FIBRILLAZIONE ATRIALE ED ICTUS CARDIOEMBOLICO:

MISURE LEGISLATIVE, STRATEGIE DI PREVENZIONE, ACCESSO ALLE CURE

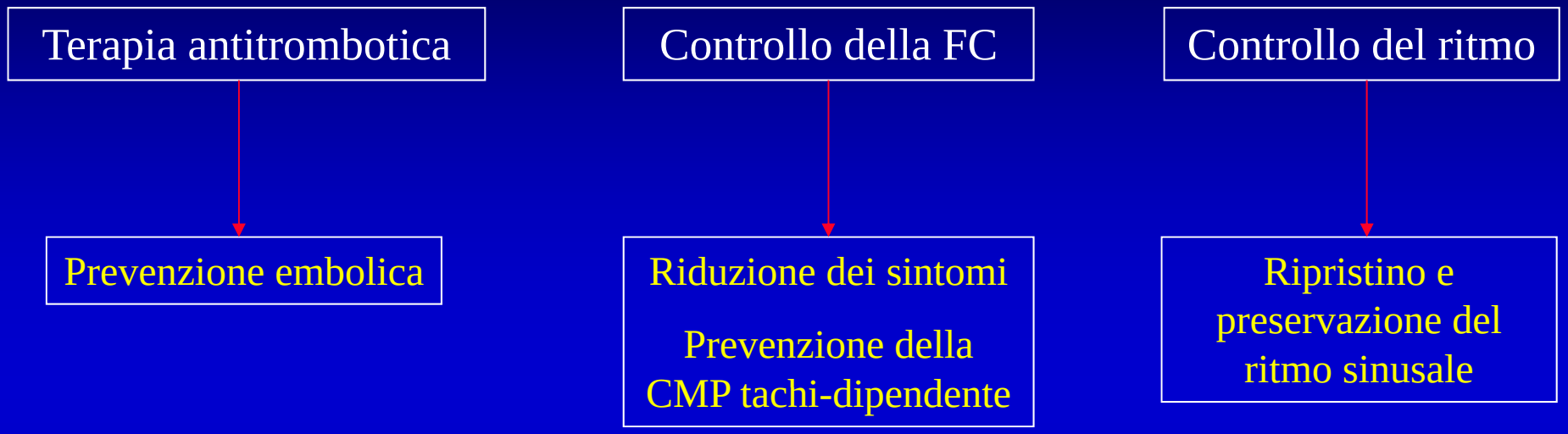
ROMA 15 MAGGIO 2013

TERAPIA NON FARMACOLOGICA DELLA FIBRILLAZIONE ATRIALE

ANDREA AVELLA

Azienda Ospedaliera S.Camillo-Forlanini II Unità Operativa Cardiologica
Centro di Elettrostimolazione ed Elettrofisiologia Cardiaca

STRATEGIE TERAPEUTICHE PER LA FA



TERAPIA FARMACOLOGICA DELLA FA

Farmaci antiaritmici	Caposaldo storico del trattamento della FA, rappresentano solitamente la prima linea di intervento terapeutico
Meccanismo d'azione	Effetto terapeutico basato sulla capacità di modificare transitoriamente i principali parametri elettrofisiologici che caratterizzano il miocardio comune ed il sistema specifico di conduzione (automatismo, velocità di conduzione, periodo refrattario).
Obiettivo terapeutico	I) Controllo della risposta ventricolare media tramite elettiva depressione della capacità conduttiva della giunzione AV. II) Controllo del ritmo tramite stabilizzazione del profilo elettrico atriale.
Vantaggi	Facile somministrazione orale o endovenosa, identificazione del farmaco più idoneo in base alle caratteristiche cliniche del paziente, titolazione individuale del dosaggio, possibilità di associare più farmaci. Strategia terapeutica erogabile in qualsiasi centro cardiologico.
Svantaggi	Efficacia parziale e progressivamente decrescente nel medio-lungo termine; limitata disponibilità di farmaci "sicuri" nel paziente affetto da cardiopatia strutturale; incidenza significativa di effetti collaterali; possibile slatentizzazione di una patologia del sistema di conduzione con conseguente necessità di associare l'impianto di un pacemaker.

TERAPIA NON FARMACOLOGICA PER LA FA

Terapia antitrombotica	Controllo della FC	Controllo del ritmo
Occlusione dell'auricola sinistra	Interruzione della conduzione AV + impianto di pacemaker	Terapia ablativa transcatetere
	Modulazione della conduzione AV	Terapia ablativa chirurgica

TERAPIA ABLATIVA DELLA FA

Premessa:

- il termine FA non identifica una sola aritmia ma piuttosto uno spettro di differenti situazioni aritmiche rilevabili spesso in contesti clinici molto diversi.

- queste diverse situazioni aritmiche costituiscono il risultato della variabile combinazione dei due elementi aritmogeni fondamentali per l'innesco e la perpetuazione dell'aritmia:

=> Attività automatica ectopica (Trigger = elemento innescante)

=> Eterogeneità della refrattarietà e delle velocità di conduzione atriali (Substrato elettrofisiologico)

TERAPIA ABLATIVA DELLA FA

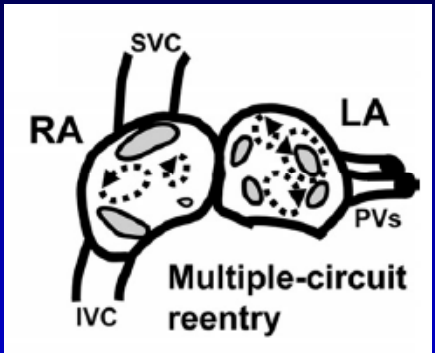
Razionale:

Cruentazione circoscritta di strutture atriali finalizzata all'eliminazione completa o parziale dei fattori responsabili dell'innesco e/o della perpetuazione della FA

Opzioni:
Ablazione transcatetere percutanea
Ablazione chirurgica

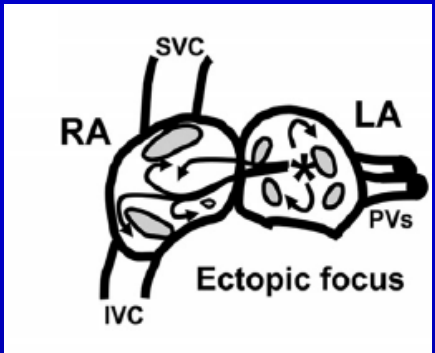
Energie utilizzabili:
Radiofrequenza, crioenergia, ultrasuoni, laser

MECCANISMI EZIOPATOGENETICI DELLA FA



Moe GK, Rheinboldt WD, Abildskov JA. A computer model of atrial fibrillation.Am Heart J 1964:200 –220.

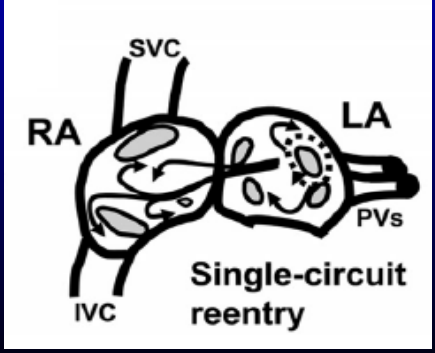
Allessie MA, Rensma PL, Lammers WJEP, Kirchoff CJHJ: The role of refractoriness, coonduction velocity, and wavelength in initiation of atrial fibrillation in normal conscious dogs. In: Attuel P, Coumel P, Janse MJ (eds): *The Atrium in Health and Disease*, Mount Kisco, NY, Futura Publishing Company Inc., 1989:27-41.



Haissaguerre M, Marcus FI, Fischer B, Clementy J. Radiofrequency catheter ablation in unusual mechanisms of atrial fibrillation: report of three cases. J Cardiovasc Electrophysiol. Sep 1994;5(9):743–751.

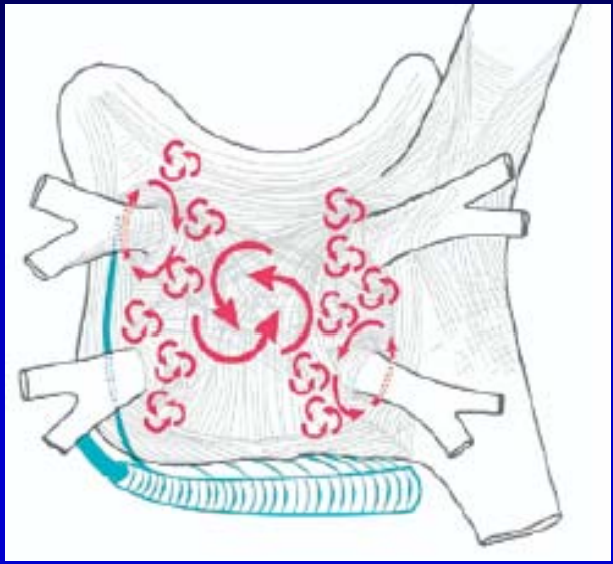
Jais P, Haissaguerre M, Shah DC, et al. Focal source of atrial fibrillation treated by discrete radiofrequency ablation. Circulation 1997;95:572–576.

Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–666.



Jalife J, Berenfeld O, Mansour M. Mother rotors and fibrillatory conduction: a mechanism of atrial fibrillation. *Cardiovasc Res* 2002;54:204-216.

Calkins et al. Catheter and Surgical Ablation of AF
Heart Rhythm, Vol 4, No 6, June 2007



Multiple Wavelet Theory

AF results from the presence of multiple reentrant wavelets occurring simultaneously in the left and right atria.

The number of wavelets at any point in time depends on the atrial conduction velocity, refractory period, and mass. Perpetuation of AF is favored by slowed conduction, shortened refractory periods, and increased atrial mass. Enhanced spatial dispersion of refractoriness promotes reentry by conduction block and conduction delay.

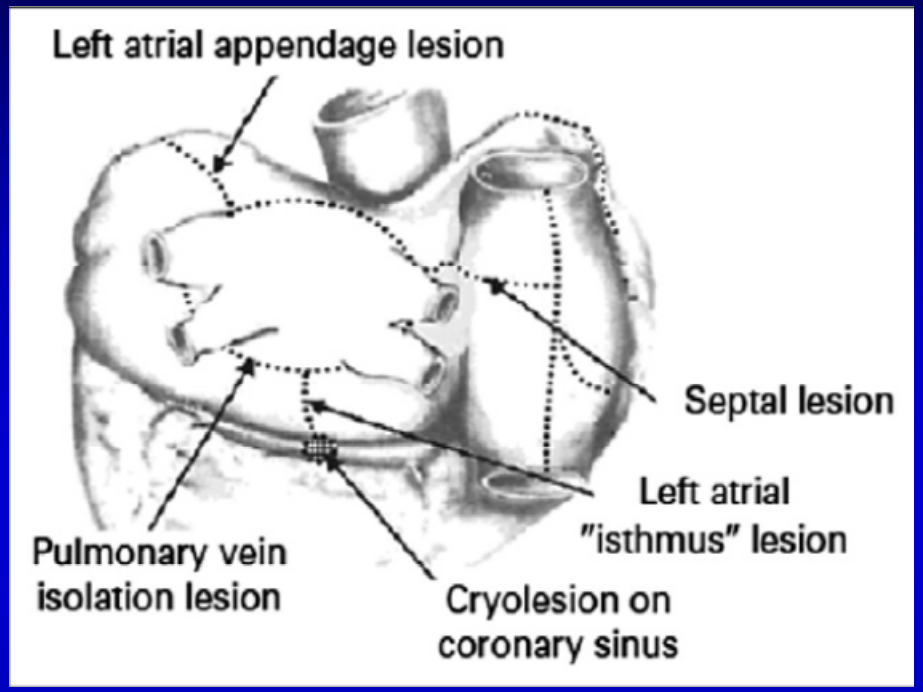
Maintenance of AF requires a critical number of circulating reentrant wavelets, each of which requires a critical mass of atrial tissue.

Razionale della terapia ablativa chirurgica per la FA

La creazione chirurgica di barriere anatomiche nelle pareti atriali può ridurre il numero di onde fibrillatorie circolanti al di sotto di un livello minimo necessario perché la FA si sostenga.

Cox JL et al. 1991 J Thorac Cardiovasc Surg => The MAZE procedure

TERAPIA ABLATIVA CHIRURGICA DELLA FA



Cox JL. Surgical treatment of atrial fibrillation: a review. *Europace* 2004;5(suppl):S20 –S29.

cohort of 308 patients treated with maze III procedure => operative mortality of 3%

Cox JL, Schuessler RB, Lappas DG, Boineau JP. An 8 1/2-year clinical experience with surgery for atrial fibrillation. *Ann Surg* 1996; 224:267–273.

8.5-year follow-up data on 178 patients treated with maze III procedure => 93% remained arrhythmia free without the aid of antiarrhythmic medication

TERAPIA ABLATIVA TRANSCATETERE DELLA FA



TERAPIA ABLATIVA TRANSCATETERE DELLA FA

- Iniziali tentativi di compartimentalizzazione atriale sinistra o biatriale con tecniche ablative caratterizzati da un'efficacia estremamente variabile (0 – 79%) e da frequenti complicanze maggiori (15%)

- Sviluppo di procedure di ablazione lineare limitata all'atrio destro finalizzate alla riduzione della massa atriale coinvolta nell'aritmogenesi

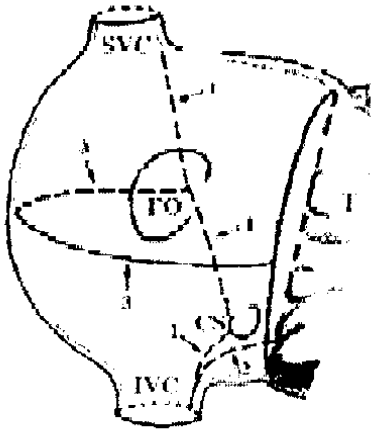
  ⇒ Efficacia senza farmaci: 6-25%

  ⇒ Efficacia con farmaci: 20-58%

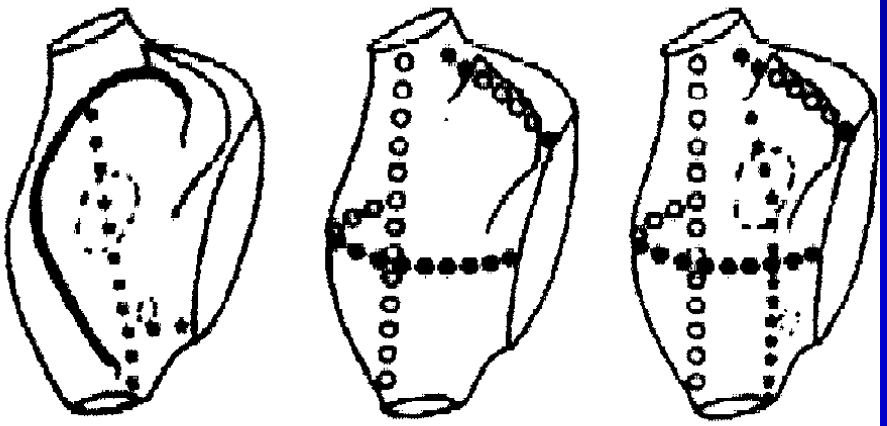
  ⇒ Efficacia prevalente in pazienti con FA idiopatica e parossistica

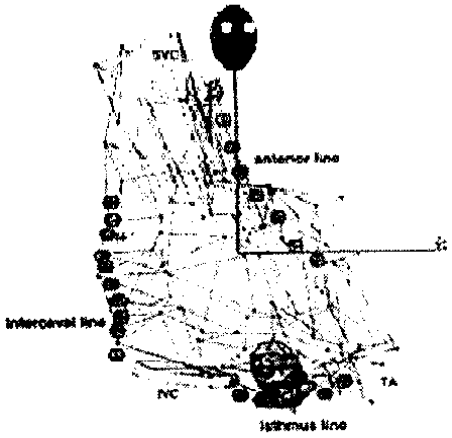
Modelli di ablazione lineare in atrio destro

Gaita 1998

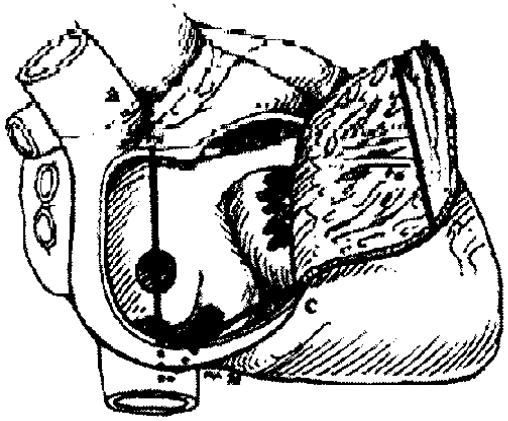


Jais 1998





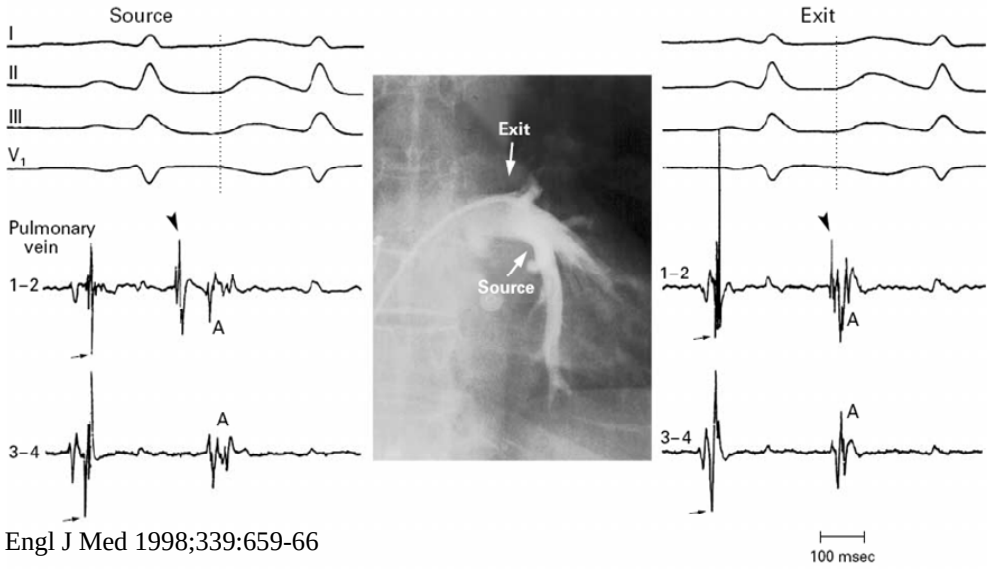
Ernst 1999



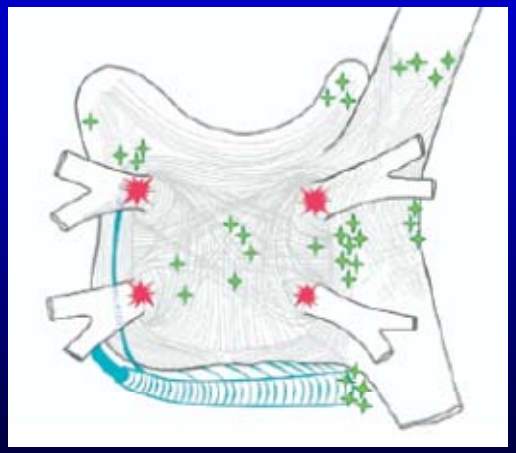
Natale 2000

SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION BY ECTOPIC BEATS ORIGINATING IN THE PULMONARY VEINS

MICHEL HAÏSSAGUERRE, M.D., PIERRE JAÏS, M.D., DIPEN C. SHAH, M.D., ATSUSHI TAKAHASHI, M.D., MÉLÈZE HOCINI, M.D., GILLES QUINIOU, M.D., STÉPHANE GARRIGUE, M.D., ALAIN LE MOUROUX, M.D., PHILIPPE LE MÉTAYER, M.D., AND JACQUES CLÉMENTY, M.D.



N Engl J Med 1998;339:659-66



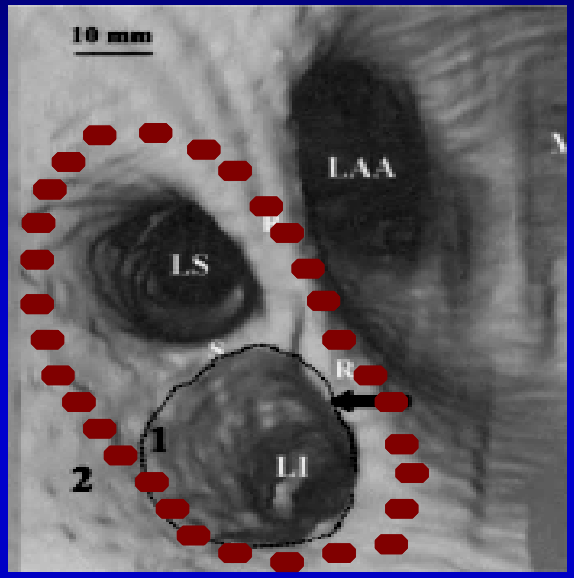
Focal Trigger Model

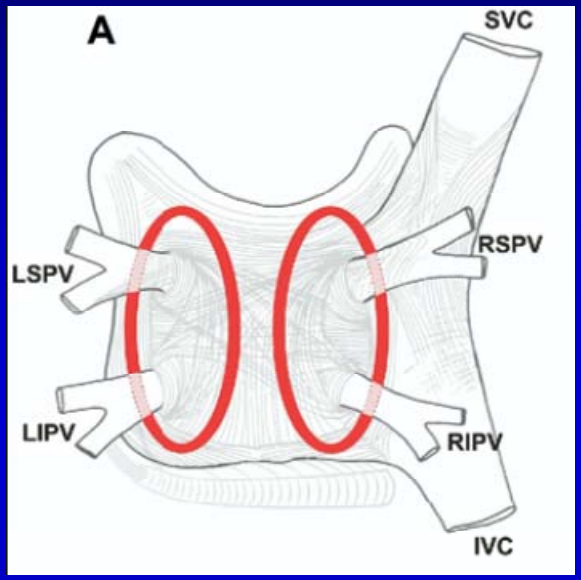
AF is often initiated by a single rapidly firing ectopic focus (focal trigger). Ablation of this trigger may eliminate AF.

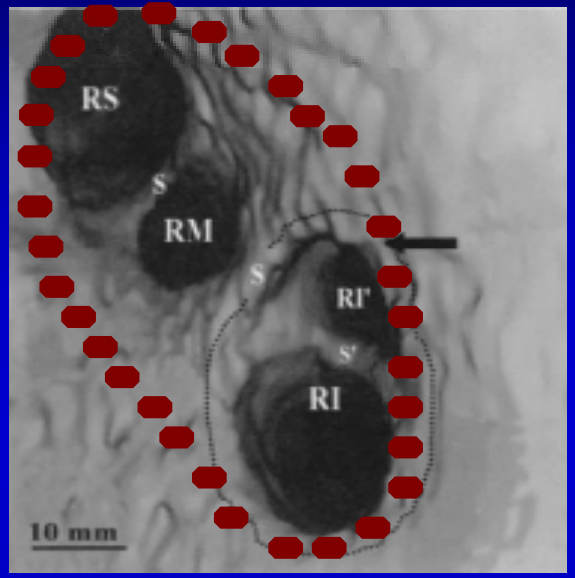
These rapidly firing ectopic foci have been mainly found at the orifices of the left or right superior PVs Thus, it is now well established that the PVs appear to be a crucial source of triggers which initiate AF.

Calkins et al. Catheter and Surgical Ablation of AF. Heart Rhythm, Vol 4, No 6, June 2007

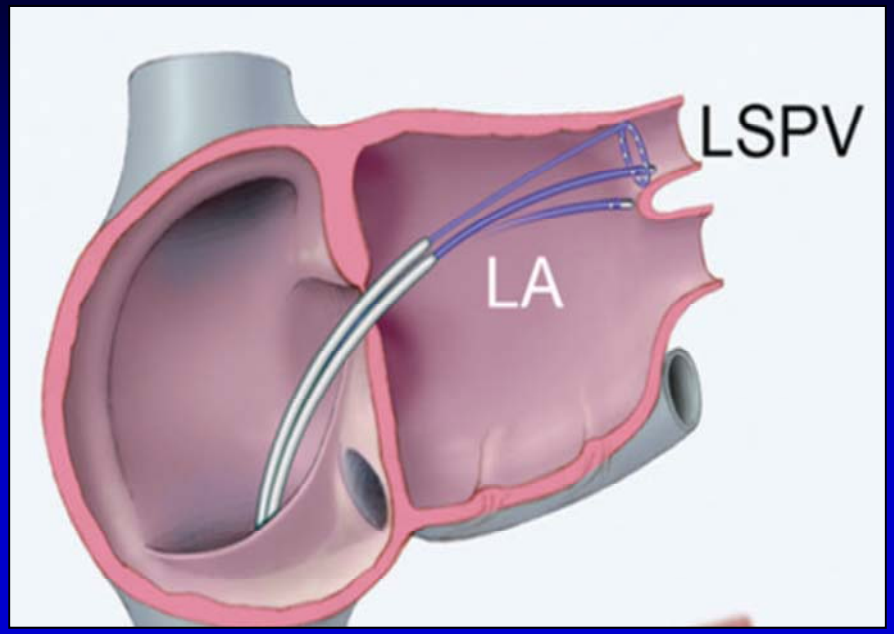
DECONNESSIONE DELLE VENE POLMONARI





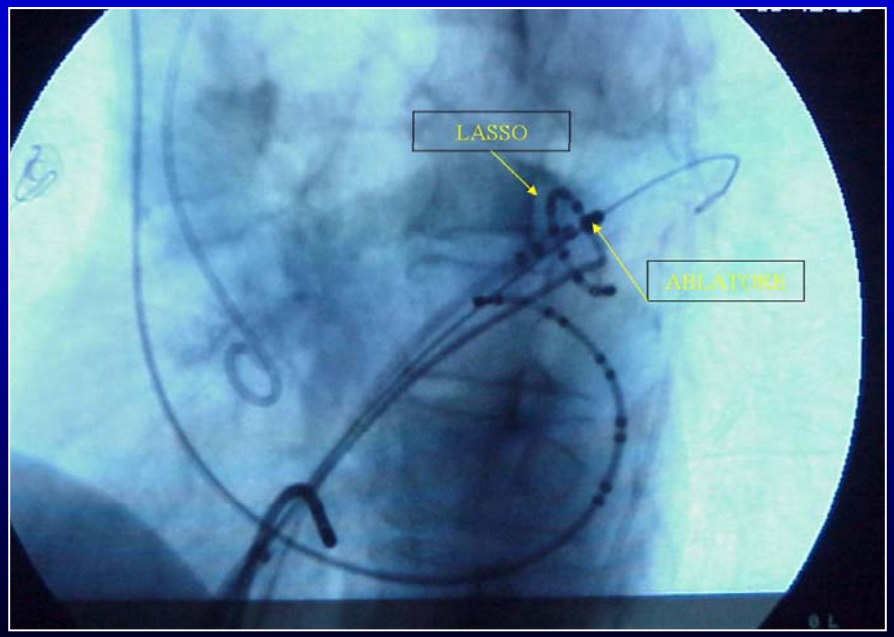


DECONNESSIONE DELLE VENE POLMONARI



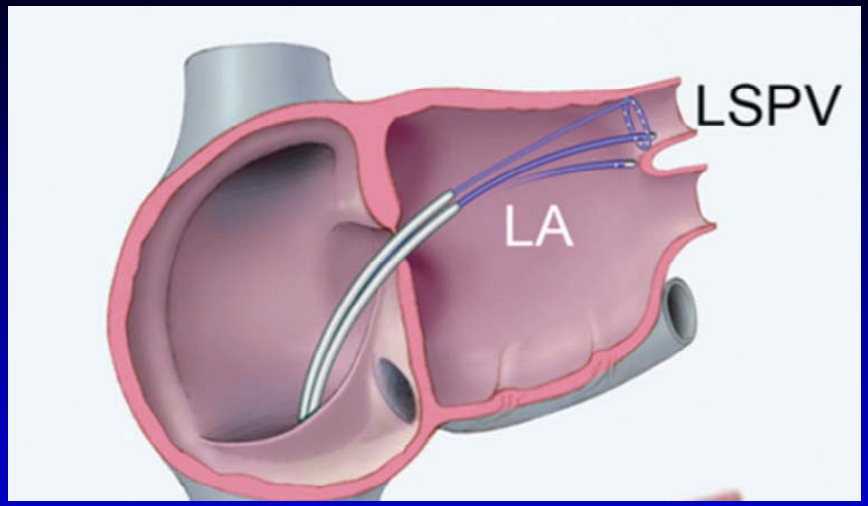


Pre





Post

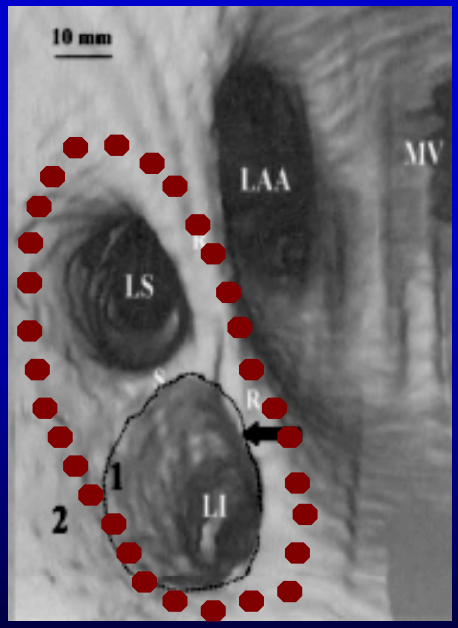


Normale Ritmo Sinusale

ECG D II

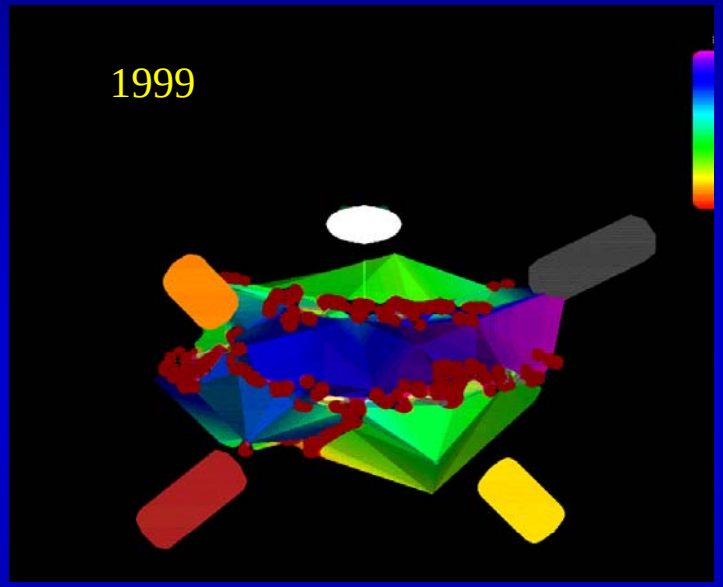
VP sinistre





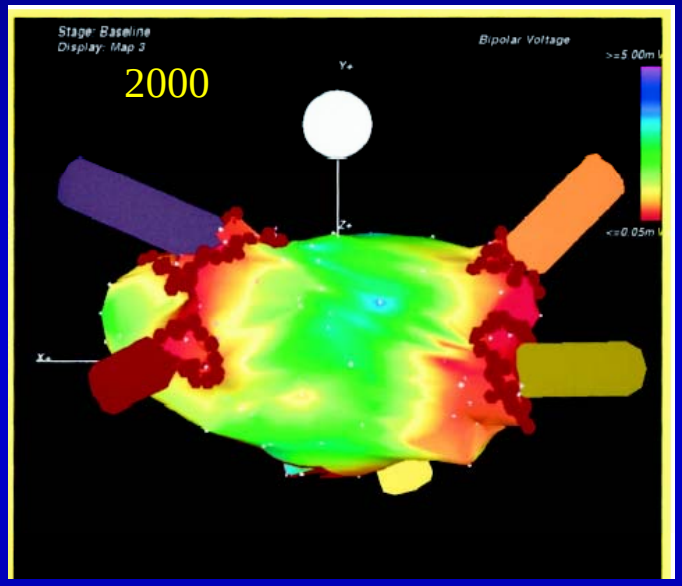
FA isolata nelle vene polmonari sinistre

Isolamento delle vene polmonari tramite ablazione circonferenziale degli osti



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 Shpun, DSc; Mariano Rillo, MD; Maria Pia Calabrò, MD; Andrea Conversano, MD; Shlomo A. Ben-Haim, MD, DSc; Riccardo Cappato, MD; Sergio Chierchia, MD



Circumferential Radiofrequency Ablation of Pulmonary Vein Ostia

A New Anatomic Approach for Curing Atrial Fibrillation

Carlo Pappone, MD, PhD; Salvatore Rosanio, MD, PhD; Giuseppe Oreto, MD; Monica Tocchi, MD; Filippo Gugliotta, BS; Gabriele Vicedomini, MD; Adriano Salvati, MD; Cosimo Dicandia, MD; Patrizio Mazzone, MD; Vincenzo Santinelli, MD; Simone Gulletta, MD; Sergio Chierchia, MD

PV ablation: strategies

Ostial PV disconnection

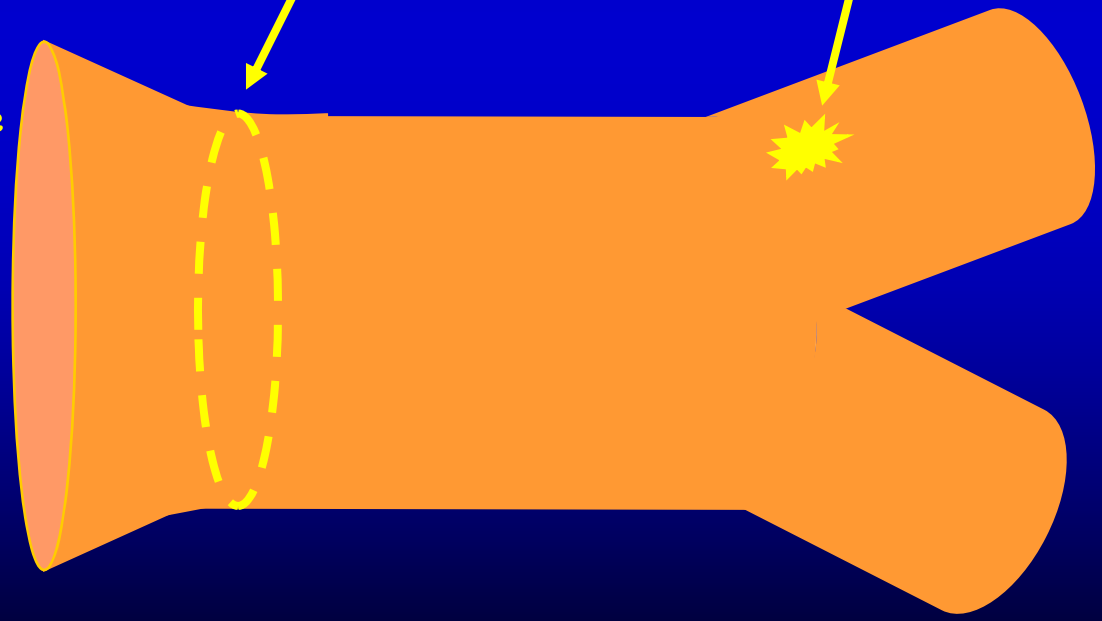
- ➔Rapid mapping with minimal arrhythmia requirement
- ➔Clear endpoint
- ➔Risk of proximal foci (10%)

Focus suppression

- ➔ Time consuming mapping
- ➔ Risk of new foci (35%)
- ➔ Higher risk of (distal) stenosis

Extra PV encircling

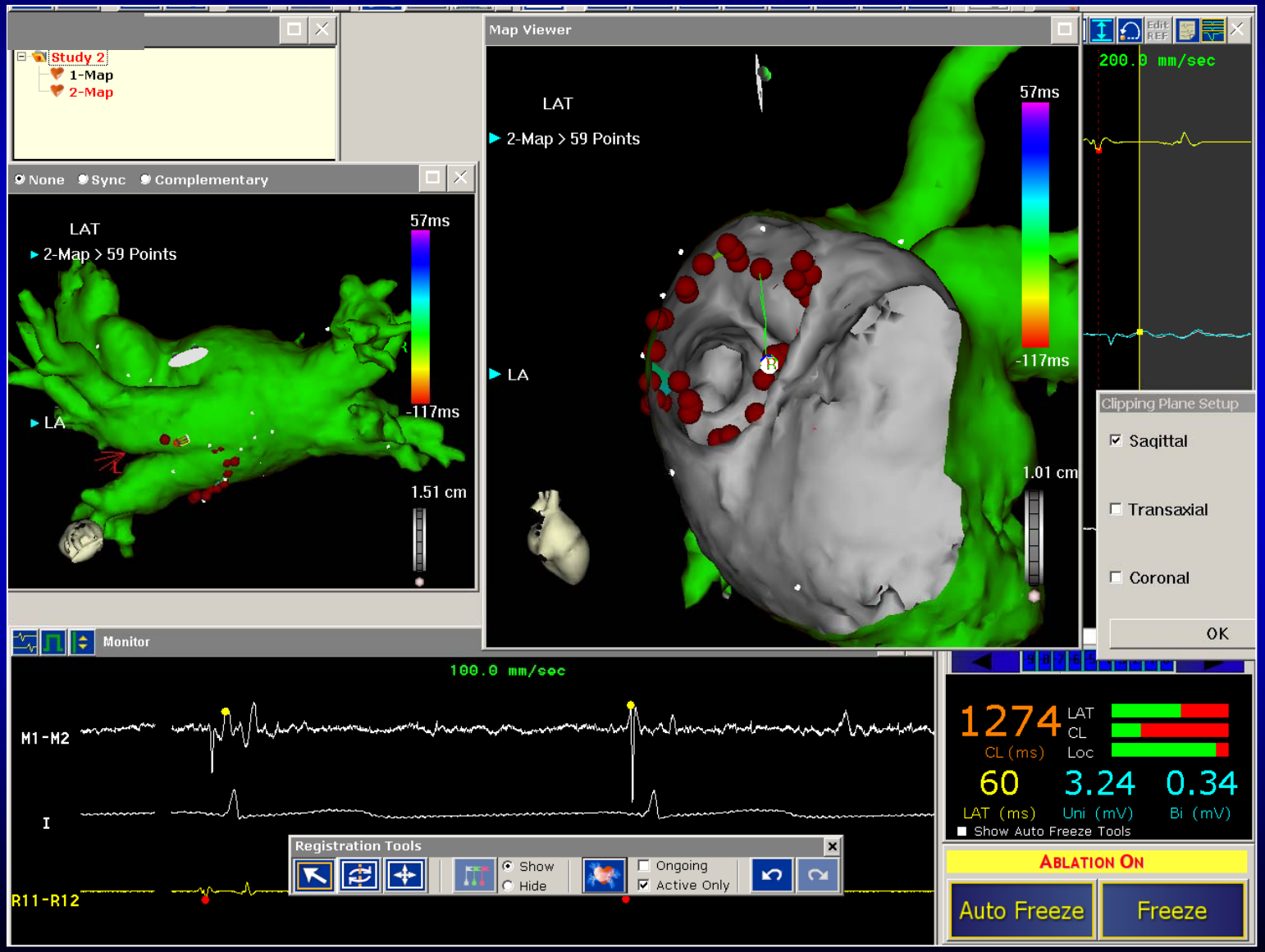
- ➔ Circumvent all PV foci
- ➔ Large circumferential line
- ➔ Difficult to achieve block



adapted from Shah JCE 2001; 24(10): 1541

DECONNESSIONE DELLE VENE POLMONARI

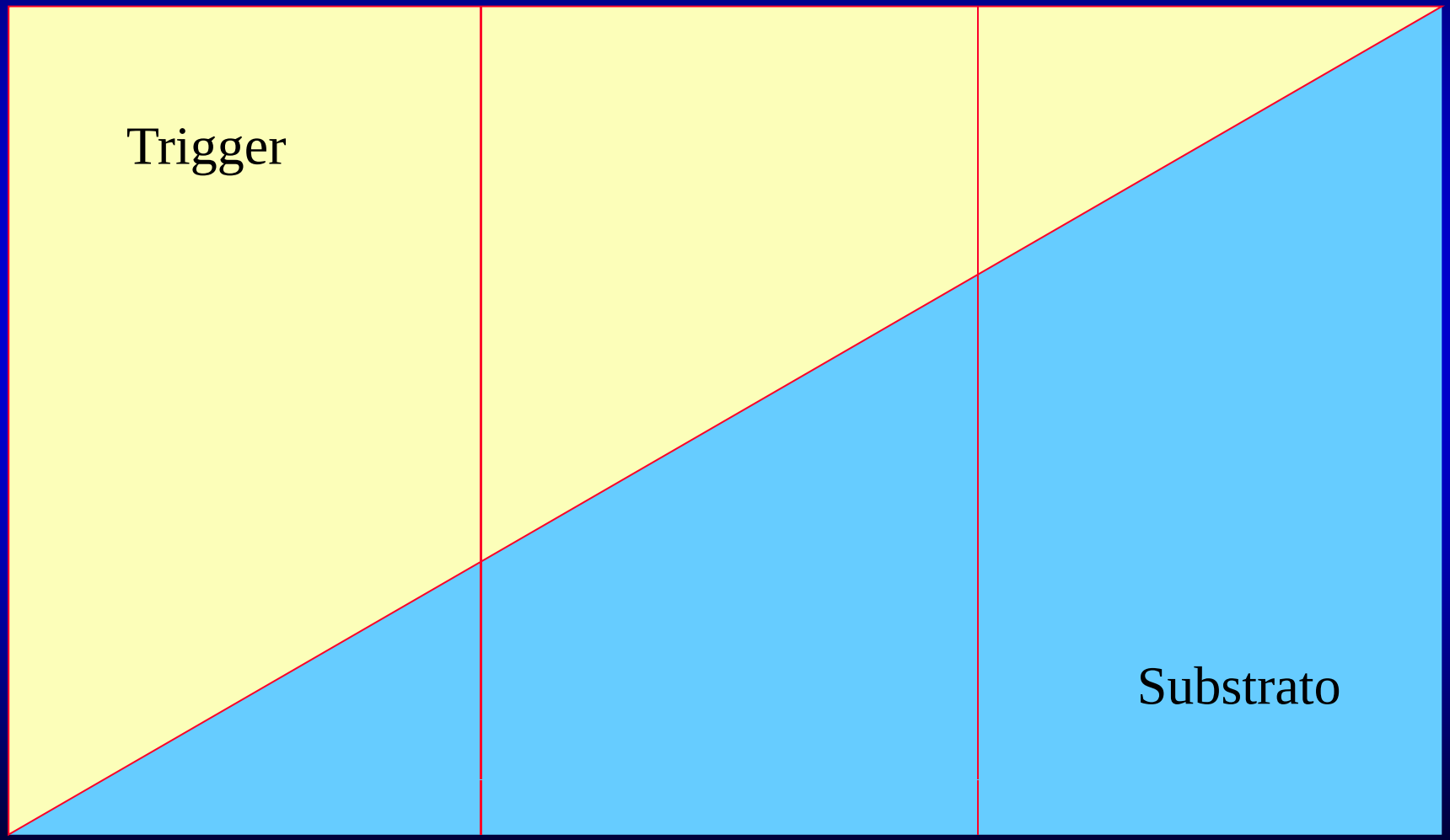
Approccio integrato anatomico ed elettrofisiologico



Ablazione della FA in atrio sn: presupposti fisiopatologici

Parossistica	Persistente	Permanente
TRIGGER ↑↑↑	TRIGGER ↑	TRIGGER ?
SUBSTRATO ATRIALE ↑?	SUBSTRATO ATRIALE ↑↑	SUBSTRATO ATRIALE ↑↑↑

Fisiopatologia della FA

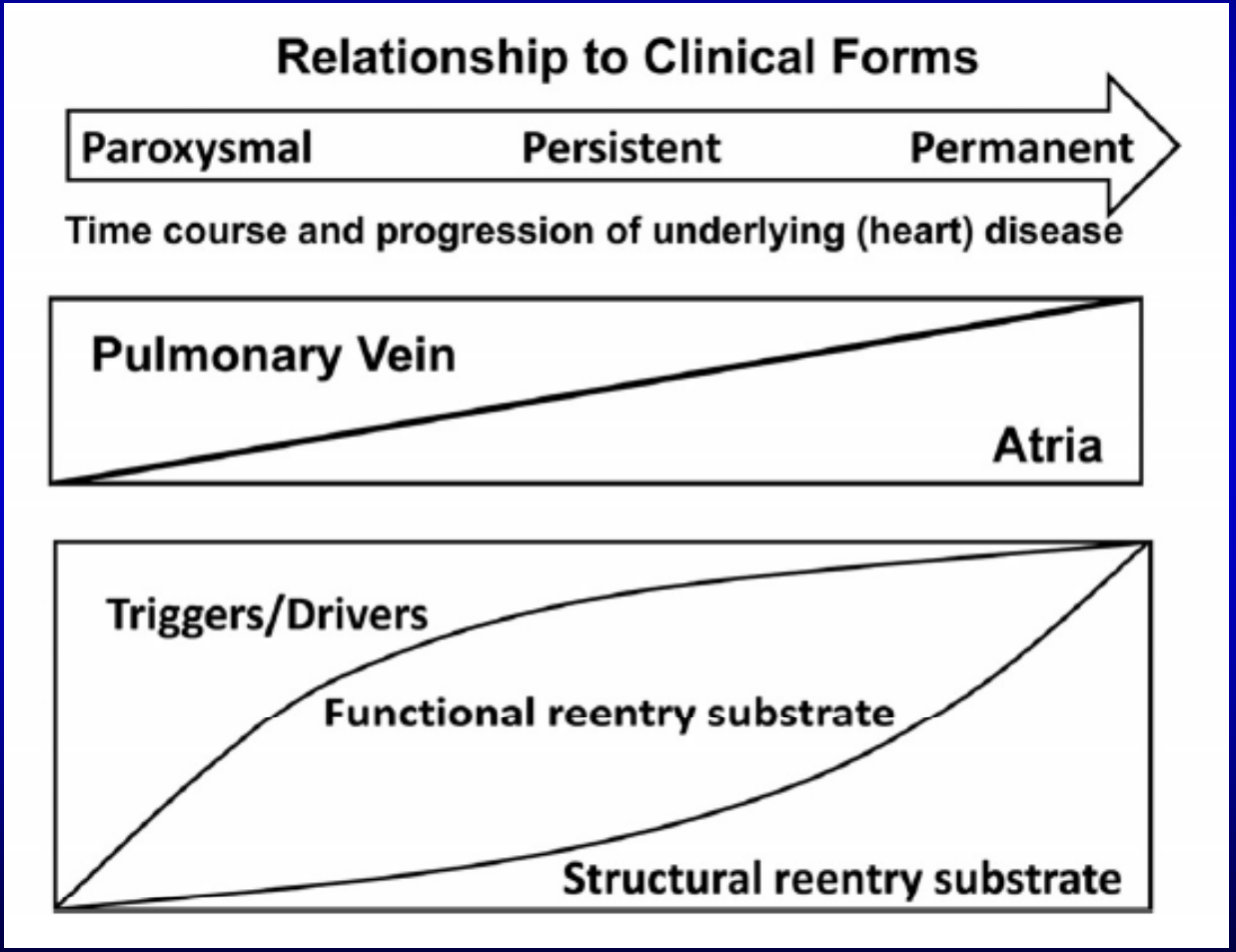


Atrial Fibrillation Pathophysiology

Implications for Management

Yu-ki Iwasaki, MD, PhD*; Kunihiro Nishida, MD, PhD*; Takeshi Kato, MD, PhD; Stanley Nattel, MD

Circulation November 15, 2011



Correlazione tra meccanismi ezipatogenetici e presentazione clinica della FA

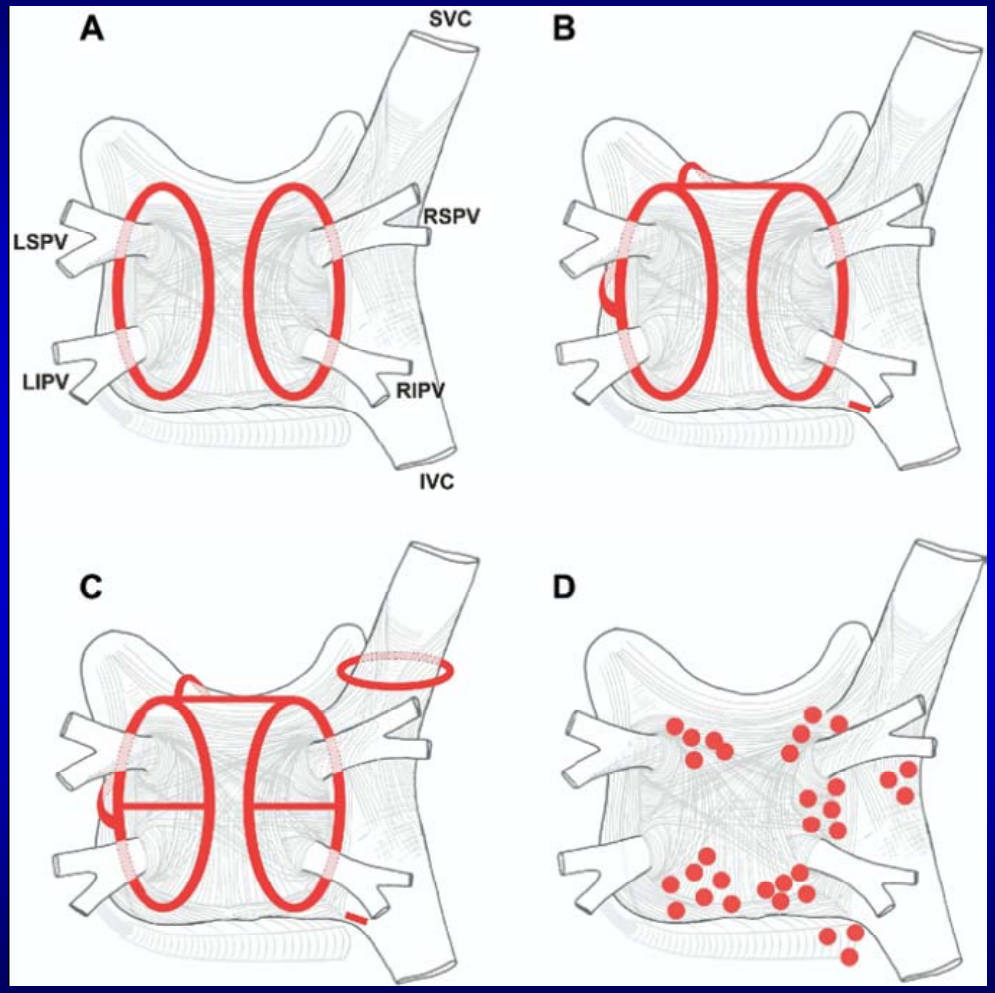
Isolamento elettrico delle vene polmonari

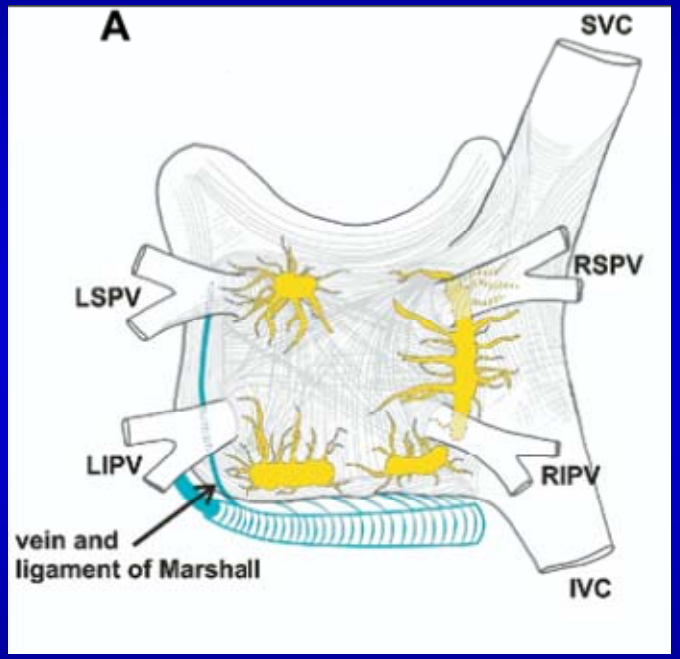
⇒ Tecnica ablativa principale per il trattamento della FA
⇒ Alta efficacia nelle forme di FA parossistica
⇒ Limitata efficacia nella FA persistente/persistente di lunga durata

Tecniche ablative supplementari

⇒ Lesioni lineari (istmo mitralico, parete posteriore e tetto dell'atrio sinistro)
⇒ Ablazione dei potenziali elettrici atriali frammentati (CFAE)
⇒ Ablazione di foci ectopici extra VP
⇒ Ablazione dei gangli autonomici cardiaci

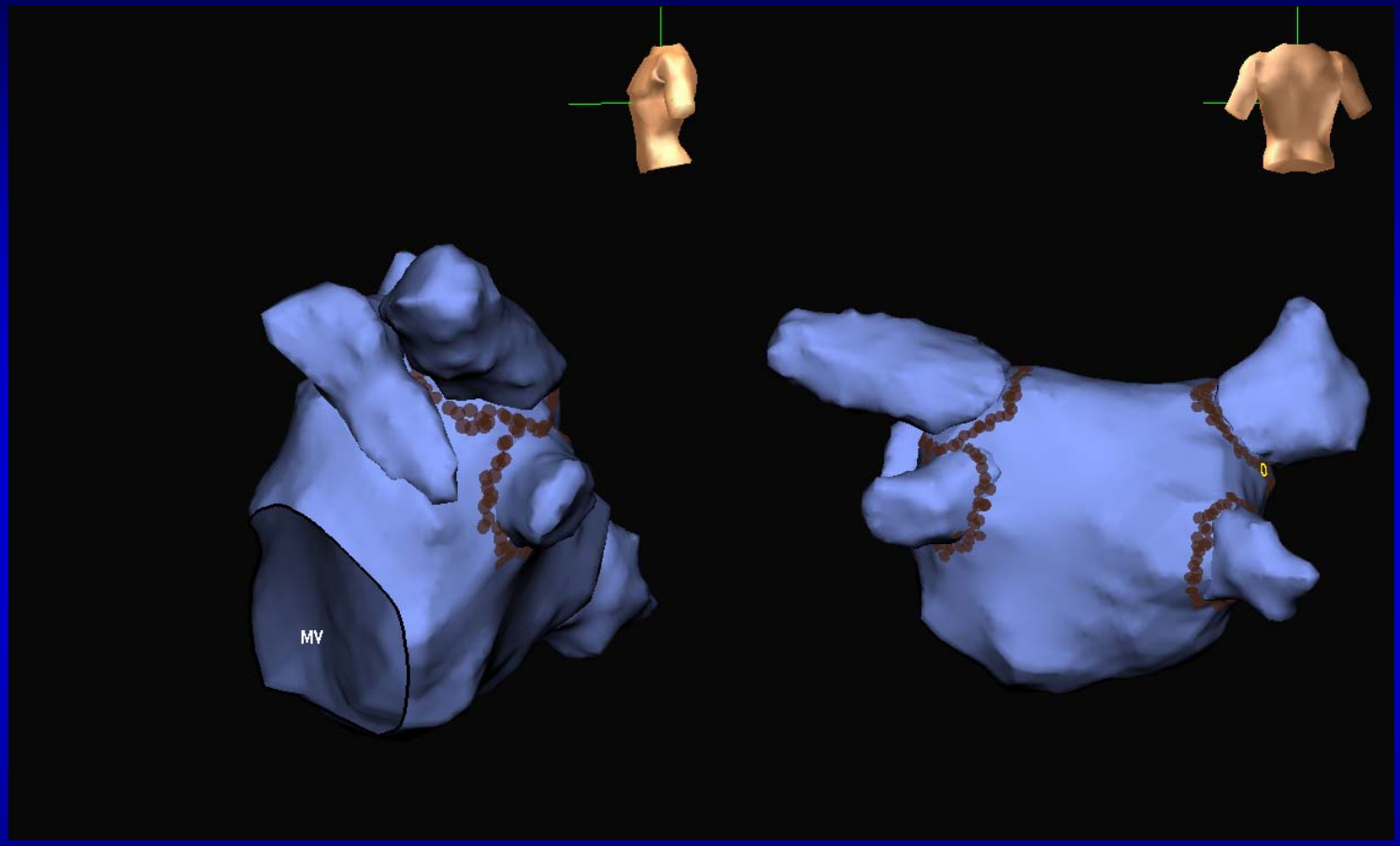
TECNICHE ABLATIVE PER IL TRATTAMENTO DELLE DIVERSE FORME DI FA





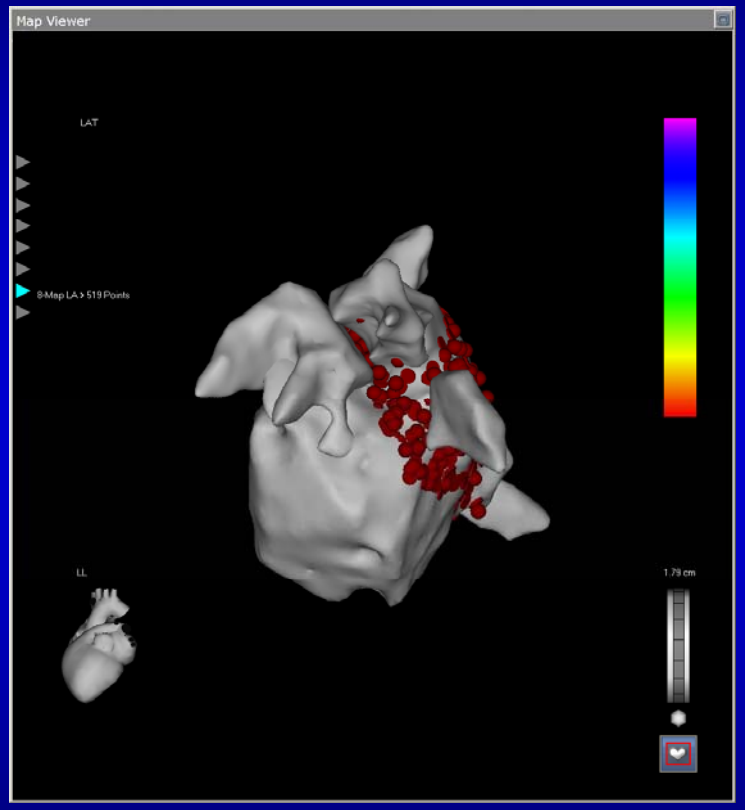
Calkins et al. Catheter and Surgical Ablation of AF
Heart Rhythm, Vol 4, No 6, June 2007

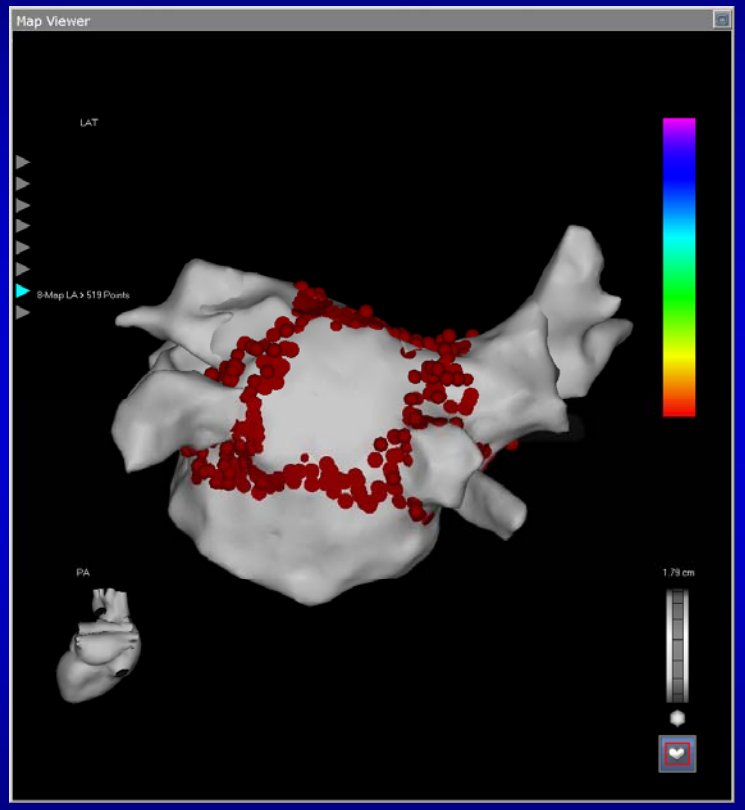
PV isolation in paroxysmal AF



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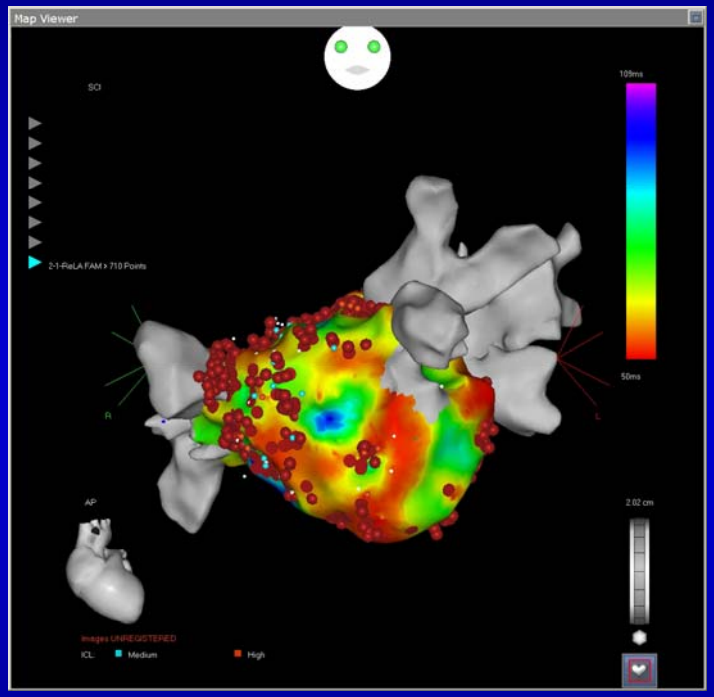
Box lesion in long-lasting persistent AF

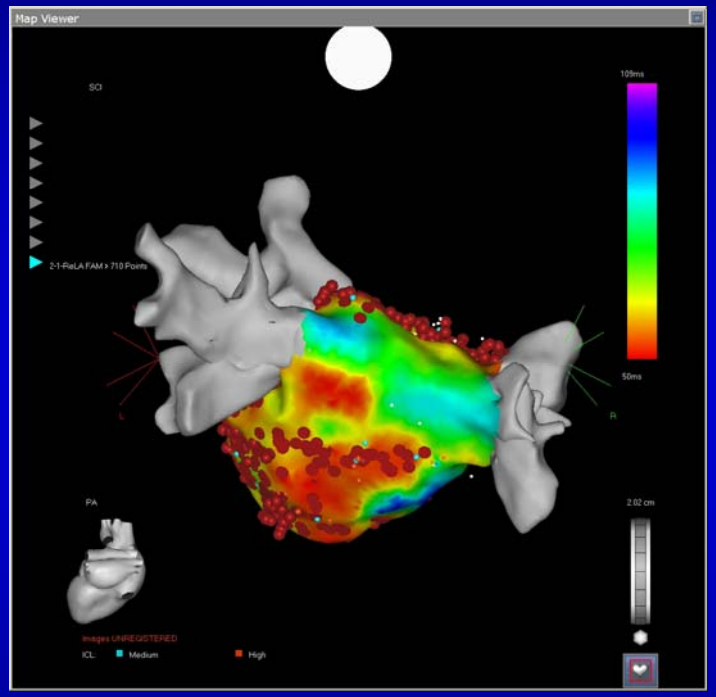




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Centro di Elettrostimolazione ed Elettrofisiologia Cardiaca

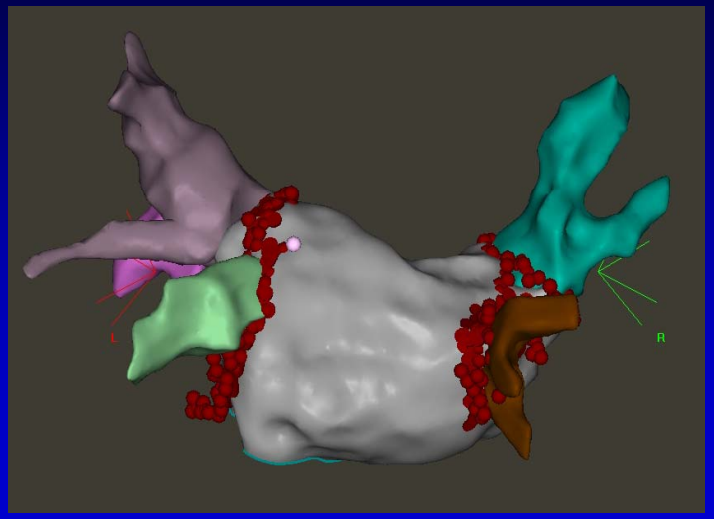
CAFE ablation in persistent AF

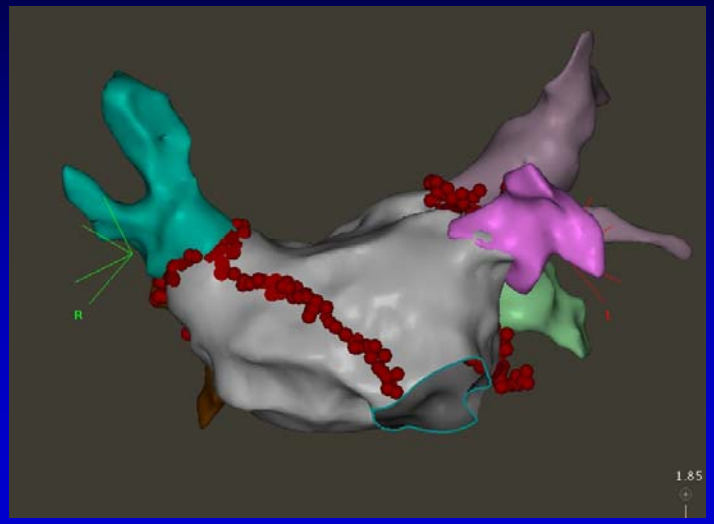


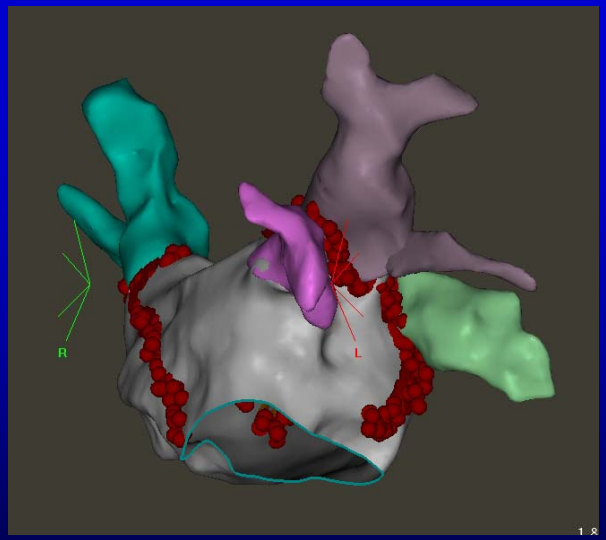


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ABLAZIONE DI FA PERSISTENTE

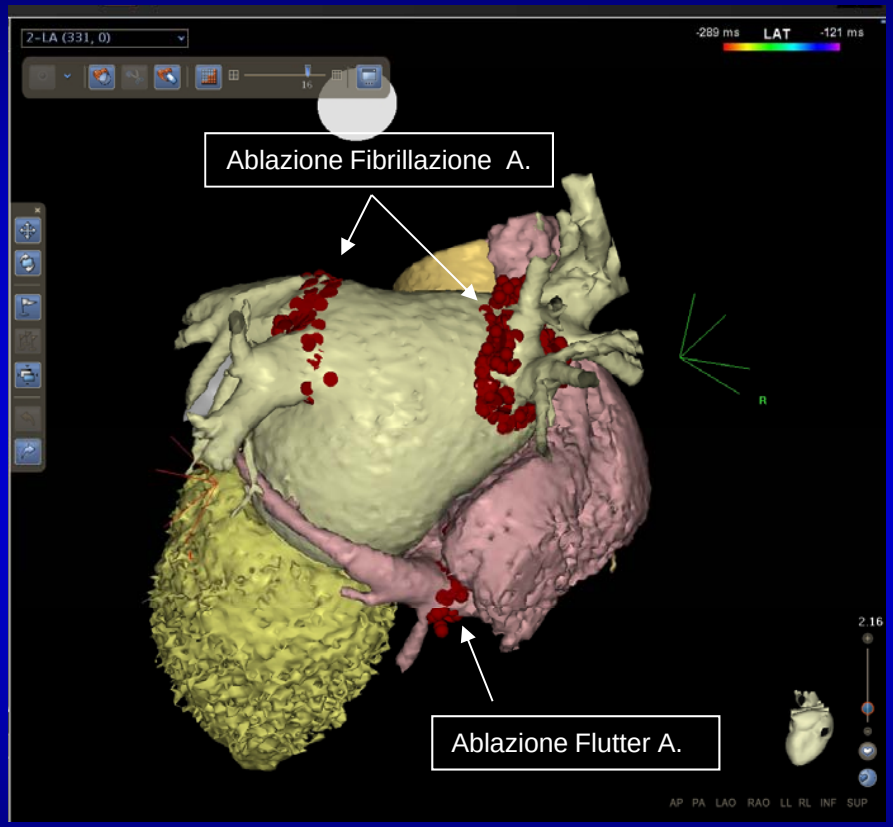






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Centro di Elettrostimolazione ed Elettrofisiologia Cardiaca

Procedura di ablazione per Fibrillazione Atriale (deconnessione delle vene polmonari) + ablazione per Flutter Atriale tipico (blocco dell'istmo cavo-tricuspidale)



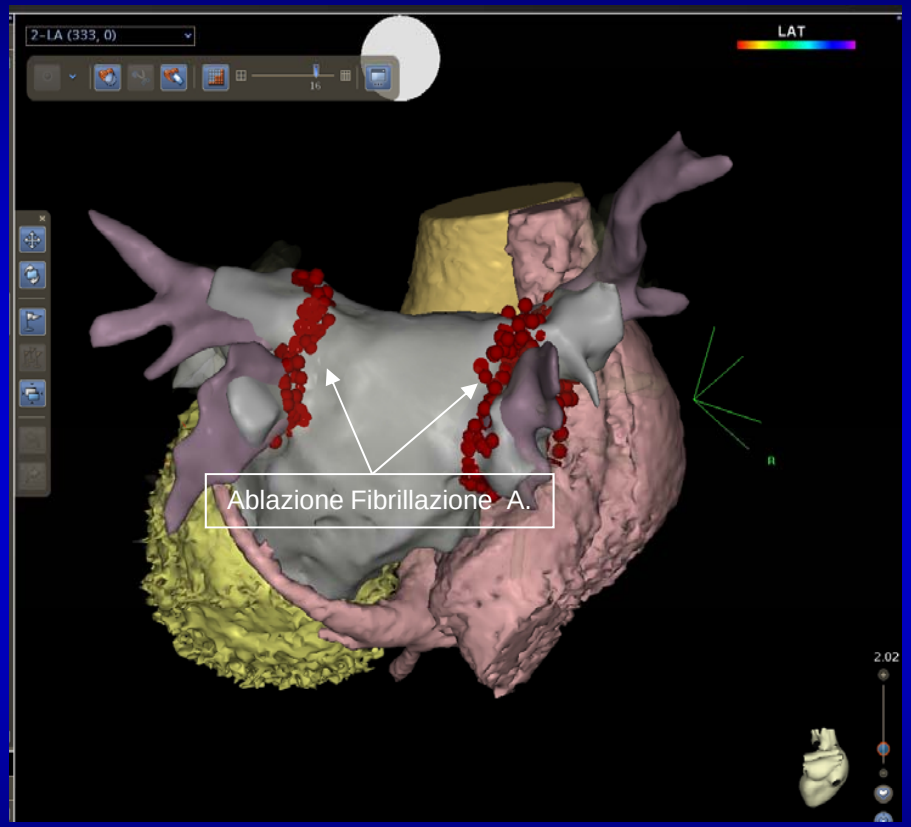


Table 18 Randomized clinical trials of catheter ablation vs. antiarrhythmic drugs or no treatment in AF

Study	Reference	Patients (n)	Age, years	Type of AF	Previous use of AAD	Ablation technique	Repeat ablation in the ablation group	Crossed to ablation in the AAD group	AF free at 1 year	
									Ablation	AAD
Krittayaphong *et al.* 2003	Online	30	55 ± 10 (ablation) 47 ± 15 (AAD)	Paroxysmal, persistent	≥1[a]	PVI + LA lines + CTI ablation + RA lines	Not stated	Not stated	79%	40%
Wazni *et al.* 2005 (RAAFT)	134	70	53 ± 8 (ablation) 54 ± 8 (AAD)	Mainly paroxysmal	No	PVI	12%[b]	49%[c]	87%	37%
Stabile *et al.* 2005 (CACAF)[d]	Online	245	62 ± 9 (ablation) 62 ± 10 (AAD)	Paroxysmal, persistent	≥2	PVI + LA lines ± CTI ablation	No exact data	57%	56%	9%
Oral *et al.* 2006[e]	Online	245	57 ± 9	Persistent	≥1 (mean 2.1 ± 1.2)	CPVA	26% for AF; 6% for LA flutter	77%	74%	4%
Pappone *et al.* 2006 (APAF)	135	198	55 ± 10 (ablation) 57 ± 10 (AAD)	Paroxysmal	≥2 (mean 2 ± 1)	CPVA + CTI ablation	6% for AF; 3% for atrial tachycardia	42%	86%	22%
Jais *et al.* 2008 (A4 study)	133	112	51 ± 11	Paroxysmal	≥1	PVI ± LA lines ± CTI ablation	Mean 1.8 ± 0.8, median 2 per patient	63%	89%	23%
Forleo *et al.* 2008[f]	Online	70	63 ± 9 (ablation) 65 ± 6 (AAD)	Paroxysmal, persistent	≥1	PVI ± LA lines ± CTI ablation	Not stated	Not stated	80%	43%
Wilber *et al.* 2010 (Thermocool)[g]	96	167	55.5 (ablation) 56.1 (AAD)	Paroxysmal	≥1 (mean 1.3)[h]	PVI ± LA lines ± CFAEs ± CTI ablation ± RA lines	12.6% within 80 days after 1st procedure[i]	59%[c]	66%	16%
Packer *et al.* 2010 (STOP-AF)[j]	Online	245	56.7 (ablation) 56.4 (AAD)	Paroxysmal	≥1[b]	Cryo-PVI ± LA lines	19% within 90 days after 1st procedure	79%	69.9%	7.3%

2010 ESC Guidelines for the management of AF

Updated Worldwide Survey on the Methods, Efficacy, and Safety of Catheter Ablation for Human Atrial Fibrillation

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Background—The purpose of this study was to provide an updated worldwide report on the methods, efficacy, and safety of catheter ablation of atrial fibrillation (AF).

Methods and Results—A questionnaire with 46 questions was sent to 521 centers from 24 countries in 4 continents. Complete interviews were collected from 182 centers, of which 85 reported to have performed 20 825 catheter ablation procedures on 16 309 patients with AF between 2003 and 2006. The median number of procedures per center was 245 (range, 2 to 2715). All centers included paroxysmal AF, 85.9% also included persistent and 47.1% also included long-lasting AF. Carto-guided left atrial circumferential ablation (48.2% of patients) and Lasso-guided ostial electric disconnection (27.4%) were the most commonly used techniques. Efficacy data were analyzed with centers representing the unit of analysis. Of 16 309 patients with full disclosure of outcome data, 10 488 (median, 70.0%; interquartile range, 57.7% to 75.4%) became asymptomatic without antiarrhythmic drugs and another 2047 (10.0%; 0.5% to 17.1%) became asymptomatic in the presence of previously ineffective antiarrhythmic drugs over 18 (range, 3 to 24) months of follow-up. Success rates free of antiarrhythmic drugs and overall success rates were significantly larger in 9590 patients with paroxysmal AF (74.9% and 83.2%) than in 2800 patients with persistent AF (64.8% and 75.0%) and 1108 patients with long-lasting AF (63.1% and 72.3%) ($P<0.0001$). Major complications were reported in 741 patients (4.5%).

Conclusions—When analyzed in a large number of electrophysiology laboratories worldwide, catheter ablation of AF shows to be effective in ≈80% of patients after 1.3 procedures per patient, with ≈70% of them not requiring further antiarrhythmic drugs during intermediate follow-up. (***Circ Arrhythm Electrophysiol.* 2010;3:32-38.**)

Key Words: atrial fibrillation ■ catheter ablation ■ antiarrhythmic drugs ■ follow-up studies

Table 3. Success Rates in Relationship With the Type of AF

			Success Without AADs		Success With AADs		Overall Success	
Type of AF	No. of Centers	No. of Patients	No. of Patients	Rate, Median (Interquartile Range)*	No. of Patients	Rate Median (Interquartile Range)*	No. of Patients	Rate Median (Interquartile Range)*
Paroxysmal	85	9590	6580	74.9 (64.9–82.6)	1290	9.1 (0.2–14.7)	7870	84.0 (79.7–88.6)
Persistent	73	4712	2800	64.8 (52.4–72.0)	595	10.0 (0.8–15.2)	3395	74.8 (66.1–80.0)
Long-lasting	40	1853	1108	63.1 (53.3–71.4)	162	7.9 (0.9–15.9)	1270	71.0 (67.4–76.3)

*Median and interquartile range are calculated using center as unit of analysis.

Recommendations for left atrial ablation

Recommendations	Class[a]	Level[b]	Ref.[c]
Ablation of common atrial flutter is recommended as part of an AF ablation procedure if documented prior to the ablation procedure or occurring during the AF ablation.	I	B	33
Catheter ablation for paroxysmal AF should be considered in symptomatic patients who have previously failed a trial of antiarrhythmic medication.	IIa	A	96, 131, 132, 133, 135, 137, 138
Ablation of persistent symptomatic AF that is refractory to antiarrhythmic therapy should be considered a treatment option.	IIa	B	33
In patients post-ablation, LMWH or i.v. UFH should be considered as 'bridging therapy' prior to resumption of systemic OAC, which should be continued for a minimum of 3 months. Thereafter, the individual stroke risk factors of the patient should be considered when determining if OAC therapy should be continued.	IIa	C	
Continuation of OAC therapy post-ablation is recommended in patients with 1 'major' ('definitive') or ≥2 'clinically relevant non-major' risk factors (i.e. CHA_2DS_2-VASc score ≥2).	IIa	B	136
Catheter ablation of AF in patients with heart failure may be considered when antiarrhythmic medication, including amiodarone, fails to control symptoms.	IIb	B	93, 94
Catheter ablation of AF may be considered prior to antiarrhythmic drug therapy in symptomatic patients despite adequate rate control with paroxysmal symptomatic AF and no significant underlying heart disease.	IIb	B	131
Catheter ablation of AF may be considered in patients with symptomatic long-standing persistent AF refractory to antiarrhythmic drugs.	IIb	C	

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
AF = atrial fibrillation; i.v. = intravenous; LMWH = low molecular weight heparin; OAC = oral anticoagulant; UFH = unfractionated heparin.

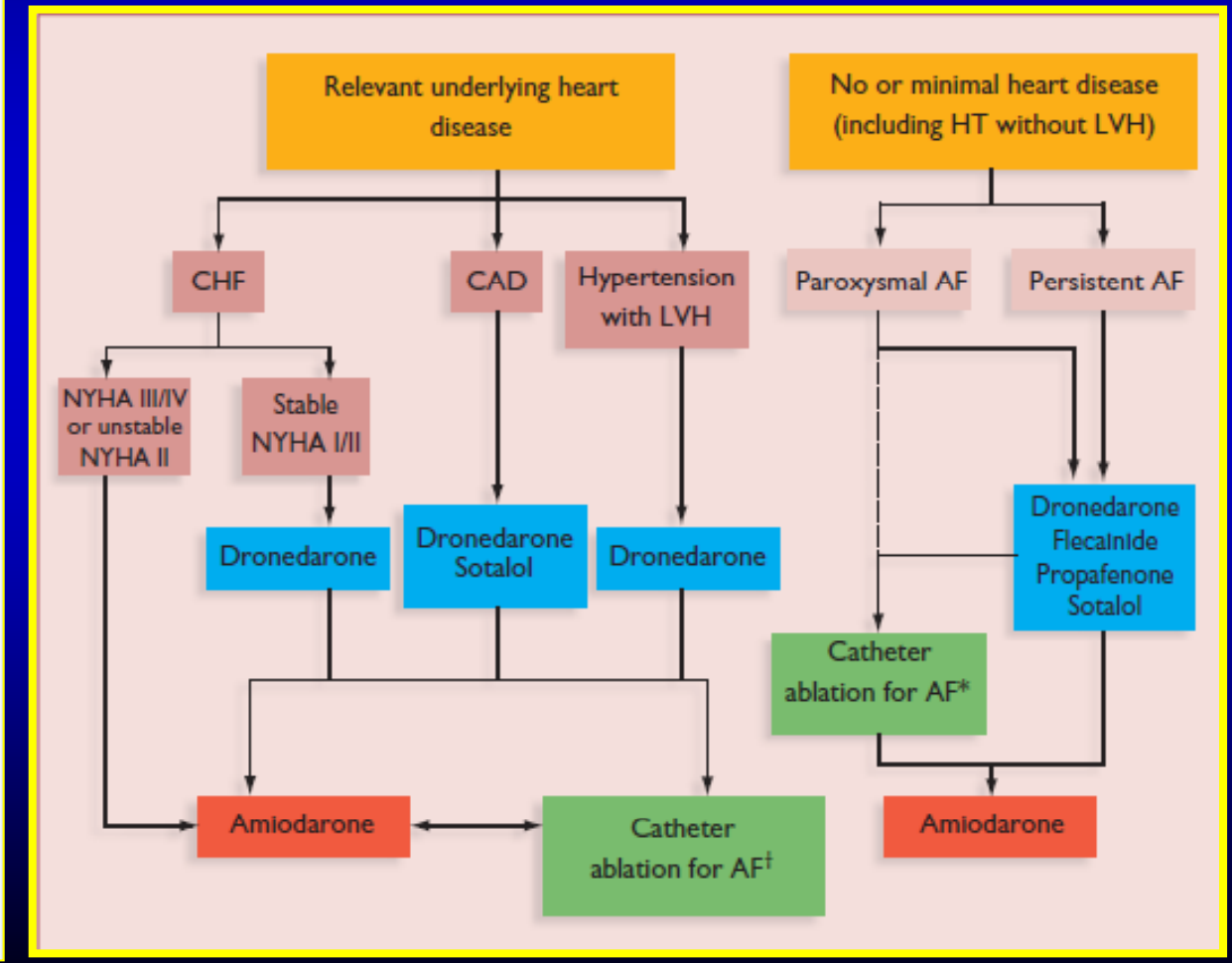
Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA)†

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

The European Society of Cardiology 2010.

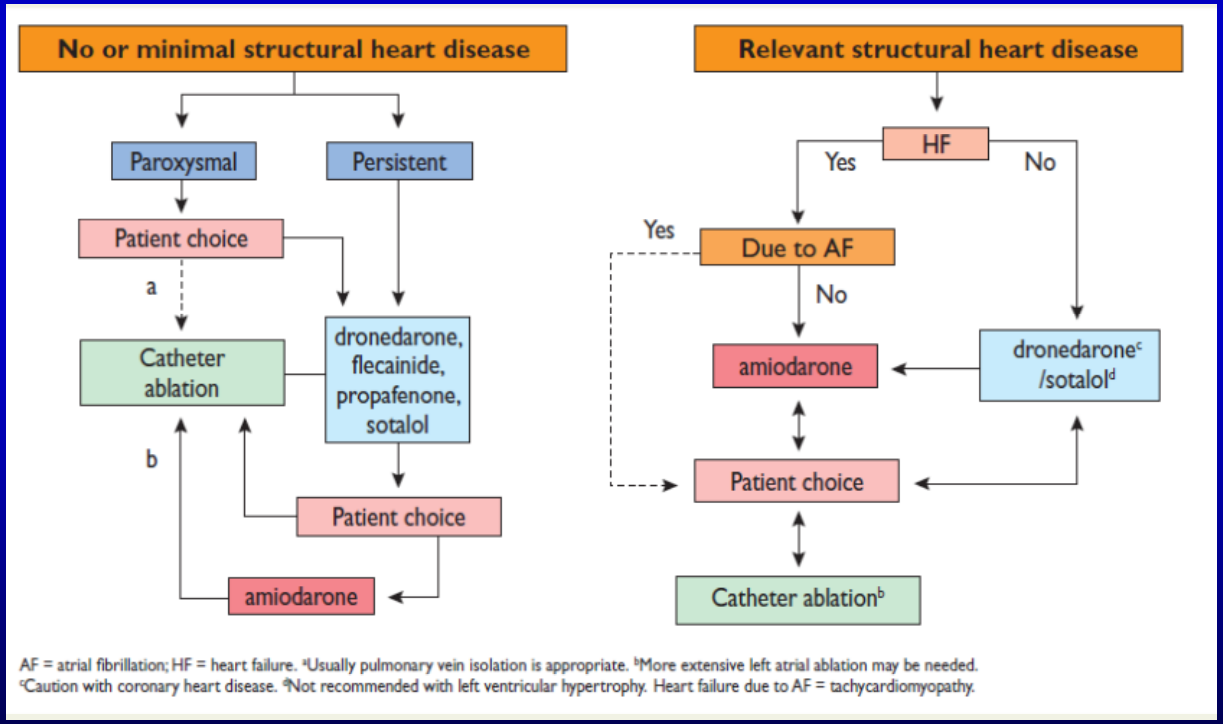


2012 focused update of the ESC Guidelines for the management of atrial fibrillation

European Heart Journal (2012) **33**, 2719–2747

Recommendations for left atrial ablation

Recommendations	Class[a]	Level[b]	Ref[c]
Catheter ablation of symptomatic paroxysmal AF is recommended in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.	I	A	192, 193
Catheter ablation of AF should target isolation of the pulmonary veins.	IIa	A	170, 172, 192, 194
Catheter ablation of AF should be considered as first-line therapy in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.	IIa	B	156–158
When catheter ablation of AF is planned, continuation of oral anticoagulation with a VKA should be considered during the procedure, maintaining an INR close to 2.0.	IIa	B	170, 181–184
When AF recurs within the first 6 weeks after catheter ablation, a watch-and-wait rhythm control therapy should be considered.	IIa	B	195



AF = atrial fibrillation; HF = heart failure. [a]Usually pulmonary vein isolation is appropriate. [b]More extensive left atrial ablation may be needed. [c]Caution with coronary heart disease. [d]Not recommended with left ventricular hypertrophy. Heart failure due to AF = tachycardiomyopathy.

Linee guida AIAC per la gestione e il trattamento della fibrillazione atriale. Aggiornamento 2013

G Ital Cardiol 2013;14(3):215-240

	Classe[a]	Livello[b]
• FA parossistica/persistente, senza o con lieve cardiopatia, sintomatica (con compromissione significativa della qualità di vita), refrattaria ad almeno un farmaco antiaritmico, quando la strategia clinica preferibile sia il mantenimento del ritmo sinusale stabile.	I	A
• FA parossistica, età relativamente giovane (<60 anni) senza o con lieve cardiopatia, senza o con lieve dilatazione atriale sinistra, sintomatica (con compromissione significativa della qualità di vita), come terapia di prima scelta, in alternativa ai farmaci antiaritmici.	IIa	A
• FA persistente di lunga durata, senza o con lieve cardiopatia, sintomatica (con compromissione significativa della qualità di vita), refrattaria ad almeno un farmaco antiaritmico, quando la strategia clinica preferibile sia il mantenimento del ritmo sinusale stabile.	IIa	C
• FA parossistica/persistente con cardiopatia strutturale, sintomatica (con compromissione significativa della qualità di vita), refrattaria ad almeno un farmaco antiaritmico, quando la strategia clinica preferibile sia il mantenimento del ritmo sinusale stabile.	IIa	C
• FA parossistica/persistente o persistente di lunga durata, quando la comparsa e la persistenza dell'aritmia comportano un significativo peggioramento della funzione di pompa del cuore, nonostante adeguata terapia farmacologica antiaritmica e per l'insufficienza cardiaca.	IIa	B
• FA persistente di lunga durata, con cardiopatia strutturale, sintomatica (con compromissione significativa della qualità di vita), refrattaria ad almeno un farmaco antiaritmico, quando la strategia clinica preferibile sia il mantenimento del ritmo sinusale stabile.	IIb	C
• Pazienti che opportunamente resi edotti dei rischi-benefici delle diverse opzioni terapeutiche scelgono la terapia ablativa per motivi psicologici o professionali.	IIb	C

[a]classe di raccomandazione.
[b]livello di evidenza.

Complicanza	Incidenza (%)
Morte	0.1
Tamponamento cardiaco	0.0-2.9
Eventi tromboembolici	0.0-1.1
Embolismo cerebrale silente	7-40.5
Stenosi vene polmonari	0.0-0.5
Paralisi nervo frenico	0.1-17
Fistola atrio-esofagea	0.03-0.25
Danno vagale periesofageo	1
Complicanze vascolari	0.2-2.5
Occlusione dell'arteria circonflessa	0.002
Intrappolamento del catetere nella mitrale	0.01
Flutter atriale atipico/tachicardia atriale	3-40

CONCLUSIONI

Nel corso degli ultimi 10 anni la terapia ablativa ha definitivamente dimostrato di poter modificare significativamente la storia naturale della FA

Ha la potenzialità di curare stabilmente soprattutto il paziente con FA parossistica, ma può ottenere risultati soddisfacenti anche nelle forme di FA persistente

In alcuni casi l'effetto terapeutico può essere transitorio e richiedere dopo mesi o anni la ripetizione della procedura.

Può causare complicanze periprocedurali significative la cui incidenza tuttavia è inversamente proporzionale all'esperienza dell'operatore.