Anatomy, Physiology and Ablation of Atrial Fibrillation

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The Foundation for The Gator Nation

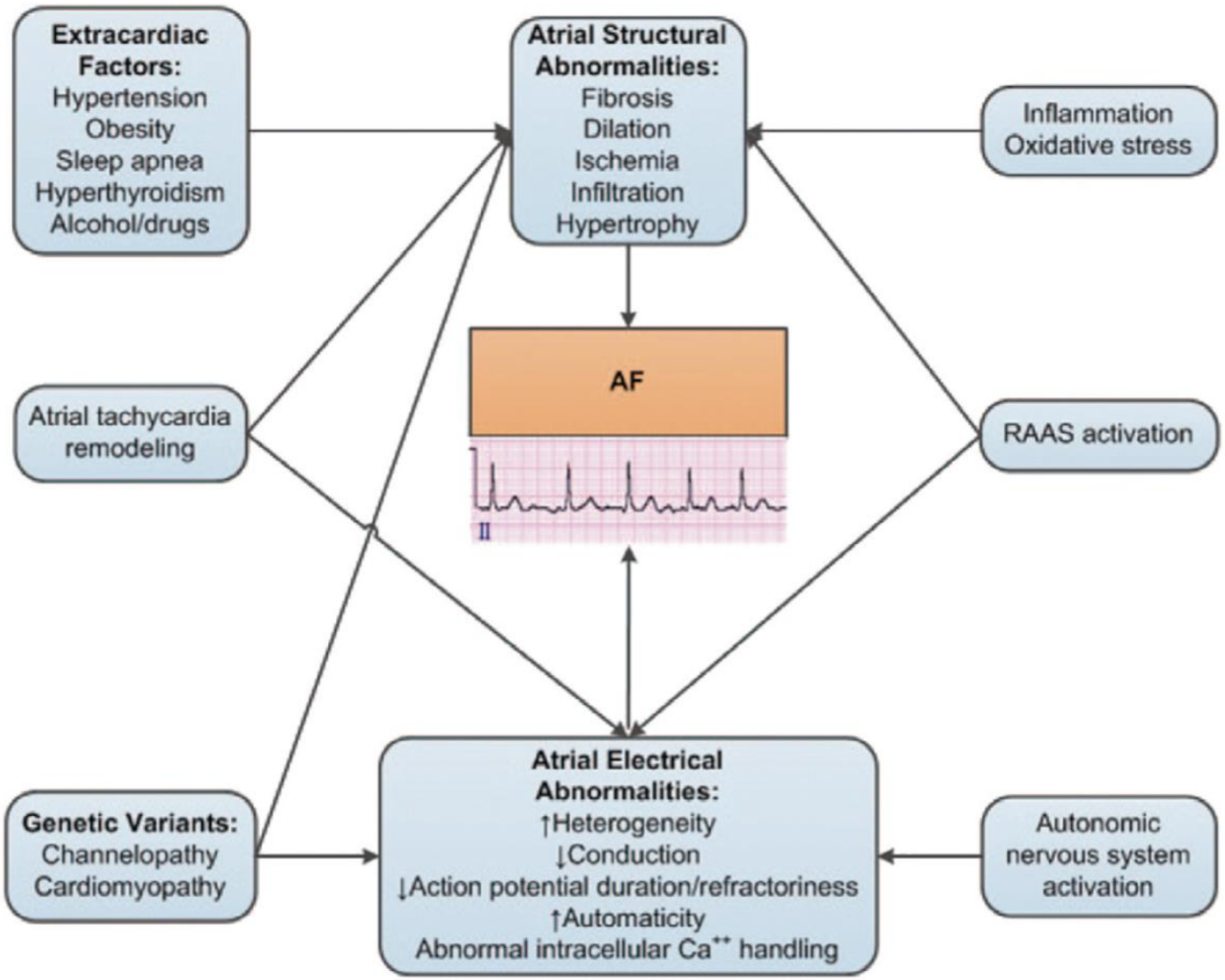
Disclosure

- Medtronic, Inc. (Clinical Events Committee, consultant)
- Biosense-Webster, Boston Scientific, Medtronic, St. Jude (UF EP Fellowship Support)

Strategies in AF Ablation

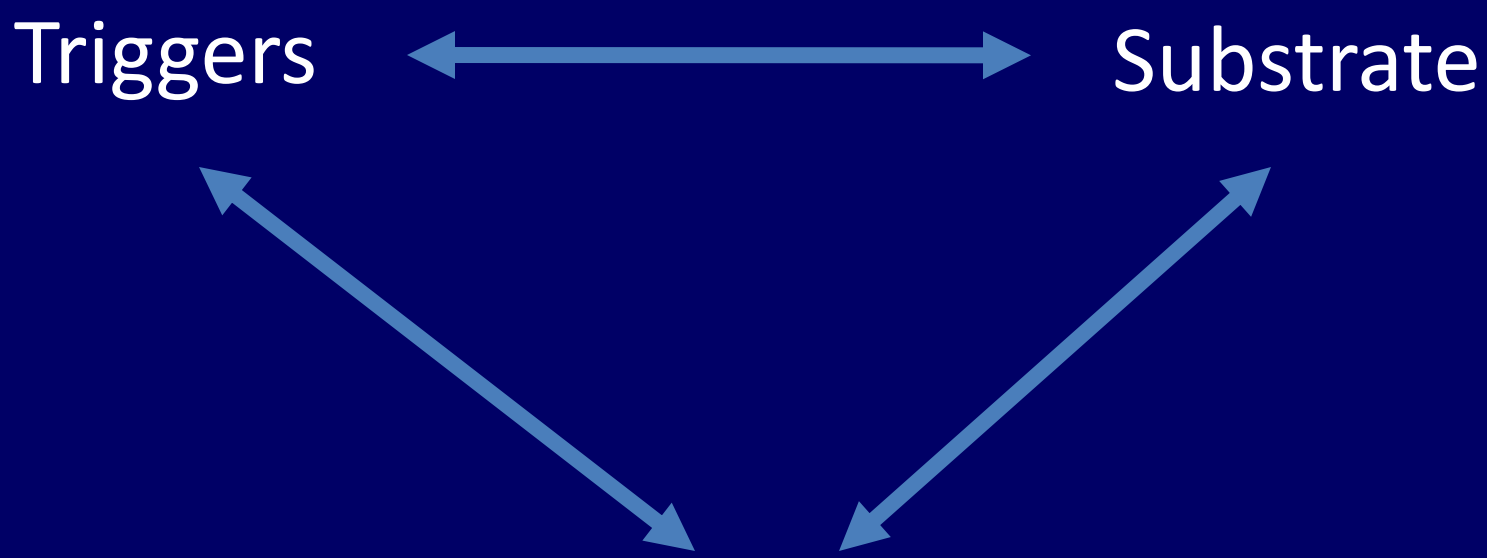
- Mechanisms of atrial fibrillation
- Pulmonary vein isolation
  - Radiofrequency techniques
  - Cryoballoon techniques
- Strategies for ablation of persistent AF
- Surgical AF ablation approaches
- Focal impulse and rotor mapping/ablation

Mechanisms of AF



2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

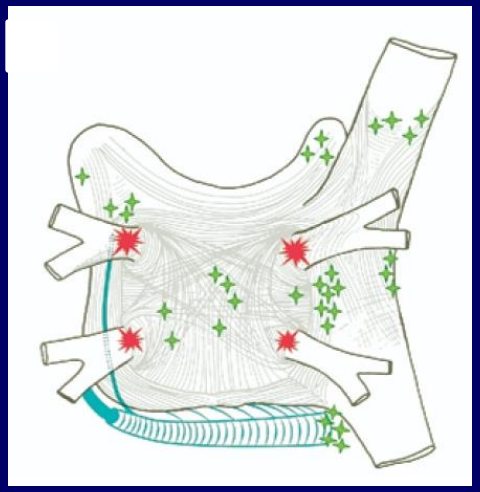
Mechanisms of Arrhythmogenesis



Pathophysiology of AF

Triggers

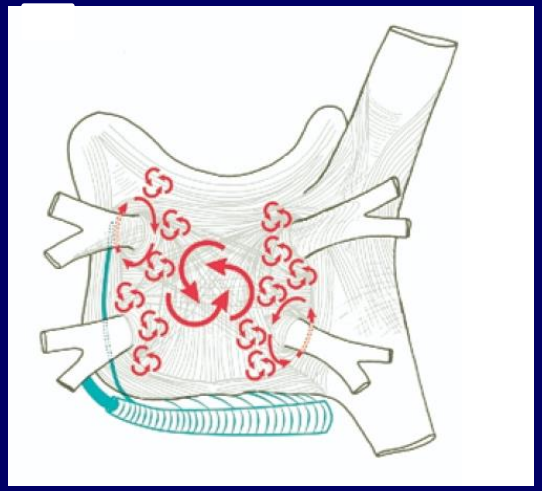
PV/non-PV Triggers



Substrate

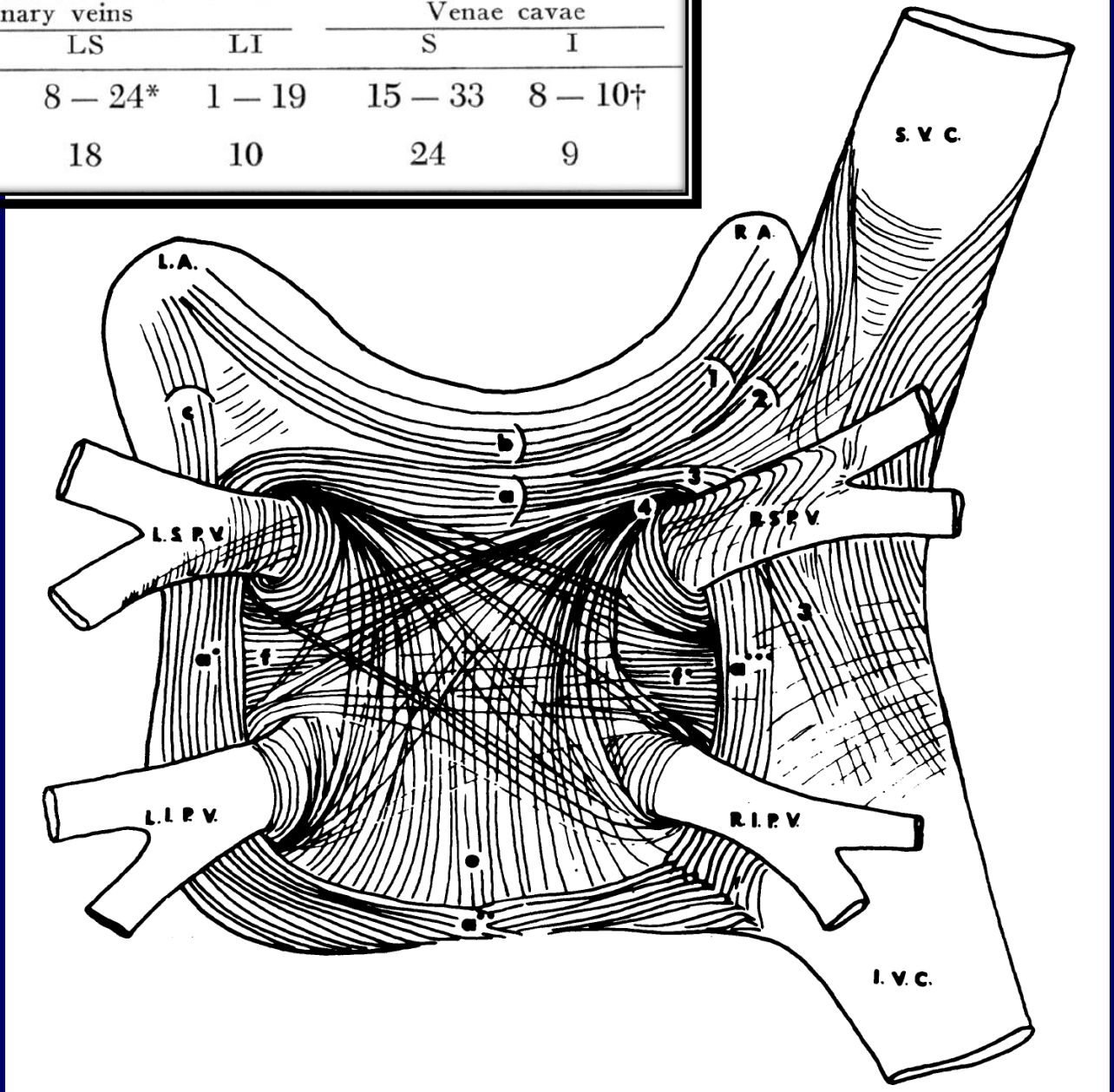
Electrophysiologic

Anatomic



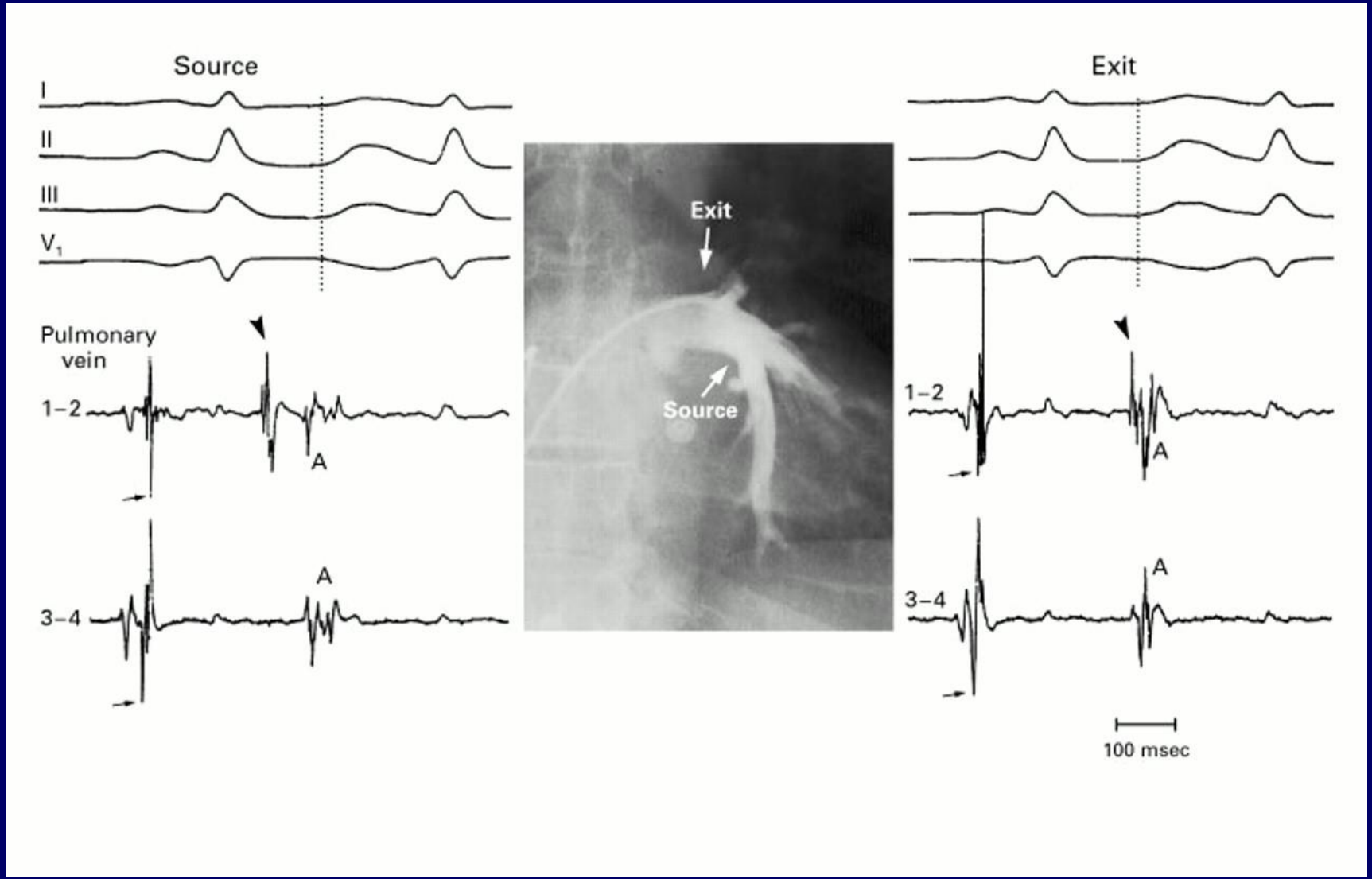
Calkins et al. Heart Rhythm 2007

	Length of the myocaordial sleeves extending over the veins (mm)					
	Pulmonary veins				Venae cavae	
	RS	RI	LS	LI	S	I
Range	5 — 25	1 — 17	8 — 24*	1 — 19	15 — 33	8 — 10†
Average	13	8	18	10	24	9



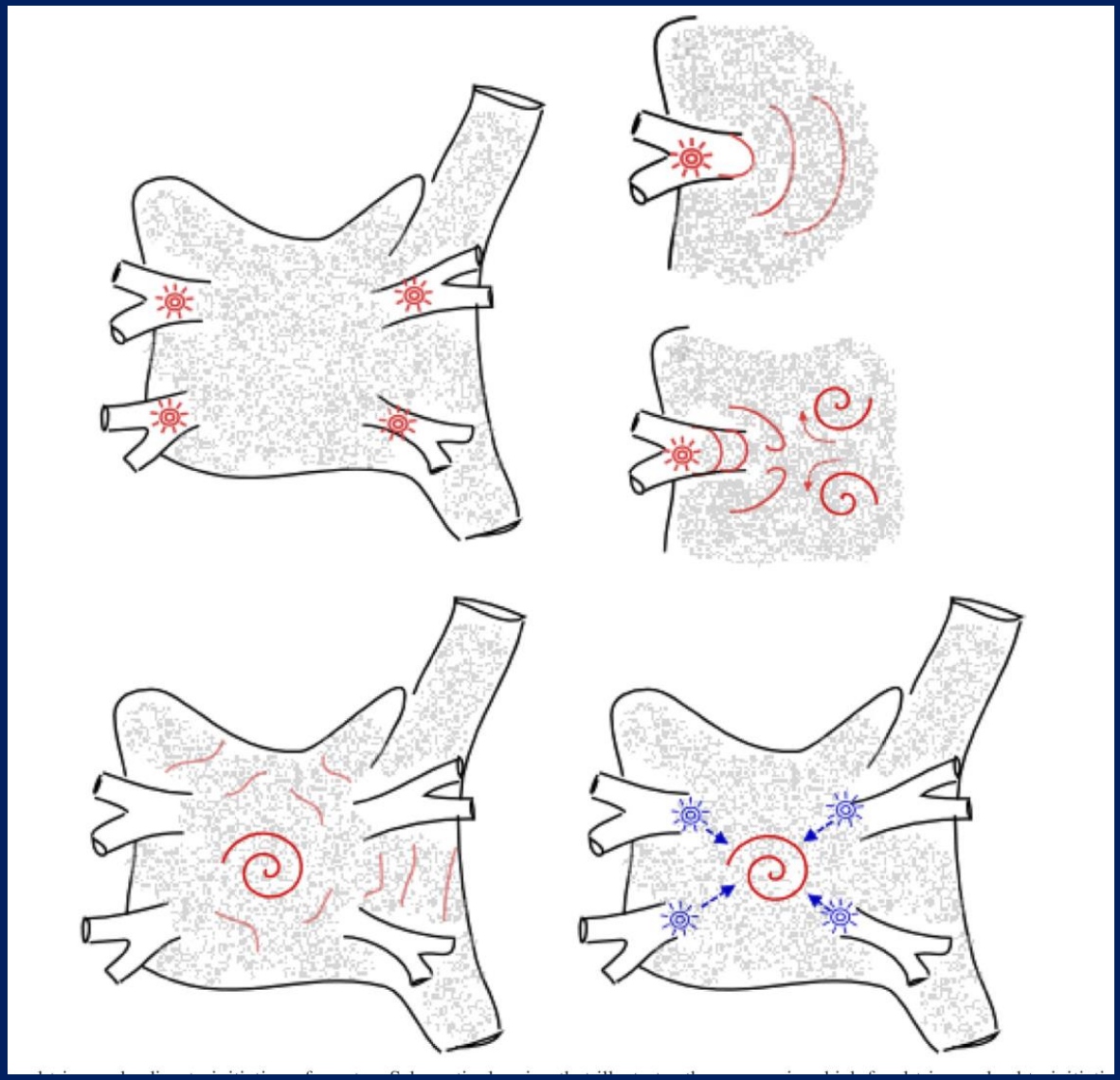
Nathan and Eliakim.
Circulation 1966;34:412-422

Angiogram of a Left Inferior Pulmonary Vein Depicting the Source and Exit of Ectopic Activity



Haïssaguerre, M. et al. N Engl J Med 1998;339:659-666

Focal Triggers Leading to Initiation of Reentry



Heart Rhythm 2012; 9:632-696

AF Ablation Efficacy Depends On Patient Population

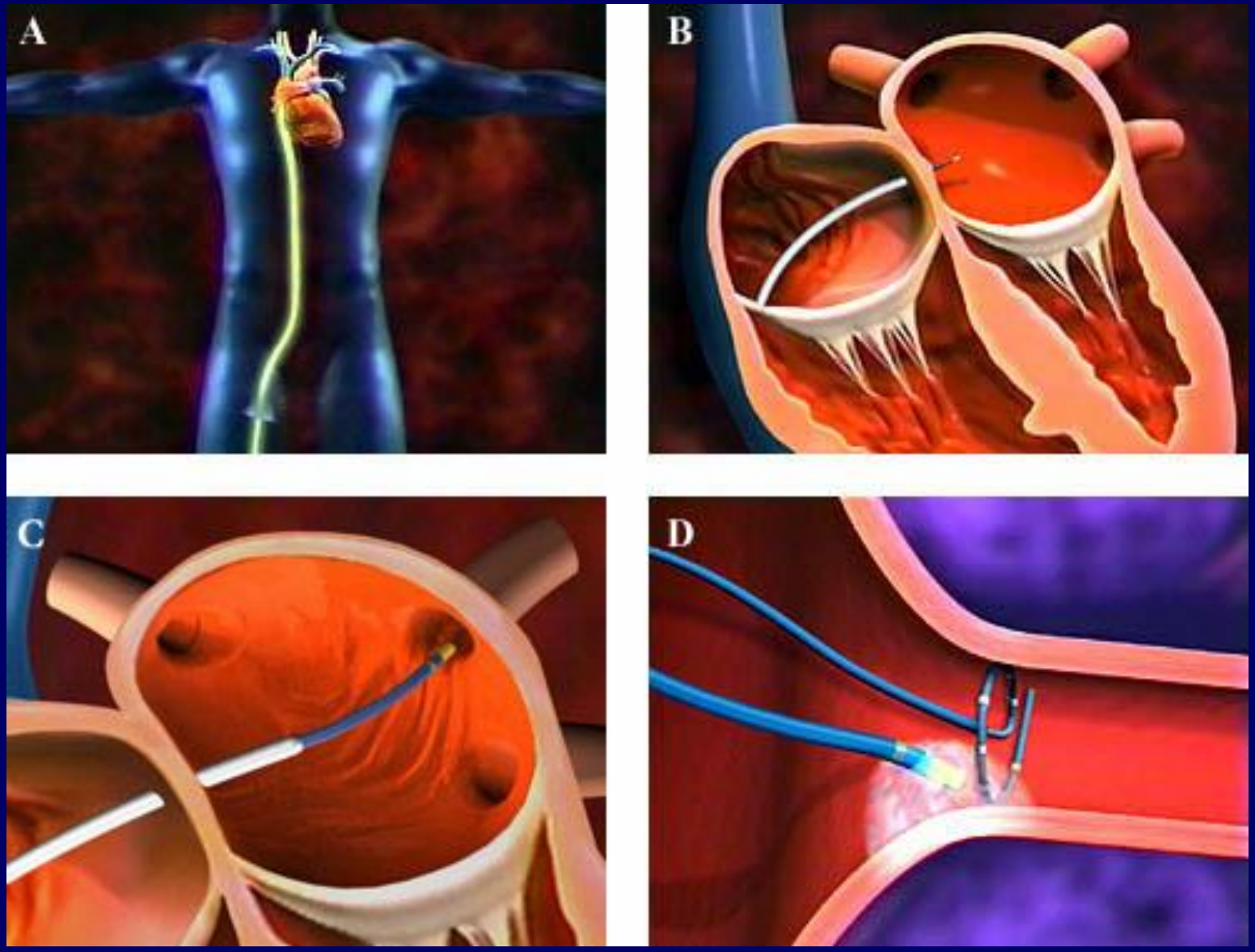
- Paroxysmal
- Persistent
- Long-standing persistent

Atrial Remodeling

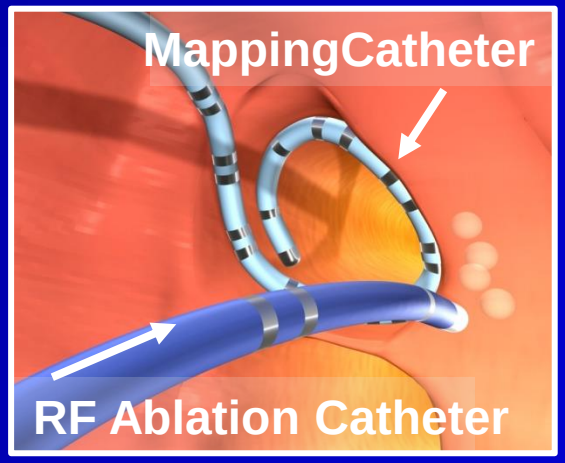
Lesion Sets for Paroxysmal AF Patients

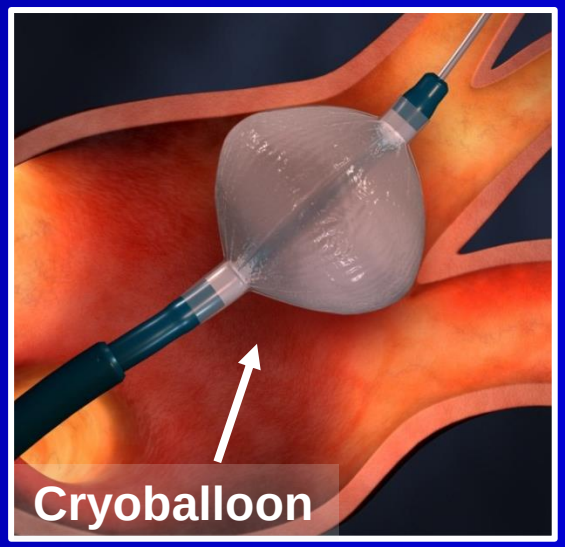
- Most paroxysmal AF patients should receive only PV isolation
  - Wide antral, not just ostial
- A minority of paroxysmal AF patients may need more extensive lesion sets
  - Concomitant atrial flutter
  - Long AF episodes
  - Large atria
  - Structural heart disease
    - HTN, obesity, etc.
  - Re-do procedures
- Should we manage “recently-persistent” AF the same as paroxysmal?

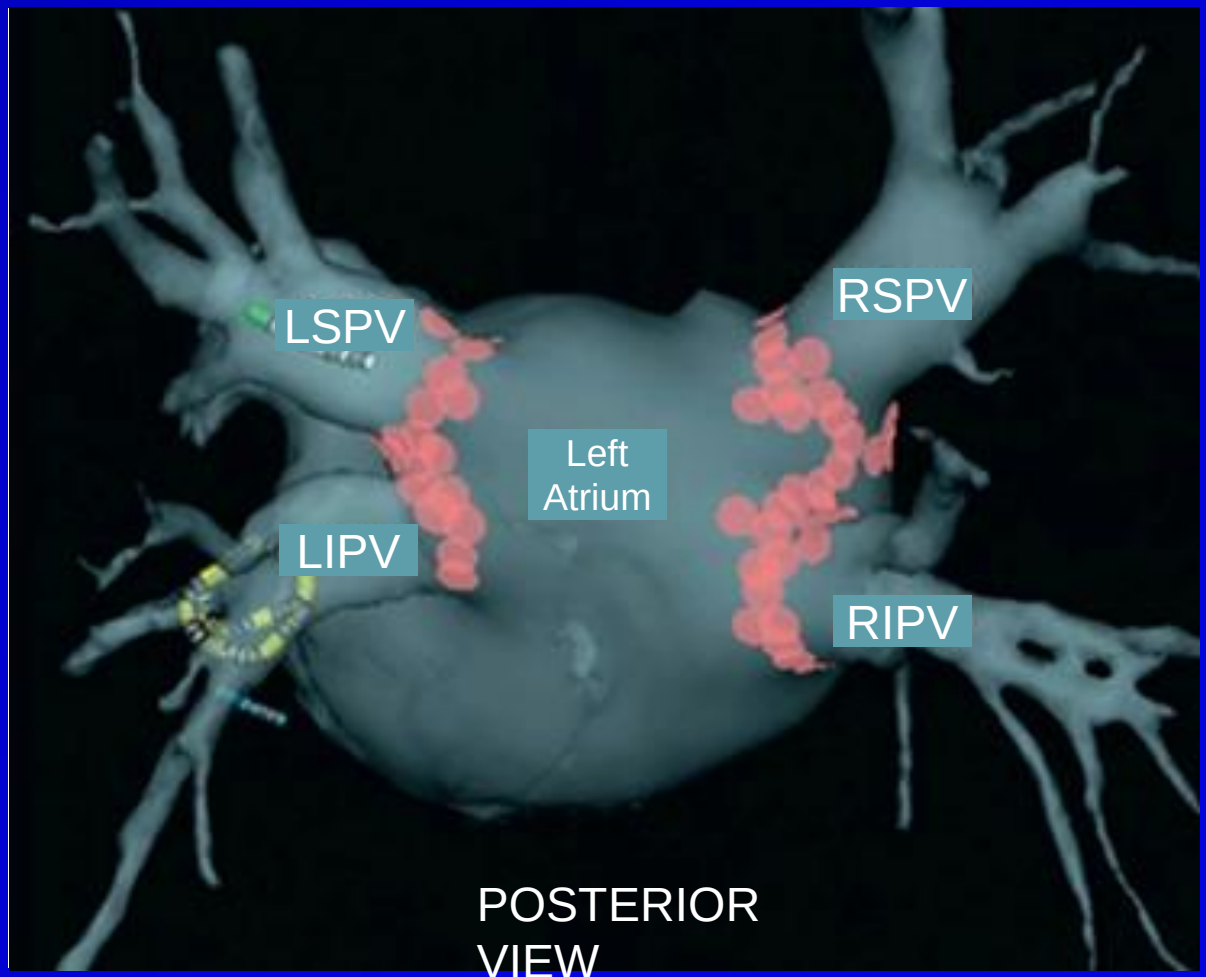
Catheter Ablation of Atrial Fibrillation



Catheter Ablation For Paroxysmal AF





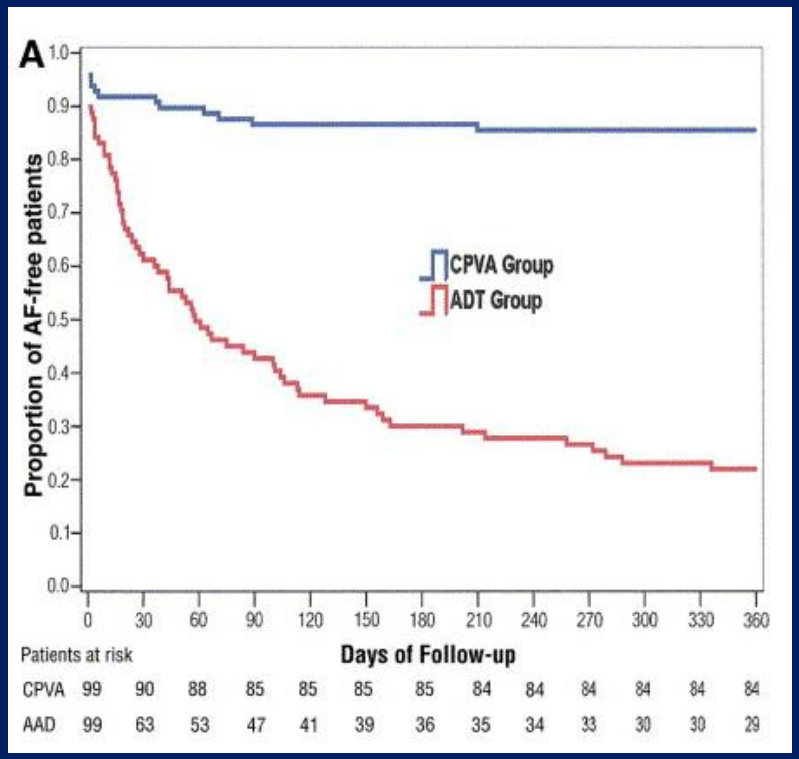


Merino, et al. *Atrial Fibrillation Ablation Guided by Computed Tomography*. Rev Esp Cardiol. 2009;62:314

Catheter Ablation Versus Antiarrhythmic Drugs for Atrial Fibrillation

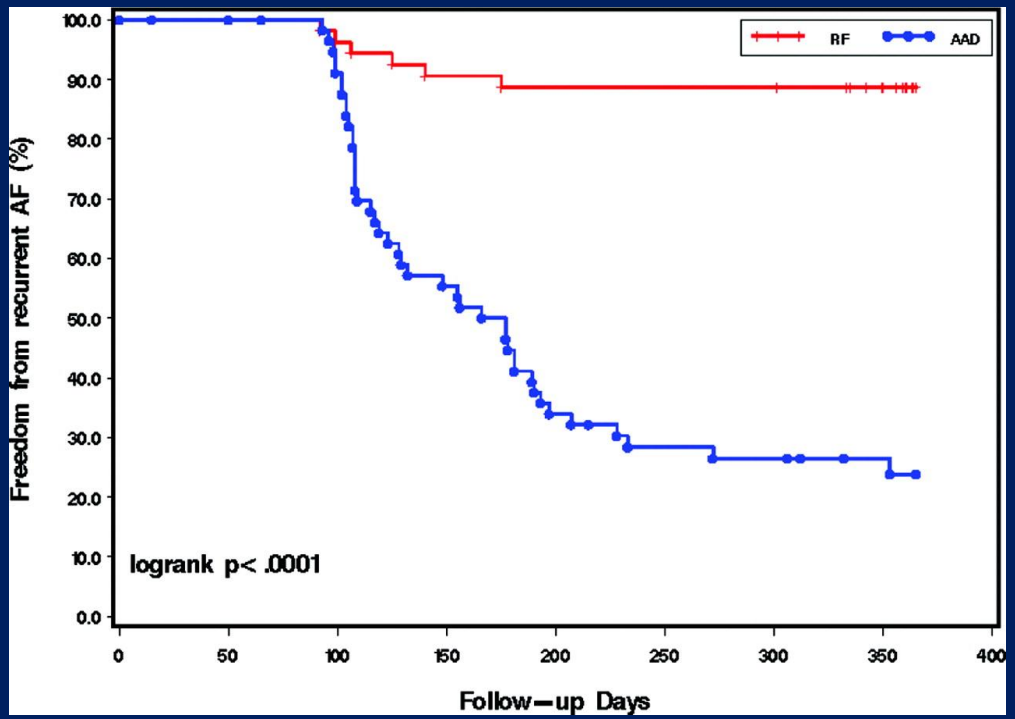
Early Studies

The APAF Study



Pappone et al. J Am Coll Cardiol 2006;48:2340-7

The A4 Study



Jais, P. et al. Circulation 2008;118:2498-2505

Early studies limited by small study populations, variable entry criteria and definitions of success, and were conducted in a single or limited number of centers.

Atrial Fibrillation Ablation

Systematic Literature Review and Meta Analysis

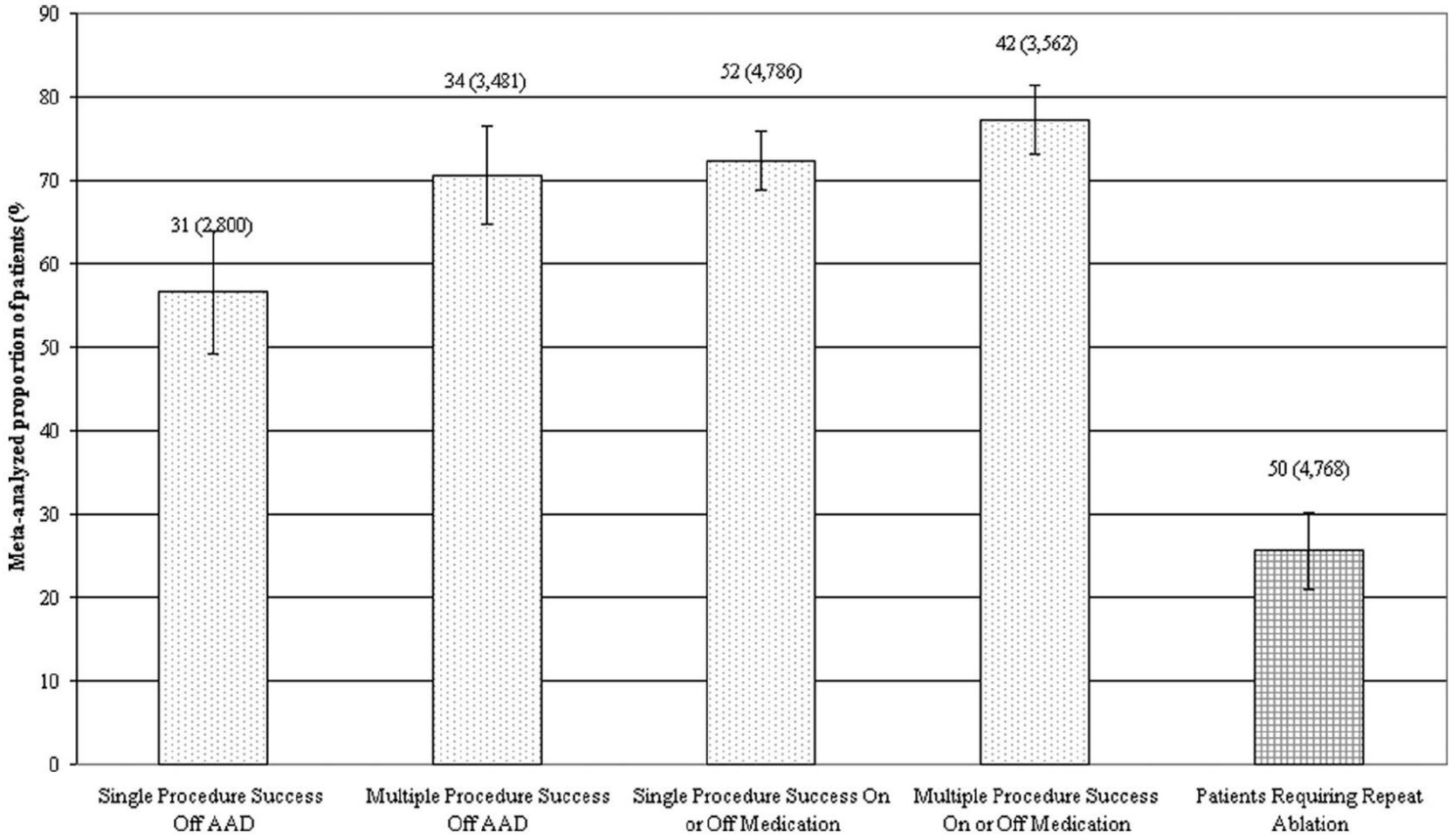


Figure 3. Efficacy of catheter ablation in patients with AF.

Calkins et al. Circ Arrhythmia Electrophysiol 2009;2:349

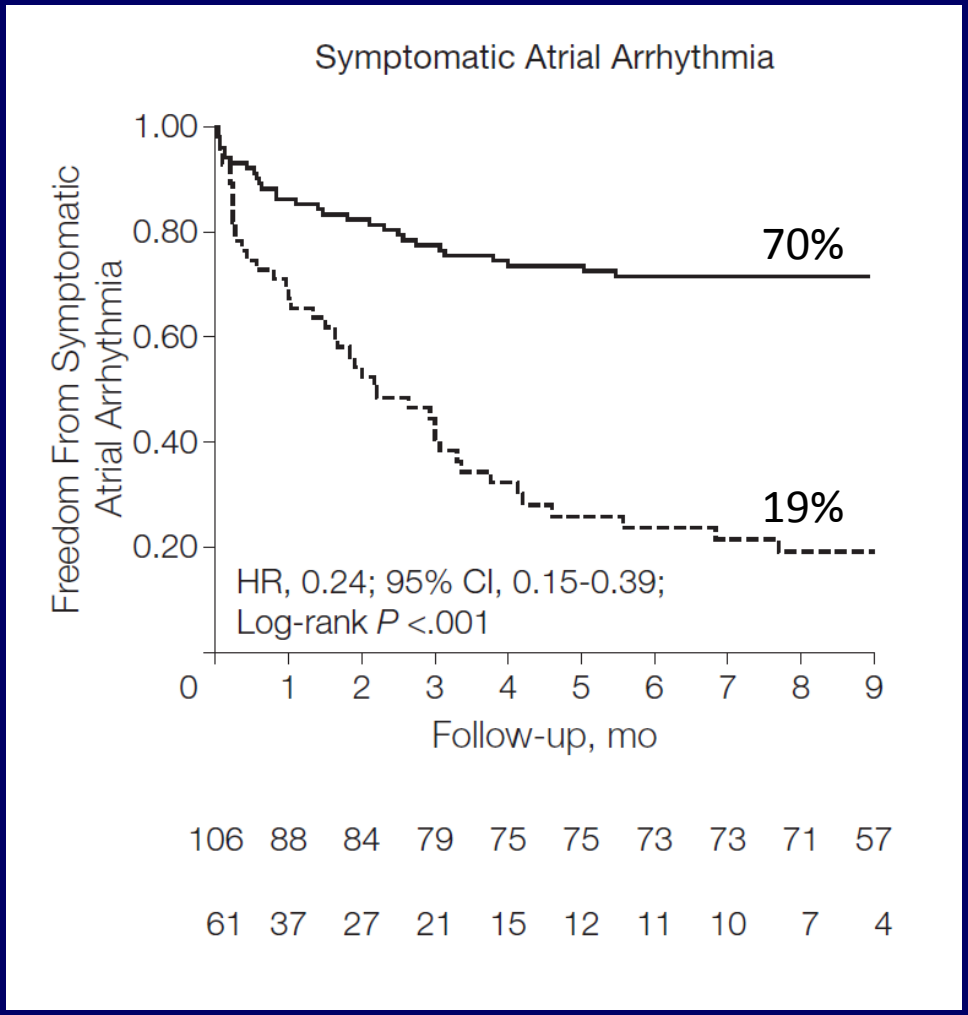
Comparison of Antiarrhythmic Drug Therapy and RF Catheter Ablation in Patients With Paroxysmal Atrial Fibrillation

Trial data from:

1) Wilber, D. J. et al. JAMA 2010;303:333-340

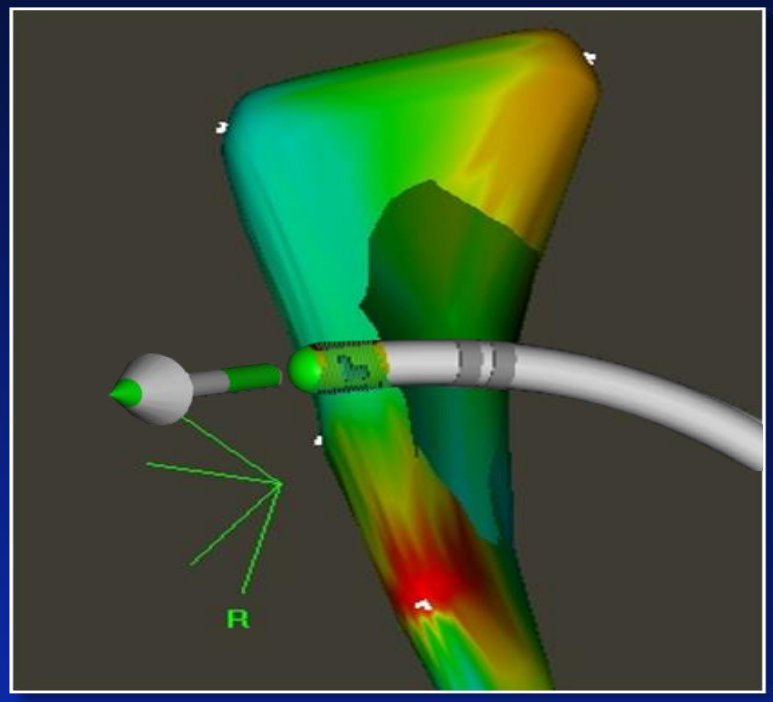
2) FDA website

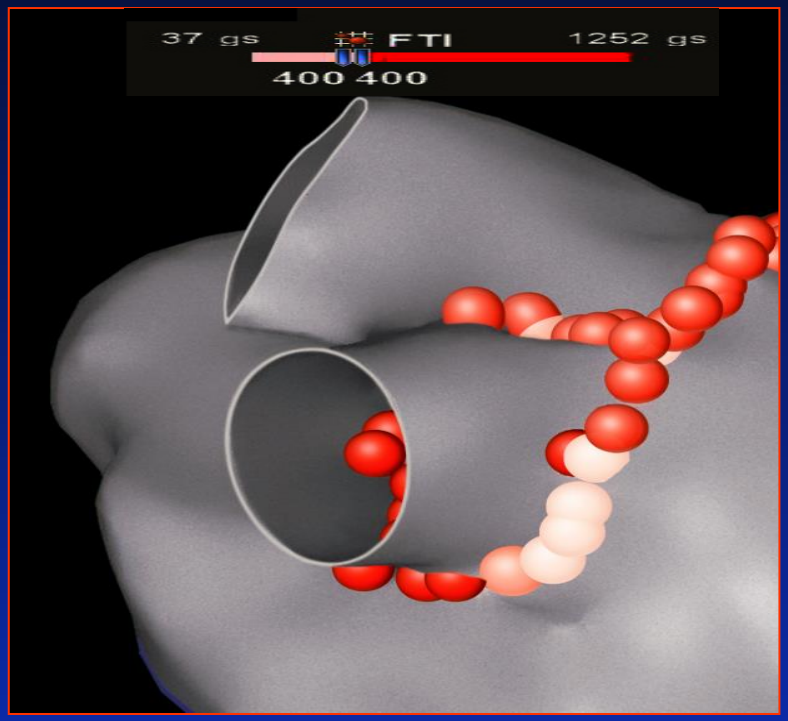
Comparison of Antiarrhythmic Drug Therapy and RF Catheter Ablation in Patients With Paroxysmal AF: *Thermocool Study*



Wilber, D. J. et al. JAMA 2010;303:333-340

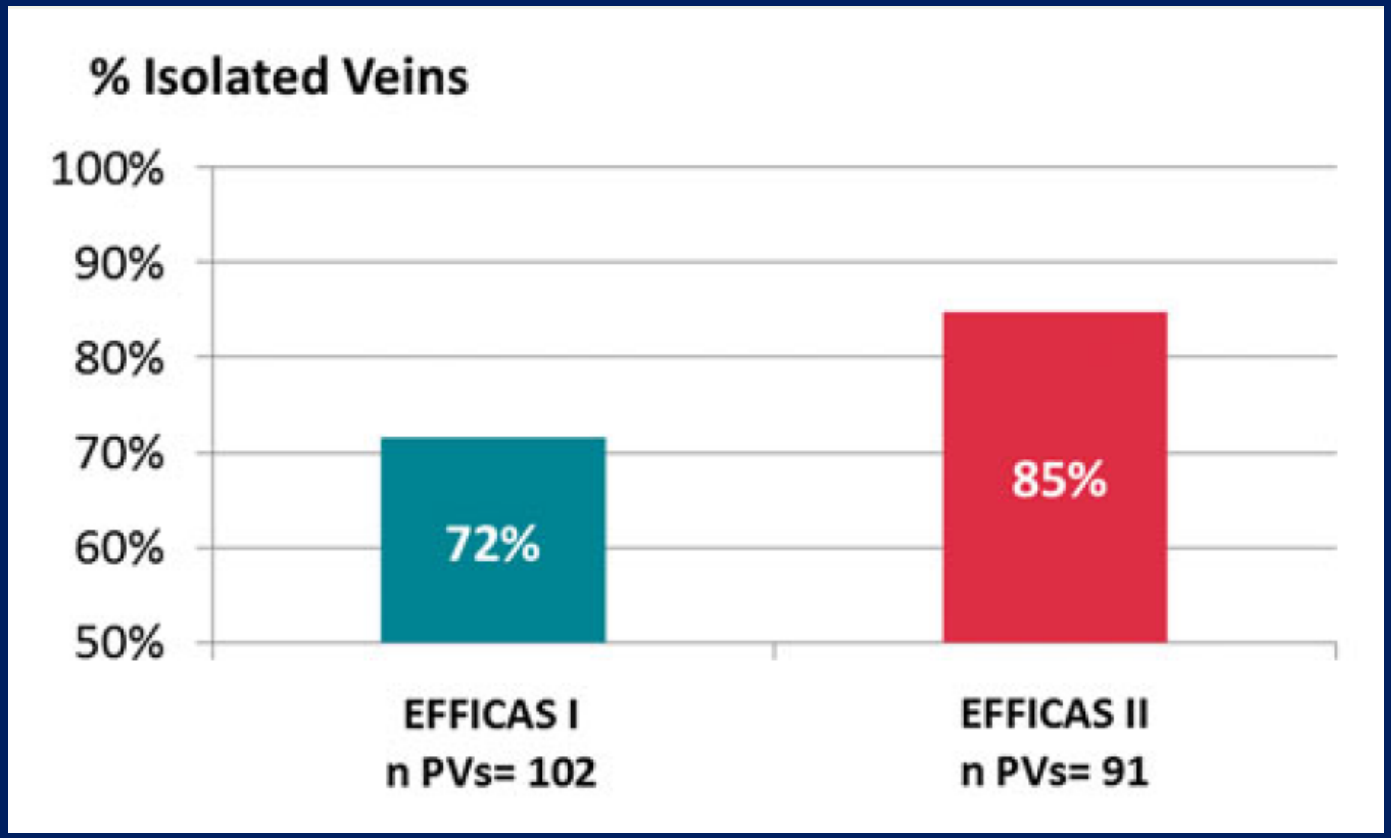
New Advances in RF Ablation – Contact Force





Biosense Webster, Inc

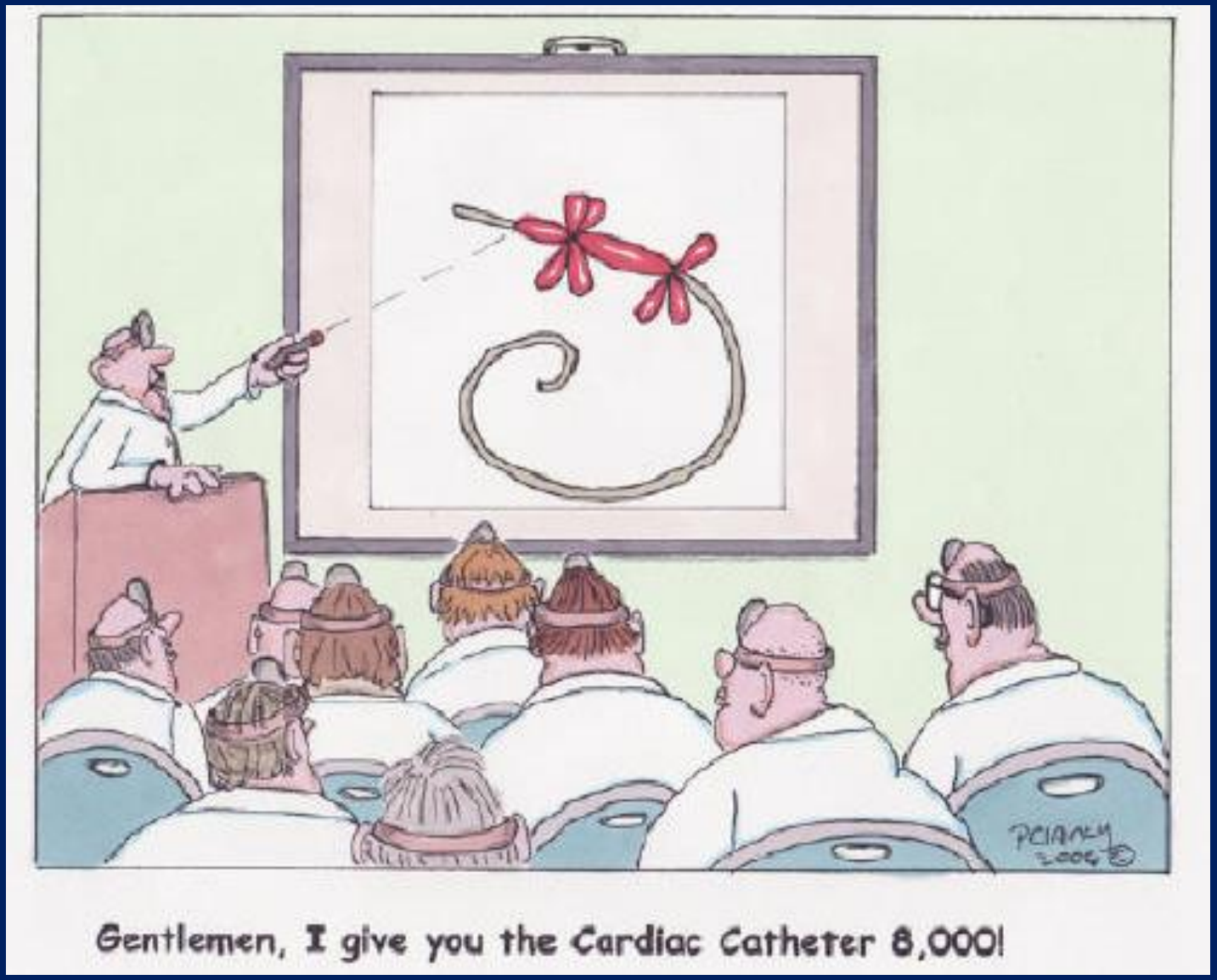
EFFICAS II: optimization of catheter contact force improves outcome of pulmonary vein isolation for paroxysmal atrial fibrillation

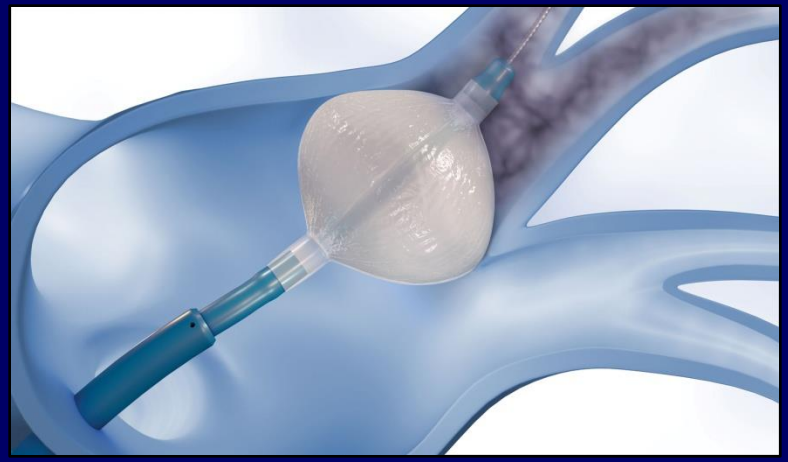


Pulmonary vein isolation at 3-month remapping. Comparison of durable isolation rates per vein in EFFICAS I, without CF guidelines, and EFFICAS II, with CF guidelines.

Kautzner et al.
Europace 2015;17:1229

Balloon Catheters

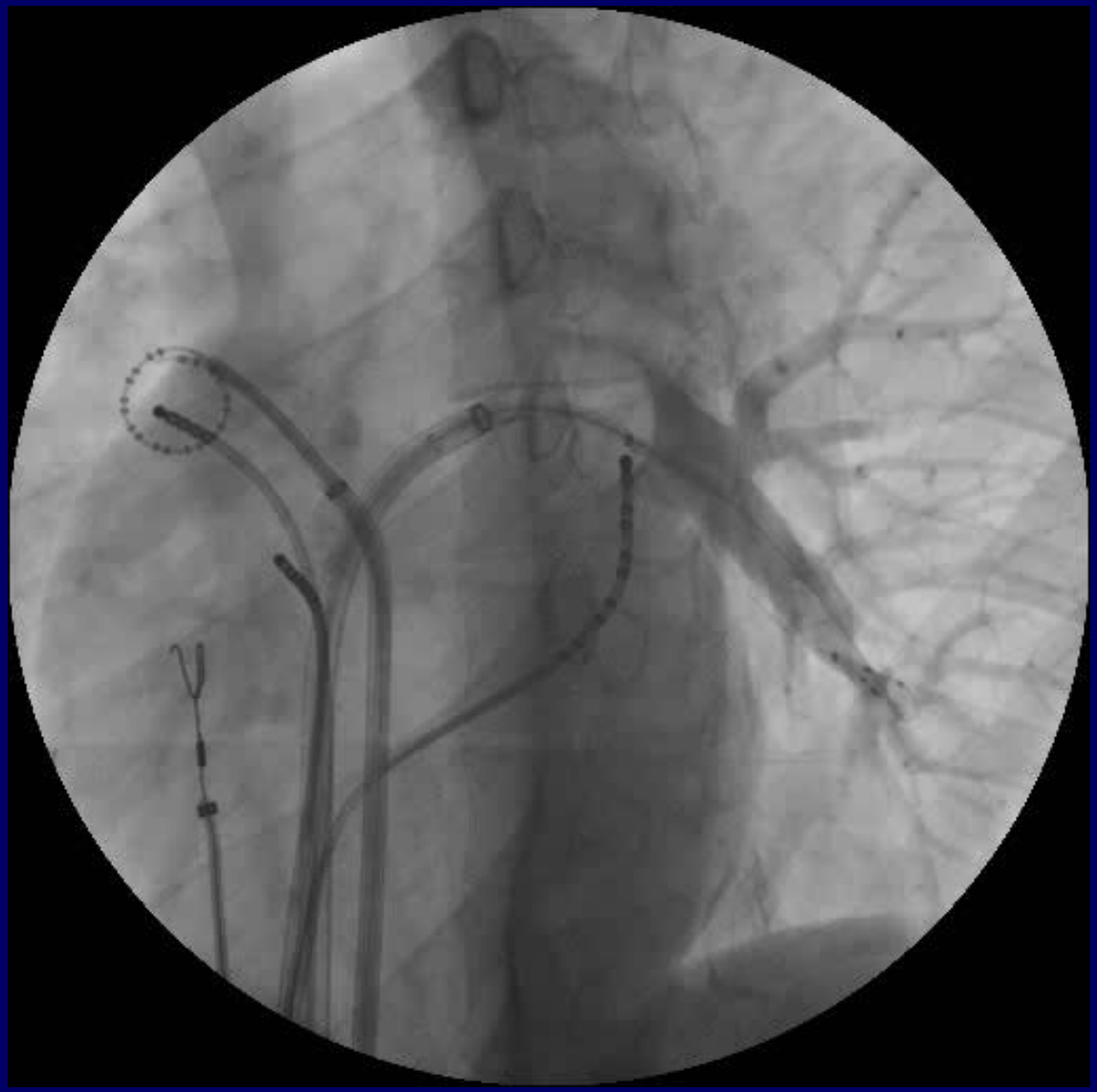




Cryoballoon

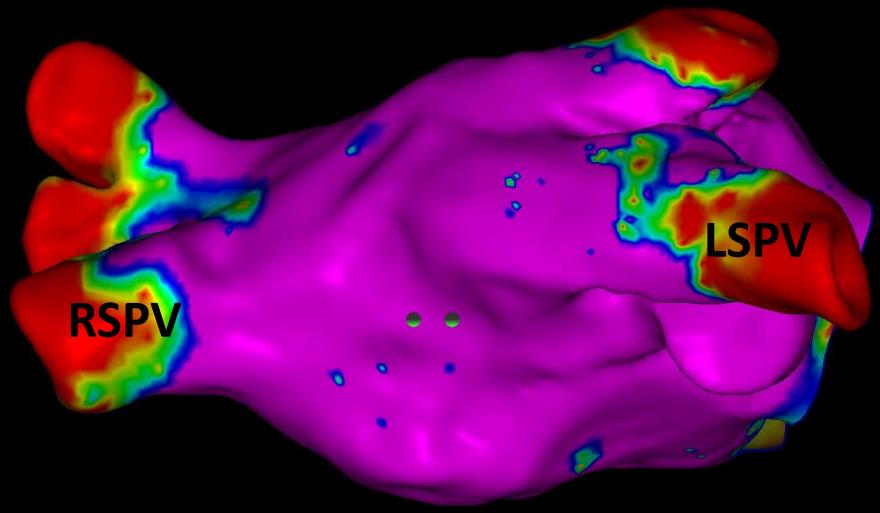
Metzner et al. *Circ Arrhythm Electrophysiol*. 2013;6:769-775

Cryoballoon Freezing of the Left Inferior Pulmonary Vein

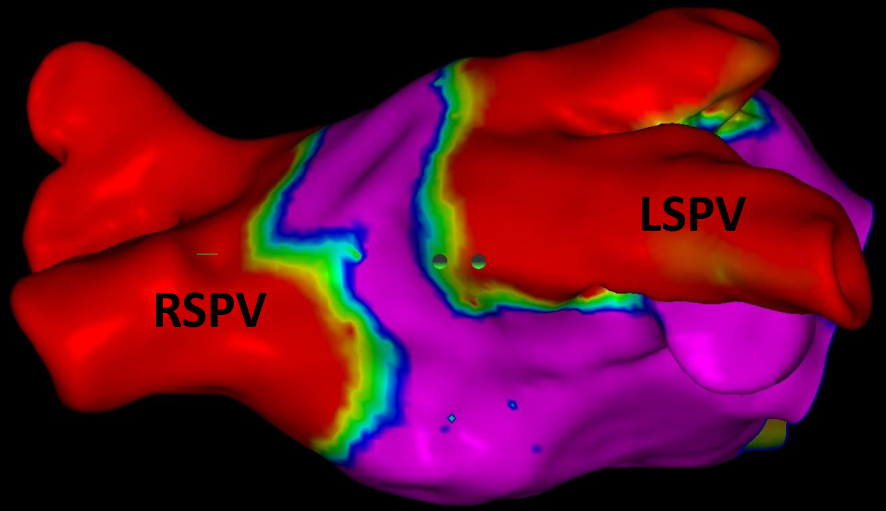


Voltage Maps Pre- and Post Cryoballoon Ablation

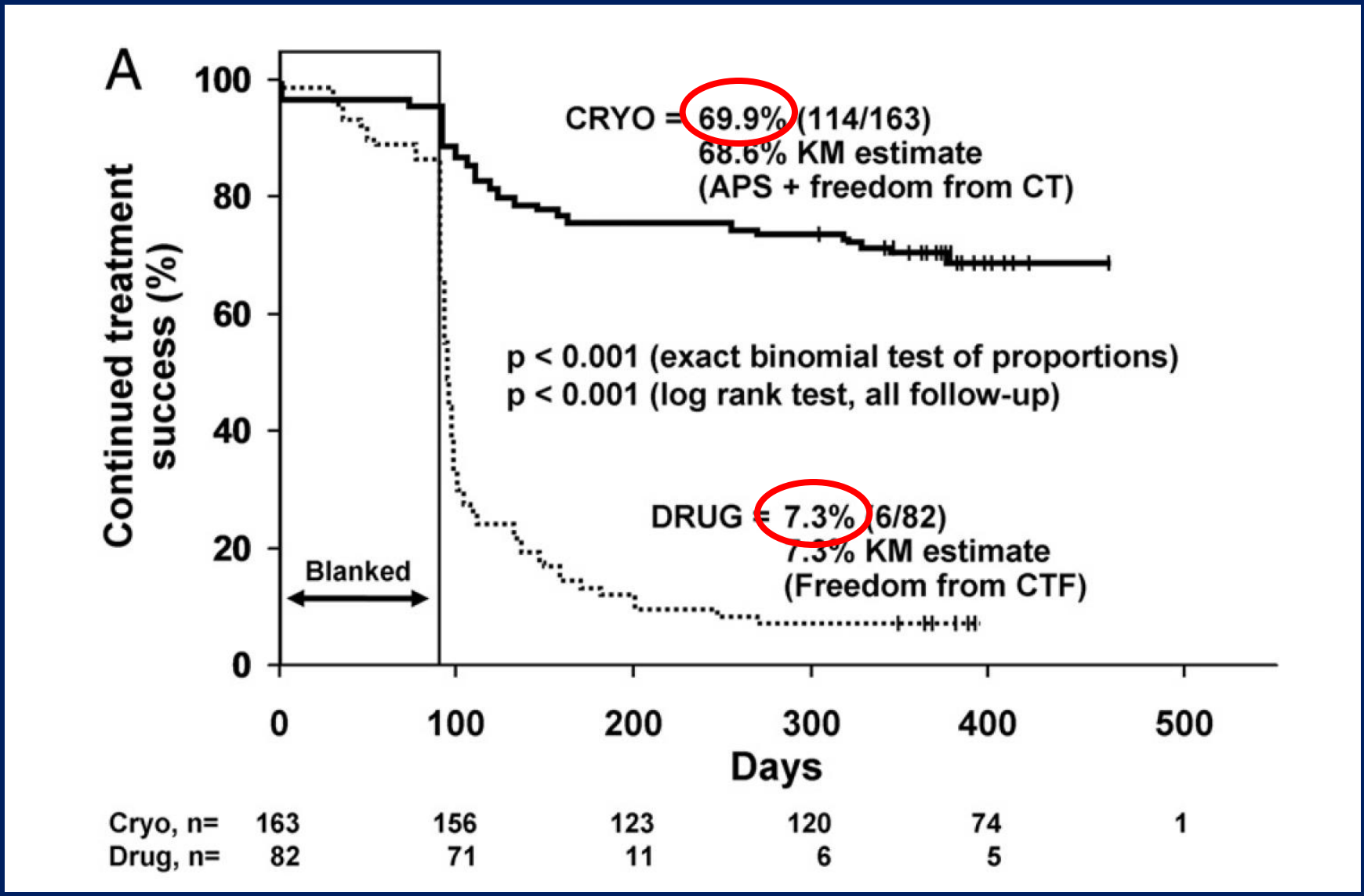
Pre-Ablation



Post-Ablation

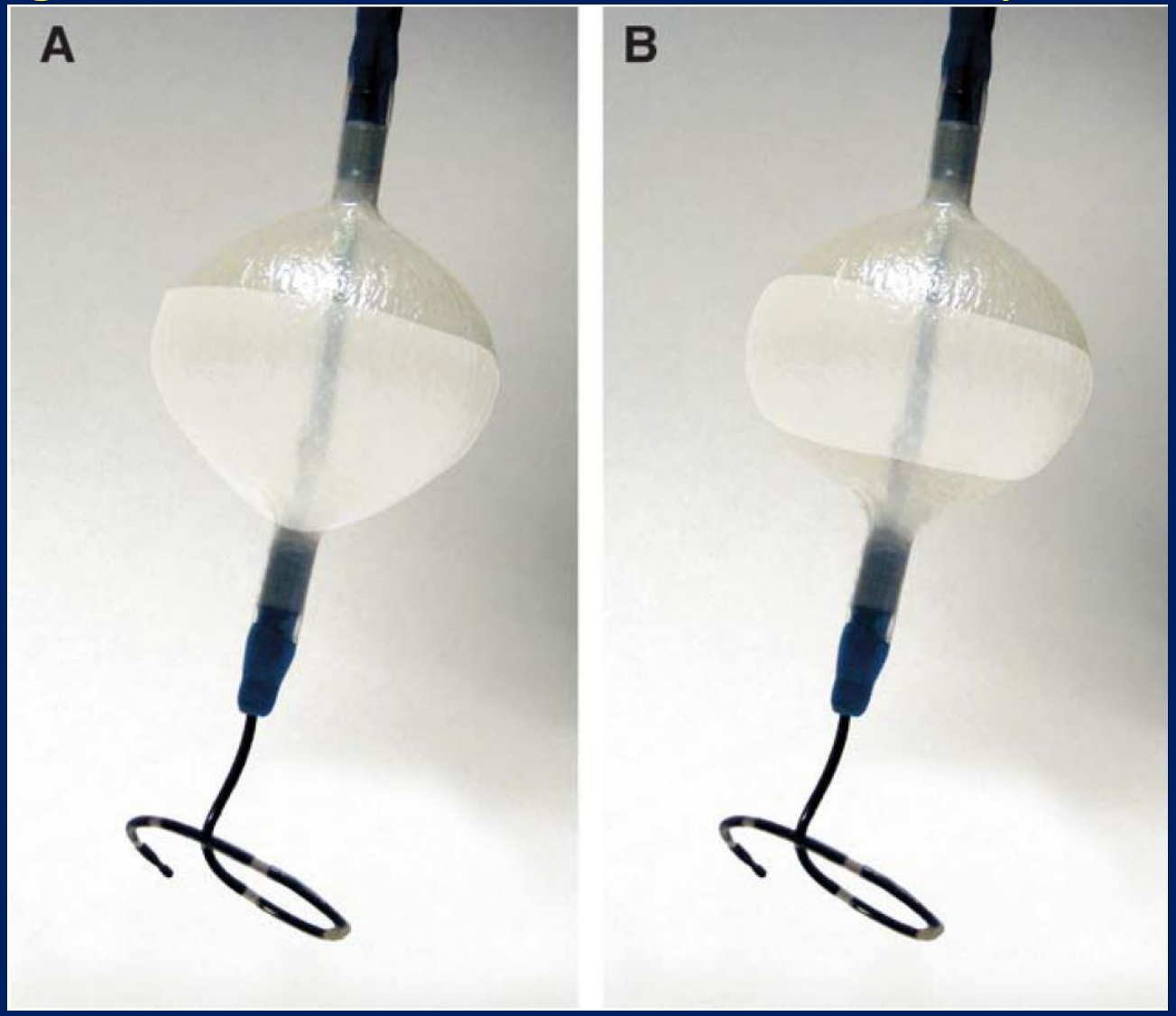


Procedural Success in the STOP AF Trial



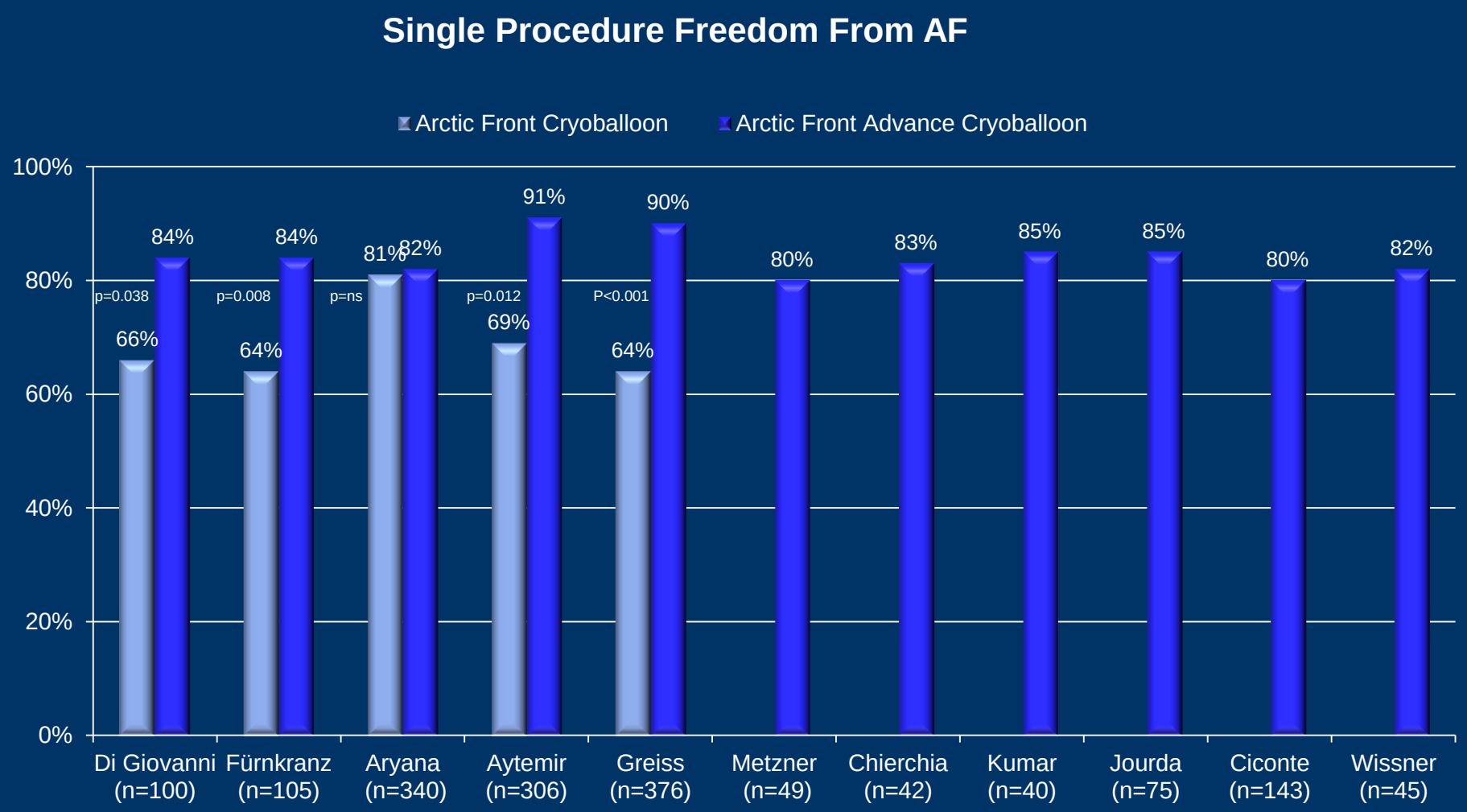
Packer et al. JACC 2013;61:1713

Increased Incidence of Esophageal Thermal Lesions Using the Second-Generation 28-mm Cryoballoon



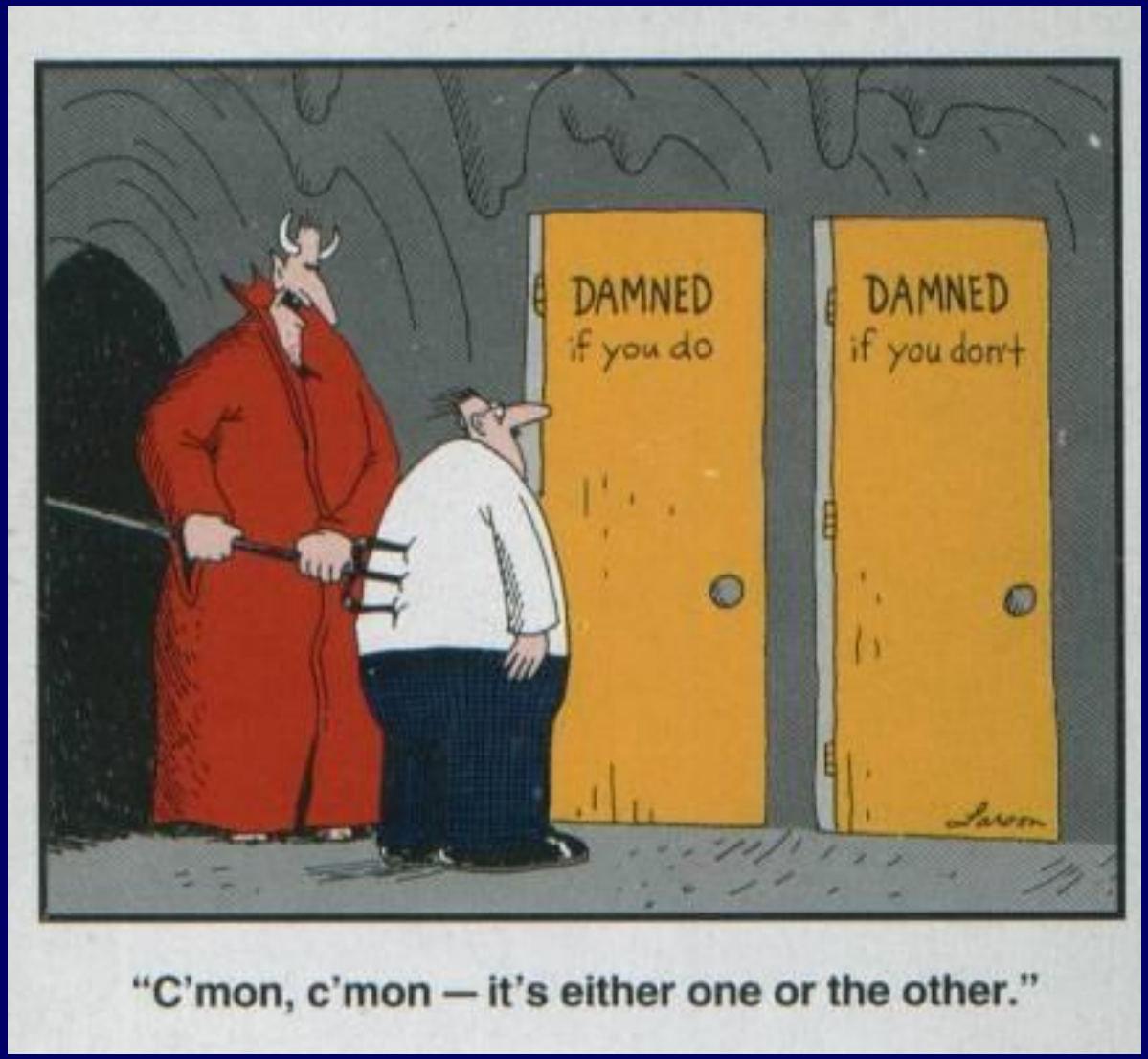
Metzner et al. *Circ Arrhythm Electrophysiol*. 2013;6:769-775

Single Procedure Freedom from AF, AT and AFL
Arctic Front Advance Cryoballoon Single Center Published Studies

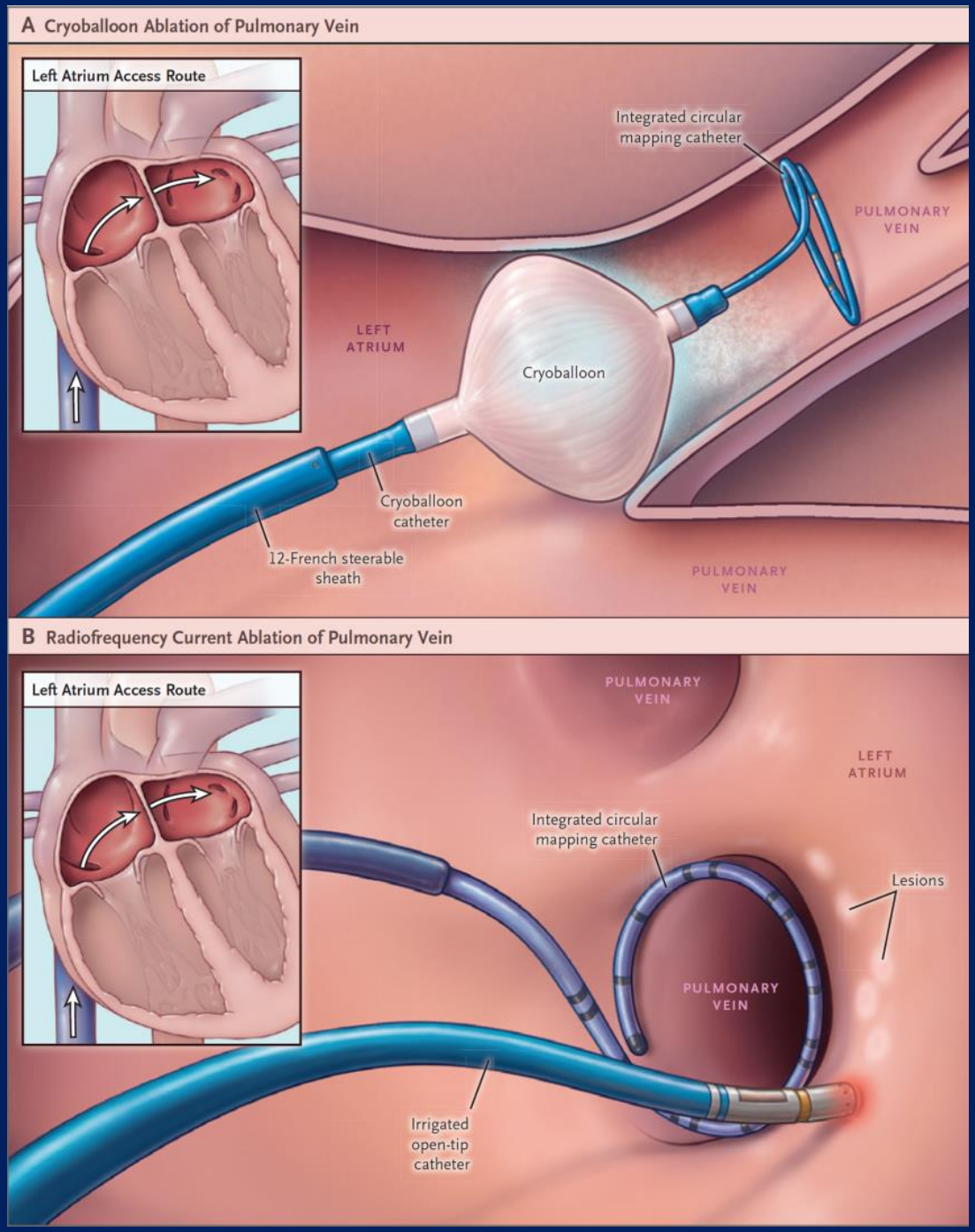


Di Giovanni, et al. *J Cardiovasc Electrophysiol.* 2014; 25(8):834-9 , Fürnkranz, et al. *Journal of Cardiovascular Electrophysiology* 2014 ;25(8):840-4, Aryana, et al. *J Interv Card Electrophysiol* 2014;41(2):177-186, Aytemir, et al. *Europace*; 2015;17(3):379-87, Metzner, et al. *Circ Arrhythm Electrophysiol.* 2014; 7(2):288-292 , Chierchia, et al. *Europace* 2014; 16(5):639-644, Kumar et al. *J Interv Card Electrophysiol* 2014;41(1):91-7, Jourda, et al. *Europace* 2015;17(2):225-31, Ciconte, et al. *Heart Rhythm* 2015;12(4):673-80, Wissner, et al. *Europace* 2015, In Press.

Cryoablation vs. RF Ablation



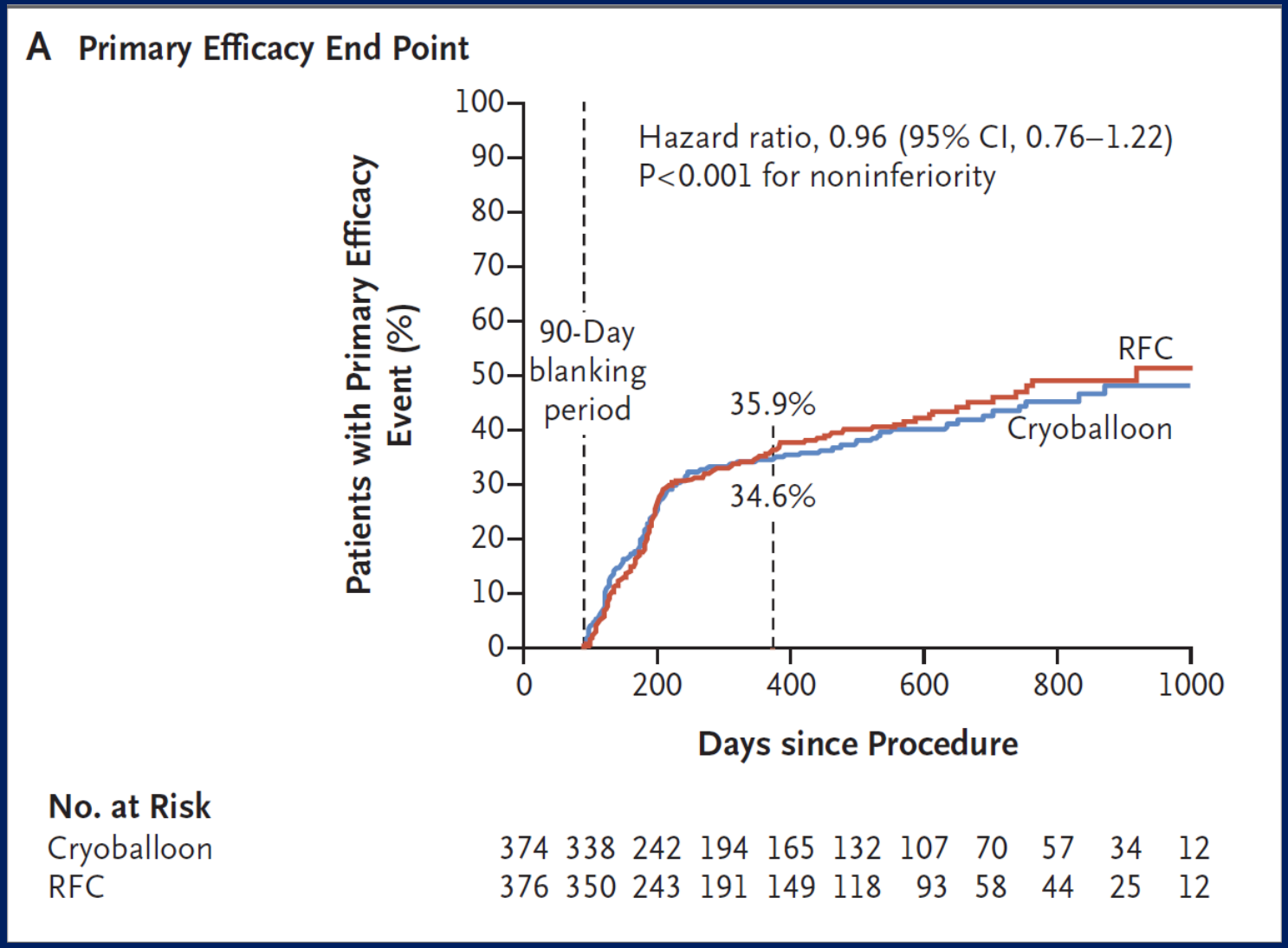
"C'mon, c'mon — it's either one or the other."



Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

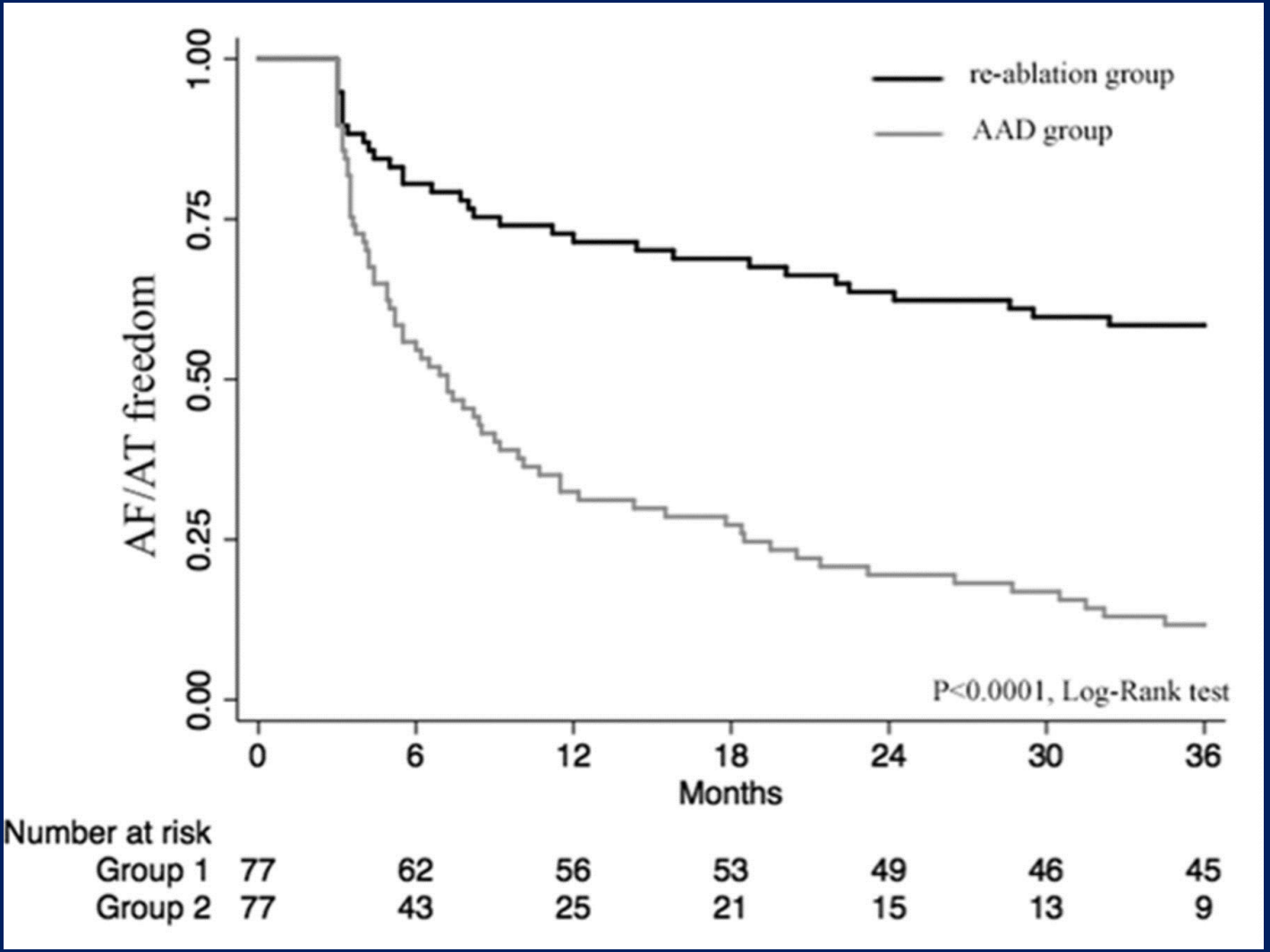
Kuck et al, NEJM 2016

Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation



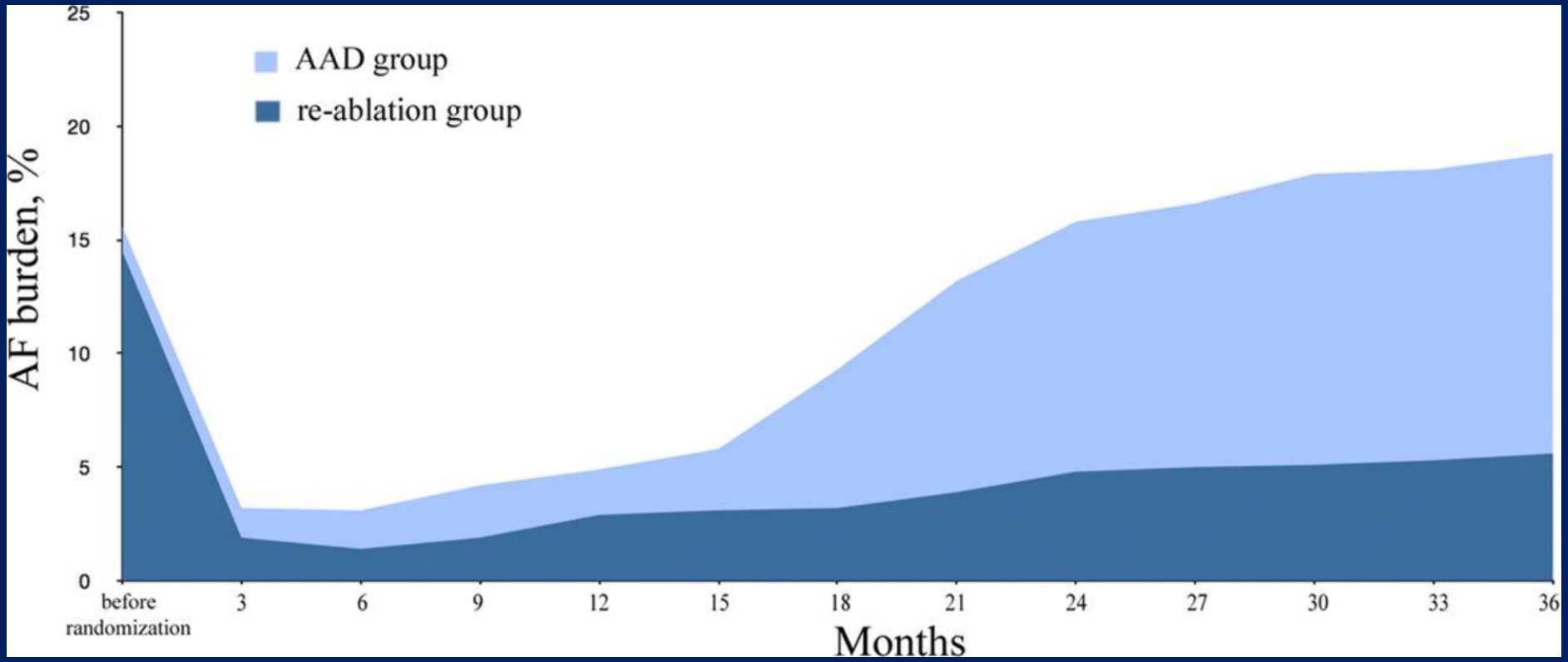
Kuck et al, NEJM 2016

A Randomized Comparison of Drug Therapy Versus Reablation *After a Failed Initial Ablation Procedure* in Patients With Paroxysmal Atrial Fibrillation



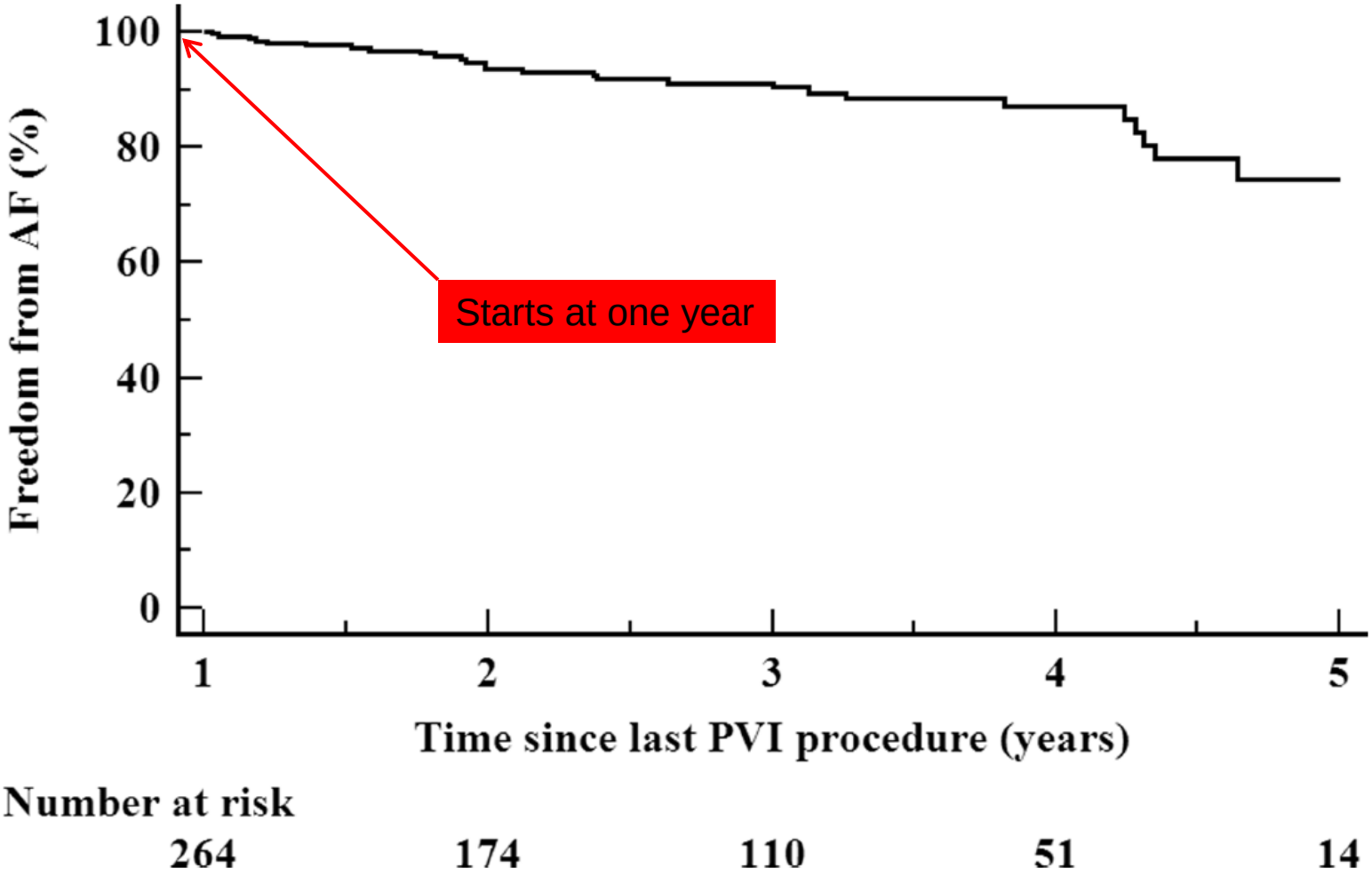
Pokushalov E et al. Circ Arrhythm Electrophysiol 2013;6:754-760

A Randomized Comparison of Drug Therapy Versus Reablation After a Failed Initial Ablation Procedure in Patients With Paroxysmal Atrial Fibrillation



Pokushalov E et al. Circ Arrhythm Electrophysiol 2013;6:754-760

Long-Term Outcome Following Successful Pulmonary Vein Isolation: Pattern and Prediction of Very Late Recurrence

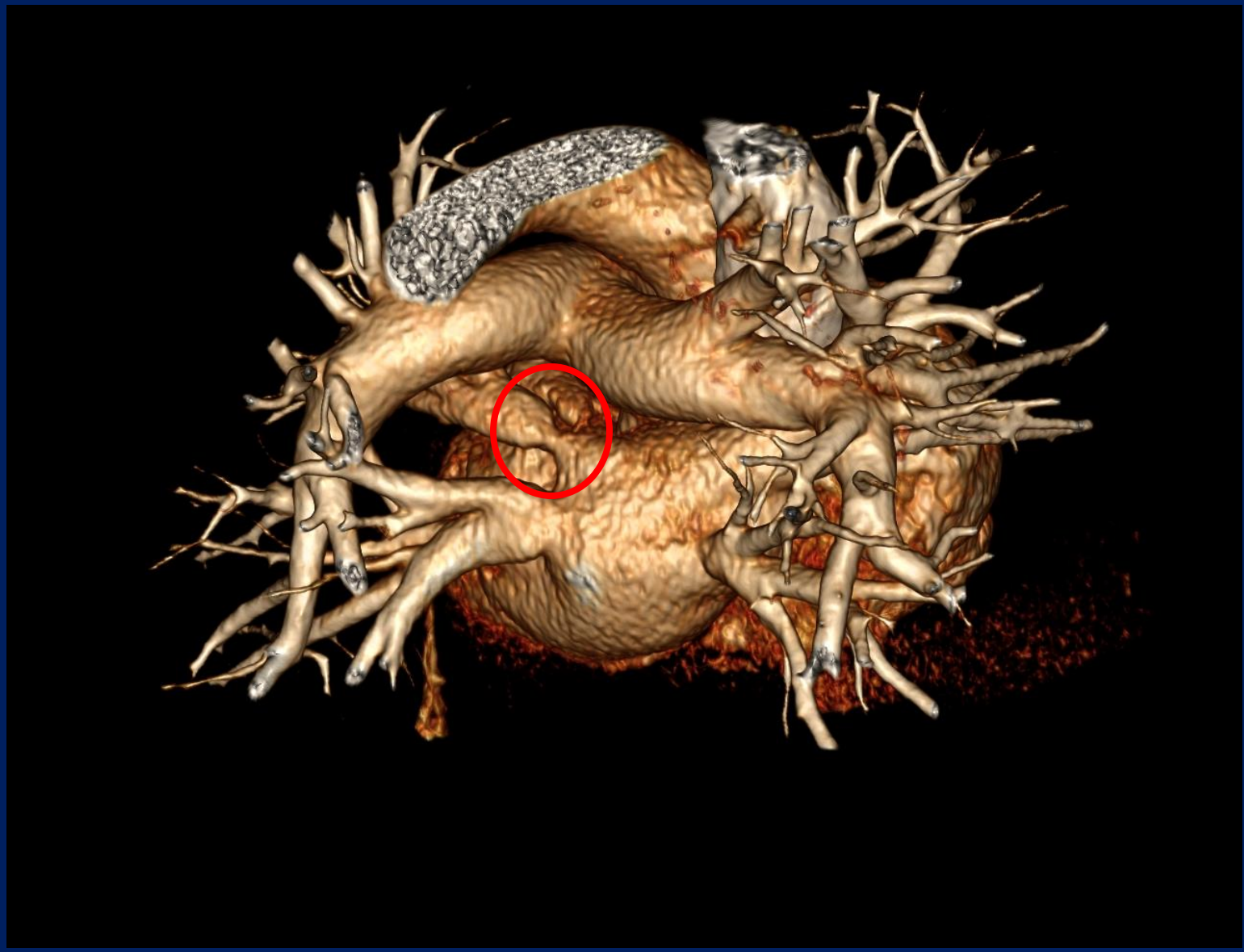


Shah et al. J Cardiovasc Electrophysiol 2008;19:661

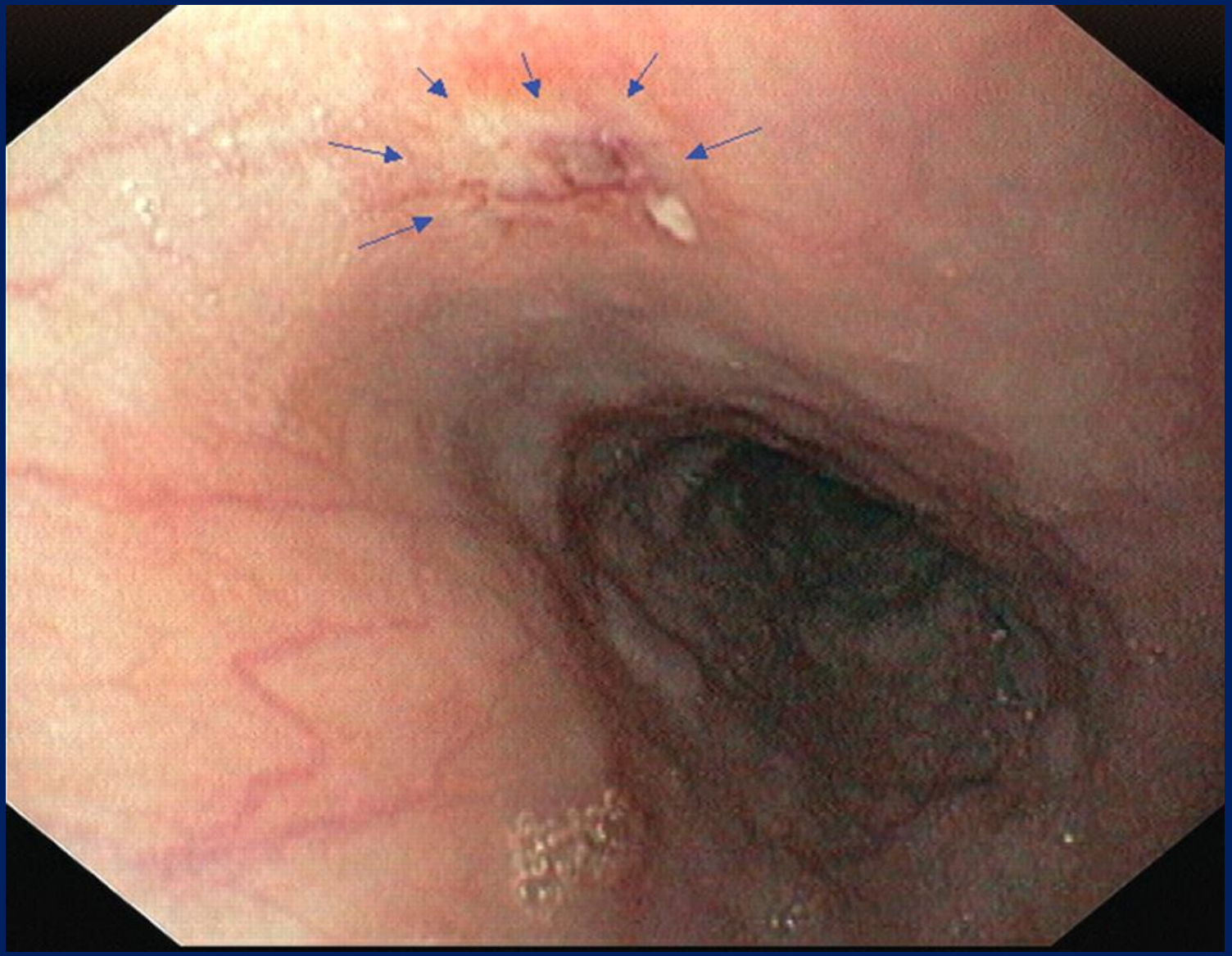
Complications of AF Ablation

- Thromboembolism/air embolism
- Cardiac tamponade
- Pulmonary vein stenosis
- Atrio-esophageal fistula
- Vascular access-related complications
  - Hematoma, pseudoaneurysm, AV fistula
- Left atrial flutters/atrial tachycardia
- Mitral valve trauma/catheter entrapment
- Phrenic nerve injury
- Radiation exposure/skin burns
- Acute coronary artery occlusion
- Periesophageal vagal injury

LUPV Stenosis

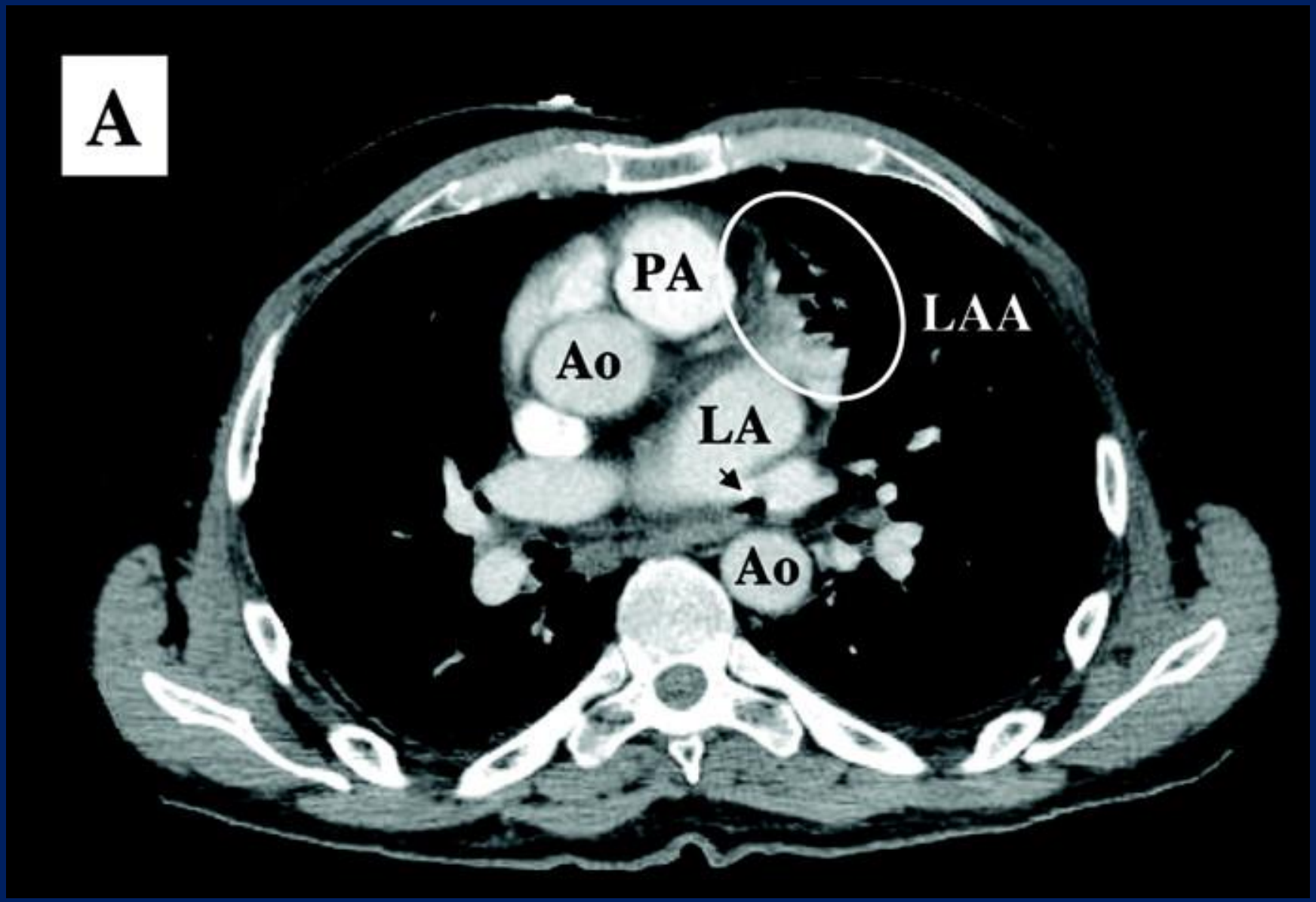


Necrotic ulcer within the anterior wall of the oesophagus in close proximity to the left atrial posterior wall 24 h after PVAI



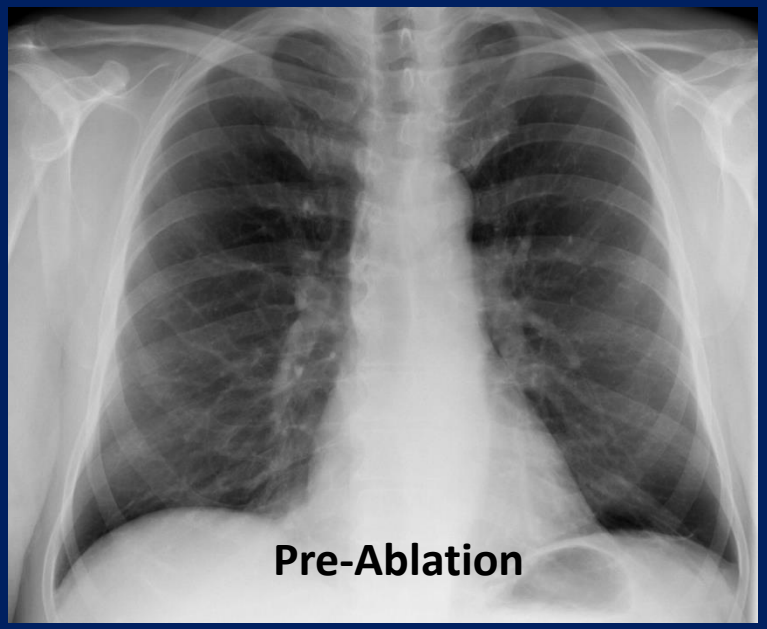
Schmidt, M. et al. Europace 2008 10:205-209

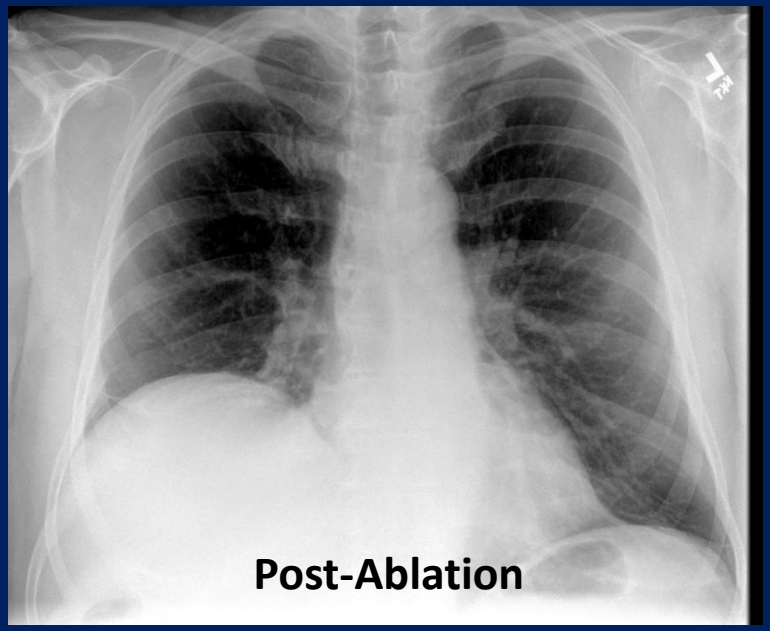
Left Atrial–Esophageal Fistula After Pulmonary Vein Isolation

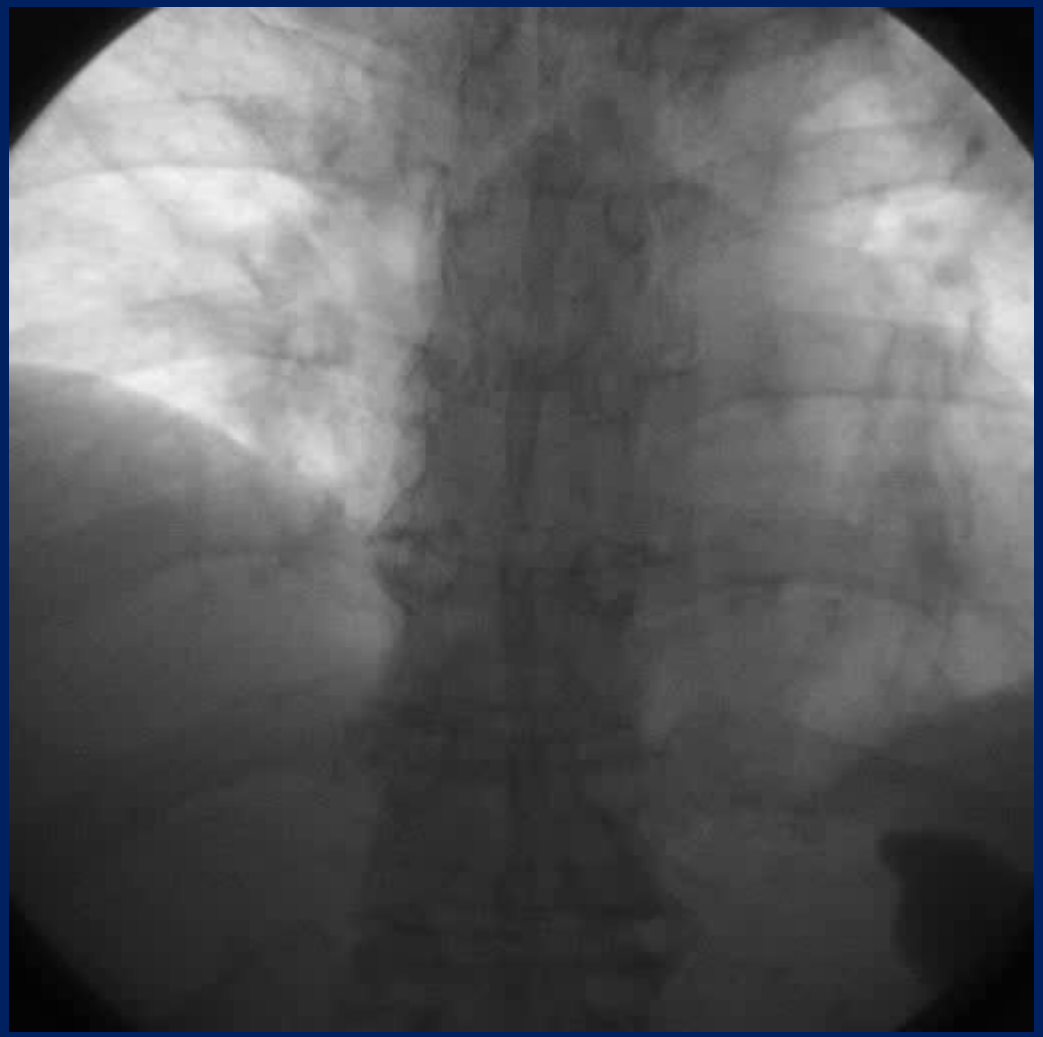


D'Avila, A. et al. Circulation 2007;115:e432-e433

Phrenic Nerve Palsy





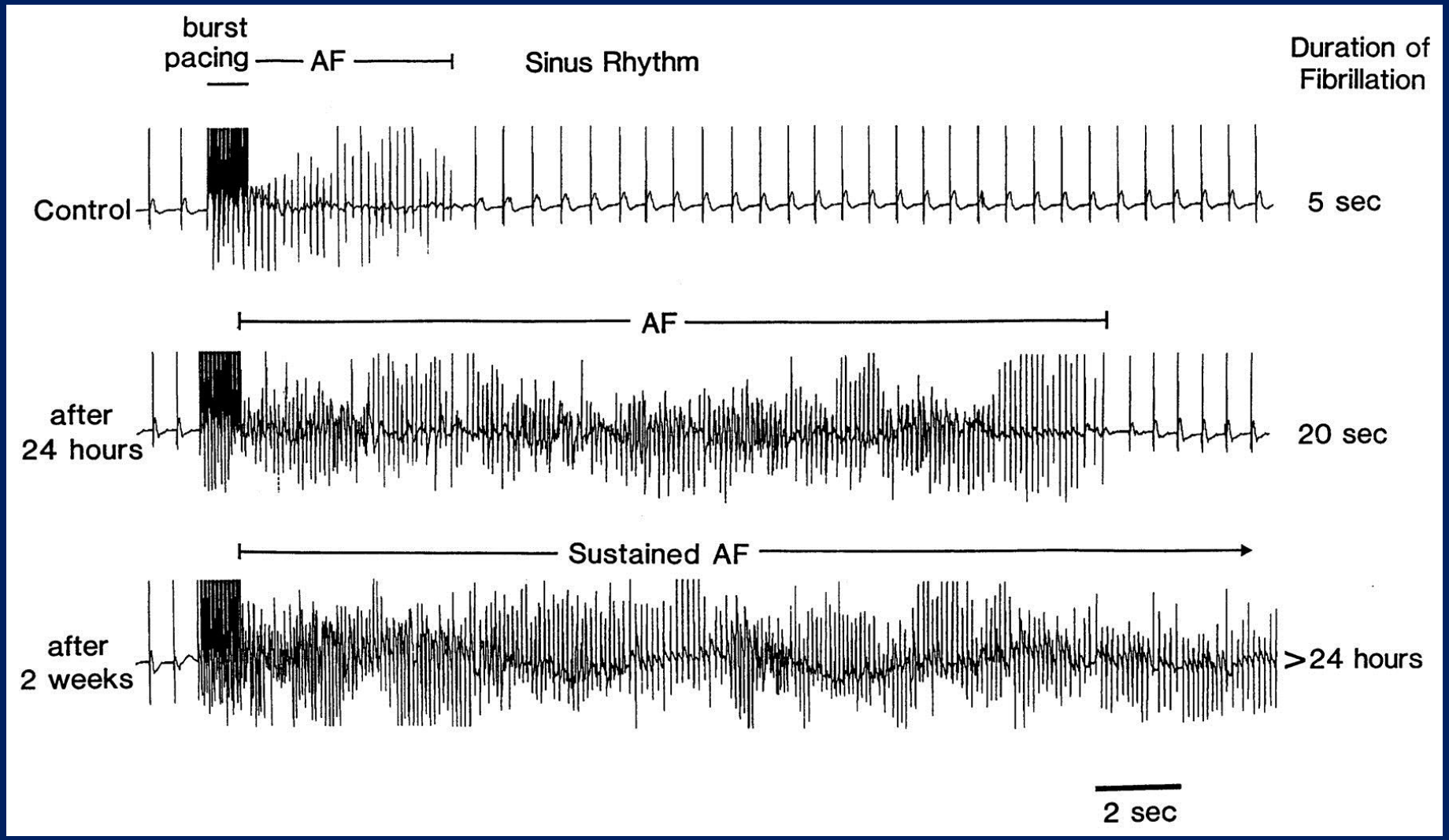


AF Ablation Efficacy Depends On Patient Population

- Paroxysmal
- Persistent
- Long-standing persistent

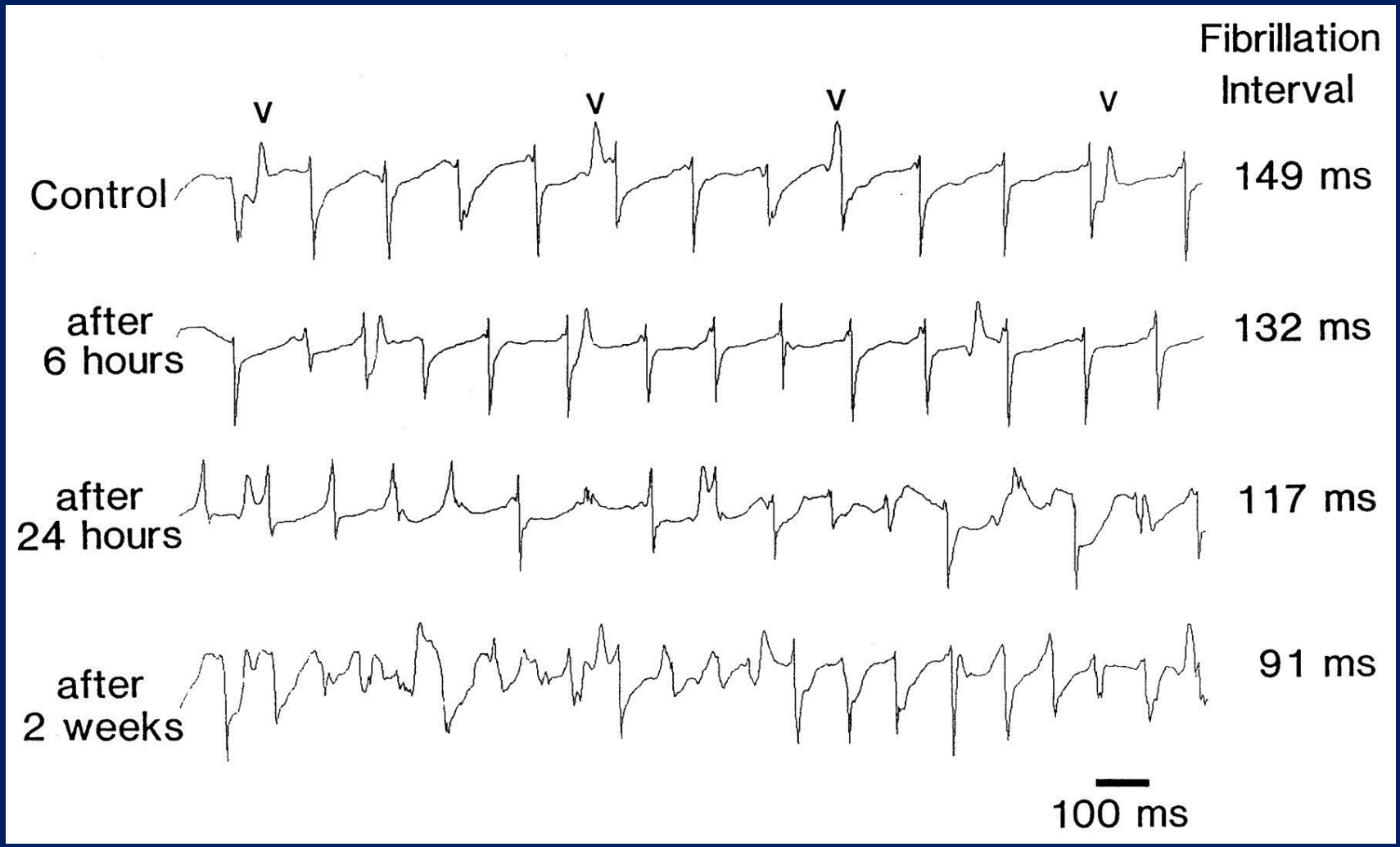
Atrial Remodeling

Atrial Fibrillation Begets Atrial Fibrillation



Wijffels, Circulation 1995;92:1954-68

Atrial Fibrillation Begets Atrial Fibrillation

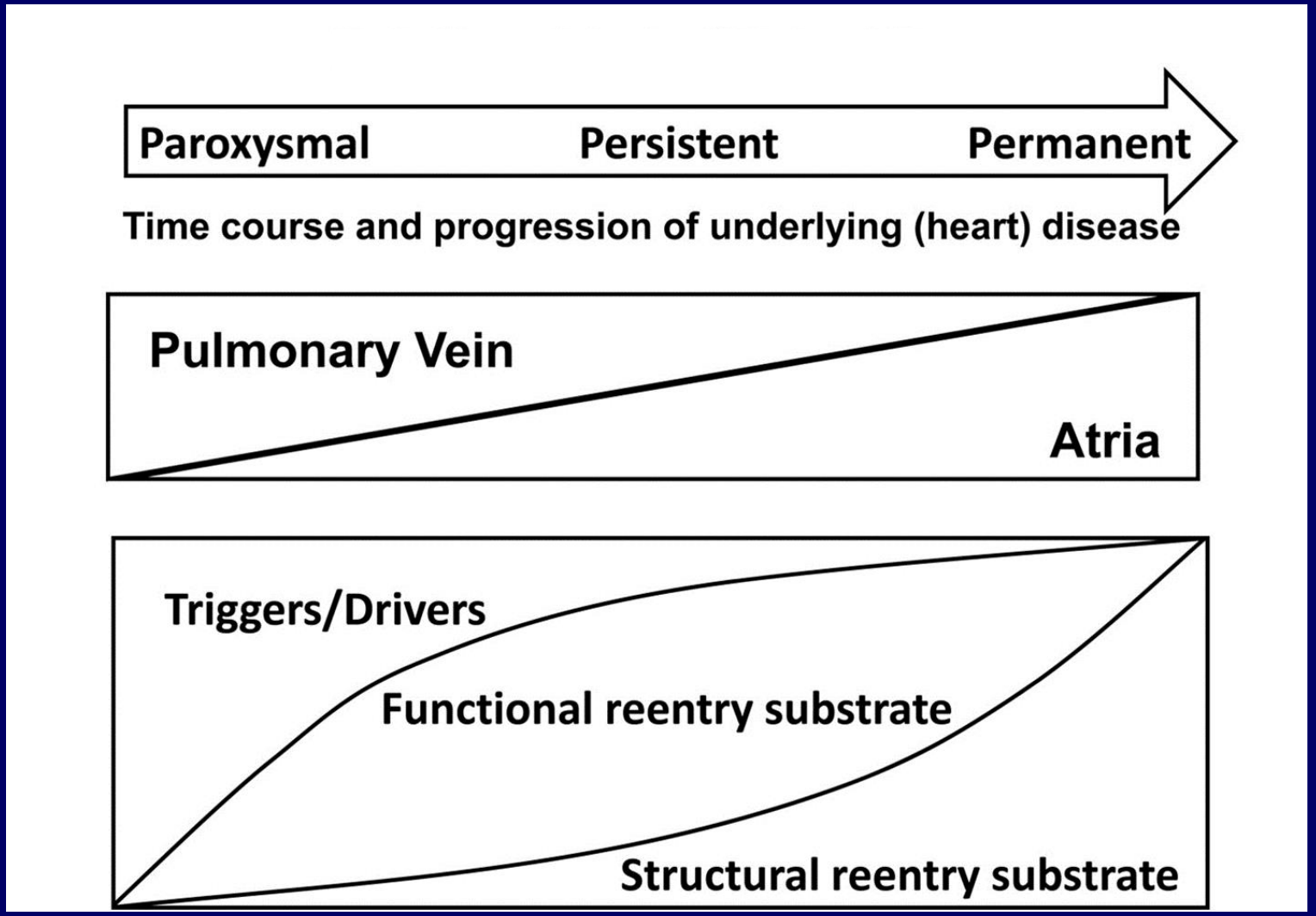


Wijffels, M. C.E.F. et al. Circulation 1995;92:1954-1968

Atrial Remodeling

- Remodeling is an adaptive regulatory process of cardiac myocytes that occurs over time in order to maintain homeostasis against external stresses
  - Electrophysiological (ionic)
  - Structural (extracellular)
  - Cellular
  - Neurohumoral
  - Genomic
- If left untreated, it may become irreversible (apoptosis, necrosis, and fibrosis)
- May be maladaptive and deleterious

Relationship of AF Mechanism to Clinical Forms



Iwasaki Y et al. Circulation 2011;124:2264-2274

Ablation of Persistent AF

- Pulmonary vein isolation

Plus??

- "Extensive substrate modification"
  - Ablation of CFEAs
  - Left-sided linear lesions (roof line, mitral isthmus line), posterior LA "box" lesions, appendage ablation
  - Cavo-tricuspid isthmus line, coronary sinus lesions, other right atrial lesions
  - Ablation of ganglionated plexi
- Rotor ablation

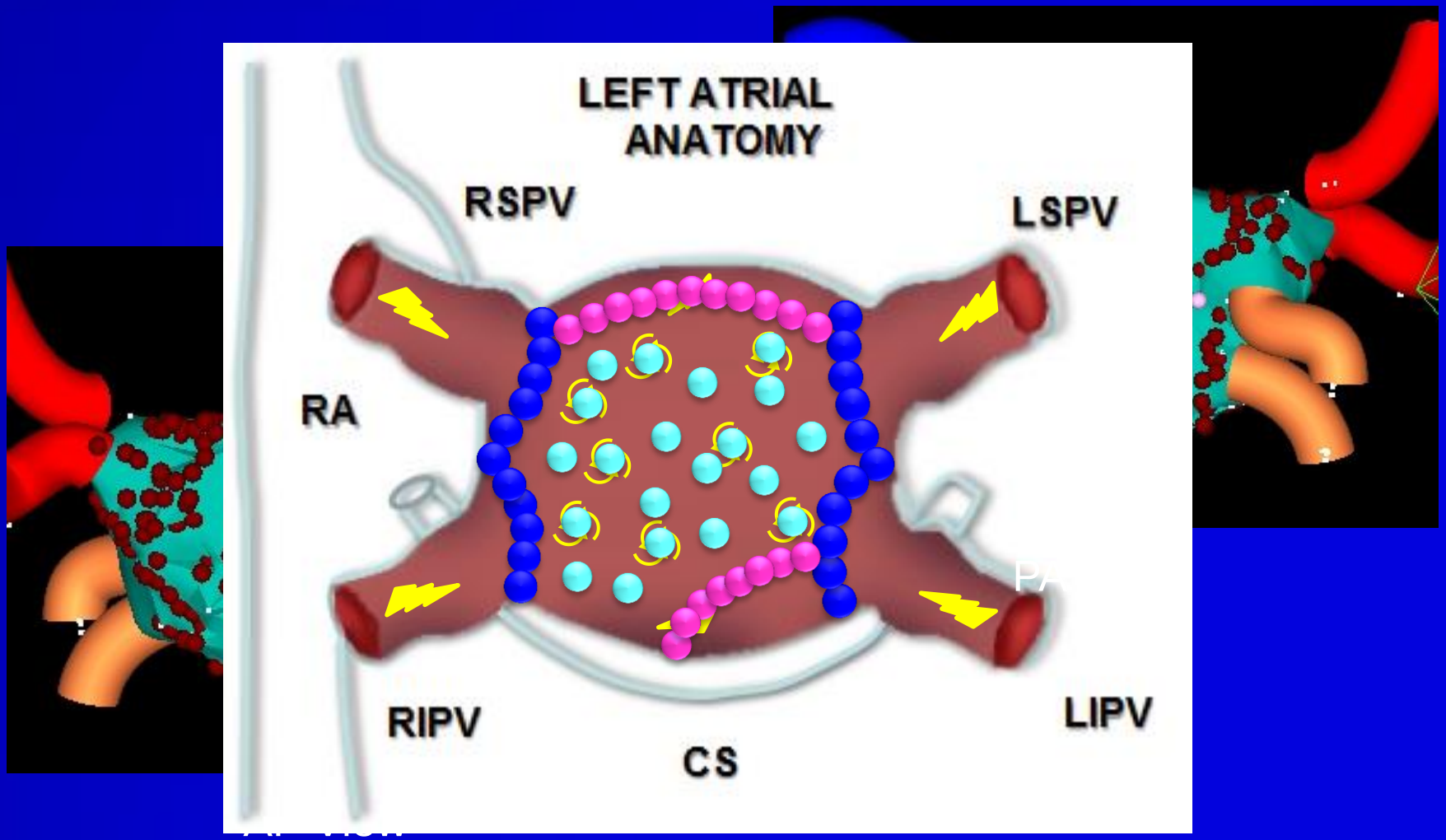
"Stepwise Approach"

Ablation Strategies for Persistent or Long-Standing Persistent AF

- PVI
- PVI + linear lesions
- PVI + complex fractionated atrial electrograms (CFAEs)
- PVI + linear lesions + CFAEs
- PVI + ablation of focal sources and rotors
- PVI + isolation of LAA
- PVI + ablation of autonomic ganglia
- PVI + isolation of area of fibrosis
- PVI + ……

Adapted from Karl-Heinz Kuck

Catheter Ablation for Persistent AF



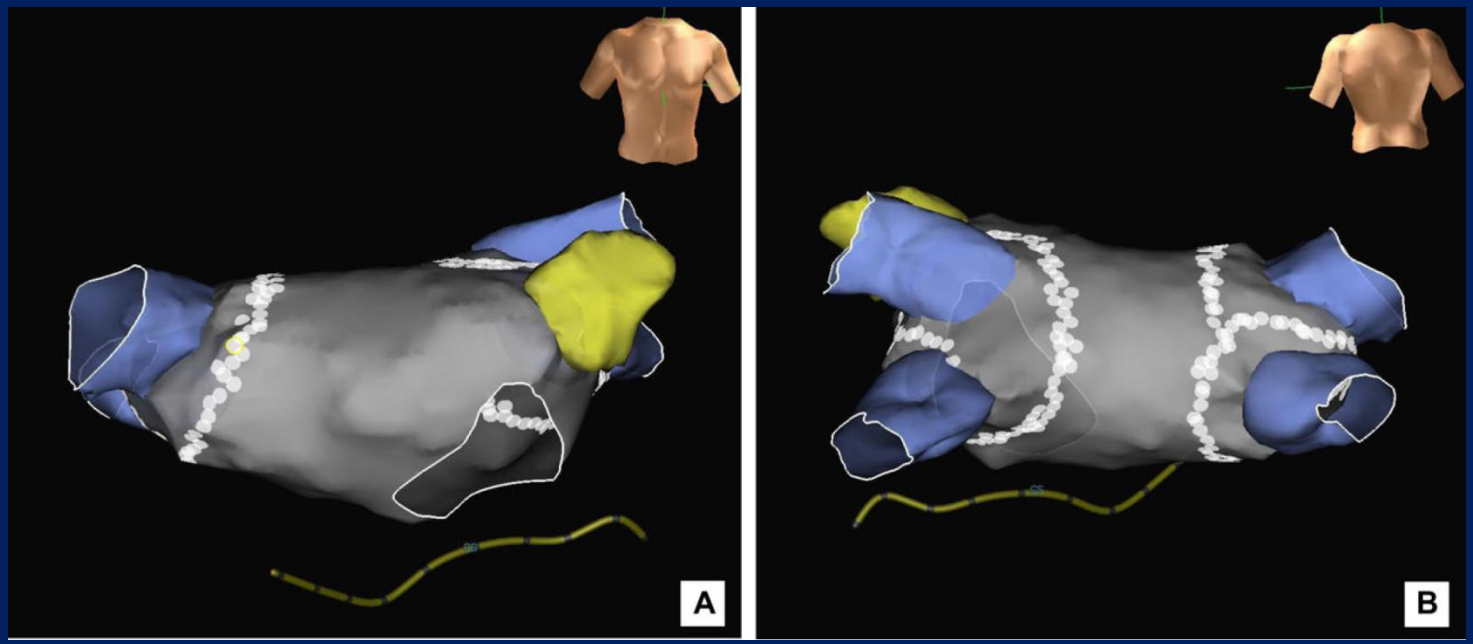
Oral H, et al. *A Randomized Assessment of the Incremental Role of Ablation of Complex Fractionated Atrial Electrograms After Antral Pulmonary Vein Isolation for Long-Lasting Persistent Atrial Fibrillation*. J Am Coll Cardiol 2009;53:782–9.

Stepwise Ablation Approach to Persistent AF

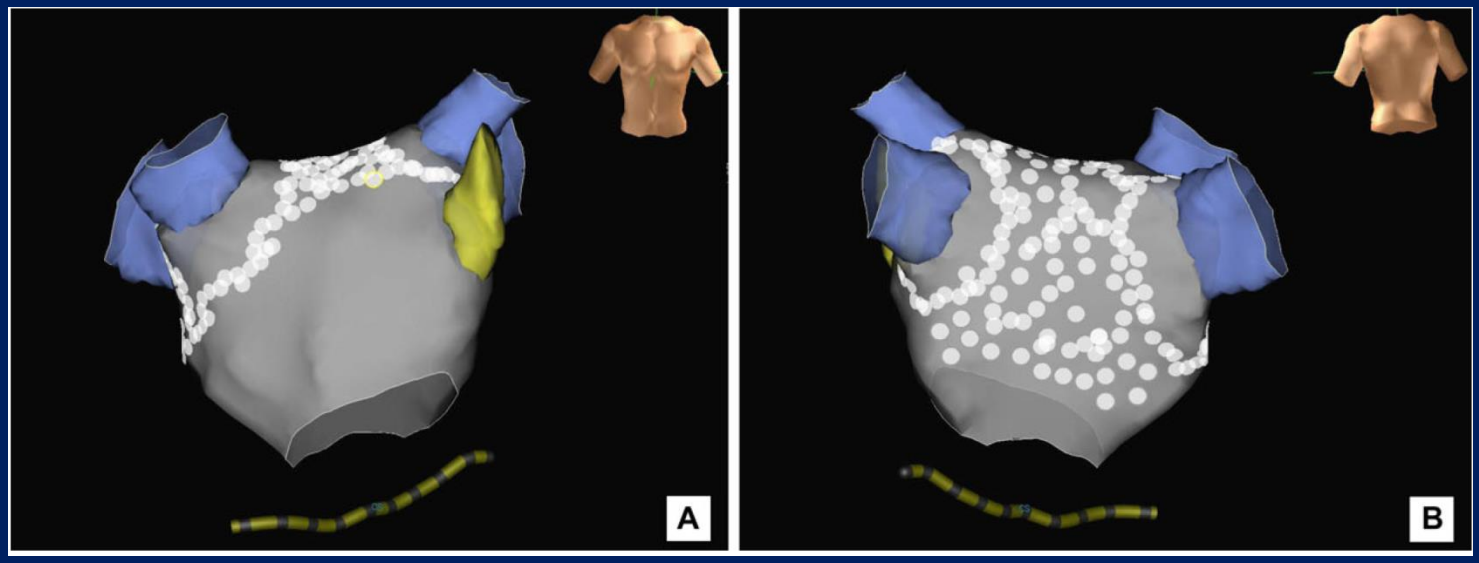
Haissaguerre et al

- Stepwise progression of lesions until AF terminates:
  - PVI
  - LA defragmentation
  - CS defragmentation/isolation
  - RA defragmentation
- Linear lesions only for macroreentry
- The longer the AF duration (especially >6 mo):
  - The more rotors are present
  - More linear lesions are needed

Standard Circumferential pulmonary vein isolation



Extensive pulmonary vein antrum isolation including the entire left atrial posterior wall down to the coronary sinus, and to the left side of the interatrial septum



J Cardiovasc Electrophysiol, Vol. 25, pp. 824-833, August 2014

Box Isolation of Fibrotic Areas

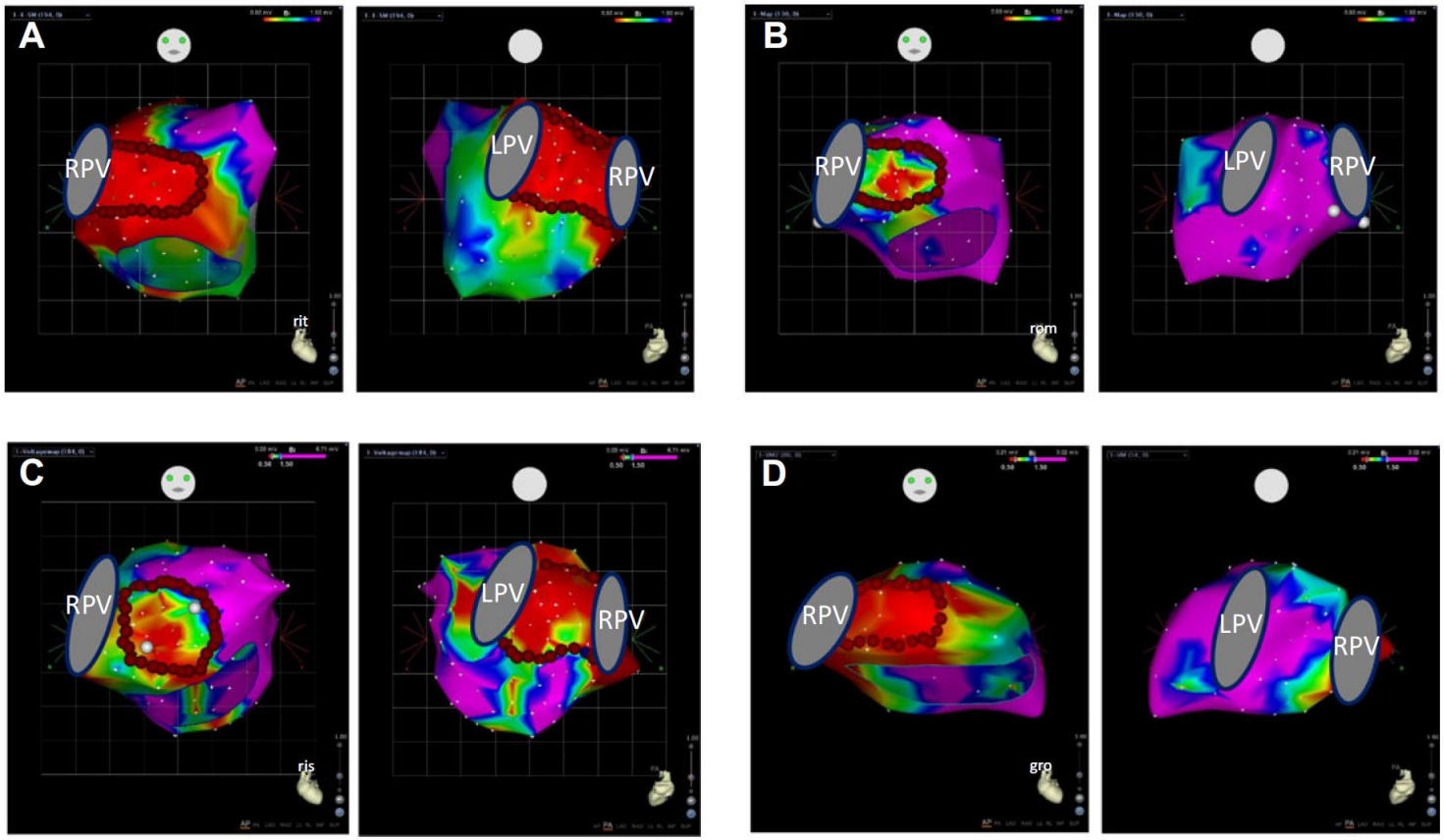
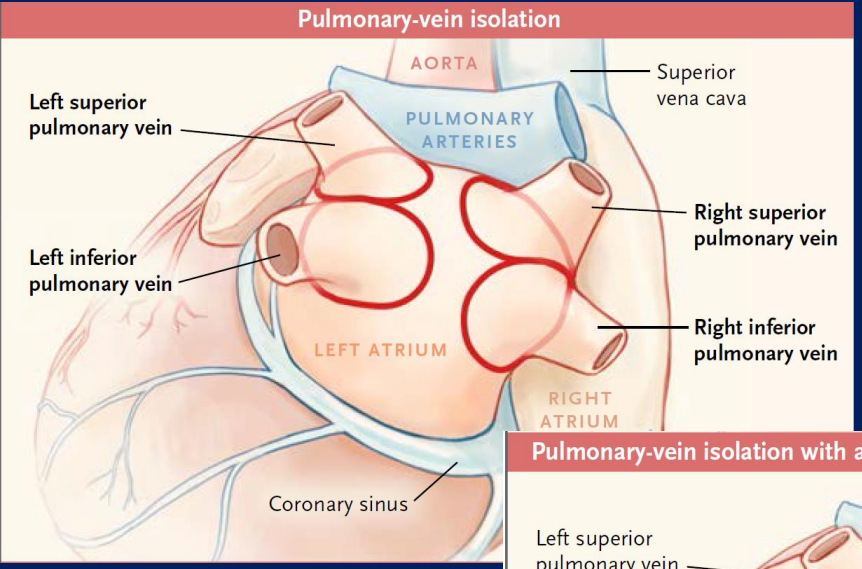
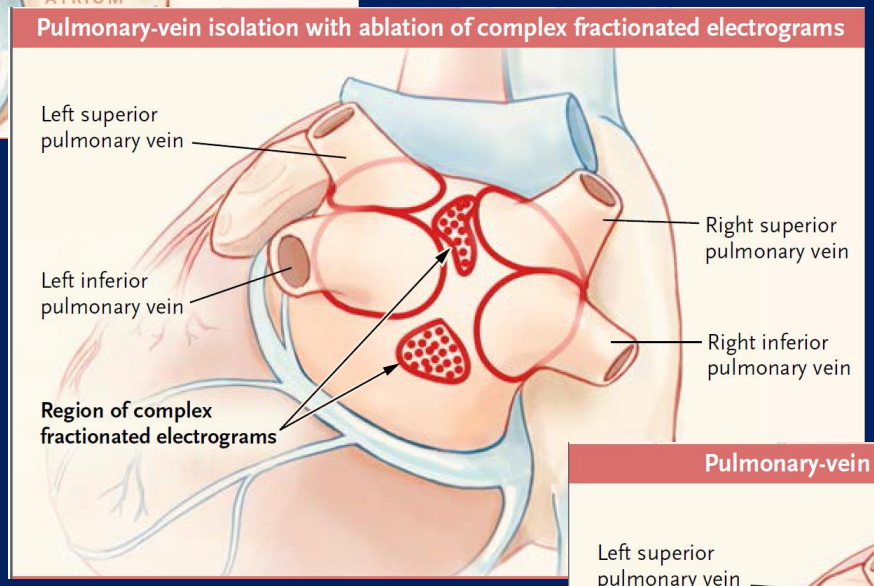


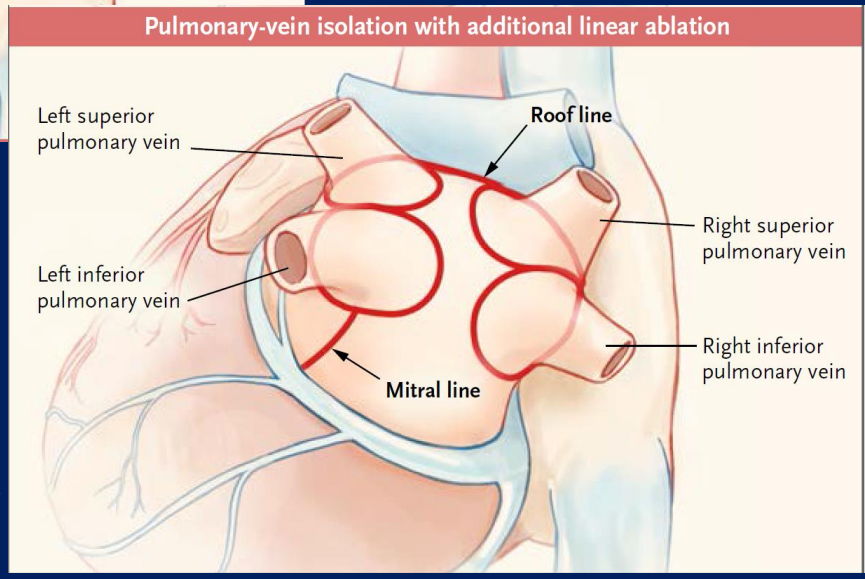
Figure 1. *Left atrial voltage mapping in four patients with recurrences of paroxysmal atrial fibrillation despite durable pulmonary vein isolation (PVI) showing the variable severity and localization of left atrial fibrosis. Box isolation of the fibrotic areas (BIFA) is done in all cases with connection to the previous PVI lines. Color coding: red for substantially reduced voltages <0.5 mV and purple >1.5 mV. LPV and RPV = left and right pulmonary veins.*

Kottkamp et al. J Cardiovasc Electrophysiol 2016;27:22

Approaches to Catheter Ablation for Persistent Atrial Fibrillation (STAR AF II)

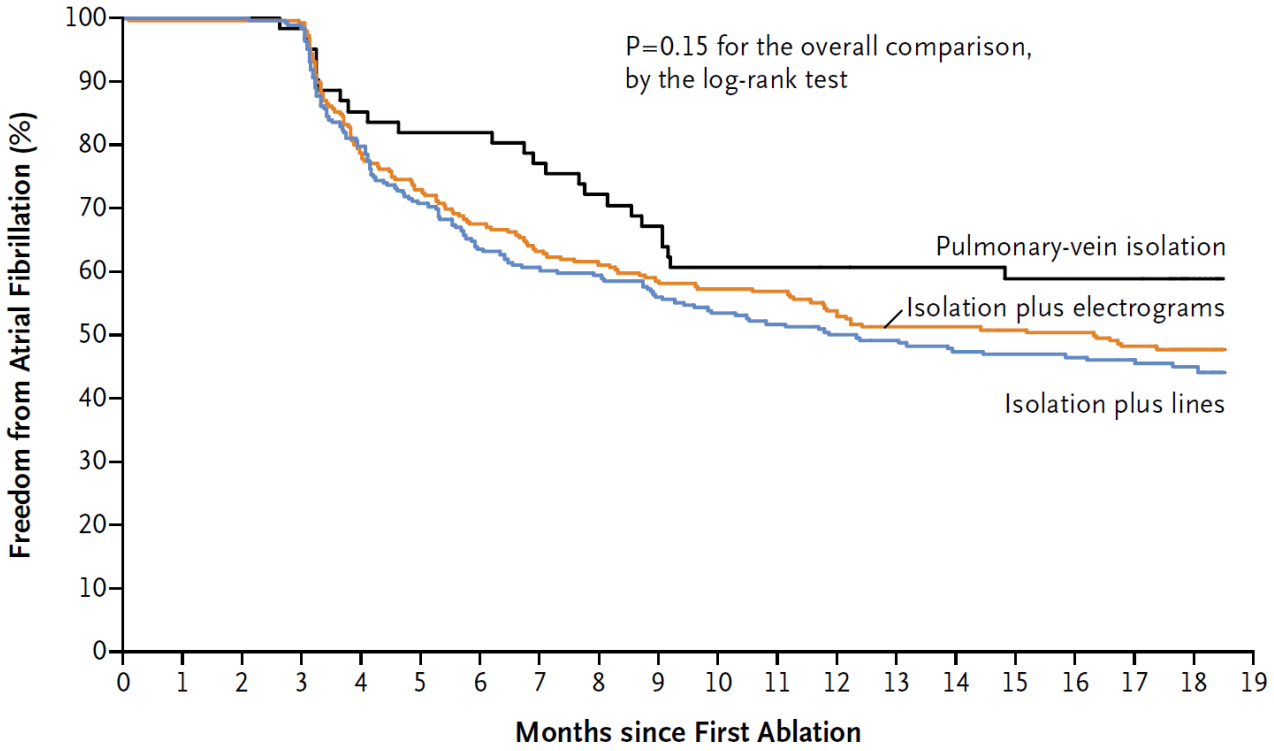






Verma and STAR AF II Investigators. N Engl J Med 2015;372:1812-22

Approaches to Catheter Ablation for Persistent Atrial Fibrillation



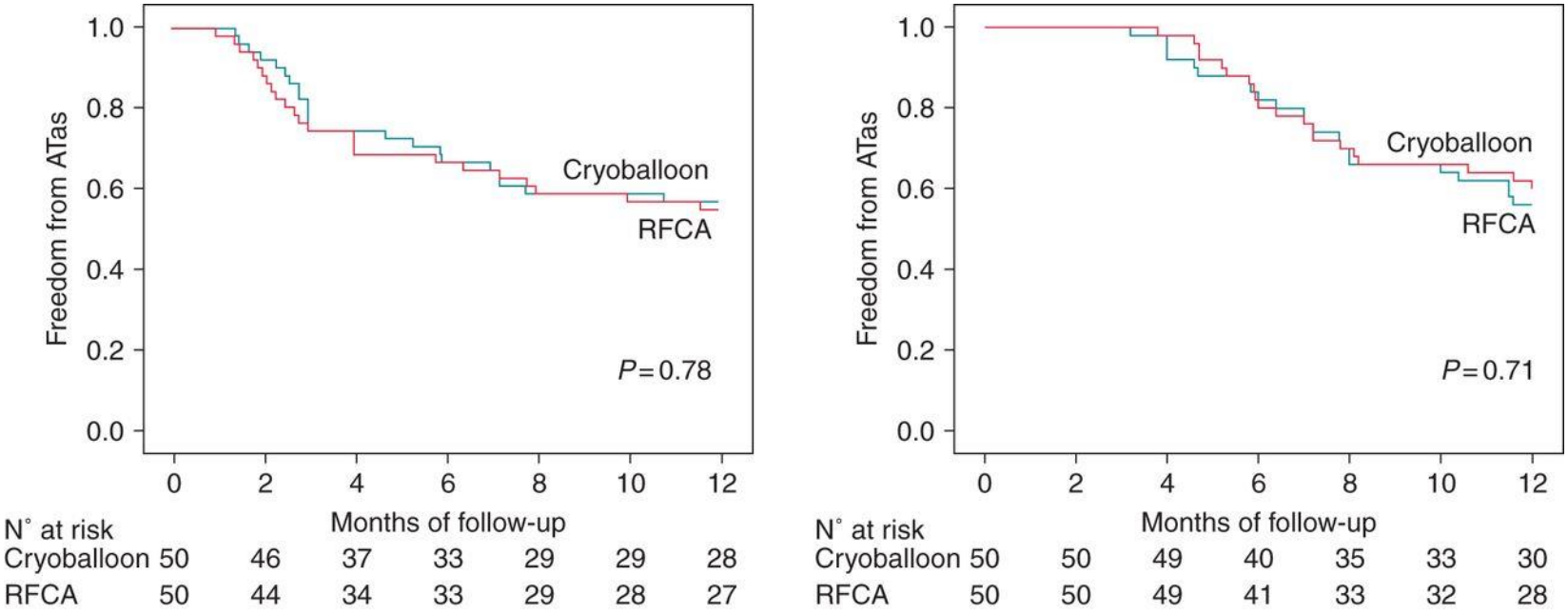
No. at Risk

Pulmonary-vein isolation	61	60	50	41	36	23
Isolation plus electrograms	244	242	161	137	124	72
Isolation plus lines	244	240	152	133	115	57

Verma and STAR AF II Investigators. N Engl J Med 2015;372:1812-22

Circumferential pulmonary vein isolation as index procedure for persistent atrial fibrillation

Freedom from ATa recurrences after 1 year follow-up according to ablation strategy (RFCA turquoise line; CB-AdvA red line) off drugs, considering (right panel) or not (left panel) a 3 months blanking period.



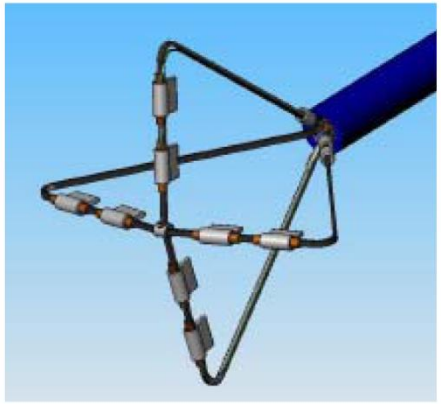
Giuseppe Ciconte et al. Europace 2015;17:559-565

How Can We Improve the Management of Persistent AF?

- Better ablation strategies for persistent AF
  - More aggressive catheter ablation
    - New catheter systems under development
  - Hybrid catheter/surgical (endocardial/epicardial) ablation
  - More targeted catheter ablation
    - FIRM ablation
  - Promotion of reverse remodeling before and after ablation
- Prevention of persistent AF
  - Earlier ablation for paroxysmal AF

Ablation of Persistent AF Using Multielectrode Catheters and Duty-Cycled Radiofrequency Energy

Figure 1. MAAC Catheter illustration and in-use



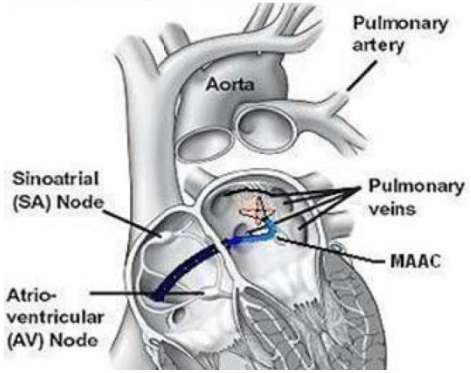
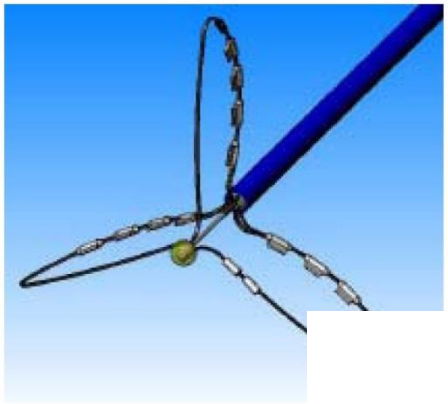


Figure 2. MASC Catheter illustration and in-use



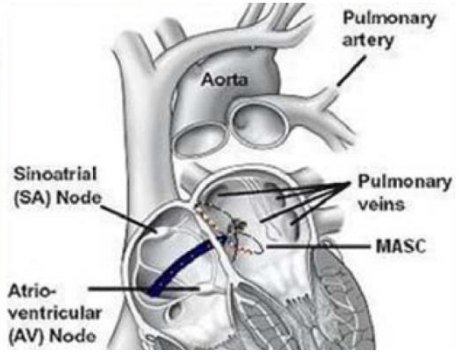
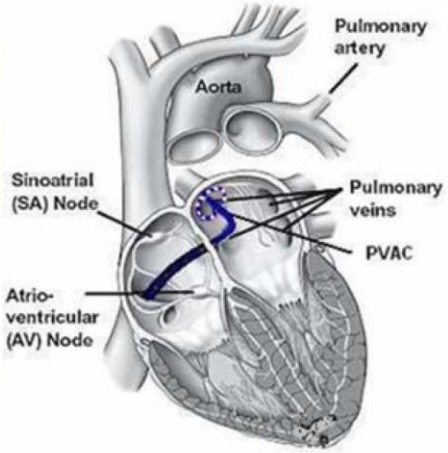
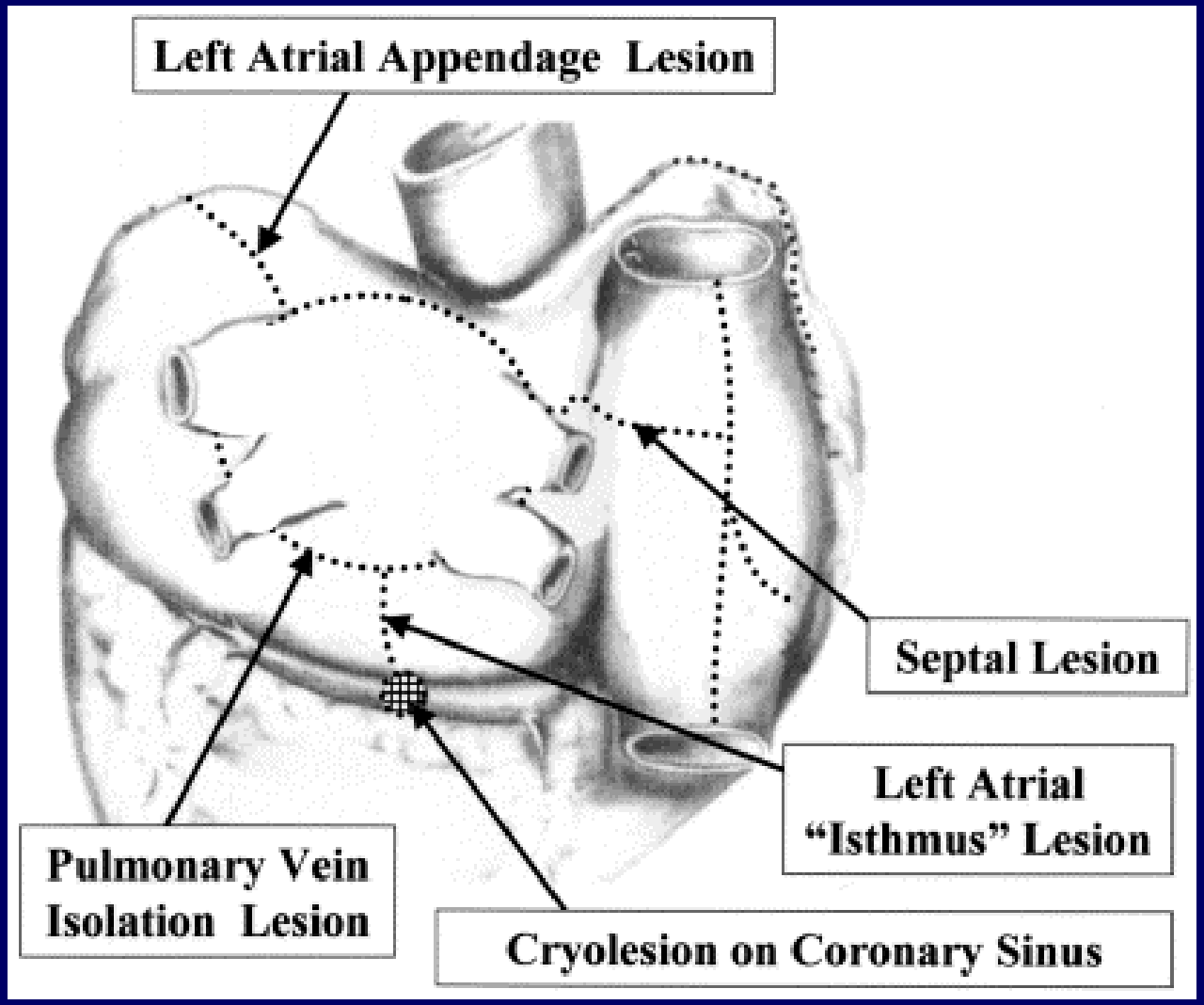


Figure 3. PVAC Catheter illustration and in-use



FDA Website

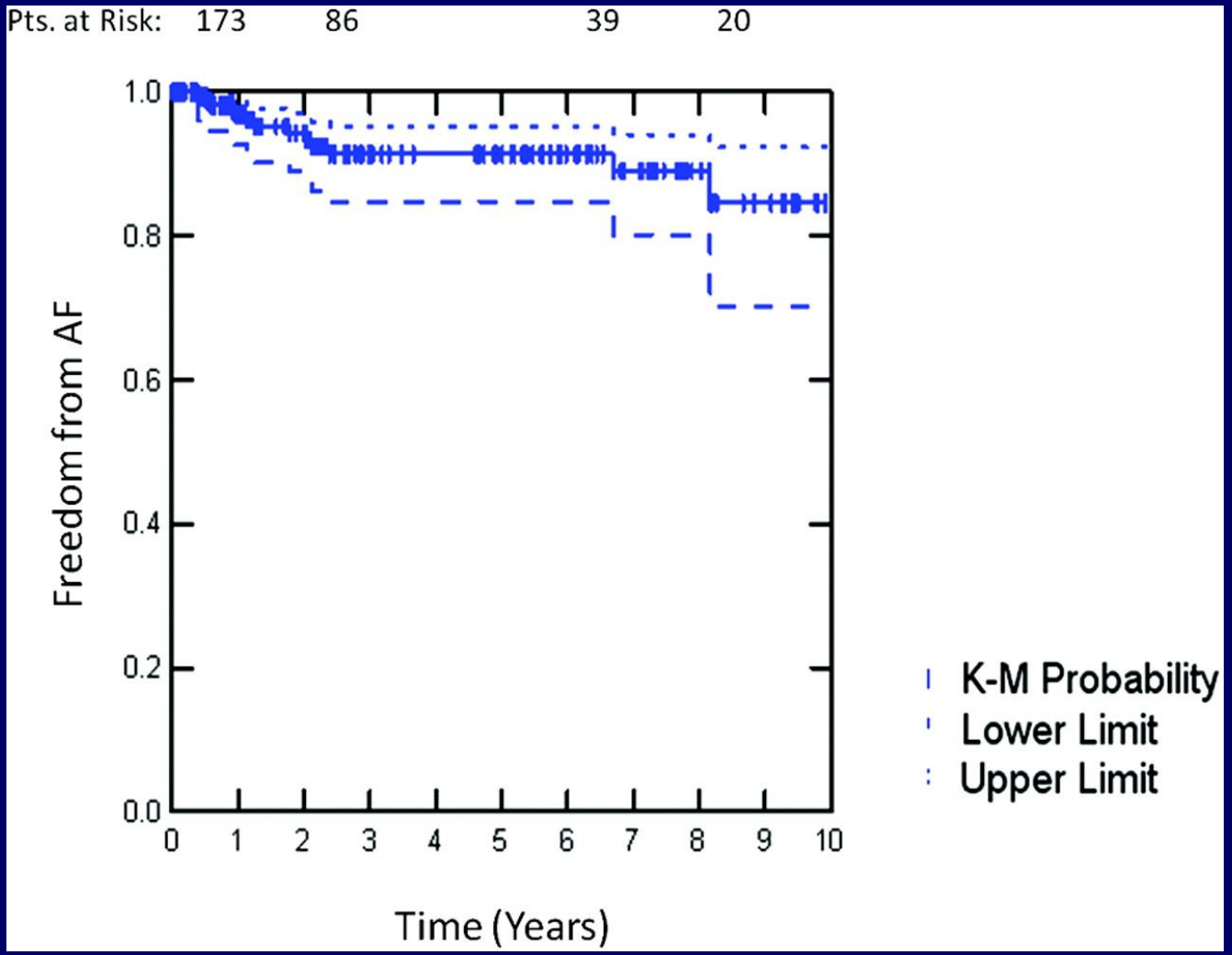
Lesions of the Standard Maze III Surgical Procedure for AF



Cox JL. J Thorac Cardiovasc Surg 2003;126:1693

The Cox-Maze Procedure for Lone AF: A Single-Center Experience Over 2 Decades

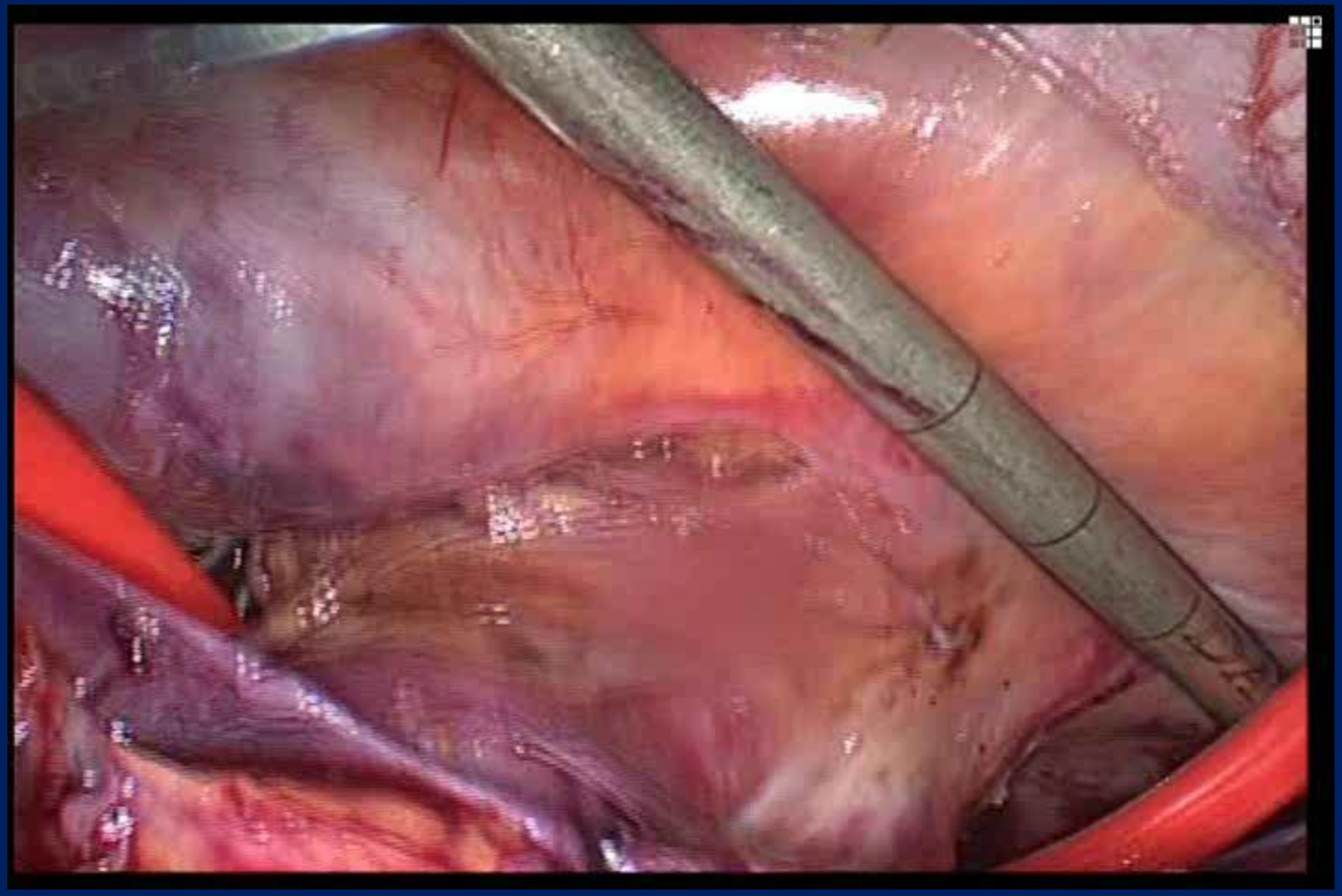
Kaplan-Meier analysis of freedom from atrial fibrillation for the Cox-Maze procedure (III+IV)

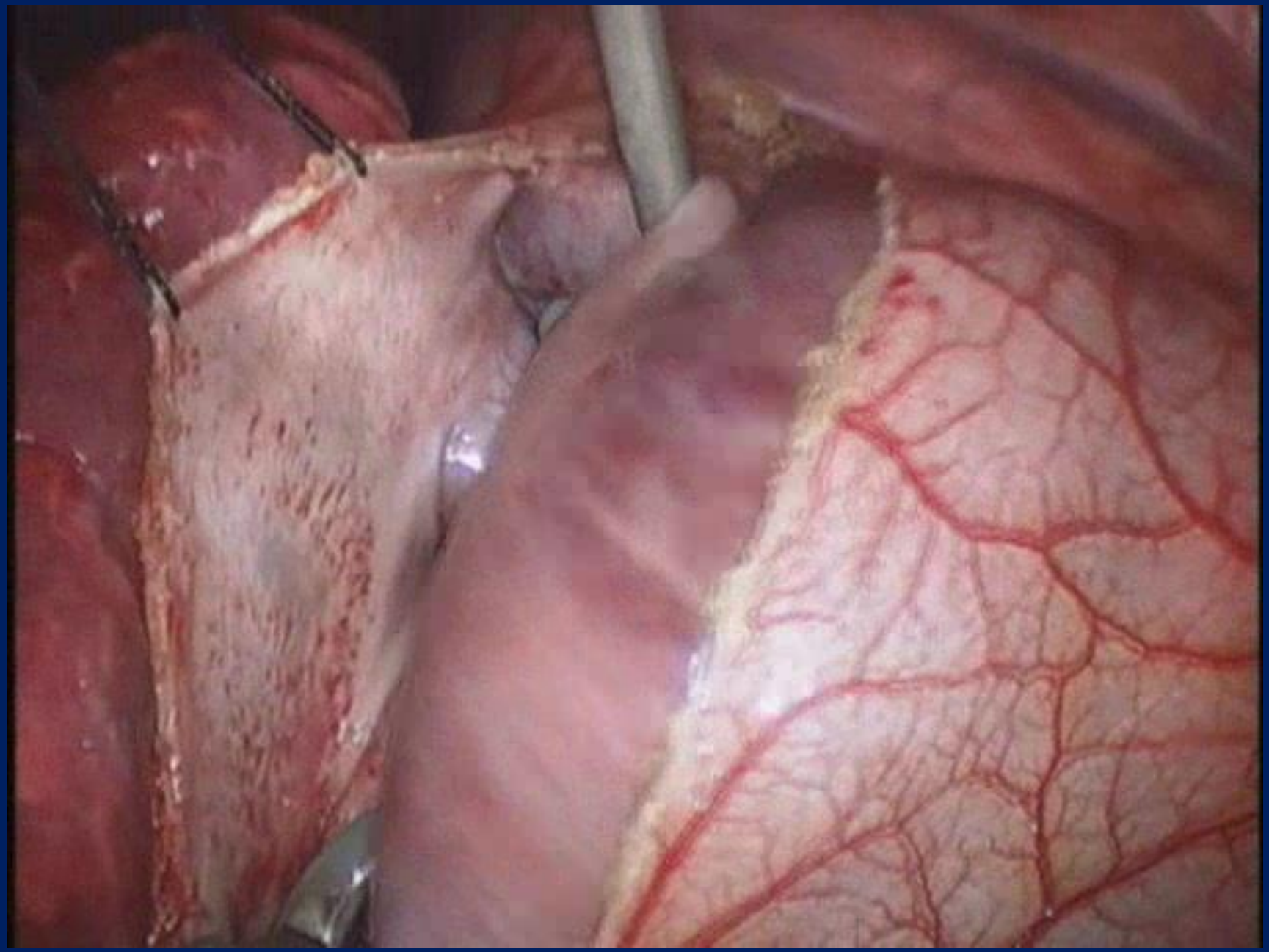


Weimar T et al. Circ Arrhythm Electrophysiol 2012;5:8-14

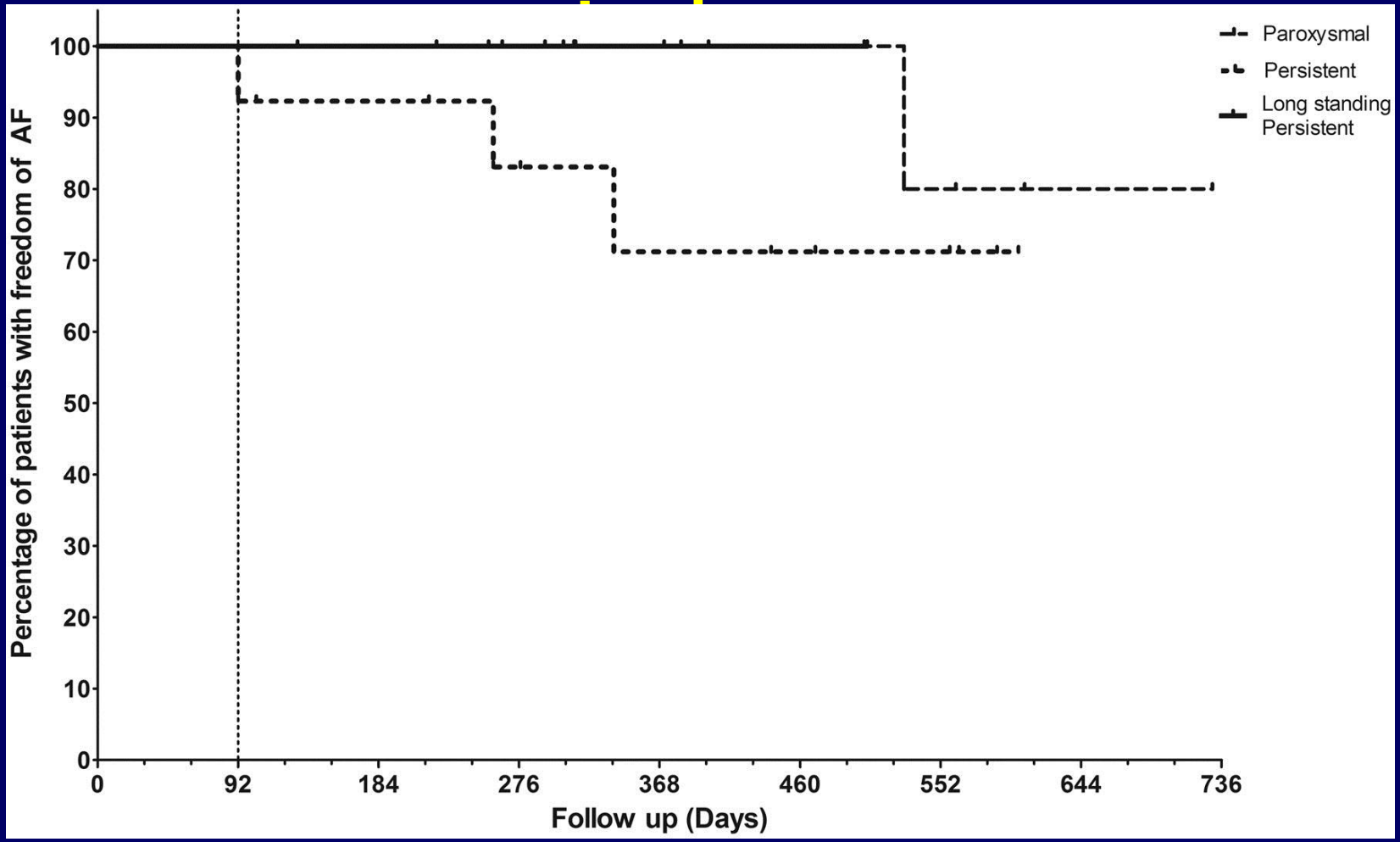
Thoracoscopic Pulmonary Vein Isolation

Pulmonary Vein Isolation



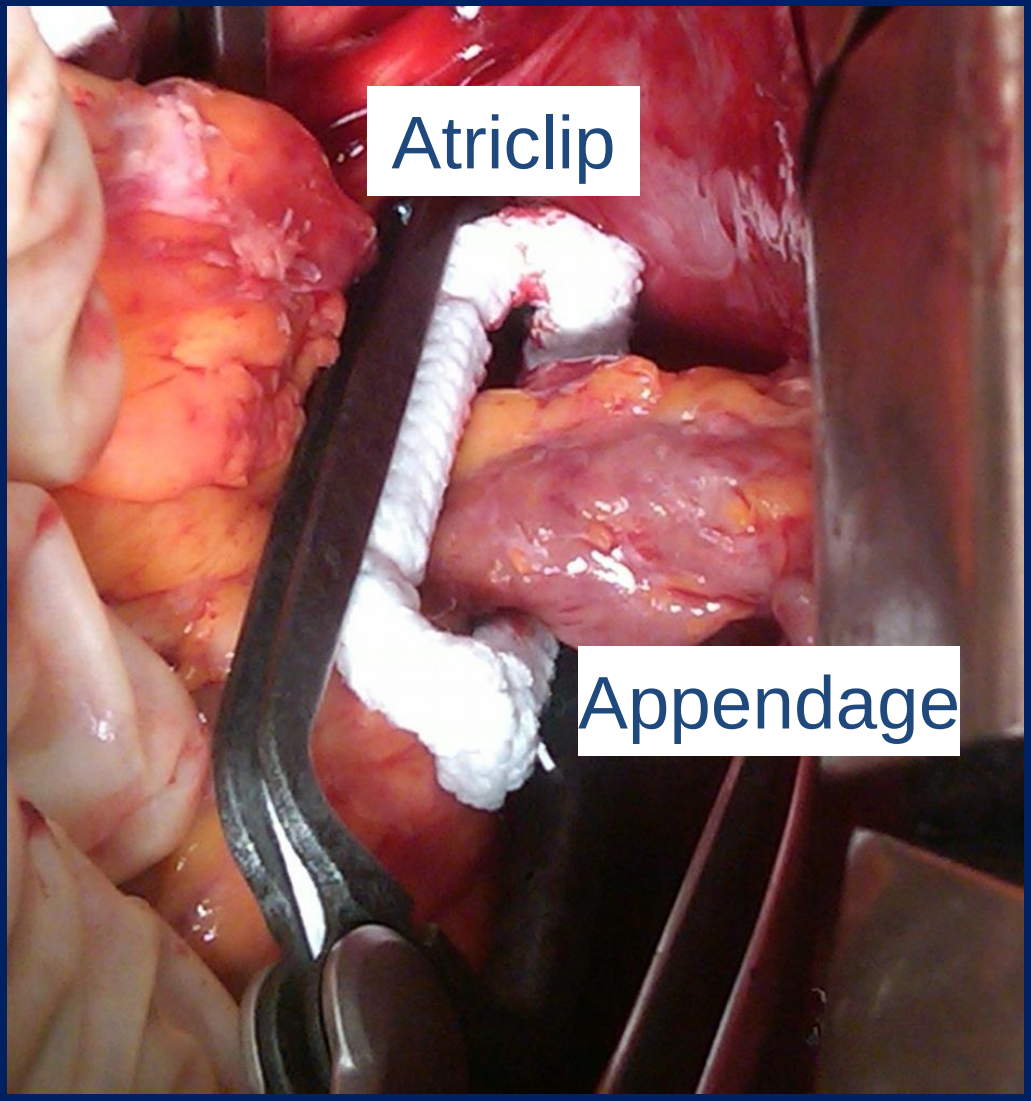


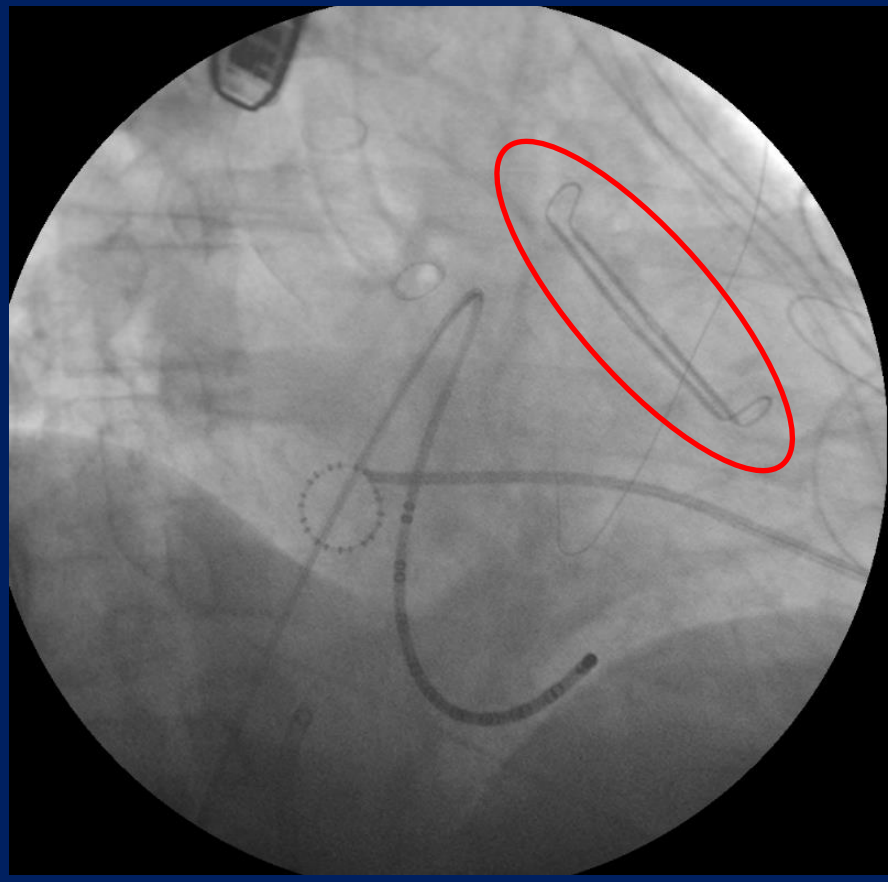
Thoracoscopic Video-Assisted Pulmonary Vein Antrum Isolation, Ganglionated Plexus Ablation, and Periprocedural Confirmation of Ablation



Krul S P et al. Circ Arrhythm Electrophysiol 2011;4:262-270

Atrial Appendage Exclusion

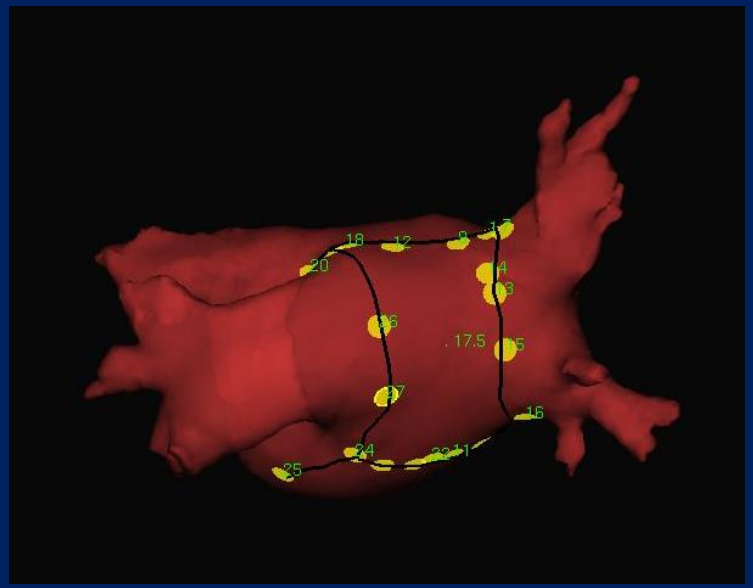




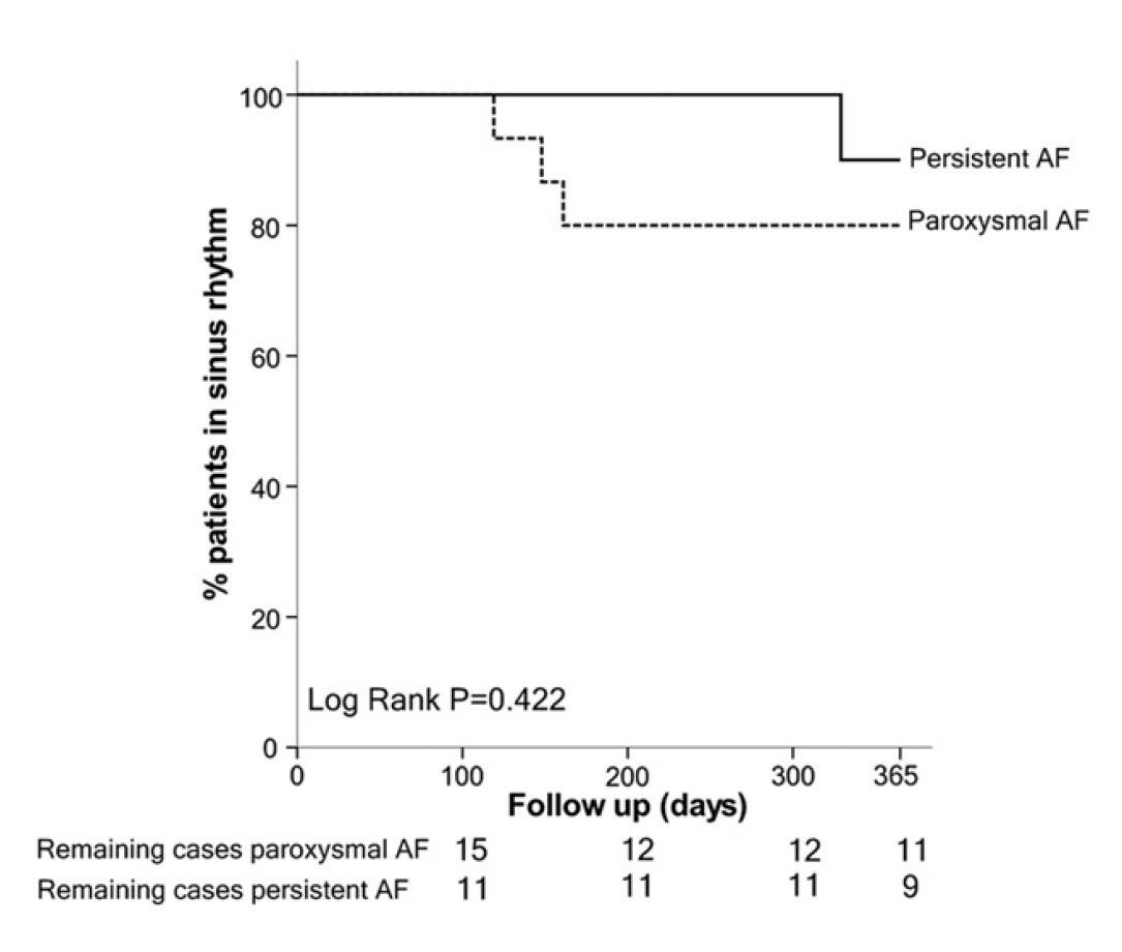
Minimally-Invasive Surgery and Catheter Ablation for Persistent AF

"Hybrid" Procedure

May be particularly useful for ablation of persistent atrial fibrillation, where the results of each technique alone are sub-optimal

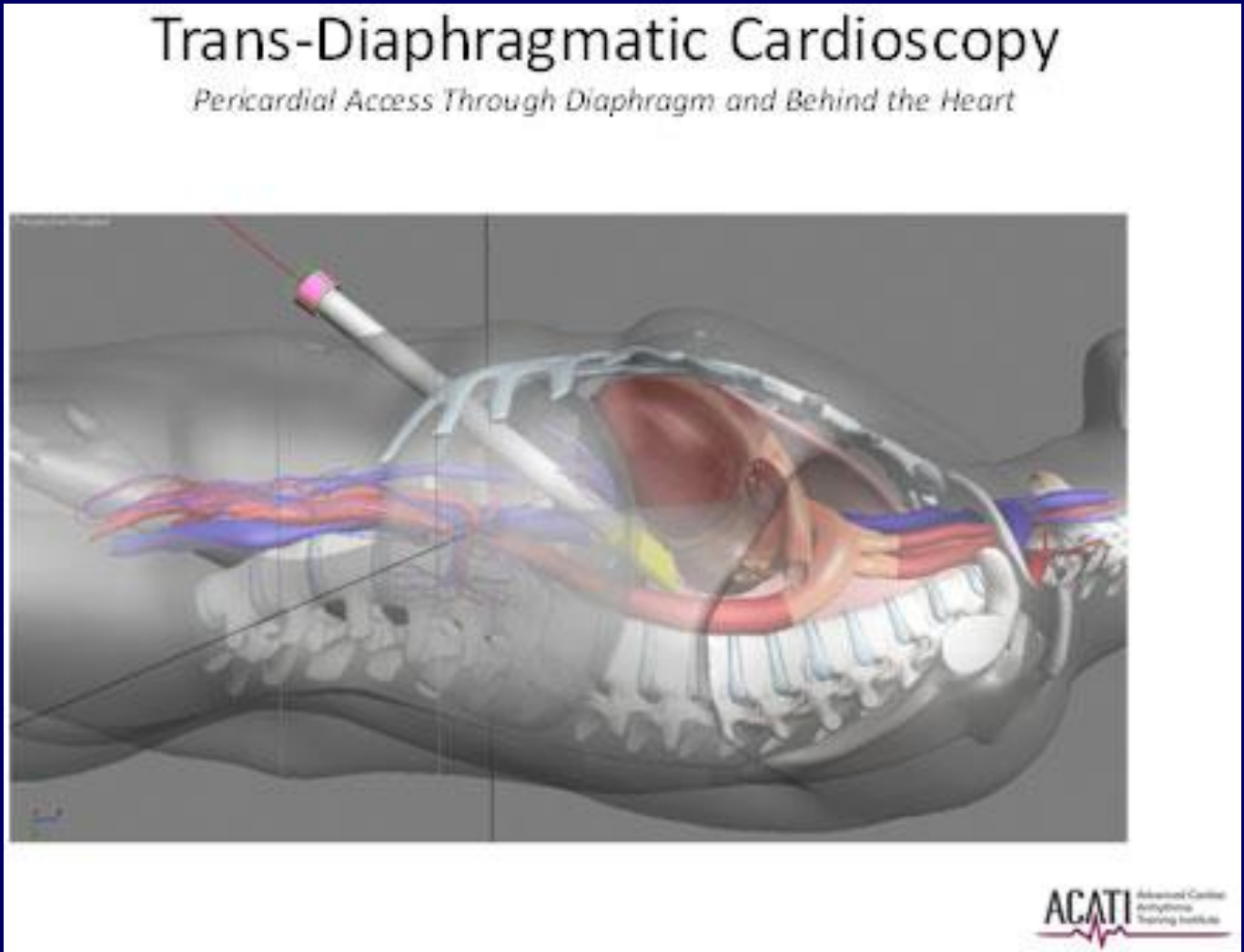


Hybrid Thoracoscopic Surgical and Transvenous Catheter Ablation of AF

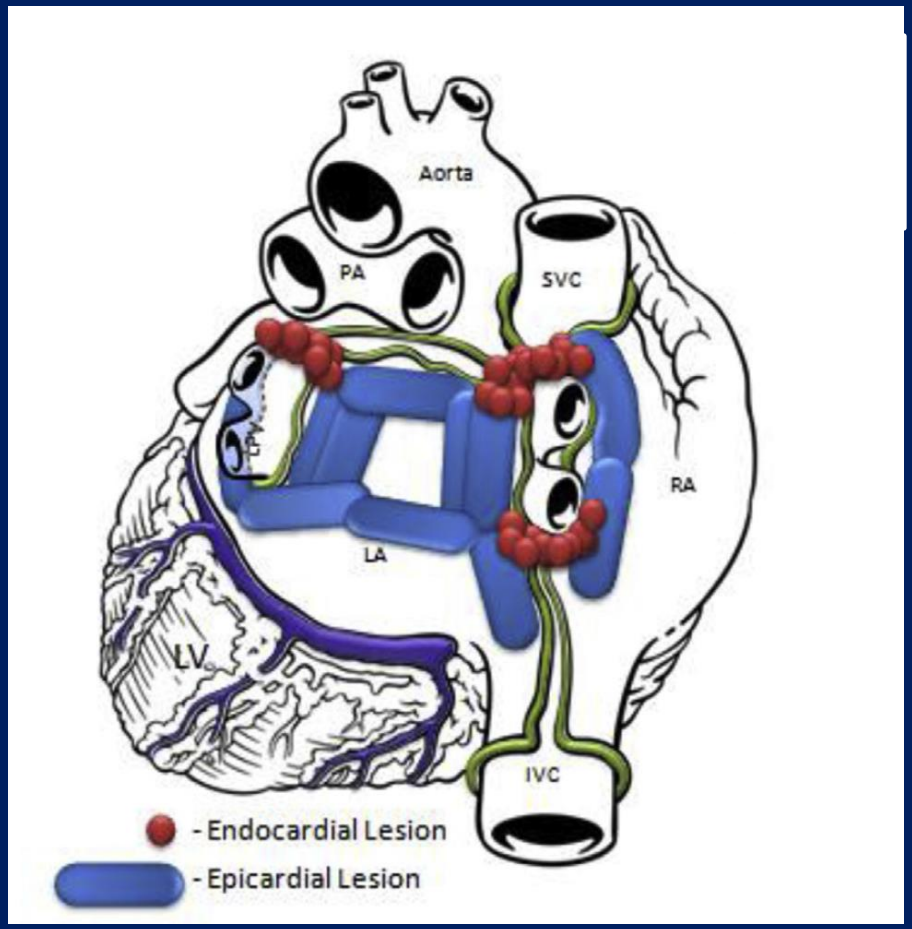


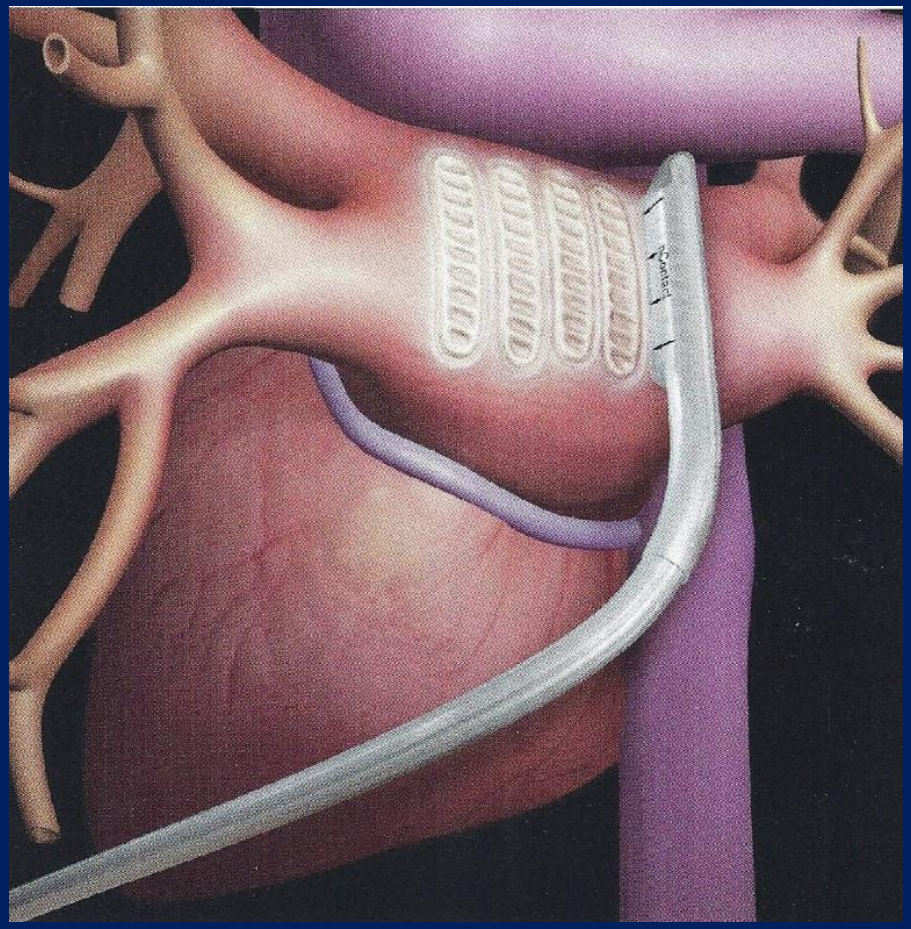
Pison et al. JACC 2012;60:54

“Convergence” Procedure



“Convergence” Procedure

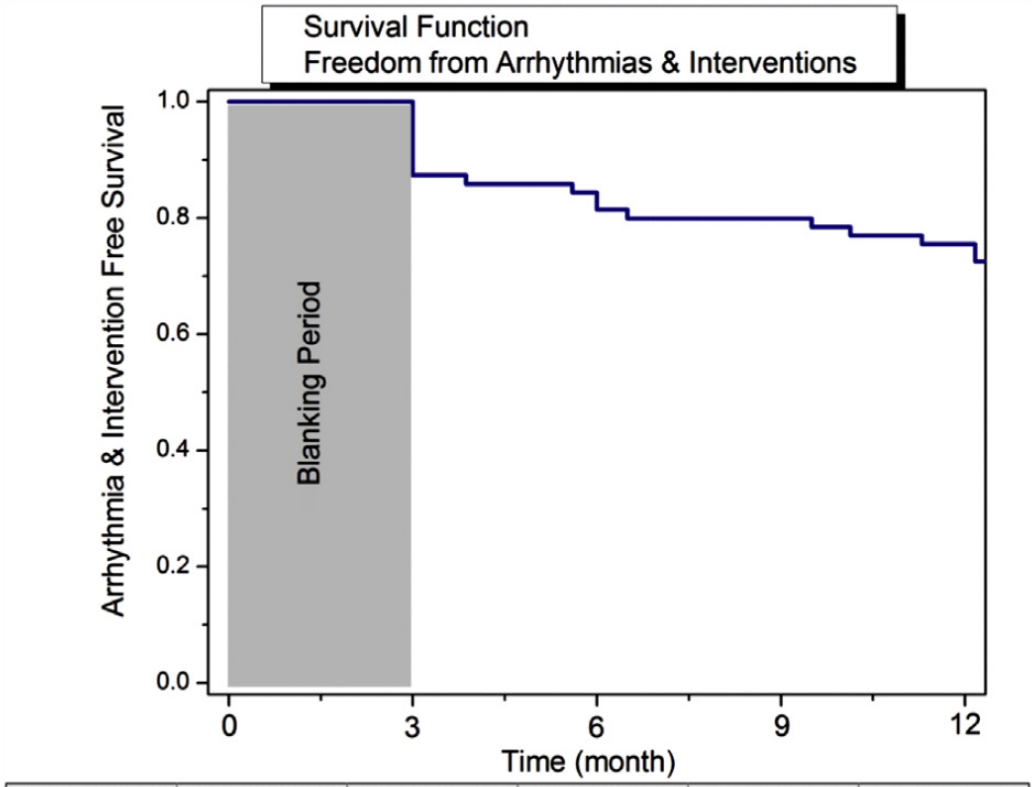




Gersak et al. J Thorac Cardiovasc Surg 2014;147:1411

European Experience of the Convergent Atrial Fibrillation Procedure:

Multicenter outcomes in consecutive patients



Time (days)	0	3	6	9	12
# at Risk	73	71	57	54	51

FIGURE 2. Arrhythmia and intervention-free survival analysis.

Gersak et al. J Thorac Cardiovasc Surg 2014;147:1411

European Experience of the Convergent Atrial Fibrillation Procedure:

Multicenter outcomes in consecutive patients

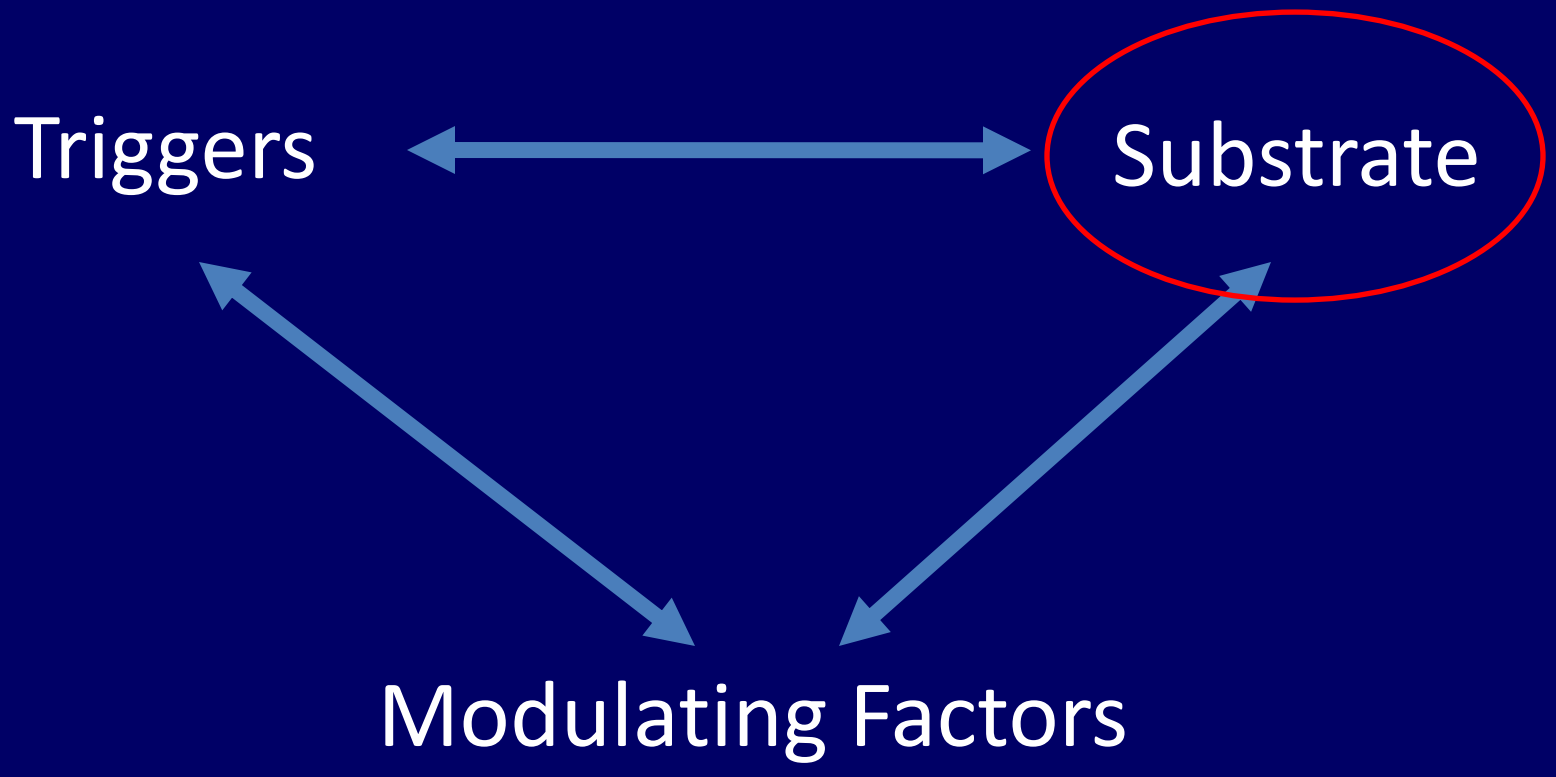
TABLE 2. Serious adverse event rates

Serious adverse event	No. (%) of 73
Operative mortality	0 (0)
<30-d Mortality	0 (0)
>30-d Mortality	0 (0)
Stroke/CVA	1 (1.4)
TIA	0 (0)
Tamponade	1 (1.4)
Pericardial effusion	1 (1.4)
Pleural effusion	1 (1.4)
Phrenic nerve palsy	0 (0)
Esophageal fistula	0 (0)
Myocardial infarction	0 (0)
Newly developed third-degree AV block	0 (0)
Acute limb ischemia	0 (0)
Bleeding requiring transfusion	2 (2.7)
Bleeding with conversion to sternotomy	2 (2.7)

Serious adverse events were observed in 8 patients (8 of 73; 11%). *CVA*, Cerebrovascular accident; *TIA*, transient ischemic attack; *AV*, atrioventricular.

Gersak et al. J Thorac Cardiovasc Surg 2014;147:1411

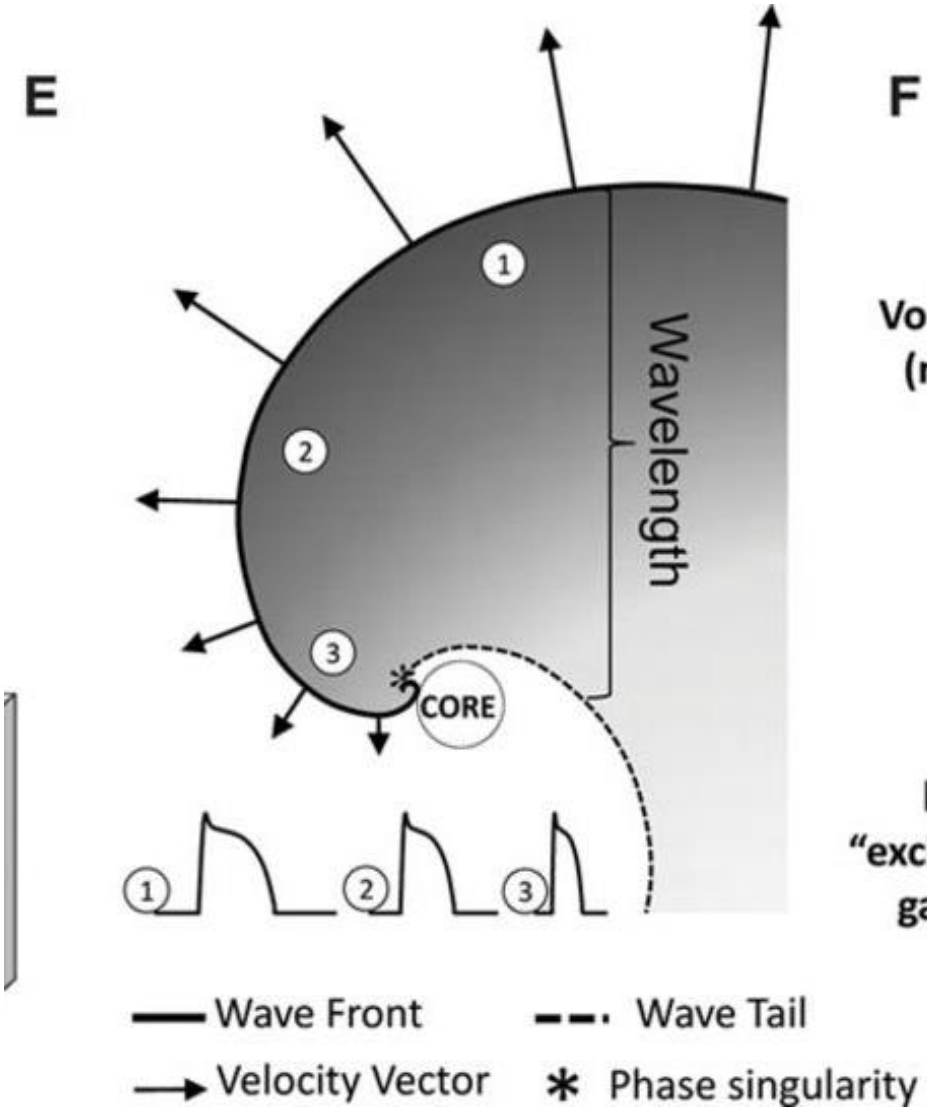
Mechanisms of Arrhythmogenesis

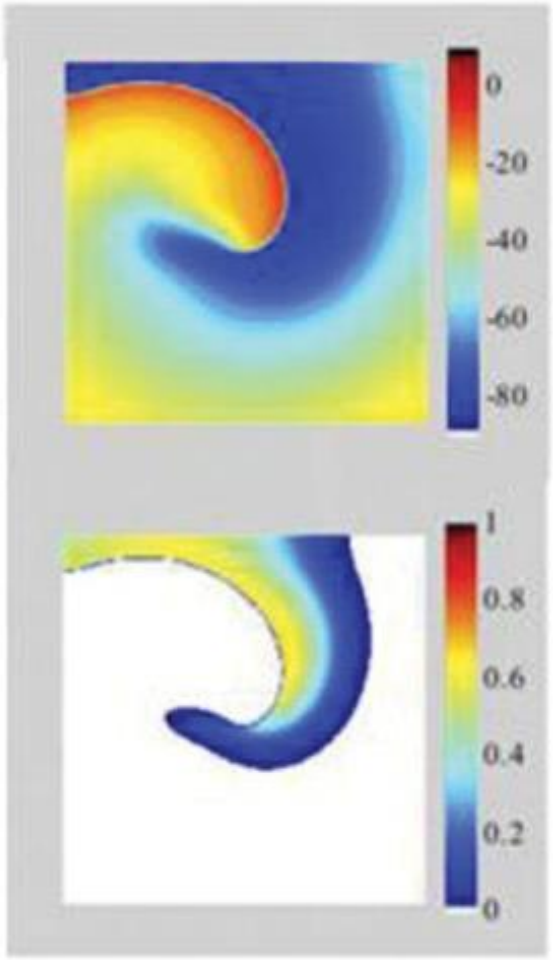


Mechanisms of AF

- Triggers initiate AF
- Drivers and rotors perpetuate AF
  - Triggers that fire incessantly are drivers

Rotors and Spirals





Sandeep V. Pandit, and José Jalife Circulation Research. 2013;112:849-862

AF Ablation Paradigm Shift

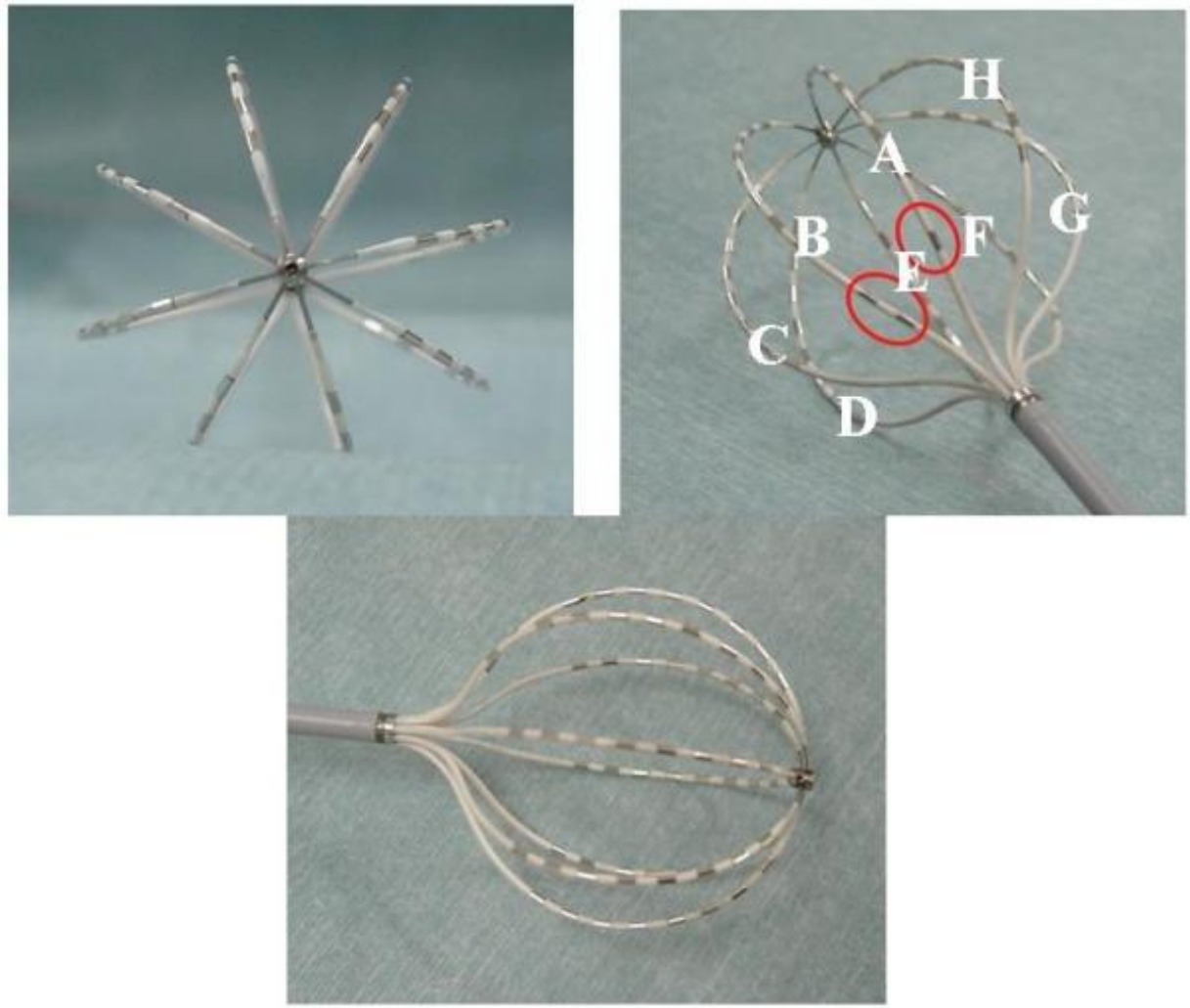
Triggers →→→→ *Substrate*

- Focal impulse and rotor modulation (FIRM) hypothesis *(Narayan et al)*:
  - AF is a substrate disease driven by a small number of drivers/rotors
    - Spatially stable over many cycles

Mapping of Focal Impulses and Rotors in Human AF

- Invasive
  - Topera: endocardial FIRM
- Noninvasive
  - Cardioinsight: epicardial FIRM
  - EP Solutions: endo- and epicardial FIRM

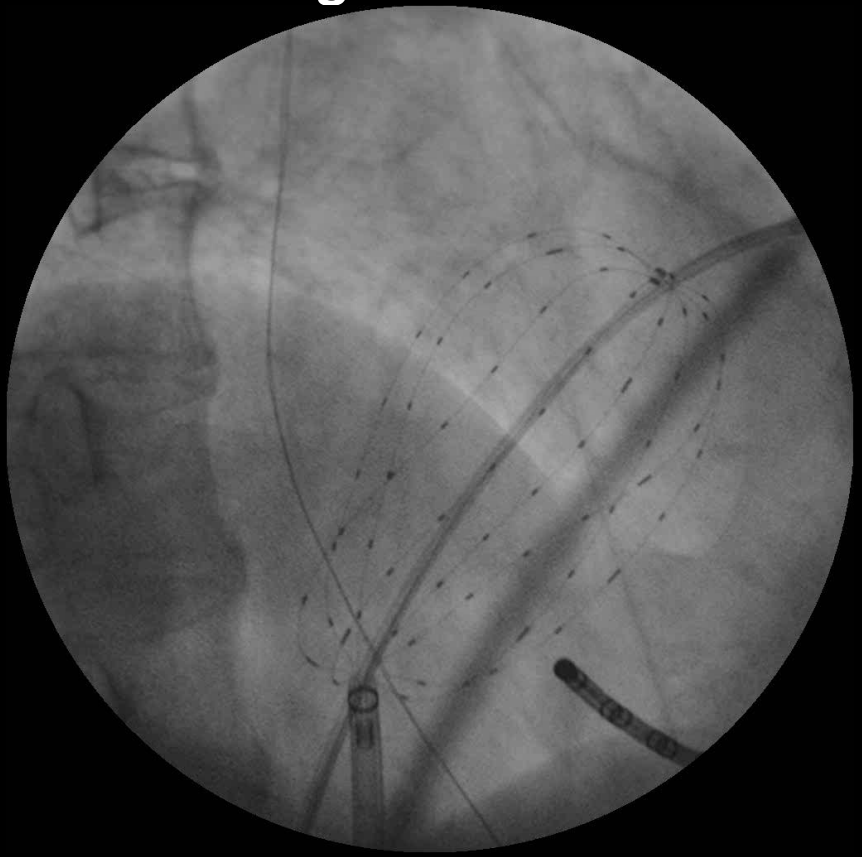
Basket Mapping Catheter



Yamada T. Indian Pacing Electrophysiol J 2007;7:97-109

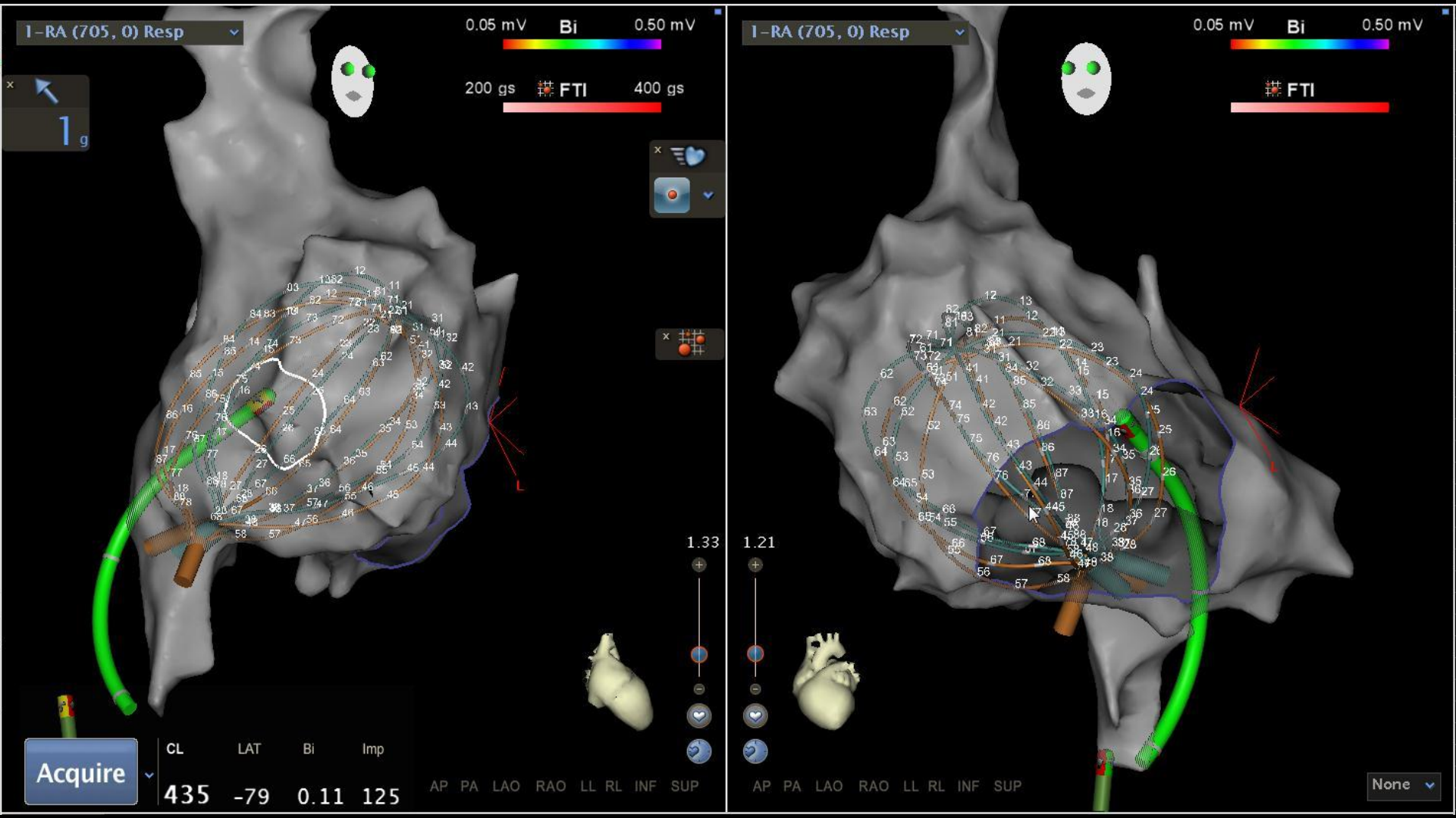
Atrial Basket Catheter Mapping

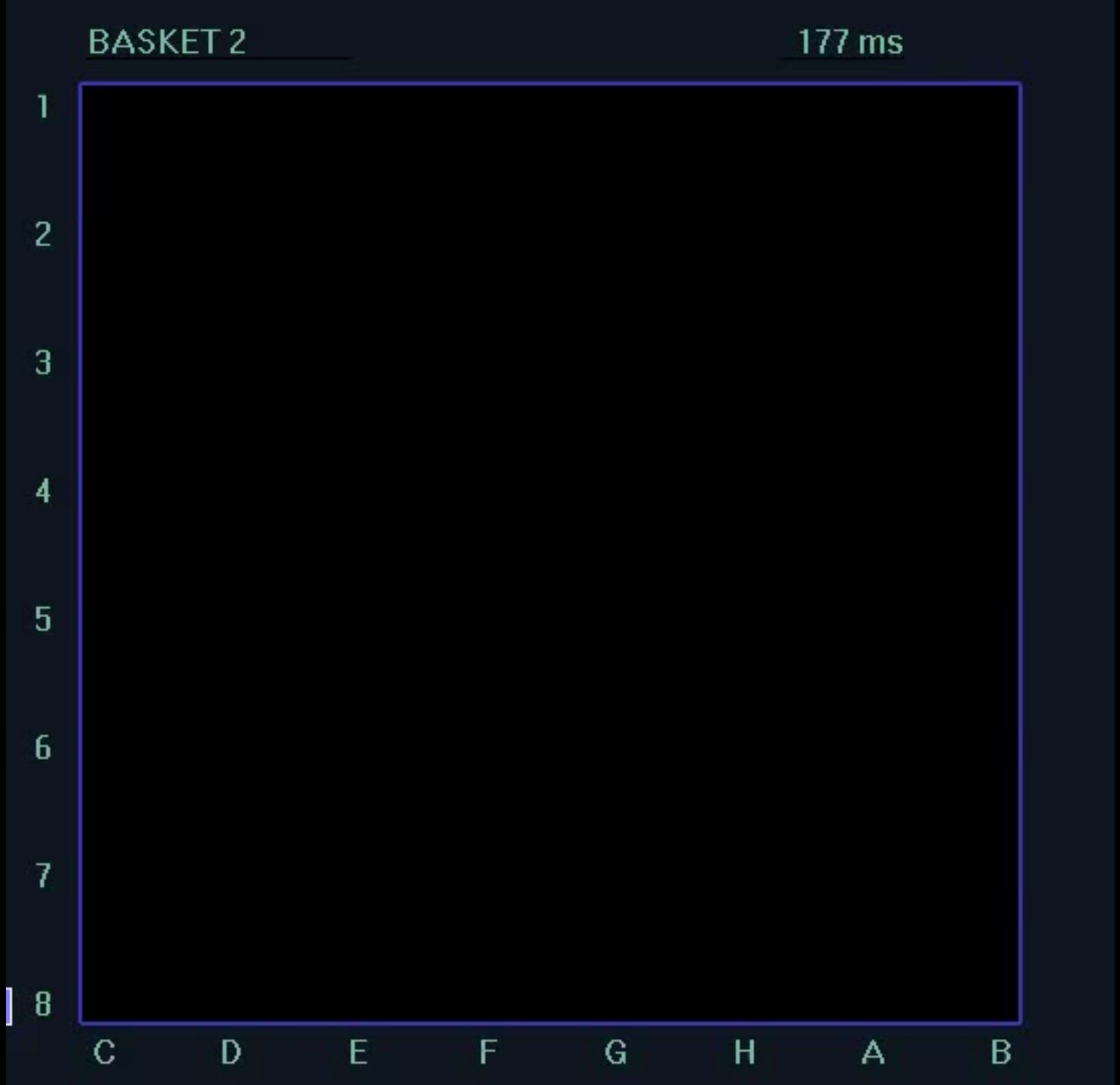
Right Atrium

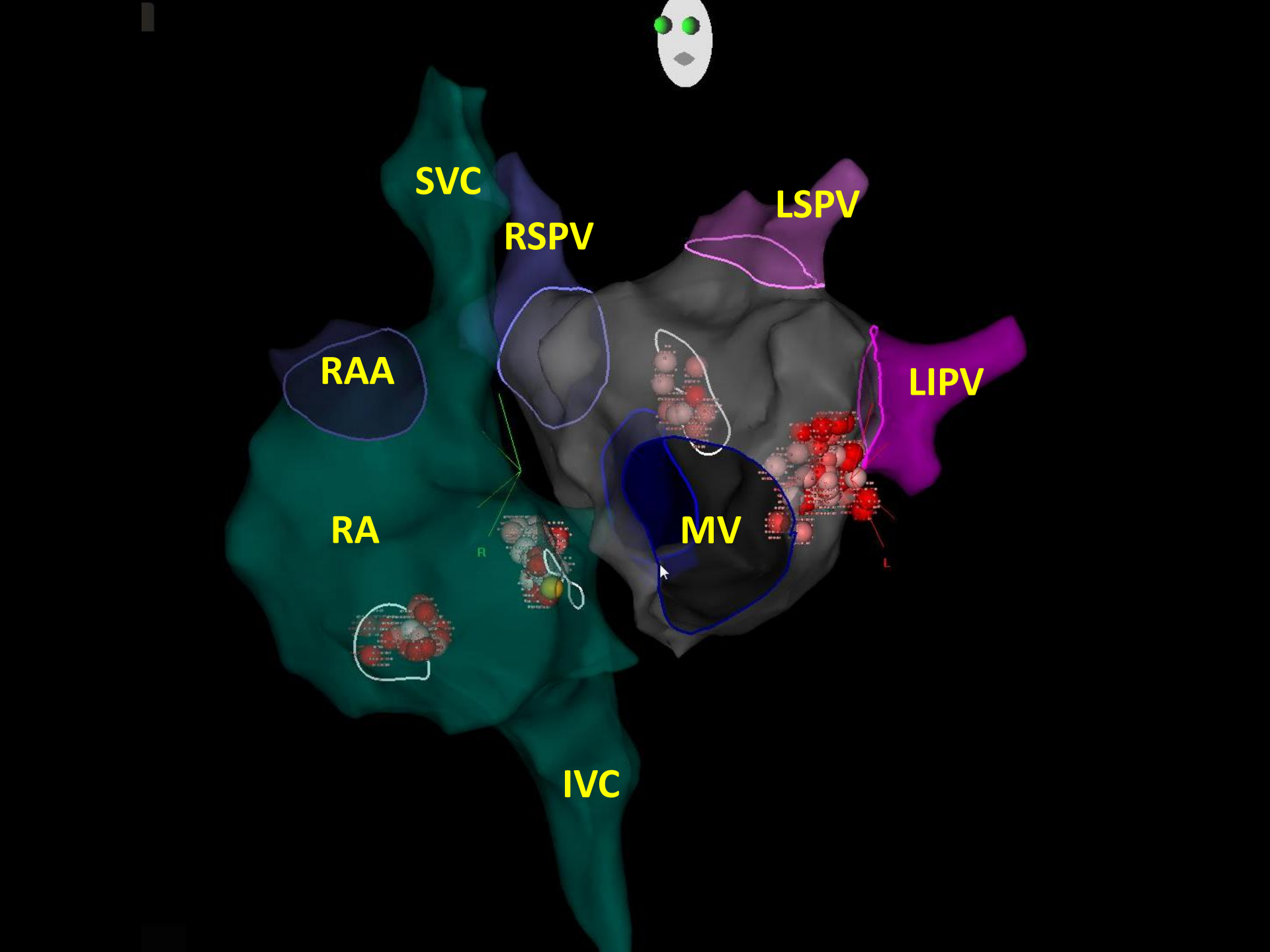


Left Atrium

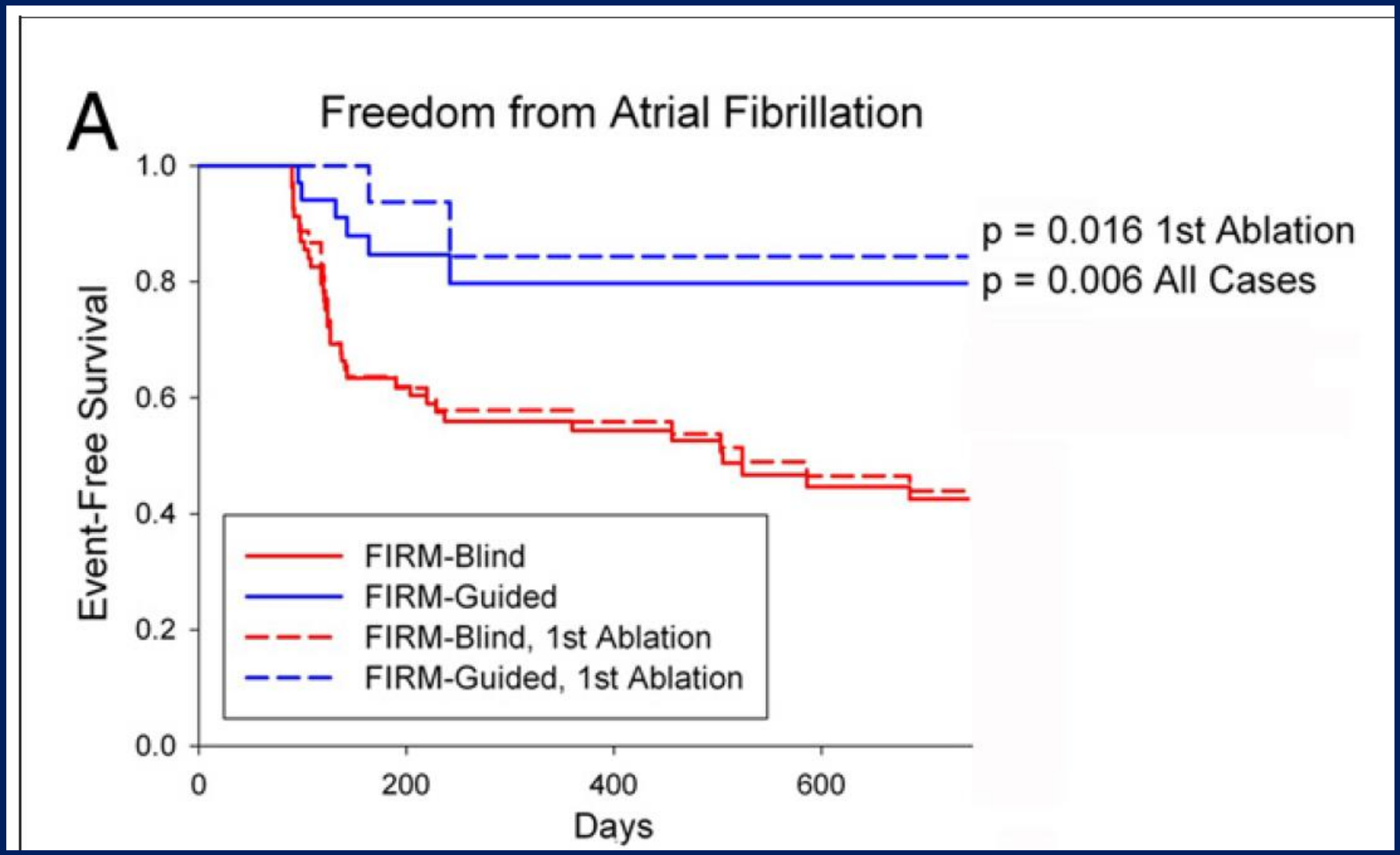
FIRM Ablation




BASKET 2
177 ms
1
2
3
4
5
6
7
8
C
D
E
F
G
H
A
B

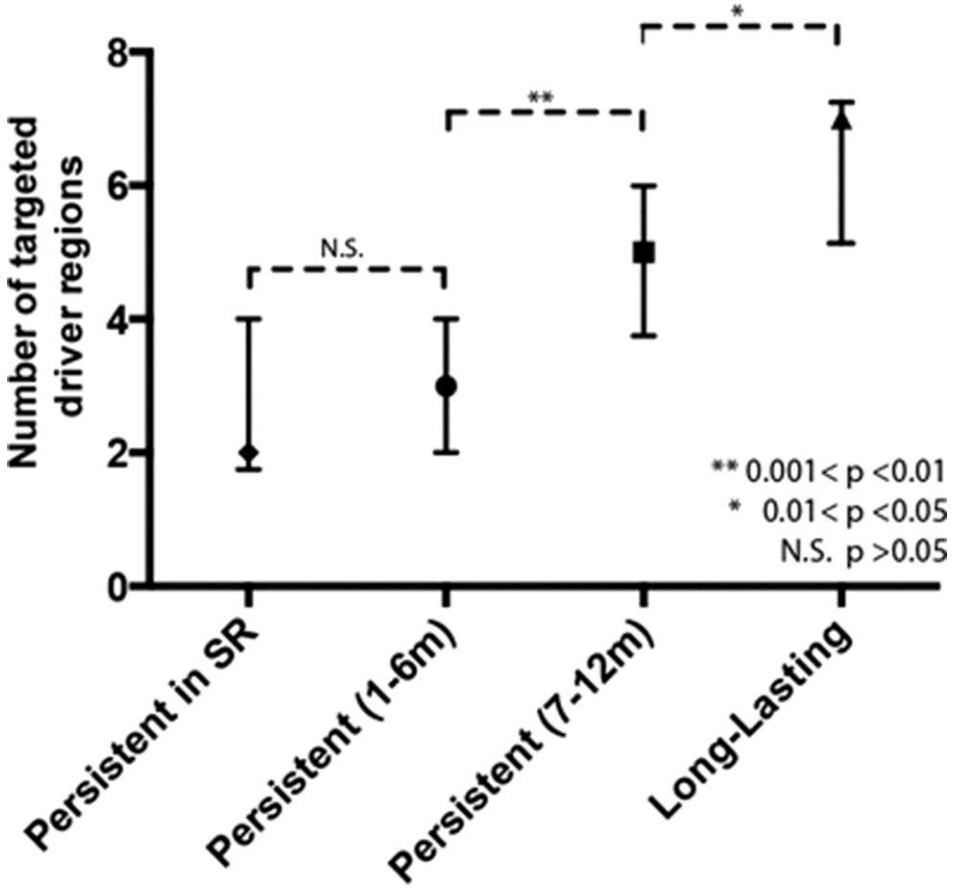

SVC
RSPV
LSPV
RAA
LIPV
RA
MV
IVC

CONFIRM (Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation) Trial



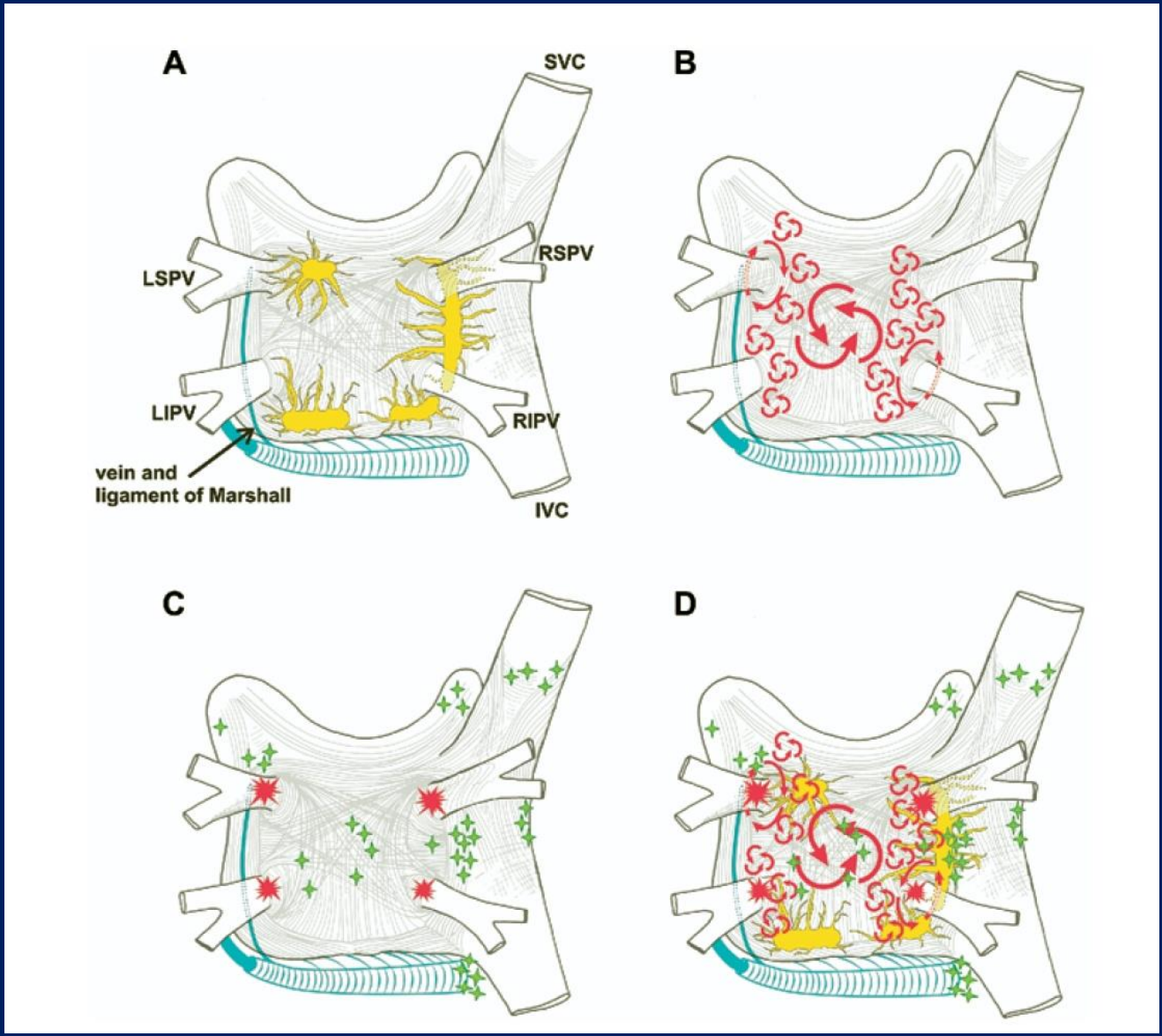
Narayan et al. JACC 2012;60:628

The number of driver regions ablated to terminate AF increases with the duration of persistent AF



Michel Haissaguerre et al. Circulation. 2014;130:530-538

Summary of Complex AF Mechanisms



Calkins et. al. Heart Rhythm 2007;4:816-861

Indications for Catheter Ablation of AF

- Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication
  - Paroxysmal: Catheter ablation is recommended* **I**
  - Persistent: Catheter ablation is reasonable **IIa**
  - Longstanding Persistent: Catheter ablation may be considered **IIb**
- Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent
  - Paroxysmal: Catheter ablation is reasonable **IIa**
  - Persistent: Catheter ablation may be considered **IIb**
  - Longstanding Persistent: Catheter ablation may be considered **IIb**

Catheter ablation of symptomatic paroxysmal AF is considered a Class 1 indication only when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced center.

Heart Rhythm 2012; 9:632-696

Catheter Ablation for Atrial Fibrillation

Class III: Harm

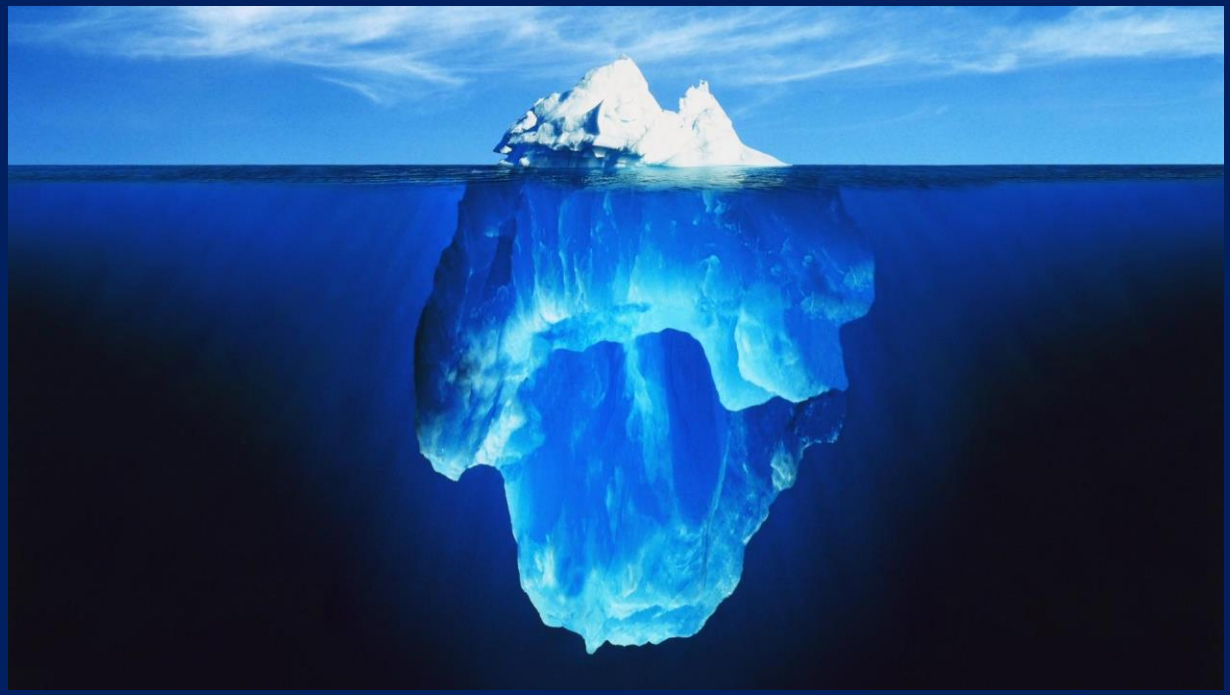
1. AF catheter ablation should not be performed in patients who cannot be treated with anticoagulant therapy during and following the procedure
2. AF catheter ablation to restore sinus rhythm should not be performed with the sole intent of obviating the need for anticoagulation

2014 AHA/ACC/HRS AF Guidelines

Atrial Fibrillation Management

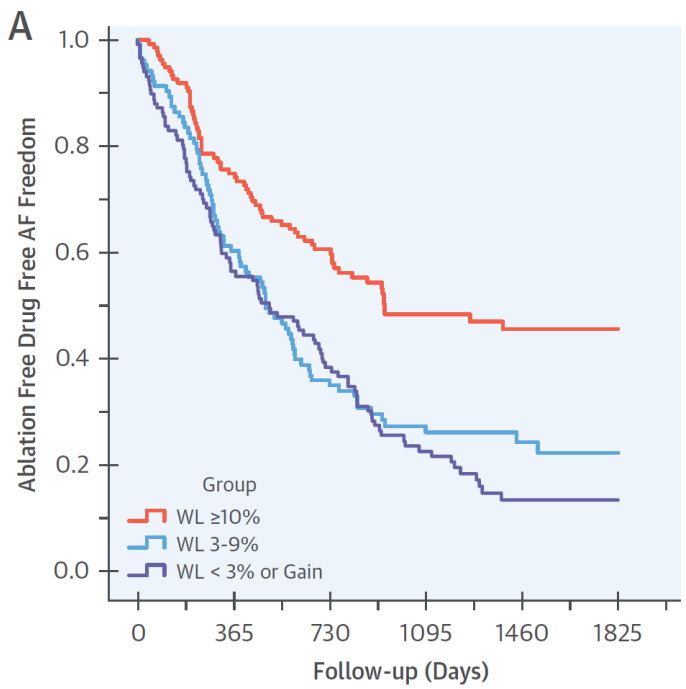
AF drugs and ablation are the tip of the iceberg

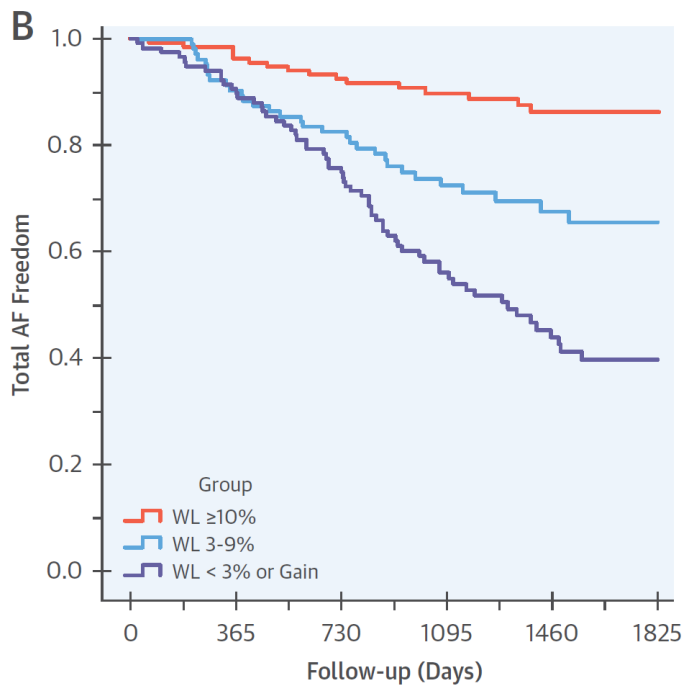
- Obesity
- Sleep apnea
- Hypertension
- CHF
- Diabetes
- Alcohol
- Exercise
- Atrial myopathy
- Genetics



Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort

FIGURE 2 Atrial Fibrillation Freedom Outcome According to Group





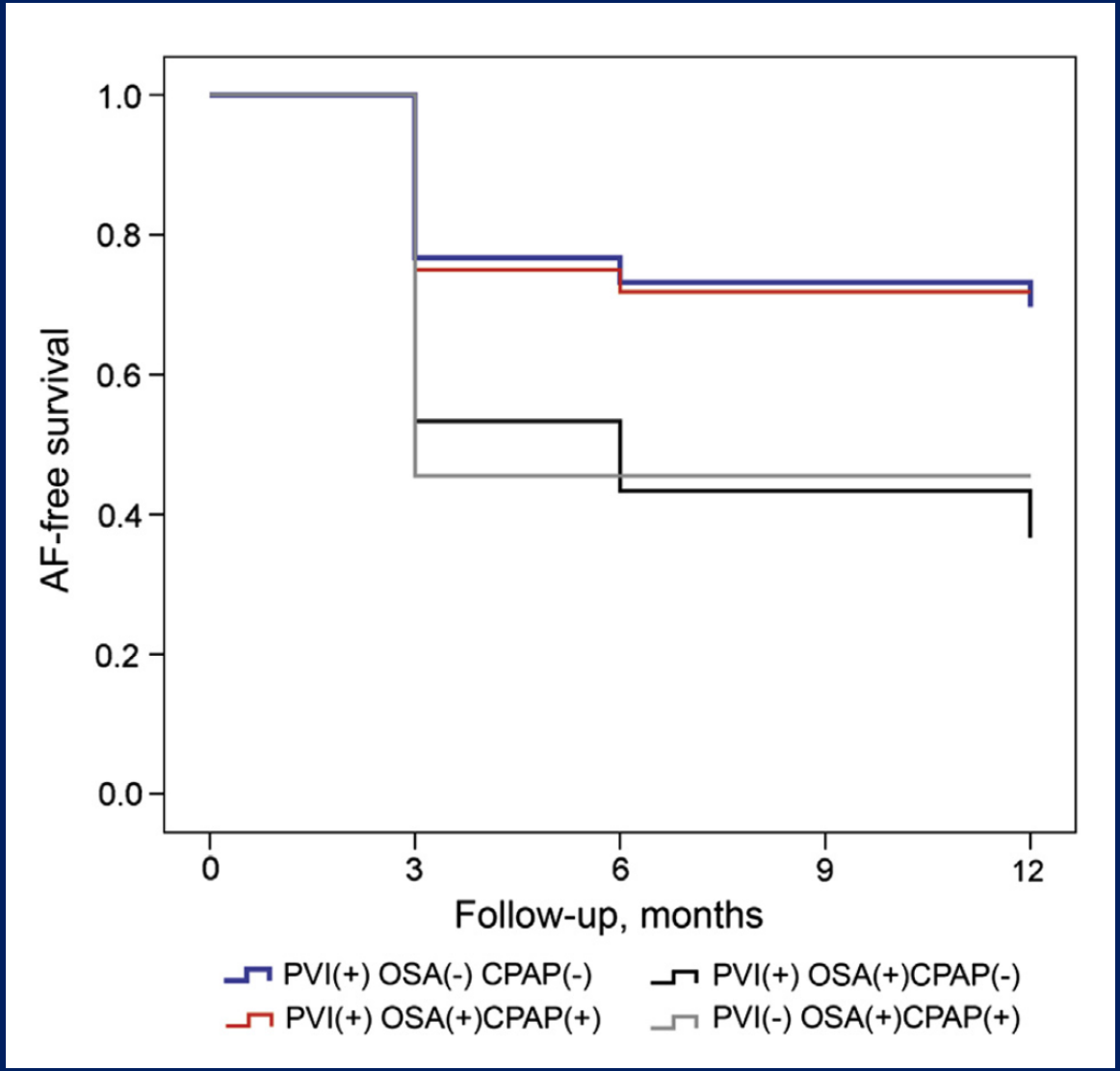
Time (Days)	0	365	730	1095	1460	1825
≥10 WL	135	101	72	42	31	18
3-9% WL	103	62	36	22	13	7
<3% WL or gain	117	66	44	22	11	9

0	365	730	1095	1460	1825
135	130	114	86	67	36
103	93	83	57	35	22
117	105	85	53	32	22

(A) Kaplan-Meier curve for AF-free survival without the use of rhythm control strategies. **(B)** Kaplan-Meier curve for AF-free survival for total AF-free survival (multiple ablation procedures with and without drugs). Abbreviations as in Figure 1.

Pathak et al. JACC 2015;65:2159

Treatment of Obstructive Sleep Apnea Reduces the Risk of Atrial Fibrillation Recurrence After Catheter Ablation



Fein et al. JACC 2013;62:300

Questions?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UNIVERSITY of
FLORIDA
The Foundation for The Gator Nation