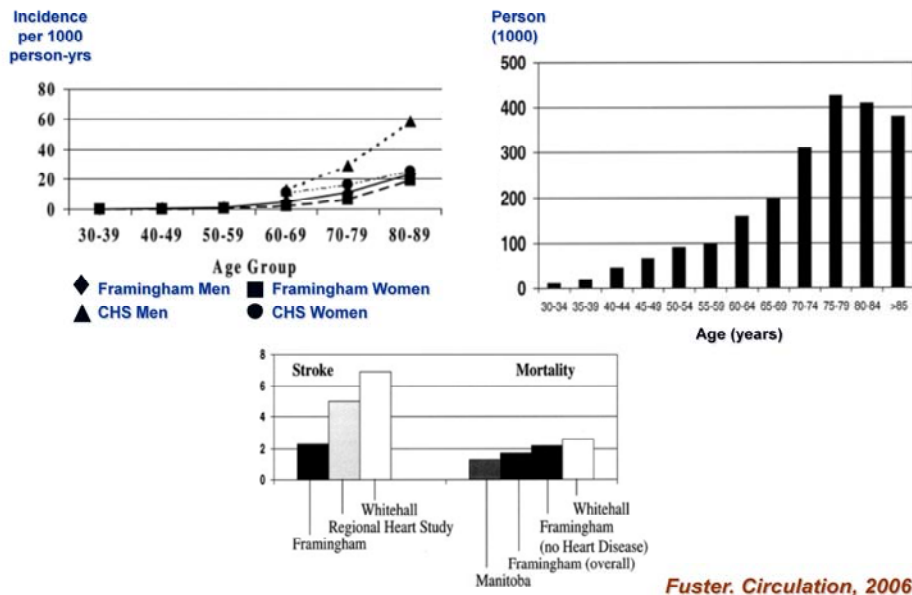


# ***Catheter Ablation of AF Electrogram-based Approach***

***Shih-Ann Chen, M.D.***

***Division of Cardiology, Taipei Veterans General Hospital  
and National Yang-Ming University, Taipei, Taiwan***

## Prevalence of AF



Atrial fibrillation is the most common cardiac arrhythmia seen in clinical practice and can induce cardiac dysfunction and strokes.

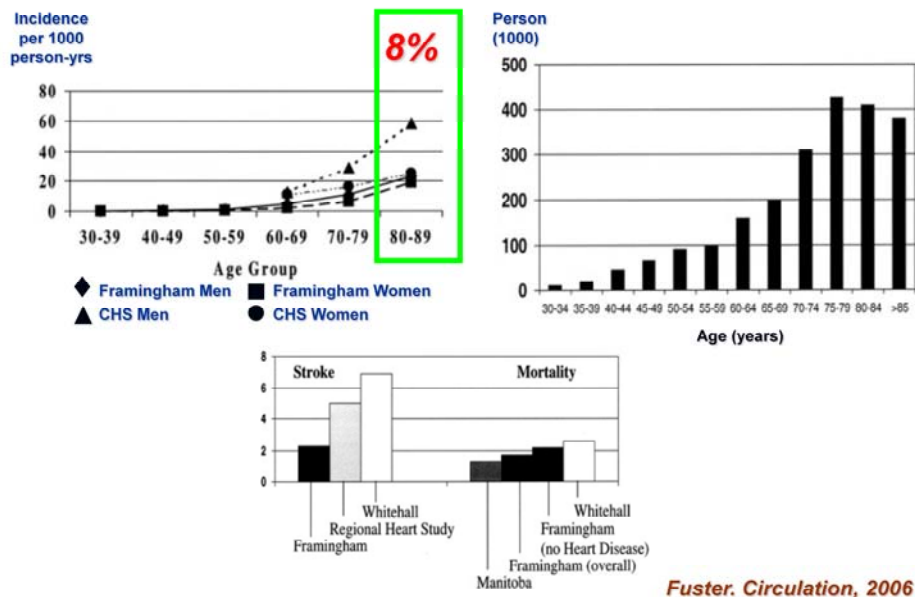
The prevalence of AF is around 0.4 to 1%, and increases with aging.

The incidence of AF in patients more than 80 years old is around 8% of population

It can cause stroke. The incidence of stroke in patients with AF is 2 to 7 times higher than those without it.

The mortality was increased 1.5 to 3-fold compared with patients without AF

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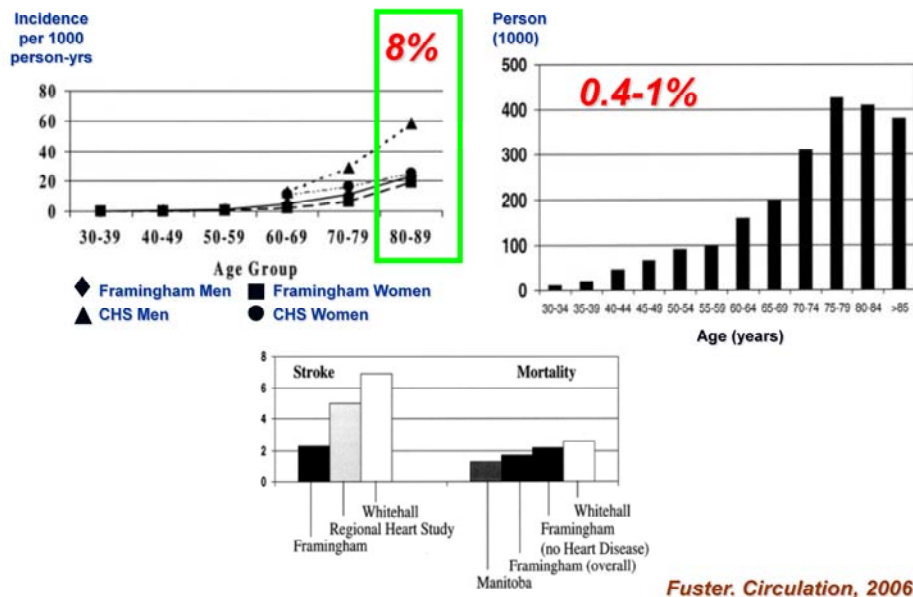
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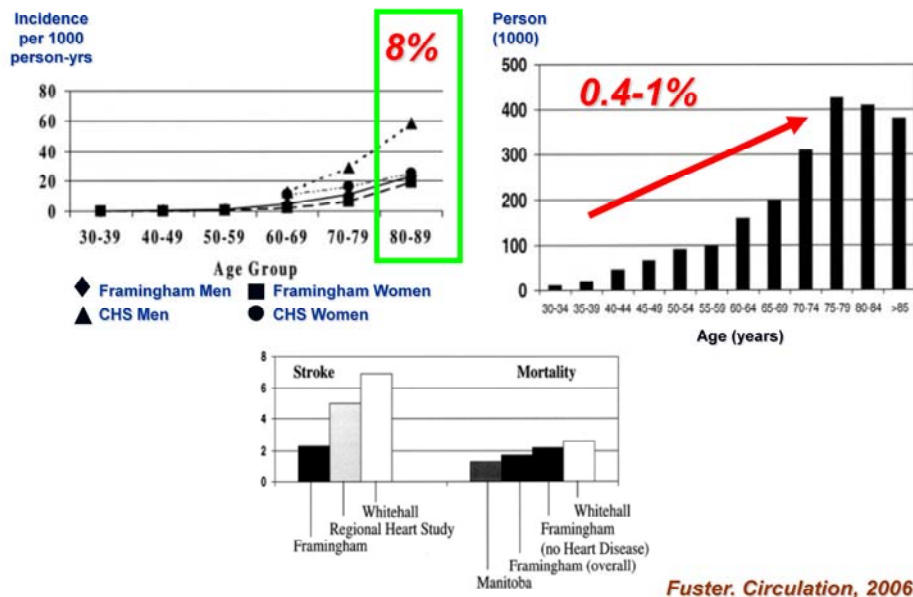
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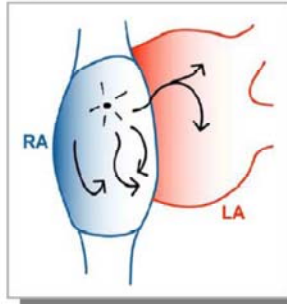
## ***Mechanism of AF***

---

***Multiple factors ?***

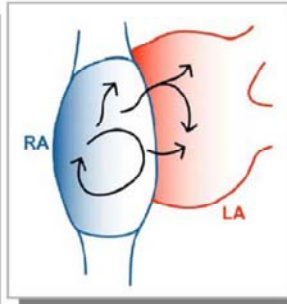
## ***Idea of AF Mechanism in Earlier 20th Century***

***Ectopic focus***



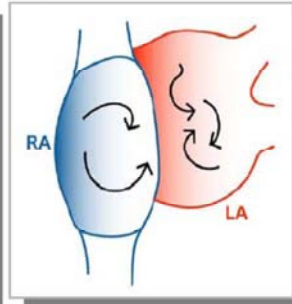
***Engelmann***

***Single circuit  
reentry***



***Lewis***

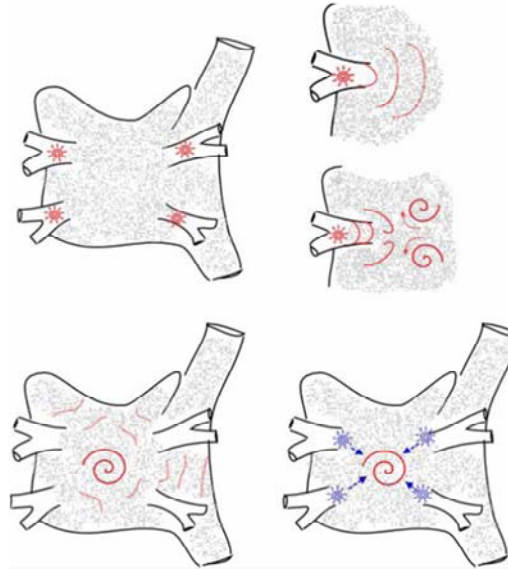
***Multiple-circuit  
reentry***



***Garrey***

***Nattel. 2005***

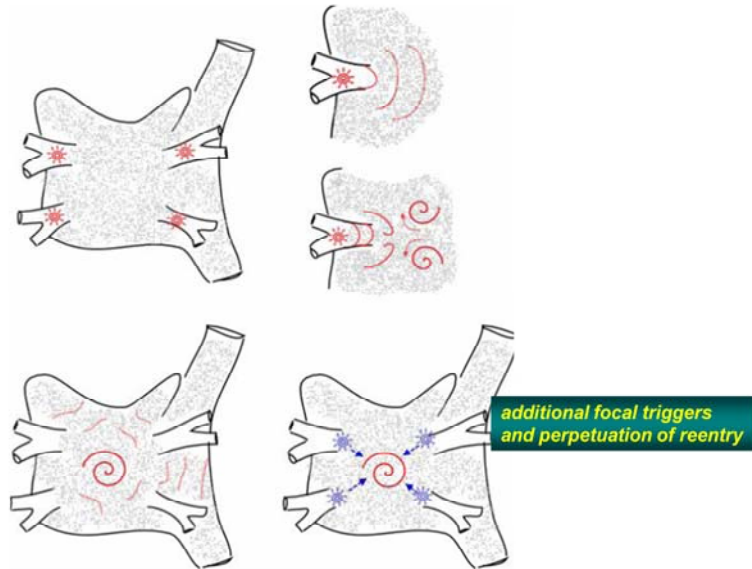
### ***Focal triggers leading to initiation of reentry***



Eventually, atrial remodeling leads to additional focal triggers and perpetuation of reentry.



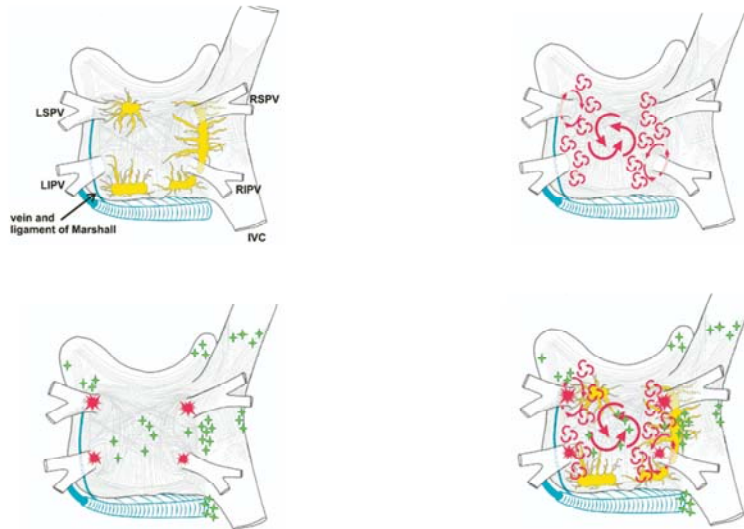
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## **Mechanisms of Atrial Fibrillation**

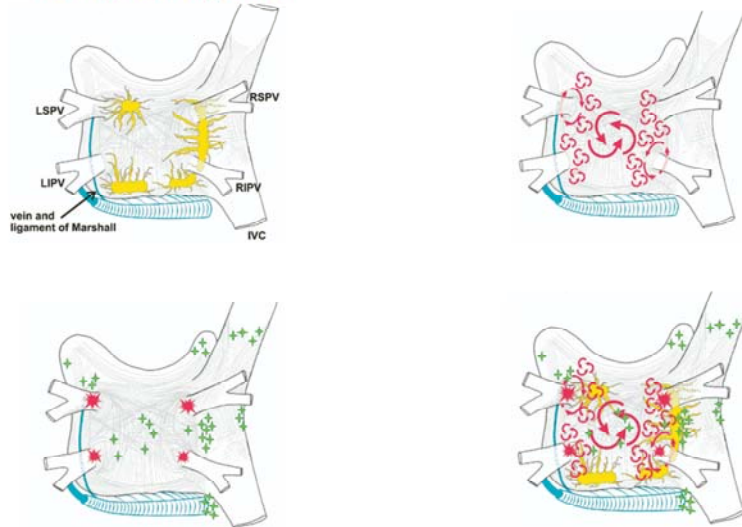
( HRS/EHRS/ECAS consensus document, 2007 )



# Mechanisms of Atrial Fibrillation

( HRS/EHRS/ECAS consensus document, 2007 )

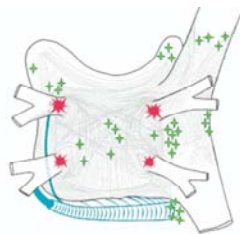
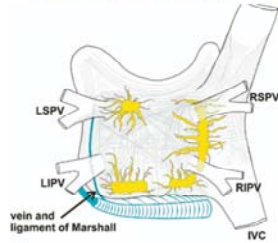
## A. *Ganglionic plexi*



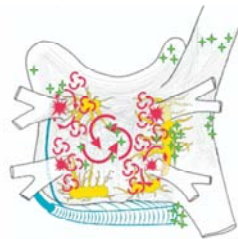
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( HRS/EHRS/ECAS consensus document, 2007 )

## A. *Ganglionic plexi*



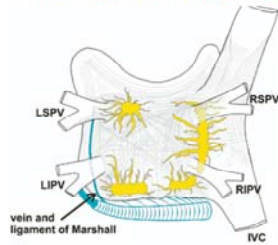
## B. *Multiple reentrant wavelets*



# Mechanisms of Atrial Fibrillation

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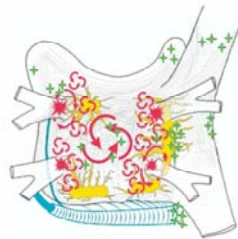
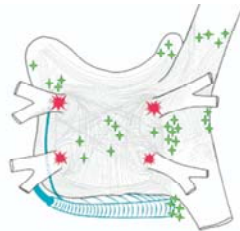
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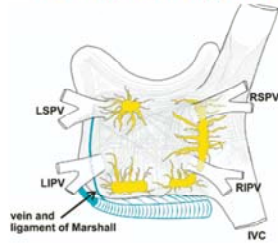
## C. *PV and non-PV triggers*



# Mechanisms of Atrial Fibrillation

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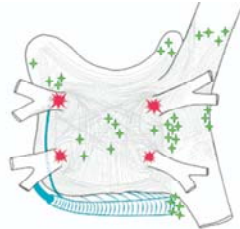
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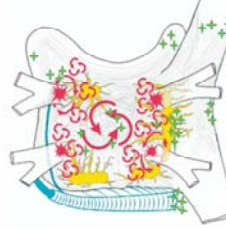
## B. Multiple reentrant wavelets



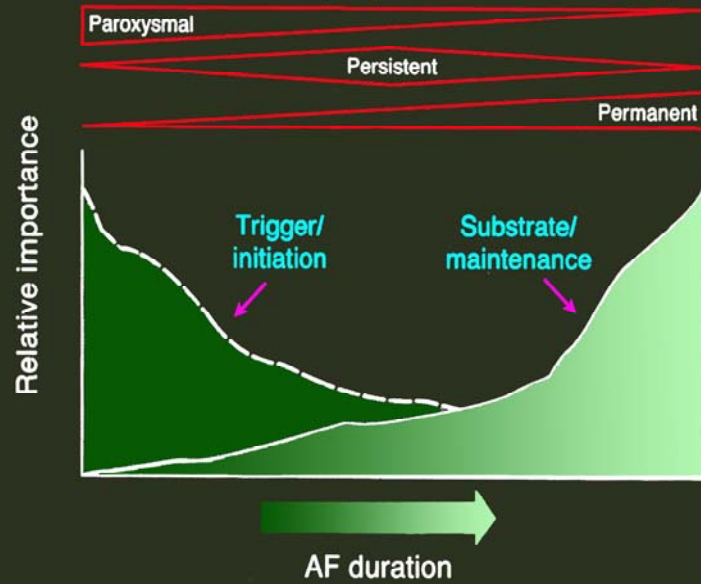
## C. PV and non-PV triggers



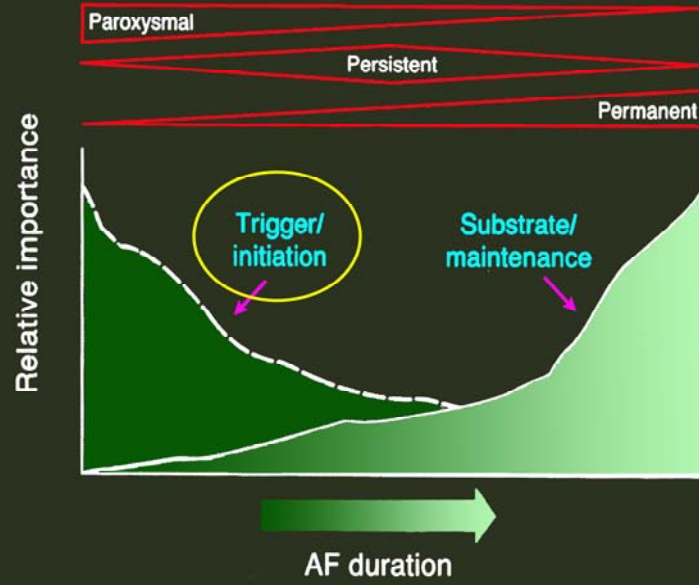
## D. Multiple mechanisms



Pathophysiological adaptation of atrial substrate as the duration of AF progress → **Remodeling**

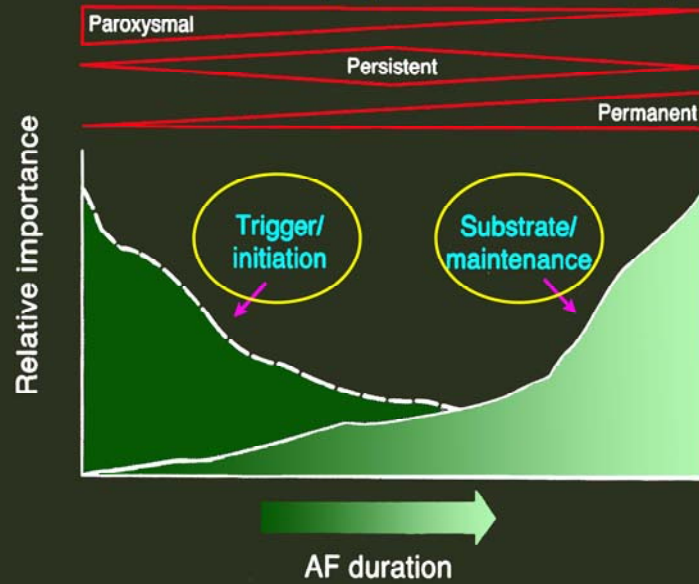


Pathophysiological adaptation of atrial substrate as the duration of AF progress → **Remodeling**





Pathophysiological adaptation of atrial substrate as the duration of AF progress → **Remodeling**



## ***Indications for Catheter AF Ablation***

- *Symptomatic AF ( paroxysmal and chronic ) refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication.*
- *Rarely, it may be appropriate to perform AF ablation as first line therapy.*
- *Selected symptomatic patients with heart failure and/or reduced ejection fraction.*

*AHA/ACC/ESC 2006, HRS/EHRS/ECAS consensus document 2007*

The ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation, written in collaboration with the Heart Rhythm Society, state that "Catheter ablation is a reasonable alternative to pharmacological therapy to prevent recurrent AF in symptomatic patients with little or no LA enlargement" (Class 2A recommendation, level of evidence C).

It is noteworthy that the only Class 1 indication in this section of the document states that treatment of precipitating or reversible causes of AF is recommended before initiating antiarrhythmic drug therapy.

Further, the maintenance of sinus rhythm treatment algorithm lists catheter ablation as second-line therapy for all categories of patients.

The Task Force supports these recommendations. In particular, the Task Force agrees that catheter ablation of AF in general should not be considered as first line therapy.

There is a consensus among the Task Force that the primary indication for catheter AF ablation is the presence of symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication (Table 1).

The Task Force also recognizes that in rare clinical situations, it may be appropriate to perform catheter ablation of AF as first line therapy. Catheter ablation of AF is also appropriate in selected symptomatic patients with heart failure and/or reduced ejection fraction. The presence of a LA thrombus is a contraindication to catheter ablation of AF. It is important to recognize that catheter ablation of AF is a demanding technical procedure that may result in complications. Patients should only undergo AF ablation after carefully weighing the risks and benefits of the procedure.

Indications for Catheter AF Ablation

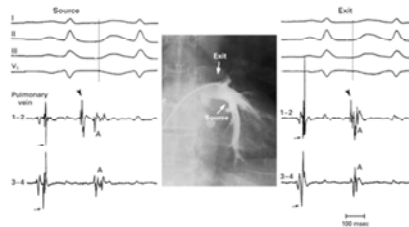
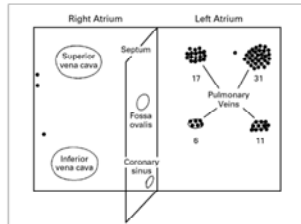
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# ***Catheter Ablation of AF***

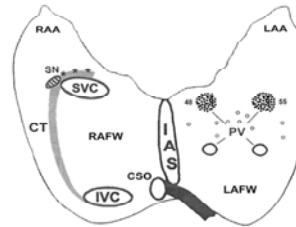
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## ***Evolution of Technique***

# Distribution of AF trigger



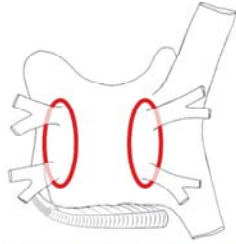
**Haissagurre et al. NEJM 1998**



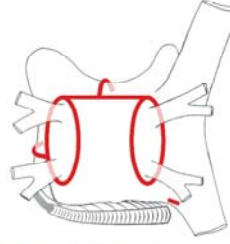
**Chen et al. Circulation 1999**

## ***Lesion Sets for Catheter Ablation of AF*** ***( Consensus Document HRS/EHRS/ECAS, 2007 )***

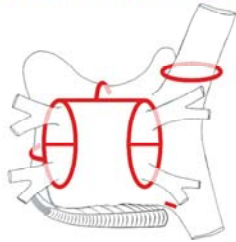
**A. PV Isolation**



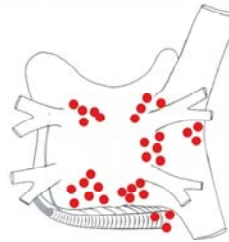
**B. PVI, Roof line, CTI**



**C. PVI, Roof, CTI, Carina, SVCI**



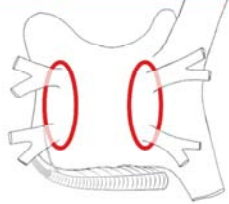
**D. DF and CFAE**



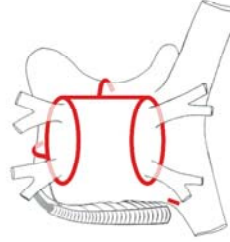
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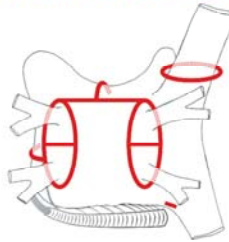
***Make sure to complete isolation***



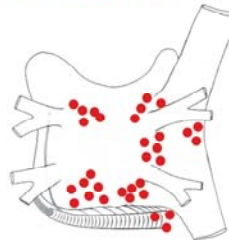
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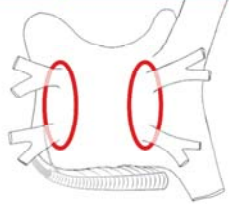
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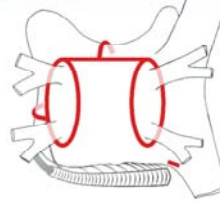
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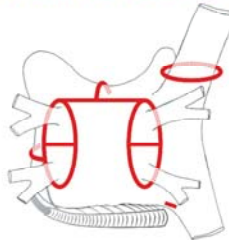


### **B. PVI, Roof line, CTI**

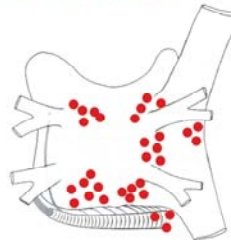
***Complete line block***



### **C. PVI, Roof, CTI, Carina, SVCI**



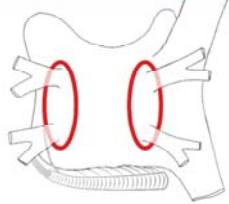
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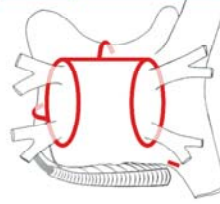
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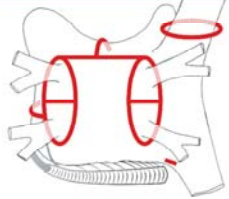
### **B. PVI, Roof line, CTI**

***Complete line block***

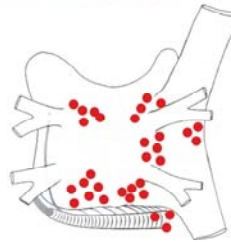


### **C. PVI, Roof, CTI, Carina, SVCI**

***Find the residual PVP or non-PV ectopy***



### **D. DF and CFAE**

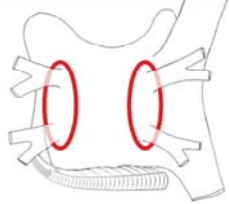




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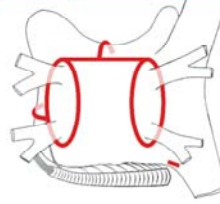
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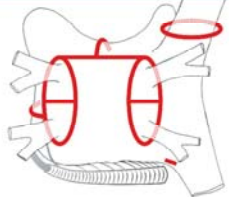
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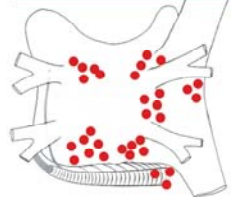
### **C. PVI, Roof, CTI, Carina, SVCI**

***Find the residual PVP or non-PV ectopy***



### **D. DF and CFAE**

***AF substrate mapping***



## ***AF Ablation Techniques (1)***

---

1. Complete PV isolation is the cornerstone for most AF ablation procedures.
2. Careful identification of the PV ostia is mandatory to avoid ablation within the PVs.
3. If a non-PV trigger is identified at the time of an AF ablation procedure, it should be targeted, if possible.

## ***AF Ablation Techniques (2)***

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4. If additional linear lesions are applied, line completeness should be demonstrated by mapping or pacing maneuvers.
5. Ablation of the cavotricuspid isthmus (CTI) is recommended only in patients with a history of typical atrial flutter (AFL) or inducible CTI dependent AFL.
6. If patients with longstanding persistent AF are approached, ostial PV isolation alone may not be sufficient.

## ***Current Catheter Ablation Techniques for Chronic AF***

- ♦ **Pure pulmonary vein isolation (PVI)**
- ♦ **Pure substrate modification without PVI**
- ♦ **PVI with adjunctive substrate modification**
  - ♦ **Anatomic approach: linear ablation**
  - ♦ **Electrogram-guided approach: based on fractionation mapping and/or frequency mapping.**

CFAE mapping may be a clinically useful tool for targeting ablation of CFAE sites as an adjunct to current methods of circumferential PV isolation.

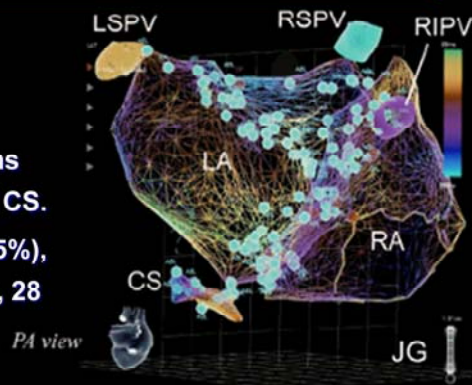
## **CFAE Ablation**

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***Adjunctive procedure ?***

## Substrate Modification: Target the Fractionated Electrograms

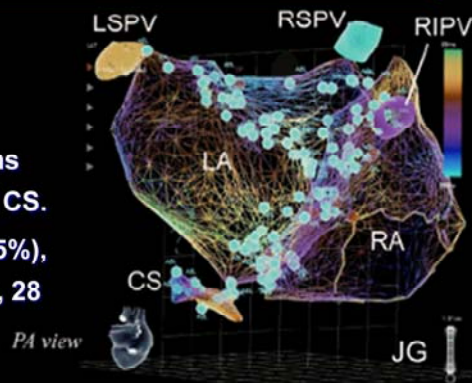
- ◆ 121 patients (age 63 yrs, 57 paroxysmal, 64 chronic) under CARTO mapping during AF.
- ◆ Target the complex electrograms at LA (mostly septum), RA, and CS.
- ◆ Acute termination in 115/121 (95%), one year F/U 63 % without drug, 28 % with ibutilide, overall 91 % successful rate.



Nademanee et al, JACC, 2004

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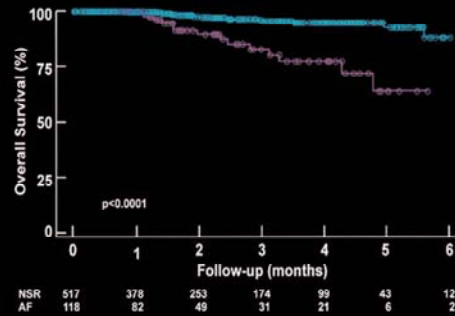
**Does CFAE represent the atrial substrate ??**  
**What are the mechanisms of CFAE ??**

*Nademanee et al, JACC, 2004*

CFAE approach

## Clinical Outcome of High Risk Group of AF Underwent CFE Ablation

- ◆ 674 patients ( $67 \pm 12$  yrs, 40%=PAF, 60%=non-paroxysmal).
- ◆ Mean LA= $45 \pm 6$  mm, LVEF<40% in 22%.
- ◆ Complication rate 0.8%; 81% remained in SR after mean follow-up period of 2.3 years, only 13% with AAD.
- ◆ SR after AF ablation is a marker of relatively low mortality and stroke risk.

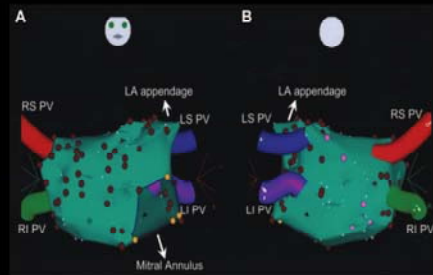


Nademanee et al. JACC 2008



## Is Pure CFAE Ablation Enough to Treat CAF?

- ❖ 100 patients with CAF underwent CFAE ablation in LA/CS, 16% with AF termination during the procedure.
- ❖ Follow up ( 14 Mo ), only 33% were in SR, 44% need second procedures



Sites Where CFAEs Were Ablated

Site	Patients, %
Left atrium	
Anterior wall	91
PV antrum or ostium	90
Septum	75
Roof	64
Posterior wall	41
Mitral isthmus	21
Coronary sinus	55

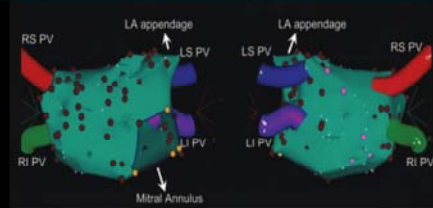
*Oral et al. Circulation 2007*

## Is Pure CFAE Ablation Enough to Treat CAF?

### Controversial Results !!

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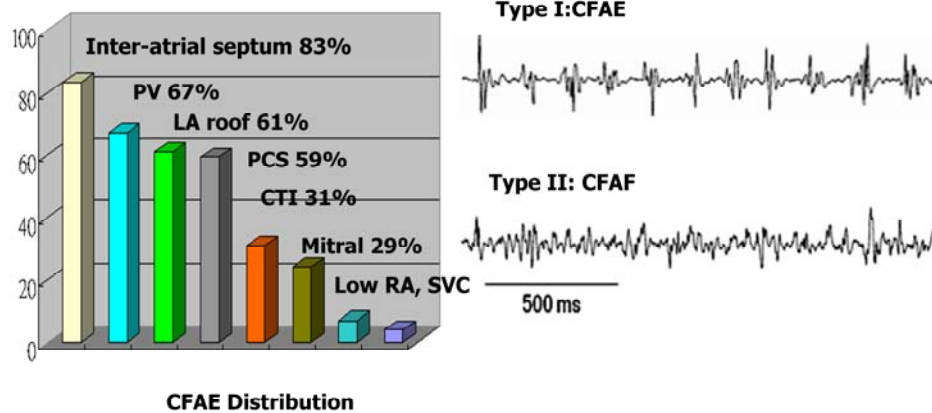
*Oral et al. Circulation 2007*

# **How to Detect CFAÉ ?**

**Visual inspection**  
**Automatic algorithm**  
**CARTO XP**  
**NavX system 7.0**

## Operator-Determined CFEs

Low amplitude, multicomponent potentials (0.05-0.25 mV) that are either continuous or separated by short isoelectric interval (< 120 msec) over a 10 seconds period.



Nademanee et al. JACC 20  
Nademanee et al. JACC 20

## Complex Fractionated Atrial Electrograms (CFAE)

- CFAE: potential AF substrate sites and target sites for AF ablation.
- CFAE are electrograms with highly fractionated potentials or with a very short cycle length (120 ms).
- CFAEs usually are low-voltage multiple potential signals between 0.06 and 0.25 mV.

**Non-CFAEs:** Discrete Eg with isoelectric segment and CL >120 ms.



**Type IIa :** Fractionated Eg with continuous activity.



**Type IIb :** Fractionated Eg with isoelectric segment and the CL < 120 ms.



Taipei VGH 2008

So, which type of electrograms could be the target during RFA ?

CFAE was thought to be fractionated Eg with continuous activity or isoelectric segment CL less than 120 ms

However, **CFAEs are generated from multi-mechanisms** with Multi-Definition

→ **Understanding the Activation Pattern Before CFAE ablation** → may avoid targeting the “bystander CFAE”, make ablation more effectively!!

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Taipei VGH 2008

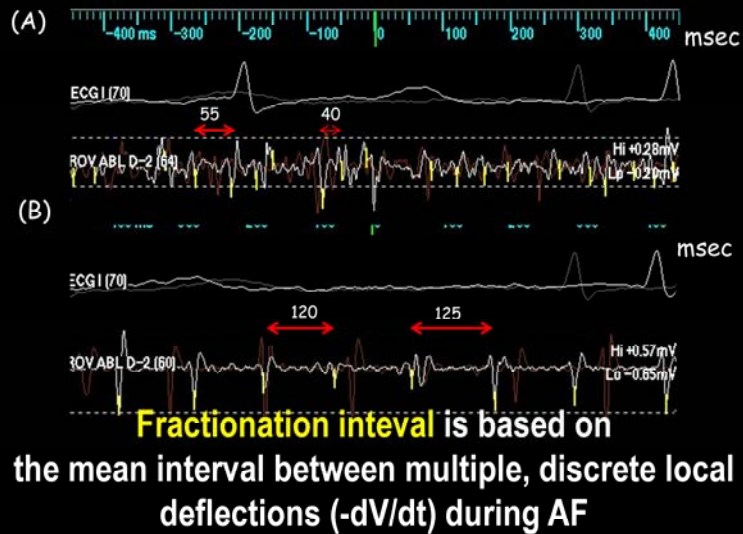
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## How to identify the most continuous fractionation with consistency (The CFE algorithm)



The magnitude of fractionation was quantified by the fraction interval algorithm. It is defined as the mean interval between multiple, and discrete deflections during atrial fibrillation

***Difference in the Automatic Algorithm of CFEs  
in 3D Mapping System***

**NavX      CARTO**

**Detection Algorithm**

Interval analysis	•	•
CFEs event frequency	X	•

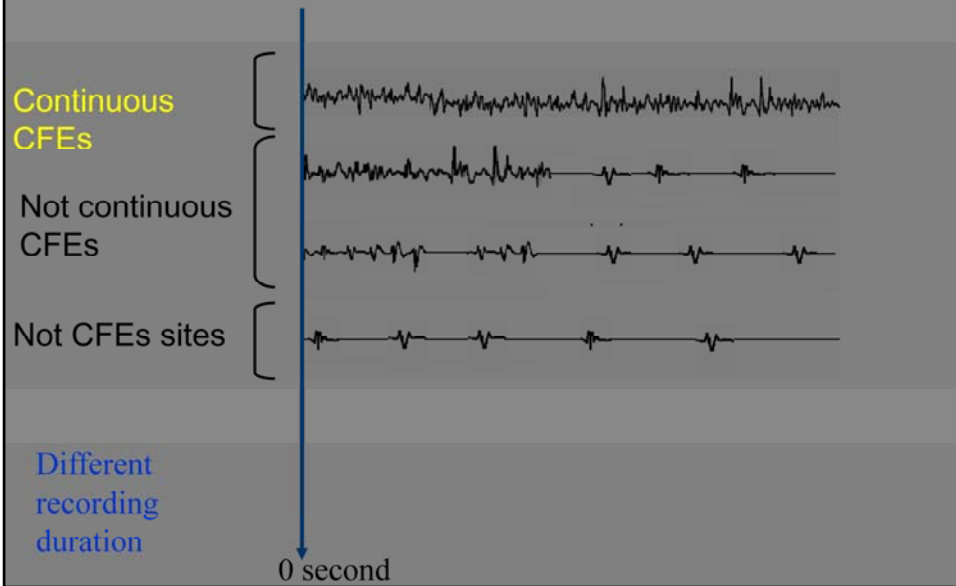
**Electrogram characteristics**

**detection**

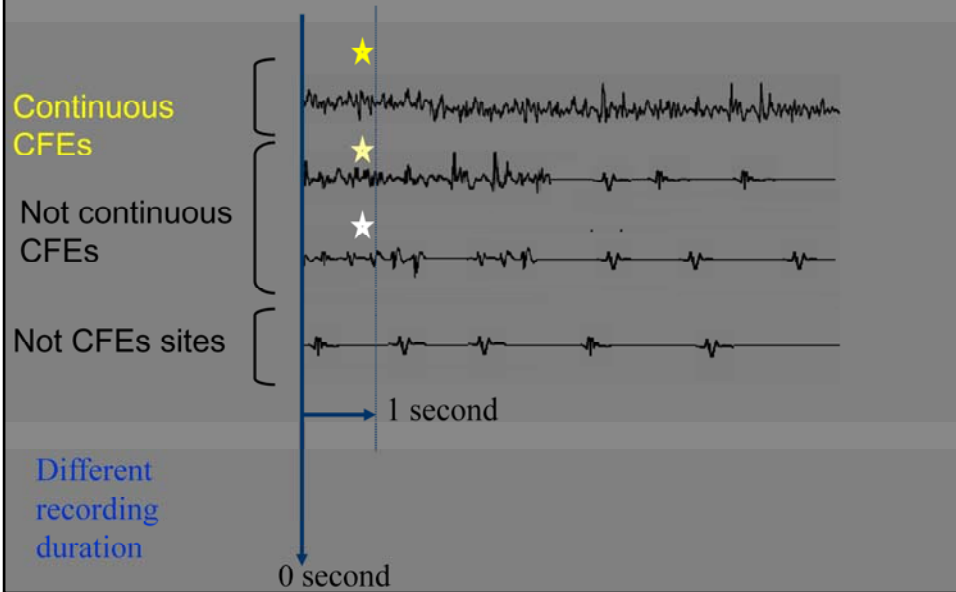
Adjustable mapping duration	•	X
Adjustable refractory period	•	•
Low voltage detection thresholds	•	•
High voltage cut off thresholds (avoid far field)	X	•
Exclude far-field by Eg width (avoid far ield)	<b>Taipei VGH, 2009</b>	



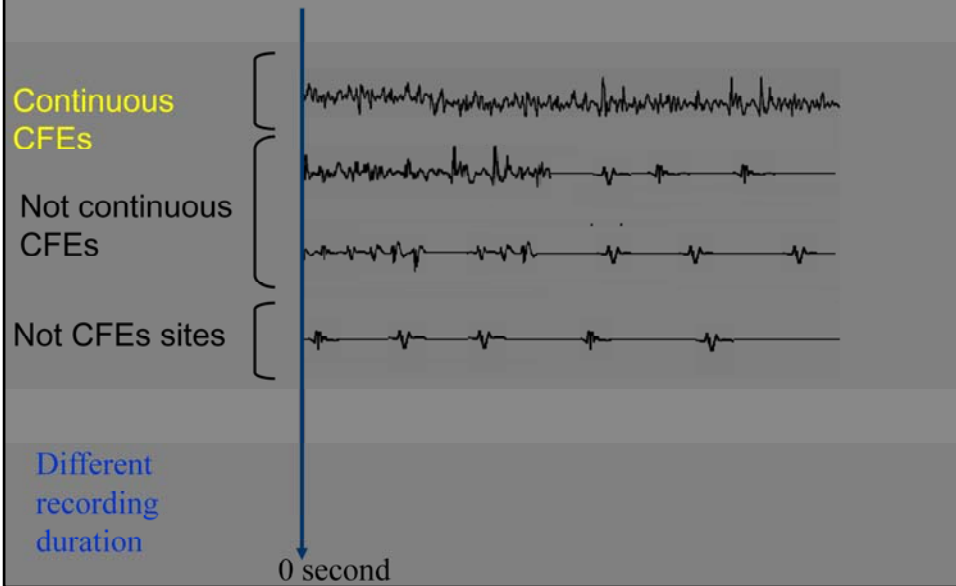
## *The requirement of long-term recording in CFE mapping in 3D mapping*



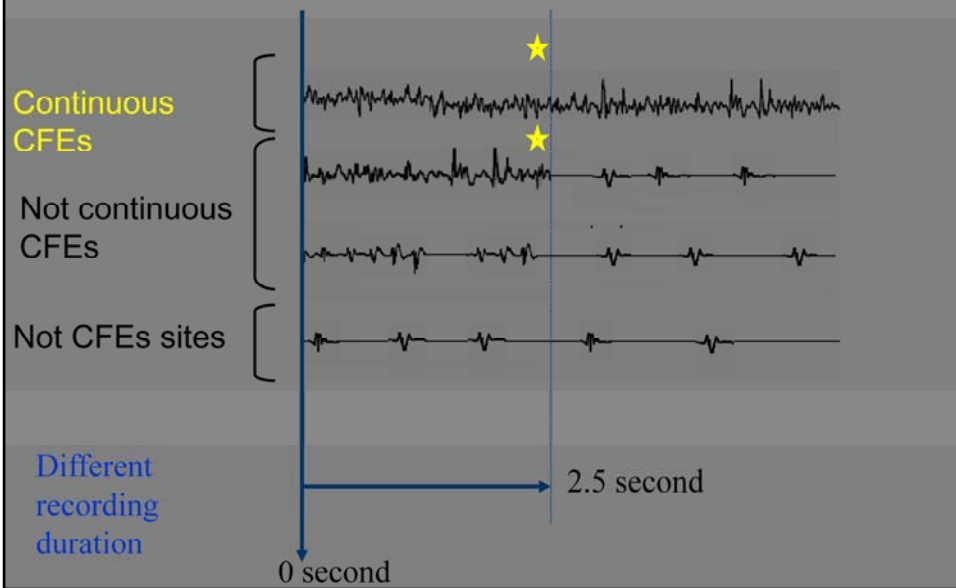
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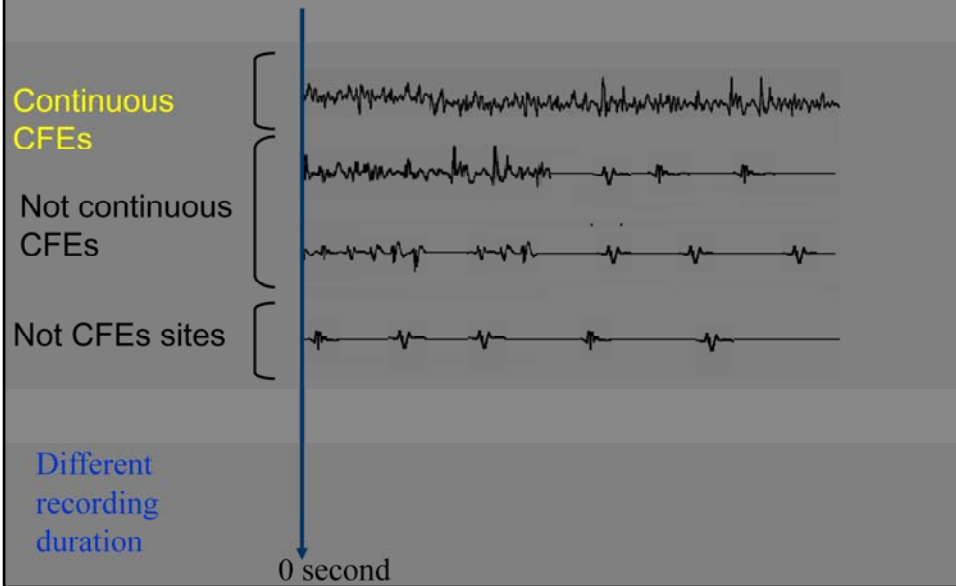
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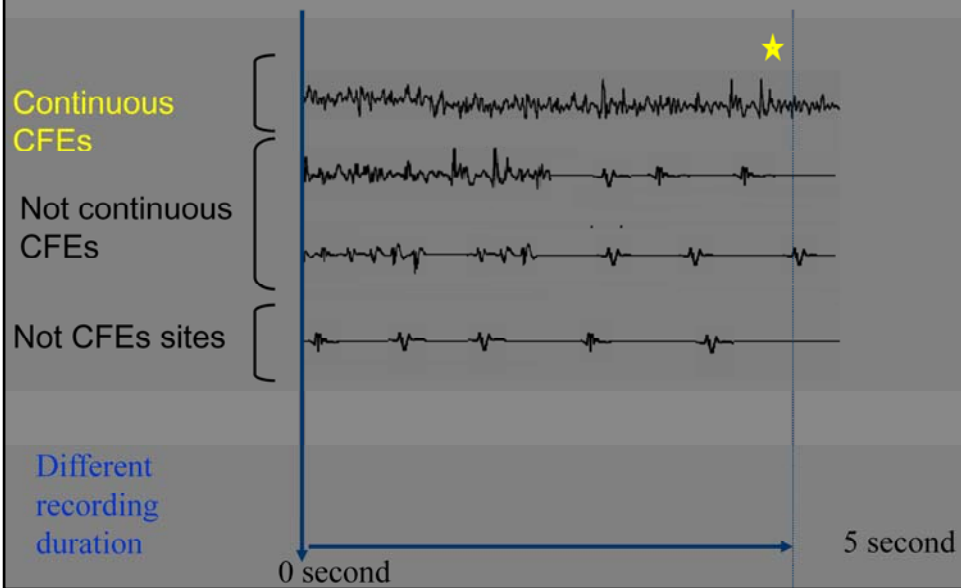
## *The requirement of long-term recording in CFE mapping in 3D mapping*



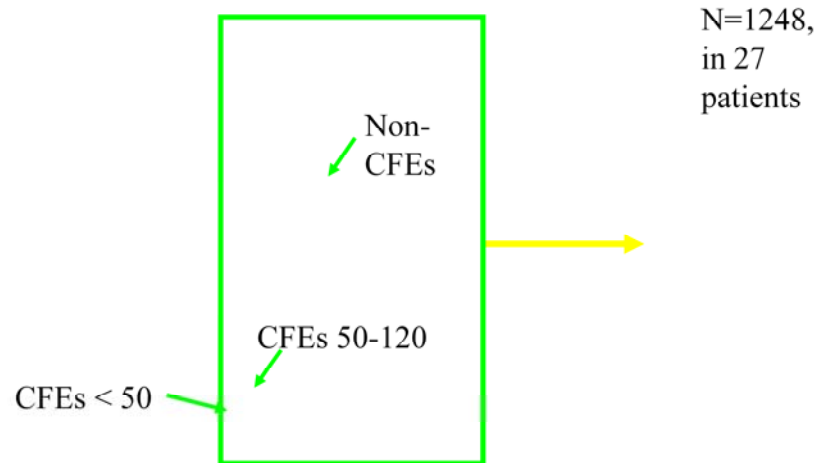
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## *The requirement of long-term recording in CFE mapping in 3D mapping*

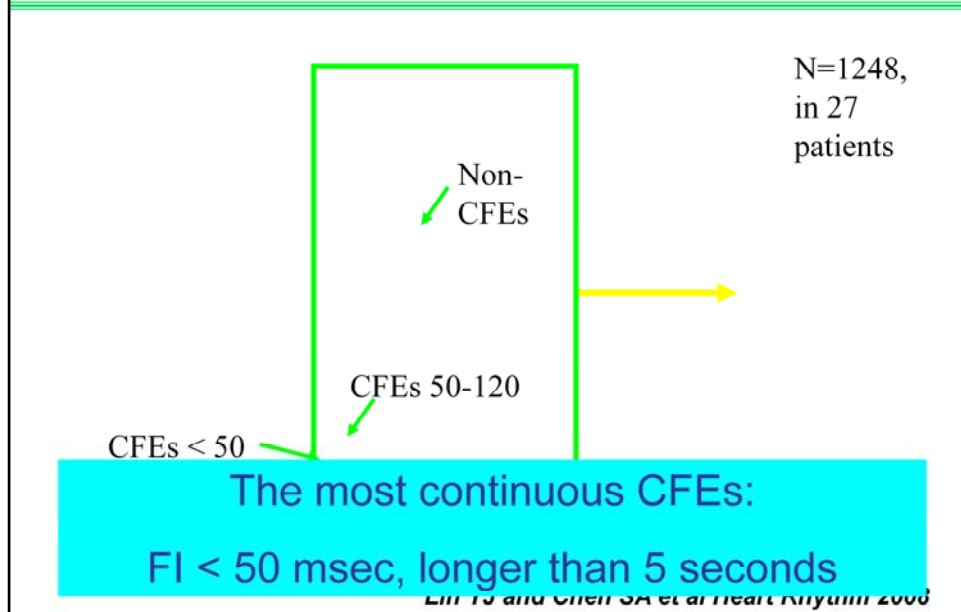


## ***Effect of Duration on the Consistency***



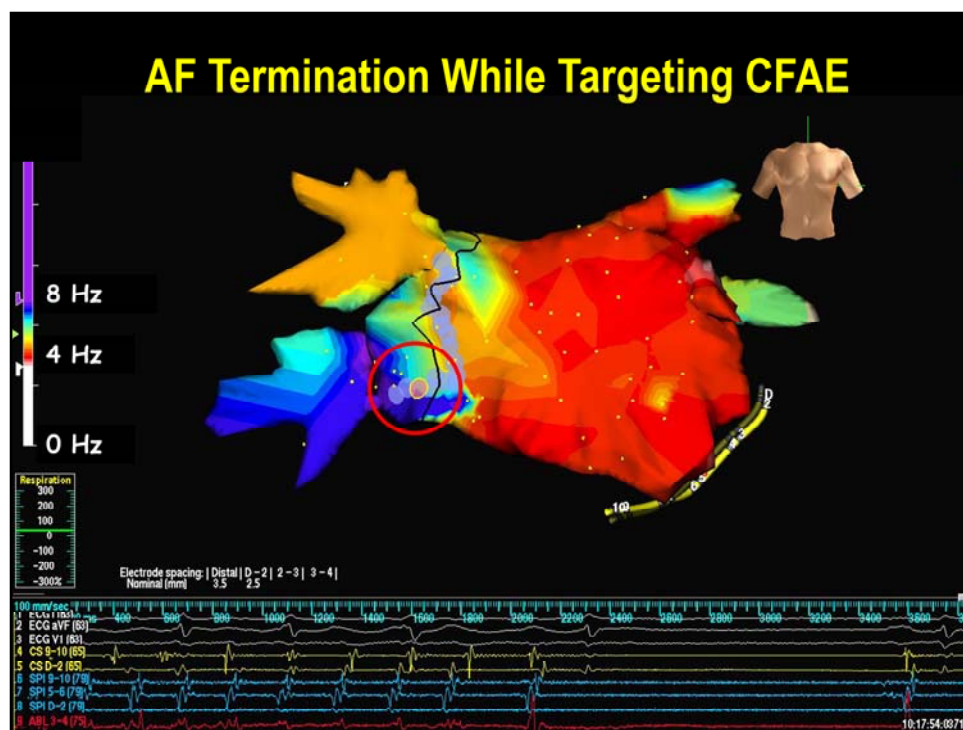
*Lin YJ and Chen SA et al Heart Rhythm 2008*

## ***Effect of Duration on the Consistency***



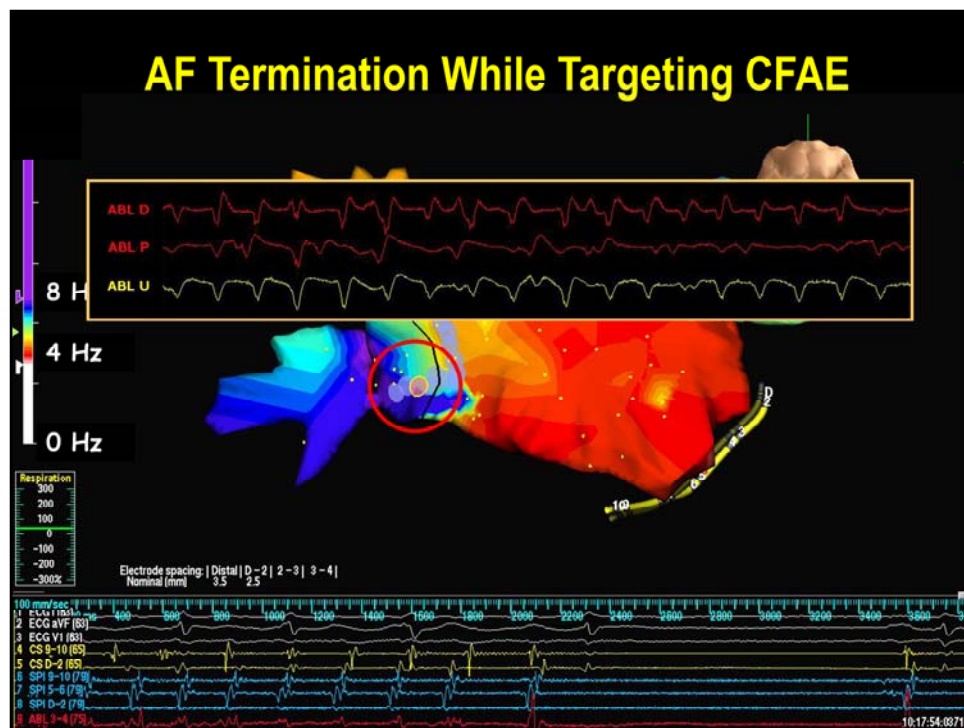


**What Is The Mechanism of CAFÉ ?**



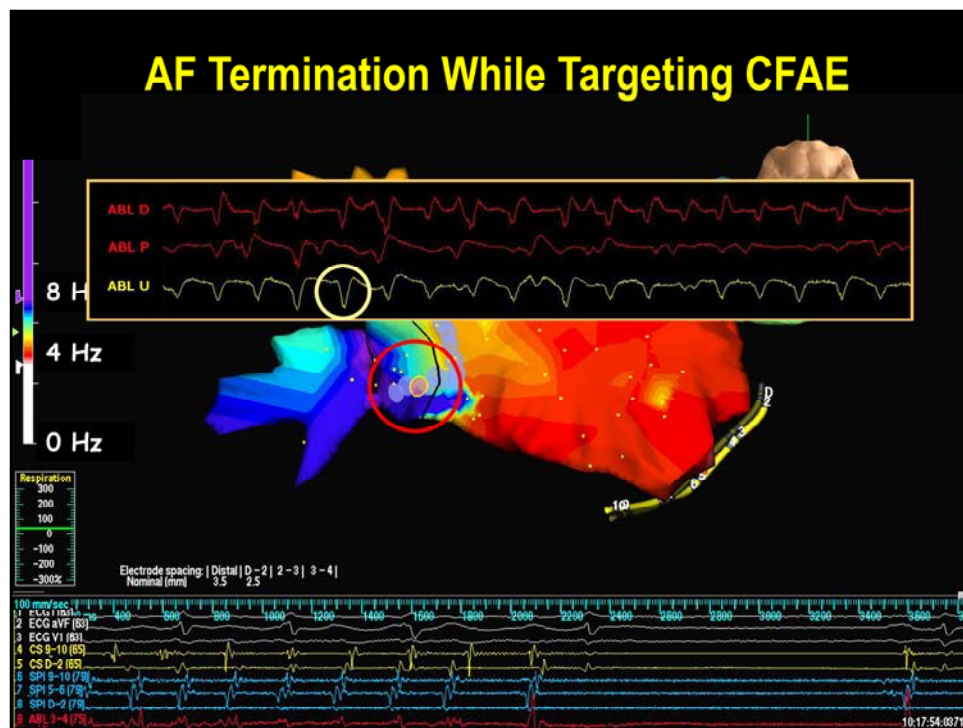
AF was terminated while encircling RPV crossing anterior septum CFE site.

The unipolar electrogram over this site showed repetitive QS pattern before termination shot.



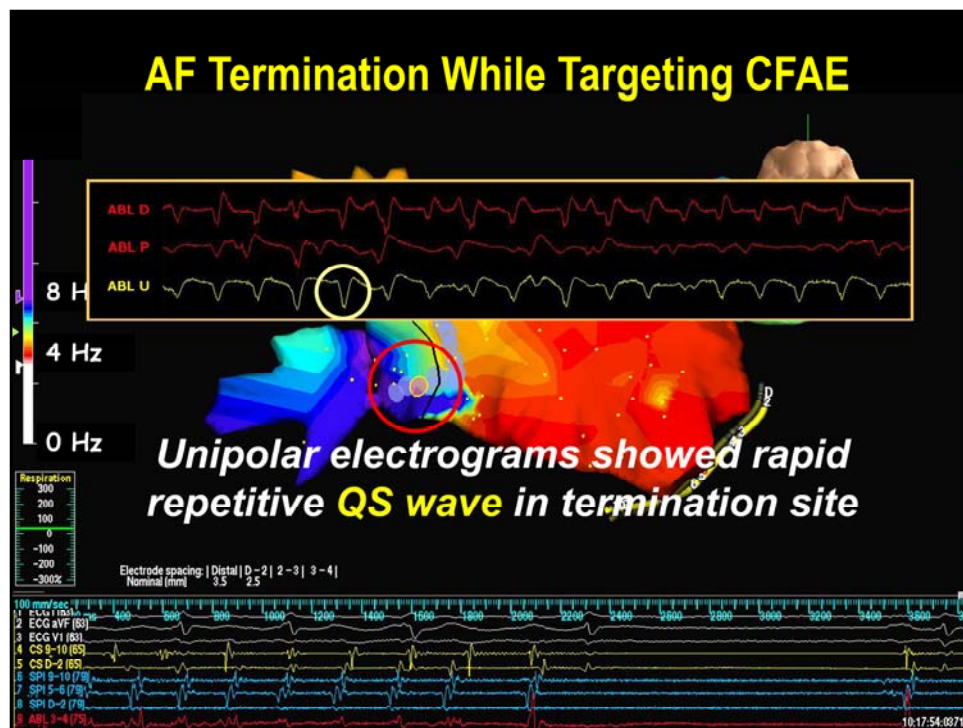
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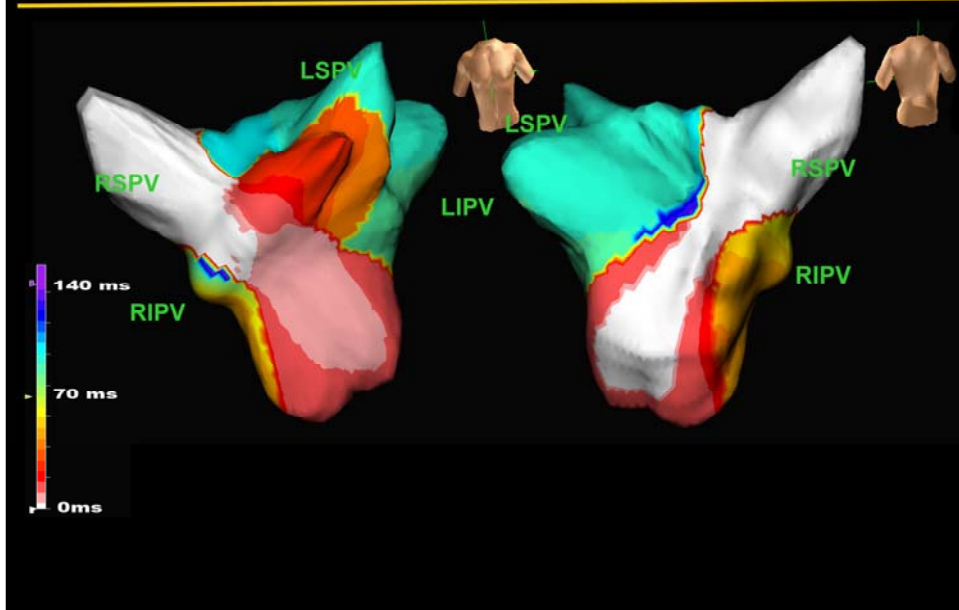
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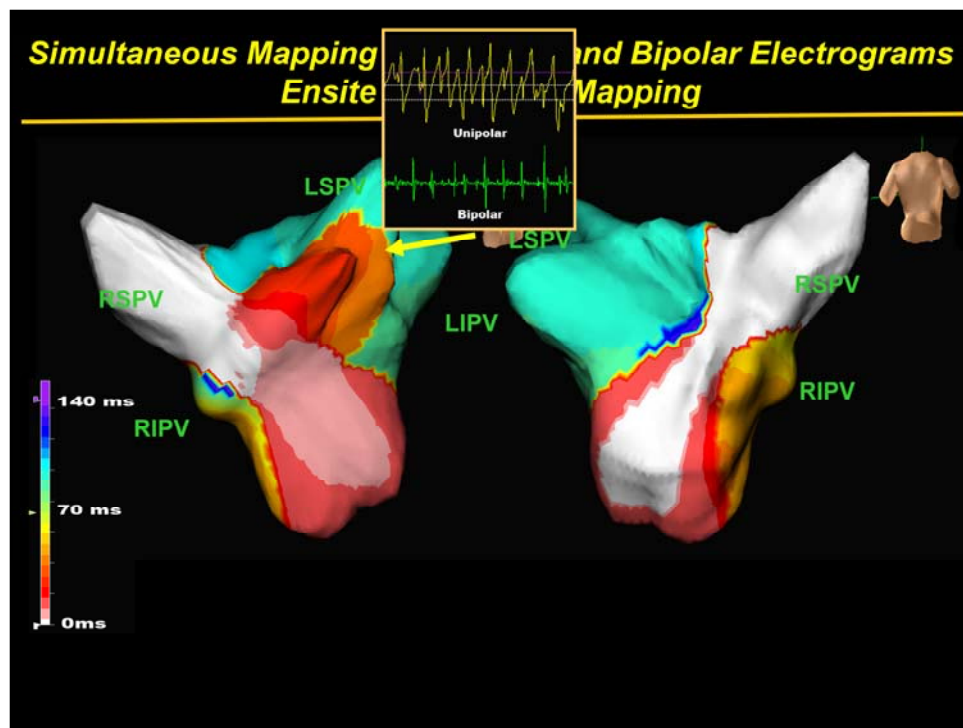
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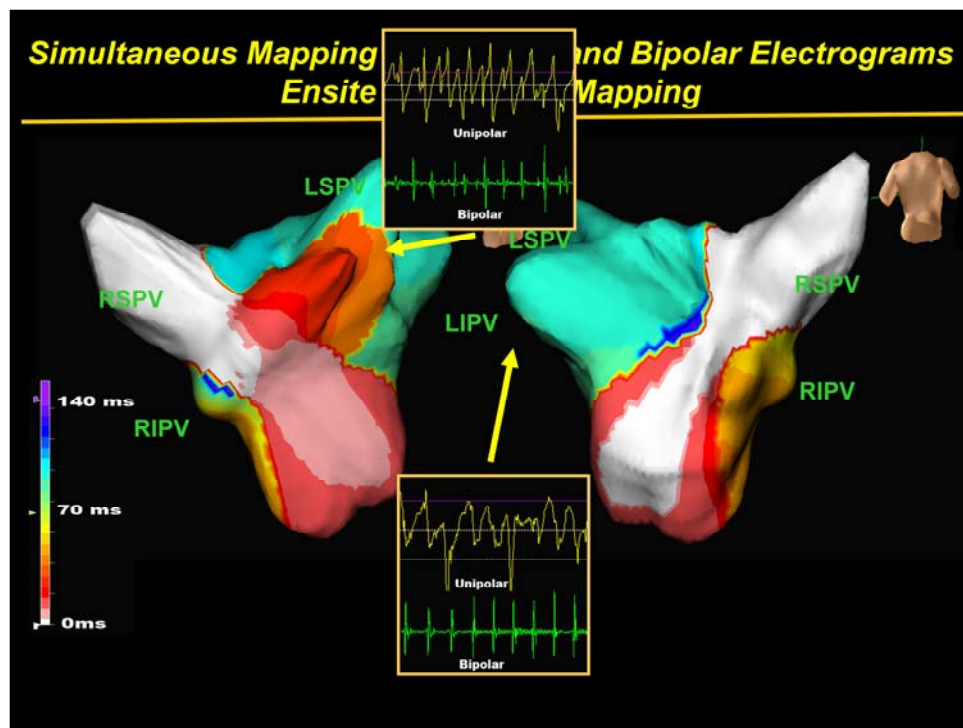
### ***Simultaneous Mapping of Unipolar and Bipolar Electrograms Ensite Noncontact Mapping***



In Ensite Array mapping, we found that bipolar CFE site with CL < 120 ms (RSPV and mid roof) showed S wave predominant unipolar electrogram.

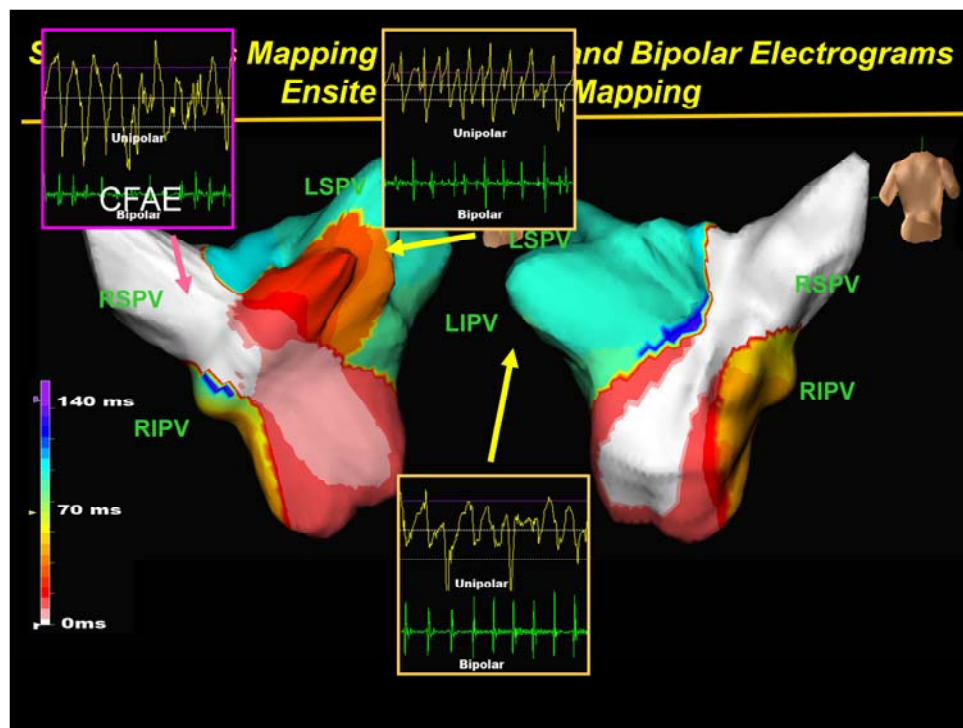


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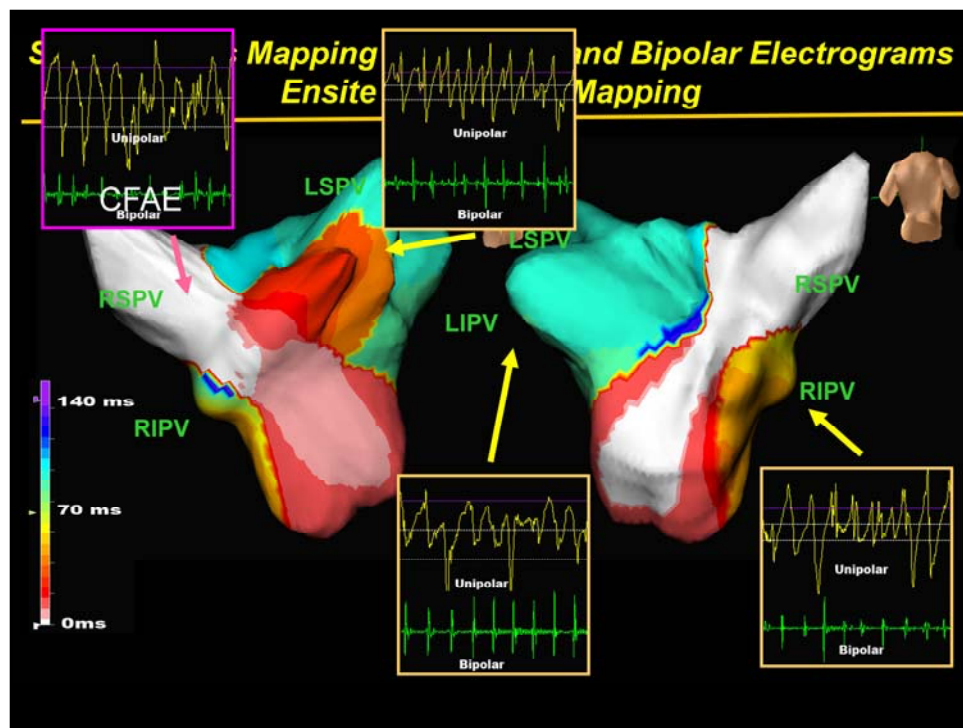


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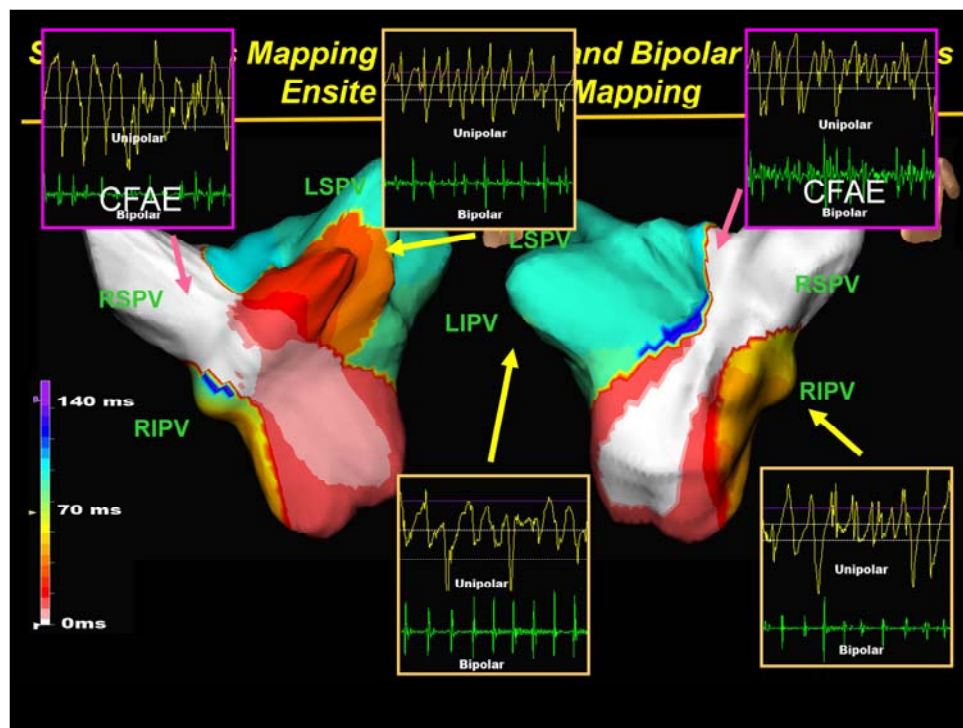




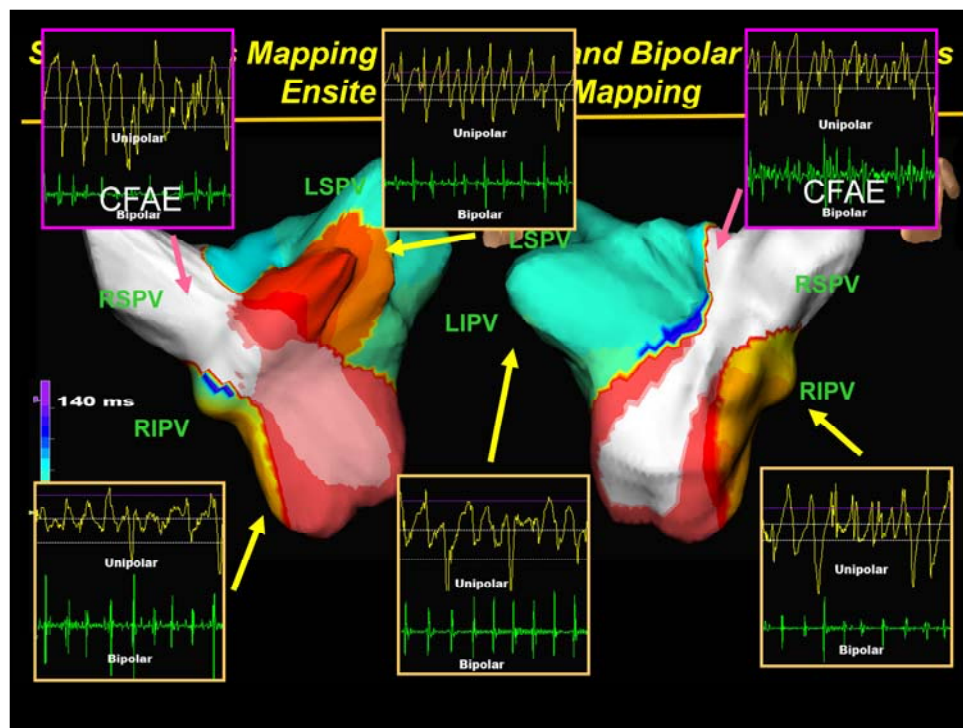
In Ensight Array mapping, we found that bipolar CFE site with CL < 120 ms (RSPV and mid roof) showed S wave predominant unipolar electrogram.



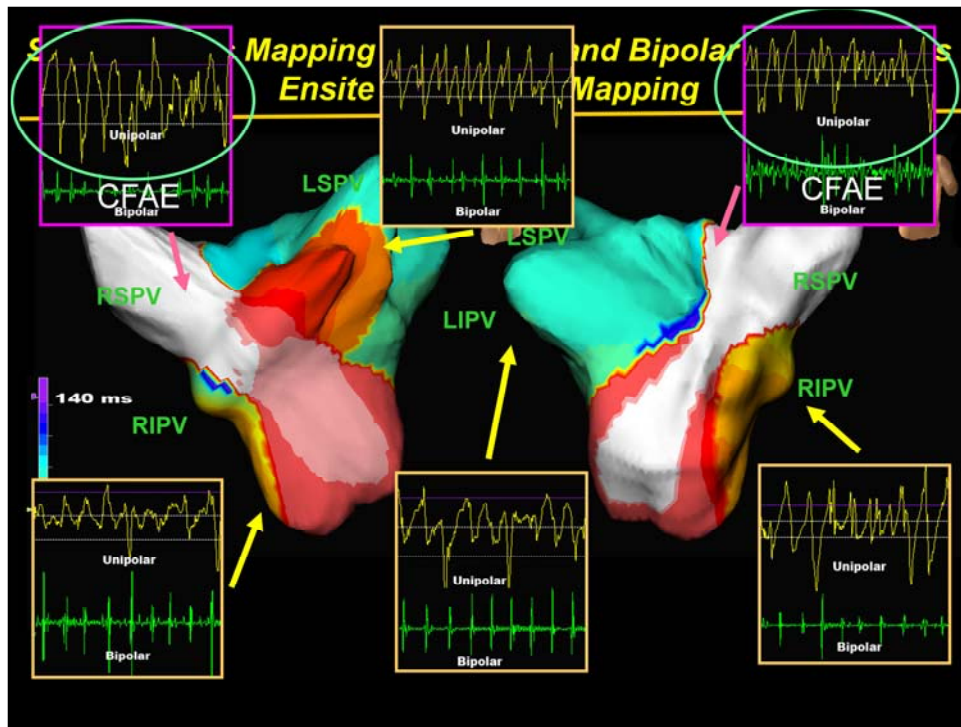
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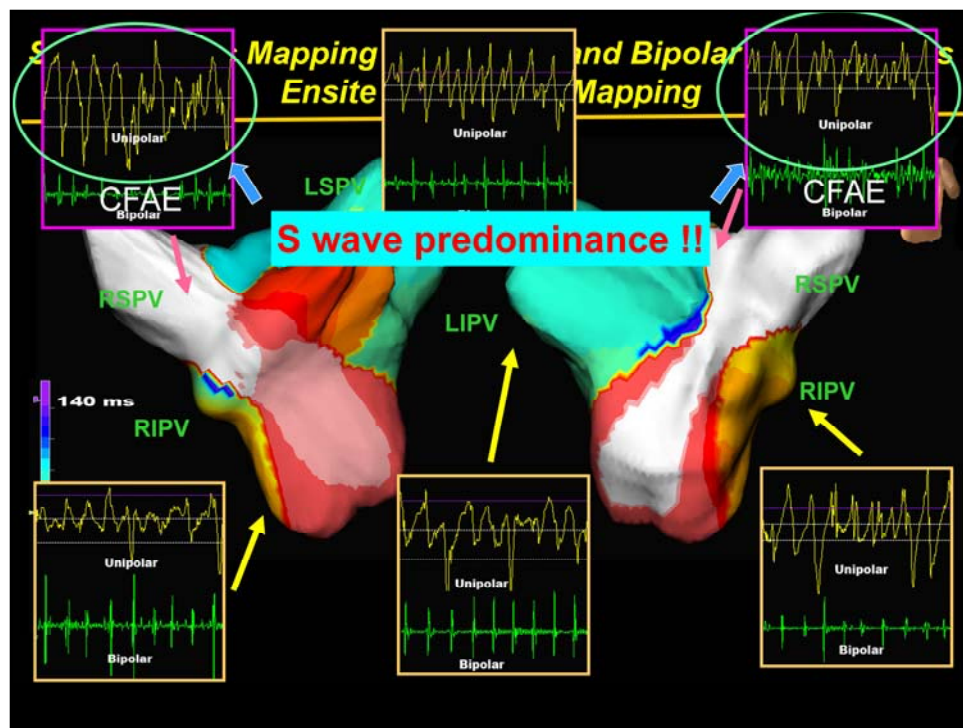
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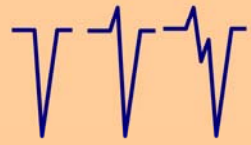


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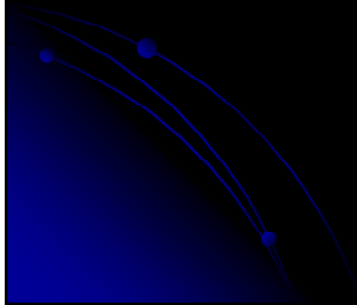
## ***Unipolar Morphology Analysis in Bipolar CFAE***



*S wave predominance*



*Non S wave predominance*





## ***Unipolar Morphology Analysis in Bipolar CFAE***



*S wave predominance*



*Non S wave predominance*

- 12 consecutive AF (Paroxysmal 8) received Ensite Array mapping, 87 sites analyzed (26 CFAE, 61 non-CFAE)



## **Unipolar Morphology Analysis in Bipolar CFAE**



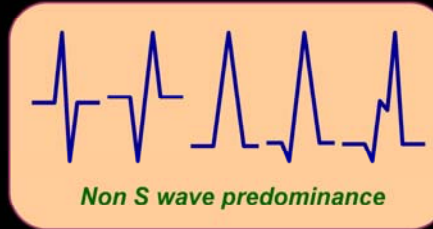
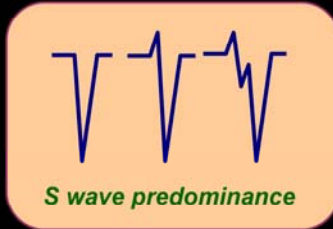
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- 12 consecutive AF (Paroxysmal 8) received Ensite Array mapping, 87 sites analyzed (26 CFAE, 61 non-CFAE)
- **S wave predominance** (>50%) in CFAE sites (24 of 26 bipolar CFAE sites)

## Unipolar Morphology Analysis in Bipolar CFAE



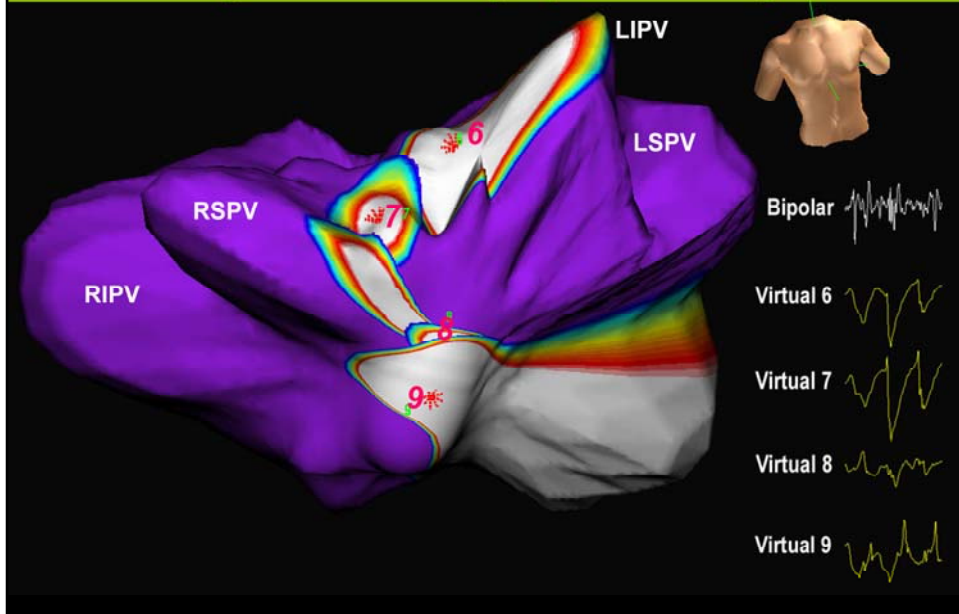
- 12 consecutive AF (Paroxysmal 8) received Ensite Array mapping, 87 sites analyzed (26 CFAE, 61 non-CFAE)
- **S wave predominance** (>50%) in CFAE sites (24 of 26 bipolar CFAE sites)
- **Non S wave predominance** ( $\leq 50\%$ ) in non-CFAE sites (56 of 61 bipolar non-CFAE sites).

## Activation Pattern in CFAE Sites

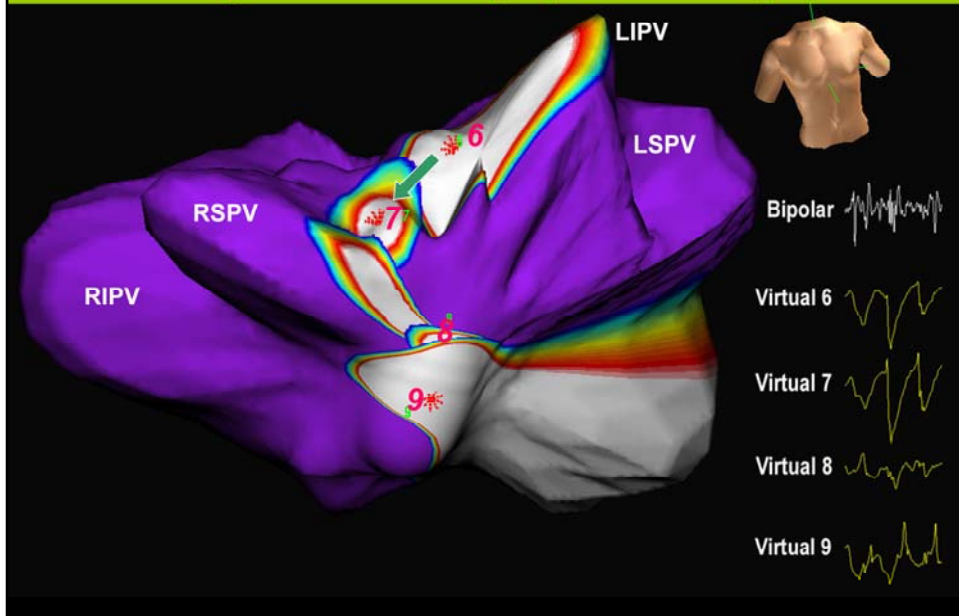
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- Eleven (**43%**) of the 26 located over *arrhythmogenic PV*.
- Eleven (**43%**) of the 26 located over *pivot points with wavefront turning*.
- Four (posterior wall, RSPVos) showed multiple wavelet pass through.

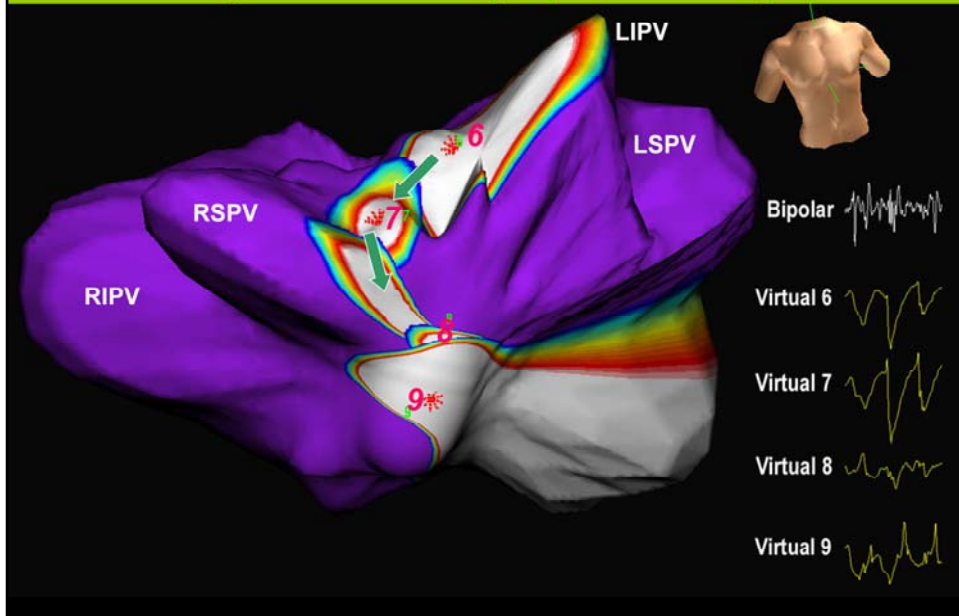
**Arrhythmogenic LIPV with negative predominant wave in  
Bipolar CFAE sites (Unipolar Virtual 6)**



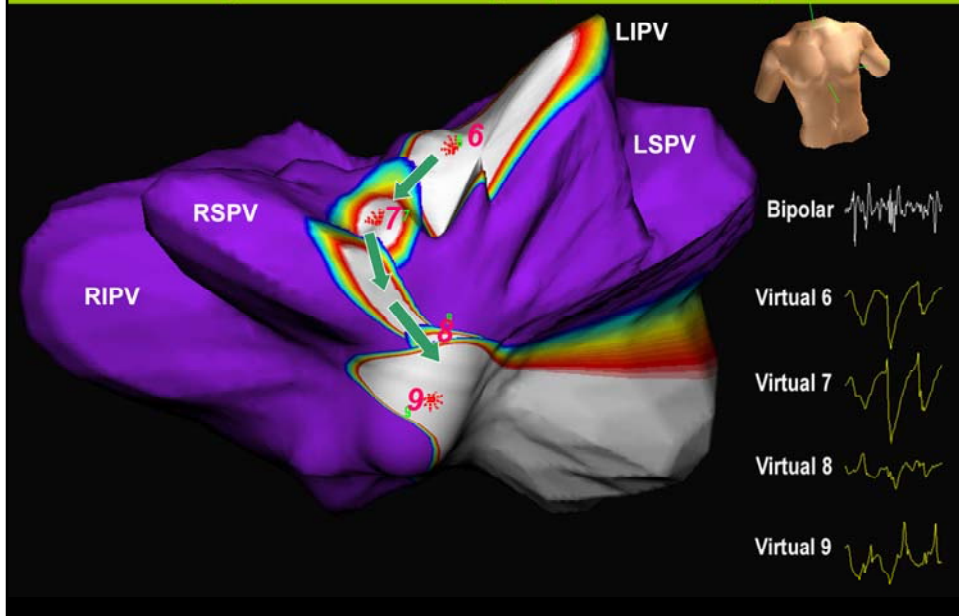
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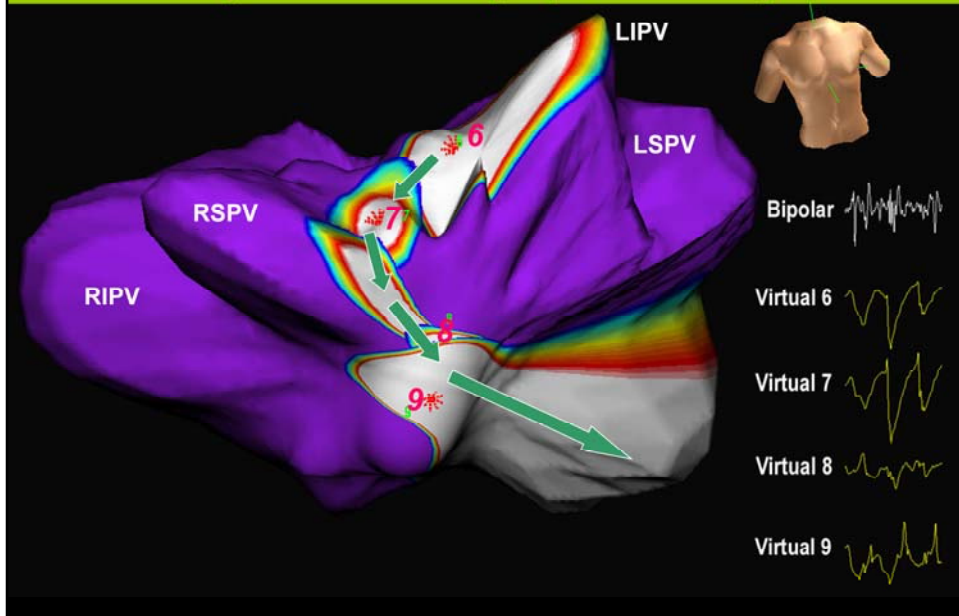
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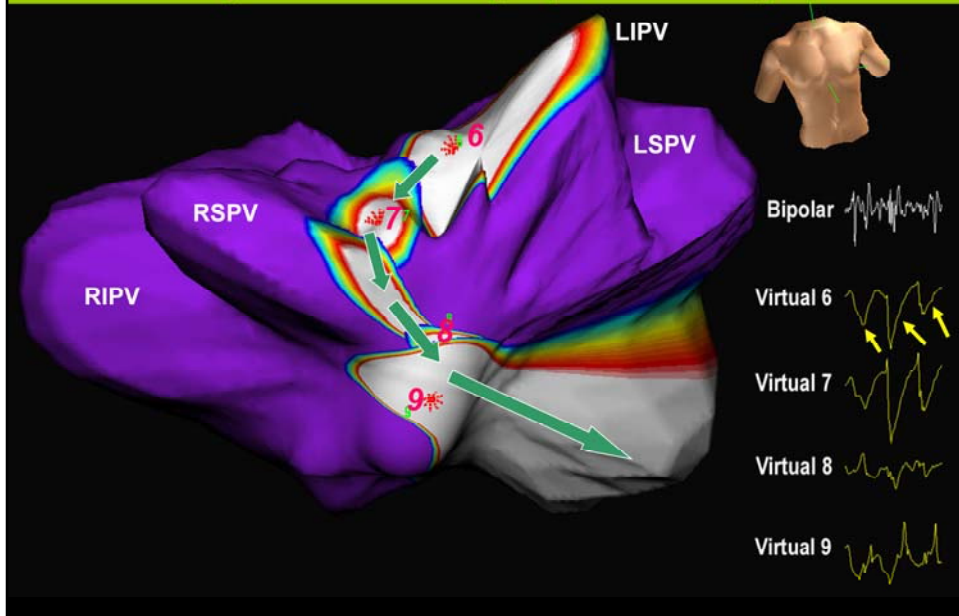


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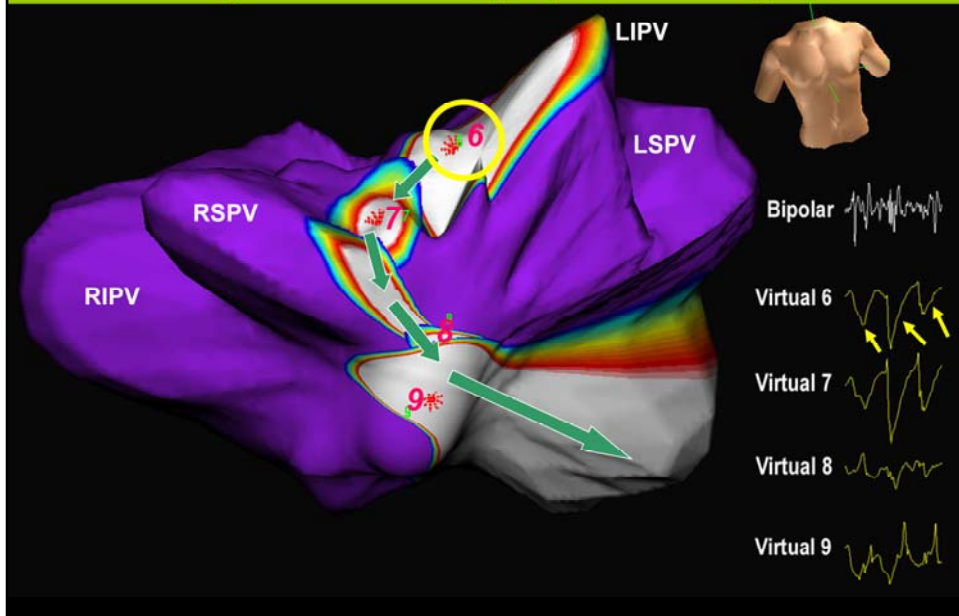




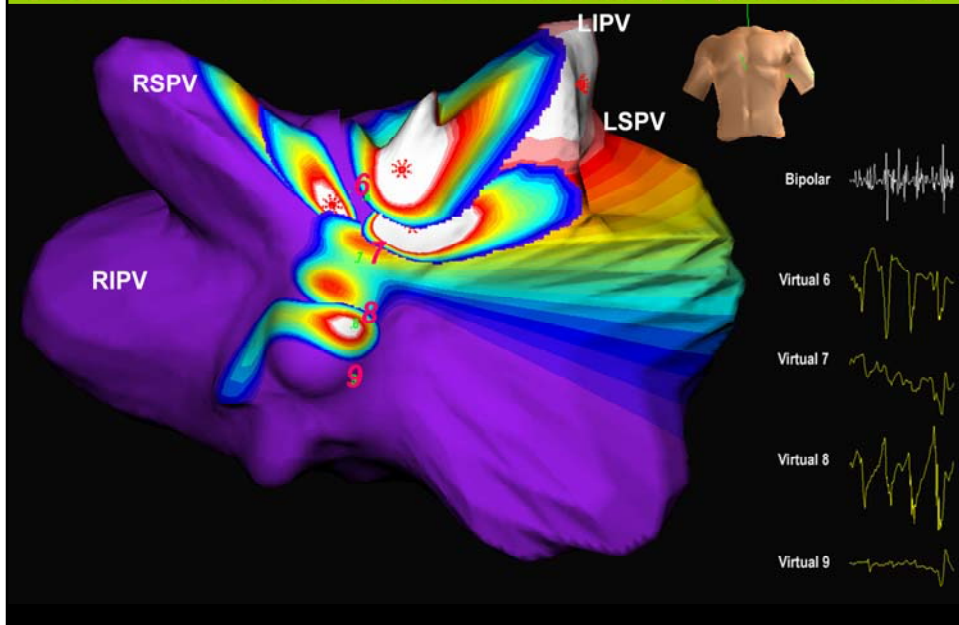
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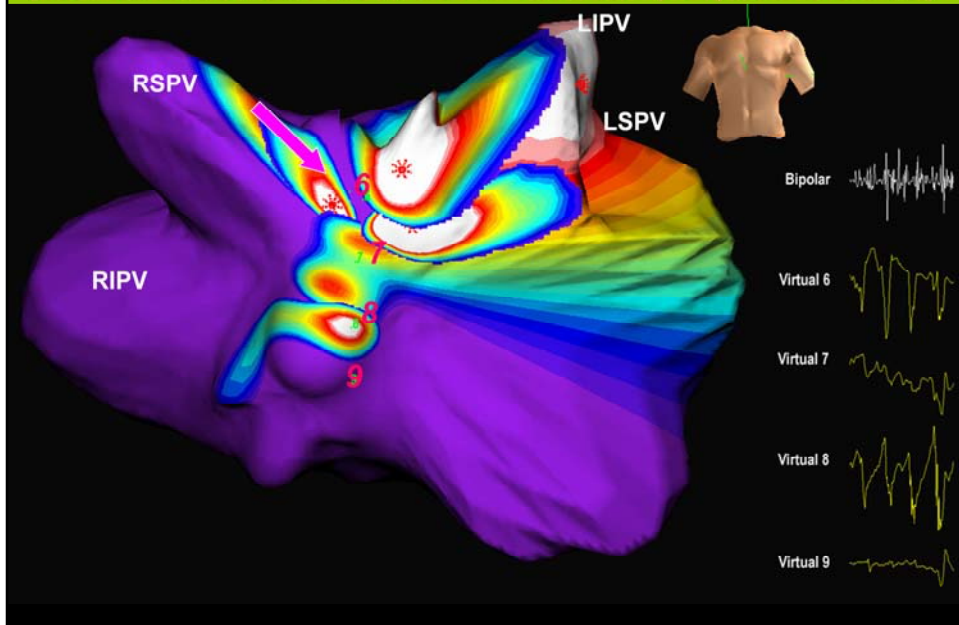
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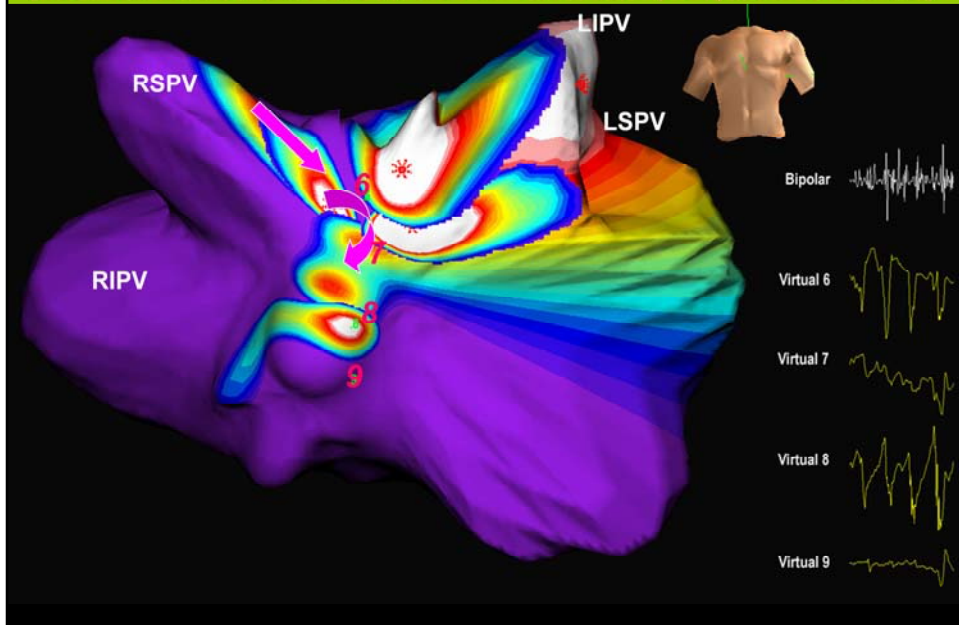
***LIPV and RSPV Ectopy Turning at Roof with negative predominant wave in Bipolar CFAE sites (Unipolar Virtual 6)***



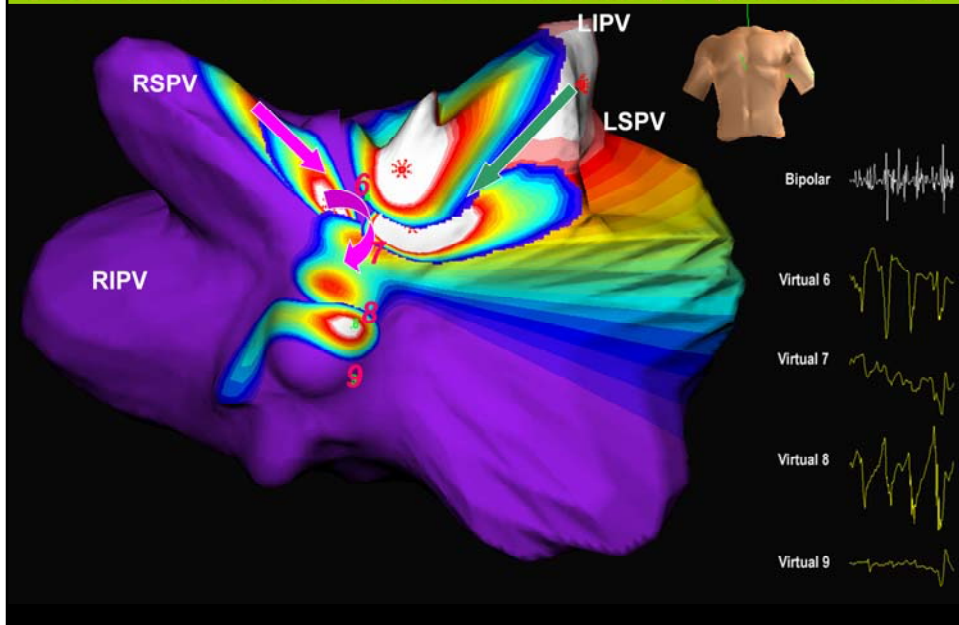
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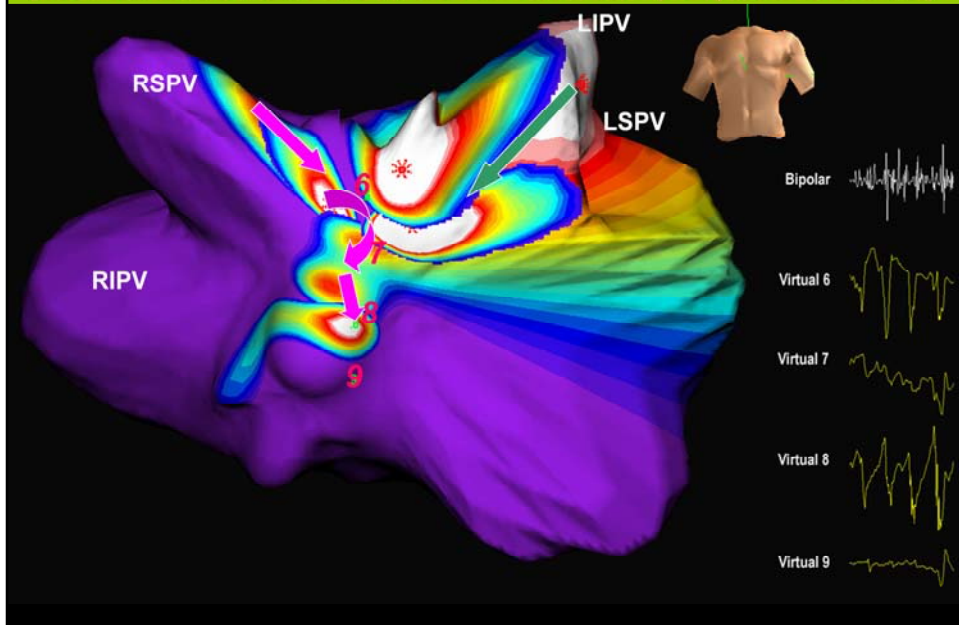
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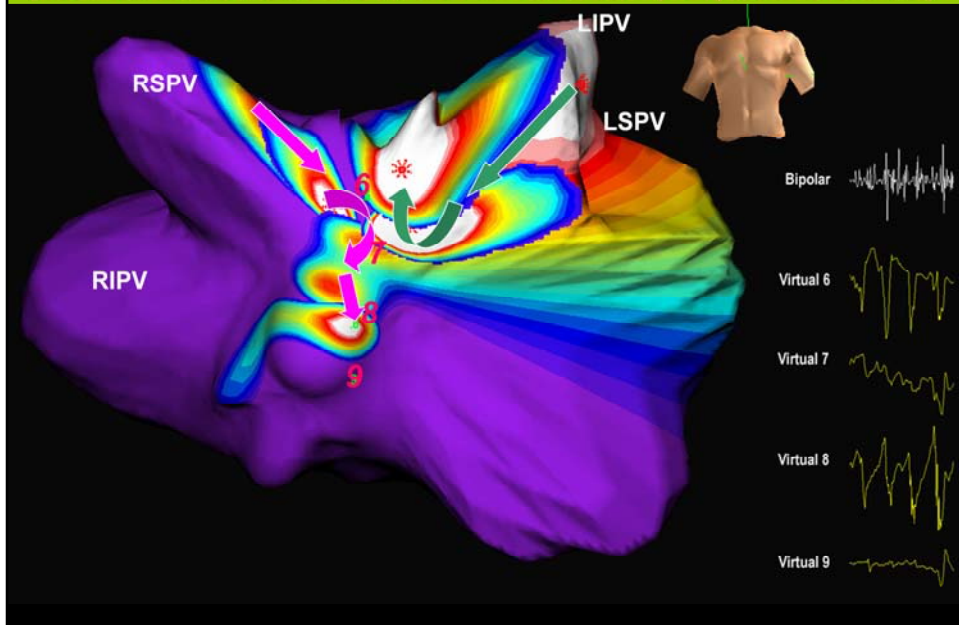


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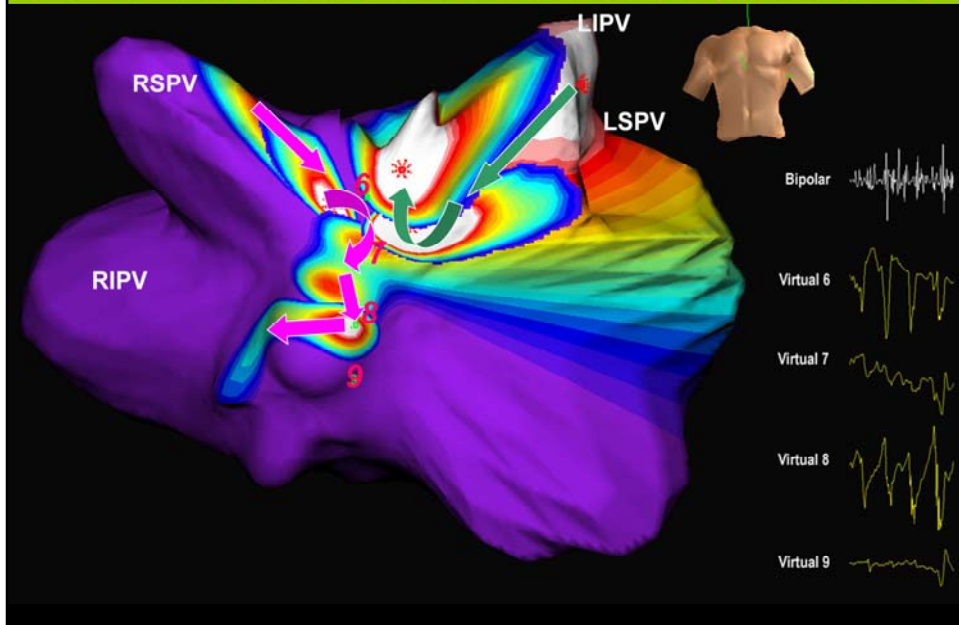


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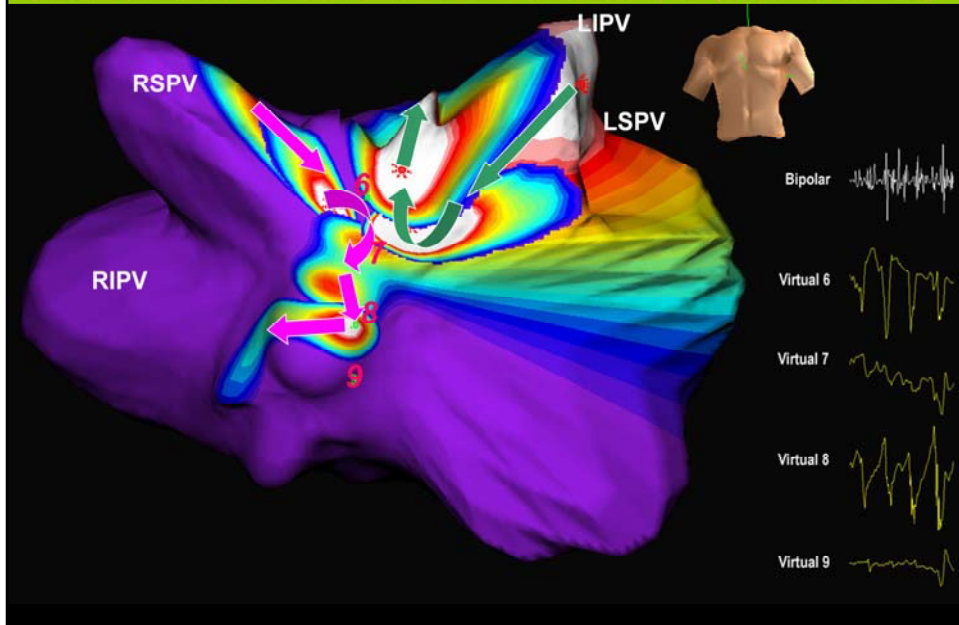




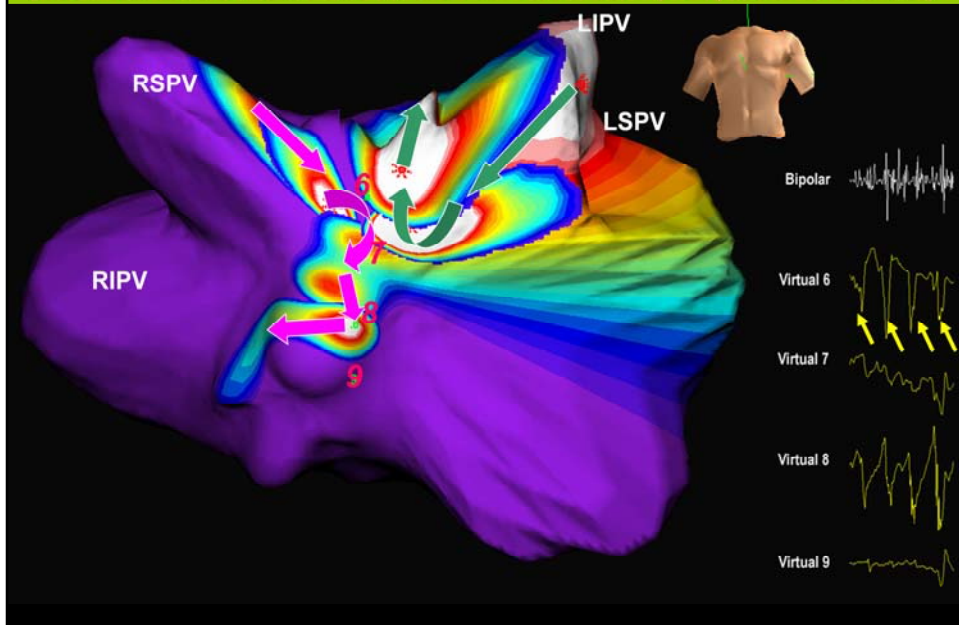
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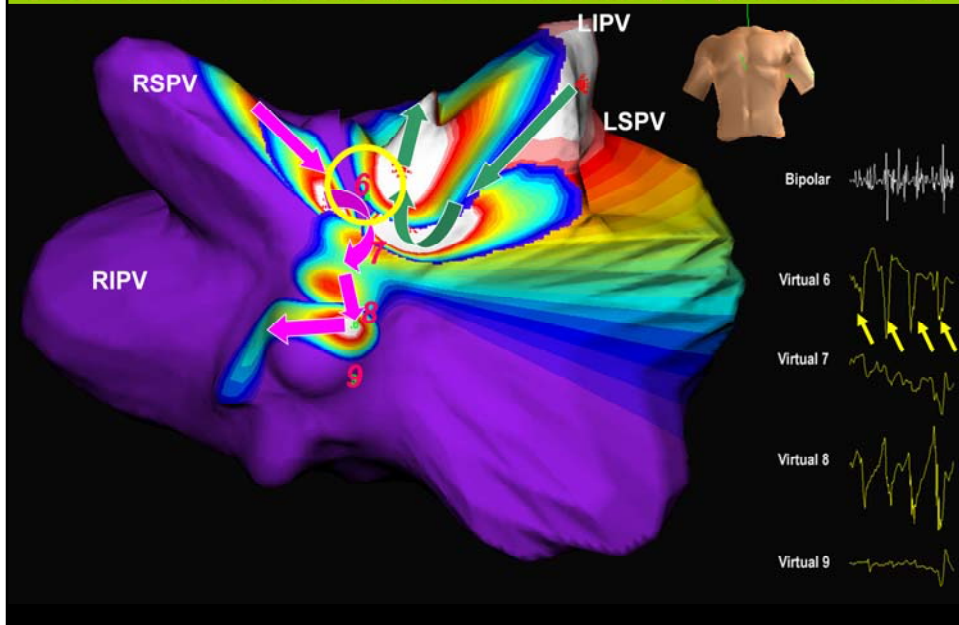
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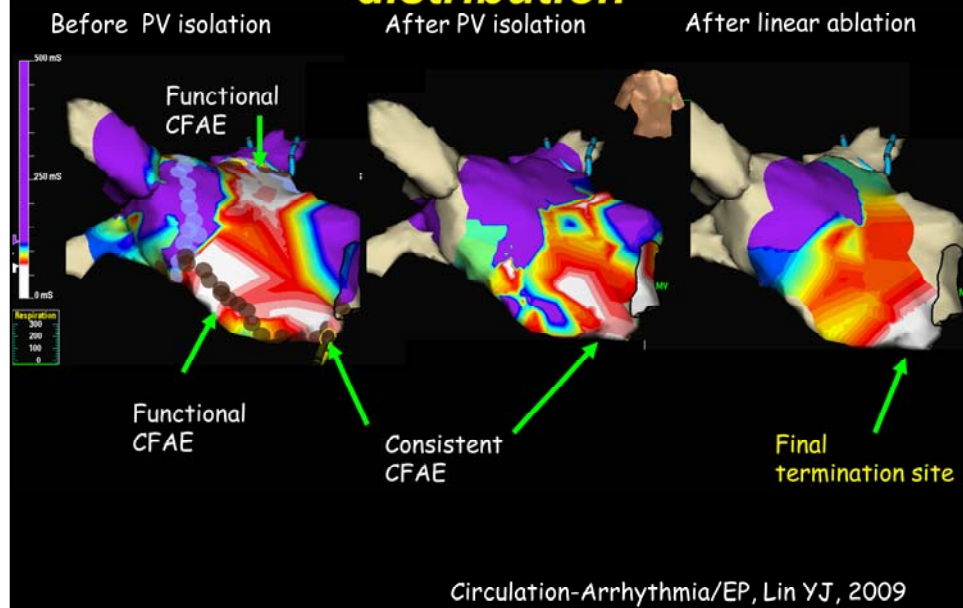
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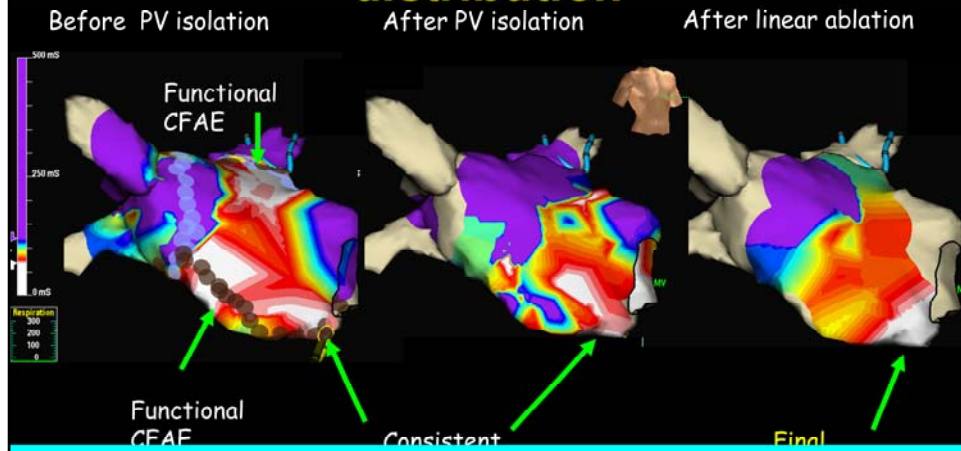
***LIPV and RSPV Ectopy Turning at Roof with negative predominant wave in Bipolar CFAE sites (Unipolar Virtual 6)***



## ***The Effect of PVI and lines on CFE distribution***



## ***The Effect of PVI and lines on CFE distribution***



The timing of CFEs mapping may affect the CFEs;  
Persistent presence of CFEs are important

Circulation-Arrhythmia/EP, Lin YJ, 2009

## *How to identify the important CFEs*

**Complex fractionation electrogram**  
**50-70% area of total atria**

### **Culprit CFEs**

Relate to procedural termination  
Higher dominant frequency  
Continuous over time

### **Bystander CFEs**

Not relate to procedural termination  
Peripheral to the high DF  
Not continuous over time

## **When to Stop the CAFÉ Ablation Procedure in Chronic AF ?**



## Catheter Ablation in Non-Paroxysmal AF

References	CFAE Definition/ Chamber	End points for CFAE site	End points for procedure
Nademanee et al. (JACC 2004)	Visual/ LA, CS, RA	<0.05 mV bipolar V	AF termination
Oral et al. (Circulation 2007)	Visual/ LA, CS	<0.1 mV bipolar V	AF termination/ elimination of CFAE
Natale et al. (HRS abstract 2007)	Visual/ LA, CS	Elimination of CFAE	AF termination/ elimination of CFAE
Haissaguerre et al. (JACC 2008)	Visual/ LA, CS, RA	Discrete Eg, slower than CL of LAA	AF termination/ elimination of CFAE
Estner et al. n=36 (AJC 2008)	Visual/ LA, CS, RA	Elimination of CFAE	AF termination/ elimination of CFAE
Chen et al. (HR 2009)	NavX automated algorithm, LA, CS	FI > 120 msec	AF termination/ elimination of CFAE

Nademanee's lab has the highest termination rate  
Whereas the highest efficacy with CFAE and lines

## Catheter Ablation in Non-Paroxysmal AF

References	Ablation procedure	Termination rate without	Long-term success rate
Nademanee et al. (JACC 2004)	Pure CFAE ablation	76% <sup>AAD</sup> To sinus rhythm	70% 12 months
Oral et al. (Circulation 2007)	Pure CFAE ablation	16% To sinus rhythm	33% 14 months
Natale et al. (HRS abstract 2007)	Adjunctive CFAE ablation	85% Mostly to AT	61% 11 months
Haissaguerre et al. (JCE 2005)	Adjunctive CFAE ablation	53% Before linear lines	95% (multiple procedures)
Estner et al. n=36 (AJC 2008)	Adjunctive CFAE ablation	23% To sinus rhythm	76% / 19 mons (multiple procedures)
Chen et al. (HR 2009)	Adjunctive CFAE ablation	52% To sinus rhythm	75% / 11 mons (single procedure)

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## Catheter Ablation in Non-Paroxysmal AF

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Can procedure termination predict long-term outcome?

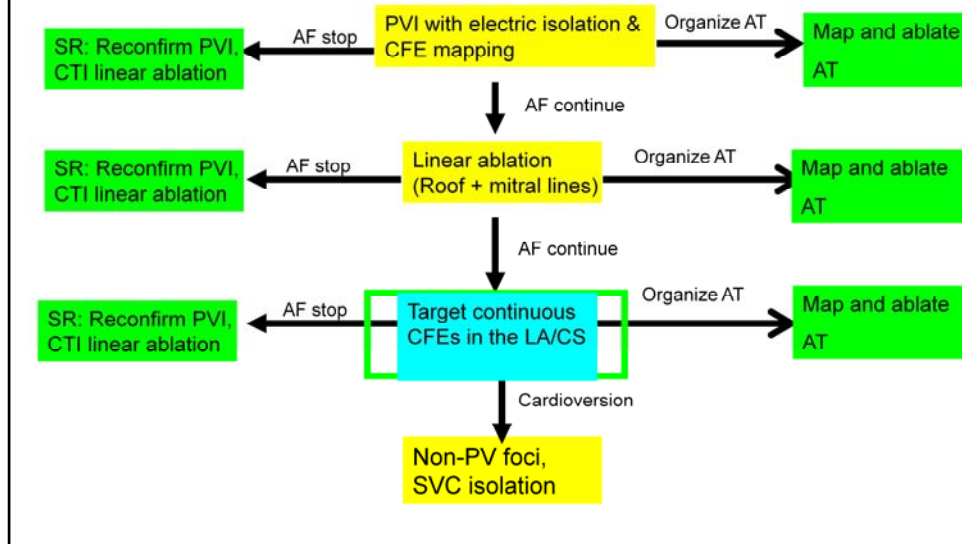
Nademanee's lab has the highest termination rate  
Whereas the highest efficacy with CFAE and lines

## **Predictors of Procedural Termination (N=88, PAF and CAF)**

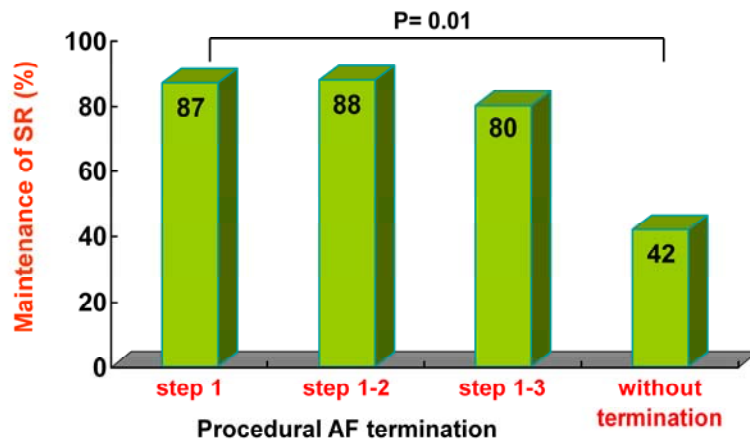
	<b>Predictors of termination</b>	<b>Predictors of recurrence</b>
<b>Significant factors from univariate Analysis</b>	AF duration, heart failure, LA size, cycle length of CS, shortest FI, DF gradient, mean LA voltage	LA size (P=0.037) High DF in RA (p=0.009)
<b>Significant factors from multivariate Analysis</b>	LA size (P=0.037) RA non-PV ectopies (p=0.009)	LA size (p=0.02) RA non-PV ectopies (p=0.01)
<b>Insignificant factors</b>	Age, Sex, underlying disease, degree of fractionation and DF in the LA	Age, Sex, underlying disease, degree of fractionation and mean DF of RA and LA, and <b>AF termination (P=0.07)</b>

*Taipei VGH, Heart Rhythm 2009*

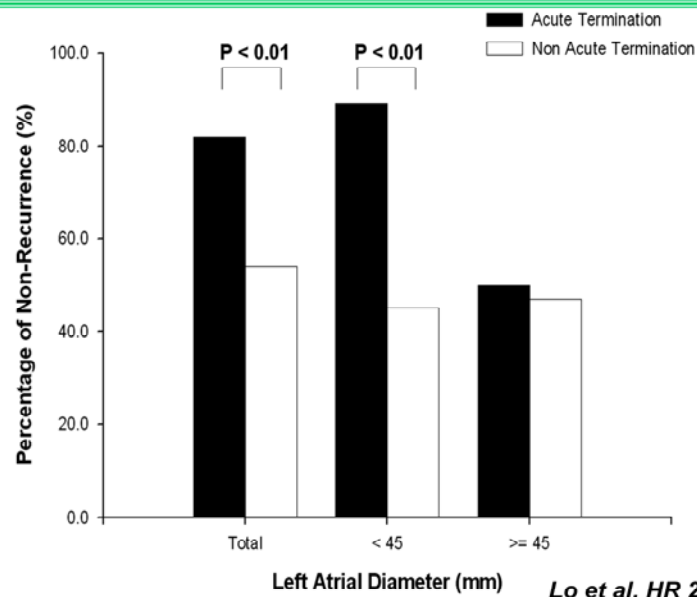
## Ablation Technique of Chronic AF (Taipei VGH)



### *Efficacy of stepwise ablation procedure*



**Procedural AF Termination and Long-term Outcome (N=85, follow-up 13 months)**



*Lo et al, HR 2009*

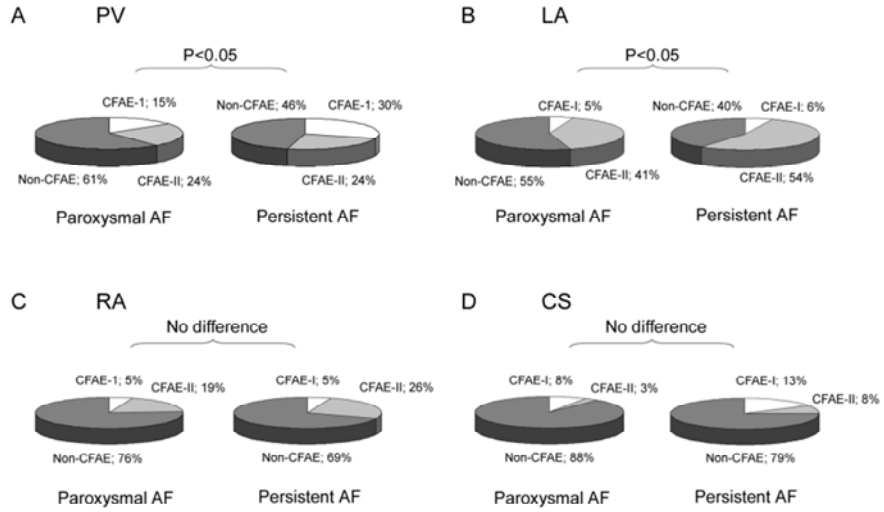
## ***Conclusion***

- ◆ Combination of PVI and adjunctive substrate modification improve success in treatment of chronic AF.
- ◆ Both frequency and fractionation mapping may provide the information to plan our ablation strategy.
- ◆ Achieving procedural termination with extensive LA modification may not be appropriate for all CAF patients.

CFAE mapping may be a clinically useful tool for targeting ablation of CFAE sites as an adjunct to current methods of circumferential PV isolation.

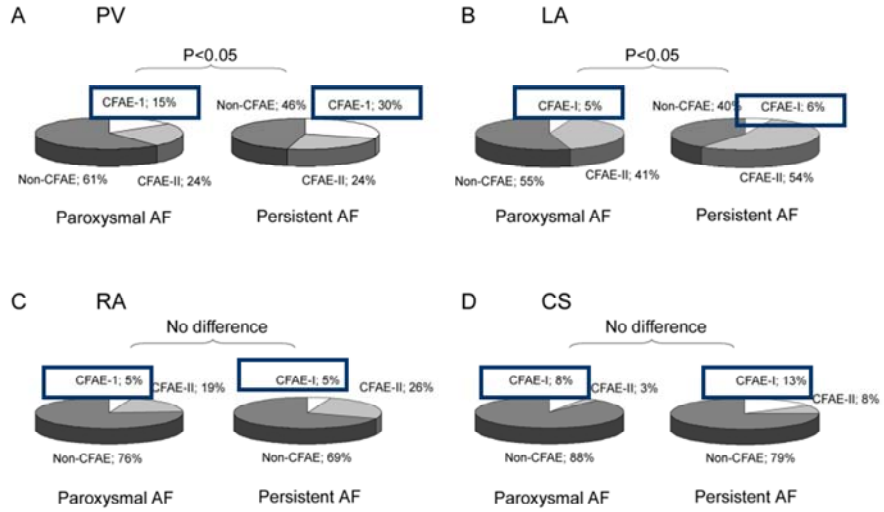


**Prevalence and Distribution of CFEs**  
**Rapid activities (I) and Continuous activities (II)**



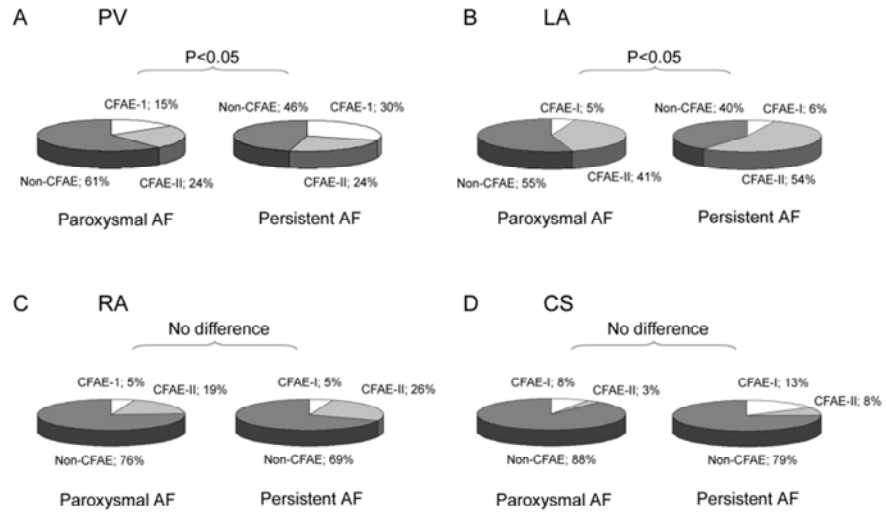
*Taipei VGH, 2006, 2007 HRS abstract*

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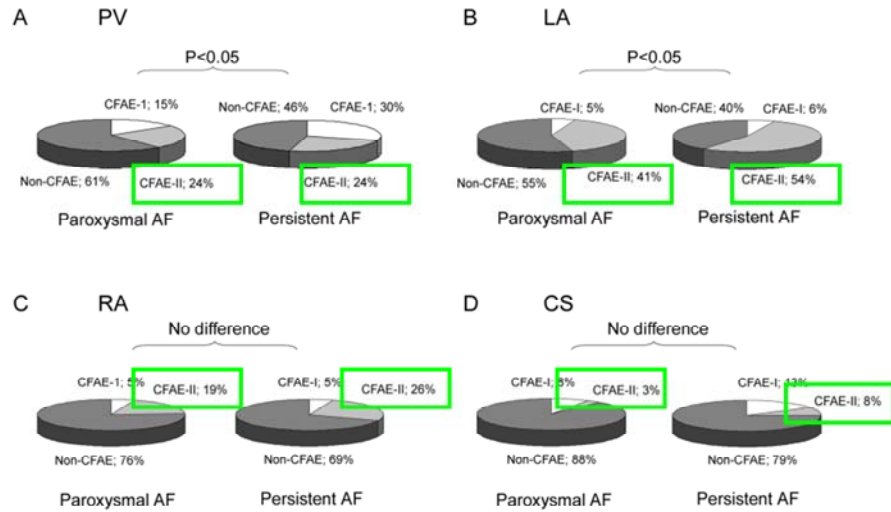
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**Prevalence and Distribution of CFEs  
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*Taipei VGH, 2006, 2007 HRS abstract*

**Prevalence and Distribution of CFEs  
Rapid activities (I) and Continuous activities (II)**



*Taipei VGH, 2006, 2007 HRS abstract*

## Characterization of CFEs by FFT

