September 19, 2024
Hot Topics in Cardiology

PULSED FIELD ABLATION FOR ATRIAL FIBRILLATION

A PROMISE FOR SAFER AND MORE EFFECTIVE ABLATION…

AND MAYBE COMMUNITY HOSPITAL INTERVENTION

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Northwell℠
Cardiovascular Institute

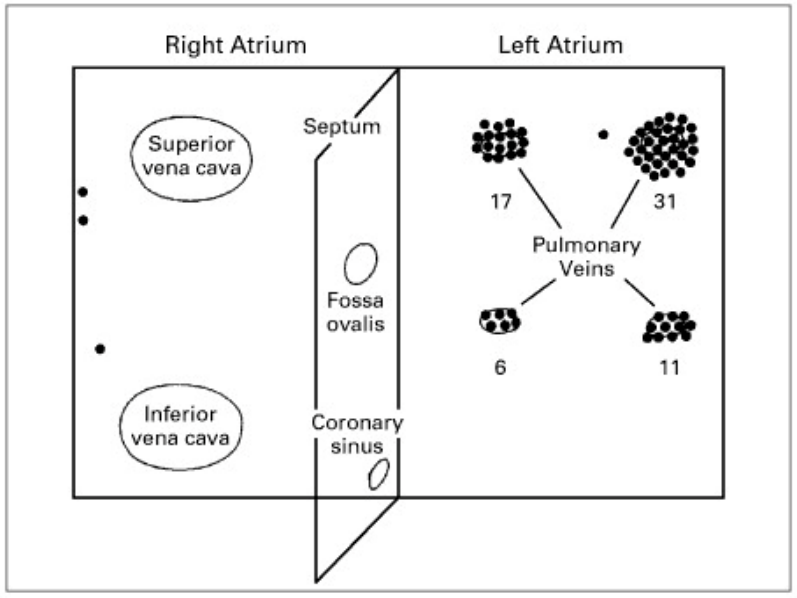
ABLATION OF ATRIAL FIBRILLATION

AF ablation based on the premise of Pulmonary Vein Isolation began 25 years ago

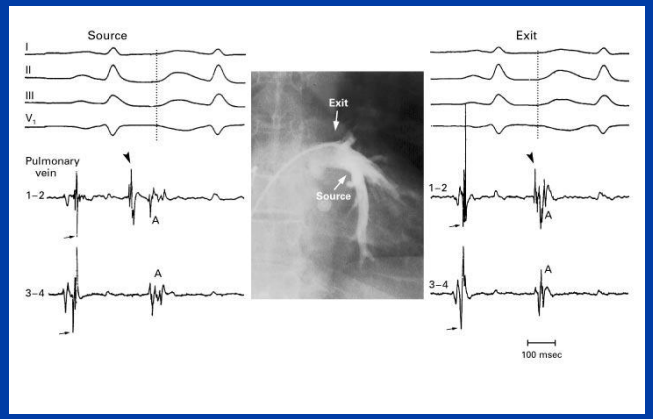
SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS

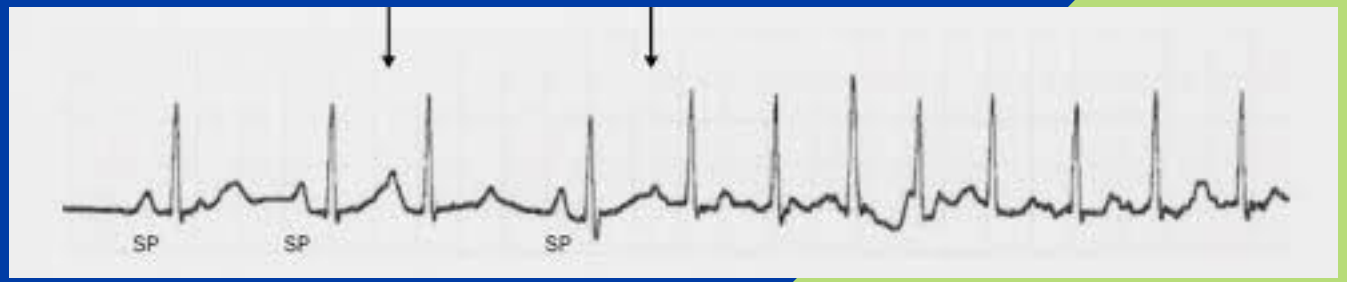
MICHEL HAÏSSAGUERRE, M.D., PIERRE JAÏS, M.D., DIPEN C. SHAH, M.D., ATSUSHI TAKAHASHI, M.D., MÉLÈZE HOCINI, M.D., GILLES QUINIOU, M.D., STÉPHANE GARRIGUE, M.D., ALAIN LE MOUROUX, M.D., PHILIPPE LE MÉTAYER, M.D., AND JACQUES CLÉMENTY, M.D.

NEJM 1998



94% of triggers in PVs (65/69)





RADIOFREQUENCY (RF) ABLATION FOR PULMONARY VEIN ISOLATION (PVI)

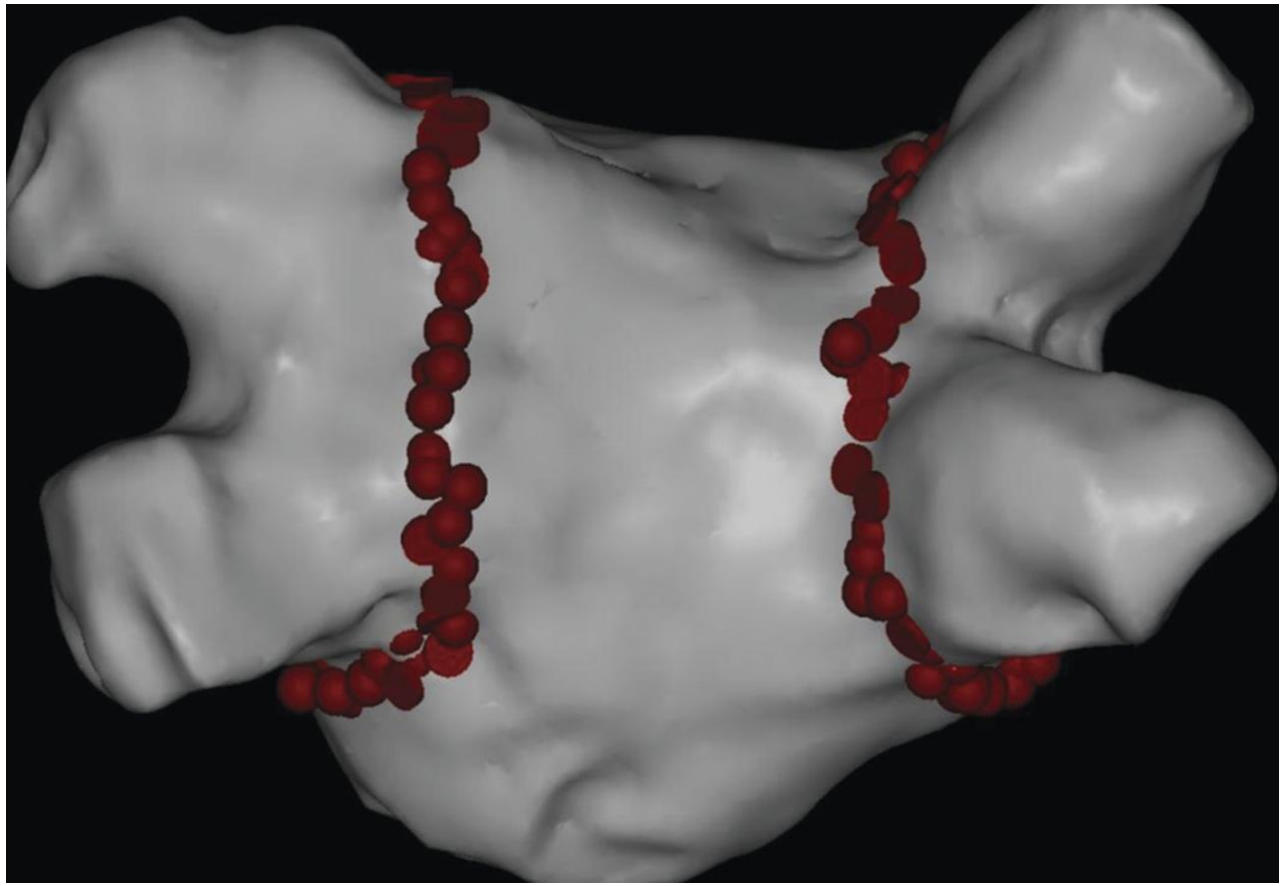
Eradication of triggers initiating AF by PVI

Requires

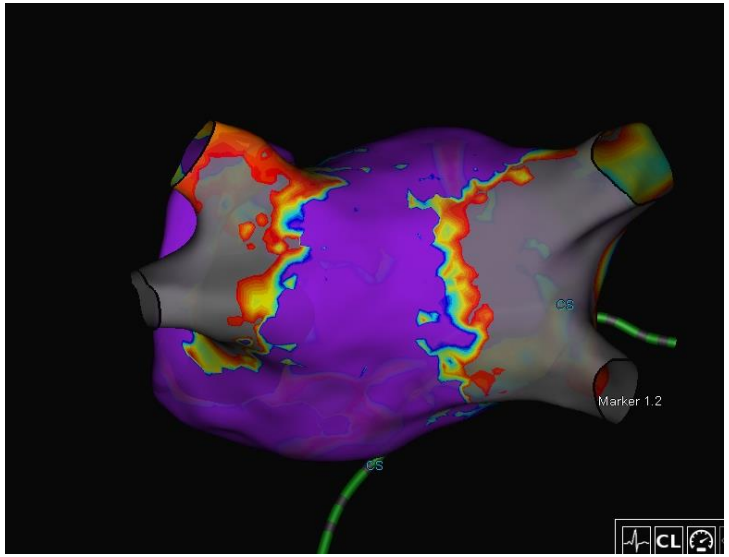
- Transseptal access to left atrium
- Accurate anatomic and electrical mapping
- Point-by-point ablation
- Durable and transmural lesions
- Avoid damage to cardiac and neighboring structure

Progress over 25 years

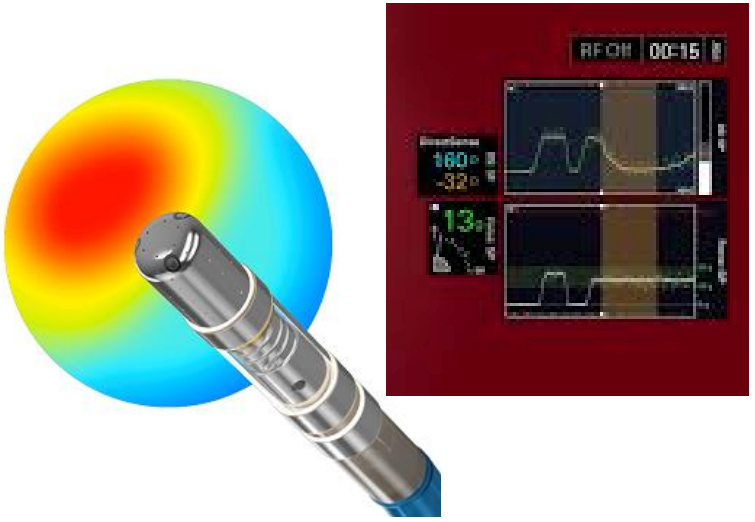
- Technological and technical advances
- AF ablation now more effective, efficient, and safe.



RADIOFREQUENCY (RF) ABLATION FOR PULMONARY VEIN ISOLATION PROGRESS OVER LAST 2.5 DECADES



1. Electro-anatomic mapping systems more precise, using both magnetic and impedance based mapping

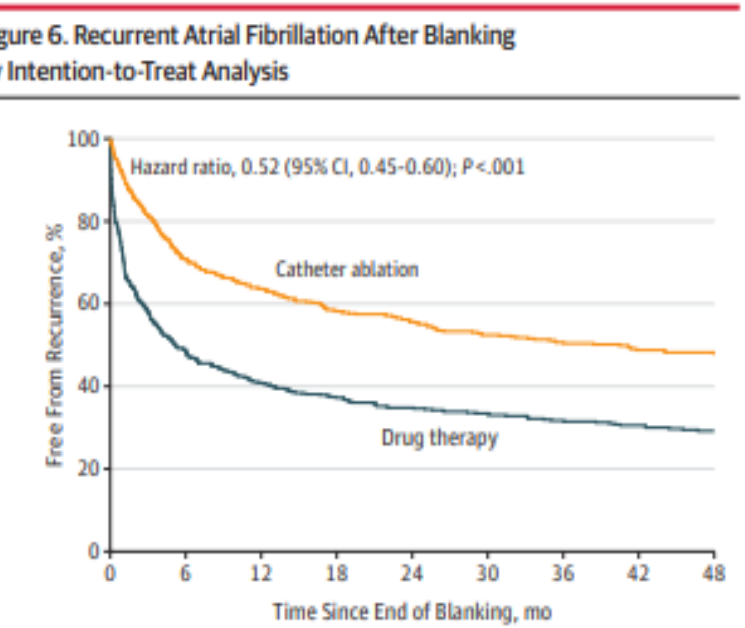


1. Ablation catheter designs
    1. More controllable
    2. Contact Force feedback
    3. Temperature monitoring
    4. Biofeedback
2. Better understanding of safe and effective power delivery

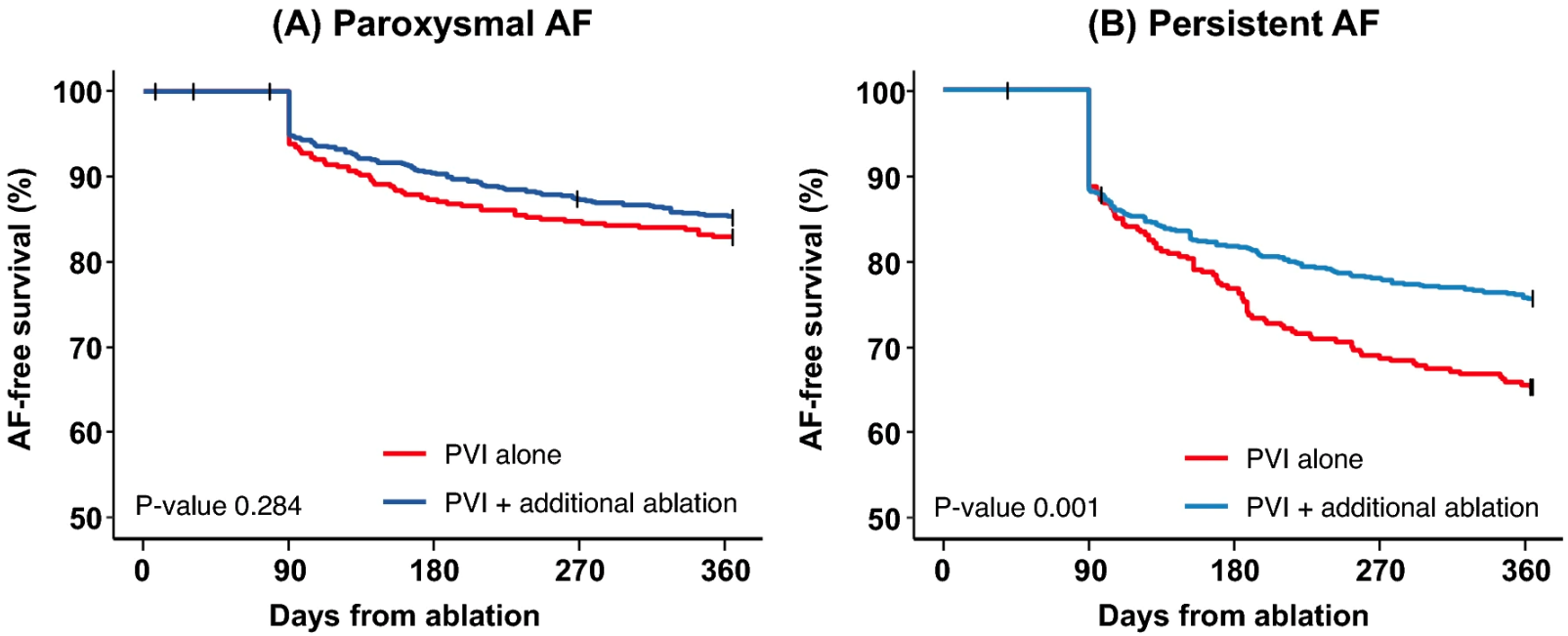
High Power Short Duration Ablation

1. Experience
2. Control environment, respirations, HR duration ablation
3. Improvements in outcomes, including safety and efficacy.
4. Triggered massive growth
    1. AF ablation now most common EP procedure done in most labs. **In Northwell alone we do >>1500 AF ablations per year**

RADIOFREQUENCY (RF) ABLATION FOR PULMONARY VEIN ISOLATION OUTCOMES



1. Packer et al. JAMA 2019;321(13):1261-1274 2.



PVI alone	390	389	340	330	323
PVI + additional ablation	707	705	638	616	602

PVI alone	318	318	244	219	208
PVI + additional ablation	717	716	584	557	541

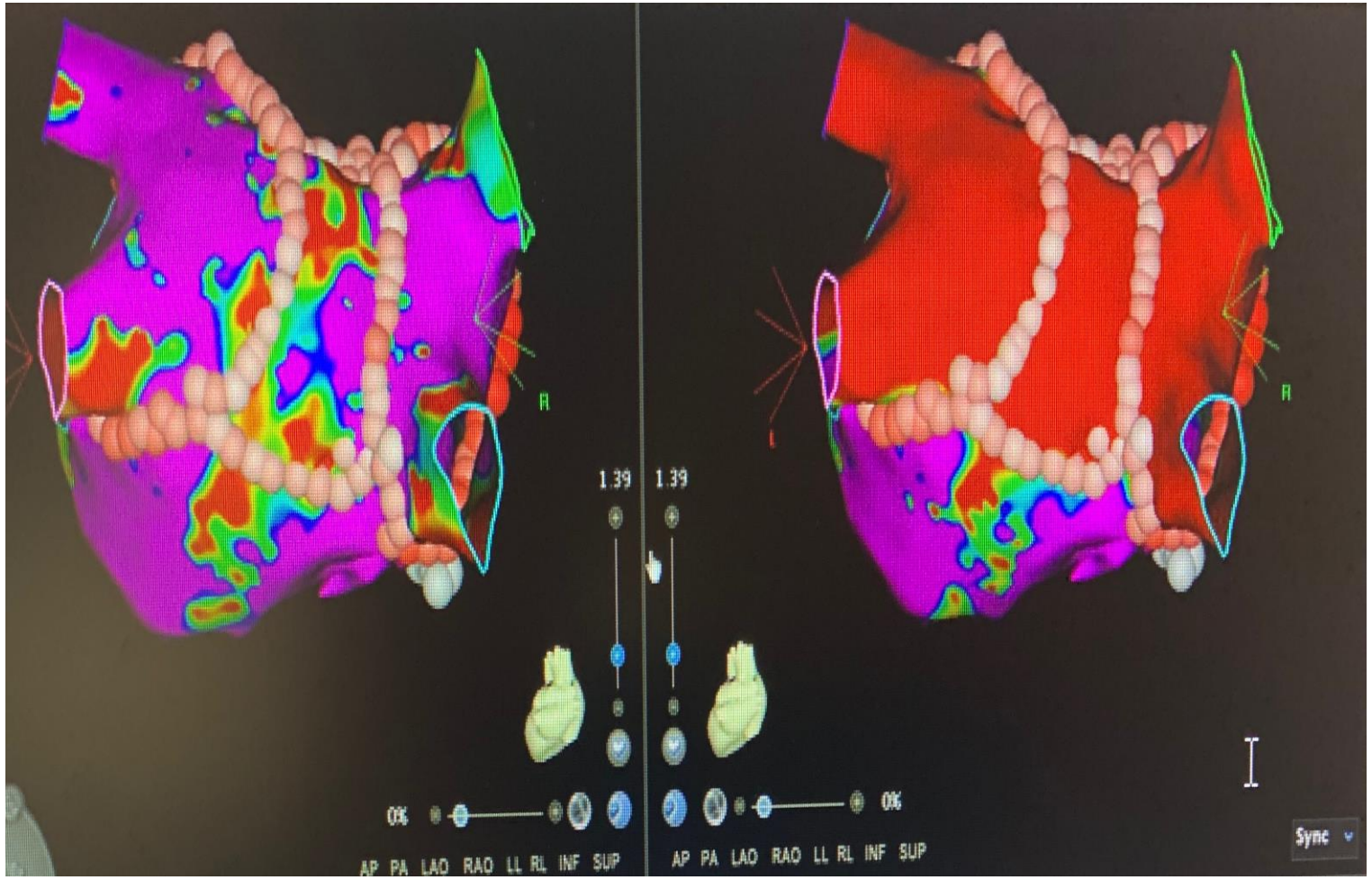
Lee *et al. Int J Arrhythm* (2021) 22:20

Success rates have improved
- Better outcomes than medical Rx
- Now >80% AF-free survival for paroxysmal AF

Persistent AF, structural heart disease, atrial myopathy

- Reduced success rates in these populations
- Often require extensive ablation outside PV antrum

PERSISTENT ATRIAL FIBRILLATION… MORE ABLATION, MORE PROBLEMS



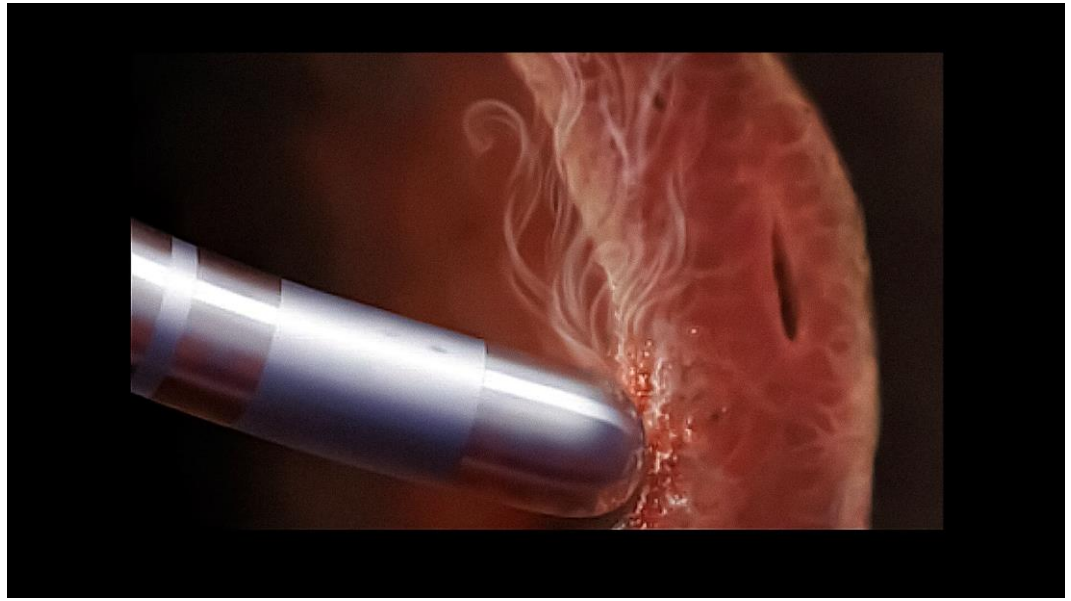
Paroxysmal AF- PVI remains primary
Persistent AF, structural heart disease, atrial myopathy
- Often require extensive ablation outside PV antrum

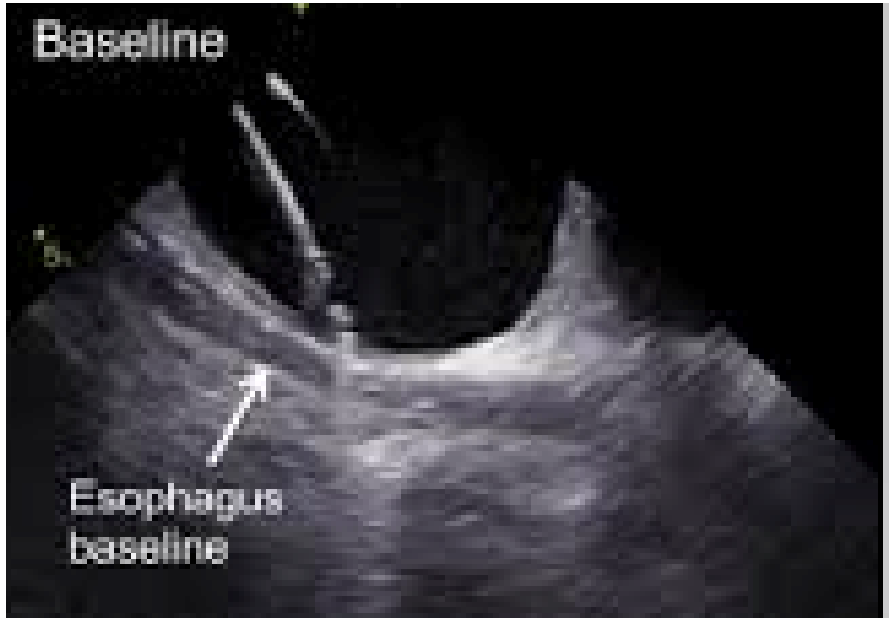
More Ablation beyond PVI
- Can improve success rates in pers AF
- Increase risk of **complications**
  - **Heat related injury** to the atria (thrombus, atrial stiffness) and surrounding structures (including phrenic nerve, esophagus

PREVENTING COMPLICATIONS FROM THERMAL ABLATION STILL ROOM FOR IMPROVEMENT

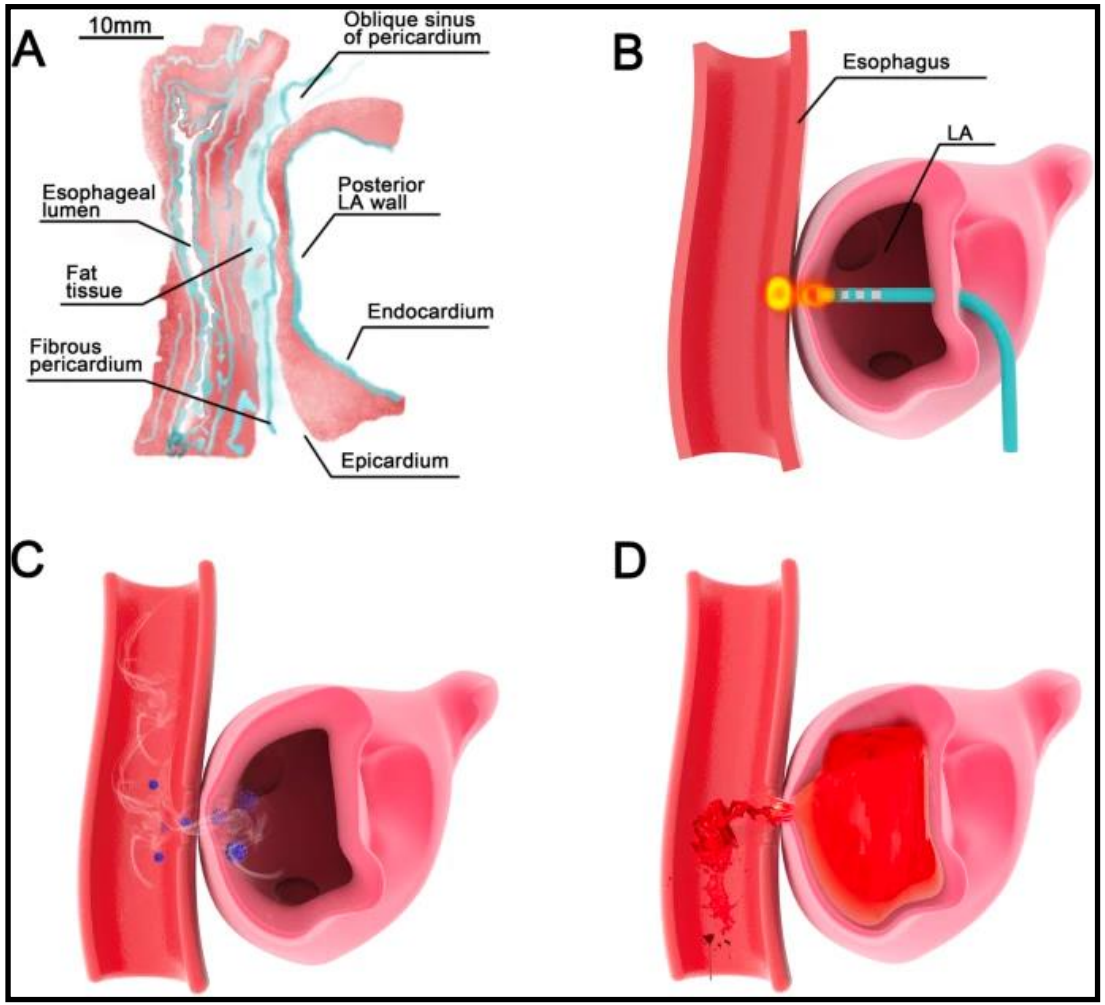
Procedure related risks- Mostly due to Thermal injury

- **Thrombosis**, and tissue damage
  - Procedure now performed on continuous anticoagulation
  - Asymptomatic cerebral lesions seen
- **Perforations/Steam pops**
  - Safer catheter designs
  - Operator experience
- **Phrenic Nerve injury**
  - More common with Cryoablation but usually transient
- **Esophageal injury**
  - Rates of clinically significant injury rare
  - Asymptomatic Esophageal Lesions (EGD-detected) > 10%
  - AE Fistula has very high morbidity and mortality





PREVENTING COMPLICATIONS FROM THERMAL ABLATION
ESOPHAGEAL INJURY



Zhang and Bian *BMC Neurology* (2020) 20:16

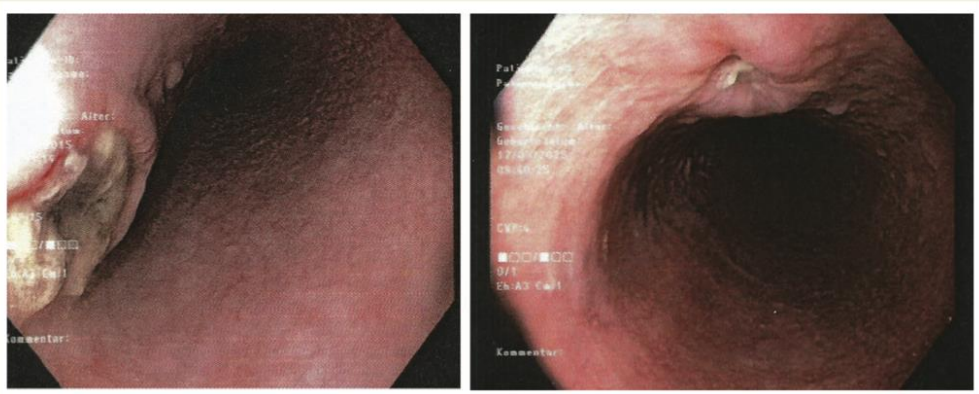


Figure 3 Oesophagogastroduodenoscopy showing an ulceration (maximum diameter 35 mm) after RF ablation without using LET monitoring (left panel) and EGD of the same patient 12 days later with ulceration in remission.

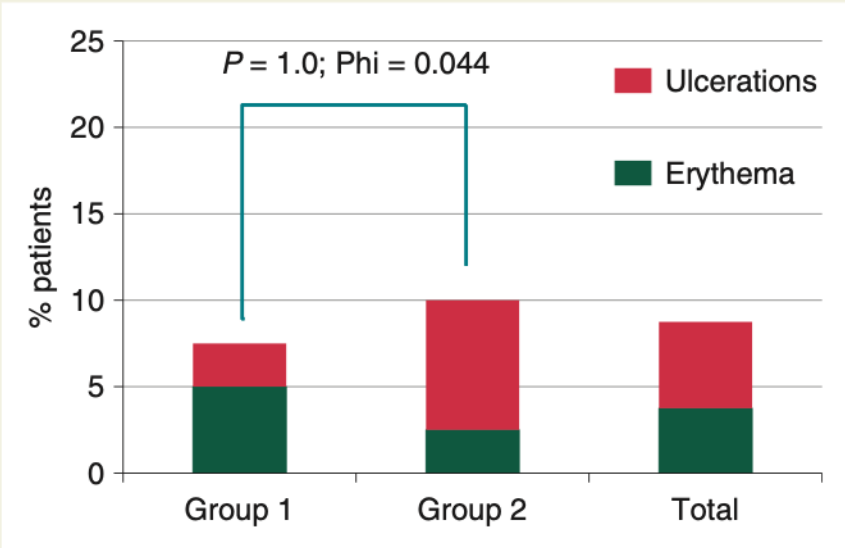
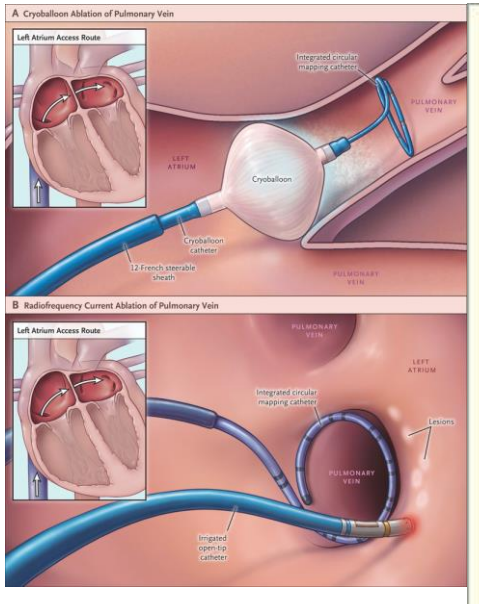


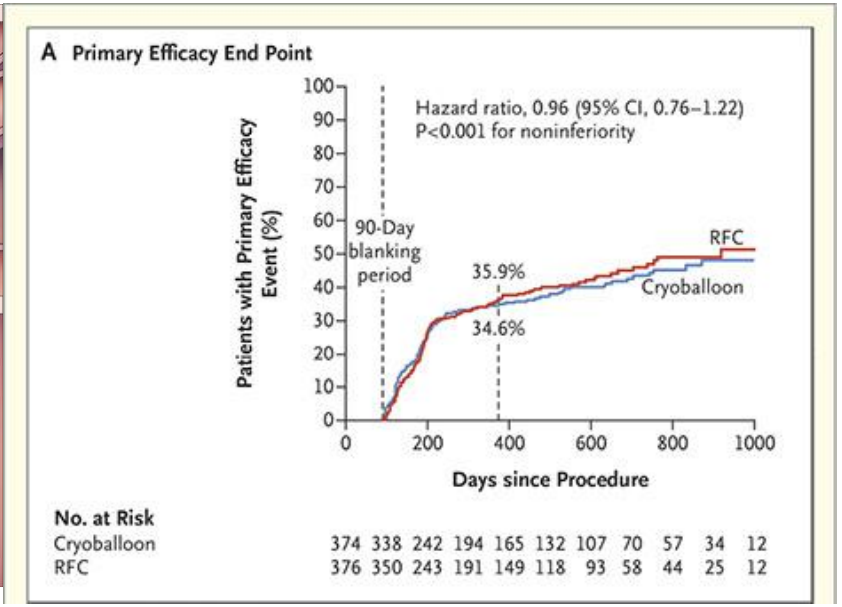
Figure 4 Incidence of EDEL in patients with and without use of temperature probe.

Halbfass et al. Europace 2017. 19:385-391

QUEST TO IMPROVE PULMONARY VEIN ISOLATION

CRYOABLATION





Cryoablation

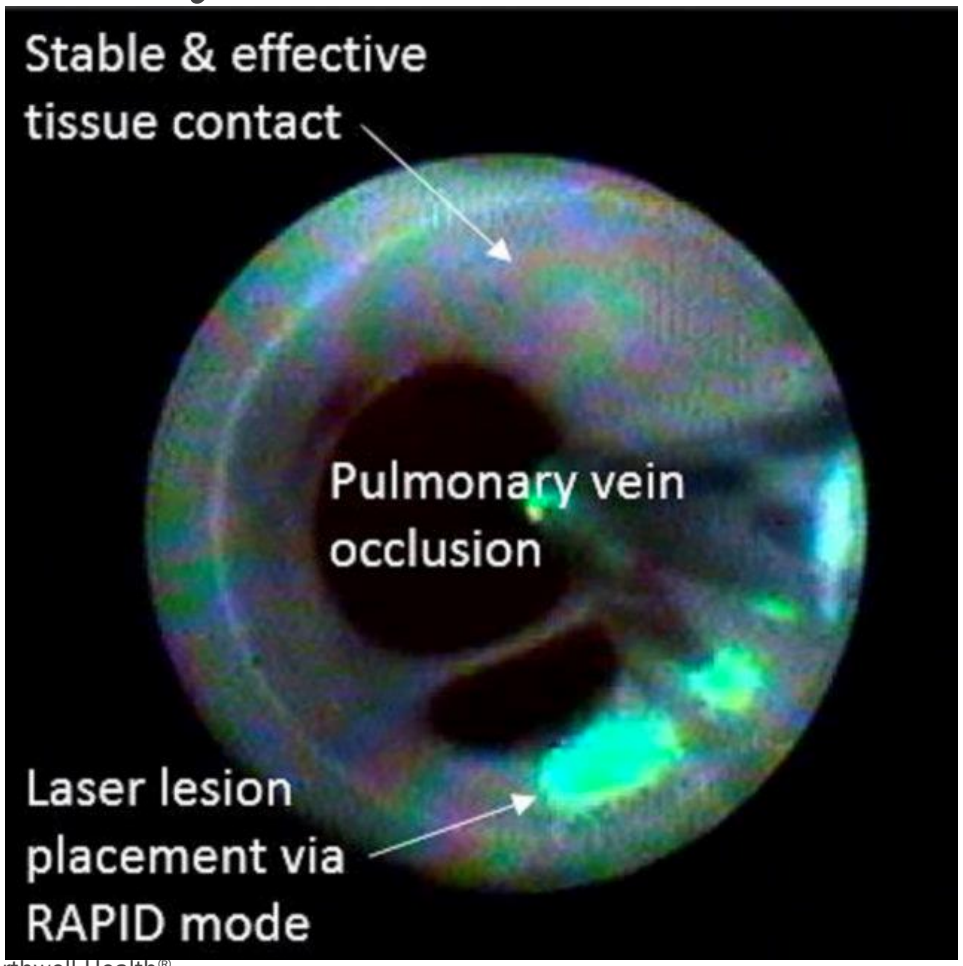
- Thermal ablation - freezes tissue
- Cryoballoon meant to fit in PV ostium for “single shot” ablation

Similar outcomes vs. RF

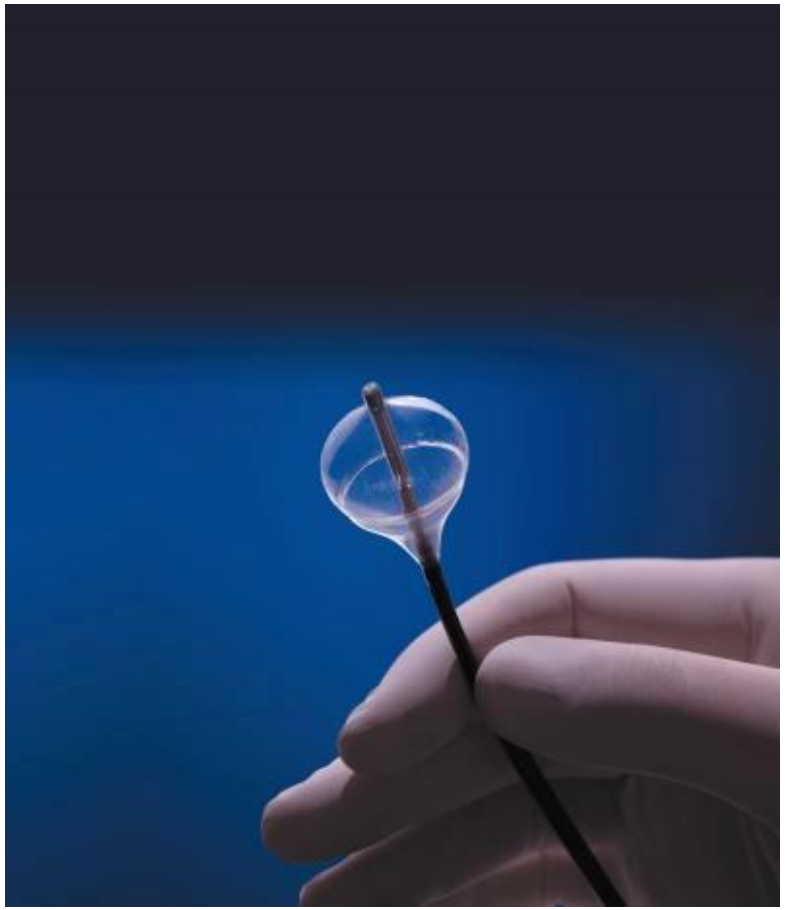
- No superiority in efficacy or safety relative to RF
- use dependent on physician preference

QUEST FOR BETTER TECHNOLOGY…
BUT NOTHING BETTER THAN "STANDARD TECHNOLOGY"

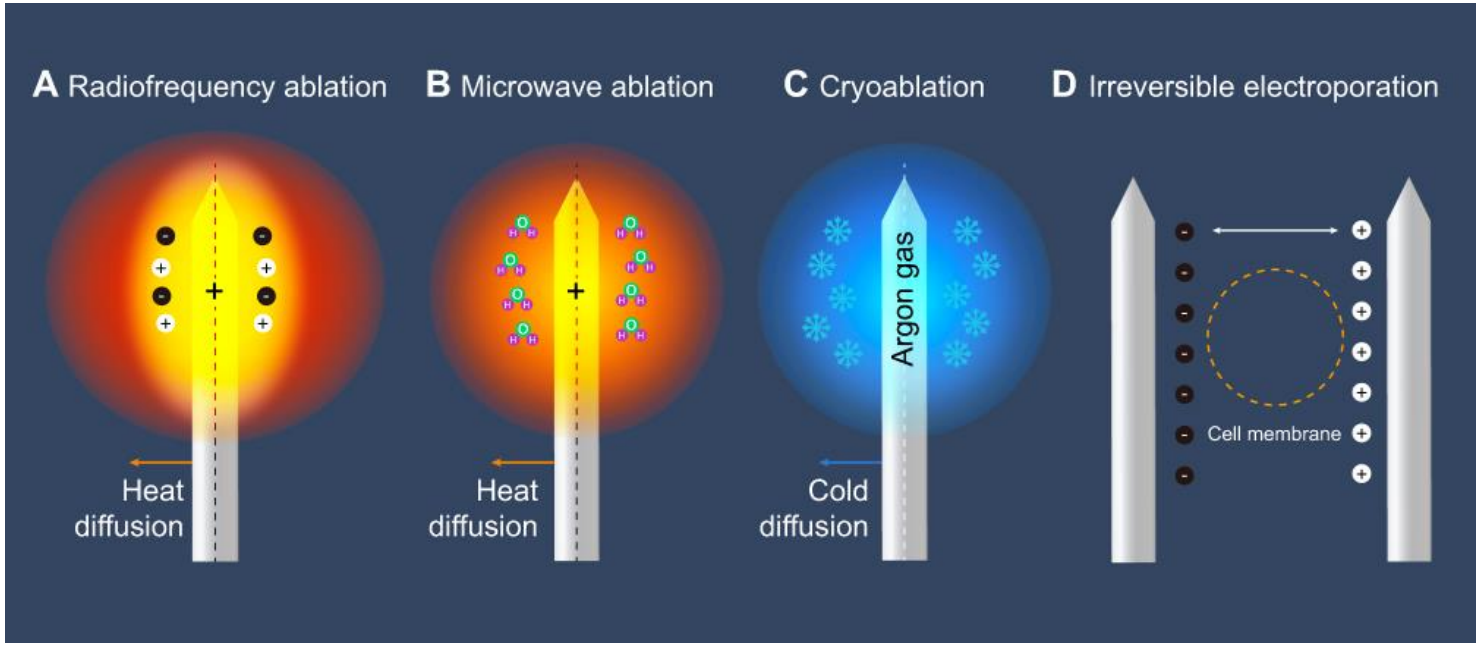
Visually Guided Laser Ablation

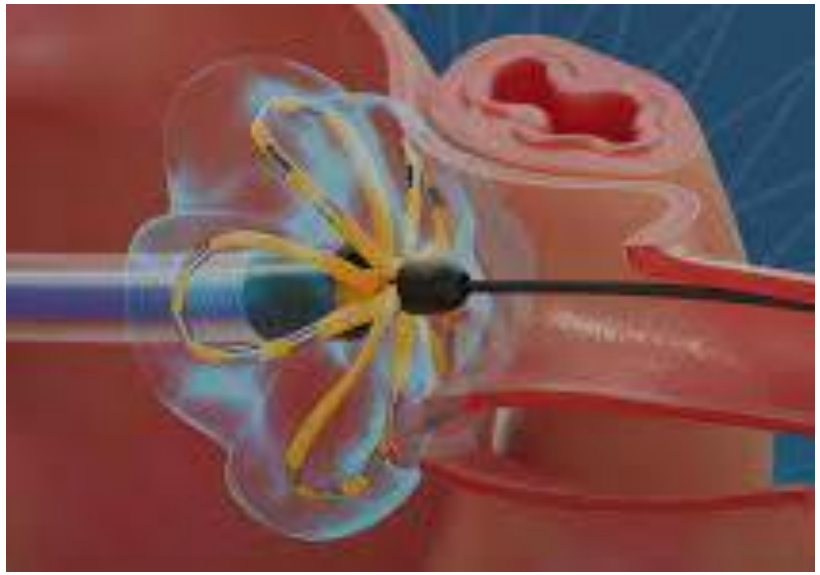


High Intensity Focused Ultrasound



ELECTRICAL ABLATION
A NON-THERMAL ENERGY SOURCE FOR ABLATION



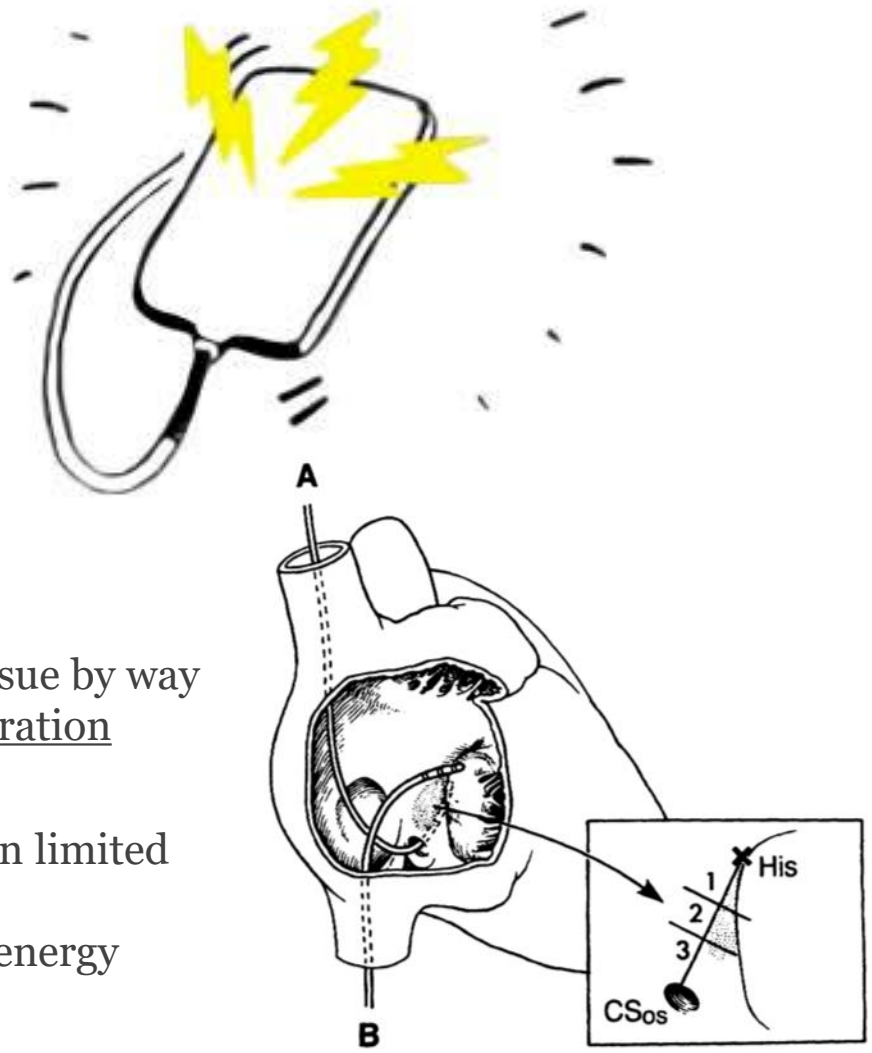


Administration of a **controlled electrical shock**

- Create programmed cell death through electroporation
- Minimal thermal effect

Zhou et al. Journal of Hepatocellular Carcinoma 2021:8 625–644

ELECTRICAL DC ABLATION



- DC ablation -
  - Destroys tissue by way of electroporation
  - Early version limited by difficulty controlling energy delivery

Percutaneous Catheter Modification of the Atrioventricular Node

A Potential Cure for Atrioventricular Nodal Reentrant Tachycardia

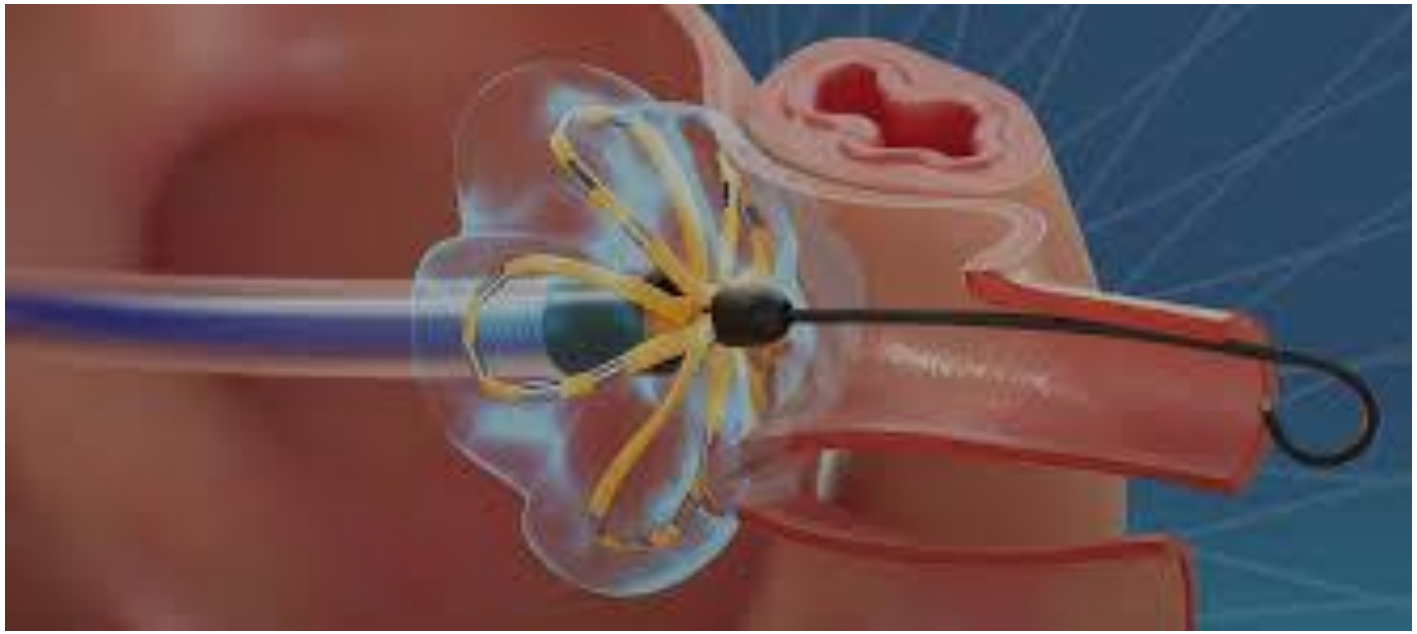
Laurence M. Epstein, MD, Melvin M. Scheinman, MD, Jonathan J. Langberg, MD, Donald Chilson, MD, Harold R. Goldberg, MD, and Jerry C. Griffin, MD

Our purpose was to describe a technique of atrioventricular (AV) node modification for patients with drug refractory AV nodal reentrant tachycardia (AVNRT). Nine patients (mean age, 45±20; range, 14–82) with recurrent drug refractory AVNRT (n=8) or sudden cardiac death thought to be precipitated by AVNRT (n=1) underwent a percutaneous catheter procedure to modify AV nodal function. The area between the electrode recording the maximal His-bundle electrogram and the ostium of the coronary sinus was divided into three zones. Perinodal direct current shocks of 100–300 J were delivered to one (n=2), two (n=3), or three (n=4) zones without complications. The procedure endpoints were modification of AV conduction (either first degree AV block or complete retrograde ventriculo-atrial [VA] block) and failure to induce AVNRT before or after isoproterenol and/or atropine administration. Six of nine patients (67%) have had no inducible or spontaneous AVNRT over a mean follow-up of 12.3±4.1 months (range, 4.5–17). One of the six underwent repeat, successful modification, because AVNRT was inducible at restudy 2 days after the initial procedure. AVNRT recurred in three patients (33%), one early (3 days) and two late (3–4 months). Two of these patients underwent complete ablation of the AV junction and permanent pacemaker placement, whereas one is controlled with drug therapy. Therefore, AV nodal modification resulted in tachycardia control without antiarrhythmic drugs in six of nine (67%) and obviated the need for complete AV junctional ablation in seven of nine patients (78%). Elimination of AVNRT appears to result from either block in the retrograde fast pathway or modification of the antegrade slow pathway, such that AVNRT cannot be sustained. Additional findings suggest that an atrio-Hisian accessory connection may not be involved in AVNRT in some of these patients. Percutaneous catheter AV nodal modification appears to be a promising technique for treatment of refractory AVNRT and may obviate need for complete AV junctional ablation in a substantial number of patients with drug/pacemaker refractory AVNRT. (*Circulation* 1989;80:757–768)

PULSED FIELD ABLATION - THE NEW FRONTIER

- Recent developments allowed Controlled Delivery using well tested waveforms and novel delivery catheters

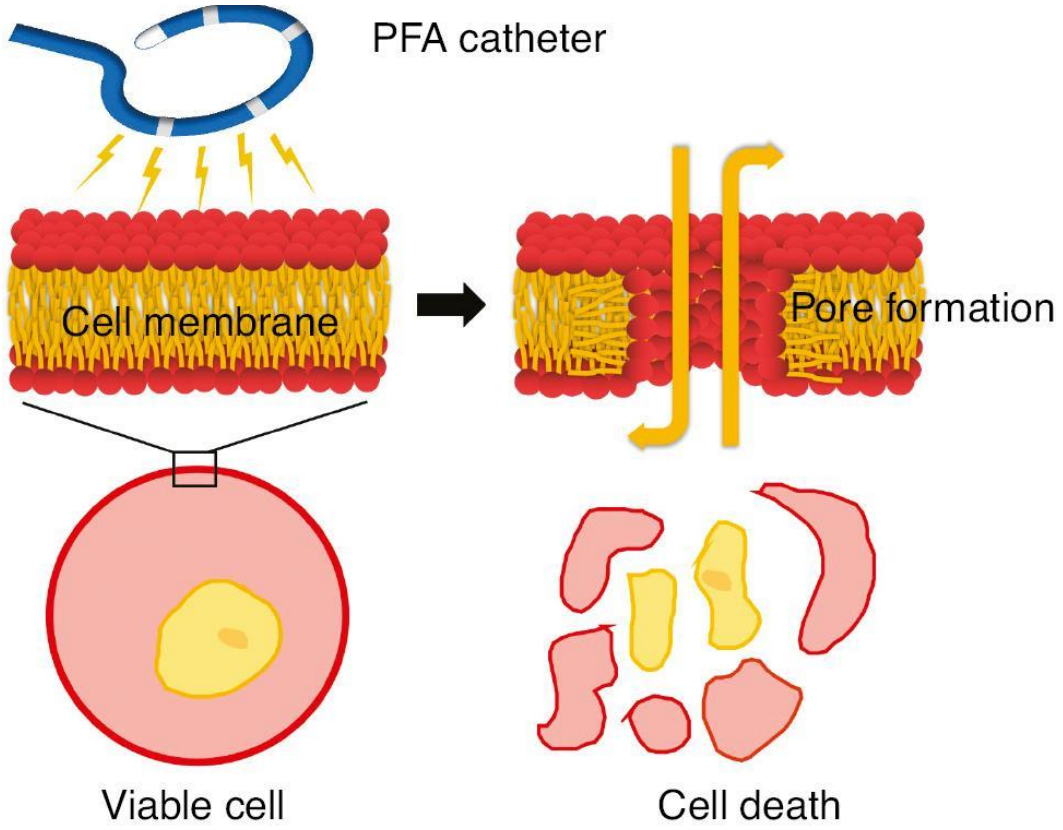
- **PFA** - used controlled applications of Electrical Energy to destroy myocardial tissue by way of electroporation



ELECTROPORATION - HOW PFA WORKS

- Short pulses of high energy delivered to destroy cardiac tissue via process of **Electroporation**
  - High energy delivered creates pores in cell membrane
  - (-) ions flow into cell, causes apoptosis

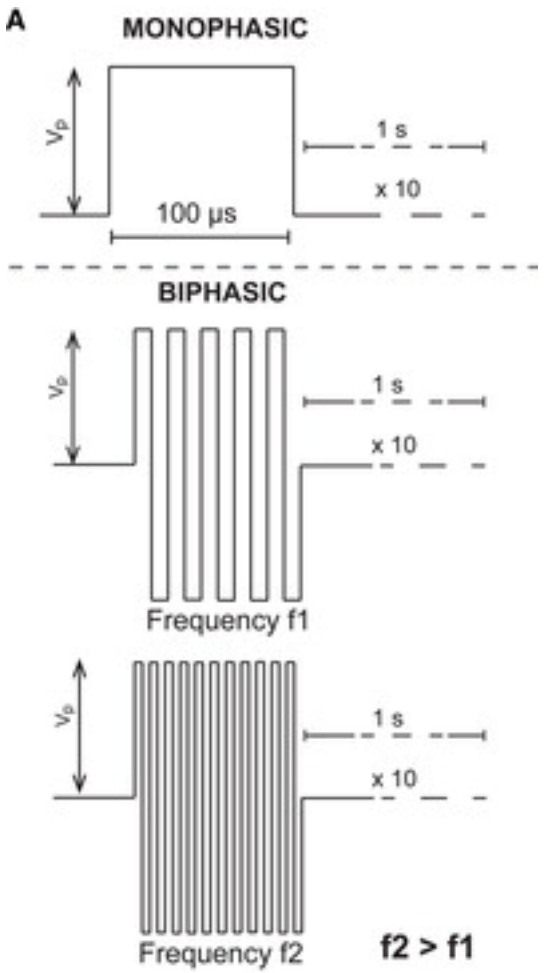
- Ablation via electroporation and apoptosis
  - -> Minimal heat creation, prevent thermal injury to tissue



Wang Y et al. Cardiovasc Innvations and Applications 2023.

PULSED FIELD ABLATION

RAPID GROWTH IN TECHNOLOGY IN RECENT YEARS

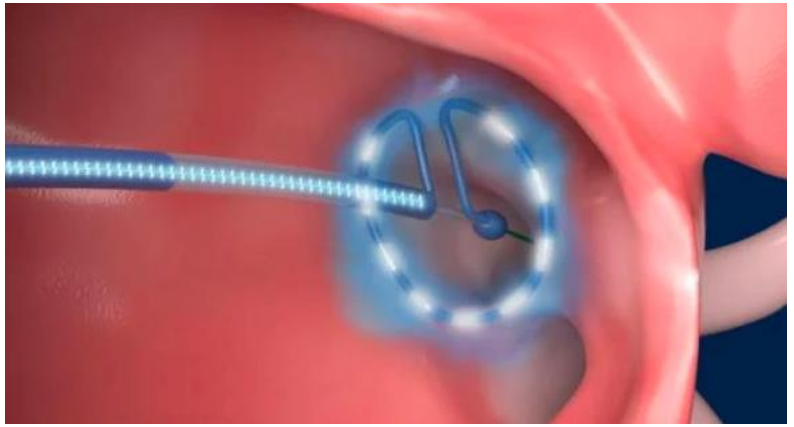


Optimize Energy Delivery

- Extent of electroporation and induced cell death is dependent on strength and duration of applied electric field.

Catheters

Designed to deliver PFA to selectively ablate around the PVs

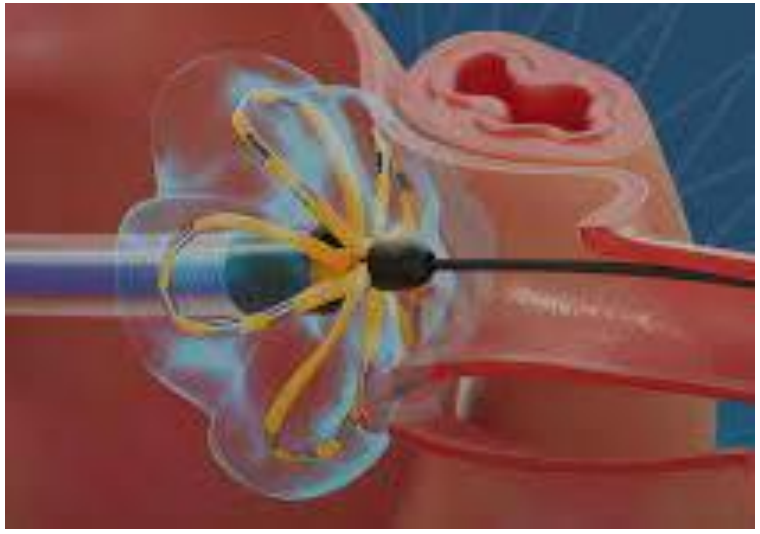


MAJOR INDUSTRY INVESTMENT IN NEW TECHNOLOGY FOR PULSED FIELD ABLATION

Currently Approved

Boston Scientific

FARAPULSE



Medtronic

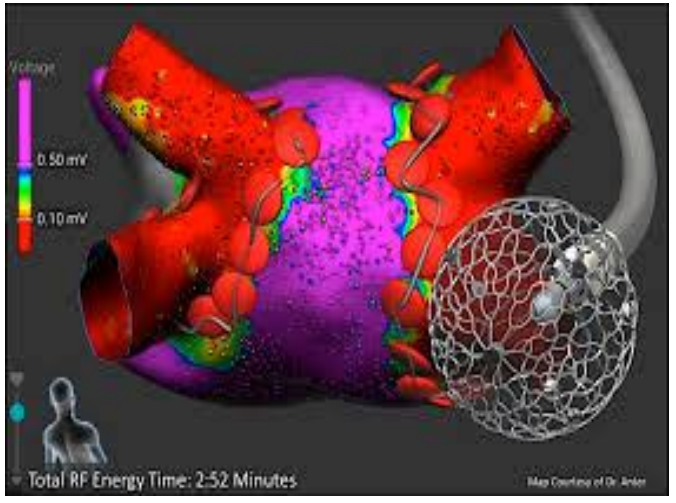
PulseSelect

In Human Studies (in development)

Biosense Webster

PART OF THE Johnson & Johnson FAMILY OF COMPANIES

VARIPULSE™ Catheter



AFFERA

Northwell Health®

ADVANTAGES OF PULSED FIELD ABLATION
THE HOLY GRAIL?

Safety

Tissue selectivity
Minimal heat
Eliminate concerns about most collateral damage

Efficiency

With microsecond pulses, procedure time can go down dramatically

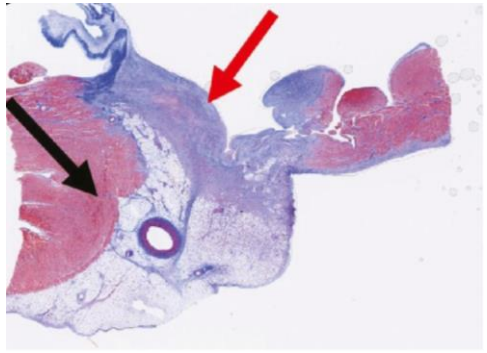
Efficacy

If permanent/durable targeted lesions could be delivered reliably and reproducibly, may improve success rates

THE SECRET SAUCE OF PULSED FIELD ABLATION (PFA)

CARDIO-SELECTIVITY

- **Cardiomyocytes** are more sensitive to electroporation
  - Require energy consumption (ATP) to maintain cell membrane potential
- Lower threshold for damage relative to other cell types
  - Vascular cells, smooth muscle, endothelial cells, nerve cells are spared



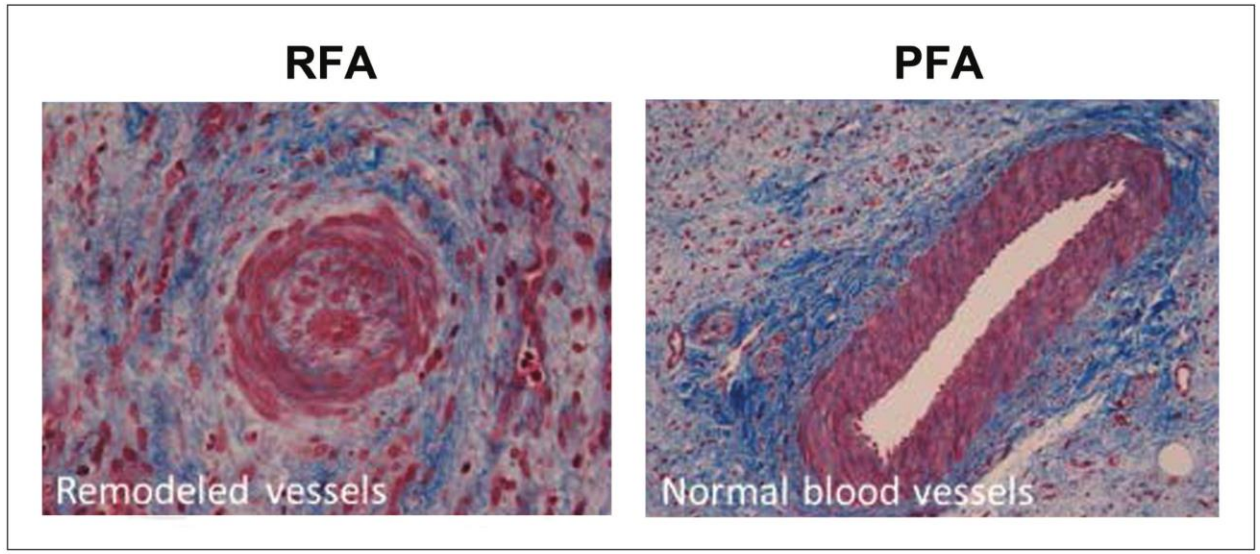


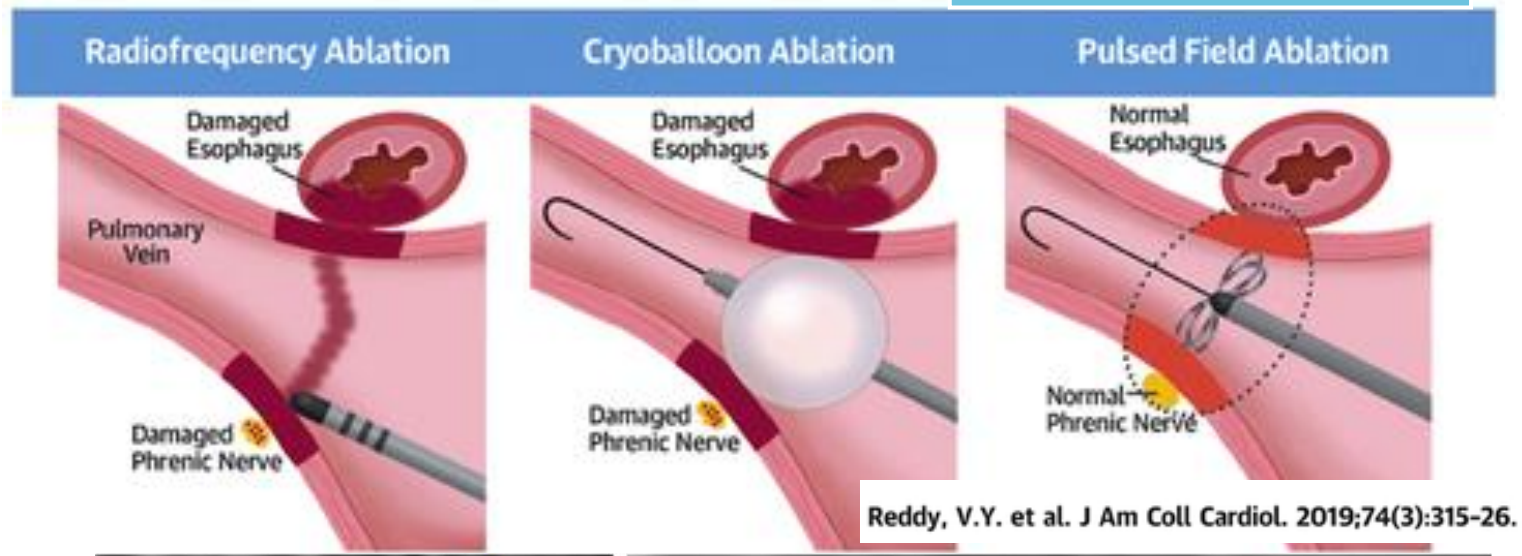
Figure 6: Photomicrographs of 2-week-old ablation lesions in the right atrial appendage (RAA) of a pig. Energy delivery was RF ablation (left panel) or PFA (right panel). The RFA resulted in significant arterial remodeling and vessel occlusion. The PFA created a homogeneous lesion in the myocardium surrounding the artery, but the artery remained unaffected. Masson's trichrome stain (blue = collagen/scar). *(Unpublished image, provided by Medtronic.)*

PULSED FIELD ABLATION (PFA)
CARDIO-SELECTIVITY

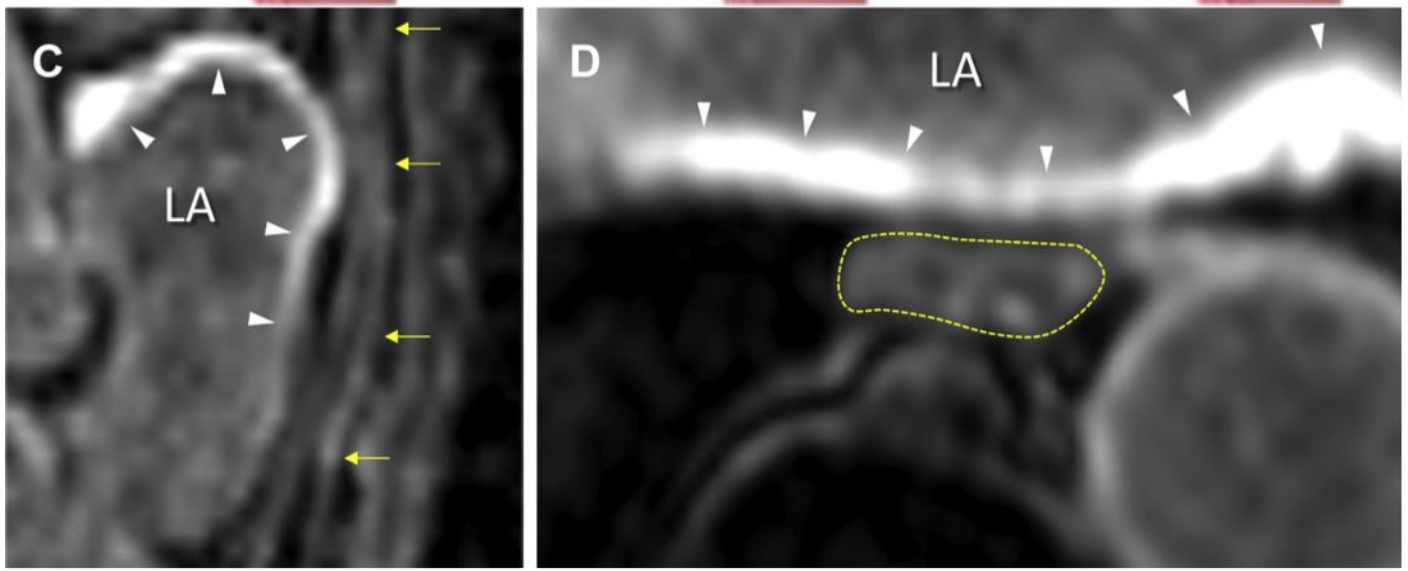
Safety

- Potential to **selectively ablate** myocardial tissue, and minimize risk of collateral damage
  - Prospective studies have shown:
    - ***No Esophageal lesions*** on EGD (0/38) or MRI (0/18)
    - ***No Phrenic Nerve injury***
    - ***No PV Stenosis*** (0/77)
    - Infrequent *Brain lesions* on MRI (2/18)

- BUT… **new risks exist**



Reddy, V.Y. et al. J Am Coll Cardiol. 2019;74(3):315-26.

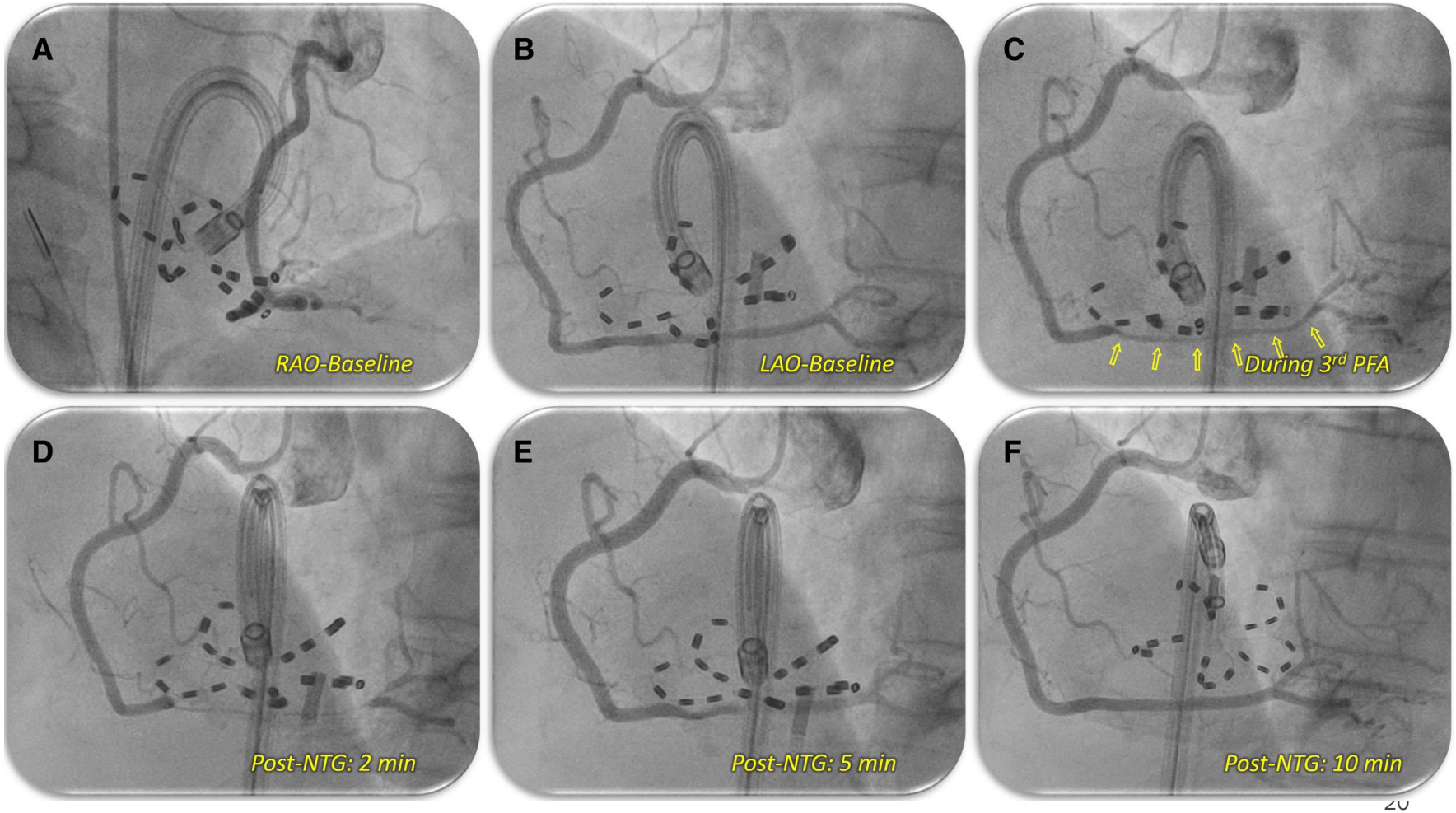


Reddy, V.Y. et al. J Am Coll Cardiol EP. 2021;7(5):614-27.

PULSED FIELD ABLATION (PFA)
SAFETY CONCERNS

Safety

- **Safety Concerns Unique to PFA**
  - **Vasospasm** when ablating near coronaries
    - Can be mitigated by Nitroglycerin

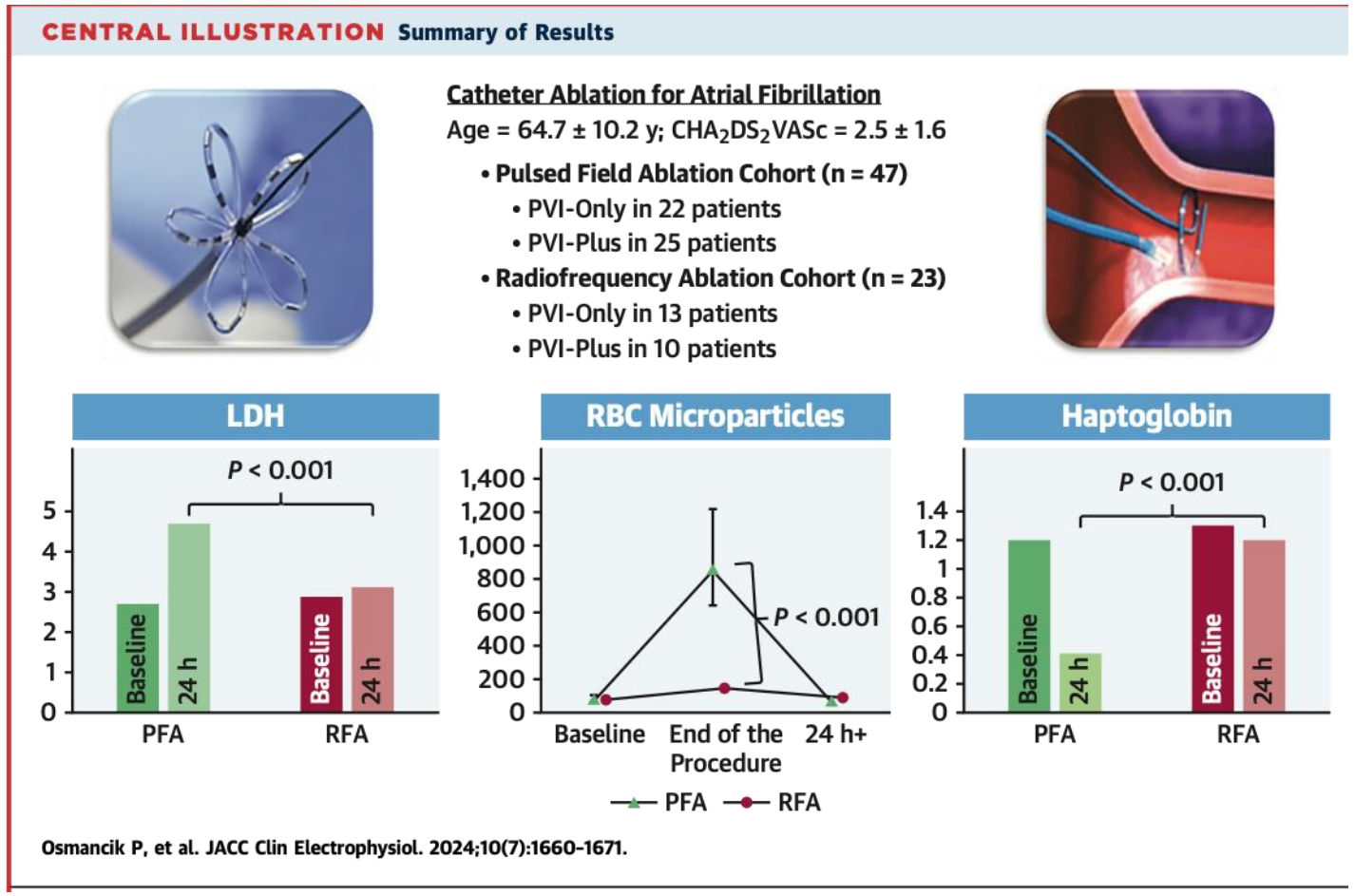


Reddy VY, Petru J, Funasako M, et al. Coronary Arterial Spasm During PFA to Treat Atrial Fibrillation. Circulation 2022;146(24)

PULSED FIELD ABLATION (PFA)
SAFETY CONCERNS

Safety

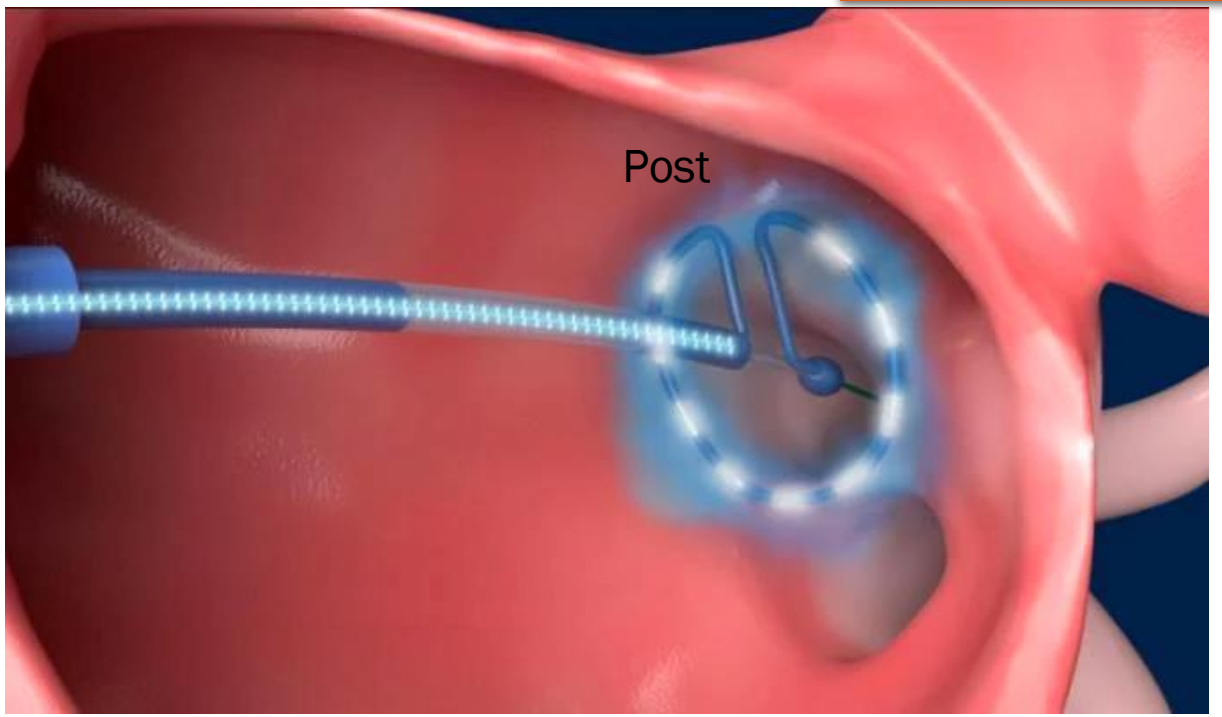
- **Safety Concerns Unique to PFA**
  - **Hemolysis**
    - Risk of ARF
    - Mitigated by IVF administration



ADVANTAGES OF PULSED FIELD ABLATION

EFFECIENCY

Efficiency



- **Rapid electrical impulses** delivered in micro-nanoseconds
- Dramatically reduces the time required for ablation.
- Total ablation time about 3 min/ patient
- LA dwell time (of PFA catheter) 34.4 +- 15.8 mins

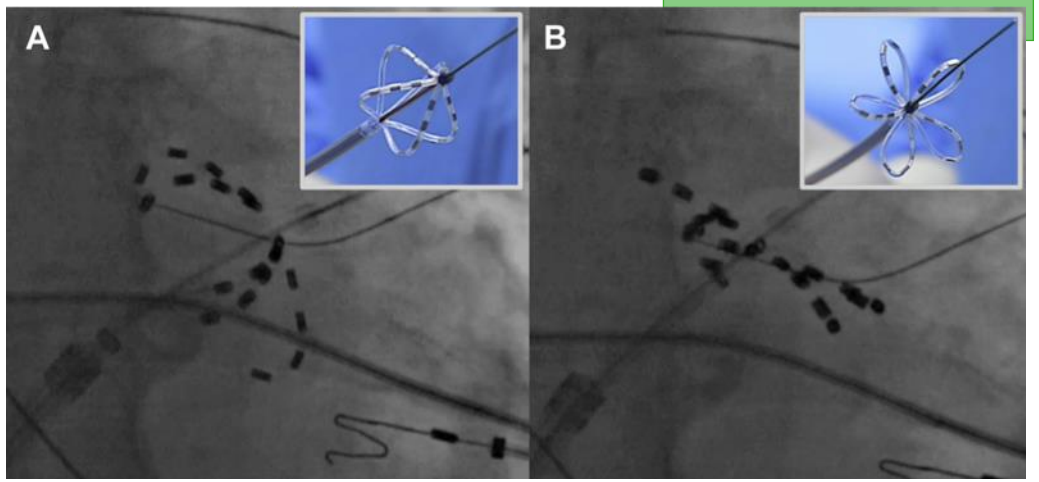
Catheters designed for one-shot PVI

- PFA catheters have been developed as one-shot devices for PVI, delivering a single packet of energy in seconds

Mehta, Haines. EP Digest July 2021
Reddy VY. JACC EP 2021;(7)5:614-27

PULSED FIELD ABLATION: EFFICACY

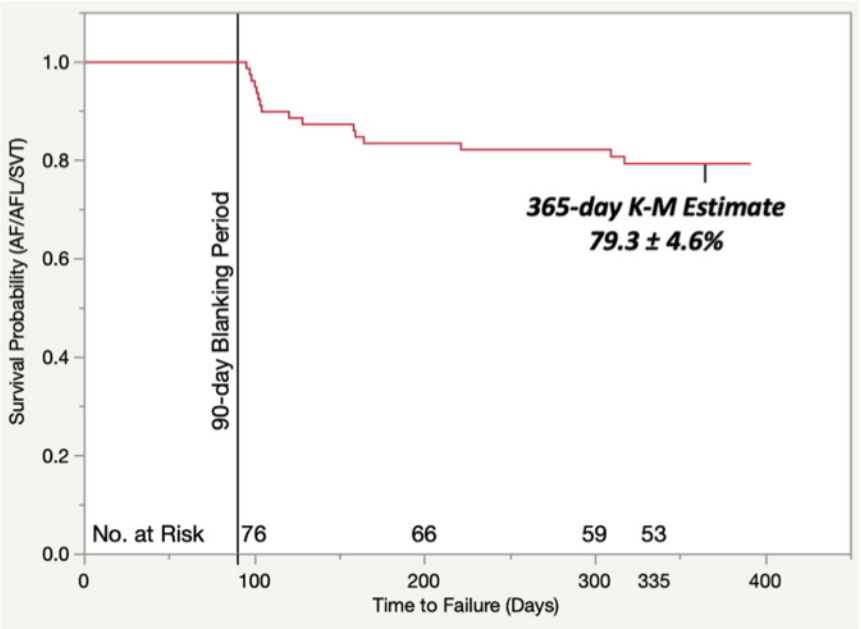
- 3 similar clinical trials IMPULSE, PEFCAT, PEFCAT II, using FARAPULSE
  - 1 yr combined outcomes
  - 121 patients with paroxysmal AF, resistant to AAD
  - First in-human use of PFA
  - Single Arm feasibility/safety trial, 2 sites



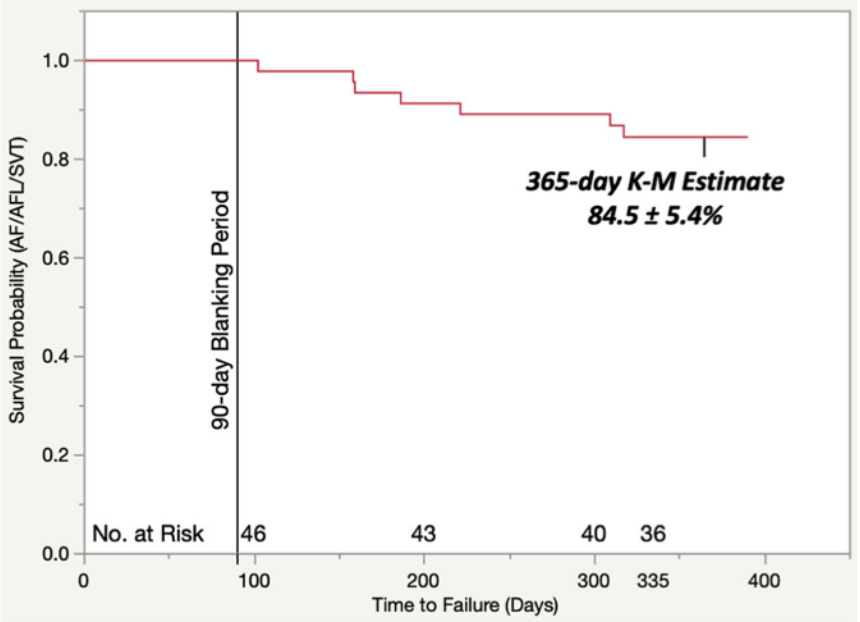
Safety

• *Esophageal Damage*	*0%*
◦ *Esophageal Dysmotility*	*0%*
◦ *Atrioesophageal Fistula*	*0%*
• *Pulmonary Vein Stenosis*	*0%*
• *Phrenic Nerve Injury*	*0%*
• *Stroke*	*0%*
◦ *Transient Ischemic Attack*	*0.9%*
• *Pericardial Effusion*	*0.8%*
• *Vascular injury*	*1.7%*
• *Death*	*0%*

Freedom from AF, AFL or AT: Single Procedure



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



Reddy, V.Y. et al. J Am Coll Cardiol EP. 2021;7(5):614-27.

OUTCOMES OF PFA ADVENT TRIAL VS. RFA

Randomized trial (1:1) of PFA (Farapulse) vs RF ablation/Cryo

- **Primary efficacy outcome**: Initial treatment failure, AT/AF >30 seconds (after blanking period), use of AADs, or repeat ablation at 1 yr
  - **Noninferior** (post prob >0.999)
  - Similar results despite operators **lack of experience** with PFA (and early generation)
  - Shorter procedure times with PFA, but longer fluoroscopy times

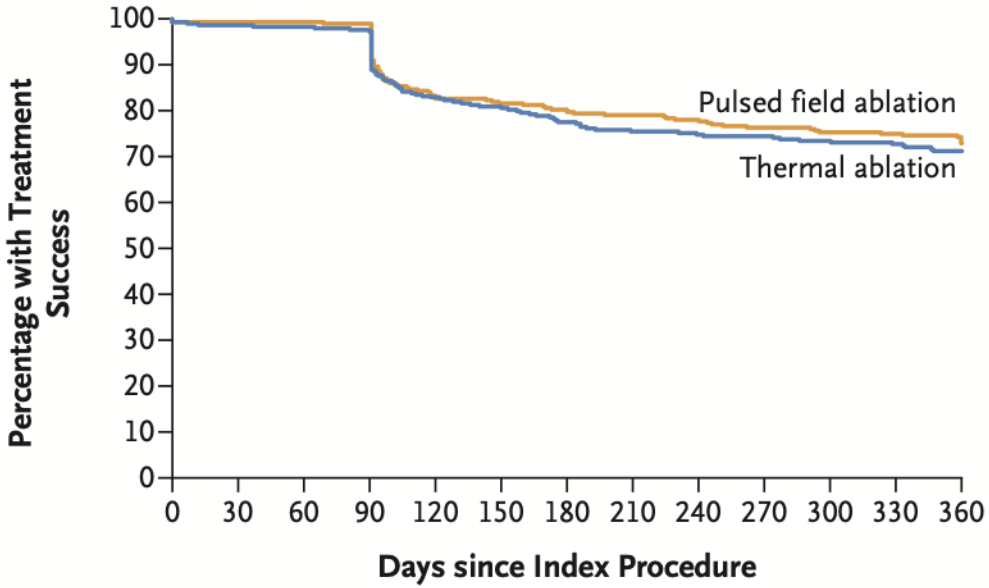
- **Primary safety outcome**: Procedure related adverse effects.
  - 2.1% PFA vs 1.5% thermal, non-inferior (0.999)
    - Brain MRI silent cerebral lesions in 3/33 with PFA, 0/37 in thermal ablation
  - Secondary safety outcome- PV stenosis
    - PV Area change: -0.9% with PFA and -12% with thermal (superior for PFA)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation

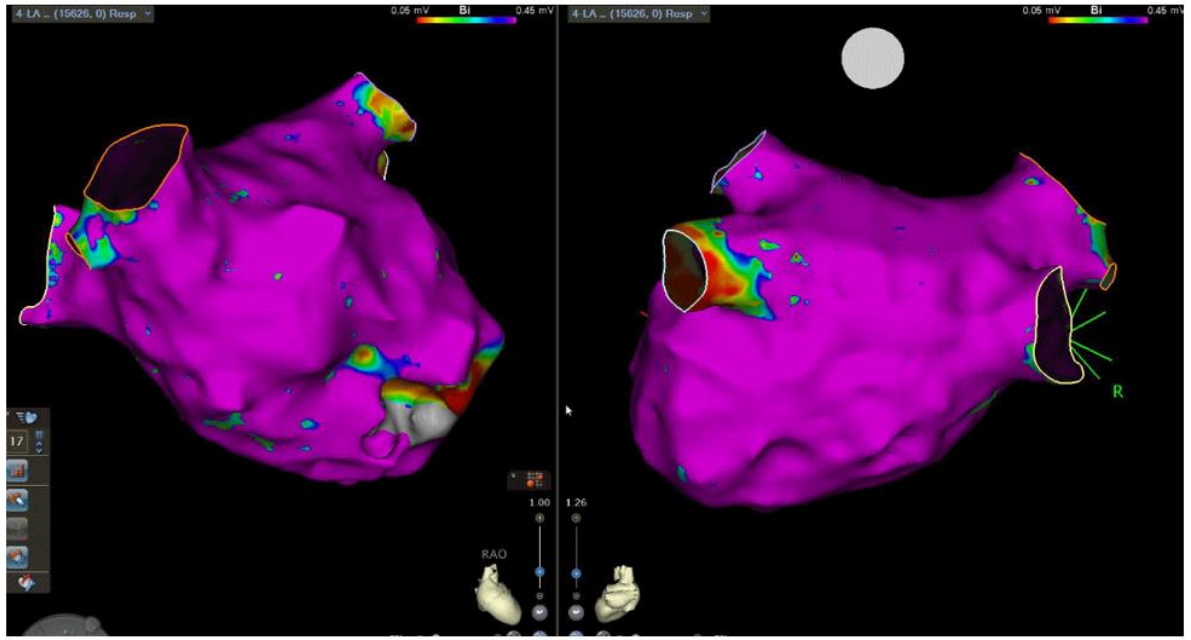
Vivek Y. Reddy, M.D., Edward P. Gerstenfeld, M.D., Andrea Natale, M.D., William Whang, M.D., Frank A. Cuoco, M.D., Chinmay Patel, M.D., Stavros E. Mountantonakis, M.D., Douglas N. Gibson, M.D., John D. Harding, M.D., Christopher R. Ellis, M.D., Kenneth A. Ellenbogen, M.D., David B. DeLurgio, M.D., Jose Osorio, M.D., Anitha B. Achyutha, M.Tech., M.S.E., Christopher W. Schneider, M.Eng., Andrew S. Mugglin, Ph.D., Elizabeth M. Albrecht, Ph.D., Kenneth M. Stein, M.D., John W. Lehmann, M.D., M.P.H., and Moussa Mansour, M.D., for the ADVENT Investigators*

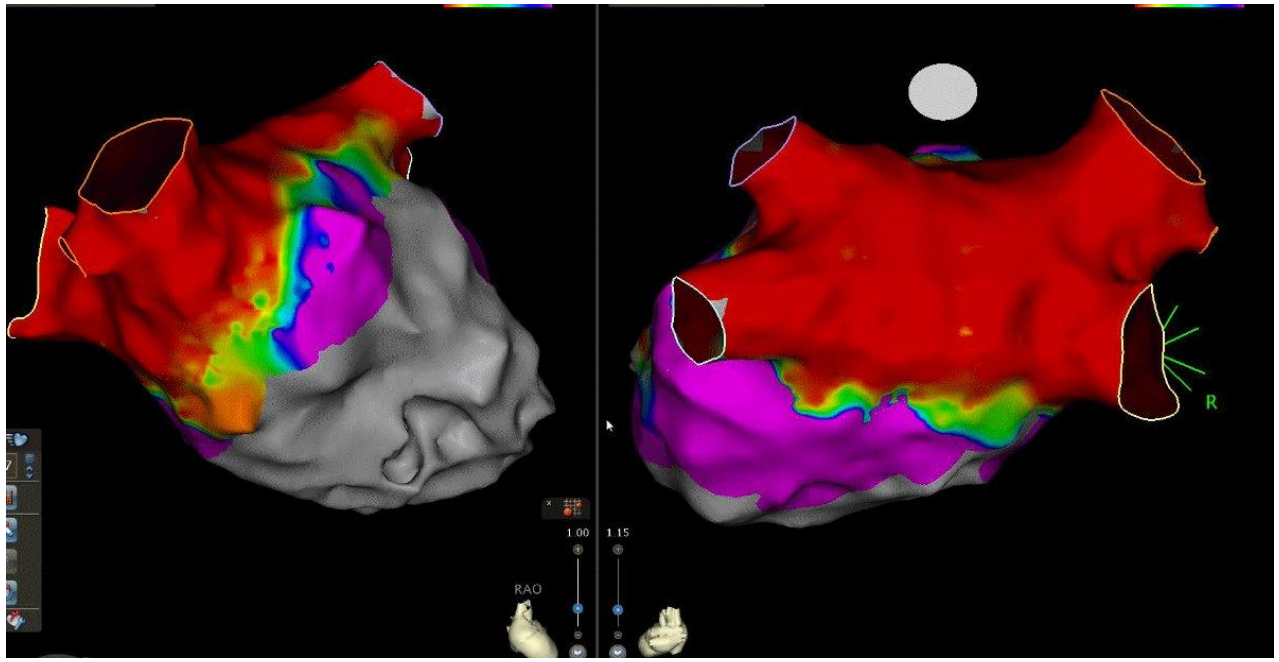


No. at Risk					
Pulsed field ablation	301	298	238	228	176
Thermal ablation	296	292	228	219	150
Treatment Success (%)					
Pulsed field ablation	99.3	99.0	79.7	76.4	73.1
Thermal ablation	98.7	97.3	77.5	74.5	71.3

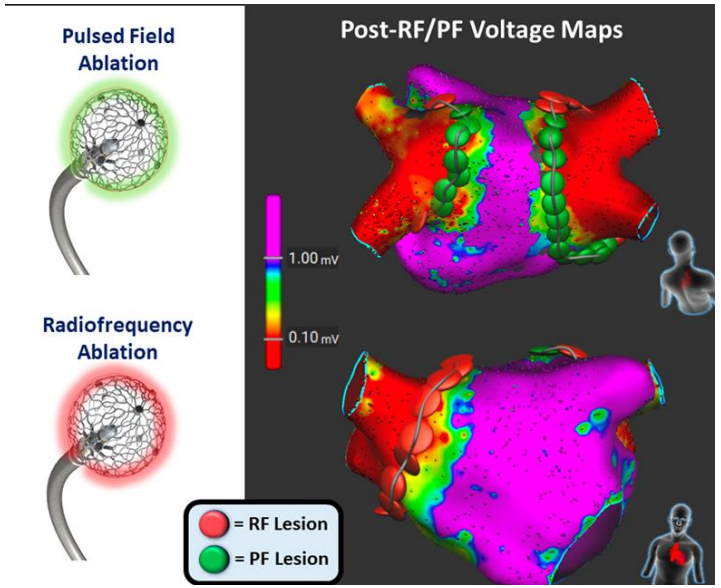
EARLY EXPERIENCE

- Simple Learning Curve
- Efficiently ablated large area of Left Atrium
  - Difficult to achieve consistently with traditional ablation methods
- Able to address non-PV substrate as well, including lines of block, SVC
  - Not as precise as focal ablation
- Predictable procedures- even among new/different operators
- Less stress, particularly when ablating posterior LA wall
  - But must be careful regarding over-ablation





ONGOING TRIALS, EMERGING PFT TECHNOLOGY
MUCH TO LEARN
NORTHWELL REMAINS INVOLVED



Farapulse catheter, Boston Scientific

Advantage Trial

Avant Garde Trial

Persistent AF, with PVI and Posterior Wall isolation

AFFERA, Medtronic

SPHERE PER-AF TRIAL

Persistent AF

Completed enrollment

Varipulse, Biosense Webster

ADMIRE Trial (pAF)

completed enrollment

SmartfIRE Trial

PF/RF using standing ablation catheter

WILL PULSED FIELD ABLATION (PFA) TAKE OVER RF AND CRYO AS THE PRIMARY TECHNOLOGY FOR AF ABLATION?

In many centers, including ours, it already has!

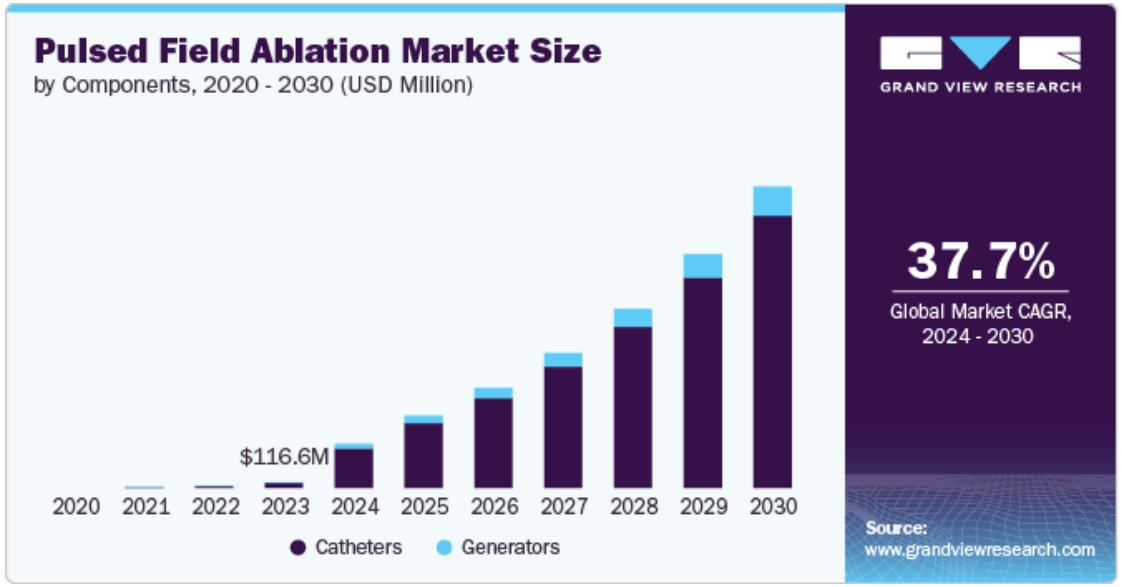
PFA is a transformative technology and will be a major market factor in the near term and long-term.

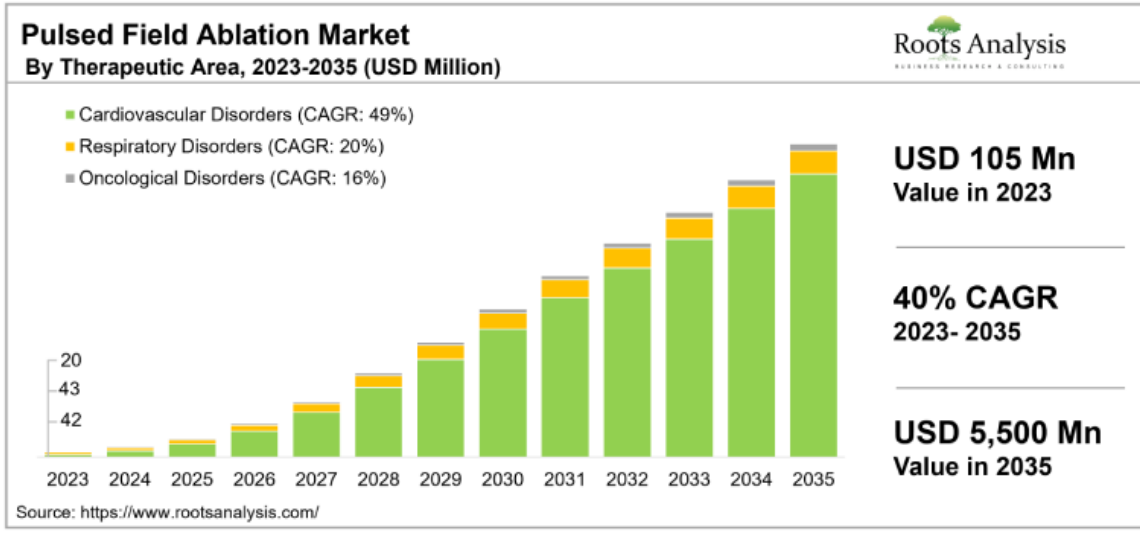
- Prior to launch in US in April 2024, PFA took off in Europe, Asia and Latin America (>25,000 pts in 31 countries)

- 2024 showed rapid adoption in US, despite cost considerations.
  - Market share rapidly taking over RF and Cryo for AF ablation

- In combination with increasing indications and rationale for early intervention
  - AF Ablation will continue to grow
  - Huge business development

- Still very early stage.
  - Imagine the gains that we will see over the **next 2 decades** of progress!





WILL PULSED FIELD ABLATION (PFA) ALLOW AF ABLATION TO BE PERFORMED IN COMMUNITY HOSPITALS?

In NY, AF ablation is currently only performed in centers with cardiac surgery

But benefits of PFA may ease transition into the community

Safety benefits

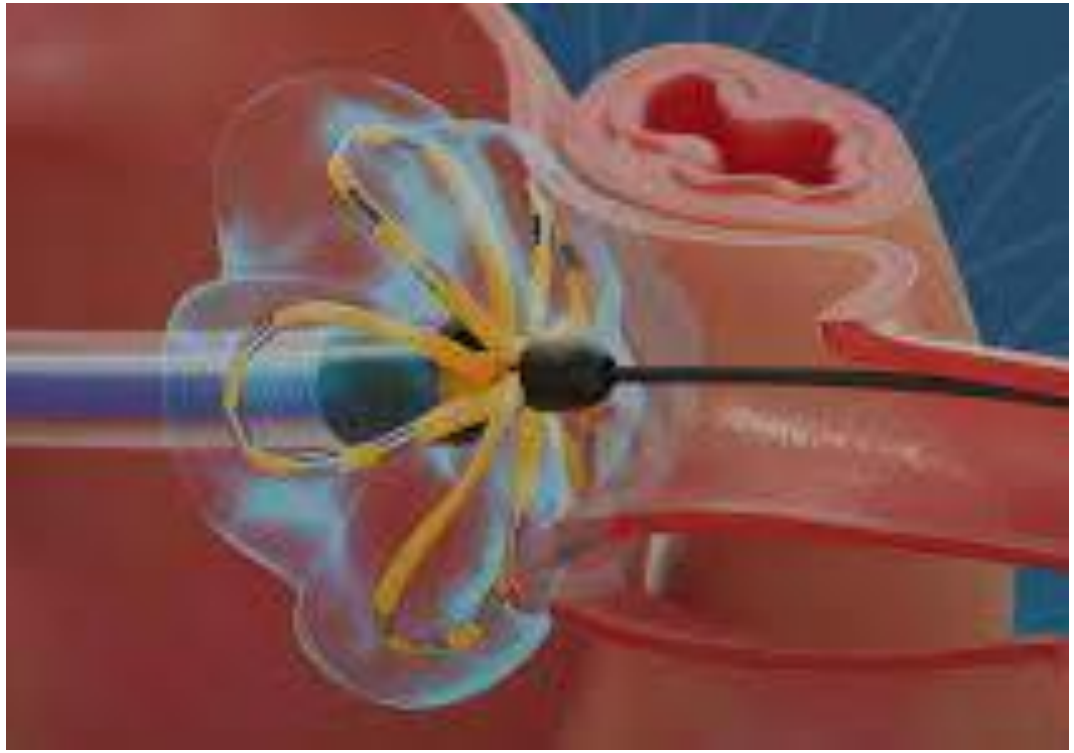
- Will drive its success and wide adoption

Efficiency

- Consistent procedure times <1 hour is possible
- May improve access and reduce wait times for ablation

Efficacy

- Though thus far has not shown improved AF outcomes
- Results are becoming more reproducible even between experiences and inexperienced operators



THANK YOU