

Výsledky studie Affera SPHERE 360 & výhled do budoucna

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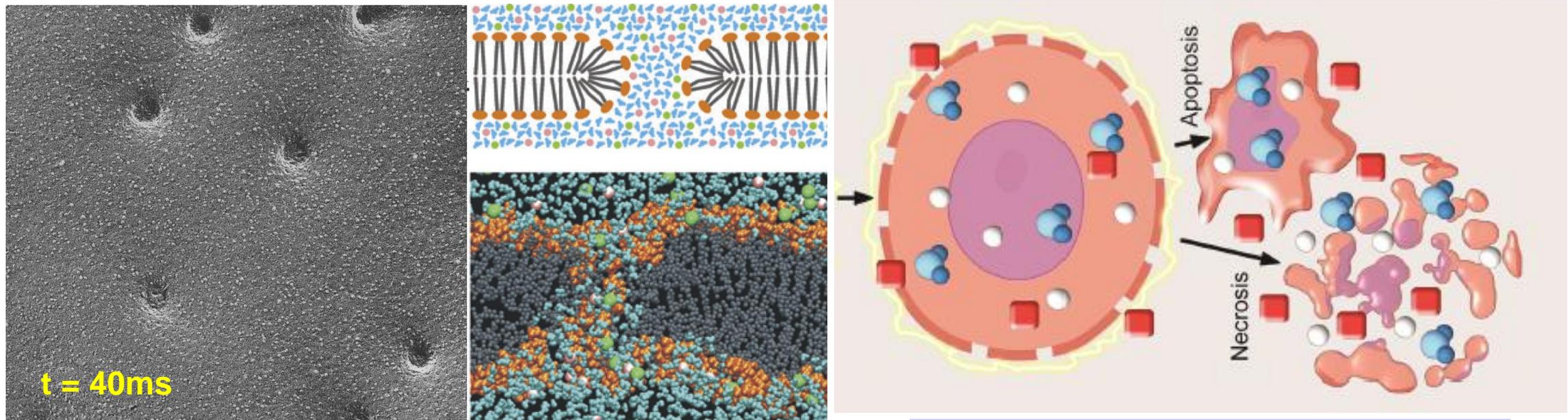
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Pulsed Field Ablation (PFA)

Fundamentals: Electroporation

- Application of intermittent, high-intensity electric fields for micro/*nano*- seconds
- Destabilizing electric potential results in cellular and tissue electroporation
- Formation of nanoscale cell membrane defects
- Pores leads to permeabilization & Cell death



E.Maor et al, *Heart Rhythm* DOI: <https://doi.org/10.1016/j.hrthm.2019.01.012> (2018)

ML Yarmush et al, *Annu. Rev. Biomed. Eng.* 16:295–320 (2014)

Chang DC, Reese TS., *Biophys J.* 58:1–12 (1990)



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Challenges for Pulsed Field Ablation (PFA)

Fundamentals: Electroporation

- **Controlling lesion size, shape and direction ?? Can we titrate to effect**
- **Complete vs incomplete ablation ? How can you tell ? (reversible vs non-transmural)**
- **Inadvertent ablation**
 - Sinus/AV node suppression
 - Coronary spasm/injury
 - Transient phrenic nerve palsy- duration?
 - Parahisian / outflow tract and epicardial ablation
- **Excessive ablation- too easy, catheters too big ?**
- **Efficacy in scarred myocardium-**
- **Proximity to conductive material : CIED/Stents/LAAO**
- **Myocardial activation, risk of VT/VF**



Why We Need to Apply RF/PF?

RF & PF Capabilities

Pulse Field

- Non-thermal lesions
- Larger reversibly affected volume
- Longer recovery period of reversibly affected area vs. Radiofrequency
- Low collateral damage risks (ability to be myocardium specific)
- Lesion stacking associated with higher lesion volume and durability, at lower potential risks
- Lower effect in ganglionic plexi

Radiofrequency

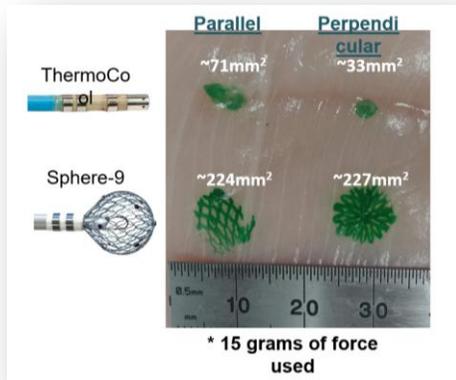
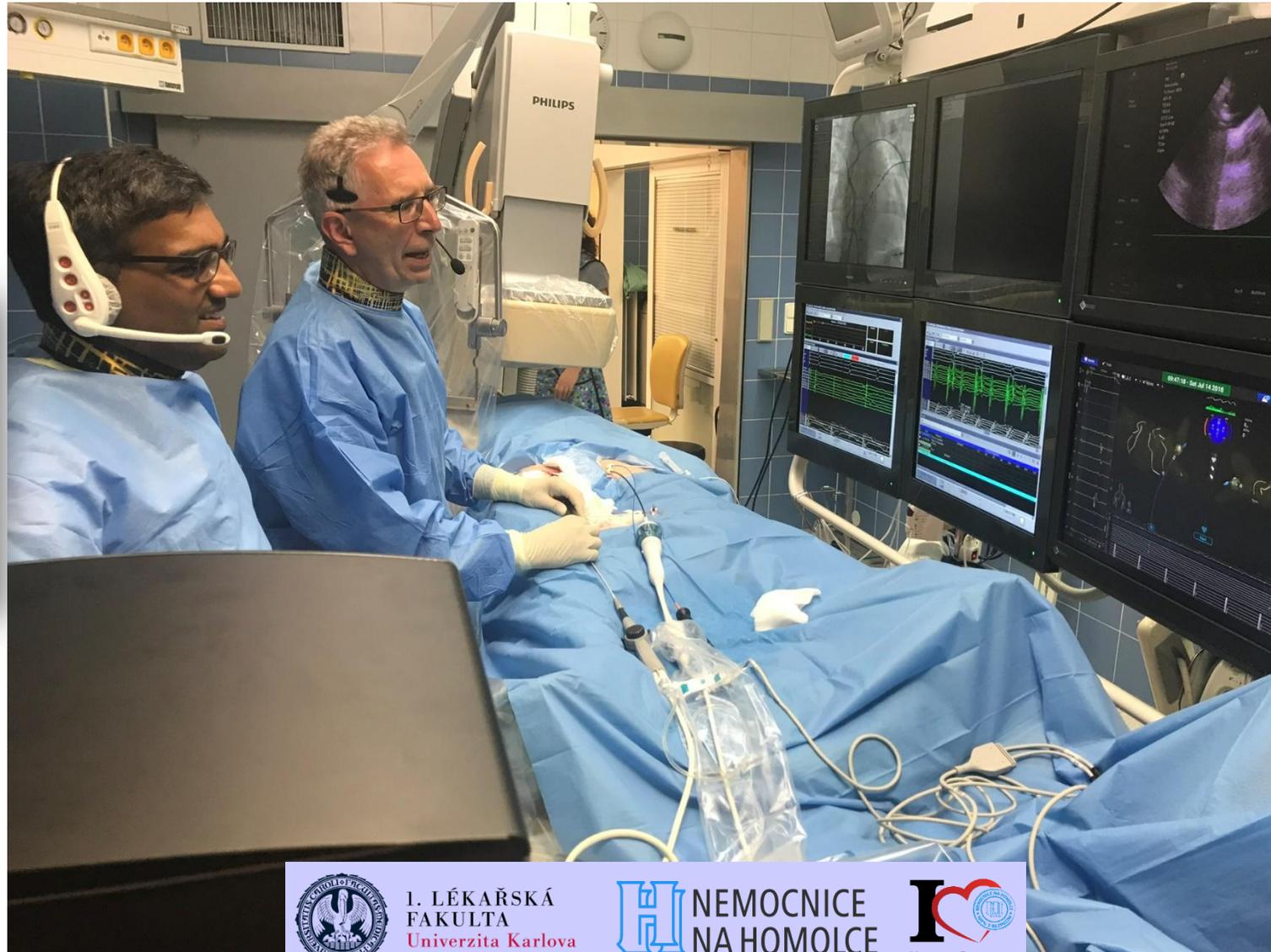
- Thermal lesion influenced by cooling in high blood flow areas
- Smaller reversibly affected volume
- Shorter recovery period of reversibly affected area Vs. Pulse Field
- Higher collateral damage risks (mechanism of thermal damage)
- Lesion stacking associated with potential risks (steam pop or damage to collateral structures)
- Higher effect in ganglionic plexi



Lattice-Tip RF Ablation Catheter

The „First in Man“ Series

14.7. 2018



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KARDIOCENTRUM

Conformable PFA Catheter

Device Description

● Rotation Free Ablation

- 4 applications per PV

● Tissue Conformable Lattice Tip

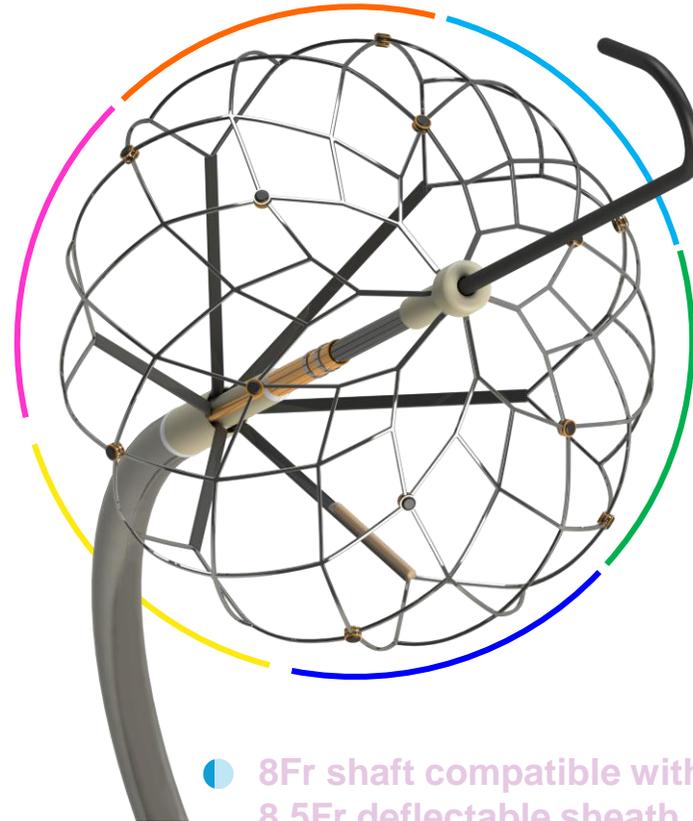
- Energy delivered thru the entire lattice

● All-in-One Mapping and Ablation

- **6 bipolar electrode pairs** provide pacing, EGM sensing, mapping and stimulation
- **Local impedance measurement** for catheter and tissue proximity
- **Single transeptal puncture**

● Electromagnetic Sensors

- Allow tracking, shape visualization, catheter orientation, tagging, & EAM/activation/voltage mapping



● 8Fr shaft compatible with 8.5Fr deflectable sheath

- Over-the-wire design

● 6 Sections

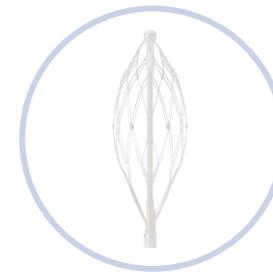
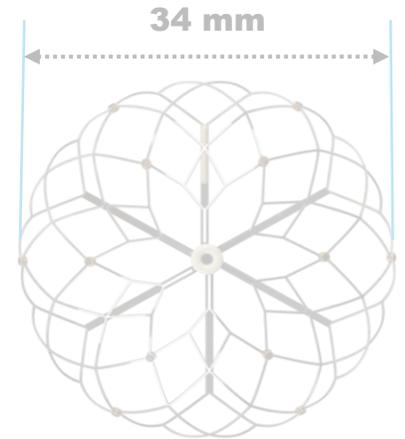
- Independently and sequentially energized

● Shape Adapting Design

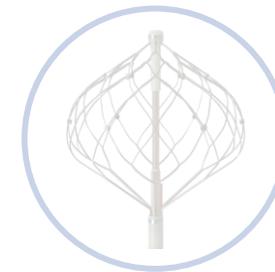
- Expandable to 34 mm
- Adaptable to varying PV anatomies

● Unipolar Biphasic Waveform

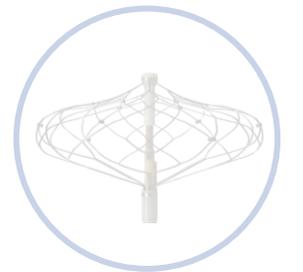
- 5.9 sec per application



Linear



Sphere



Disc

Expand/collapse to various shapes



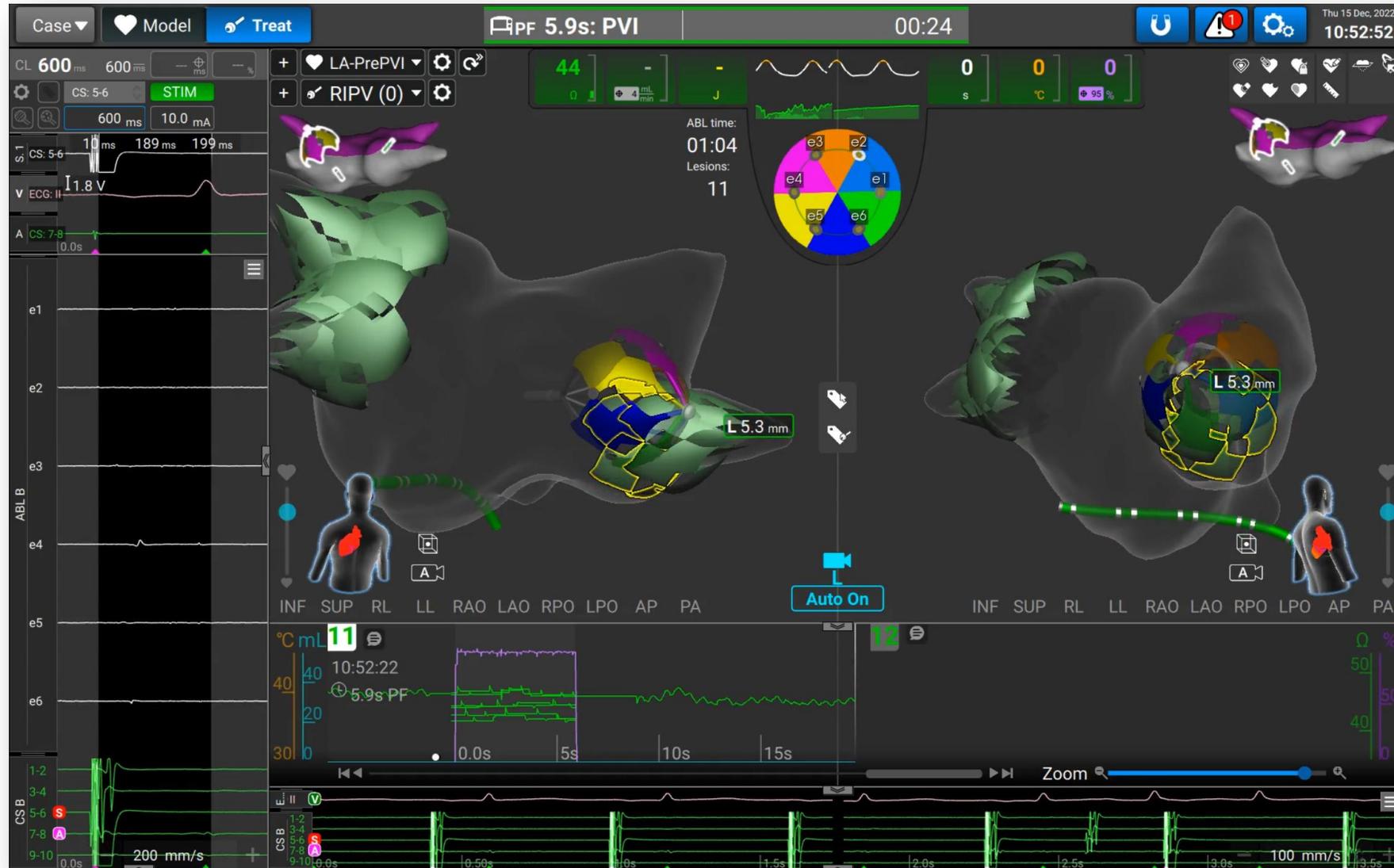
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Conformable PFA Catheter

Guided by EAM System



FIH Clinical Trial

Objective and Study Design

Objective: to evaluate the safety and efficacy of PVI conducted with Affera Sphere-360 ablation system for treating paroxysmal atrial fibrillation in a prospective, multi-center study

Design:

- Index PFA procedure with Sphere-360 Catheter
- PVI with **~4 applications per PV**
- Optional **Day 75 invasive remapping procedure**

		Blanking period			Post-blanking period								
		1-M	2-M	3-M	4-M	5-M	6-M	7-M	8-M	9-M	10-M	11-M	12-M
All pts	Visits	X		X			X						X
(n=85)	TTM				Weekly & symptomatic		Monthly and symptomatic						
	24h Holters						X						X
(n=15)	ILR*	Continuous monitoring → Simulated Holter / TTM Follow-Up											

*Subcohort with ILR had them implanted a median of 43 days prior to the ablation. Analysis of ILR data was performed using EGMs to simulate the TTM and HM schedule and also sub-analysis using full continuous EGM monitoring data were employed in determining recurrence and burden.



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FIH Clinical Trial

Clinical Study Outcomes

Primary

- Efficacy: Acute electrical isolation of all PVs using study device
- Safety: Incidence of prespecified serious device-related adverse events following index ablation procedure

Secondary

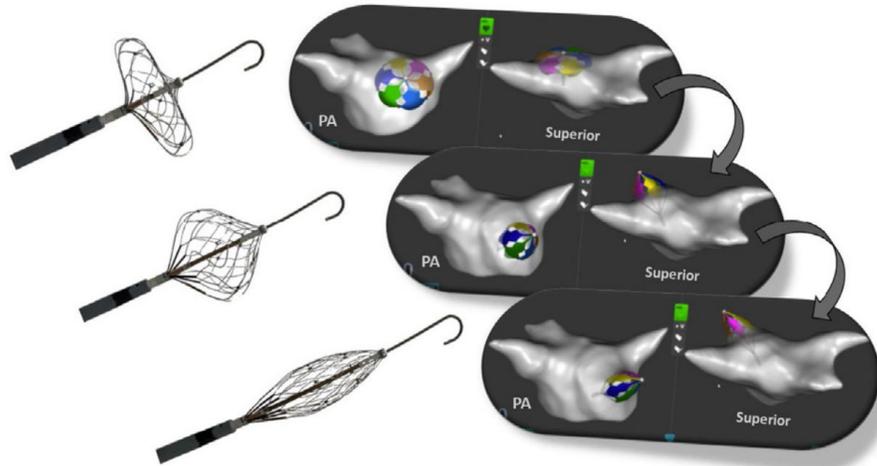
- Chronic (12-month) freedom from atrial arrhythmia recurrence
- Proportion of subjects experiencing device- or procedure-related adverse events
- **Lesion durability** by invasive remapping



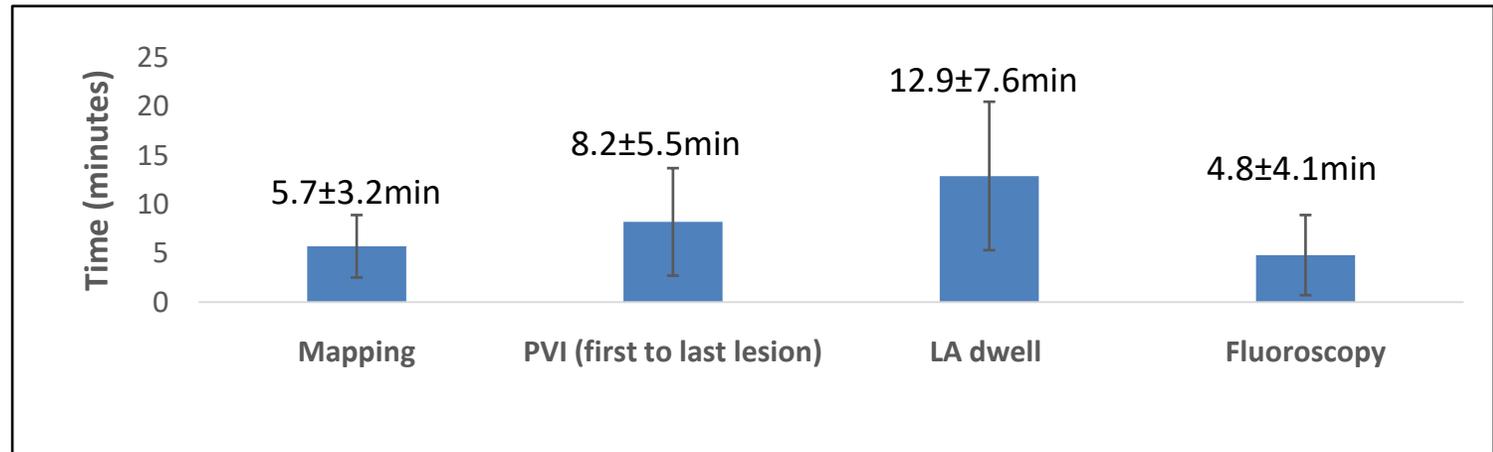
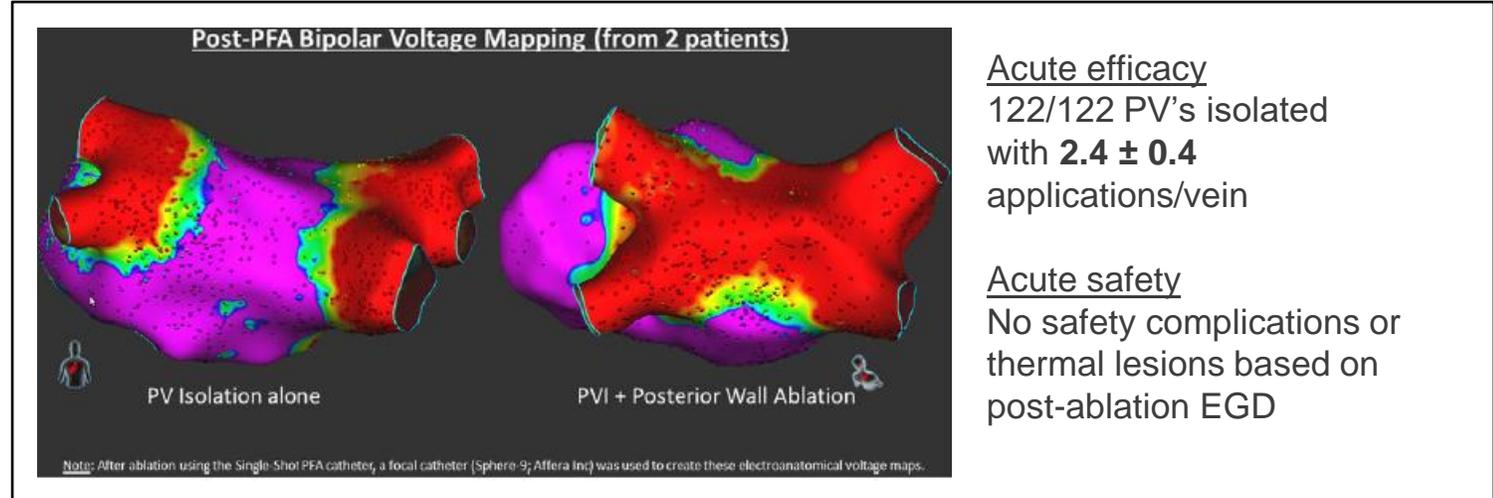
"Single-Shot" PFA Catheter for Ablation integrating Mapping

- 30 patients treated in first-in-human clinical trial at 3 centers with 5 operators: NCT05144503 and NCT05115214

Anatomical Rendering of RIPV by changing shape and advancing catheter into veing



- **Sphere-PVI: 8-Fr single-shot** large lattice catheter
- Compressible/conformable lattice framework expandable **up to 34 mm diameter**
- 6 sections independently and sequentially energized for ablation
- PV anatomy using Affera™ Mapping Software
- Bi-phasic pulse trains of 5sec, 1.3-2.0 kV



Reddy, Vivek Y., et al. FIH CLINICAL EXPERIENCE OF A NOVEL CONFORMABLE" SINGLE-SHOT" PFA CATHETER FOR PULMONARY VEIN ISOLATION." Heart Rhythm 19.5 (2022): S142.

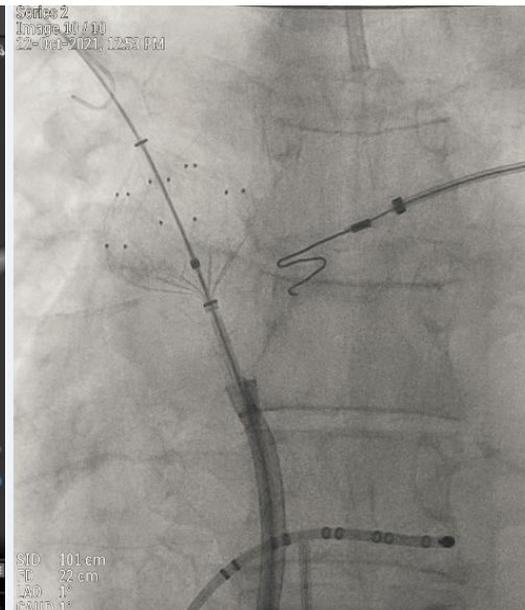
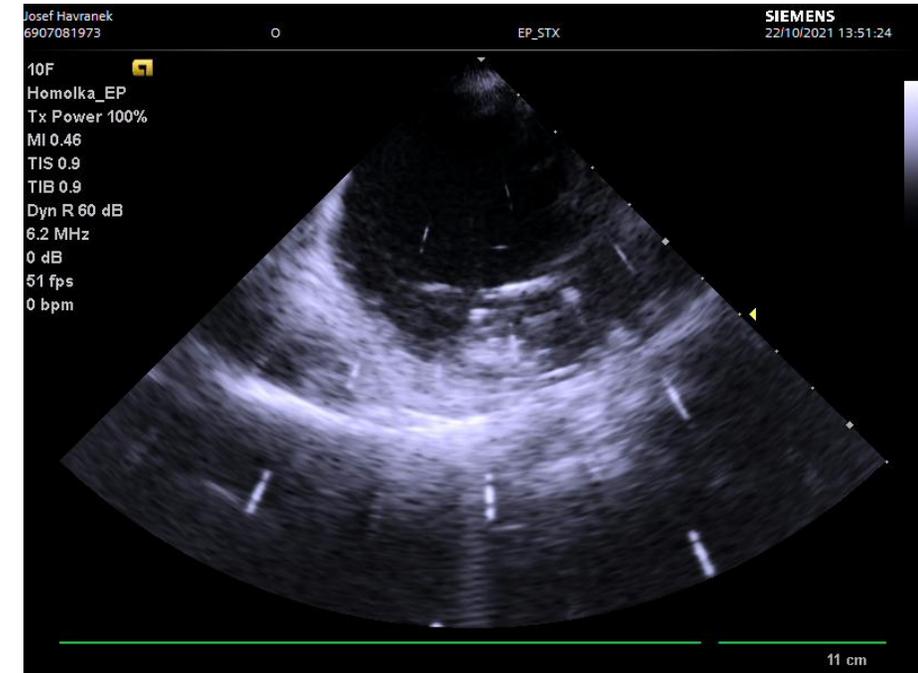
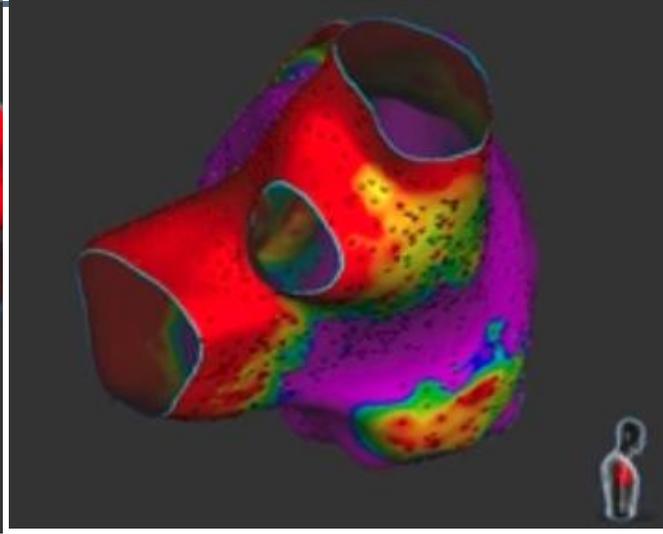
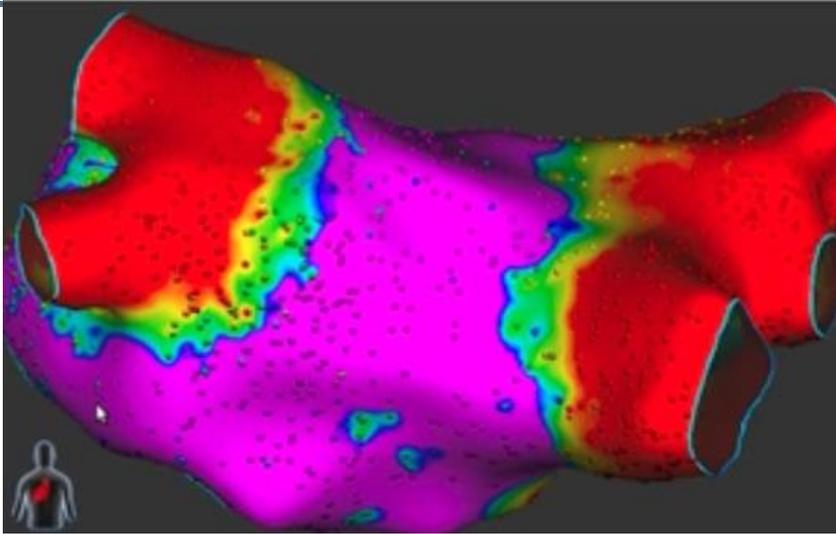


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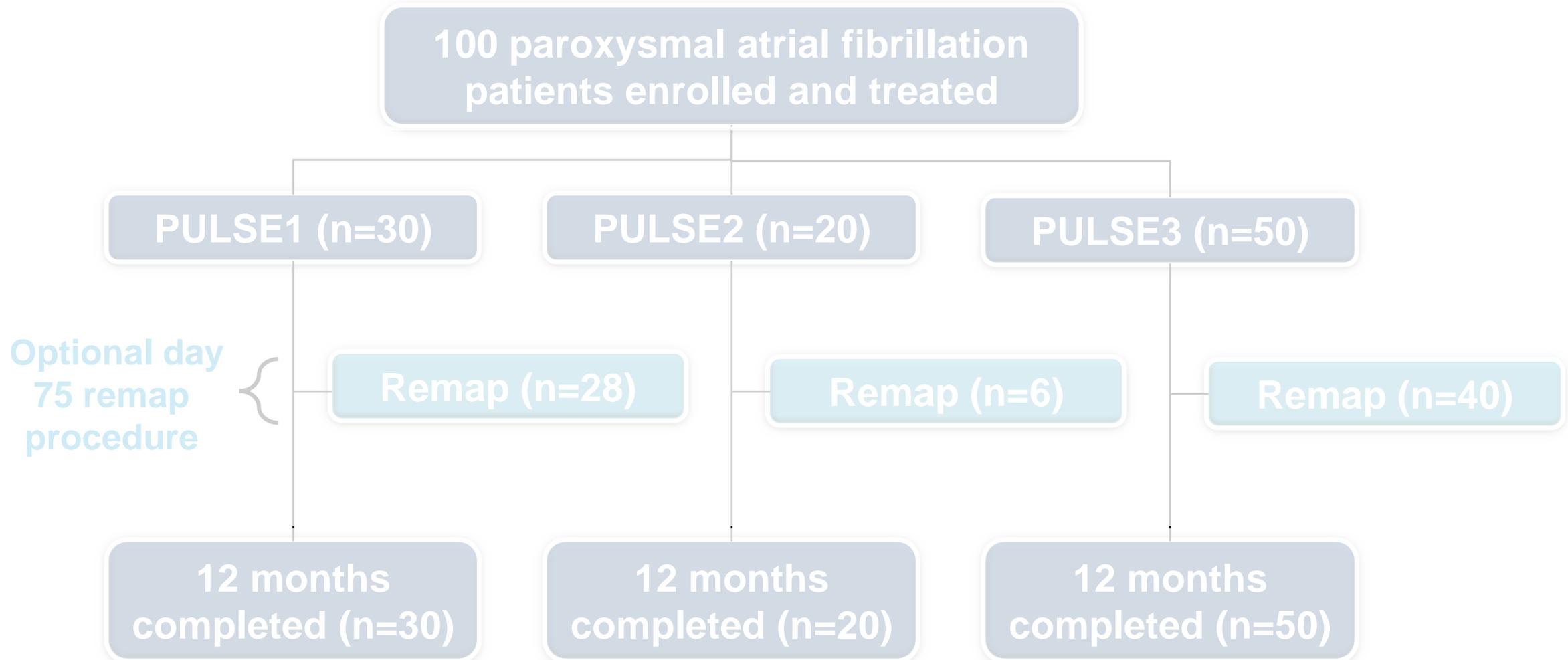
"Single-Shot" PFA Catheter for Ablation integrating Mapping



First-in-Human Clinical Experience Of A Novel Conformable 'Single-Shot' Pulsed Field Ablation Catheter For Pulmonary Vein Isolation.
V.Reddy, G.Rackauscas, J.Kautzner, P.Neuzil, HRS 2022

FIH Clinical Trial

Subject Flow



96.3% TTM and 100% Holter monitoring compliance

FIH Clinical Trial

Baseline and Procedural Characteristics

Selected Baseline Characteristics	Total Cohort (n = 100)
Male sex	60 (60%)
Age (years)	58.4 ± 10.6
Time from AF diagnosis to enrollment (years) *	3.4 ± 3.7
Left atrial diameter (mm)	41.0 ± 4.4
Left ventricular ejection fraction (%) †	59.7 ± 5.7
Body mass index (kg/m ²)	29.1 ± 4.2
Diabetes (Type 2)	7 (7%)
Hypertension	70 (70%)
CHA ₂ DS ₂ -VASc †	1.8 ± 1.3
Prior antiarrhythmic Class I-IV drugs †	99 (100%)

*Data available for 95 patients

†Data available for 99 patients

Selected Procedural Characteristics	Total Cohort (n = 100)
Procedure time (minutes) *	57.9 ± 20.6
Fluoroscopy time (minutes) †	6.8 ± 5.7
Left atrial dwell time (minutes) ‡	22.2 ± 11.8
Transpired ablation time (minutes) #	11.5 ± 7.1
PVI application time (minutes)	1.5 ± 0.5
Number of applications per PV	4.0 ± 1.3

* Includes a 20-minute wait period or infusion of adenosine

† 4 patients with zero fluoroscopy, 26 with ≤ 3 minutes of fluoroscopy

‡ Includes mapping time

Time from first to last application

Numbers are presented as Number of Subjects (% Subjects) or Mean ± SD



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Safety

Primary and Secondary Events

Primary and Secondary Safety Events		Total Cohort (n = 100)
Primary Safety Endpoint (device-related SAEs)	Subjects with any primary safety event	0 (0%)
	Within 7 days	
	Death	0
	Myocardial infarction	0
	Persistent phrenic nerve palsy	0
	Transient ischemic attack	0
	Stroke/cerebrovascular accident	0
	Thromboembolism	0
	Major vascular access complications/bleeding	0
	Heart block	0
	Gastroparesis	0
	Severe pericarditis	0
	Hospitalization (initial and prolonged) due to cardiovascular or pulmonary AE*	0
	Within 30 days	
Cardiac tamponade/perforation†	0	
Within 180 days		
Pulmonary vein stenosis‡	0	
Atrio-esophageal fistula‡	0	
Secondary Safety Outcome (device/procedure-related SAEs)	Diplopia and vertigo	1 (1%)

* Occurring up to 30 days after index ablation is considered primary safety event

† Occurring up to 180 days after index ablation is considered primary safety event

‡ Symptom remission in 2 days. MRI evaluation ruled out embolic event

Safety

Other Analyses

	Assessment	Total Cohort (n = 100)
Esophageal sub-study (n=18)	Esophageal observations	
	Minor erythema*	1 (6%)
	Injury to mucosa*	1 (6%)
	Post-anesthesia intubation irritation†	1 (6%)
	Thermal injuries	0 (0%)
Brain MRI sub-study (n=40)	Brain MRI findings	
	Acute ischemia with FLAIR hyperintensity ‡	4 (10%)
	Acute ischemia without FLAIR hyperintensity ‡	3 (8%)

* Incidental findings not device- or procedure-related

† Procedure-related

‡ Mutually exclusive

Numbers are presented as Number of Subjects (% Subjects)



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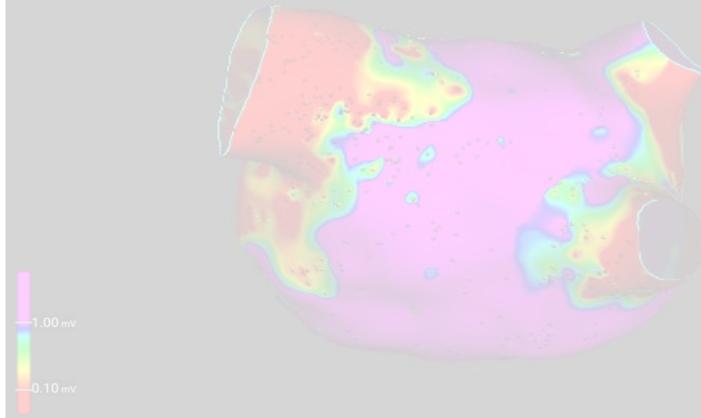
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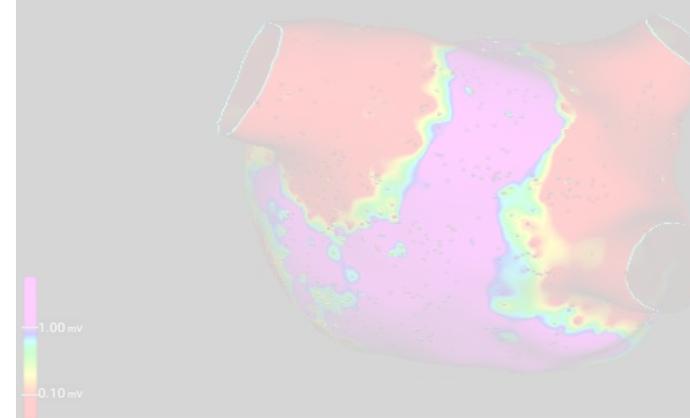
Outcomes

Electroanatomical Maps

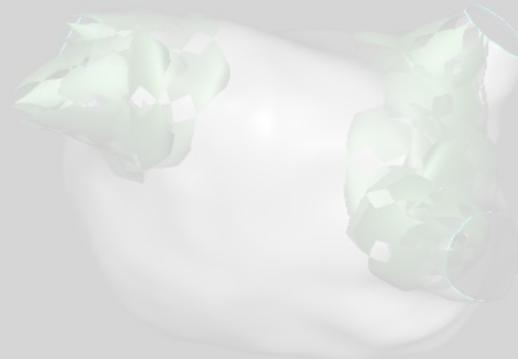
Pre-ablation



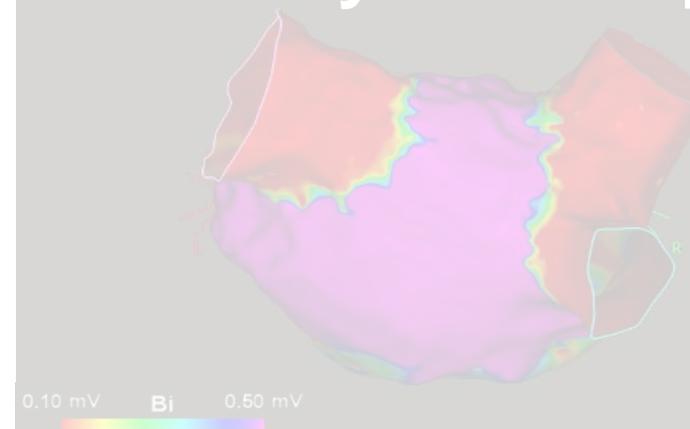
Post-ablation



Ablation tags

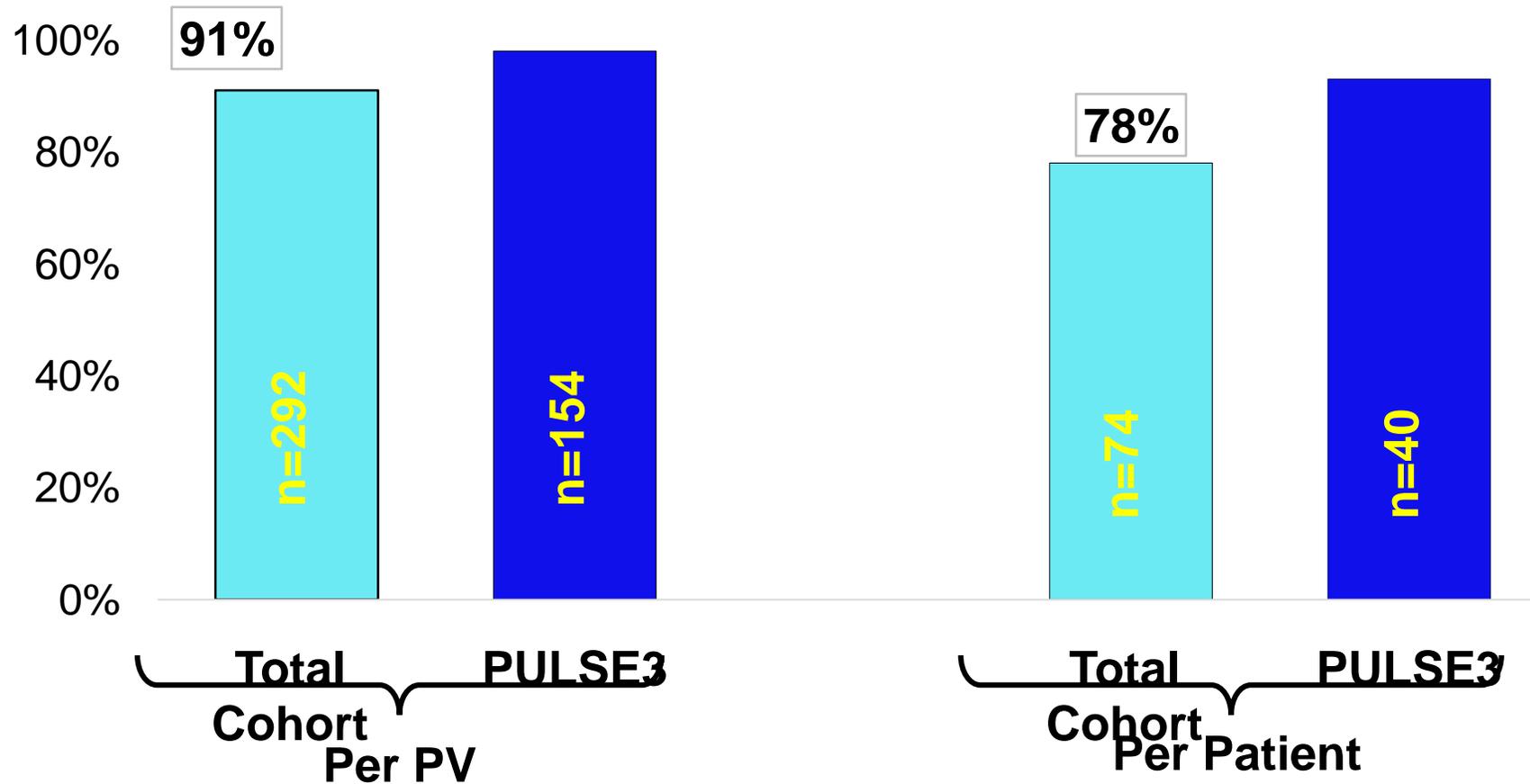


Day 75 remap



Durability of PVI

Remapping after 75 Days

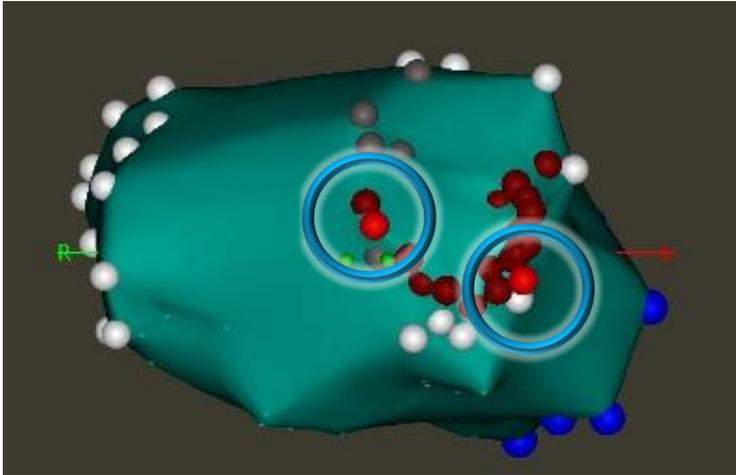


Only 3 reconnected PVs when treated with PULSE3

Durability of PVI

PULSE3 Reconnections

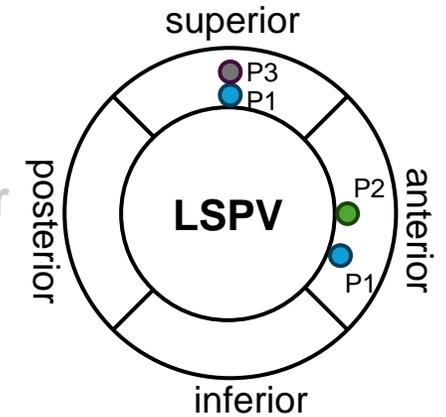
Patient 1



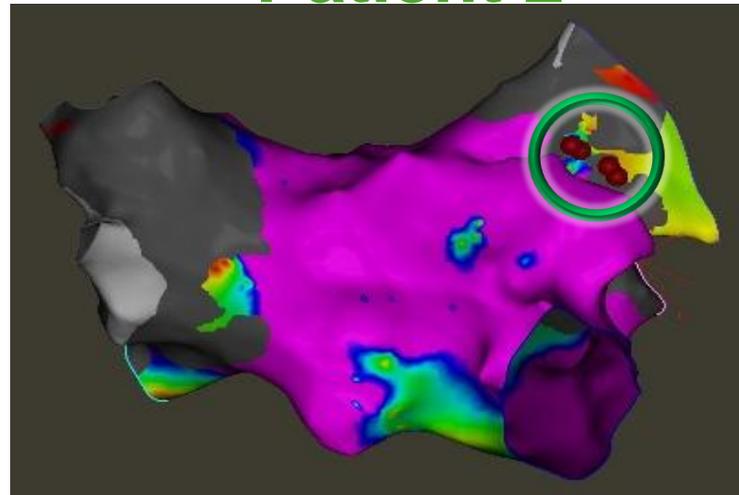
Three Reconnected PVs in 3 PULSE3 patients

- Only 3 reconnections (encompassing 4 gaps) out of 154 treated PVs, all LSPVs
- All reconnections occurred in **anterior/superior** aspect of the LSPV
- 2 of 3 veins were reconnected at discrete gaps, that were re-isolated with 1st RF delivery

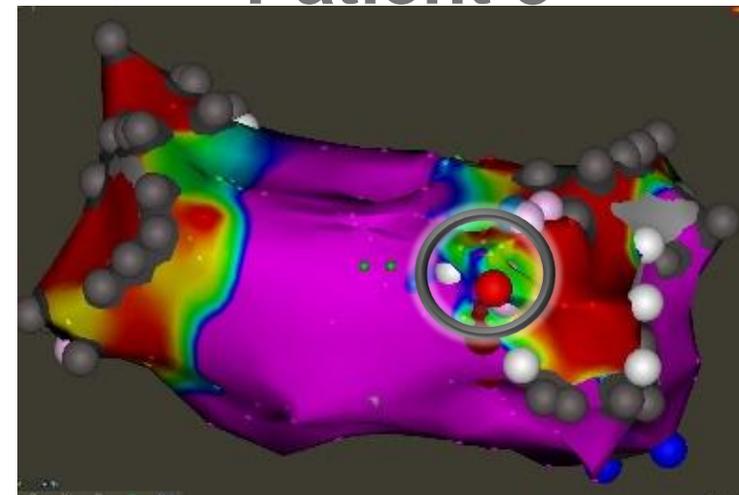
Gap Locations



Patient 2



Patient 3



Outcomes

Primary and Secondary Effectiveness

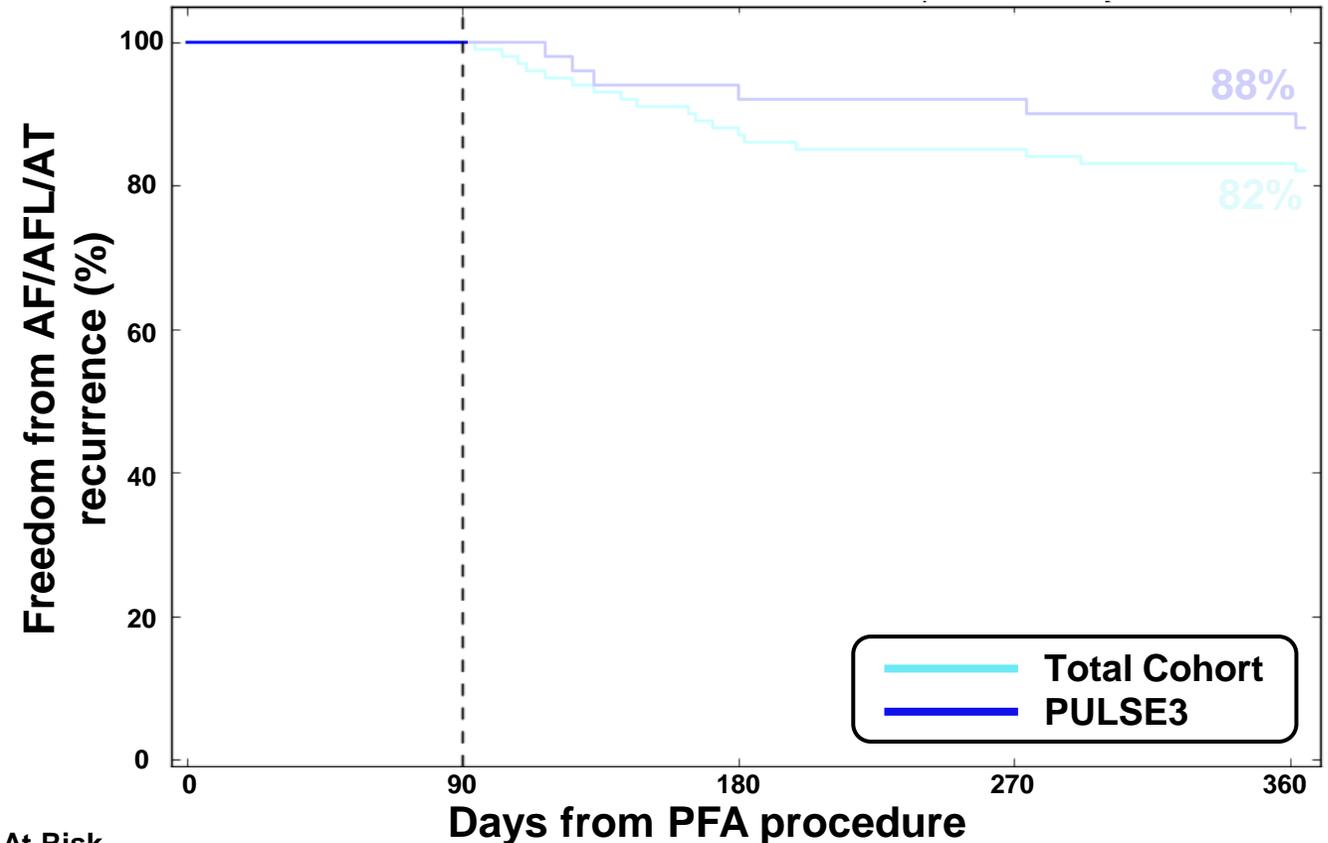
Acute success: 100% (n=395)
All targeted PVs were successfully isolated.

Kaplan-Meier estimate

Includes data from TTMs, Holter monitoring, or from simulated ILR

Total Cohort: 82%
(95% CI: 73.0 – 88.3%)

PULSE3: 88%
(95% CI: 75.2– 94.4%)

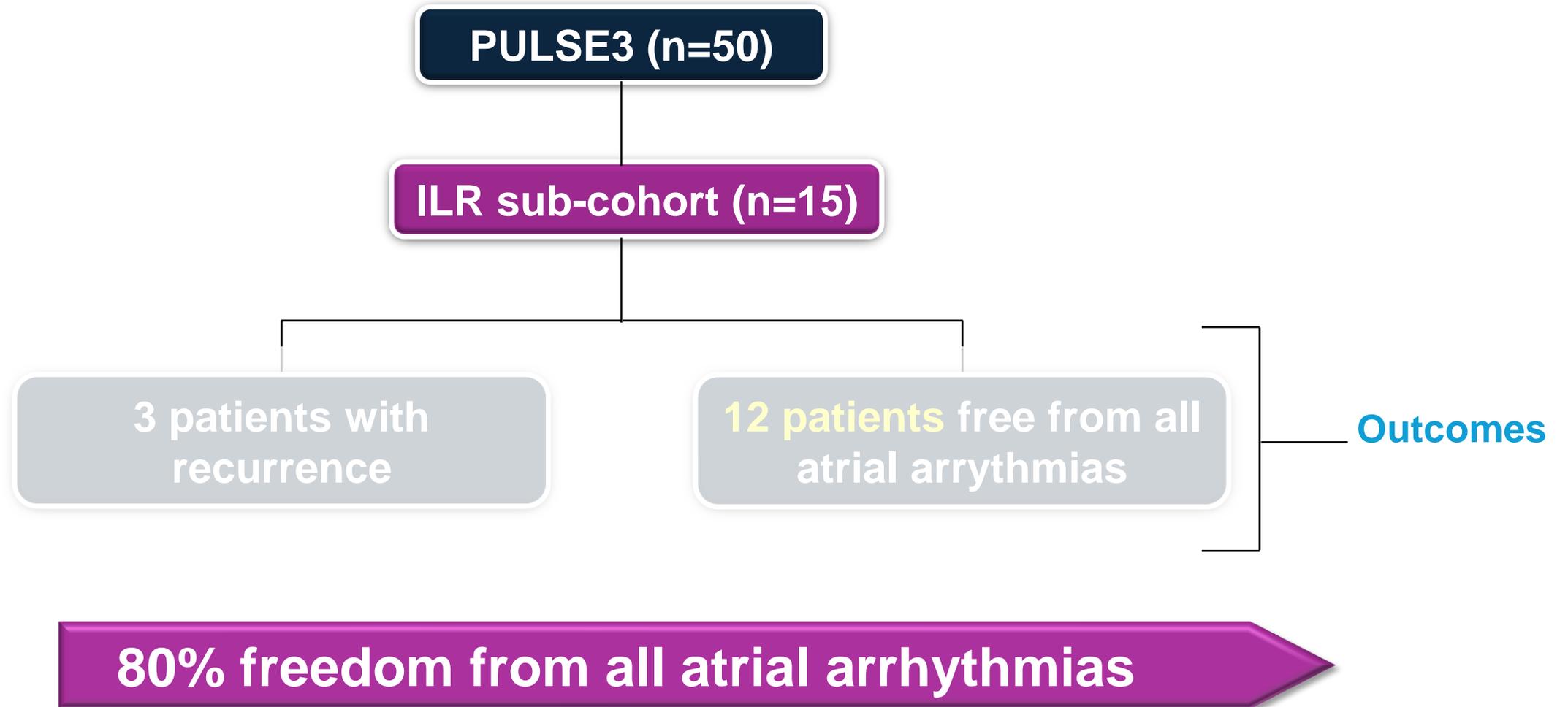


Number At Risk

Total Cohort	100	100	82	67	66
PULSE3	50	50	41	28	28

PULSE3 ILR Sub-study (n=15)

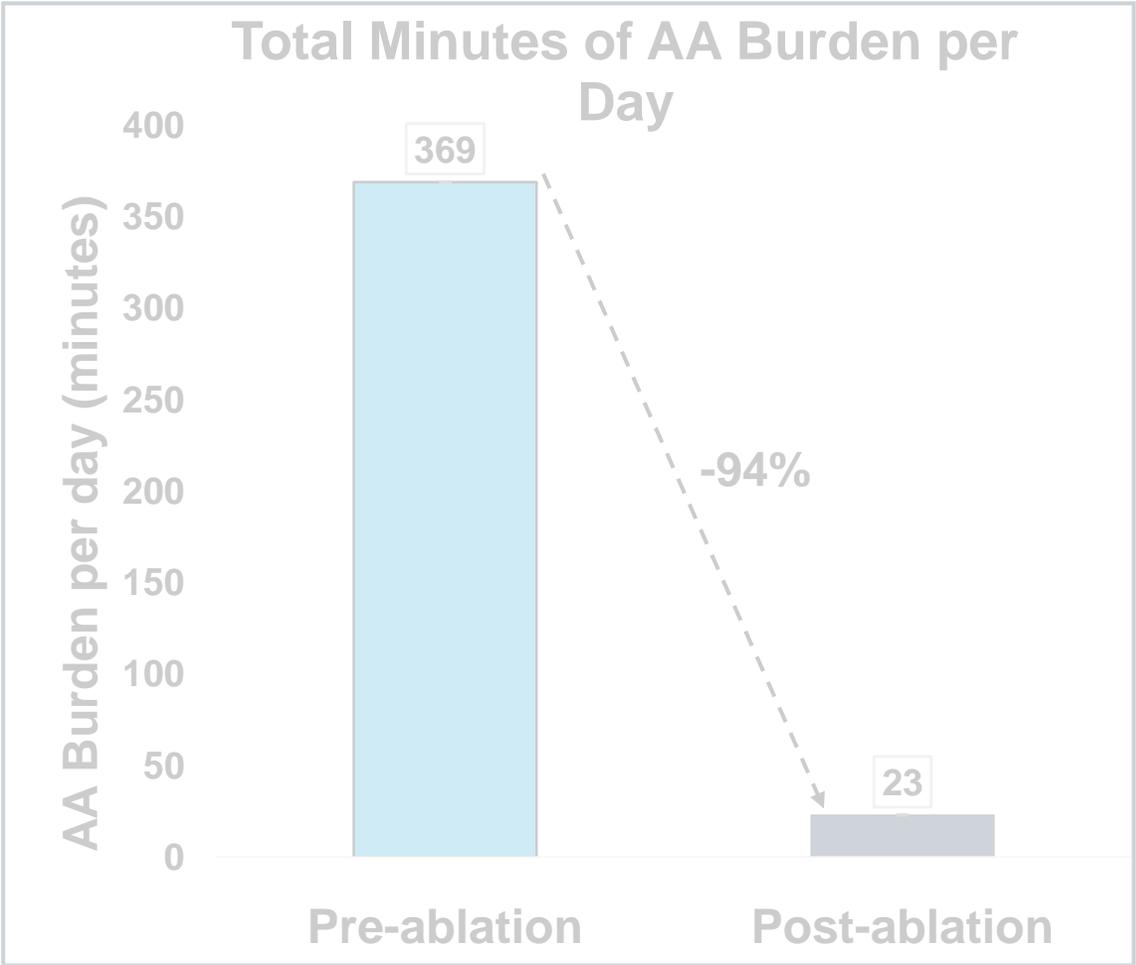
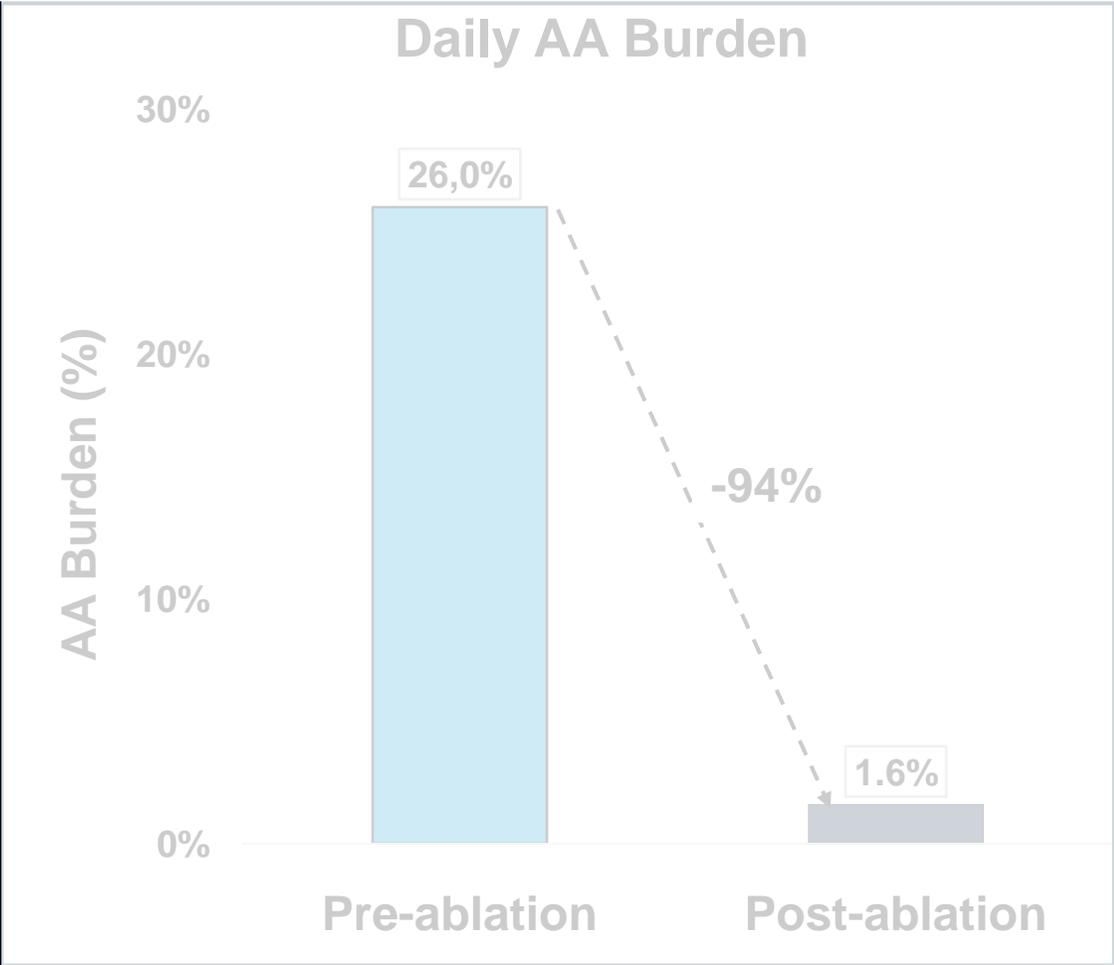
Analysis Using Full ILR Continuous Data



PULSE3 ILR Sub-study (n=15)

AA Burden in ILR Sub-cohort with Recurrence

PULSE3 ILR sub-cohort (n=15) → with recurrence (n=3)



In this FIH European study, the conformable PFA catheter:

- Was **efficient, safe, and effective** for PVI
- Had a **predictable workflow** requiring only ~4 applications per PV (~16 per procedure)
- **0% primary safety event rate** with minimal findings in esophageal & brain MRI sub-studies
- Demonstrated excellent PVI durability
 - PULSE3: **98% of PVs remained isolated** and **93% of patients had durable PVI**
- **Freedom from AA recurrence was 82% & 88%** in the total & PULSE3 cohort, respectively
 - Even using continuous monitoring, **freedom from all AAs was 80%**
 - Among patients with recurrence, there was a **significant decrease in AA burden**
- The **FDA Pivotal Trial** will start later this year



Future for AFFERA !!!



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