

Fibrillazione Atriale

Trattamento interventistico

Milano 5/10/18

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University of Turin



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Policlinico di Monza
Istituto ad Alta Specializzazione

Mechanisms of AF

Trigger

Atrial premature contractions (P/T)

AF

Autonomic Nervous System

Vagal /Adrenergic




Substrate

Anatomical:

Critical mass, fibrosis, hypertrophy, Loss of connecting

Electrophysiological

Short ERP, ERP dispersion, intraatrial conduction delay and block



Tomorrow

Today

Yesterday

Antiarrhythmic therapy in atrial fibrillation

1749 Quinine

1785 Digitalis

'700

1936 Procainamide

1954 Disopyramide

1962 Beta Blocking agents

1972 Amiodarone

1978 Propafenone

1982 Flecainide

1984 Sotalol

1995 Ibutilide

1996 Dofetilide

1998 Azimilide

'900

1996 ablation

surgical/ transcatheter

2010 Vernakalant

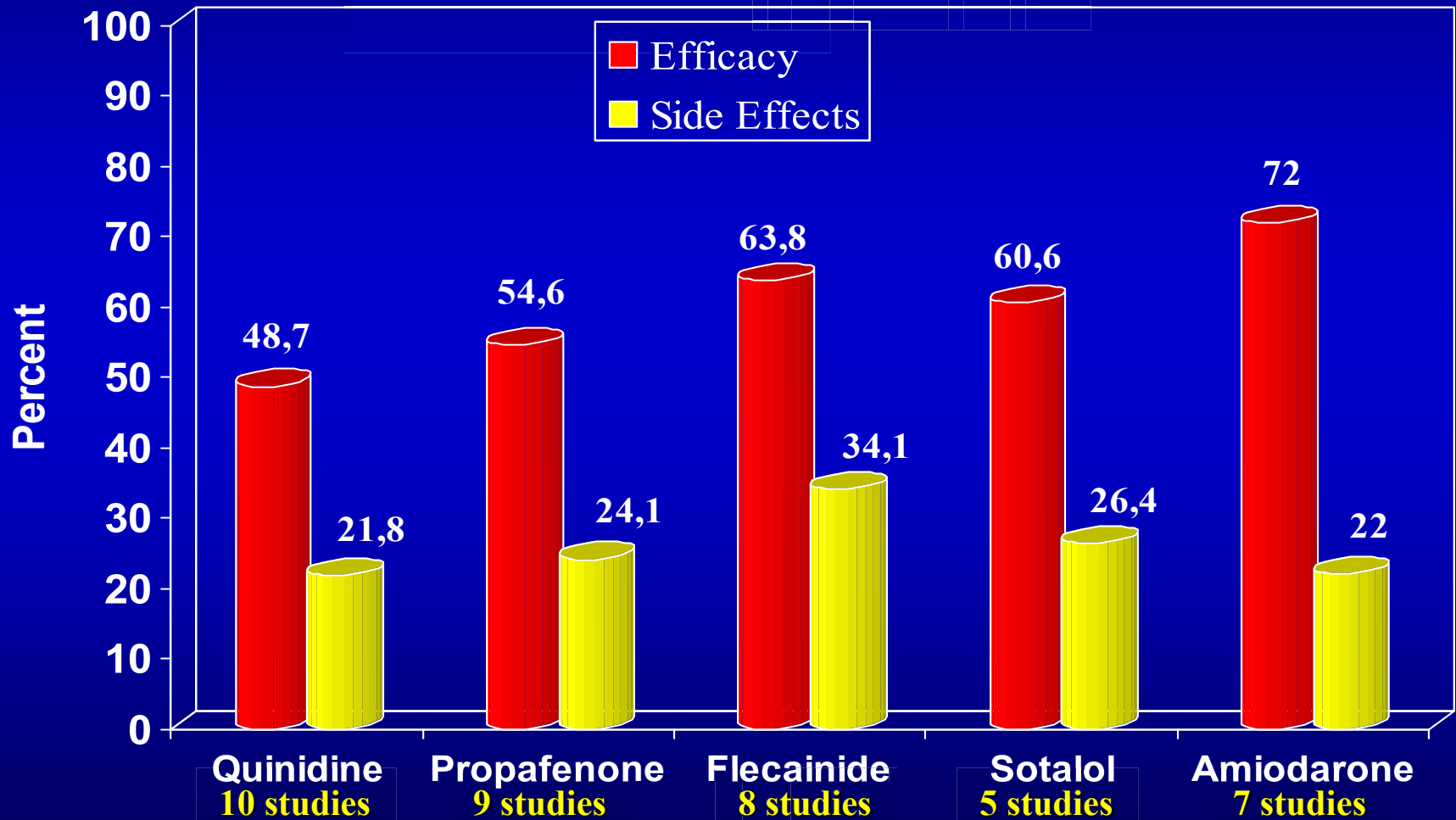
2010 Dronedarone

2000

Antiarrhythmic drugs in atrial fibrillation

(39 studies between 1968 and 2000)

AAD for AF (~1 year F-up)

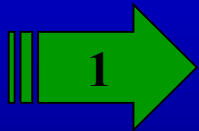


Electrophysiologic targets of AF ablation

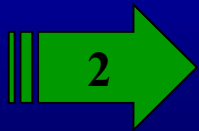
Multiple wavelets theory



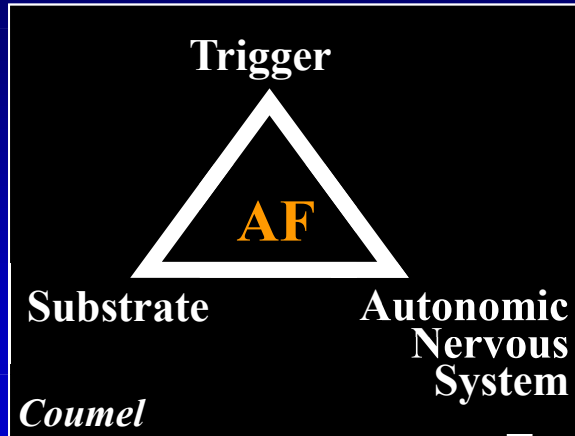
Substrate:



Linear lesions



Ablation of fractionated electrograms



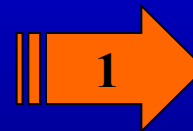
Ganglia ablation

Focal theory

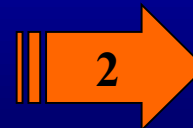


Triggers:

- VVPP
- SVC
- CS



Electrophysiologic guided PV isolation

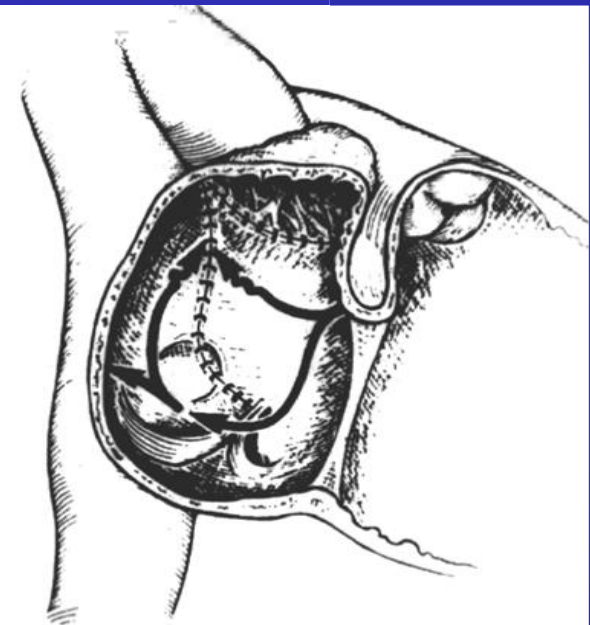
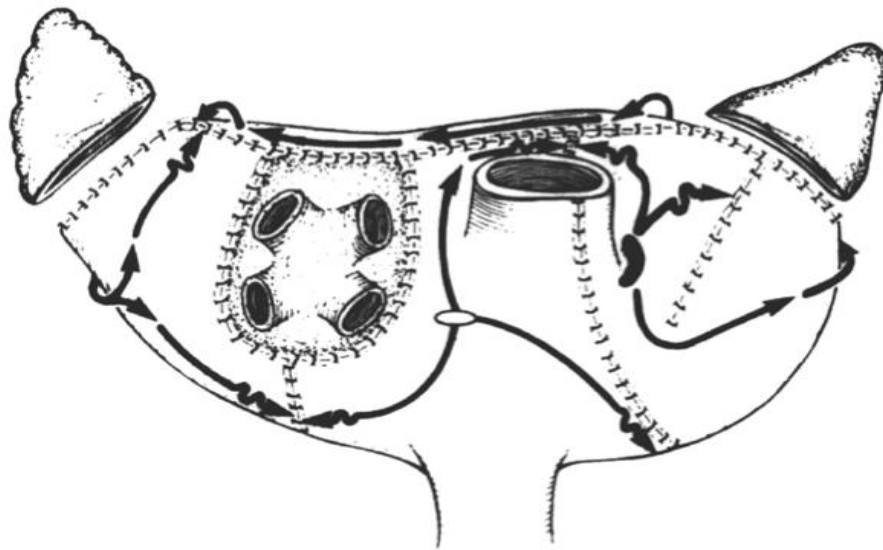


Circumferential PV isolation (Anatomical encircling)

Who started and when ?

J. Cox, Maze procedure started in 1990

Substrate modification: linear lesions



178 pts (103 paroxysmal, 75 chronic)

Follow-up : 3 - 102 months

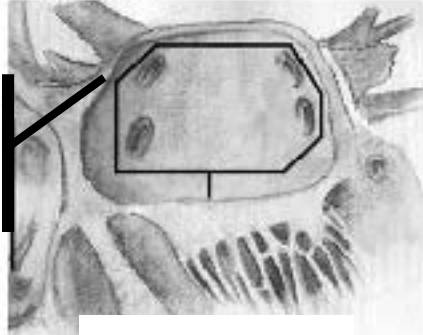
Success rate: 93%

Complications: PM implant 30 pts, 1 stroke, 2 MI
4 deaths

J.L.Cox Annals of Surgery September 1996

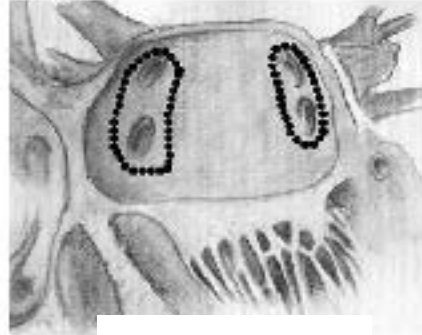
Different surgical approaches for AF ablation

Scalpel



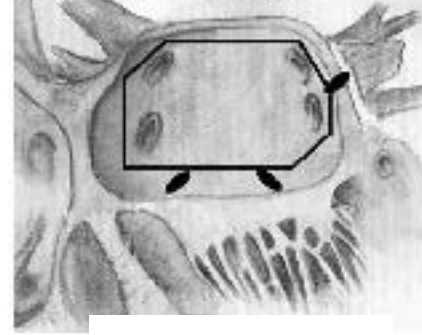
COX 93%

RF



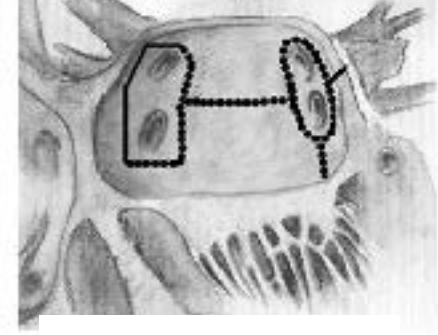
MELO 69%

Scalpel + Cryo



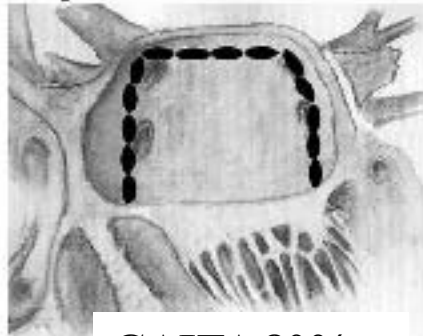
SUEDA 68%

Scalpel + RF



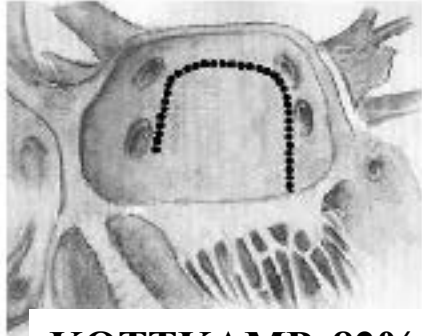
BENUSSI 77%

Cryo



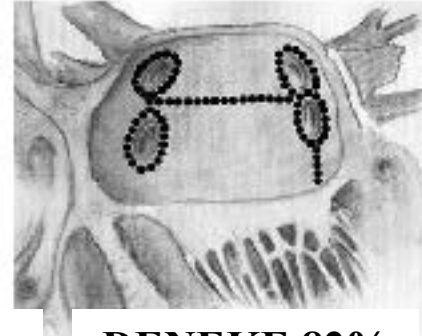
GAITA 80%

RF



KOTTKAMP 82%

Cooled RF

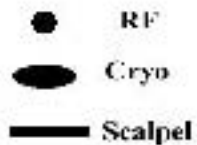


DENEKE 82%

Cryo

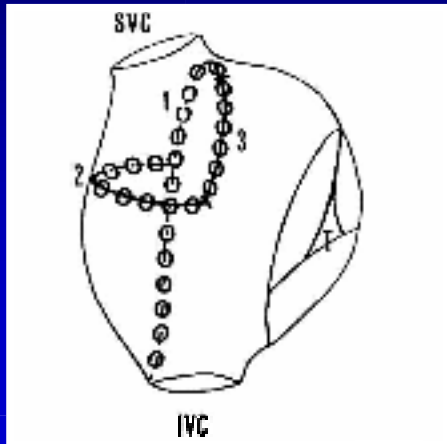


GAITA 85%

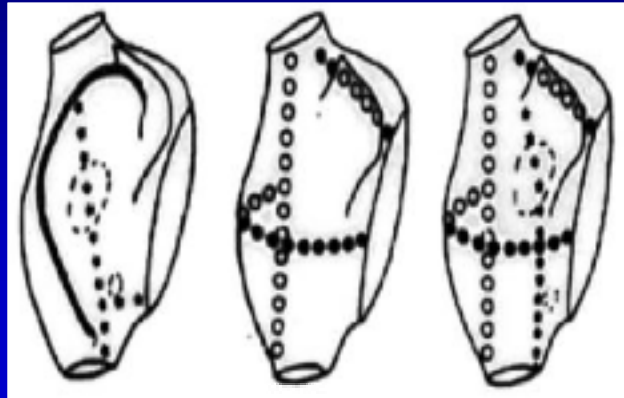


Mean Efficacy 79.5%

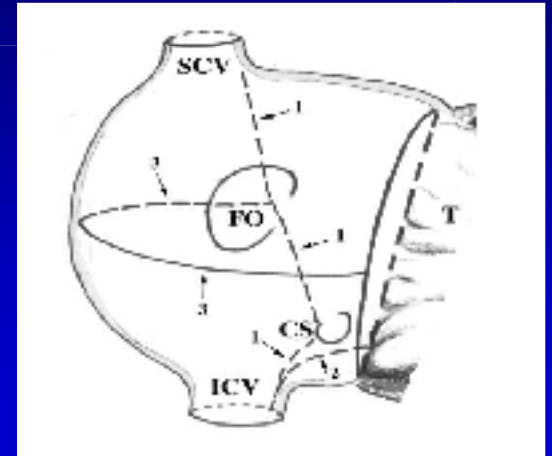
Beginning of era of TC ablation



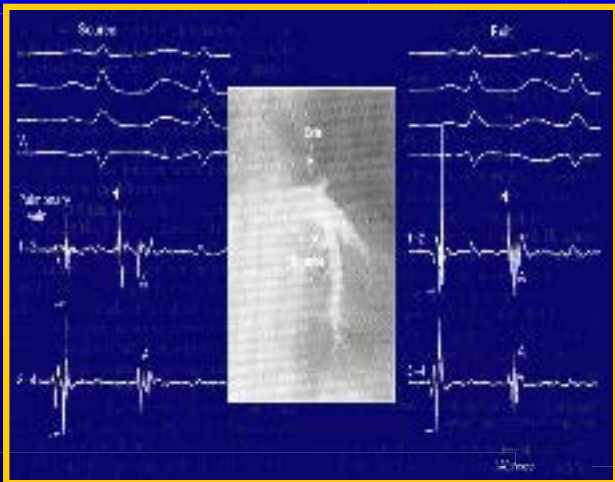
Haissaguerre 1996



Jais 1998



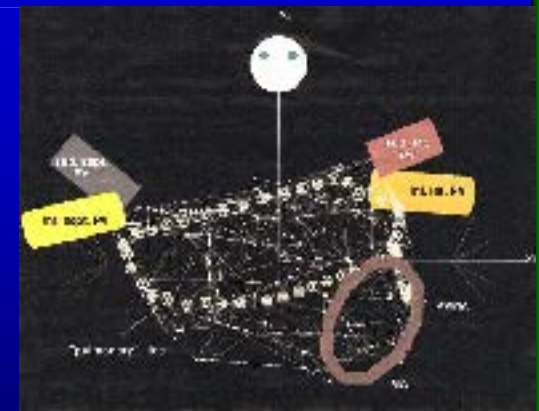
F. Gaita 1998



Haissaguerre 1998



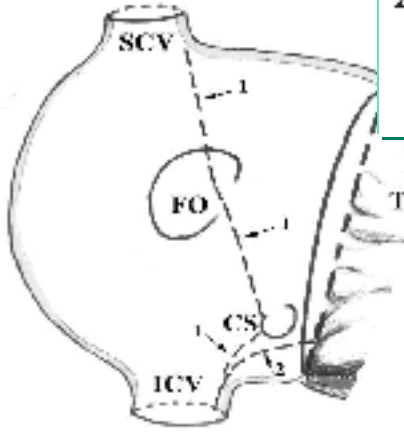
Pappone 1999



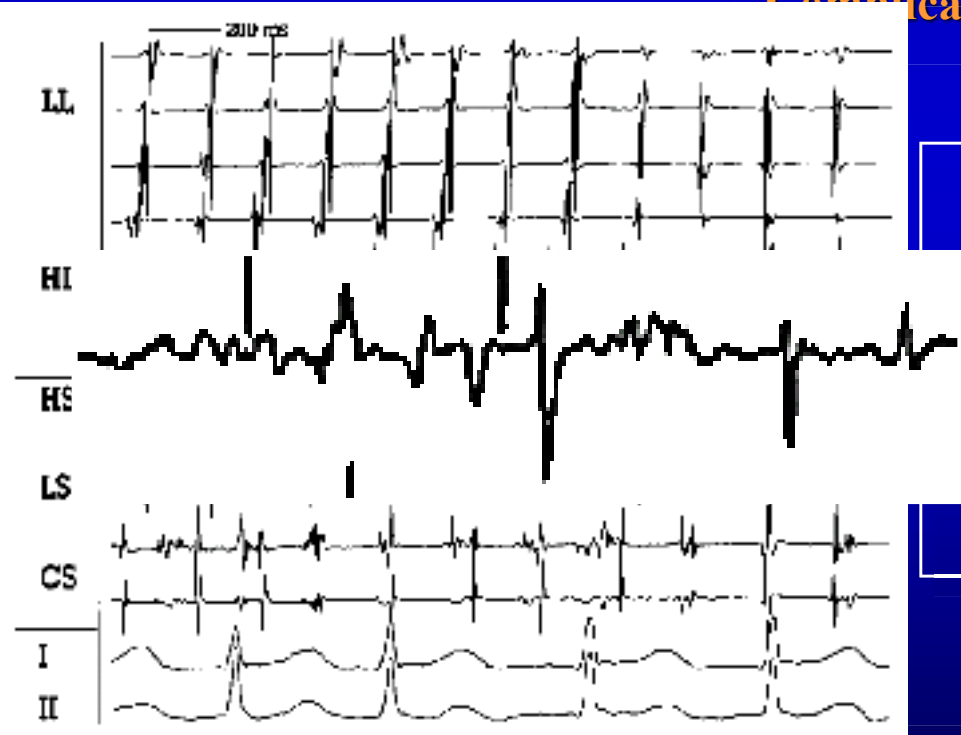
Kuck 1999

Atrial Mapping and Radiofrequency Catheter Ablation in Patients With Idiopathic Atrial Fibrillation

Electrophysiological Findings and Ablation Results



Follow-up (months)	11 ± 4	36 ± 6
Success	56%	39%
Without drugs	25%	11%
With drugs	31%	28%
Complications	none	none



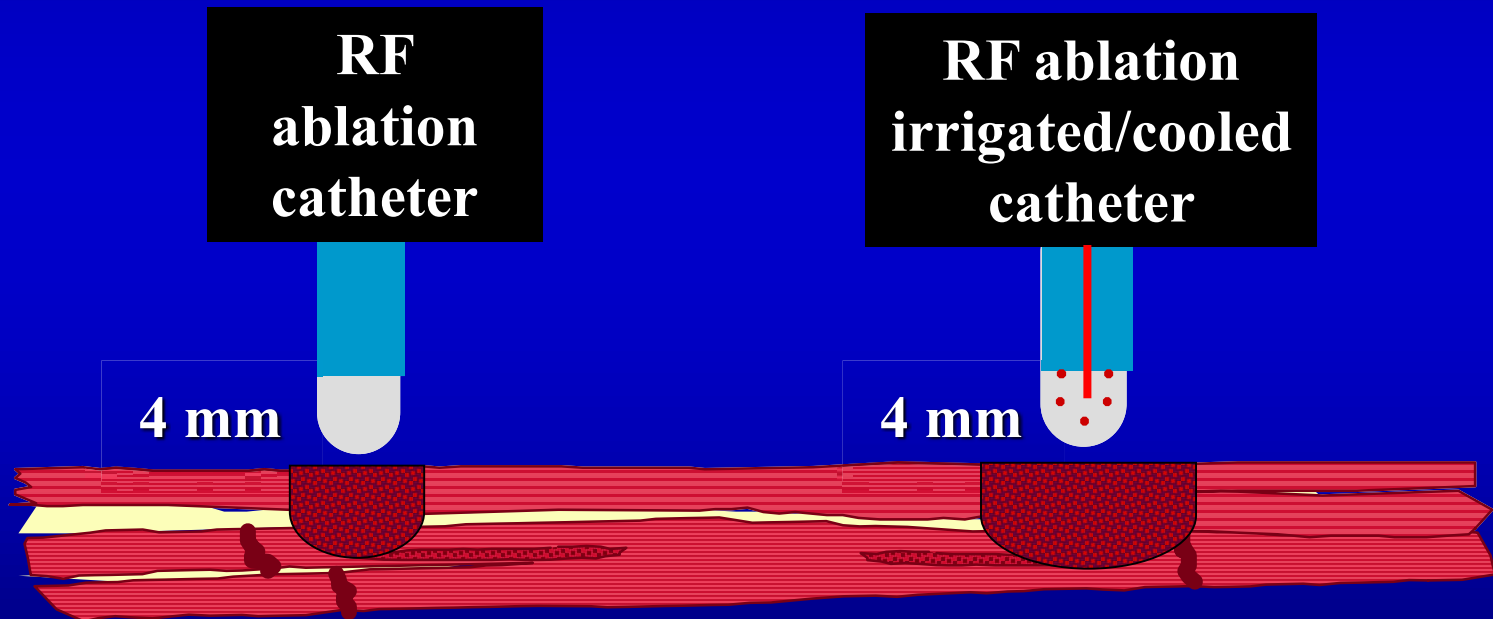
Predictors of success:
 ablation in areas with
shortest FF interval,
vagal ↓
 demonstrated by heart rate variability

Why right atrium ablation to cure AF?

**At that time due to a lack of
technology (4 mm tip ablation
catheters) we were unable to safely
reproduce the surgical maze with
catheters**

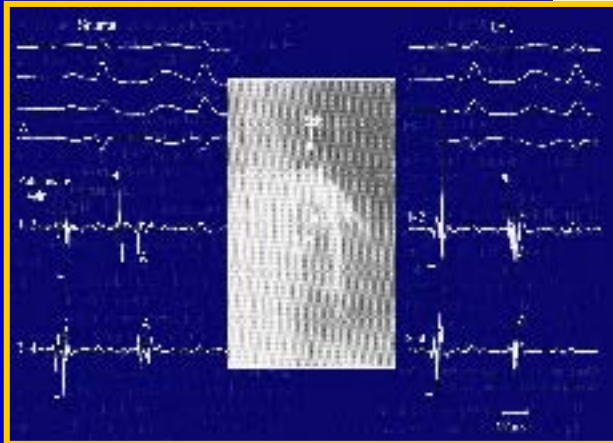
Cornerstone: “the right tools”

4 mm irrigated/temperature control catheter produces larger and safer lesions, decreasing the risk of cerebral vascular accidents



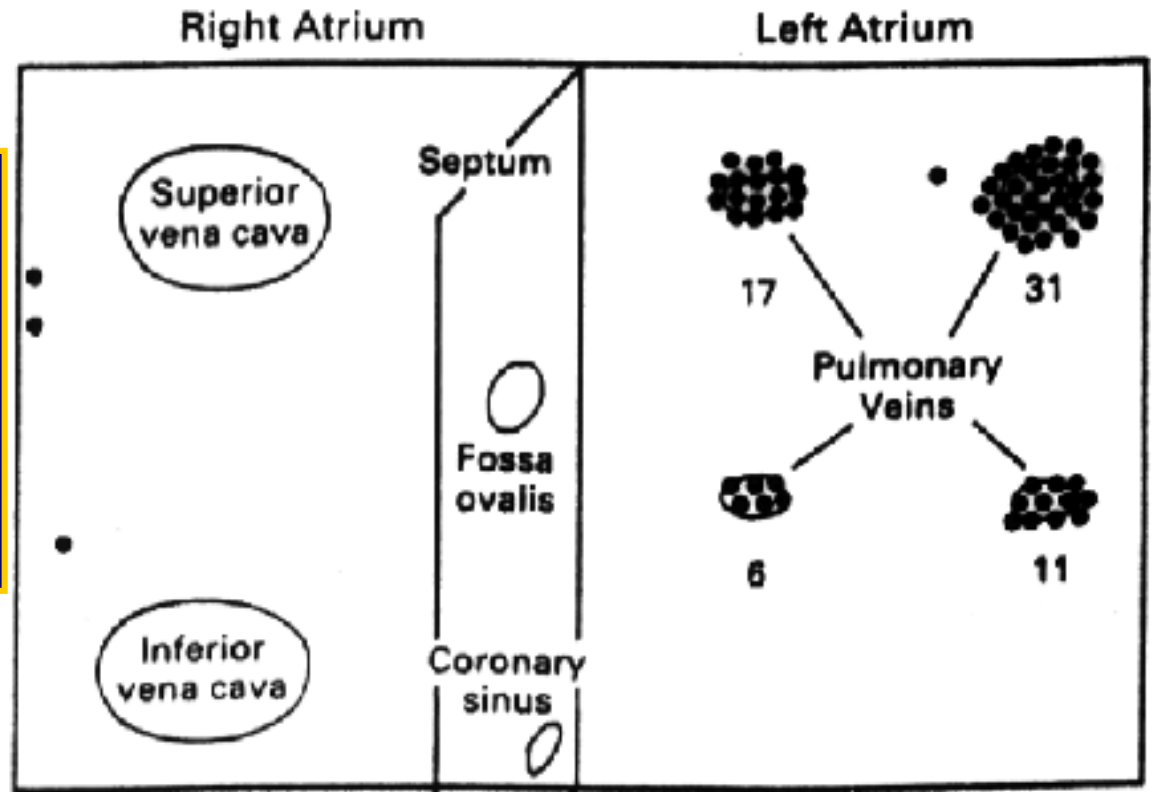
Tsai Circ.1999;

Interest moves from the *substrate* to the *triggers*



45 pts with
idiopathic PAF

Follow-up:
8±6 months



62% success rate w/out AAD

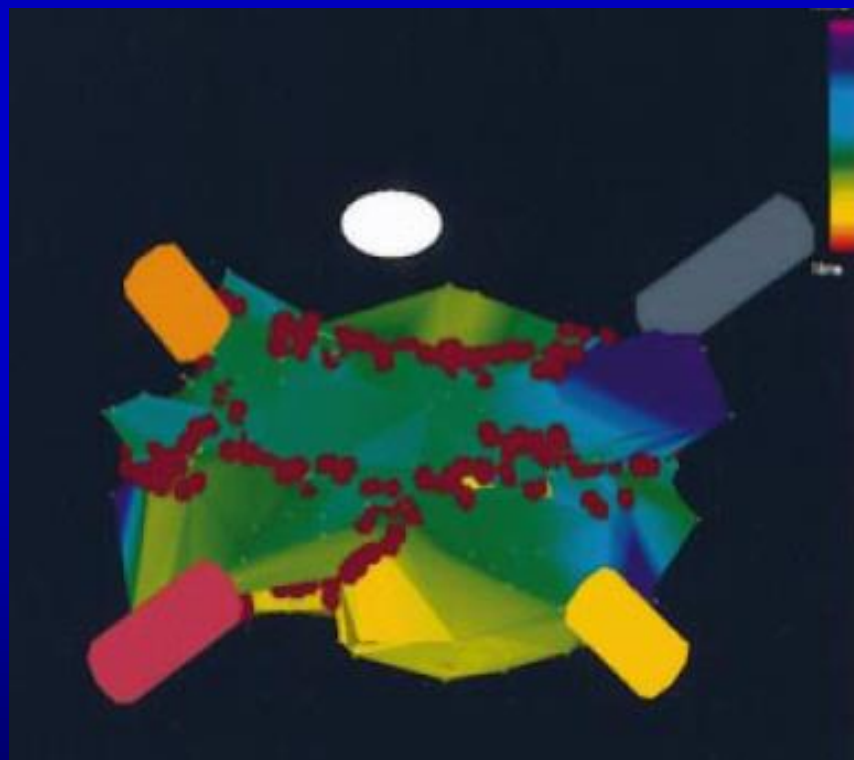
Haissaguerre et al. N Engl J Med 1998;339:659-66

Electroanatomic mapping systems

Substrate modification

Catheter Ablation of Paroxysmal Atrial Fibrillation Using a 3D Mapping System

Carlo Pappone, MD; Giuseppe Oreto, MD; Filippo Lamberti, MD; Gabriele Vicedomini, MD; Maria Luisa Loricchio, MD; Shlomo Shpurn, DSc; Mariano Rillo, MD; Maria Pia Calabrò, MD; Andrea Conversano, MD; Shlomo A. Ben-Haim, MD, DSc; Riccardo Cappato, MD; Sergio Chierchia, MD
(*Circulation*. 1999;100:1203-1208.)



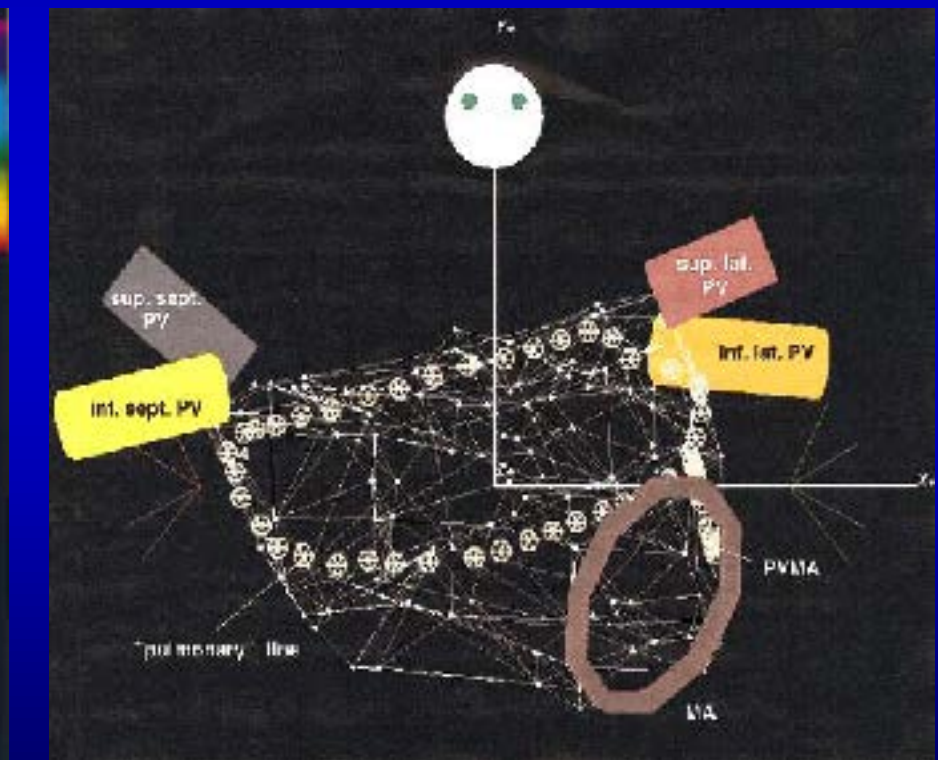
27 pts: success in 16 pts (59%)

Modification of the Substrate for Maintenance of Idiopathic Human Atrial Fibrillation

Efficacy of Radiofrequency Ablation Using Nonfluoroscopic Catheter Guidance

Sabine Ernst, MD; Michael Schlöter, PhD; Teifan Ouyang, MD; Afshar Khznedani, MD; Riccardo Cappato, MD; Joachim Hebe, MD; Marcus Volkmer, MD; Matthias Antz, MD; Karl Heinz Kuck, MD

(*Circulation*. 1999;100:2085-2092.)



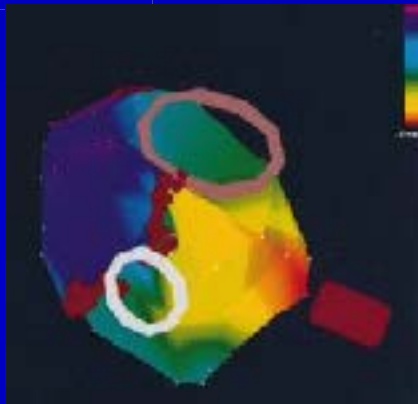
32 pts: success in 2 pts (6%)

Catheter ablation of PAF using 3D mapping

Population: 27 pts with PAF > 1 year

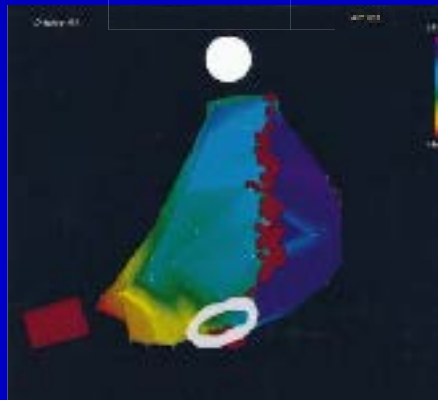
RA linear ablation

8 pts (30%)



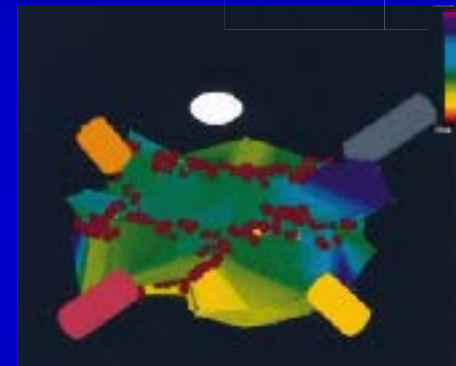
Biatrial ablation

14 pts (51%)



LA ablation

5 pts (18%)



F-up: 6±15.3 mos

success	w/o drug	12 pts (44%)
	with drug	4 pts (15%)
improvement	with drug	4 pts (15%)
unchanged		7 pts (26%)

Conduction block: 21/27 (77%)

Complications: 1 DDD PM implant

Pappone et al. Circ 1999;100:1203-1208

Modification of the substrate for idiopathic human AF

Population: 45 pts: PAF 37 (82%) Permanent 8 pts



LA ablation
First 13 pts (%)

+ RA
ablation

Biatrial ablation
12 out of 13 pts

Recurrence rate: 100%

Recurrence rate: 100%

Complete linear lesions
0/7pts studied

Complete linear lesions
3/8 pts studied

Complications:
1 pericardial tamponade 1 cerebral infarct

Complications:
1 pseudo-aneurysm
2 pericardial effusion

RA linear ablation (3 lines)
32 pts

Recurrence rate: 94%

Complete linear lesions 56% (18/32)

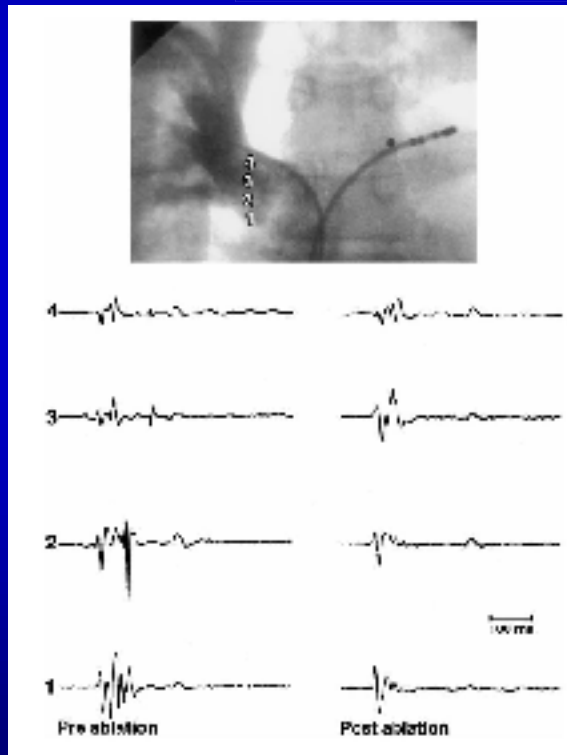
Complications:
3 RA isolation
7 PM implant
1 retroperitoneal hematoma
1 pneumothorax
3 Pericardial effusions

Ernst S, Kuch KH et al Circ 1999;100:2085-2092

Focal ablation of atrial fibrillation

90 pts with paroxysmal AF (97% PV foci - 3% atrial foci)

Rhythm outcome at 8 ± 5 month follow-up



AF elimination:

64 pts (71%) with **no AAD**

12 pts (13%) on **with AAD**

84%

49 pts required 2 or more sessions.

Complications:

pulmonary vein stenosis

air embolism

hemopericardium

reversible neurological deficit

blurred binocular vision

5 pts

5 pts

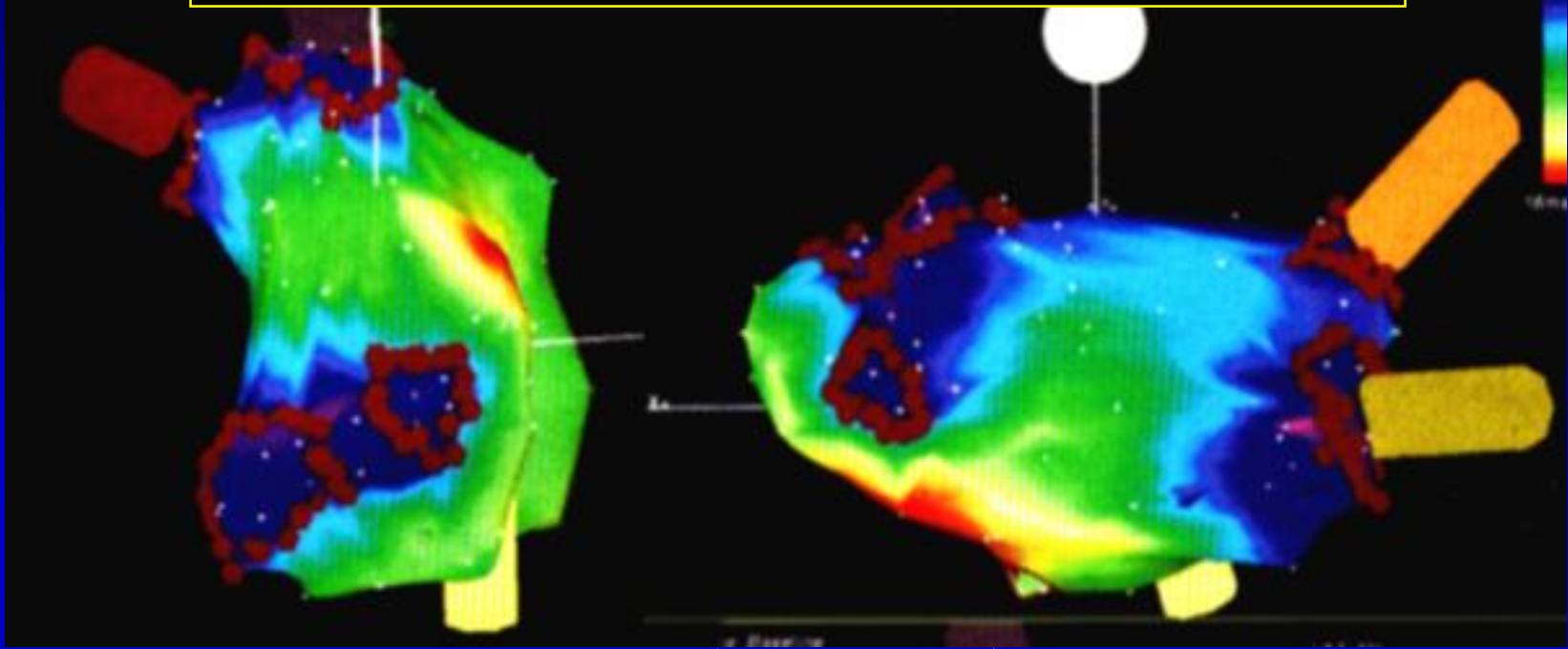
1 pt.

1 pt.

1 pt.

14%

Anatomical encircling of PPVVs



26 pts with **idiopathic AF**

Mean procedure duration 6 hours

RF pulses 118 ± 16

Success:

w/o drugs

62 %

with drugs

23 %

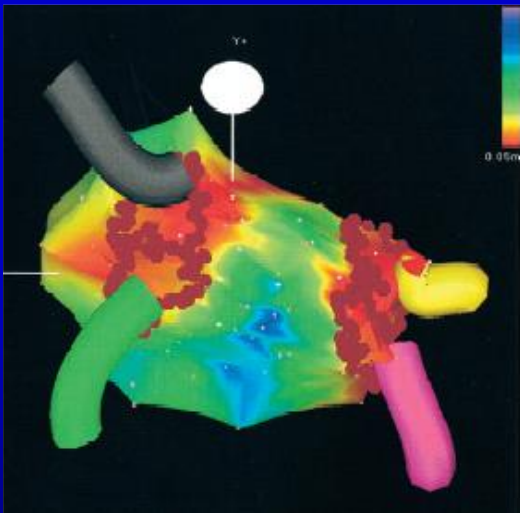
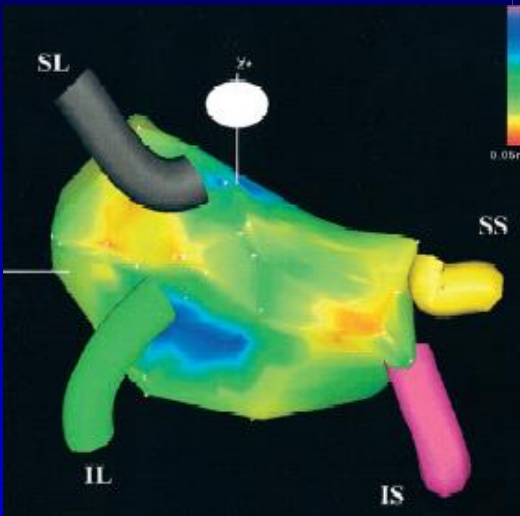
85%

Complications 4% (cardiac tamponade)

Pappone et al. Circulation 2000;102:2619-2628

Anatomical encircling PPVVs

Population: 251 pts → 179 PAF
→ 72 Persistent AF



PAF	
w/o drug:	148pts (82%)
with drug :	4pts (3%)
} 85%	

Persistent	
w/o drug:	40 pts (48%)
with drug :	9 pts (20%)
} 68%	

Complications: 2 pericardial tamponade

Evolution of AF CATHETER ablation strategy over the years (Oct 1996-May 2001) = 305 pts

1996-1997

RA lines

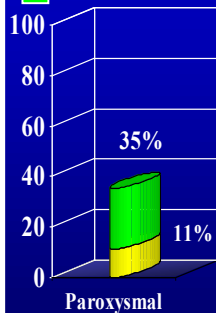
Pts = 35

Procedure duration: 6 h.

RX: 88'

Complications = 0%

■ Success w/o drugs
■ Success with drugs



1998

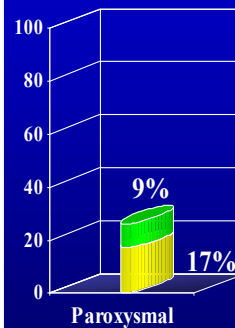
"Culprit" PV

Pts = 25

Procedure duration: 4,30 h.

RX: 94'

Complications = 1,3%



1999-2001

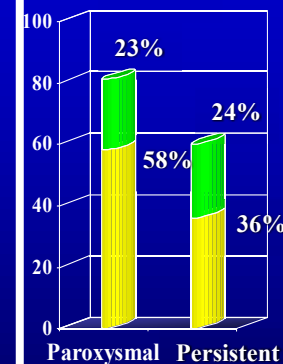
all PV+Carto

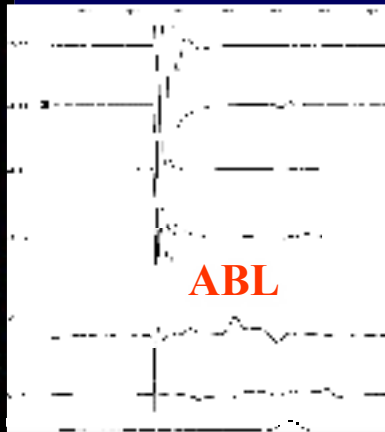
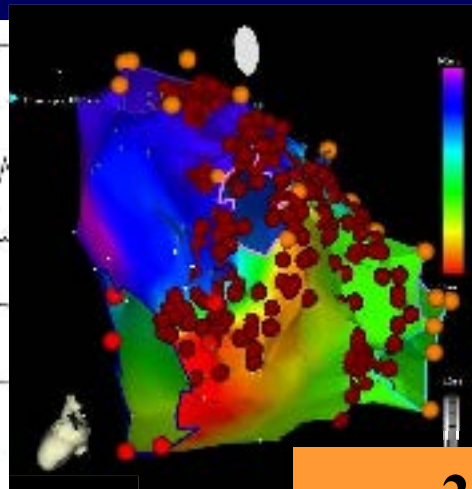
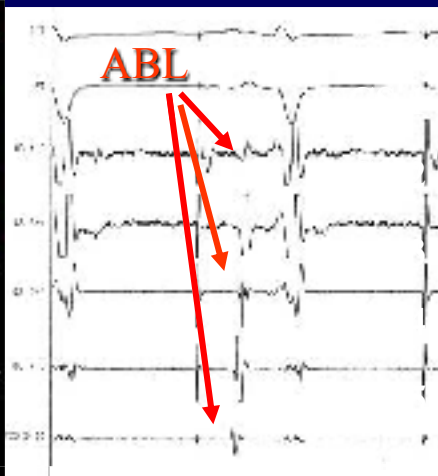
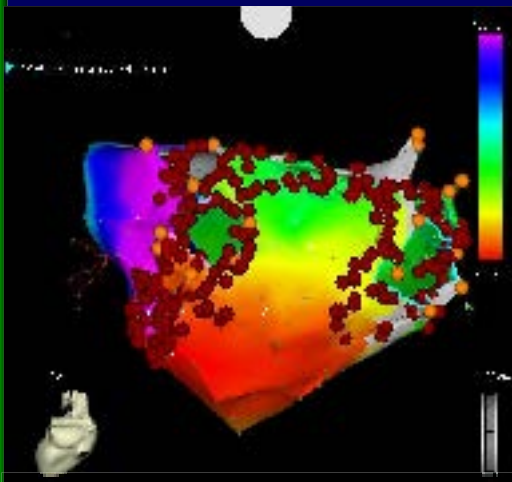
Pts = 245

Procedure duration: 4 h.

RX: 62'

Complications = 1,4%





Cardiology Dept. Civil Hospital Asti
Mauriziano Hospital Torino

406pts

PAF 271pts

Persistent AF 135pts

25% of pts
underwent to a
second procedure

Success:

w/o AAD

with AAD

211pts (78%)

27pts (10%)

88%

74 pts (55%)

32 pts (24%)

79%

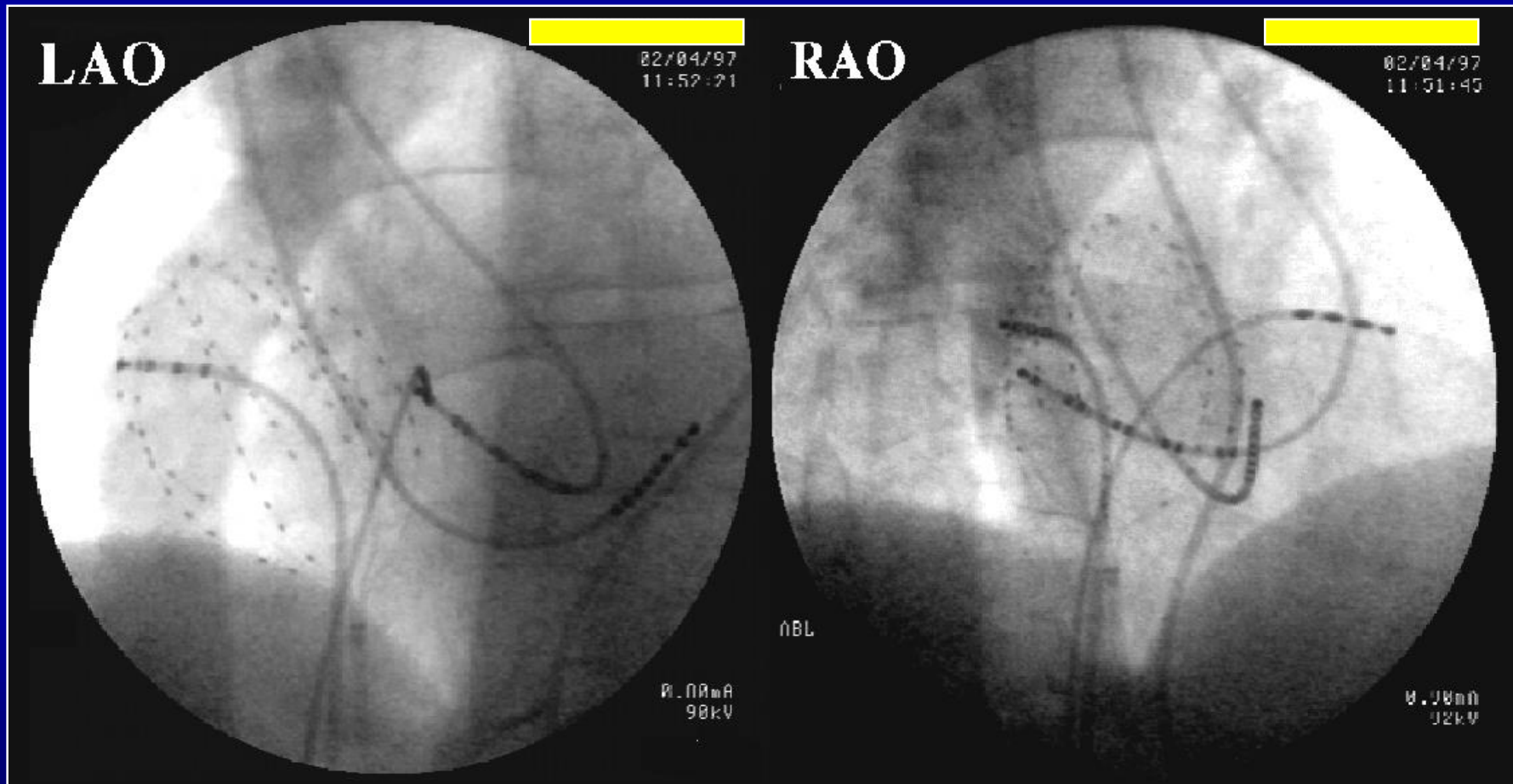
Complications: 1 TIA

2 pericardial effusion

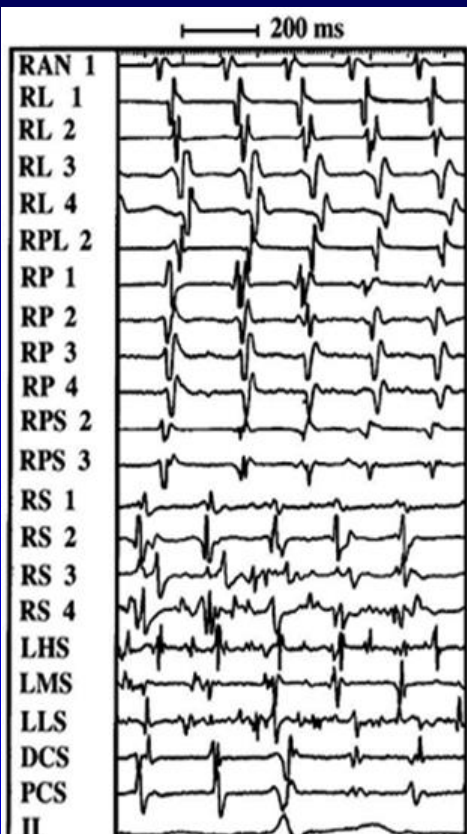
The question in 2000

Can pulmonary vein isolation
effectively treat also patients
with **persistent AF** and
structural heart disease?

Different Patterns of Atrial Activation in Idiopathic Atrial Fibrillation: Simultaneous Multisite Atrial Mapping in Patients With Paroxysmal and Chronic Atrial Fibrillation

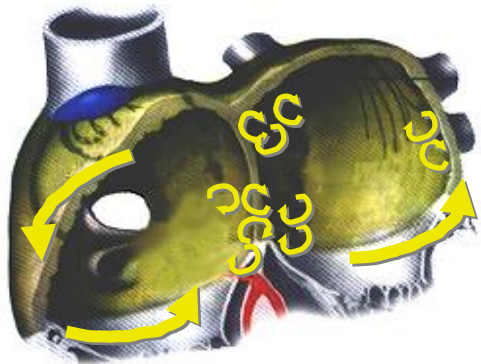
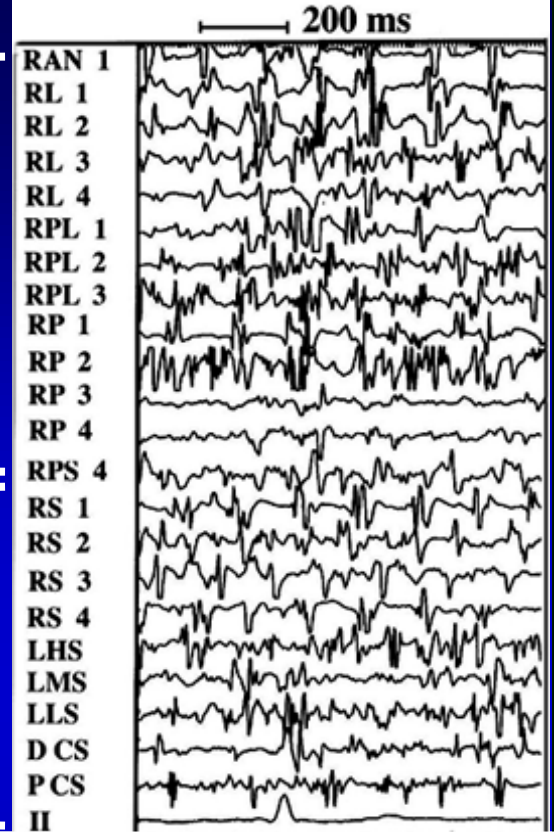


Gaita F. Scaglione M. Calo L. Riccardi R. JACC 2001

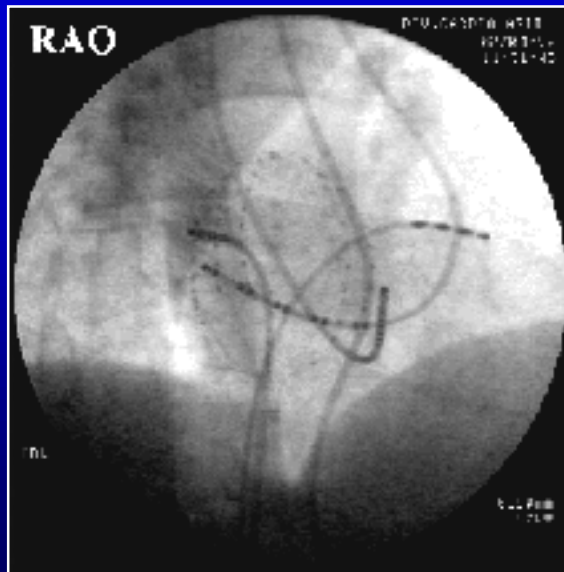


RIGHT ATRIUM

LEFT ATRIUM



Paroxysmal AF



Persistent AF

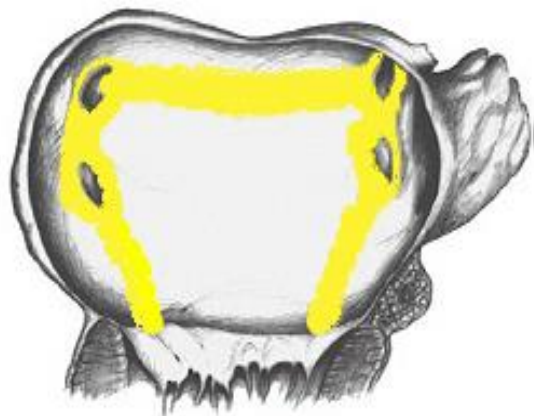
Linear Cryoablation of the Left Atrium Versus Pulmonary Vein Cryoisolation in Patients With **Permanent** Atrial Fibrillation and Valvular Heart Disease

Correlation of Electroanatomic Mapping and Long-Term Clinical Results

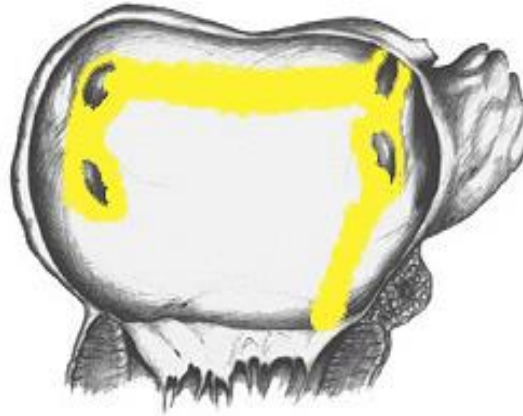
Fiorenzo Gaita, MD; Riccardo Ricciardi, MD; Domenico Caponi, MD; Dipen Shah, MD; Lucia Garberoglio, MD; Laura Vivalda, MD; Alessandro Dulio, BS; Andrea Chiecchio, PhD; Eric Manasse, MD; Roberto Gallotti, MD

Circulation 2005;111:136-42

105 pts, Permanent AF and Valvular Heart Disease



reversed **U**
Lesion



7
Lesion



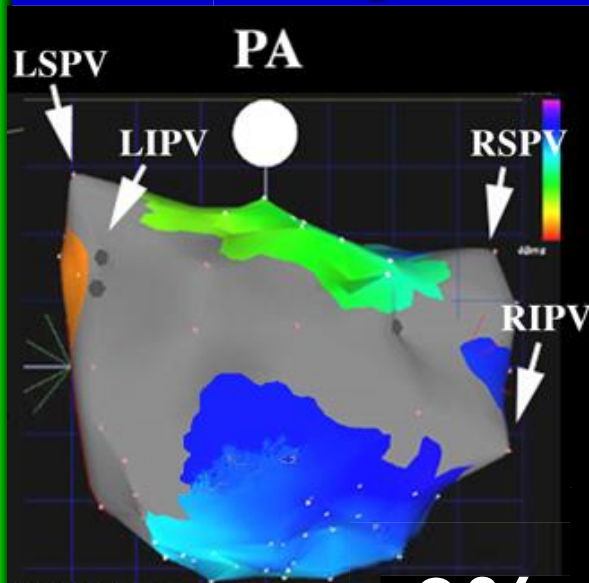
VP
Isolation

Linear Cryoablation of the Left Atrium Versus Pulmonary Vein Cryoisolation in Patients With Permanent Atrial Fibrillation and Valvular Heart Disease

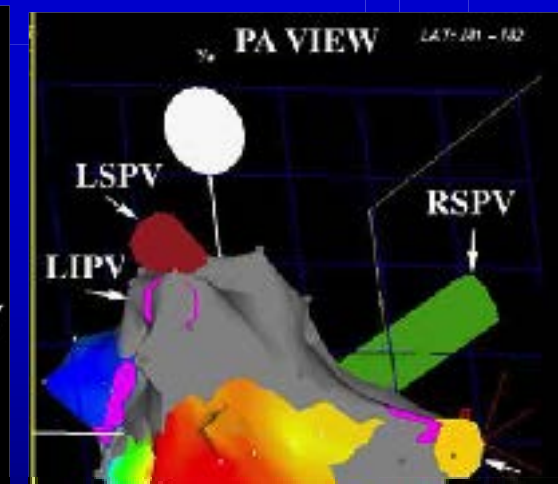
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3D left atrial mapping 3 months after procedure
105 pts, Permanent AF and Valvular Heart Disease

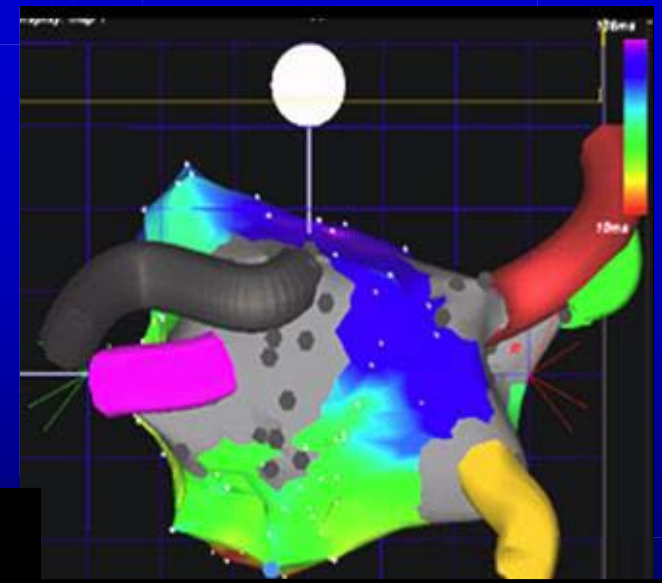


"U" lesion 0%



Complete Lesions

7 scheme 65%



PVI isolation 81%

Linear Cryoablation of the Left Atrium Versus Pulmonary Vein Cryoisolation in Patients With Permanent Atrial Fibrillation and Valvular Heart Disease

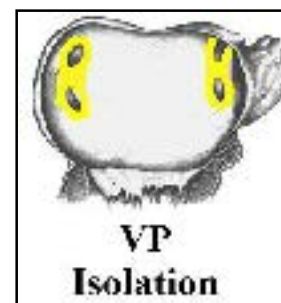
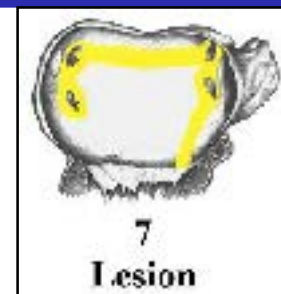
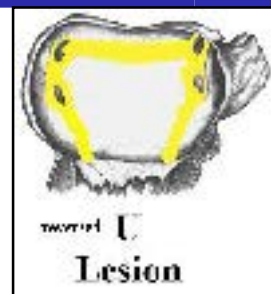
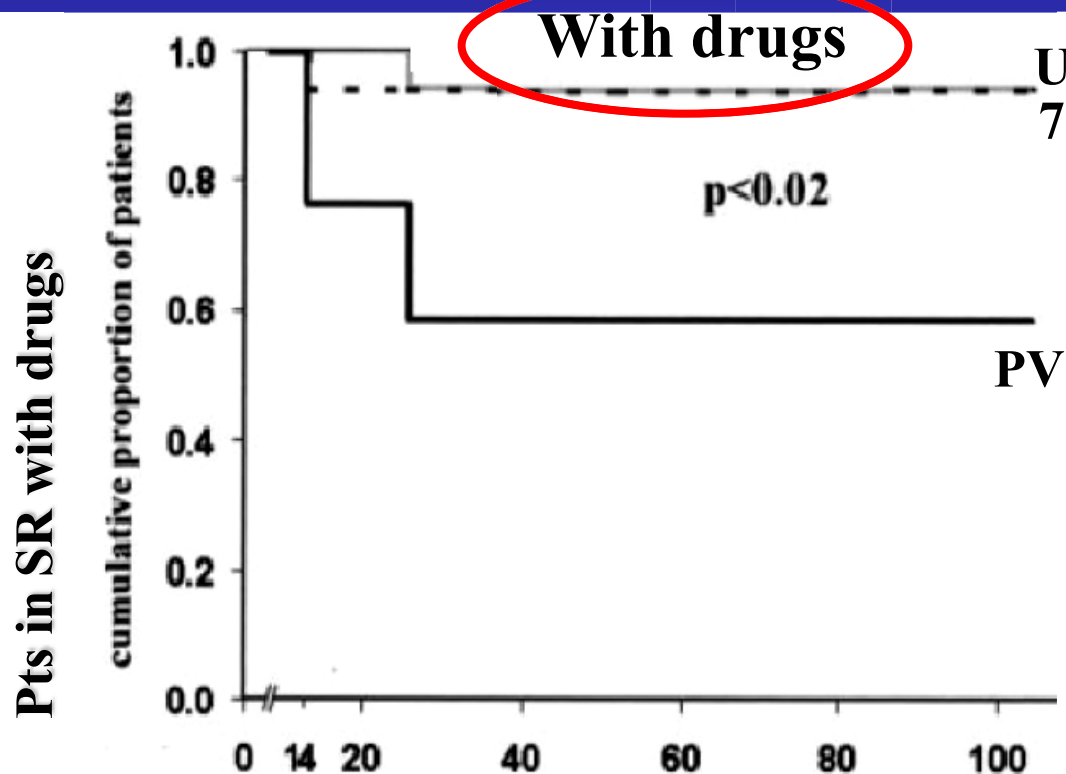
Circulation

2005;111:136-42

Correlation of Electroanatomic Mapping and Long-Term Clinical Results

Permanent AF
and Valvular
Heart Disease

Fiorenzo Gaita, MD; Riccardo Ricciardi, MD; Domenico Caponi, MD; Dipen Shah, MD;
Lucia Garberoglio, MD; Laura Vivalda, MD; Alessandro Dulio, BS; Andrea Chiecchio, PhD;
Eric Manasse, MD; Roberto Gallotti, MD



U pts	17	17	17	17	17	17
7 pts	17	17	17	17	17	17
PVI pts	17	17	17	17	17	17

Linear Cryoablation of the Left Atrium Versus Pulmonary Vein Cryoisolation in Patients With Permanent Atrial Fibrillation and Valvular Heart Disease

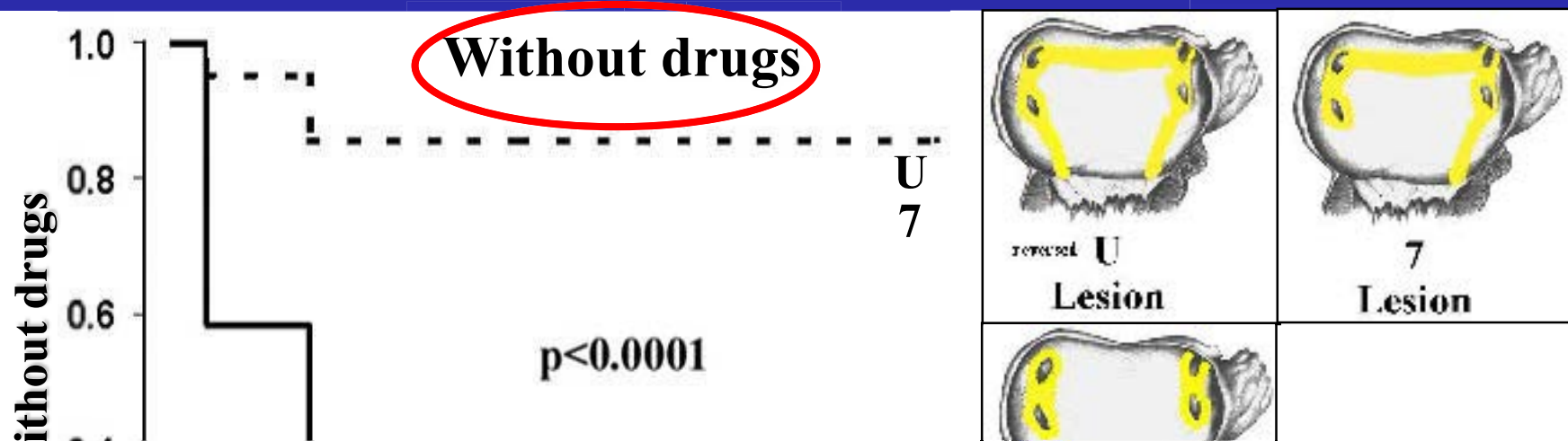
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Correlation of Electroanatomic Mapping and Long-Term Clinical Results

Permanent AF
and Valvular
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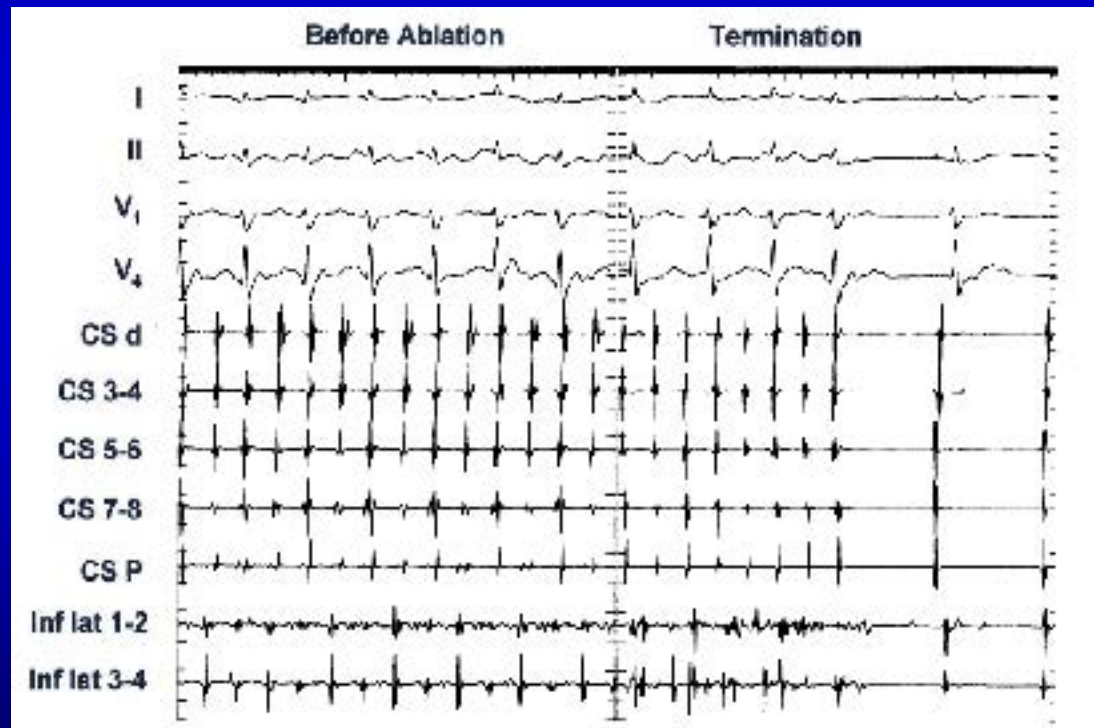
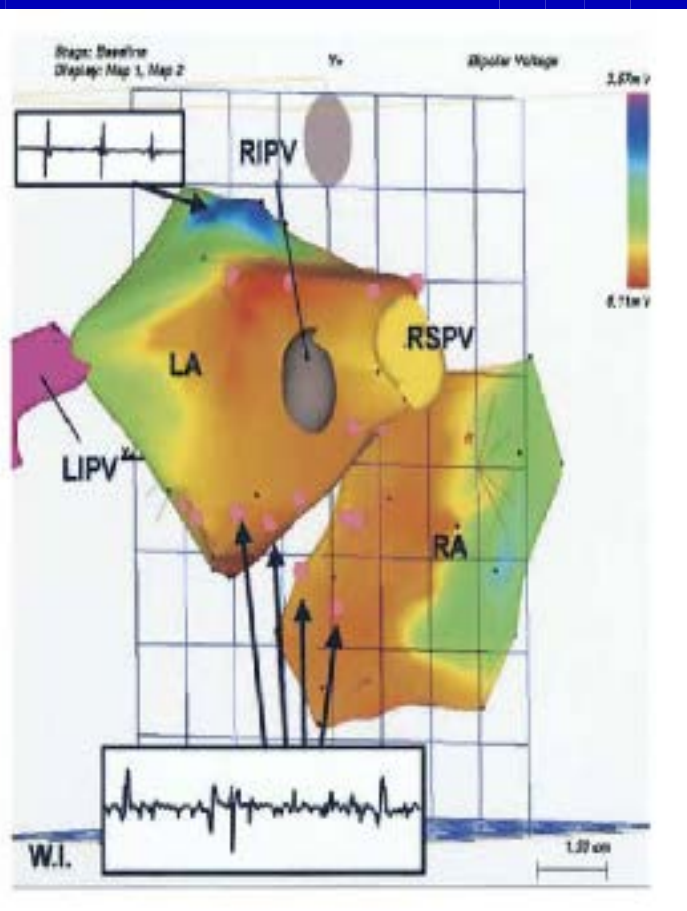
For Long Standing Atrial Fibrillation
PV isolation alone is not sufficient:
we have to modify the substrate
adding linear lesions

A New Approach for Catheter Ablation of Atrial Fibrillation: Mapping of the Electrophysiologic Substrate

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JACC 2004; 43:2044

121 pts (57 PAF). Complex Fractionated Atrial Electrograms

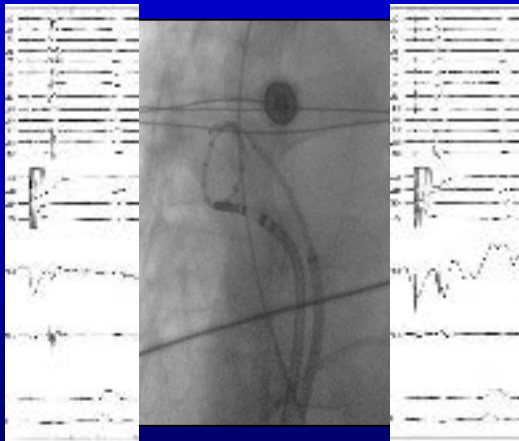
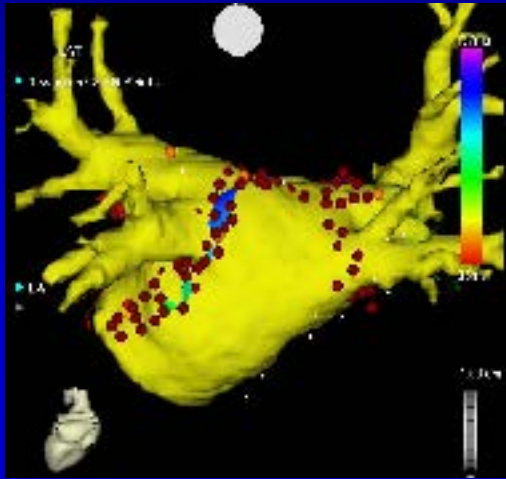


84% success rate w/out AAD (16% redo)

**What about ablation
in patients with
structural heart disease?**

AF ablation in structural heart disease

HCM vs. other CMP vs. lone AF



Total population : 78 pts

F-up: 19 ± 10 months

% of success		HCM (n = 26)	Other cardiopathies (n = 26)	idiopathic AF (n = 26)
Success	Total	64%	65%	77%
	PAF			
	AF			
	Pers/Perm			

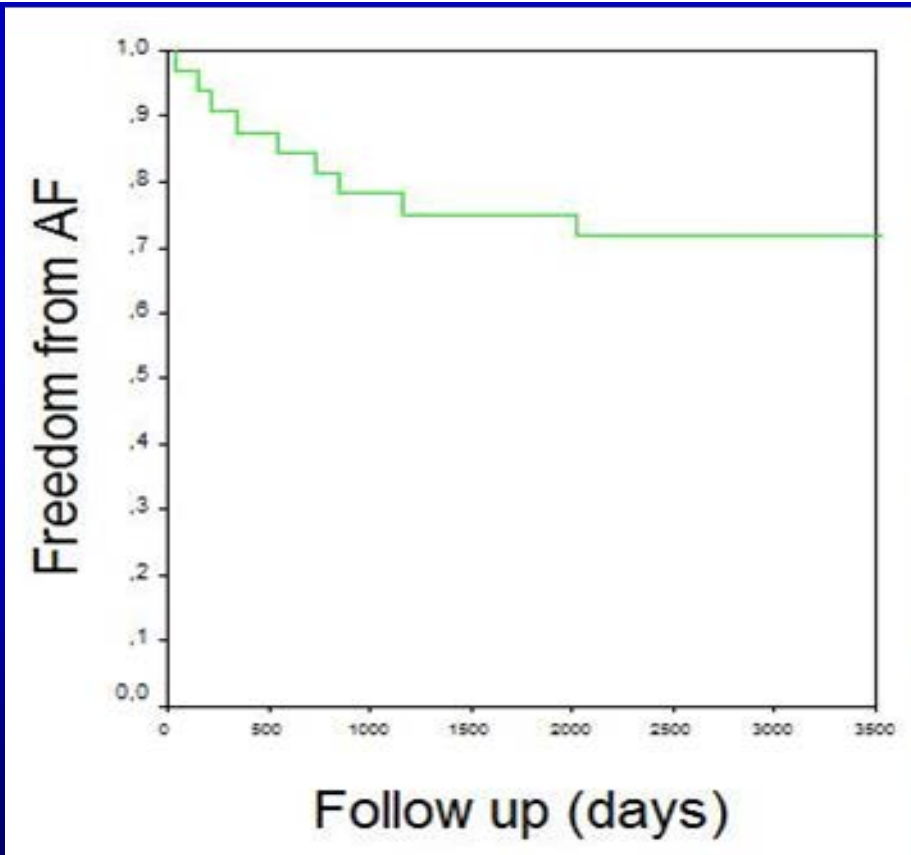
Major complications:

none

**WHAT ABOUT
LONG-TERM EFFICACY
OF AF ABLATION ?**

Very Long-Term Results of Surgical and Transcatheter Ablation of Long-Standing Persistent Atrial Fibrillation

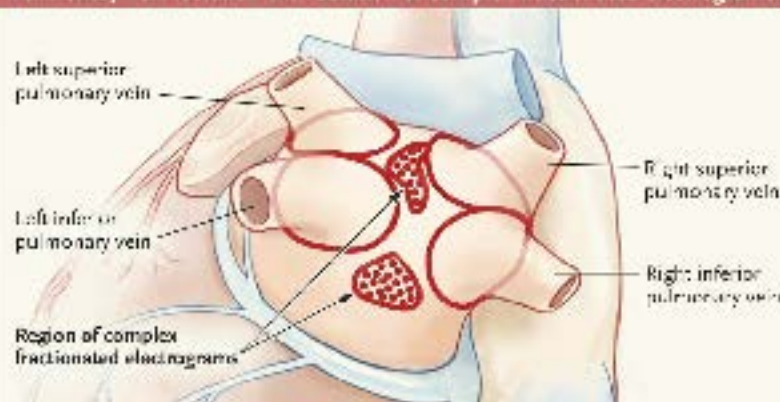
Fiorenzo Gaita, MD, Elisa Ebrille, MD, Marco Scaglione, MD, Domenico Caponi, MD, Lucia Garberoglio, MD, Laura Vivalda, MD, Alessandro Barbone, MD, PhD, and Roberto Gallotti, MD



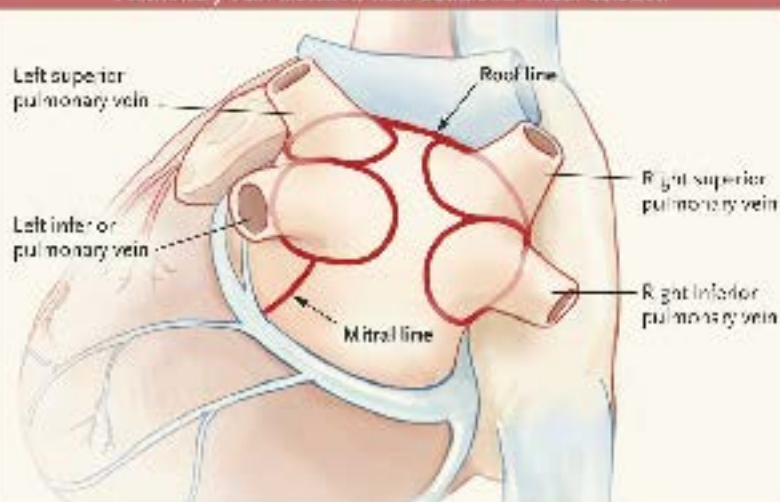
**Mean FU 10 ± 3 years
73% in SR**

Approaches to Catheter Ablation for Persistent Atrial Fibrillation

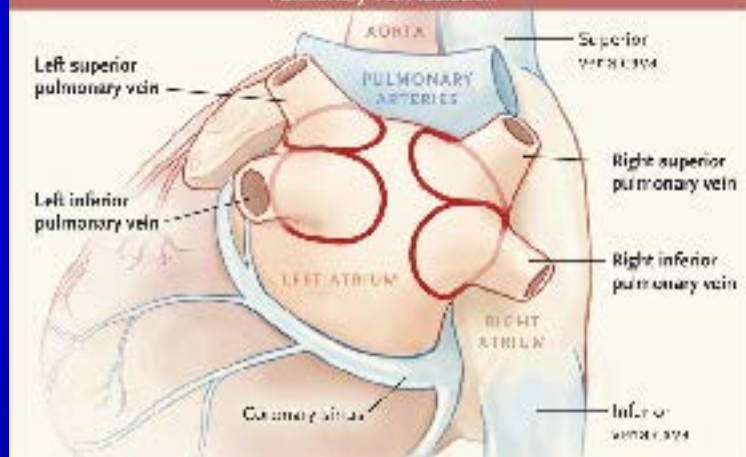
Pulmonary-vein isolation with ablation of complex fractionated electrograms

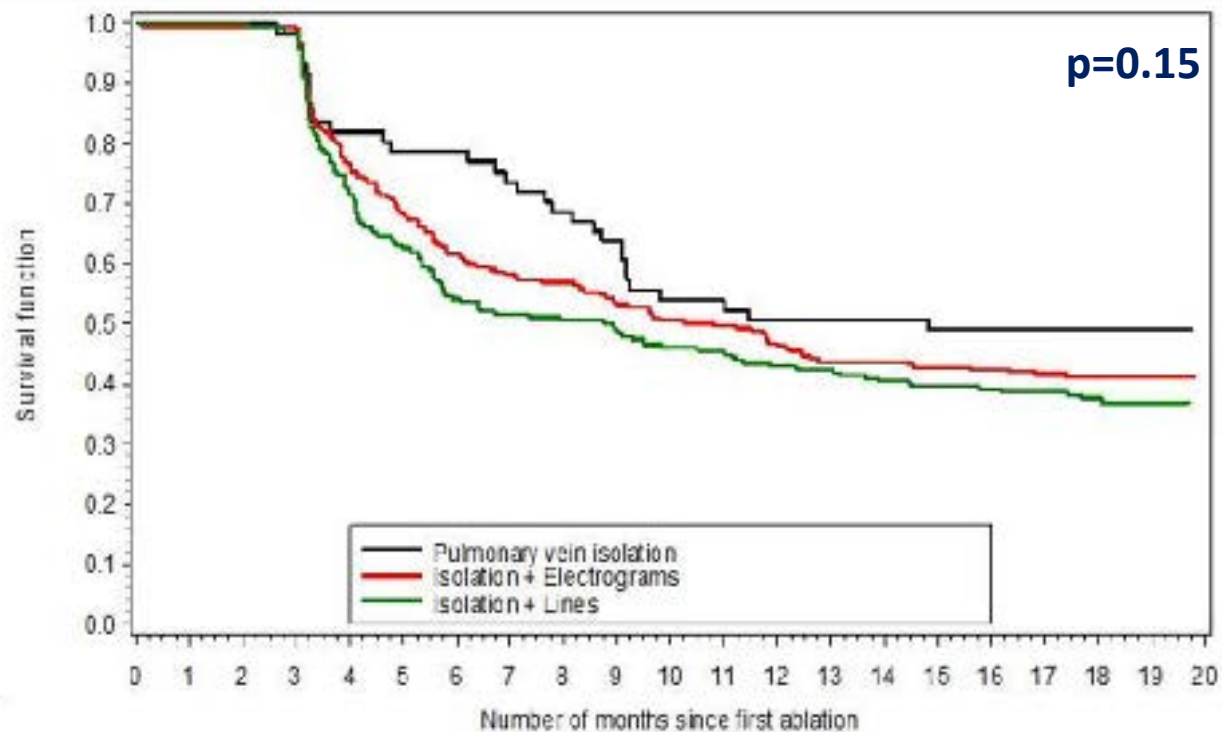


Pulmonary-vein isolation with additional linear ablation



Pulmonary-vein isolation





No. at Risk

Pulmonary vein isolation	61	60	50	41	36	23
Isolation + Electrograms	244	242	181	137	124	72
Isolation + Lines	244	240	152	133	115	57

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

Procedural Adverse Events 6%.

Table 3. Procedural Adverse Events.*

Adverse Event	Isolation Alone (N=64)	Isolation plus Electrograms (N=254)	Isolation plus Lines (N=250)	Total (N=568)
	<i>number of events</i>			
Hematoma at access site	2	0	3	5
Arteriovenous fistula or pseudo-aneurysm at access site	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
Death due to atrioesophageal fistula	0	1	0	1

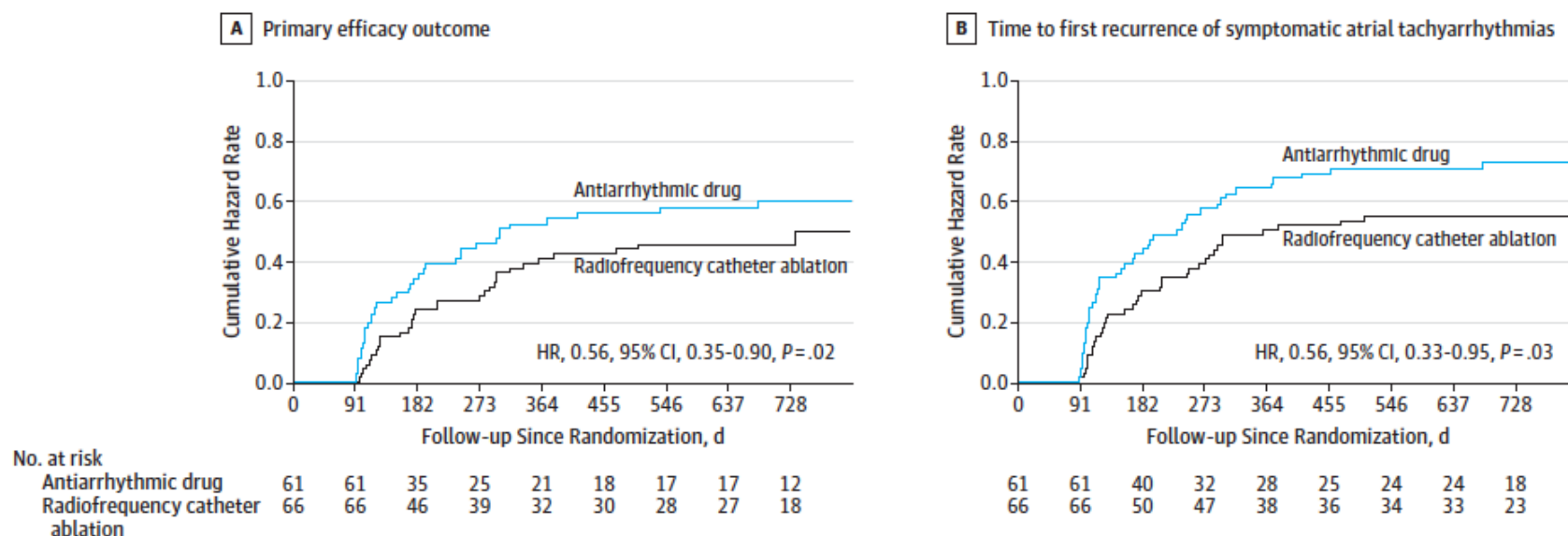
* Adverse events are reported for patients who underwent an ablation procedure, regardless of whether they completed at least 3 months of follow-up. There were no significant differences between groups.

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

Figure 2. Kaplan-Meier Curves of Time to First Recurrence of Any Atrial Tachyarrhythmias (A) and Time to First Recurrence of Symptomatic Atrial Tachyarrhythmias (B)



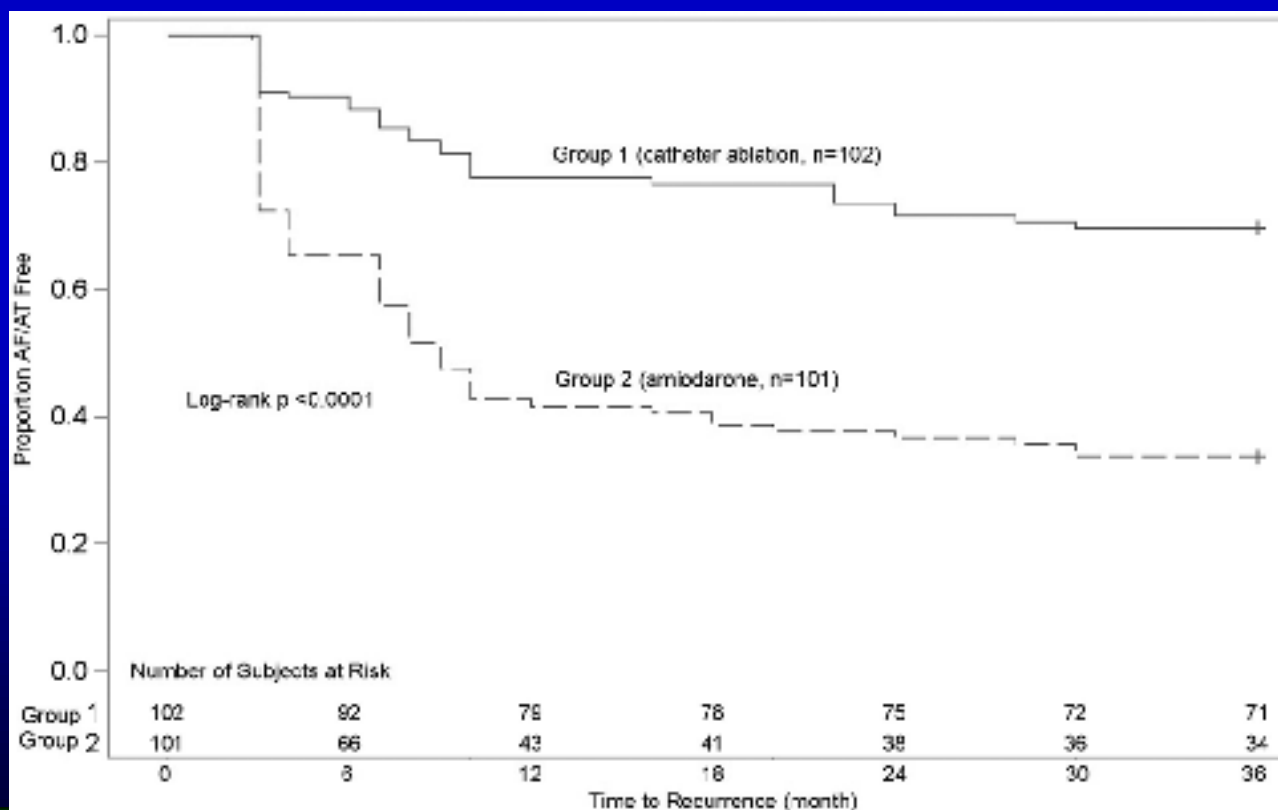
Tachyarrhythmias include atrial fibrillation, tachycardia, and flutter. HR indicates hazard ratio.

Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device

Results From the AATAC Multicenter Randomized Trial

Luigi Di Biase, MD, PhD; Prasant Mohanty, MBBS, MPH; Sanghamitra Mohanty, MD; Pasquale Santangeli, MD; Chintan Trivedi, MD, MPH; Dhanunjaya Lakkireddy, MD; Madhu Reddy, MD; Pierre Jais, MD; Sakis Themistoclakis, MD; Antonio Dello Russo, MD; Michela Casella, MD; Gemma Pelargonio, MD; Maria Lucia Narducci, MD; Robert Schweikert, MD; Petr Neuzil, MD; Javier Sanchez, MD; Rodney Horton, MD; Salwa Beheiry, RN; Richard Hongo, MD; Steven Hao, MD; Antonio Rossillo, MD; Giovanni Forleo, MD; Claudio Tondo, MD; J. David Burkhardt, MD; Michel Haissaguerre, MD; Andrea Natale, MD

Circulation. 2016 Apr 26;133(17)





Recurrence of Atrial Arrhythmias in the Catheter Ablation Versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) Trial

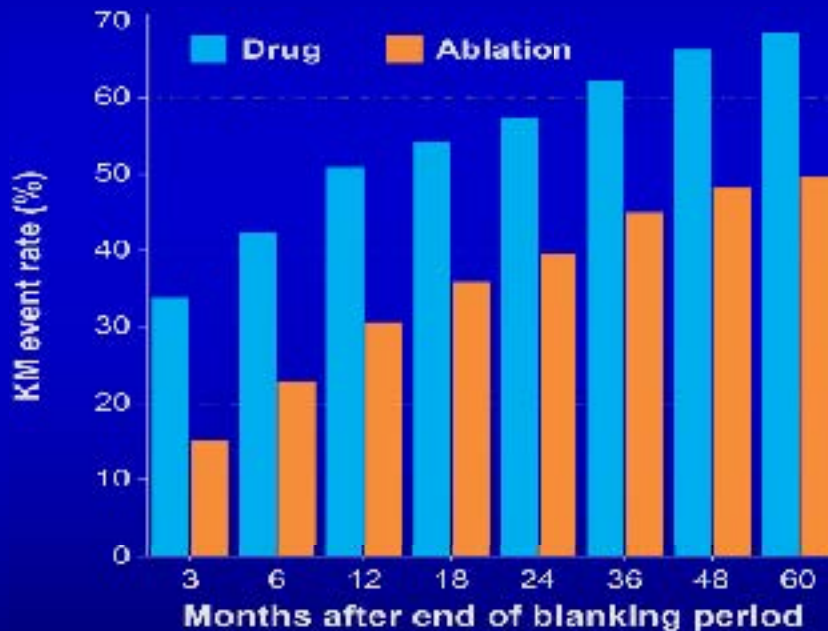
Jeanne E. Poole MD, George Johnson BSEE, Kristi H. Monahan RN, Hoss Rostami BSMSE, Adam Silverstein MS, Hussein Al-Khalidi PhD, Mauri Wilson RN, Yves Rosenberg MD, MPH, Tristram D. Bahnson MD, Richard A. Robb PhD, Daniel B. Mark MD, MPH, Kerry L. Lee PhD, Douglas L. Packer MD for the CABANA Investigators and ECG Rhythm Core Lab

Background

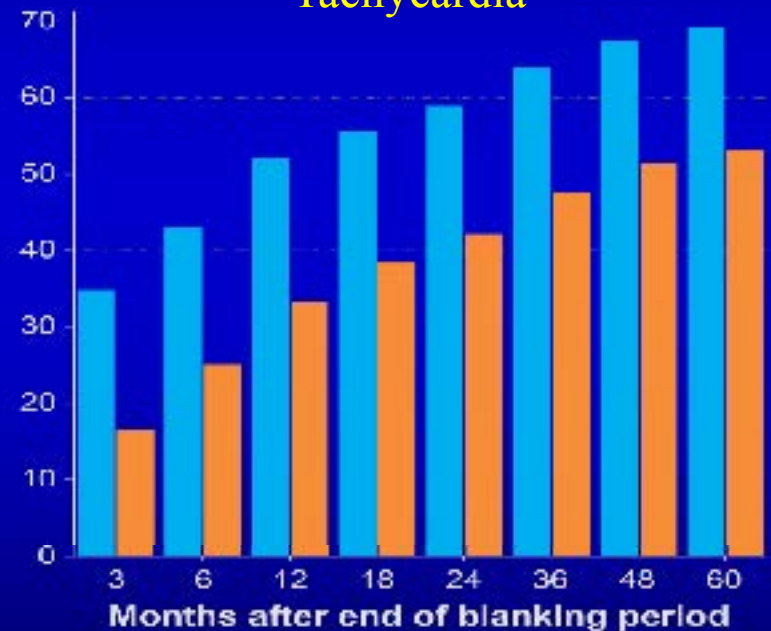
- CABANA randomized 2204 symptomatic patients with paroxysmal or persistent atrial fibrillation (AF) 1:1 to percutaneous left atrial catheter ablation versus medical therapy
 - Patients were ≥ 65 years or < 65 years with ≥ 1 risk factor for stroke
- Primary endpoint - Composite of death, disabling stroke, serious bleeding, or cardiac arrest

Cumulative First Recurrence Event Rates After 90-day Blanking

Atrial Fibrillation
($P < 0.0001$)

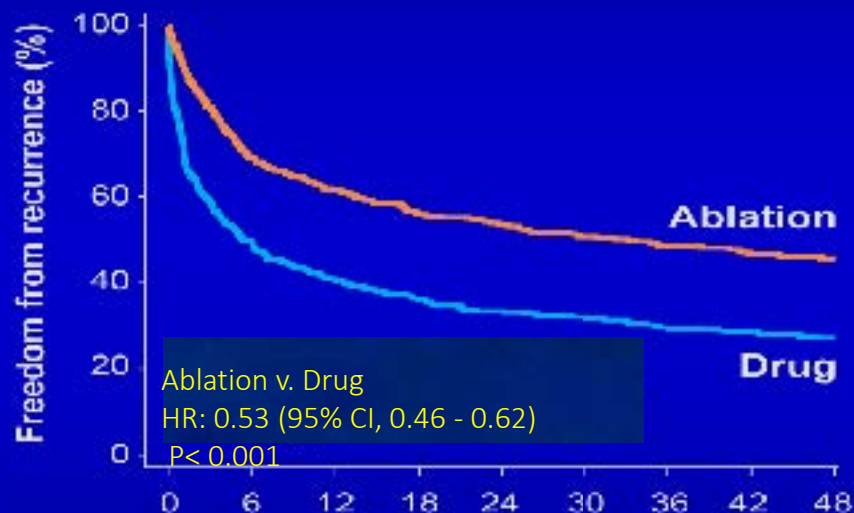


**Atrial Fibrillation/Flutter/
Tachycardia**
($P < 0.0001$)



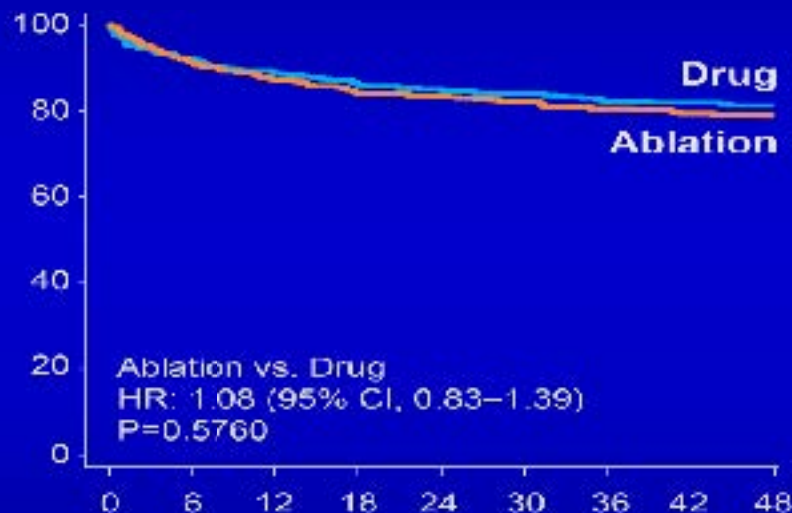
Both CABANA and non-CABANA study recorders

Atrial Fibrillation/Flutter



	Months since end of blanking								
Number at risk:	0	6	12	18	24	30	36	42	48
Drug	628	511	455	410	370	335	307	282	22
Ablation	611	522	473	432	397	360	328	297	132

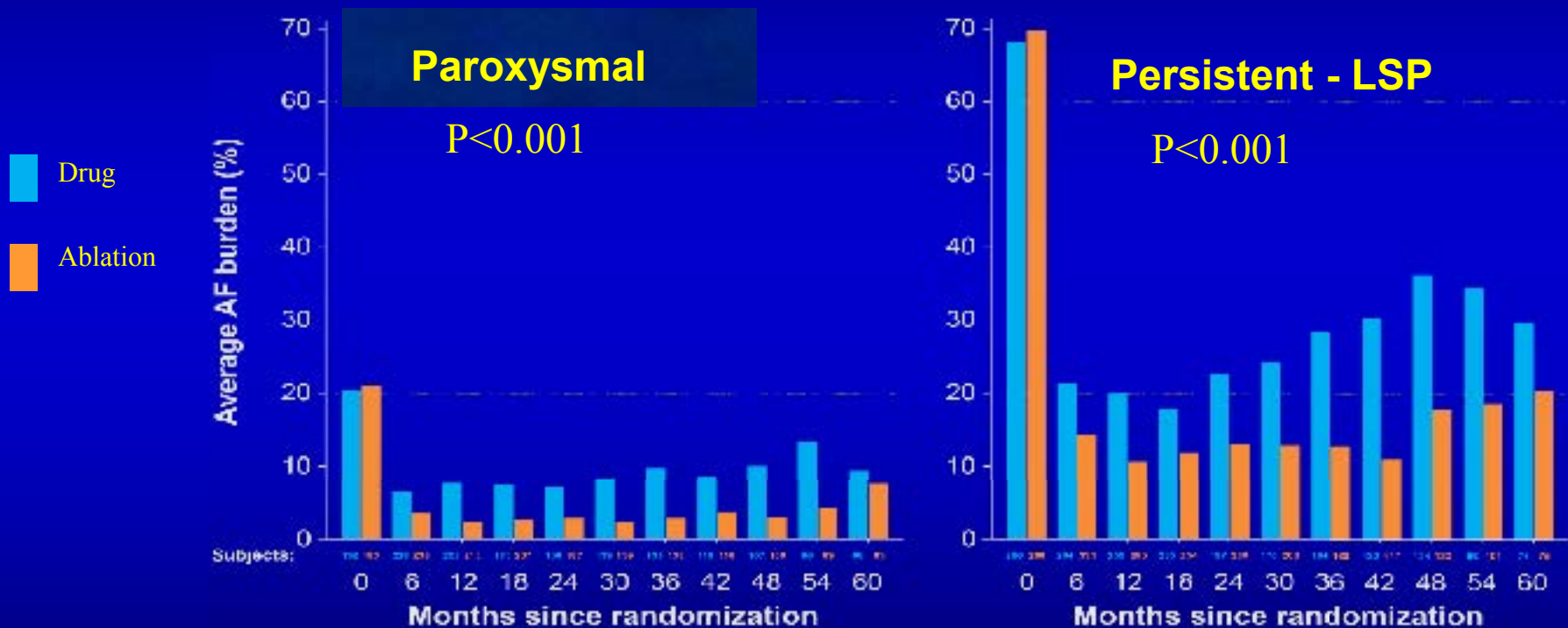
Atrial Flutter/Tachycardia



	Months since end of blanking								
Number at risk:	0	6	12	18	24	30	36	42	48
Drug	628	597	541	480	436	393	356	321	278
Ablation	611	552	524	478	440	405	347	300	251

*Cabana study recording system only

Percent AF Burden Holter Analysis by Baseline Pattern of AF



*Cabana study recording system only

Conclusions

- Catheter ablation was associated with a significant relative risk reduction (~50%) in recurrence of atrial arrhythmias
- Holter-determined AF burden was significantly lower in patients randomized to catheter ablation compared to drug-therapy across 5 years of follow-up

Conclusions

- Secondary endpoint - All cause mortality:
 - 15% reduction with ablation was observed (ITT)
(HR 0.85; 95% CI 0.60-1.21; p=0.377) non stat significant
- Analyses by *treatment received and per protocol* showed significant benefits of ablation for both the primary endpoint and for mortality

**So what is the
state of the art of
Atrial Fibrillation Ablation
in 2018 ?**

AF ablation per year today



25.000

93% RF

6% cryo

1% other



213.000

91% RF

7% cryo

2% other



250.000

92% RF

6% cryo

2% other



800.000

92% RF

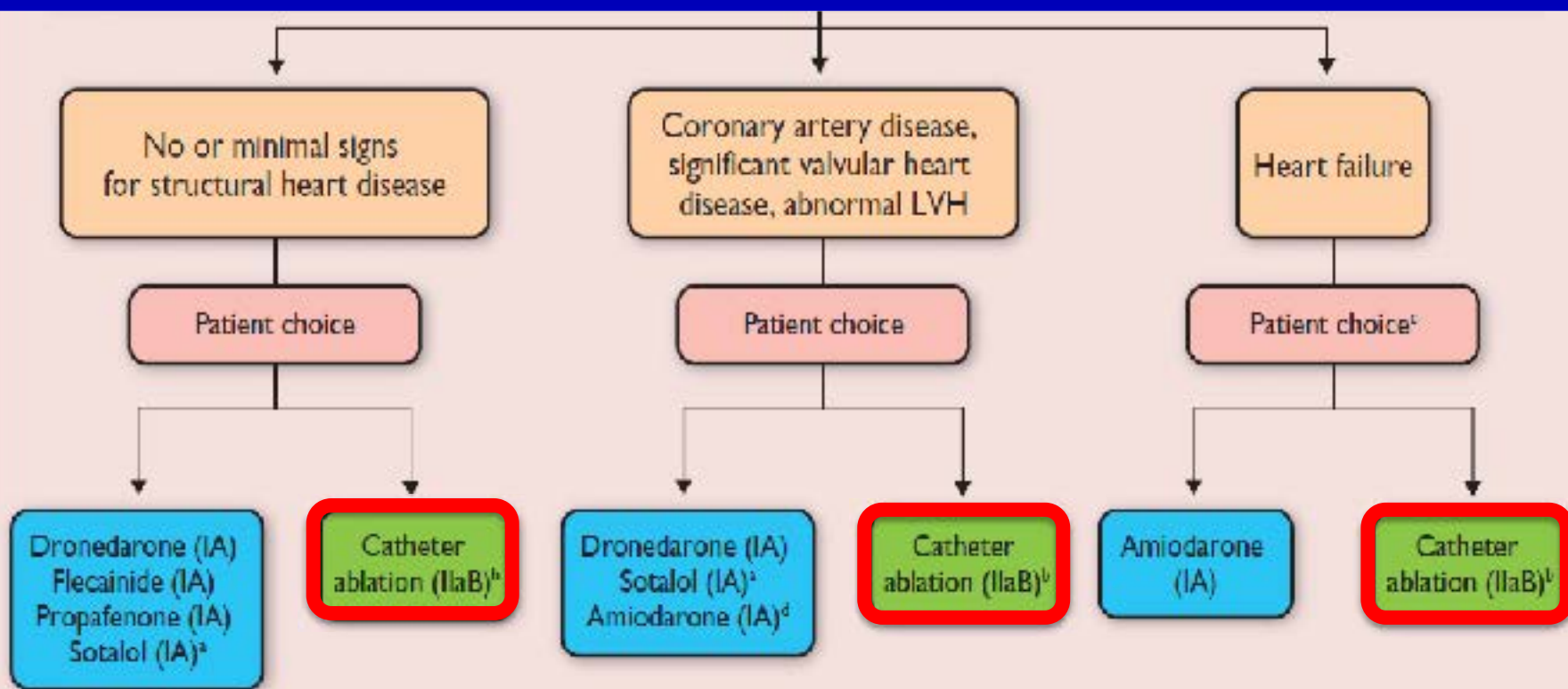
6% cryo

2% other

2016

AF guidelines ESC

Long term rhythm control therapy in AF



Thank you for your attention !

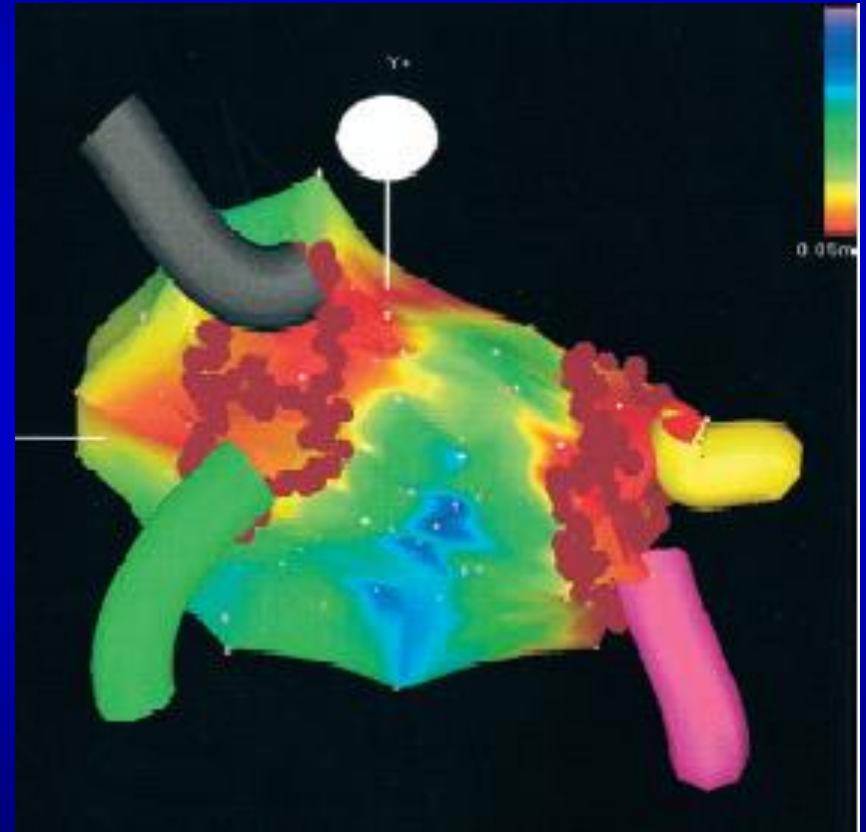


Target for Paroxysmal AF

Pulmonary vein isolation

Trigger

AF



Courtesy of Dr. Damian Sanchez-Quintana

Carlo Pappone

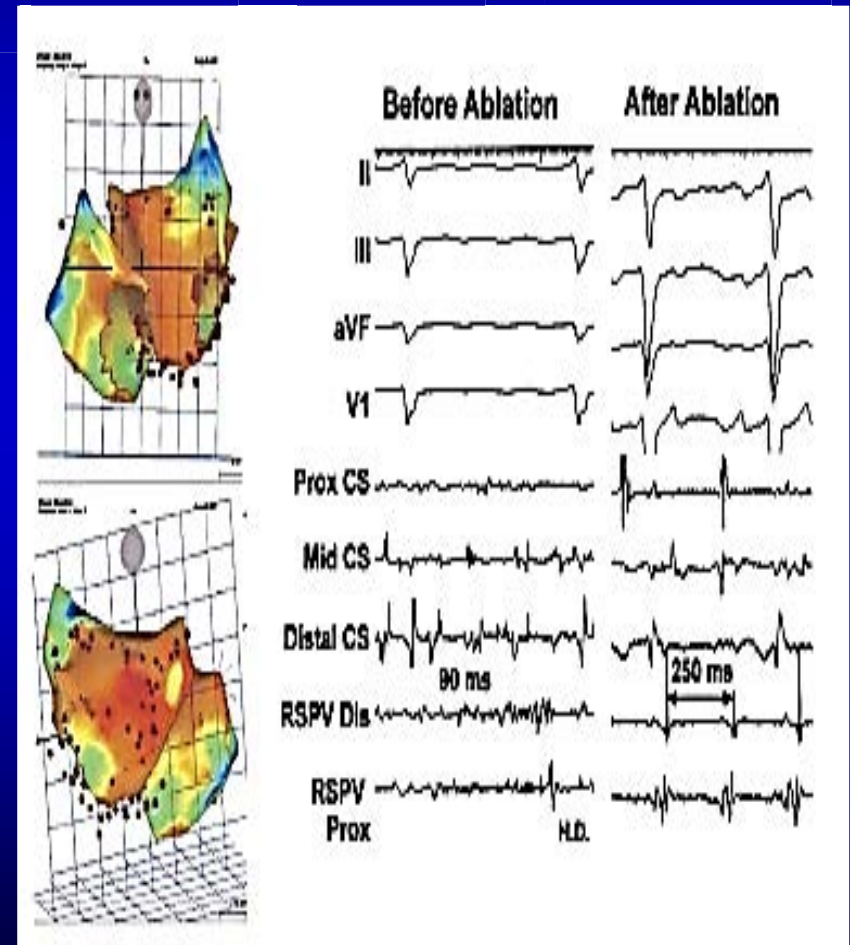
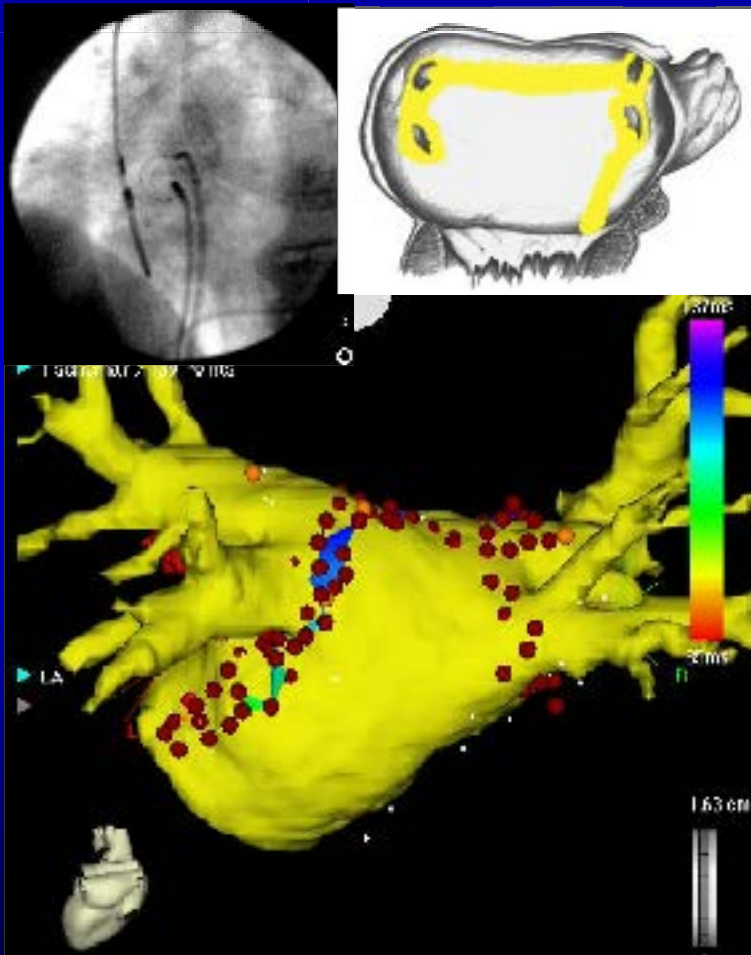
Substrate

Target for pts with structural heart disease or Persistent AF

AF

PVI + Linear Lesions (7 scheme)

+ Complex fractionated electrogram



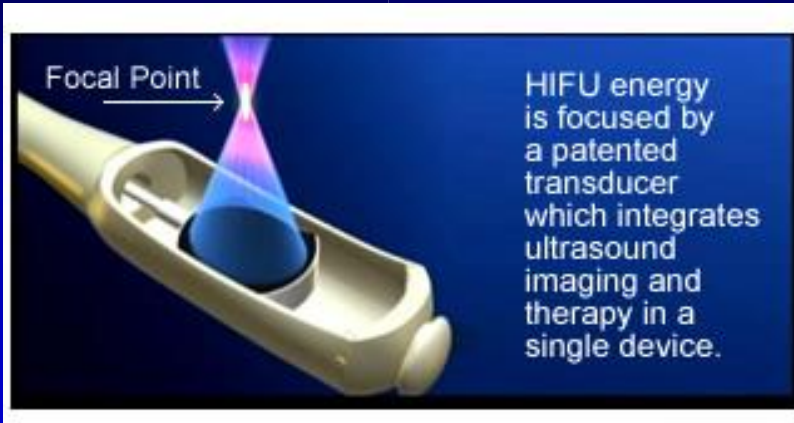
A signpost with three directional signs. The top sign is a blue arrow pointing right with the word 'Tomorrow' in white. The middle sign is a dark blue rectangle with the word 'Today' in white. The bottom sign is a dark blue arrow pointing left with the word 'Yesterday' in white. The signpost is a silver pole with three horizontal bars.

Tomorrow

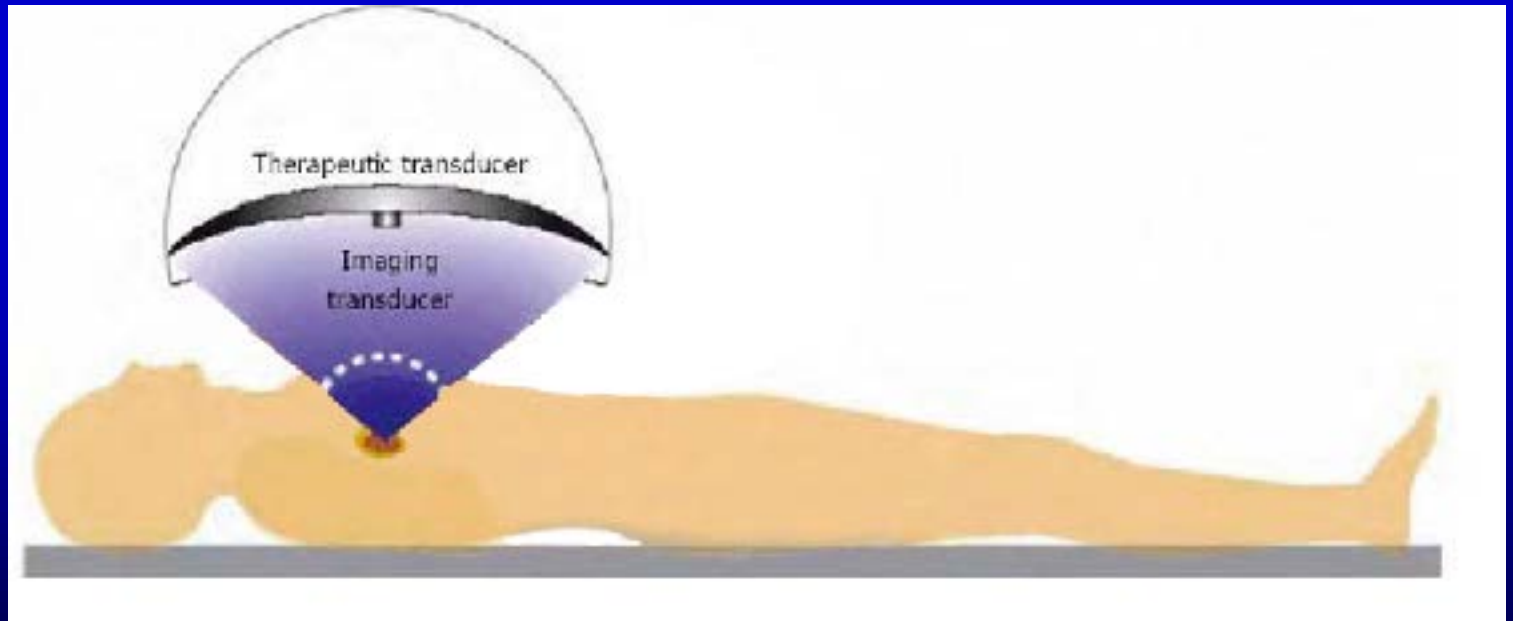
Today

Yesterday

External ablation for AF?



Focused ultrasound therapy?



Waiting for the future...

**What can we do today to
improve our results?**

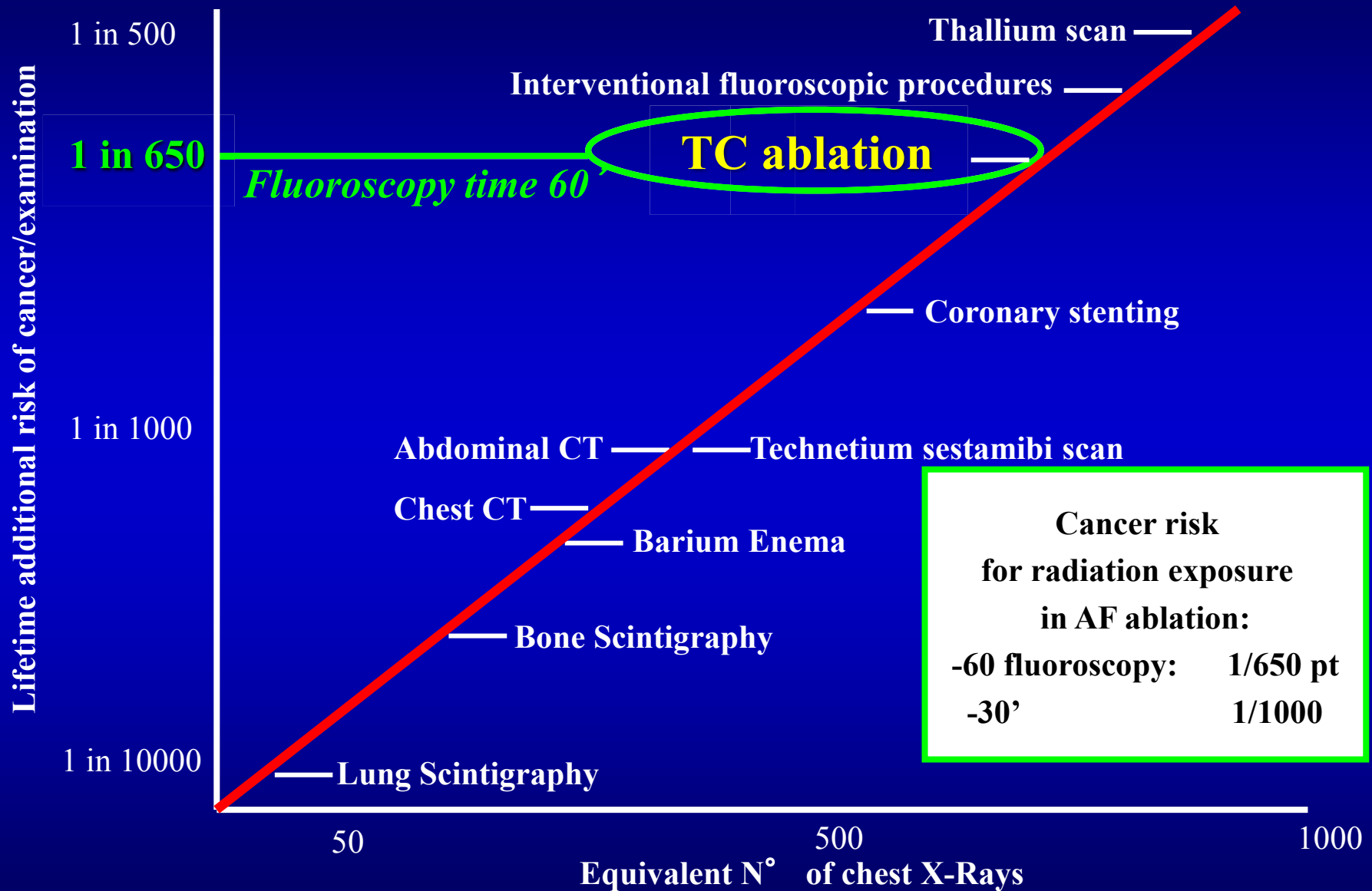
The New York Times 30 Jan, 2014

We Are Giving Ourselves Cancer
By X-Ray Exposure



Ben Jones

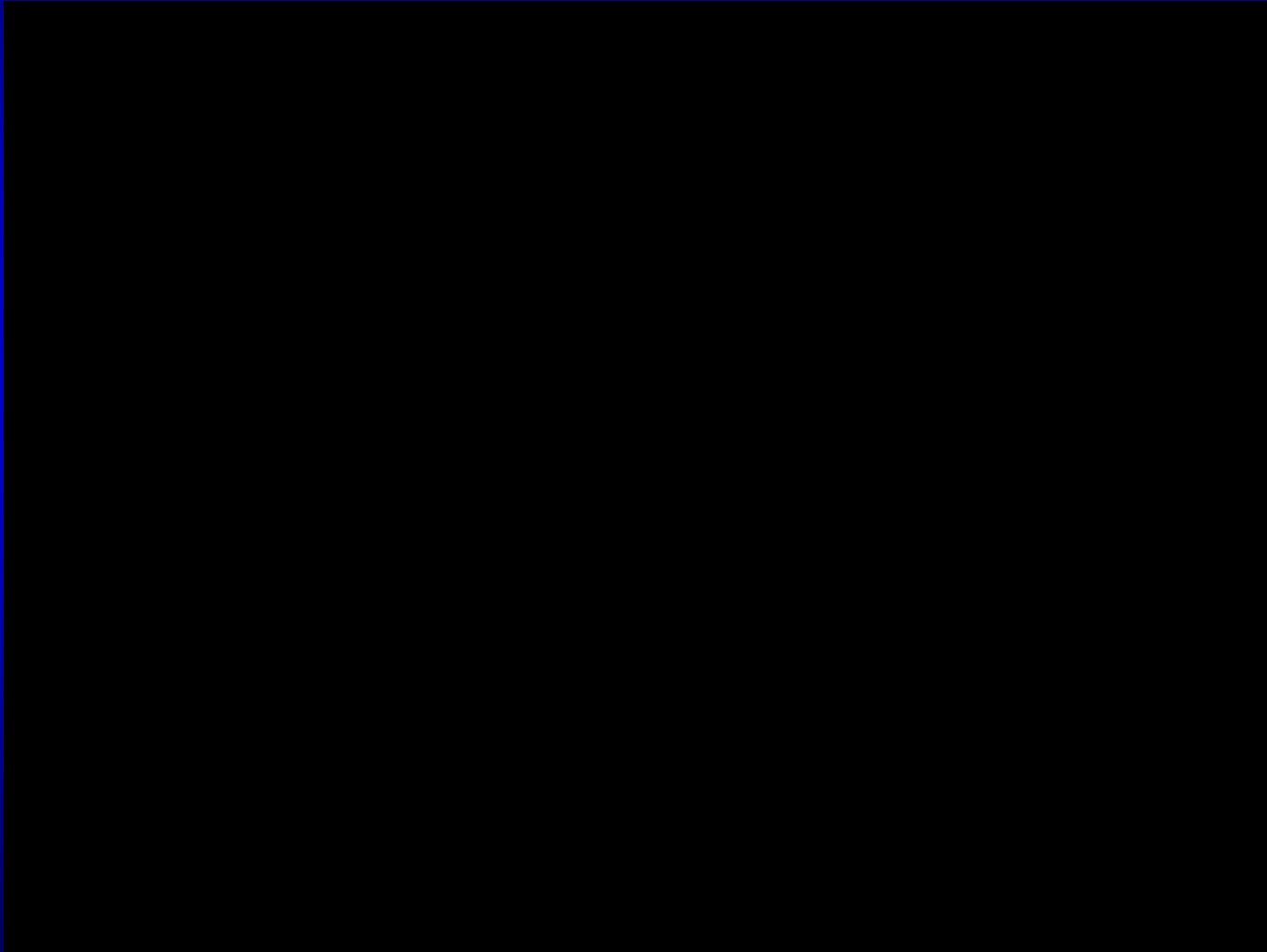
Radiation exposure: additional cancer risk for patients



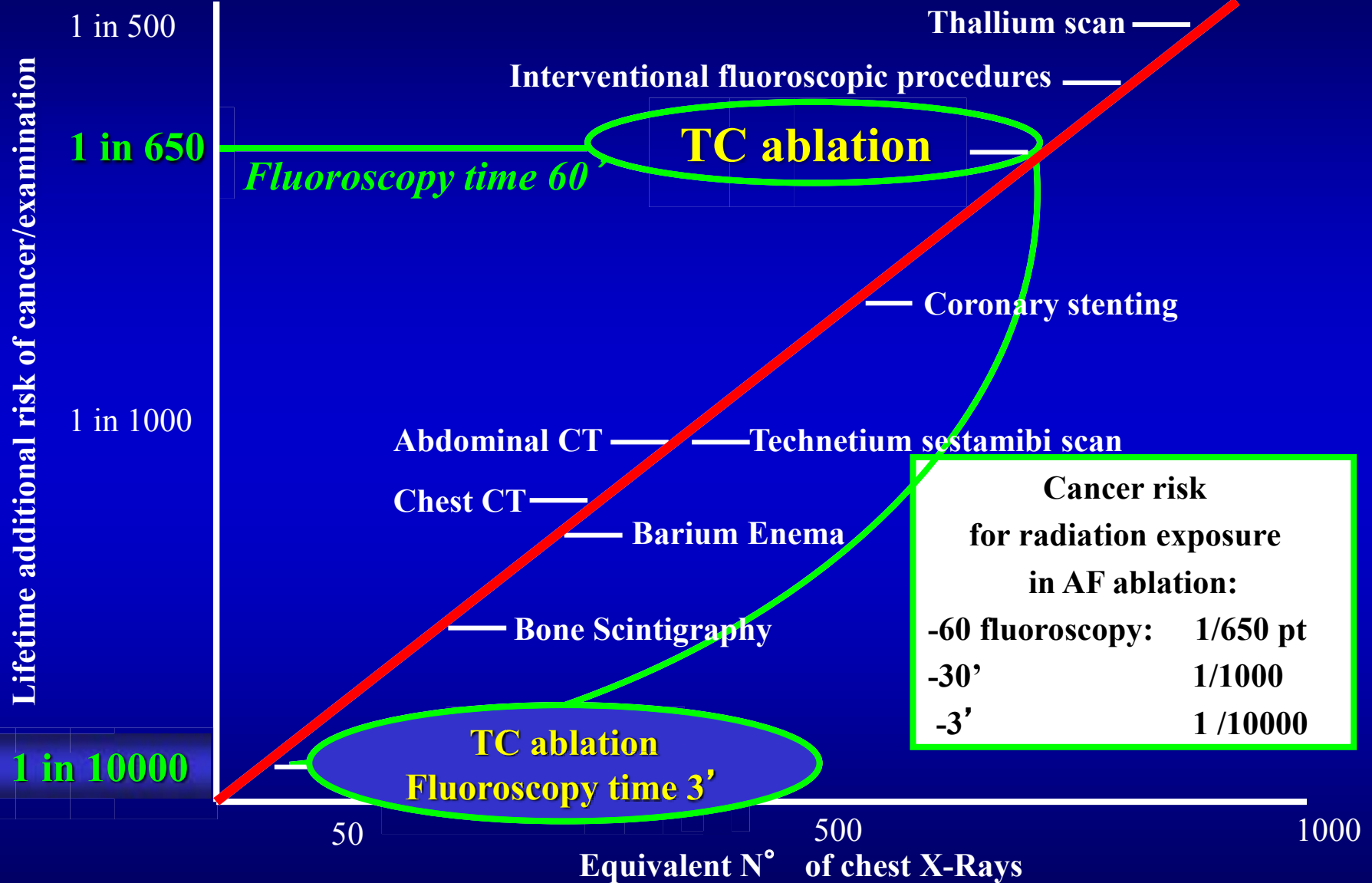
**Cancer risk
for radiation exposure
in AF ablation:**

-60 fluoroscopy:	1/650 pt
-30'	1/1000

AF transcatheter ablation



Radiation exposure: additional cancer risk for patients



2016

European Heart Rhythm Association/Heart Failure Association joint consensus document on arrhythmias in heart failure, endorsed by the Heart Rhythm Society and the Asia Pacific Heart Rhythm Society



EUROPEAN SOCIETY OF CARDIOLOGY®

Gregory Y.H. Lip* (Chairman; UK), Frank R. Heinzel (Germany), Fiorenzo Gaita

