



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

**ROMA**

Centro Congressi  
di Confindustria

**Auditorium  
della Tecnica**

**9<sup>a</sup> Edizione**

**30 Settembre**

**1 Ottobre**

**2022**



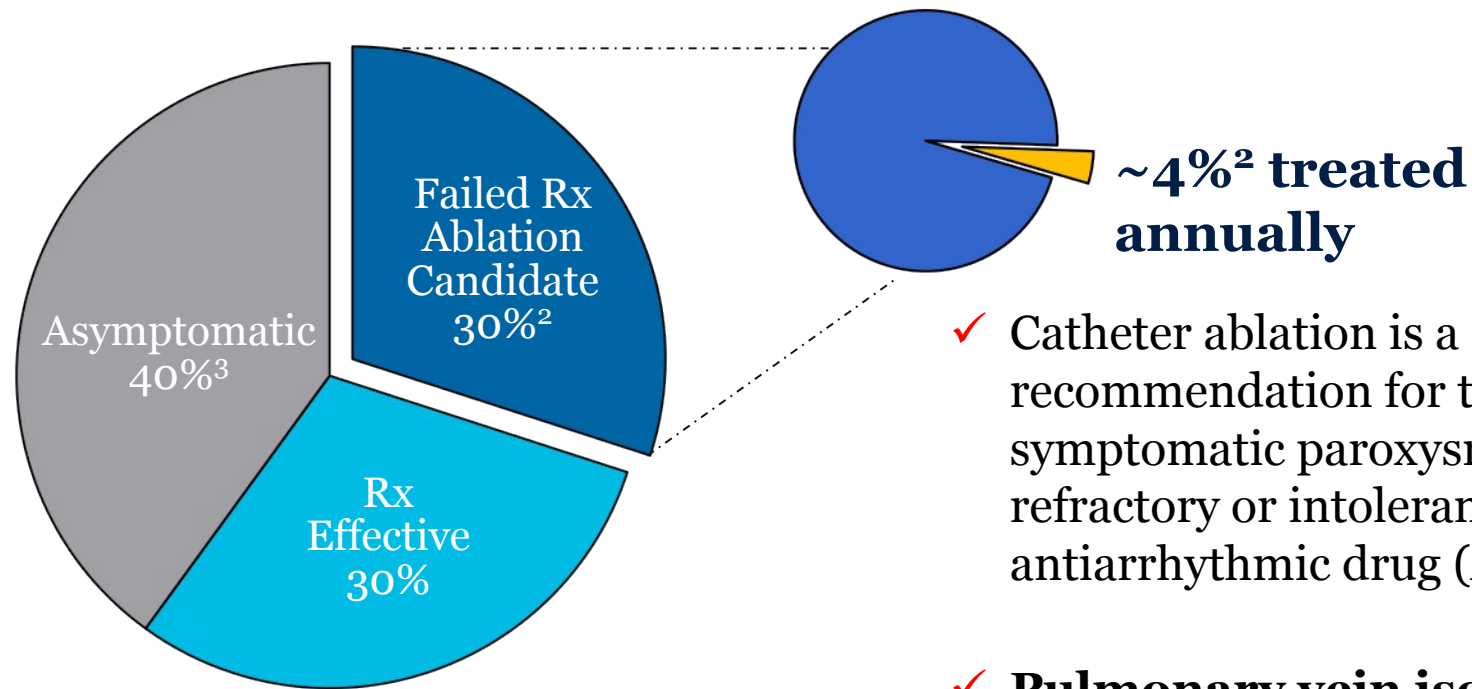
**QUALE LAMA PER SCONFIGGERE LA FIBRILLAZIONE ATRIALE**

# Elettroporazione: l'ultima frontiera

**Saverio Iacopino, FACC, FESC**

Chairman of Electrophysiology Units GVM  
Head of Arrhythmology Department  
Maria Cecilia Hospital, Cotignola (RA), Italy

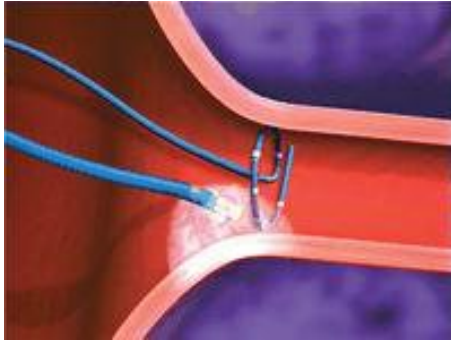
# AF Clinical/Referral Challenge



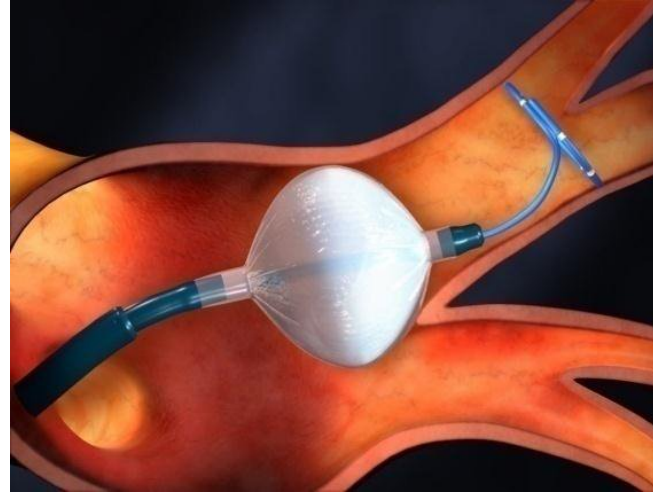
- ✓ Catheter ablation is a **Class I Level A** recommendation for treatment of symptomatic paroxysmal AF (PAF) refractory or intolerant to  $\geq 1$  Class I or III antiarrhythmic drug (AAD)<sup>4</sup>
- ✓ **Pulmonary vein isolation (PVI) is the cornerstone of AF ablation strategy<sup>5</sup>**
- ✓ Consensus guidelines and statements recommend PVI during the index CA procedure in **patients with PAF and persistent AF**

1. Rahman , et al. Nat. Rev. Cardiol. 2014; 11: 639–654
2. Wyse, et al. Circ. 1996; 93:1262-1277
3. Savelieva, et al. Pace. 2000; 23: 145-148
4. Calkins, H., et al. Heart Rhythm. 2012; 9(4): p. 632-696.e20
5. Raviele et al. J Cardiovasc Electrophysiol, 2012;23:890-923

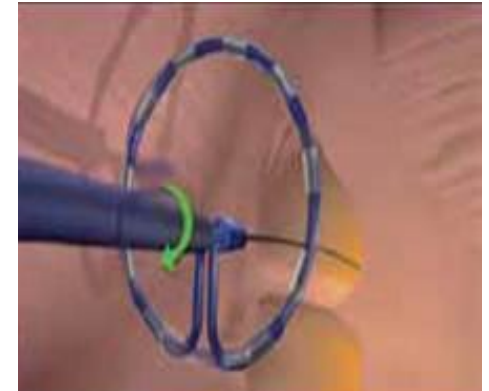
# Different Technology for CA of AF



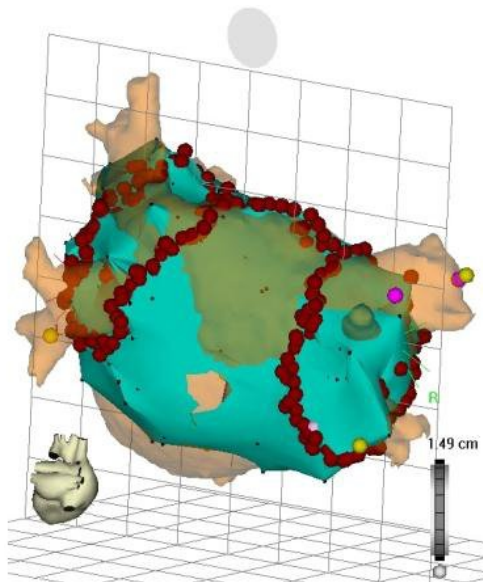
Segmental Ostial CA



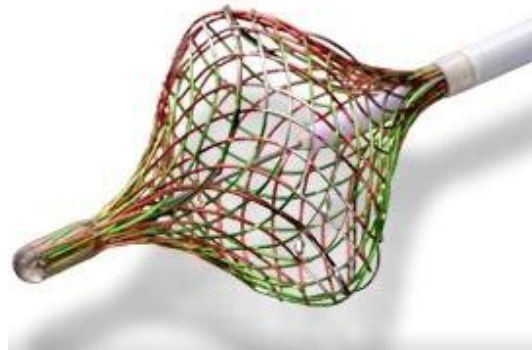
CRYOABLATION



PVAC



Circumferential Ostial CA



MESH



Cardiofocus

# Afib Ablation: Results

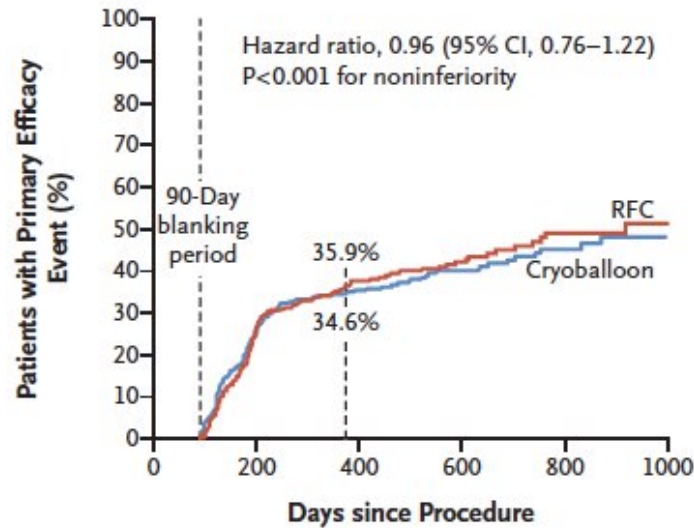
- ✓ Clinical Variability (Afib type; cardiomyopathy; atrial remodeling; LV dysfunction, atrial fibrosis)
- ✓ Ablation Strategy
- ✓ Acute and Long-term evaluation of results (antiarrhythmic drugs; diagnostics)
- ✓ Different EP Lab Experience



# Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Karl-Heinz Kuck, M.D., Josep Brugada, M.D., Alexander Fürnkranz, M.D., Andreas Metzner, M.D., Feifan Ouyang, M.D., K.R. Julian Chun, M.D., Arif Elvan, M.D., Ph.D, Thomas Arentz, M.D., Kurt Bestehorn, M.D., Stuart J. Pocock, Ph.D., Jean-Paul Albenque, M.D., Ph.D., and Claudio Tondo, M.D., Ph.D., for the FIRE AND ICE Investigators\*

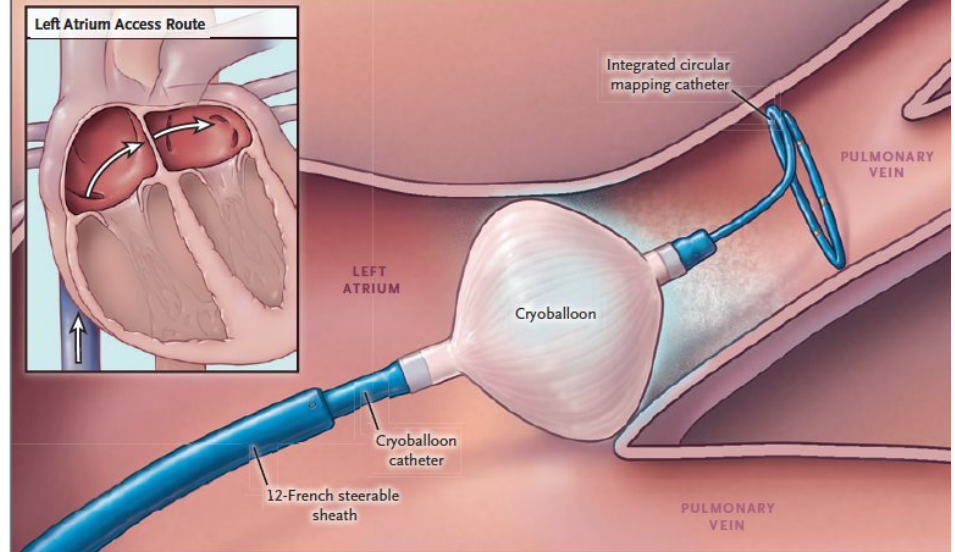
## A Primary Efficacy End Point



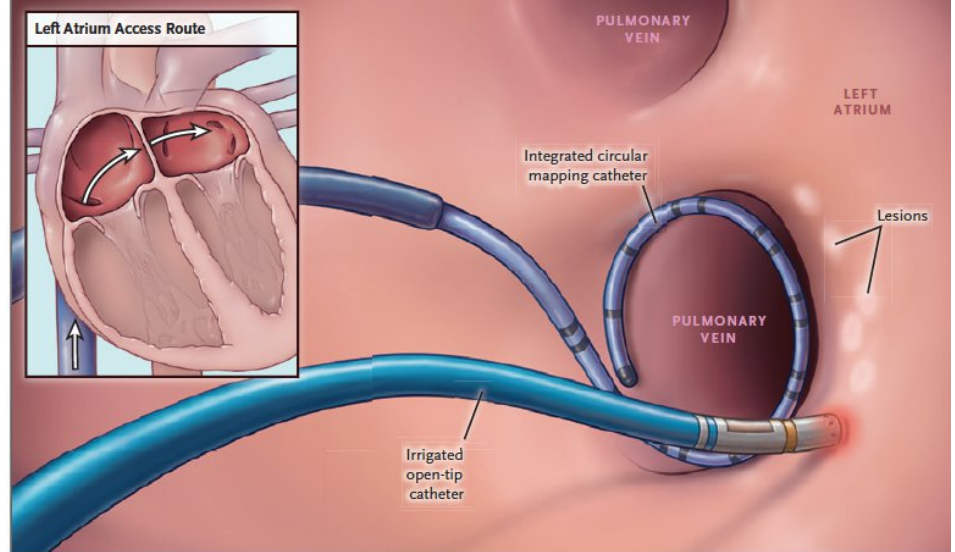
No. at Risk  
Cryoballoon  
RFC

374	338	242	194	165	132	107	70	57	34	12
376	350	243	191	149	118	93	58	44	25	12

## A Cryoballoon Ablation of Pulmonary Vein



## B Radiofrequency Current Ablation of Pulmonary Vein

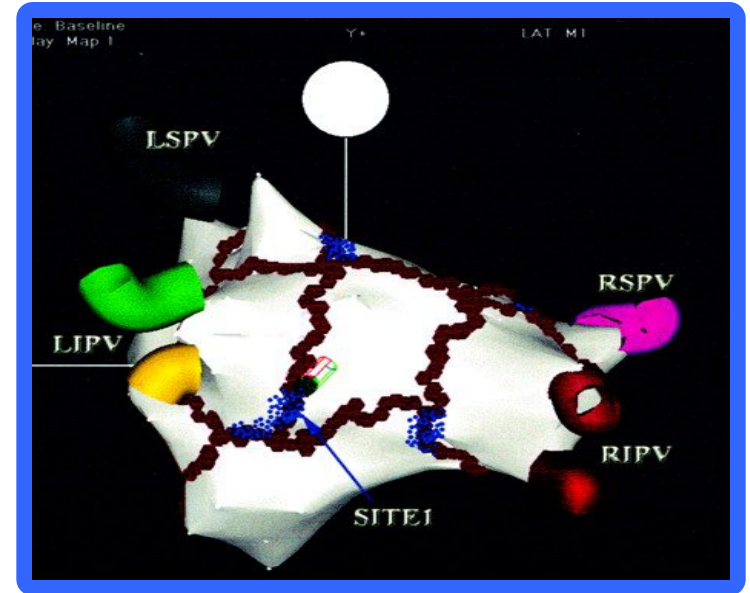


# Cryoablation vs RF Catheter Ablation



28 mm **CRYOBALLON**  
LA electroanatomic map

(area of electrical isolation, mean of **40+/-**  
**3.9%** of the map's surface)

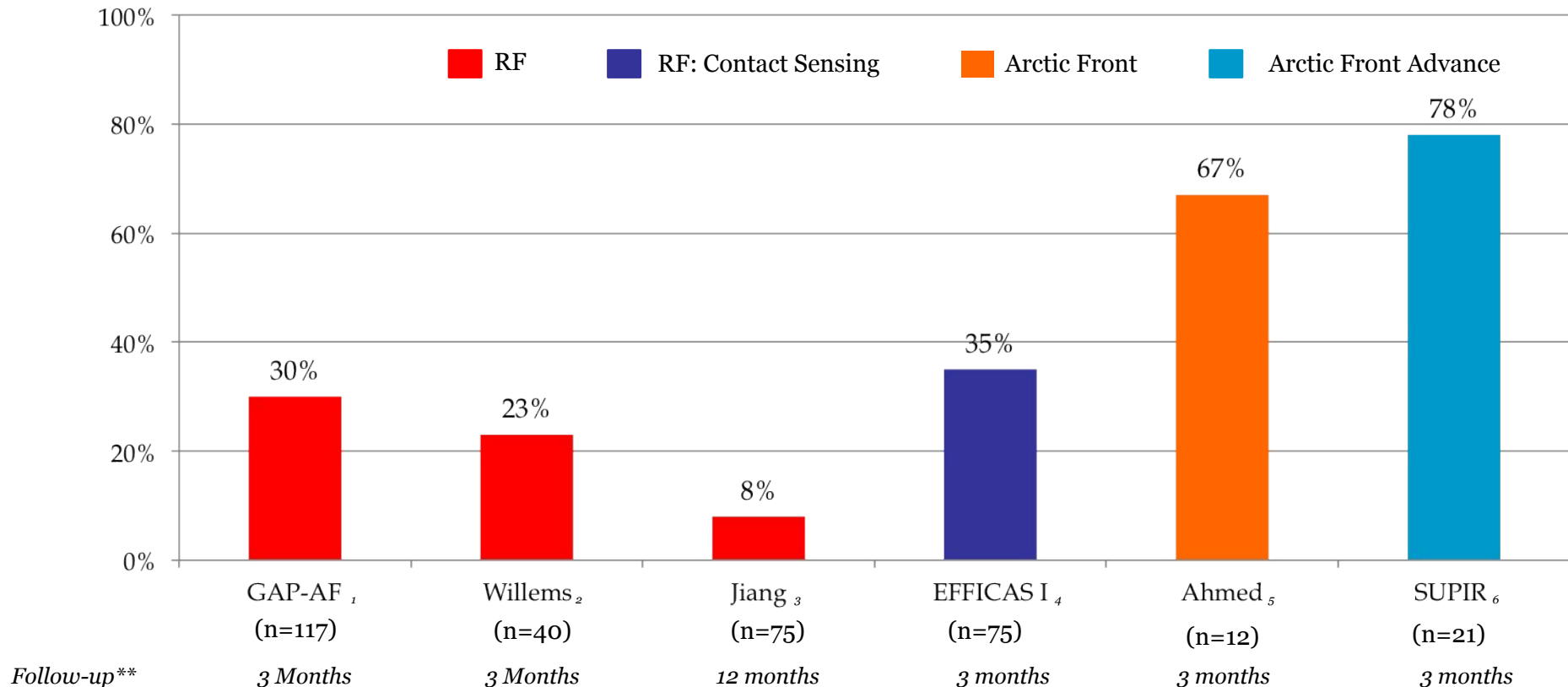


**CARTO 3D**  
LA electroanatomic map

# PV Lesion Durability with RF and Cryo

## PV re-conduction Using Repeat Electrophysiology and Mapping

% of Patients with PVI\* During Remapping Procedure



<sup>1</sup>Late Breaking Clinical Trials session I at the EHRA EUROPACE 2013 meeting in Athens, Greece

<sup>2</sup>Williems, et al. J Cardiovasc Electrophysiol 2010; 21(10):1079-84.

<sup>3</sup>Jiang, et al. Heart Rhythm. 2014;11(6):969-76

<sup>4</sup>Neuzil et al. Circ Arrhythm Electrophysiol.(2):327-33

<sup>5</sup>Ahmed, et al. J Cardiovasc Electrophysiol, 2010;21(7):731-7,

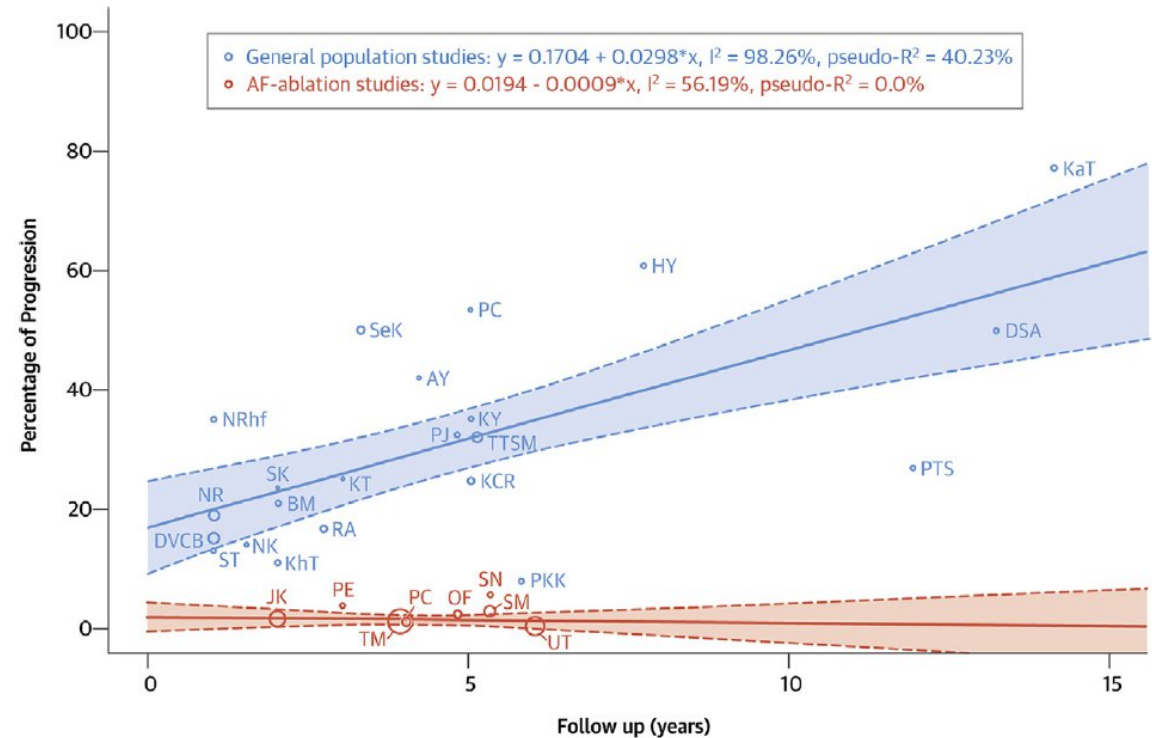
<sup>6</sup>Petru, et al. International Symposium on Progress in Clinical Pacing 2014

# Preventing Progression Of AF

## HOW TO TREAT?

- ✓ Systematic review in general population (primarily medical therapy only) vs. catheter ablation studies
- ✓ Weighted progression from paroxysmal to persistent or permanent AF by follow-up duration
- ✓ The percentage of AF progression increases over time (i.e., with longer follow up duration) in general population studies (n = 21), but remains flat in AF-ablation studies (n = 8)

Ablation reduces the percentage of AF progression vs. medical therapy alone

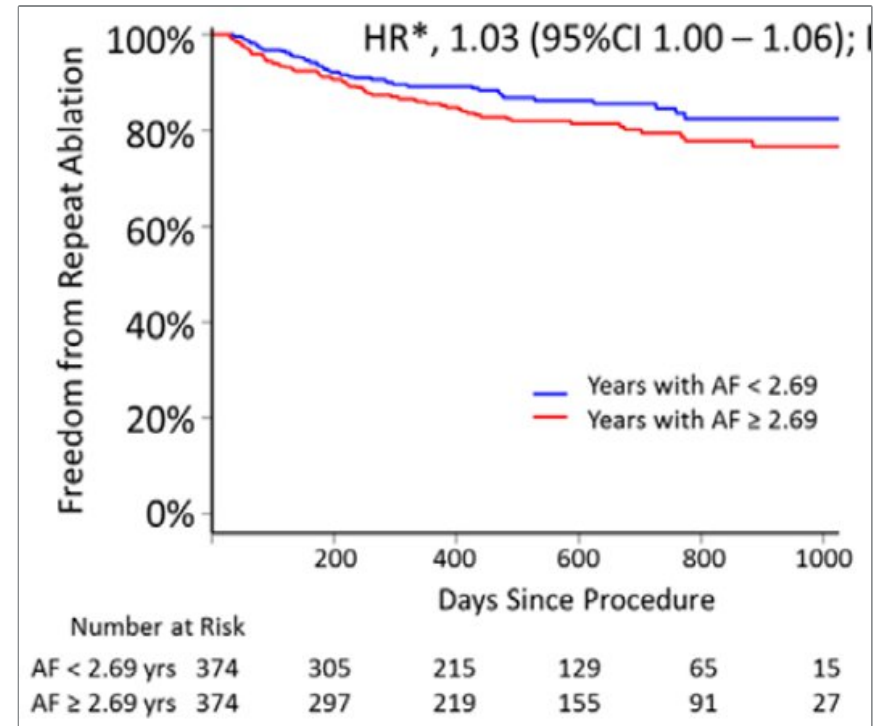


Proietti et al. A systematic review on the progression of paroxysmal to persistent atrial fibrillation: shedding new light on the effects of catheter ablation. JACC: Clinical Electrophysiology. 2015; 1(3):105-115.



# Earlier ablation Decreases the Risk of Repeat Ablation – Fire and Ice

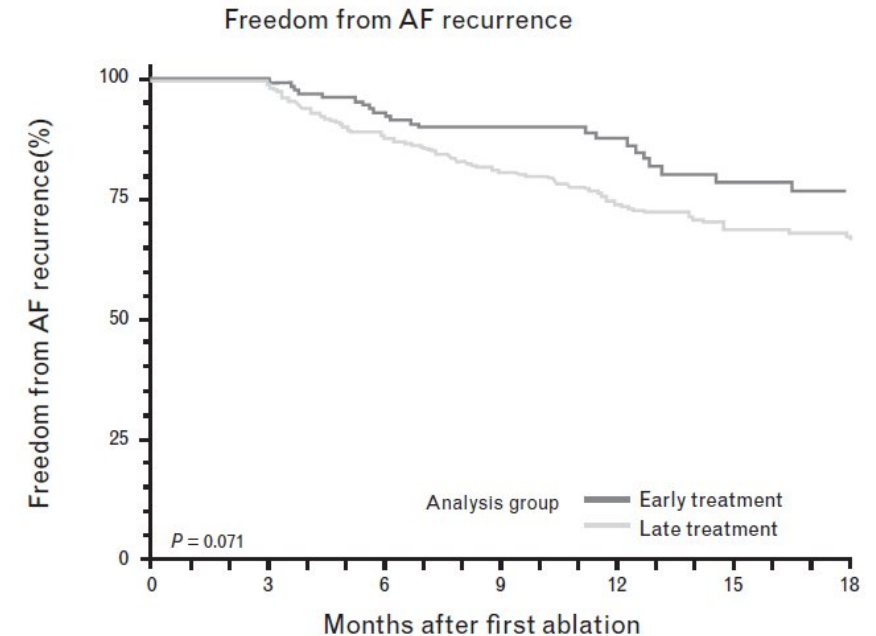
- ✓ 750 subjects with symptomatic PAF:
  - ✓ Refractory to class I or III antiarrhythmic drugs
  - ✓ Cryoballoon or RF catheter ablation
- ✓ Each additional year between AF diagnosis and ablation procedure was associated with a 3% increased risk of repeat ablation (HR = 1.03; P = 0.039)
- ✓ Higher freedom of AF predictor for patients who did not undergo cardioversions



# Earlier Ablation Decreases Risk of AF Recurrence

## 1STOP ITALIAN CRYOBALLOON REGISTRY

- ✓ **130 (25%)** patients in the **early treatment group** ( $\leq 15$  months post-AF diagnosis)
- ✓ **380 (75%)** patients in the **late-treatment group** ( $> 15$  months post-AF diagnosis)
- ✓ **Freedom from AF recurrence** at a mean follow-up of  $\sim 16$  months was:
  - ✓ **78.5% in the early-treatment group**
  - ✓ **68.4% in the late-treatment group**



No. at risk							
Early treatment	130	129	121	89	70	48	36
Late treatment	380	377	334	240	179	131	104

Risk of AF recurrence in the multivariable analysis was significantly higher in the late-treatment group (HR: 1.77, 95% CI: 1.00-3.13;  $P = 0.048$ )

# Cryo-FIRST: Multicenter Randomized (1:1) Controlled Trial

**218**

First-Line  
Patients with  
Symptomatic  
PAF

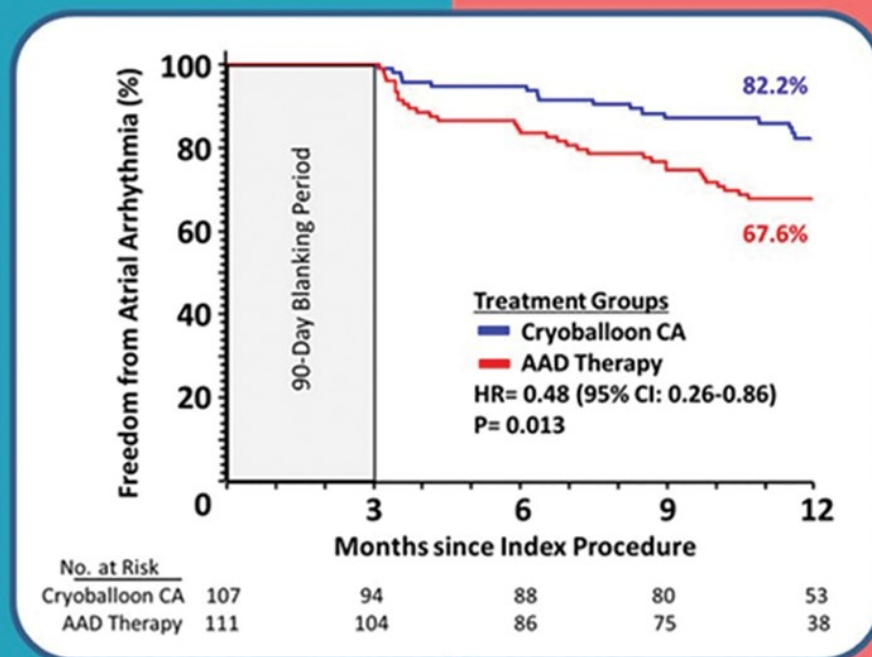
**CRYOBALLOON CATHETER  
ABLATION (CA) WITH  
ARCTICFRONT ADVANCE  
N=107**



**ANTIARRHYTHMIC  
DRUG (AAD) THERAPY  
N=111**

**82.2%**

**67.6%**



**60% Reduction in the Incidence Rate  
of Symptomatic Palpitations with  
Cryoballoon CA**

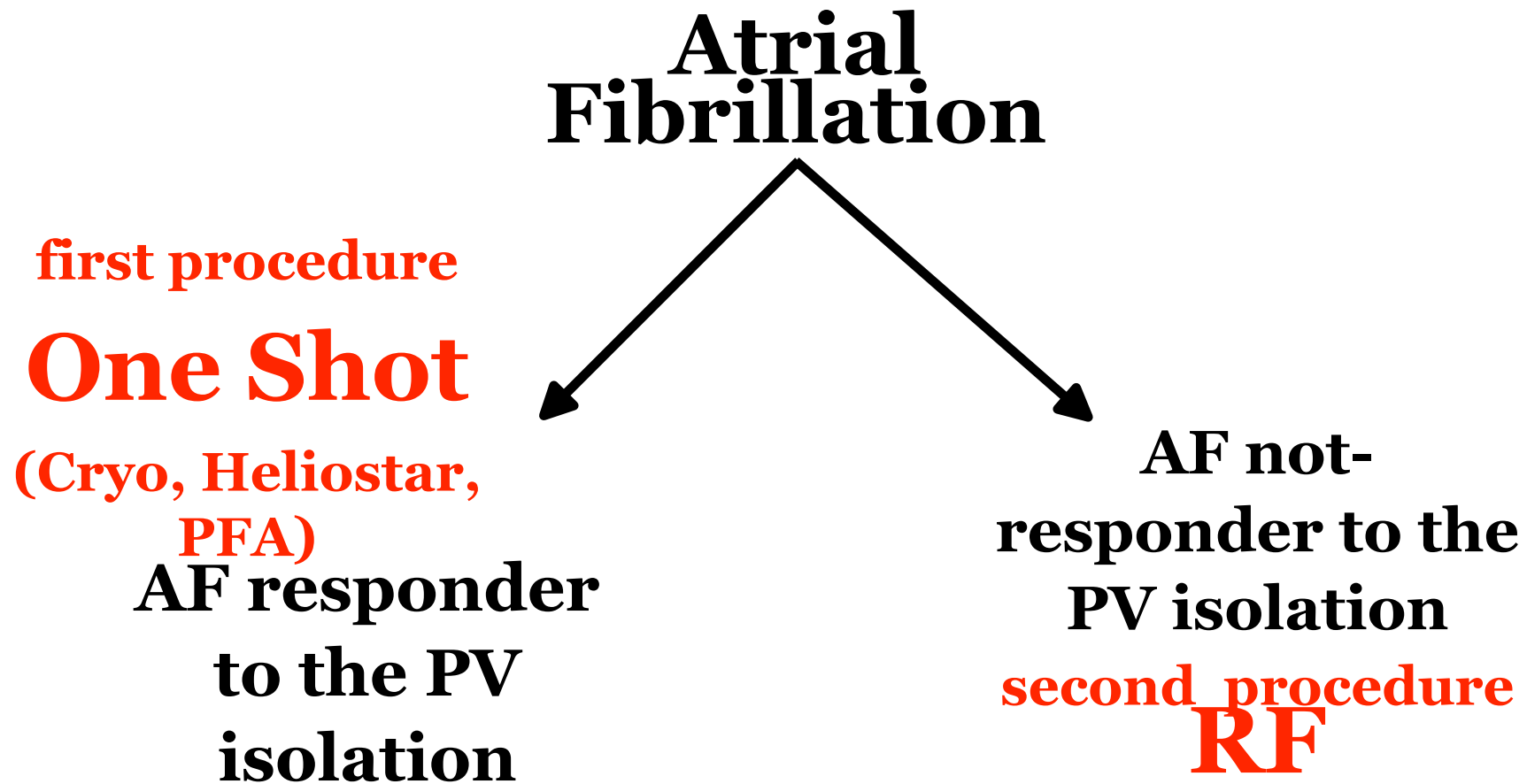
**No Difference in the Incidence Rate  
of Serious Adverse Events**



**Cryoballoon CA Results in Superior Efficacy Compared to AAD Therapy and has a  
Comparable Safety Profile in Treatment Naïve Patients with  
Symptomatic Paroxysmal AF**

# AF Ablation

## Maria Cecilia Hospital Approach



LA dim > 60 mm indication for **Hybrid Ablation (staged)**

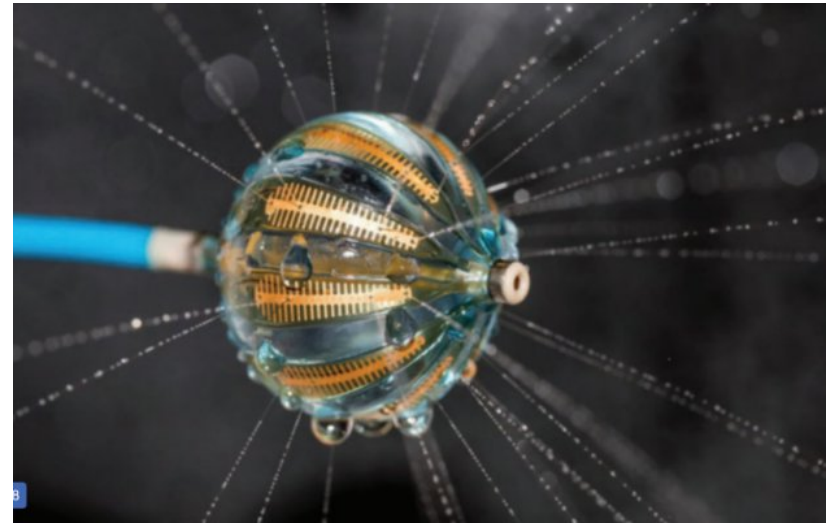
# New Balloon Ablation Catheter Technologies



POLARx™ Cardiac Cryoablation System



Apama multi-electrode RFA

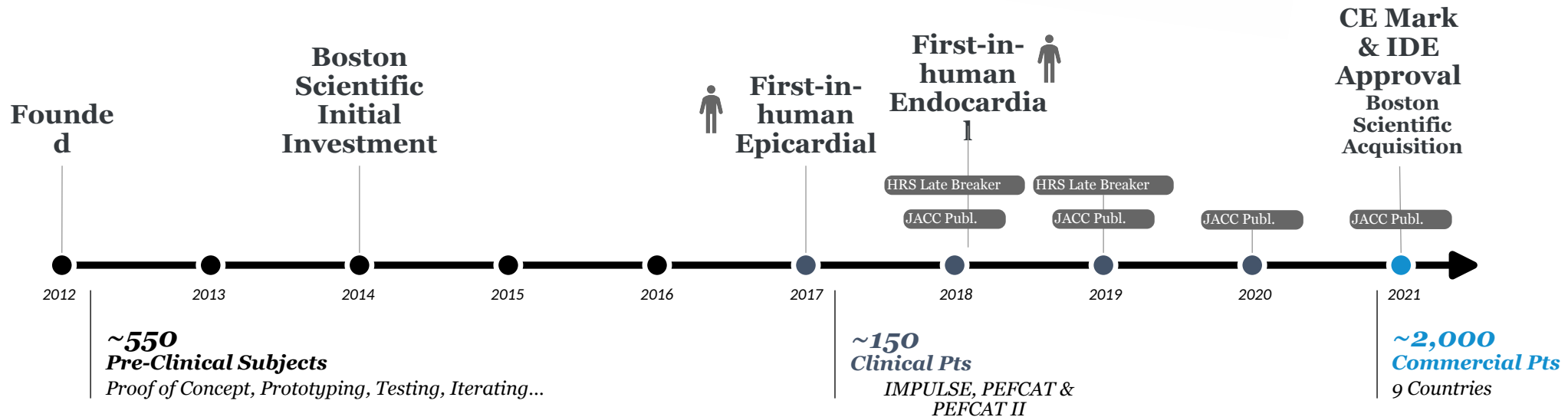


Helios II multi-electrode RFA



# FARAPULSE Dedicated History

## Pioneering PFA Technology



### BUILDING

the ideal PFA system  
from the ground-up



### OPTIMIZING

pre-clinical & clinical safety,  
efficacy & lesion durability



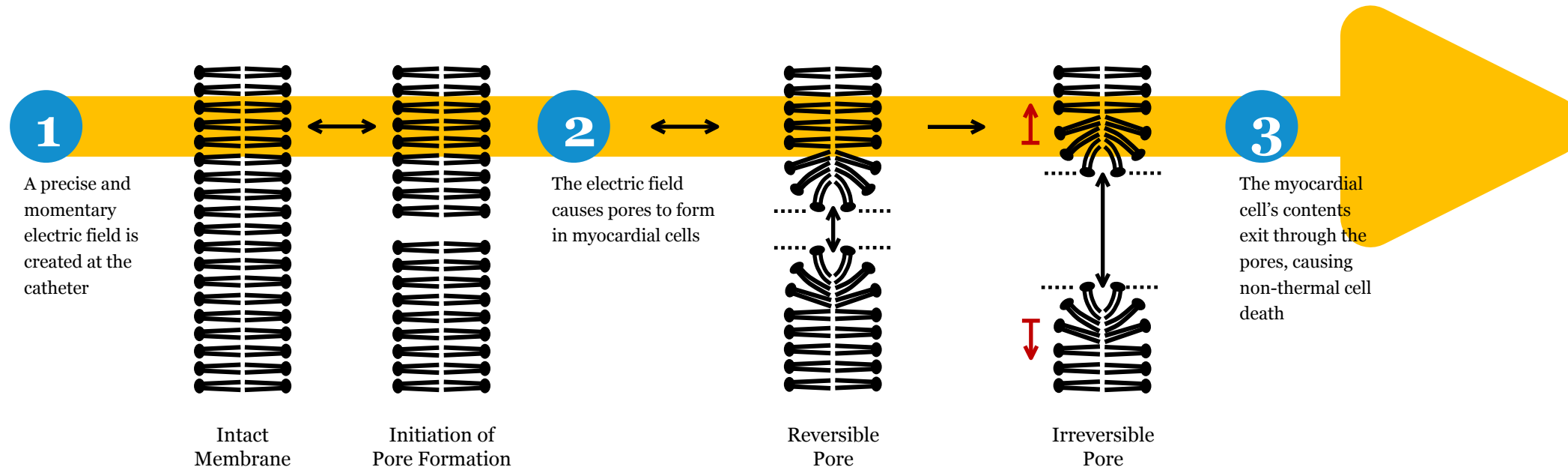
### VALIDATING

system in randomized  
trials & commercial use

# PFA - Mechanism of Action

## PFA is Non-Thermal (Not Heating or Cooling)

Irreversible Electroporation:  
cell membrane pore formation & cell death occurs with sufficient electric field



# Extensive Preclinical Set the Foundation

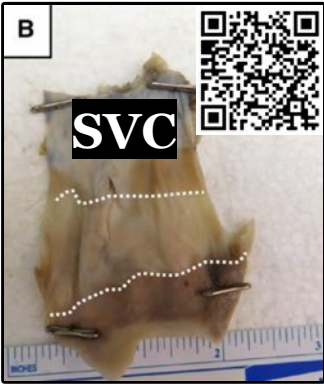
Safety, Usability, & Lesion Durability to Optimize System

## The FARAPULSE PFA System was developed through extensive pre-clinical testing

Comprehensive study of safety, usability and acute & durable effectiveness have led to a fully-optimized endocardial PFA system

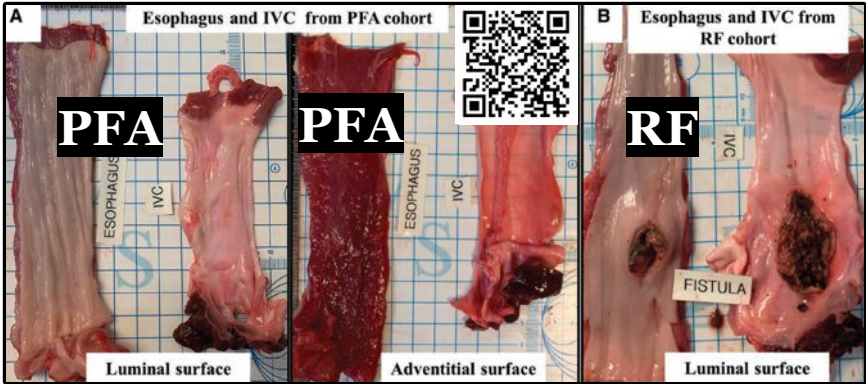
<i>Study Objective</i>	<i>Subjects</i>
<i>Collateral Safety</i>	<i>70</i>
<i>Validation</i>	<i>85</i>
<i>Device/Therapy</i>	<i>415+</i>
<i>Other</i>	<i>180</i>
<i>TOTAL</i>	<i>750+</i>

### LESION DURABILITY



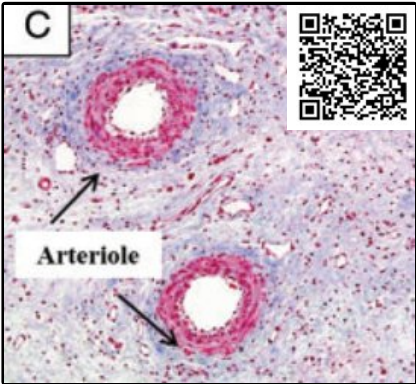
Koruth et al. Circulation AE.2019;12:e00778

### ESOPHAGEAL SAFETY



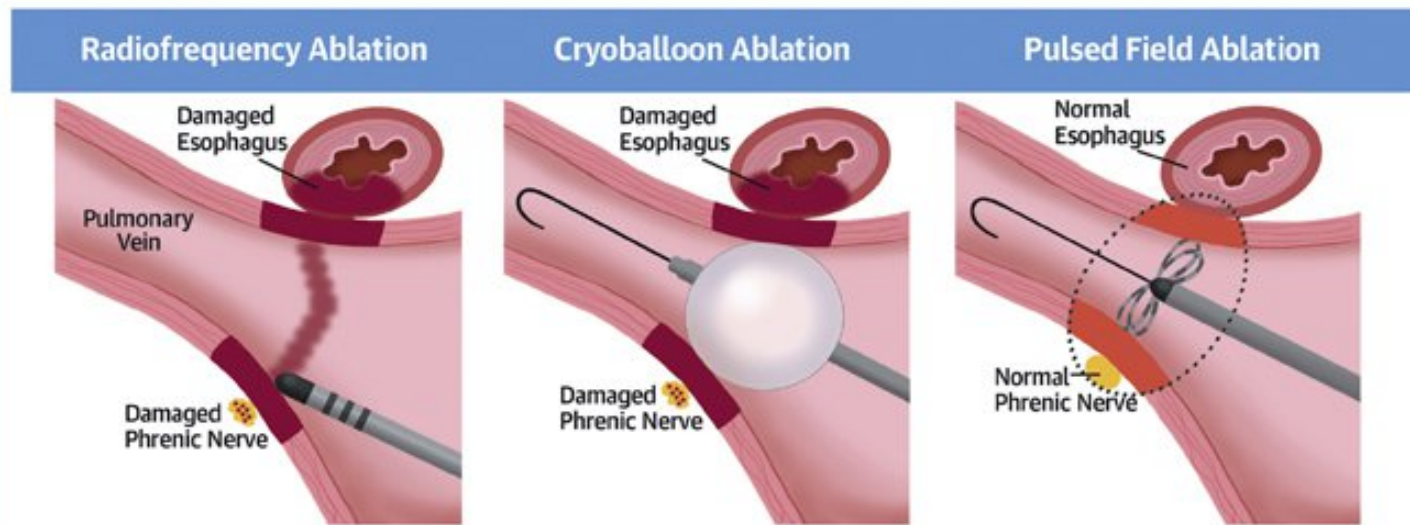
Koruth et al. Circulation AE. 2020;13:e008303

### NERVE & VASCULAR SAFETY

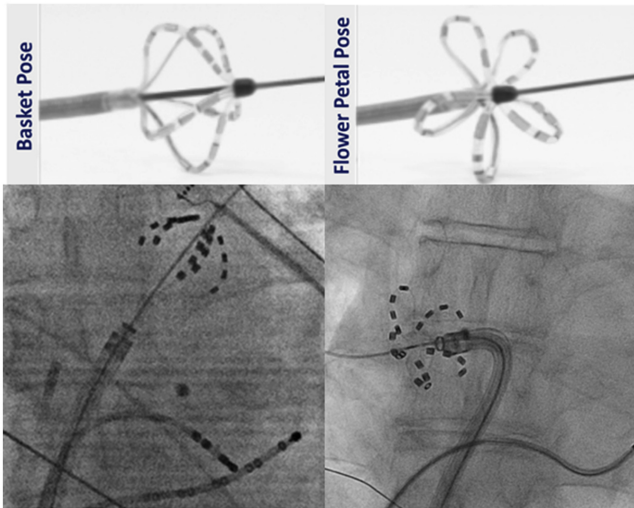


Koruth et al. Europace. 2019;0:1-6

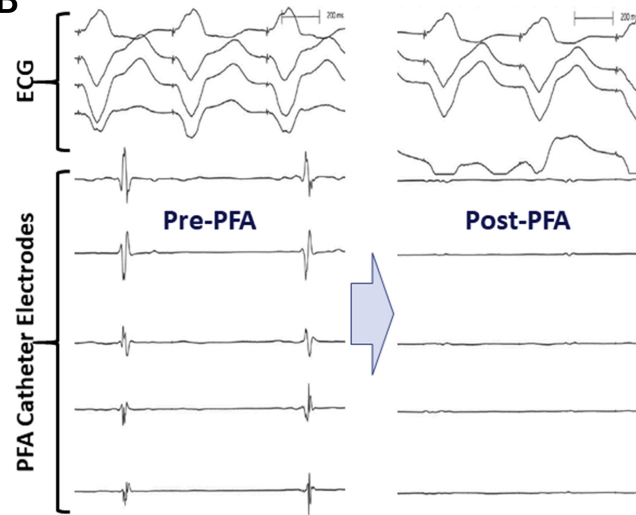
# PVI by Pulsed Field Ablation



A



B



# Catheter Variable Deployment

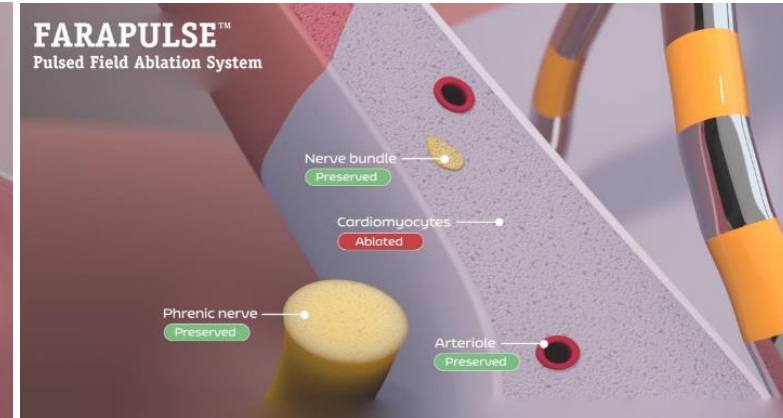
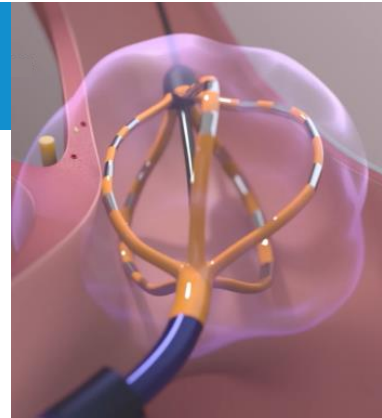
Basket/Flower Designed to Treat Variety of Anatomies

## Basket Position

Ostial positioning & centering capability

Visual:

RSPV – ablating cardiomyocytes & preserving phrenic nerve

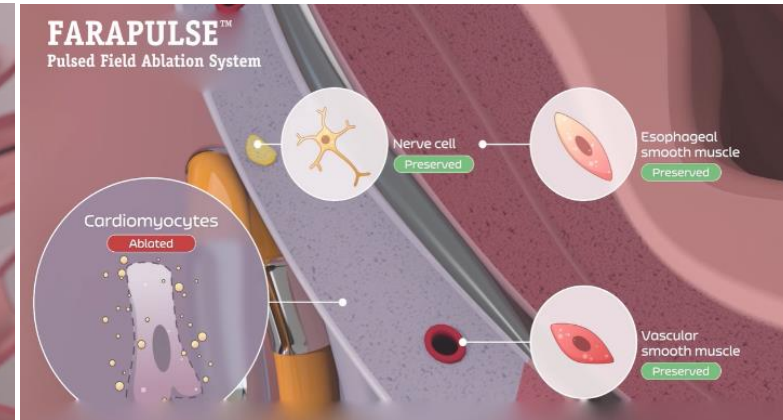
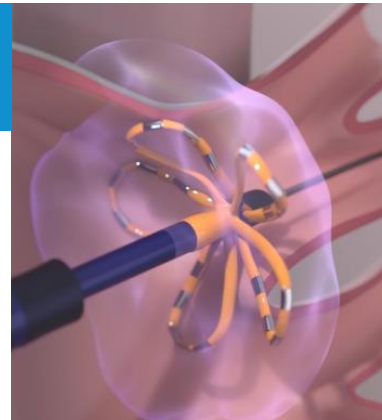


## Flower Position

Antral positioning & radially widest

Visual:

LSPV – ablating cardiomyocytes & preserving esophageal tissue



**4 pairs per vein** (8 total applications):

Basket: 2x applications – Rotate

Basket: 2x applications

**Change deployment to flower configuration**

Flower: 2x applications – Rotate

Flower: 2x applications



# Cerebral Safety

## Additional Safety Assessments



**Three FARAPULSE PVI  
AF studies quantitated  
SCE/SCL burden post-  
ablation**

### **IMPULSE, PEFCAT, PEFCAT II<sup>1</sup>**

2/18 (11%) DW-positive

### **FARA-FREE<sup>2</sup>**

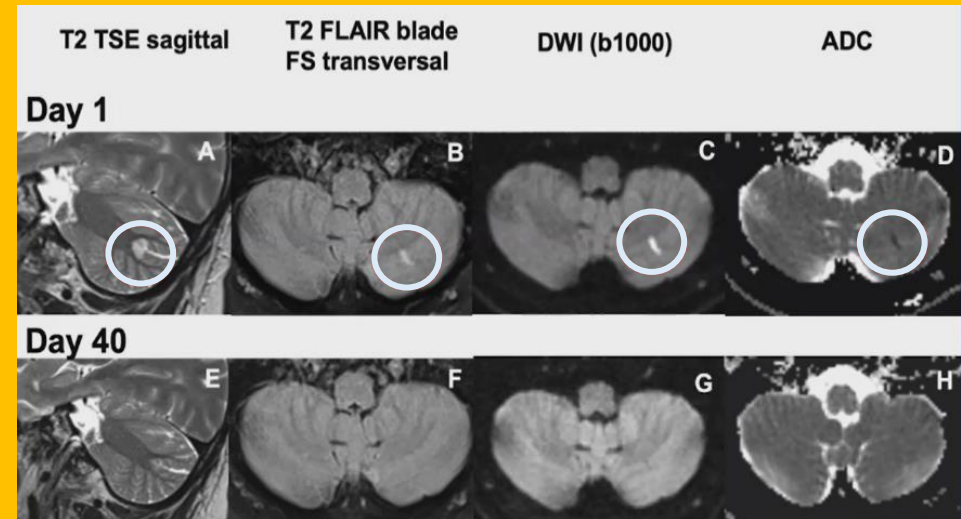
SCE: 1/15 (7%) DW-positive

SCL: 0/15 (0%) FLAIR positive

### **Alfried Krupp Krankenhaus, Essen<sup>3</sup>**

SCE: 1/30 (3%) (FLAIR positive)

40-day post PVI showed complete lesion  
regression (FLAIR negative)



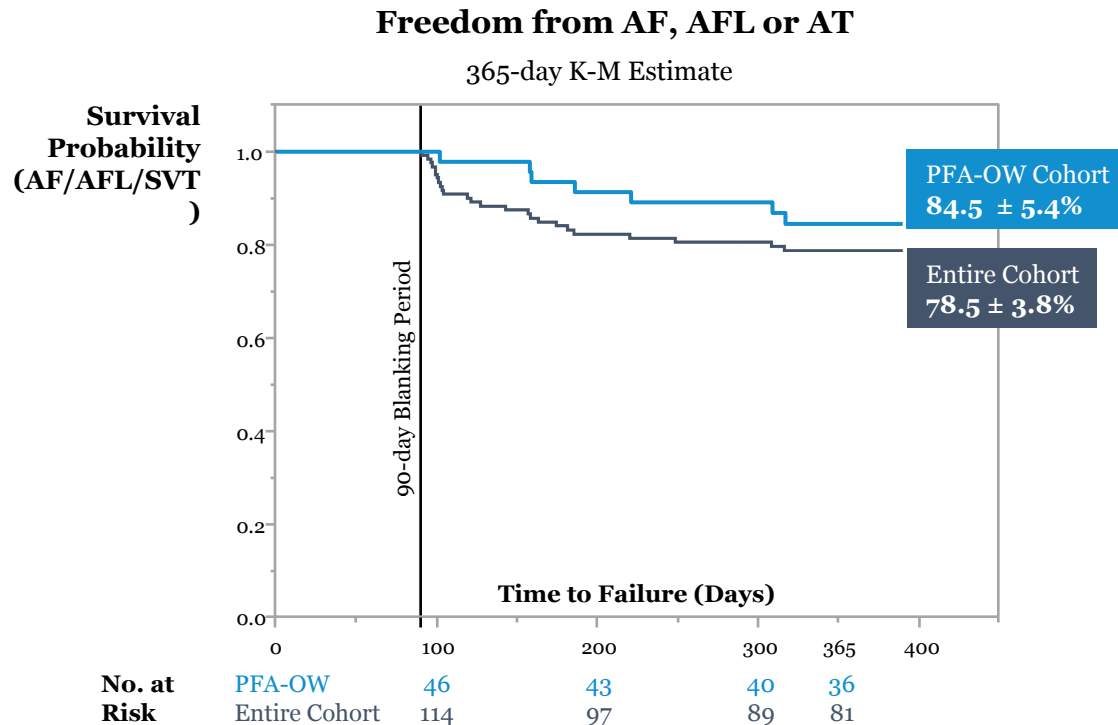
<sup>1</sup>Reddy et al. JACC: Clinical Electrophysiology 7.5 (2021): 614-627

<sup>2</sup>Presented by A. Anic. DGK 2021 (April) – FARA-FREE

<sup>3</sup>Image presented at DGK 2021. Clin Res Cardiol (2021)

# Durable PVI with Optimized Dose

$85 \pm 5\%$  Freedom from Atrial Arrhythmia at 1 Year



**97**  
patients to 1 year of follow-up

**$85 \pm 5\%$**   
freedom from atrial arrhythmia in patients treated with the optimized PFA dose<sup>1</sup>

➔ **High Compliance**

86% TTM (per week)  
98% Holter (per monitor)

➔ **6/7 recurrences**

demonstrated durable PVI at remap,  
suggesting extra-PV triggers for AF

<sup>1</sup>Reddy et al. JACC: Clinical Electrophysiology 7.5 (2021): 614-627

# PFA Studies Demonstrated Efficient Procedures

Translated to Real-World with Short Learning Curve

## Study Procedure Times: PFA, Cryo & RF IMPULSE, PEFCAT, & PEFCAT II vs. Fire & Ice

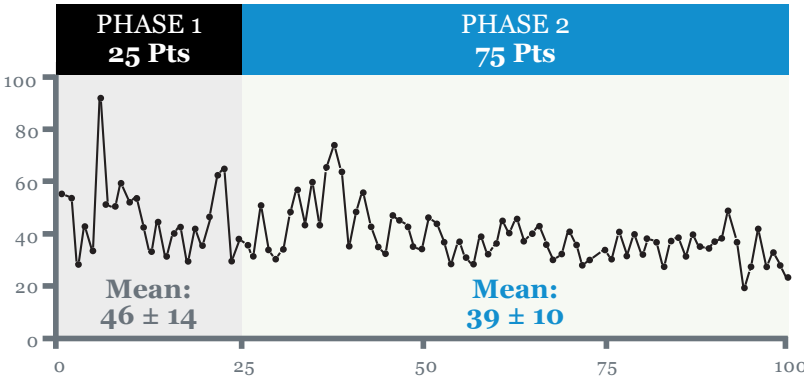
	<i>FARAPULSE</i> <sup>1</sup>	<i>Cryo</i> <sup>2</sup>	<i>RF</i> <sup>2</sup>
<b>Procedure Time</b>	<b>96 minutes*</b> 96.2 ± 30.3	<b>124 minutes</b> 124.4 ± 39	<b>141 minutes</b> 140.9 ± 54.9
<b>Left Atrial Dwell Time</b>	<b>34 minutes</b> 34.4 ± 15.8	<b>92 minutes</b> 92.3 ± 31.4	<b>109 minutes</b> 108.6 ± 44.9
<b>Fluoroscopy Time</b>	<b>14 min</b> 13.7 ± 7.8	<b>22 min</b> 21.7 ± 13.9	<b>17 min</b> 16.6 ± 17.8

\* Inclusive of time required (~19 min) to perform protocol-mandated voltage mapping.

Cumulative PFA therapy delivery time did not exceed 3 min/patient.

## Clinical & Real-World Experience Demonstrated Efficiency, Short Learning Curve & Reproducible Procedures

## Single Center Experience with 6 operators & 100 patients in Two Phases<sup>3</sup>



	TOTAL 100 Pts, 393 PVs	PHASE 1 25 Pts, 98 PVs	PHASE 2 75 Pts, 295 PVs
Procedure Time (min)	41 ± 11	46 ± 14	39 ± 10
Fluoroscopy Time (min)	9.6 ± 3.9	11.1 ± 4.7	9.2 ± 3.5
Number of Applications / Vein	8 ± 1	8 ± 1	8 ± 0
Single-Shot Isolation	388 (99%)	95 (97%)	293 (99%)
Patients, all PVs single-shot isolation	96 (96%)	22 (88%)	74 (99%)

<sup>1</sup>Reddy et al. JACC: Clinical Electrophysiology 7.5 (2021): 614-627

<sup>2</sup> Kuck, KH. et al. N Engl J Med 2016; 374:2235-2245

<sup>3</sup>K. R. Julian Chun CCB, Frankfurt, Germany. Presented at DGK 2021.

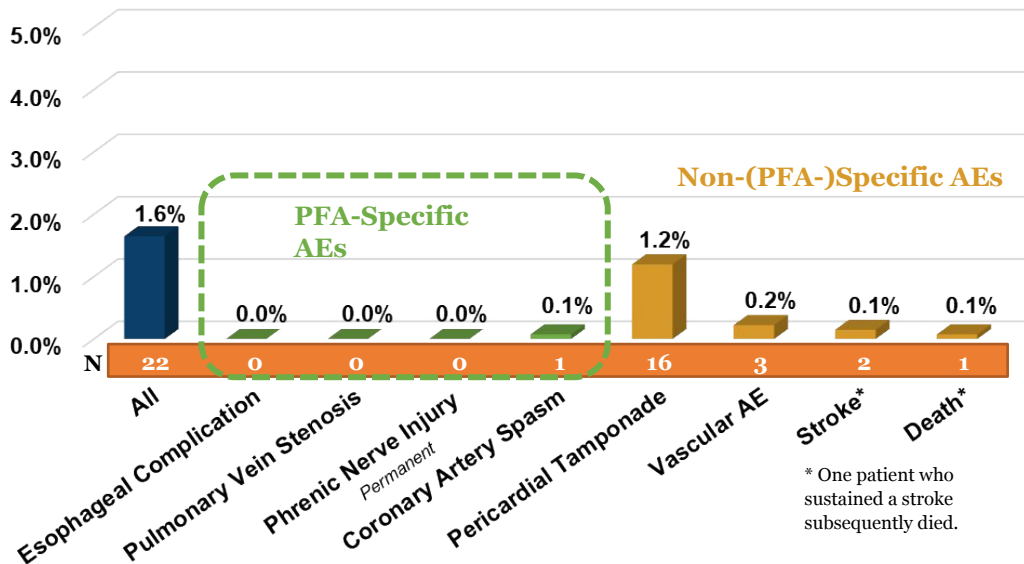
# Real-World Data: MANIFEST-PF

## Safety

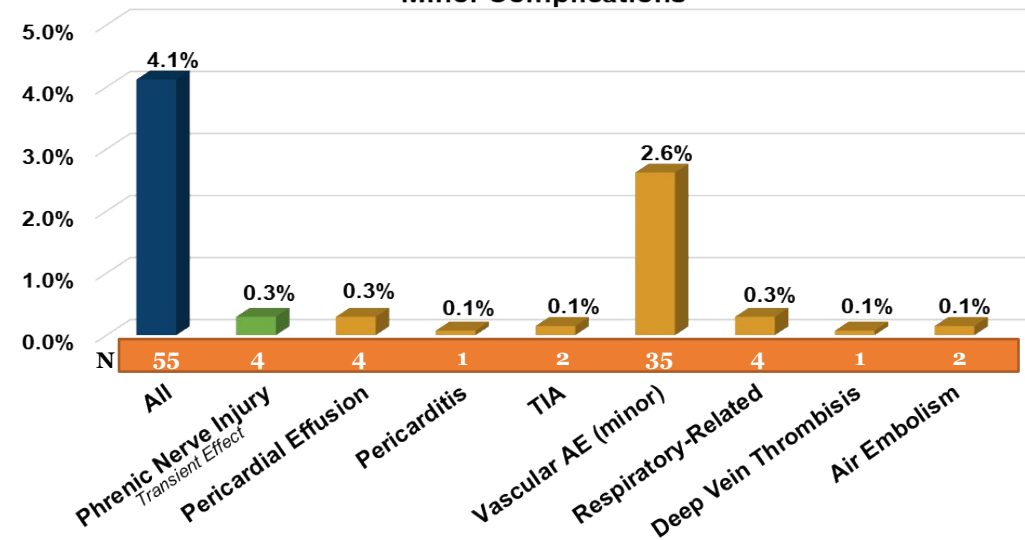
In **1,334 AF patients (24 EU Centers)** treated with the pentaspline PFA catheter:

- Results demonstrated tissue selectivity of PFA ☺ no esophageal injury, PV stenosis, or permanent phrenic nerve injury
- No late complications were reported**

Major Complications



Minor Complications



V.Y. Reddy et al. at ESC 2022. “Multi-national Registry on the One-Year Safety and Efficacy of the “Real-World” use of Pulsed Field Ablation to Treat Atrial Fibrillation”

# PFA - Maria Cecilia Hospital Experience

<i>Clinical and baseline data</i>	<i>N=19</i>
<i>Age</i>	<i>61±7</i>
<i>LVEF</i>	<i>57±5</i>
<i>Male</i>	<i>14 (73.7%)</i>
<i>First line therapy</i>	<i>7 (36.8%)</i>
<i>AF Type:</i>	
• <i>Paroxysmal</i>	<i>15 (78.9%)</i>
• <i>Early persistent</i>	<i>2 (10.5%)</i>
• <i>Long lasting persistent</i>	<i>2 (10.5%)</i>
<i>Symptomatic AF</i>	<i>18 (94.7%)</i>
<i>Structural Heart disease</i>	<i>1 (5.3%)</i>
<i>CAD</i>	<i>1 (5.3%)</i>
<i>HF</i>	<i>0 (0.0%)</i>
<i>CKD</i>	<i>0 (0.0%)</i>
<i>COPD</i>	<i>1 (5.3%)</i>
<i>Obesity:</i>	
• <i>Normal weight</i>	<i>3 (15.8%)</i>
• <i>Pre-obesity</i>	<i>8 (42.1%)</i>
• <i>Obesity</i>	<i>8 (42.1%)</i>
<i>Diabetes</i>	<i>2 (10.5%)</i>
<i>Hypertension</i>	<i>11 (57.9%)</i>
<i>Antiarrhythmics</i>	<i>11 (57.9%)</i>

<i>Procedural times</i>	<i>N=19</i>
<i>Fluoroscopy time, min</i>	<i>21±8</i>
<i>Procedural time, min</i>	<i>93±48</i>
<i>Time to PVI, min</i>	<i>24±3</i>
<i>Lab occupancy time, min</i>	<i>114±41</i>
<i>Primary physician time, min</i>	<i>77±36</i>
<i>Support time, min</i>	<i>82±37</i>

<i>Procedural data</i>	<i>N=19</i>
<i>Sinus rhythm at the procedure</i>	<i>12 (63.2%)</i>
<i>De novo procedure</i>	<i>17 (89.5%)</i>
<i>Mapping system used</i>	<i>3 (15.8%)</i>
<i>2 accesses</i>	<i>17 (89.5%)</i>
<i>Non invasive ventilation support:</i>	
• <i>Nasal cannula</i>	<i>8 (42.1%)</i>
• <i>Oxygen mask</i>	<i>3 (15.8%)</i>

**First pass isolation:  
98.7% per PV, 94.7% per  
patient**



OneView



07/07/2022  
17:13:50  
0 - 6/6

R

FL - EP

cm 25  
A  
D 28  
LAO 28° / CAUD 1°

H

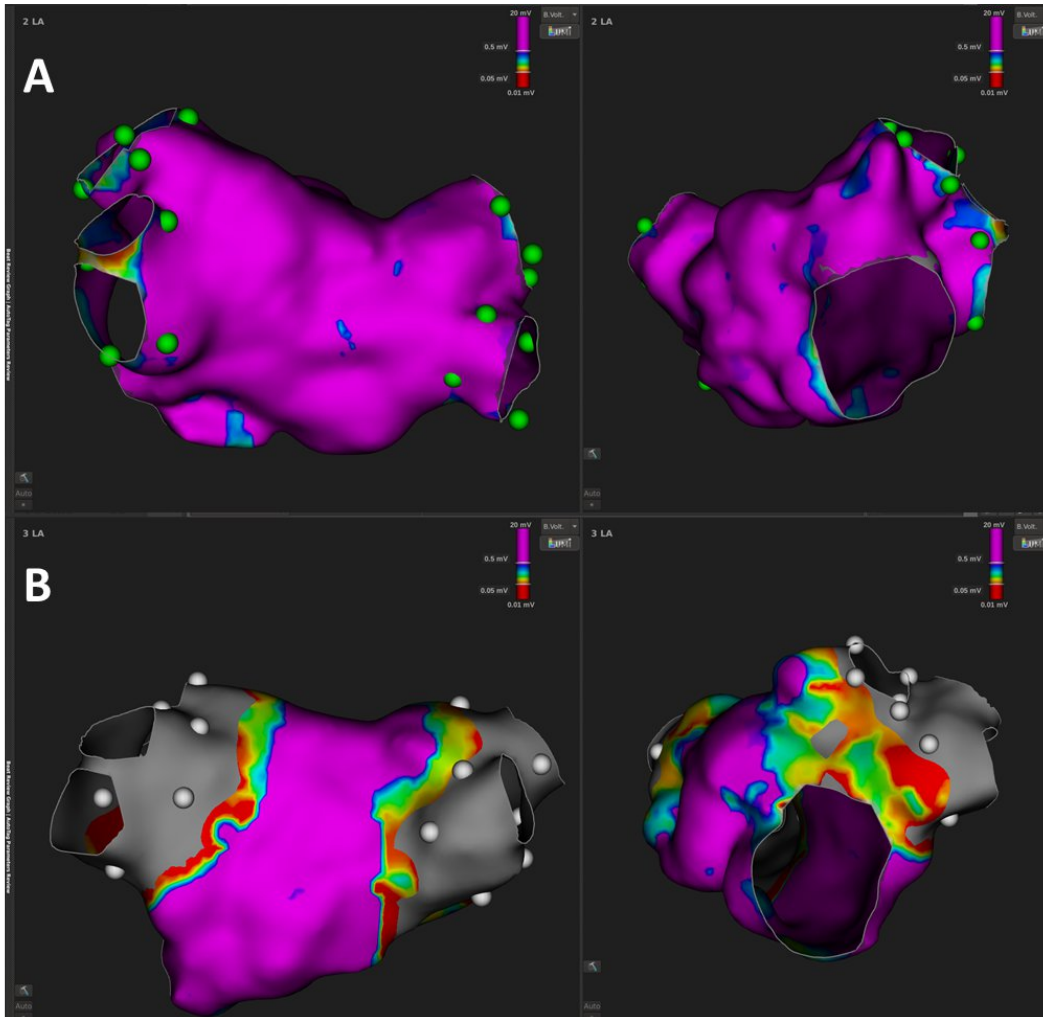
MARIA CECILIA HOSPITAL  
Default  
AXIOM Artis  
VC21C 161026  
HFS  
////



EE 10%  
DDO 40%

WC 1850  
VW 2500

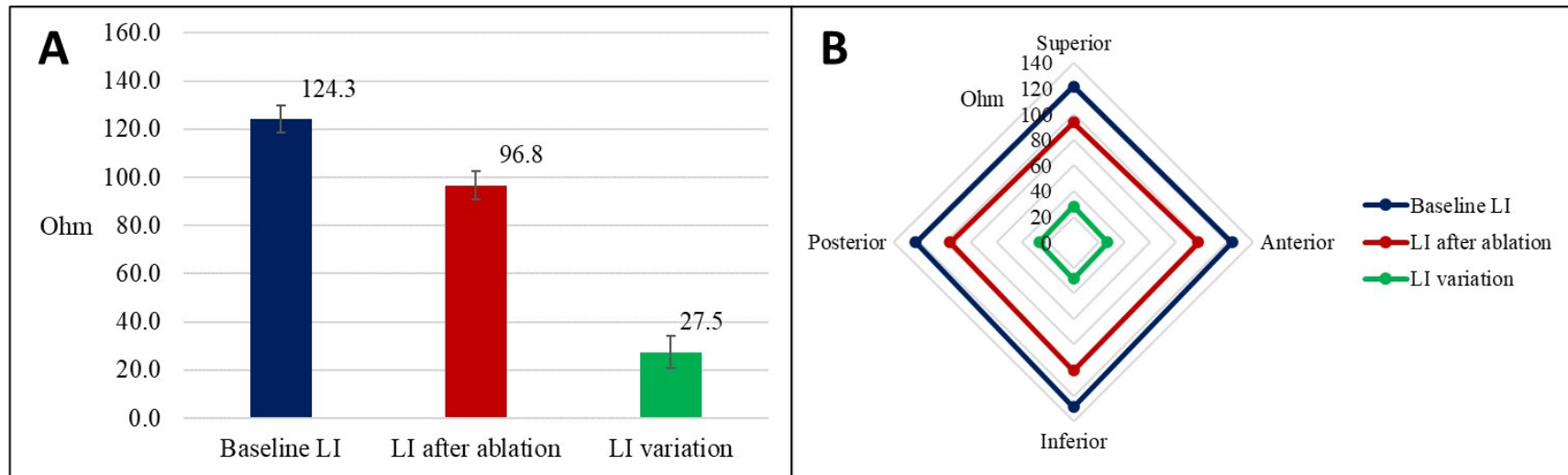
# “Lesion effects in terms of local impedance variations after pulsed-field ablation during pulmonary vein isolation”



**Figure 1A:** Modified PA (left) and LAO (right) view of the left atrial voltage map before PFA was undertaken. The green tags indicate the exact vein segment position where the IntellaNAV™ catheter measured the LI values.

**Figure 1B:** Modified PA (left) and LAO (right) view of the left atrial voltage map after PFA. The grey color of the veins shows their electrical disconnection. The same green tags previously used to take the baseline LI values, are now used (grey tags) to record how the LI changed post ablation

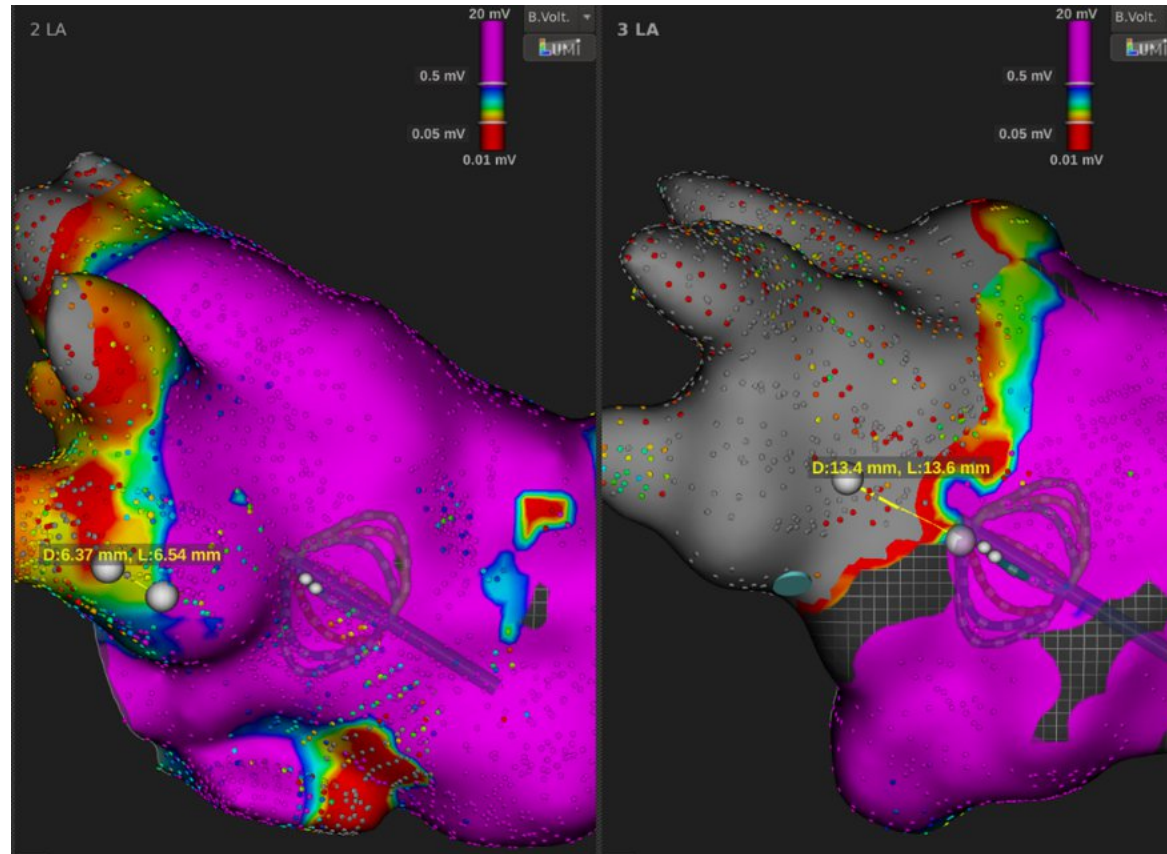
# “Lesion effects in terms of local impedance variations after pulsed-field ablation during pulmonary vein isolation”



**Figure 2A.** Baseline LI, LI after ablation and LI variation.

**Figure 2B.** Radar plot shows the LI values according to location sites. The apexes of the chart represent different location sites (anterior, inferior, posterior, superior) (5–14 g, 15–24 g, and  $\geq 25$  g), whereas the lines represent different degrees of LI information (blue line for baseline LI values, red line for LI values after PFA and green line for LI variation values).

# “Lesion effects in terms of local impedance variations after pulsed-field ablation during pulmonary vein isolation”



Example of circumferential PVI area resulting from PFA involving the antral portion of PVs. Left panel: pre- PFA. Right panel: post- PFA.



# Conclusion

- ✓ **PVI remains the cornerstone of PAF ablation**
- ✓ Novel tools might render the procedures safer and faster
- ✓ Early ablation therapy of PAF seems to yield excellent results on a short-mid term F-Up
- ✓ the **PVI procedure was safe, effective, and efficient** with regards to the treatment of patients with paroxistical and persistent AF
- ✓ **Pulsed-field ablation (Farapulse)**, involves irreversibly electroporating cell membranes, without thermal damage, by using short-duration, high-voltage electrical impulses to create lesions
- ✓ **Patient selection is the best predictor of success!**