IJC Heart & Vasculature 58 (2025) 101674

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.sciencedirect.com/journal/ijc-heart-and-vasculature

Pulsed field ablation using a circular electrode array catheter in patients with atrial fibrillation: A workflow optimization study evaluating the role of mapping

Melanie A. Gunawardene [a,b,c,d,*], Jens Hartmann [a,c], Jannis Dickow [a,c], Rahin Wahedi [a,c], Tim Harloff [a,c], Johanna Jezuit [a,c], Eike P. Tigges [a,c], Mario Jularic [a,c], Borislav Dinov [b], Nele Gessler [a,c,d,e], Stephan Willems [a,c,d]

[a] Asklepios Hospital St. Georg, Department of Cardiology and Intensive care medicine, Hamburg, Germany
[b] University Hospital Giessen, Department of Cardiology, Giessen, Germany
[c] Semmelweis University, Budapest, Hungary
[d] DZHK (German Center for Cardiovascular Research), partner site Hamburg/Kiel/Lübeck, Berlin, Germany
[e] Asklepios Proresearch, Hamburg, Germany

ARTICLE INFO

Keywords:
Pulsed field ablation
Three-dimensional mapping
Atrial fibrillation
Pulmonary vein isolation

ABSTRACT

Background: Pulsed field ablation (PFA) with a circular-electrode-array catheter (cPFA) has shown to be effective and safe. However, data on procedural workflow are limited.
Objective: to analyze the process of streamlining cPFA-procedures including evaluation of fluoroscopy versus 3D-map guidance and lesion characteristics.
Methods: Consecutive AF-patients underwent cPFA-based pulmonary vein isolation (PVI) in three phases (learning-phase-I: visualization of cPFA in 3D-map; phase-II: operator blinded to 3D-map with fluoroscopy-guidance only; phase-III: optimized mapping and ablation). Additionally, hemolysis-parameters were collected.
Results: A total of 35 patients (57 % paroxysmal-AF, age 63.4 ± 9.4 years) were enrolled: n = 10 phase-I, n = 15 phase-II, n = 10 in phase III. Total procedure and fluoroscopy time was 51.9 ± 9.4 and 6.7 ± 3.1 min, respectively. First-pass PFA isolation-rate was lowest in the fluoroscopy-only phase-II (I:86 %, II:81 %, III:100 %, p = 0.0079). Insufficient PV ablation with remaining conduction occurred mostly anterior (n = 8/15, 53 %) and at the carina (n = 4/15; 27 %). Following additional PFA, all 142 PVs (100 %) were acutely isolated.
Procedure times between phase II and III did not differ (49 ± 8 vs. 46 ± 3 mins p = 0.23). Fluoroscopy times were longer in phase-II (phase-I: 5.8 ± 1.3, phase-II: 9.2 ± 2.9, phase-III: 3.8 ± 1.0 mins, p < 0.0001). No complications occurred. Pre- and post-ablation hemoglobin (14.4 ± 1.4 vs. 13.5 ± 1.2 g/dl, p = 0.0169) and LDH (188 ± 39 vs. 210 ± 29 U/l, p = 0.0007) were different.
Conclusion: The cPFA-catheter allows for fast and efficient PVI. A fluoroscopy-only approach creates distal PV ablation lesions that are associated with residual PV conduction along the carina and anterior antrum. However, with visualization and mapping, creation of wide antral ablation lesions is feasible without prolonging procedural duration.

1. Introduction

Pulsed field ablation (PFA) is a novel energy source to perform preferential myocardial ablation in patients with atrial fibrillation (AF), [1].

After initial introduction of the first PFA system [2], a variation of

Abbreviations: AF, atrial fibrillation; ICD, implantable cardioverter defibrillator; LA, left atrium; LAO, left-anterior oblique view; LDH, Lactate dehydrogenase; LCPV, left common pulmonary vein; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; NOAC, novel oral anticoagulants; PFA, pulsed field ablation; PV, pulmonary vein; PVI, pulmonary vein isolation; RAO, right-anterior oblique view; RIPV, right inferior pulmonary vein; RMPV, right middle pulmonary vein; RSPV, right superior pulmonary vein.

* Corresponding author at: Department of Cardiology, Asklepios Klinik St. Georg, Lohmühlenstr. 5, 20099 Hamburg, Germany.
E-mail address: melanie.gunawardene@gmail.com (M.A. Gunawardene).

https://doi.org/10.1016/j.ijcha.2025.101674
Received 6 January 2025; Received in revised form 8 March 2025; Accepted 27 March 2025

different catheter designs and PFA waveforms is currently underway [1]. PFA promises predictable, efficient and safe performance of catheter ablation in AF patients, including so called "single-shot" devices [3–5]

However, each PFA system requires individual assessment of feasibility, efficiency, safety and workflow adaption, as each system comes along with unique features and different form factors. A circular electrode array PFA catheter for pulmonary vein isolation (PVI) has recently been investigated in a first multicenter trial showing an acute PVI rate of 100 % [6].

The freedom from treatment failure rates reported in this study were consistent with thermal ablation and the primary safety adverse event rate was as low as 0.7 % [6]. In the PULSED-AF trial, however, no details on the number of reconnected pulmonary veins (PV), the number of patients with reconnected PV or the patterns of reconnections were provided [6].

The circular electrode array catheter can be used with and without three-dimensional (3D) mapping visualization. However, in 95 % of paroxysmal and 92 % of persistent AF procedures in the approval study, 3D-mapping was used with this PFA catheter design [7].

The catheter itself is not magnetically integrated but can be visualized via impedance tracking. However, up to now, clinical data on procedural workflow strategies, usefulness of 3D mapping and description of lesion characteristics are still limited.

The aim of this study was to report the process of streamlining procedures including workflow optimization and evaluation of 3D-map guidance with characterization of lesion formation with a newly introduced circular electrode array PFA catheter.

2. Methods

2.1. Study design

This study is a prospective, single-center study. Consecutive patients eligible for catheter ablation of AF (including paroxysmal and persistent (AF)), were enrolled into the study from June to August 2024. The study was investigator-initiated without external funding; the authors are responsible for design, execution, and conduct of the study. The statistical analyses and interpretation of the data were approved by all authors, who attest to the accuracy of the data and of all analyses. Written informed consent was obtained from all patients. The study was conducted in accordance with the provisions of the Declaration of Helsinki and its amendments. The institutional review board and ethics committee approved the study (Hamburg ethics: *2023–101043-BO-ff*).

2.2. Catheter ablation

2.2.1. Peri-procedural management

Prior to ablation, intracardiac thrombus formation was ruled out by transesophageal echocardiography. Oral anticoagulation was minimally interrupted at the morning of the procedure and restarted 6 h after sheath removal.

Procedures were performed under deep sedation using a continuous infusion of propofol (1 mg/ml) and boluses of midazolam (1 mg/ml) and sufentanyl (0.1 mg/ml). Intravenous heparin (25000 IU/5 ml) was applied to reach an activated clotting time of at least 300 s. To minimize vagal responses, 1 mg of intravenous atropine (0.5 mg/ml) was administered to all patients prior to ablation. If patients presented in AF at the beginning of the procedure, electrical cardioversion was performed prior to mapping and ablation.

2.2.2. Access and Pulsed field ablation system

The procedures were conducted by three experienced operators. All operators had prior experience with cryoballoon and PFA single shot devices.

Two ultrasound-guided venous punctures of the right groin were performed in all patients. After femoral venous access, a decapolar diagnostic catheter (Inquiry™, 2–5-2 mm spacing; Abbott, MN, USA) was placed into the coronary sinus. After transseptal puncture and left atrial angiography, the left atrial sheath was exchanged by a 10-French deflectable sheath (Medtronic, FlexCath Contour 13 mm or 20 mm curve, MN, USA) and the PFA-catheter (Medtronic PulseSelect™ PFA ablation system, MN, USA) was introduced to the left atrium (LA). The PFA system has been described in detail before [7]. All patients of this study underwent PFA-guided PVI. No additional ablation was performed. If patients presented in AF electrical cardioversion was performed prior to mapping and ablation.

PVI was performed in all patients using at least 8 PFA applications at an output of 1.5 kV with the aim of at least four initial ostial applications, followed by 4 antral applications around each PV. The catheter was rotated between a train of applications to ensure circumferential PV ostial and antral coverage to 3′, 6′, 9′ and 12′ o'clock, as recommended. Procedures included a PVI-only approach, no additional substrate modification was performed. At the right superior PV, a single test pulse with reduced energy delivery was applied before further ablation to rule out phrenic capture (manually and by fluoroscopy).

2.2.3. Work flow of pulsed field ablation and mapping strategies

The study included 3 phases to optimize and adapt the workflow of the ablation approach and to evaluate PVI and lesion formation (Fig. 1).

Phase I – initial visualization and learning phase: after the transseptal puncture, an anterior-posterior LA angiogram was performed and the deflectable sheath introduced. After introduction of the PFA catheter to the LA, a 3D map of the LA was performed using the now visualized circular PFA catheter as mapping catheter (Ensite-X®, NavX mode, Abbott,MN, USA). Mapping was performed in sinus rhythm after electrical cardioversion without pacing via the coronary sinus. Afterwards, PVI was performed while visualizing the PFA catheter in the 3D map using 8 PFA applications per PV. The PFA catheter was rotated by 90° from 3′ to 6′, 9′ and 12′ to ensure lesion continuity due to the electrode gap between electrode 1 and 9 of the catheter's "horse shoe" configuration (Fig. 2A). After PVI of all veins, a remap was performed to assess PV isolation (with the use of the PFA catheter's 1–9 electrodes) and lesion formation along the PV ostia, again using the circular PFA catheter as the mapping catheter. If required (either due to insufficient ablation with detection of a conduction gap or because of incompleteness of a wide antral lesion), additional PFA was performed until complete PVI with wide antral lesions were present. PVI was confirmed in all patients following ablation by positioning the PFA catheter at each PV to assess entrance block in sinus rhythm.

Phase II – blinded phase: after the transseptal puncture, an anterior-posterior LA angiogram was performed and the deflectable sheath introduced. After introduction of the PFA catheter to the LA, the operator was blinded to the 3D map that was running in the background. The operator performed PVI of all PVs solely by a fluoroscopic guidance with 8 PFA applications. After finishing ablation and confirmation of fluoroscopic-guided isolation of all veins, the operator was unblinded to the 3D map and able to see shadows of the prior ablation sites. The operator then performed a remap of all PVs using the circular PFA catheter as the mapping catheter and to evaluate the quality of PV isolation status and lesion formation. If required (either due to conduction gap or incomplete wide antral lesion), additional PFA was performed until complete PVI with wide antral lesions were present. PVI was confirmed in all patients following ablation by positioning the PFA catheter at each PV to assess entrance block in sinus rhythm.

Phase III: optimized phase: after transseptal puncture, left anterior oblique (LAO) 30° and right anterior oblique (RAO) 30° angiograms of the LA were performed to visualize the precise PV anatomy, including all branches. After introduction of the PFA catheter to the LA, three-dimensional PV mapping at the same time as ablation was performed using as many PFA applications as necessary to create antral ablation lesions, with a minimum of 8 applications. Ninety-degree rotation and lesion overlap of the PFA catheter was ensured by visualization in the 3D

Fig. 1. Workflow optimization.

map and taking a shadow for every ablation position. Additionally, each PV-branch was wired in the so called "snake" configuration separately and consecutively ablated (Fig. 2B and 2C). The "snake" configuration was used for wiring and positioning only, no ablation was performed in this configuration. With the "snake" configuration the catheter was first positioned more distally in the PV. Next, the catheter was pulled back in its circular shape to the PV ostium to improve positioning for ablation (Fig. 2B). At least 2 PFA lesions each were applied with the sheath deflected at the anterior and posterior carina for superior veins, and with a non-deflected sheath positioning for the inferior PVs. Anterior movement of the sheath was performed in the beginning of ablation to target the ridge or anterior aspect of the PV ostium.

While ablating, the circular PFA catheter was moved after every PFA application within the map to assess electrograms at the PV ostia, antrum and carina region and ablate if remaining electrograms were detected. Finally, a remap of the PV was performed to assess PVI, before moving to the next PV for ablation. PVI was confirmed in all patients following ablation by positioning the PFA catheter at each PV to assess entrance block in sinus rhythm.

2.3. Safety

All *peri*-procedural complications were recorded. Additionally, hemolysis parameters were collected one day before and one day after the procedure via blood testing. These included creatinine (mg/dl), glomerular filtration rate (ml/min), haptoglobin (g/l), bilirubin (mg/dl), hemoglobin (g/dl) and lactate dehydrogenase (LDH) values (U/l).

2.4. Statistics

Continuous data are shown as mean ± standard deviation or as median and interquartile range. For group comparisons, Student's *t* test (paired or unpaired) or the Mann-Whitney *U* test for unpaired variables were used. Categorical data are described as absolute and relative frequencies; they were compared with the chi-square or Fisher's exact test. Statistical significance was assumed at a P-value < 0.05. Statistical analyses was performed using the GraphPad Prism 10.0 software (GraphPad Software Inc., San Diego, CA, USA).

3. Results

3.1. Baseline and procedural characteristics

A total of 35 consecutive patients were enrolled in this study cohort: n = 10 in phase I, n = 15 in phase II and n = 10 in the optimized phase III. Baseline characteristics of the patients are shown in Table 1. Twenty patients (57 %) suffered from paroxysmal AF, 15 (43 %) from persistent AF with a mean CHA_2DS_2-VA score of 1.3 ± 1.1. Mean age was 63.4 ± 9.4 years. No patient had an implanted pacemaker or implantable cardioverter defibrillator (ICD). Prior antiarrhythmic drug therapy was present in 8 patients (23 %; class III amiodarone in 2 patients and class IC flecainide in 6 patients). First-line ablation was therefore performed in 27 (77 %) patients. Twenty-nine patients were pre-treated with novel oral anticoagulants (NOACs), (83 %), while 5 had no prior OAC therapy (27 %).

Procedural parameters are shown in Table 2. Thirteen patients presented in AF and received electrical cardioversion prior to mapping and ablation. In total 3,028 ± 1,879 mapping points were collected per patient to create the 3D LA-maps. Total procedure time in all patients was 51.9 ± 9.4 min and time in the LA was 36.1 ± 9.2 min. The mean fluoroscopy time was 6.7 ± 3.1 min and the mean LA fluoroscopy time was 5.0 ± 2.8 min. Ablation time was 24.8 ± 7.5 min with an ablation fluoroscopy time of 4.0 ± 2.6 min for the complete cohort.

All 142 PVs (100 %; including 4 left common PVs (LCPV) and 6 right

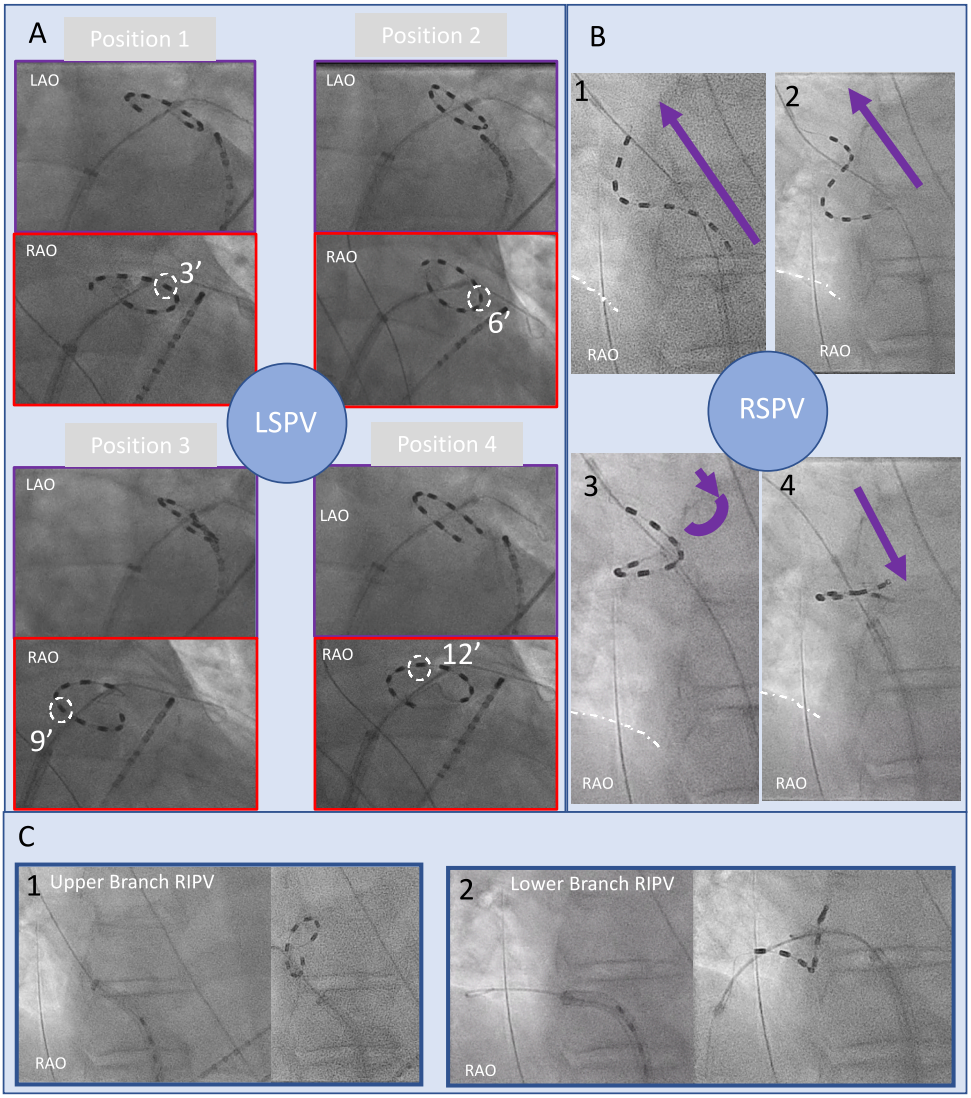

Fig. 2. Technical aspects of catheter maneuverability. A. **Rotation of PF catheter during ablation at the PV ostium.** This figure shows the rotation of the horse-shoe-figured/circular electrode array PFA catheter while ablating in the LSPV at 3′, 6′, 12′ and 9′ o'clock to cover the whole PV antrum and to aim for continuous ablation lesions. Each position is shown in LAO (purple) and RAO (red) as two views are needed to validate positioning. Note, that anterior (counterclockwise) movement of the sheath was performed to ablate the ridge region at the first ablation site (position 1). **B: Positioning of the PF catheter at the pulmonary vein.** After wiring the PV, the "snake configuration" was used at the RSPV to advance the catheter's electrodes into the PV (**B1-B2**). Then, the slider on the catheter's handle was slightly pulled back to regain circular shape of the catheter (**B3**). Afterwards, the circular PF catheter was pulled back to the ostium of the PV for the first ablation position (**B3-B4**). **C: Addressing all PV branches.** This is an example of a RIPV with two branches (upper and inferior branch). As shown in the images **C1** and **C2**, both branches were separately wired and the PFA catheter was positioned in both branches for separate ablation. Again the "snake" configuration was used for optimization of catheter positioning in the inferior branch (**C2**). LAO indicates left-anterior oblique view: LSPV, left superior pulmonary vein; PV, pulmonary vein; RAO, right-anterior oblique view; RSPV, right superior pulmonary vein. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

middle PVs (RMPV)) were acutely isolated at the end of the procedure (Fig. 7).

3.2. Initial phase I

In phase I, 42 PVs were present (1LCPV, 3 RMPVs). After the initial 8 PFA applications per PV, 6/42 (14 %) failed to be isolated and revealed a conduction gap during remapping, mostly located at the anterior PV ostium (n = 4/6, 66.7 %, 2 left superior PV (LSPV), 1 right inferior PV (RIPV), 1 left inferior (LIPV); 1 gap right inferior PV (RIPV) inferior; 1 gap LSPV posterior, Fig. 3). Another 7 PVs required additional PFA applications to create wide antral ablation lesions. Therefore, a total of 13 out of 42 PVs required ablation with 4 ± 2 additional PFA applications resulting in a total of 9 ± 2 PFA applications per PV. In total, a mean of 40 ± 6 applications per patient were needed to isolate all PVs and create wide antral lesions.

Mean procedure duration in phase I was 61 ± 10 min with a mean fluoroscopy time of 5.8 ± 1.3 min (Fig. 4). LA-catheter time and ablation time were 44 ± 10 and 29 ± 10 min, respectively.

3.3. Blinded phase II

In phase II, 63 PVs were present (3 RMPVs). During fluoroscopy-only ablation 8 ± 0.4 PFA applications were delivered per PV: in two LIPVs, 2 additional PFA applications were applied due to remaining signals after 8 applications. During un-blinded remapping, 12/63 (19 %) PVs showed insufficient ablation with failed first pass isolation with a fluoroscopy-only-, 8-application-approach:

Table 1
Baseline Patient Characteristics.

	All n = 35	Initial Phase I n = 10	Blinded Phase II n = 15	Optimized Phase III n = 10
Age (years)	63.4 ± 9.4	61.9 ± 11.9	64.3 ± 19.6	63.4 ± 6.8
Male gender	20 (57)	5 (50)	7 (47)	8 (80)
Hypertension	15 (43)	4 (60)	8 (77.8)	3 (30)
Diabetes mellitus	3 (9)	1 (10)	1 (7)	1(10)
Chronic kidney disease	2(6)	0	1 (7)	1(10)
Congestive heart failure	8 (23)	2 (20)	3 (20)	3 (30)
BMI (kg/m^2)	27.7 ± 4.0	26.7 ± 3	26.1 ± 4.5	28.1 ± 3.1
CHA_2DS_2-VA score	1.3 ± 1.1	1.2 ± 1.1	1.5 ± 1.1	1.2 ± 0.9
Type of AF				
- PAF	20 (57)	6 (60)	7 (47)	7 (70)
- Persistent AF	15 (43)	4 (40)	8 (53)	3 (30)
Left atrial diameter (mm)	43 ± 5	43 ± 6	44 ± 6	42 ± 6
Left ventricular ejection fraction (%)	58 ± 8	60 ± 1	57 ± 8	57 ± 6

Values are mean ± standard deviation, median [first-third quartile] or n (%).
AF indicates Atrial fibrillation; BMI, body mass index; **CHA_2DS_2-VA score** is a clinical estimation of the risk of stroke in patients with atrial fibrillation; scores range from 0 to 9, with higher scores indicating a greater risk of stroke = **C**ongestive heart failure, **H**ypertension, **A**ge > 75 years, **D**iabetes, previous **S**troke, transient ischemic attack, or thromboembolism, **V**ascular disease, **A**ge 65–75 years; PAF, paroxysmal atrial fibrillation

Table 2
Procedural parameters.

Procedural Parameters	All n = 35	Initial Phase I n = 10	Blinded Phase II n = 15	Optimized Phase III n = 10
Procedural Data				
Rhythm at the beginning of the procedure	22 (63) 13 (37)	7 (70) 3 (30)	8 (53) 7 (46)	7 (70) 3 (30)
- Sinus Rhythm				
- Atrial fibrillation				
Total Procedure time (min)	52 ± 9	61 ± 10	49 ± 8	46 ± 3
Total Fluoroscopy time (min)	6.7 ± 3.1	5.8 ± 1.3	9.2 ± 2.9	3.8 ± 1.0
Pulsed Field ablation				
LA ablation time (min)	25 ± 8	29 ± 10	22 ± 7	25 ± 3
LA Fluoroscopy time during PFA (min)	4 ± 2.6	2.5 ± 1.3	6.2 ± 2.2	1.8 ± 0.6
Total PFA applications per patient for PVI (at end of procedure)	39 ± 6	40 ± 6	37 ± 6	39 ± 5
LSPV	10 ± 3	11 ± 3	9 ± 2	12 ± 3
LIPV	9 ± 3	9 ± 3	10 ± 3	9 ± 1
RSPV	9 ± 2	8 ± 1	8 ± 1	10 ± 3
RIPV	9 ± 2	10 ± 2	9 ± 2	9 ± 2
LCPV	16 ± 3	16	N/A	15 ± 3
RMPV	8 ± 0	8 ± 0	8 ± 0	N/A
All complications	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
• Pericardial tamponade	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
• Phrenic nerve palsy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
• Access complications (groin)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
• Coronary spasm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
• Acute renal failure	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Values are mean ± standard deviation, [n] or n (%), median [first-third quartile].
LA indicates left atrium; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; N/A, not applicable; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; PFA, pulsed field ablation, PVI, pulmonary vein isolation;

Insufficient ablation with remaining conduction were located at the LSPV n = 4 (1 ridge, 3 anterior carina), LIPV n = 2 (both anterior), right superior PV (RSPV) n = 1 (anterior) and RIPV n = 2 (1 anterior, 1 posterior carina), (Fig. 3). Two RIPV were not isolated during remapping, as only the upper branch was wired and ablated with PFA but not the inferior branch (Fig. 3). Additionally, in one case, the operator was only able to successfully position and ablate the LIPV after unblinding and using the 3D map for guidance and catheter positioning **(**Fig. 3**).**

A total of additional 5 ± 2 PFA applications were applied in these cases to isolate the PVs and create wide antral ablation lines. In total, 9 ± 2 PFA applications per PV and 37 ± 6 applications per patient were needed to isolate all PVs and create wide antral lesions. Mean procedure duration in phase II was 49 ± 8 min with a mean fluoroscopy time of 9.2 ± 2.9 min **(**Fig. 4**)**. LA-catheter time and ablation time were 33 ± 7 and 22 ± 7 min, respectively.

3.4. Optimized phase III

In phase III, 37 PVs were present (3 LCPV). All PVs were isolated after a first pass with 11 ± 3 PFA applications using the strategy to map, ablate and remap directly at each PV. Mean procedure duration in phase III was 46 ± 3 min with a mean fluoroscopy time of 3.8 ± 1.0 min **(**Fig. 4**)**. LA-mapping and ablation time was 32 ± 3 min.

3.5. Comparison of phases

Failure to first-pass PFA isolation was highest in the blinded phase II fluoroscopy-only approach and lowest in the optimized III phase (first pass PFA isolation rates: phase I 86 %, phase II 81 %, phase III 100 %, (p = 0.0079). A total of 15 residual conduction gaps were found in phase I and II, mostly located anterior (n = 8/15, 53 %) and at the carina (n = 4/15; 27 %) region of the PV ostium (Fig. 6).

The number of first-pass PFA applications were higher in phase III (11 ± 3 applications) as compared to phase I (8 ± 0 applications; p < 0.0001) and II (8.1 ± 0.4 applications, p < 0.0001). There was no difference between number of first pass PFA deliveries in phase I and II (p = 0.24).

There was no difference in the mean number of total PFA deliveries per patient between the three different phases (phase I: 40 ± 6, phase II: 37 ± 6, phase III: 39 ± 5; p = 0.6159). The posterior wall or roof was not accidentally ablated in any patient of this cohort.

Procedure times were significantly longer in phase I (61 ± 10 mins) as compared to phase II (49 ± 8 mins, p = 0.0028) and III (46 ± 3 mins, p = 0.0002). Procedure times between phase II and III did not differ (p = 0.2279), **(**Fig. 4**)**.

Fluoroscopy times were longer in phase II (9.2 ± 2.9 mins) as compared to phase I (5.8 ± 1.3 mins, p = 0.0018) and III (3.8 ± 1.0 mins, p < 0.0001). Phase III fluoroscopy time was shorter than in phase I (p = 0.0012), **(**Fig. 4**)**.

3.6. Safety and complications

Phrenic nerve capture during ablation was found in all 35 patients during PFA ablation at the RSPV. No transient or persistent phrenic nerve palsy occurred. No vagal responses were seen. There were no periprocedural complications, including no pericardial tamponades, no access complications, no clinical apparent coronary spasm.

3.7. Hemolysis parameters

Creatinine (pre-ablation 0.9 ± 0.2 mg/dl vs. post-ablation 0.9 ± 0.2 mg/dl, p = 0.33), glomerular filtration rate (pre: 79 ± 12 ml/min vs. post: 79 ± 12.7 ml/min post, p = 0.85), haptoglobin (pre: 1.1 ± 0.4 g/l vs. post: 0.9 ± 0.4 g/l post, p = 0.13) and bilirubin (pre: 0.76 ± 0.26 mg/dl vs. post: 0.94 ± 0.42 mg/dl, p = 0.22) values before and one day after PFA did not differ (Fig. 5). Pre- and post-ablation hemoglobin

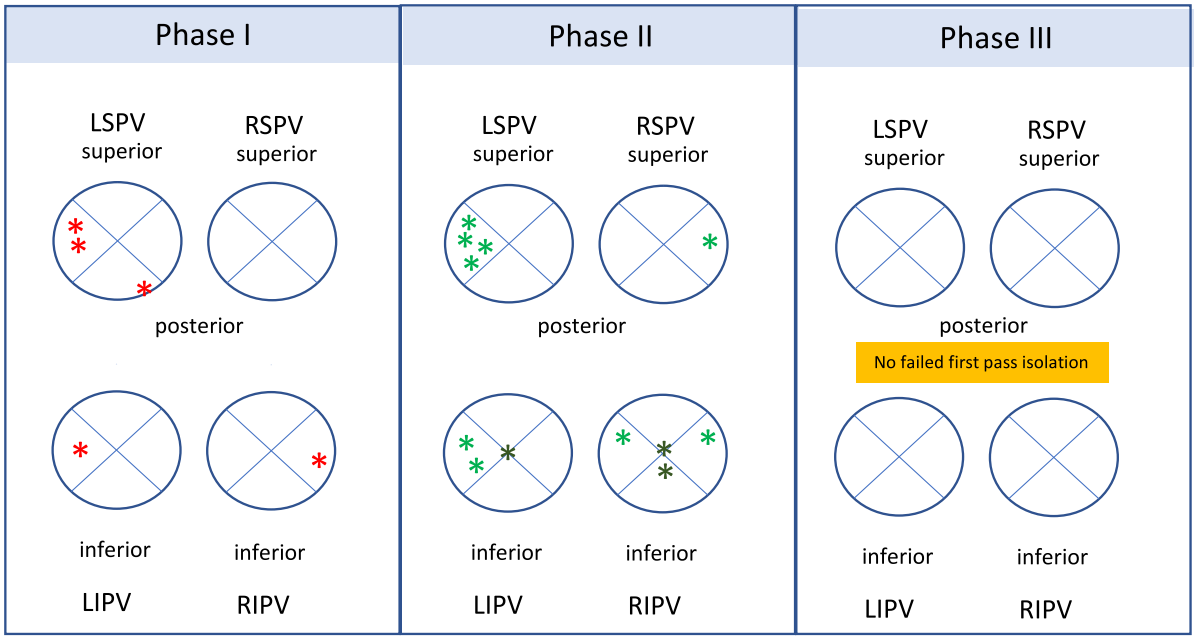

Fig. 3. Conduction sites after failed first pass isolation in phase I, II and III. The asterixis "*" mark the site of conduction during remapping after initial ablation with 8 PFA applications per pulmonary vein. Of note, at the end of the procedure all conduction sites were successfully ablated and all PVs were isolated. LIPV, left inferior pulmonary vein; LPV, left pulmonary veins; LSPV, left superior pulmonary vein; PV, pulmonary vein; RIPV, right inferior pulmonary vein; RPV, right pulmonary veins, RSPV, right superior pulmonary vein.

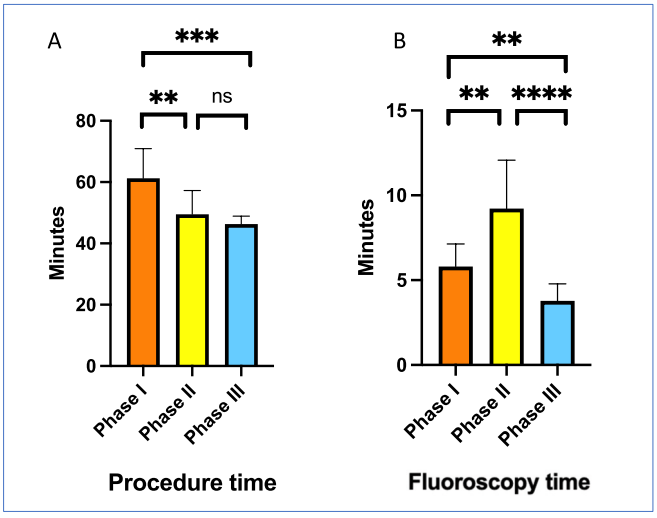

Fig. 4. Procedure and fluoroscopy times. Fig. 4. shows the different laboratory markers pre- and post-ablation on the following day. LDH indicates lactate dehydrogenase, * p-Value = 0.0169, *** p-value = 0.0007.

values (pre: 14.4 ± 1.4 g/dl vs. post: 13.5 ± 1.2 g/dl, p = 0.0169) and LDH values (pre: 188 ± 39 U/l vs. post: 210 ± 29 U/l, p = 0.0007) were different (Fig. 5**).**

4. Discussion

Major findings of this study are:

1) PFA procedures with a circular electrode array catheter allowed for fast, efficient and safe treatment of AF with a steep learning curve in our cohort.
2) Insufficient isolation with remaining PV conduction was frequently seen in a fluoroscopy-only approach. The gaps were mostly found at the anterior aspect of the PV and the carina region. With the use of three-dimensional mapping and a pre-defined ablation strategy, occurrence of conduction gaps could be prevented.
3) A higher number of PFA applications, as initially recommended, were necessary to successfully isolate all PVs, increase first pass PVI and create antral ablation lesions.
4) With the use of three-dimensional mapping, procedures could be streamlined and quality of PV isolation lesions optimized – without prolonging procedural duration.
5) In regards to hemolysis parameters, hemoglobin and LDH levels differed before and after PFA. There was no acute renal failure in any patient.

To the best of our knowledge, this is the first report on the circular electrode array PFA catheter investigating the role of mapping.

4.1. *Workflow optimization and role of mapping*

In current practice, PVI can be performed with thermal or non-thermal energy sources using a point-by-point or an anatomical catheter [8]. These anatomical catheters are frequently named "single shot" devices as they facilitate a single positioning at the PV with an on–/off-energy delivery mode [9,10].

However, the circular PFA catheter used in this study is not a classic single-shot catheter. Although it is an anatomical device designed to be positioned at the PV ostium and ablate a large area, our study showed that the catheter creates more distal lesions and does not cover the whole PV antrum with a single position as other "single shot" devices may [4,10]. Due to the smaller, more segmental footprint of a per se anatomical catheter, it requires more planning of lesion sets and rotations. In our study, this included movements of the sheath to position the whole superior to inferior and septal to lateral axis of the PV antrum. Our study showed, that this maneuverability around the PV ostium is difficult to perform with a sole guidance by fluoroscopy. In the initially blinded, fluoroscopy-only phase II, 19 % of PVs were not isolated after 8 PFA applications and required additional ablation. This shows that PV anatomy is more complex than one may consider [11] – the PFA catheter

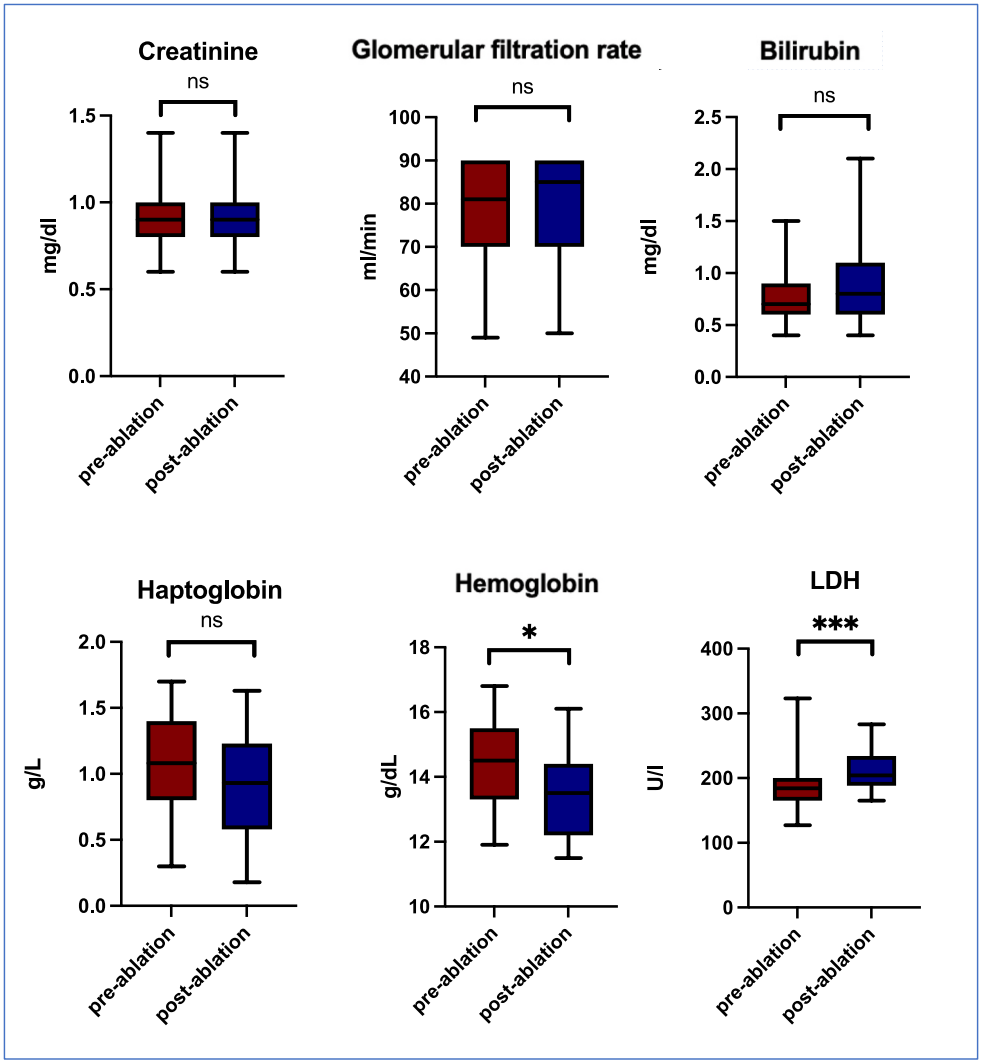

Fig. 5. Hemolysis parameters pre- and post- pulsed field ablation.

did not always have sufficient contact to the PV ostium and the anterior and carina region were often spared. Additionally, the rather small size of the "horse-shoe" PFA catheter yields further limitations. The electrodes are not positioned continuously in a circle and a gap between electrode 1 and 9 is present. Therefore, sufficient lesion overlap to overcome this distance between the electrodes and rotational movements seem crucial to achieve durable PVI with PFA. Due to the lack of complete antrum coverage, we found PVs not to be isolated. Wiring different branches of the PV and applying PFA may enhance antral coverage and lesion overlaps, thus achieving complete antral PVI. Therefore, it is essential to understand the precise, individual anatomy of the patient. Several approaches can be utilized to obtain detailed PV anatomy, including pre-procedural imaging techniques such as computed tomography or magnetic resonance imaging, as well as *peri*-procedural imaging options like selective PV angiography or intracardiac ultrasound [8].

We demonstrated that an optimized workflow with visualization and integration into 3D mapping resulted in higher first pass isolations with PFA. This was most likely explained by two reasons: 1) lesion planning and positioning of the PFA catheter were more predictable, 2) more applications were delivered as the area covered by the PFA catheter was visualized and could be optimized and 3) by constantly rotating the catheter and moving it within the 3D map of the PV, possible residual electrograms could be evaluated.

Procedure times in phase II went down most likely because a pre-ablation 3Dmap was not actively performed (only running in the background, not visualized to the operator). At the same time the fluoroscopy times increased due to blinding and a fluoroscopy-only approach. With the use of 3D mapping, in general, more information is gathered and fluoroscopy times can be reduced, as shown in this study and by others [12,13]. Badertscher et al. compared the use of 3D-mapping versus no 3D-mapping in patients undergoing AF ablation with a pentaspline PFA catheter and found no difference in freedom from atrial arrhythmias after 267 [IQR 164–419] days in this non-randomized study [14]. However, as mentioned before, every PFA system is different and requires its own evaluation [1]. Data on randomized comparison on the usefulness of additional 3D-mapping are currently missing for all PFA systems.

Of note, intracardiac echocardiography (ICE) was not used in our study, which could bring additional benefits regarding information on the underlying anatomy [15]. Yet, a propensity-score matched study by Dello Russo et al. showed that the use of ICE to guide PFA was not associated with an improvement of procedural metrics [16].

4.2. *Sites of conduction*

Insufficient isolation sites were mostly found anteriorly or at the carina region of the PV in our study. This is in alignment with the initial findings reported on a pentaspline PFA catheter where acute PV-reconnection was found in 6.25 % of PVs during 3D-mapping, mostly

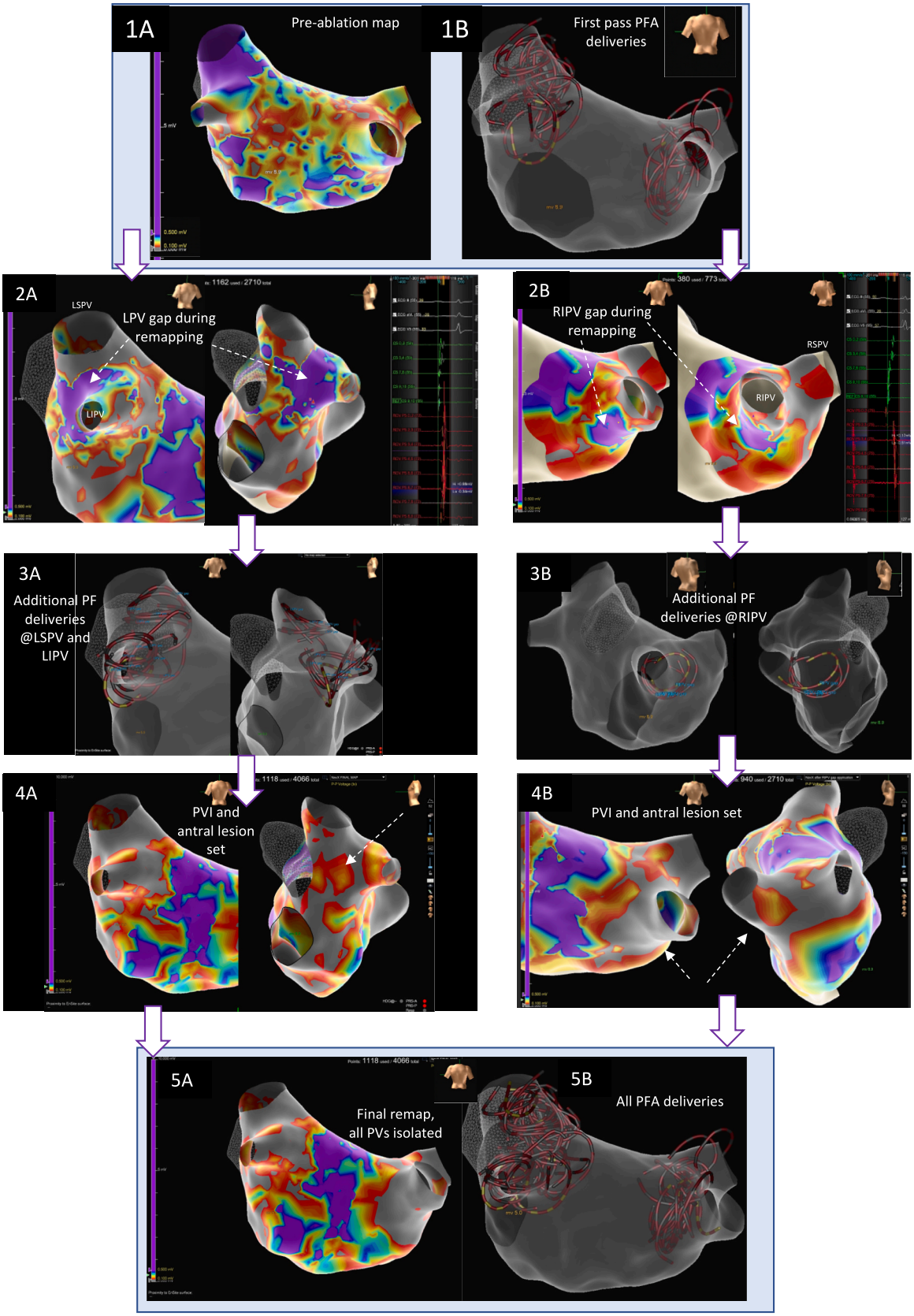

Fig. 6. Example of conduction gaps after first pass PFA with 8 applications. In this phase I patient, initial mapping in AF was performed with the PFA catheter as the mapping catheter (**1A**), followed by ablation with 8 PFA applications per PV (**1B**). During remapping insufficient ablation with conduction gaps of the left pulmonary veins (anterior carina, **2A**) and RIPV (inferior, **2B**) were detected. Additional PFA was delivered (**3A and 3B**). The remap of the left and right PVs is shown (**4A and 4B**). In the final remap, all veins were successfully isolated (**5A and 5B**).

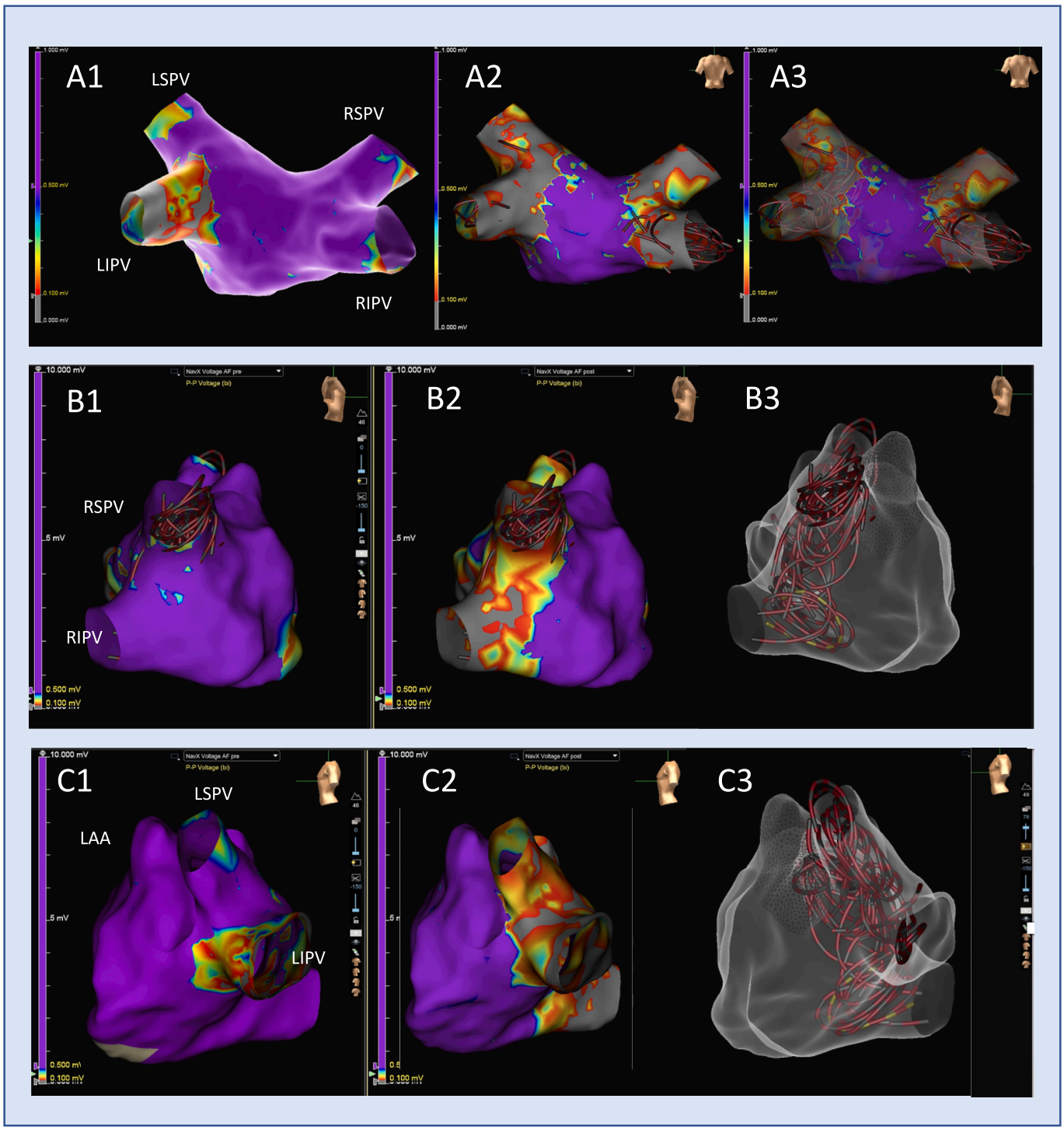

Fig. 7. Wide antral pulmonary vein isolation. A: A1: Example of Pre-ablation left atrial map created with PFA catheter. **A2:** Post-PFA left atrial map demonstrating wide antral ablation lesions and catheter positions **(A3). B:** Example of antral ablation lesion set for right pulmonary veins **B1:** pre-ablation, **B2** post-PFA and catheter positioning **B3. C:** Example of antral ablation lesion set for left pulmonary veins **C1:** pre-ablation, **C2** post-PFA and catheter positioning **C3.**

at the anterior, superior aspect of the PV [4]. Further, fluoroscopy-guided PVI with the pentaspline PFA catheter frequently resulted in insufficient isolation areas in the left anterior antral PV segments and enlarged LA isolation areas on the posterior wall in a small study of 40 patients, reported by Bohnen et al [17]. One commonality of the two devices is their over-the-wire design that leads to posterior movement of the catheter once the PV is wired, away from the anterior part of the ostium.

Therefore, this region may require a distinct ablation approach with visualization of the PFA catheter into 3D mapping systems. However, in our study, PFA lesions did not extend into the posterior wall in any patient, most likely due to the smaller catheter size and more distal PFA lesions.

Prior studies also investigated lesion characteristics of thermal balloon single-shot devices, demonstrating that balloon-guided PVI was associated with antral lesion formation [18]. Perrotta et al. reported that cryoballoon-guided PVI resulted in the largest isolated surface area [18]. Of note, we did not report on the acute lesion size in this study and no

dedicated mapping catheter was used to create 3D anatomy. Further studies and comparisons to other technologies are needed to evaluate the degree and quality of antral lesion that are created with the circular array PFA catheter.

This study did not incorporate a waiting period to evaluate potential acute reconnection of the PV following PVI with PFA. Although many Investigational Device Exemption (IDE) studies, including the PULSED-AF trial [6], have traditionally included waiting periods, it has been discussed that the standard waiting period used for thermal ablation energy sources may not be applicable to PFA. Due to the occurrence of myocardial stunning immediately after PFA, which may persist beyond the conventional 20-minute waiting period, acute PV reconnections may be missed despite a waiting period [19].

In 144 patients undergoing repeat ablation after index-PVI with a pentaspline PFA-catheter, 3D electroanatomical mapping detected 404 of 567 PVs (71 %) with durable isolation [20]. Data on chronic PVI durability and PV reconnection with the circular PFA catheter, however, are yet unknown.

4.3. Streamlining

Regarding catheter ablation of AF, PFA procedures are faster than conventional ablation

technologies with an overall comparable long-term outcome [21]. The *5-S study*, reported by Schmidt et al., demonstrated a steep learning curve with PFA in 191 AF patients that was most likely attributable to streamlining the processes of the procedure as compared to changes in the ablation time over the course of the study [3]. In the EUPORIA registry, freedom from atrial arrhythmias after PFA was independent of operator experience [22]. This underlines that PFA is easy to adapt in clinical routine. Despite the small sample size in our study, procedural duration also decreased significantly over the course of the study.

4.4. Safety

There were no complications in this study. This is in alignment with the findings of the PULSED-AF trial that demonstrated very low major complications rate of only 0.7 % [6]. PFA promises preferential myocardial ablation, sparing adjacent tissues but rare complications such as coronary spasms may occur [2,23,24]. Although phrenic nerve capture was not present with the test pulse, it was seen in all patients during ablation at the RSPV. This however did not result in any phrenic nerve palsy.

In this study, no PFA-specific complications – no renal failure, no clinical apparent coronary spasm was seen. Of note, in the published 17,000 patients of the MANIFEST-PF cohort, PFA-specific complications were rare: 0.14 % coronary spasm and 0.03 % hemolysis-related renal failure [5]. Therefore, they could have been missed in this small study cohort.

Hemolysis-related renal failure has been reported after PFA-PVI and seemed to be associated with the number of PFA applications [5,25]. Until now, hemolysis markers in patients undergoing ablation with the here used circular PFA catheter have not been reported. While renal function, haptoglobin and bilirubin showed no difference before and after ablation, pre- and post-ablation hemoglobin levels dropped and LDH levels increased in our patient cohort. However, these two markers are not specific for hemolysis only and could also be explained by other circumstances. Patients in our study were fasting for 1–2 days and periprocedural fluids were administered. This could explain the drop in hemoglobin levels. The LDH increase can not only be found in hemolysis but can also be explained by cell death and destruction of myocardial cells through ablation [26]. However, it has been reported that LDH values are higher after PF ablation as compared to radiofrequency current ablation [26]. Although renal failure after PFA is rare, it can be prevented by fluid infusions and limiting the number of PFA applications [27]. The threshold for the number of applications in patients undergoing ablation with the circular PFA catheter needs to be awaited as data are missing.

5. Limitations

The present study has a few limitations. First, the design of our single-center study was explorative and observational with a small sample size limiting the generalizability of the results. Although the study cohort is small, we were able to demonstrate the learning curve and the evaluation of the usefulness of 3D mapping was evident. Further, procedural quality may improve even further with more experience.

Only intra-procedural parameters are shown in this manuscript – no chronic PVI durability was assessed. However, the information on acute isolation rates in this study can already guide the ablation approach and possibly improve chronic PVI success. Another limitation of this study is that only the circular array PFA catheter has been used to evaluate PVI in our study. No additional mapping catheter was used to verify the findings detected by the PFA catheter. However, the circular array PFA catheter electrodes are smaller and positioned closer together compared to other PFA catheters, such as the pentaspline catheter that has shown to allow reliable endpoint assessment for PVI [28]. More studies are needed in this regard.

Next, the study consists of consecutive patients during clinical routine, no randomization was performed.

6. Conclusion

The circular PFA-catheter allows for fast and efficient PVI. A fluoroscopy-only approach creates distal PV ablation lesions that are associated with insufficient isolation and residual conduction along the carina and anterior aspect of the PV. However, with visualization and mapping, creation of wide antral ablation lesions is feasible without prolonging procedural duration.

7. Financial support

none.

CRediT authorship contribution statement

Melanie A. Gunawardene: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jens Hartmann:** Writing – original draft, Resources, Conceptualization. **Jannis Dickow:** Writing – review & editing, Resources, Investigation. **Rahin Wahedi:** Writing – review & editing, Investigation. **Tim Harloff:** Writing – review & editing, Investigation. **Johanna Jezuit:** Writing – review & editing, Investigation. **Eike P. Tigges:** Writing – review & editing, Visualization, Resources, Investigation. **Mario Jularic:** Writing – review & editing, Resources, Investigation. **Borislav Dinov:** Writing – review & editing, Conceptualization. **Nele Gessler:** Writing – review & editing, Resources, Project administration, Investigation, Conceptualization. **Stephan Willems:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors thank the St. Georg Heart Staff Team, including all co-

workers of the hospital who are involved in planning and conducting these ablation procedures.

Disclosures regarding this study: MG consultant and advisory board member of Medtronic, Boston Scientific and Abbott, SW consultant Boston Scientific, Abbott

References

[1] K.-R.-J. Chun, D. Miklavčič, K. Vlachos, S. Bordignon, D. Scherr, P. Jais, et al., State-of-the-art pulsed field ablation for cardiac arrhythmias: ongoing evolution and future perspective, Europace 26 (6) (2024 Jun).

[2] V.Y. Reddy, P. Neuzil, J.S. Koruth, J. Petru, M. Funosako, H. Cochet, et al., Pulsed Field Ablation for Pulmonary Vein Isolation in Atrial Fibrillation, J Am Coll Cardiol. 74 (3) (2019) 315–326.

[3] B. Schmidt, S. Bordignon, S. Tohoku, S. Chen, F. Bologna, 5S Study : Safe and Simple Single Shot Pulmonary Vein Isolation with Pulsed Field Ablation Using Sedation. June (2022).

[4] M.A. Gunawardene, B.N. Schaeffer, M. Jularic, C. Eickholt, T. Maurer, U.F. Pape, et al., Pulsed - field ablation combined with ultrahigh - density mapping in patients undergoing catheter ablation for atrial fibrillation : Practical and electrophysiological considerations, J Cardiovasc Electrophysiol. 33 (3) (2022) 345–356.

[5] E. Ekanem, P. Neuzil, T. Reichlin, J. Kautzner, P. van der Voort, P. Jais, et al., Safety of pulsed field ablation in more than 17,000 patients with atrial fibrillation in the MANIFEST-17K study, Nat Med. 30 (7) (2024 Jul) 2020–2029.

[6] A. Verma, D.E. Haines, L.V. Boersma, N. Sood, A. Natale, F.E. Marchlinski, et al., Pulsed Field Ablation for the Treatment of Atrial Fibrillation: PULSED AF Pivotal Trial, Circulation 147 (2023) 1422–1432.

[7] A. Verma, D.E. Haines, L.V. Boersma, N. Sood, A. Natale, F.E. Marchlinski, et al., Pulsed Field Ablation for the Treatment of Atrial Fibrillation: PULSED AF Pivotal Trial, Circulation 147 (19) (2023 May) 1422–1432.

[8] S. Tzeis, E.P. Gerstenfeld, J. Kalman, E.B. Saad, A. Sepehri Shamloo, J.G. Andrade, et al., 2024 European Heart Rhythm Association/Heart Rhythm Society/Asia Pacific Heart Rhythm Society/Latin American Heart Rhythm Society expert consensus statement on catheter and surgical ablation of atrial fibrillation, Europace 1 (26) (2024 Apr) 1–107.

[9] K.-H. Kuck, J. Brugada, A. Fürnkranz, A. Metzner, F. Ouyang, K.R.J. Chun, et al., Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation, N Engl J Med. 9(374(23)):2235–45 (2016).

[10] K.J. Chun, B. Schmidt, A. Metzner, R. Tilz, T. Zerm, I. Koester, et al., The " single big cryoballoon " technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation : a prospective observational single centre study, Eur Heart J. 15–8 (2008).

[11] S.Y. Ho, J.A. Cabrera, D. Sanchez-Quintana, Left atrial anatomy revisited, Circ Arrhythm Electrophysiol. 5 (1) (2012 Feb) 220–228.

[12] H.L. Estner, I. Deisenhofer, A. Luik, G. Ndrepepa, C. von Bary, B. Zrenner, et al., Electrical isolation of pulmonary veins in patients with atrial fibrillation: reduction of fluoroscopy exposure and procedure duration by the use of a non-fluoroscopic navigation system (NavX), Eur Eur Pacing, Arrhythmias, Card Electrophysiol J Work Groups Card Pacing, Arrhythmias, Card Cell Electrophysiol Eur Soc Cardiol. 8 (8) (2006 Aug) 583–587.

[13] A. Voskoboinik, E.S. Kalman, Y. Savicky, P.B. Sparks, J.B. Morton, G. Lee, et al., Reduction in radiation dose for atrial fibrillation ablation over time: A 12-year single-center experience of 2344 patients, Heart Rhythm 14 (6) (2017 Jun) 810–816.

[14] Badertscher P, Serban T, Isenegger C, Krisai P, Voellmin G, Osswald S, et al. Role of 3D electro-anatomical mapping on procedural characteristics and outcomes in pulsed-field ablation for atrial fibrillation. EP Eur [Internet]. 2024 Apr 1;26(4): euae075. Available from: Doi: 10.1093/europace/euae075.

[15] A. Enriquez, L.C. Saenz, R. Rosso, F.E. Silvestry, D. Callans, F.E. Marchlinski, et al., Use of Intracardiac Echocardiography in Interventional Cardiology: Working With the Anatomy Rather Than Fighting It, Circulation 137 (21) (2018 May) 2278–2294.

[16] A. Russo, C. Tondo, V. Schillaci, M. Casella, S. Iacopino, S. Bianchi, et al., Intracardiac echocardiography-guided pulsed-field ablation for successful ablation of atrial fibrillation: a propensity-matched analysis from a large nationwide multicenter experience, J Interv Card Electrophysiol an Int J Arrhythm Pacing 67 (5) (2023) 1257–1266, https://doi.org/10.1007/s10840-023-01699-2.

[17] M. Bohnen, R. Weber, J. Minners, A. Jadidi, M. Eichenlaub, F.-J. Neumann, et al., Characterization of circumferential antral pulmonary vein isolation areas resulting from pulsed-field catheter ablation, Europace 25 (1) (2023 Feb) 65–73.

[18] L. Perrotta, A. Konstantinou, S. Bordignon, A. Fuernkranz, D. Dugo, K.J. Chun, et al., What Is the Acute Antral Lesion Size After Pulmonary Vein Isolation Using Different Balloon Ablation Technologies? Circ J. 81 (2) (2017 Jan) 172–179.

[19] A. Verma, S.J. Asivatham, T. Deneke, Q. Castellvi, R.E. Neal 2nd, Primer on Pulsed Electrical Field Ablation: Understanding the Benefits and Limitations, Circ Arrhythm Electrophysiol. 14 (9) (2021 Sep) e010086.

[20] T. Kueffer, S. Bordignon, K. Neven, Y. Blaauw, J. Hansen, R. Adelino, et al., Durability of Pulmonary Vein Isolation Using Pulsed-Field Ablation: Results From the Multicenter EU-PORIA Registry, JACC Clin Electrophysiol. 10 (4) (2024 Apr) 698–708.

[21] V.Y. Reddy, E.P. Gerstenfeld, A. Natale, W. Whang, F.A. Cuoco, C. Patel, et al., Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation, N Engl J Med. 389 (18) (2023) 1660–1671.

[22] Schmidt B, Bordignon S, Neven K, Reichlin T, Blaauw Y, Hansen J, et al. EUropean real-world outcomes with Pulsed field ablatiOn in patients with symptomatic atRIAl fibrillation : lessons from the multi-centre EU-PORIA registry. Europace [Internet]. 2023;25(7):1–11. Available from: Doi: 10.1093/europace/euad185.

[23] H. Cochet, Y. Nakatani, S. Sridi-cheniti, G. Cheniti, F.D. Ramirez, T. Nakashima, et al., Pulsed field ablation selectively spares the oesophagus during pulmonary vein isolation for atrial fibrillation, Europace (2021) 1–9.

[24] Gunawardene MA, Schaeffer BN, Jularic M, Eickholt C, Maurer T, Akbulak RÖ, et al. Coronary Spasm During Pulsed Field Ablation of the Mitral Isthmus Line. JACC Clin Electrophysiol. 2021;Sep 23;S2405-500X(21)00785-4.

[25] Venier S, Vaxelaire N, Desbiolles A, Garban F, Jacon P, Carabelli A, et al. Severe acute kidney injury related to haemolysis after pulsed field ablation for atrial fibrillation. Europace [Internet]. 2024;26(1):1–9. Available from: Doi: 10.1093/europace/euad371.

[26] P. Osmancik, B. Bacova, D. Herman, M. Hozman, I. Fiserova, S. Hassouna, et al., Periprocedural Intravascular Hemolysis During Atrial Fibrillation Ablation: A Comparison of Pulsed Field With Radiofrequency Ablation, JACC Clin Electrophysiol. 10 (7 Pt 2) (2024 Jul) 1660–1671.

[27] S. Mohanty, M. Casella, P. Compagnucci, P.G. Torlapati, D.G. Della Rocca, V.M. La Fazia, et al., Acute Kidney Injury Resulting From Hemoglobinuria After Pulsed-Field Ablation in Atrial Fibrillation: Is it Preventable? JACC Clin Electrophysiol. 10 (4) (2024 Apr) 709–715.

[28] T. Kueffer, S.H. Baldinger, H. Servatius, A. Madaffari, J. Seiler, A. Muehl, et al., Validation of a multipolar pulsed field ablation catheter for endpoint assessment in pulmonary vein isolation procedures, EP Eur [internet]. (2022), https://doi.org/10.1093/europace/euac053.201. May 18;24(Supplement_1):euac053.201. Available from:.