State-of-the-Art AF Management:

A Labor of Love

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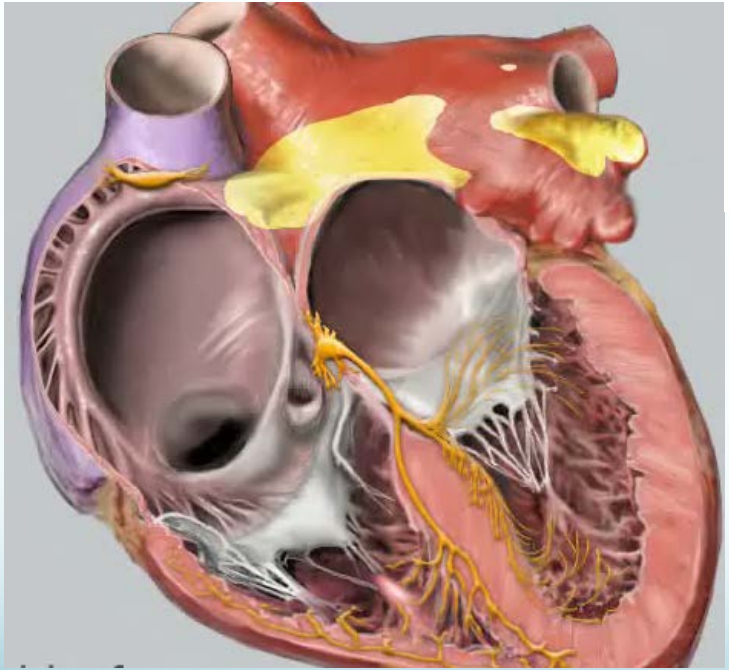
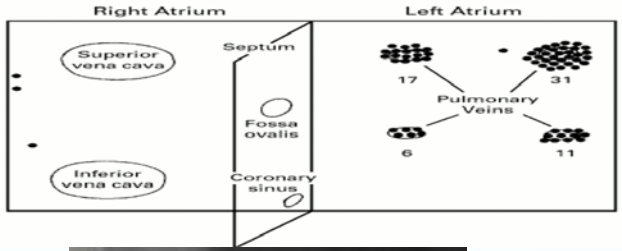
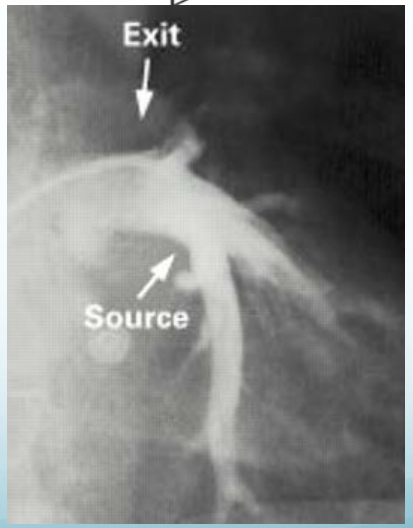
Atrial Fibrillation
Mechanisms: Pulmonary veins







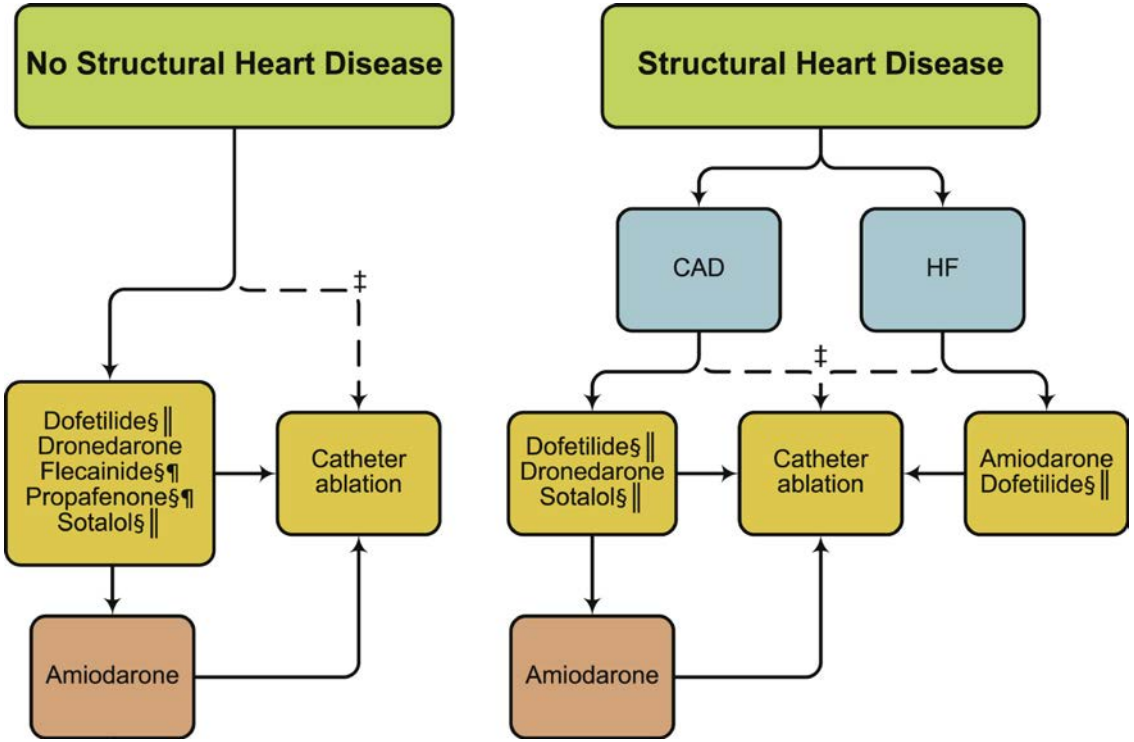
Haissaguerre M *N Engl J Med* 1998 15 (2), 250-262

Treatment Goals

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

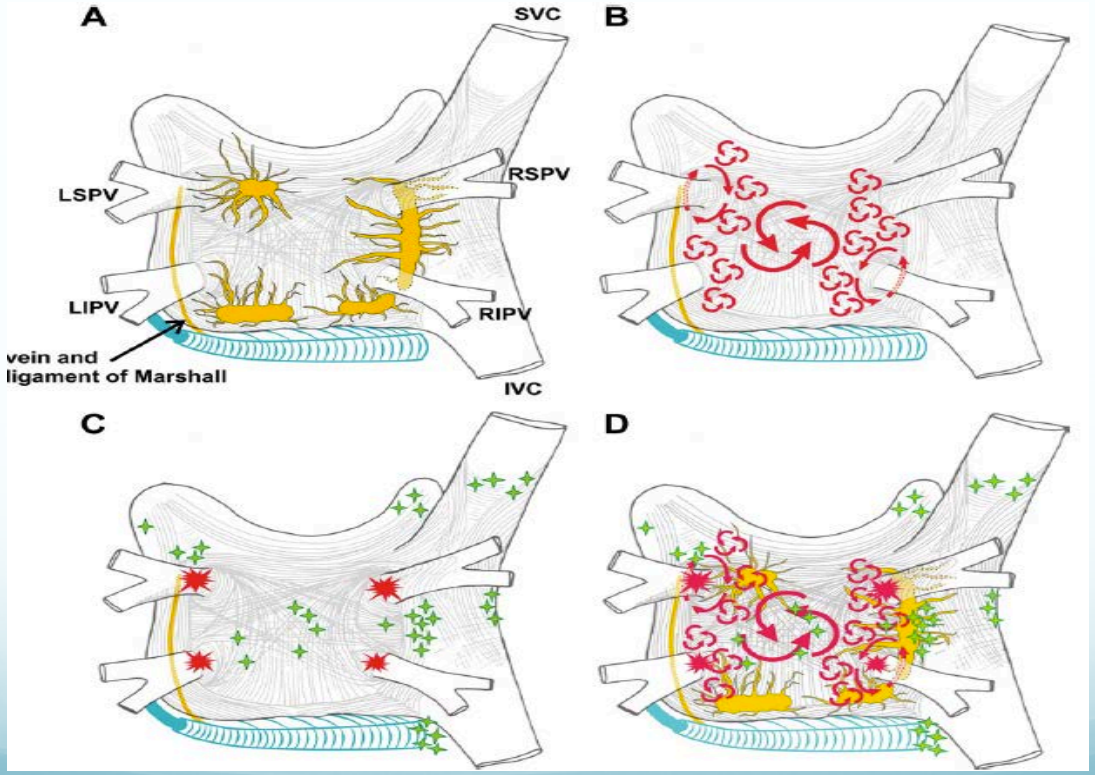
- #1: Symptom suppression
- #2: Improve outcomes:
  - Prevent strokes
  - Prevent tachycardia-induced cardiomyopathy
  - Prevent dementia?
  - Reduce mortality?
- Approaches:
  - Rhythm control
  - Rate control/anticoagulation

Goal #1: Improve symptoms
Rhythm Control: Drugs



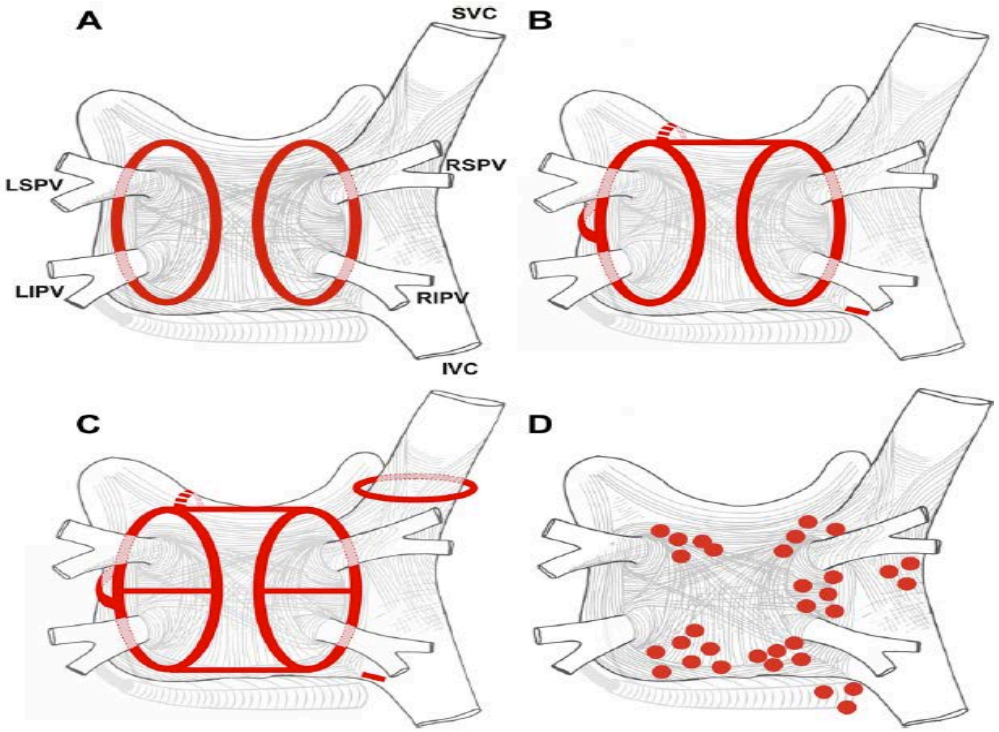
J Am Coll Cardiol. 2014;64(21):2246-2280. doi:10.1016/j.jacc.2014.03.021

Atrial Fibrillation
Mechanisms: Beyond PV ectopy



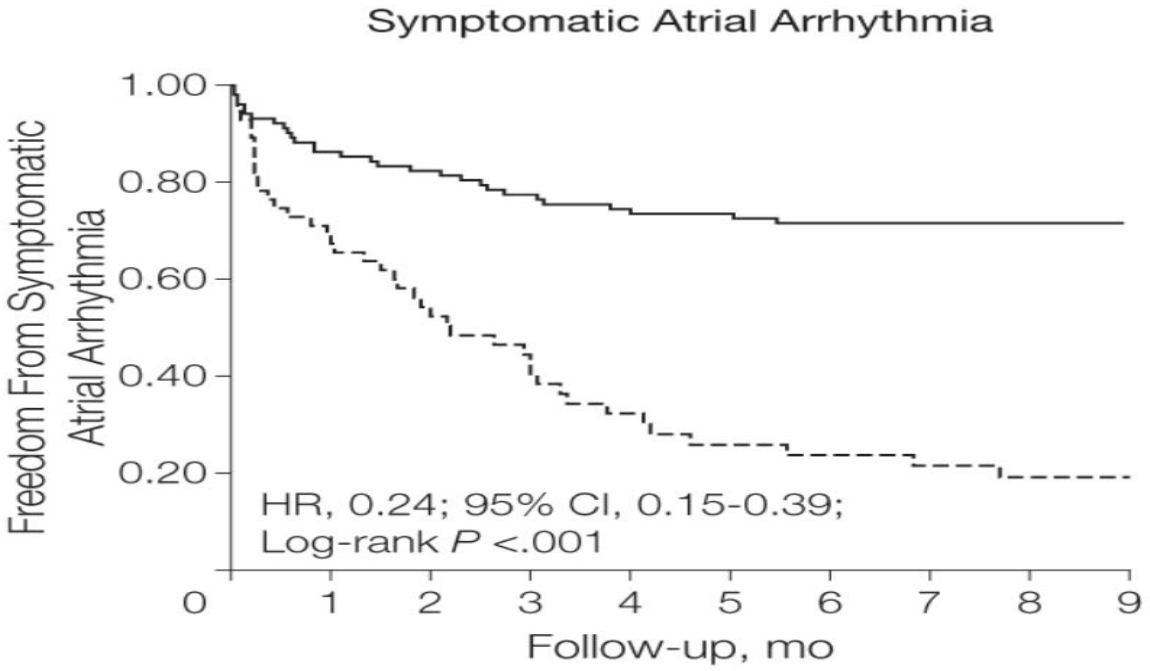
Calkins et al et al *Heart Rhythm* 2017

Atrial Fibrillation Ablation Strategies



Calkins et al *Heart Rhythm* 2017

Symptom control

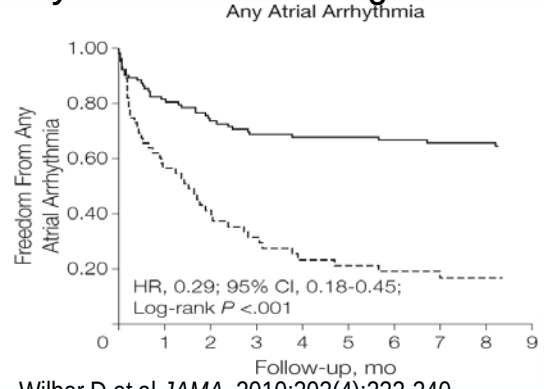


Wilber et al Thermocool AF: *JAMA*. 2010;303(4):333-340

PV isolation: More effective than drugs

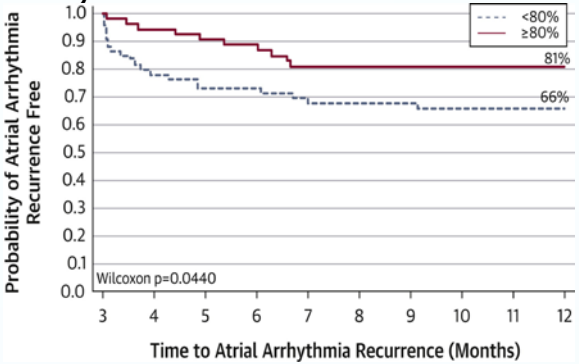
HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

Paroxysmal AF-Failed Drug



Wilber D et al *JAMA.* 2010;303(4):333-340

Paroxysmal AF-Contact-force

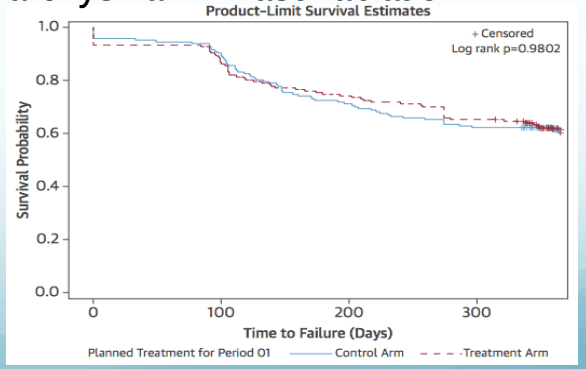


Natale et al *J Am Coll Cardio*l. 2014;64(7):647-656

Paroxysmal AF-Cryo-ablation

Packer D et al *J Am Coll Cardiol*. 2013;61:1713-23

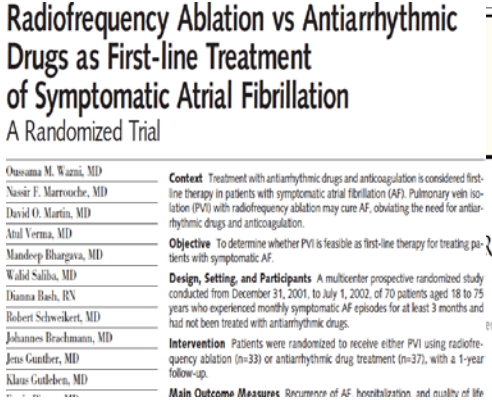
Paroxysmal AF-Laser-ablation



Dukkipati S et al *J Am Coll Cardiol* 2015;66:1350–60

Ablation as first-line?

Wazni et al *JAMA* 2005;293:2634



Radiofrequency Ablation vs Antiarrhythmic Drugs as First-line Treatment of Symptomatic Atrial Fibrillation

A Randomized Trial

Oussama M. Wazni, MD; Nassir F. Marrouche, MD; David O. Martin, MD; Atul Verma, MD; Mandeep Bhargava, MD; Walid Saliba, MD; Dianna Bash, RN; Robert Schweikert, MD; Johannes Brachmann, MD; Jens Gunther, MD; Klaus Gutleben, MD

Context Treatment with antiarrhythmic drugs and anticoagulation is considered first-line therapy in patients with symptomatic atrial fibrillation (AF). Pulmonary vein isolation (PVI) with radiofrequency ablation may cure AF, obviating the need for antiarrhythmic drugs and anticoagulation.

Objective To determine whether PVI is feasible as first-line therapy for treating patients with symptomatic AF.

Design, Setting, and Participants A multicenter prospective randomized study conducted from December 31, 2001, to July 1, 2002, of 70 patients aged 18 to 75 years who experienced monthly symptomatic AF episodes for at least 3 months and had not been treated with antiarrhythmic drugs.

Intervention Patients were randomized to receive either PVI using radiofrequency ablation (n=33) or antiarrhythmic drug treatment (n=37), with a 1-year follow-up.

Main Outcome Measures Recurrence of AF, hospitalization, and quality of life

Nielsen et al *NEJM* 2012;367:1587

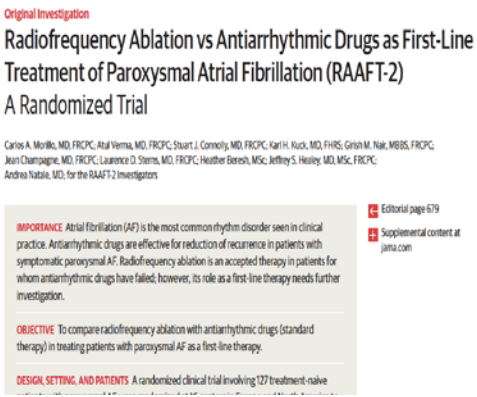
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 25, 2012 VOL. 367 NO. 17

Radiofrequency Ablation as Initial Therapy in Paroxysmal Atrial Fibrillation

ens Cosedis Nielsen, M.D., D.M.Sc., Arne Johannessen, M.D., D.M.Sc., Pekka Raatikainen, M.D., Ph.D., Gerhard Hindricks, M.D., Ph.D., Håkan Walfridsson, M.D., Ph.D., Ole Kongstad, M.D., Ph.D., Steen Pehrson, M.D., D.M.Sc., Anders Englund, M.D., Ph.D., Juha Hartikainen, M.D., Ph.D., Leif Spange Mortensen, M.Sc., and Peter Steen Hansen, M.D., D.M.Sc.

Morillo et al *JAMA* 2014;311:692



Original Investigation

Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2)

A Randomized Trial

Carlos A. Morillo, MD, FRCPC; Atul Verma, MD, FRCPC; Stuart J. Connolly, MD, FRCPC; Karl H. Kuck, MD, FHRS; Girish M. Nair, MBBS, FRCPC; Jean Champagne, MD, FRCPC; Laurence D. Sterns, MD, FRCPC; Heather Beresh, MSc; Jeffrey S. Healey, MD, MSc, FRCPC; Andrea Natale, MD; for the RAAFT-2 Investigators

Editorial page 679

Supplemental content at jama.com

IMPORTANCE Atrial fibrillation (AF) is the most common rhythm disorder seen in clinical practice. Antiarrhythmic drugs are effective for reduction of recurrence in patients with symptomatic paroxysmal AF. Radiofrequency ablation is an accepted therapy in patients for whom antiarrhythmic drugs have failed; however, its role as a first-line therapy needs further investigation.

OBJECTIVE To compare radiofrequency ablation with antiarrhythmic drugs (standard therapy) in treating patients with paroxysmal AF as a first-line therapy.

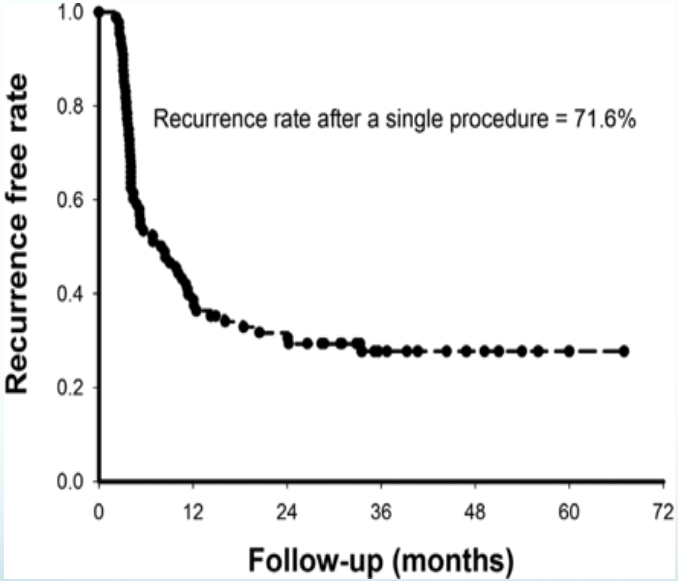
DESIGN, SETTING, AND PATIENTS A randomized clinical trial involving 127 treatment-naive

Primary endpoint: Symptomatic AF

Primary endpoint: AF burden

Primary endpoint: Time to documented atrial tachyarrhythmia

PV isolation: Unsatisfactory for Persistent AF



Chao et al *Circ Arrhythm Electrophysiol.* 2012;5:514520

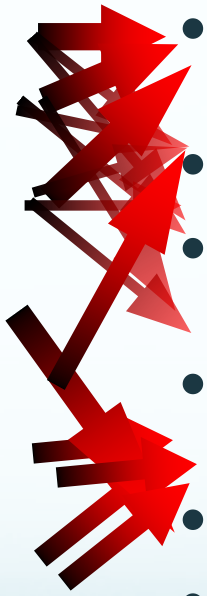
Table 3 Recommendations regarding ablation technique

- Ablation strategies that target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures.
- If the PVs are targeted, electrical isolation should be the goal.
- Achievement of electrical isolation requires, at a minimum, assessment and demonstration of entrance block into the PV.
- Monitoring for PV reconduction for 20 minutes following initial PV isolation should be considered.
- For surgical PV isolation, entrance and/or exit block should be demonstrated.
- Careful identification of the PV ostia is mandatory to avoid ablation within the PVs.
- If a focal trigger is identified outside a PV at the time of an AF ablation procedure, ablation of that focal trigger should be considered.
- If additional linear lesions are applied, operators should consider using mapping and pacing maneuvers to assess for line completeness.
- Ablation of the cavotricuspid isthmus is recommended in patients with a history of typical atrial flutter or inducible cavotricuspid isthmus dependent atrial flutter.
- If patients with longstanding persistent AF are approached, operators should consider more extensive ablation based on linear lesions or complex fractionated electrograms.
- It is recommended that RF power be reduced when creating lesions along the posterior wall near the esophagus.

Calkins et al et al *Heart Rhythm* 2012

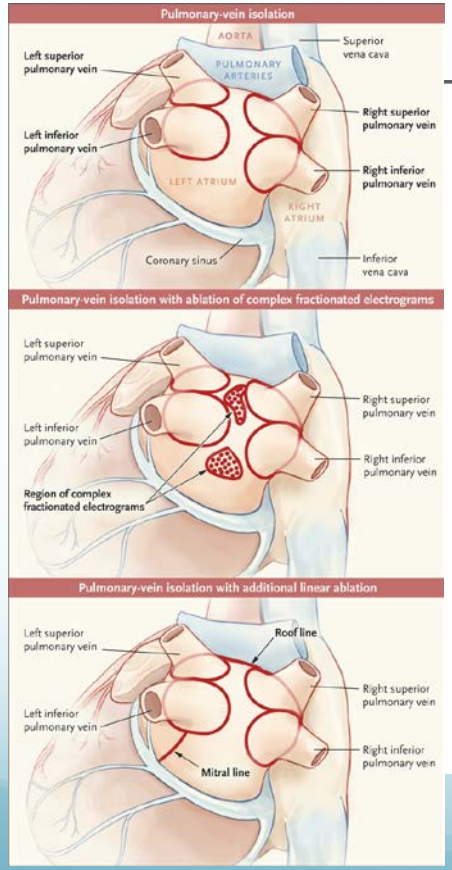
Strategies and targets

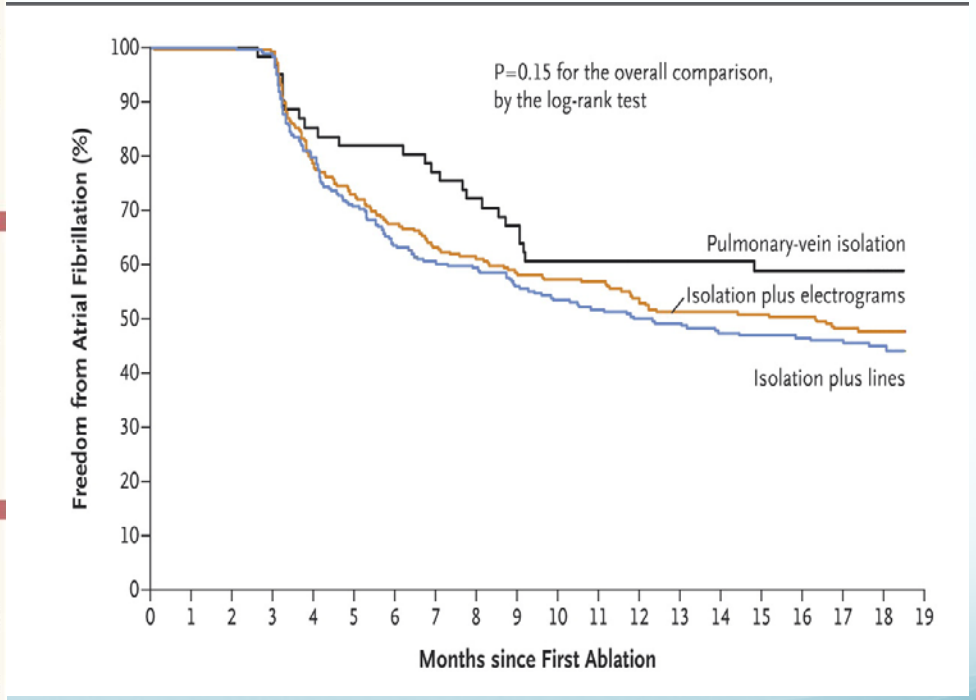
- Pulmonary vein isolation
- Wide area circumferential ablation
- Antral isolation
- Complex and fractionated potential ablation
- Ganglionic vagal ablation
- Left atrial posterior linear ablation
- Mitral isthmus linear ablation



- Ectopic foci from the pulmonary veins
- Vagal innervation
- Triggers from the vein of Marshall
- Rotors in the posterior left atrium
- Elimination of iatrogenic flutter
- Rotor-anchoring and wavebreak sites

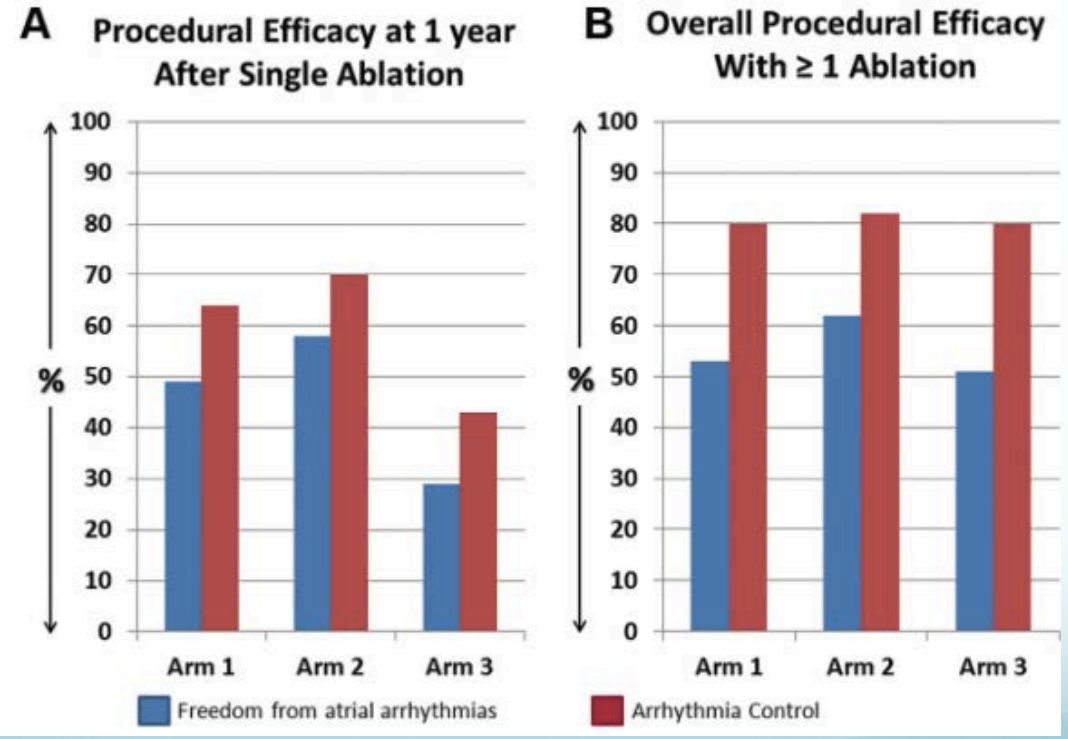
Persistent AF: Beyond the Pulmonary Veins?





Verma A et al. *N Engl J Med* 2015;372:1812-1822.

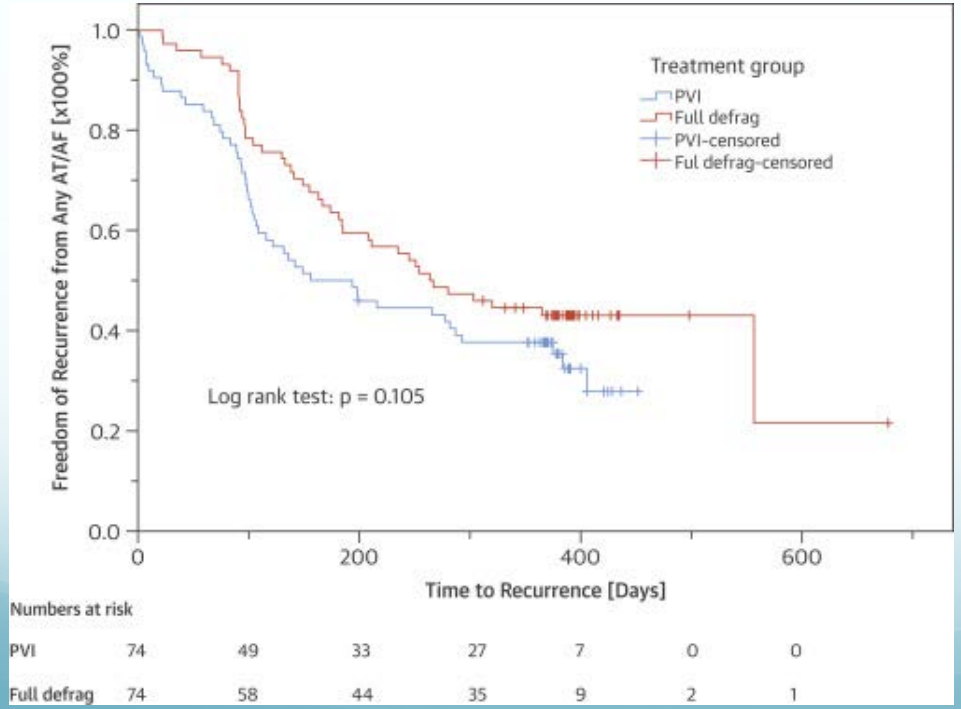
Persistent AF: Beyond the Pulmonary Veins?

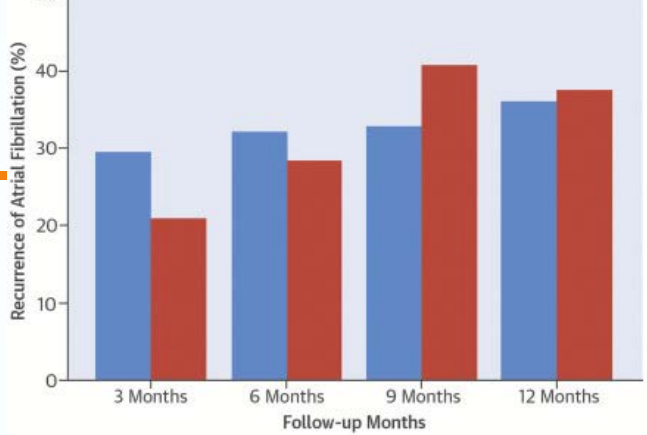


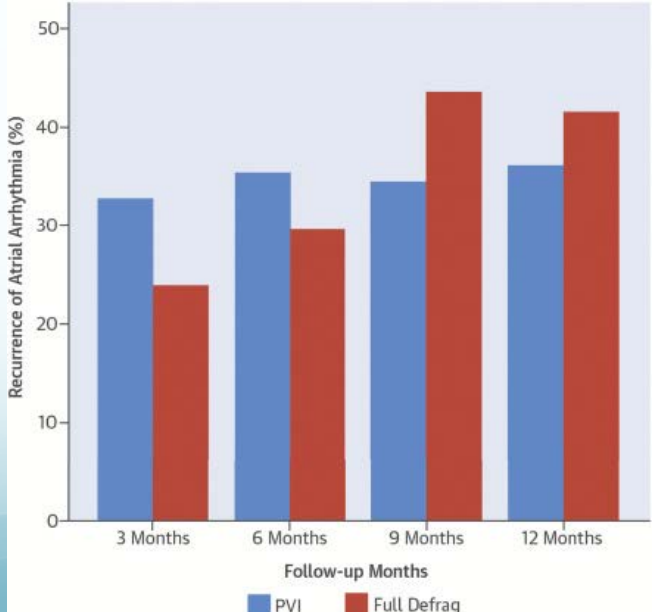
Dixit S et al *Circ Arrhythm Electrophysiol*. 2012;5:287-294

Persistent AF ablation
Additional lesions?

- Defragmentation -no impact. CHASE-AF
  - *J Am Coll Cardiol* 2015: 66 (24): 2743-2752

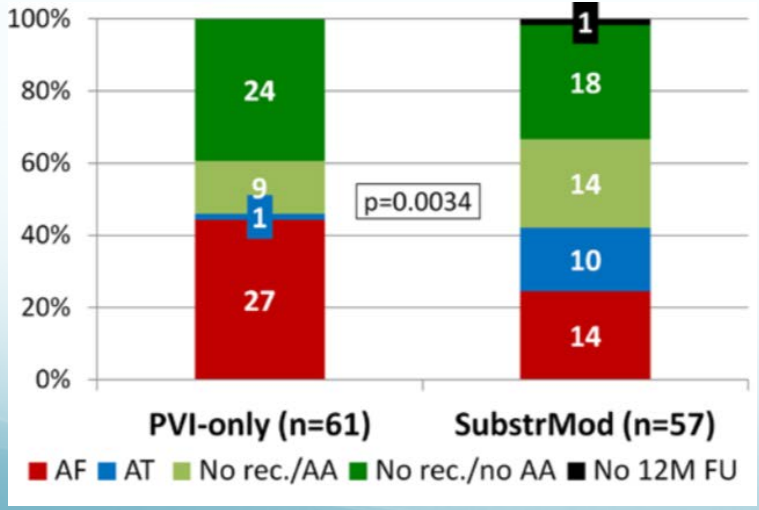


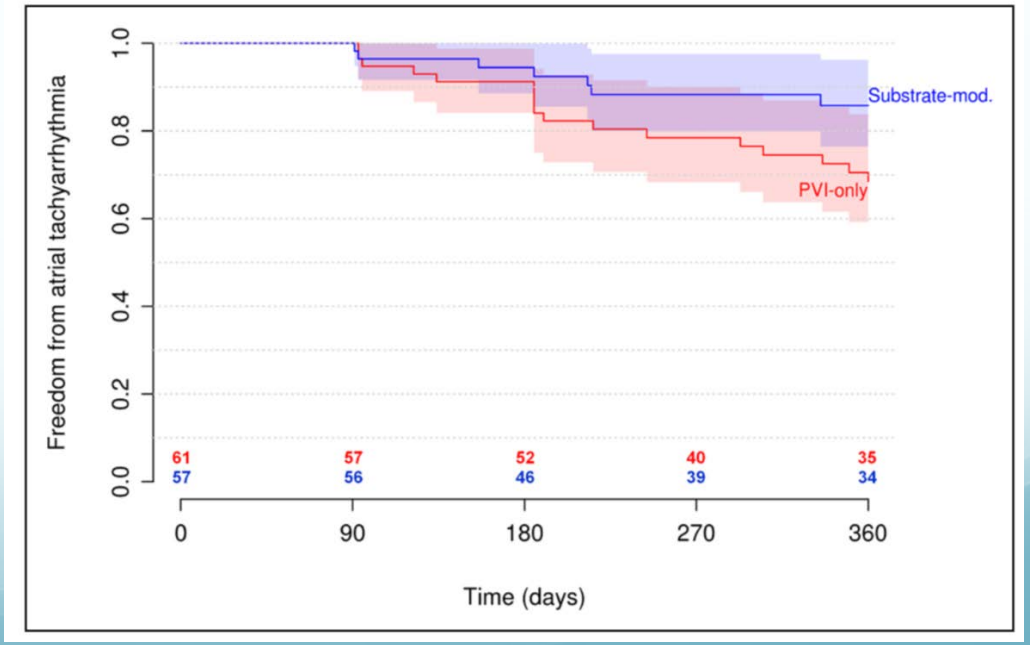




Persistent AF ablation
Additional lesions?

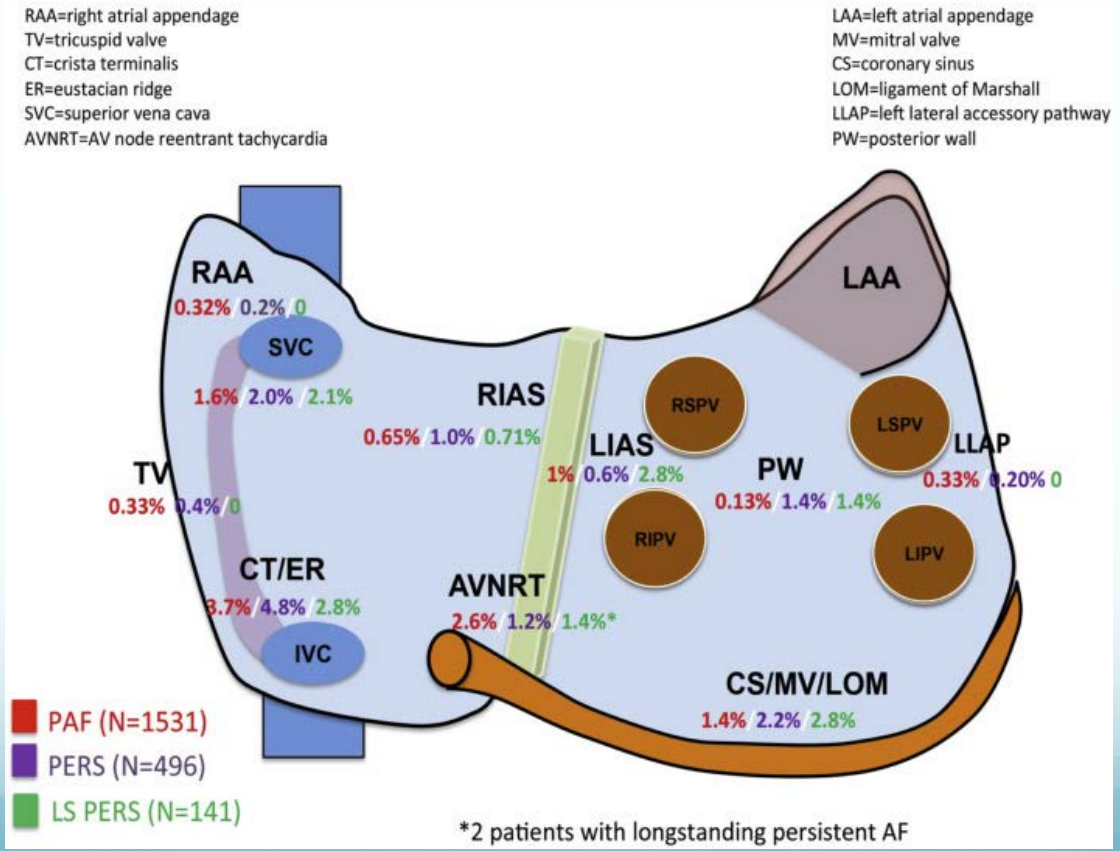
- Substrate modification. Randomized Alster-Lost-AF Trial *Circ Arrhythm Electrophysiol*. 2017;10:e005114.





Extrapulmonary triggers

Santangeli P, Marchlinski F. *Heart Rhythm.* 2017 Jul;14(7):1087-1096



Longstanding Persistent AF: Left atrial appendage?

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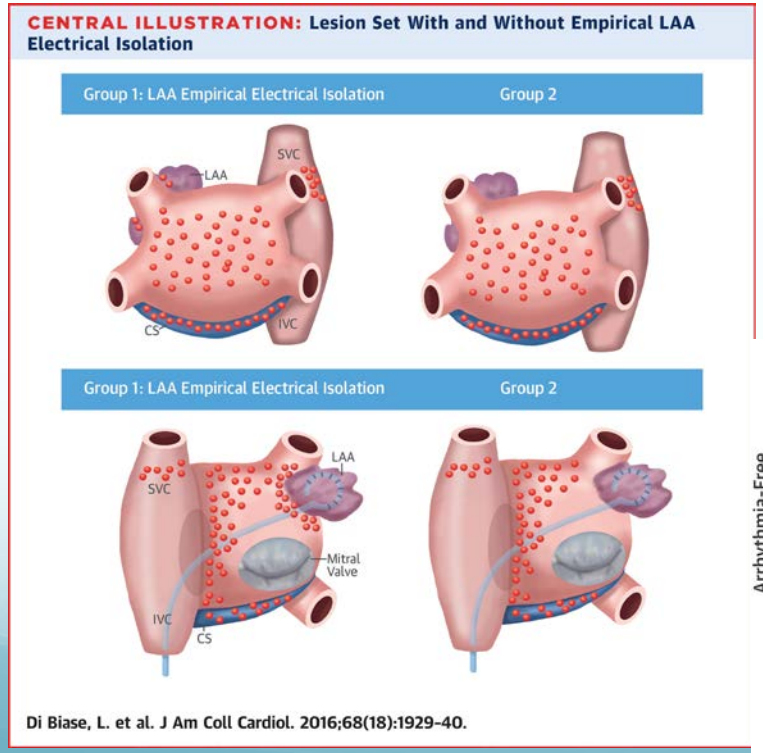
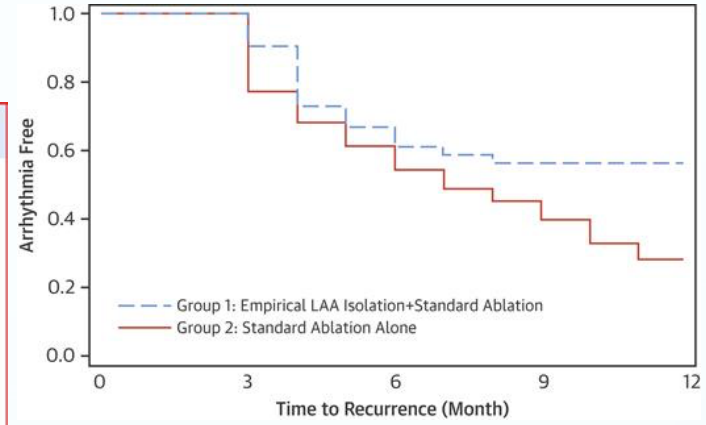
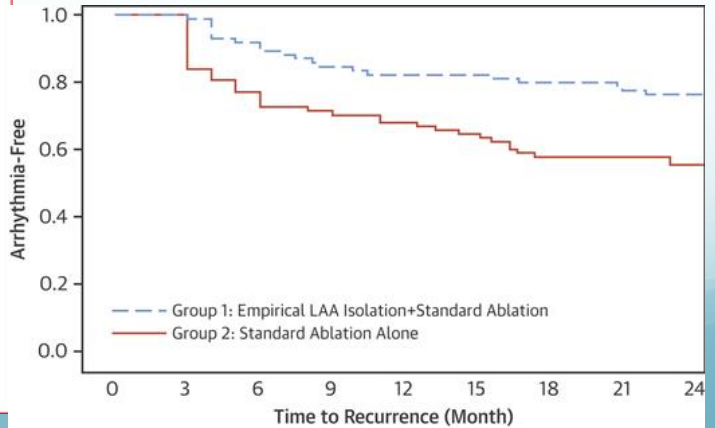


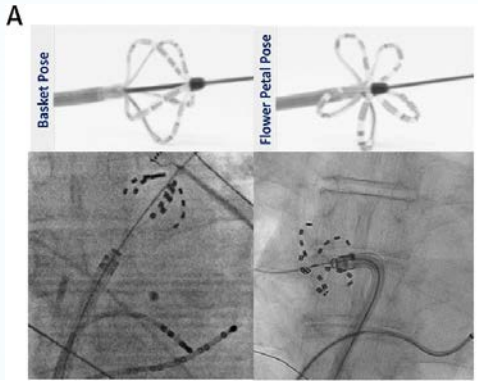


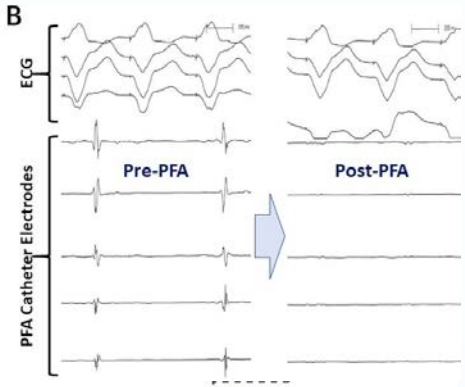


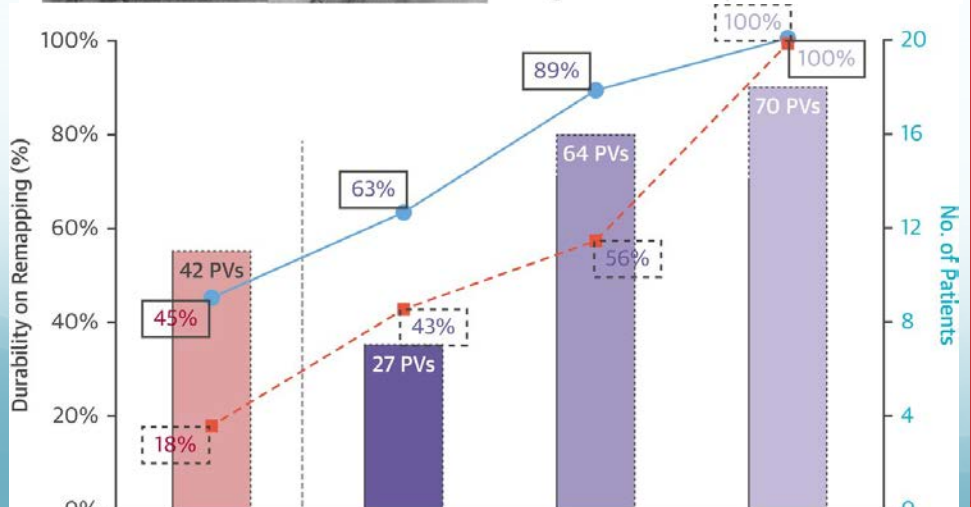
Emergent techniques and technologies

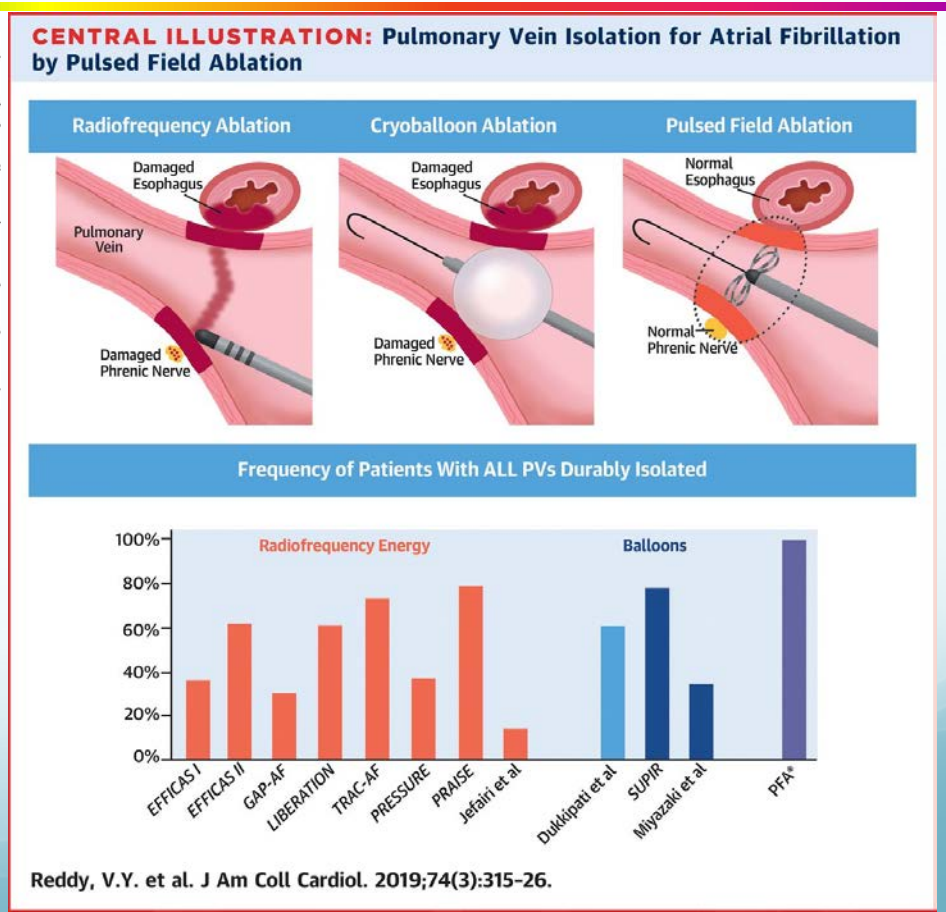
- More on PV isolation:
  - Pulsed electrical fields
  - Lattice radiofrequency (Affera)
  - Radiofrequency balloon (Apama)
  - Cyberheart
  - Cardiofocus HeartLight X3
  - Vytronus® robotic ablation
- Ablative technology
  - Diamond tip
- Propagation Mapping
  - Acutus®
  - ICAN
- Techniques:
  - LAA isolation
  - VOM ethanol infusion

Pulsed-Field ablation





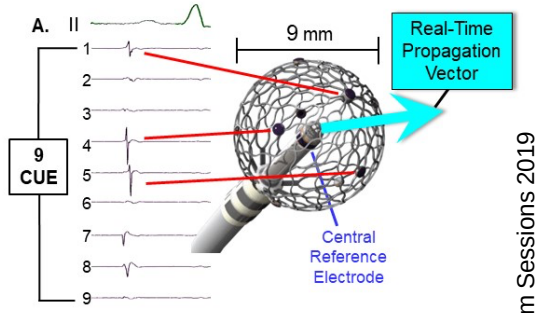


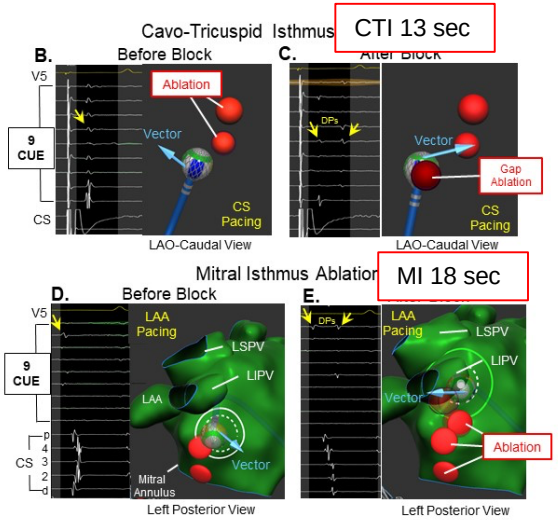


Reddy, V.Y. et al. J Am Coll Cardiol. 2019;74(3):315-26.

Affera® Lattice electrode ablation catheter

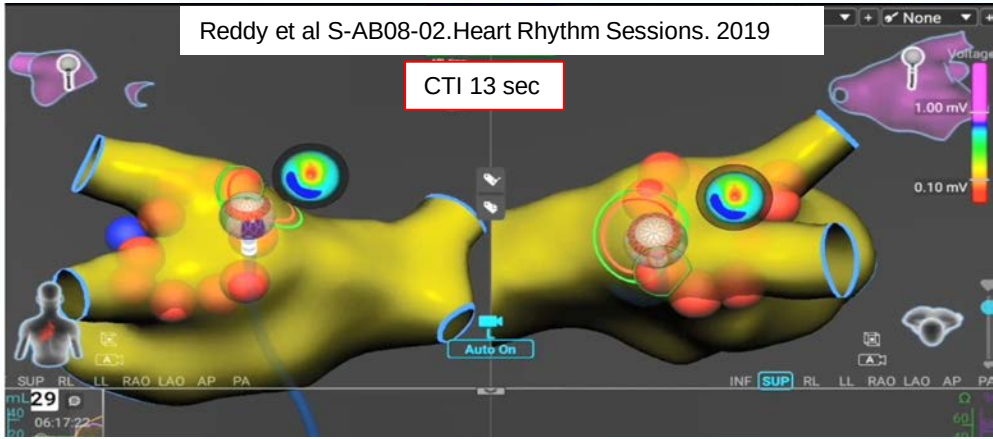
Ultra-rapid ablation

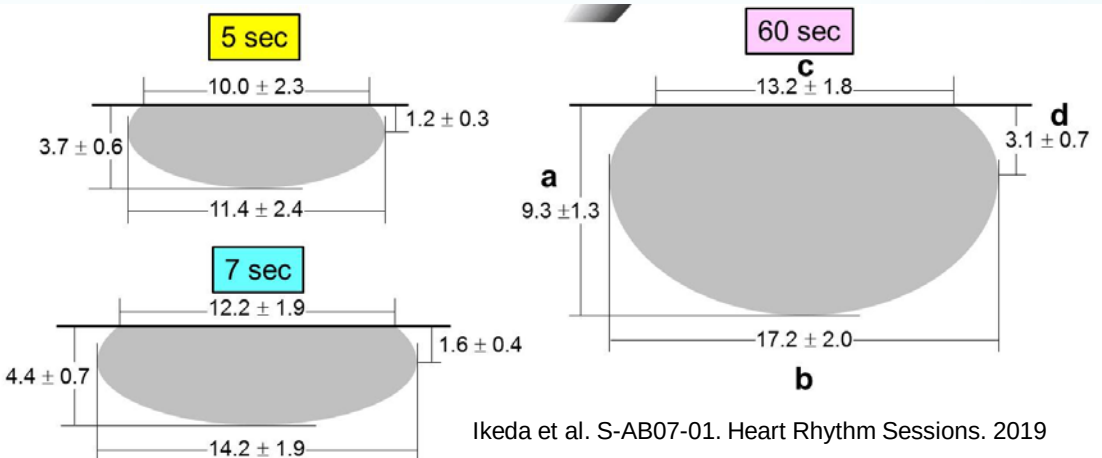




Nakagawa et al S-PO01-046. Heart Rhythm Sessions 2019

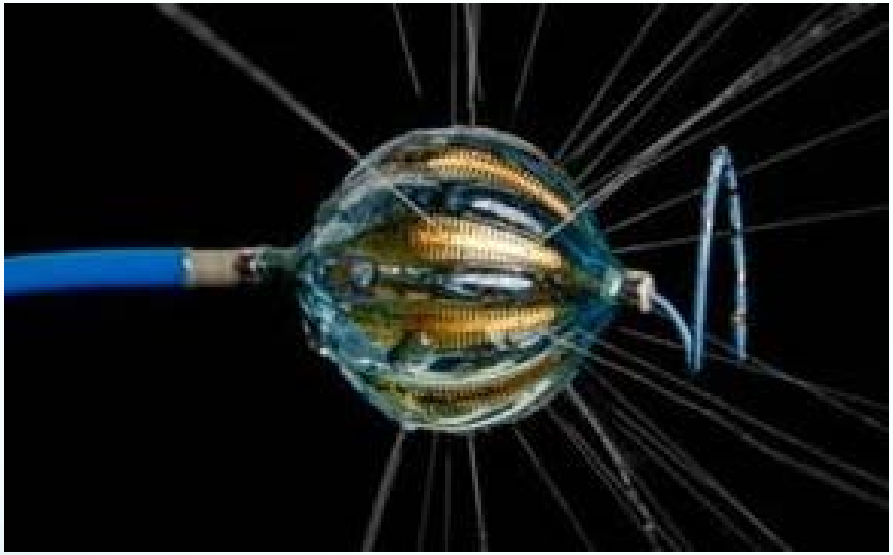
Reddy et al S-AB08-02.Heart Rhythm Sessions. 2019





Ikeda et al. S-AB07-01. Heart Rhythm Sessions. 2019

Radiofrequency balloons for PVI

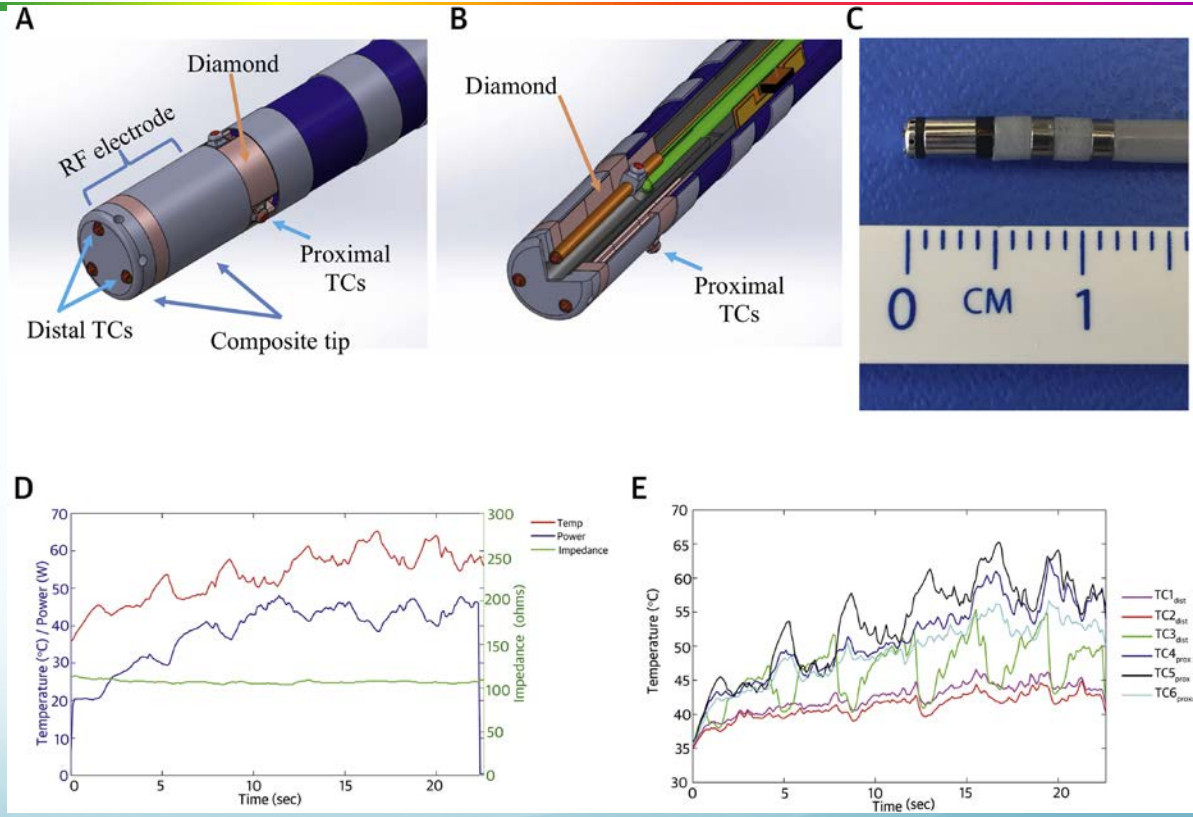


- HelioStar® RF balloon.
- In IDE clinical trial in the US.

- Apama® RF balloon
- In IDE clinical trial in the US.

Temperature-controlled RF (EPIX®)

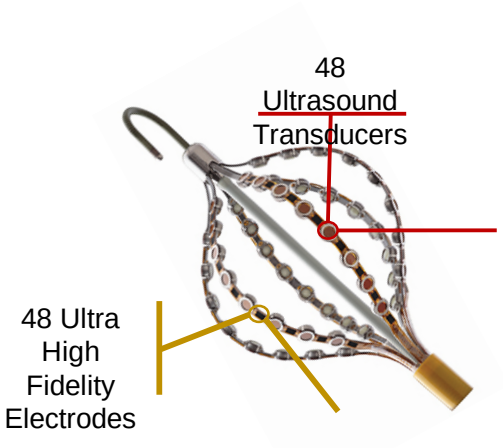
- Diamond tip dissipates heat
- Thermocouples effectively reflect tissue temperature
- RF titrated to tissue temperature
- Contact force sensing not needed



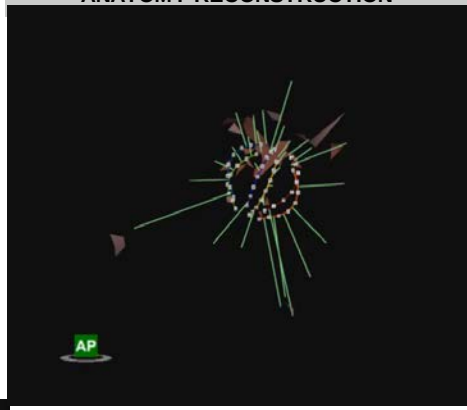
J Am Coll Cardiol 2017;70:542–53

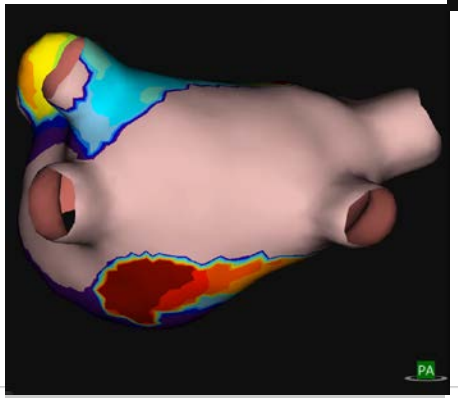
AcQMap® High Resolution Imaging and Mapping System

- Non-contact 3D electro-anatomic Visualization System capable of mapping all types of complex atrial arrhythmias
- Ultrasound anatomy reconstruction in as little as 2-3 minutes
- Full-chamber mapping, clear view of cardiac activation
- Charge source mapping reveals conduction patterns in the substrate
- Rapid re-mapping to assess effect of ablation
- CE Mark - April 2014
- FDA clearance - October 16, 2017



ULTRASOUND: 115,000 SIG/SEC
ANATOMY RECONSTRUCTION





11 MILLION SIG/SEC
CHARGE MAPPING

Brief Summary: Please review the Instructions for Use prior to using these devices for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use. The following presentation may contain information that is considered off-label in the U.S."

Current *Procedural* limitations in AF ablation

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- Technical limitations of the PV isolation procedure:
  - Inability to achieve durable PV isolation
  - Procedure time and complexity
  - Procedure risks
- Mechanistic limitations of the PV isolation procedure:
  - Are all mechanisms of AF ablated with PV isolation?
  - How much PV antrum/posterior wall should be included in a PVI
- What other targets besides PV isolation should be ablated?
  - Rotors?
  - Focal triggers?
  - Innervation?
  - Scar?
  - LAA?
- What ablation strategy should be used in each individual patient?
  - Paroxysmal vs persistent
  - Lone vs “accompanied’ AF
  - LA scar vs healthy
  - Young vs old.

Current *Clinical* limitations in AF ablation

HOUSTON Methodist DEBAKEY HEART & VASCULAR CENTER

- Patient selection
  - Paroxysmal vs persistent vs longstanding persistent
  - Impact of structural heart disease
    - Atrial scar
    - Ventricular dysfunction
- Timing of the procedure
  - Guided by symptoms?
- Prognostic implications:
  - Do we prevent stroke, dementia, reduce mortality?
  - Can we stop oral anticoagulants in high-risk patients?

Case Study

- 73 year-old woman
- Paroxysmal AF since age 62. Sporadic AF episodes managed with pill-in-the-pocket propafenone until age 65.
- CHADS-Vasc: age, female, HTN, vascular
- TIA at age 71: CHADS-Vasc: 6
- Rivaroxaban led to GU bleeding: spontaneous ureteral bleeding, leading to urinary obstruction and transient AKI, requiring transfusion
- AF becomes persistent at age 71, rate control in the 100s at rest, with progressive DOE and functional decline

Challenges and possible approaches

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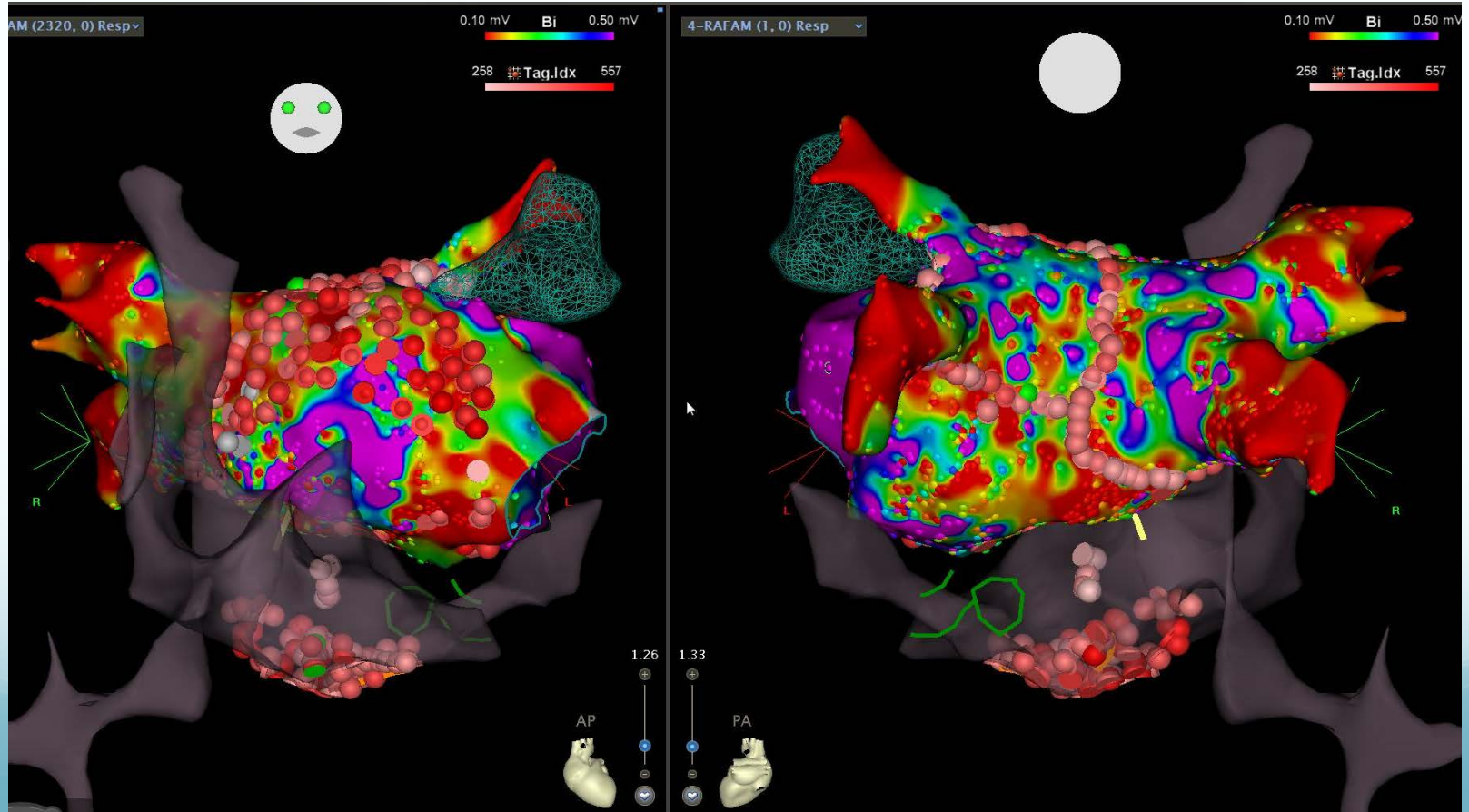
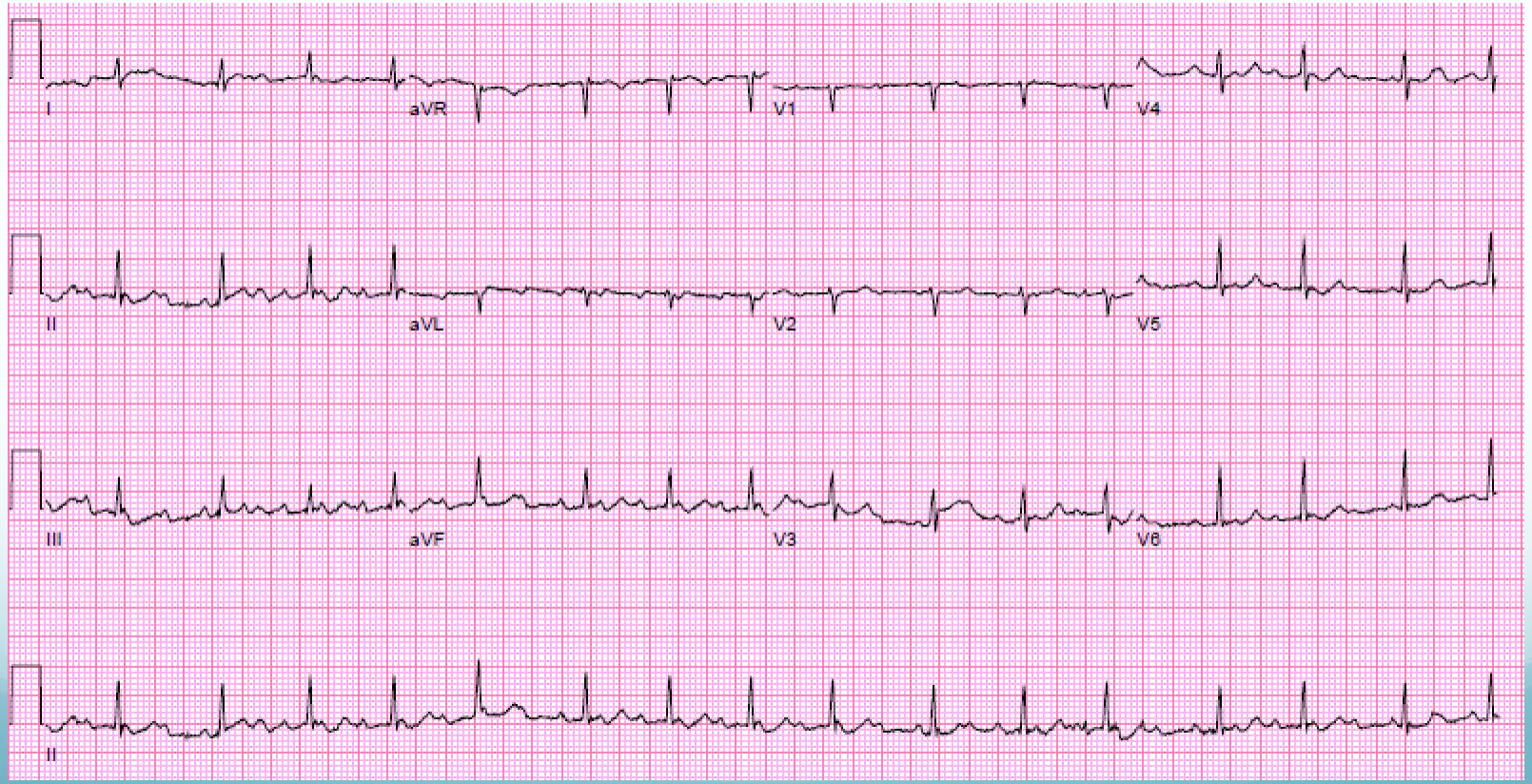
- Needs stroke protection in the face of OAC-induced bleeding
- Needs rhythm control
- Ablation challenges:
  - Longstanding persistent AF
  - Enlarged LA
    - LA diameter 6 cm
    - LA volume 189 cc.
- A strategy of aggressive ablation – including LAA isolation- combined with LAA occlusion was planned
  - 2-stage procedure

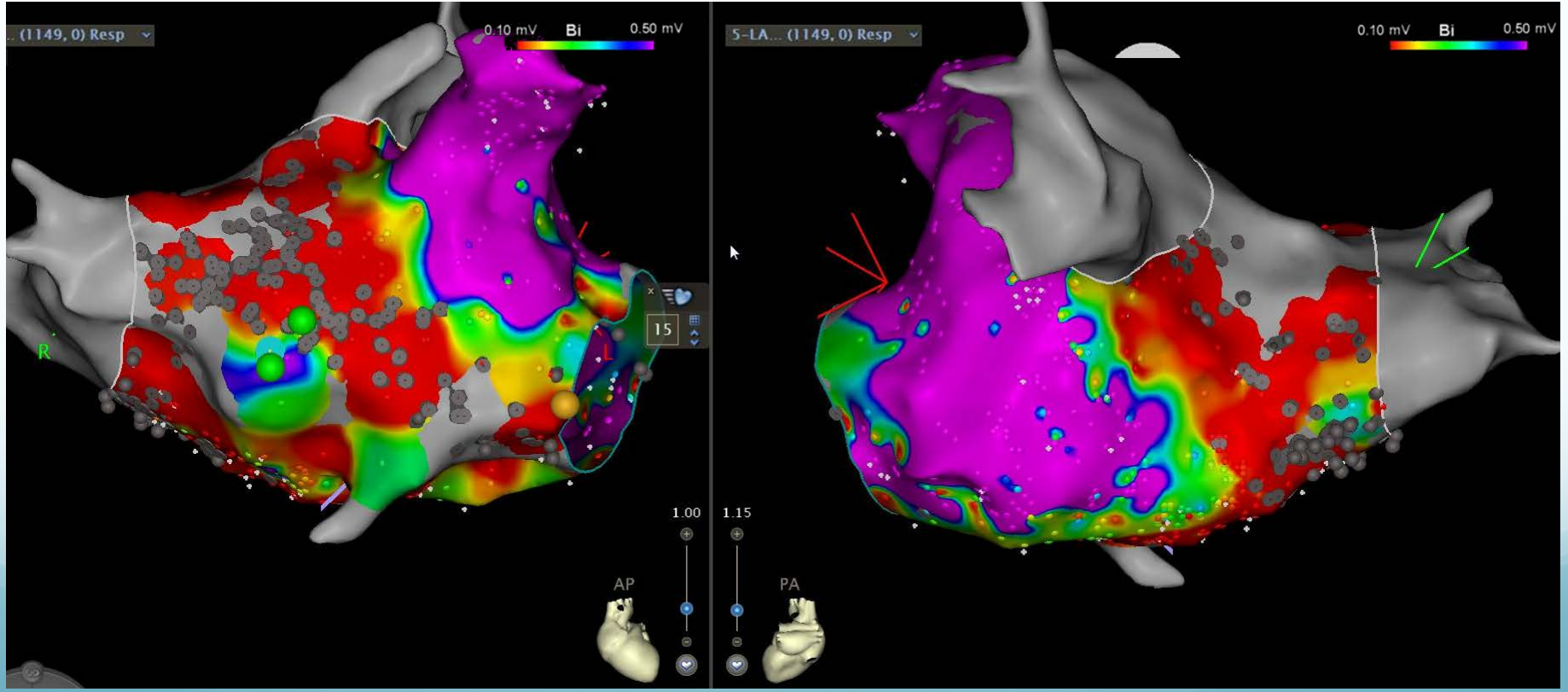
First procedure



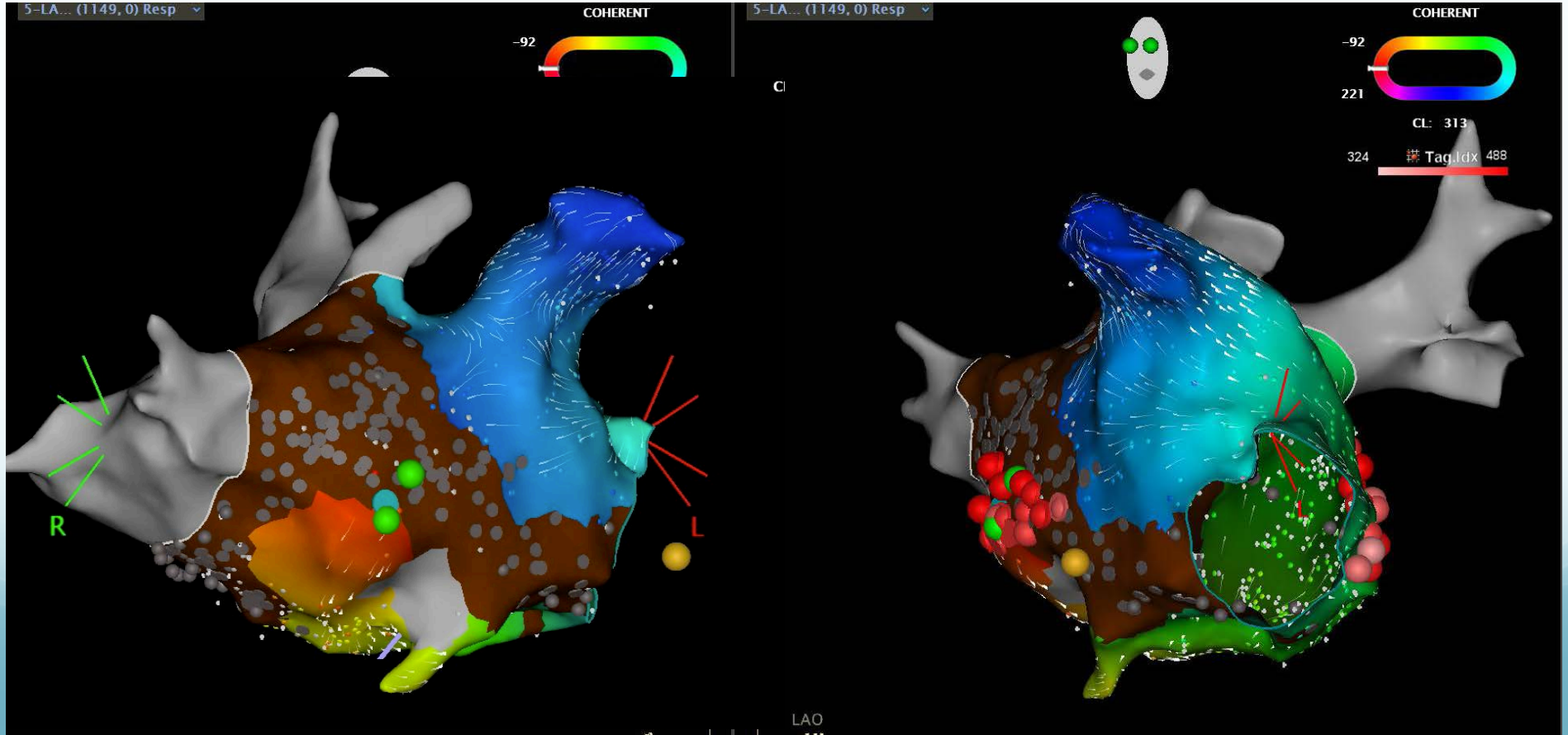
One week post ablation EKG



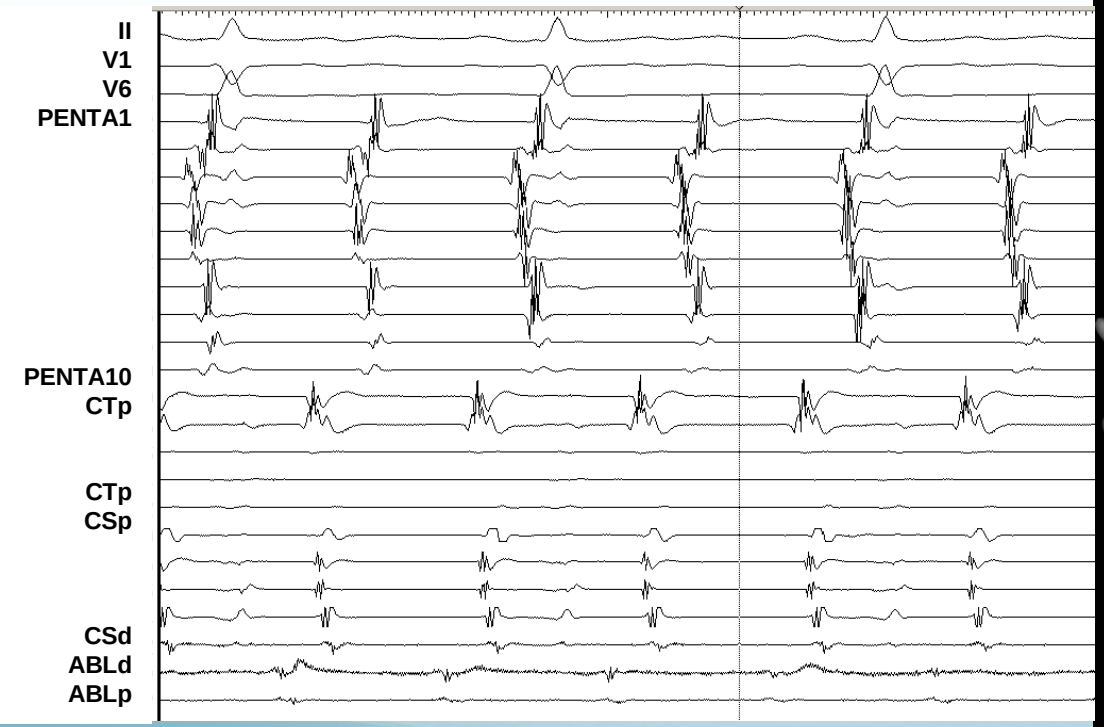
One month later: bipolar voltage map

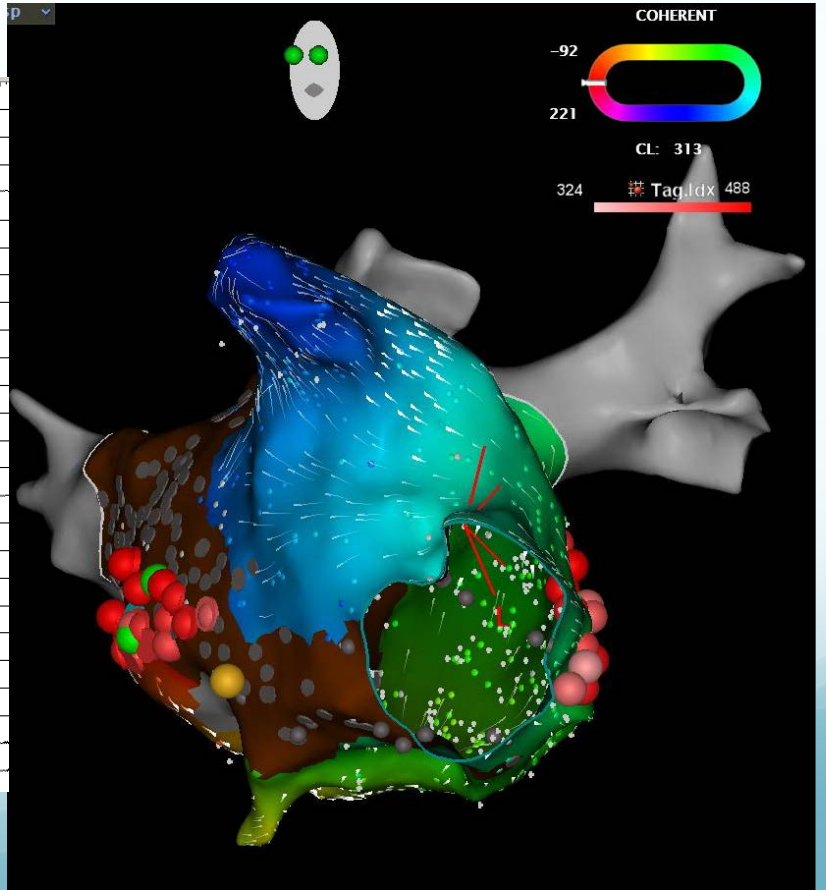


One month later: propagation

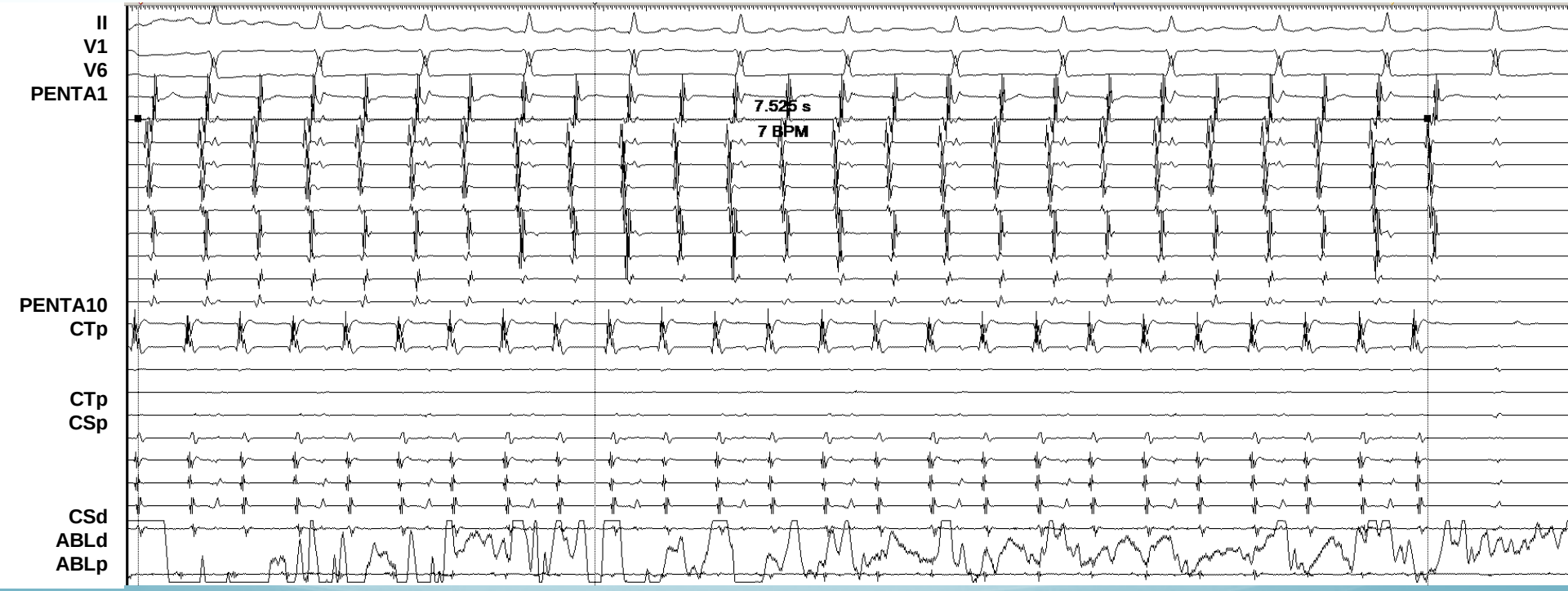


One month later: propagation

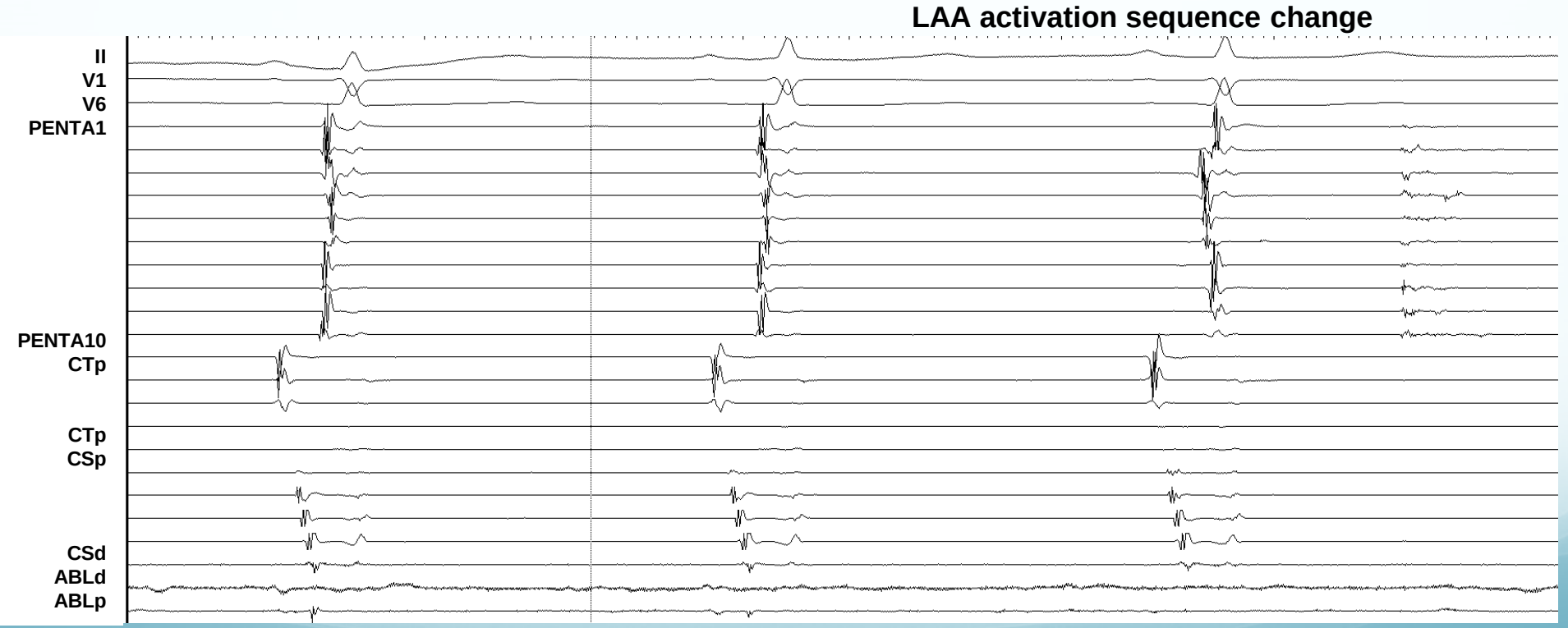




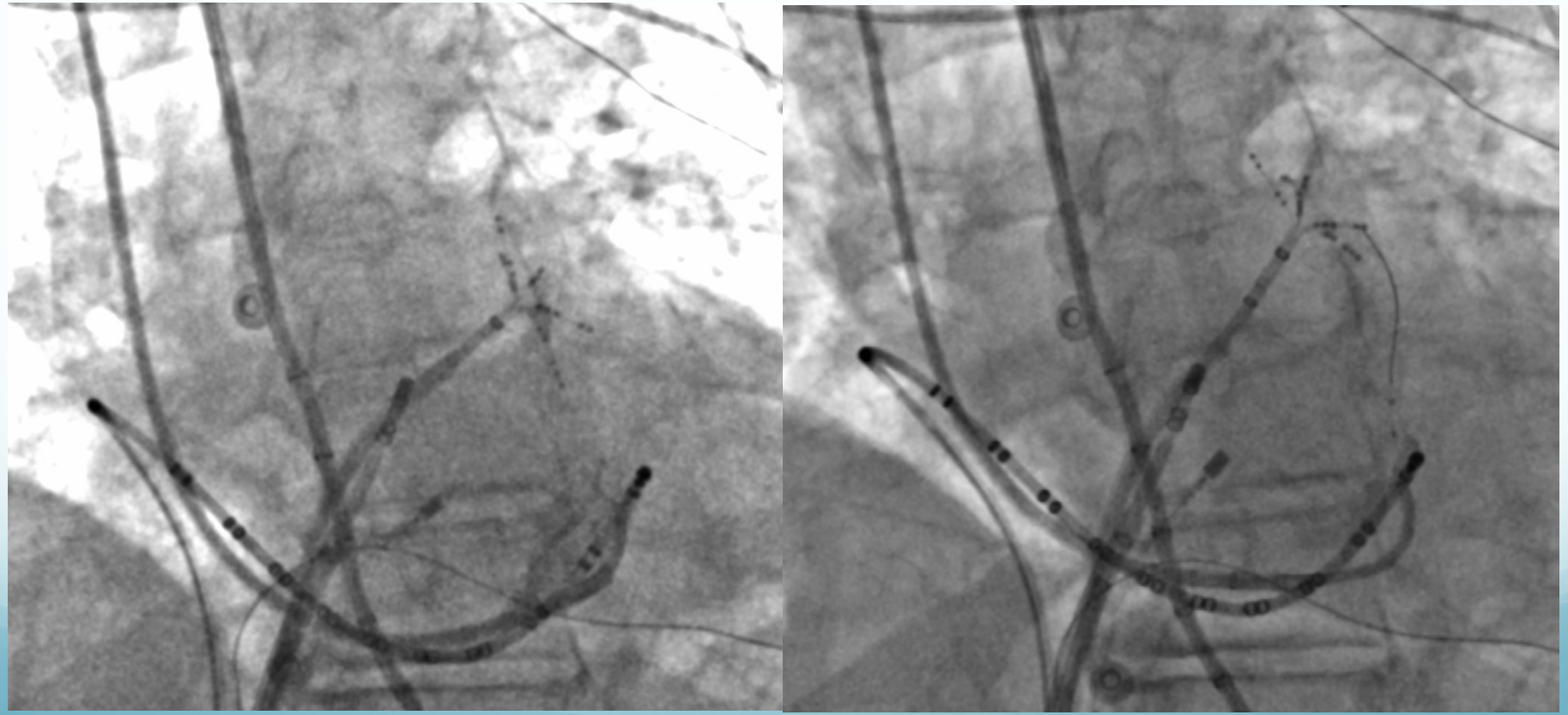
Ablation at septal site



Reinforcing septal line



Vein of Marshall ethanol



Vein of Marshall ethanol

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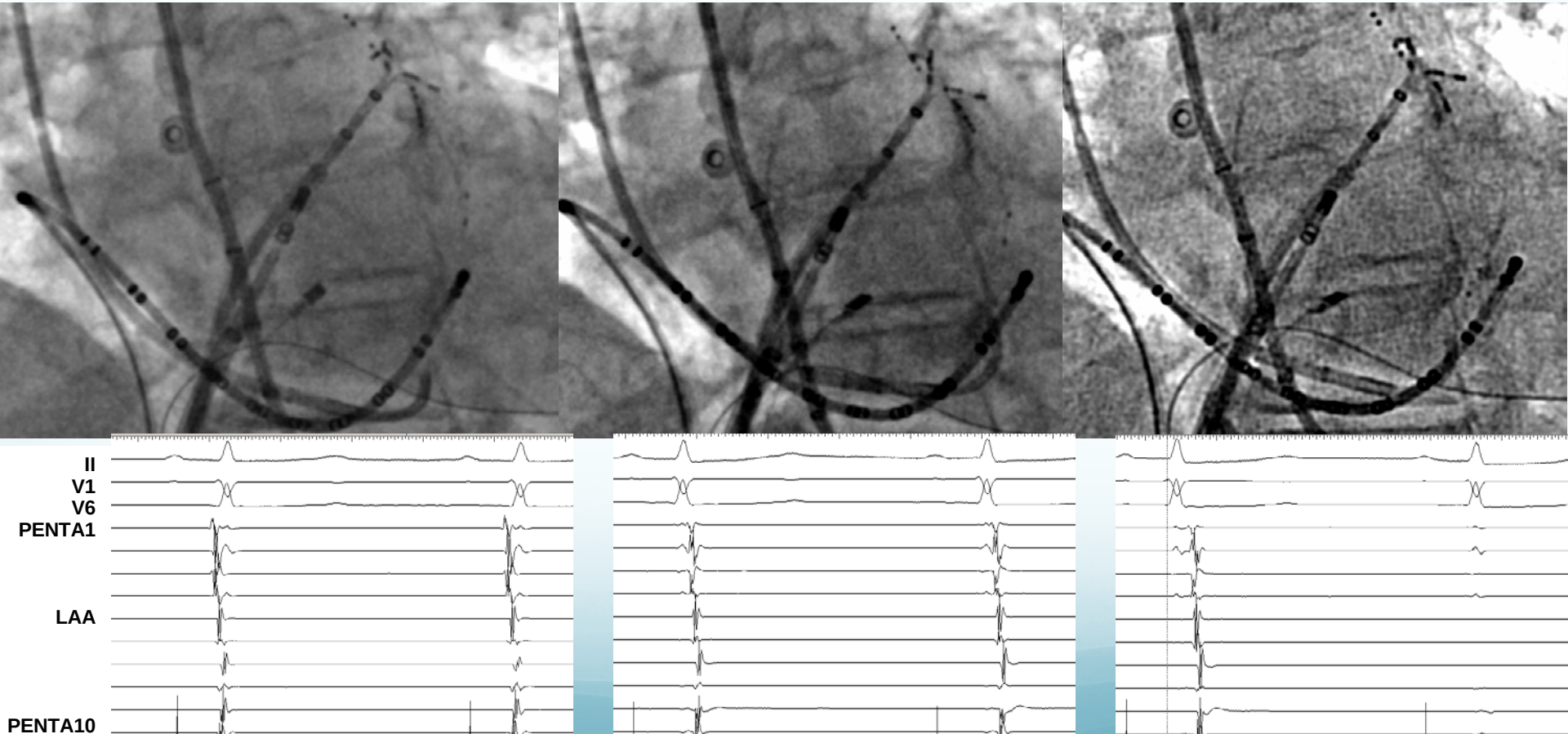

Vein of Marshall ethanol: VENUS trial

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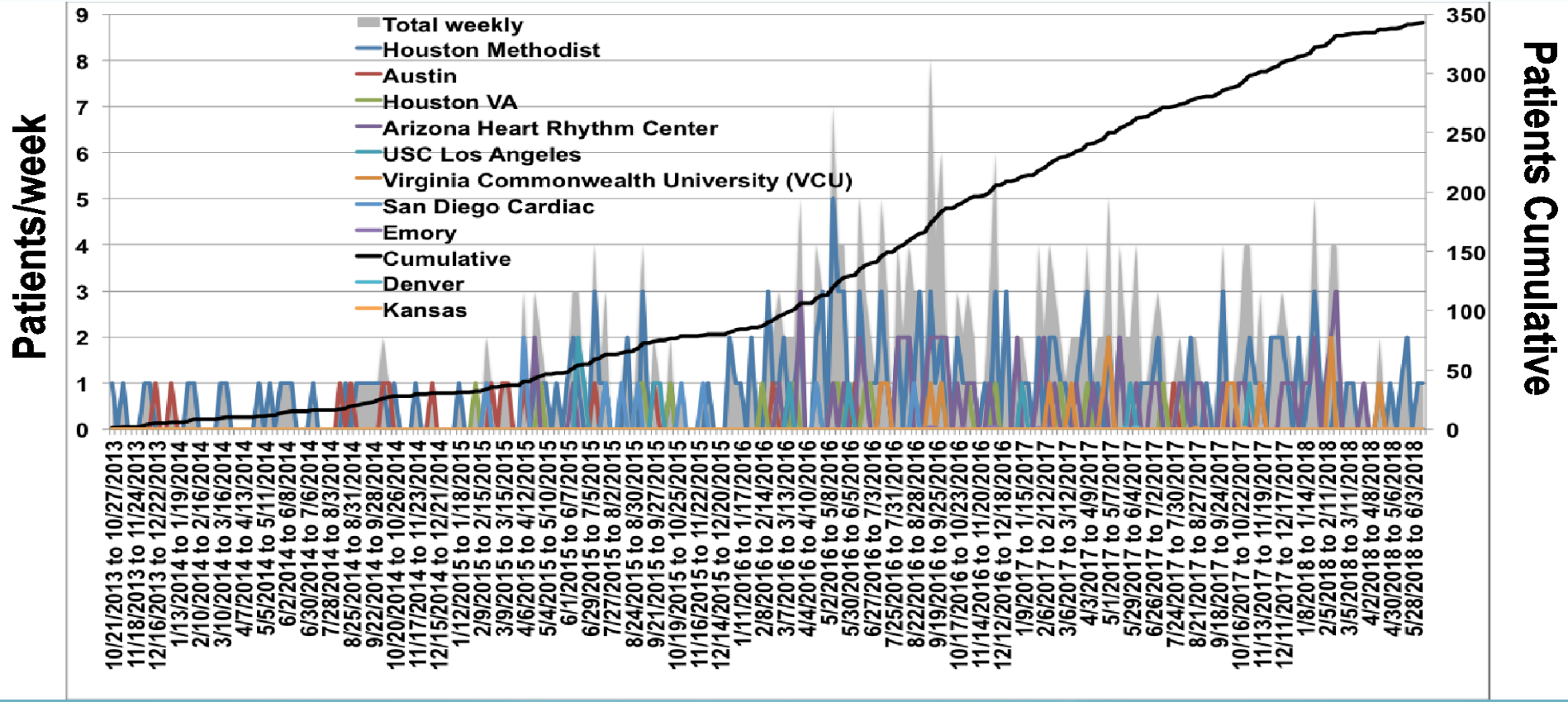

Treatment Goals

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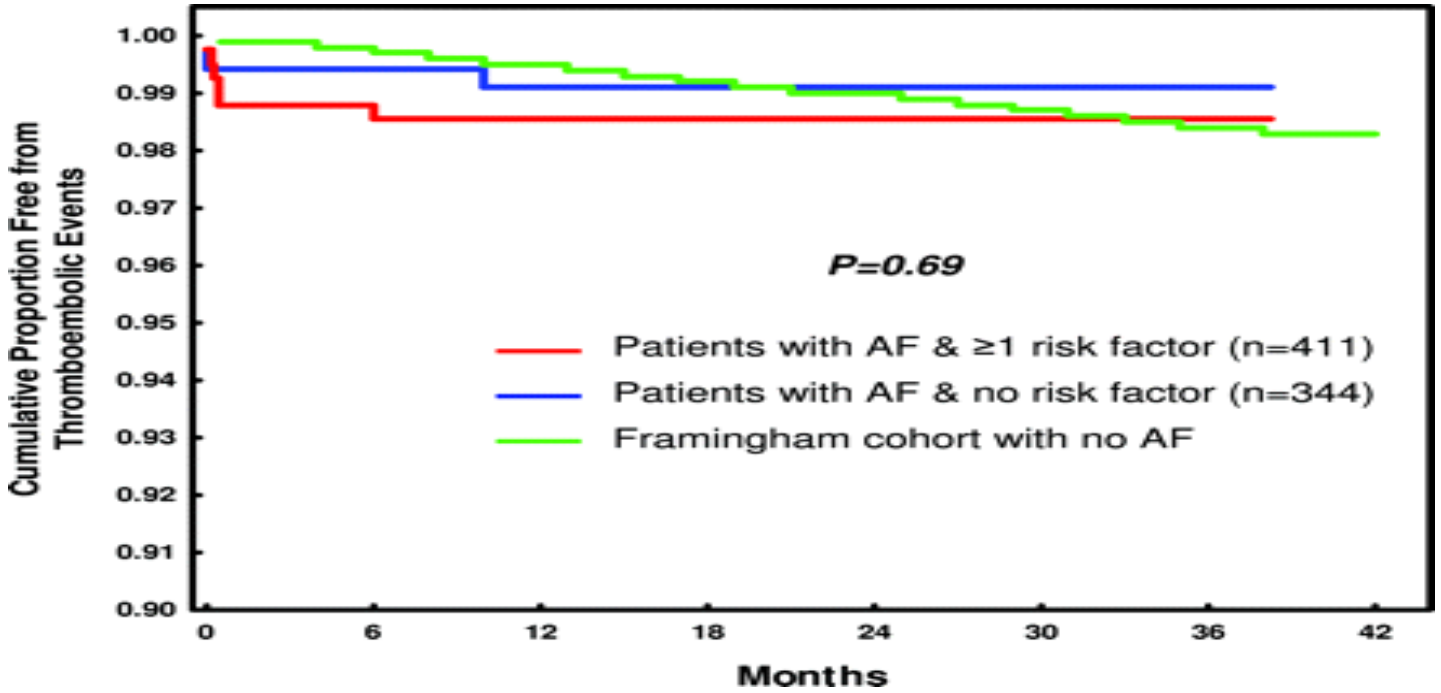
- #1: Symptom suppression
- #2: Improve outcomes:
  - Prevent strokes
  - Prevent tachycardia-induced cardiomyopathy
  - Prevent dementia?
  - Reduce mortality?

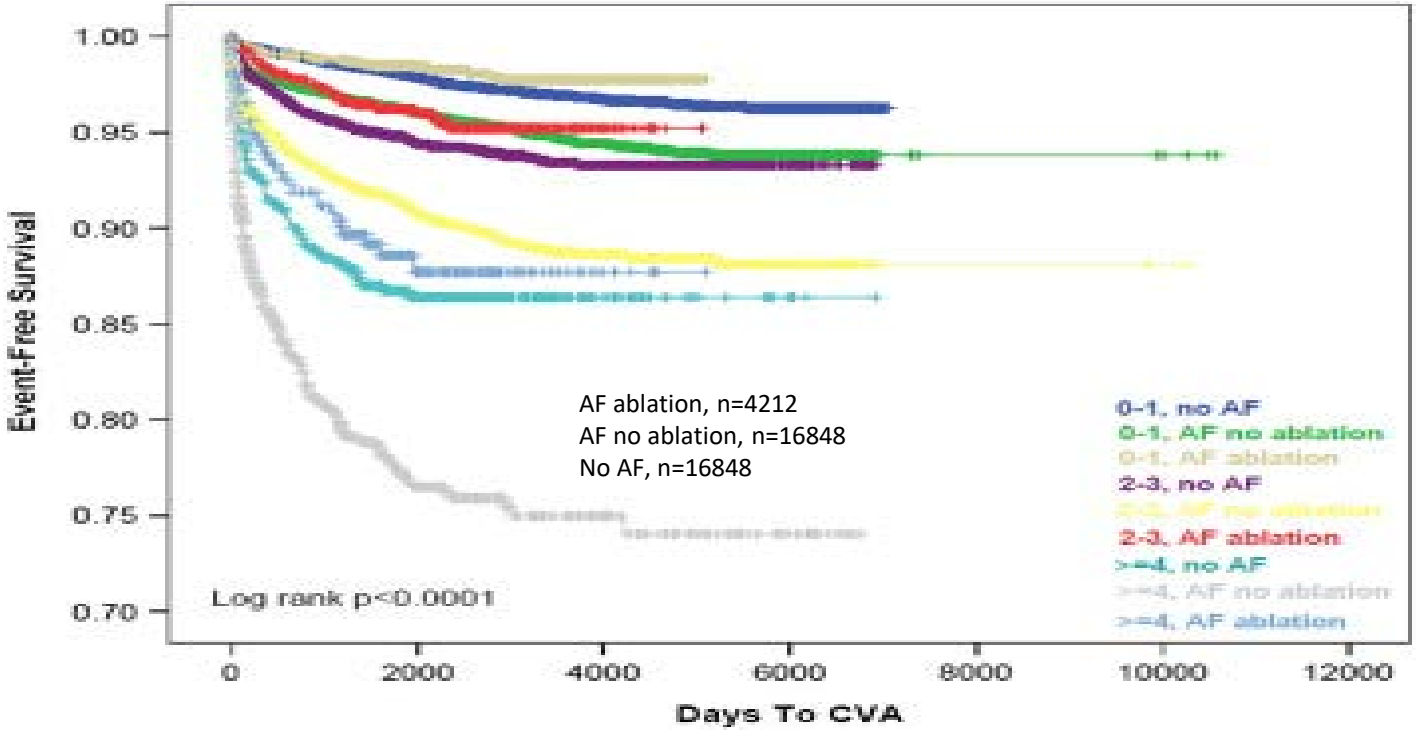
Ablation and Stroke prevention

- Observational studies:



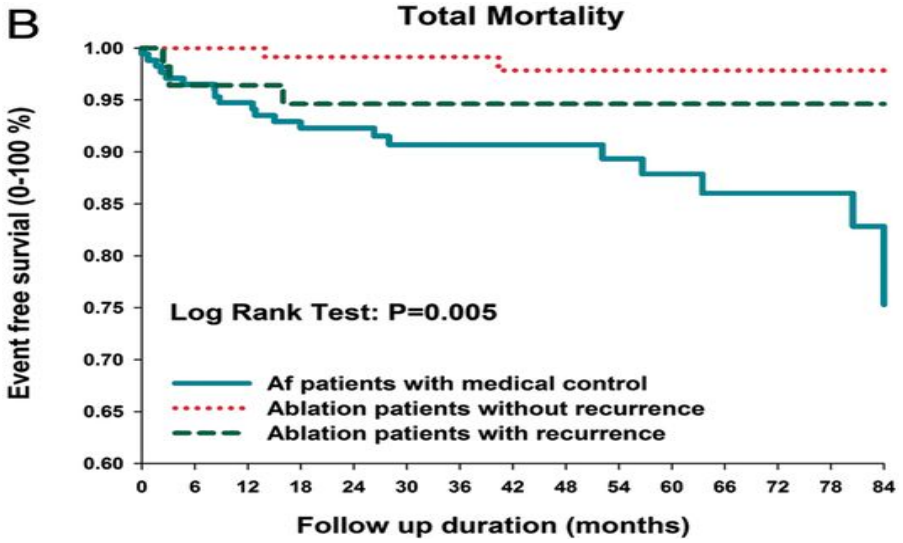
Oral et al *Circulation* 2006;114:759

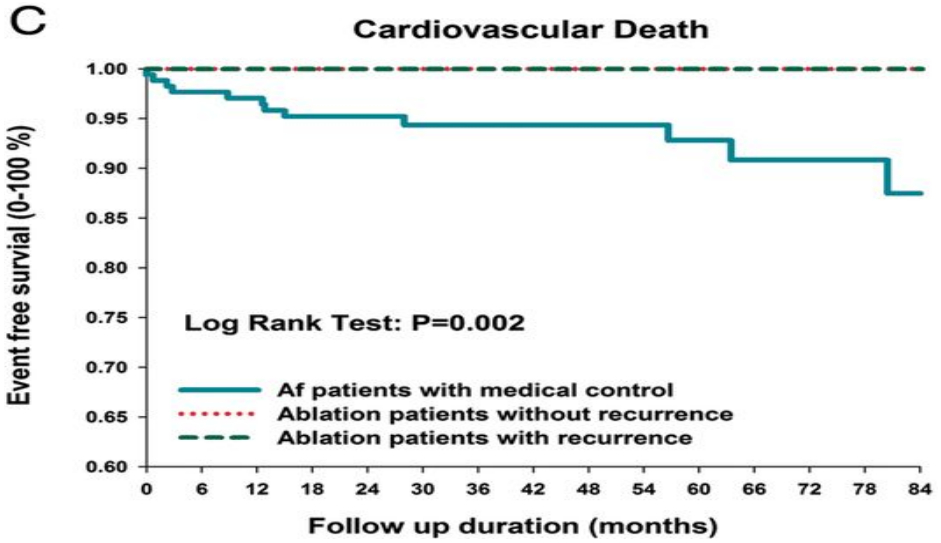
Stroke prevention
AF ablation ~ no AF



Bunch TJ et al *Heart Rhythm* 2013;10:1272

Ablation and Mortality

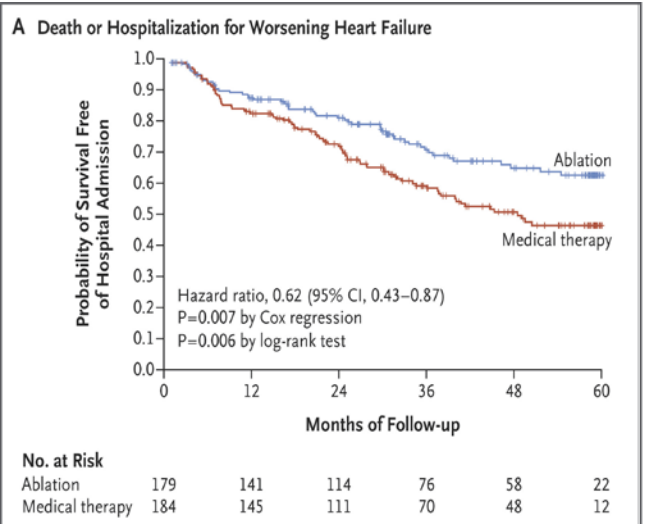


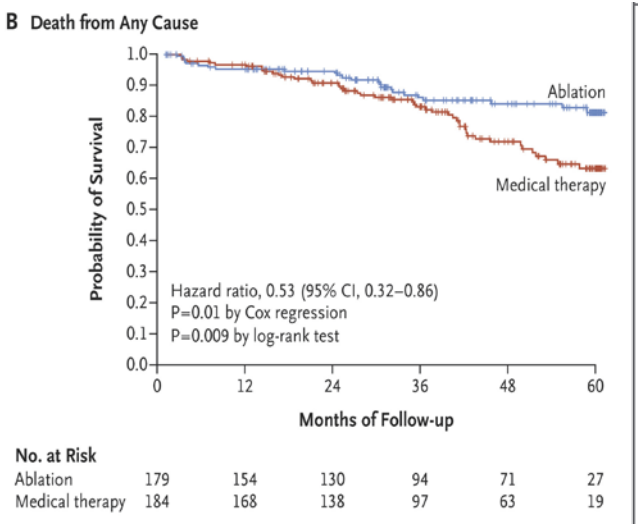


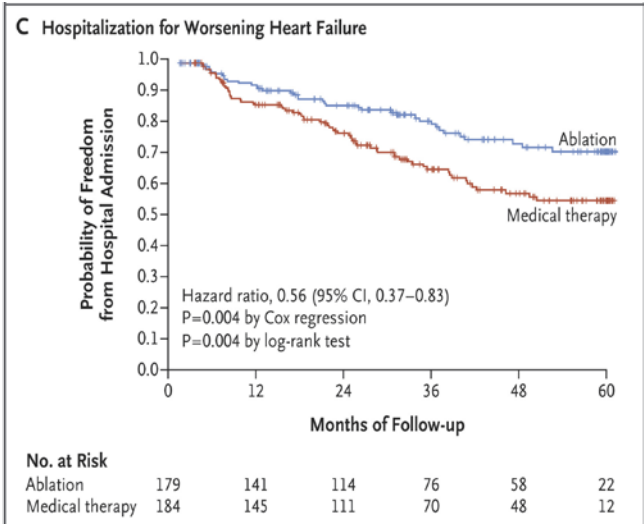
Lin et al *Europace*. 2013;15:676–684

Does AF ablation improve survival?

- AATAC: EF <40%. Lower death from all causes in ablation group (8% vs 18% in amiodarone), 53% reduction. Di Biase et al *Circulation.* 2016;133:1637–1644.
- CASTLE AF: Heart failure population, EF <35%

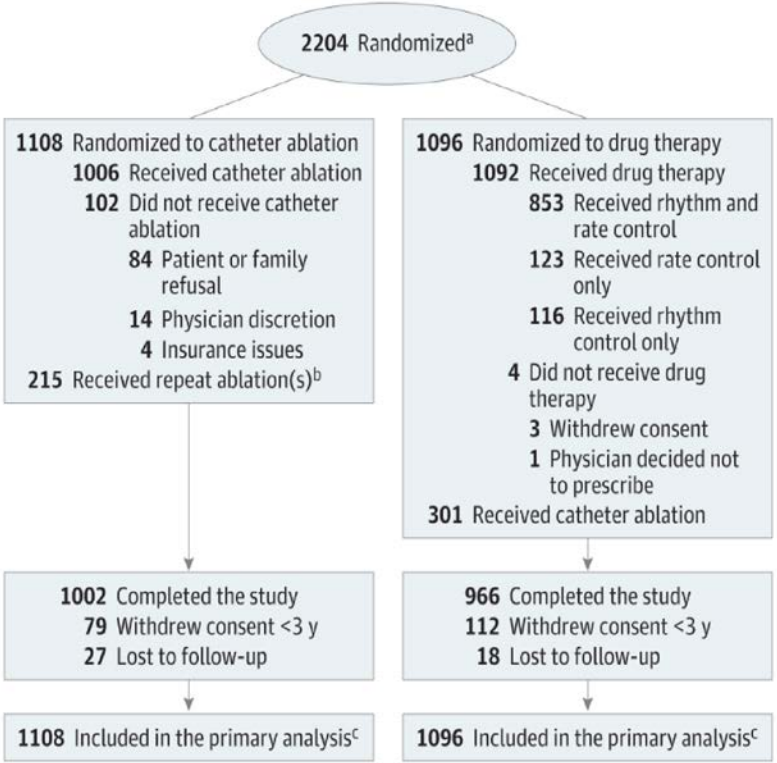






Marrouche et al *N Engl J Med* 2018; 378:417-427

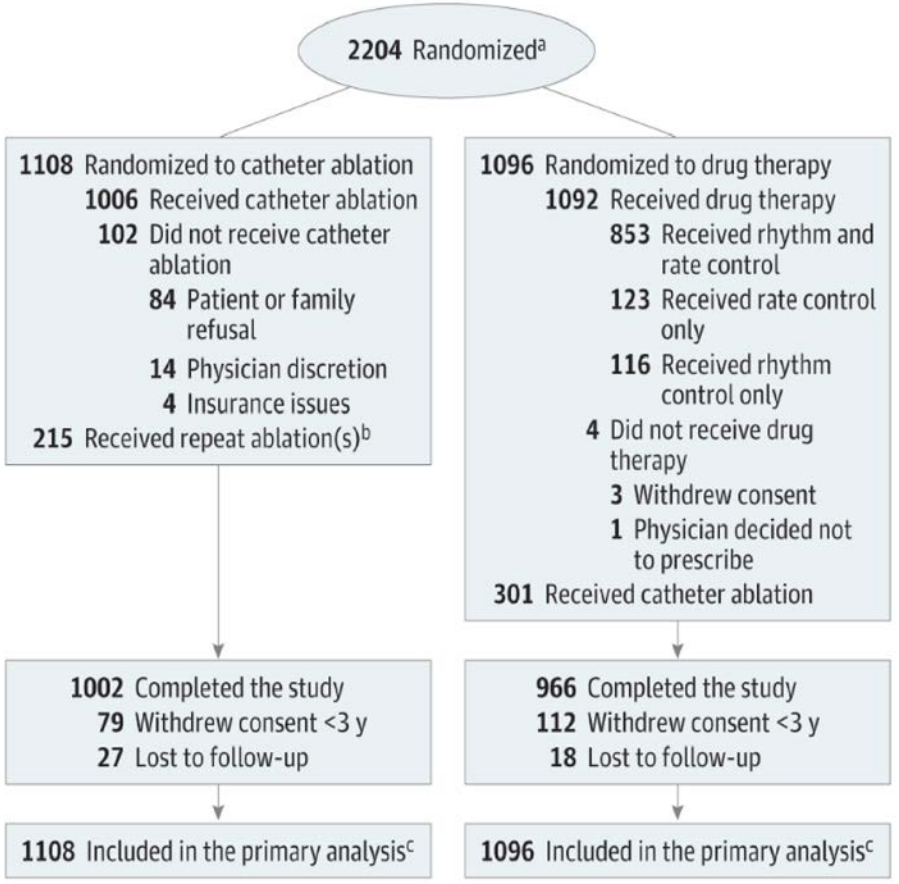
CABANA Trial



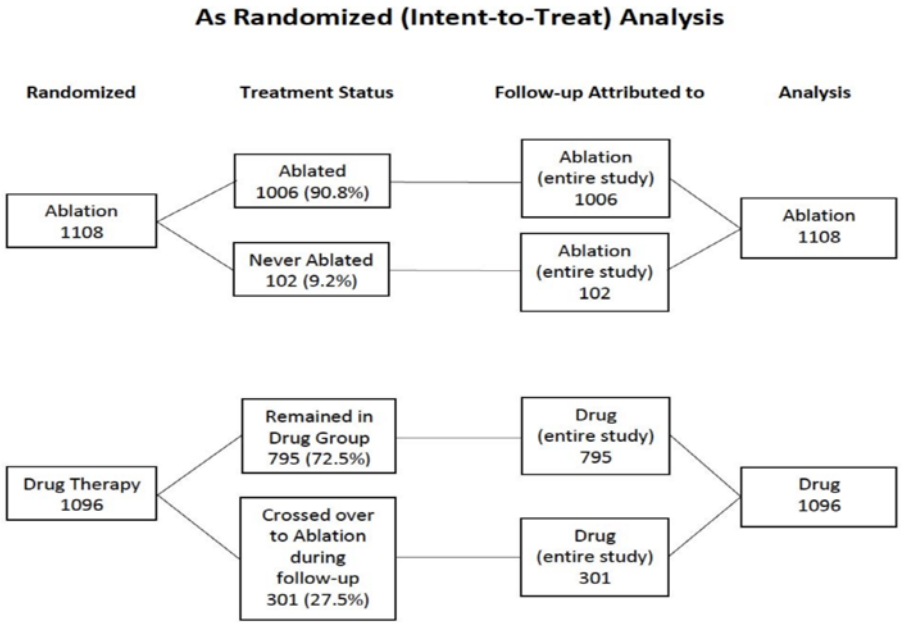
Packer et al *JAMA*. 2019;321(13):1261-1274

CABANA analyses

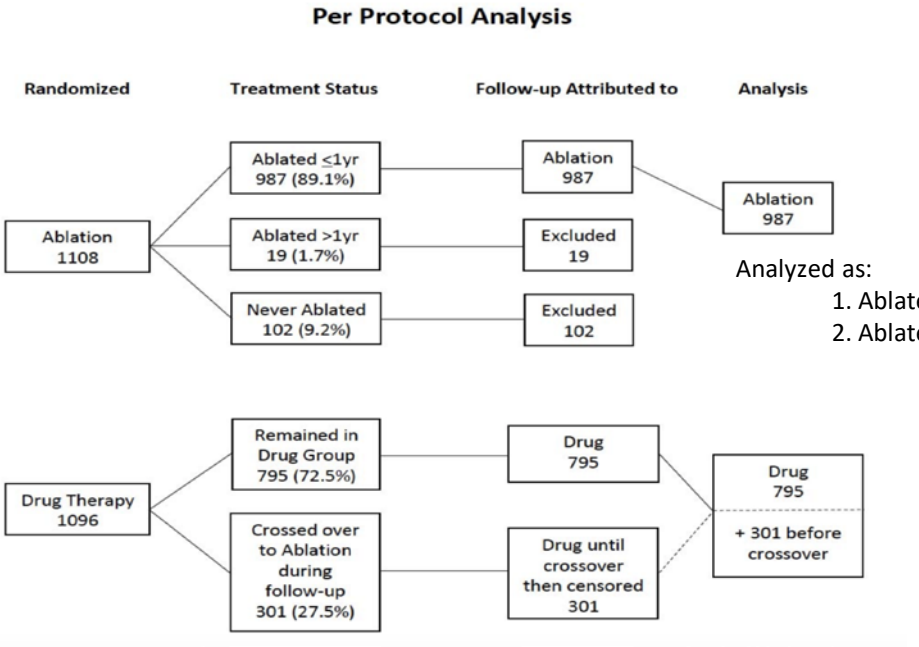
- Primary analysis as “intention to treat”.
- “Per-protocol” comparisons were performed in which :
  - Drug group consisted of all patients randomized to drug therapy, with the follow-up of patients who received drug therapy and crossed over to catheter ablation censored at the time of ablation (n=301).
  - Catheter ablation group included patients randomized to catheter ablation who received an ablation within the 6-month time window following randomization. (censored 102 patients)
- ”Treatment received”: all catheter-ablation treated patients vs drug-treated patients



CABANA "Intention-to-Treat" Analysis



CABANA "Per-protocol" Analysis



Analyzed as:

1. Ablated within 6 mo
2. Ablated within 12 mo

CABANA "Treatment Received" Analysis

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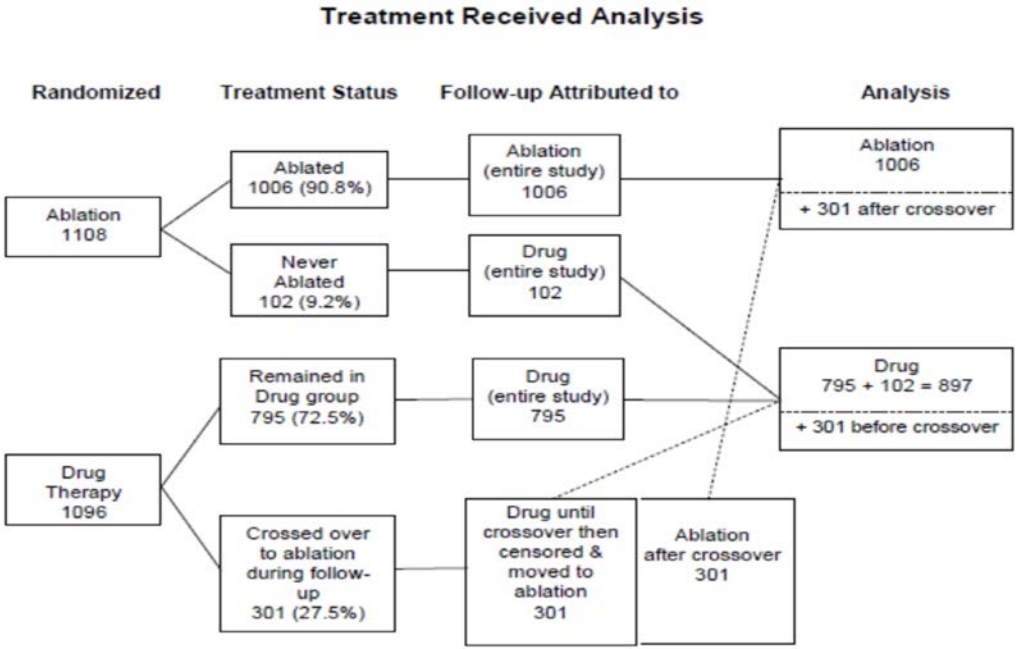

Outcomes by Intention-to-treat

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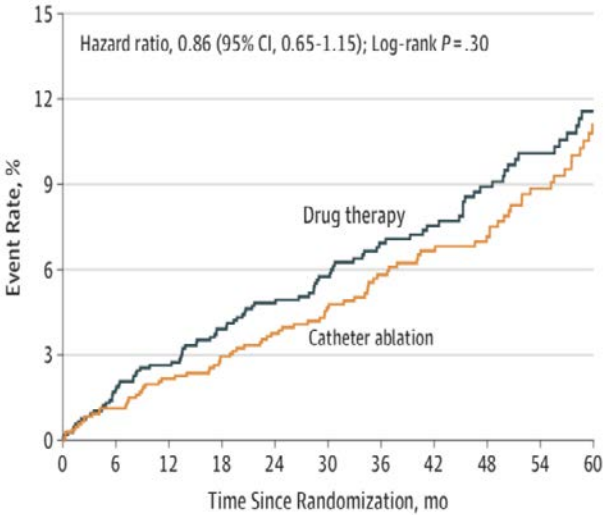
Table 2. Primary and Secondary Outcomes by Intention-to-Treat Analysis

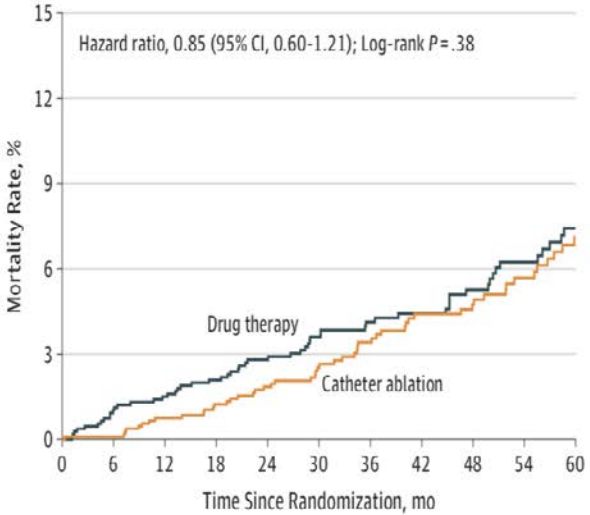
	Events, No. (%)		Kaplan-Meier 4-Year Event Rate, %				
	Catheter Ablation Group (n = 1108)	Drug Therapy Group (n = 1096)	Catheter Ablation Group (n = 1108)	Drug Therapy Group (n = 1096)	Absolute Reduction	Hazard Ratio (95% CI)[a]	*P* Value
Primary end point (death, disabling stroke, serious bleeding, or cardiac arrest)[b]	89 (8.0)	101 (9.2)	7.2	8.9	1.7	0.86 (0.65-1.15)[c]	.30
Components of primary end point							
Death	58 (5.2)	67 (6.1)	4.7	5.3	0.6	0.85 (0.60-1.21)	.38
Disabling stroke	3 (0.3)	7 (0.6)	0.1	0.7	0.6	0.42 (0.11-1.62)	.19
Serious bleeding	36 (3.2)	36 (3.3)	3.0	3.7	0.7	0.98 (0.62-1.56)	.93
Cardiac arrest	7 (0.6)	11 (1.0)	0.7	1.1	0.4	0.62 (0.24-1.61)	.33
Secondary end point							
Death or cardiovascular hospitalization	573 (51.7)	637 (58.1)	54.9	62.7	7.8	0.83 (0.74-0.93)	.001

Outcomes by Intention-to-treat

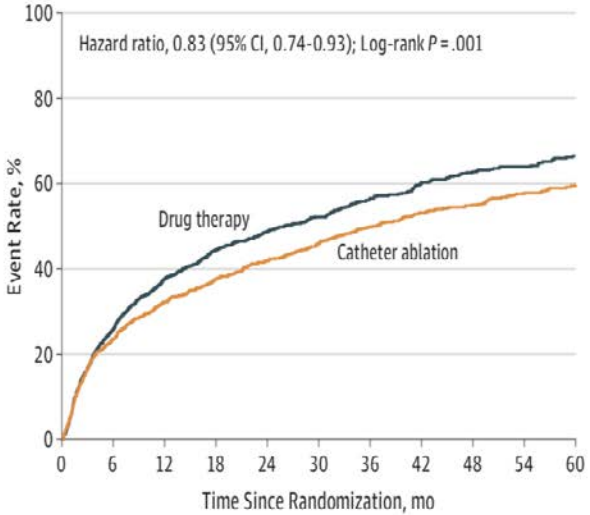
Primary Endpoint:
death, disabling stroke, serious bleeding, or cardiac arrest



All-cause mortality



Death-Hospitalization



Outcomes by Per-protocol analysis

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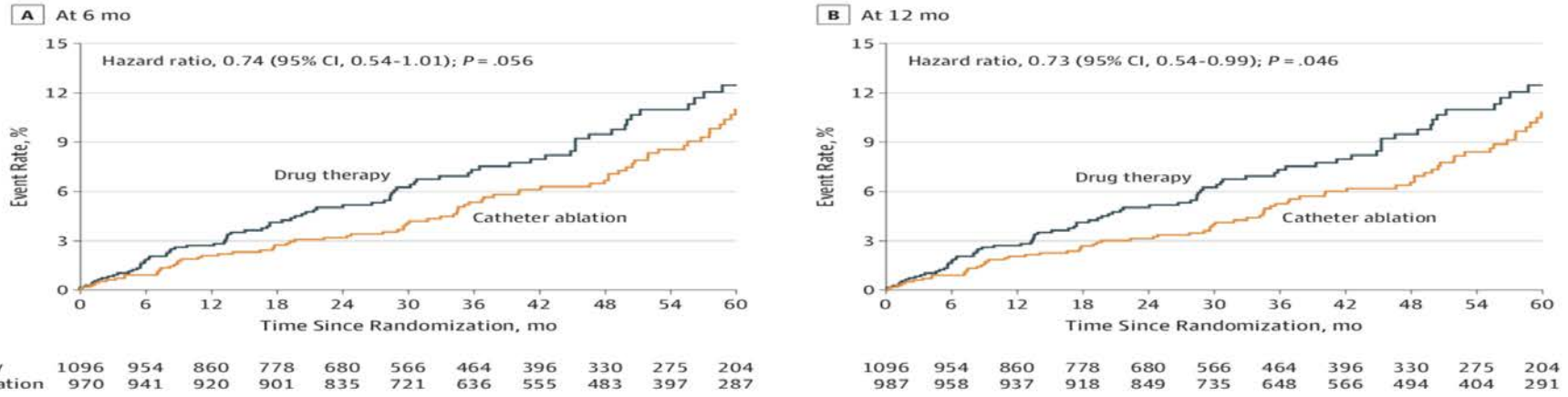
Primary Endpoint:
death, disabling stroke, serious bleeding, or cardiac arrest



No. at risk

Drug therapy	1096	954	860	778	680	566	464	396	330	275	204
Catheter ablation	970	941	920	901	835	721	636	555	483	397	287

Drug therapy	1096	954	860	778	680	566	464	396	330	275	204
Catheter ablation	987	958	937	918	849	735	648	566	494	404	291

Kaplan-Meier estimates of the cumulative risk of death, disabling stroke, serious bleeding, or cardiac arrest (primary end point) by 6-month (A) and 12-month (B) per-protocol analysis. Figure includes patients randomized to catheter ablation who were ablated within 6 months (A) or 12 months (B) after randomization. It also includes all patients randomized to drug therapy, with follow-up censored at crossover to ablation. A, The median (25th, 75th percentiles) length of patient follow-up was 4.1 years (2.6, 5.2) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group. B, The median (25th, 75th percentiles) length of patient follow-up was 4.2 years (2.6, 5.2) in the catheter ablation group and 4.0 years (2.5, 5.2) in the drug therapy group.

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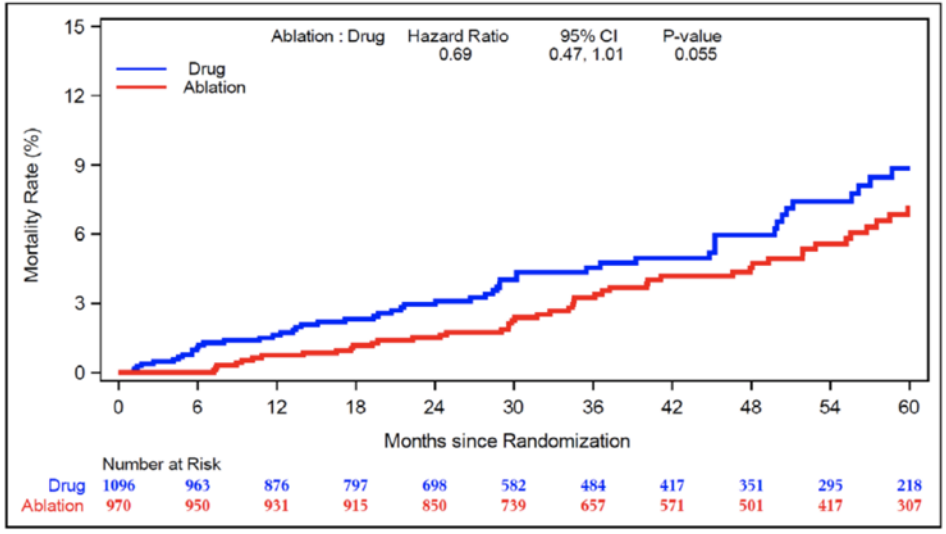
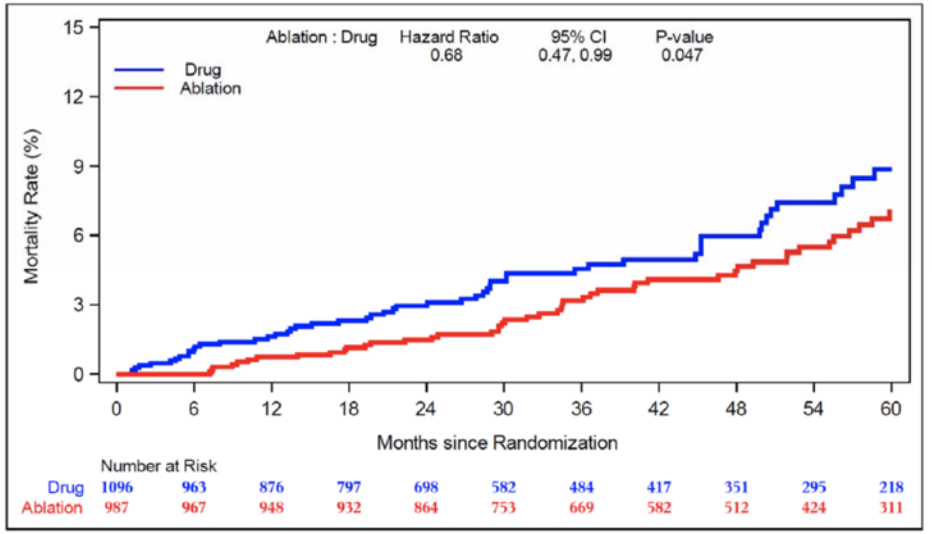
Mortality by Per-protocol analysis

eFigure 1A. Kaplan-Meier Estimates of Mortality (6 Month *Per-Protocol*)
Kaplan-Meier estimates of all-cause mortality by *Per-Protocol* analysis.



eFigure 1B. Kaplan-Meier Estimates of Mortality (12 Month *Per-Protocol*)
Kaplan-Meier estimates of all-cause mortality by *Per-Protocol* analysis.



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Conclusions

- AF ablation is a valuable tool in the management of AF:
  - Greatest impact on symptoms and quality of life
  - Can reduce death-hospitalization
- Valuable as first-line treatment but drug therapy may be more acceptable
- Does not worsen outcomes
- Most effective in paroxysmal AF

Conclusions

- Novel technologies promise to continue improving the safety, efficacy and speed of PV isolation
- The limitations of PV isolation largely remain unaltered by technology
- Rotor mapping remains in search of a role
- Techniques like LAA isolation and VOM ethanol need to refine:
  - Their indications
  - Optimal timing and procedural logistics
- Combination of LAA isolation plus LAA occlusion is particularly attractive from standpoint of rhythm control and stroke prevention