Treatment of atrial fibrillation by advanced ablation technology

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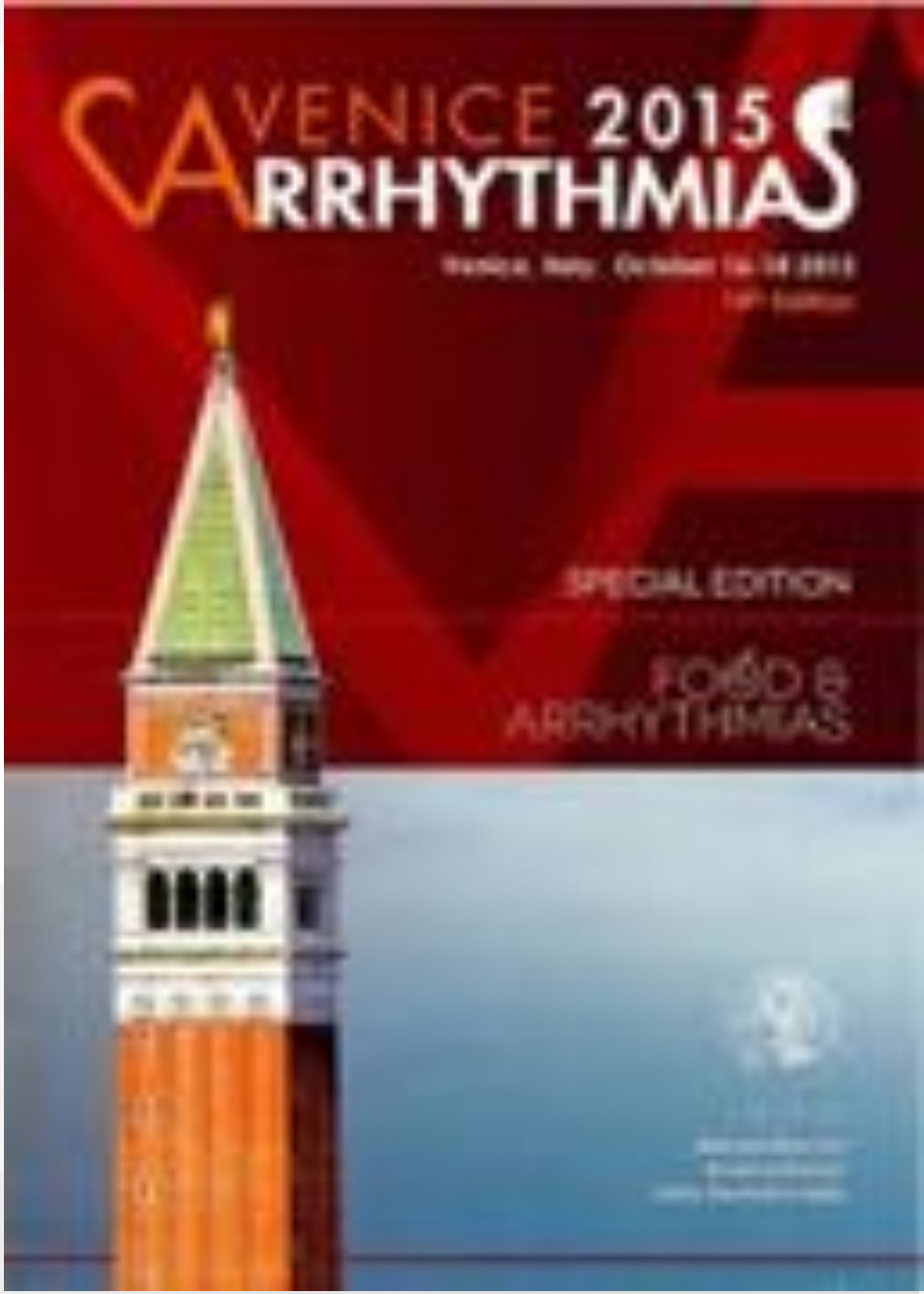
Conflict of interests

- Lecture fees and congress support by:
- Medtronic, Biotronik, St. Jude Medical

Treatment of atrial fibrillation by advanced ablation technology



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Advanced ablation of AF

- Definitions, targets, general results
- Special approaches: „Single shot“ devices
- Fibrosis imaging
- Complex fractionated atrial electrograms (CFAE)
- Ganglionated Plexi (GP), Fad pads
- Left atrial appendage (LAA)
- Rotors

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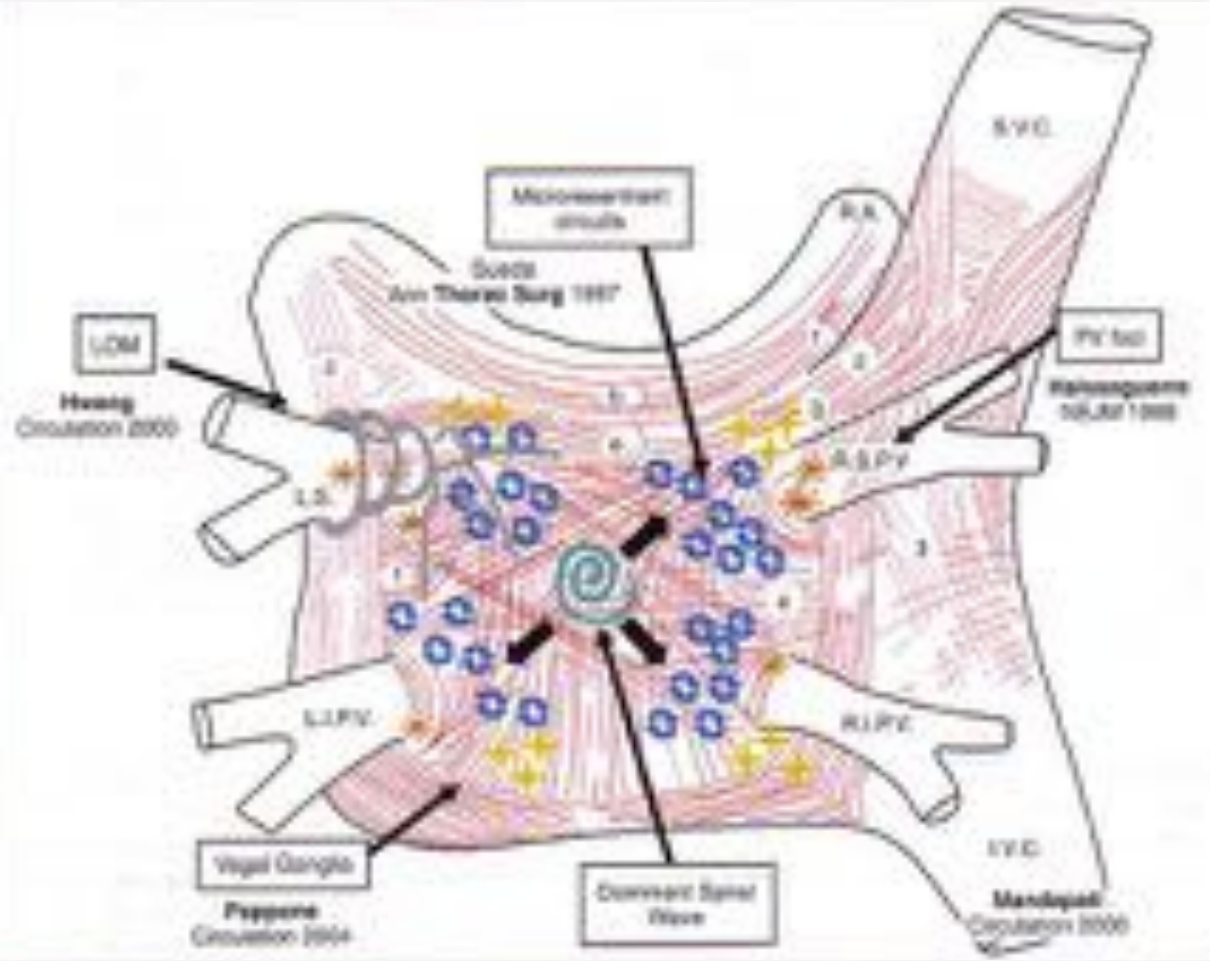
A new classification of clinical types of atrial fibrillation as proposed by the Consensus Conference of AFNET/ European Heart Rhythm Association (from Kirchhof et al.)

AF type	Clinical presentation	Possible pathophysiology
Defined types of AF		
Monogenic AF	AF in patients with inherited cardiomyopathies including channelopathies	The arrhythmogenic mechanisms conveying sudden death in these diseases also contribute to the occurrence of atrial fibrillation
Focally induced AF	Patients with repetitive atrial runs and frequent, short episodes of paroxysmal atrial fibrillation. Often highly symptomatic, younger patients with distinguishable atrial waves (coarse AF), atrial ectopy, an ever atrial tachycardia deteriorating in AF	Localized triggers, in most cases originating from the pulmonary veins, initiate AF. AF due to one or few re-entrant circuits is also considered to be part of this type of AF
Post-operative AF	Atrial fibrillation occurring after cardiac/pulmonary surgery in patients who were in sinus rhythm before surgery and had no prior history of AF	Acute factors: inflammation, surgical trauma, high sympathetic tone, electrolyte changes, and volume overload, potentially interacting with a chronic predisposition
Complex types of AF		
Valvular AF	Atrial fibrillation manifesting before senescence (e.g. <80 years) in patients with mitral stenosis or patients after mitral valve surgery	Left atrial pressure (stenosis) and volume (regurgitation) load contributes to atrial enlargement and structural atrial damage in these patients.
AF in the elderly	AF which first manifests at an age >80 years	Ageing of the atria (possibly including 'accelerated ageing'). Interstitial fibrotic infiltration, loss of cardiomyocytes, increased arterial and myocardial stiffness contribute to this type of AF
Polygenic AF	This type of AF is defined by the presence of common gene variants which are associated with early onset AF in the population	Currently under study, possibly including shortening of the left atrial action potential and/or left atrial cardiomyocytes with abnormal automaticity
Unclassified AF	AF which does not fulfil any of the other definitions. These forms of AF may be rather common, illustrating the need for a better classification	Shortening of atrial refractoriness (e.g. tachycardia-induced atrial remodelling or enhanced parasympathetic tone) or localized conduction disturbances due to atrial fibrosis induced by structural heart disease may contribute to this type of AF

Kuck et al., EHJ, 2014

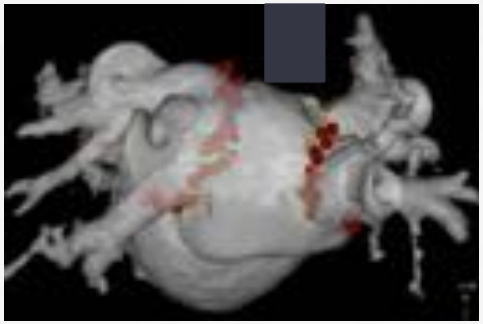
Arrhythmogenic targets of AF in the LA

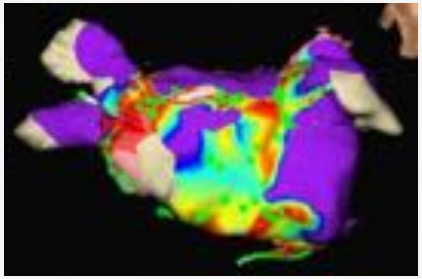


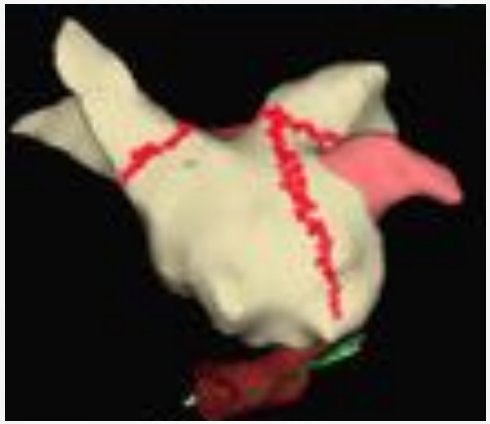
Summary of the electrophysiologic substrate in posterior left atrial wall amenable to catheter ablation using the linear approach.

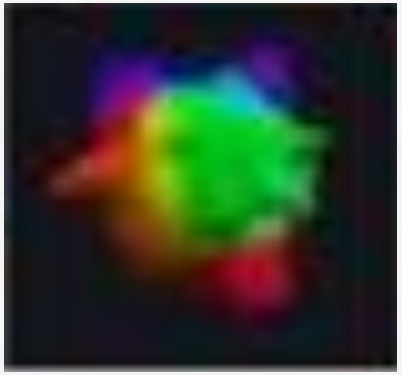
Huang,SKS.,Wood,MA; Catheter Ablation of Cardiac Arrhythmias; Saunders Elsevier.2006.

AF Ablation Strategies

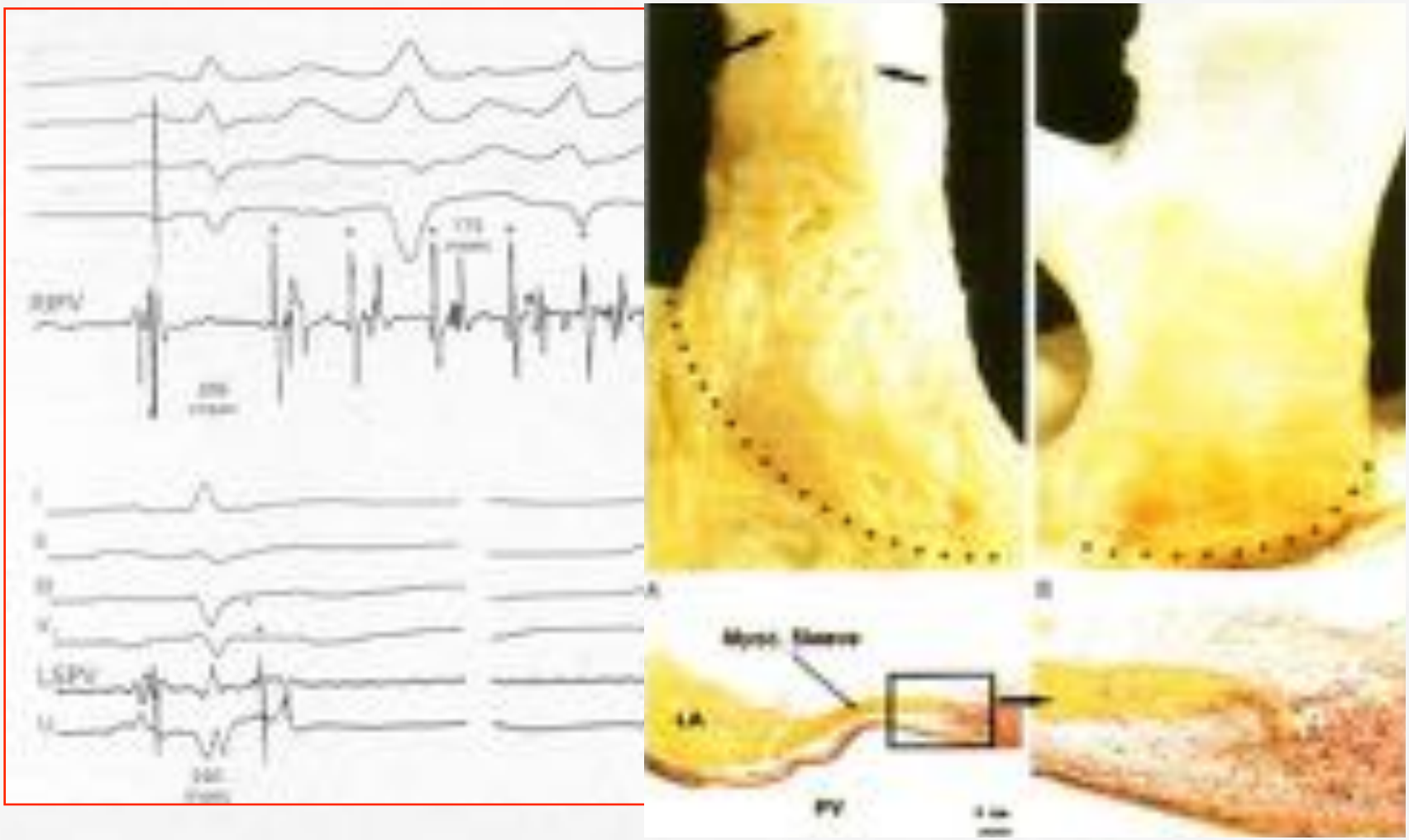








Pioneer work: „Spontaneous initiation of AF by ectopic beats origination in the pulmonary veins“



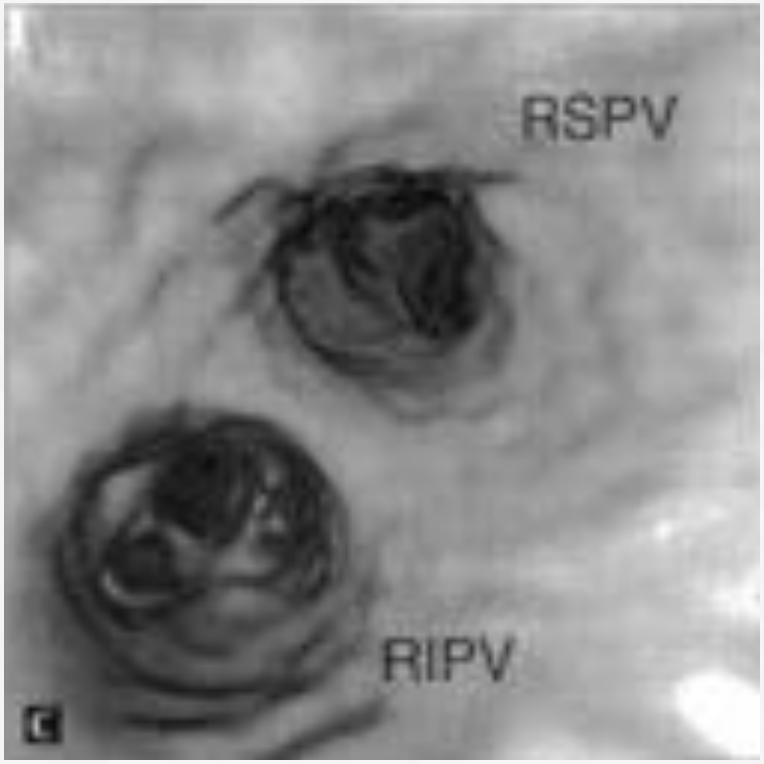
Haissaguerre, N Engl J Med 1998.

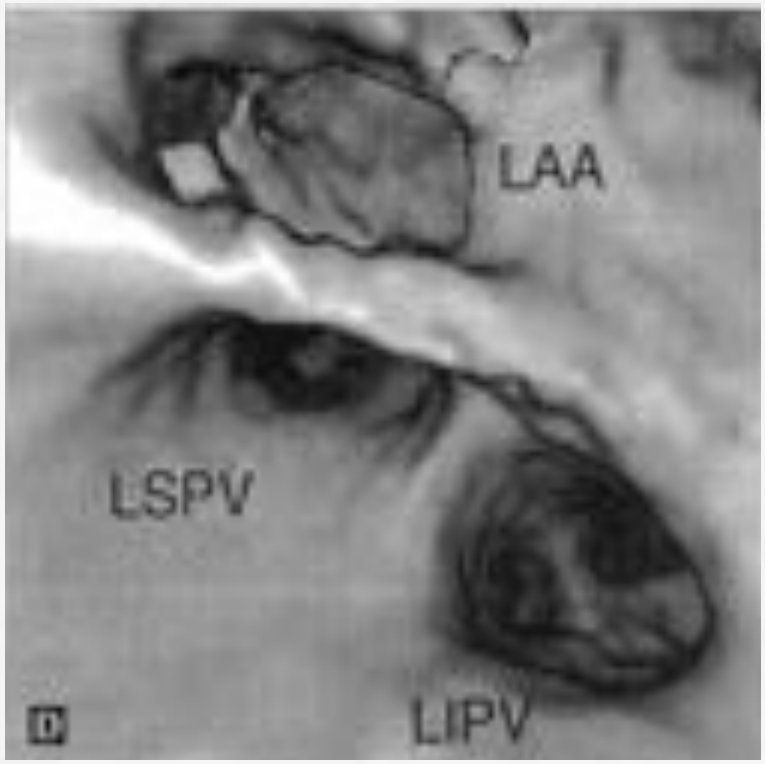
Recommendations for left atrial ablation

Catheter ablation of AF should target isolation of the pulmonary veins.	IIa	A	170, 172, 192, 194

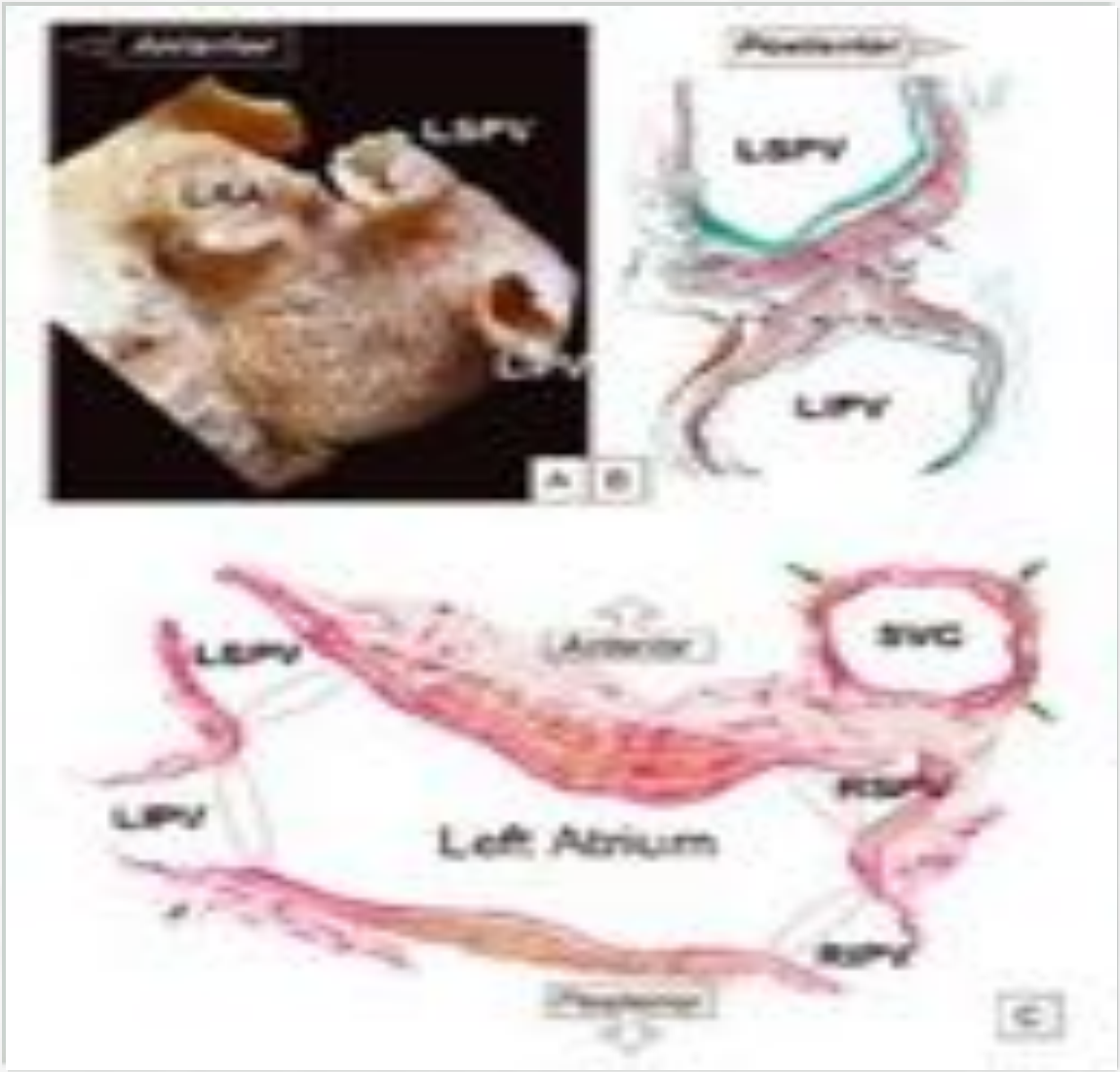
European Heart Journal (2012) 33, 2719-2747.

MRI relationsship of the pulmonary vein ostia and left atrial appendage





LA and PV's - anatomic relations

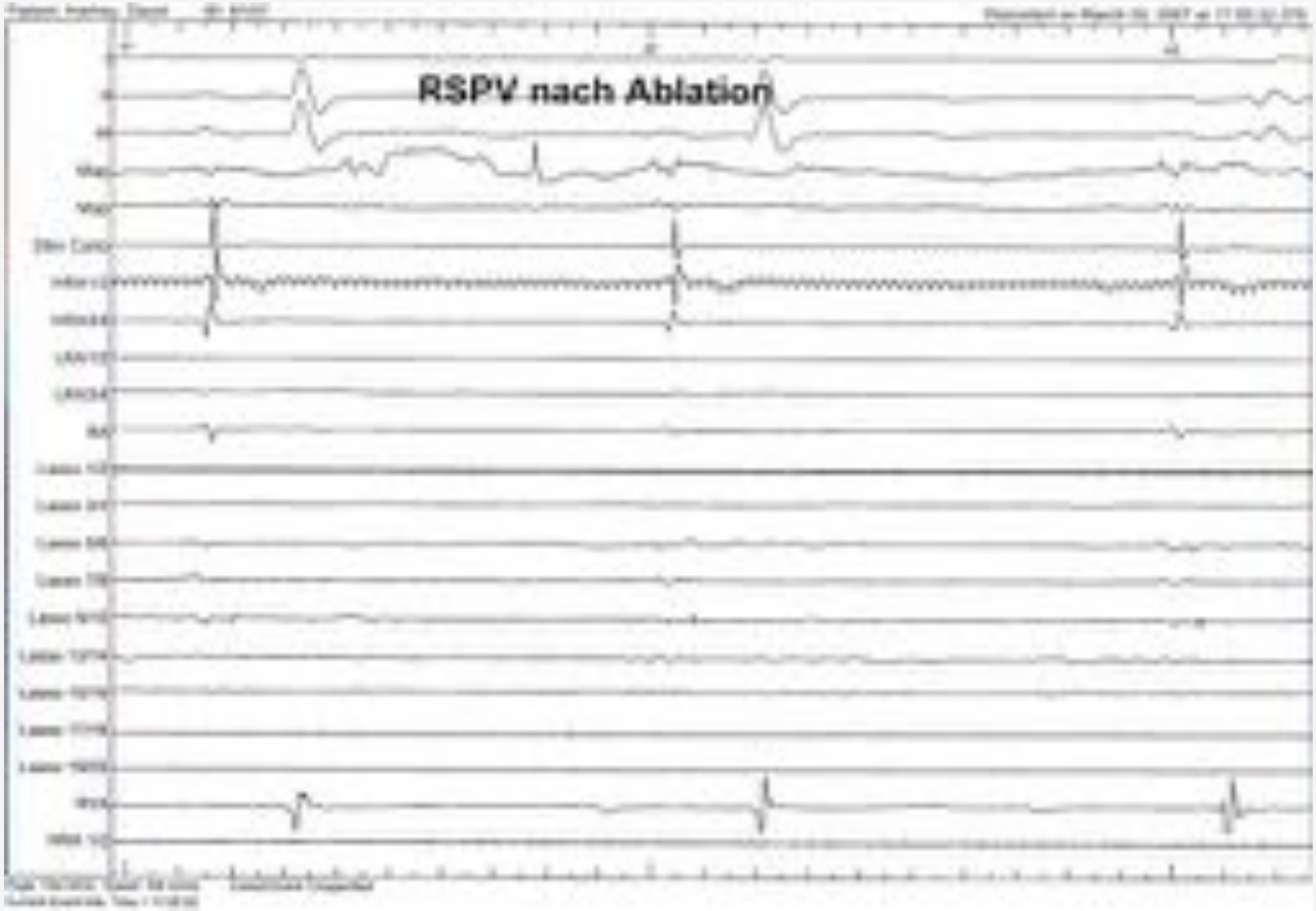


Venice Chart International Consensus Document on Atrial Fibrillation Ablation: 2011 Update

Patrick et al, Cardiovasc Electrophysiol, Vol, pp. 500-525, August 2012

Electrical isolation of the PV

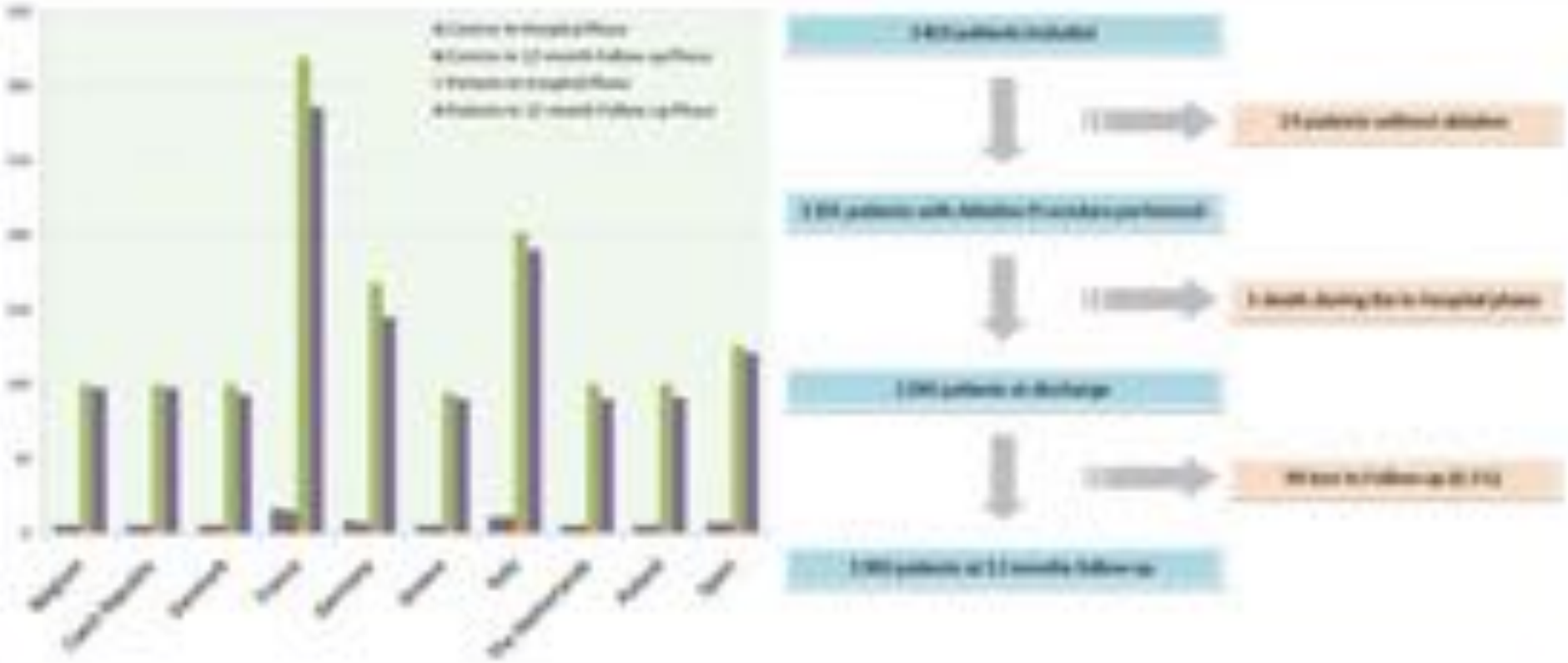
Electrical isolation of the PV



The Atrial Fibrillation Ablation Pilot Study: a European Survey on methodology and results of catheter ablation for atrial fibrillation conducted by the European Heart Rhythm Association

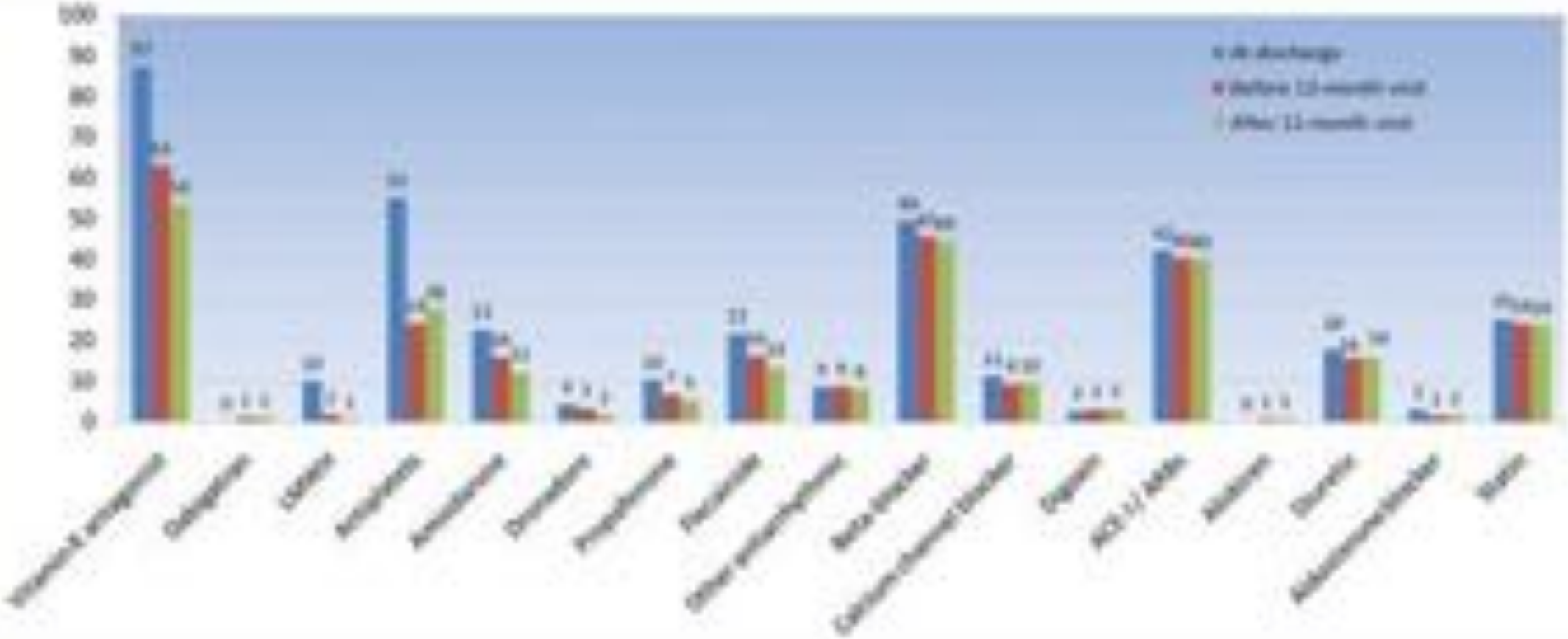
Arbelo E et al., Eur Heart J 2014

Distribution of centres and patients included in the Atrial Fibrillation Ablation Pilot by country



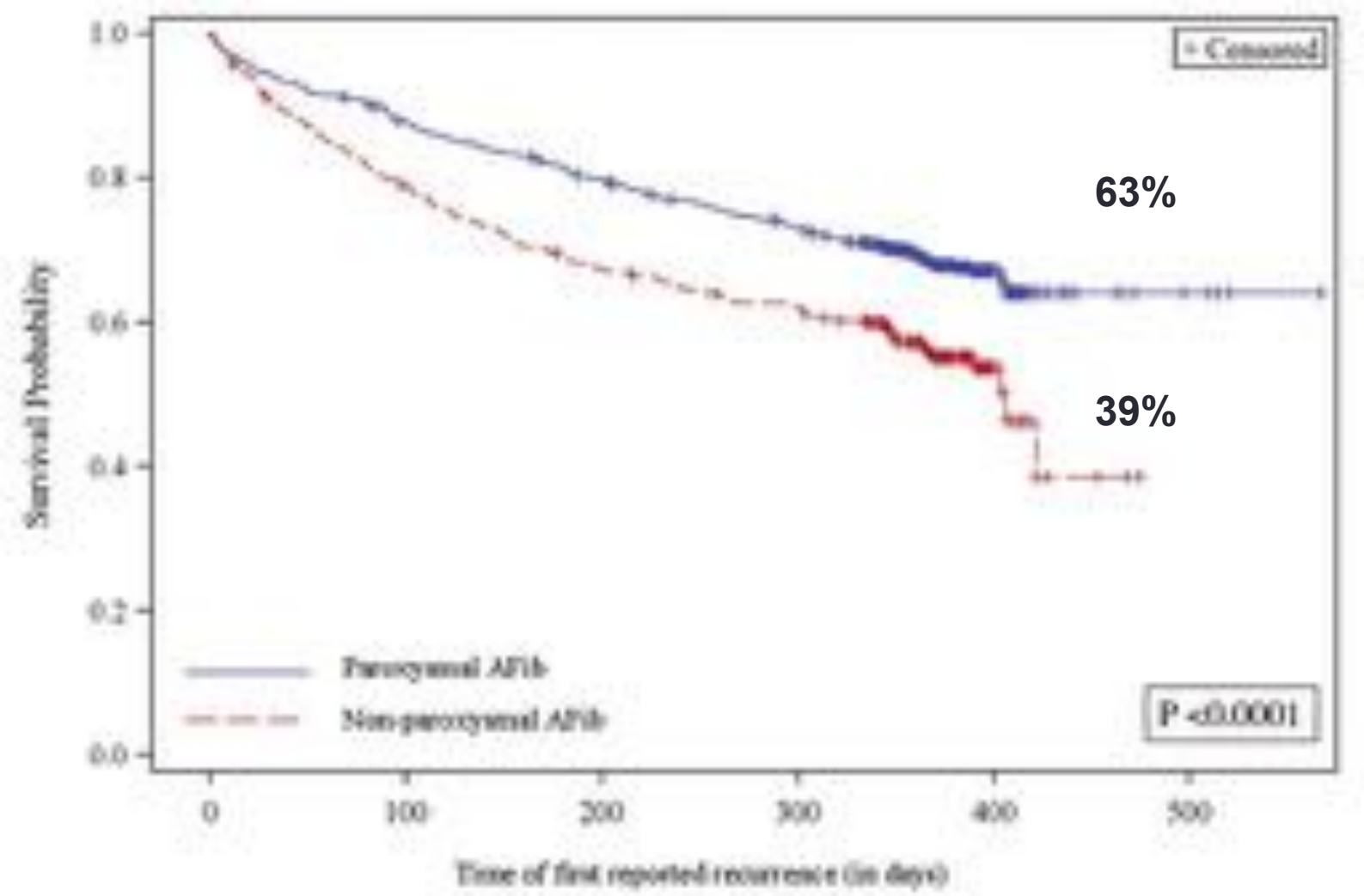
Arbelo E et al, EHJ, 2014

Rate of use of pharmacological treatment at discharge and at the 12-month follow-up



Arbelo E et al, EHJ, 2014

Kaplan– Meier arrhythmia-free survival curve by type of atrial fibrillation



Arbelo E et al, EHJ, 2014

The atrial fibrillation ablation - Pilot Study

72 centres in 10 European countries
from Oct 2011 - May 2012

1391 1st AF ablations

Arrhythmia documentation by:

- ECG	76%
- Holter	52%
- Transtelephonic monitoring	8%
- Implanted system (Reveal)	4,5%

Over 50% of the patients become asymptomatic
21% of the patients were readmitted due to post ablation arrythmias

Arbelo E et al, EHJ, 2014

Success rates in relationship with the type of atrial fibrillation

Type AF	No. countries	No. centres	No. patients
Paroxysmal	10	70	871
Persistent	10	61	265
Long-lasting persistent	10	40	90
Overall	10	70	1226

	Success without antiarrhythmic drugs (AADs)*		Success with antiarrhythmic drugs (AADs)*		Overall success*	
Type AF	*n* (%)	Median (IQR) between countries	*n* (%)	Median (IQR) between countries	*n* (%)	Median (IQR) between countries
Paroxysmal	381 (43.7)	42.0 (39.4–51.9)	256 (29.4)	29.6 (4.8–42.5)	647 (74.3)	72.1 (70.7–75.4)
Persistent	80 (30.2)	27.0 (17.9–47.1)	99 (37.4)	41.2 (17.6–55.6)	191 (72.1)	70.5 (64.7–76.5)
Long-lasting persistent	33 (36.7)	42.9 (31.6–50.0)	18 (20.0)	22.2 (14.3–28.9)	52 (57.8)	56.3 (25.0–64.7)
Overall	494 (40.3)	41.1 (28.6–50.0)	373 (30.4)	28.9 (18.5–41.6)	890 (72.6)	70.5 (58.8–75.4)

Arbelo E et al, EHJ, 2014

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„all in one device“
PVAC-Catheter

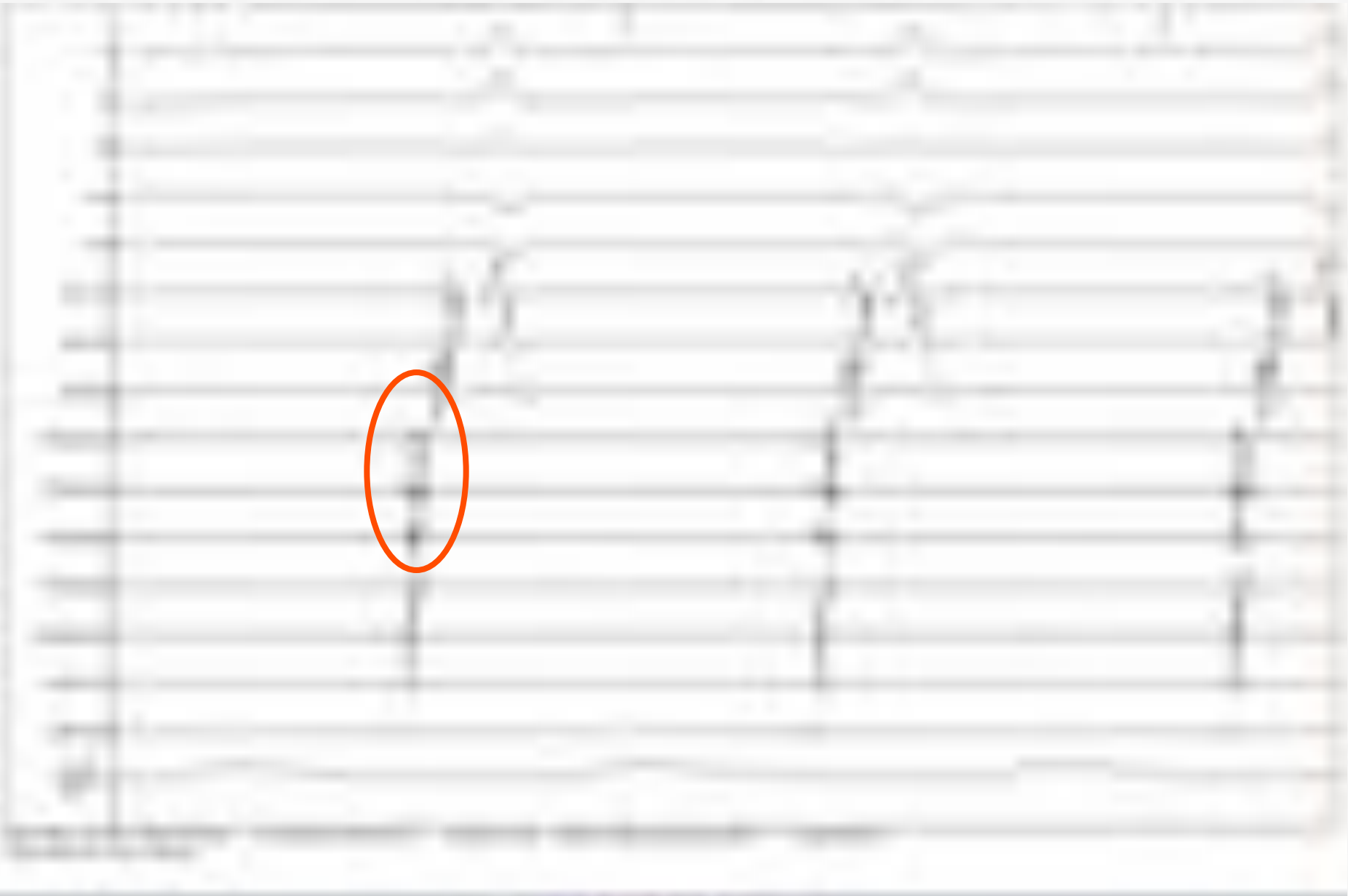
1st Generation

„Lasso“-Map and RF-Ablation

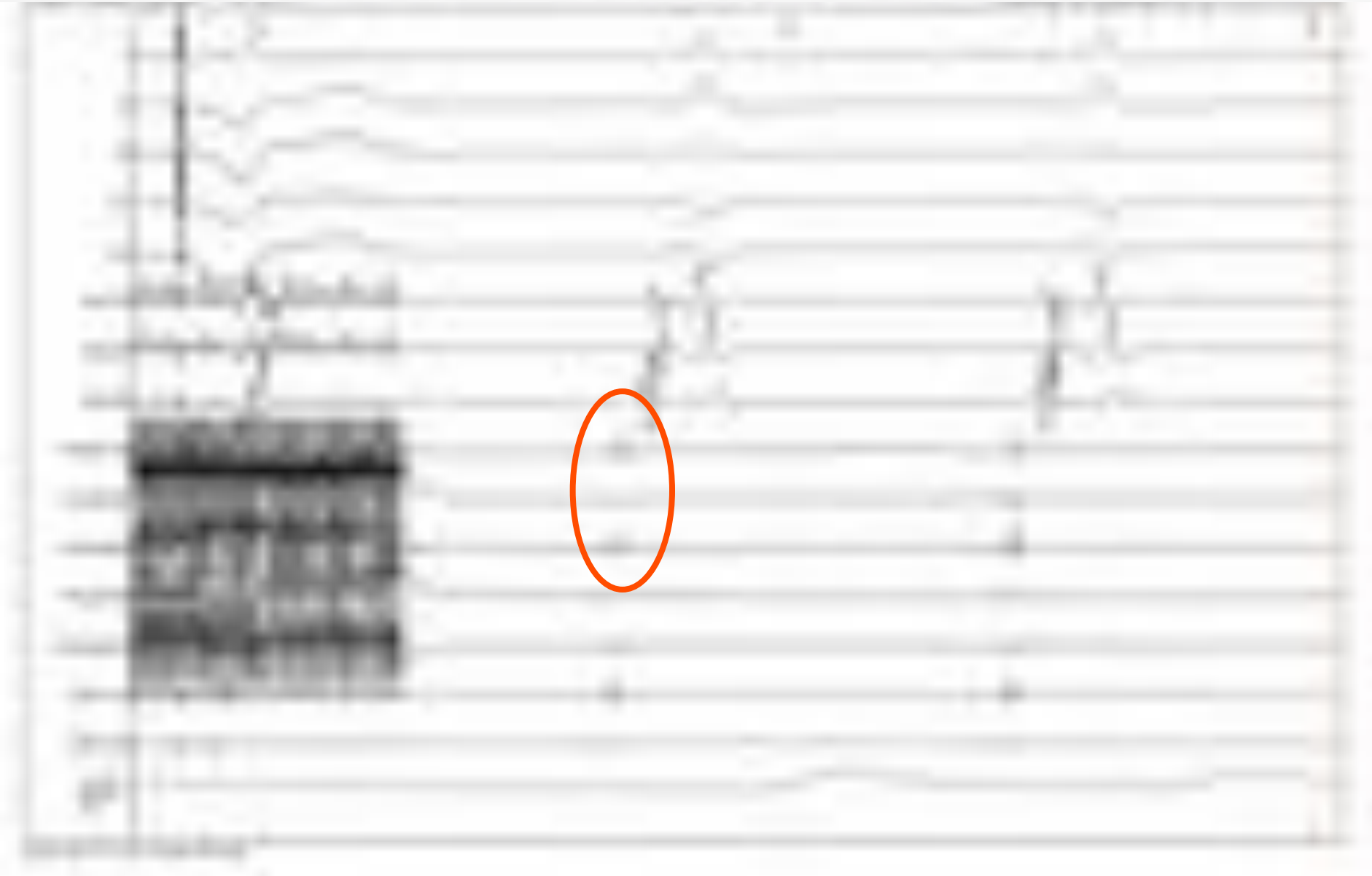
1st edition: 10 –polar circular catheter for mapping and ablation using duty-cycled and alternating (unipolar and bipolar) energy

ICE: PVAC in RIPV

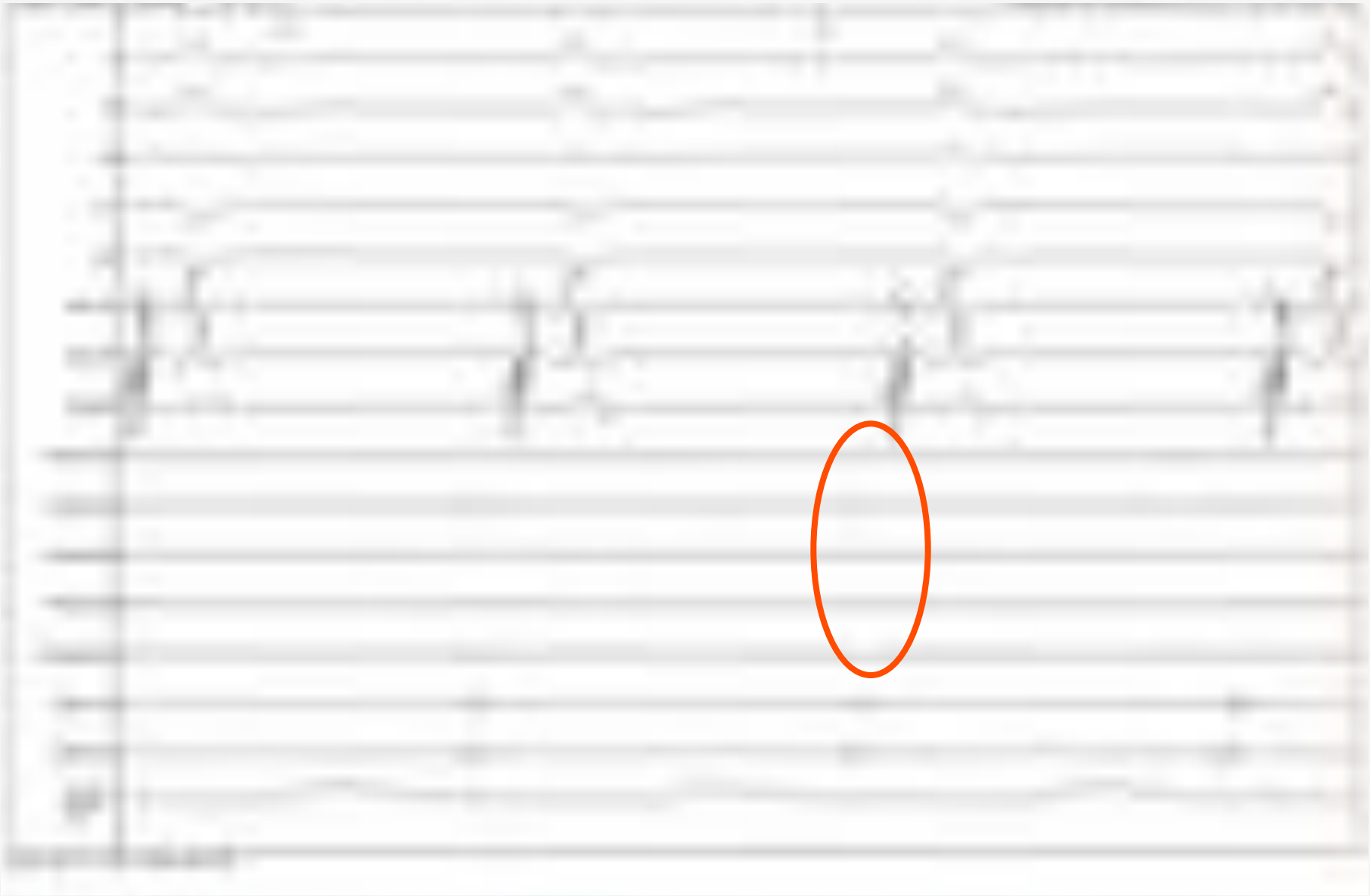
LA/PV-Signals on PVAC – before ablation



LA/PV-Signals on PVAC – after 1st ablation



LA/PV-Signals on PVAC – final result - entry block

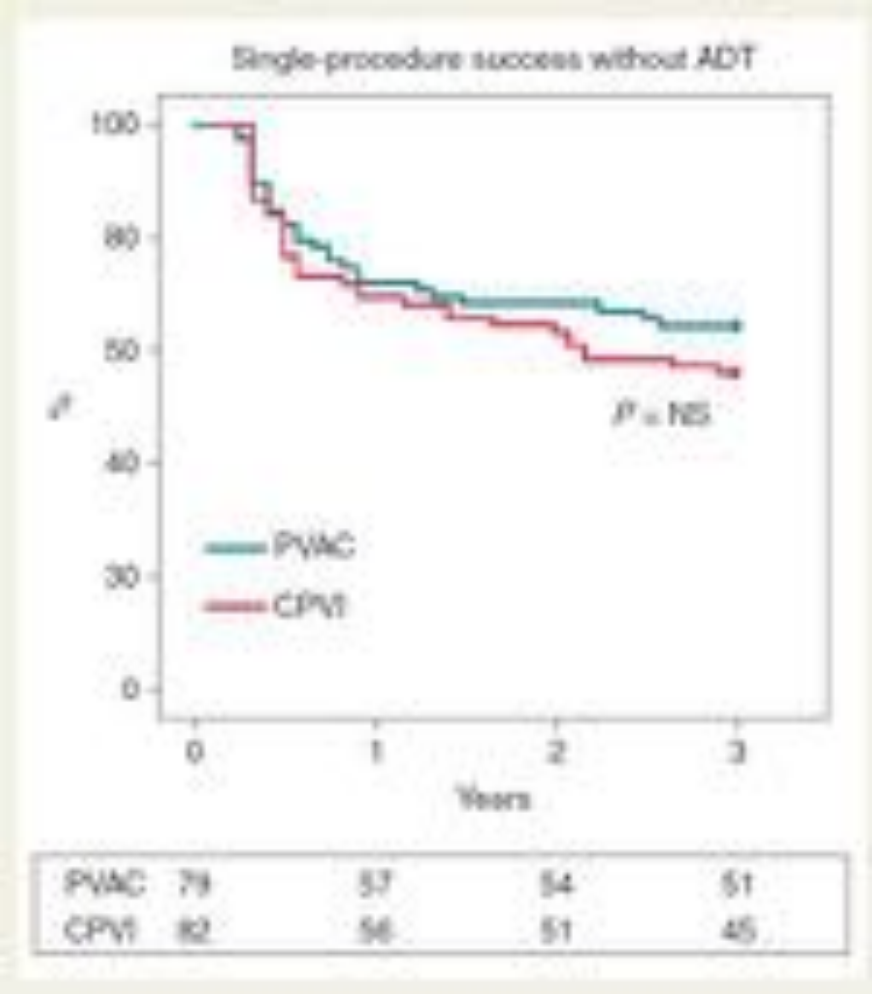


LA/PV-Signals on PVAC – exit block

Duty-cycled multi-electrode radiofrequency vs. conventional irrigated point-by-point radiofrequency ablation for recurrent atrial fibrillation: comparative 3-year data

De Greef et al, Europace 2014

Kaplan-Meier plot representing the time to documented recurrence during the 3 years follow-up period



At 3 years,single-procedure success off-drugs in PVAC-guided ablation was comparable to conventional PVI (65% vs. 55%, P ¼ NS).

De Greef et al, Europace 2014

PVAC vs. point by point RF ablation in AF

	Technique	Patients (N)	Success %	FU duration
Paroxysmal atrial fibrillation (PAF)				
Bulava et al[illegible]	PVAC	11	36	200 ± 13 days
	Point by point	11	71	
Khaykin et al.[illegible]	PVAC	11	47	6 months
	Point by point	19	54	
Bauernfeind et al.[illegible]	PVAC	89	42	347 ± 139 days
	Point by point	96	66	
Chun et al.[illegible]	PVAC	30	73	6 months
	Point by point	43	49	
Tang et al.[illegible]	PVAC	17	34	>12 months (> or >1)
	Point by point	47	68	
Persistent atrial fibrillation (PERS) AF				
Chun et al.[illegible]	PVAC	9	56	6 months
	Point by point	28	25	
Tang et al.[illegible]	PVAC/PVAC/PVAC	22	46	>12 months (> or >1)
	Point by point + substrate	23	61	
PAF → PERS AF				
Bünner et al.[illegible]	PVAC	40	72	214 ± 99 days
	Point by point	40	68	

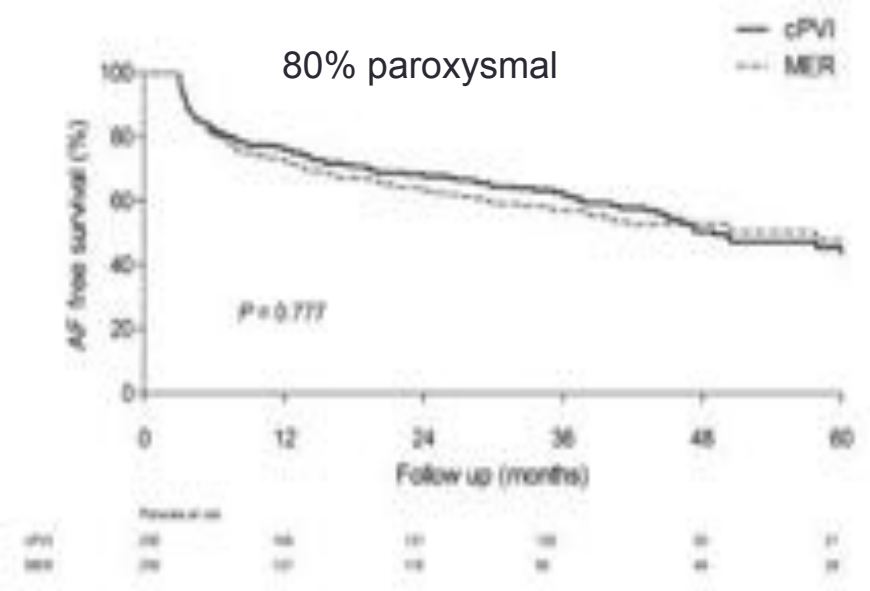
FU, follow-up.

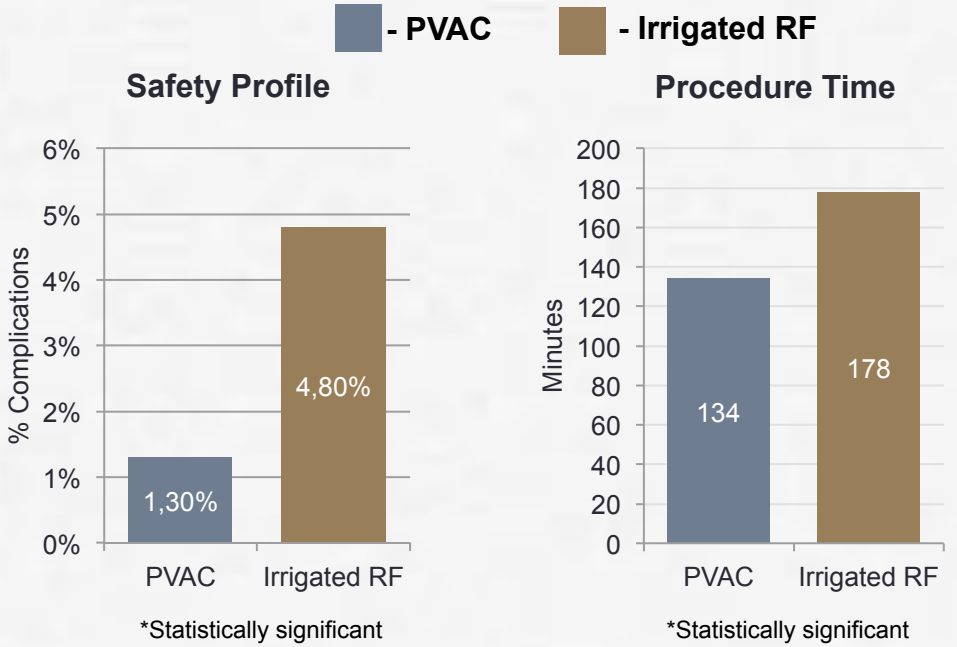
Point by point average success **59,5%**
PVAC average success **67,5%**

De Greef et al, Europace 2014

5 year Follow-Up with PVAC vs. Irrigated RF

Single Procedure Success off Drugs





Ablation characteristics.

	cPVI group (n = 230)	MER group (n = 230)	P
Procedure duration (min)	177.7 (±48.7)	133.9 (±38.8)	<0.001
Ablation time (min)	45.3 (±30.3)	32.6 (±12.0)	<0.001
Fluoroscopy time (min)	29.7 (±12.3)	31.9 (±12.3)	0.064

Data are presented as means ± their SD. *P*-value between cPVI and MER group, Student's t-test. cPVI: conventional point-by-point pulmonary vein isolation; MER: multi-electrode catheter pulmonary vein isolation.

Complications.

	cPVI group (n = 230)	MER group (n = 230)	P
Femoral vascular access	5 (2.2%)	0 (0%)	0.025
Pneumonia	4 (1.7%)	1 (0.4%)	0.177
Atrial perforation	2 (0.9%)	0 (0%)	0.156
Retinal infarction	0 (0%)	1 (0.4%)	0.317
Transient global amnesia	0 (0%)	1 (0.4%)	0.317
Stroke/TIA	0 (0%)	0 (0%)	–
Total	11 (4.8%)	3 (1.3%)	0.030

Data are presented as absolute numbers with their respective percentages. *P*-value between cPVI and MER group (χ^2-test). cPVI: conventional point-by-point pulmonary vein isolation; MER: multi-electrode catheter pulmonary vein isolation; TIA: transient ischemic attack.

Gal et al. Int J Cardiol 176 (2014)

Advanced duty-cycled multielectrode RF ablation: Benefits of "Gold"

9 Electrodes

10 Electrodes

3.75mm Spacing

3mm Spacing

20° Forward Tilt

Perpendicular

- What Benefits Does Gold Offer?
  - Thermal conductivity
    - Platinum = 71.6 W/m°C
    - Gold = 317 W/m°C
  - Precise temperature control across the electrode*
  - Ability to drive more power, if desired*
  - Create deeper lesions, if desired*

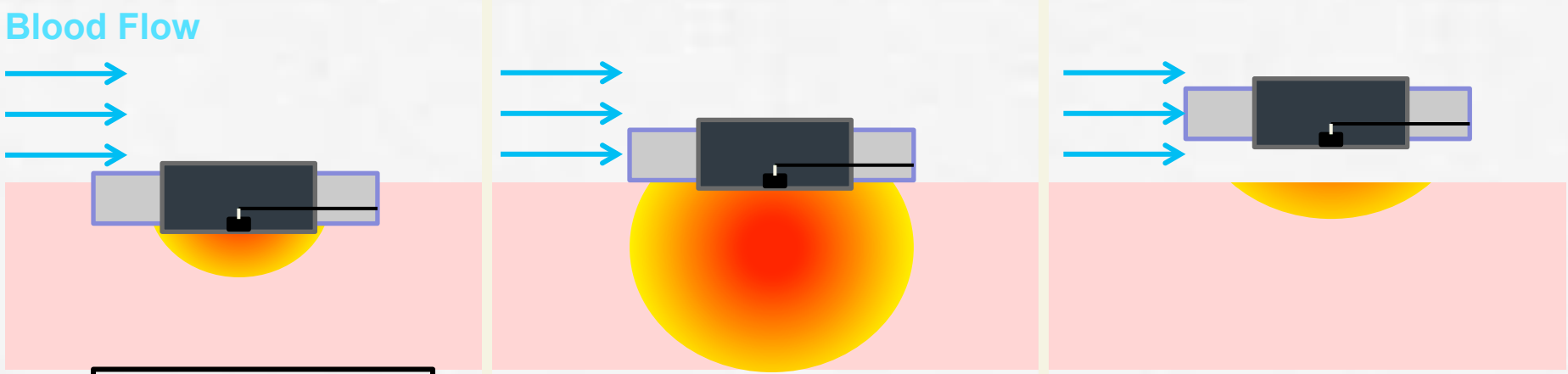
Create more consistent lesions independent of cardiac flow conditions

Contact Assessment using Temperature and Power

Low Power
Power: <3W
Temp: 60°C

Good Contact
Power: >3W
Temp: 50-65°C

No Contact
Power: 9W (Max)
Temp: <50°C



Excess Contact

Good Contact

Poor Contact

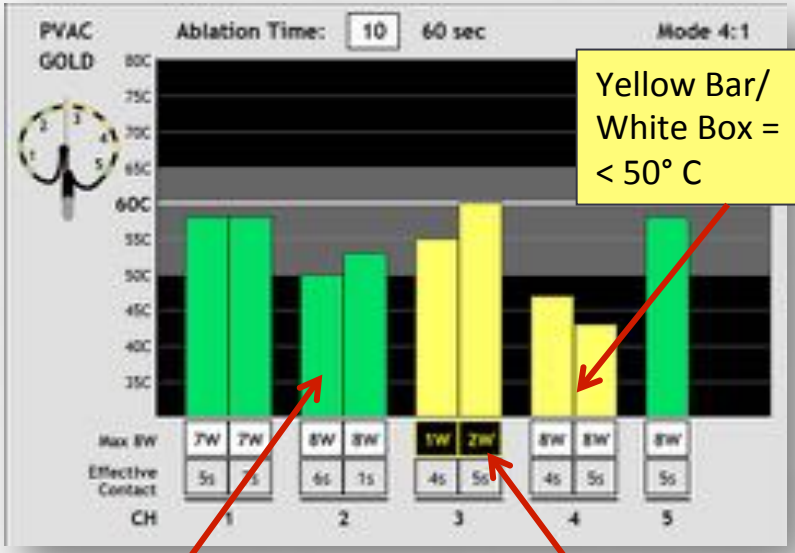
Contact Assessment- During ablation

GENius
Temperature Only

Green Bar =
55 - 65° C

Blue Bar =
< 55° C

GENius with ContactIQ
Temperature and Power



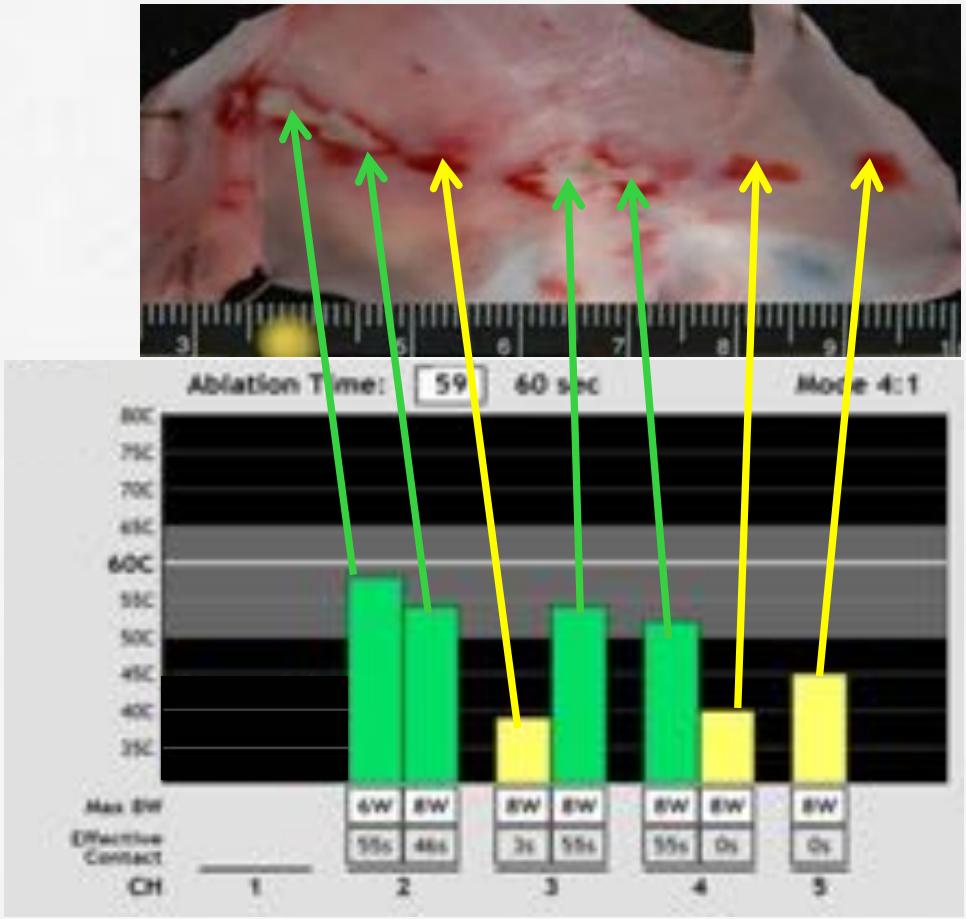
Yellow Bar/
White Box =
< 50° C

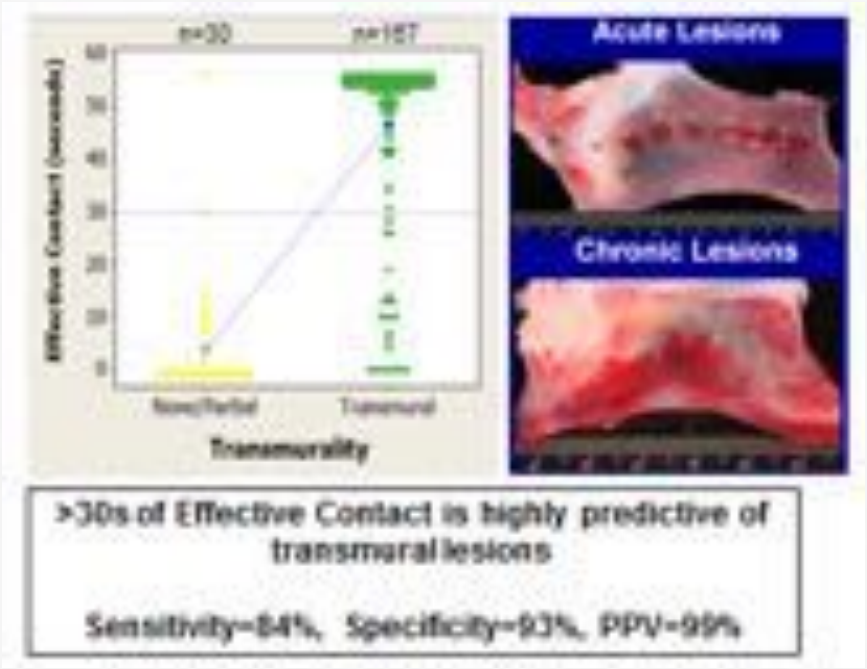
Green Bar =
50 - 65° C +
Power ≥ 3W

Yellow Bar/Black Box =
50 - 65° C +
Power < 3W

Effective contact seconds

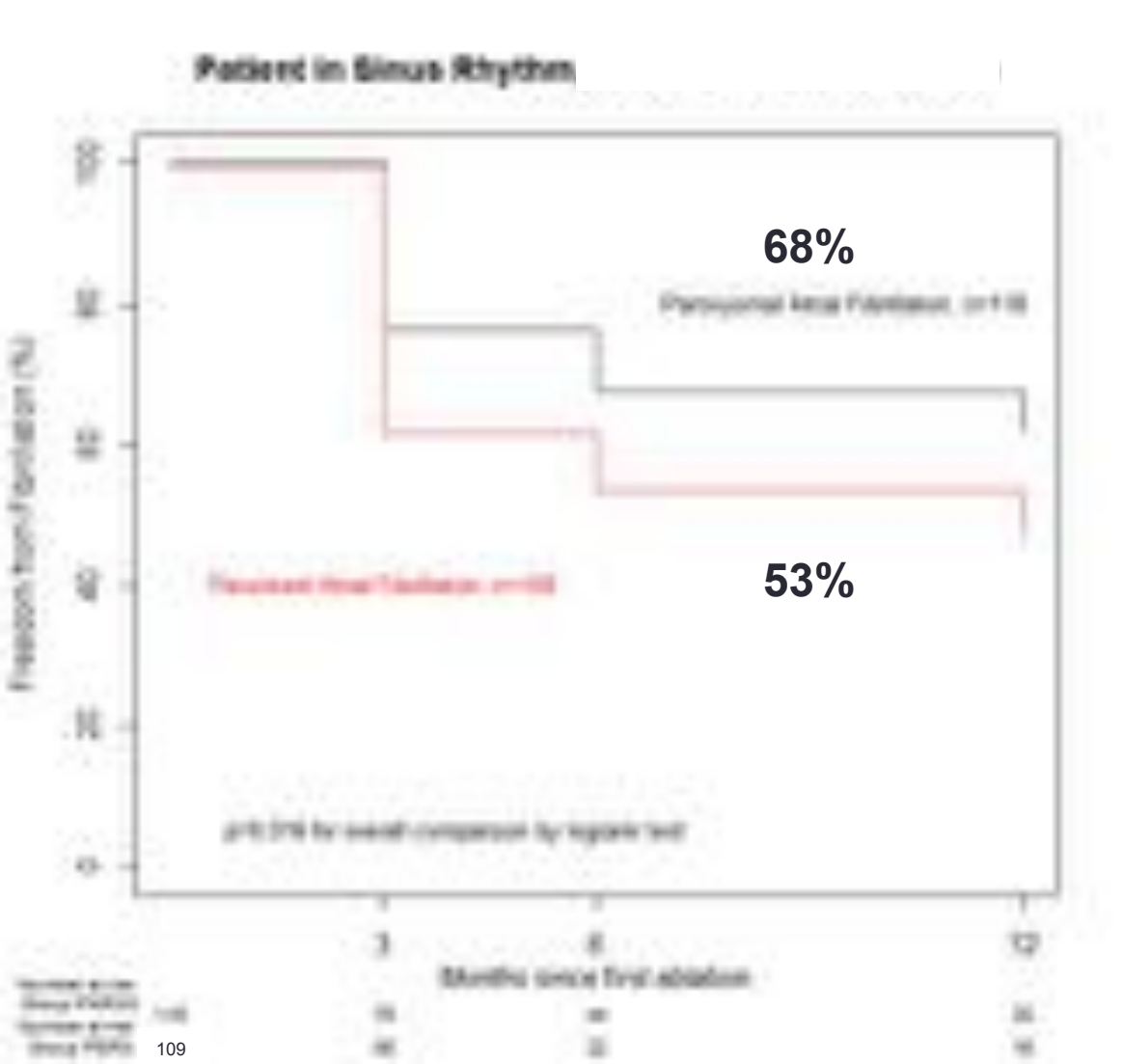
PVAC GOLD shows that greater than 30 seconds of Effective Contact is highly predictive of transmural lesions in a preclinical model.



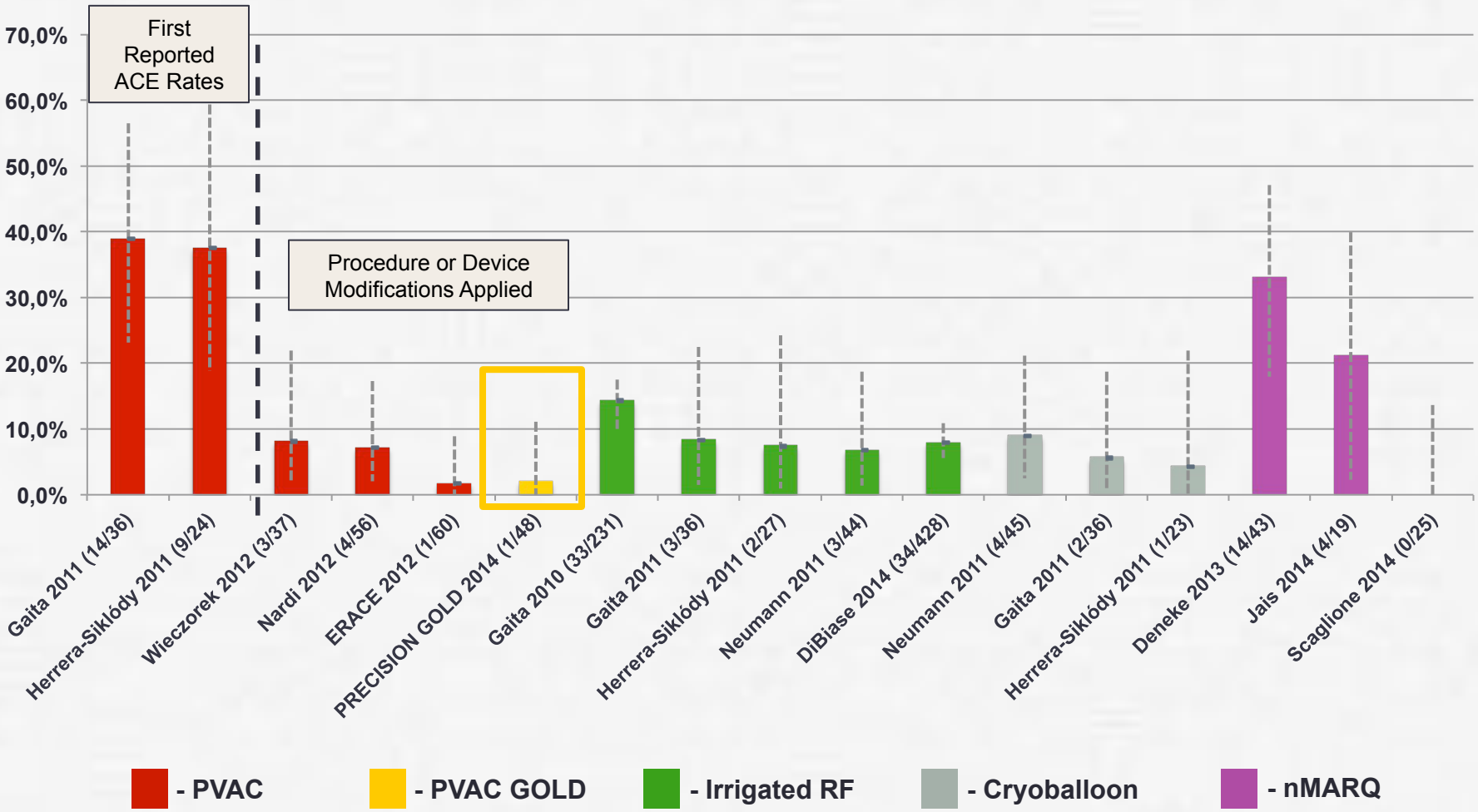


Hocini M et al, Strong Correlation Between RF Biophysics, Contact Assessment, and Lesion Quality in a Temperature-Controlled, Multi-electrode Ablation System, Cardiostim Abstract 2014

Dresden experience – PVAC Gold ® - 227 patients

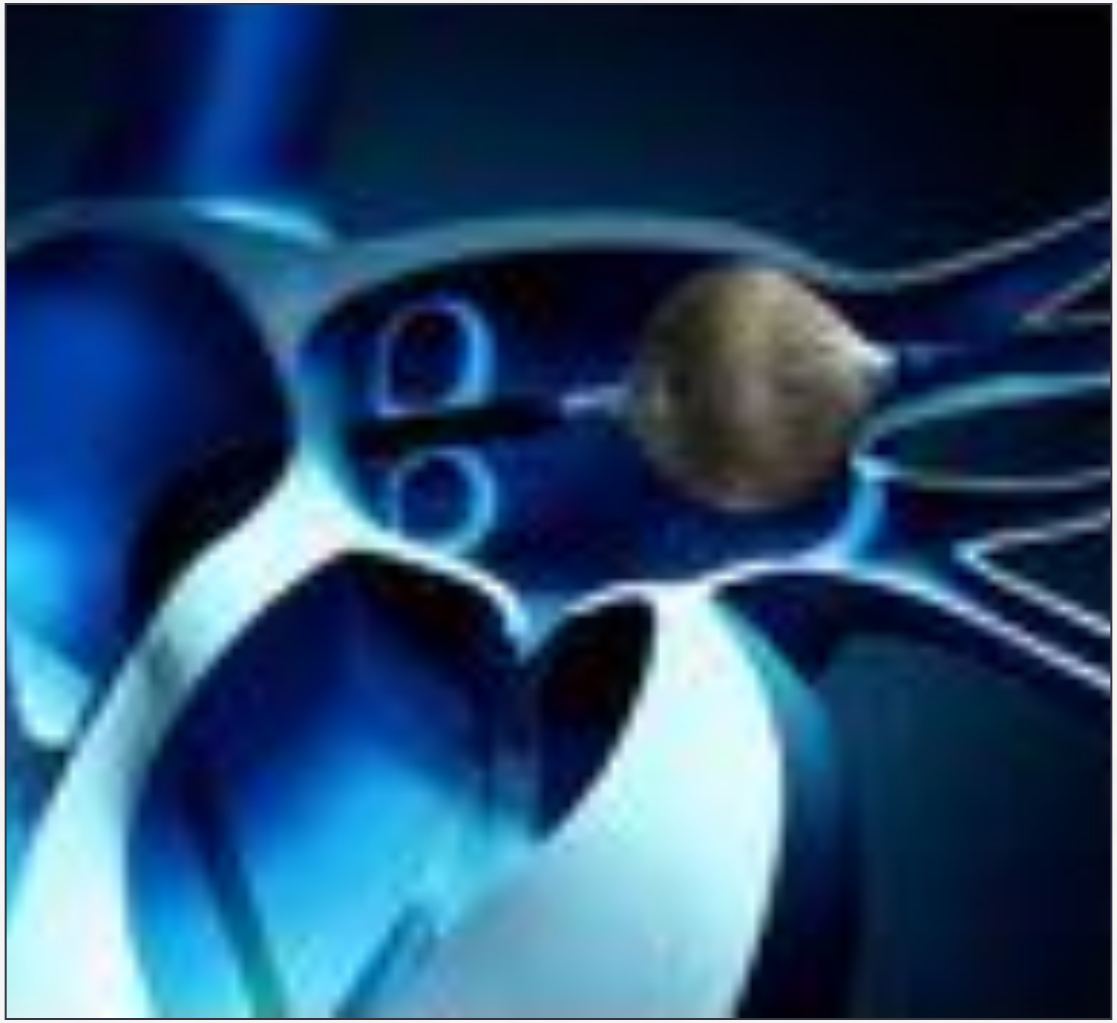


ACE rates using various technologies



Caution: Clinical results across studies/protocols may not be comparable.
All studies included used 1.5T MRI scanner and used a consistent lesion definition as per Gaita/Herrera-Siklódy (DWI + ADC + FLAIR)

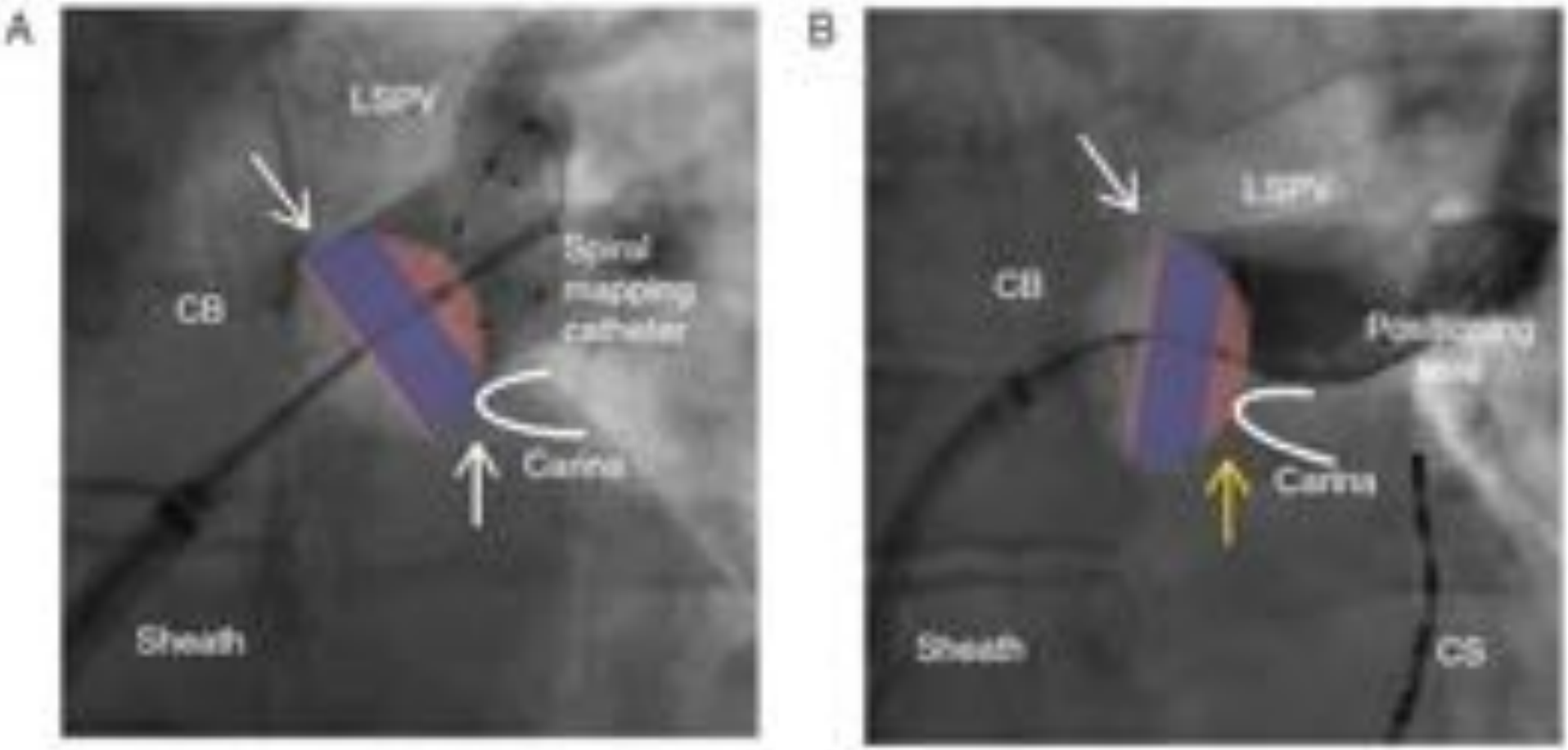
„balloon based technique“
Cryoablation (Cryocath)



Lemola,K. et al; PACE 2008,Vol 31, 2:235- 244

Advances in Cryo technology

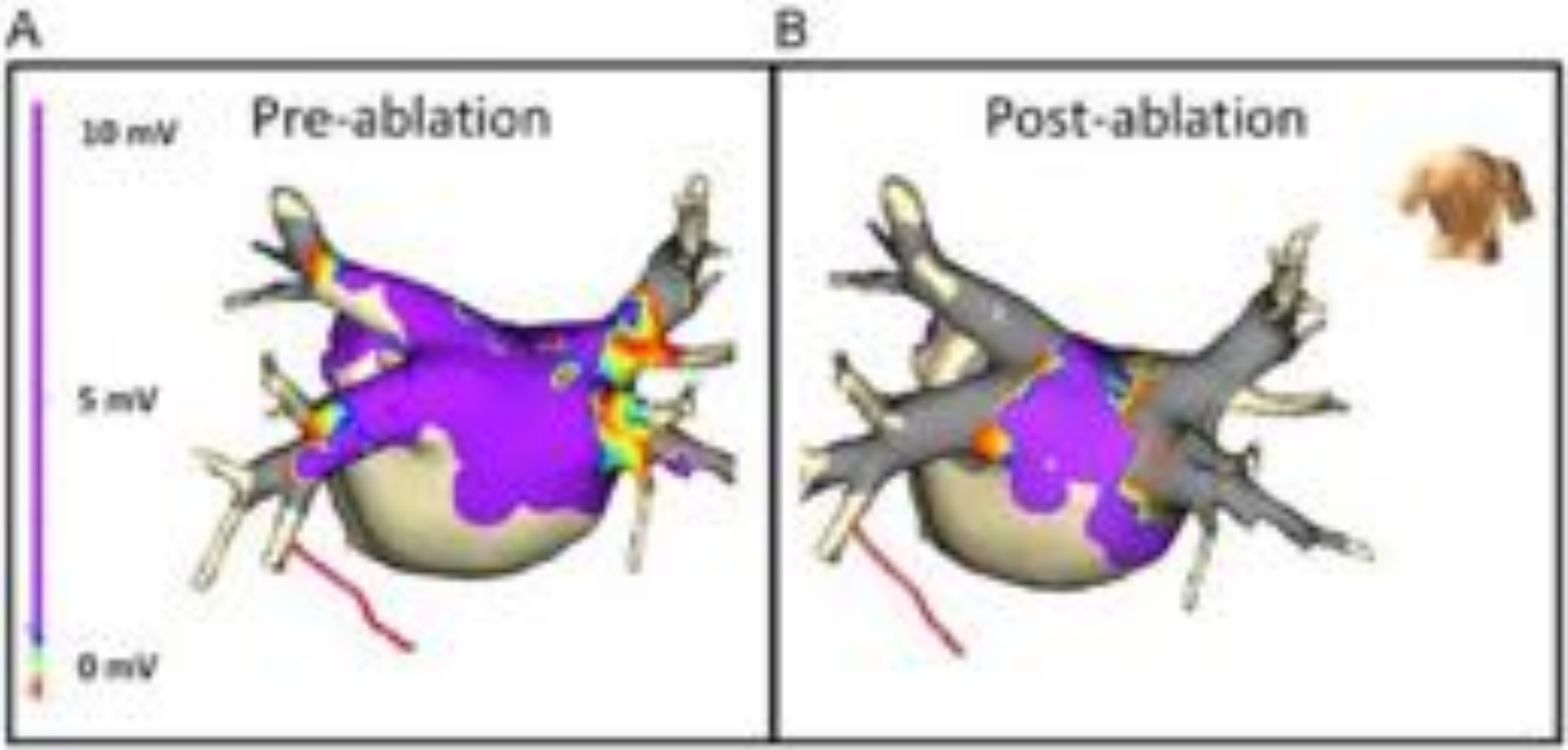
Optimal balloon positioning with CBG1 and CBG2



(A and B) Occlusion of LSPV with a CB, demonstrated by PV angiography. Illustration of the ideal freezing zone of CBG1 (blue area) and CBG2 (red area, includes the blue area).

Straube et al., Europace, 2014

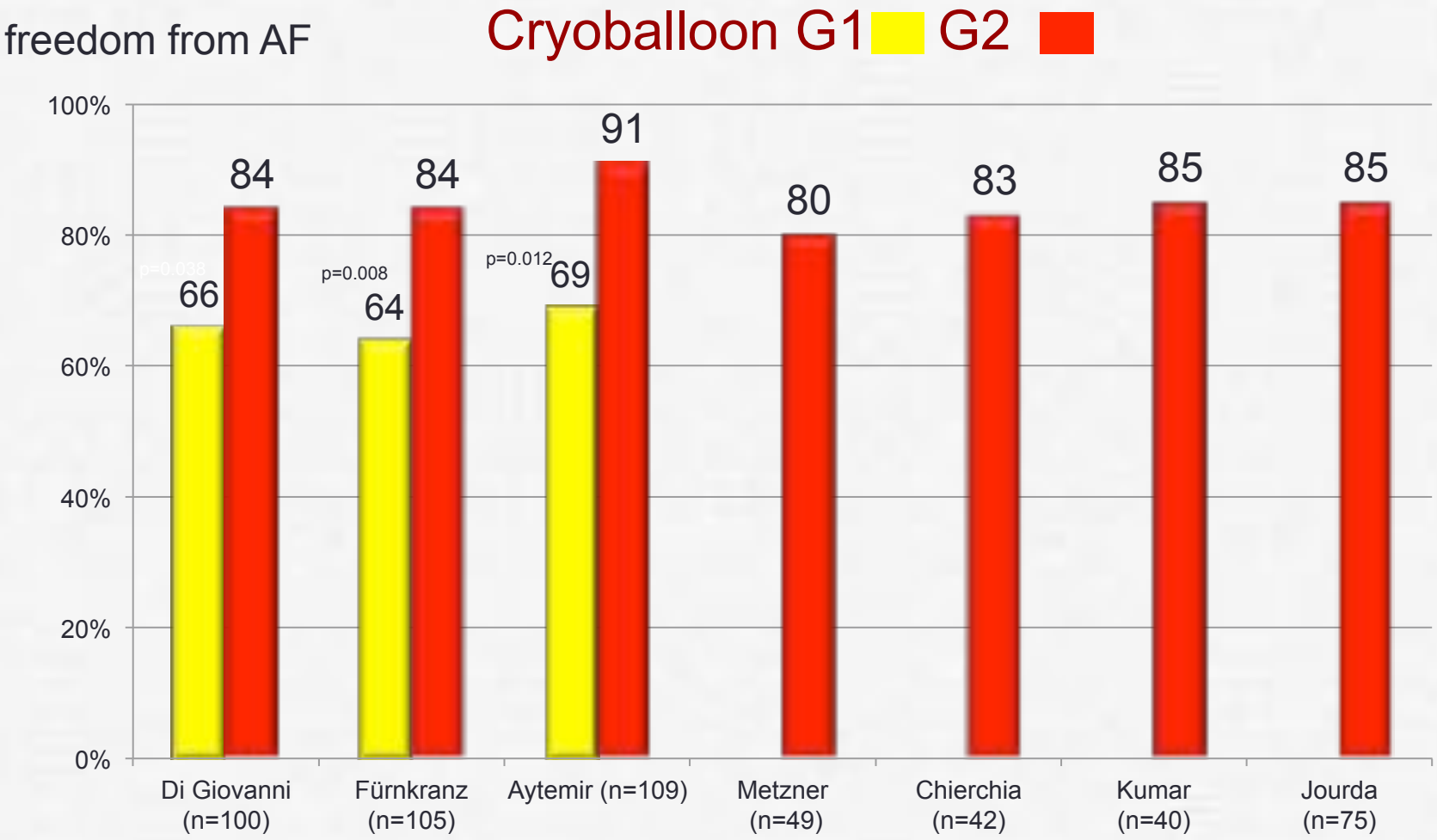
Pre- and postablation images recorded with the 3-dimensional electroanatomic mapping system



The scale on the NavX voltage map was set from 0.2 to1.2mV. The purple region represents voltage 41.2 mV, and the gray region represents voltage o 0.2 mV. A: A preablation voltage map demonstrating the posterior left atrial(LA) and 4 pulmonary veins. B: A postablation voltage map demonstrating cryoballoon lesion demarcationon the posterior LA wall.

Koenigsberg DN et al, HeartRhythm, 2015

REPRODUCIBLE OUTCOME DATA WITH THE CRYOBALLOON IN PAROXYSMAL AF AT 1 YEAR



Di Giovanni, JCE 2014; Fürnkranz, JICE 2014; Aytemir, Europace 2014; Metzner, Circ AEP 2014; Chierchia, Europace 2014; Kumar, JICE 2014; Jourda, Europace 2014

G2: 91% of veins isolated at 3.4 months post-ablation (68/75 veins in 21 pat.)

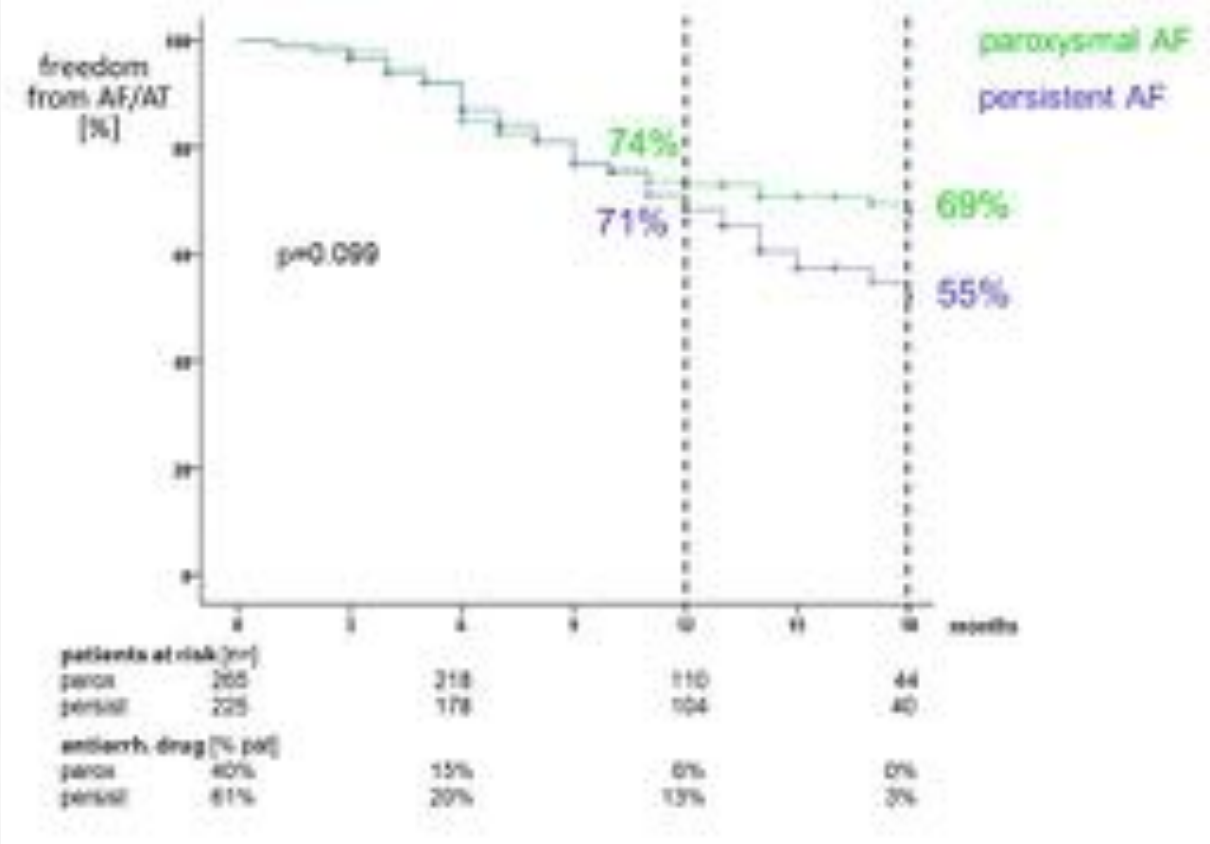
Reddy, JCE 2015

2ND GEN. CB: PAROXYSMAL VS. PERSISTENT AF
FREEDOM FROM AF/AT: SINGLE CB PROCEDURE SUCCESS

n=560 pts., 63.5 yrs., 45% pers. AF, LA 43 vs. 47 mm p<0.01, LA volume 120 vs. 149 ml p<0.01

recurrence: ≥ 30sec AF/AT and/or symptoms after blanking period

FU at 3, 6, 9, 12 months, thereafter every 6 months (incl. holter)



FU 11 ± 5 mo

FU 11 ± 6 mo.

FU in 490/560 patients (88%) complete

AAD

Dorwarth, Straube, Hoffmann, DGK 4/2015

2nd Gen CB → high rate of freedom from AF/AT also in pers. AF

Second-generation cryoballoon ablation for paroxysmal atrial fibrillation: 1-year follow-up

Chiercha GB et al., 2014

Inclusion: 42 patients — 30 male (71 %), 12 female (29%) — mean age 57,9 ± 21,1 years

Treatment (all patients) with the large 28 mm CB-A; total 168 PV`s were depicted on pre-procedural CT scan and 100% isolated with CB only (=100%).

Freedom from AF off-antiarrhythmic drug treatment after a single procedure (mean 11,6 ± 2months follow up) **78%**

_if the blanking period was considering (3 months) **83%**

Most frequent complication:

phrenic nerve palsy (PNP) in 19 % of individuals

Chierchia GB et al, Europace, 2014

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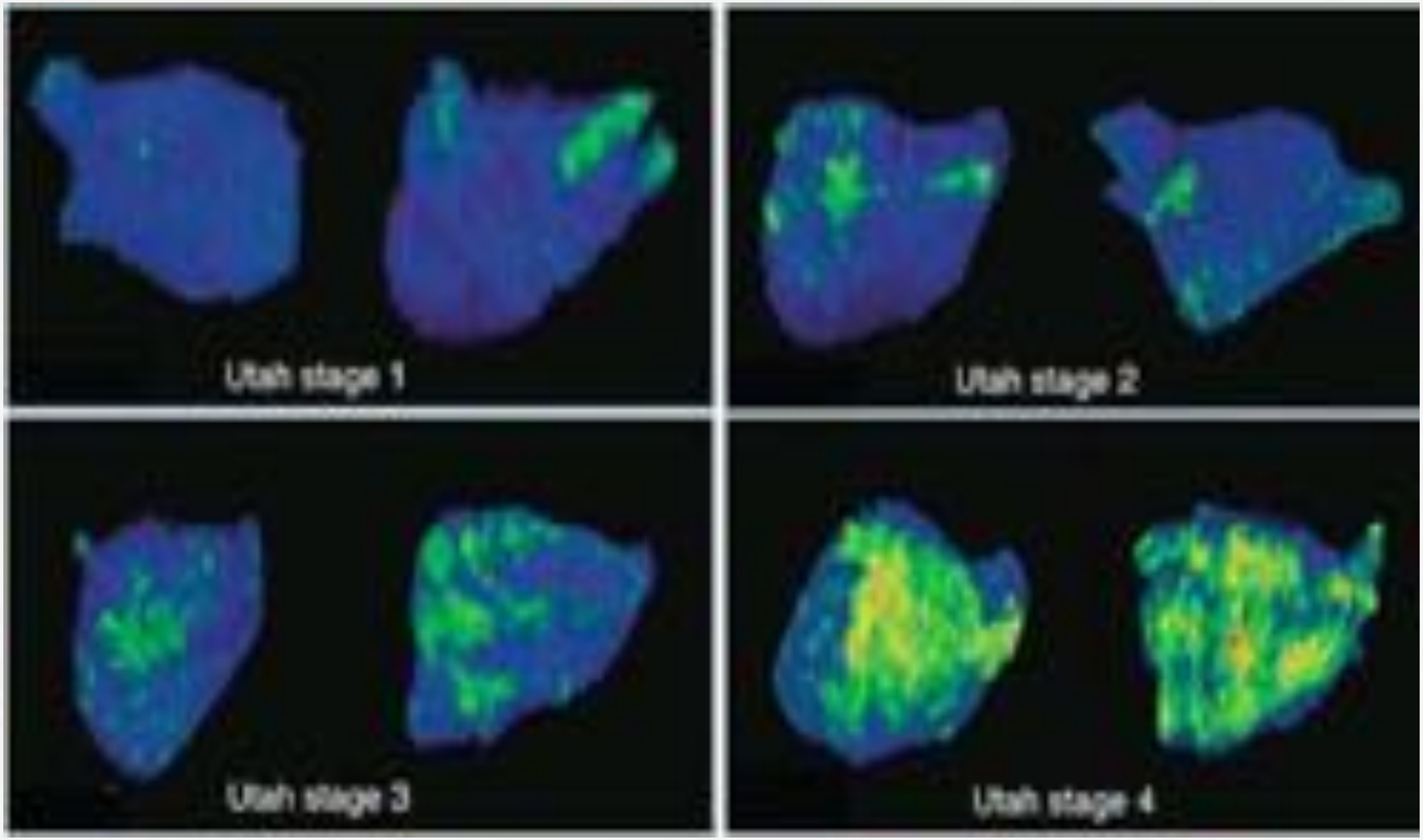
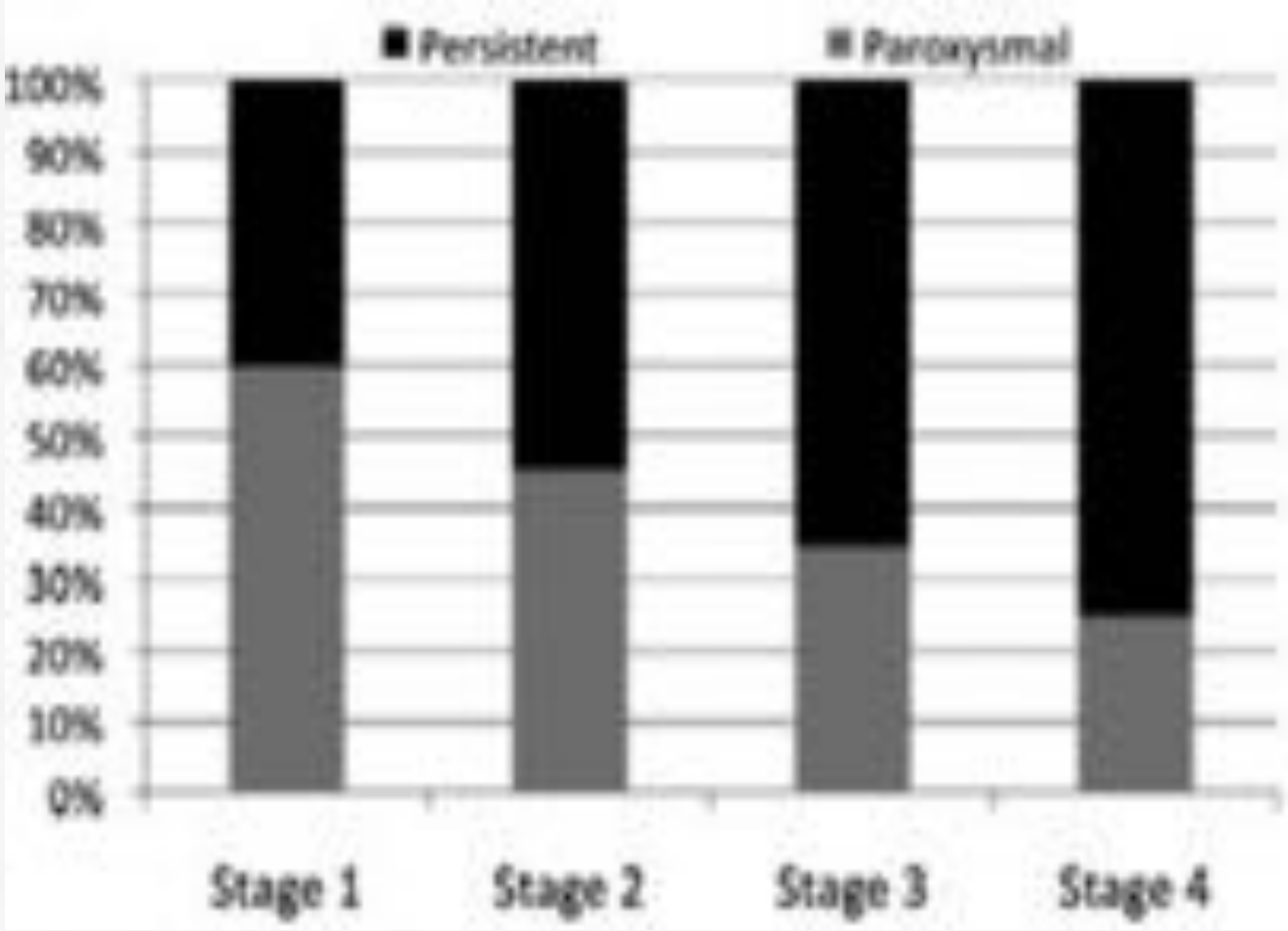
- Special approaches: „Single shot“ devices
- **Fibrosis imaging**
- Complex fractionated atrial electrograms (CFAE)
- Ganglionated Plexi (GP), Fad pads
- Left atrial appendage (LAA)
- Rotors

Pre-Ablation Fibrosis/Structural Remodeling Based Staging



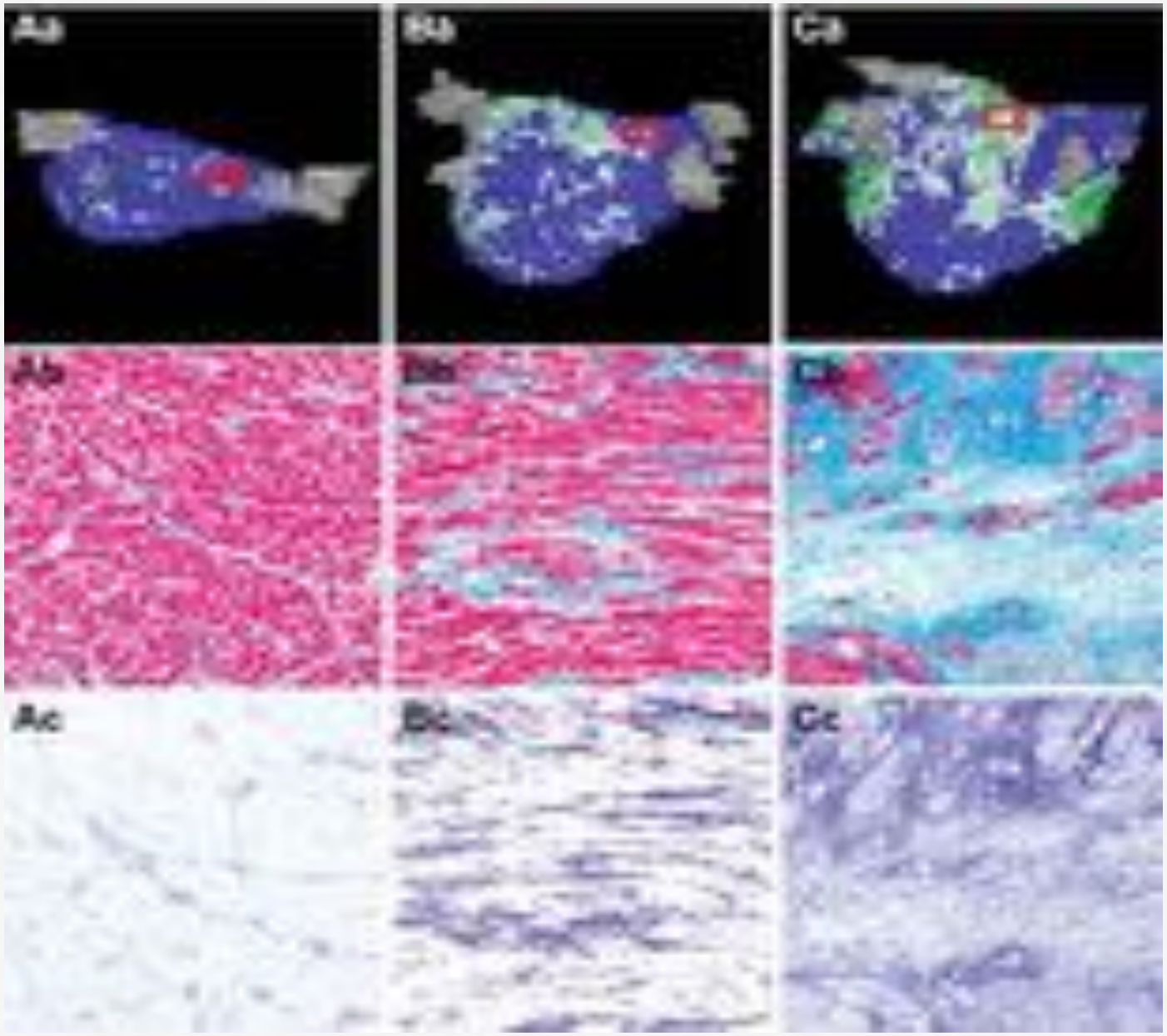
Akoum N. et al; J Cardiovasc Electrophysiol, Vol. 22, pp. 16-22, January 2011.

AF Phenotype and Degree of Fibrosis



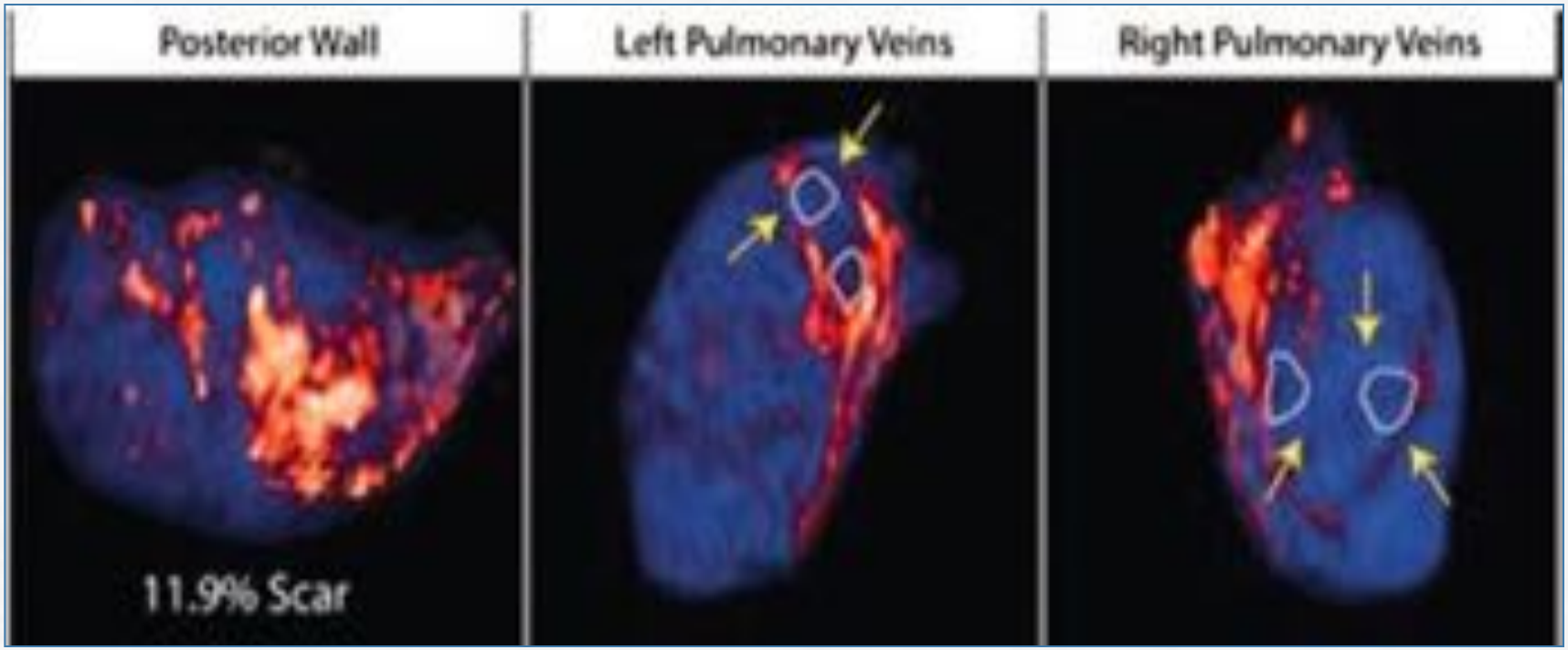
Akoum N. et al; J Cardiovasc Electrophysiol, Vol. 22, pp. 16-22, January 2011.

Histological Basis for LA Wall Fibrosis



McGann C. et al; Circ Arrhythm Electrophysiol. 2014;7:23-30.

Evaluation of pulmonary vein encirclement with ablation scar



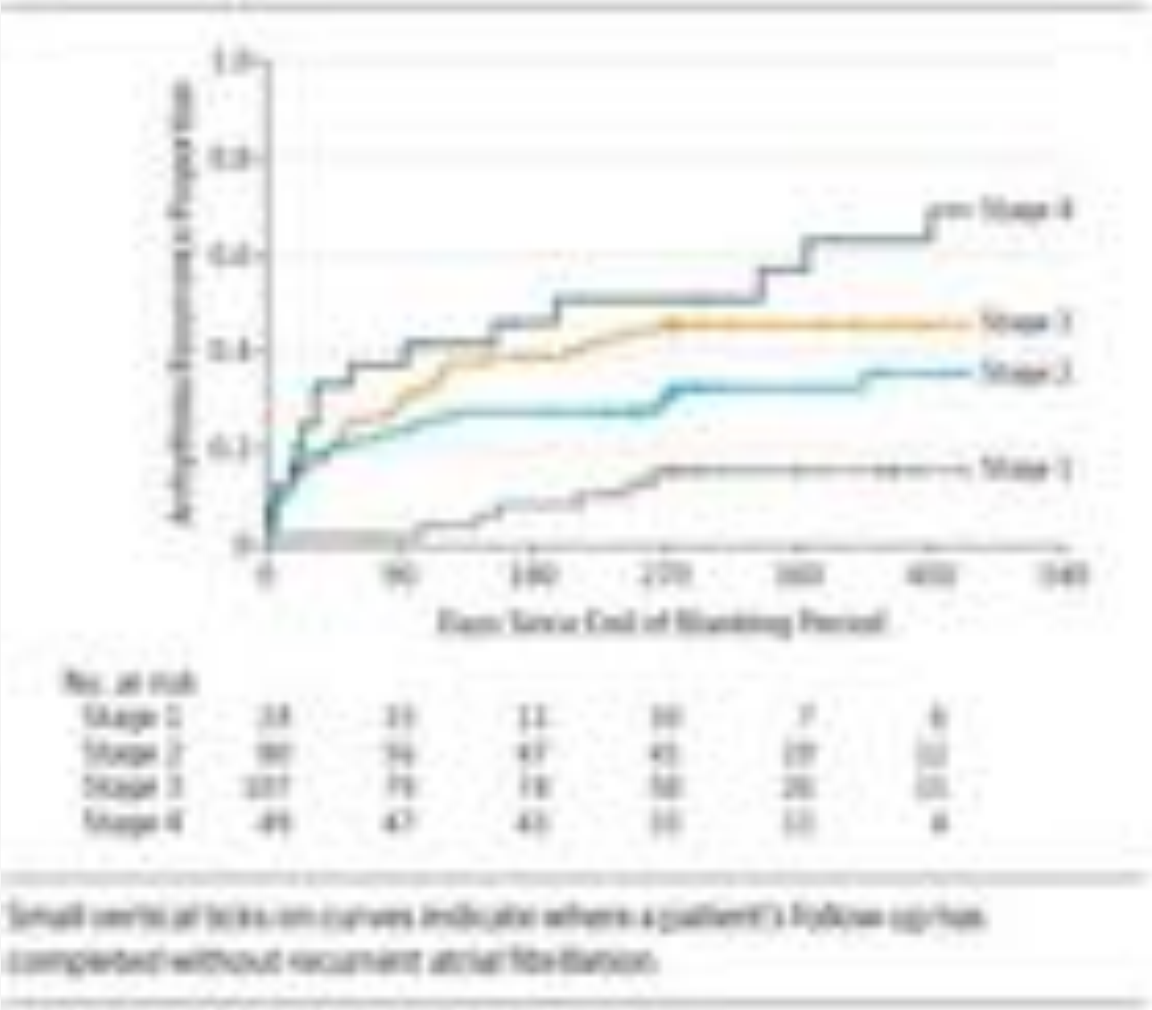
Akoum N. et al; J Cardiovasc Electrophysiol, Vol. 22, pp. 16-22, January 2011.

Association of Atrial Tissue Fibrosis Identified by Delayed Enhancement MRI and Atrial Fibrillation Catheter Ablation

The DECAAF Study

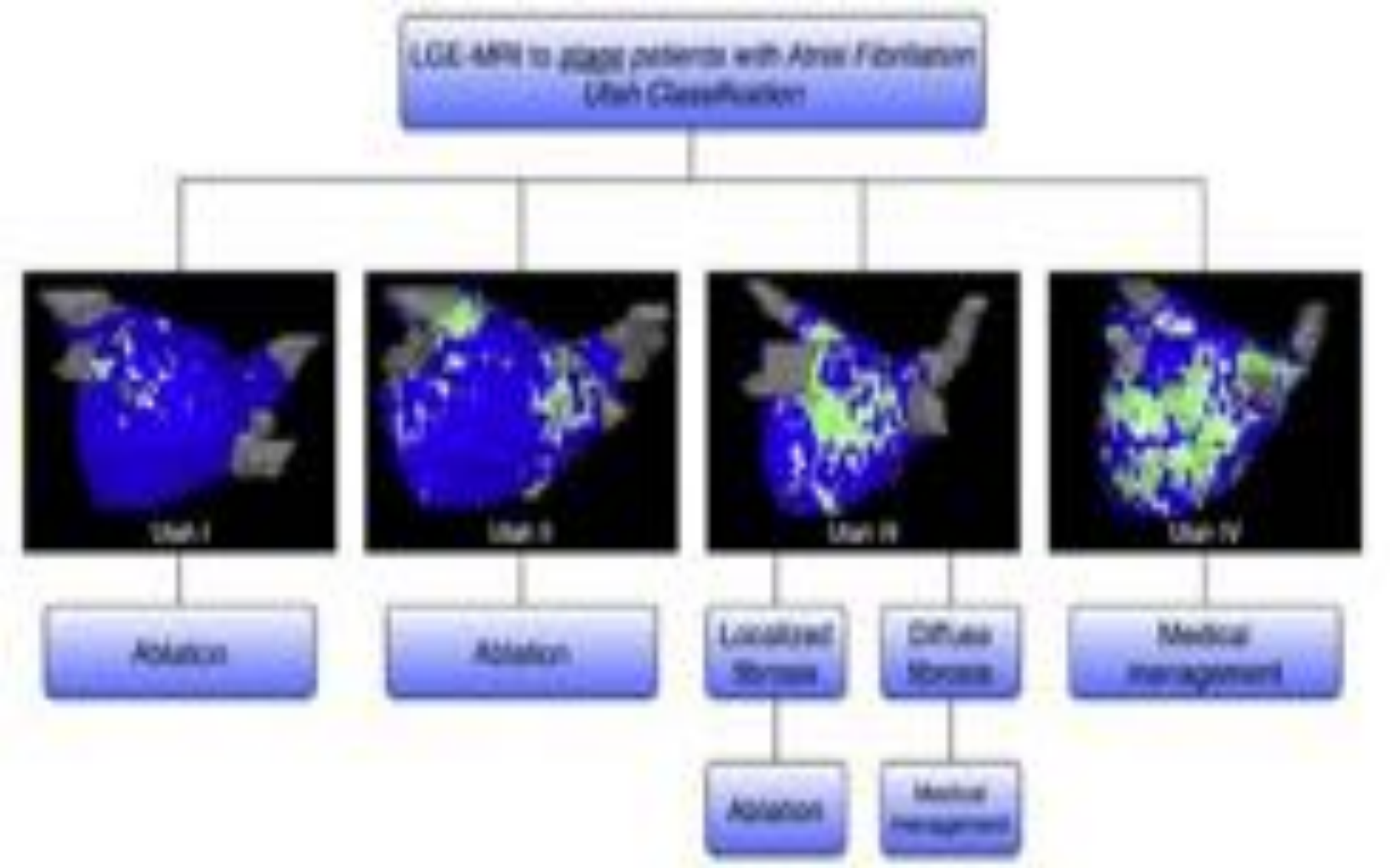
Marrouche N. et al; JAMA. 2014;311(5):498-506.

Cumulative Incidence of Arrhythmia Recurrence Without Covariate Adjustment Through Day 475 After the Blanking Period



Marrouche N. et al; JAMA. 2014;311(5):498-506.

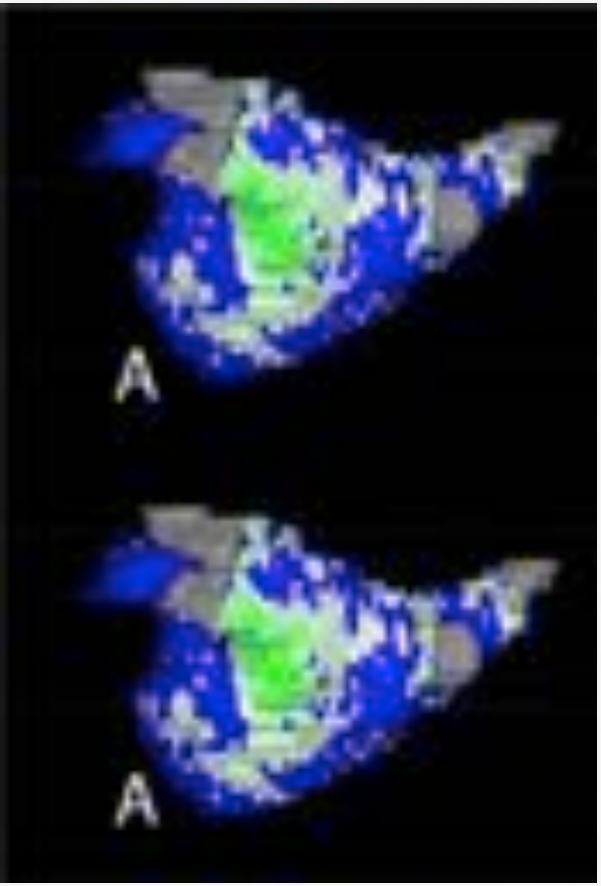
Personalized treatment of atrial fibrillation



Han FT. et al; Canadian Journal of Cardiology 29 (2013) 1194e1202.

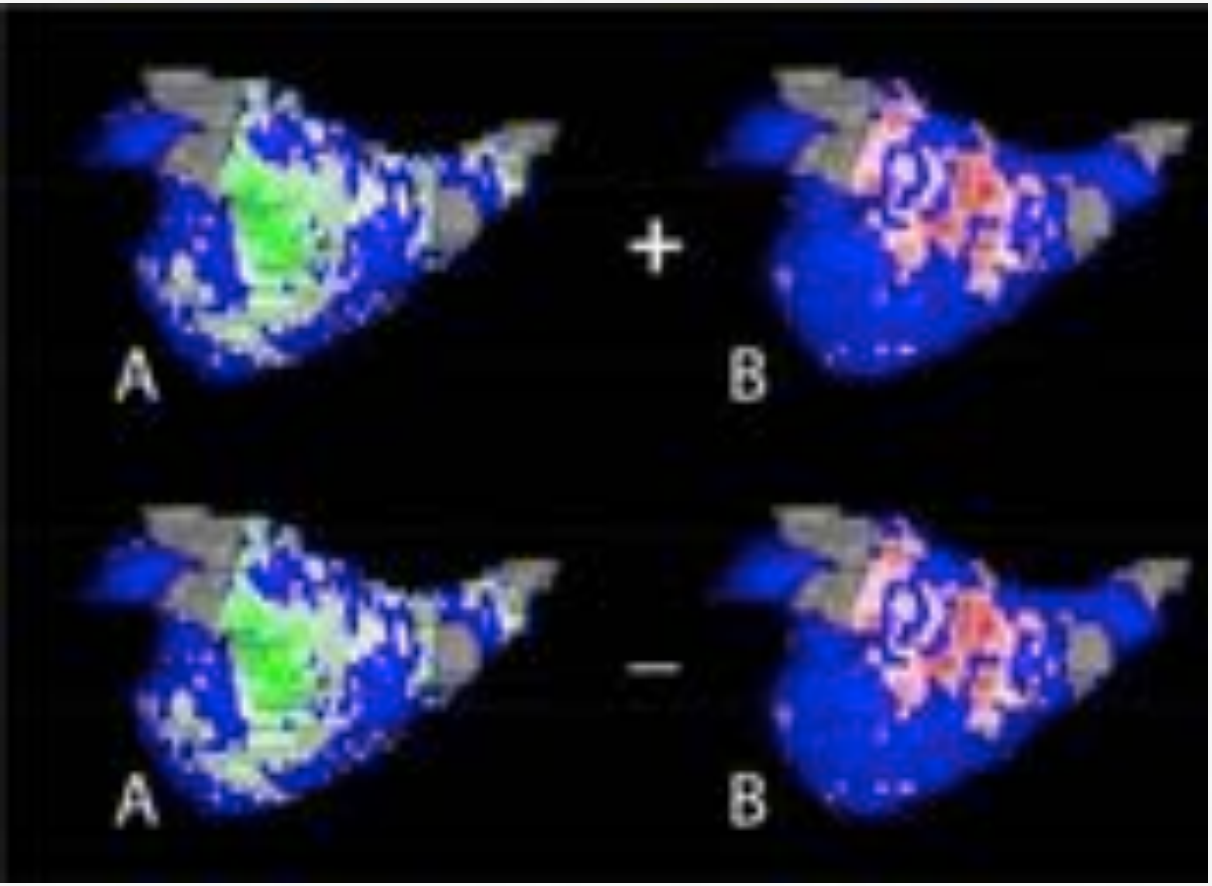
USA: 6 **Europe: 8** **Australia: 1**

DECAAF – Subanalyse



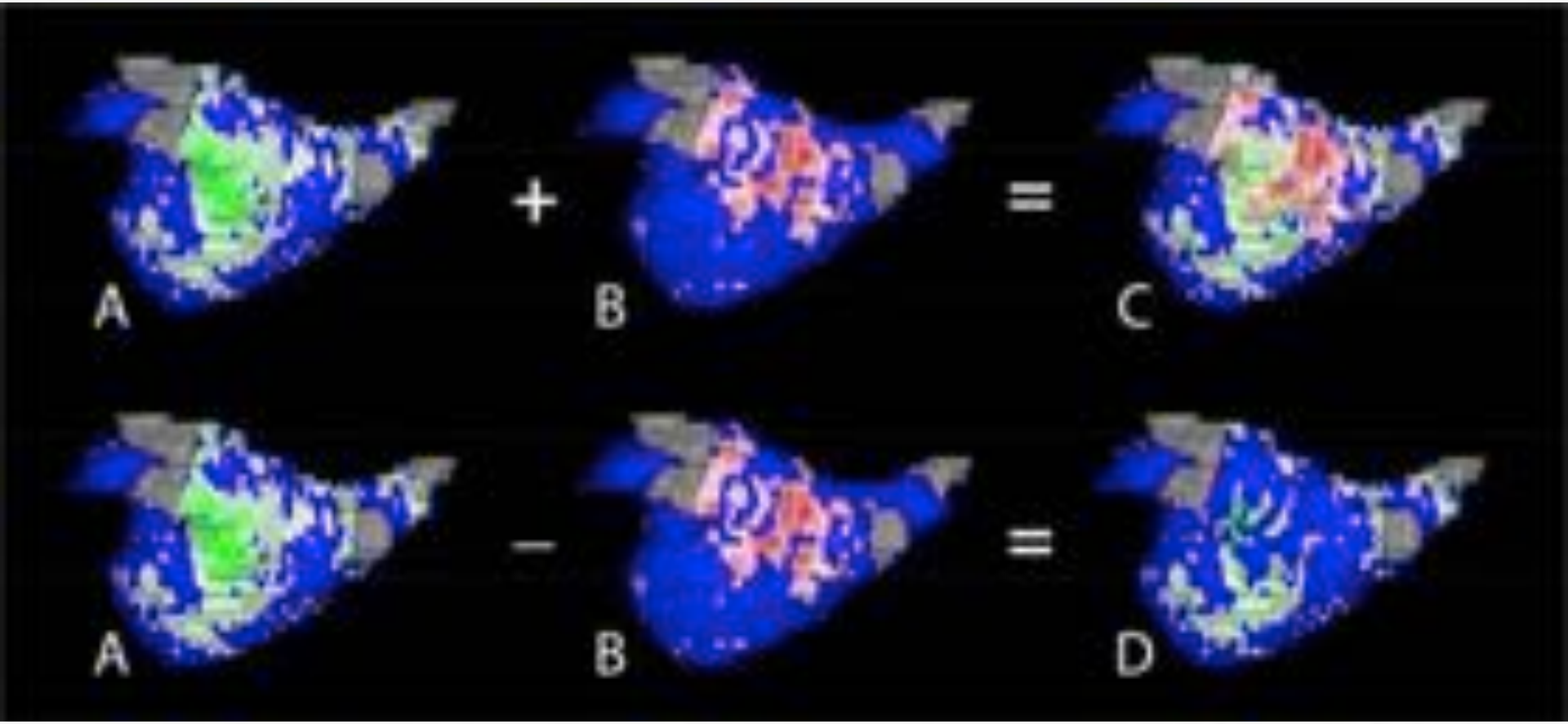
Akoum et al.; (J Cardiovasc Electrophysiol, Vol. 26, pp. 473-480, May 2015)

DECAAF – Subanalyse



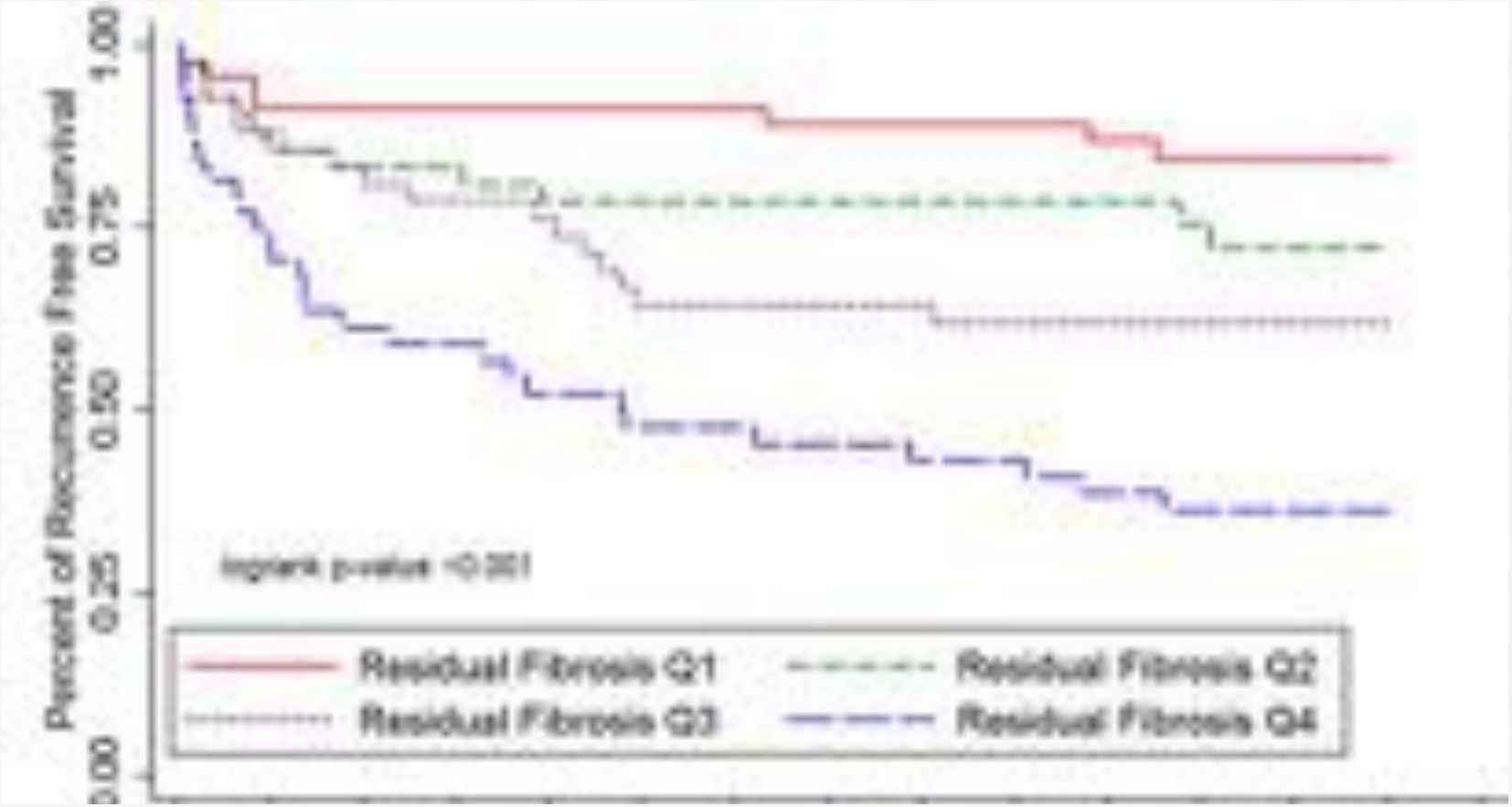
Akoum et al.; (J Cardiovasc Electrophysiol, Vol. 26, pp. 473-480, May 2015)

DECAAF – Subanalyse



Akoum et al.; (J Cardiovasc Electrophysiol, Vol. 26, pp. 473-480, May 2015)

DECAAF – Subanalyse



Akoum et al.; (J Cardiovasc Electrophysiol, Vol. 26, pp. 473-480, May 2015)

Efficacy of LGE-MRI-Guided Fibrosis Ablation vs. Conventional Catheter Ablation of Atrial Fibrillation (DECAAF II)

The University of Utah

DECAAF II

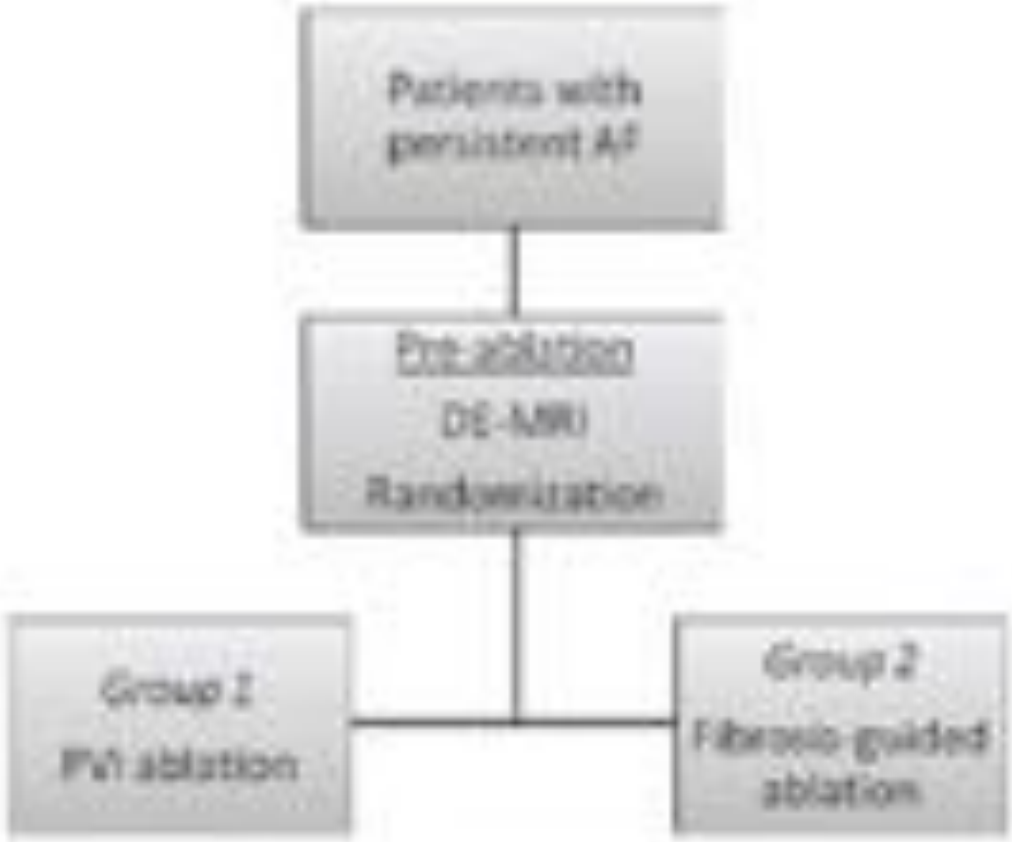
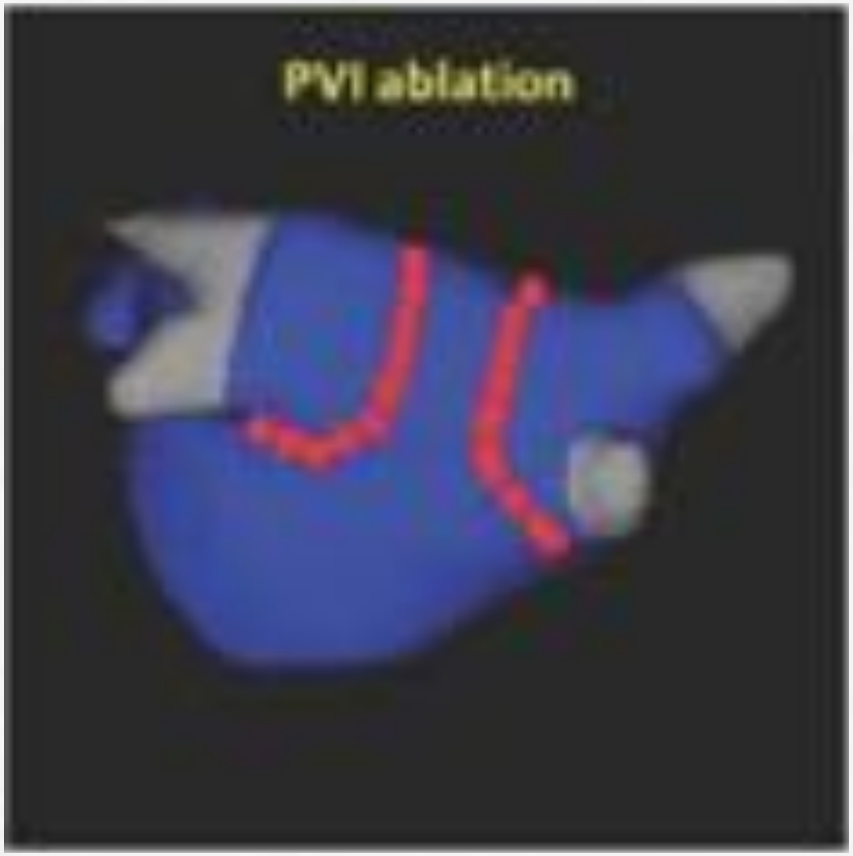
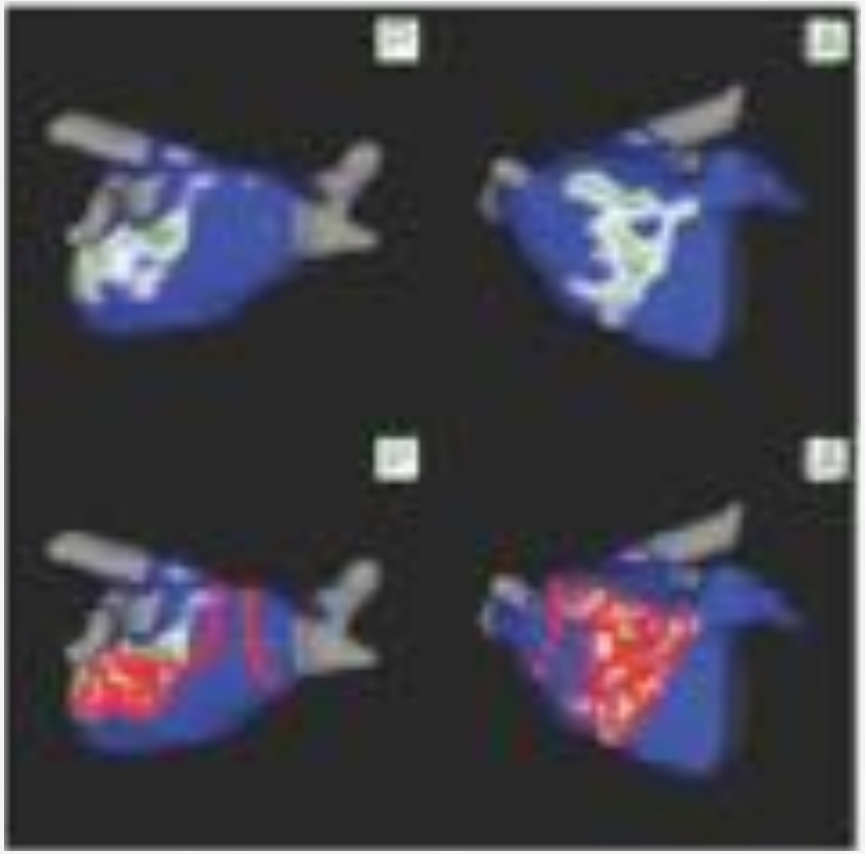


Figure 1. DECAAF II Study Treatments

DECAAF II

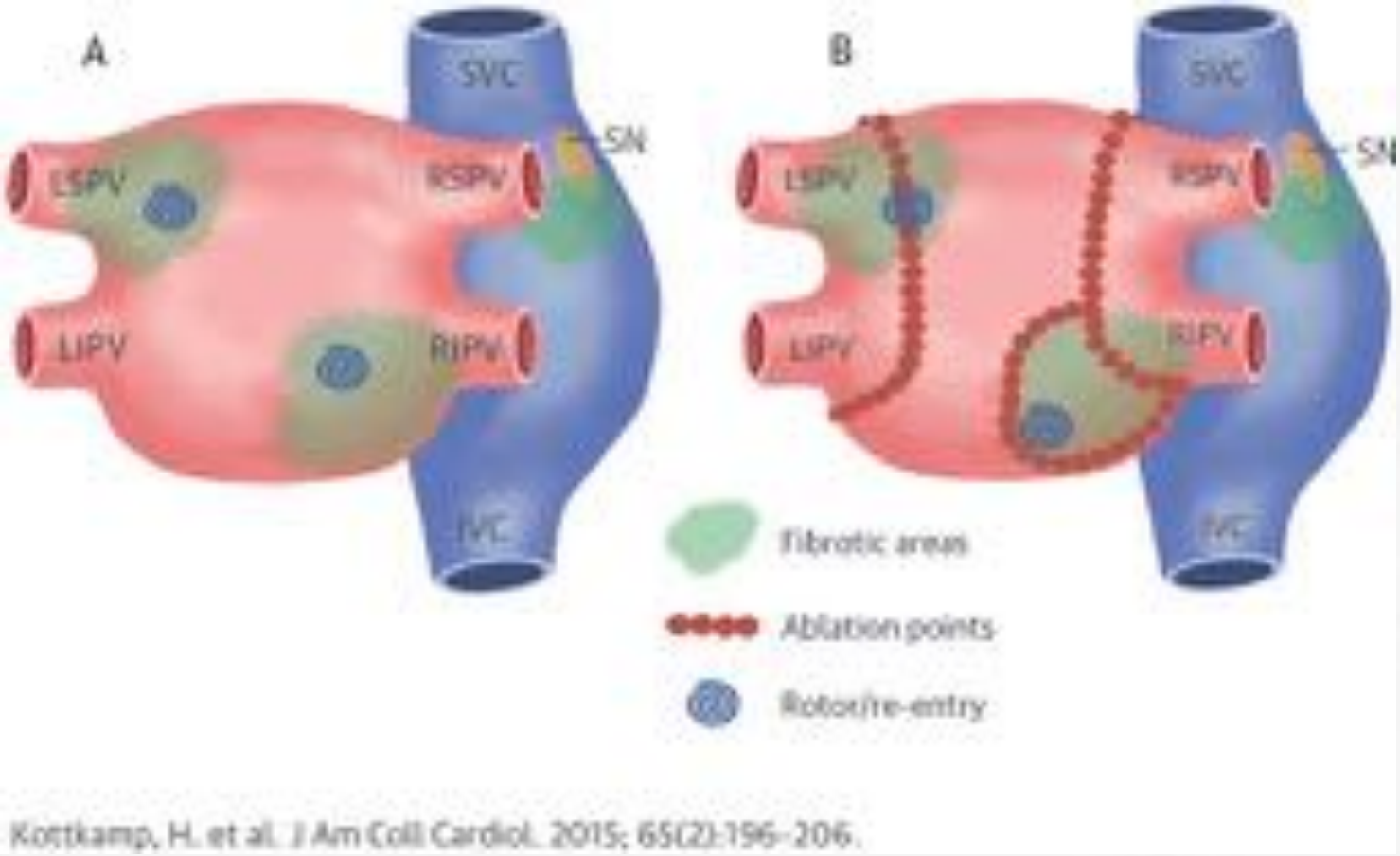


Group1



Group 2

Personalized therapy of atrial fibrillation



Kottkamp H et al. J Am Coll Cardiol 2015

Advanced ablation of AF

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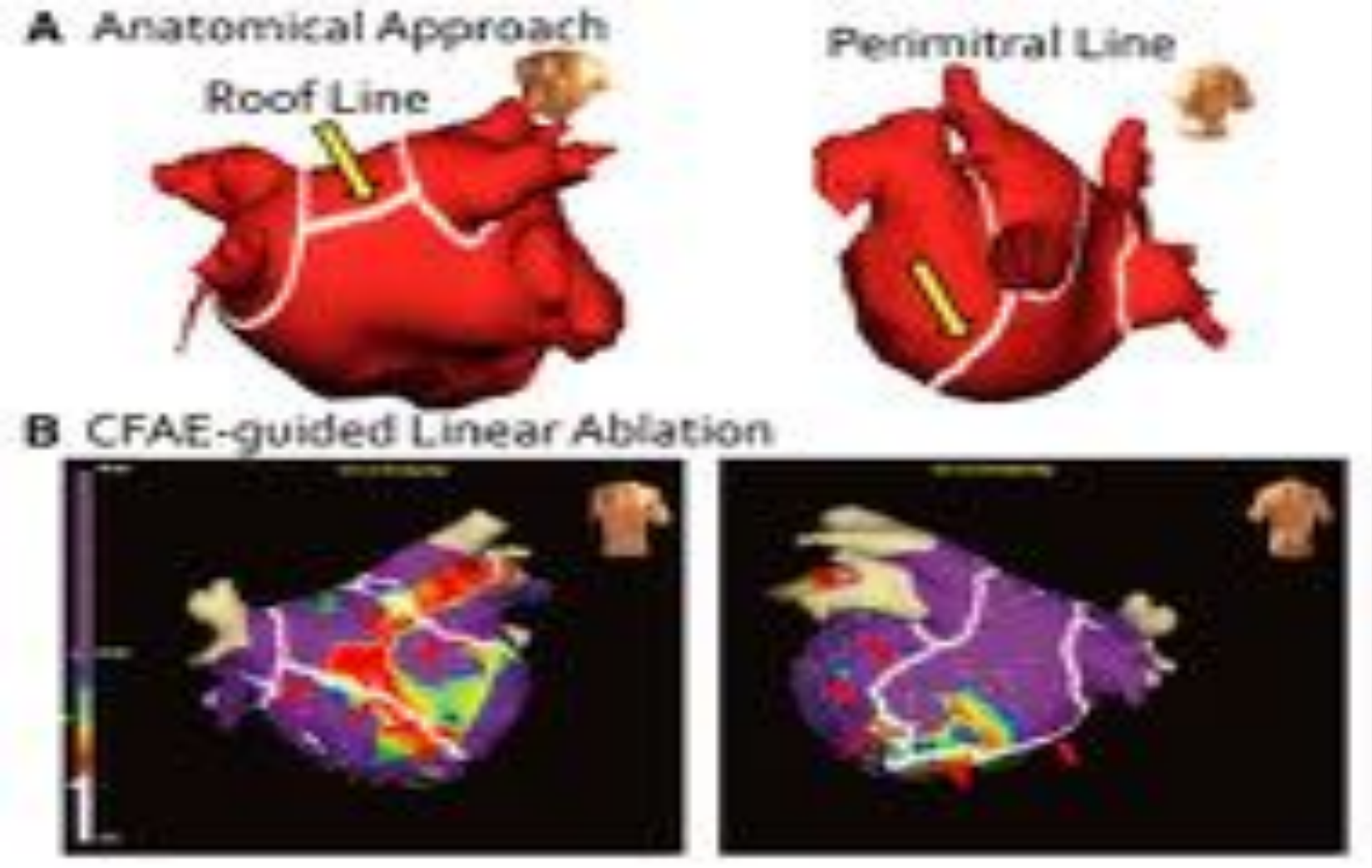
Catheter Ablation of Longstanding Persistent Atrial Fibrillation – Are We on the Right Path? –

CFAE-Guided Ablation

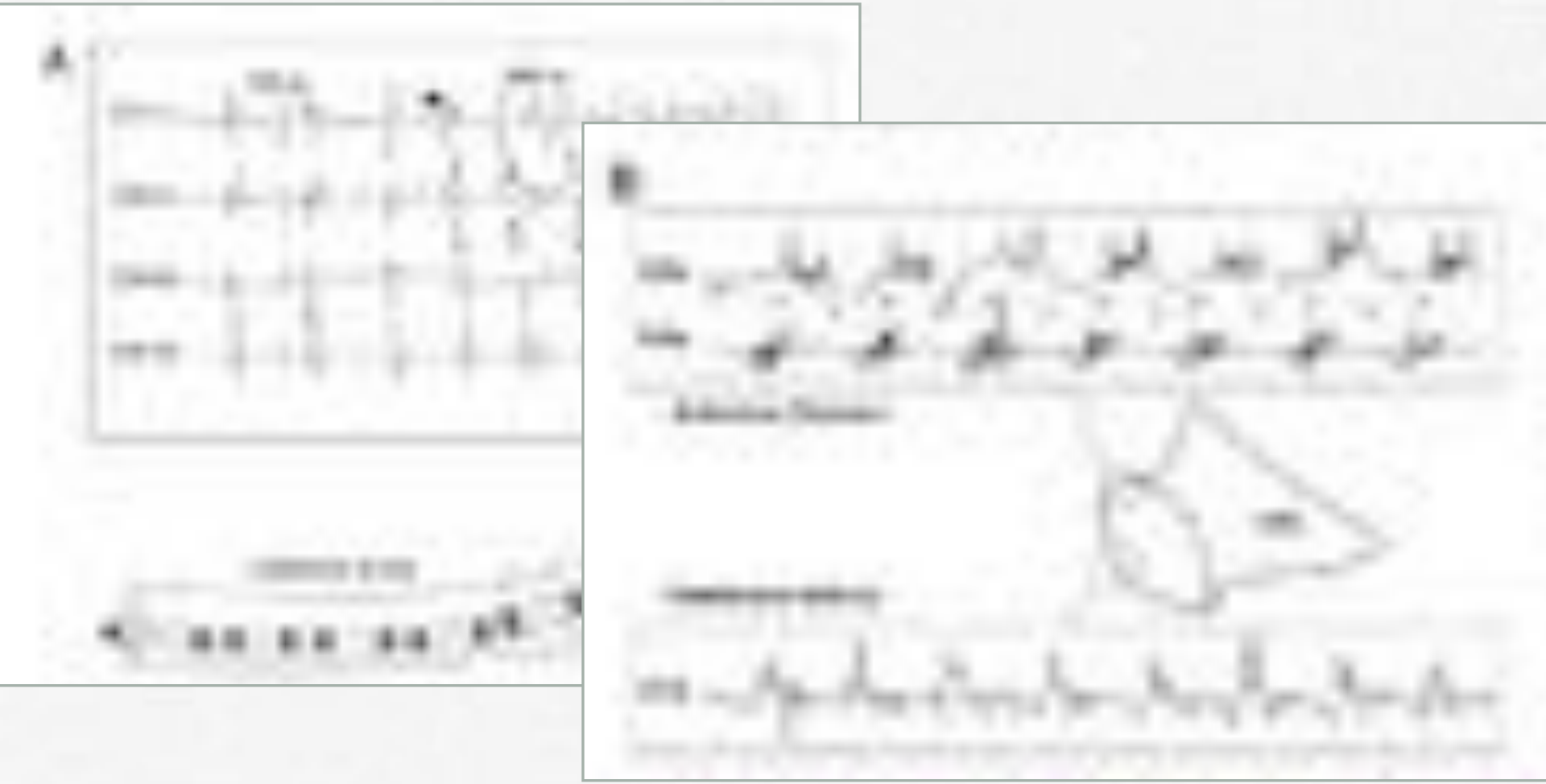


Comparison of anatomical approach (A) vs. CFAE-guided linear ablation (B)

Kim Young-Hoon; Circ J 2012; 76: 1299 – 1306.

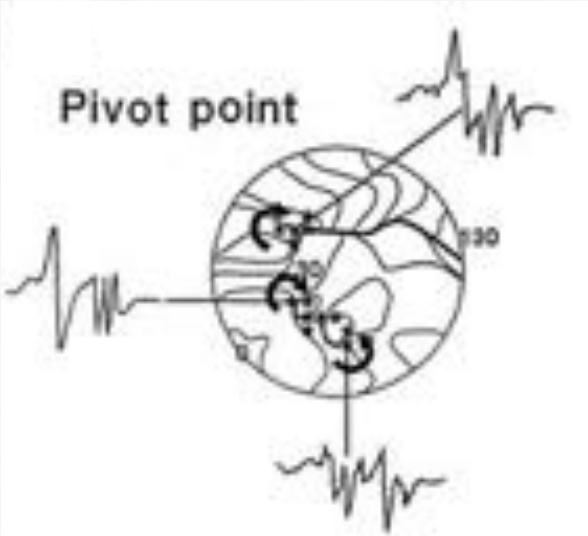
LA electrophysiological targets in persistent AF:

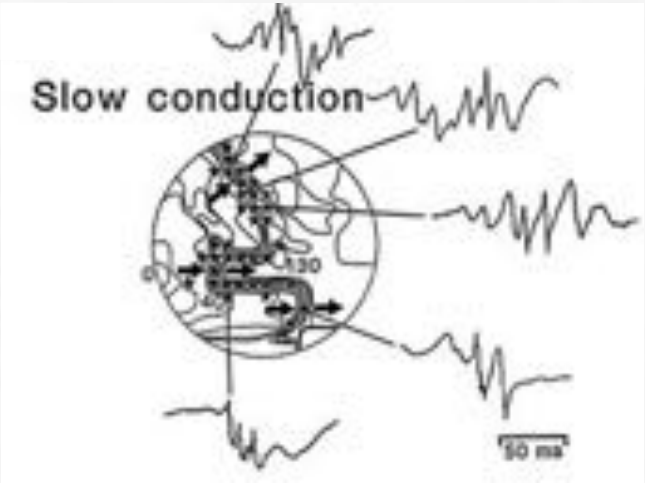
Complex fractionated atrial electrograms (CFAE)

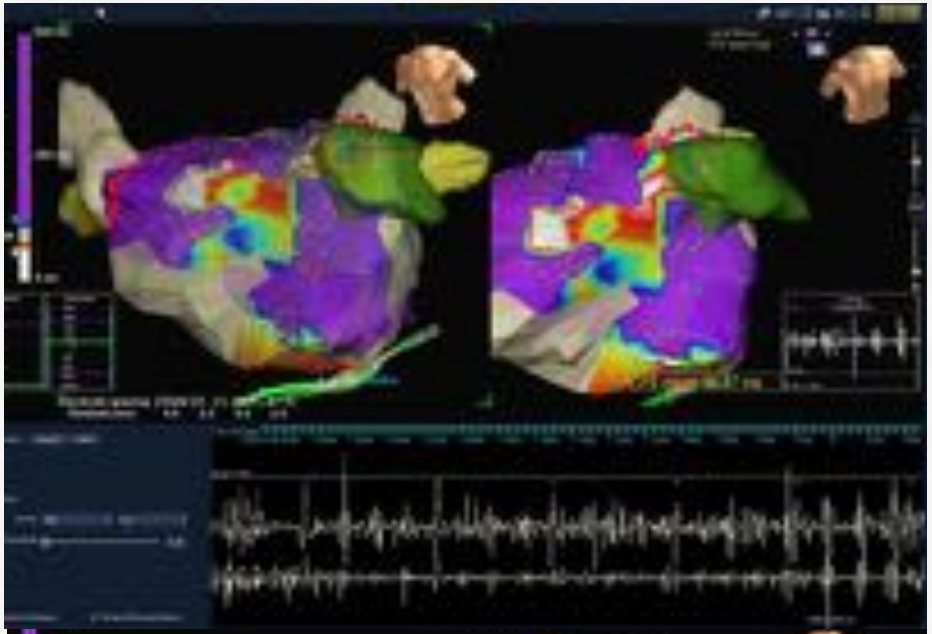


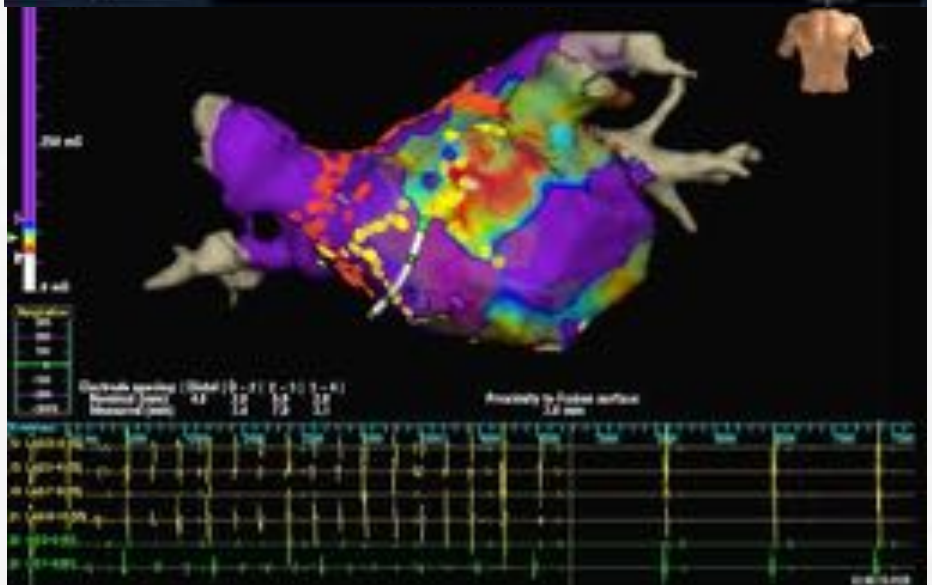
O´Neill et al; Circulation 2007, 116:1515-1523.

CFAE ablation





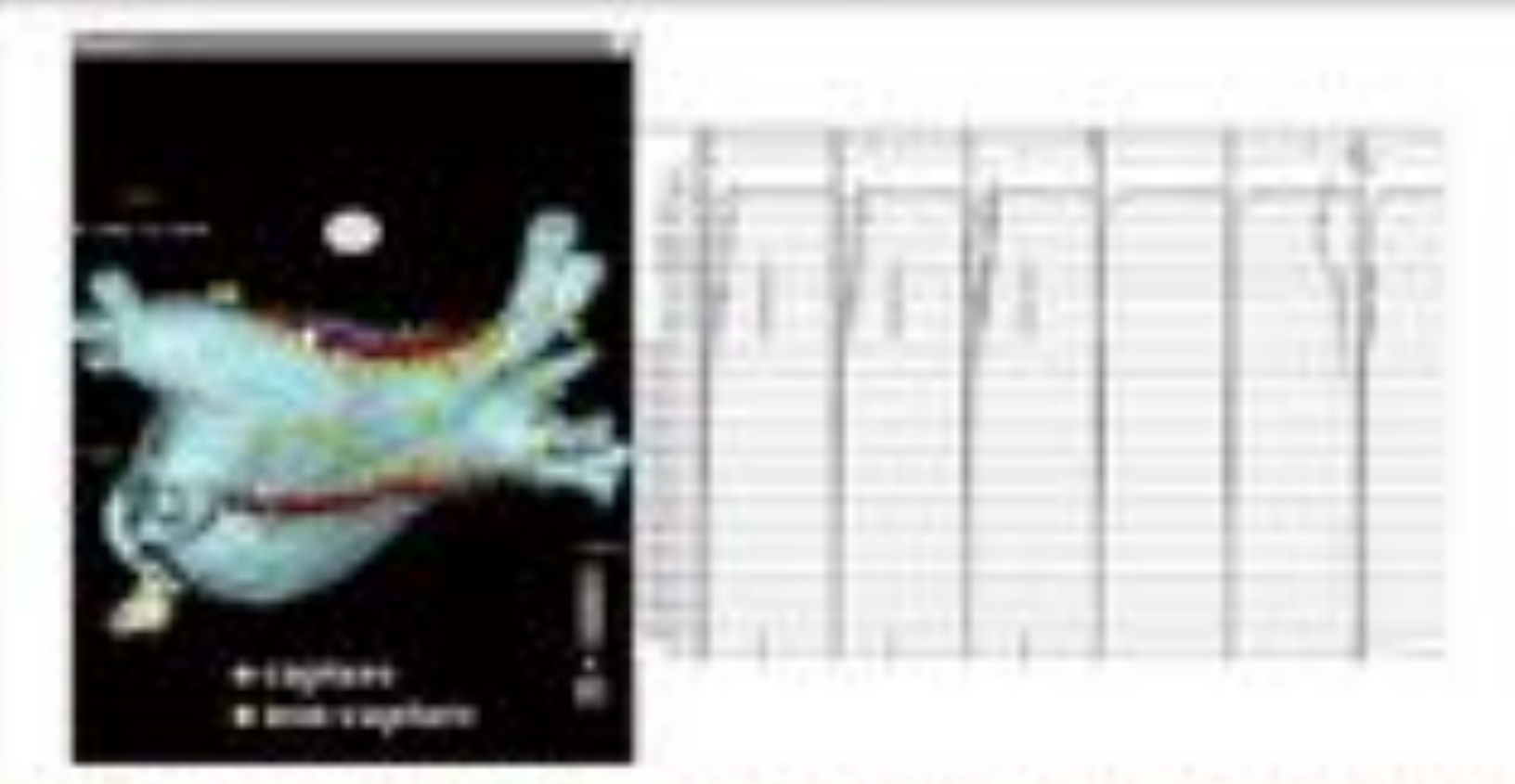




Konings K T et al. Circulation. 1997;95:1231-1241

Long-standing and permanent AF

Exit block of the box lesion



Kumagai, K; Circ J 2011; 75:2350-2311.

Inverse Relationship Between Fractionated Electrograms and Atrial Fibrosis in Persistent Atrial Fibrillation

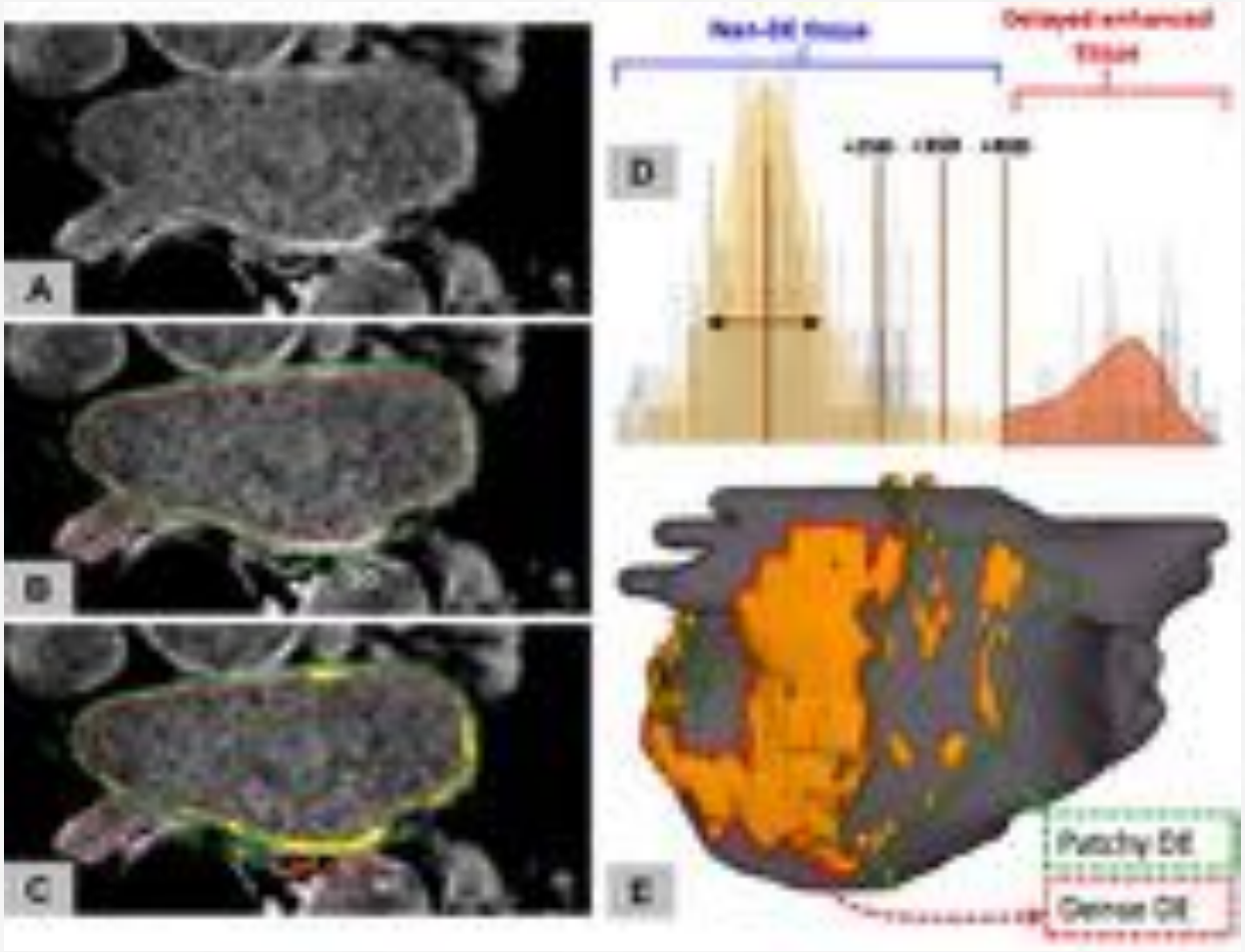
Jadidi AS. Et al; J Am Coll Cardiol 2013;62:802–12.

Detection, Segmentation, and 3-Dimensional Reconstruction of Atrial DE (Delayed Enhancement)

A) High-resolution (1.25 1.25 2.5 mm) delayed enhancement (DE) magnetic resonance imaging.

(B) Segmentation of the left atrial wall between the inner (red) and outer (green) markers.

(C) Regions of DE are depicted in yellow.

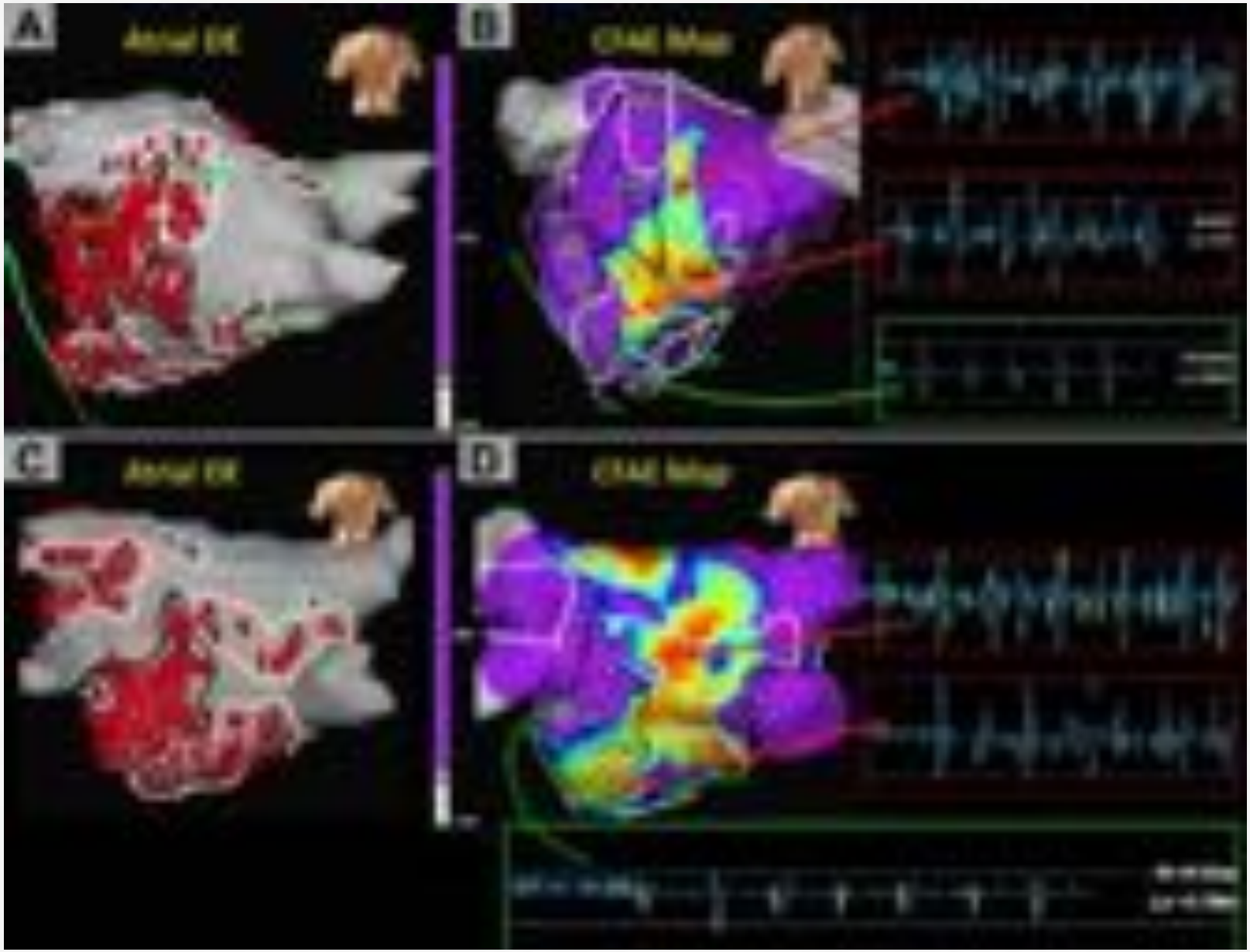


(D) Voxel intensity histogram analysis of left atrial wall identifies DE as voxel intensities >4 SD than the mean in-plane voxel intensity.

(E) Three-dimensional (3D) reconstruction of left atrial blood pool and DE areas. Dense DE regions are measured using the red marker in E with corresponding red arrows in C, and patchy DE regions are measured using the green marker in E with corresponding green arrows in C. ao = descending aorta.

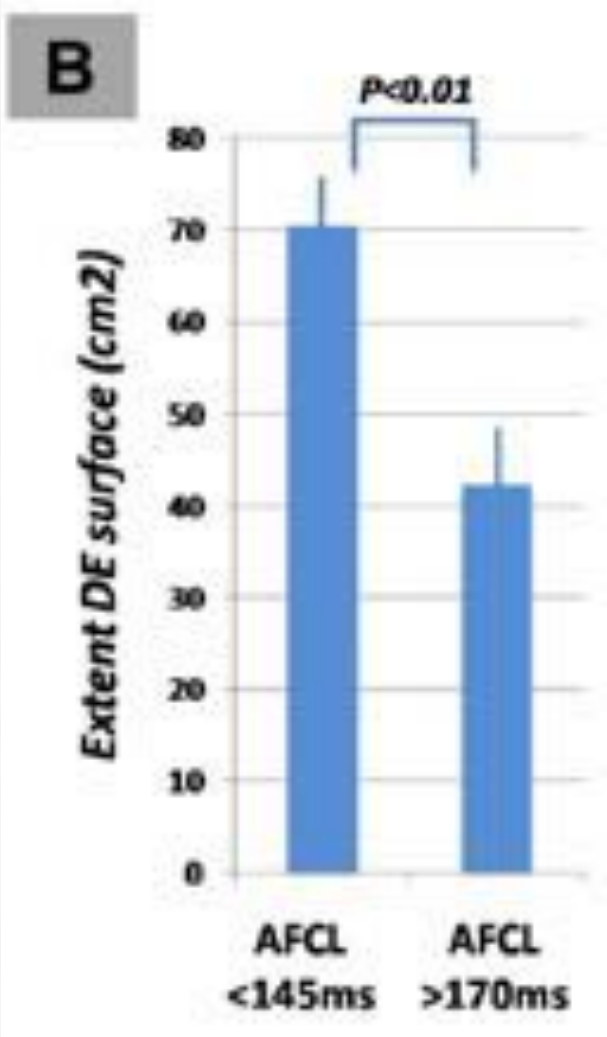
Jadidi AS. Et al; J Am Coll Cardiol 2013;62:802–12.

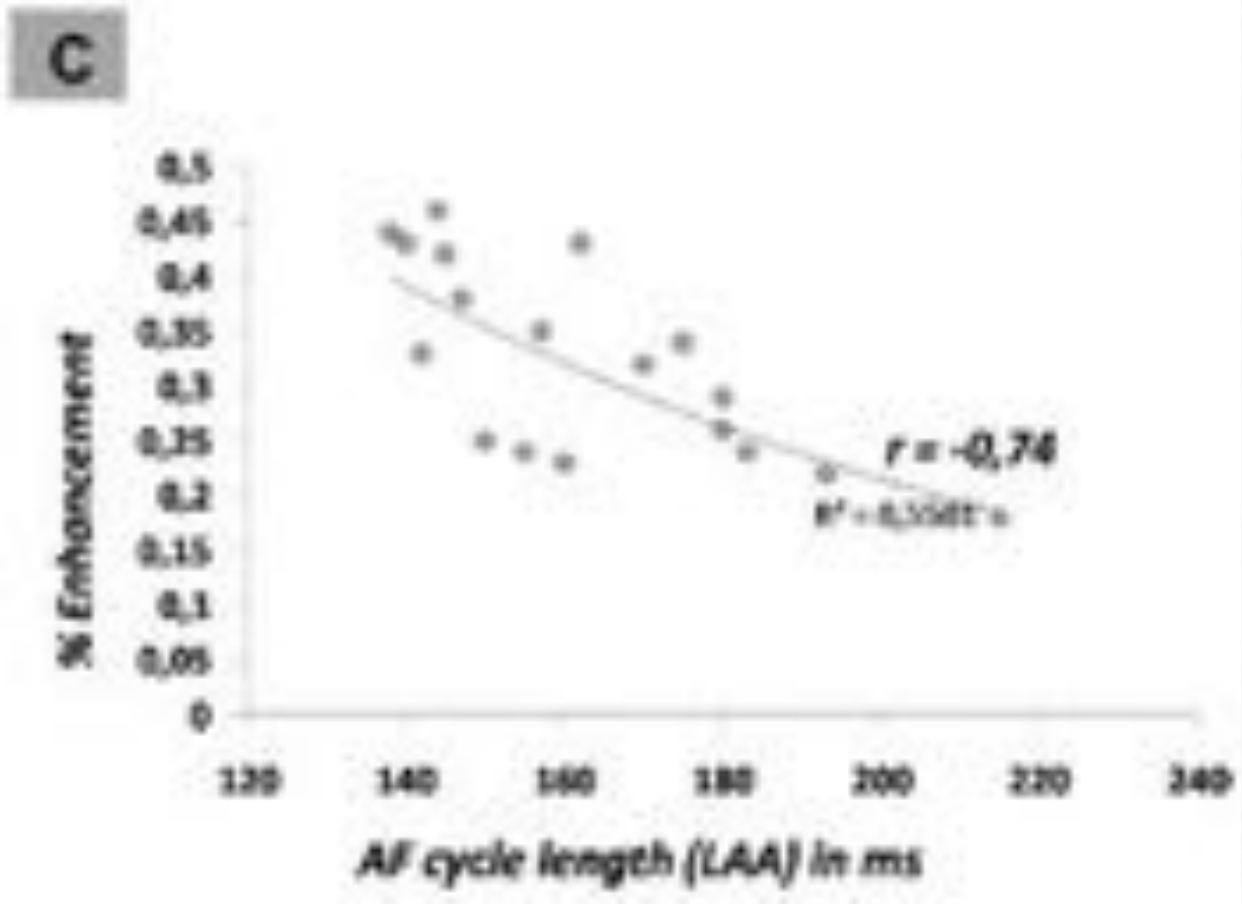
Relationship of Atrial DE to Continuous CFAE Sites



Jadidi AS. Et al; J Am Coll Cardiol 2013;62:802–12.

Shorter AFCL is associated with increased amount of DE





Jadidi AS. Et al; J Am Coll Cardiol 2013;62:802–12.

Conclusions

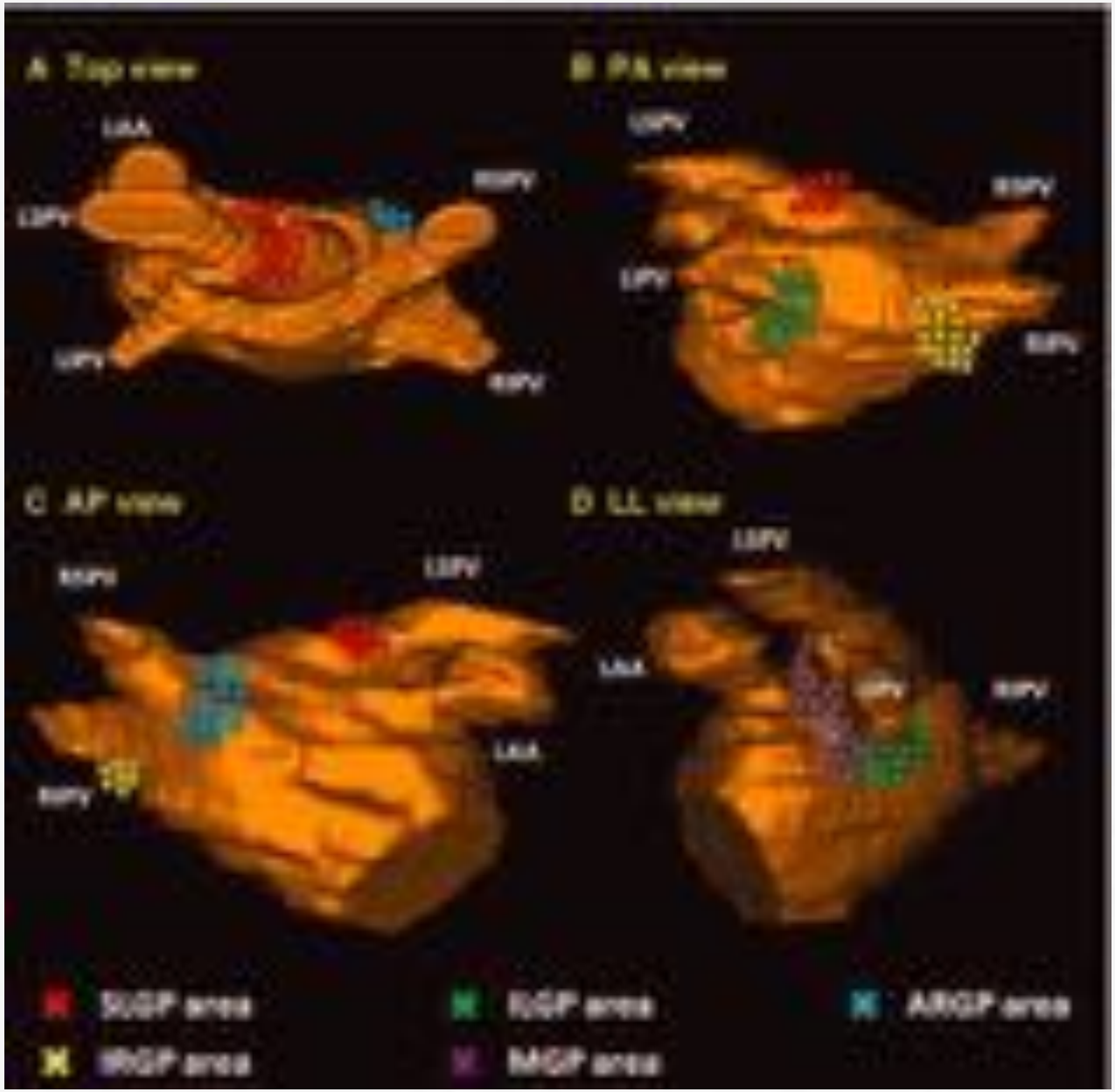
- However, **19% of CFAE occur within or around dense DE** sites.
- These findings may be of clinical importance for choosing the ablation strategy in patients with persistent AF.
- **The region of slow conduction (with fractionated or rapid activity)** within or around the areas of atrial fibrosis may be a promising **ablation target** in patients with persistent AF.
- Alternatively, novel global biatrial mapping systems are currently in the clinical evaluation phase and will allow for a more mechanistically oriented ablation strategy in persistent AF that targets the patient-specific AF sources and drivers.

Jadidi AS. Et al; J Am Coll Cardiol 2013;62:802–12.

The Effect of Fat Pad Modification during Ablation of Atrial Fibrillation: Late Gadolinium Enhancement MRI Analysis

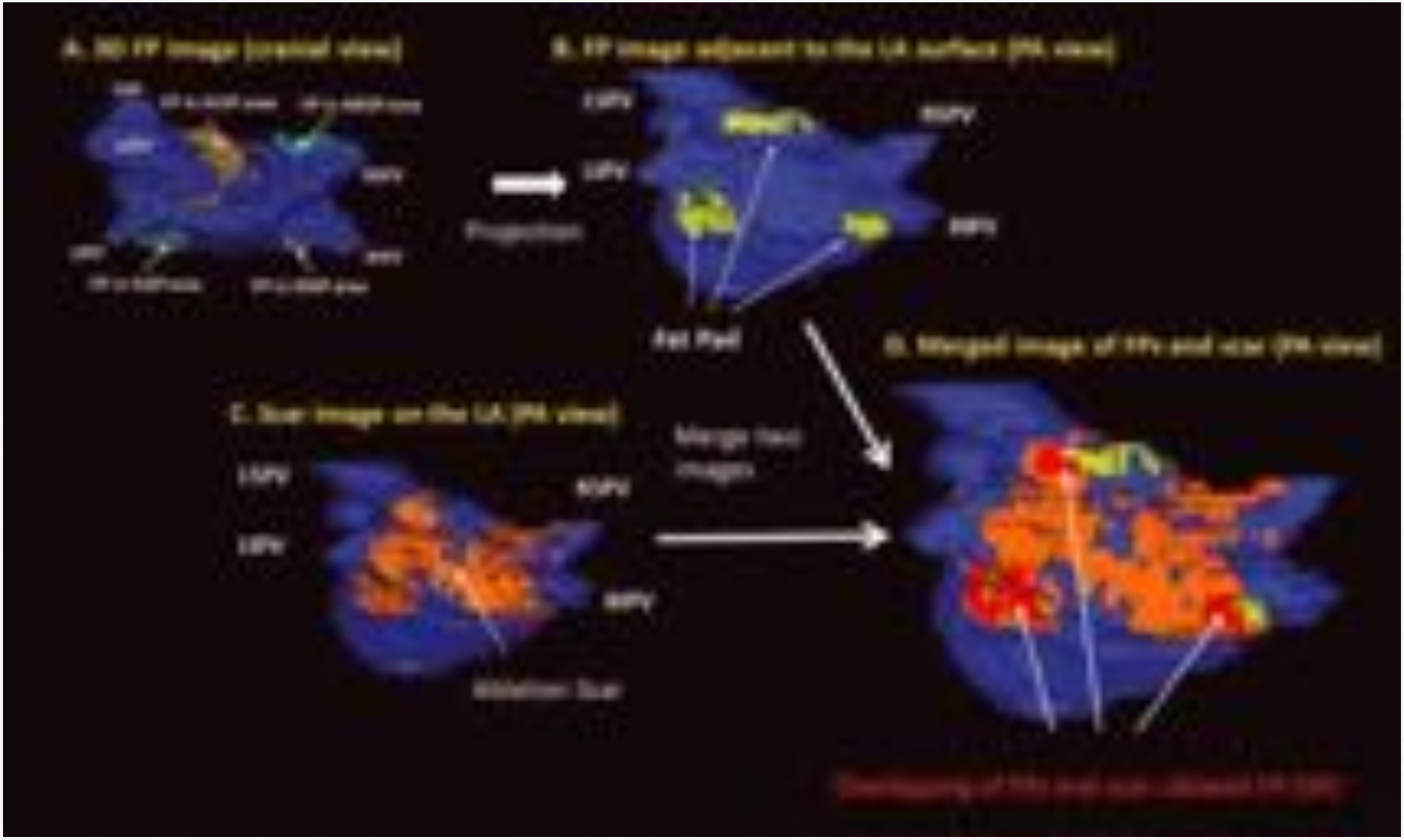
Higuchi K. et al; PACE 2013; 36:467–476.

Definition of GP Areas

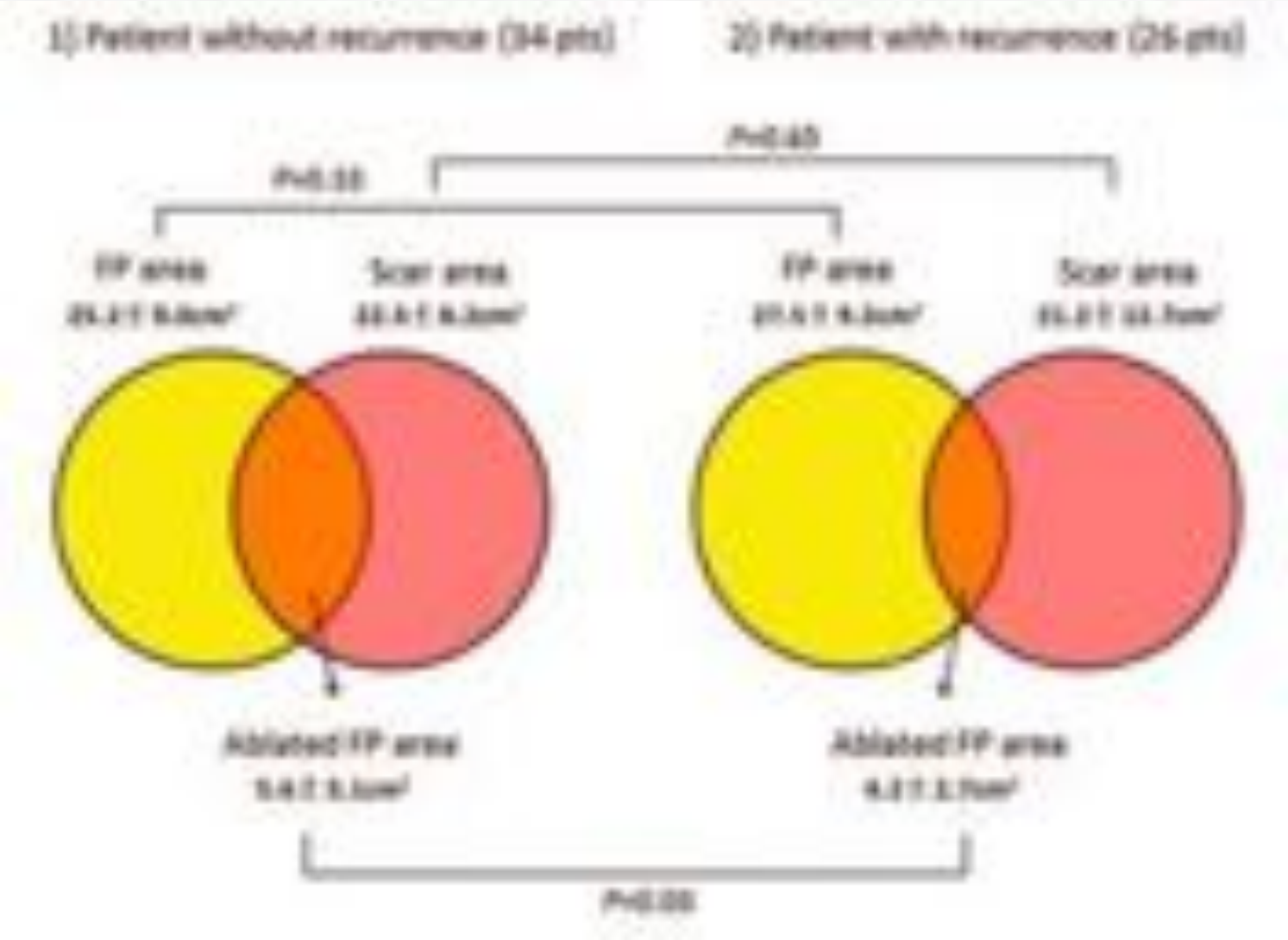


Higuchi K. et al; PACE 2013; 36:467–476.

Merging LA, Scar, and FP Image



Higuchi K. et al; PACE 2013; 36:467–476.



Higuchi K. et al; PACE 2013; 36:467–476.

Optimal Method and Outcomes of Catheter Ablation of Persistent AF: The STAR AF 2 Trial

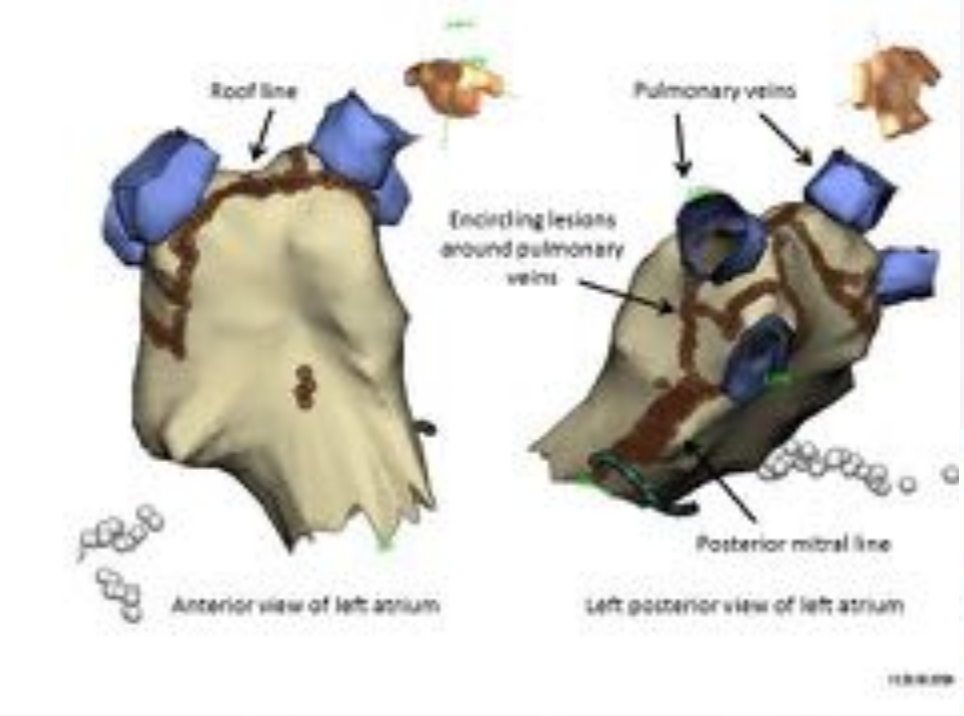
presented at ESC 2014 Barcelona

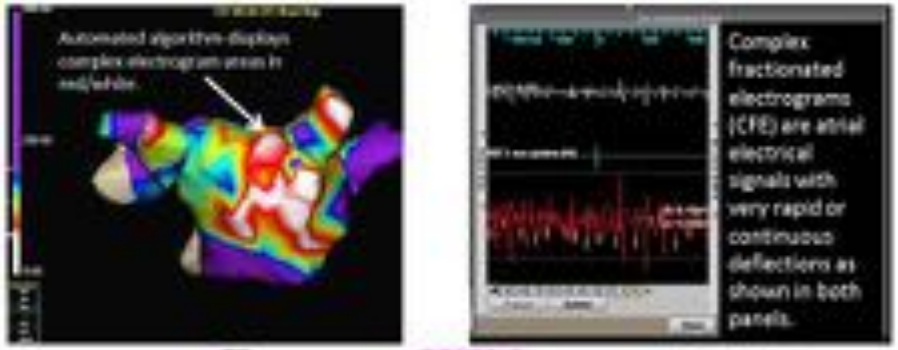
Atul Verma, Jiang Chen-yang, Tim Betts, John Radcliffe, Jian Chen, Isabel Deisenhofer, Roberto Mantovan, Laurent Macle,
Carlos Morillo, Prashanthan Sanders
on behalf of the STAR AF 2 Investigators

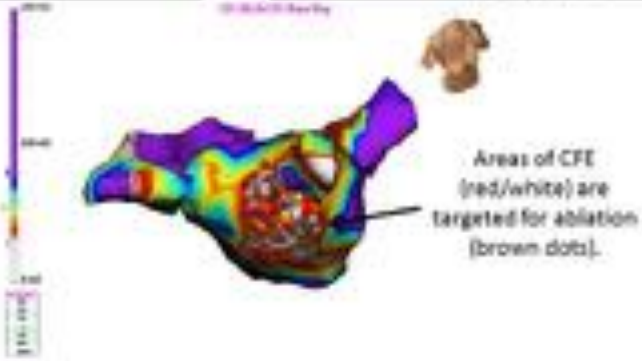
ClinicalTrials.gov NCT01203748

The STAR AF 2 trial was funded by St Jude Medical Inc.

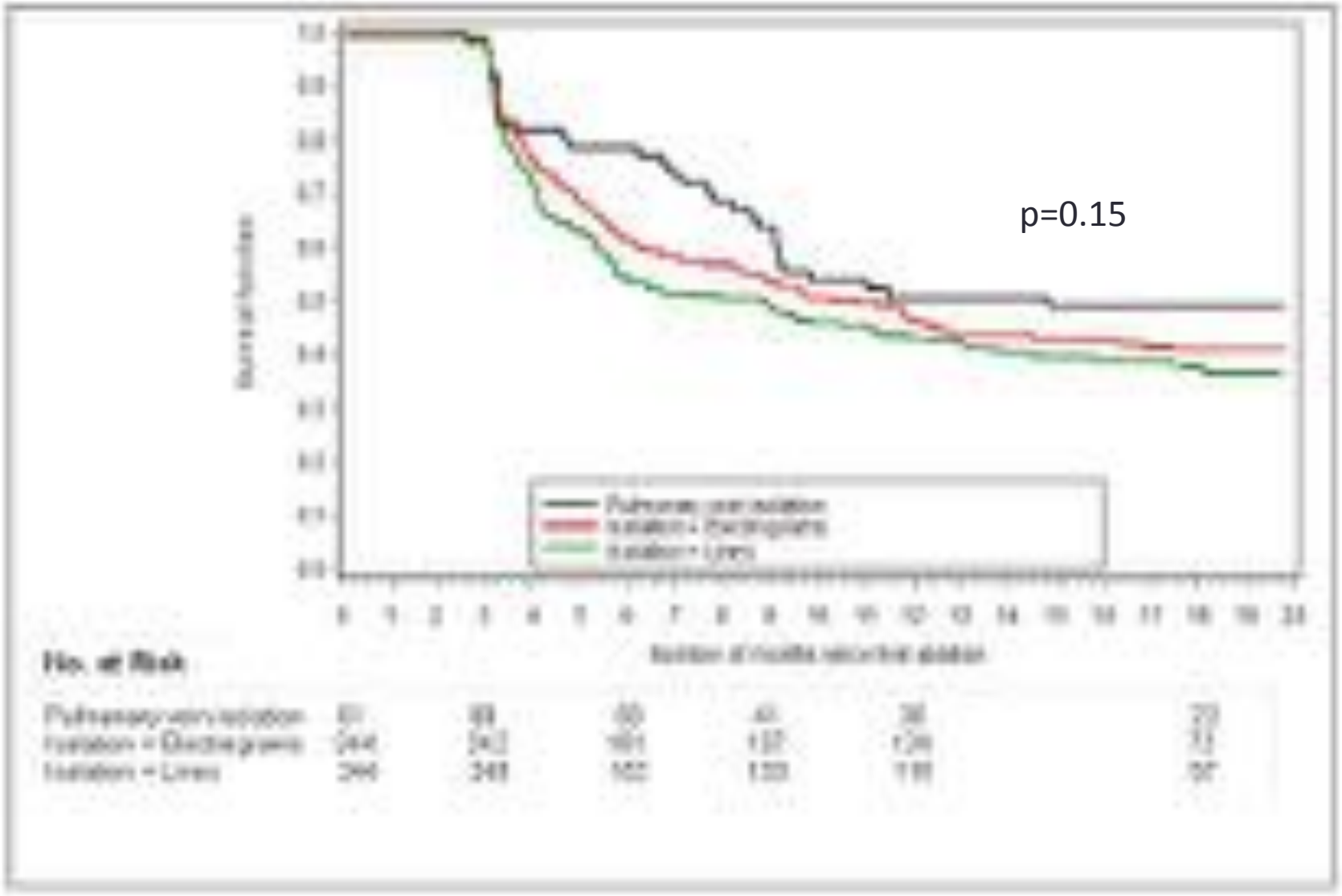
Methods


Roof line
Pulmonary veins
Encircling lesions around pulmonary veins
Posterior mitral line
Anterior view of left atrium
Left posterior view of left atrium


Automated algorithm displays complex electrogram areas in red/white.
Complex fractionated electrograms (CFE) are atrial electrical signals with very rapid or continuous deflections as shown in both panels.


Areas of CFE (red/white) are targeted for ablation (brown dots).

Primary Outcome



Documented AF > 30 seconds after <u>one</u> procedure with or without AAD

Primary and Secondary Outcomes

	PVI	PVI+CFE	PVI+LINES	p value
Freedom from AF after 1 procedure	59 %	48 %	44 %	0.15
Freedom from AF/AFL/AT after 1 procedure	49 %	41 %	37 %	0.15
Freedom from AF after 2 procedures	72 %	60 %	58 %	0.18
Freedom from AF/AFL/AT after 2 procedures	60 %	50 %	48 %	0.24
Percentage of patients still on AAD at 18 mo	11 %	12 %	12 %	0.35

* AAD = antiarrhythmic drugs

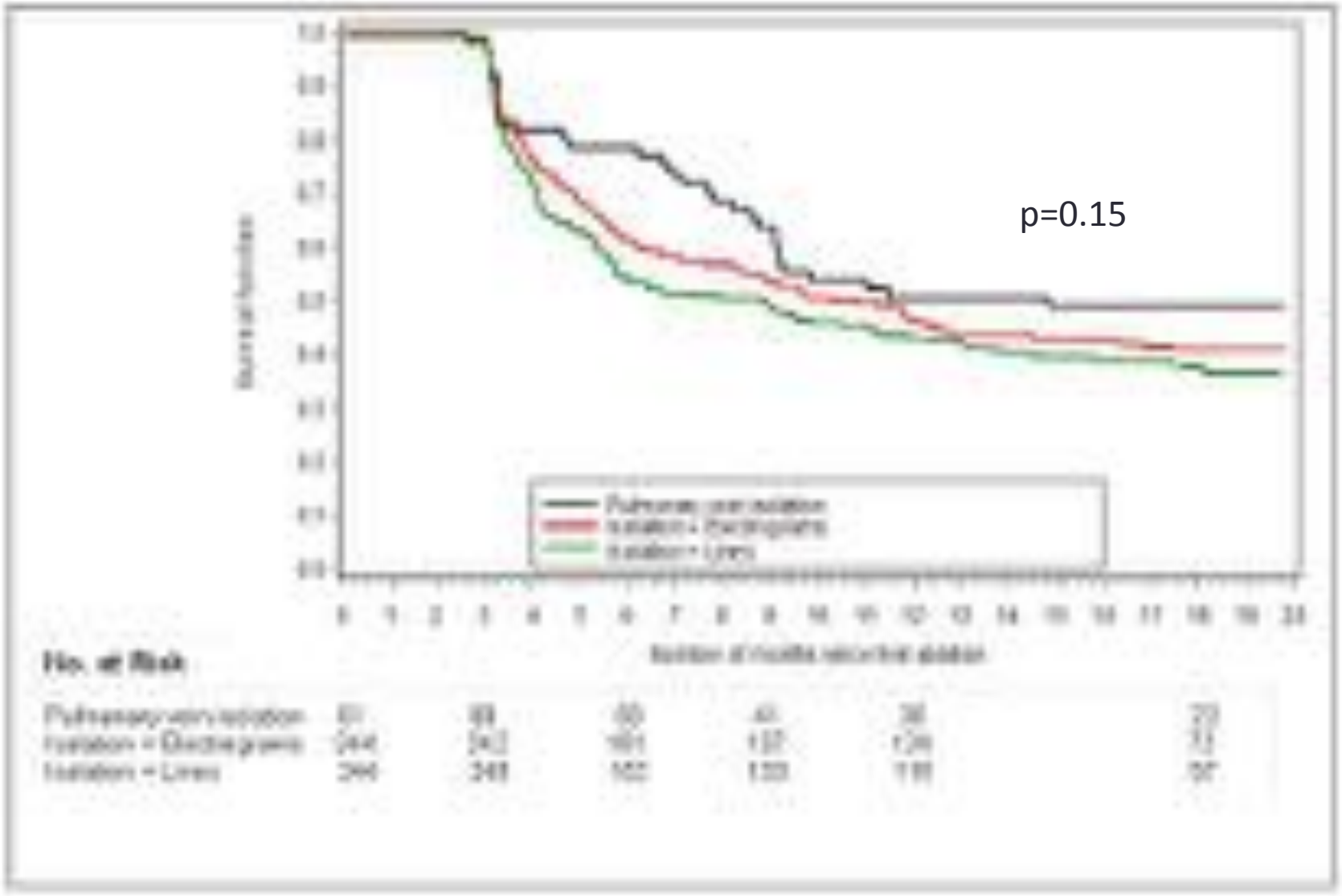
Complications

Category	PVI (n=64)	PVI+CFE (n=254)	PVI+Lines (n=250)	Total (n=568)
Access site hematoma	2	0	3	5
Access site arteriovenous fistula or pseudoaneurysm	0	3	3	6
Pericarditis	0	1	2	3
Fluid overload	0	1	3	4
Sedation related complication	0	3	5	8
Skin burn	1	0	0	1
Cardiac tamponade	1	0	2	3
Transient ischemic attack or Stroke	0	2	1	3
Atrial esophageal fistula - procedural death	0 6%	1 4%	0 7%	1 6%

Conclusions

- Largest randomized trial to examine outcomes of catheter ablation in persistent AF
- Additional CFE or Lines ablation increased procedural time (may increase risk)
- No benefit in AF reduction when additional substrate ablation (CFE or Lines) was performed on top of PVI
- PVI alone achieved freedom from recurrence in about 50% of patients – comparable to published success rates from randomized, multicenter trials in paroxysmal AF

STAR-AF Trial, ESC Barcelona 2014



Documented AF > 30 seconds after <u>one</u> procedure with or without AAD

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- Ganglionated Plexi (GP), Fad pads
- **Left atrial appendage (LAA)**
- Rotors

Neues vom ESC London 2015

- **BELIEF-Trial:**

- **Verbessert die empirische LAA Isolation zusätzlich zur komplexen linksatrialen Ablation die Langzeit-Prognose bei Pat. mit lang persistierendem AF?**
- **Multicenter, randomisiert**

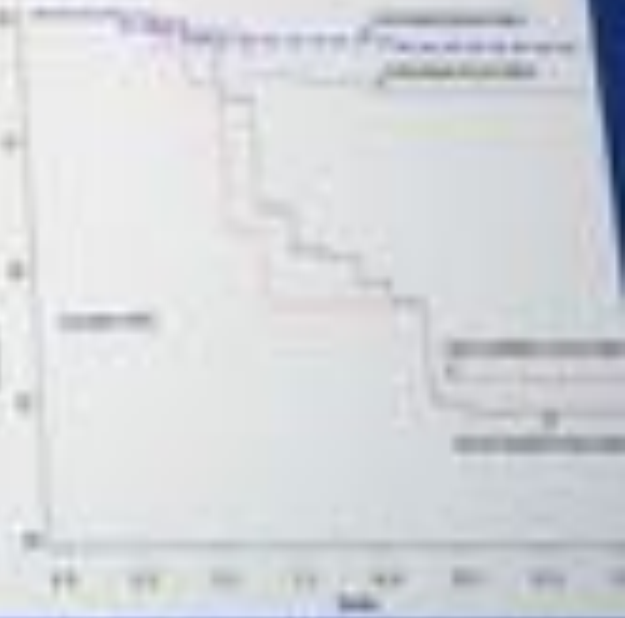
De Biase et al

Circulation

American Heart Association.

Left Atrial Appendage : An Underrecognized Trigger Site of Atrial Fibrillation

Luigi Di Biase, J. David Burkhardt, Prasant Mohanty, Javier Sanchez, Sanghamitra Mohanty, Rodney Horton, G. Joseph Gallinghouse, Shane M. Bailey, Jason D. Zagrodzky, Pasquale Santangeli, Steven Hao, Richard Horgo, Sabwa Behaley, Sakis Themistoclakis, Aldo Bonso, Antonio Rossillo, Andrea Corrado, Antonio Raviele, Amin Al Ahmad, Paul Wang, Jennifer E. Cummings, Robert A. Schweikert, Gemma Pelargonio, Antonio Dello Russo, Michela Casella, Pietro Santarelli, William R. Lewis and Andrea Natale

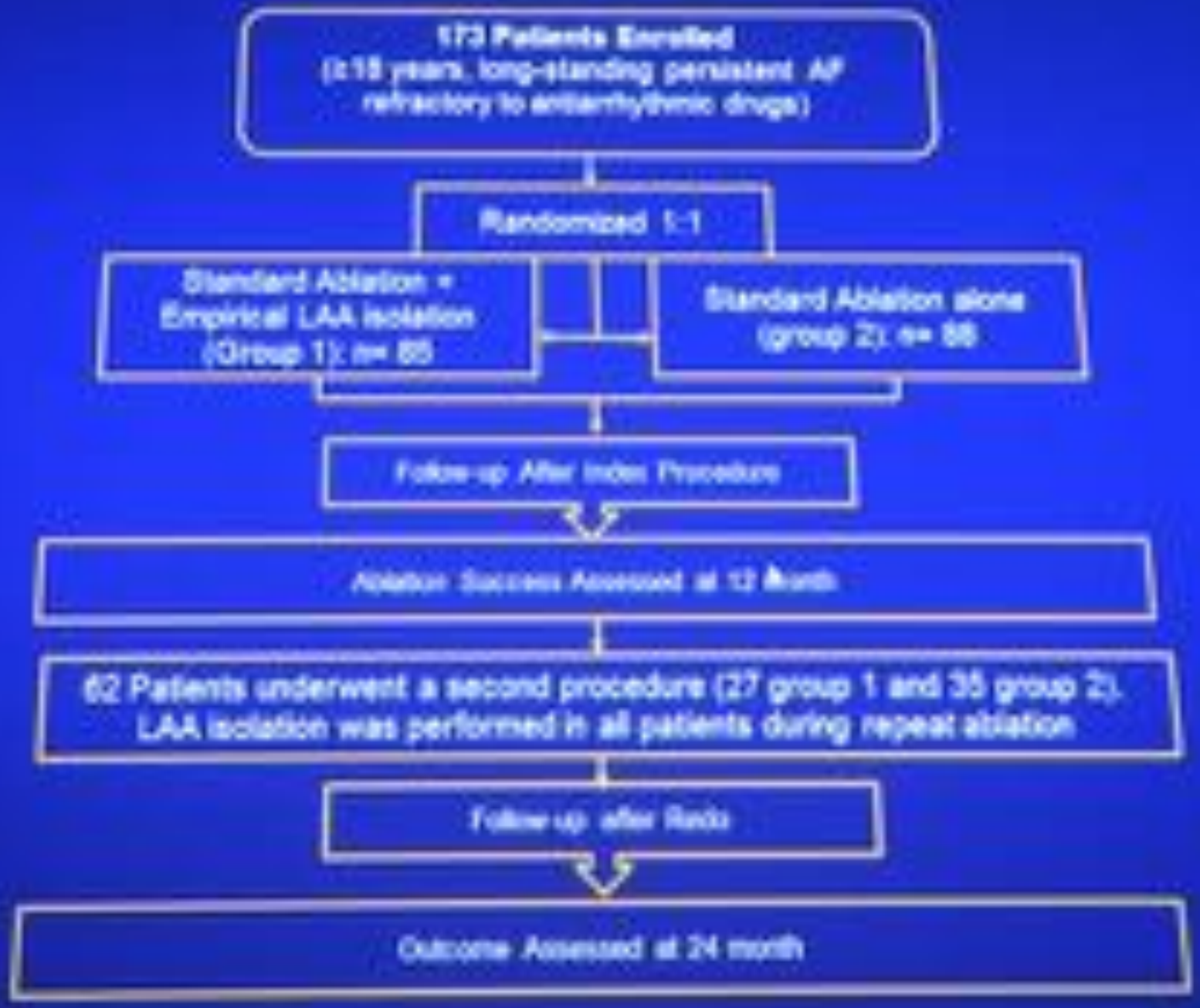


Di Biase et al. Circulation. 2010;122:109-118.

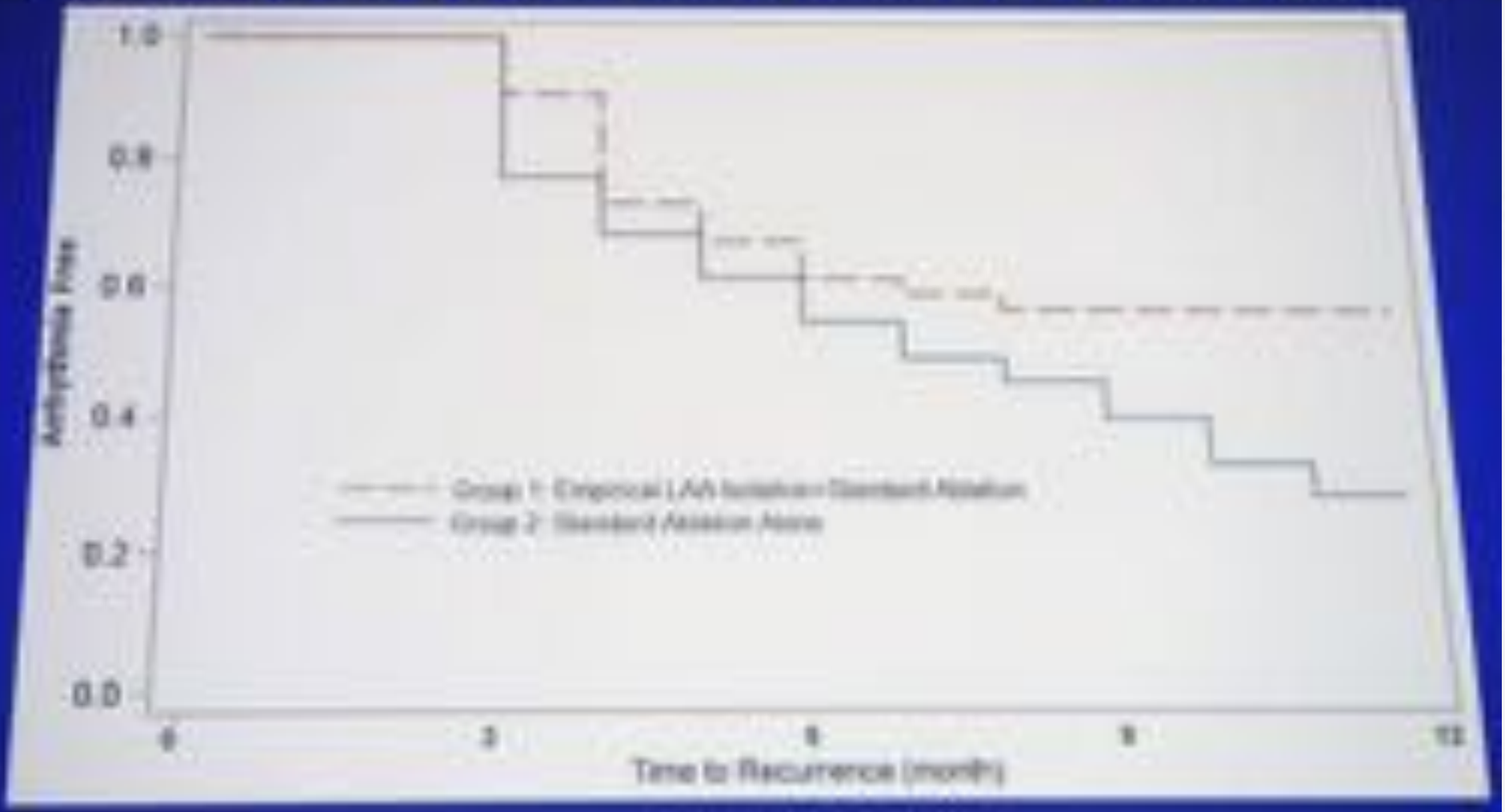
BELIEF-Trial Methods ESC 2015 London

- This was a randomized, parallel-group study assessing whether empirical electrial isolation of the LAA in addition to a standard ablation with an extended pv antrum, could improve the freedom from atrial arrhythmia in LSP AF patients
- Power Calculation: The study had 80% power to detect at least 20% difference in success rate (50% to 70%) at 12 month follow-up (using log-rank test), with two-sided Type I error of 0.05.
- 173 patients were enrolled and randomly assigned (1:1 ratio) to:
  - Extensive ablation plus ***Empirical Electrical LAA Isolation*** (group 1, *n*=85)
  - Extended PV antrum and non PV triggers ablation (group 2, *n*=88)
- Patients ≥18 years of age, with LSP AF refractory to antiarrhythmic drugs were included in the study

Study Design

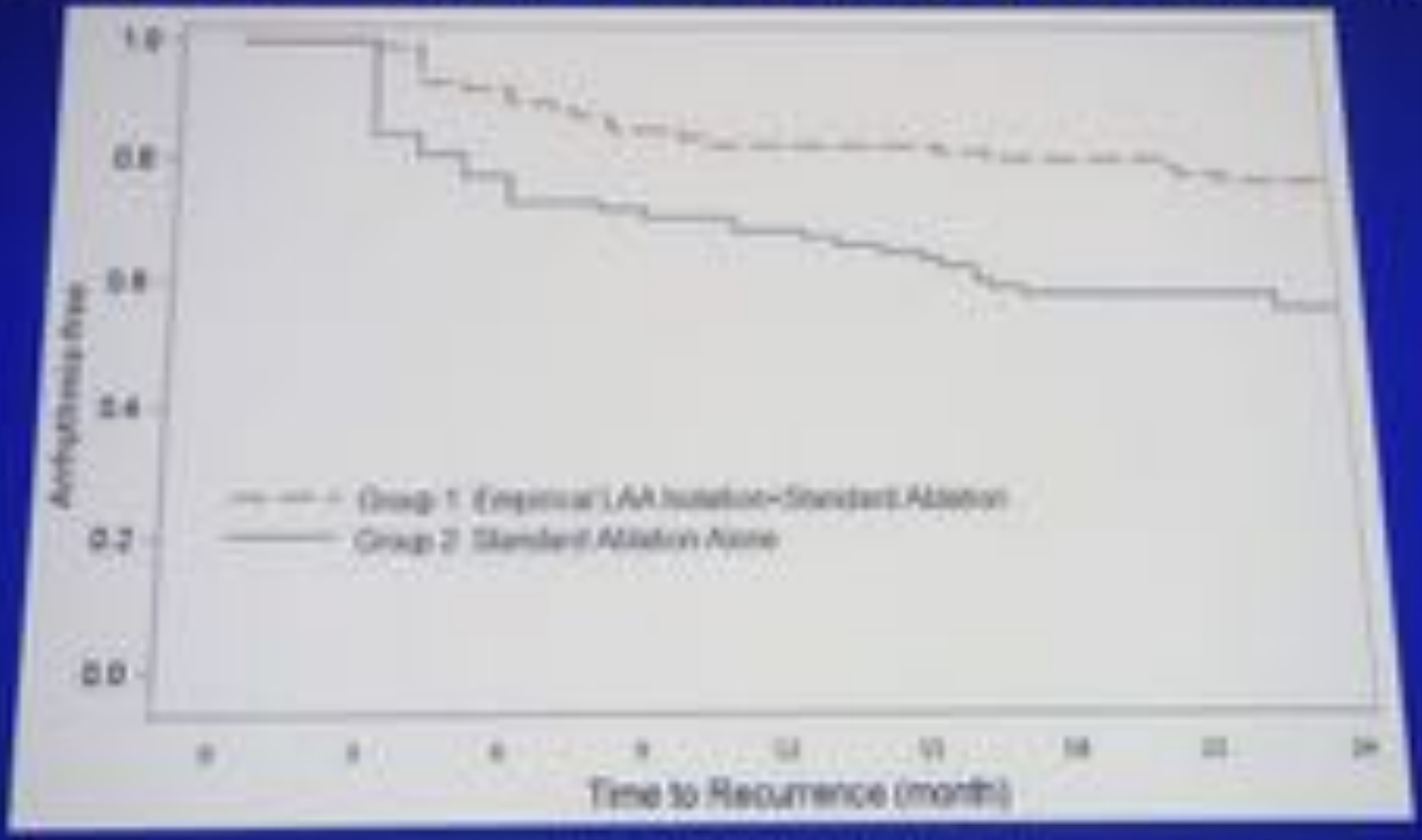


Kaplan–Meier curves: single procedure success rate



At the 12 month follow-up, 48(56%) in group 1 and 25 (28%) in group 2 were recurrence-free off-AAD after a single procedure. (Log-rank p=0.001, unadjusted HR 1.92 [1.3 to 2.9]).

Cumulative Overall Success After 1.3 Procedures



The cumulative success after multiple procedures was 65 (76%) in group 1 and 49 (56%) in group 2

ALL THE PATIENTS UNDERWENT LAA ISOLATION

(Log-rank p= 0.003, unadjusted HR 2.24 [95% CI 1.3-3.8])

Relative contribution of different ablation targets in the AF disease continuum

CONCLUSIONS

- The results of this randomized study show that both after a single and redo procedures in patients with long standing persistent AF, the ***EMPIRICAL ELECTRICAL ISOLATION*** of the ***LAA*** improve the long-term freedom from atrial arrhythmias without increasing complications.

- Future studies examining the physiopathology of these findings are necessary.

AF ablation: Mapping and Imaging

- The substrate
- Intracardial signals
- Point by point vs circular mapping
- 3D imaging
- Lines
- Ganglionated Plexi (GP)
- Complex fractionated atrial electrograms (CFAE)
- Left atrial appendage (LAA)
- Fad pads
- **Magnetic robotic ablation**
- Rotors
- Technical improvements and safety

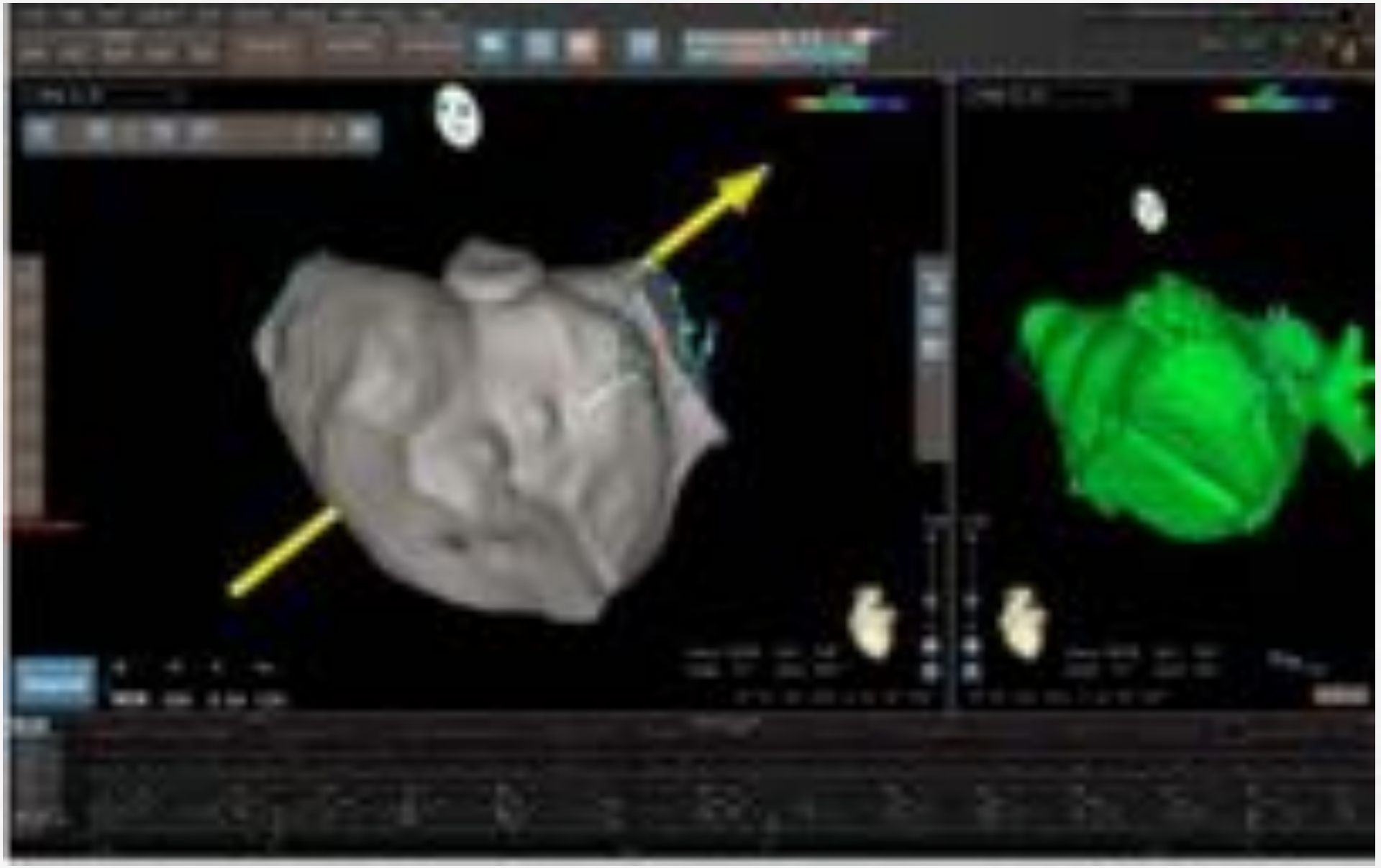
Remote-controlled magnetic pulmonary vein isolation using a new three-dimensional non-fluoroscopic navigation system: A single-centre prospective study

Da Costa A. et al; Archives of Cardiovascular Disease (2013) 106, 423—432.

Remote magnetic navigation system

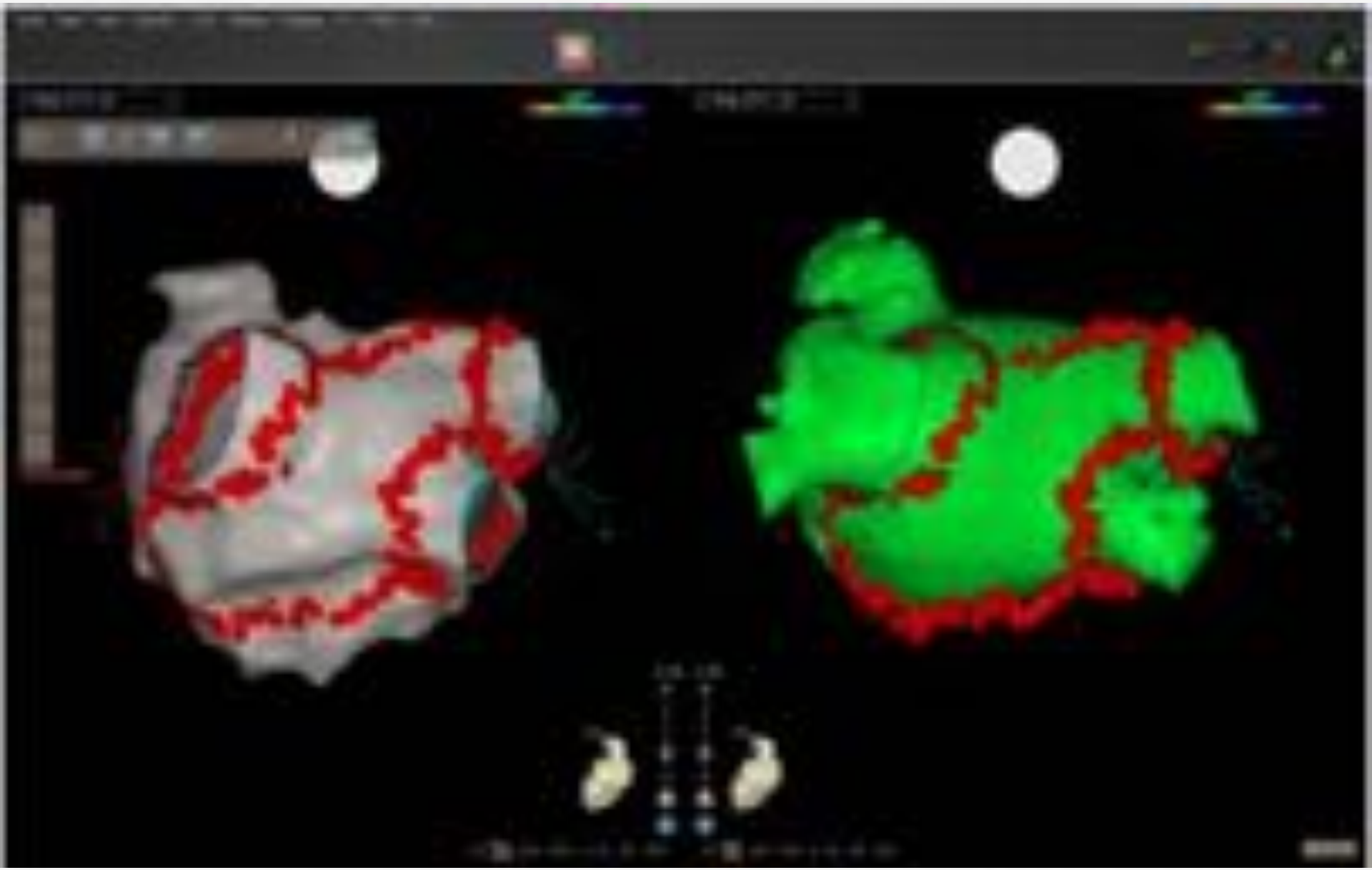
Da Costa A. et al; Archives of Cardiovascular Disease (2013) 106, 423—432.

Carto 3 system features



Da Costa A. et al; Archives of Cardiovascular Disease (2013) 106, 423—432.

Carto 3 system features



Da Costa A. et al; Archives of Cardiovascular Disease (2013) 106, 423—432.

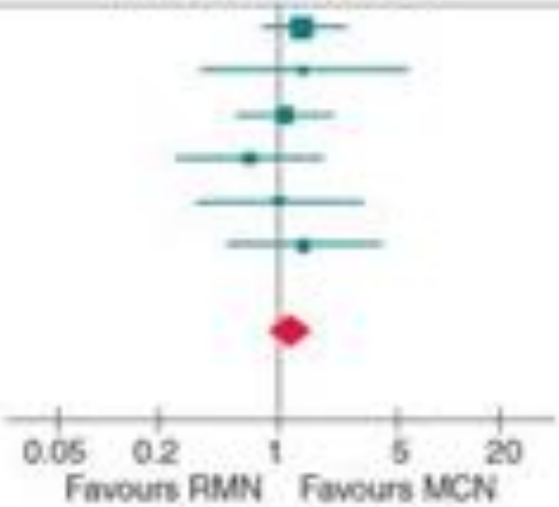
Remote magnetic with open-irrigated catheter vs. manual navigation for ablation of atrial fibrillation: a systematic review and meta-analysis

Proietti R. et al; Europace (2013) 15, 1241–1248.

Remote magnetic navigation vs. MCN; outcome: atrial tachyarrhythmia recurrence

Study or subgroup	RMN Events	RMN Total	MCN Events	MCN Total	Weight	Odds ratio M-H, Random, 95% CI
Arya 2011	29	70	96	286	38.1%	1.40 [0.82, 2.39]
Choi MS 2011	4	41	5	70	5.8%	1.41 [0.36, 5.56]
Luthje 2011	50	107	24	54	25.2%	1.10 [0.57, 2.12]
Miyazaki 2010	9	30	17	44	11.1%	0.68 [0.25, 1.83]
Natale 2011	8	43	8	44	9.3%	1.03 [0.35, 3.04]
Sorgente 2010	15	35	10	29	10.5%	1.43 [0.52, 3.94]
Total (95% CI)		**326**		**527**	**100.0%**	**1.18 [0.85, 1.65]**
Total events	115		160			

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.88$, df = 5 ($P = 0.86$); $I^2 = 0\%$
Test for overall effect: $Z = 1.00$ ($P = 0.32$)

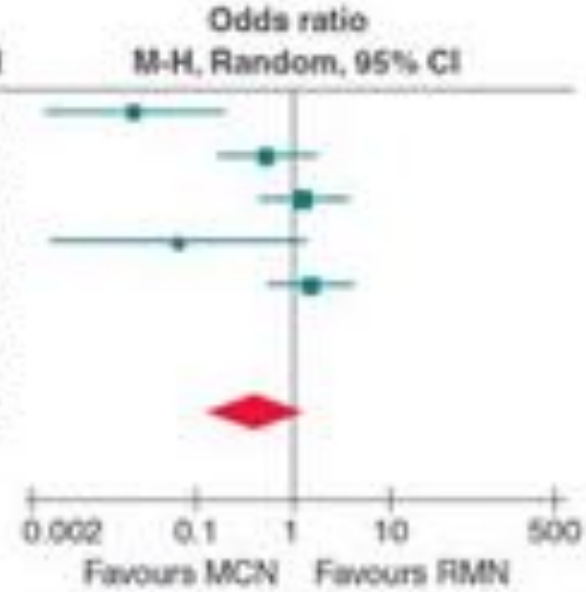


Proietti R. et al; Europace (2013) 15, 1241–1248.

Remote magnetic navigation and MCN; outcome: PVI

Study or subgroup	RMN Events	RMN Total	MCN Events	MCN Total	Weight	Odds ratio M-H, Random, 95% CI
Arya 2011	61	70	285	286	16.3%	0.02 [0.00, 0.19]
Choi MS 2011	34	41	63	70	23.4%	0.54 [0.17, 1.67]
Luthje 2011	96	107	47	54	24.3%	1.30 [0.47, 3.57]
Miyazaki 2010	26	30	44	44	11.4%	0.07 [0.00, 1.28]
Solheim 2011	10	23	22	65	24.6%	1.50 [0.57, 3.97]
Sorgente 2010	35	35	29	29		Not estimable
Total (95% CI)		**306**		**548**	**100.0%**	**0.41 [0.11, 1.47]**
Total events	262		490			

Heterogeneity: $\tau^2 = 1.51$; $\chi^2 = 17.36$, df = 4 ($P = 0.002$); $I^2 = 77\%$
Test for overall effect: $Z = 1.37$ ($P = 0.17$)

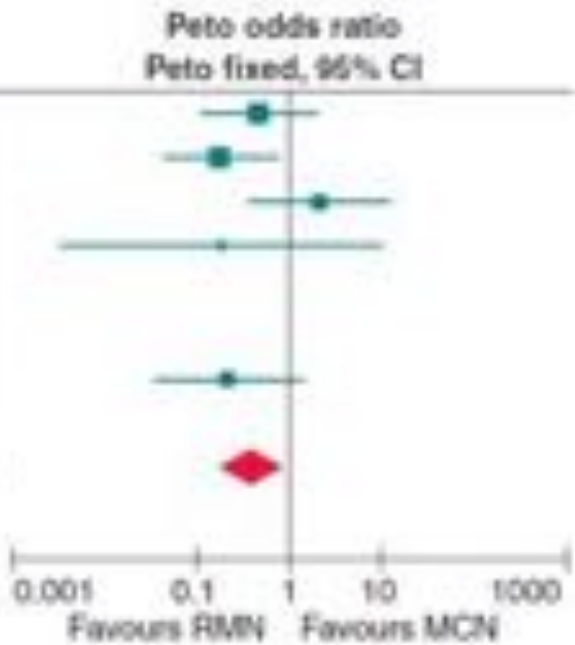


Proietti R. et al; Europace (2013) 15, 1241–1248.

Remote magnetic navigation vs. MCN; outcome: major complications

Study or subgroup	RMN Events	RMN Total	MCN Events	MCN Total	Weight	Peto odds ratio Peto fixed, 95% CI
Arya 2011	1	70	11	286	28.4%	0.48 [0.11, 2.03]
Choi MS 2011	0	41	9	70	30.0%	0.18 [0.04, 0.74]
Luthje 2011	5	107	1	54	20.0%	2.18 [0.39, 12.22]
Miyazaki 2010	0	30	1	44	3.7%	0.19 [0.00, 10.08]
Natale 2011	0	43	0	44		Not estimable
Solheim 2011	0	23	0	65		Not estimable
Sorgente 2010	1	35	4	29	17.9%	0.22 [0.04, 1.38]
Total (95% CI)		**349**		**592**	**100.0%**	**0.41 [0.19, 0.88]**
Total events	7		26			

Heterogeneity: $\chi^2 = 5.54$, df = 4 ($P = 0.24$); $I^2 = 28\%$
Test for overall effect: $Z = 2.28$ ($P = 0.02$)



Proietti R. et al; Europace (2013) 15, 1241–1248.

AF ablation: Mapping and Imaging

- The substrate
- Intracardial signals
- Point by point vs circular mapping
- 3D imaging
- Lines
- Ganglionated Plexi (GP)
- Complex fractionated atrial electrograms (CFAE)
- Left atrial appendage (LAA)
- Fad pads
- Magnetic robotic ablation
- **Rotors**
- Technical improvements and safety

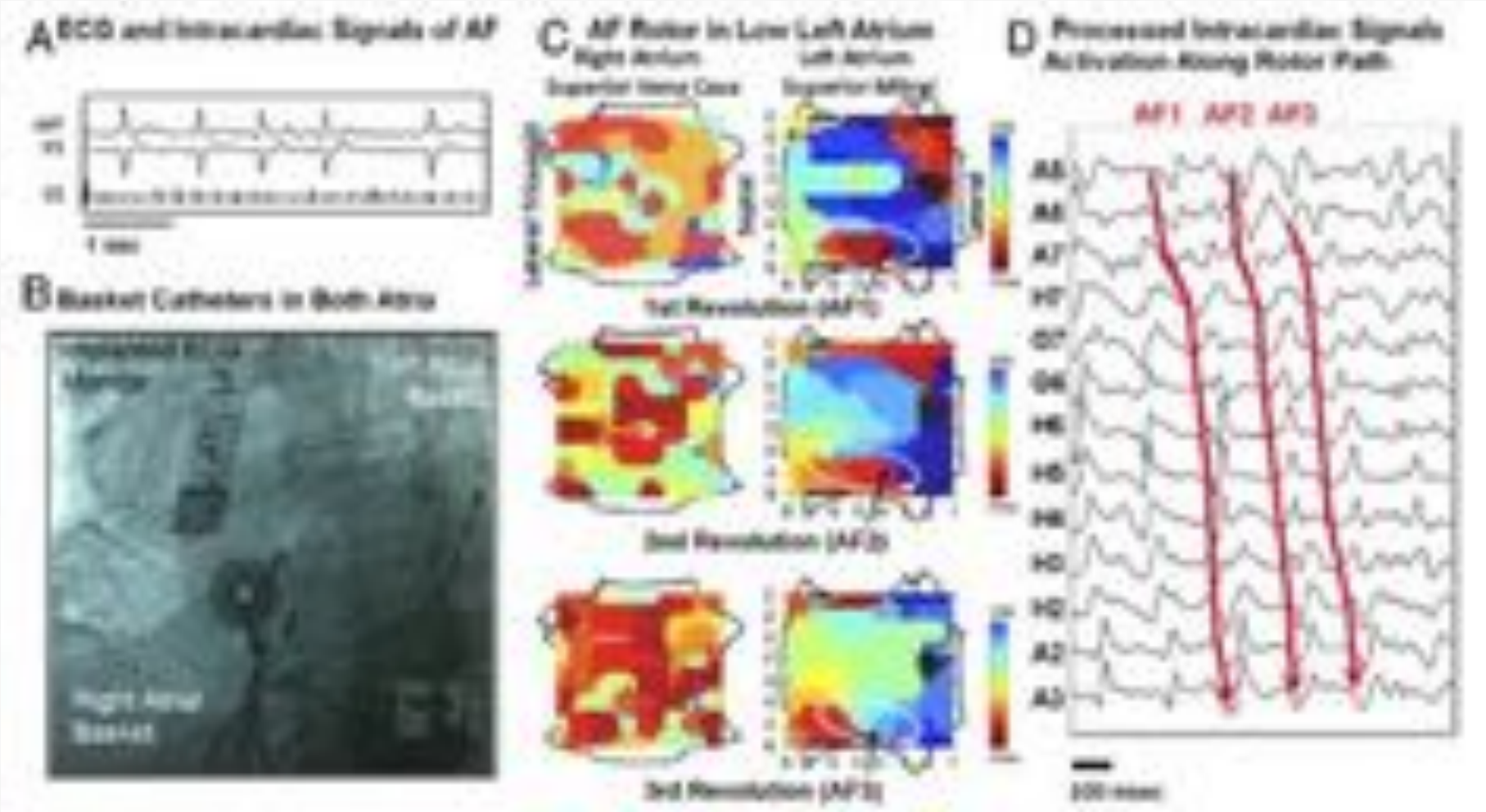
Advanced ablation of AF

- Definitions, targets, general results
- Special approaches: „Single shot“ devices
- Fibrosis imaging
- Complex fractionated atrial electrograms (CFAE)
- Ganglionated Plexi (GP), Fad pads
- Left atrial appendage (LAA)
- **Rotors**

CONFIRM

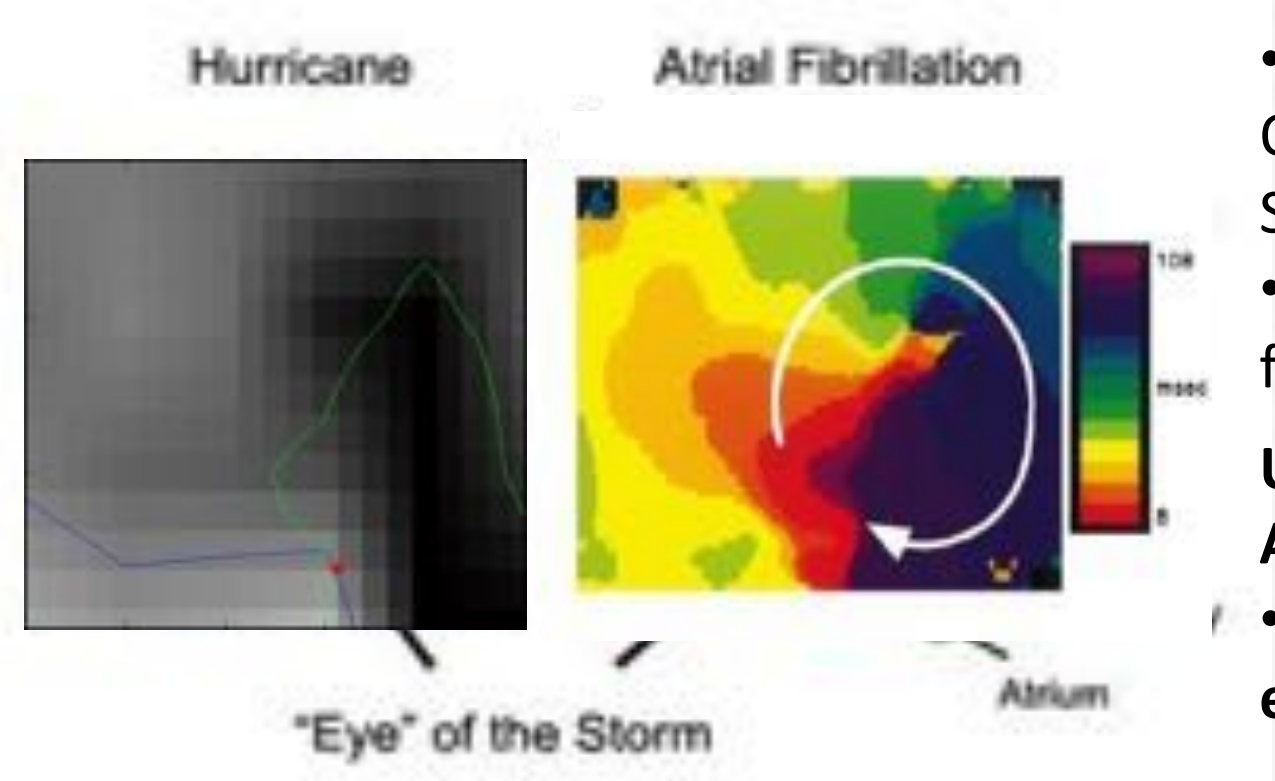
The FIRM principle: Focal Impulse and Rotor Modification

Computational Mapping of “Electrical Rotor” During Atrial FibrillationConclusions



Narayan et al: JACC Vol. 60, No. 7, 2012 Narayan et al; August 14, 2012:628–36.

Localized Sources Often Sustain Human Atrial Fibrillation



- Direct evidence from Optically Mapped Sheep atria [1,2]
- Indirect Evidence from Canine atria [3]

Until 2011, Human AF:

- **Little or no prior evidence for rotors**

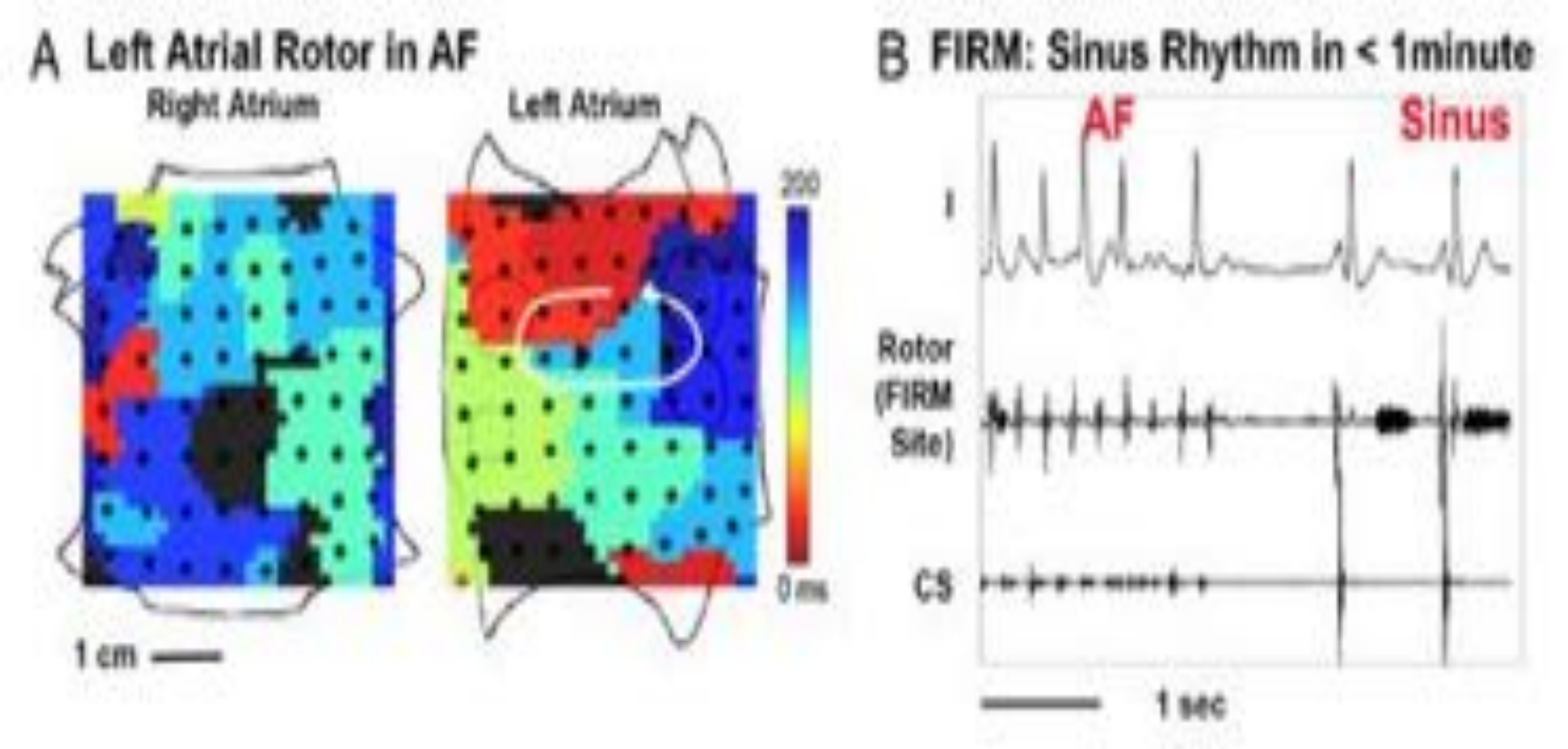
CONFIRM (2011): AF rotors/sources typically sustain human AF
Focal Impulse and Rotor Modulation (FIRM) – Multicenter Validation

(1) Vaquero/Jalife Heart Rhythm 2008;872-879; (2) Skanes Circulation 1998; 1236-48; (3) Ryu, Stambler JCE 2005; 16: 1348-1358; (4) Lin Circ 2005; 112:1692-700; (5) Cuculich, Rudy. Circ 2010; 1364-1372; (6) Allessie Circ EP 2010; 1674-1682; (7) Narayan, Shivkumar, Miller et al, J Am Coll Cardiol **2012**; 60(7): 628-636

CONFIRM

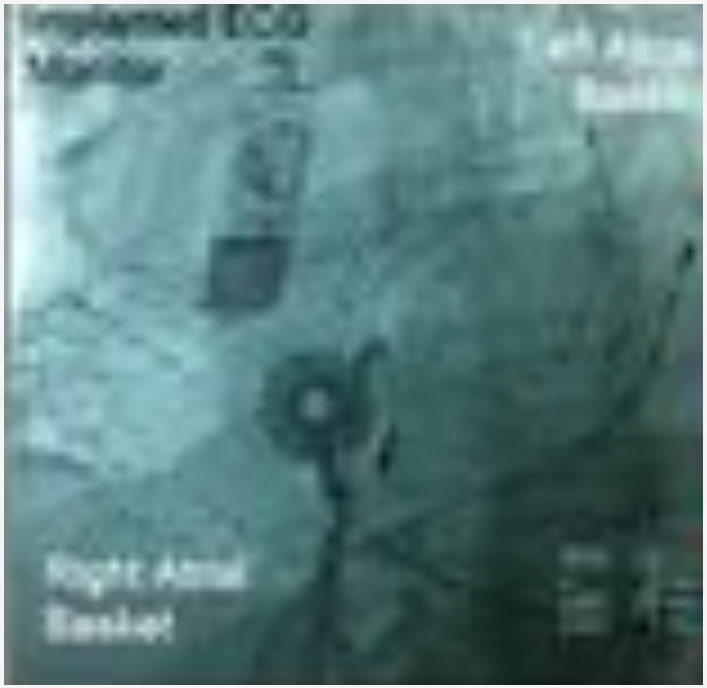
The FIRM principle: Focal Impulse and Rotor Modification

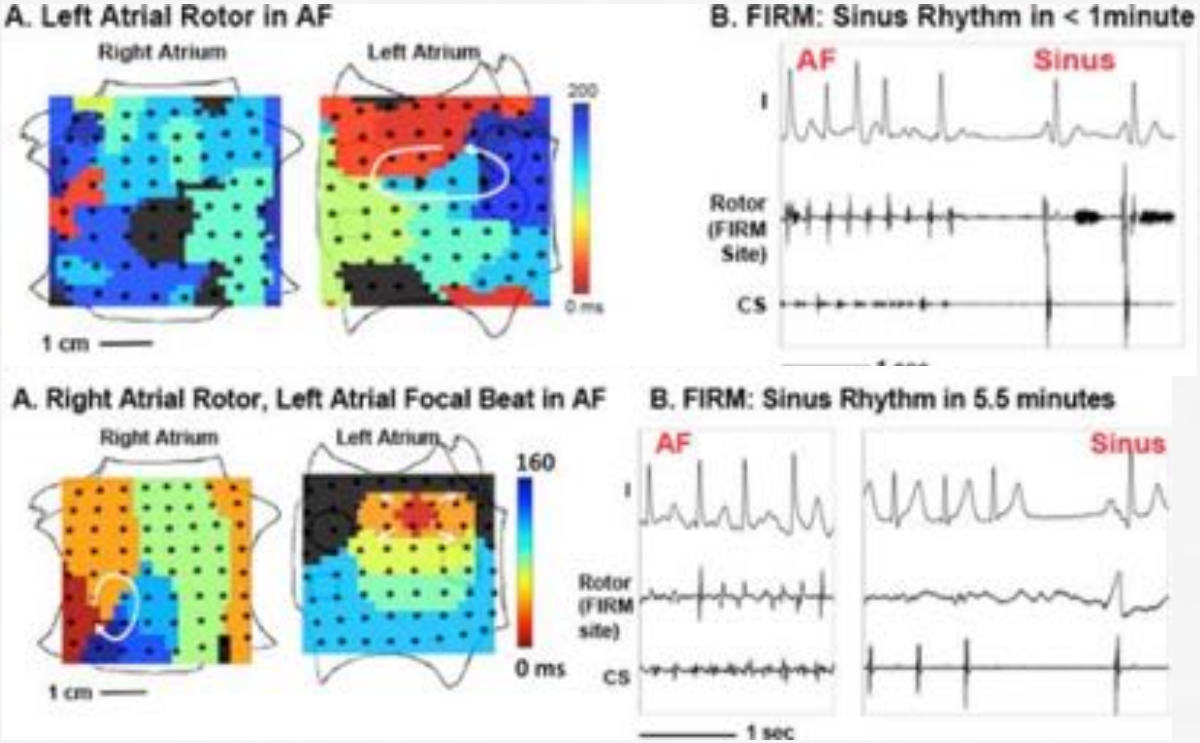
Computational Mapping of “Electrical Rotor” During Atrial Acute Termination of AF to Sinus Rhythm By FIRM Ablation Fibrillation Conclusions



Narayan et al: JACC Vol. 60, No. 7, 2012 Narayan et al; August 14, 2012:628–36.

CONFIRM Trial
FIRM-Ablation = „Focal Impulse and Rotor Modulation“





N = 92 Pat./107 Ablationen, parox. + persist. (72%) VHF, „FIRM“ + PVI vs. PVI allein: Rotoren in 97% der Fälle, 2,1±1,0 Rotoren. 273 d FU, überwiegend mit ILR

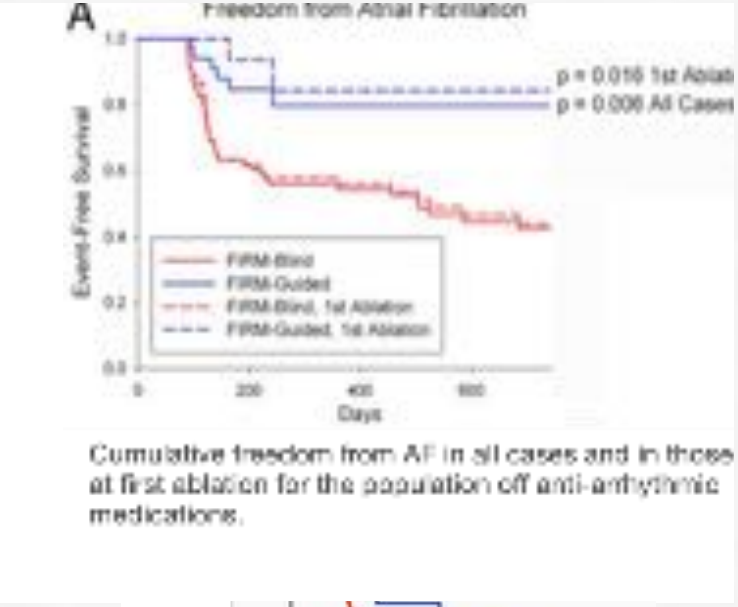
Narayan et al, JACC 2012

Clinical Outcomes: The CONFIRM Trial

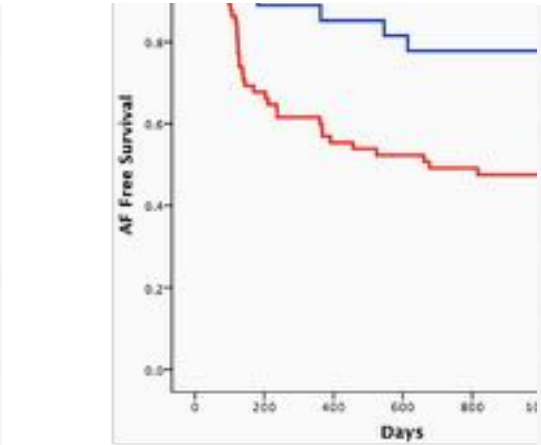
Study Size: 92 patients (mostly Persistent)

1-Year Single procedure results:

- **44.9%** for the control arm (PVI only)
- **82.4%** of FIRM-guided cases were free of AF vs.
- Superior results also achieved in high-risk patients (sleep apnea, heart failure, metabolic syndrome, etc.)



Cumulative freedom from AF in all cases and in those at first ablation for the population off anti-arrhythmic medications.

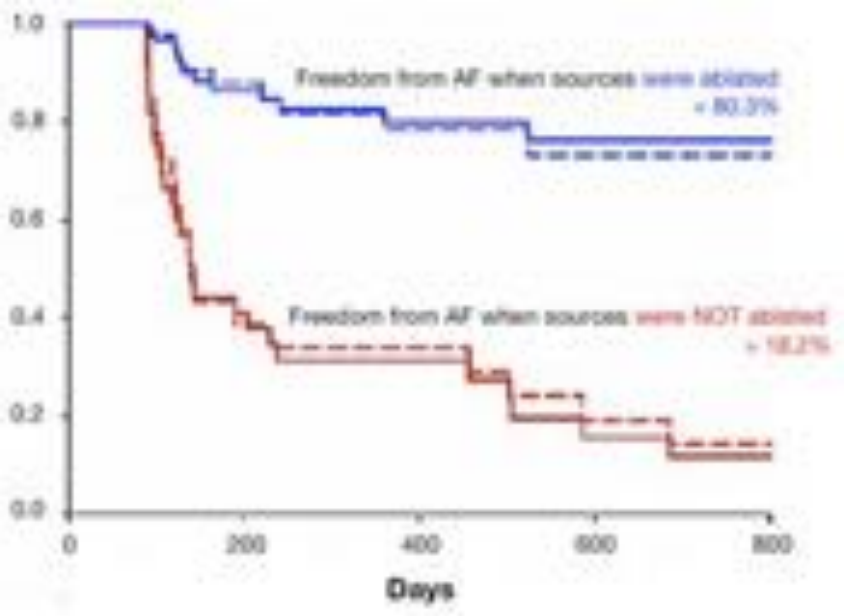


3-Year freedom from AF with F guidance (blue) and PVI only

Narayan SM,et al; J Am Coll Cardiol; 60(7):628-636., 2012

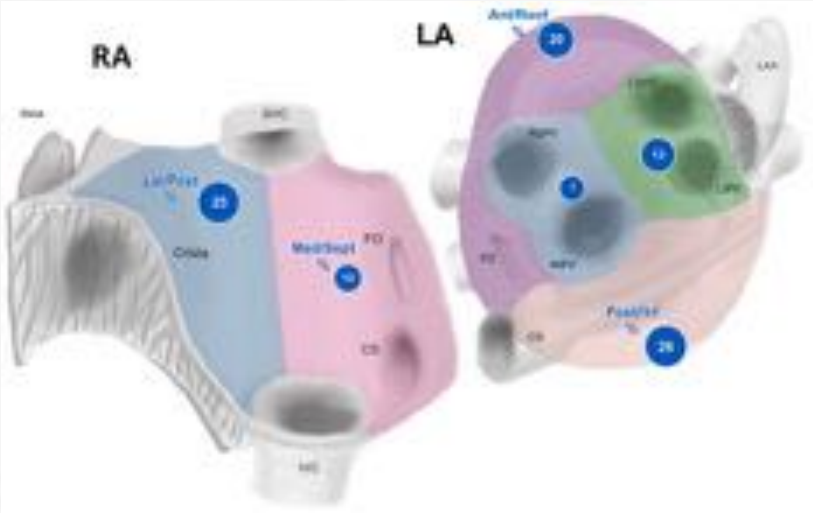
Narayan SM et al; J Am Coll Cardiol; DOI 10.1016., 2014

Rotors Are Vital to Sustaining AF – On Treatment analysis of CONFIRM



Key Points/Key Findings:

- Rotors were critical to success
- Each patient had an average of 2.3 rotors
- Locations more widely distributed in Persistent AF
- > 50% were outside of PVI ablation zones



Narayan et al., Circulation Arrhyth Electrophys; 6(1):58-67, 2013
Narayan et al., On-Treatment Analysis of CONFIRM. J Am Coll Cardiol. 2013

Multi-Center Validation Study

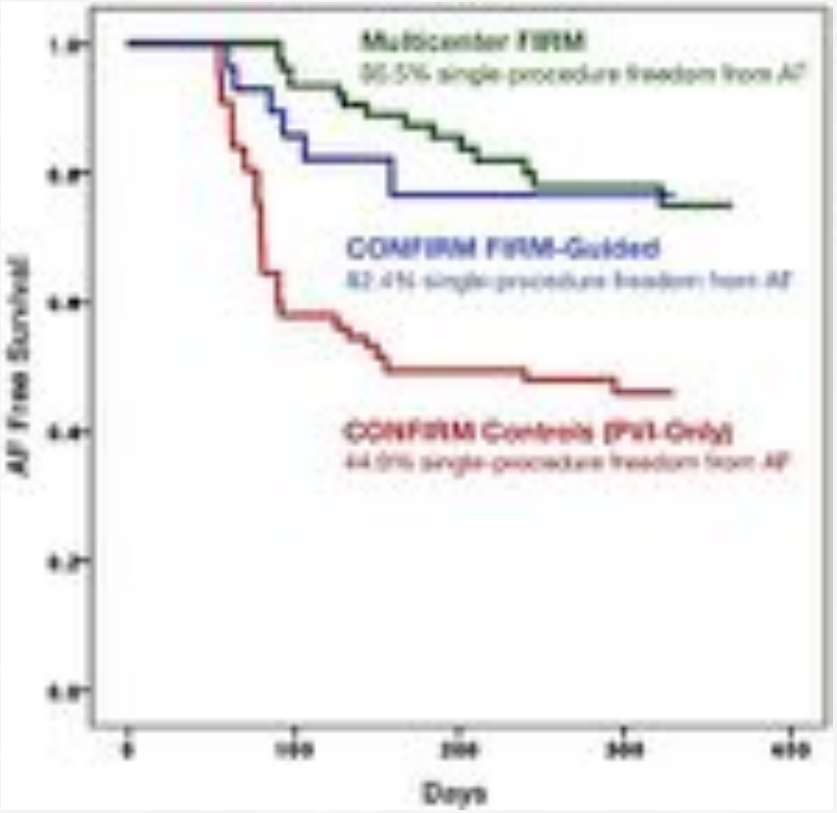
Study Size: 78 patients (mostly Persistent AF)

Purpose:

- Determine if the CONFIRM Trial results can be replicated by 10 independent centers

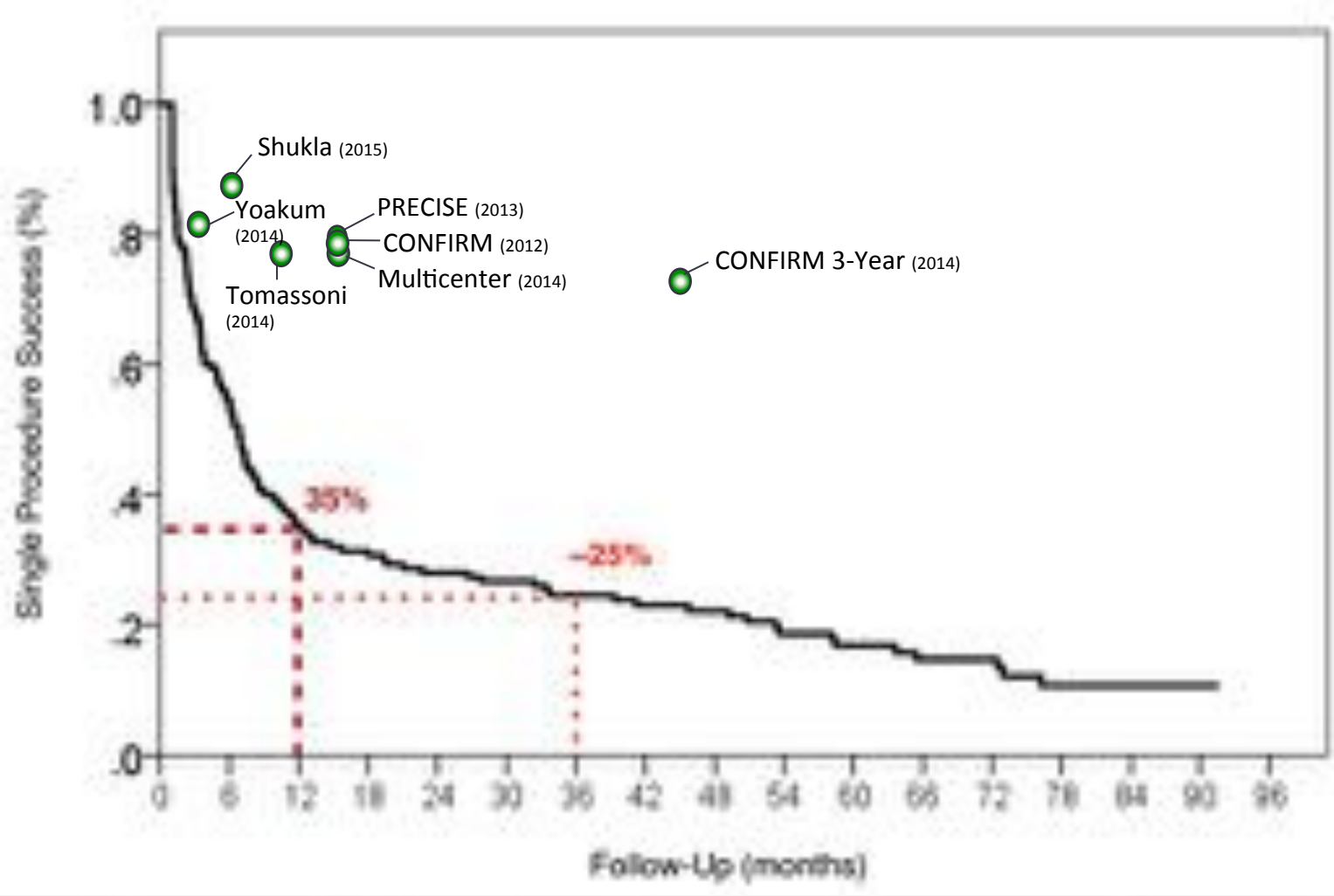
1-Year Single procedure results:

- ***80.5%*** of FIRM-guided cases were free of AF
- ***87.5%*** of patients with no prior ablation were free from AF
- Rotor distributions similar to the CONFIRM trial



Miller et al; AHA Scientific Sessions, Nov 2013.

Summary of Clinical Outcomes

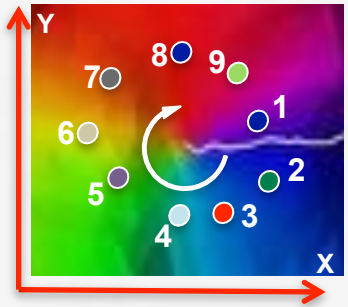


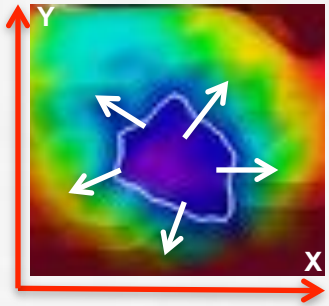
Scherr et al. Circ Arrhythm Electrophysiol. December 20, 2014.

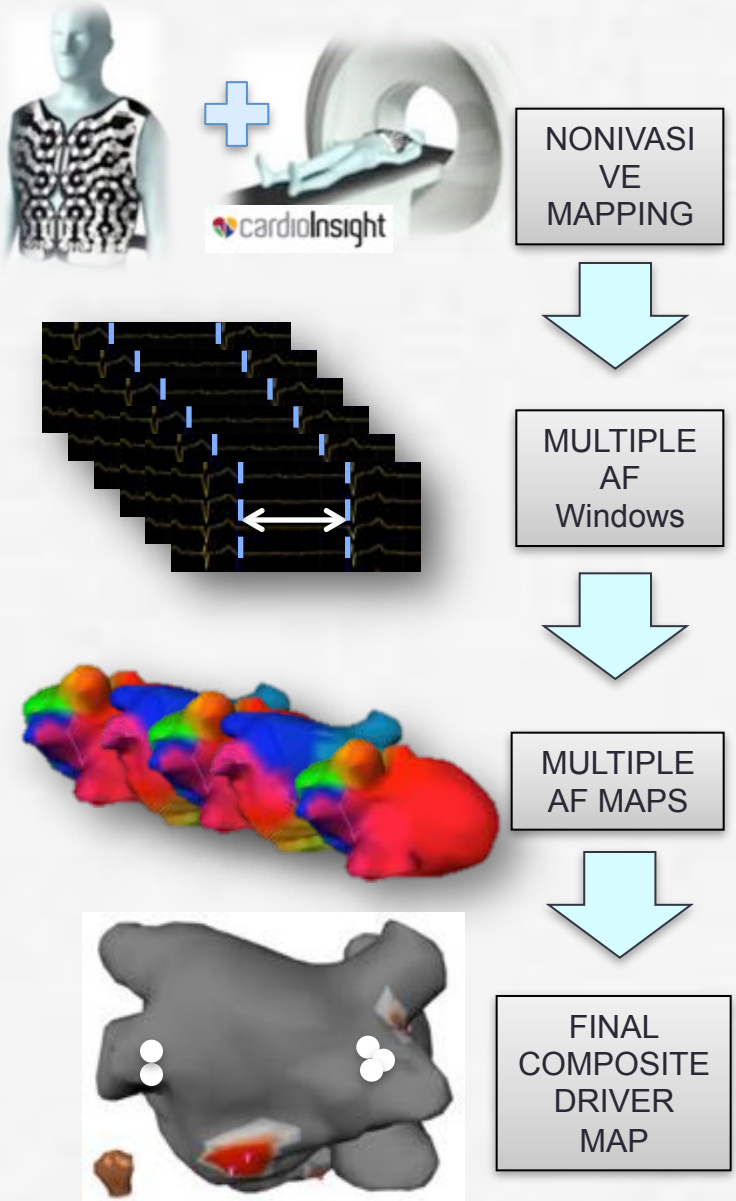
Comparison CFAE- and Rotor Ablation

By the courtesy of Sonia Ammar, Deutsches Herzzentrum München

- CT Scan with the 252 electrodes vest
- AF ‘windows’ (over several minutes) are analyzed to identify consistent drivers (bedside or in the EP lab)
- Drivers are defined as local reentrant circuits (≧1.5 rotations) or focal breakthroughs (> 2 that appear at the same spatial location per window)

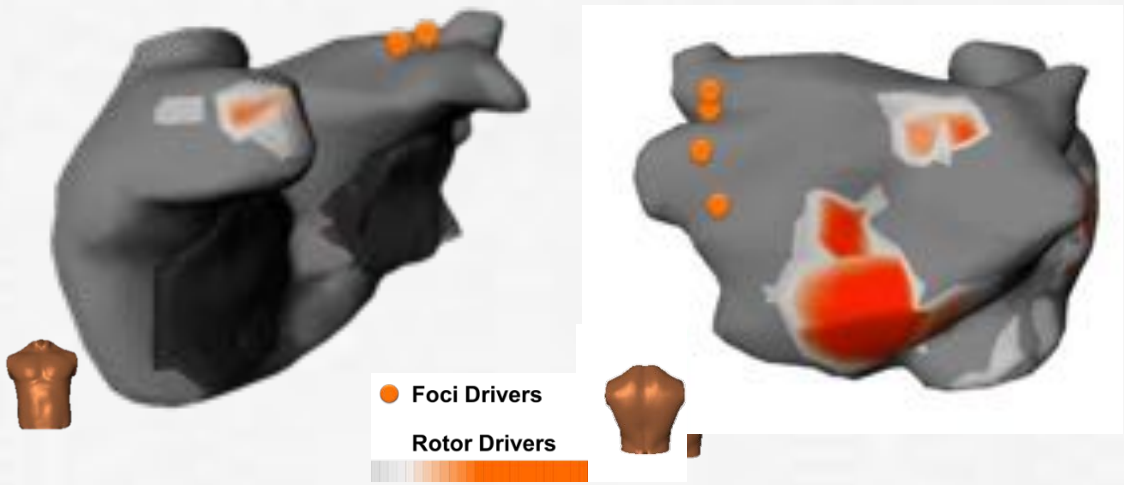






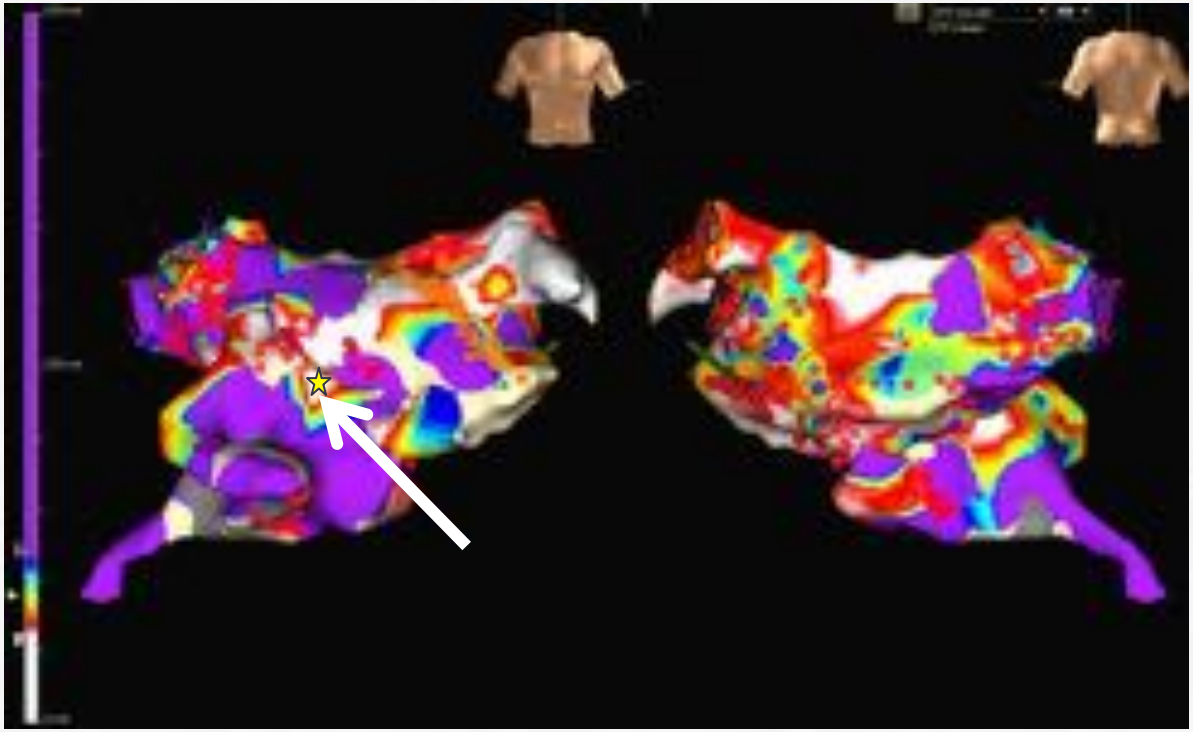
ecVUE & ecSYNC are not yet cleared or approved for use by the FDA

A: ECVUE Driver Map



A: Sites of AF drivers:
1) Inferior LA and CS
2) Right PVs and septum
3) Left PVs
4) Cavotricuspidal isthmus
5) RAA.

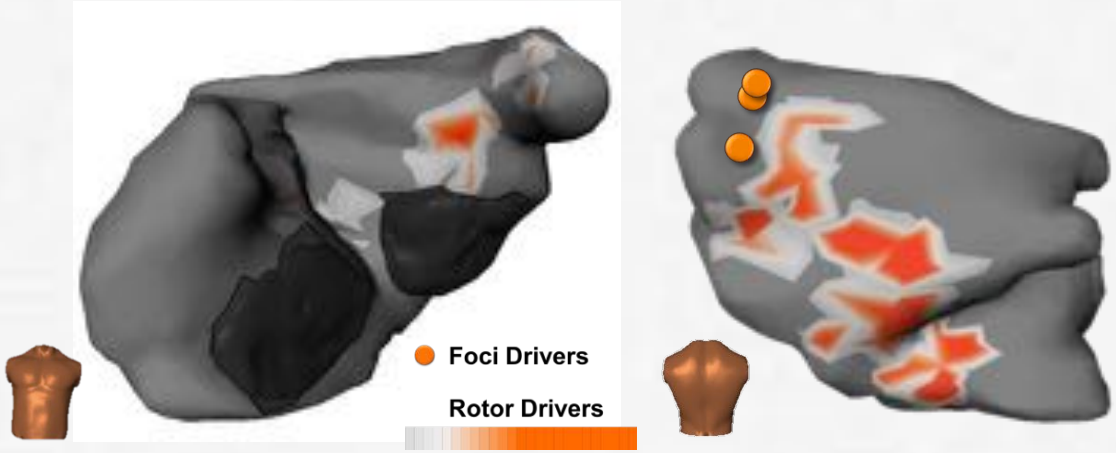
B: NavX CFAE Map



B: Total CFAE area: 325.8 cm^2 (79% of total mapped area).

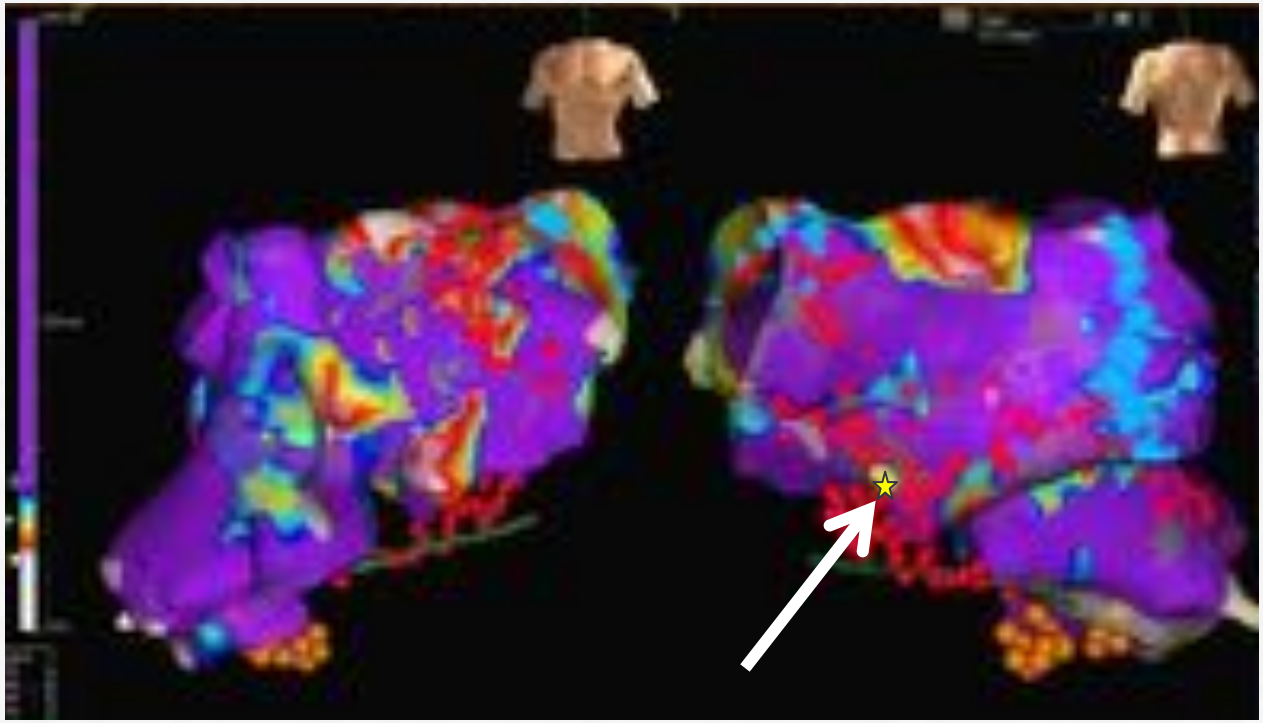
→ AF terminated to a perimitral reentry during ablation in the RAA (yellow asterix).

A: ECVUE Driver Map



A: Sites of AF drivers:
1) Left PVs and LAA
2) lateral RA
3) Inferior LA and CS
4) Cavotricuspidal isthmus
5) Right PVs and septum.

B: NavX CFAE Map



B: Total CFAE area: 182cm^2 (54% of mapped area).

→ AF terminated to a peritricuspid reentry during ablation in the inferior LA (yellow asterix).

Results: procedural data

AF termination	N= 16 patients
AF termination with drivers ablation only	11/16 (70%)
AF termination with drivers ablation + PVI	12/16 (75%)

Results: drivers locations

Driver locations, N= 63	N= 16 patients
Nbr of drivers/patient	4±1 /patient
Inferior left atrium, coronary sinus	15/16
Right atrium	15/16
Right PVs and septum	14/16
Lefts PVs	12/16
Left atrial appendage	9/16

Driver regions with >75% CFAE	**49/63 (78%)**
Driver regions with 50% CFAE	**7/63 (11%)**
Driver regions with <25% CFAE	7/63 (11%)

Ongoing and Future Clinical Studies

Current/Ongoing & Future Studies

- **Company Sponsored**
- REAFFIRM
  - Purpose: Evaluate the long-term effectiveness of FIRM + PVI versus PVI alone for de novo PerAF procedures
  - Design: Randomized controlled multicenter trial; 200 patients from ~25 centers throughout Europe (with some in the U.S.)
  - Status: Currently enrolling
- FIRM-Only for Paroxysmal AF
  - Purpose: Evaluate the long-term effectiveness of FIRM-only ablation versus PVI for the treatment of paroxysmal AF
  - Design: Randomized controlled multicenter trial; ~200 patients from multiple centers (primarily Germany)
  - Status: planned initial enrollment in 2015
- Health Economics
  - Various studies evaluating the cost effectiveness and economic benefits of FIRM-guided ablation

- **Investigator Initiated**
- PRECISE (long-term outcomes of FIRM-only ablation for paroxysmal AF)
- Early Recurrence of Atrial Fibrillation (ERAF) with FIRM-guided ablation + PVI compared to PVI alone
- Long-term clinical outcomes of FIRM + PVI with and without acute termination
- Correlation of rotors identified by RhythmView with optically mapped rotors (in the same human heart)
- Various other small clinical outcome studies

Reaffirm-Studie

Randomized Evaluation of Atrial Fibrillation Treatment with Focal Impulse and Rotor Modulation Guided Procedures

PI: Johannes Brachmann Coburg

Reaffirm-Study-Design

Assess the safety and effectiveness of FIRM procedures followed by conventional ablation including PVI versus a standard PVI procedure for the treatment of persistent atrial fibrillation

- 200 subjects
- Prospective
- 1:1 randomization (eCRF)
- Open-label
- International, multicenter

PI: Johannes Brachmann

Endpoints

- Primary safety endpoints
  - Acute success: Freedom from SAE related to procedure within 10 days post-procedure
  - Long-term success: Freedom from cumulative SAE related to the procedure within 1 year of index procedure

Endpoints

- Primary effectiveness endpoints
  - Long-term success
    1. Single procedure freedom from AF/AT recurrence at 3 months, and
    2. Single procedure freedom from AF/AT recurrence from 3 – 12 Months after the index procedure

Ablation of Rotor and Focal Sources Reduces Late Recurrence of Atrial Fibrillation Compared With Trigger Ablation Alone Extended Follow-Up of the CONFIRM Trial

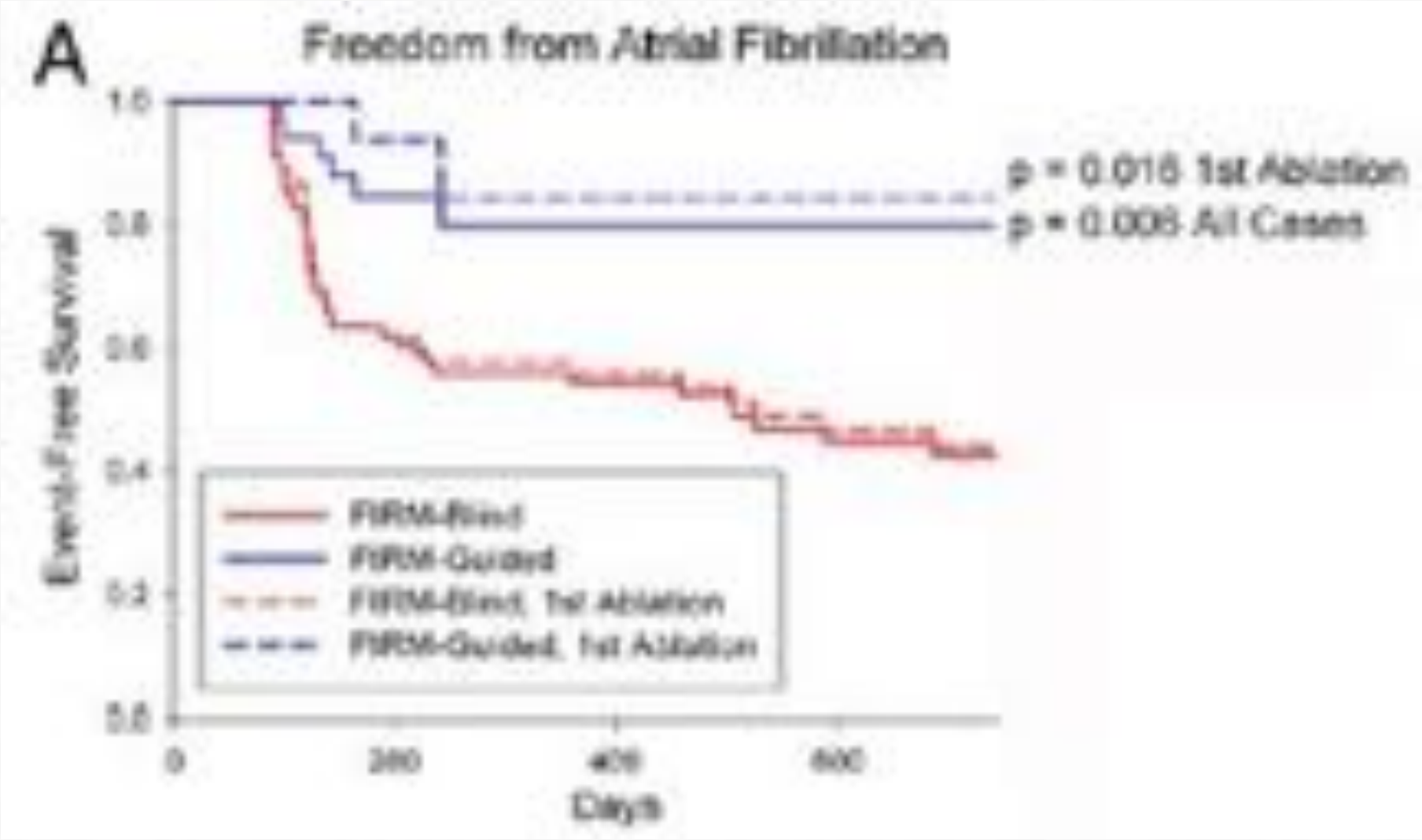
(Conventional Ablation for Atrial Fibrillation With or Without Focal Impulse and Rotor Modulation)

Narayan S. et al; J Am Coll Cardiol 2014;63:1761–8.

CONFIRM

The FIRM principle: Focal Impulse and Rotor Modification

Cumulative Freedom From Primary Endpoint



Narayan et al: JACC Vol. 60, No. 7, 2012 Narayan et al; August 14, 2012:628–36.

Conclusions

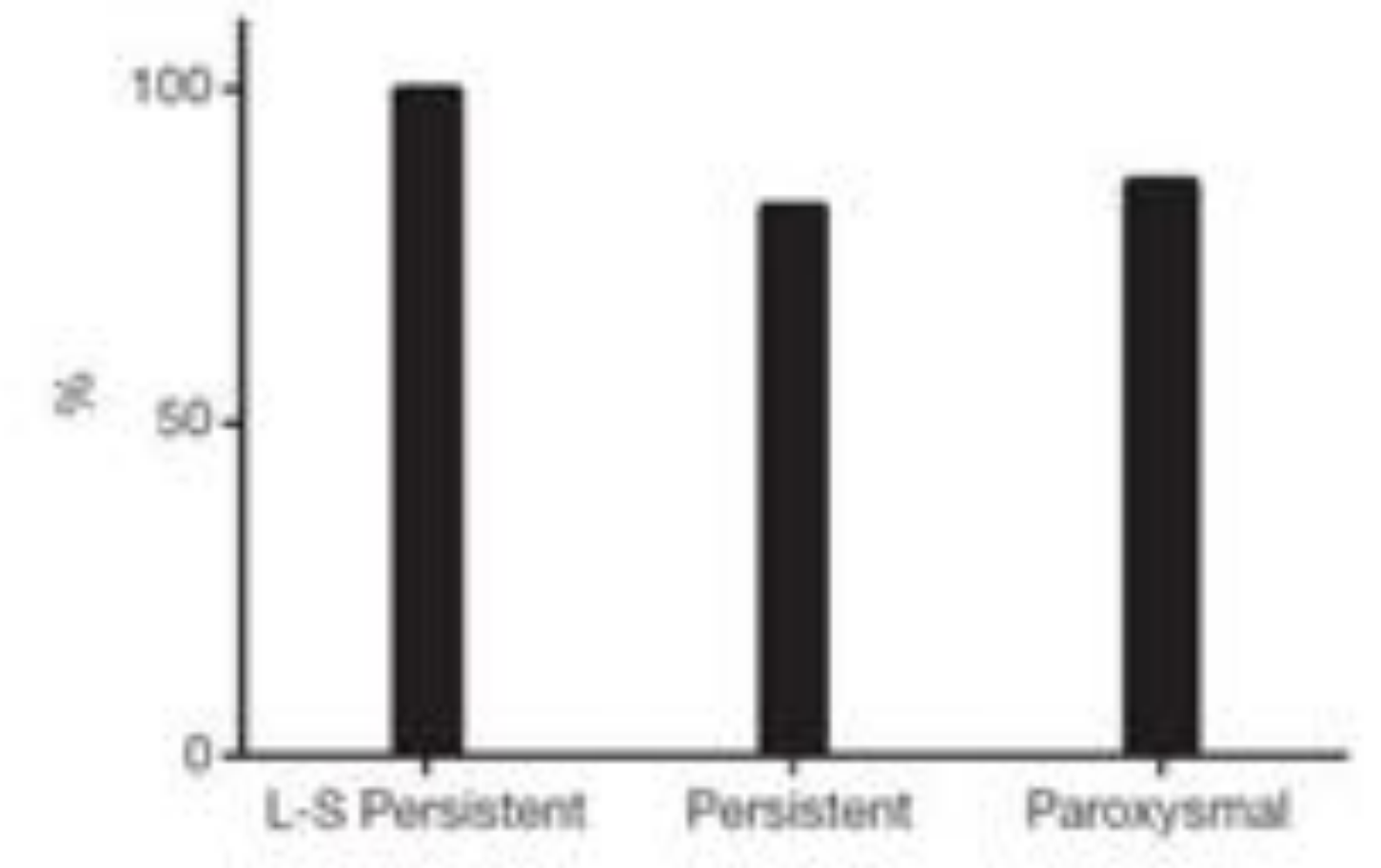
- FIRM-guided ablation is more durable than conventional trigger-based ablation in preventing 3-year AF recurrence.
- Future studies should investigate how ablation of patient-specific AF-sustaining rotors and focal sources alters the natural history of arrhythmia recurrence.

Narayan S. et al; J Am Coll Cardiol 2014;63:1761–8.

Effectiveness and safety of simultaneous hybrid thoracoscopic and endocardial catheter ablation of lone atrial fibrillation

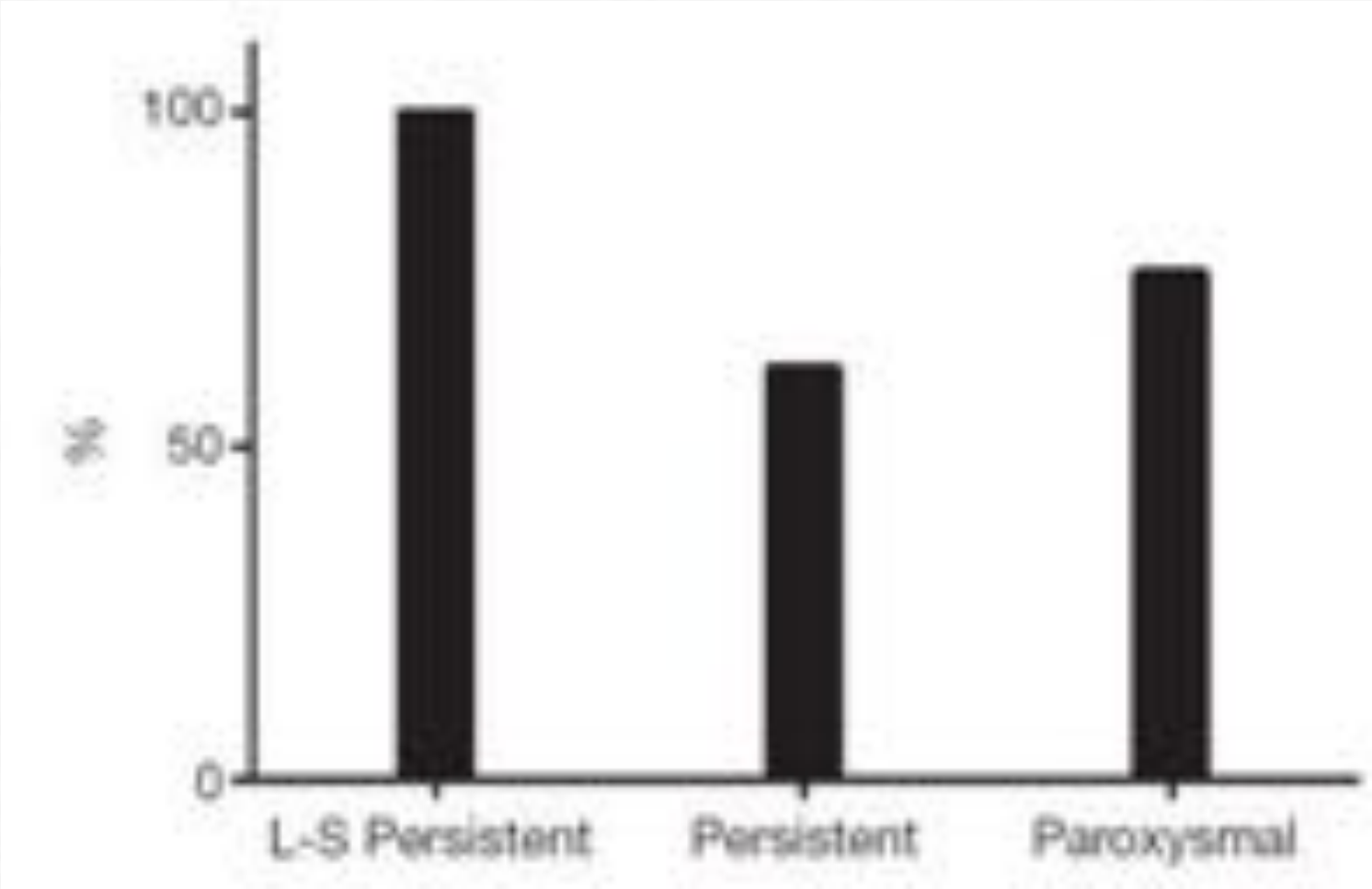
Pison L et al., AnnCardiothoracSurg, 2014

Success rate off antiarrhythmic drugs (Off-ADD)



Pison L et al., AnnCardiothoracSurg, 2014

Single-procedure success rate



Pison L et al., AnnCardiothoracSurg, 2014

Results

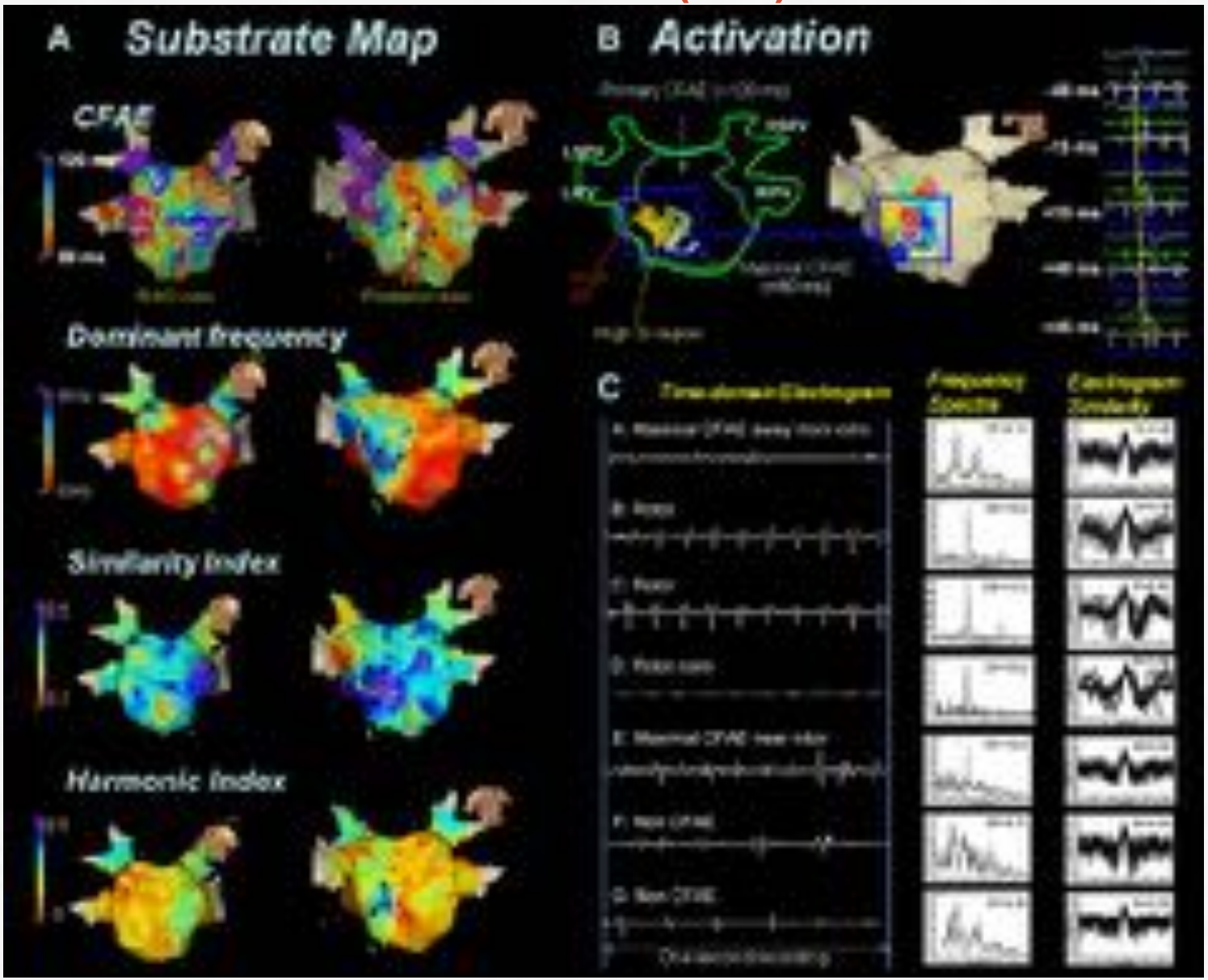
No death or conversion to cardiopulmonary bypass occurred. No patient demonstrated paralysis of the phrenic nerve. Overall, the incidence of perioperative complications was 8% (n=6). At the end of follow-up, sixty-eight patients (87%) were in sinus rhythm (SR) with no episode of AF, atrial flutter or atrial tachycardia lasting longer than 30 seconds and off antiarrhythmic drugs (ADD). Among patients with longstanding persistent AF, 15 (100%) were in SR and off AAD. Success rates were 82% (n=28) in persistent and 76% (n=22) in paroxysmal AF (P=0.08). No patient died and no thromboembolic/bleeding events or procedure-related complications occurred during the follow-up.

Pison L et al., AnnCardiothoracSurg, 2014

Prevalence, Characteristics, Mapping, and Catheter Ablation of Potential Rotors in Nonparoxysmal Atrial Fibrillation

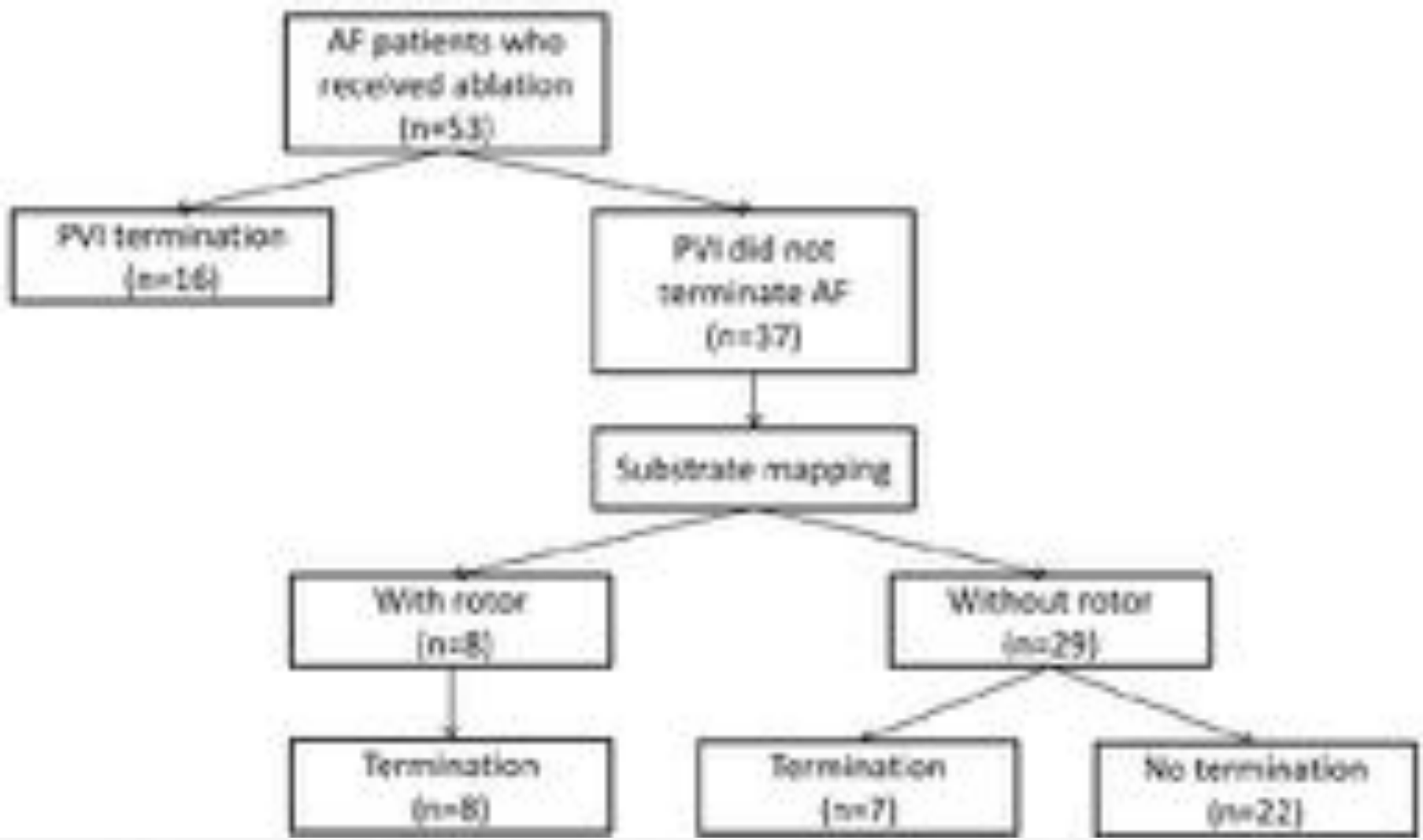
Lin YJ et al., CircArrhythmElectrophysiol, 2013

Illustration of the substratemapping after the pulmonary vein isolation (PVI)



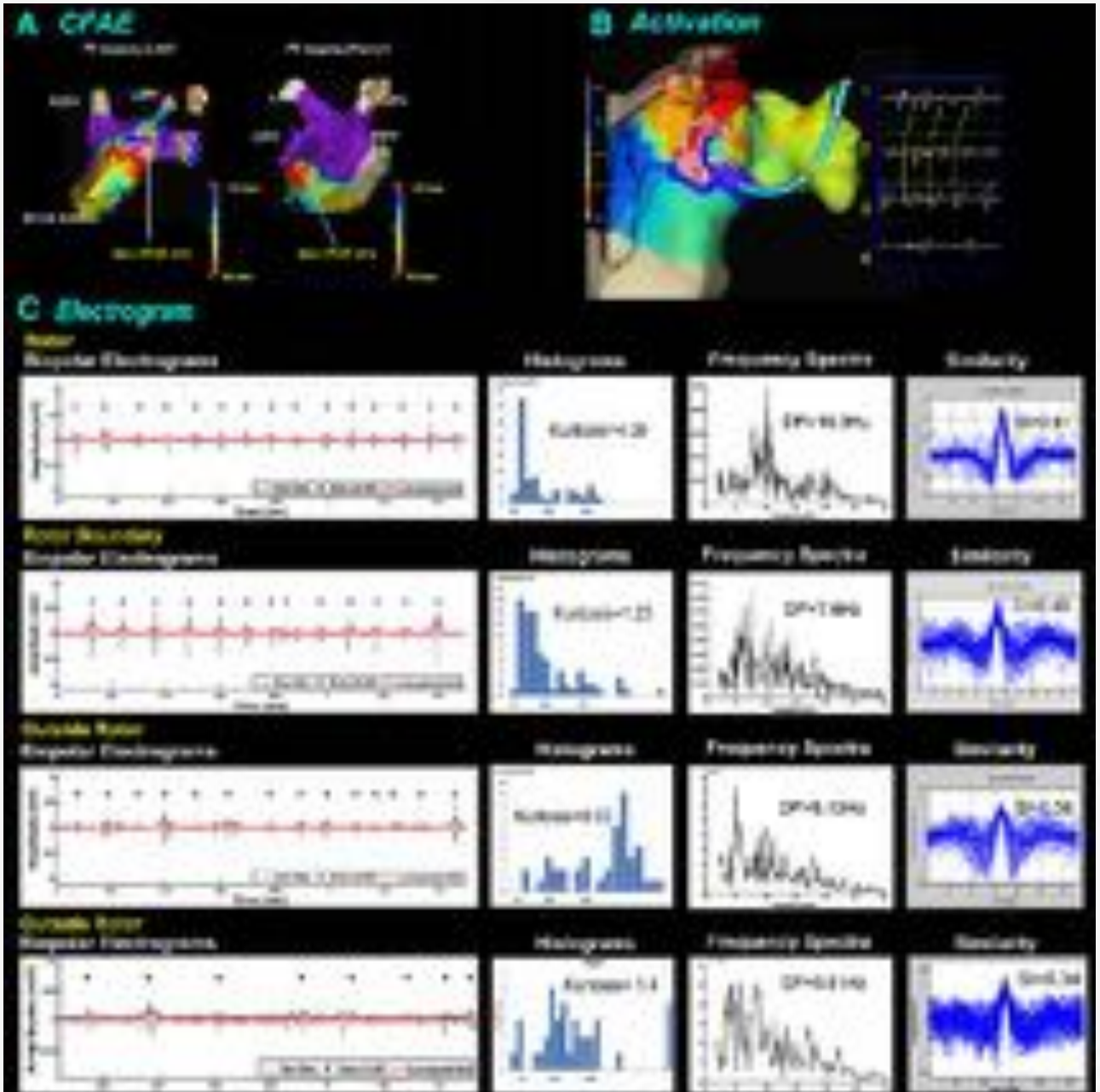
Lin YJ et al., CircArrhythmElectrophysiol, 2013

Catheter ablation results of the pulmonary vein isolation (PVI) and substrate



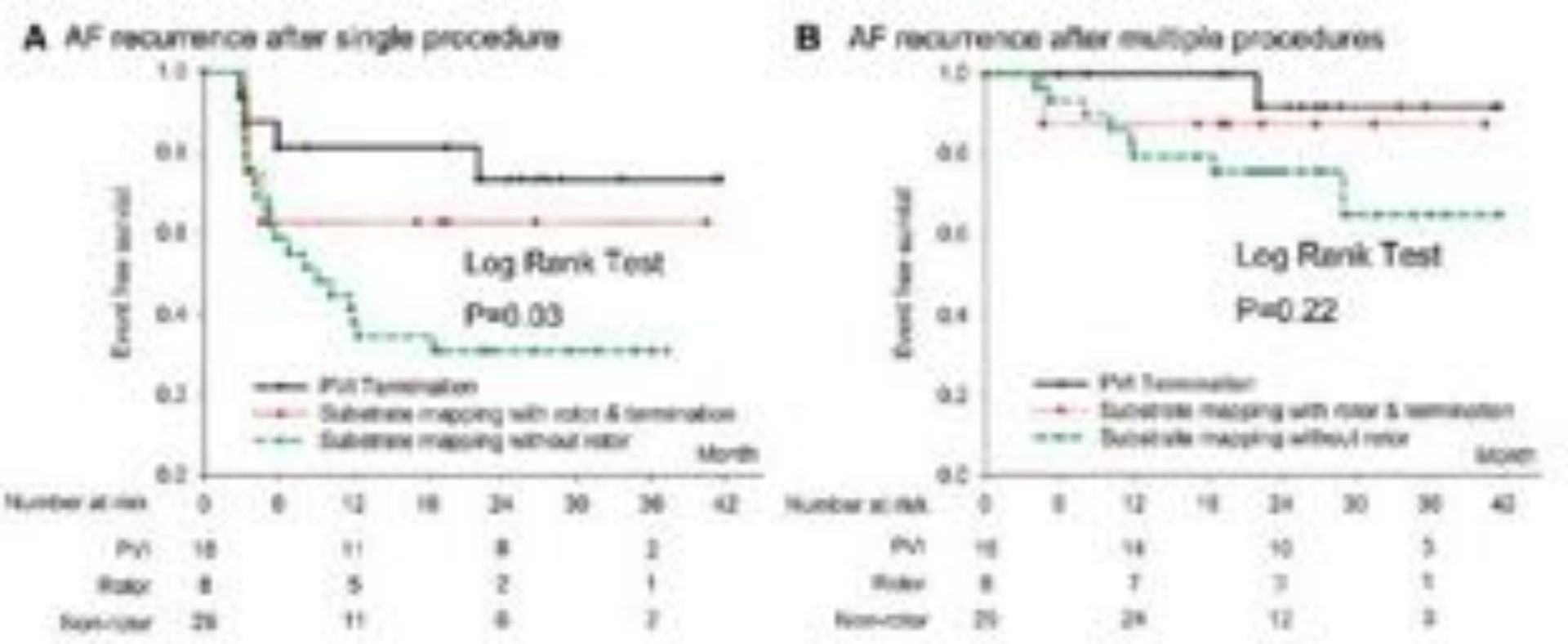
Lin YJ et al., CircArrhythmElectrophysiol, 2013

The complex fractionated atrial electrograms (CFAEs) in 1 persistent patient with atrial fibrillation after pulmonary vein isolation



Lin YJ et al., CircArrhythmElectrophysiol, 2013

Freedom of atrial arrhythmia



Kaplan–Meier curves demonstrating the freedom of atrial arrhythmia recurrence after a single (**A**) and multiple procedures (**B**).AF indicates atrial fibrillation; and PVI, pulmonary vein isolation.

Lin YJ et al., CircArrhythmElectrophysiol, 2013

Advanced ablation of AF
Conclusions

- The overall success of AF ablation is unsatisfactory and amounts to 65% for paroxysmal and 40% for persistent forms
- „Make it as simply as possible“ is the purpose of single shot devices like PVAC or Cryo reaching 65 and 80% resp. with advanced technology
- Fibrosis MRI shows a clear correlation between degree of fibrosis and outcome; if isolation of scar areas by ablation improves outcome is still unclear
- The same is true for CFAE and GP/FD ablation

Advanced ablation of AF
Conclusions

- Rotors have been shown to maintain AF (mechanism not completely understood) and can now be visualized by computational mapping using baskets/electrode vests; their abolition seems to improve results, but data still have to be reconfirmed
- **Facit:** PV isolation remains the corner stone of AF ablation and should be gained first by simple and safe techniques (single shot) or conv. RF ablation
- Complex techniques (s. above) have not demonstrated a clear benefit over PVI, but can be used additionally in an individualized, exploratory approach

Thanks for your attention and greets from Düsseldorf !