fibroblast Activation Using 68Ga- FAPI PET/CT after Pulmonary Vein Isolation with Pulsed Field Compared with Cryoballoon Ablation
Kupusovic J, Kessler L, Bruns F, et al.

Journal of Nuclear Cardiology (March, 2023), available here

- Fibroblast activation was used as a surrogate for ablation damage after FARAPULSE(n=15) and CBA (n=11) ablation.
- Fibroblast activation tissue response was less pronounced in the PFA patient cohort vs CBA.

A Randomized Controlled Trial of Pulsed Field Ablation versus Standard-of-Care Ablation for Paroxysmal Atrial Fibrillation: The ADVENT Trial Rationale and Design
Reddy VY, Lehmann JW, Gerstenfeld EP, et al.

Heart Rhythm O2 (March, 2023), available here

- The ADVENT (Randomized Controlled Trial for Pulsed Field Ablation versus Standard of Care Ablation for Paroxysmal Atrial Fibrillation) trial was a multicenter, prospective, single-blind, randomized controlled trial comparing PVI using PFA vs conventional thermal (cryoballoon and contact force radiofrequency) ablation for the treatment of drug-resistant paroxysmal AF.

Pulsed Field Ablation in Real-World Atrial Fibrillation Patients: Clinical Recurrence, Operator Learning Curve and Re-Do Procedural Findings
Ruwald MH, Johannessen A, Lock Hansen M, et al.

Journal of Interventional Cardiac Electrophysiology (February, 2023), available here

- 121 patients underwent PVI with FARAPULSE. The mean procedure time was significantly reduced from the initial cases from 85 ± 34 min to 72 ± 18 min.
- There was one phrenic nerve palsy with partial remission at follow-up. The KM event-free estimate at 365 days was 80% (88% paroxysmal, 69% persistent).
- In 5/8 re-do procedures, the gaps were primarily located in the right pulmonary veins.

2022 CLINICAL PUBLICATIONS

Pulsed-Field Ablation for the Treatment of Left Atrial Reentry Tachycardia

Kueffer T, Seiler J, Madaffari A, et al.

*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the FARAPULSE PFA System

Journal of Interventional Cardiac Electrophysiology (December, 2022), available here

- Left atrial reentry tachycardia were treated with FARAPULSE (n=22).
- Lesion used to treat the ATs included, 20 roof lines, 13 anterior lines, and 6 mitral isthmus lines with no reported complications.

Findings from Repeat Ablation using High-Density Mapping after Pulmonary Vein Isolation with Pulsed Field Ablation

Tohoku S, Chun J, Bordignon S, et al.

EUROPACE (November, 2022), available at here

- In redo patients initially treated with FARAPULSE using the 5S strategy, the incidence of pulmonary vein (PV) reconnection was assessed (inclusive of learning curve).
- Among the 360 patients, 25 patients (19 paroxysmal) underwent a redo procedure in 6.1 ± 4 months.
- The PV durable isolation rate was 90.9% as assessed by high-density mapping.
- The mechanism of all but one atrial tachyarrhythmia was macro-reentry.
- The mean % of isolated posterior wall surface area was 72.7 ± 19.0%.
- There was a low rate of PV reconnection (9.1%) in redo patients and the unique features of the FARAWAVE catheter design and optimized workflow enabled wide antral lesion creation without regression over time.

Pulsed Field Ablation-Based Pulmonary Vein Isolation in Atrial Fibrillation Patients with Cardiac Implantable Electronic Devices: Practical Approach and Device Interrogation (PFA in CIEDs)

Chen S, Chun J, Bordignon S, et al.

*PRECAUTION: Implantable pacemakers and implantable cardioverter/defibrillators may be adversely affected by irreversible electroporation current

Journal of Interventional Cardiac Electrophysiology (November, 2022), available here

- A pilot patient cohort (n=20) underwent PFA ablation for AF (PVI) with different CIEDs.
- CIEDs included pacemaker, implantable cardioverter-defibrillators (ICD), or cardiac resynchronization therapy plus defibrillator (CRT-D).
- CIED pre- and post-PFA interrogation of the devices showed no significant alterations to the parameters or function of the CIEDs and no lead dislodgement.

Initial Experience with Pulsed Field Ablation for Atrial Fibrillation

Magni F, Mulder B, Groenveld H, et al.

Frontiers in Cardiovascular Medicine (November, 2022), available here

- 100 subjects (80% paroxysmal AF) underwent AF ablation with FARAWAVE.
- The learning curves of 2 operators (junior/senior) who performed >20 procedures showed no difference in procedure time, senior (46.9 ± 9.7 min) and junior (45.9 ± 9.9 min).
- The 2 complications that occurred were bleeding at the access site.

2022 CLINICAL PUBLICATIONS

Pulsed Field Ablation in Patients with Complex Consecutive Atrial Tachycardia in Conjunction with Ultra-High-Density Mapping: Proof of Concept

Gunawardene M, Schaeffer B, Jularic M, et al.

*Ablation beyond pulmonary vein isolation is outside the use of labeled indication of the FARAWAVE PFA Catheter with the FARAPULSE PFA System

Journal of Cardiovascular Electrophysiology (September, 2022), available here

- Fifteen patients with atrial tachycardia (AT) underwent high density mapping to ID critical sites for AT maintenance.
- FARAWAVE ablation was performed with 100% success, 63% terminated with the first application and 2 ATs in the right atrial requiring RF ablation.
- No procedure-related complications occurred.

Pulsed-Field Ablation-Based Pulmonary Vein Isolation: Acute Safety, Efficacy and Short-Term Follow-up in a Multi-Center Real World Scenario

Lemoine MD, Fink T, Mencke C, et al.

Clinical Research in Cardiology (September, 2022), available here

- 138 patients (62% persistent AF) from 2 centers were treated with FARAWAVE.
- Mean procedure time was 78 ± 22 min including pre- and post-procedure HD voltage mapping. FARAWAVE LA dwell time was 23 ± 9 min with a fluoroscopy time of 16 ± 7 min.
- There were 3 groin complications (2.2%), 1 pericardial tamponade (0.7%) and 1 transient ST-elevation (0.7%).
- The one-year freedom from recurrence rate was 90% in paroxysmal patients (n = 47) and 60% in persistent AF patients (n = 82).

Cerebral Safety After Pulsed Field Ablation for Paroxysmal Atrial Fibrillation

Reinsch N, Füting A, Höwel D, et al.

Heart Rhythm (September, 2022), available here

- In 30 patients treated with FARAWAVE, Nation Institute of Heath Stroke Scale (NIHSS) scores were assessed 2- and 30-days post PVI. One day after PVI, DW-MRI and FLAIR imaging was done to document the occurrence of silent cerebral events (SCE)/silent cerebral lesions (SCL).
- NIHSS scores were 0 for all patients. Cerebral MRI scans were normal in 29/30 (97%) of patients. In one patient (3%), a single cerebral lesion was observed. 40-days post-procedure, a follow-up MRI cerebral scan showed complete lesion regression.

2022 CLINICAL PUBLICATIONS

Catheter Ablation Induced Phrenic Nerve Palsy by Pulsed Field Ablation—Completely Impossible? A Case Series

Pansera F, Bordignon S, Bologna F, et al.

European Journal Case Report (September, 2022), available here

- Case series on three patients that had FARAWAVE PFA-induced phrenic nerve (PN) injury during PVI. Cases 1 and 3 had PAF without evidence of structural heart disease and case 2 had Pers AF and ischemic cardiomyopathy with preserved ejection fraction.
- Transient right hemidiaphragm palsy was seen during PFA delivery in the RSPV (Cases 1 and 2) and the RIPV (Case 3).
- The palsy lasted < 1 min and was followed by spontaneous full recovery in all cases (Case 1, 40 sec, Cases 2 and 3 lasted a few seconds).
- Transient PN palsy fully recovered rapidly suggesting PN hyperpolarization of neuronal cells or depletion of acetylcholine in the motoric endplate. Further studies are needed to understand the mechanism.

Multi-National Survey on the Methods, Efficacy, and Safety on the Post-Approval Clinical Use of Pulsed Field Ablation (MANIFEST-PF)

Ekanem E, Reddy VY, Schmidt B, et al.

Europace (August, 2022), available here

- The MANIFEST-PF registry was a retrospective survey of 24 centers with 90 operators, 1758 patients that assessed the real-world performance (use case, acute effectiveness, safety) of FARAPULSE.
- Procedure time was 65 min, fluoroscopy time was 13.7 min. There was a 99.9% mean acute PVI success rate.
- There were no esophageal complications reported, no phrenic nerve injury persisting beyond hospital discharge and no reported PV stenosis. There was a 1.6% rate of major complications, a 3.87% rate of minor complications and 0.46% rate of energy specific adverse events.
- Root cause analysis showed that most of the pericardial tamponades and stroke were attributable to catheter workflow and manipulation, independent of energy modality. Complications were plotted on a timeline, and it indicated an improvement in complication rate over time.

Pulsed Field Ablation for Pulmonary Vein Isolation: Real-World Experience and Characterization of the Antral Lesion Size Compared with Cryoballoon Ablation

Blockhaus C, Guelker J, Feyen L, et al.

Journal of Interventional Cardiac Electrophysiology (August, 2022), available here

- Single-center study looking at procedural characteristics and the size of acute PVI antral lesions with high-density mapping in 43 patients treated with PFA compared to 20 patients treated with cryoballoon ablation.
- All patients had 100% acute vein isolation with no early reconnections. The acute antral lesion size of PFA lesions (67.03 ± 12.69%) were significantly larger compared to cryoballoon (57.39 ± 10.91%).
- In the PFA group there was no acute phrenic nerve injury, and 1 (4.34%) patient stroke.

2022 CLINICAL PUBLICATIONS

Validation of a Multipolar Pulsed-Field Ablation Catheter for Endpoint Assessment in Pulmonary Vein Isolation Procedures

Kueffer T, Baldinger S, Servatius H, et al.

EUROPACE (June, 2022), available here

- In 56 patients undergoing PVI with FARAWAVE, the accuracy of FARAWAVE to detect residual PV connections was assessed with high-density mapping.
- Acute PVI was achieved in 100% of PVs.
- The accuracy of the PV assessment with FARAWAVE was 91%. In 14/213 (6.6% of veins), FARAWAVE incorrectly indicated residual PV conduction due to high-output pace-capture.
- Lowering the output to 5 V/1 ms reduced this observation to 0.9% (2/213) and increased the accuracy to 97%.
- FARAWAVE offered reliable endpoint assessment for PVI and lowering the pacing output increased the accuracy from 91% to 97%.
- At a median of 3.2 months, 3/56 (5.4%) underwent a redo procedure. The durable PV isolation rate was 10/12 (83%).

5S Study: Safe and Simple Single Shot Pulmonary Vein Isolation with Pulsed Field Ablation Using Sedation

Schmidt B, Bordignon S, Tohoku S, et al.

Circulation: Arrhythmia and Electrophysiology (June, 2022), available here

- Single-center study looking at the adoption and the process of streamlining the procedure in the first 191 patients treated with FARAPULSE PFA. Electrogram validation was performed with a circular mapping catheter (CMC) in the first 25 patients, cerebral MRI was performed in 53 patients and esophageal endoscopy was performed in 52 patients.
- Electrogram information was 100% congruent between the CMC and FARAWAVE. PVI rate was 100%. No esophageal temperate rise or esophageal thermal injuries were observed. Two minor strokes occurred in the first 25 patients, likely due to air embolism during catheter exchanges.
- After the first 25 patients, the procedure times were significantly reduced from an average of 46 ± 14 min to 38 ± 13 min. During short term follow-up, 9% (17/191) of patients had atrial arrhythmia recurrence.

Characterization of Circumferential Antral Pulmonary Vein Isolation Areas Resulting from Pulsed-Field Catheter Ablation

Bohnen M, Weber R, Minners J, et al.

Europace (June, 2022), available here

- In 40 patients, pre- and post-procedure 20-pole circular mapping catheter voltage mapping was done to evaluate PV isolation and area of isolation.
- Isolation gaps were located most frequently in the anterior antral PV segments of the left PVs.
- Additional areas of isolation beyond the antral PV segments were found on the posterior wall and roof regions.

2022 CLINICAL PUBLICATIONS

First Experience with Pulsed Field Ablation as Routine Treatment for Paroxysmal Atrial Fibrillation
Füting A, Reinsch N, Höwel D, et al.

Europace (May, 2022), available here

- Single-center 30 patient study looking at phrenic nerve injury and high-density mapping pre-and post-ablation.
- Acute PVI rate was 100%, the median procedure time was 116 min and the FARAWAVE catheter dwell time was 29 min. There was no esophageal or phrenic nerve injury.
- 97% of patients were in sinus rhythm after 90 days.

Troponin Release After Pulmonary Vein Isolation Using Pulsed Field Ablation Compared to Radiofrequency and Cryoballoon Ablation
Krisai P, Knecht S, Badertscher P, et al.

Heart Rhythm (May, 2022), available here

Troponin T is a measure of myocardial cell death. Troponin T was measured in 60 patients one day before and the morning after PVI ablation with FARAWAVE, radiofrequency or cryoballoon ablation. No additional lesion sets were performed.

- Post-procedure Troponin T levels with PFA were 1.6x and 1.9x higher vs. RF and Cryo, respectively with no significant difference between the RF and cryo groups.

Pulsed Field Ablation Combined with Ultra-High-Density Mapping in Patients Undergoing Catheter Ablation for Atrial Fibrillation: Practical and Electrophysiological Considerations
Gunawardene M, Schaeffer B, Jularic M, et al.

Journal of Cardiovascular Electrophysiology (March, 2022), available here

20 consecutive patients underwent PVI with FARAWAVE. Additional ablations were performed off-label in a sub-set of patients. PFA lesion size and decrease in voltage were assessed with high-density voltage mapping.

- High density mapping showed PV reconnection in 5 cases (6.25%). Gaps were located at the anterior-superior PV ostia and were successfully closed with additional PFA. Voltage was significantly decreased following PFA with almost no complex electrogram fractionation at the lesion border zones.
- High-density mapping for FARAWAVE PFA lesion showed wide, antral, circumferential lesion with significantly decreased atrial tissue voltage and little evidence of fraction in the lesion border zones.

2021 CLINICAL PUBLICATIONS

Does Pulsed Field Ablation Regress Over Time? A Quantitative Temporal Analysis of Pulmonary Vein Isolation

Kawamura I, Neuzil P, Shivamurthy P, et al.

Heart Rhythm (June, 2021), available here

- Patients with PAF underwent PVI with FARAWAVE. A comparison of voltage maps immediately after PFA and at a median of 84 days (interquartile range 69–90 days) later revealed that there was no significant difference in either the left and right-sided PV antral isolation areas or nonablated posterior wall area.
- The distances between low-voltage edges on the posterior wall were also not significantly different between the 2 time points.
- The level of PV antral isolation after PFA with FARAWAVE persisted without regression.

Pulsed Field Ablation Prevents Chronic Atrial Fibrotic Changes and Restrictive Mechanics After Catheter Ablation for Atrial Fibrillation

Nakatani Y, Sridi-Cheniti S, Cheniti G, et al.

Europace (May, 2021), available here

- Cardiac magnetic resonance was performed pre-ablation, acutely (< 3 h), and 3 months post-ablation in 41 patients with PAF undergoing PVI with PFA (n = 18) or thermal ablation (n = 23, 16 radiofrequency ablations, 7 cryoballoon ablations).
- Tissue changes were more homogeneous after PFA than after thermal ablation, with no sign of microvascular damage or intramural hemorrhage. In the chronic stage, the majority of acute LGE had disappeared after PFA, whereas most LGE persisted after thermal ablation.
- The maximum strain on PV antra, the LA expansion index, and LA active emptying fraction declined acutely after both PFA and thermal ablation but recovered at the chronic stage only with PFA.
- In this study, PFA induced large acute LGE lesions which mostly disappeared in the chronic stage, suggesting a reparative process involving less chronic fibrosis.

Pulsed Field Ablation of Paroxysmal Atrial Fibrillation: 1-Year Outcomes of IMPULSE, PEFCAT, and PEFCAT II

Reddy VY, Dukkipati SR, Neuzil P, et al.

JACC-EP (May, 2021), available here

- In 3 multicenter studies (IMPULSE, PEFCAT and PEFCAT II), PAF patients underwent PVI using a basket and flower PFA catheter.
- Invasive remapping was performed at 2 to 3 months, and reconnected PVs were reisolated with PFA or radiofrequency ablation. After a 90-day blanking period, arrhythmia recurrence was assessed over 1-year follow-up.
- In 121 patients, acute PVI was achieved in 100% of PVs with PFA alone.
- PV remapping, performed in 110 patients at 93.0 ± 30.1 days, demonstrated durable PVI in 84.8% of PVs (64.5% of patients), and 96.0% of PVs (84.1% of patients) treated with the optimized biphasic energy PFA waveform.
- The 1-year Kaplan-Meier estimates for freedom from any atrial arrhythmia for the entire cohort and for the optimized biphasic energy PFA waveform cohort were 78.5 ± 3.8% and 84.5 ± 5.4%, respectively.

2021 CLINICAL PUBLICATIONS

How Does the Level of Pulmonary Venous Isolation Compare between Pulsed Field Ablation and Thermal Energy Ablation (Radiofrequency, Cryo, or Laser)?

Kawamura I, Neuzil P, Shivamurthy P, et al.

Europace (May, 2021), available here

- In a clinical trial (NCT03714178), PAF patients under-went PVI with FARAWAVE using a biphasic waveform, and after 75 days, detailed voltage maps were created.
- Comparative voltage mapping data were retrospectively collected from consecutive PAF patients who (i) underwent PVI using thermal energy, (ii) underwent re-ablation for recurrence, and (iii) had durably isolated PVs. The left and right PV antral isolation areas and non-ablated posterior wall were quantified.
- There was no significant difference between the PFA and thermal ablation cohorts in either the left- and right-sided PV isolation areas, or the non-ablated posterior wall area.

Pulsed Field Ablation Selectively Spares the Oesophagus During Pulmonary Vein Isolation for Atrial Fibrillation

Cochet H, Nakatani Y, Sridi-Cheniti S, et al.

Europace (February, 2021), available here

- Cardiac magnetic resonance (CMR) imaging was performed before, acutely (< 3 h) and 3 months post-ablation in 41 PAF patients undergoing PVI with PFA (N = 18, FARAPULSE) or thermal methods (N = 23, 16 radiofrequency, 7 cryoballoon).
- Esophageal and aortic injuries were assessed by using late gadolinium-enhanced (LGE) imaging. Phrenic nerve injuries were assessed from diaphragmatic motion on intra-procedural fluoroscopy.
- Acutely, thermal methods induced high rates of esophageal lesions (43%), all observed in patients showing direct contact between the esophagus and the ablation sites.
- Esophageal lesions were observed in no patient ablated with PFA (0%, P < 0.001 vs. thermal methods), despite similar rates of direct contact between the esophagus and the ablation sites (P = 0.41).
- Acute lesions were detected on CMR on the descending aorta in 10/23 (43%) after thermal ablation, and in 6/18 (33%) after PFA (P = 0.52). CMR at 3 months showed a complete resolution of esophageal and aortic LGE in all patients.

Pulsed Field Ablation: A Promise That Came True

Ante A, Breskovic T, Sikiric I.

Current Opinion in Cardiology (January, 2021), available here

- Pulsed field ablation is a nonthermal ablative modality that uses short living, strong electrical field created around catheter to create microscopic pores in cell membranes (electroporation). When adequately dosed/ configured it shows a preference for myocardial tissue necrosis.
- First in human series using pulsed field ablation for atrial fibrillation ablation have been completed and data published for several platforms. Acute safety outcomes are similar across the platforms with a low complication rate for complications typically reported for thermal ablation methods (esophageal injury, pulmonary vein stenosis, phrenic nerve palsy).
- Promising acute data on pulmonary vein isolation had been corroborated with satisfactory 1-year clinical follow-up for a single platform (i.e., FARAPULSE), whereas reports are pending for the rest. Research efforts are being expanded to a development of focal catheters, and therefore, pulsed field ablation application for ventricular arrhythmias.

2020 CLINICAL PUBLICATIONS

Pulsed Field Ablation in Patients with Persistent Atrial Fibrillation
Reddy VY, Anic A, Koruth J, et al.

JACC (September, 2020), available here

- PersAFOne was a single-arm study evaluating biphasic, bipolar PFA with FARAWAVE for PVI and LAPW ablation to assess the safety and lesion durability of pulsed field ablation (PFA) for both PVI and LAPW ablation in persistent AF.
- In 25 patients, acute PVI (96 of 96 pulmonary veins) were 100% acutely successful with the FARAWAVE catheter. Using the focal PFA catheter, acute cavotricuspid isthmus block was achieved in 13 of 13 patients.
- Post-procedure EGD and repeat cardiac computed tomography revealed no mucosal lesions or PV narrowing, respectively.
- Invasive remapping at 2 to 3 months demonstrated durable isolation (defined by entrance block) in 82 of 85 PVs (96%) and 21 of 21 LAPWs (100%) treated with the pentaspline catheter.

Ostial Dimensional Changes After Pulmonary Vein Isolation: Pulsed Field Ablation vs. Radiofrequency Ablation
Kuroki K, Whang W, Eggert C, et al.

Heart Rhythm (May, 2020), available here

- Data were analyzed from 4 PAF ablation trials using either PFA or RFA.
- Baseline and 3-month cardiac computed tomography scans were reconstructed into 3-dimensional images, and the long and short axes of the PV ostia were quantitatively and qualitatively assessed in a randomized blinded manner.
- PV ostial diameters decreased significantly less with PFA than with RFA (% change; long axis: 0.9% ± 8.5% vs. −11.9% ± 16.3%; $P < .001$ and short axis: 3.4% ± 12.7% vs. −12.9% ± 18.5%; $P < .001$).
- PV narrowing/stenosis was present in 0% and 0% vs. 12.0% and 32.5% of PVs and patients who underwent PFA and RFA, respectively.
- In this study, unlike after RFA, the incidence and severity of PV narrowing/stenosis after PV isolation was virtually eliminated with PFA.

2019 CLINICAL PUBLICATIONS

Pulsed Field Ablation for Pulmonary Vein Isolation in Atrial Fibrillation
Reddy VY, Neuzil P, Koruth JS, et al.

JACC (July, 2019), available here

- Two trials were conducted to determine whether PFA allows durable pulmonary vein (PV) isolation without damage to collateral structures, in patients with PAF.
- Ablation was performed using proprietary bipolar PFA waveforms: either monophasic with general anesthesia and paralytics to minimize muscle contraction, or biphasic with sedation because there was minimal muscular stimulation. No esophageal protection strategy was used. Invasive electrophysiological mapping was repeated after 3 months to assess the durability of PV isolation.
- 81 patients, all PVs were acutely isolated by monophasic (n = 15) or biphasic (n = 66) PFA. With successive waveform refinement, durability at 3 months improved from 18% to 100% of patients with all PVs isolated. Beyond 1 procedure-related pericardial tamponade no additional primary adverse events over the 120-day median follow-up, including: stroke, phrenic nerve injury, PV stenosis, and esophageal injury.

2018 CLINICAL PUBLICATIONS

Ablation of Atrial Fibrillation with Pulsed Electric Fields
Reddy VY, Koruth J, et al.

JACC-EP (April, 2018), available here

- The first acute clinical experience of AF ablation with PFA, both epicardial box lesions during cardiac surgery, and catheter-based PVI.
- PFA was performed using a custom over-the-wire endocardial catheter for percutaneous transseptal PV isolation, and a linear catheter for encircling the PVs and posterior left atrium during concomitant cardiac surgery.
- Catheter PV ablation was successful in 15 patients (100%) 57 PVs Using 3.26 lesions/PV and surgical box lesions were successful in 6 of 7 patients (86%) 2 lesions/patient. No complications.

2023 PRECLINICAL PUBLICATIONS

Efficacy of Pulsed Field vs Radiofrequency for the Reablation of Chronic Radiofrequency Ablation Substrate: Redo Pulsed Field Ablation
Younis A, Buck E, Santangeli P, et al.

JACC: Clinical Electrophysiology (November, 2023), available here

- PFA is highly efficient for ablation following prior RFA, which may be beneficial in patients presenting for redo procedures.
- PFA resulted in lesions in the ventricle that were deeper than RFA when ablating over chronic superficial RFA lesions.

Electrophysiology, Pathology, and Imaging of Pulsed Field Ablation of Scarred and Healthy Ventricles in Swine
Kawamura I, Reddy V, Santos-Gallego C, et al.

Circulation: Arrhythmia and Electrophysiology (January, 2023), available here

- 6 swine were infarcted to assess penetration of scar, risk of arrhythmias and lesion imaging evaluation.
- FARAPULSE PFA successfully penetrated scar without significant differences in the lesion depth of infarcted tissue (5.9 ± 1.0 mm) vs healthy (5.7 ± 1.3 mm) myocardium.
- In ungated QRS PFA applications, sustained ventricular arrhythmias requiring defibrillation occurred in 4/187 (2.1%) applications with zero occurring during gated applications.
- Dark-blood late-gadolinium-enhanced sequences allowed for improved endocardial border detection.

2022 PRECLINICAL PUBLICATIONS

Effect of Epicardial Pulsed Field Ablation Directly on Coronary Arteries
Higuchi S, Im S, Stillson C, et al.

JACC: Clinical Electrophysiology (December, 2022), available here

- 4 swine, FARAWAVE lesions were delivered directly to the left anterior descending artery, left circumflex artery or normal myocardium.
- Angiography was performed to quantify the degree of coronary artery narrowing and histology was performed at 4 and 8 weeks.
- Acute luminal narrowing immediately after PFA was 47% which gradually resolved over 30 minutes.
- Epicardial lesions had a median depth of 4.1 mm and 87.5% of the arteries had minimal to mild stenosis via neointimal hyperplasia.

Pulsed Field Ablation of Left Ventricular Myocardium in a Swine Infarct Model
Im S, Higuchi S, Lee A, et al.

JACC: Clinical Electrophysiology (June, 2022), available here

- 10 swine were infarcted to evaluate how PFA and RF perform in areas of myocardial scar.
- In myocardial scar, lesion depth was not different between the FAWAVAVE or the FOCAL PFA catheter.
- In myocardial scar, lesion depth was significantly greater for PFA vs. RF.
- In a pre-clinical animal model, unlike RF, FARAPULSE PFA was able to effectively ablate surviving islands of myocardium in infarct-related ventricular substrate.

2020 PRECLINICAL PUBLICATIONS

Pulsed Field Ablation vs Radiofrequency Ablation: Esophageal Effects in a Novel Preclinical Model
Koruth JS, Kuroki K, Kawamura I, et al.

Circulation: Arrhythmia and Electrophysiology (January, 2020), available here

- A novel preclinical model was created to nonsurgical assess the response to esophageal injury. This was accomplished by delivering the energy source from within the inferior vena cava, against the esophagus (which was purposefully mechanically deviated towards the IVC).
- Biphasic pulsed field ablation induced no chronic histopathologic esophageal changes, whereas radiofrequency catheter ablation demonstrated a spectrum of esophageal lesions including esophageal ulcers, abscess, and fistula.

2019 PRECLINICAL PUBLICATIONS

Preclinical Evaluation of Pulsed Field Ablation: Electrophysiological and Histological Assessment of Thoracic Vein Isolation
Koruth JS, Kuroki K, Iwasawa J, et al.

Circulation: Arrhythmia and Electrophysiology (December, 2019), available here

- In this study, the safety, efficacy, and durability of achieving catheter-based electrical isolation of PVI using optimized monophasic and biphasic PFA waveforms and describe procedural and histological characteristics of PFA in swine atrial tissue.
- Both waveforms created confluent myocardial lesions that demonstrated a myocardial-specific ablative effect.
- Biphasic PFA was more durable than monophasic PFA and radiofrequency ablation lesions.

Endocardial Ventricular Pulsed Field Ablation: A Proof-of-Concept Preclinical Evaluation
Koruth JS, Kuroki K, Iwasawa J, et al.

EP Europace (December, 2019), available here

- Assessment of safety and feasibility of FARAPULSE PFA in swine ventricles with a prototype steerable endocardial catheter.
- Gross measurements, available for 28 of 30 ablation sites, revealed average lesion dimensions to be 6.5 ± 1.7 mm deep and 22.6 ± 4.1 mm, with a maximum depth and width of 9.4 mm and 28.6 mm respectively. In PFA lesions, fibrous tissue homogeneously replaced myocytes. When present in the lesion zone, nerve fascicles and vasculature were preserved.

FARAWAVE™ Pulsed Field Ablation Catheter

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

INTENDED USE The FARAPULSE Pulsed Field Ablation (PFA) System is intended for the isolation of the pulmonary veins in the treatment of paroxysmal atrial fibrillation by rendering targeted cardiac tissue electrically non-conductive to prevent cardiac arrhythmia initiation or maintenance.

INDICATIONS FOR USE The FARAWAVE Catheter is indicated for the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

INTENDED PATIENT POPULATION The FARAPULSE PFA System is intended for adult patients who are age 18 or older who have drug-refractory, recurrent, symptomatic PAF.

CONTRAINDICATIONS The FARAWAVE Catheter is contraindicated for use: in patients with active systemic infection; in patients with a mechanical prosthetic heart valve through which the catheter must pass; in patients with conditions where insertion into or manipulation in the cardiac chambers is unsafe as these conditions (e.g., presence of intracardiac thrombus or myxoma, history of recent cardiac surgery with atriotomy, etc.) may increase the risk of systemic embolism or cardiac perforation; in patients with a bleeding disorder, or who are unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation; in patients who have vena cava embolic protection filter devices and/or known femoral thrombus who require catheter insertion from the femoral approach; in patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe, such as but not limited to, a recent previous cardiac surgery (e.g., ventriculotomy or atriotomy, Coronary Artery Bypass Graft [CABG], PTCA/PCI/coronary stent procedure/unstable angina) and/or in patients with congenital heart disease where the underlying abnormality increases the risk of the ablation (e.g. severe rotational anomalies of the heart or great vessels); via transseptal approach in patients with an intra-atrial baffle or a foramen ovale patch.

WARNINGS If the visibility of the EP catheter is compromised for any reason, the user should stop and not resume ablation therapy until catheter visibility is established in order to prevent patient injuries such as perforation, heart block and injury to adjacent structures. Cardiac mapping and ablation procedures should be performed only by physicians thoroughly trained in invasive cardiology, in the techniques of mapping and ablation, and in the specific approach to be used, in a fully-equipped electrophysiology lab. Device specific physician in-service training is made available by the manufacturer. Administer appropriate levels of peri-procedural anticoagulation therapy for patients undergoing left-sided and transseptal cardiac procedures. There is an increased risk of thromboemboli if appropriate anticoagulation levels are not maintained while the transseptal sheath and/or catheter is in the left side of the heart. Administer anticoagulation therapy during and post procedure according to the institution's standards to minimize bleeding and thrombotic complications. Carefully read all equipment and ancillary device instructions required for the procedure prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient complications. Do not use the device if past the "Use By" date on the device package. Do not use if sterile barrier is damaged or unintentionally opened before use, as use of non-sterile devices may result in patient injury. Before using, inspect the FARAWAVE Catheter for any defects or physical damage, including electrical insulation on the cables and the catheter shaft that, if used, may cause patient and/or user injury. Do not use defective or damaged devices. Replace damaged equipment if necessary. No modification of this equipment is allowed. Electromagnetic Interference (EMI) from any source during normal operation may adversely affect the visualization and tracking of the catheter during the procedure, which can cause patient injuries such as perforation, heart block and injury to adjacent structures. Use of the FARAWAVE Catheter with generators other than a compatible BSC PFA Generator can lead to unexpected energy delivery resulting in either insufficient ablation treatment or over-delivery of energy leading to possible patient hazardous events such as thrombus formation, tissue damage, etc. Patients undergoing ablation are at risk for complete AV block which requires the implantation of a temporary and/or permanent pacemaker. When the catheter is in the patient, neither the patient nor the catheter connector should be allowed to come in contact with grounded metal surfaces to minimize the potential for electrical shock. Ensure that the cable/catheter connection remains dry throughout the procedure in order to prevent electric shock or other patient injuries as well as to prevent loss of device function. Fibrin may accumulate in or on the sheath/catheter assembly during the procedure. Aspirate when removing the catheter. In the presence of anticoagulation, there may be an increased risk of bleeding from all causes. Electrical recording or stimulation equipment must be isolated. Current leakage from any electrical equipment that is connected to the patient must not exceed 10 microamps for intracardiac electrodes. Care must be taken to ensure that any equipment used in connection with the FARAWAVE Catheter be type CF, be defibrillation proof, meet IEC 60601-1 electrical safety requirements, and comply with all local regulatory requirements for specified intended use to reduce the potential risk of inadvertent electrical shock. Do not directly touch the patient when ablation energy is being delivered to prevent the risk of electric shock. Stimulation of cardiac tissues caused by pacing stimulus and/or ablation energy may lead to inadvertent induction of arrhythmias. These arrhythmias may require defibrillation that could also result in skin burns. Warnings for patients with implantable pacemakers (PPMs) and Implantable Cardioverter Defibrillators (ICDs): PPMs, ICDs, and leads can be adversely affected by ablation energy. It is important to refer to the device manufacturer's instruction for use prior to performing ablation procedures. Do not apply ablation energy directly to a lead or to tissue immediately in contact with a lead because it could potentially damage the lead or lead function. Temporarily reprogram the pacemaker or defibrillator per the manufacturer guidelines during ablation. The device could be damaged by the ablation procedure. Interrogate the device fully after the ablation per the manufacturer guidelines and reprogram to preoperative sensing and pacing parameters. Program the ICD Tachy therapy to "Off" to prevent inappropriate shock and/or possible damage to the device from the ablation procedure. Remember to turn Tachy Therapy to "On" once ablation is complete. Have temporary external sources of pacing and defibrillation available. Perform a complete analysis of the implanted device function after ablation. Fluoroscopic or appropriate imaging guidance and care must be taken during catheter advancement, manipulation, and withdrawal to avoid lead dislodgement. Monitor pre- and post-measurements for sensing and pacing thresholds and impedances to determine the integrity of the lead-patient function. Ablation in contact with any other electrodes alters the function of the catheter and can lead to embolism. At no time should a FARAWAVE Catheter be advanced, withdrawn, rotated, deployed or undeployed when resistance is felt, without determining the cause. Valve damage, vascular and/or cardiac perforation is a risk with any intracardiac catheter. Catheter entrapment within the heart or blood vessels is a possible complication of cardiac ablation procedures. The potential for catheter entrapment may be increased when the catheter is over torqued and/or positioned in the chordae tendineae. The occurrence of this complication may necessitate surgical intervention and/or repair of injured tissue and/or valve damage. Do not use the FARAWAVE Catheter in the proximity of Magnetic Resonance Imaging (MRI) equipment because the MRI equipment may adversely impact the function of a PFA Generator and the ablation system may adversely impact the image quality. This can also lead to loss of visibility during ablation which can cause patient injuries such as perforation, heart block and injury to adjacent structures. Catheter ablation procedures present the potential for significant radiation exposure, which can result in acute radiation injury as well as an increased risk for somatic and genetic effects, to both patients and laboratory staff due to the radiation beam intensity and duration of the fluoroscopic imaging. Catheter ablation should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure, and steps have been taken to minimize this exposure. Due to radiation exposure during catheter ablation, the safety and effectiveness of this device has not yet been established in pregnant and/or nursing women and pediatric patients. There are no data to support the safety and effectiveness of this device in the pediatric population. Prior to the procedure, always identify the patient's risk of volume overload. Monitor the patient's fluid balance throughout the procedure and after the procedure to avoid fluid volume overload. Some patients may have factors that reduce their ability to handle the volume overload, making them susceptible to developing pulmonary edema or heart failure during or after the procedure. Patients with congestive heart failure or renal insufficiency, and the elderly are particularly susceptible. Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter that may result in embolism. Excessive curves or kinking of the catheter may damage internal wires and components, including the flush lumen. This damage may affect mechanical and electrical performance leading to patient injury. Do not attempt to bend, kink, or shape the patient-contact portions or flush lumen of the FARAWAVE Catheter. Doing so could cause electrical or mechanical catheter failure resulting in patient injury. Kinking of the flush lumen may compromise flow through the device leading to potential thrombus formation and embolism. Use both fluoroscopy, or other visualization techniques such as echocardiography, and electrograms to monitor the advancement of the catheter to the area of the endocardium under investigation to avoid conduction pathway injury, cardiac perforation or tamponade. The FARAWAVE Catheter tip and guidewire move forward during device undeployment. Device deployment and undeployment should be visualized using fluoroscopy. Failure to do so may result in catheter damage and/or patient injury. Do not deliver ablation energy with the catheter outside the target site. Ablation Generators can deliver significant electrical energy and may cause patient injury such as arrhythmia and heart block. Always verify that the tubing set, catheter, sheath and all connections have been properly cleared of air prior to inserting the catheter into the vasculature. Air entrapped in the tubing, catheter or sheath can cause potential injury or cardiac arrest. The operator is responsible for removing all air from the system. Patients undergoing left-sided ablation procedures should be closely monitored during and post procedure for clinical manifestations of infarction, pulmonary vein injury, nerve damage, and/or embolism. Patients undergoing an ablation procedure have the potential for greater anticoagulation and therefore Activated Coagulation Time (ACT) should be monitored closely due to the increased risk for bleeding/ hemorrhage and/or embolism. Patients with hemodynamic instability or cardiogenic shock are at increased risk for life-threatening adverse events and ablation must be done with extreme caution. The FARAWAVE Catheter is not intended to be used for internal cardioversion. Doing so may result in perforation, arrhythmias, embolism, thrombus and/or patient death. Inspect irrigation saline for air bubbles and remove any air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause embolism. If there is uncertainty regarding the patient's anticoagulation status or rhythm prior to the procedure, there should be a low threshold to perform a Transesophageal Echocardiogram (TEE) prior to the procedure to confirm absence of mural thrombus and/or thrombus in the left atrial appendage. Guiding catheters and/or long introducer sheaths present the potential for thromboembolic events. Pre-flush and maintain lumen patency with heparinized intravenous infusion. Do not wipe this catheter with organic solvents such as alcohol or immerse the handle and/or cable connector in fluids. This may result in electrical or mechanical catheter failures. It may also result in an allergic reaction from the patient. Pre-procedural anticoagulation therapy is at the discretion of the physician. However, patients with a history of thromboembolic events may require therapeutic anticoagulation therapy, pre-, during and post-ablation to reduce the incidence of major complications. Peri-procedural anticoagulation therapy is recommended for patients undergoing left-sided and transseptal cardiac procedures and should be considered for selected patients undergoing right-sided procedures. The safety and/or efficacy of epicardial use of the FARAWAVE Catheter has not been evaluated in a clinical trial. Care should be used during multiple sheath/catheter exchanges through the transseptal puncture to avoid causing a residual atrial septal defect that would require repair. Do not leave the FARAWAVE Catheter in the patient for more than four (4) hours. Failure to remove the device before four hours after first insertion could result in formation of thrombus with attendant stroke risks. Use of the FARAWAVE Catheter with delivery devices other than the FARADRIVE Sheath can result in poor access to endocardial locations, inefficient ablation delivery and inadequate procedural outcomes. Cardiac ablation has the potential of causing unintended myocardial injury. Clinical indications of myocardial ischemia should be closely monitored during the procedure (e.g., ECG changes). The FARAWAVE Catheter has not been studied clinically in the mitral isthmus or cavotricuspid isthmus areas. Ablations in areas adjacent to coronary arteries may lead to coronary artery spasm and/or injury, and the resulting myocardial injury can be fatal. Ensure that the guidewire is properly inserted into the catheter for adequate support during use. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire fully inserted, at or past the FARAWAVE Catheter tip. Failure to do so may result in catheter damage and/or patient injury. When positioning on cardiac structures, the guidewire should be retracted to prevent cardiac perforation or tissue damage. Ensure the tip of the device is not against tissue prior to advancing or retracting the guidewire to prevent cardiac perforation or tissue damage. The risk of igniting flammable gases or other materials is potential outcome of ablation procedures. Precautions must be taken to restrict flammable materials from the electrosurgical suite. Take care when manipulating the guidewire to prevent cardiac or vessel trauma. To avoid cardiac damage, do not use excessive force when manipulating the catheter in vivo. Specifically, use caution when maneuvering while undeployed. Note that mapping and recording data do not require the use of force on the tissue. Minimize catheter exchanges and always advance and withdraw components through the valve slowly to minimize the vacuum created during withdrawal and to reduce the risk of air embolism. Follow advancement or withdrawal of catheters with appropriate aspiration and flushing according to institutional standards or consensus statements. Instruct users with co-implanted devices to refer to ancillary device labeling as well as the manufacturer of the ancillary device for recommended compatibility and settings. Use caution when advancing, retracting or otherwise manipulating system components to avoid damaging tissue or vessels or interfering with previously implanted medical devices. When advancing or undeploying the FARAWAVE catheter, do not retract the guidewire simultaneously. If resistance is felt during retraction of the guidewire, do not continue to retract the guidewire until cause of resistance is determined as this may result in cardiac trauma. If resistance is felt, it may be necessary to advance guidewire under imaging guidance before continuing to retract. Ensure that the guidewire is not contacting ablation electrodes prior to starting ablation to prevent inappropriate energy delivery. Always un-deploy the catheter and withdraw the catheter into the sheath before removing the catheter from the Left Atrium (LA). Deploying the catheter in the septal puncture site or crossing the septum while the catheter is unsheathed or deployed may cause serious atrial septal defects or other cardiac and vessel trauma. Use visualization (such as fluoroscopy) to verify undeployment. Avoid deploying the catheter in constrained parts of the anatomy to prevent cardiac trauma or damage to the device. Prior to starting ablation verify that the catheter has been positioned and deployed correctly to prevent inappropriate application of ablation energy. Do not deploy the catheter while the distal end is inside the sheath as it could lead to catheter damage which may result in patient harm. PV potentials recorded from the electrodes on the FARAWAVE Catheter will likely show a significant reduction in amplitude after the first application of PFA. This should not be used as an indication that no further ablation is necessary. The nominal dose of PFA should be delivered in accordance to the parameters listed in the Operational Instructions section, regardless of absence of PV signal. Potential biohazard after use. Handle and dispose of in accordance with applicable regulations.

PRECAUTIONS Do not attempt to use with devices, including guidewires, larger than the delivery lumen diameter specified on the package label. Care must be taken to ensure all luer fittings are secure to prevent leaking. It is essential that a cardiac defibrillator with paddles connected is readily available in the procedure room for use if Ventricular Fibrillation is noted subsequent to ablation. There is limited data to support the safety and effectiveness of this device in patients older than 75 years. Catheter deployment and undeployment should occur under imaging guidance. Catheter may be fully deployed or undeployed even though the slider switch is not fully engaged. Failure to monitor deployment may result in catheter damage and need for catheter exchange. Device deployment friction is increased when attempting to deploy the device when the catheter shaft is bent. FARAWAVE Catheter deployment should always occur with the catheter shaft as straight as possible. Do not apply excessive force to the deployment mechanism when deploying the catheter as doing so may damage the catheter. Avoid allowing the distal end of the catheter to be put into an acute bend, particularly when advancing the catheter beyond the sheath or deploying the catheter. A catheter exchange may be necessary if the catheter deploys improperly.

ADVERSE EVENTS Potential adverse events associated with use of the FARAWAVE Catheter includes, but are not limited to: • Pain or discomfort, for example: Angina, Chest pain, Non-cardiovascular pain, • Cardiac arrest, • Death, • Electric shock, • Hypotension, • Infection/inflammation/exposure to biohazardous material, • Edema/heart failure/pleural effusion, • Renal failure/insufficiency, • Respiratory distress/insufficiency/dyspnea • Arrhythmia (new or exacerbated), Conduction pathway injury (heart block, nodal injury, etc.), • Nerve injury, for example: Phrenic nerve injury, Vagal nerve injury, • Gastrointestinal disorders, • Vessel trauma, including: Perforation, Dissection, Coronary artery injury, Vasospasm, Occlusion, Hemothorax, • Cardiac trauma, for example: Cardiac perforation/cardiac tamponade/pericardial effusion, Valvular damage, Stiff left atrial syndrome, • Injury related to tissue damage and/or adjacent structures, for example: Esophageal injury, Pulmonary injury, Catheter entrapment, Physical trauma, • Fistula, for example: Atrio-esophageal fistula, Bronchopericardial fistula, • PV stenosis and its symptoms, for example: Cough, Shortness of breath, fatigue, Hemoptysis, • Surgical and access complications, for example: Hematoma/seroma, AV fistula, Bleeding, Pseudoaneurysm, Pneumothorax, Residual atrial septal defect, • Thrombus/thrombosis, • Muscle spasm, • Injury due to embolism/thromboembolism/air embolism/foreign body embolism, Cerebrovascular Accident (CVA)/stroke, Transient Ischemic Attack (TIA), Myocardial infarction, Neurological impairment and its symptoms, for example: Cognitive changes, visual disturbances, headache, motor impairment, sensory impairment, and speech impairment, Pulmonary embolism, Asymptomatic cerebral embolism, • Hemolysis, • Procedural related side effects, for example: Allergic reaction (including anaphylaxis), Genitourinary complication, Side effects related to medication or anesthesia, Radiation injury/tissue burn, Vasovagal response, Fluid volume overload. The potential adverse events may be related to the ablation catheter(s) and/or the interventional procedure. The severity and/or the frequency of these potential adverse events may vary and may result in prolonged procedure time and/or additional medical and/or surgical intervention, implantation of a permanent device such as a pacemaker, and in rare cases, may result in death. 97173260 (Rev. A)

FARADRIVE™ Steerable Sheath

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

INTENDED USE / INDICATIONS FOR USE The FARADRIVE Sheath is intended for percutaneous catheter introduction into the vasculature and into the chambers of the heart, including the left side of the heart through the interatrial septum.

CONTRAINDICATIONS Use of the FARADRIVE Sheath is contraindicated for use: in patients with active systemic infection; in patients with conditions where insertion into or manipulation in the cardiac chambers is unsafe as these conditions (e.g., presence of intracardiac thrombus or myxoma, history of recent cardiac surgery with atriotomy, etc.) may increase the risk of systemic embolism or cardiac perforation; in patients with a mechanical prosthetic heart valve through which the catheter must pass; via transseptal approach in patients with an intra-atrial baffle or a foramen ovale patch; in patients with a bleeding disorder, or who are unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation; in patients who have vena cava embolic protection filter devices and/or known femoral thrombus who require catheter insertion from the femoral approach; in patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe, such as but not limited to, a recent previous cardiac surgery (e.g., ventriculotomy or atriotomy, Coronary Artery Bypass Graft [CABG], PTCA/PCI/coronary stent procedure/unstable angina) and/or in patients with congenital heart disease where the underlying abnormality increases the risk of the ablation (e.g. severe rotational anomalies of the heart or great vessels).

WARNINGS Cardiac mapping and ablation procedures should be performed only by physicians thoroughly trained in invasive cardiology, in the techniques of mapping and ablation, and in the specific approach to be used, in a fully-equipped electrophysiology lab. Device specific physician in-service training is made available by the manufacturer. Do not attempt to use the FARADRIVE Sheath prior to reading these instructions for use. All instructions should be understood and followed carefully. Observe all contraindications, warnings, and precautions noted in this user manual. Failure to do so may result in patient complications. Carefully read all equipment and ancillary device instructions required for the procedure prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient complications. Do not use the device if past the "Use By" date on the device package. Do not use if sterile barrier is damaged or unintentionally opened before use, as use of non-sterile devices may result in patient injury. Before using, inspect the FARADRIVE Sheath for any defects or physical damage that may cause patient and/or user injury if the sheath is used. Do not use defective or damaged devices. Replace damaged device(s) if necessary. Administer appropriate levels of peri-procedural anticoagulation therapy for patients undergoing left-sided and transseptal cardiac procedures and for selected patients undergoing right-sided procedures. There is an increased risk of thromboemboli if appropriate anticoagulation levels are not maintained while the transseptal sheath and/or catheter is in the left side of the heart. Administer anticoagulation therapy during and postprocedure according to the institution's standards to minimize bleeding and thrombotic complications. If there is uncertainty regarding the patient's anticoagulation status or rhythm prior to the procedure, there should be a low threshold to perform a Transesophageal Echocardiogram (TEE) prior to the procedure to confirm absence of mural thrombus and/or thrombus in the left atrial appendage. Prior to inserting the device into the patient, pre-assemble the FARADRIVE Sheath and Dilator to remove residual air; failure to do so may result in air embolus. To minimize the risk of air embolism, observe and remove any air prior to introducing the sheath and during the procedure. Infusion through the flush line should only occur after all air has been removed. Always maintain a constant sterile, heparinized saline infusion to prevent coagulation within the sheath which may result in embolism. If constant infusion is interrupted, aspirate and flush the sheath with heparinized saline to minimize the potential for thrombus formation that may result in patient injury. Prevent any obstruction of the flush line to ensure effective heparinized saline flush. Introducing catheters and sheaths into the circulatory system entails the risk of air emboli. Air embolism can occlude blood vessels resulting in serious consequences such as tissue infarction and/or end organ failure. Always advance/withdraw the FARADRIVE Sheath slowly. Always advance/withdraw catheters slowly through the FARADRIVE Sheath valve and minimize catheter exchanges. At no time should components be advanced, retracted, or otherwise manipulated when resistance is met without first determining the cause. Use fluoroscopy or additional imaging modalities to assess system integrity and catheter position as needed and take remedial action as necessary. Prior to the procedure, always identify the patient's risk of volume overload. Monitor the patient's fluid balance throughout the procedure and after the procedure to avoid fluid volume overload. Some patients may have factors that reduce their ability to handle the volume overload, making them susceptible to developing pulmonary edema or heart failure during or after the procedure. Patients with congestive heart failure or renal insufficiency, and the elderly are particularly susceptible. Advancement or withdrawal of catheters should be followed with appropriate aspiration and flushing. Following insertion of catheter into the hemostatic valve aspirate via the side-port until air bubbles are no longer seen to prevent air embolism from occurring. Do not use with cardiovascular catheters less than 7F, as an air embolism or patient injury can occur. To minimize the risk of air embolism, do not flush or aspirate the FARADRIVE Sheath with the dilator present as doing so may damage the valve leading to patient injury. Monitor the spontaneously-breathing patient for risk factors which may lead to negative left atrial pressures. Negative left atrial pressure may increase the risk of air ingress through the hemostasis valve particularly during insertion and removal of the catheter. Such risk factors may include, among others, pre-existing low left atrial pressure (e.g., noted at time of transseptal puncture), hypovolemia, airway collapse, deep breathing, snoring, or apnea, and may be more prevalent under sedation. Use additional caution when using drugs with respiratory depressive effects in such patients. Do not use if kinked or damaged, as this may result in patient injury. Do not kink flush lumen; flow through the device lumen could be diminished or compromised resulting in embolism or other patient injury. Take care to minimize damage to the femoral vein and access site upon insertion, manipulation, or withdrawal of the FARADRIVE Sheath. Complications associated with femoral vein catheterization include hematoma and thrombosis. Air ingress may be recognized by the visual presence of air bubbles in the side port tubing, shaft, or by an audible sucking sound emanating from the hemostasis valve. Imaging modalities employed during the procedure, such as fluoroscopy or intracardiac echocardiography, may also demonstrate the presence of air. If air embolism is suspected, begin appropriate management immediately as indicated by treatment guidelines or consensus statements. To minimize unintended back-bleeding through the side port, make sure the stopcock is in a closed position to the FARADRIVE Sheath at all times unless aspirating or flushing. The Transseptal Procedure (TSP) presents a potential risk for perforation/tamponade; echocardiography and/or fluoroscopic images should be used to guide the transseptal puncture and a real-time arterial blood pressure monitor should be applied. TSP may induce an air embolus; use proper aspiration and flushing techniques to minimize air embolus. Care should be used during multiple sheath/catheter exchanges through the transseptal puncture to avoid causing a residual atrial septal defect that would require repair. The FARADRIVE Sheath should not be used when in the presence of active Magnetic Resonance (MR). Use of the FARADRIVE Sheath in the presence of active MR could lead to patient injuries such as perforation, heart block and injury to adjacent structures. Cardiac catheterization procedures present the potential for significant radiation exposure, which can result in acute radiation injury as well as an increased risk for somatic and genetic effects, to both patients and laboratory staff due to the radiation beam intensity and duration of the fluoroscopic imaging. Cardiac catheterization should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure, and steps have been taken to minimize this exposure. Due to radiation exposure during cardiac ablation, the safety and effectiveness of this device has not yet been established in pregnant and/or nursing women and pediatric patients. There are no data to support the safety and effectiveness of this device in the pediatric population. Do not leave the FARADRIVE Sheath in the patient for more than four (4) hours. Failure to remove the device before four hours after first insertion could result in formation of thrombus with attendant stroke risks. To avoid patient injury, manipulate the sheath carefully when performing the transseptal puncture especially if the patient has any of the following conditions: Enlarged aortic root. Marked right atrial enlargement. Small left atrium. Marked skeletal deformity or distortion of the thoracic configuration (e.g., scoliosis). Potential biohazard after use. Handle and dispose of in accordance with applicable regulations.

PRECAUTIONS Do not attempt to use with devices, including guidewires, larger than the delivery lumen diameter specified on the package label.

ADVERSE EVENTS Potential adverse events associated with use of the FARADRIVE Sheath includes, but are not limited to: • Pain or discomfort, for example: Angina, Chest pain, Non-cardiovascular pain, • Cardiac arrest, • Death, • Hypotension, • Infection/inflammation/exposure to biohazardous material, • Edema/heart failure/pleural effusion, • Respiratory distress/insufficiency/dyspnea, • Arrhythmia (new or exacerbated), Conduction pathway injury (heart block, nodal injury, etc.), • Vessel trauma, including: Perforation, Dissection, Coronary artery injury, Vasospasm, Occlusion, Hemothorax, • Cardiac trauma, for example: Cardiac perforation/cardiac tamponade/pericardial effusion, Valvular damage, Stiff left atrial syndrome, • Injury related to tissue damage and/or adjacent structures, for example: Esophageal injury, Pulmonary injury, Catheter entrapment, Physical trauma, • Surgical and access complications, for example: Hematoma/seroma, AV fistula, Bleeding, Pseudoaneurysm, Pneumothorax, Residual atrial septal defect, • Thrombus/thrombosis, • Injury due to embolism/thromboembolism/air embolism/foreign body embolism, Cerebrovascular Accident (CVA)/stroke, Transient Ischemic Attack (TIA), Myocardial infarction, Neurological impairment and its symptoms, for example: Cognitive changes, visual disturbances, headache, motor impairment, sensory impairment, and speech impairment, Pulmonary embolism, Asymptomatic cerebral embolism, • Procedural related side effects, for example: Allergic reaction (including anaphylaxis), Genitourinary complication, Side effects related to medication or anesthesia, Radiation injury/tissue burn, Renal failure/insufficiency, Vasovagal response, Fluid volume overload. The potential adverse events may be related to the ablation catheter(s) and/or the interventional procedure. The severity and/or the frequency of these potential adverse events may vary and may result in prolonged procedure time and/or additional medical and/or surgical intervention, implantation of a permanent device such as a pacemaker, and in rare cases, may result in death. 97162573 (Rev. A)

FARASTAR™ Pulsed Field Ablation Generator

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

INTENDED USE The FARAPULSE Pulsed Field Ablation (PFA) System is intended for the isolation of the pulmonary veins in the treatment of paroxysmal atrial fibrillation by rendering targeted cardiac tissue electrically non-conductive to prevent cardiac arrhythmia initiation or maintenance. The FARASTAR PFA Generator is part of the FARAPULSE PFA System.

INDICATIONS FOR USE The FARASTAR Generator is indicated for the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

CONTRAINDICATIONS The FARAPULSE PFA System is contraindicated for use: in patients with active systemic infection; in patients with a mechanical prosthetic heart valve through which the catheter must pass; in patients with conditions where insertion into or manipulation in the cardiac chambers is unsafe as these conditions (e.g., presence of intracardiac thrombus or myxoma, history of recent cardiac surgery with atriotomy, etc.) may increase the risk of systemic embolism or cardiac perforation; in patients with a bleeding disorder, or who are unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation; in patients who have vena cava embolic protection filter devices and/or known femoral thrombus who require catheter insertion from the femoral approach; in patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe, such as but not limited to, a recent previous cardiac surgery (e.g., ventriculotomy or atriotomy, Coronary Artery Bypass Graft [CABG], PTCA/PCI/coronary stent procedure/unstable angina) and/or in patients with congenital heart disease where the underlying abnormality increases the risk of the ablation (e.g. severe rotational anomalies of the heart or great vessels); via transseptal approach in patients with an intra-atrial baffle or a foramen ovale patch.

WARNINGS To avoid the risk of electric shock, the FARASTAR PFA Generator must always be connected to a supply mains with protective earth. The Equipotential ground provides a direct connection between the chassis of the FARASTAR PFA Generator and the equalization bus of the electrical installation. It is not a protective earth connection point. The conductive parts of electrodes and associated connectors for system applied parts, including the neutral electrode, should not come into contact with any other conductive parts including earth ground. Electric shock can occur if this happens. The FARASTAR PFA Generator must only be used with equipment and accessories listed in this manual or patient injury or death may occur. Use of the FARASTAR PFA Generator with devices other than the FARAWAVE PFA Catheter can lead to unexpected energy delivery resulting in either insufficient ablation treatment or over-delivery of energy leading to possible patient hazardous events such as thrombus formation, tissue damage, etc. Use only with equipment and cabling that are listed in this manual or tested during installation of the equipment. Use with untested equipment or cables could result in increased EM emission or decreased EM immunity. Before using, inspect the FARASTAR PFA Generator for any defects or physical damage. Do not use defective or damaged devices. Replace damaged equipment if necessary. No modification of this equipment is allowed. The FARASTAR PFA Generator must be installed by a qualified/trained Boston Scientific representative. For assistance with installation, please contact your local Boston Scientific representative or Technical Support. Cardiac mapping and ablation procedures should be performed only by physicians thoroughly trained in invasive cardiology, in the techniques of mapping and ablation, and in the specific approach to be used, in a fully-equipped electrophysiology lab. The FARASTAR PFA Generator User's Manual is a fundamental part of the FARASTAR PFA Generator and should accompany it at all times. Users must refer to this manual for correct and complete information on the use of the FARASTAR PFA Generator. The FARASTAR RSM includes its own User's Manual. See this manual for specifics regarding the usage of the FARASTAR RSM. Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of this equipment, including cables specified by Boston Scientific. Otherwise, degradation of the performance of this equipment could result in patient or user harm. The FARASTAR PFA Generator internally produces voltages that are high enough to be potentially fatal. There are no user serviceable parts in the FARASTAR PFA Generator and it should not be opened. Maintenance should only be carried out by trained authorized personnel. Do not attempt to service the FARASTAR PFA Generator while in use with a patient. Cardiac ablation has the potential of causing unintended myocardial injury. Clinical indications of myocardial ischemia should be closely monitored during the procedure (e.g., ECG changes). The FARAWAVE PFA Catheter has not been studied clinically in the mitral isthmus or cavotricuspid isthmus areas. Ablations in areas adjacent to coronary arteries may lead to coronary artery spasm and/or injury may occur, and the resulting myocardial injury can be fatal. Direct patient contact should be avoided during ablation delivery as this may result in a mild electrical sensation and/or electric shock to the user. Do not touch the FARASTAR PFA Generator console and the patient simultaneously as this may cause excessive leakage currents on the patient which could lead to arrhythmias. Ensure that any additional equipment used with the FARAPULSE PFA System has been certified to IEC 60601-1. Use of non-certified equipment can increase the risk of patient harm due to failure of protective isolation barriers that could place hazardous voltages on the patient or operator or cause excessive leakage currents that may increase the risk of cardiac arrhythmias. Do not use a power bar or extension cord when connecting the FARASTAR PFA Generator and accessories (FARASTAR RSM) to the hospital AC source as this could cause an increase in leakage currents. Ensure the FARASTAR PFA Generator and FARASTAR RSM are plugged into separate AC mains connections. Do not use a power bar to connect any combination of FARASTAR PFA Generator or FARASTAR RSM together to an AC mains supply as doing this could cause an increase in leakage currents. Ensure that equipment is used at 120V/60Hz. Ablation with the FARASTAR PFA Generator may result in Ventricular Fibrillation. It is essential that a cardiac defibrillator with paddles or patches connected is readily available in the procedure room for use if Ventricular Fibrillation is noted subsequent to ablation. The FARASTAR stimulator outputs are primarily used to synchronize energy delivery and are not meant to replace the functions of the primary cardiac stimulator used by the Electrophysiology Lab, delay in arrhythmia treatment and/or arrhythmia may occur. Always have external sources of pacing and defibrillation available during ablation. Catheter electrodes are subjected to potentially harmful electrical energy. During preparation of the system do not deliver energy. If the user comes into contact with the catheter electrodes during delivery, electric shock can occur. Warnings for patients with implantable pacemakers (PPMs) and Implantable Cardioverter Defibrillators (ICDs): PPMs, ICDs, and leads can be adversely affected by ablation energy. It is important to refer to the device manufacturer's instruction for use prior to performing ablation procedures. Do not apply ablation energy directly to a lead or to tissue immediately in contact with a lead because it could potentially damage the lead or lead function. Temporarily reprogram the pacemaker or defibrillator per the manufacturer guidelines during ablation. The device could be damaged by the ablation procedure. Interrogate the device fully after the ablation per the manufacturer guidelines and reprogram to preoperative sensing and pacing parameters. Program the ICD Tachy therapy to "Off" to prevent inappropriate shock and/or possible damage to the device from the ablation procedure. Remember to turn Tachy Therapy to "On" once ablation is complete.Have temporary external sources of pacing and defibrillation available. Perform a complete analysis of the implanted device function after ablation. Fluoroscopic or appropriate imaging guidance and care must be taken during catheter advancement, manipulation, and withdrawal to avoid lead dislodgement. Monitor pre- and post-measurements for sensing and pacing thresholds and impedances to determine the integrity of the lead-patient function.

PRECAUTIONS Ensure prior to use that the FARASTAR PFA Generator is connected to the proper mains power supply. This equipment is intended for use in hospitals except near active High Frequency (HF) surgical equipment (including diathermy and electrocautery equipment), or Radiofrequency (RF) shielded room of a Medical Electrical (ME) system for Magnetic Resonance Imaging (MRI) where the intensity of Electromagnetic Interference (EMI) is high. Do not use the FARASTAR PFA Generator no closer than 30 cm (12 inches) to any Wireless Power Transfer (WPT) and 5G cellular devices, otherwise electromagnetic interference from those devices could result in degradation of the performance of this equipment. The emissions characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). Perform pulsed field ablation procedures only within environmental parameters as outlined in section 10.2. It is the user's responsibility to ensure that the equipment used with the system meets all local applicable electrical safety standards. Use of this equipment adjacent to or stacked with other equipment should be avoided as it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally. For purpose of disconnection, the mains connection is on the back of the console. Do not connect any device to the fiber optic port. Do not use the FARASTAR PFA Generator if a malfunction is suspected. Contact Boston Scientific if a malfunction is suspected. Do not use the FARASTAR PFA Generator in oxygen rich environment or in the presence of flammable gases or explosive gas mixtures. Ensure that the mains power supply cord is not damaged before plugging it into an electrical mains power supply. Replace the power supply cord if any damage is noticed. In the event of an external defibrillation pulse is delivered to the patient, the FARASTAR PFA Generator may become unresponsive and will require a reboot of the system. Avoid intentional or accidental liquid spills on the FARASTAR PFA Generator. Do not place cups or containers of liquid on the generator. Do not handle the generator with wet hands or gloves. Do not use the generator near irrigation equipment. Store the FARASTAR PFA Generator away from direct sunlight, heat sources or dust. Do not expose the LCD display of the generator to direct sunlight for long time periods. Ensure that the vents on the back of the generator are unobstructed. Avoid moving the generator when powered on. During transport, avoid jarring the device. Do not scratch the LCD display of the FARASTAR PFA Generator. Before cleaning the generator, ensure that it is powered OFF and disconnect the mains cord from the device. Clean the FARASTAR PFA Generator and the FARASTAR RSM by wiping down surfaces using a non-abrasive cloth with a mild detergent solution (not containing enzymes, abrasives, bleach, or alkali) or isopropyl alcohol. For the screen, use a standard screen cleaner. Do not position the FARASTAR PFA Generator in such a manner that it is difficult to access or unplug in the event of an emergency. To maintain system isolation, only Classified Medical Electrical Equipment may be connected to the FARAPULSE PFA System. The FARASTAR RSM must be used to pass ECG and/or EGM signals to the EP Recording System, during use of the FARAPULSE PFA System, to avoid potentially damaging the EP Recording System components. Disconnect all patient inputs from the Mapping System prior to pulsed field ablation. Leaving patient inputs connected during pulsed field ablation delivery may damage the Mapping System.

ADVERSE EVENTS Any potential clinical complications are in large part expected to be related to the accessories and/or therapeutic catheter that are used with the generator, rather than the generator itself. In order to identify potential adverse events, the user is instructed to read the pertinent instructions for use associated with the catheters and accessories that will be employed during the ablation procedure. Potential adverse events associated with use of the FARASTAR PFA Generator include, but are not limited to: Pain or discomfort, for example: Angina, Chest pain, Non-cardiovascular pain, • Cardiac arrest, • Death, • Electric shock, • Hypotension, • Infection/inflammation/exposure to biohazardous material, • Procedural related side effects, for example: Allergic reaction (including anaphylaxis), Genitourinary complication, Side effects related to medication or anesthesia, Radiation injury/tissue burn, Vasovagal response, Fluid volume overload, • Renal failure/insufficiency, • Respiratory distress/insufficiency/dyspnea, • Arrhythmia (new or exacerbated), Conduction pathway injury (heart block, nodal injury, etc.), • Nerve injury, for example: Phrenic nerve injury, Vagal nerve injury, • Gastrointestinal disorders, • Vessel trauma, including: Perforation, Dissection, Coronary artery injury, Vasospasm, Occlusion, Hemothorax, • Cardiac trauma, for example: Cardiac perforation/cardiac tamponade/pericardial effusion, Valvular damage, Stiff left atrial syndrome, • Injury related to tissue damage and/or adjacent structures, for example: Esophageal injury, Pulmonary injury, Catheter entrapment, • Physical trauma/laceration, • Fistula, for example: Atrio-esophageal fistula, Bronchopericardial fistula, • PV stenosis and its symptoms, for example: Cough, Shortness of breath, fatigue, Hemoptysis, • Thrombus/thrombosis, • Muscle spasm, • Injury due to embolism/thromboembolism/air embolism/foreign body embolism, Cerebrovascular Accident (CVA)/stroke, Transient Ischemia Attack (TIA), Myocardial infarction, Neurological impairment and its symptoms, for example: Cognitive changes, visual disturbances, headache, motor impairment, sensory impairment, and speech impairment, Pulmonary embolism, Asymptomatic cerebral embolism, • Hemolysis. The potential adverse events may be related to the PFA generator, ablation catheter(s), and/or the interventional procedure. The severity and/or the frequency of these potential adverse events may vary and may result in prolonged procedure time and/or additional medical and/or surgical intervention, implantation of a permanent device such as a pacemaker, and in rare cases, may result in death. 97172186 (Rev. A)

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