



# **Vorhofflimmern und Schlaganfall – Ablation, Antikoagulation, Vorhofohrverschluß – was wann für wen ?**

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16.11.2013



# Incidence of Atrial Fibrillation, Standard population of industrialised countries

> 60 years	5 %
> 70 years	7-8 %
> 80 years	10 %



# Atrial Fibrillation and Mortality

- Mortality is at least 3 times higher in AF patients as compared to non AF patients
- This is mainly due to stroke and due to bleedings from oral anticoagulation
- No major difference in stroke rate between PAF, PsAF, LsAF
- AF patients are more likely to develop dementia\*

\*Cognitive Impairment Associated With Atrial Fibrillation: A Meta-analysis  
Kalantarian et al , Ann Intern Med. 2013;158(5 Part 1):338-346



# Atrial Fibrillation, Categories

- Paroxysmal Atrial Fibrillation ( $> 30$  sec)
- Persistent Atrial Fibrillation ( $> 7$  days)
- Long standing persistent Atrial Fibrillation ( $> 6$  months)
- Permanent Atrial Fibrillation ( $> 12$  months)



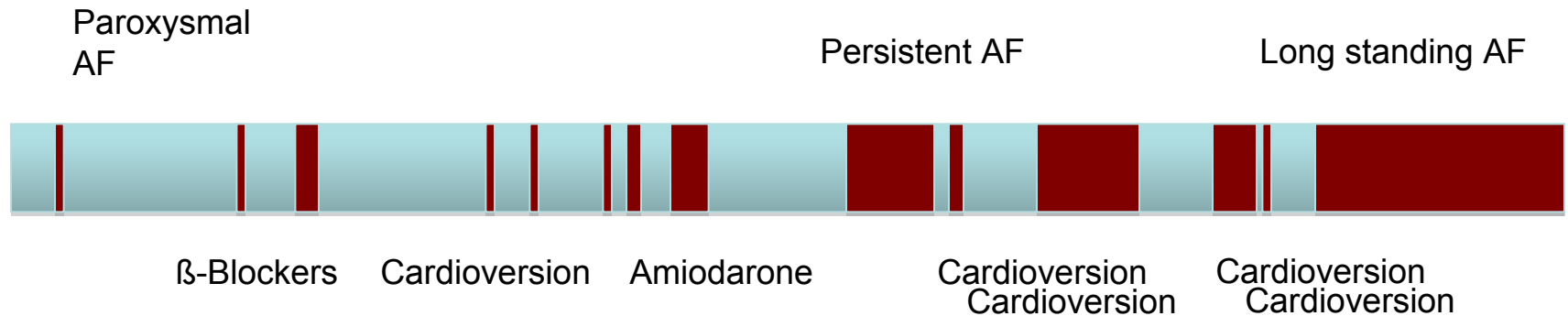
# Etiology of Atrial Fibrillation

## multiple factors

- Mechanical stress / La dilatation
- Genetic alterations
- Atrial fibrosis
- Inflammation
- Autonomic hyperactivation
- Macroreentry



# AF disease progression without ablation during several years:





## How about AF symptoms during disease progression ?

(fast and irregular heart beat, breathing problems, exercise insufficiency)

- Usually high symptom level in some patients with PAF and PsAF
- Often low symptom level in patients with LsAF





# AF, Treatment Goals

- No stroke
- No dementia
- No symptoms
- No disease progression





# Therapy of AF

- OAK / LAA Occlusion
- Drugs
- Cardioversion
- Ablation

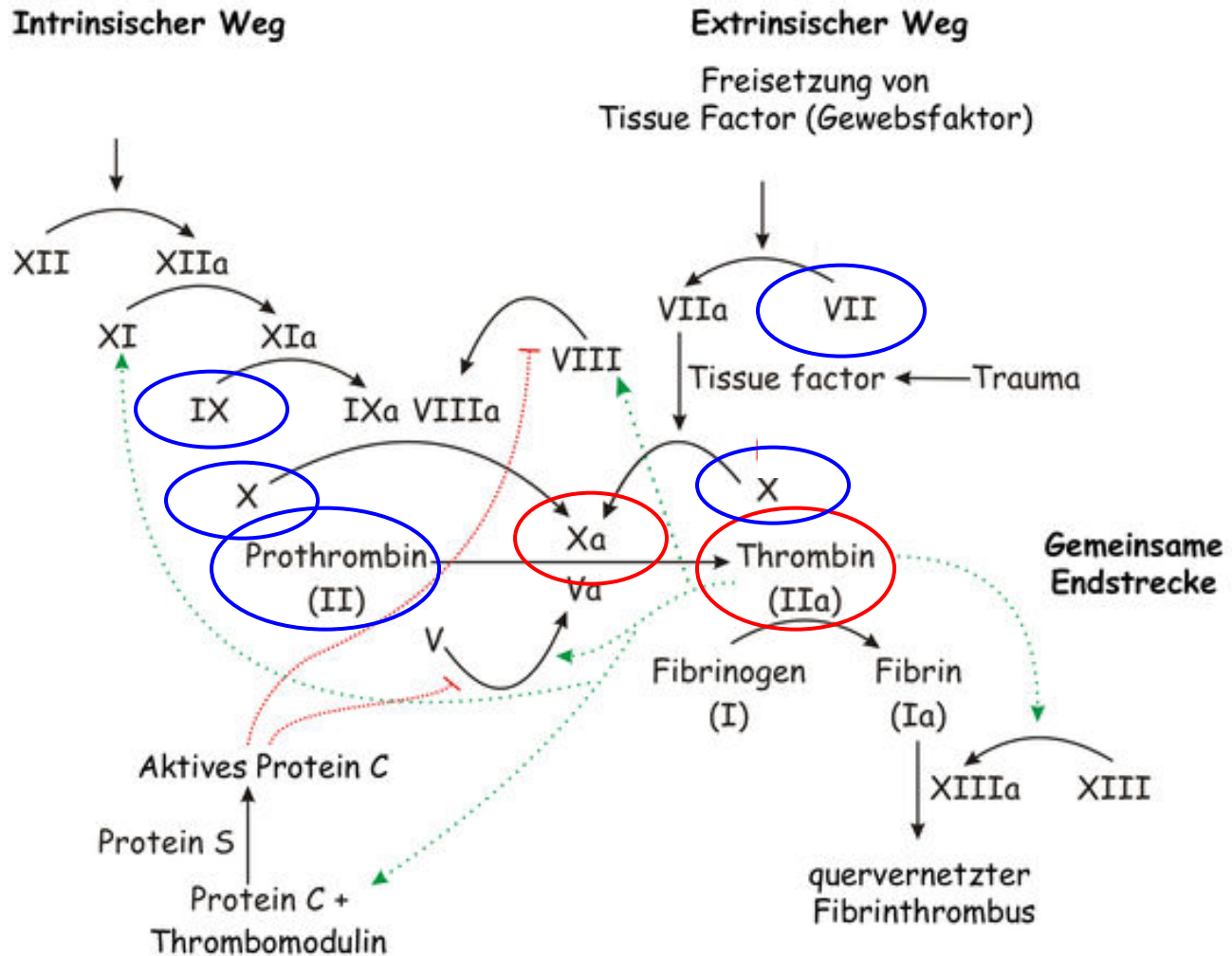


# Orale Antikoagulation

- Cumarine:
  - Coumadin (Warfarin)
  - Phenprocoumon (Falithrom/Marcumar)
- Direct Oral Anticoagulants (DOAK's)
  - a) Faktor 10a Antagonists
    - Apixaban (Eliquis),
    - Rivaroxaban(Xarelto)
  - b) Thrombininhibitoren
    - Dabigatran (Pradaxa)



# Plasmatische Gerinnung

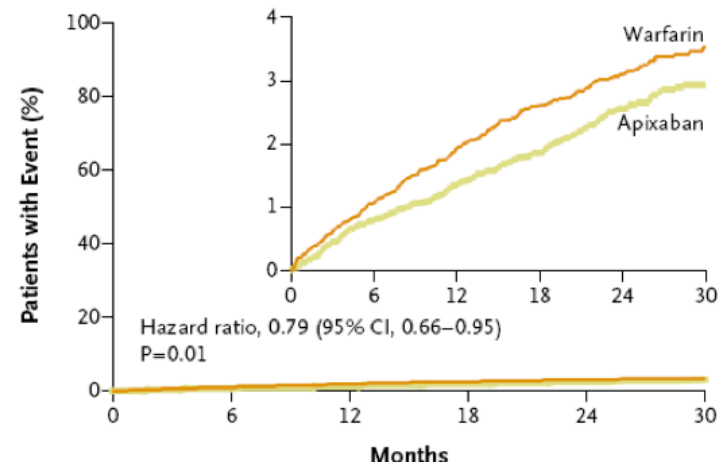




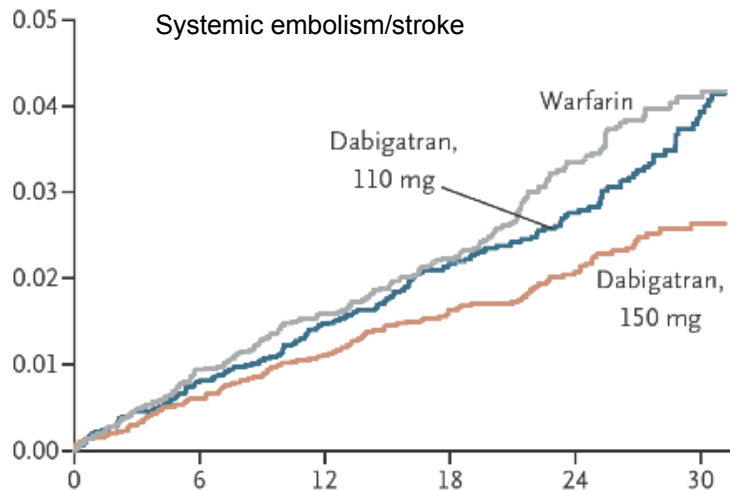
# DOAK's vs. Warfarin

- RELY (Dabigatran)
- ARISTOTLE (Apixaban)
- ROCKET AF (Rivaroxaban)

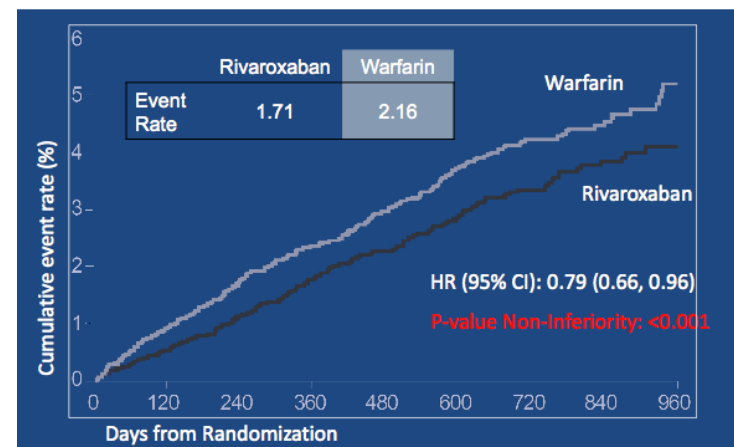
Primary Outcome: Stroke or Systemic Embolism



Granger et al, N Engl J Med 2011; 365:981-992



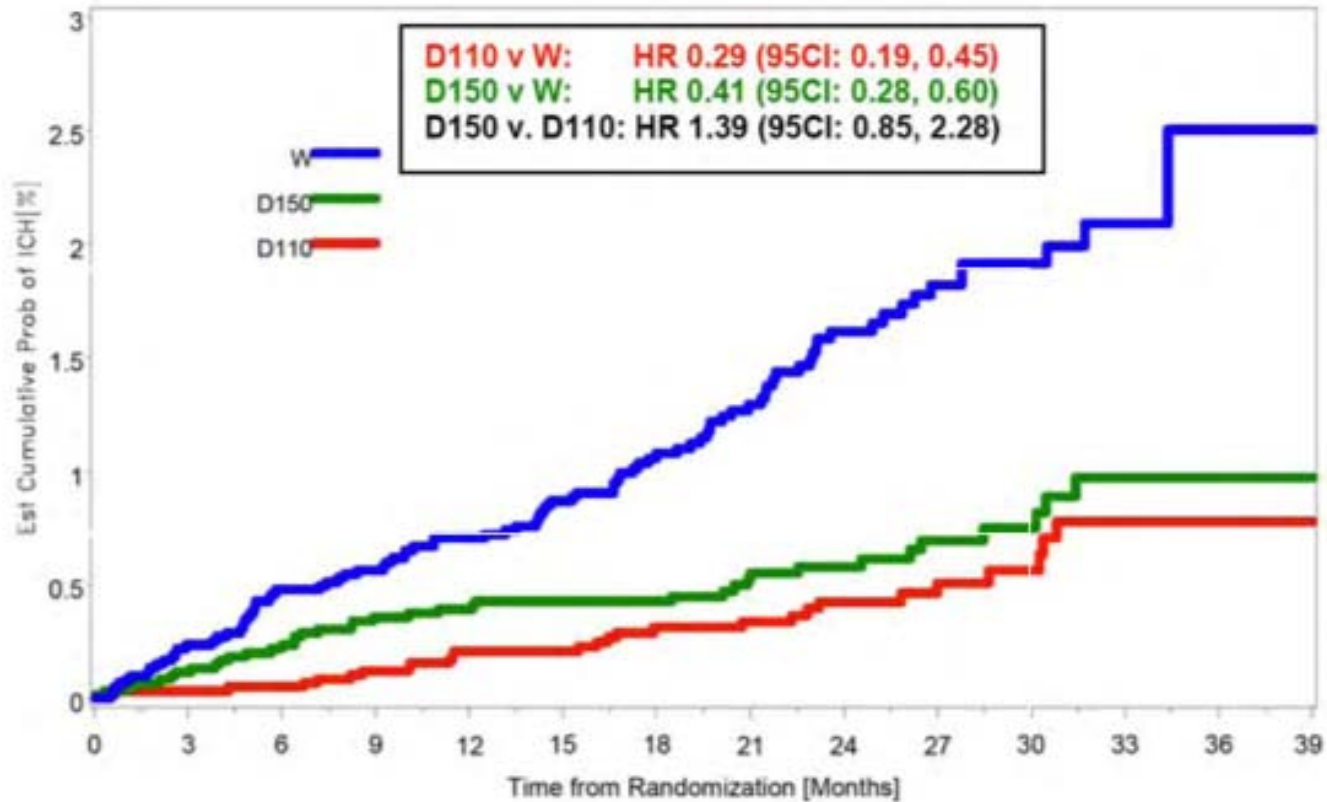
Conolly et al, N Engl J Med 2009; 361:1139-1151



Mahaffey et al, N Engl J Med 2011; 365:883-891



# RELY, intracerebral bleeding



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39
D110	6015	5874	5806	5734	5665	5432	4575	3717	3123	2365	1437	476	81	
D150	6078	5931	5847	5756	5694	5454	4626	3761	3182	2385	1456	480	88	
W	6022	5871	5779	5694	5617	5306	4501	3594	3007	2279	1322	359	73	



## Case 1

- 70 years, male
  - Paroxysmal atrial fibrillation (PAF)
  - No heart failure
  - Does not want to take vitamine k antagonists because he is lazy
- 
- What do you do ?
  - You are not lazy but your drug budget is stressed...



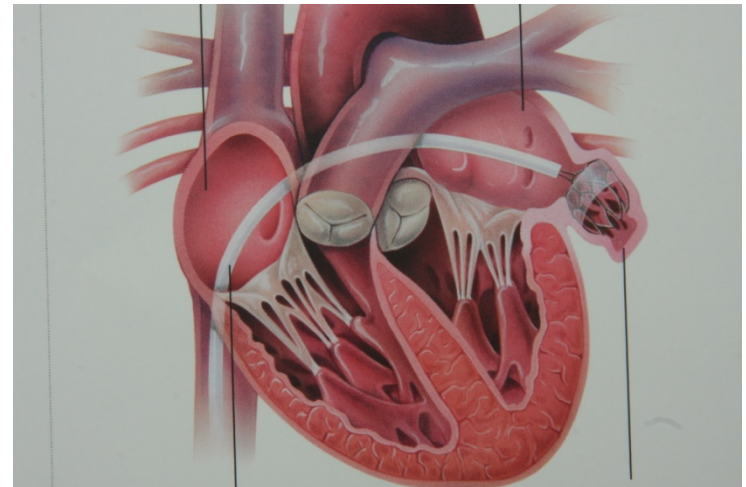
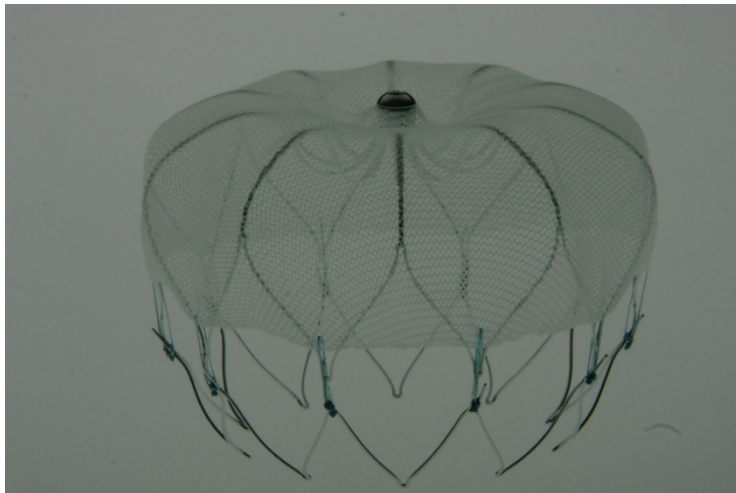
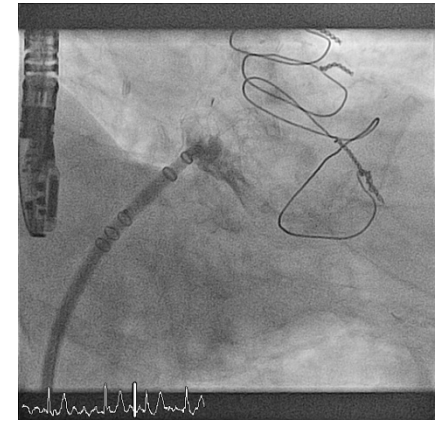
# Case 1

- Still VKA
- Change to DOAK
- LAA occlusion



## Left Atrial Appendage Occlusion Watchman device

- Reduces stroke rate similar to warfarin (PROTECT-AF non inferiority trial)

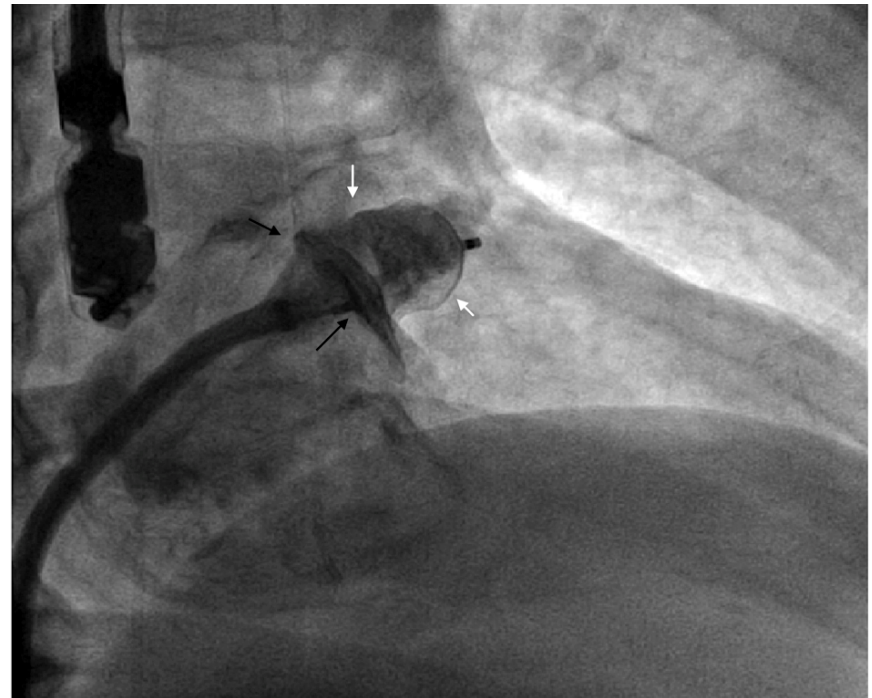


Holmes D R et al, Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomized non-inferiority trial, Lancet 2009;374:534-42



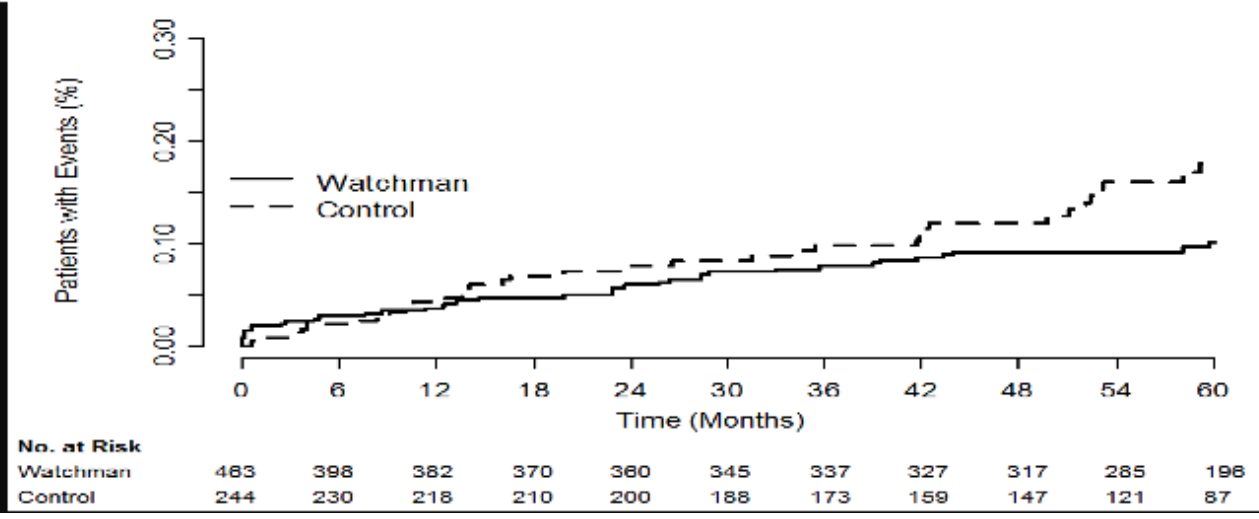


# Amplatzer™ Cardiac Plug



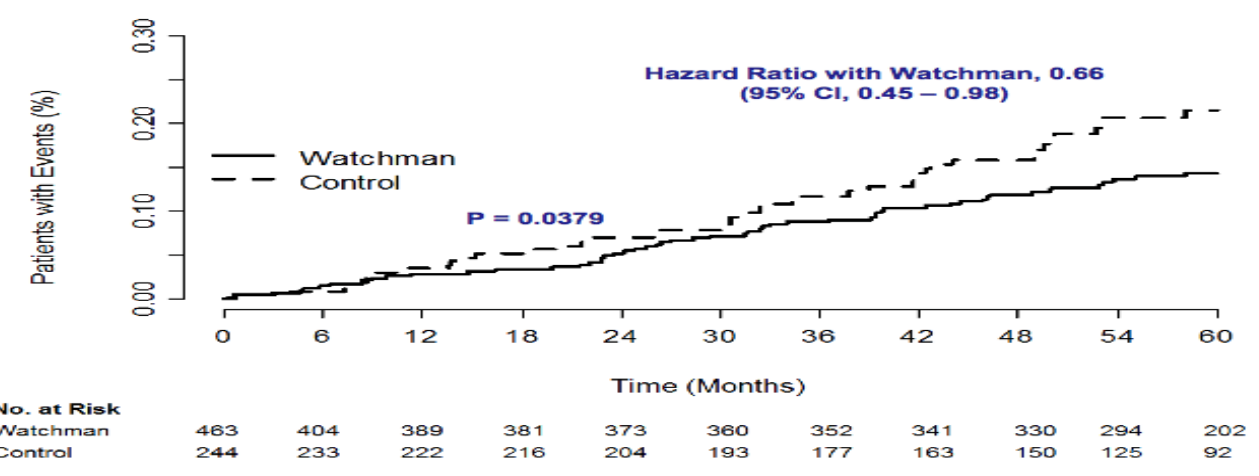


# Watchman device, Protect AF Trial – long term follow up



Adapted from HRS LBC2 2013 by Dr. Vivek Reddy SH-158101-AA- MAY 2013

Primary efficacy endpoint:  
Stroke  
CV death (& unknown)  
Systemic embolism



Adapted from HRS LBC2 2013 by Dr. Vivek Reddy SH-158101-AA- MAY 2013

All cause mortality



## Case 2

- 76 years, male
  - Ex professional cyclist, still 3 times per week on the bike
  - Permanent atrial fibrillation (PmAF)
  - LA 60mm, EF 65%, LVEDV 420ml, SV 273ml
  - Resting heart rate 28´ min, up to 8 s asystoly, does not want to take VKA any longer because he is afraid of injuries when falling off his bike
- What to do ?



## Case 2, cyclist 76 years

- Continue VKA
- Change to DOAK
- LAA occlusion
  
- Catheter ablation of atrial fibrillation yes/no
  
- Pacemaker yes/no



# Therapy of AF - Drugs

- Metoprolol / Bisoprolol
- Amiodarone / Dronedarone
- Flecainid / Propafenone



# Cardioversion

- First episode of paroxysmal or persistent atrial fibrillation
- Post ablation



## Case 3

- 43 years, male
- Bus driver
- Paroxysmal atrial fibrillation (PAF) since 36 hours after excessive drinking
- EF normal, LA normal

What to do ?



## Case 3

- 43 years, male
- Bus driver
- Paroxysmal atrial fibrillation (PAF) since 36 hours after excessive drinking
- EF normal, LA normal

What to do ?

TEE / cardioversion / 3 month OAK





## Case 4

- 63 years, female
  - Pulmonary vein isolation because of persistent atrial fibrillation 2 month ago
  - Cardioversion day 2, cardioversion day 10, now again PsAF since two weeks
- What to do ?



## Case 4, 63 years, female, post ablation

- TEE/CV
- Change to frequency control
- Need to know more

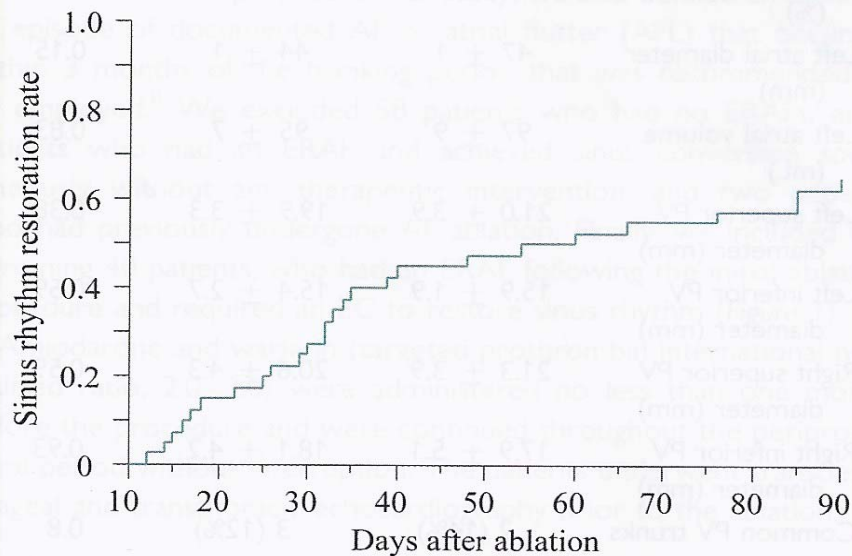


# Cardioversion

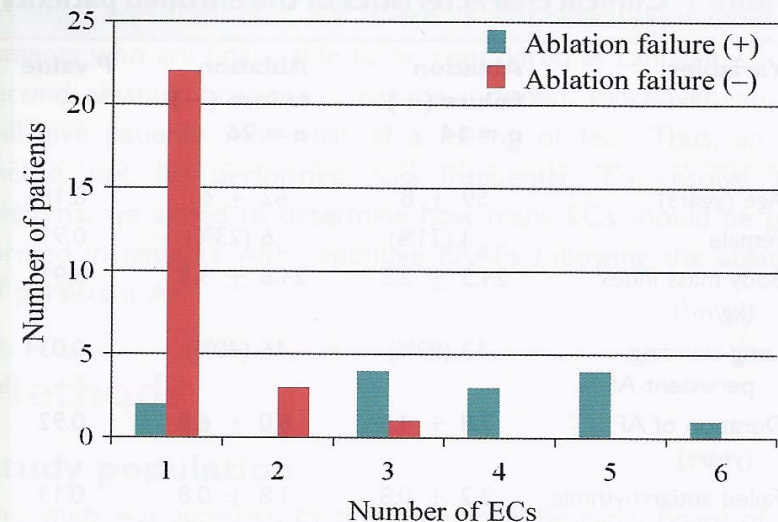
- Post ablation:

How many electrical cardioversions should be applied for repetitive recurrences of atrial arrhythmias following ablation of persistent atrial fibrillation?

Sairaku et al. Europace (2011) 13, 1703-1708 (108 pts -> 40 ERAF )



**Figure 3** Kaplan–Meier estimate of the time to restoration of sinus rhythm for three consecutive months after ablation.



**Figure 2** Distribution of the patients according to the number of electrical cardioversions applied in the patients with or without an ablation failure. ECs, electrical cardioversions.



How many ECs should be applied for repetitive recurrences of atrial arrhythmias?

1707

**Table 2 Predictors of ablation failure (n = 40)**

Variables	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age >65 years	0.78 (0.34 – 1.63)	0.53		
Female	0.95 (0.41 – 2.05)	0.91		
Body mass index >25 kg/m <sup>2</sup>	1.37 (0.70 – 2.71)	0.36		
Long-standing persistent AF	2.85 (1.14 – 12.6)	0.049	2.16 (0.49 – 15.77)	0.36
Duration of AF of >5 years	1.35 (0.69 – 2.85)	0.39		
Number of failed AADs of ≥2	1.49 (0.67 – 4.07)	0.37		
Hypertension	1.51 (0.78 – 3.06)	0.23		
Diabetes	1.13 (0.52 – 2.35)	0.75		
Structural heart disease	0.77 (0.17 – 2.27)	0.66		
Left ventricular ejection fraction <50%	1.15 (0.53 – 2.41)	0.7		
Left atrial diameter >45 mm	1.37 (0.71 – 2.70)	0.35		
Left atrial volume >90 mL	1.46 (0.76 – 2.89)	0.26		
Mean diameter of the PVs >20mm	0.92 (0.43 – 1.86)	0.82		
Atypical PV anatomy	1.07 (0.45 – 2.37)	0.87		
Interleukin-6 > 7.0 pg/mL	1.25 (0.65 – 2.44)	0.51		
Time to early recurrence of AF of ≥ 10 days	0.87 (0.43 – 1.69)	0.69		
Number of electrical cardioversions of ≥3	12.2 (4.24 – 60.67)	<0.0001	11.32 (3.83 – 58.22)	0.0019

OR, odds ratio; CI, confidence interval; AF, atrial fibrillation; AADs, antiarrhythmic drugs; PV, pulmonary vein.

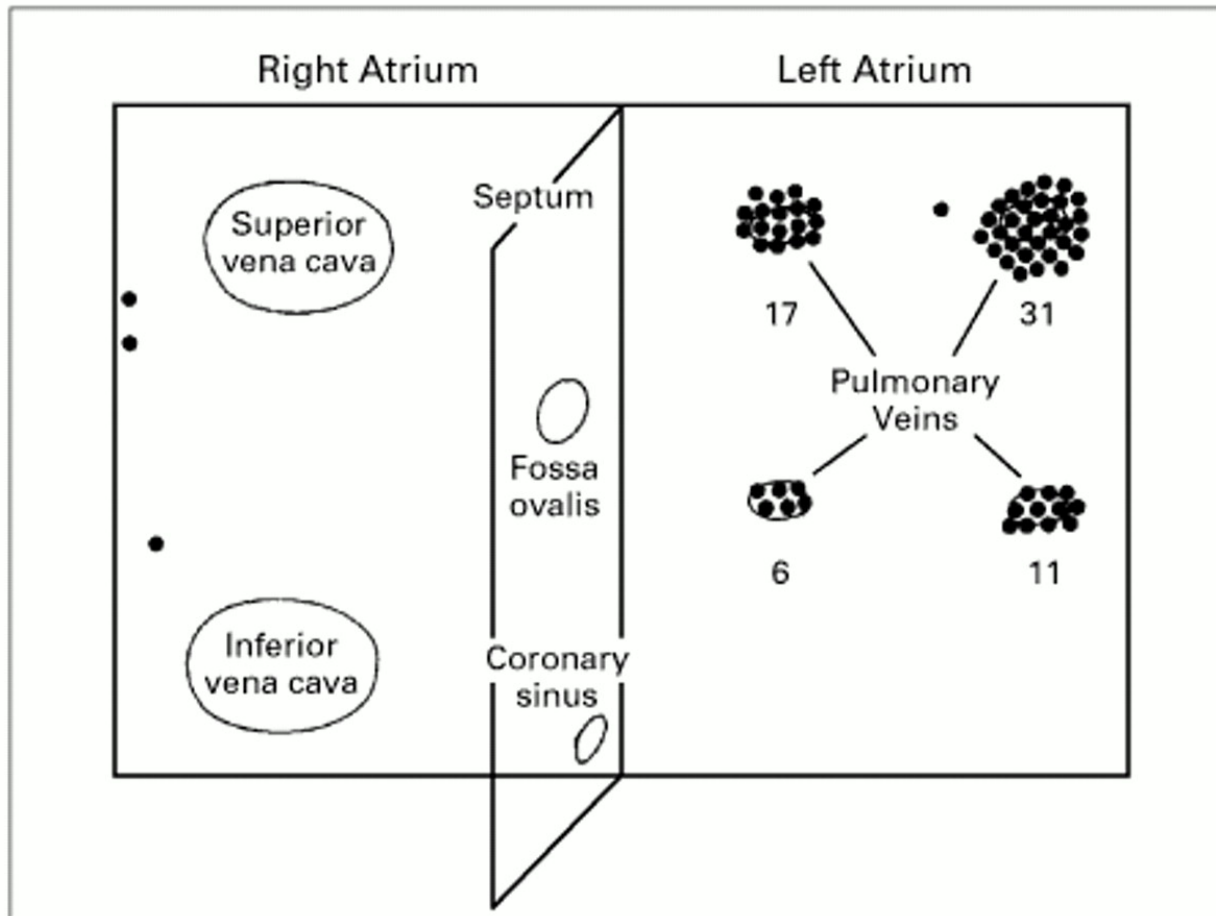


# Ablation of Atrial Fibrillation

1. Pulmonary vein isolation (RF, Cryo, PVAC, nMARQ)  
Ganglionated plexus ablation
2. Additional substrate modification of LA:
  - Linear Lesions
  - CAFE Ablation
  - Ganglionated Plexus Ablation
3. Rotor Ablation

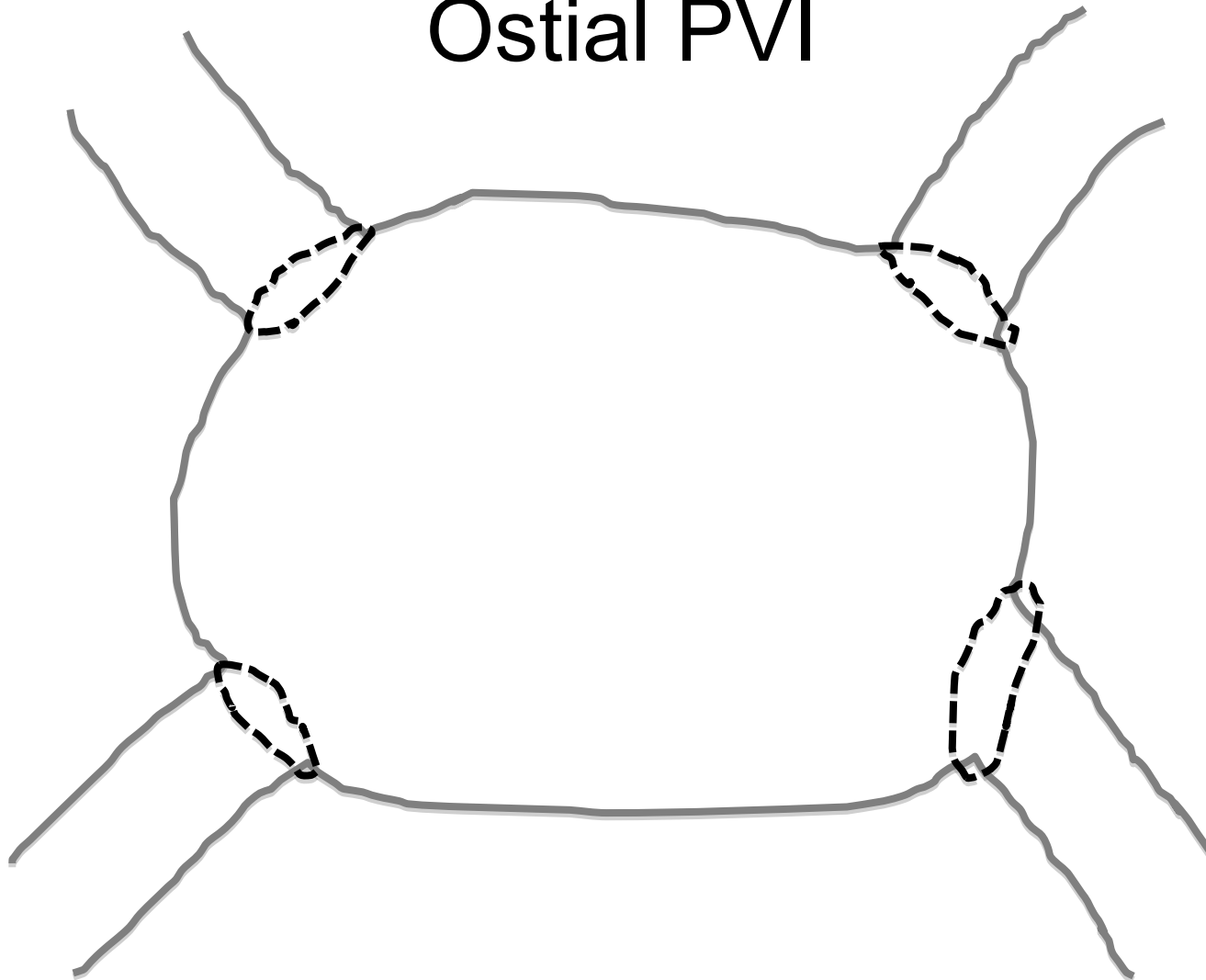


## Diagram of the Sites of 69 Foci Triggering Atrial Fibrillation in 45 Patients





# Ostial PVI

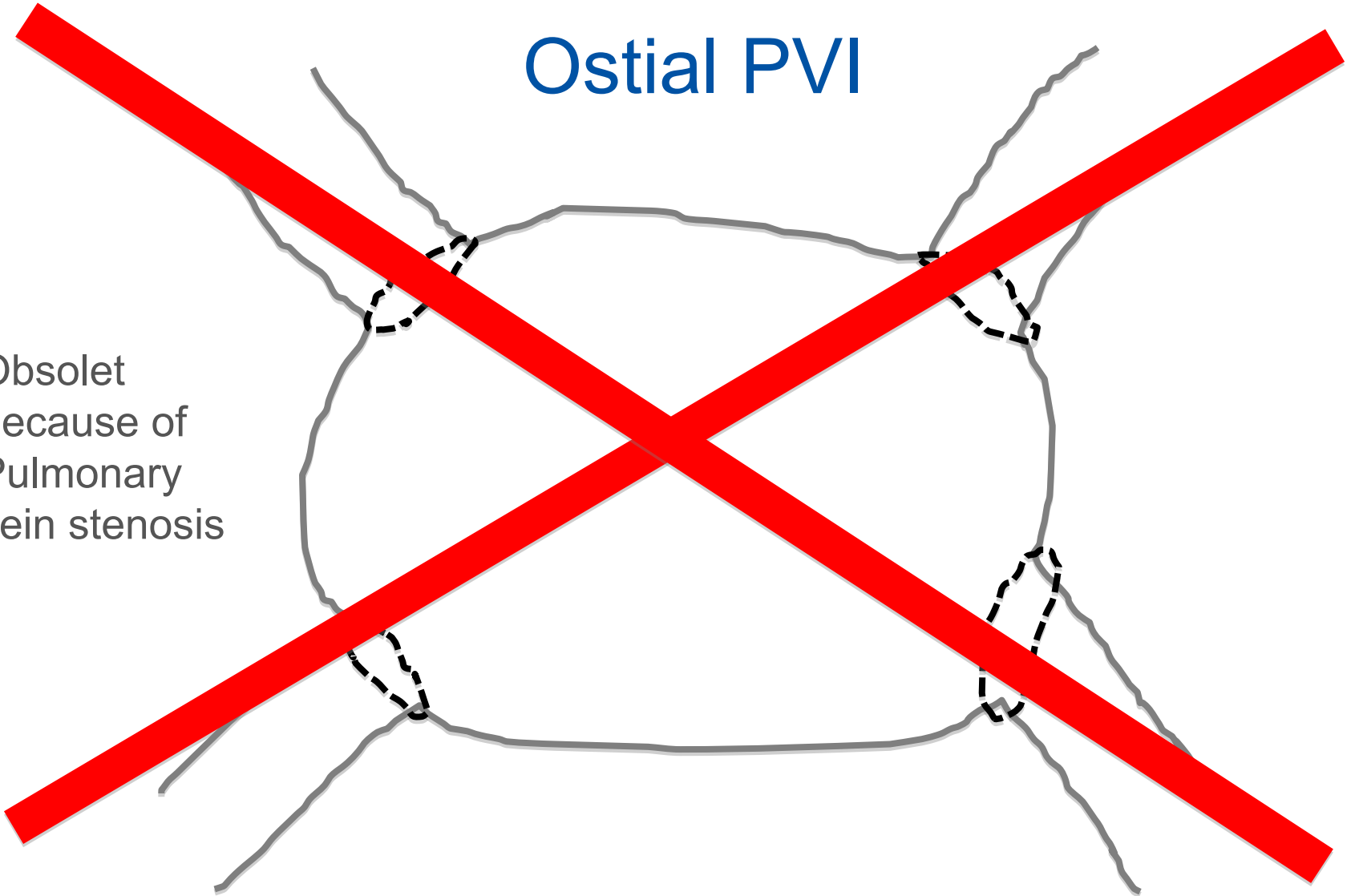






# Ostial PVI

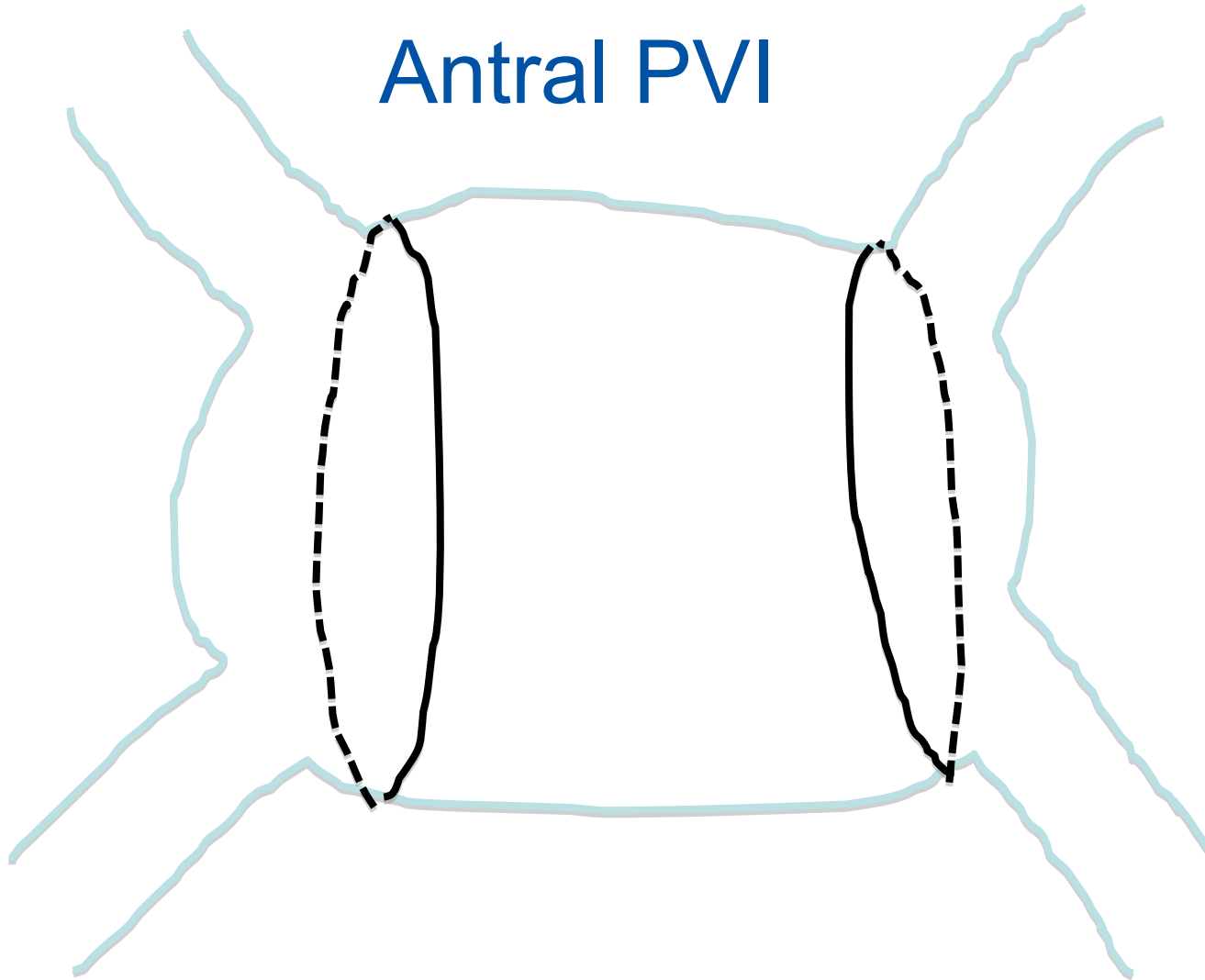
Obsolet  
because of  
Pulmonary  
vein stenosis





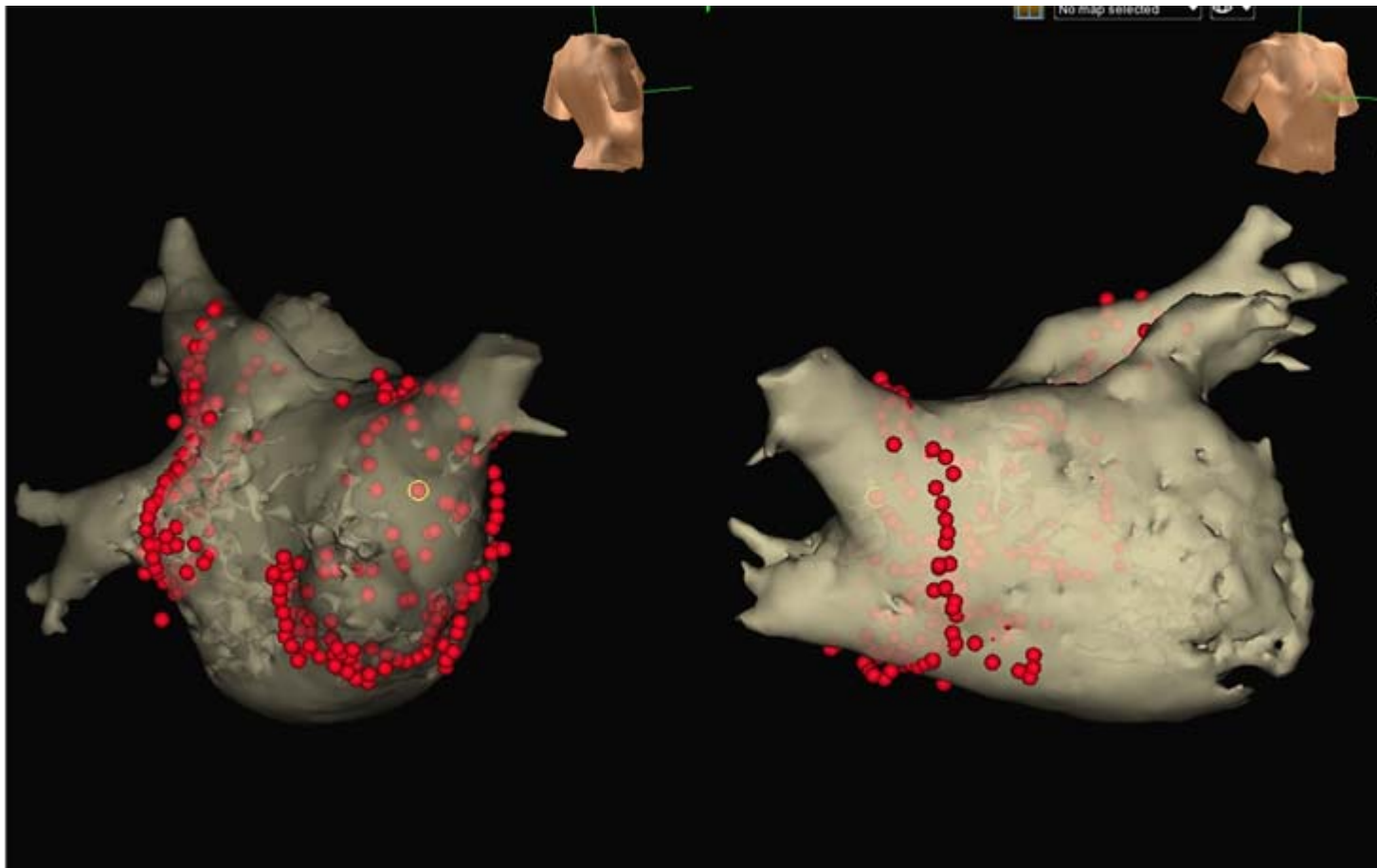


# Antral PVI



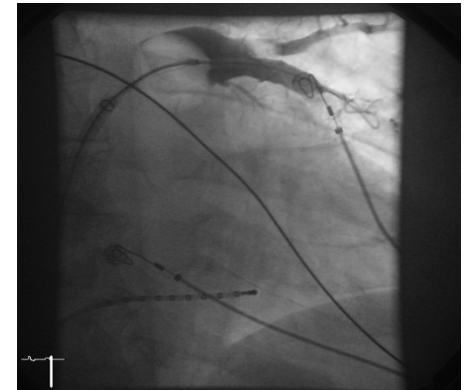
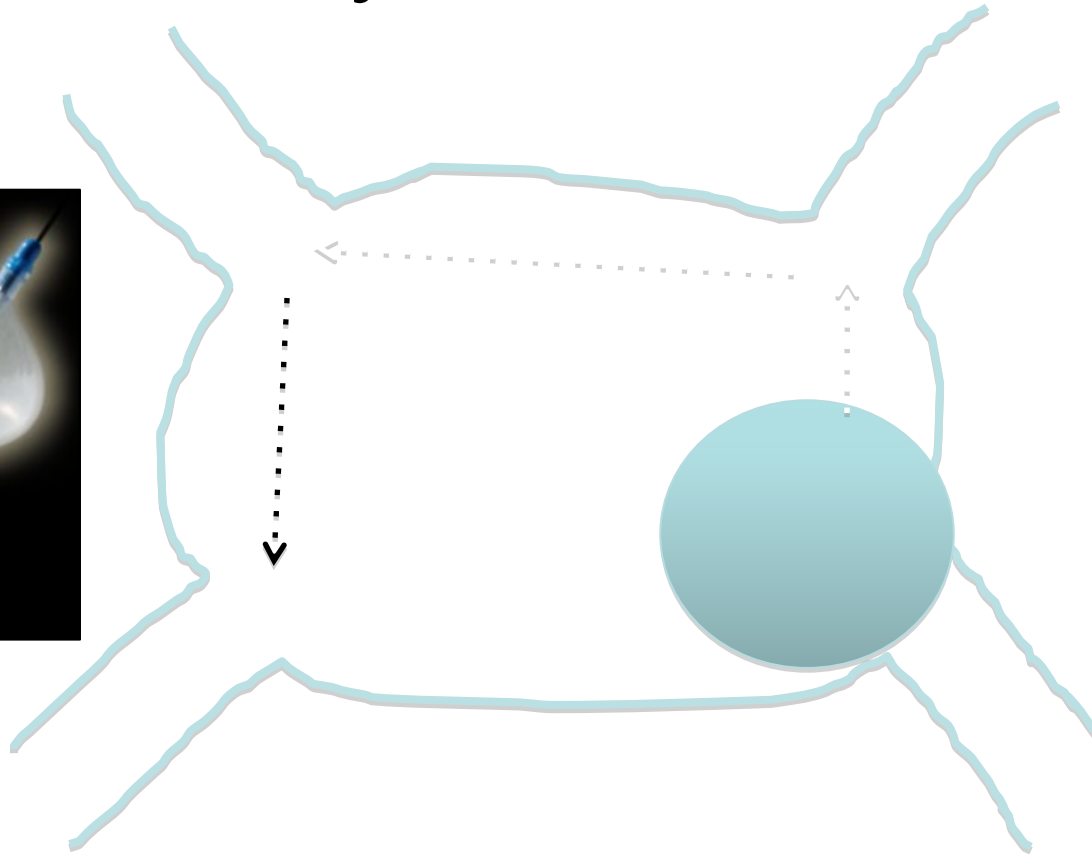


# Antral Pulmonary Vein Isolation



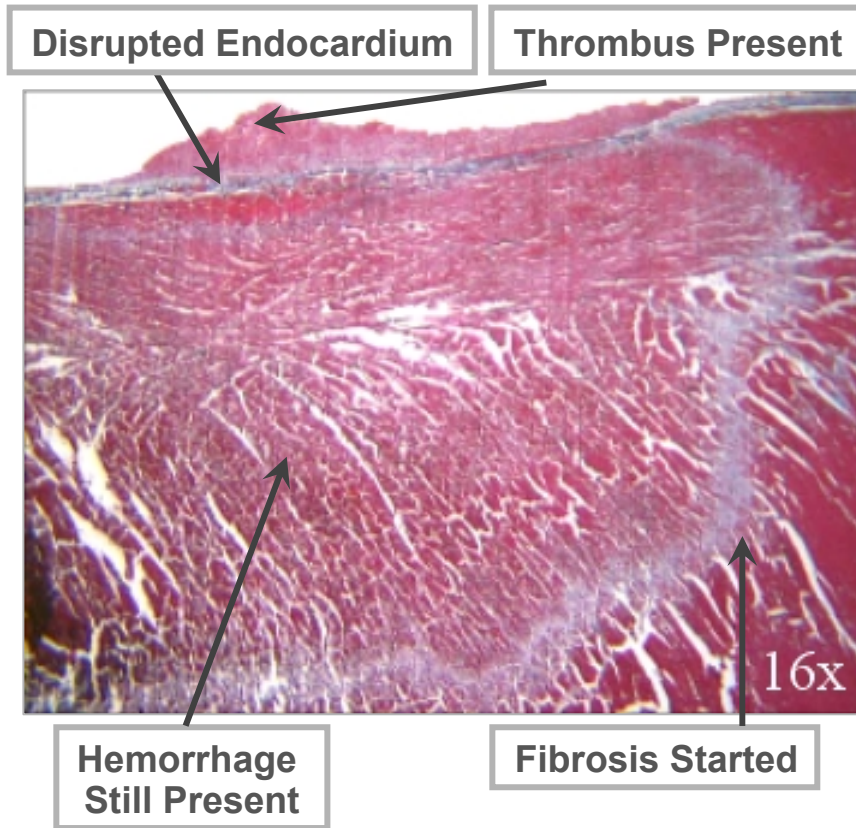


# Cryoballon PVI

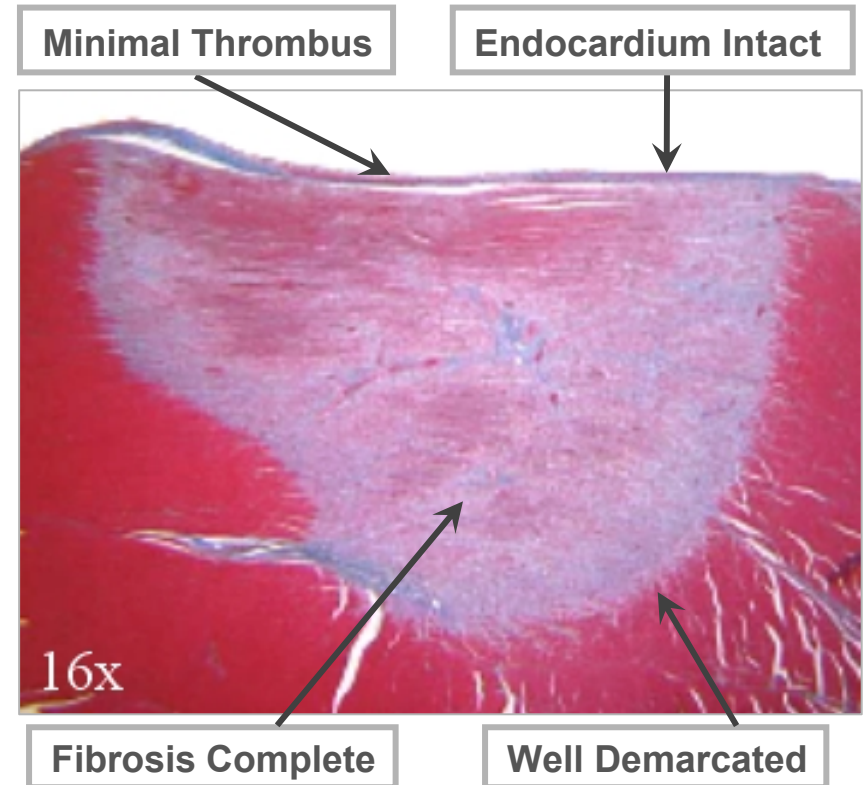




# Effect on the Connective Tissue Matrix



RF Lesion at 1 Week (canine model)  
+70° C • 50 W • 60 seconds

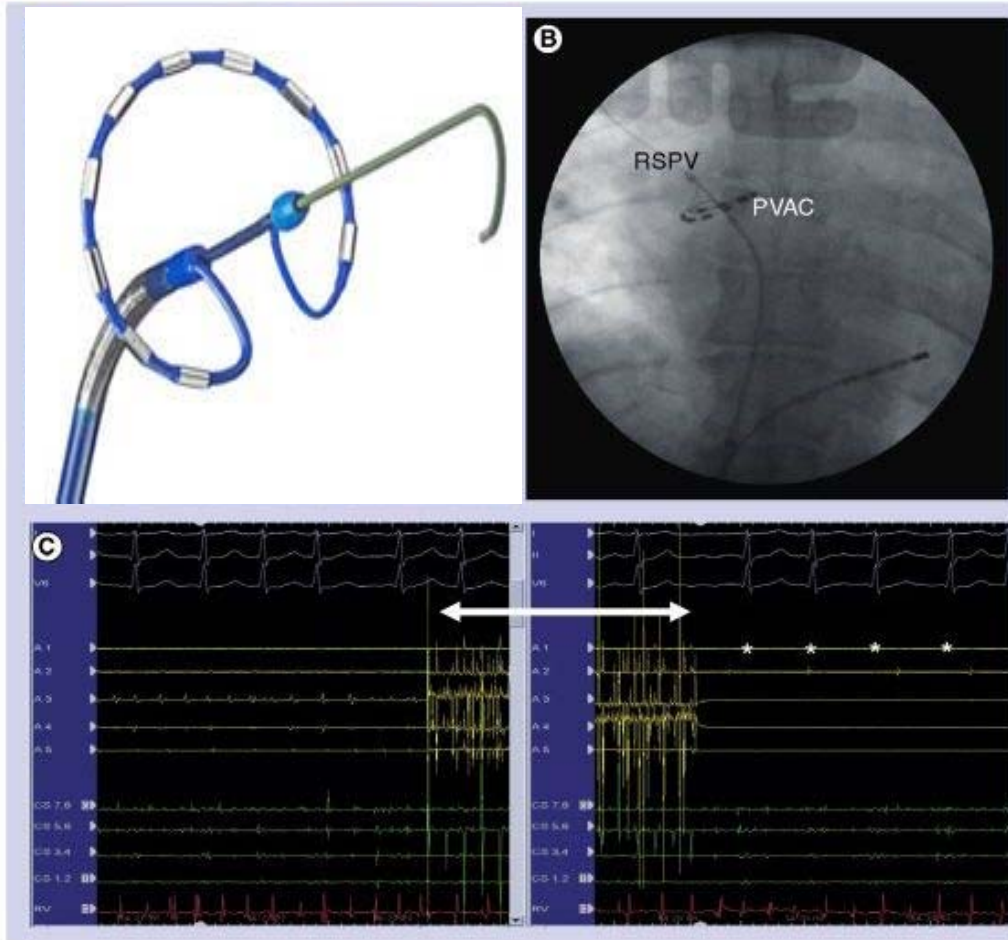


Cryoablation at 1 Week (canine model)  
-75° C • 1 x 4 minutes

Khairy P, et al. *Circulation*. 2003;107:2045-2050.



# PVAC (pulmonary vein ablation catheter) PVI



Ablation Frontiers  
/ Medtronic

Source: Expert Rev Cardiovasc Ther © 2011 Expert Reviews Ltd





## PVAC PVI, safety

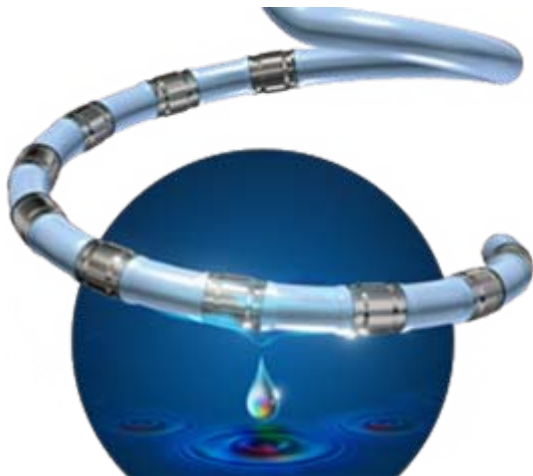
Incidence of Asymptomatic Intracranial Embolic Events After Pulmonary Vein Isolation Comparison of Different Atrial Fibrillation Ablation Technologies in a Multicenter Study

**Herrera Siklódy et. al. *Am Coll Cardiol.* 2011;58(7):681-688. doi:10.1016/j.jacc.2011.04.010**

Post-procedure magnetic resonance imaging detected a single new embolic lesion in 2 of 27 patients in the irrigated RF group (7.4%) and in 1 of 23 in the cryoballoon group (4.3%). However, in the PVAC group 9 of 24 patients (37.5%) demonstrated  $2.7 \pm 1.3$  new lesions each ( $p = 0.003$  for the presence of new embolic events among the 3 groups).

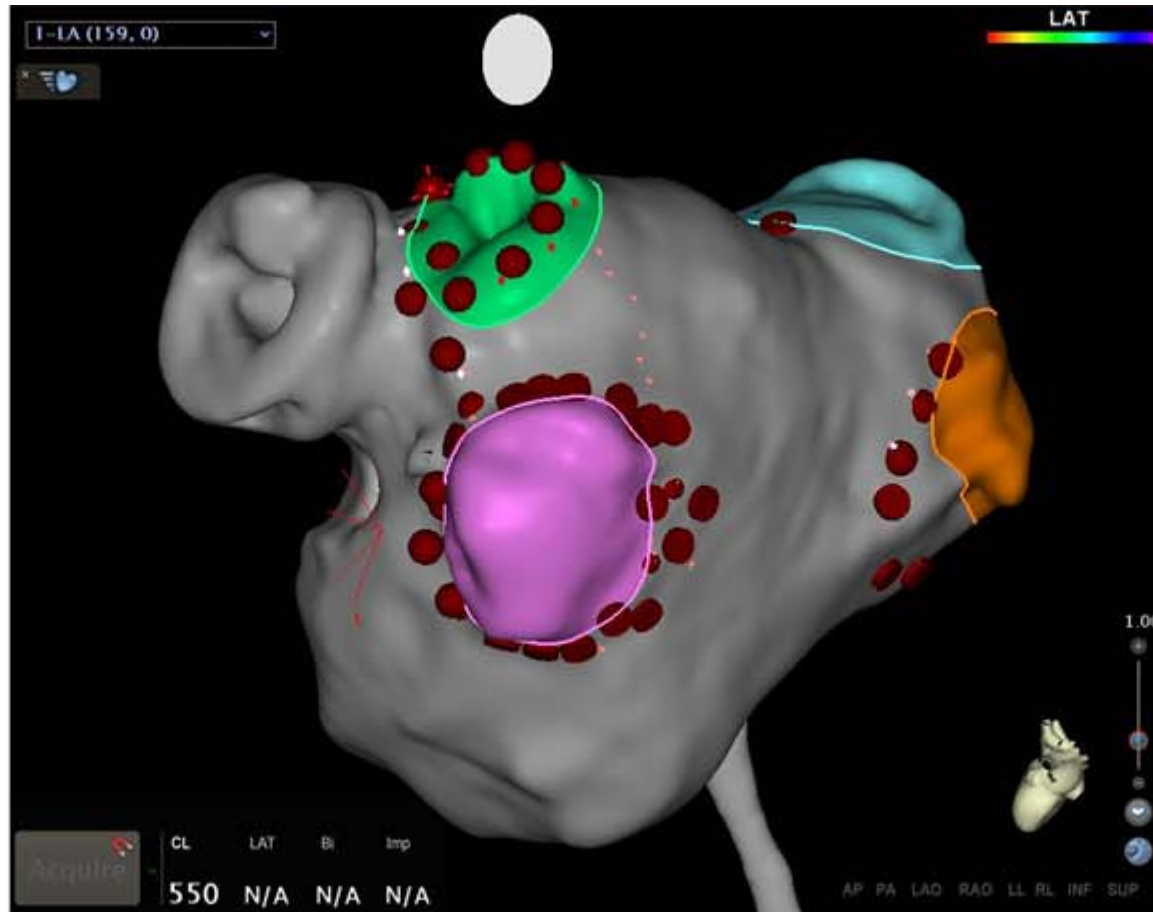


# nMARQ PVI





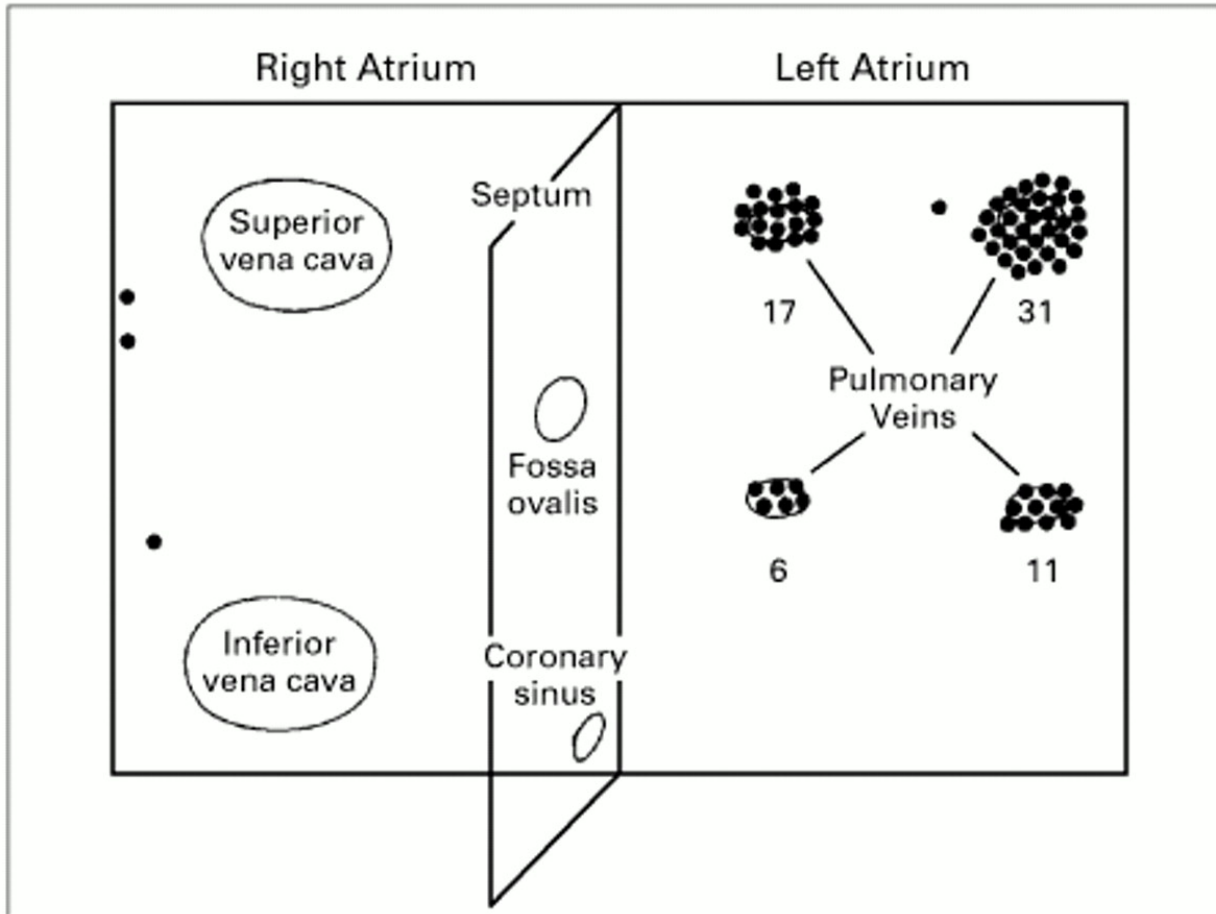
# nMARQ PVI







## AF triggers from the pulmonary veins – why ?



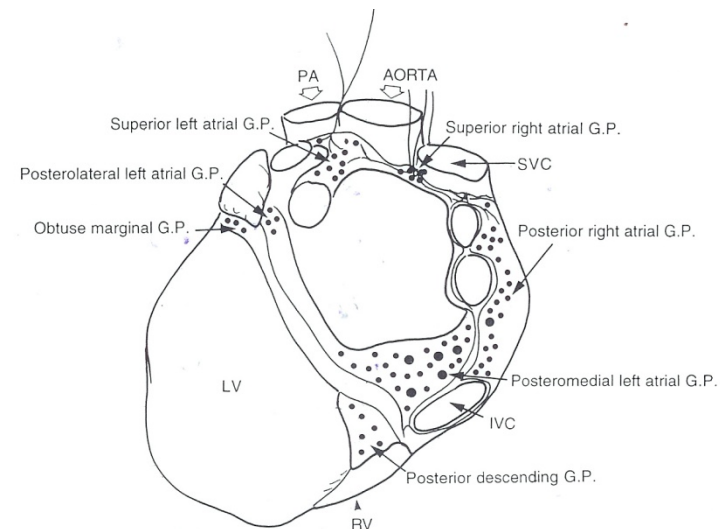
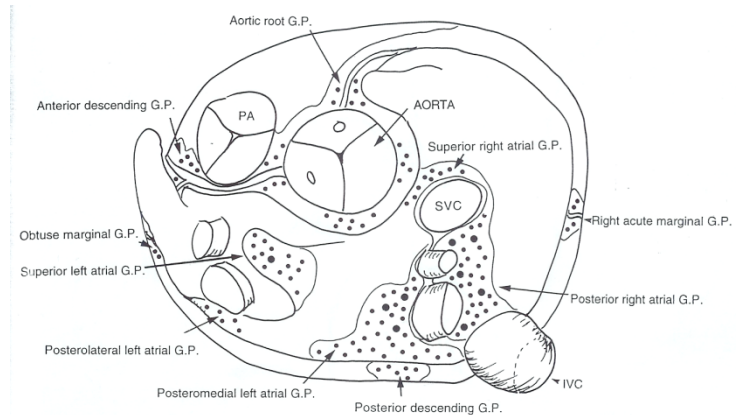


# Human intrinsic cardiac nervous system, location of ganglionated plexus

Gross and Microscopic Anatomy of the Human Intrinsic Cardiac Nervous system,

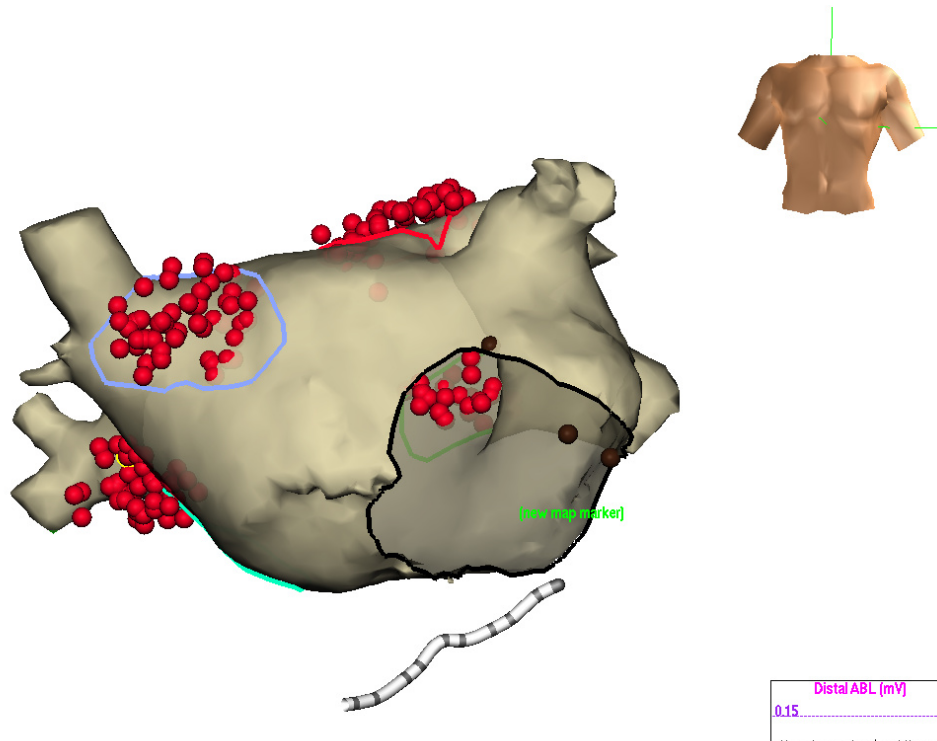
J.A.Armour et al

The Anatomical Record 247:289-298 (1997)





# RF Ganglionated plexus ablation



Zhang et al,  
**Efficacy of cardiac autonomic denervation for atrial fibrillation: a meta-analysis.** Zhang Y, Wang Z, Zhang Y, Wang W, Wang J, Gao M, Hou Y.  
J Cardiovasc Electrophysiol.  
2012 Jun;23(6):592-600

3D EnSite NavX Map combined with CT scan



## Case 5

- 83 years, female, biological age 73
  - Hypertension
  - No heart failure in sinus rhythm NYHA 0
  - Exercise insufficiency under paroxysmal atrial fibrillation several hours a day, EHRA III-IV
  - LA 45mm
- What to do ?



## Case 5, 83 years, female, PAF EHRA III

- Amiodarone / Dronedarone
- Catheter ablation

If yes:

- Standard antral RF pulmonary vein isolation
- RF GPA
- Cryoballoon ablation
- nMARQ
- PVAC

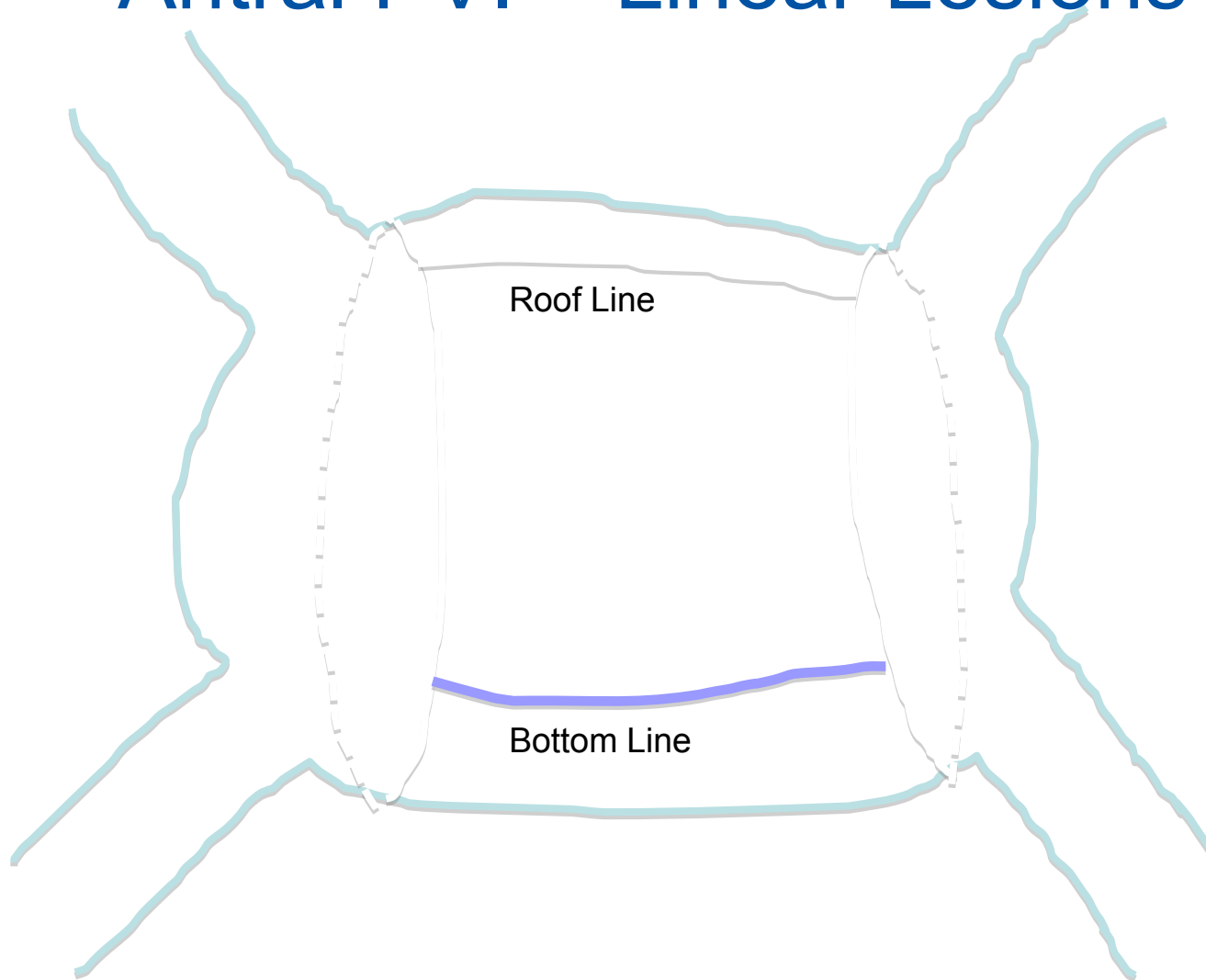


# Ablation of Atrial Fibrillation

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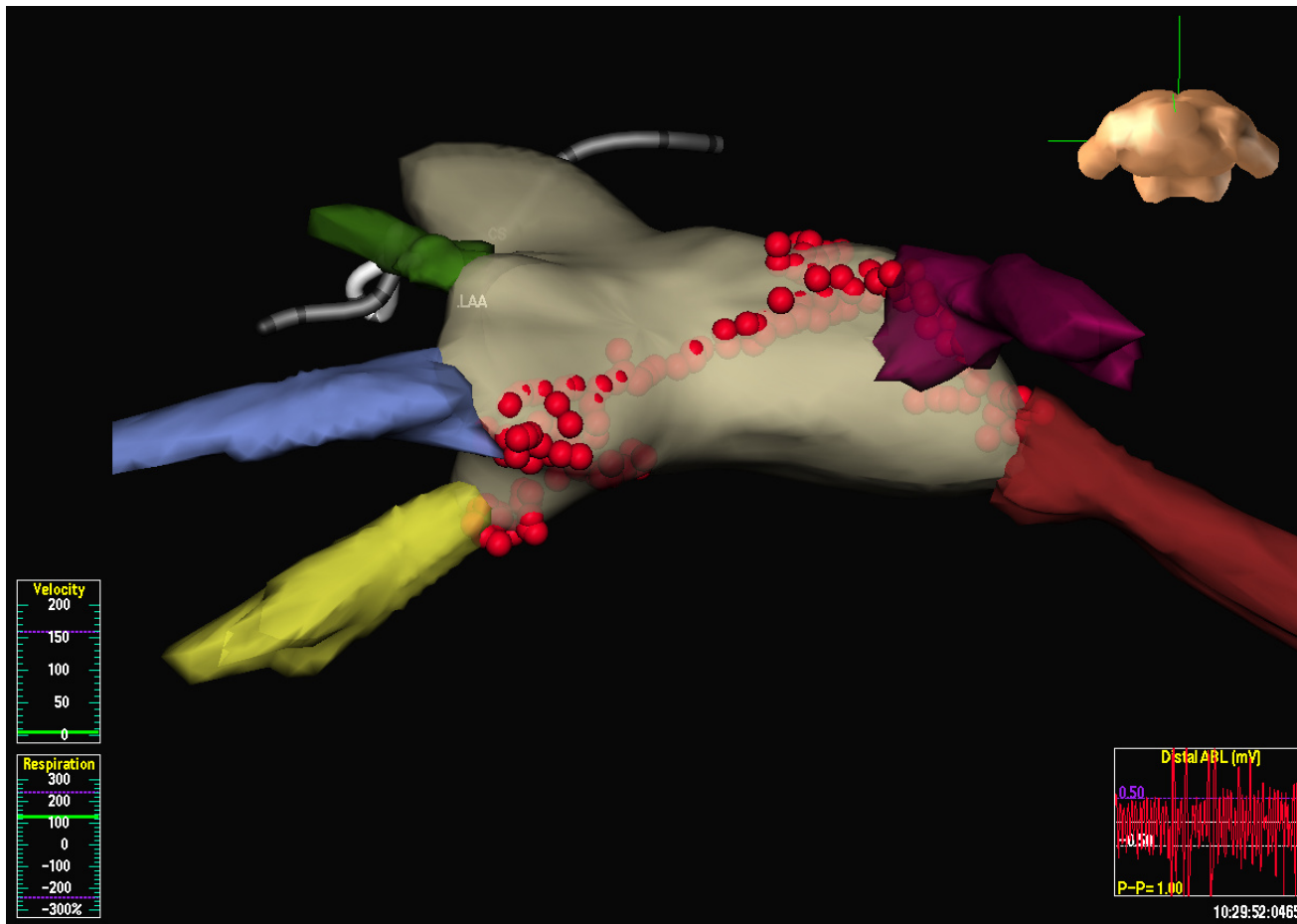


# Antral PVI + Linear Lesions





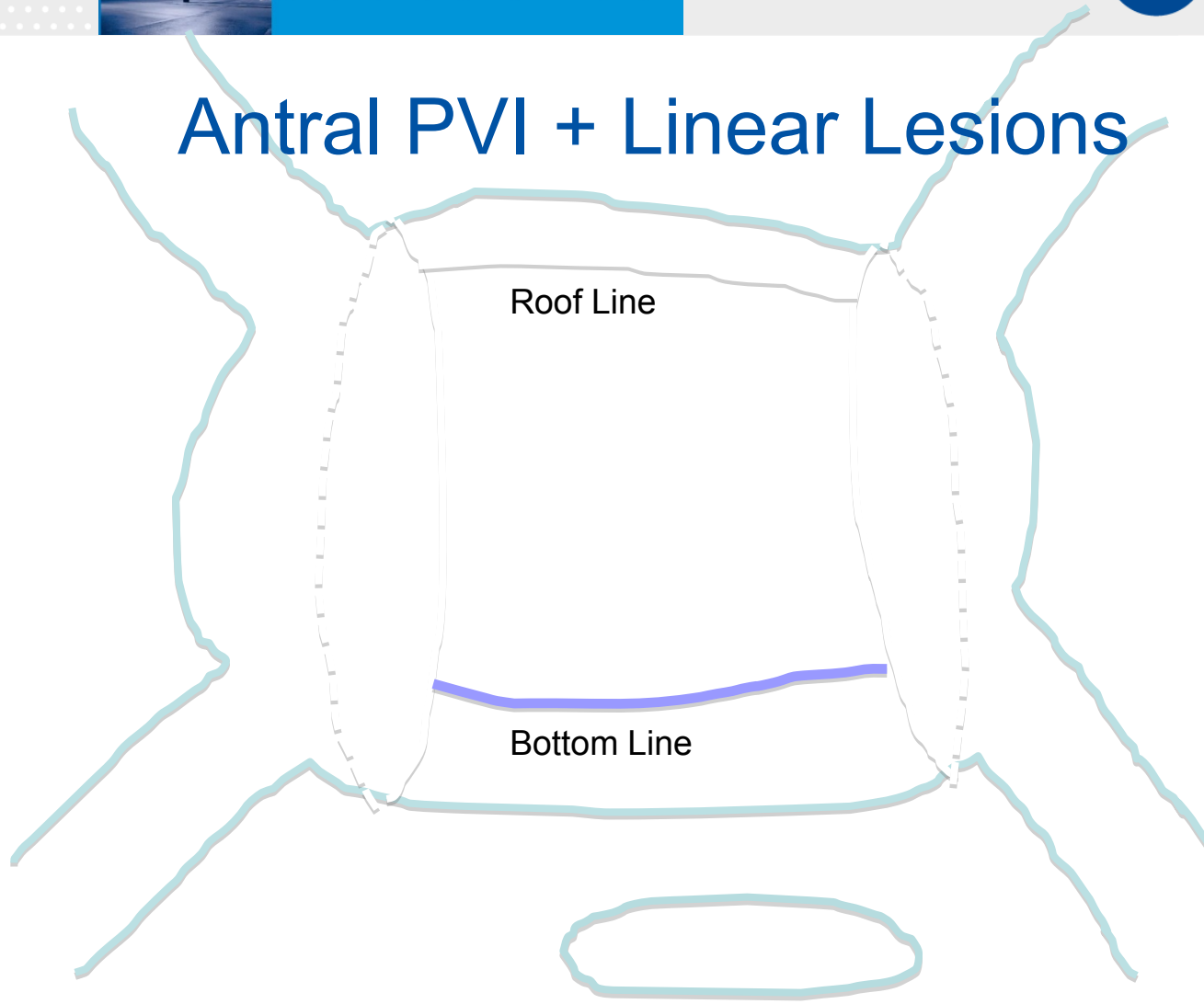
# Roof Line





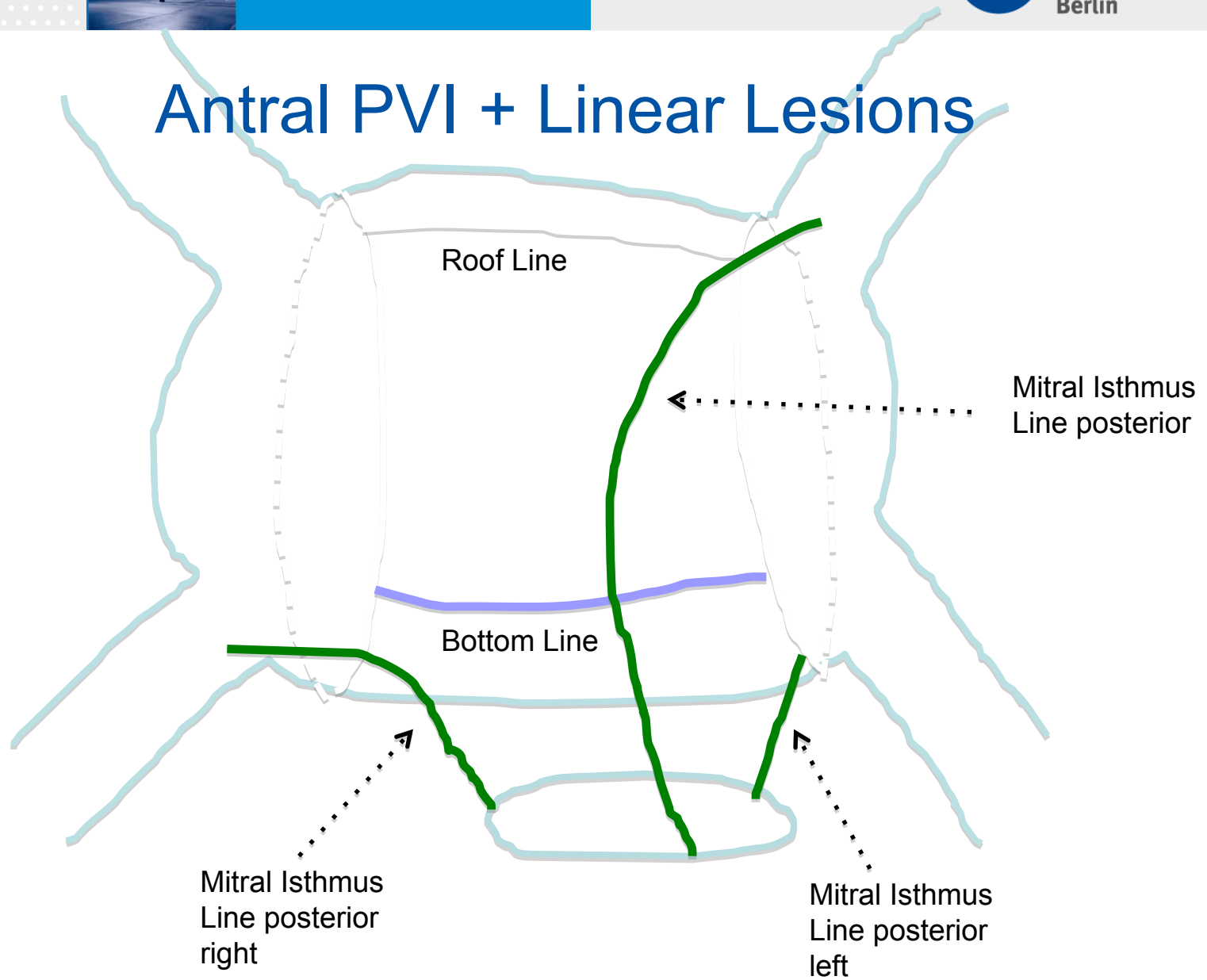


# Antral PVI + Linear Lesions



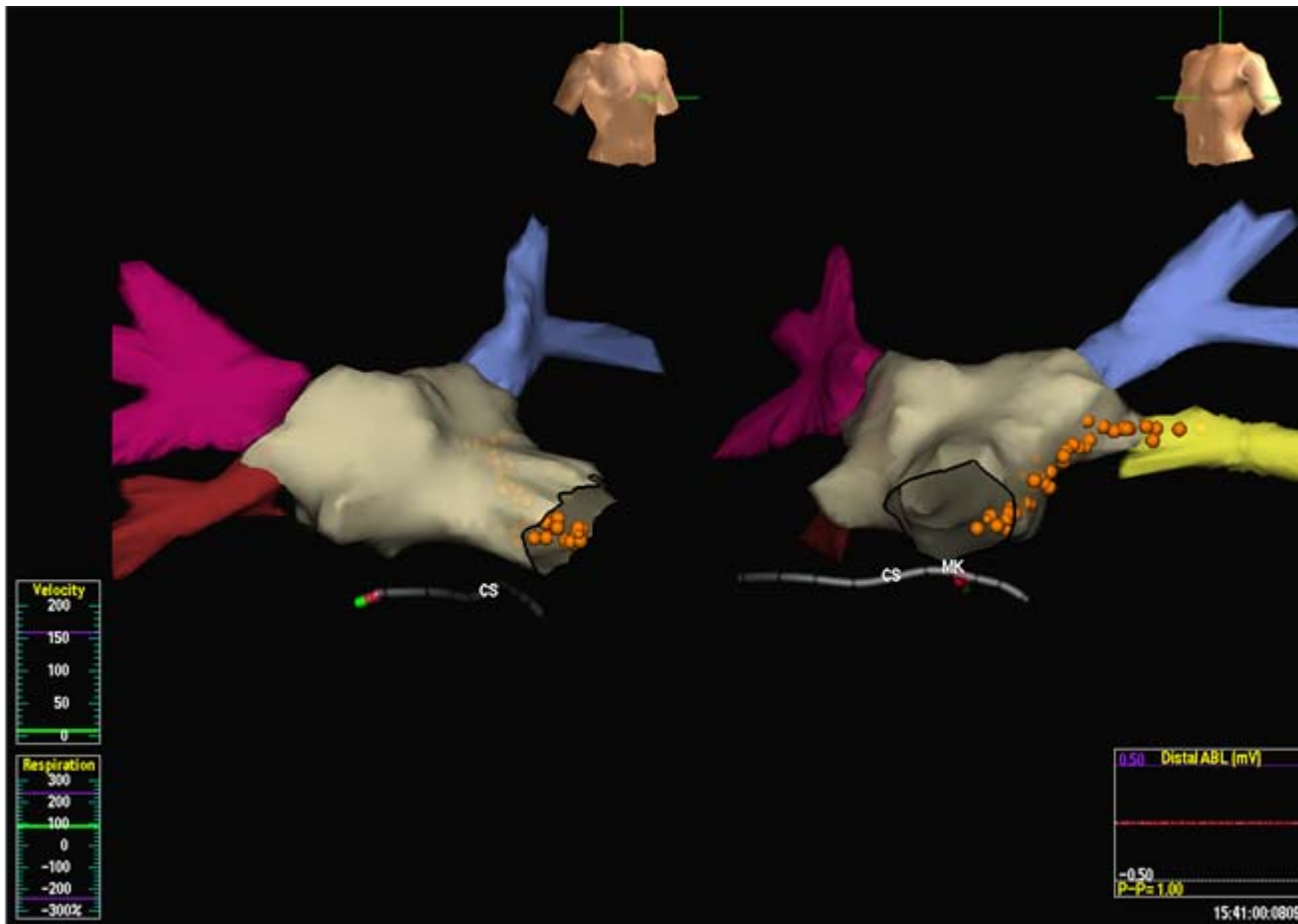


# Antral PVI + Linear Lesions





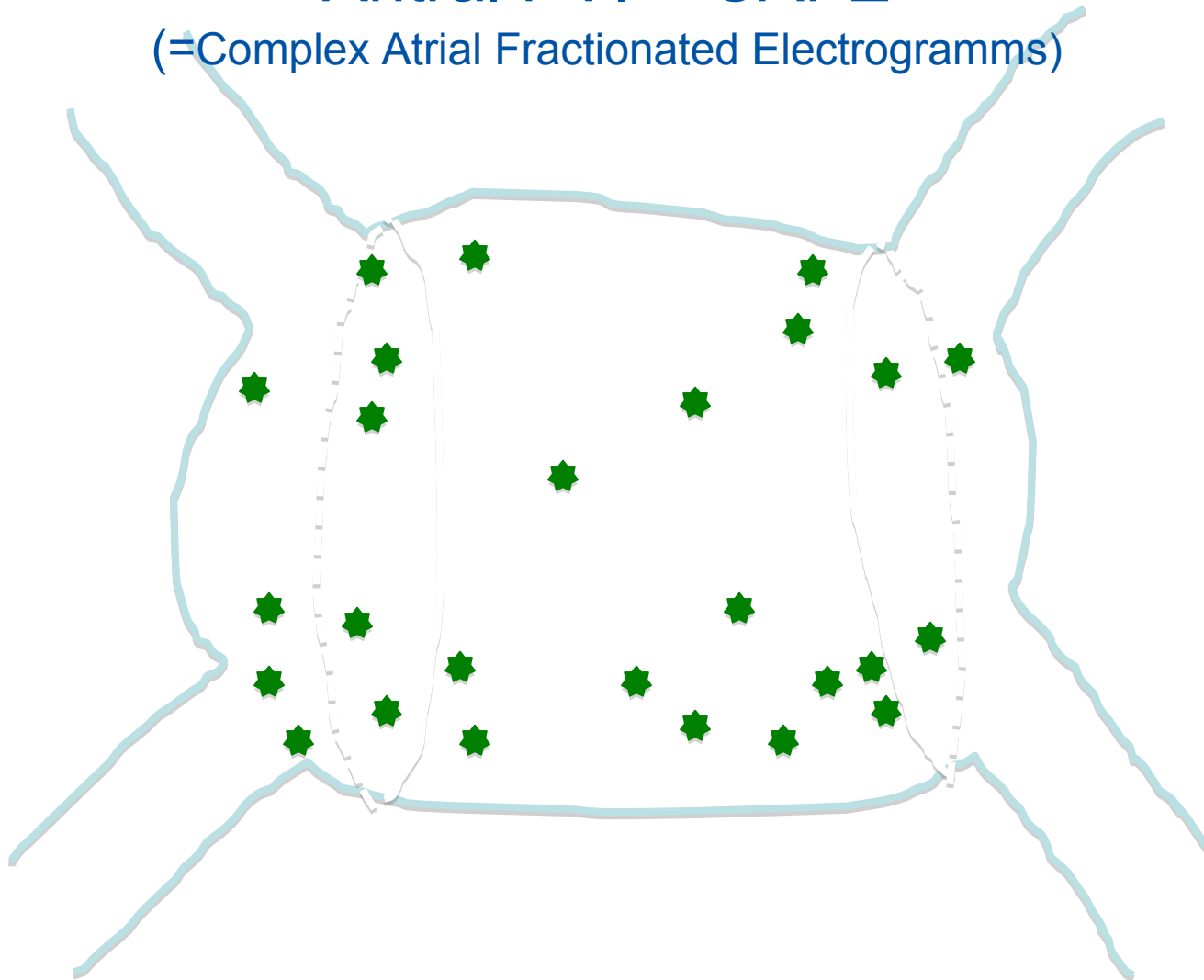
# Posterior Mitral Isthmus Line





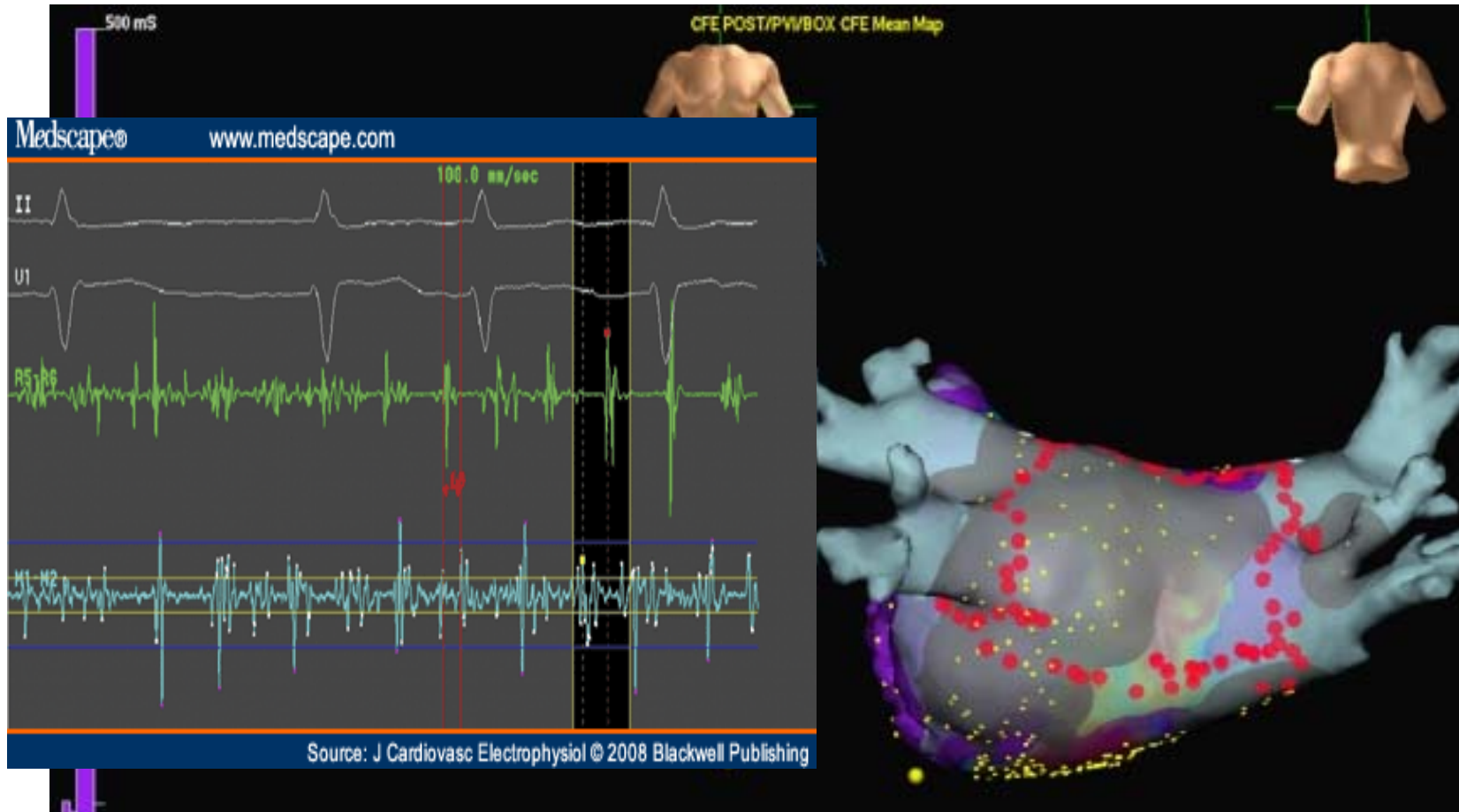
# Antral PVI + CAFE

(=Complex Atrial Fractionated Electrogramms)





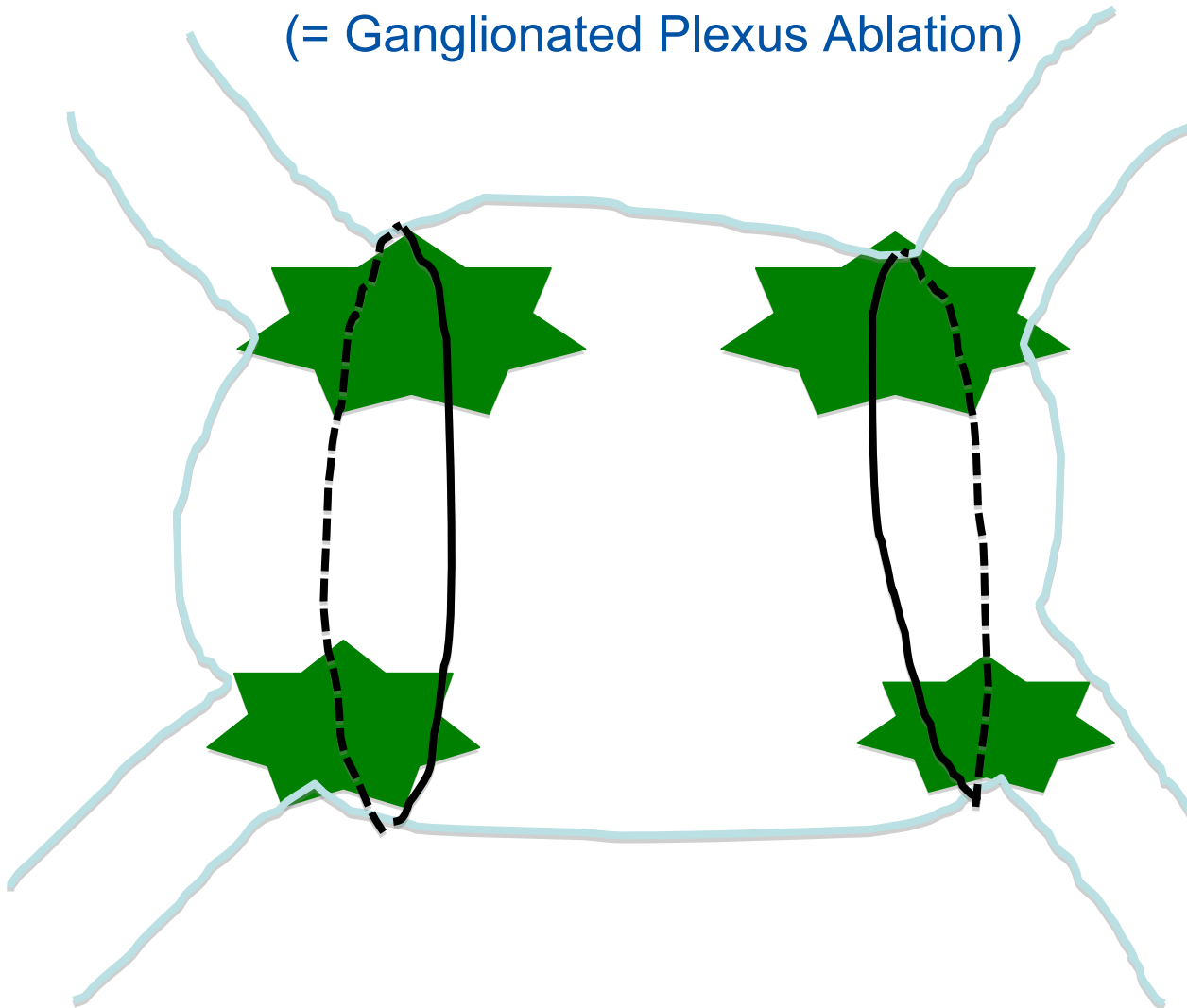
# Antral PVI + Lines + CAFE





# Antral PVI + GPA

(= Ganglionated Plexus Ablation)

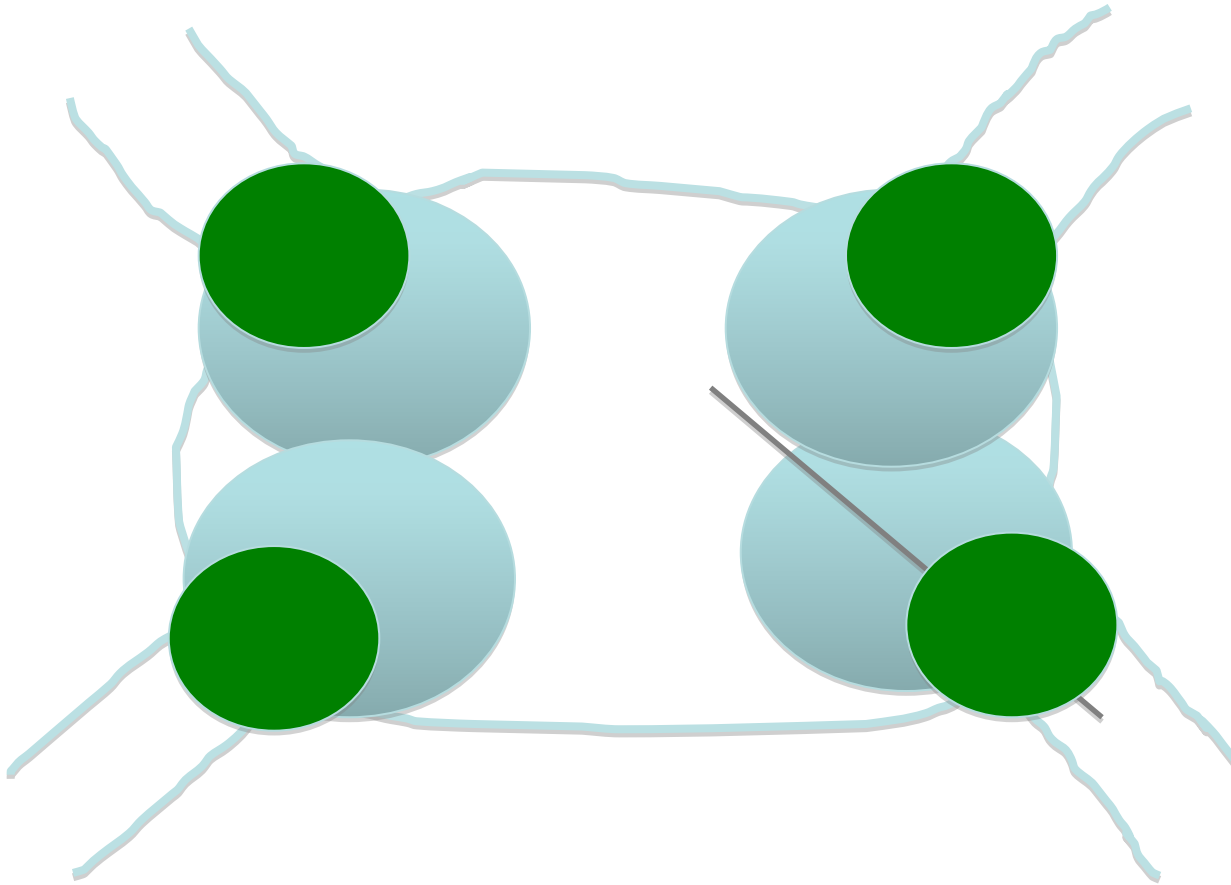


Katritsis et al,  
**Autonomic Denervation Added to Pulmonary Vein Isolation for Paroxysmal Atrial Fibrillation: A Randomized Clinical Trial**  
J Am Coll Cardiol.  
2013 Aug S0735-1097(13)03089-1.

Zhou et al,  
**A meta-analysis of the comparative efficacy of ablation for atrial fibrillation with and without ablation of the ganglionated plexi.**Zhou  
Pacing Clin Electrophysiol.  
2011 Dec;34(12):1687-94.



# Cryoballoon PVI, both balloons



Schmidt,  
Doorwarth,  
Hoffmann et al.  
**.A novel double  
cryoballoon  
strategy in  
persistent atrial  
fibrillation: a  
pilot study.** Clin  
Res Cardiol.  
2012  
Oct;101(10):777-  
85. Epub 2012  
Apr



## Case 6

- 68 years, female
- Hypertrophic obstructive cardiomyopathy (HOCM), post TASH
- LA 58mm, EF 70%, EDV 60ml, ESV 42ml, SV 18ml
- MI II°
- NYHA II in sinus rhythm
- Now persistent atrial fibrillation, EHRA IV

What to do ?





## Case 6, 68 years, female, HOCM, PsAF

- Frequency control
- Catheter ablation

If catheter ablation:

- RF PVI + lines
- RF PVI + CAFE
- RF PVI + GPA
- Two cryoballoons




# AF ablation succes rate

PAF 70 – 92%

PsAF 50 – 72 %

LsAF 30 – 60%



drops rapidly  
with disease  
progression

Pokushalv et al

Europace 2010:12,342-46

Boersma et al

Heart Rhythm 2008:5,1635-42

Pappone et al

JACC 2003:42,185-197

Nademanee K et al

JACC 2004:43,2044-53

Kottkamp H et al

JACC 2004:44:869-877

Haissaguerre M et al

JCE 2005:16:1125-1137



# Disease progression of AF

Paroxysmal AF

Persistent AF

Long standing AF



Increasing Structural Changes

- LA dilatation
- Atrial fibrosis
- Autonomic hyperactivation
- Genetic alterations

Decreasing ablation succes rate

70%

50%

30%

Symptoms

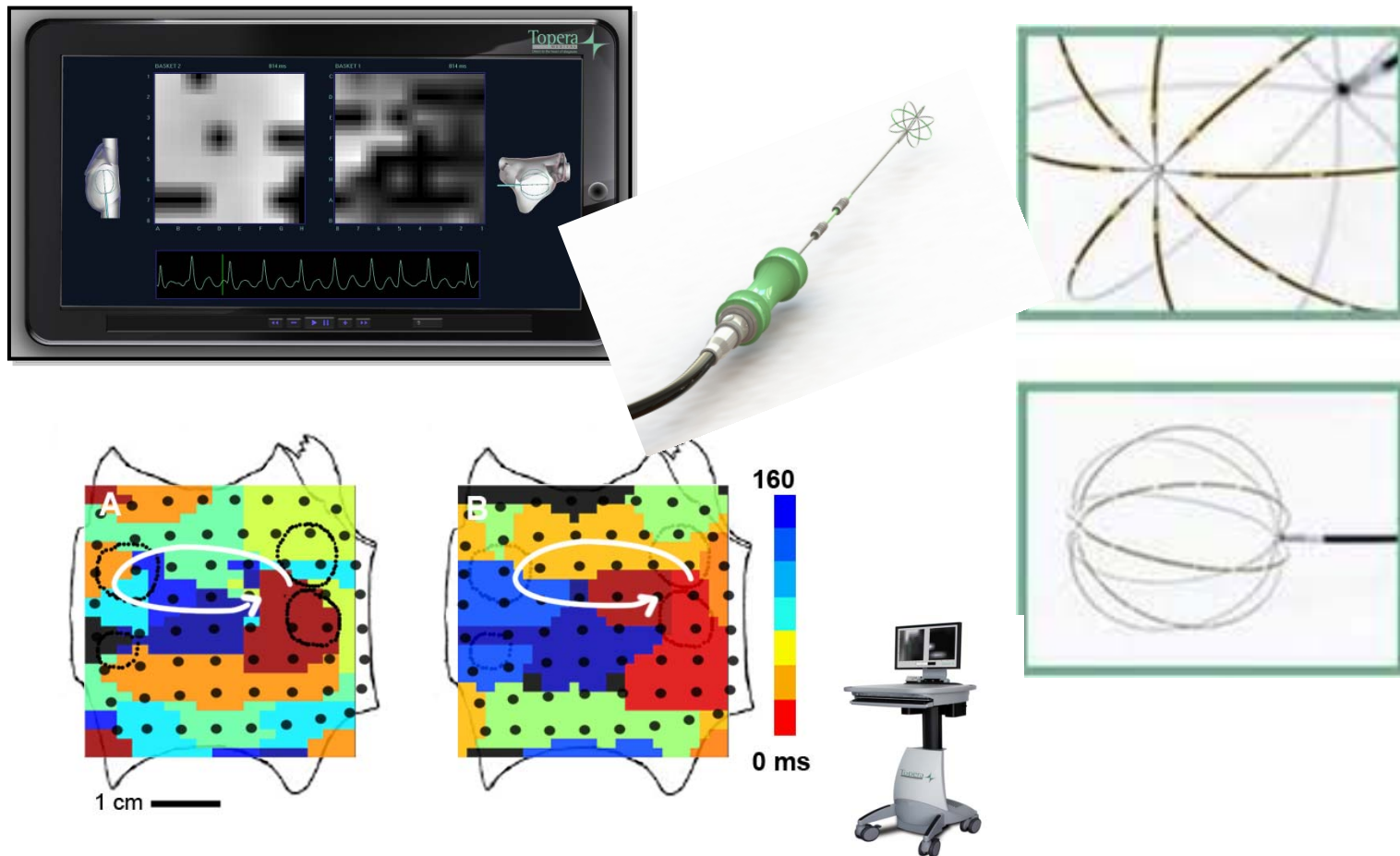


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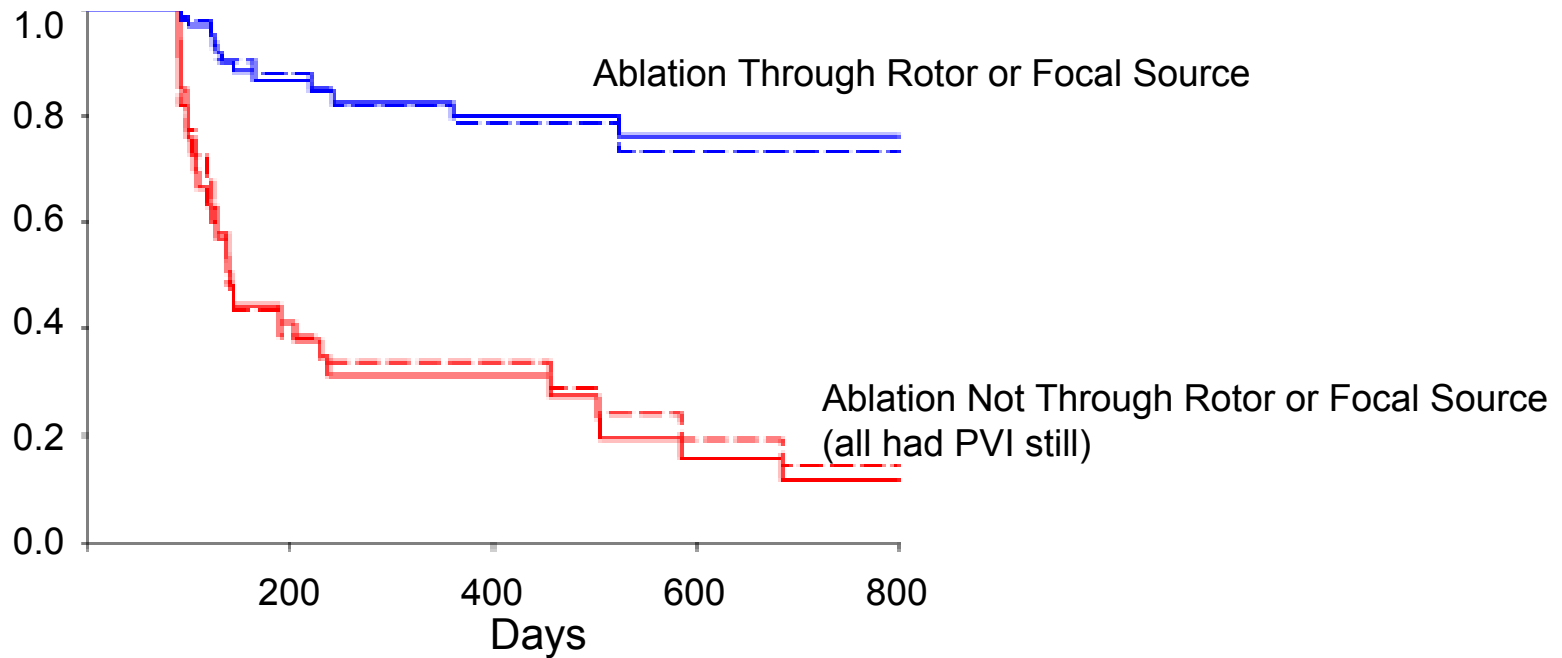


# Fokal Impulse and Rotor Mapping (FIRM)





## Freedom from Atrial Fibrillation



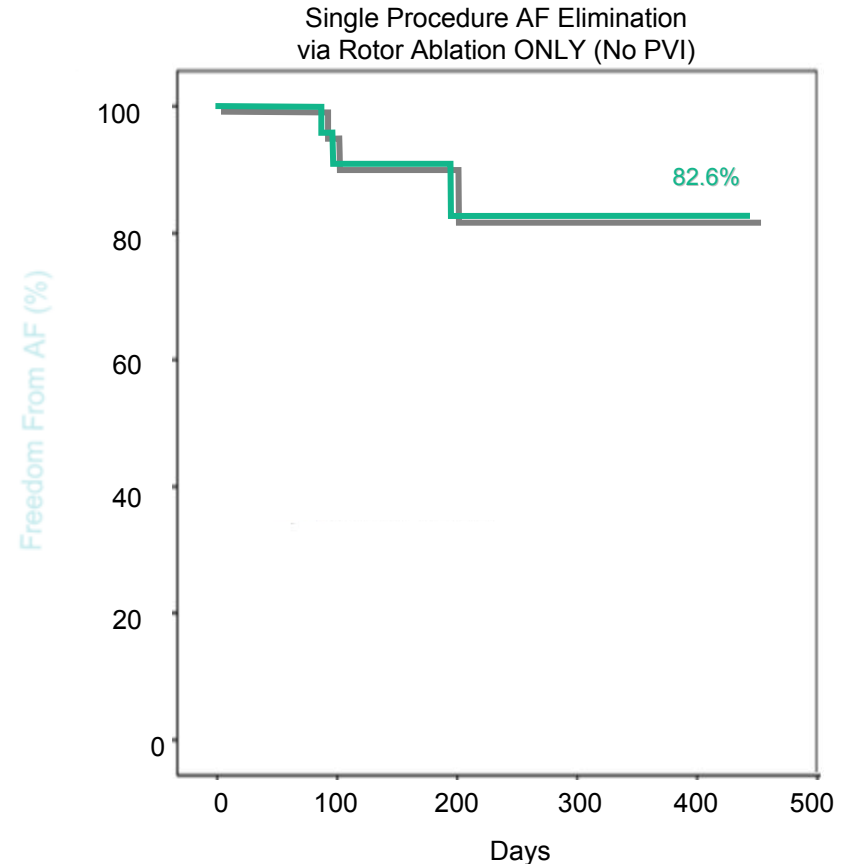


## PRECISE-PAF, Rotor Ablation Without PVI

- HRS Late Breaking Clinical Trial (May 2013)
- Prospective Design In 31 PAF Patients (Persistent AF excluded)
- 5 clinical sites
- Veins confirmed 'open' at procedure end
- Implanted Loop Recorders In 64%, OR

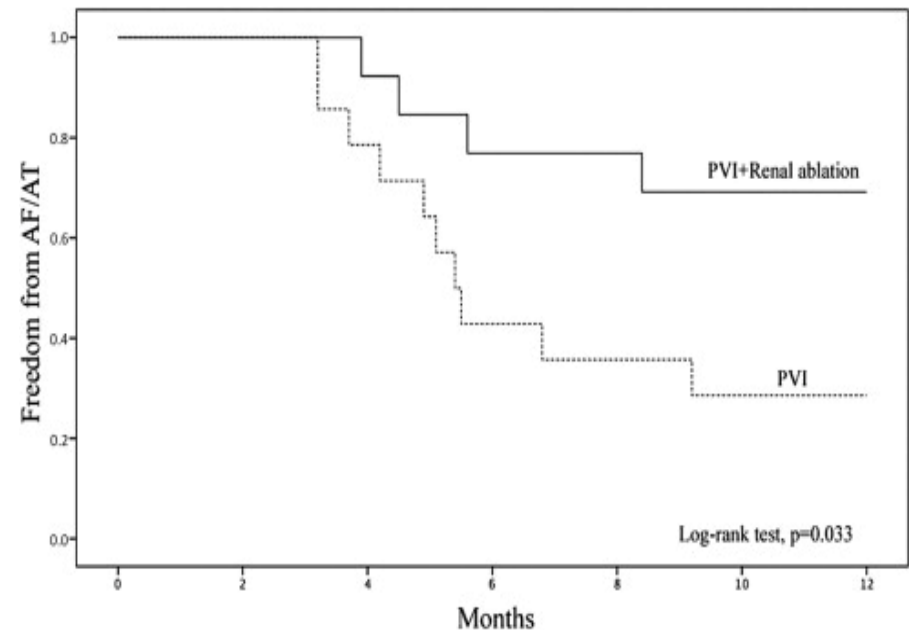
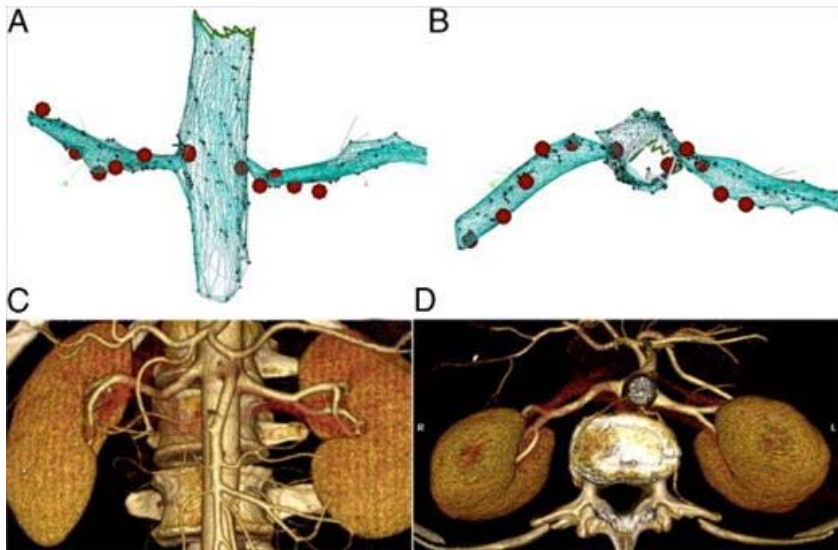
**Short Ablation Time (mean 17 min)**

**Results Similar to CONFIRM  
without PVI**





## Have we been targeting the wrong organ ?



Pokushalov et al,  
A Randomized Comparison of Pulmonary Vein Isolation With Versus Without Concomitant Renal Artery Denervation in Patients With Refractory Symptomatic Atrial Fibrillation and Resistant Hypertension  
J Am Coll Cardiol. 2012;60(13):1163-1170

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## Summary / Take home messages

- Think of DOAK's / LAA Occlusion
- Ablate early but do not ablate PmAF
- PVI or GPA with PAF
- PVI + Substrate Modification with PsAF
- Cardiovert up to three times post ablation
- Be ready for new techniques...



# Vielen Dank für Ihre Aufmerksamkeit !

