

*23<sup>rd</sup> Prague Workshop on Catheter Ablation*

# **Experience With Single Shot Pulse Field Ablation System**

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Heart**

# Disclosures

- Consultant and/or Grant support:

Abbott, Ablacon\*, Acutus Medical\*, **Affera\***, Apama Medical\*, APN Medical\*, Aquqheart\*, Atacor\*, Autonomix\*, Axon\*, Backbeat\*, **Biosense-Webster**, Biosig\*, BioTel Heart, Biotronik, Boston Scientific, CardiaCare\*, Cardiofocus, Cardionomics, CardioNXT/AFTx\*, Circa Scientific\*, Corvia Medical\*, Dinova-Hangzhou Nuomao Medtech\*, East End Medical\*, EBR, EPD\*, EPIX\*, EpiEP\*, Eximo\*, **Farapulse\***, Fire1, Impulse Dynamics, Intershunt\*, Javelin\*, Kardium\*, Keystone Heart\*, LuxMed\*, Manual Surgical Sciences\*, Medlumics\*, **Medtronic**, Middlepeak\*, Newpace\*, Nuvera\*, Phillips, Pulse Biosciences, Sirona Medical\*, Surecor\*, Thermedical, Valcare\*, Vizarmed\*

\* I have an equity stake in these companies

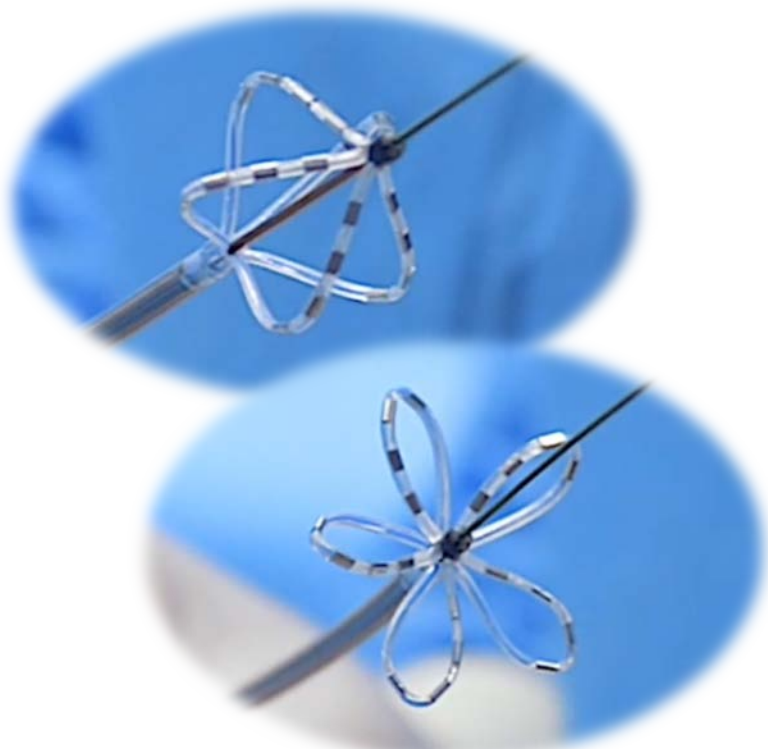
- I will be discussing investigational devices without FDA or CE-Mark approval.



# Pulsed Field Ablation Catheter Ablation Technology

## Focal PFA

Lattice-Tip: RF/PF

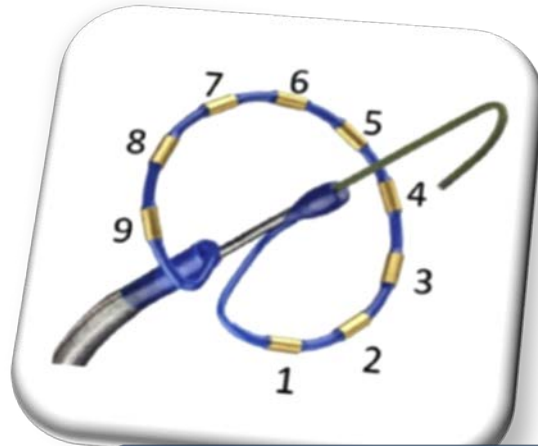


FDA Trial (*ADVENT*) Ongoing

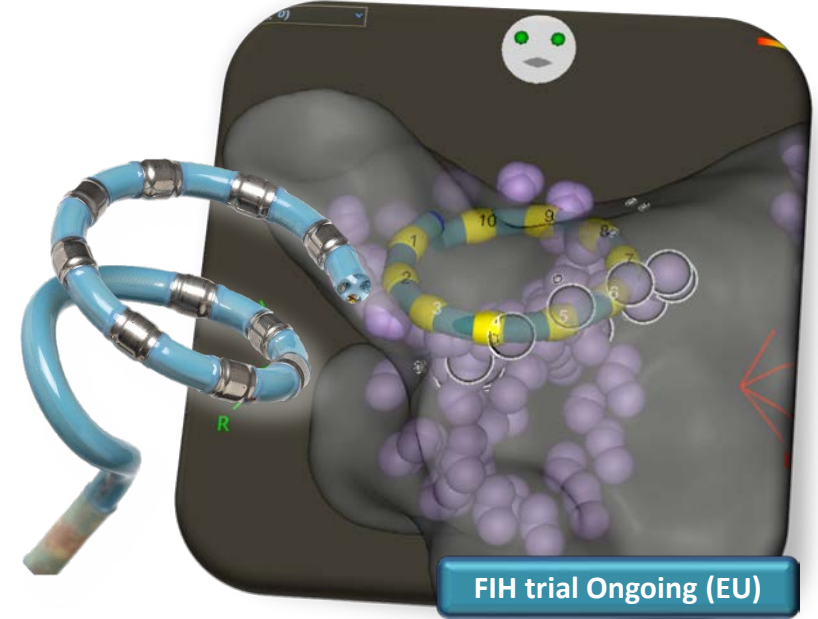
CE-Mark approved



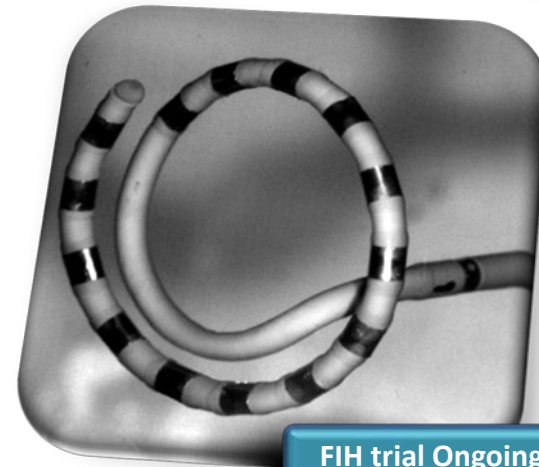
FIH trials Ongoing (EU)



FDA Trial (*PULSED-AF*) Ongoing



FIH trial Ongoing (EU)



FIH trial Ongoing (EU)



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# PFA Ablation Technology

## Pentaspine Multielectrode PFA Catheter (CE-Mark)

### FARAWAVE Catheter

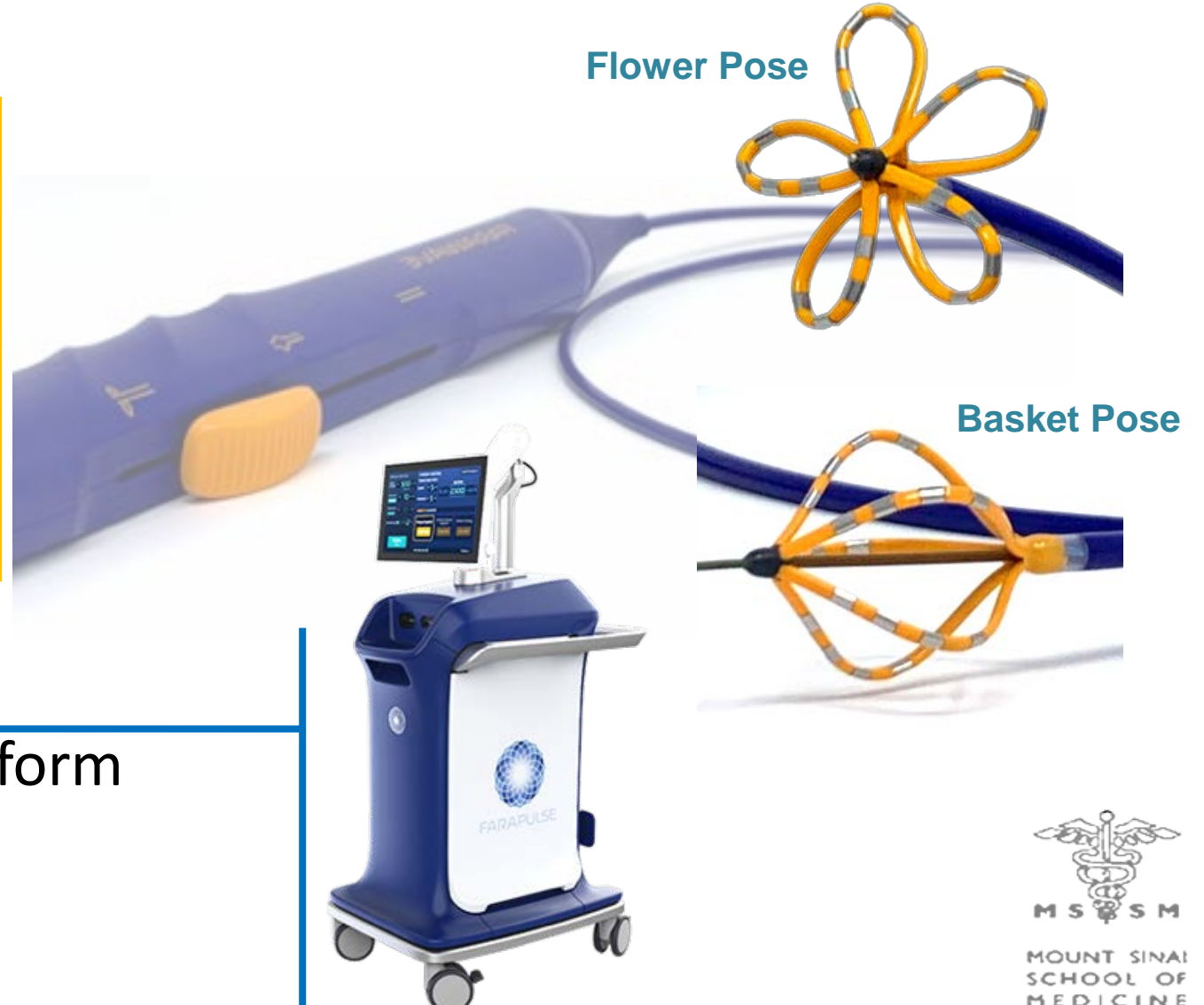
- 12F over-the-wire
- Variable shape
- Two sizes: 31mm and 35mm
- Bipolar delivery

### FARADRIVE Sheath

13F ID

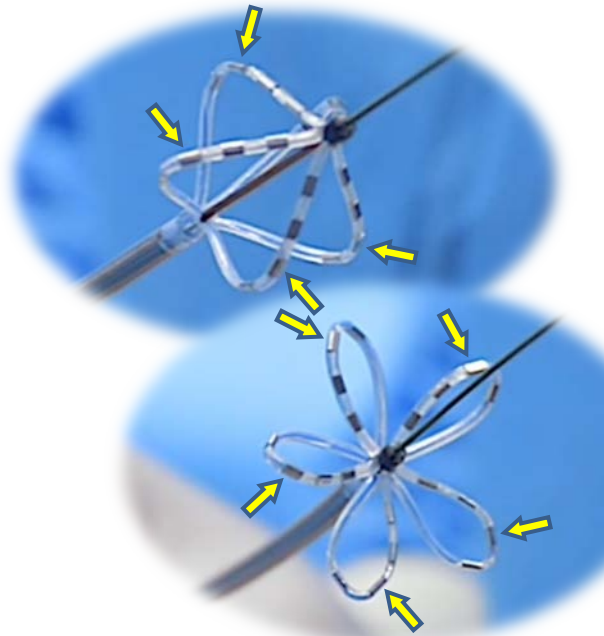
### FARASTAR Generator

- Catheter-specific biphasic waveform
- Power Titration: 1800 – 2000 V

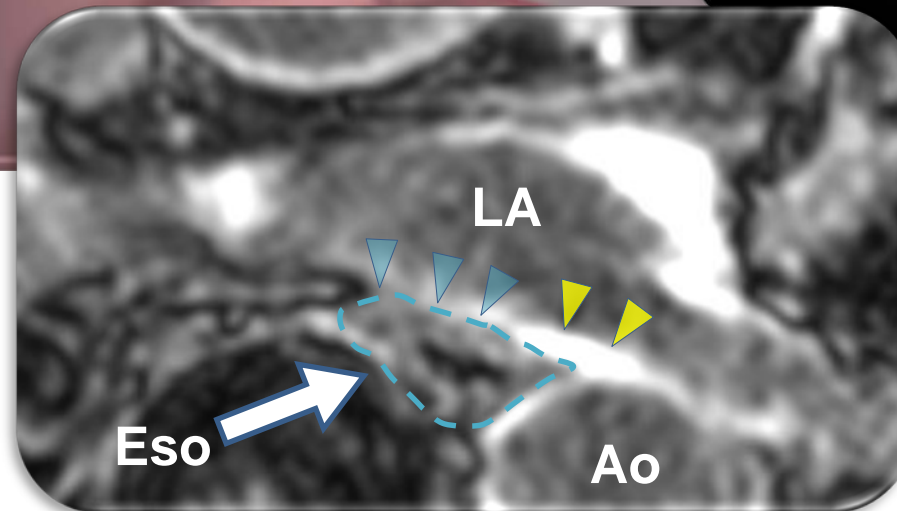
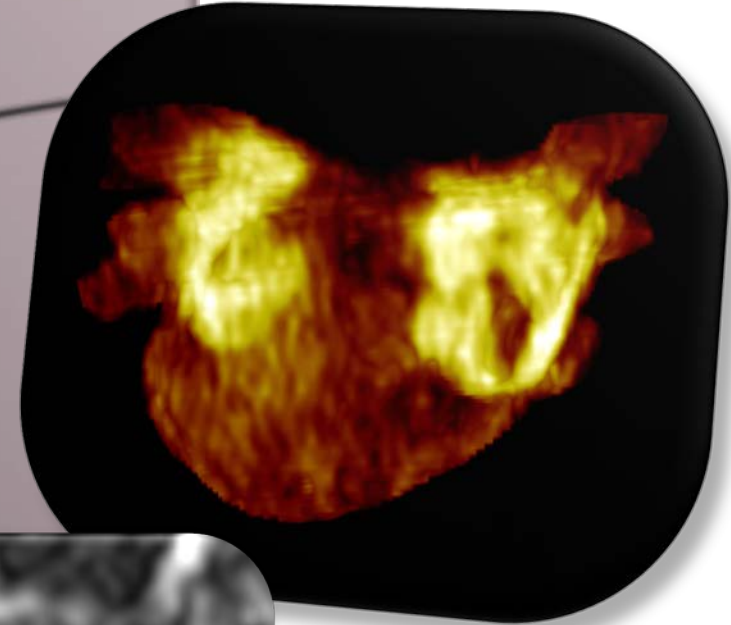
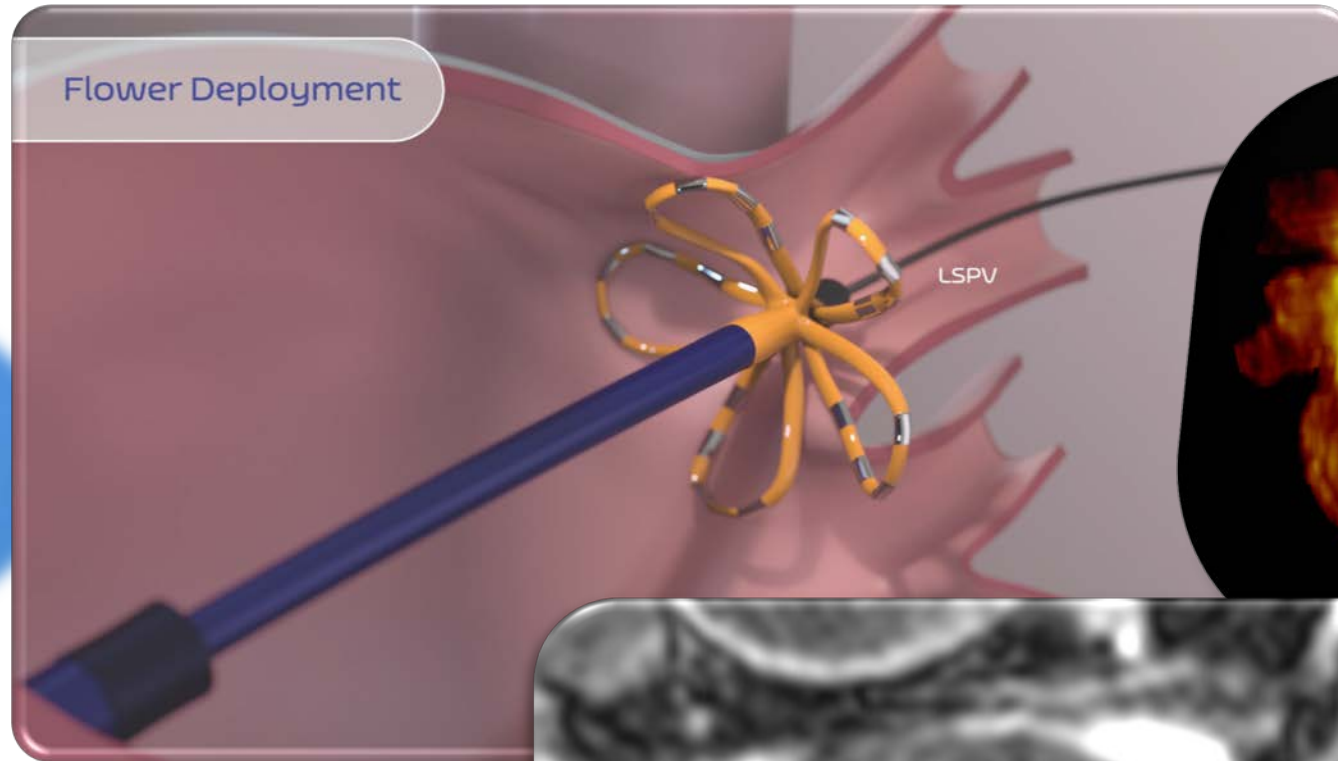
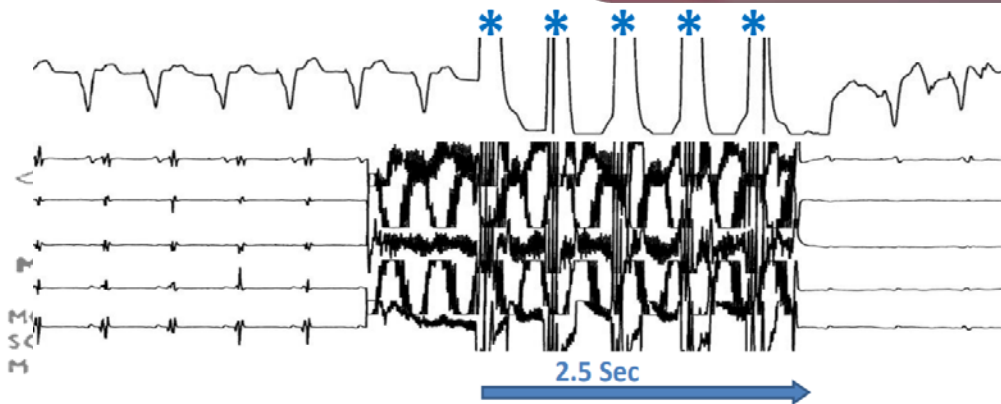


# PVI in Paroxysmal AF

## Multielectrode Basket/Flower PFA Catheter



EGMs from 3<sup>rd</sup> electrode



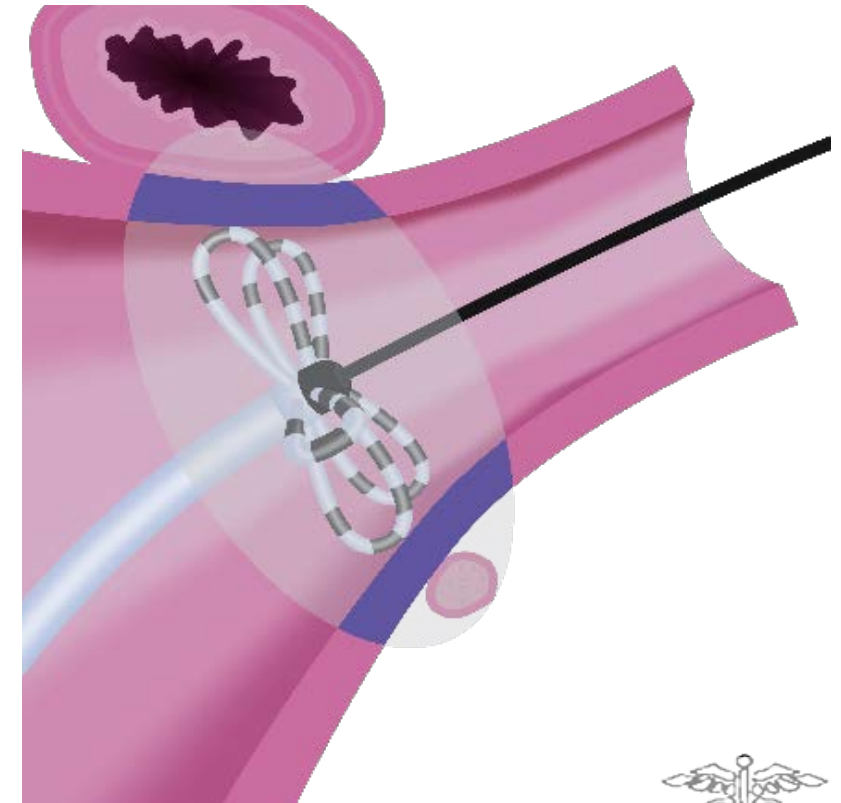
VY.Reddy, P.Neuzil, J.Koruth, et al, *JACC* 74:315–26 (2019)



# PAF: *IMPULSE*, *PEFCAT* & *PEFCAT II*

## Baseline Demographics

	Total (N = 121)	PFA <sub>ow</sub> (N=49)
Age, years	57.4±10.3	56.9±10.4
Male	89 (73.6%)	32 (65.3%)
LA diameter, mm	40.5±4.5	40.0±5.0
LVEF	62.5±5.7	61.2±7.2
Sleep apnea	4 (3.3%)	2 (4.1%)
COPD	4 (3.3%)	0 (0%)
Hypertension	68 (56.2%)	29 (59.2%)
Diabetes	11 (9.1%)	3 (6.1%)
Dyslipidemia	41 (33.9%)	17 (34.7%)
Stroke or TIA	6 (5.0%)	3 (6.1%)
CAD (MI / CABG)	4 (3.3%)	2 (4.1%)
Antiarrhythmics	118 (97.5%)	49 (100%)
Class I	83 (68.6%)	38 (77.6%)
Class III	23 (19.0%)	8 (16.3%)
Beta blockers	44 (36.4%)	18 (36.7%)



# PAF: *IMPULSE*, *PEFCAT* & *PEFCAT II*

## Procedural Characteristics

	Total Cohort (n=121)	PFA <sub>ow</sub> (N=49)
PVI Success	475 of 475 (100%)	195 of 195 (100%)
No. of Lesions / PV		
Combined PVs	7.2 ± 2.2	8.7 ± 1.5
LCPV	12.9 ± 6.1	18.5 ± 4.7
LSPV	7.3 ± 2.4	8.6 ± 1.7
LIPV	6.9 ± 2.2	8.5 ± 1.6
RSPV	7.2 ± 2.4	8.6 ± 1.6
RIPV	6.9 ± 2.5	8.5 ± 1.6
Procedure time	96.2 ± 30.3	97.2 ± 29.1
Mapping time	19.3 ± 12.0	19.0 ± 13.5
Catheter dwell time	34.4 ± 15.8	33.7 ± 12.2
Fluoroscopy time	13.7 ± 7.8	13.4 ± 7.6
CTI Block Success	4 of 4 (100%)	4 of 4 (100%)
Catheter dwell time	8.5 ± 7.7	8.5 ± 7.7



→ PVI was typically achieved with a single application

→ Remap results drove dose optimization throughout the studies

→ Protocol-mandated mapping

# PAF: *IMPULSE, PEFCAT & PEFCAT II*

## Primary Safety Events

	Total Cohort (n=121)	PFA <sub>ow</sub> (N=49)
<b>Total Patient Cohort, n = 121</b>		
Death	0 (0)	0 (0)
Myocardial infarction	0 (0)	0 (0)
Diaphragmatic paralysis	0 (0)	0 (0)
Stroke	0 (0)	0 (0)
TIA	1 (0.8%)	0 (0)
Other thromboembolism	0 (0)	0 (0)
Cardiac perforation or tamponade	1 (0.8%)	0 (0)
Vascular complications (AV fistula)	2 (1.7%)	1 (2.0%)
PV stenosis >70%	0 (0)	0 (0)
Atrio-esophageal fistula,	0 (0)	0 (0)
Pericarditis requiring intervention	0 (0)	0 (0)
Pulmonary edema, n (%)	0 (0)	0 (0)





# Additional Safety Assessments

## Esophageal Findings

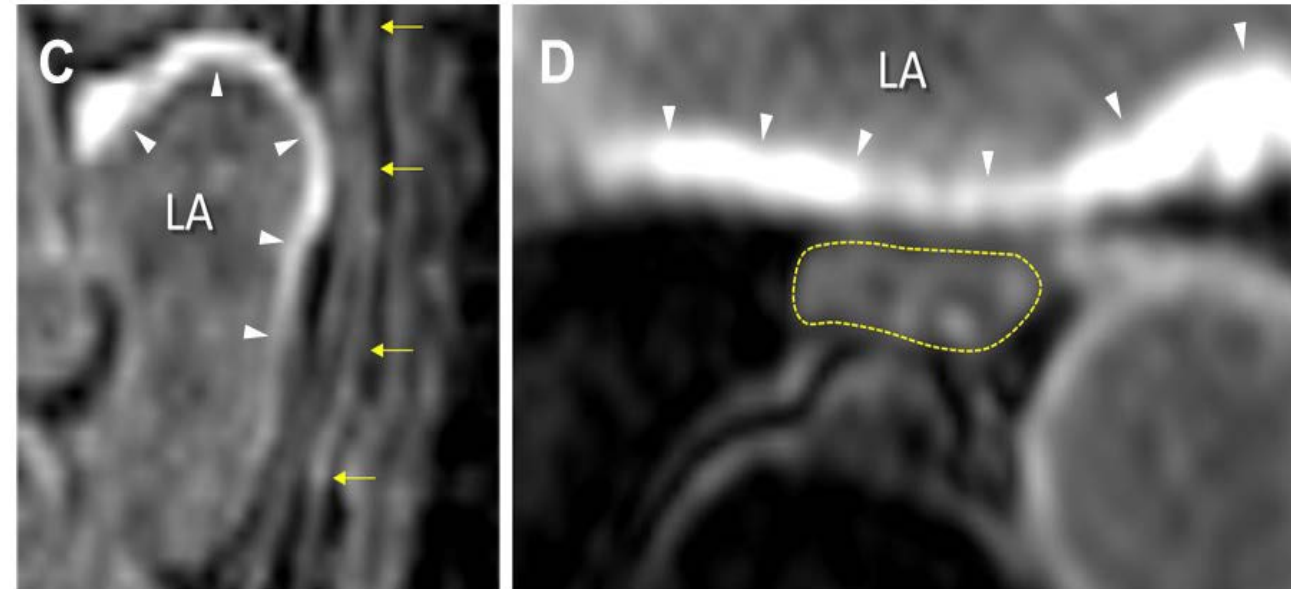
	No. of Pts Assessed	Findings
<b>Eso findings</b>		
EGD	38	<b>No eso lesions</b>
Chest MRI	18	No eso enhancement
Brain MRI	18	16 of 18 negative
<b>Phrenic nerve</b>		
Pacing	121	No paresis / palsy
X-Ray at 3 mo	110	No paresis / palsy
<b>PV stenosis</b>		
EAM at 3 mo	110	No PV stenosis or narrowing
CT at 3 mo	74	



# Additional Safety Assessments

## Esophageal Findings

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# Additional Safety Assessments

## Brain: Silent Cerebral Ischemic Events

	No. of Pts Assessed	Findings
<b>Eso findings</b>		
EGD	38	No eso lesions
Chest MRI	18	No eso enhancement
<b>Brain MRI</b>	<b>18</b>	<b>16 of 18 negative</b>
<b>Phrenic nerve</b>		
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### ➔ Post-procedure MRIs in 18 pts

- Screening in Asymptomatic pts (n=17)
  - 1 of 17: DWI-positive / FLAIR-negative
- Imaging in 1 symptomatic pt (TIA)
  - 1 of 17: DWI-positive / FLAIR-negative

### Additional: Brain MRI Series with PFA

- MRI<sub>Baseline</sub> ➔ PVI (n=15 pts) ➔ MRI<sub>24 hrs</sub>
- Reviewed by independent radiologists
- 1 of 15: DWI-positive / FLAIR-negative

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A.Anic, Presented at DGK: 87th Annual Meeting of the German Cardiac Society (April 2021)

VY.Reddy, SR.Dukkipati, P.Neuzil, et al, JACC-EP (In Press)



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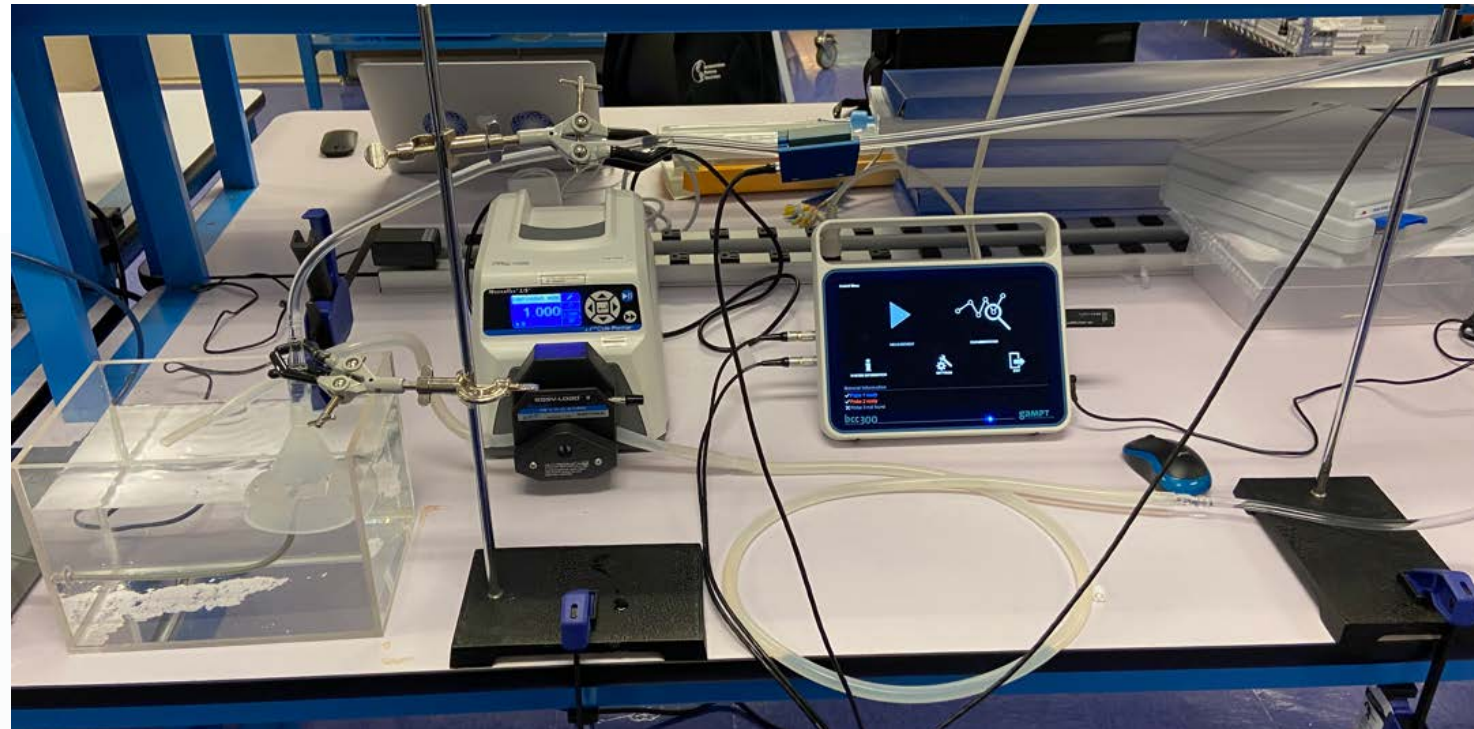
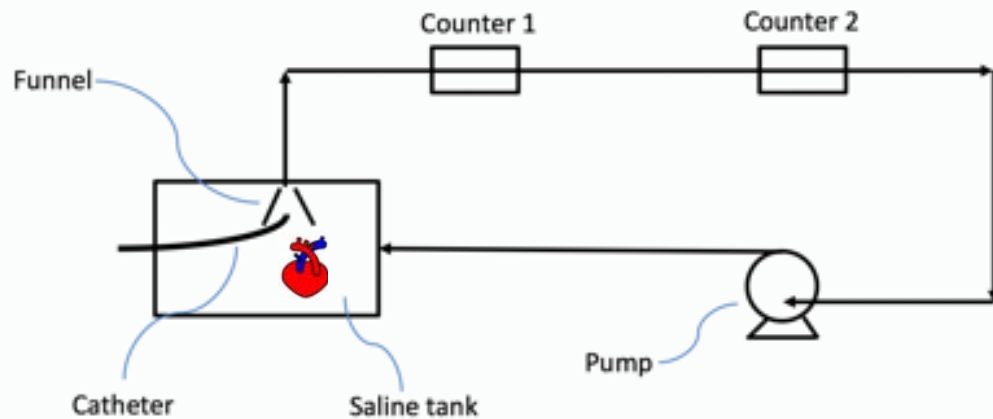
# PFA vs RFA: Microbubbles

## Benchtop Study

Clinical PFA system used in >140 AF patients<sup>1,2</sup> was used

- 13F over the wire 5-spline catheter
- Optimized biphasic, bipolar PFA waveform and generator

Benchtop model with ultrasound bubble counters described previously<sup>3</sup>



1-Reddy VY et al, D-PO01-136, Heart Rhythm Journal. 2020; 17(6), S87-S200.  
2-Reddy VY et al, Journal of Coll Am Cardiology (Sept 2020)  
3-van Es et al, *Cardiovasc. Electrophysiol.* 30 (2019) 2071 – 2079.

# PFA vs RFA: Microbubbles

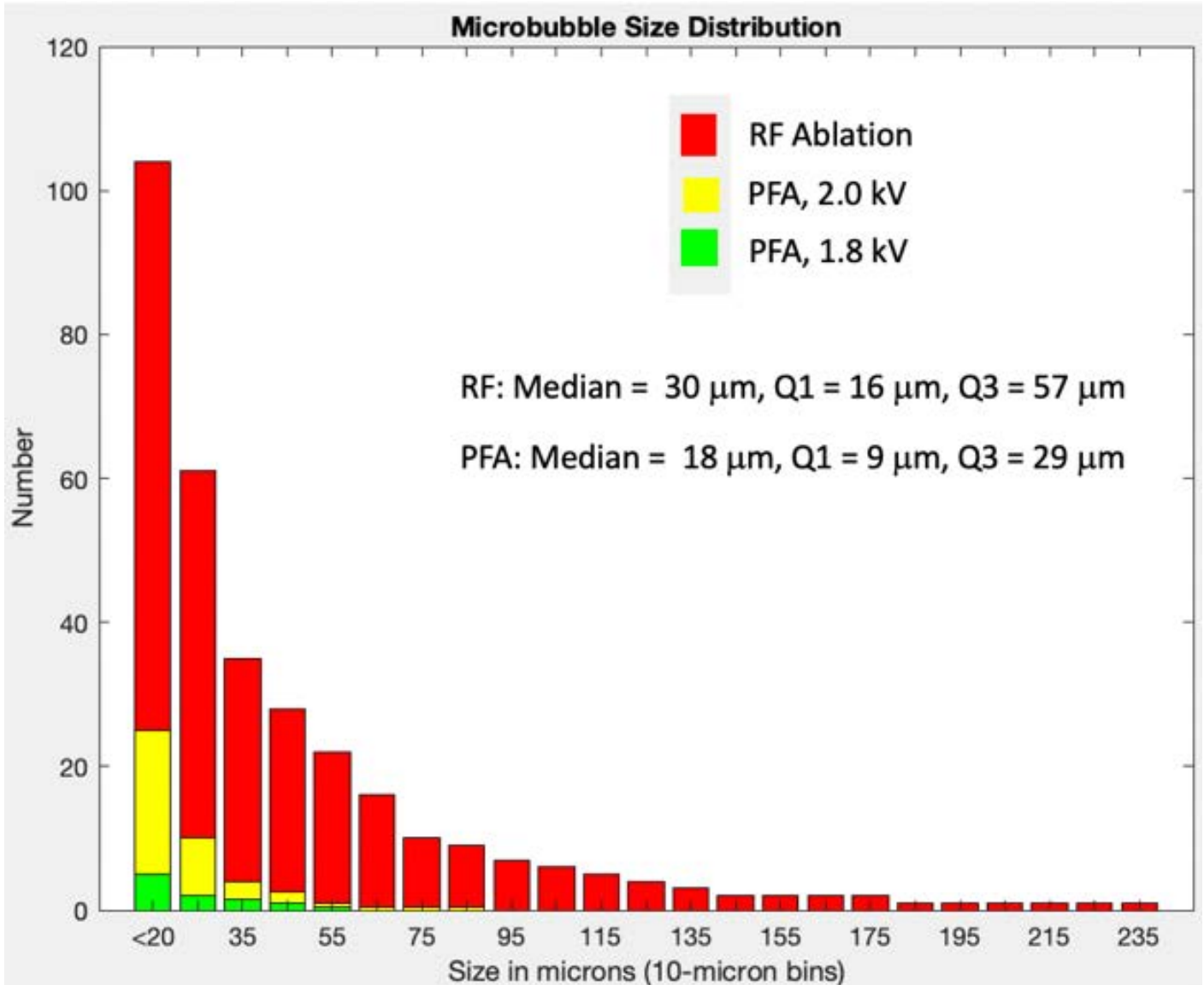
## Benchtop Study

**PFA** 18  $\mu\text{m}$  (9-29 IQR)

**RF** 30  $\mu\text{m}$  (16-57 IQR)



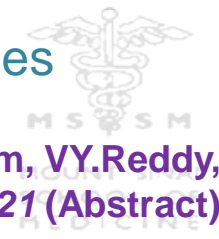
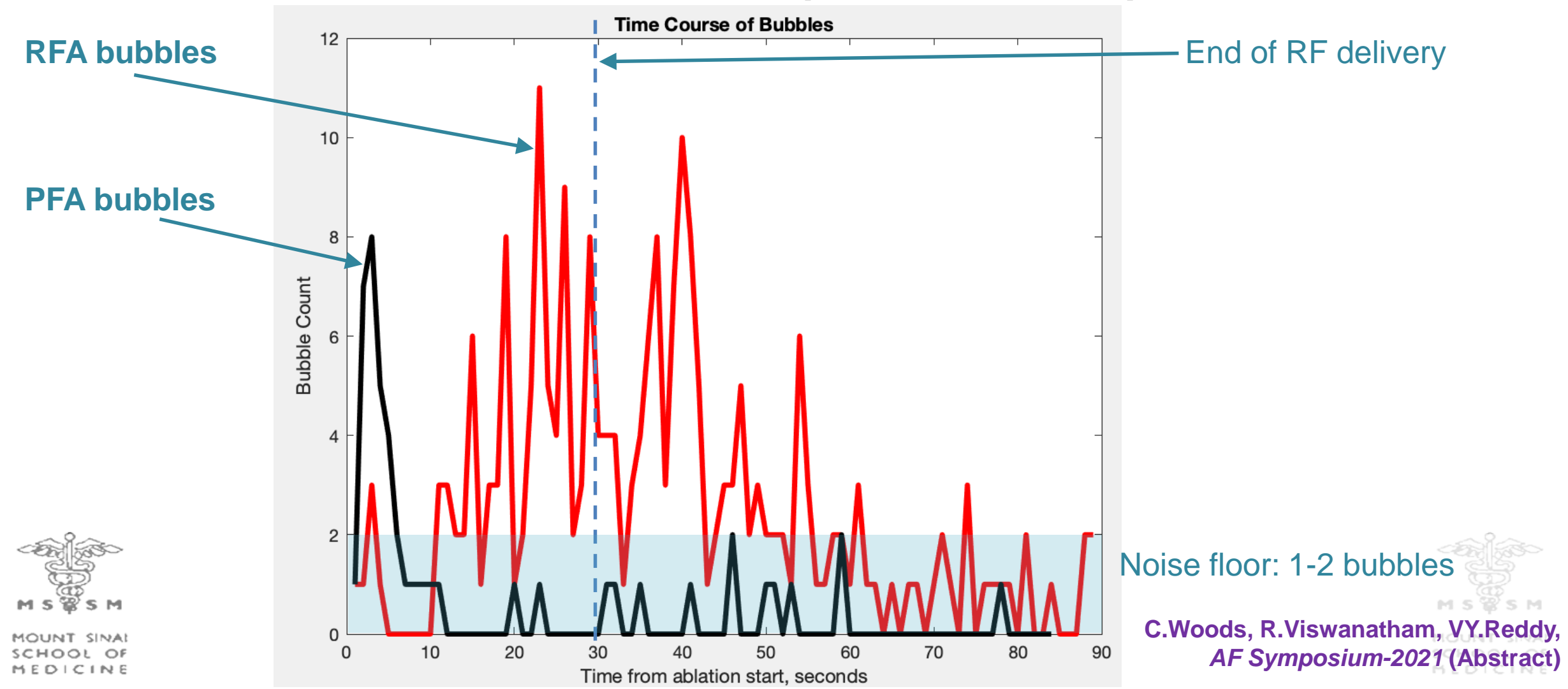
C.Woods, R.Viswanatham, VY.Reddy,  
AF Symposium-2021 (Abstract)



# PFA vs RFA: Microbubbles

## Benchtop Study

### Bubble Counter Observations (Quantitative)



C.Woods, R.Viswanatham, VY.Reddy,  
AF Symposium-2021 (Abstract)

# Additional Safety Assessments

## Phrenic Nerve Assessment

	No. of Pts Assessed	Findings
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Chest MRI	18	No eso enhancement
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VY.Reddy, SR.Dukkipati, P.Neuzil, et al, *JACC-EP* (In Press)

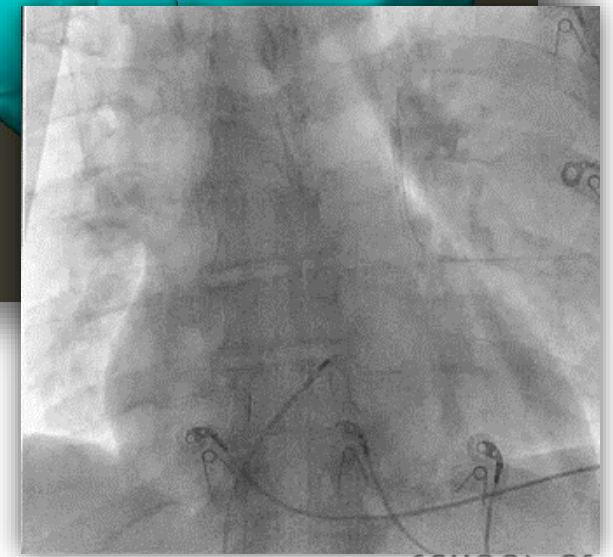
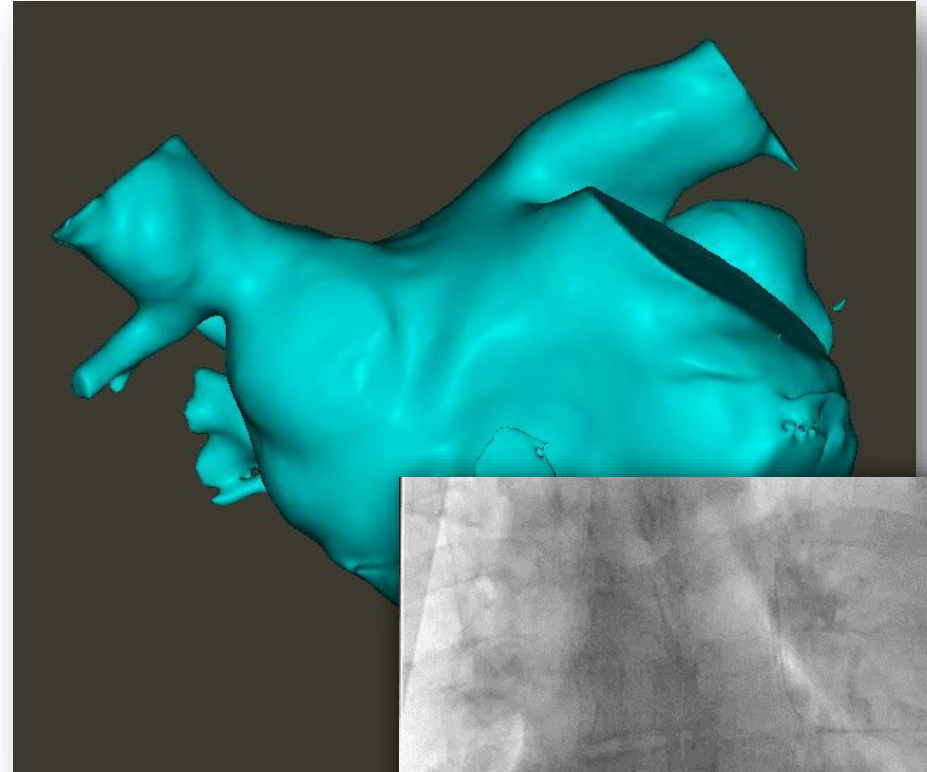


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# A Recent Case

## Asymptomatic Transient Phrenic Nerve Paresis

- 62 yo man with PAF
  - BMI = 22.7 ; Weight = 76 kg
  - LA Diameter = 36 mm
  - RSPV: 13 x 17 mm
- PVI:
  - Pentaspline PFA catheter (31 mm device)
  - LSPV → LIPV → RIPV
  - RSPV: 13 PF applications
    - **Not 8** b/c prolapsing of splines
- Phrenic Nerve Paresis noted
  - Last RSPV PF application: minimal Phrenic capture
  - End of case: right diaphragm didn't move (not paradoxical)
  - But: phrenic capture did occur with pacing
  - Next morning: good movement (plus deep inspiration)



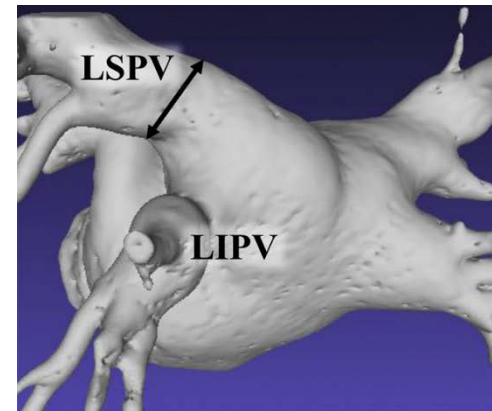


# Pulmonary Vein Stenosis

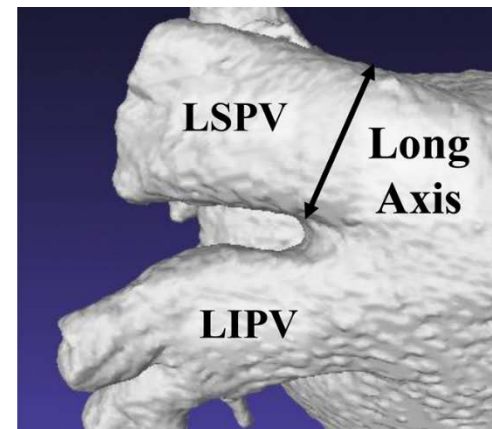
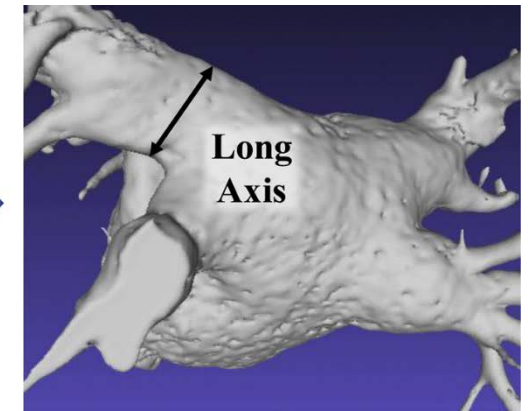
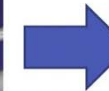
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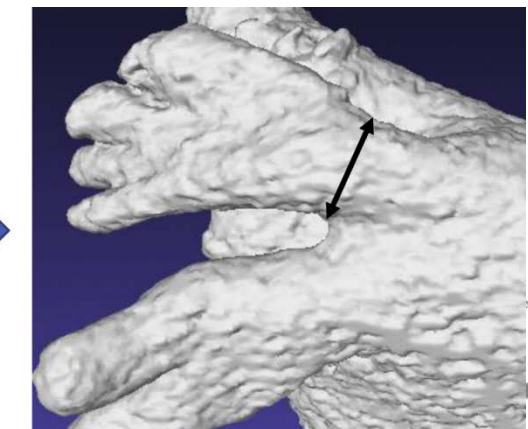
### PV Narrowing / Stenosis Qualitative + Quantitative Analysis



PFA



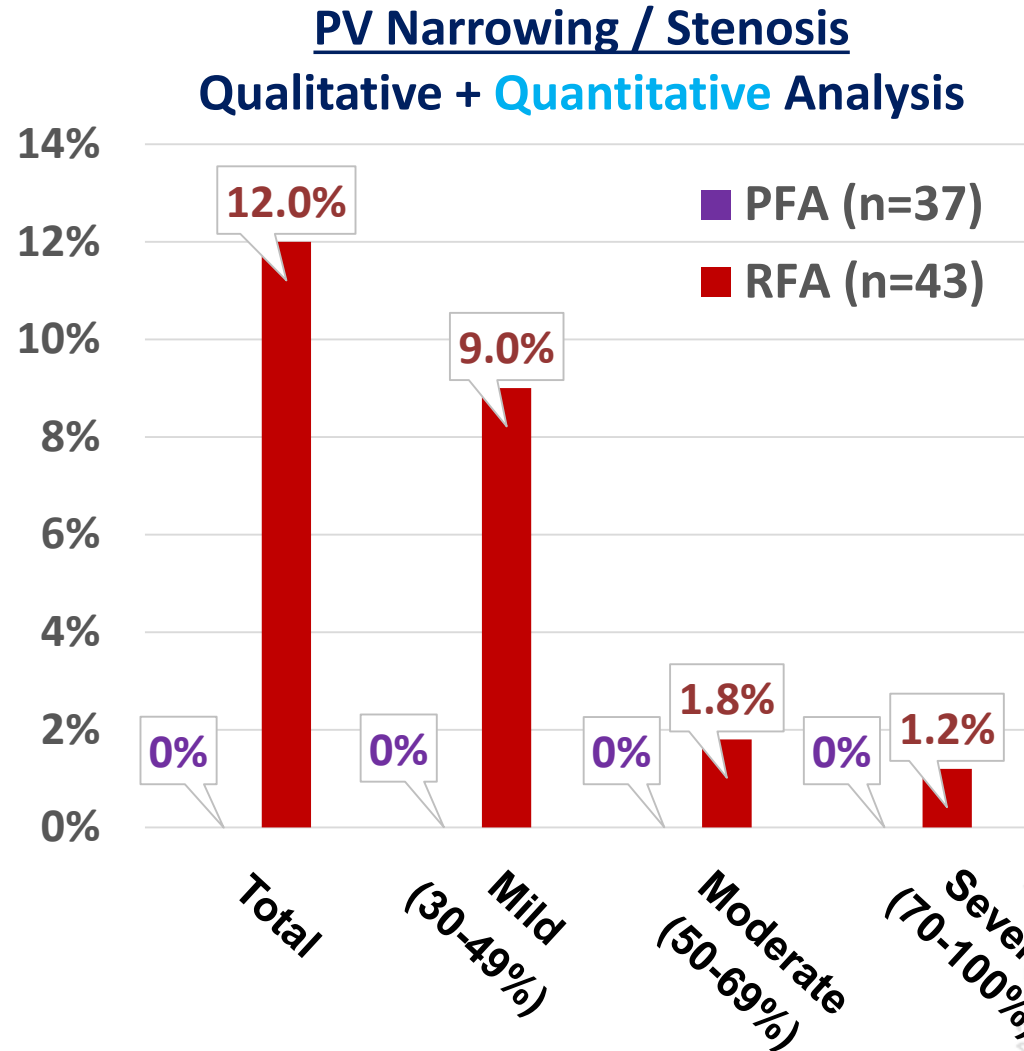
RFA



# Pulmonary Vein Stenosis

## PFA vs RFA

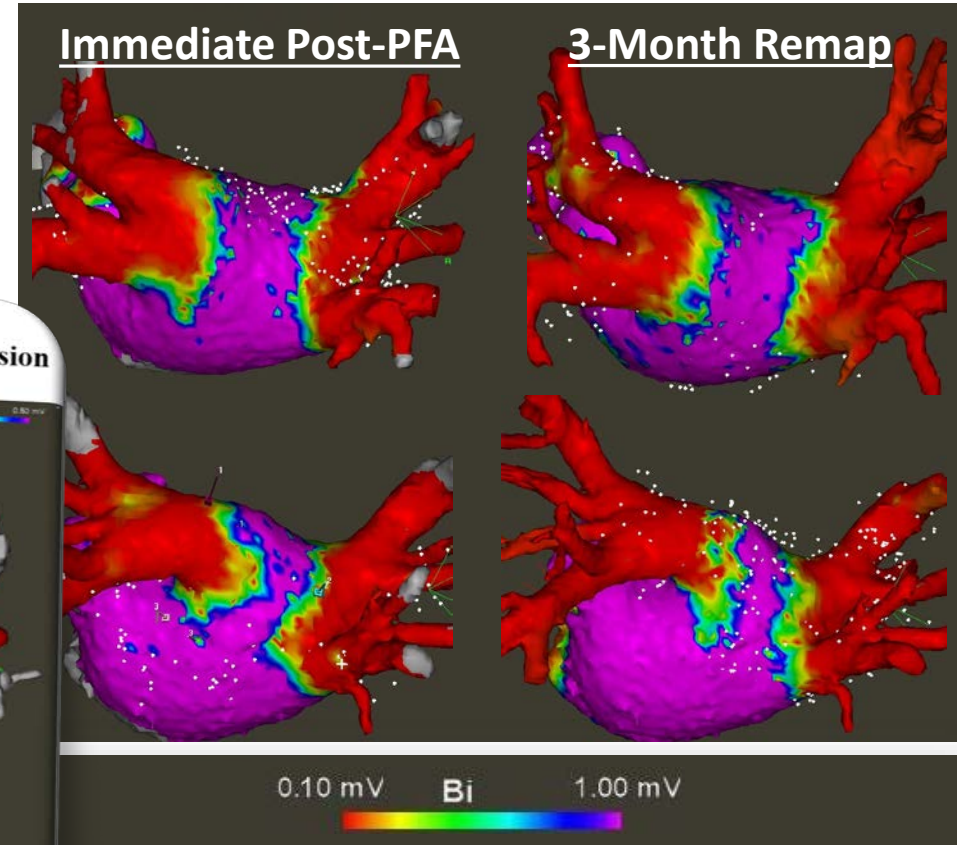
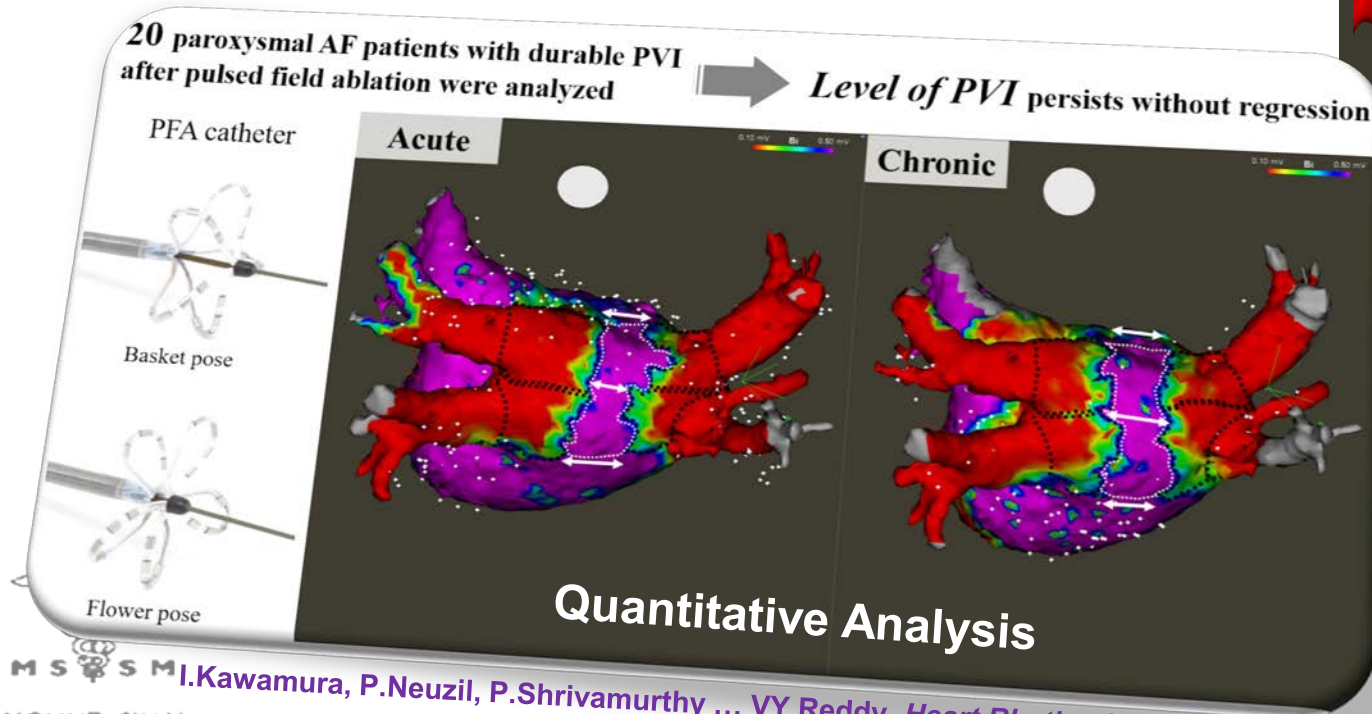
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# PFA for Paroxysmal AF

## Efficacy

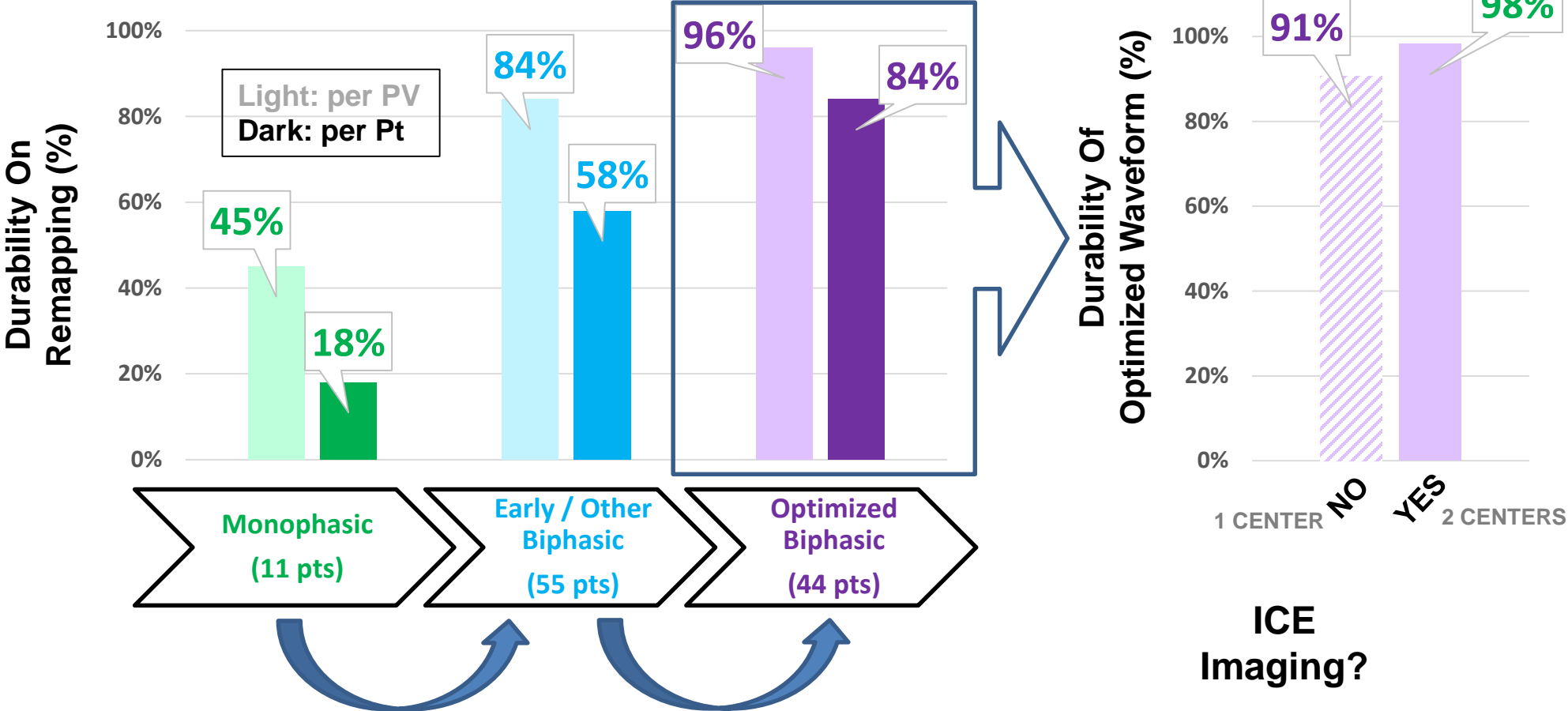
- Acute PVI in 454 of 454 PVs (**100%**)
- Is PVI **Durable**?
  - Protocol-driven redo procedure (not clinically-driven)



# Remapping Outcomes

## PFA<sub>OW</sub> vs Earlier PFA Delivery (N = 110 pts)

AVERAGE 92±29 days



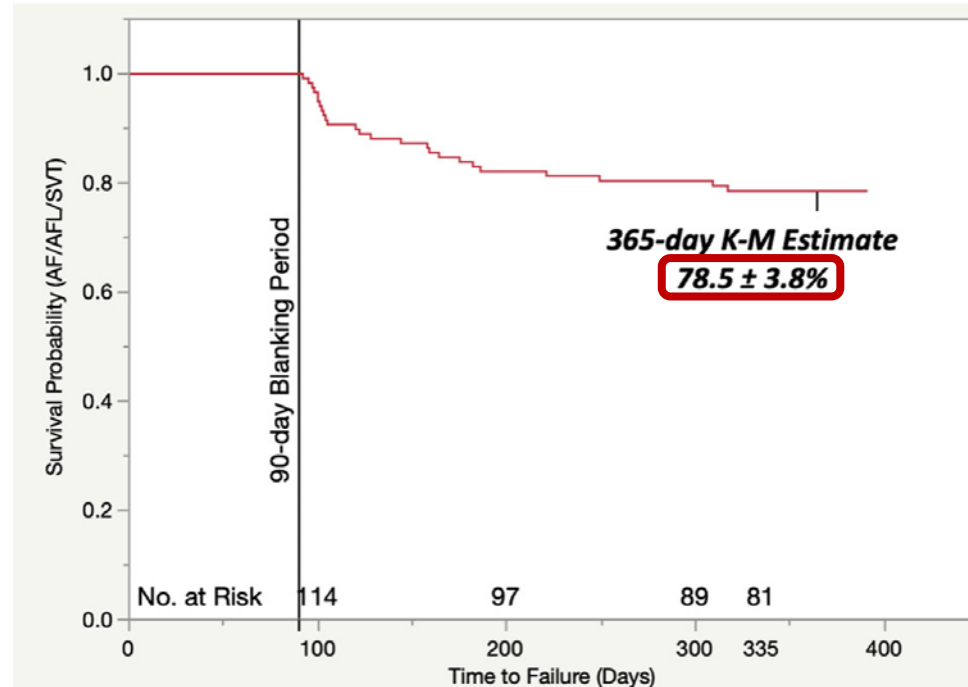
# Clinical Arrhythmia Recurrence

## Full Cohort vs PFA<sub>OW</sub> 1-Year Outcomes

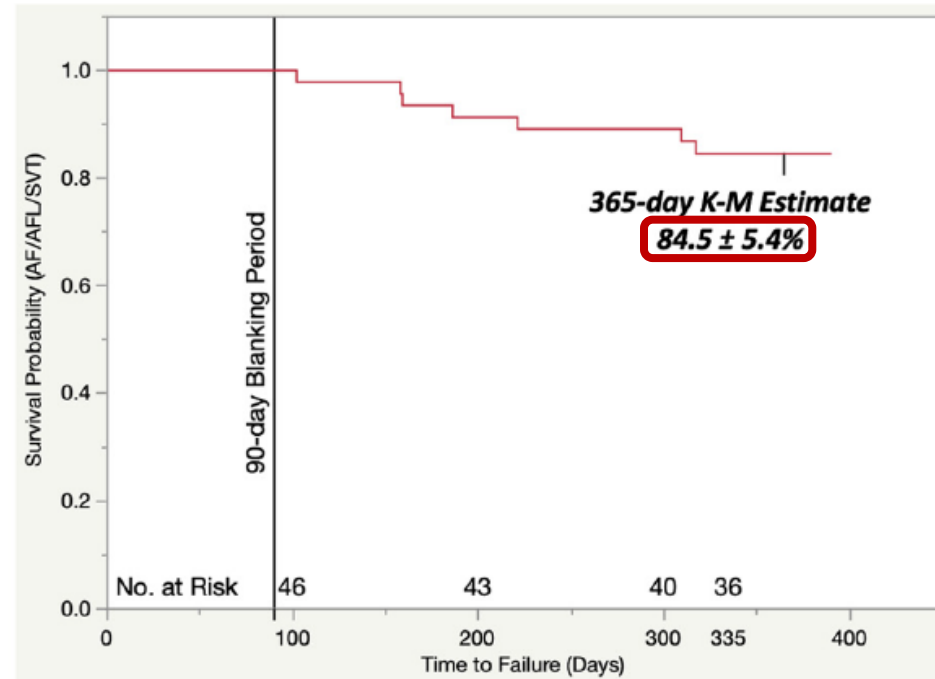
### Compliance with Monitoring

- TTM (weekly): 86.1%
- Holters (6 & 12M): 98.2%

Freedom from AF, AFL or AT: Entire Cohort



Freedom from AF, AFL or AT: PFA-OW Cohort



# Clinical Arrhythmia Recurrence

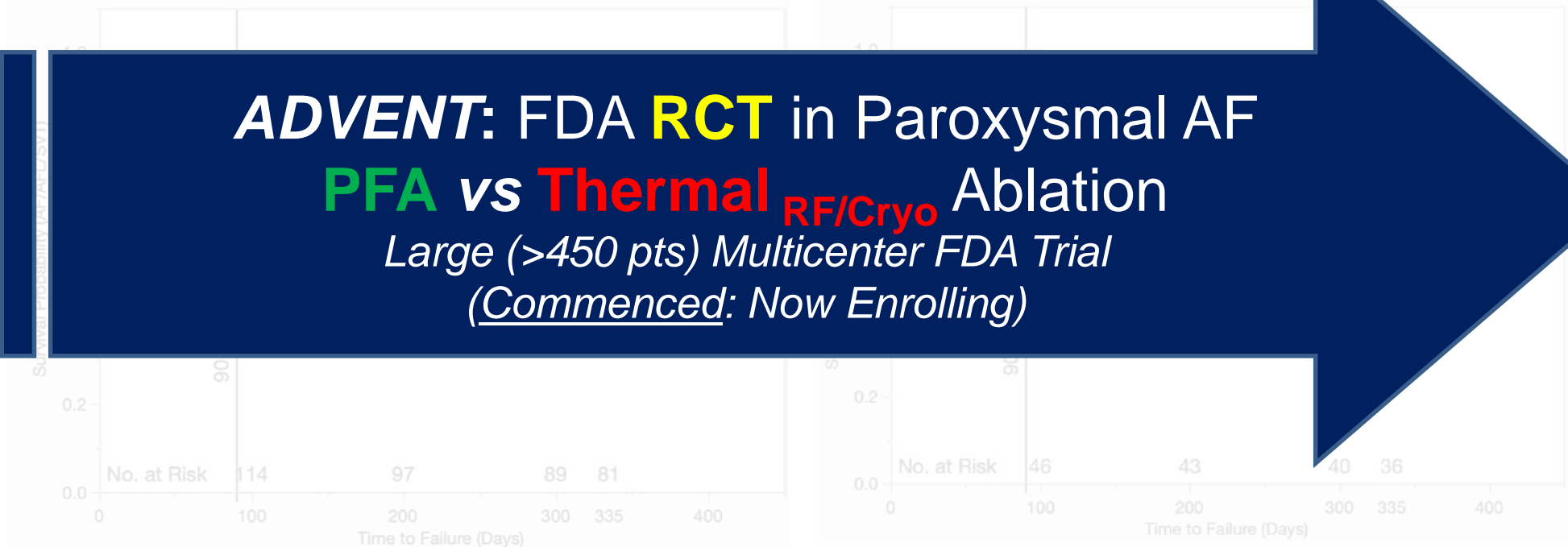
## Full Cohort vs PFA<sub>OW</sub> 1-Year Outcomes

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- > TTM (weekly): 86.1%
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Freedom from AF, AFL or AT: Entire Cohort

Freedom from AF, AFL or AT: PFA<sub>OW</sub> Cohort

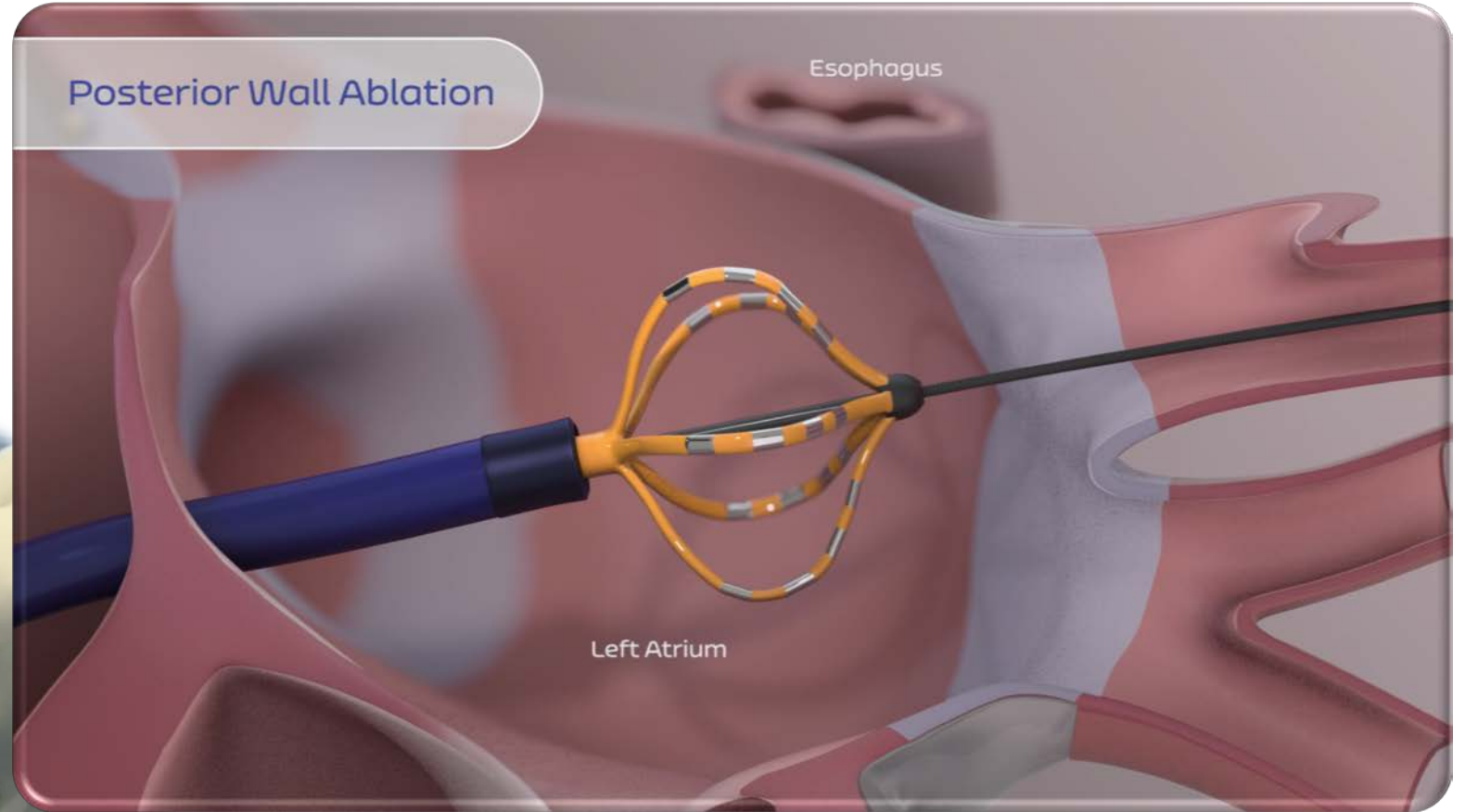
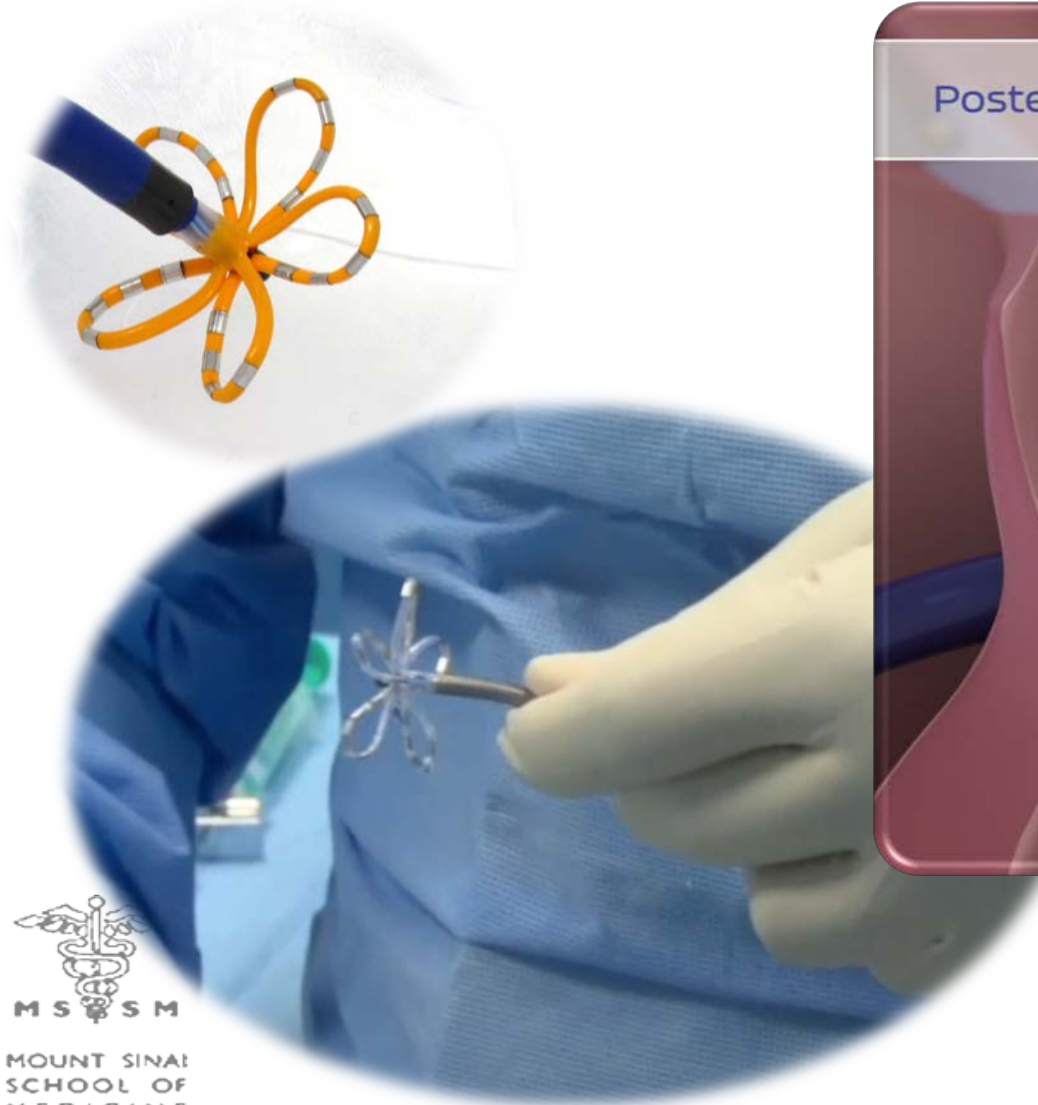


**ADVENT: FDA RCT** in Paroxysmal AF  
**PFA vs Thermal RF/Cryo** Ablation  
*Large (>450 pts) Multicenter FDA Trial  
(Commenced: Now Enrolling)*



# *PersAFOne* (NCT#04170621)

## FIH Study of Persistent AF (PVI + PWA + CTI)

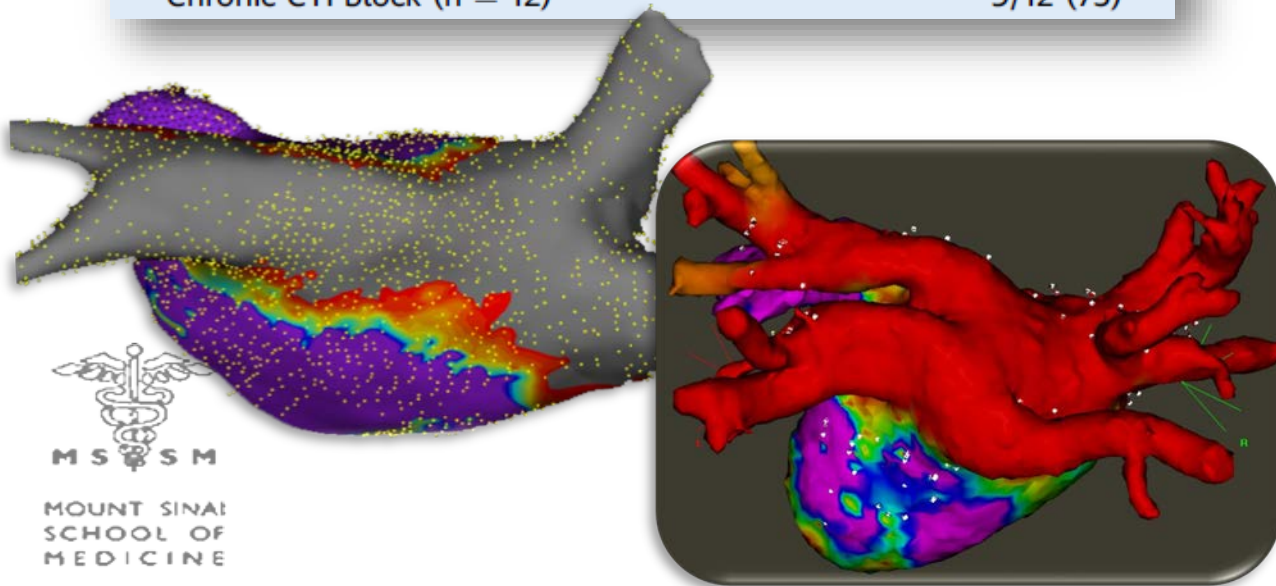


# PersAFOne

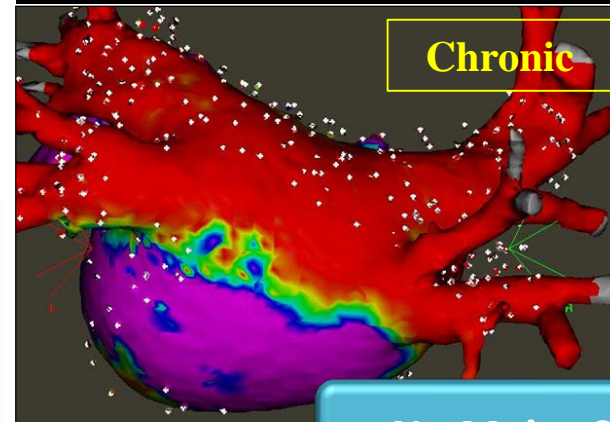
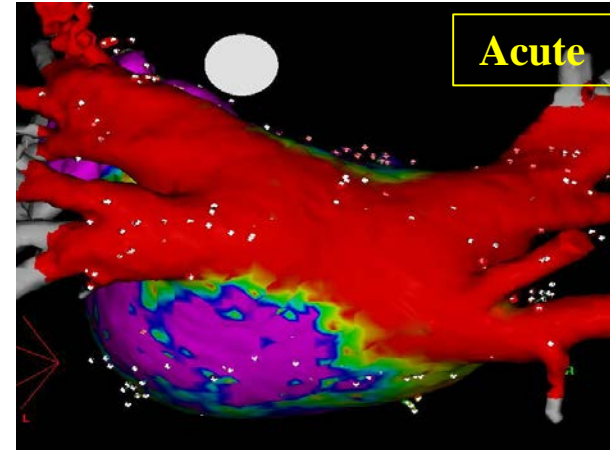
## Clinical Outcomes: Efficacy

**TABLE 3 Primary and Secondary Endpoints (N = 25)**

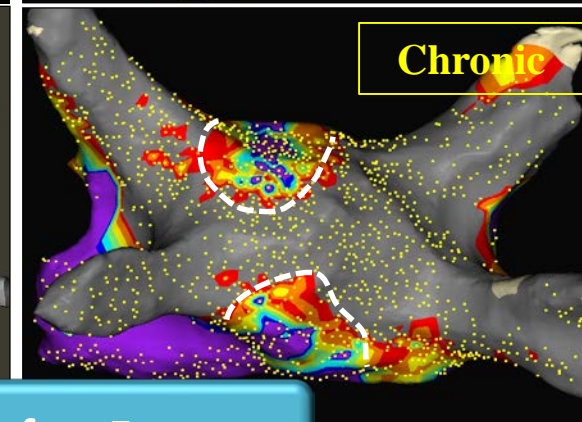
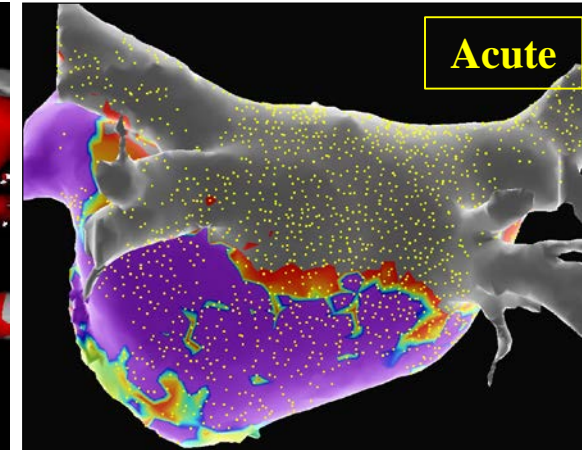
Primary feasibility endpoint (n = 25)	
Acute PV isolation	96/96 (100)
Secondary feasibility endpoints (n = 25)	
Chronic PV isolation (n = 22)	82/85 (96)
Chronic LAPW isolation (n = 22)	
Full cohort (n = 22)	21/22 (95)*
Treated using pentaspline catheter only (n = 21)	21/21 (100)*
Acute CTI block (n = 8)	8/8 (100)
Chronic CTI block (n = 12)	9/12 (75)



18/21 Unchanged



3/21 Localized Regression



No Major Safety Events

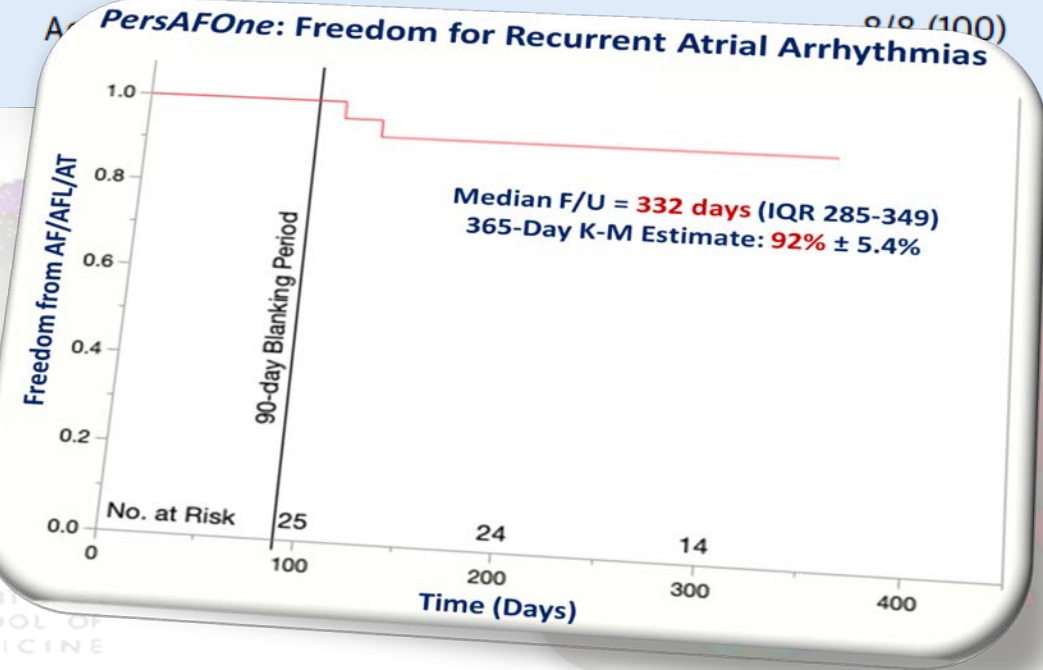


# PersAFOne

## Clinical Outcomes: Efficacy

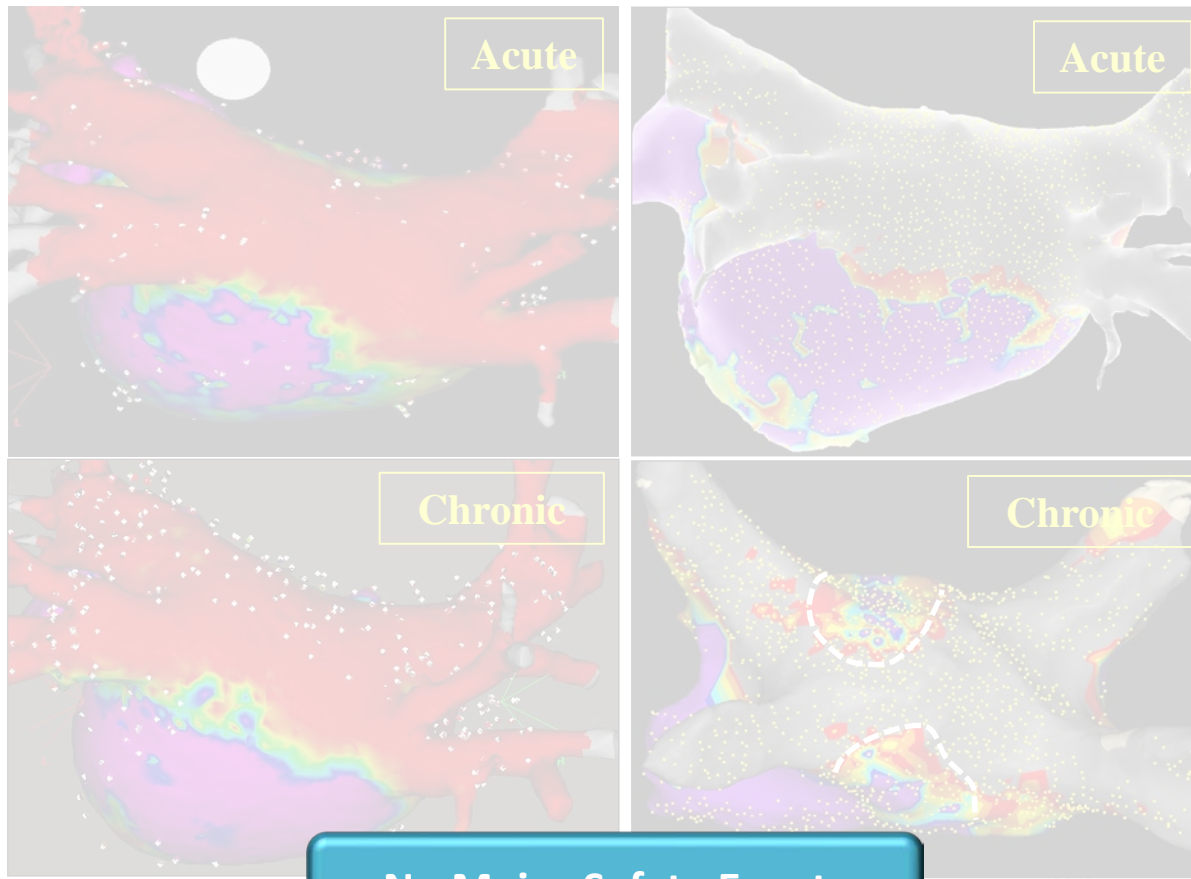
**TABLE 3 Primary and Secondary Endpoints (N = 25)**

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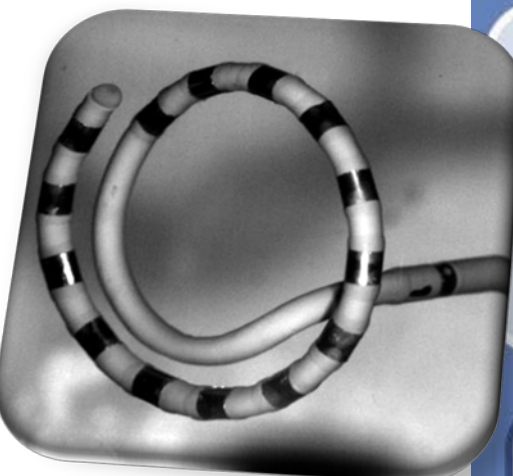


No Major Safety Events

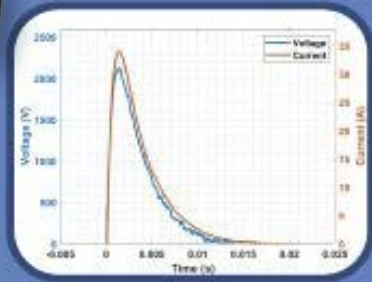
VY.Reddy, A.Anic, J.Koruth, ... P.Neuzil, JACC 76:1068-1080 (2020)

# PFA: Other Technologies

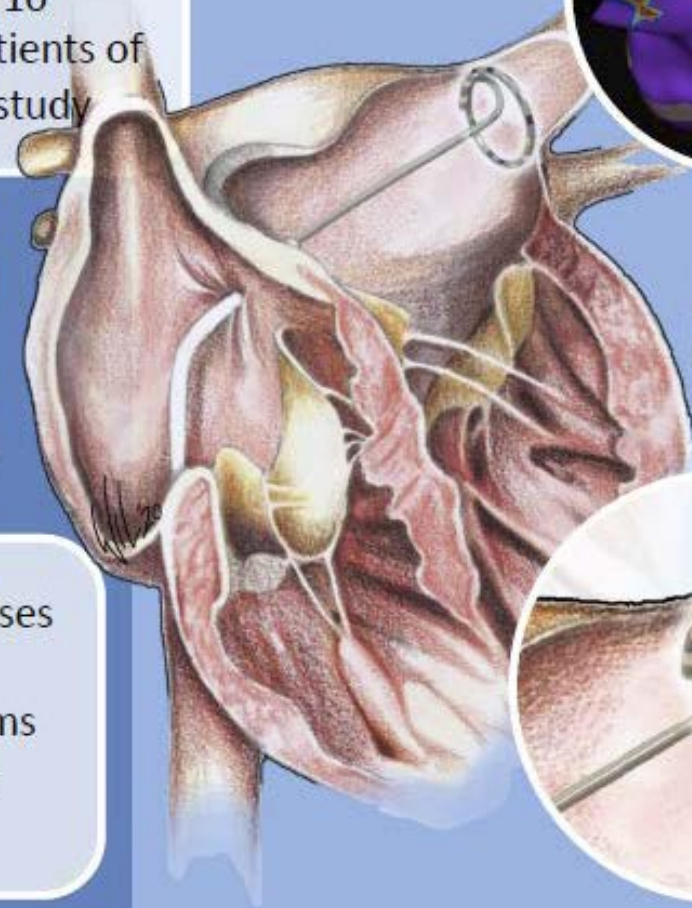
## PV Loop Catheter – *Single Pulse IRE*



Single pulse IRE ablation successfully isolated all pulmonary veins in 10 atrial fibrillation patients of this first-in-human study



- Mean  $2.4 \pm 0.4$  pulses per PV
- Pulse duration 6 ms
- No complications occurred



- Advantages:
- Non-thermal
  - Feasible and safe
  - Ultra rapid
  - No complications

- Disadvantages
- ST segment elevations
  - Gas bubbles
  - High voltage required
  - Myocardial stunning



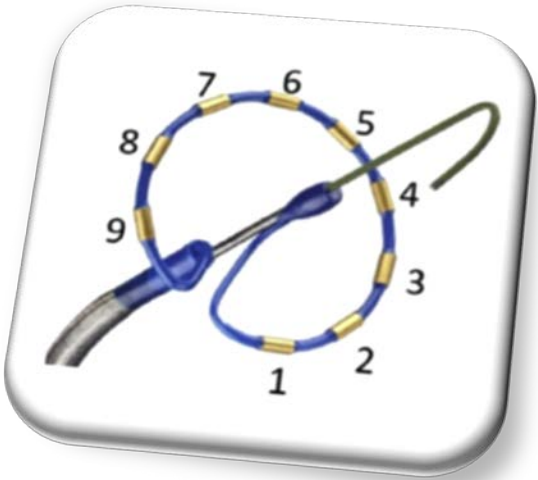
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# PFA: Other Technologies

## PV Loop Catheter – *PULSED-AF* Pilot Trial



- 14 patients: PAF (n=13) or PerAF (n=1)

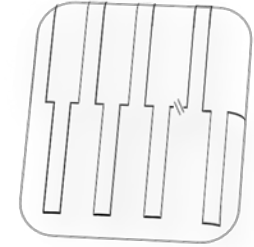
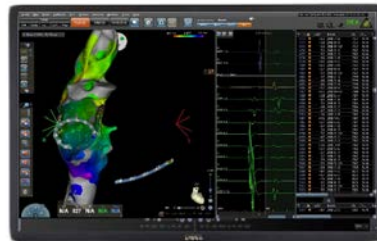
Procedural Characteristics	N = 14
Acute PV Isolation (n = 56 PVs)	14 / 14 (100%)
Procedure Time (skin-to-skin), min	212 ± 10
PFA Device LA Dwell Time, min	91 ± 21
Fluoroscopy Time, min	31 ± 11
Conscious Sedation Use	5 / 14 (36%)
Neuromuscular Blockade Use	1 / 14 (7%)
PFA System-Related SAEs	0 / 14 (0%)
PFA Procedure-Related SAEs*	1 / 14 (7%)

\* Groin puncture bleeding



# PFA: Other Technologies

## EAM-Enabled PV Loop Catheter – *inspIRE* Trial



- **Bipolar, Biphasic pulses**
- Touch screen monitor for **electrode selection** and on/off control.



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# PFA: Other Technologies

## EAM-Enabled PV Loop Catheter – *inspIRE* Trial



# Final Thoughts

## Pentastpline PFA Catheter

- In all 121 pts, acute isolation was easily achieved in all PVs
  - All left common PVs successfully treated
- Acute PFA isolation is a poor predictor of durable isolation
  - Discordance appears much greater than RF/Cryo
  - Need to do remapping studies to assess PFA technologies
- Safety profile is very encouraging
  - Consistent with PFA's promise
- Clinical recurrence is very low with good PVI durability
  - Long-Term (1-year) Outcomes are good
  - Suggests no "hidden shortcomings" of the mechanism
- *PersAFone*: Outcomes in persistent AF is quite compelling
  - Larger studies of PFA:PVI+PWA are warranted





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