

When should a line not be crossed: The role of non-linear ablation

Dr. Mark O'Neill

Consultant Cardiologist & Electrophysiologist

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Outline

- What are complex fractionated atrial egms?
- What is the acute impact of ablation?
- What is the clinical impact of ablation?
- When should we recommend CFE ablation?

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Characterization of Atrial Fibrillation in Man: Studies Following Open Heart Surgery*

WELLS, J.L., JR., ET AL. *Characterization of Atrial Fibrillation in Man*. The nature of localized atrial activation during atrial fibrillation was characterized in 34 patients following open heart surgery. Bipolar atrial electrograms (AEG) recorded in each patient with atrial fibrillation exhibited a myriad of sizes, shapes, polarities, amplitudes, and beat-to-beat intervals. On the basis of the AEG morphology and the nature of its baseline, we have classified the recordings into four Types. Type I was characterized by discrete AEG complexes separated by an isoelectric baseline free of perturbation, Type II by discrete AEG complexes but with perturbations of the baseline between complexes, Type III by AEGs which failed to demonstrate either discrete complexes or isoelectric intervals, and Type IV in which AEGs of Type III alternated with periods characteristic of Type I and/or Type II. In 22 patients, the AEGs were recorded a second time, and in 11 of these patients the type of atrial fibrillation changed between the first and second recording period. An atrial flutter-fibrillation pattern in the ECG was associated with a relatively ordered atrial activation pattern and a relatively slow atrial rate. Human atrial fibrillation is not an electrophysiologically homogeneous process when compared among different patients or ad seriatim in the same patient. (PACE, Vol. 1, October-December, 1978)

“It is clear from this study that human atrial fibrillation is not an electrophysiologically homogeneous process.”



Figure 5. ECG lead III recorded simultaneously with a filtered (12-500 Hz) bipolar atrial electrogram (AEG) during Type I atrial fibrillation.

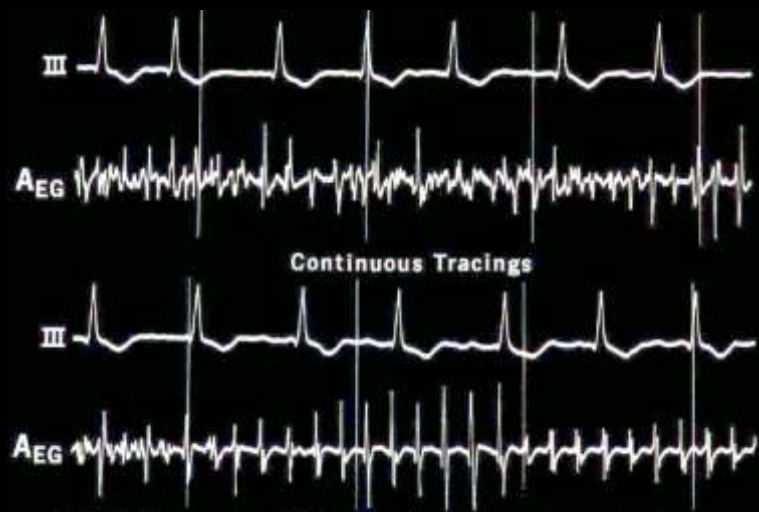
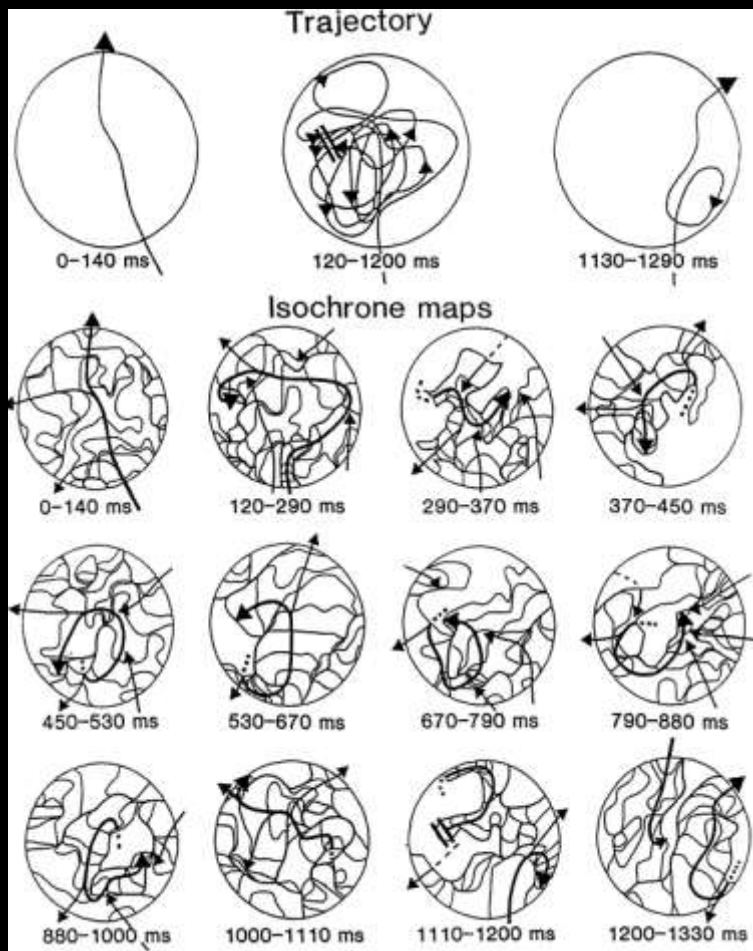


Figure 6. Continuous tracings of ECG lead III recorded simultaneously with a filtered (12-500 Hz) bipolar atrial electrogram (AEG) during Type IV atrial fibrillation. Note the change in pattern from an initial Type III to a Type I.

High-Density Mapping of Electrically Induced Atrial Fibrillation in Humans

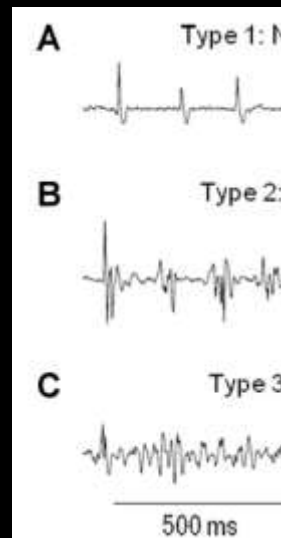


- 25 patients undergoing surgery for WPW
- Induced AF
- Contact recordings
- 3 types of AF
 - Single broad front
 - 1 or 2 non-uniformly conducting wavelets
 - Multiple wavelets
- Different numbers and dimensions of intra-atrial reentrant circuits in human AF

Mapping during continuous electrical activity

Prevalence and Characteristics of Continuous Electrical Activity in Patients with Paroxysmal and Persistent Atrial Fibrillation

- 44 Patients (PAF 25)
- >5s LA recordings x 24
- CEA:depol>1s, no IEI
- Higher prevalence and duration of CEA at non-antral sites in PsAF
- High prevalence of CEA at non-antral sites in PAF
- A poor guide for ablation?

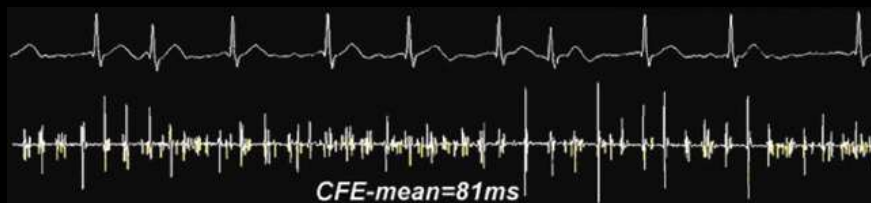
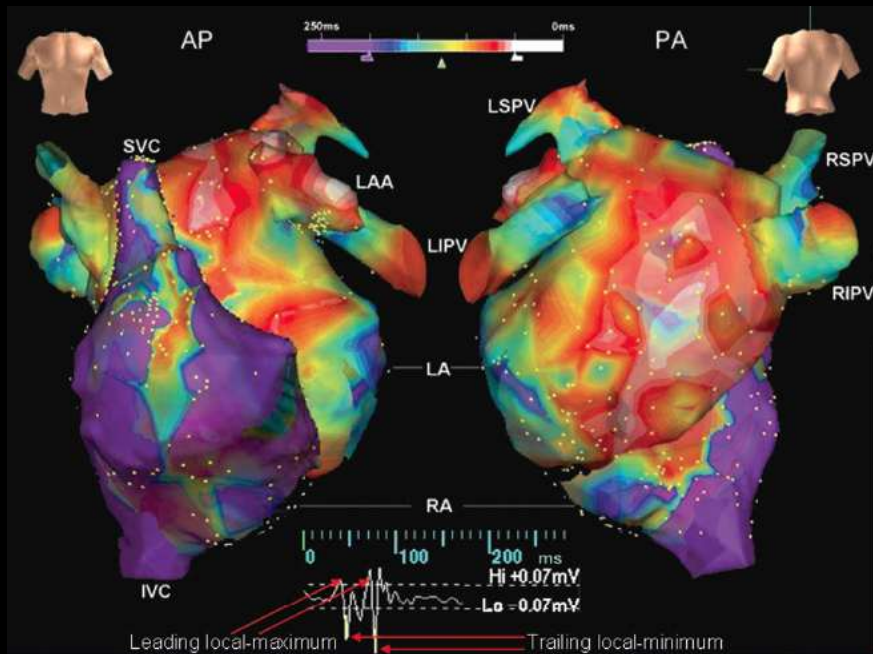


	Electrogram Type		
	CEA (-)		CEA (+)
	1	2	
Left atrium (n = 1056)			
Antrum (n = 352)	7 (2)	113 (32)	232 (66)
Right (n = 176)	4 (2)	54 (31)	118 (67)
Left (n = 176)	3 (2)	59 (33)	114 (65)
Nonantrum (n = 704)	39 (6)	222 (32)	443 (63)
Septum (n = 132)	4 (3)	24 (18)	104 (79)
Posterior wall (n = 132)	11 (8)	31 (23)	90 (68)
Anterior wall (n = 132)	3 (2)	40 (30)	89 (67)
Roof (n = 88)	6 (7)	24 (27)	58 (66)
Base of LA appendage (n = 44)	1 (2)	16 (36)	27 (61)
Inferior wall (n = 44)	0	17 (39)	27 (61)
Posterior mitral annulus (n = 88)	5 (6)	41 (46)	42 (48)
LA appendage (n = 44)	9 (23)	29 (66)	6 (14)*
Coronary sinus (n = 88)	12 (14)	40 (45)	36 (41)**
Total (n = 1144)	58 (5)	375 (33)	711 (62)

	Paroxysmal AF (n = 25)	Persistent AF (n = 19)	P
Left atrium			
Antrum (n = 352)	125/200 (63%)*	107/152 (70%)**	0.12
Nonantral LA sites (n = 660)	212/375 (57%)*	227/285 (80%)**	<0.0001
Posterior wall (n = 132)	43/75 (57%)	47/57 (82%)	0.002
Roof (n = 88)	28/50 (56%)	30/38 (79%)	0.02
Anterior wall (n = 132)	39/75 (52%)	50/57 (88%)	<0.0001
Septum (n = 132)	55/75 (73%)	49/57 (86%)	0.08
Inferior wall (n = 44)	14/25 (56%)	13/19 (68%)	0.40
Posterior mitral annulus (n = 88)	17/50 (34%)	25/38 (66%)	0.003
Base of LA appendage (n = 44)	14/25 (56%)	13/19 (68%)	0.40
LA appendage (n = 44)	2/25 (8%)	4/19 (21%)	0.42
Coronary sinus (n = 88)	22/50 (44%)	14/38 (37%)	0.46
Total (n = 1,144)	362/650 (56%)	352/494 (71%)	<0.0001

The Effect of Electrogram Duration on Quantification of Complex Fractionated Atrial Electrograms and Dominant Frequency

14 AF ablation patients, 8s recordings
CFE-mean and spectral analysis

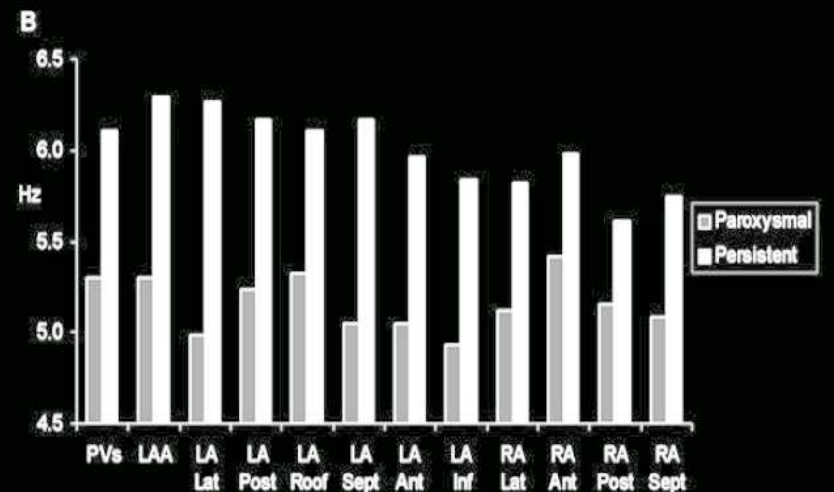
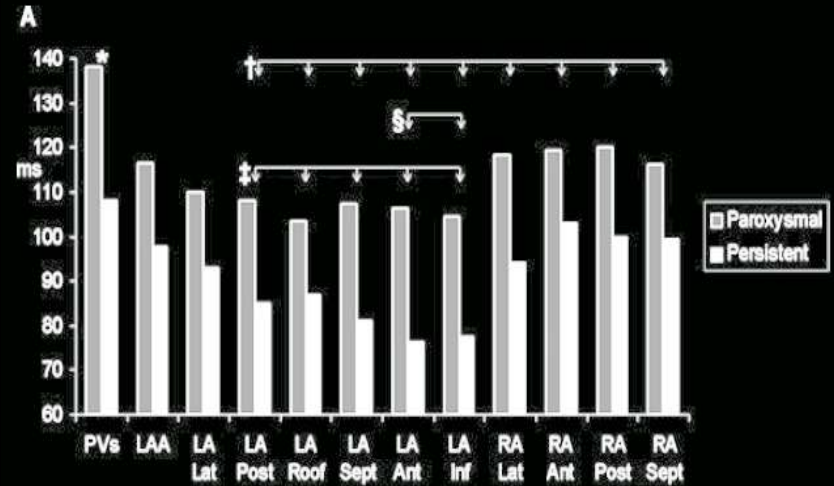
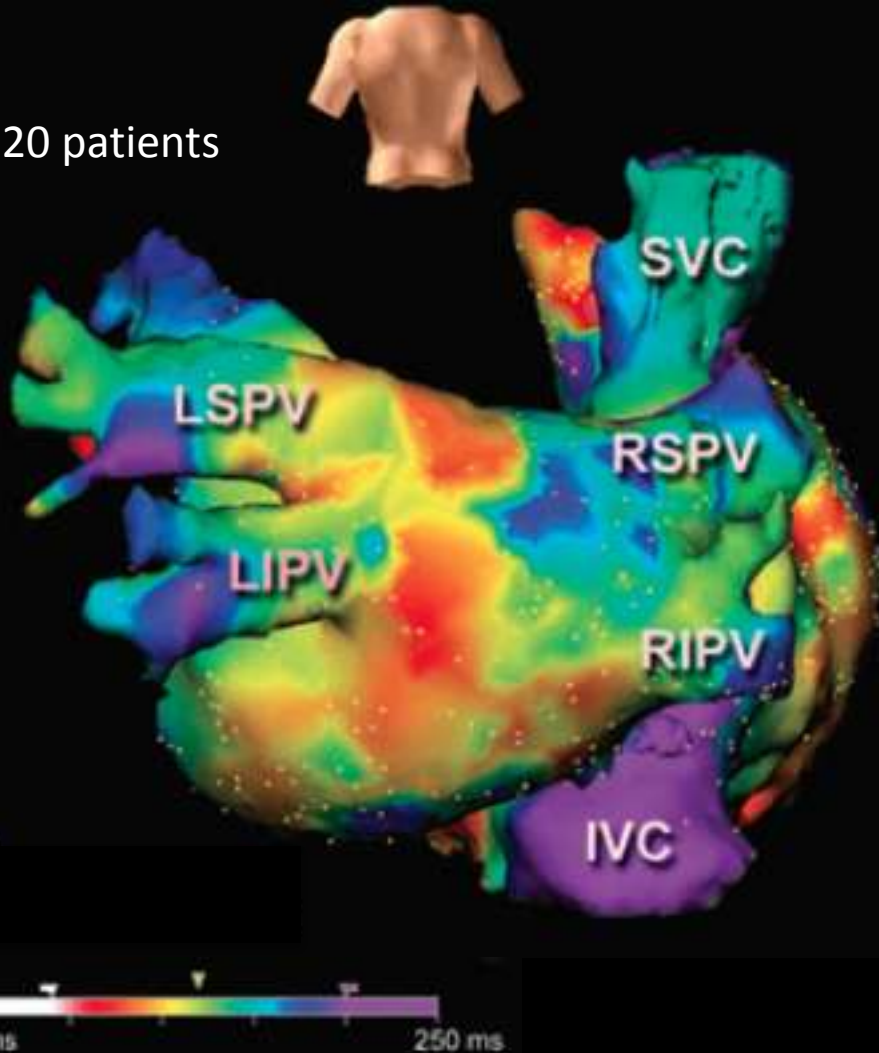


Findings

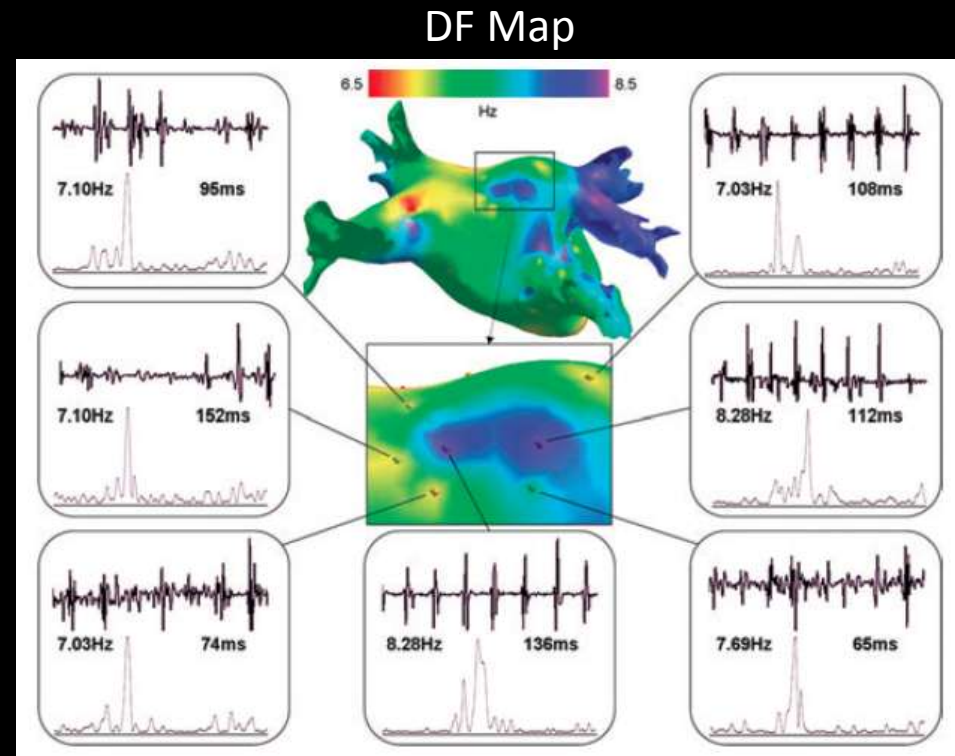
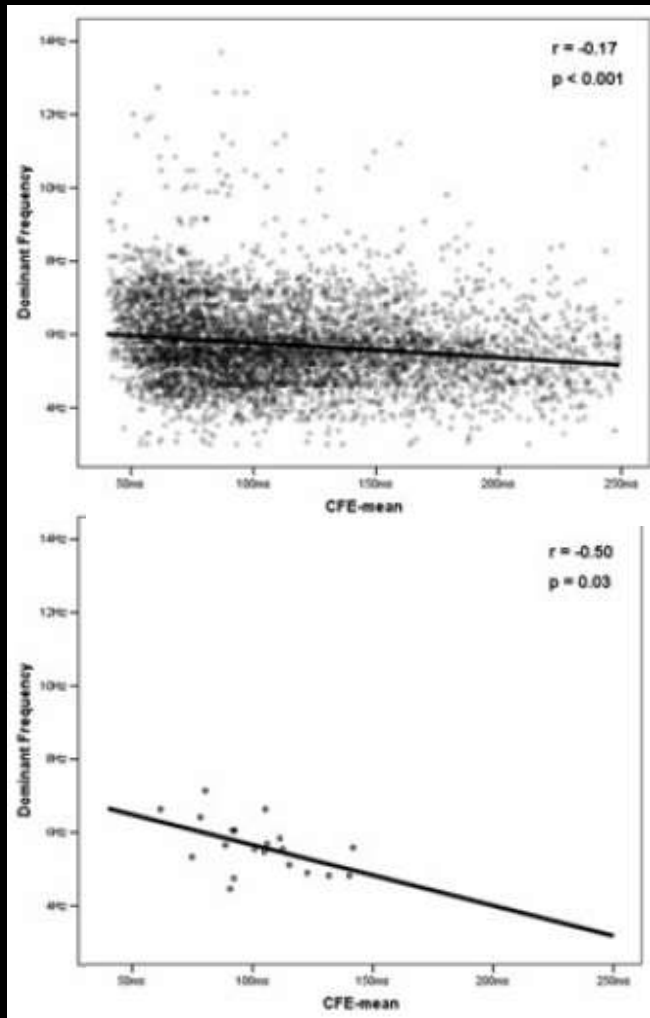
- Mean absolute differences between subsampled (1-7s) and index (8s) values ranged from 3.3 to 20.1ms for CFE mean and 0.11 to 1.18 for DF
- Using these analysis methods, CFE-mean (average interval between consecutive deflections) and DF are inconsistent when using recording windows of <5s

High-Density Mapping of Atrial Fibrillation in Humans: Relationship Between High-Frequency Activation and Electrogram Fractionation

20 patients



High-Density Mapping of Atrial Fibrillation in Humans: Relationship Between High-Frequency Activation and Electrogram Fractionation



Fractionation close to sites of high DF

High-density activation mapping of fractionated electrograms in the atria of patients with paroxysmal atrial fibrillation

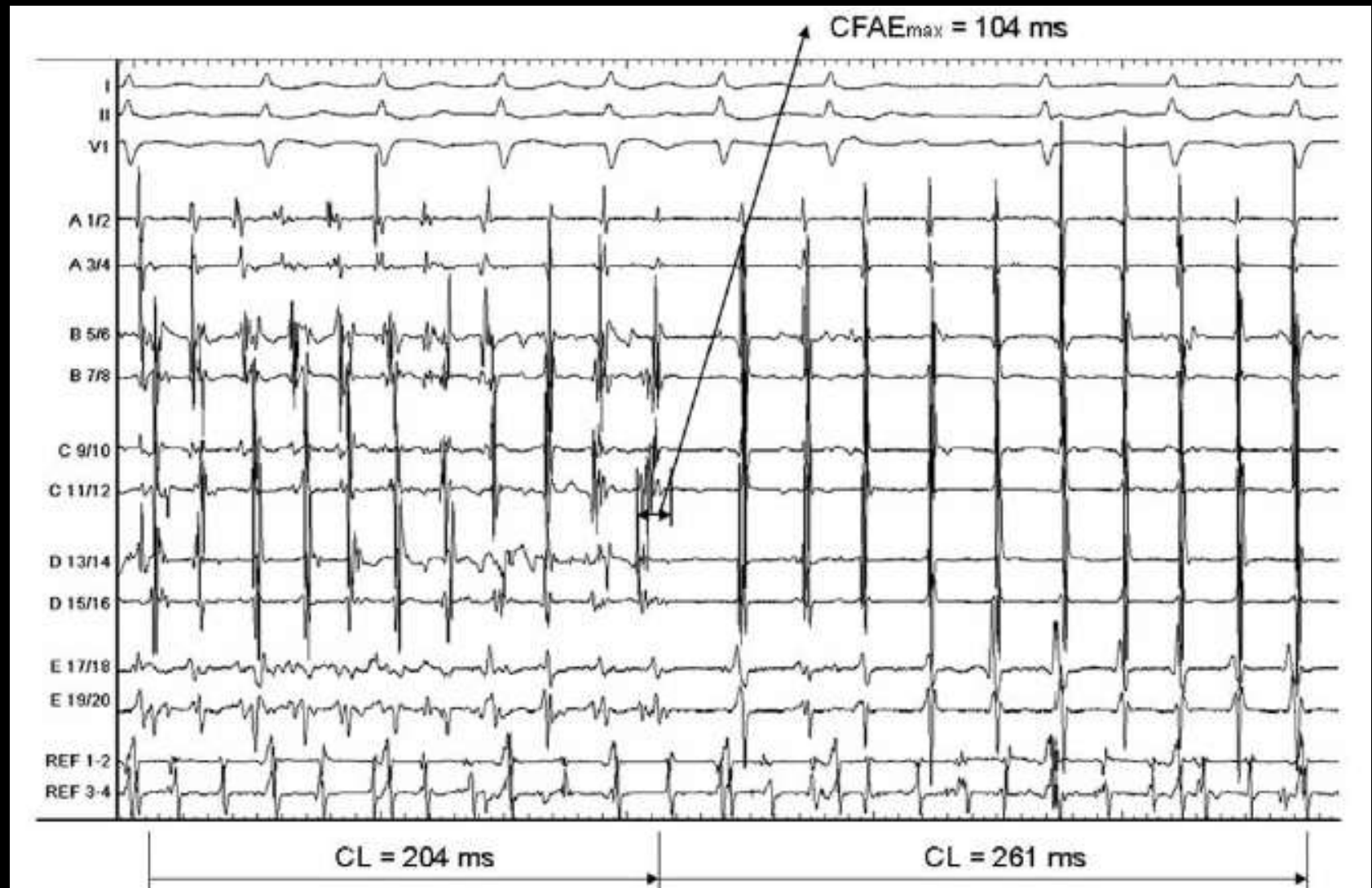
Design

- To assess regional activation using a high density mapping catheter
- 20 patients with PAF
- 10 sites mapped
- 2 different activation patterns seen
 - 84% simultaneous
 - 16% non-simultaneous, indicating complex activation, local reentry

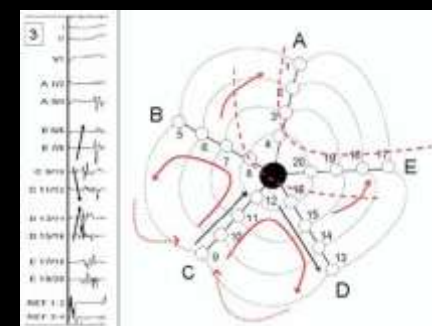
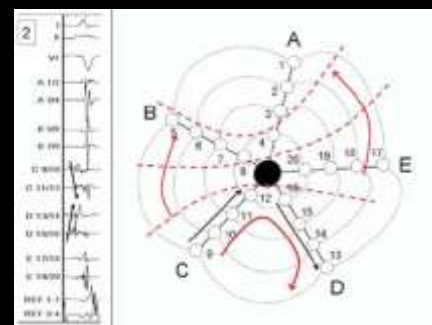
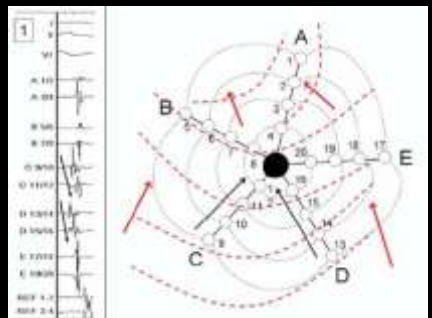
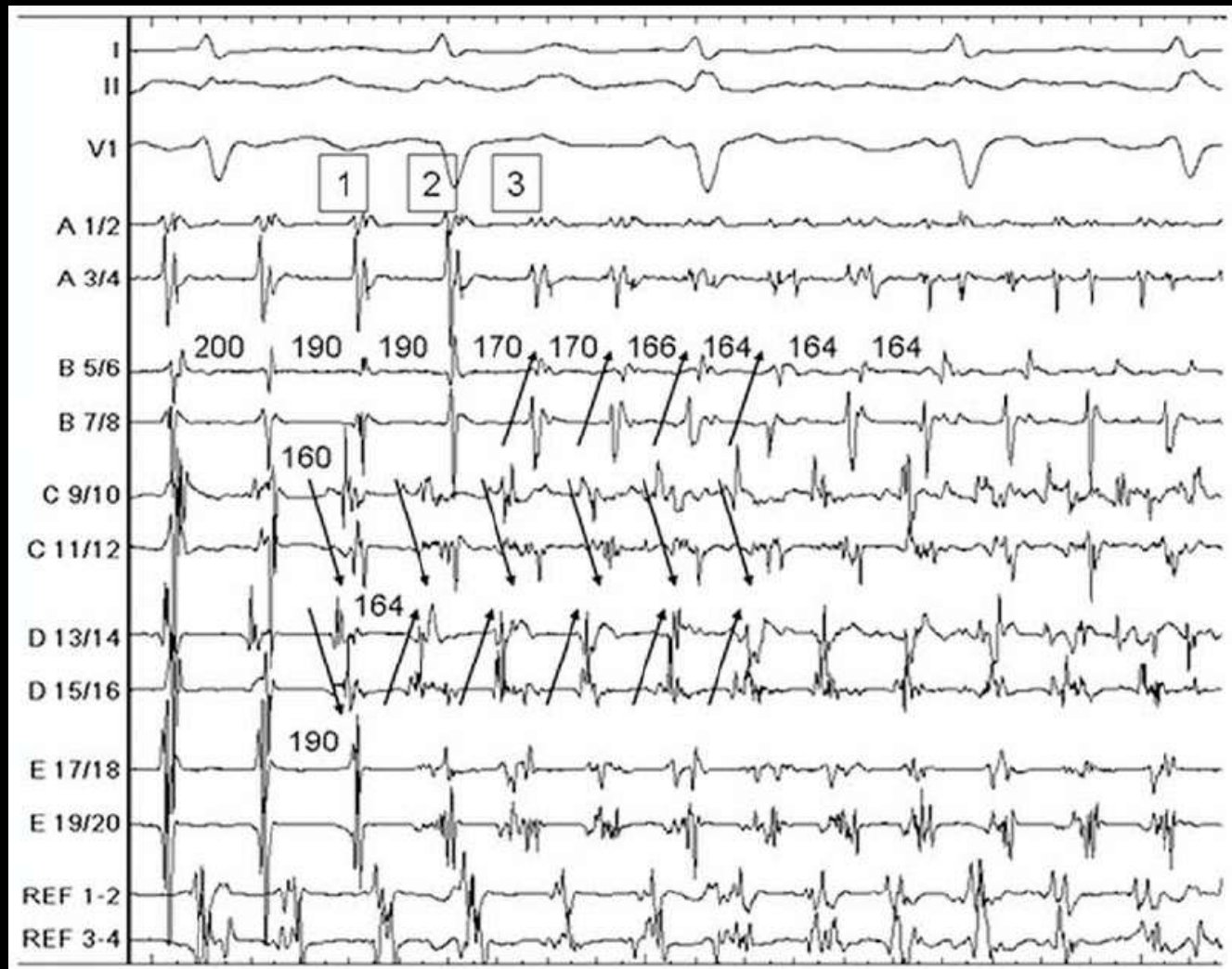
Active or Passive?

- The same anatomic region could have nonfractionated activity during an episode of long AFCL and fractionated activity when AFCL shortens
- CFEs per se may not necessarily indicate critical regions for arrhythmia perpetuation
- How do we distinguish the wheat from chaf?

High-density activation mapping of fractionated electrograms in the atria of patients with paroxysmal atrial fibrillation



High-density activation mapping of fractionated electrograms in the atria of patients with paroxysmal atrial fibrillation



To summarise so far...

- CFEs are ubiquitous in atrial fibrillation patients
- Local rapid activation may indicate the presence of an AF perpetuator eg rotor
- Continuous or fragmented activity may represent pivot points or regions of very slow conduction, responsible for continued fibrillatory conduction
- CFE may often be a passive phenomenon
- Fractionation may occur due to tissue anisotropy, wavefront collision or wave break, which can be transient phenomena
- Signals that meet the CFE definition may be AFCL-influenced

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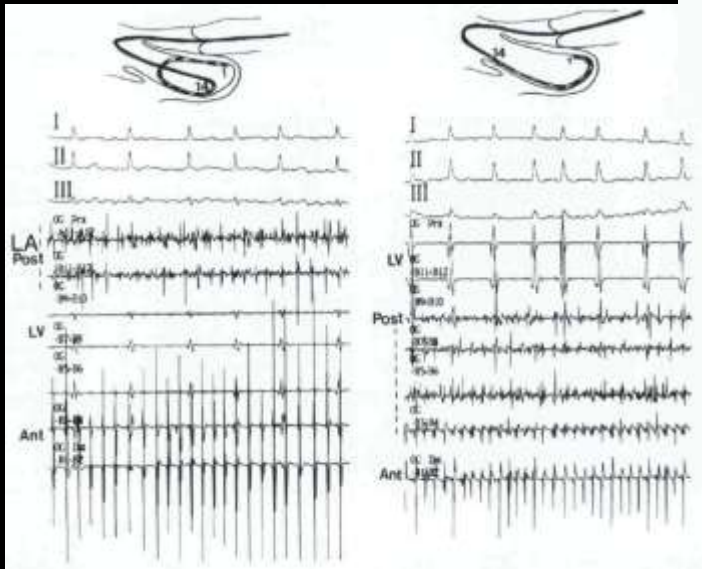
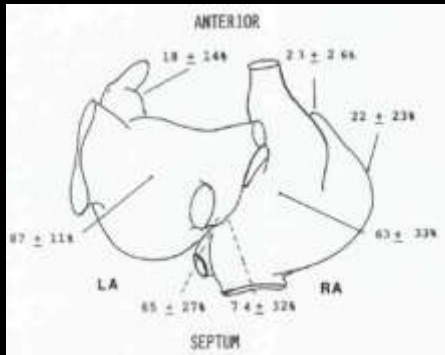
Rationale behind CFE ablation

- Continuous and/or fractionated atrial egms may indicate sites of conduction block, wavefront collision, slow conduction or pivot points for reentry
- Wavebreak & fibrillatory conduction typically occur within mm of a rotor core
- Ablation should limit wavelet reentry, may interrupt rotor or trigger activity and therefore impact the process of fibrillation

Regional Disparities of Endocardial Atrial Activation in Paroxysmal Atrial Fibrillation

PIERRE JAÏS, MICHEL HAÏSSAGUERRE, DIPEN C. SHAH, SALAH CHOUAIRI, and JACQUES CLÉMENTY

Hôpital Cardiologique du Haut-Lévêque, Bordeaux, France



Despite some limitations, this study quantifies the temporal and spatial distribution of CEA in both atria in humans. The areas exhibiting the most consistently disorganized electrograms could be considered preferential targets for catheter-based AFib ablation.

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



- 2 or more deflections and/or perturbation of the baseline with continuous deflection of a prolonged activation complex over a 10s recording period (1A)
- Very short CL (<120ms) over 10s (1B)

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

AF Classification	Number of Patients (Types)	Number of Patients at Various Location of CFAE Distribution
Type I AF: CFAEs localize in only one area	23 (16 PAF and 7 CAF)	10 pulmonary veins (4 RSPV; 3 LSPV; 1 LIPV and 2 both RSPV and LSPV) 8 interatrial septum 4 proximal CS 1 inferolateral aspect of the right atrium (Fig. 4)
Types II AF: CFAEs localize in two areas	43 (21 PAF and 22 CAF)	19 pulmonary veins and septum 9 septum and proximal CS 4 pulmonary veins and left posteroseptal mitral annulus 3 pulmonary vein and cavotricuspid isthmus 5 septum and mitral annulus 3 septum and the roof of the left atrium
Type III AF: CFAEs localize in ≥ 3 areas	55 (20 PAF and 35 CAF)	46 interatrial septum (83%) 37 pulmonary veins (67%) 34 left atrial roof (61%) 32 proximal CS and its os (59%) 13 mitral annulus (24%) 17 cavotricuspid isthmus (31%) 4 inferolateral aspect of the right atrium (7%) 2 SVC and right atrial junction (4%)

Radiofrequency Ablation of Complex Fractionated Atrial Electrograms (CFAE): Preferential Sites of Acute Termination and Regularization in Paroxysmal and Persistent Atrial Fibrillation

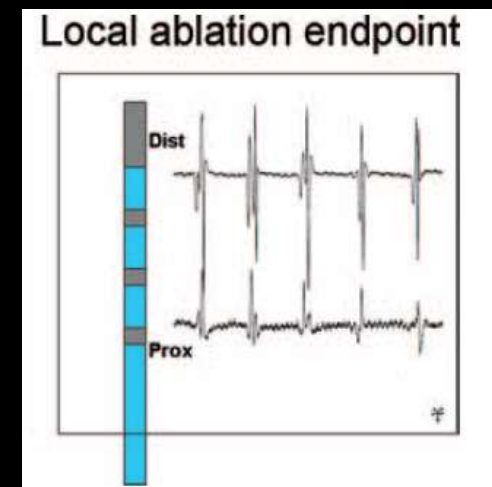
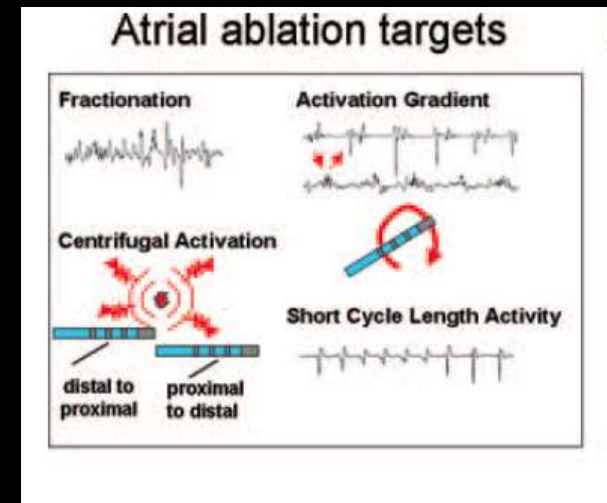
- 66 patients, PAF and PsAF
- PAF in SR: segmental PVI plus induction, then CFE ablation
- PAF in AF + PsAF: CFE ablation as first step
- 12 ± 3 m f/u; 54% PsAF and 65% of PAF in SR

	Paroxysmal AF (n = 36)	Persistent AF (n = 30)	P
Termination (n patients)	19	9	0.012
Regularization (n patients)	13	15	NS
No effect	4	6	NS
	89%	80%	

	Paroxysmal AF		Persistent AF		Total	
	Term	Reg	Term	Reg	Term	Reg
PV	13	10	2	12	15	22
Anterior LA/LAA	11	8	3	11	14	19
Septum	6	8	2	9	8	17
Posterior MA	5	5	2	2	7	7
Roof	3	4	1	2	4	6
CS	1	3	3	5	4	8
SVC/crista terminalis	1	0	0	2	1	2
Total	40	38	13	43	53	81

Catheter Ablation of Long-Lasting Persistent Atrial Fibrillation: Critical Structures for Termination

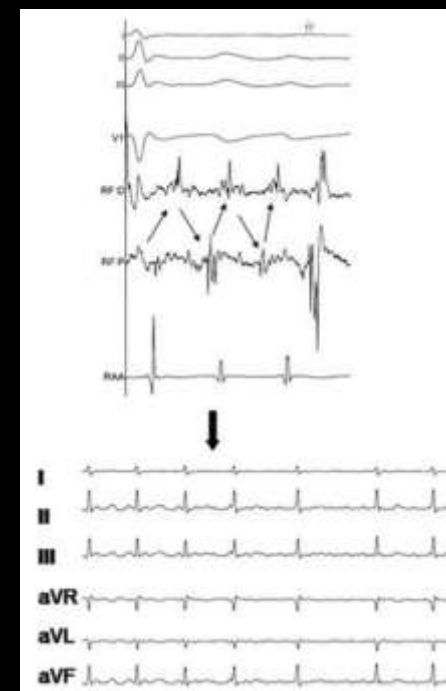
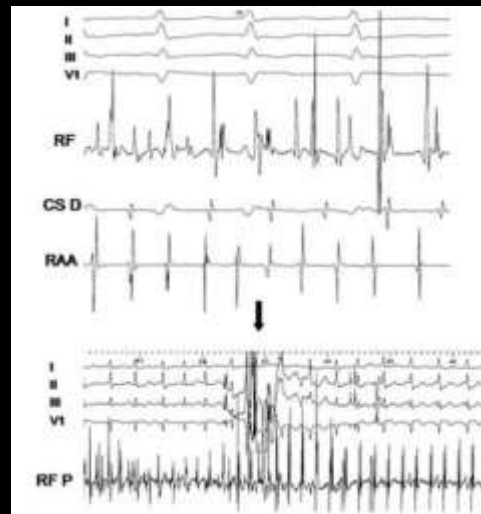
- 60 patients (17 ± 27 m)
- Randomized ablation sequence
- PV, thoracic veins, LA followed by linear ablation
- Termination in 52/60, via AT in 45/52



Stepwise Catheter Ablation of Chronic Atrial Fibrillation: Importance of Discrete Anatomic Sites for Termination

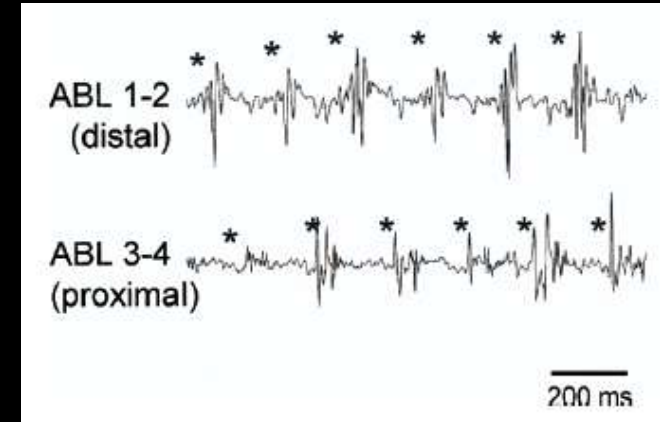
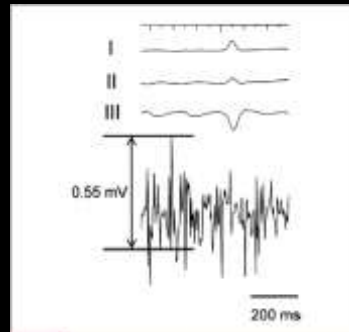
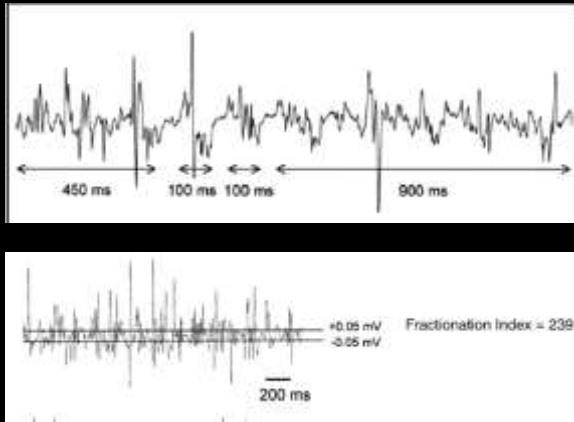
Study

- 80 patients with CAF
- Termination in 50/69 during stepwise approach
- Termination in 19/69 at a discrete site
 - Electrophysiological signatures
 - Point and activation mapping



Electrogram Type	Anatomical Site	Type I CEA	Type II Fraction	Type III Burst	Type IV Source	Type V Gradient
Septum		1	1		1	
LAA ant-sup				1	2	1
post-inf		1	1	2		
CS distal		1		2		
CS ostium					1	1
Posterior LA			1			
Anterior LA				1		
CTI						1
Total number of patients		3	3	6	4	3

Characterization of Electrograms Associated With Termination of Chronic Atrial Fibrillation by Catheter Ablation



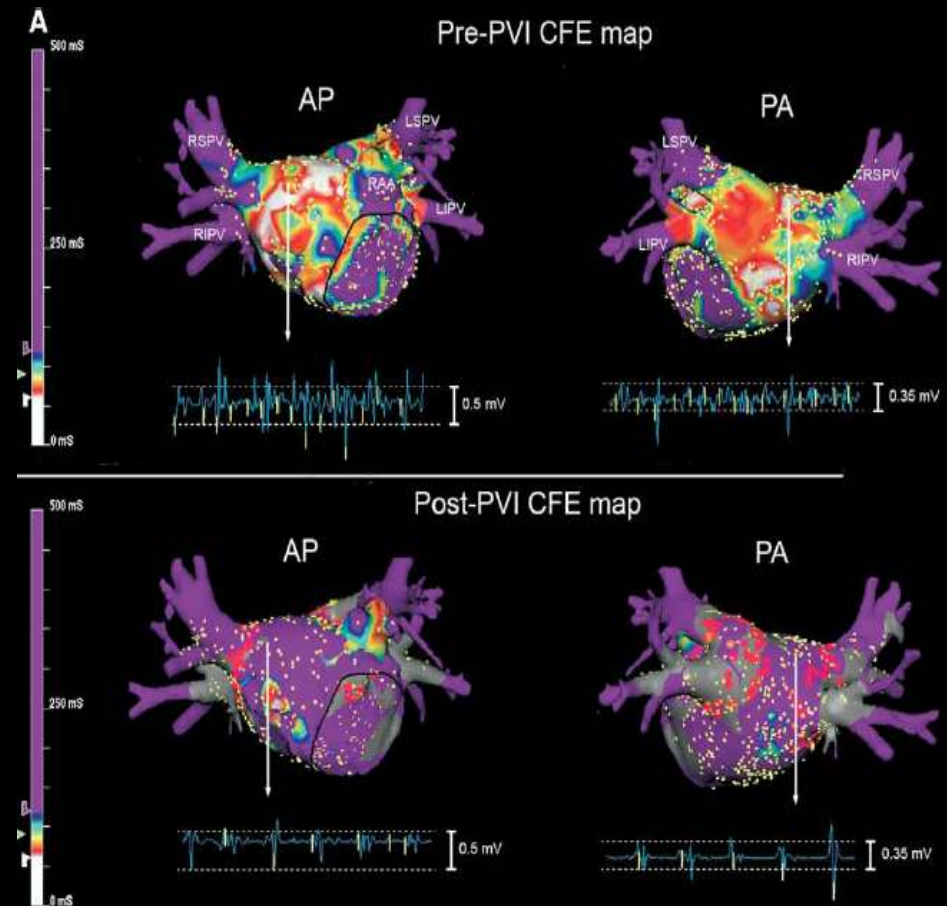
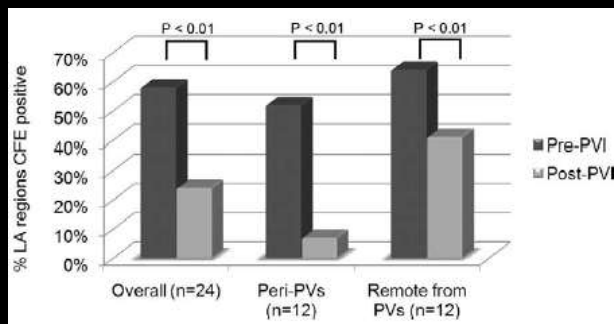
40 CAF patients, 29 with termination during egm-guided ablation phase

Table 4 Characteristics of Electrograms and Impact of Ablation

	Ablation Regions With AF Termination (n = 29)	Ablation Regions With a ≥ 6 -ms Increase in AFCL (n = 37)	Ablation Regions With a < 6 -ms Increase in AFCL (n = 105)	p Value
Percentage of continuous activity (%; median [1st, 3rd quartile])	80 (60, 90)	70 (43, 86)	50 (25, 85)	0.0018*
Voltage of continuous activity (mV)	0.20 \pm 0.11	0.16 \pm 0.09	0.20 \pm 0.11	0.12†
Local DF (Hz)	7.87 \pm 3.38	7.71 \pm 3.10	7.29 \pm 2.43	0.52†
DF difference with LAA (Hz)§	1.79 \pm 3.22	1.51 \pm 3.12	0.91 \pm 2.45	0.23†
Fractionation index	164 \pm 63	150 \pm 66	157 \pm 50	1.0†
Mean absolute value of dV/dt (V/s ²)	0.015 \pm 0.006	0.015 \pm 0.009	0.015 \pm 0.007	0.91†
Local mean cycle length (ms)	166 \pm 21	178 \pm 26	169 \pm 23	0.21†
Cycle length difference with LAA (ms)	-8 \pm 22	-5 \pm 10	-9 \pm 17	0.58†
Activation gradient (patients [%])	7 (24%)	9 (24%)	10 (10%)	0.03‡

Effect of pulmonary vein isolation on the distribution of complex fractionated electrograms in humans

- 22 patients with PsAF
- 47% of LA CL<120ms (CFE)
- Reduced to 23% post ablation (PVI+triggers)
- Increase in LA AFCL from 144ms to 214ms
- Reduction in CFE burden in both PV (50v6%) and non-PV (61v39%) regions



To summarise so far...

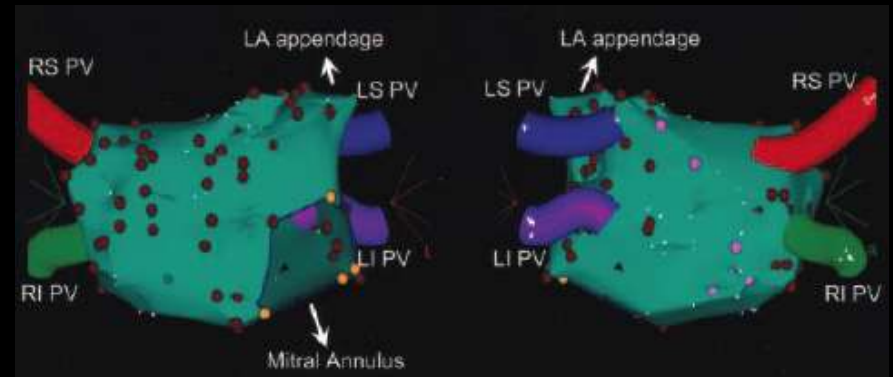
- CFE sites can be identified throughout the atrium and targeted for ablation
- Atrial ablation is essential to achieve AF termination in most persistent AF patients
- There are often recognisable egm characteristics at sites of termination
- PVI alters CFE distribution acutely

Outline

- What are complex fractionated atrial egms?
- What is the acute impact of ablation?
- What is the clinical impact of ablation?
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Radiofrequency Catheter Ablation of Chronic Atrial Fibrillation Guided by Complex Electrograms

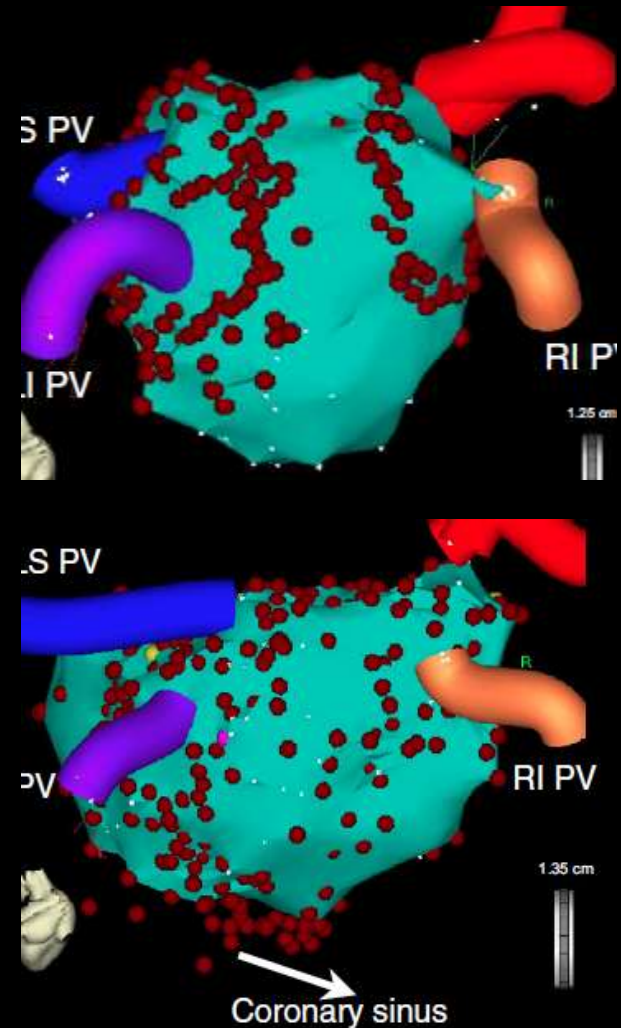
- 100 patients
- RF targeting CFEs at PV antra (not isolation), LA, CS until AF termination or elimination of all CFEs
- Ablation of macroreentrant circuits where possible
- Repeat ablation in 44 patients



- 13±7m after final ablation, 57/100 patients in SR without AAD
- AF termination did not predict clinical outcome
- CFE ablation alone has modest efficacy in patients with chronic AF

A Randomized Assessment of the Incremental Role of Ablation of Complex Fractionated Atrial Electrograms After Antral Pulmonary Vein Isolation for Long-Lasting Persistent Atrial Fibrillation

- 119 consecutive patients
- AF termination in 19/119 (Group A)
- Randomisation of remainder
 - no further ablation (Group B)
 - ablation of CFEs in LA and CS for up to 2 hours (Group C)
- 157 procedures in total



A Randomized Assessment of the Incremental Role of Ablation of Complex Fractionated Atrial Electrograms After Antral Pulmonary Vein Isolation for Long-Lasting Persistent Atrial Fibrillation

Ablation of CFEs (Group C)

- AF terminated in 9/50 patients
- To SR in 5, AT in 4
- In remaining 41, ibutilide infusion (11) or DCC (30)

Maintenance of SR at 10±3m

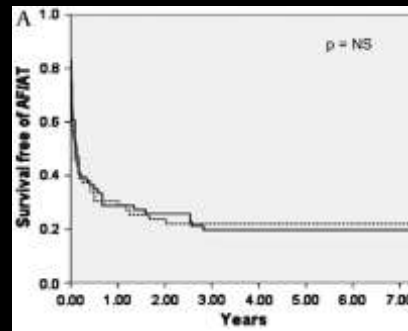
- 19/50 (38%) of patients in group B, repeat in 18
- 18/50 (36%) of patients in group C, repeat in 17
- 15/19 (79%) of patients in group A, repeat in 1

9±4m after the final procedure, among the 100 randomised patients, 68% who underwent APVI and 60% who also had CFE ablation were in sinus rhythm.

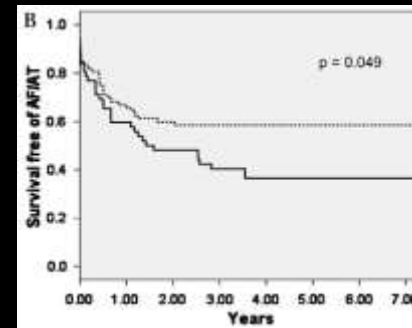
Up to 2h of additional ablation of CFEs outside of the antral regions in patients who Remained in AF after APVI did not improve the clinical efficacy.

Long-term efficacy of catheter ablation for atrial fibrillation: impact of additional targeting of fractionated electrograms

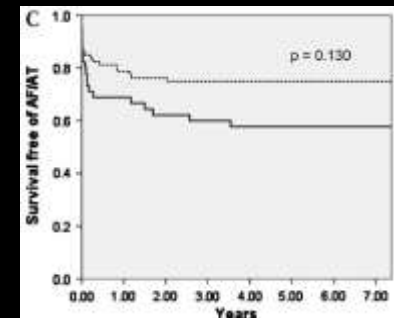
- Retrospective case analysis 2002-2007
- 285 patients, 530 procedures (1.9)
- Freedom from arrhythmia
 - 86% for PAF
 - 68% for PsAF
- The addition of CFE ablation to PV isolation may improve outcomes



CFE during 1st
Procedure (49%)



During 1st cluster
of procedures
(59%)



During any
Procedure
(65%)

Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint

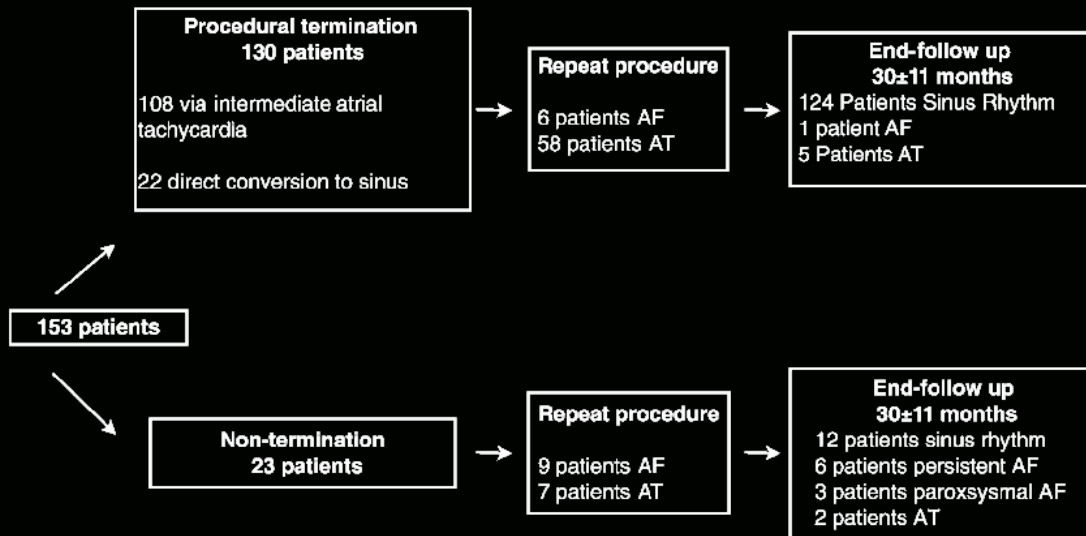


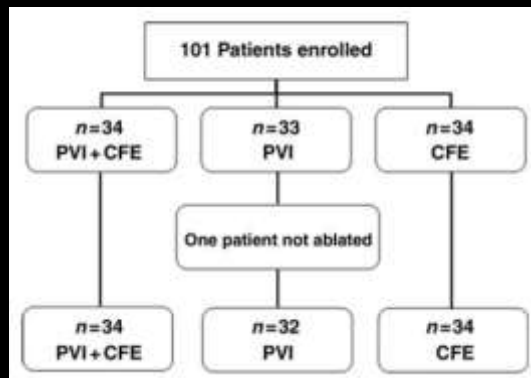
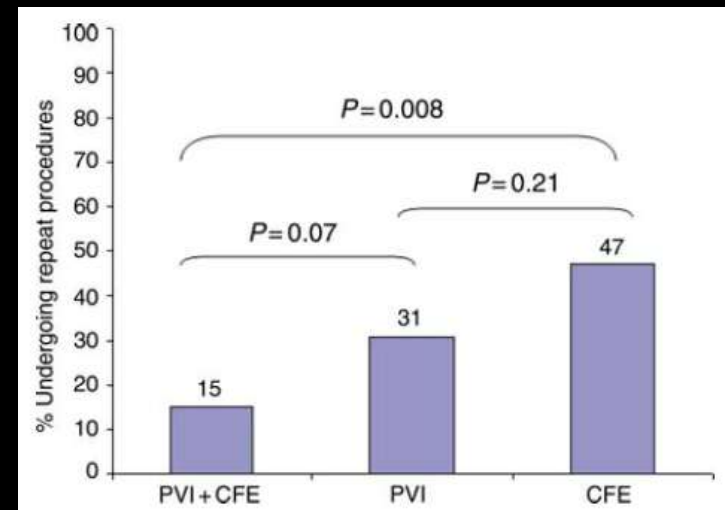
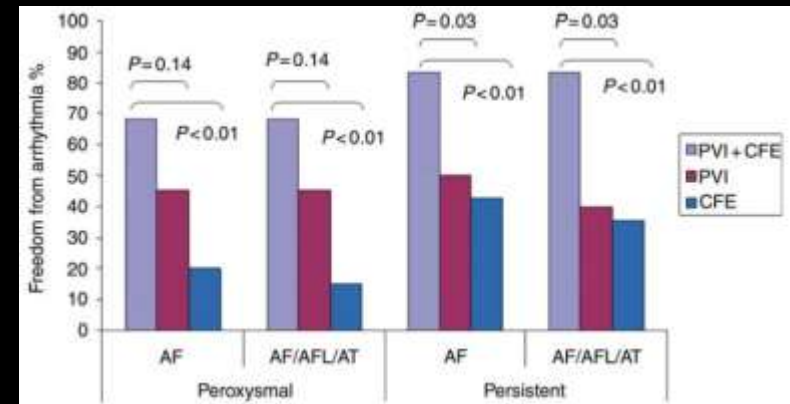
Table 3 Breakdown of anatomical sites of termination of atrial fibrillation by catheter ablation

Site of AF termination	Number of patients
Left atrium (n = 118)	
Inferior LA	11
CS os	2
CS (epicardial)	17
Left atrial appendage	25
Mitral isthmus	17
Pulmonary veins	14
Interatrial septum	12
Roof	8
Posterior LA	6
Anterior LA	4
Lateral LA	2
Right atrium (n = 12)	
Right atrial appendage	4
Intercaval	3
Cavotricuspid isthmus	2
Superior vena cava	2
Foramen ovale	1

Termination of AF by catheter ablation using a stepwise approach has a better long term clinical outcome than when AF fails to be terminated

Substrate and Trigger Ablation for Reduction of Atrial Fibrillation (STAR AF): a randomized, multicentre, international trial[†]

- 8 Centres
- High burden PAF 64/100
 - >4 episodes in 6m
 - 2>6h in duration
- Persistent AF 36/100
- Comparison of three ablation strategies, NavX



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Current Recommendation

HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Personnel, Policy, Procedures and Follow-Up

1. Ablation strategies which target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures.
2. If the PVs are targeted, complete electrical isolation should be the goal.
3. Careful identification of the PV ostia is mandatory to avoid ablation within the PVs.
4. If a focal trigger is identified outside a PV at the time of an AF ablation procedure, it should be targeted, if possible.
5. If additional linear lesions are applied, line completeness should be demonstrated by mapping or pacing maneuvers.
6. Ablation of the cavotricuspid isthmus is recommended only in patients with a history of typical atrial flutter or inducible cavotricuspid isthmus dependent atrial flutter.
7. If patients with longstanding persistent AF are approached, ostial PV isolation alone may not be sufficient.

Guidelines for the management of atrial fibrillation

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

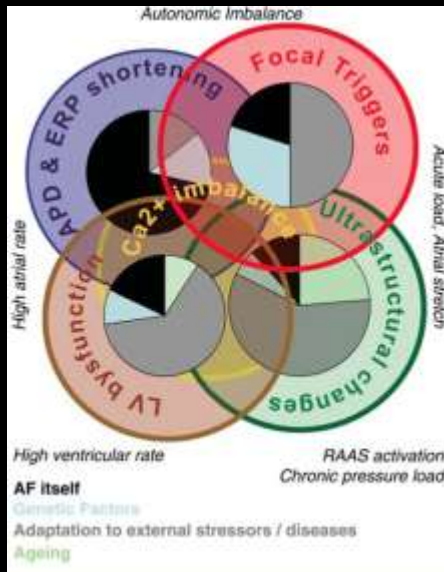
Alternative techniques for substrate modification

Atrial tissue generating **complex fractionated atrial electrograms (CFAEs)** has been ablated, without any attempt to isolate the PVs. While reports from single centres are favourable, prospective randomized trials have not shown benefit. Interestingly, arrhythmia recurrences after such procedures are dominated by arrhythmias originating in the PVs. Several groups have described radiofrequency ablation of **ganglionic plexi** as an add-on to PV isolation. The value of this technique is not yet established.

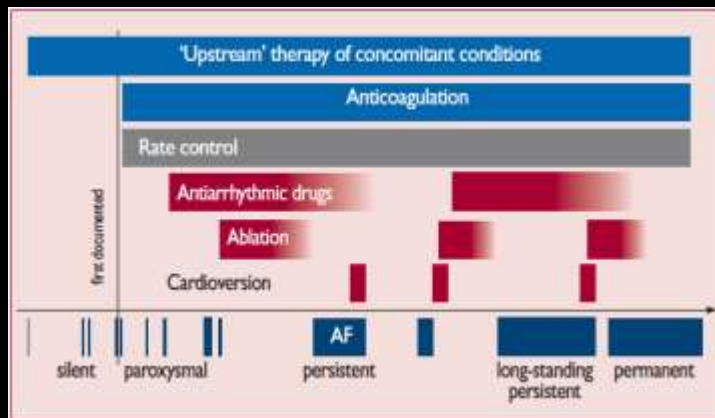
EHRA AF Guidelines EHJ 2010

Mechanisms in Atrial Fibrillation

Kirchhof et al
EHJ 2009;30:2969-80

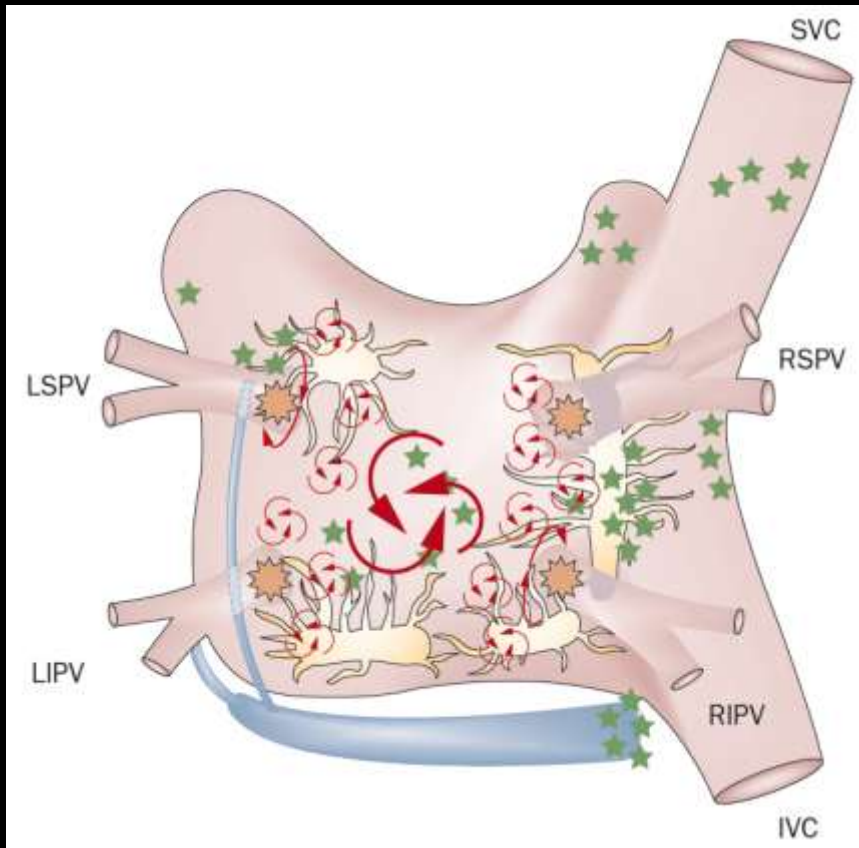


- Contributors: focal triggers, electrical remodelling, localised reentrant drivers, ultra-structural remodelling, altered Ca_i handling, inherited influences
- Variable combination in a given patient
- Several mechanisms active before AF occurs
- Many AF-promoting processes are caused by atrial damage unrelated to AF *per se*, but are then aggravated by AF itself
- Successful therapy requires identification of all AF causing factors and “graded” therapy of all relevant pathological processes



Camm et al. EHJ 2010;Sept 25 epub

When to target non-PV (CFE) sites?



- PAF
 - Clear non-PV source eg. LoM, SVC, CS, atrial site
 - Only following confirmed PVI
- PsAF
 - Majority of patients
 - Site-specific clustering at LAA, inferior LA, CS os, septum

The scientific theory I like best
is that the rings of Saturn are
composed of lost airline luggage.

Mark Russell
American Writer
1932-