EGM-Guided Ablation: CFE, Ganglia, Rotors…

ISHNE 2009

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Disclosures

- Consulting fees/honoraria
  - Biosense Webster, Medtronic, St Jude Medical, Sanofi Aventis, Astra Zeneca, Servier
- Speakers bureau
  - Biosense Webster, Medtronic, St Jude Medical
- Research grants
  - Biosense Webster, Medtronic, St Jude Medical
- Equity, Ownership, Salary, Royalties
  - None

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EGM-Guided Ablation

- Complex Fractionated Electrograms (CFE)
- STAR AF data
- Ganglionated Plexi (GP)
- Dominant Frequency (DF)

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Question #1

- Of the following EGM-based targets, which do you feel offer the greatest potential value as a hybrid strategy to PVI?

1. CFE
2. Ganglionated Plexi
3. Dominant Frequency
4. None of the above

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Question #2

- In which AF patients do you think CFE are most useful to study/ablate?

1. All AF
2. Paroxysmal AF
3. Persistent AF

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Question #3

- What do you think are the biggest barriers to using CFE ablation for AF (either alone or in combination)?

1. Not a consistent definition of CFE
2. Not a stable target for ablation
3. Not enough data showing its benefit
4. Too much extra procedural time
5. None of the above

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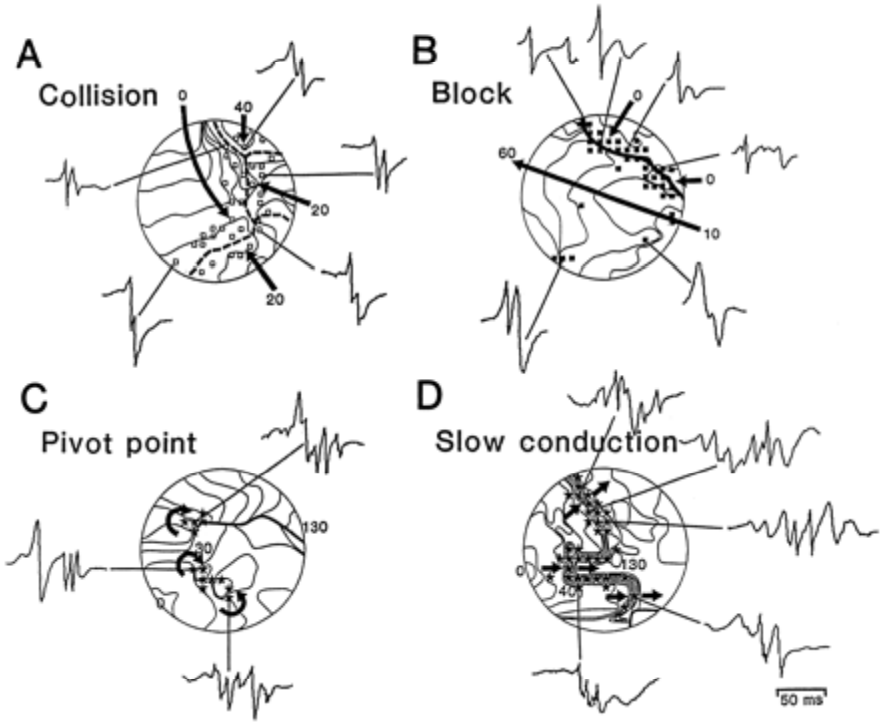
Complex Fractionated Electrograms (CFE)

Theory Behind CFEs



Konings et al, Circulation 1997

- Intraoperative mapping of RA during induced AF
- Identified 4 types of atrial potentials during AF
- Fragmented potentials correlated to pivot points where multiple wavelets arc around a region of functional block
- OR areas of slow conduction

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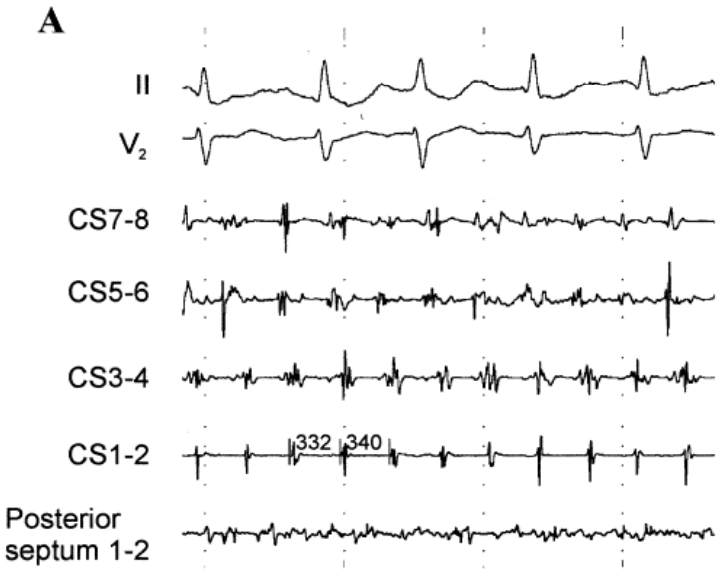
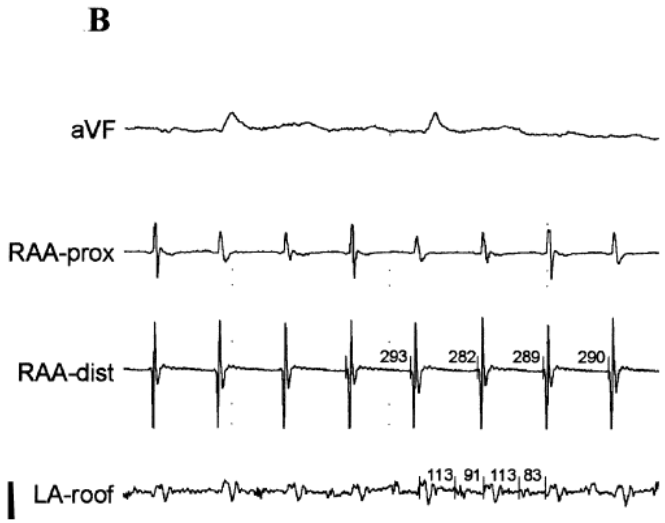
Definition of CFE – Nademanee JACC 2004



(A)atrial electrograms that are Fractionated & composed of two deflections or more and have a perturbation of the baseline with continuous deflections



(B) atrial electrograms with a very short cycle length (<120 ms) with or without multiple potentials when compared with the atrial CL from other parts of the atria

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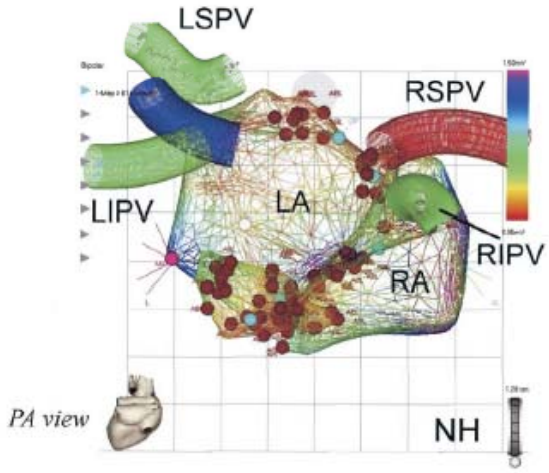
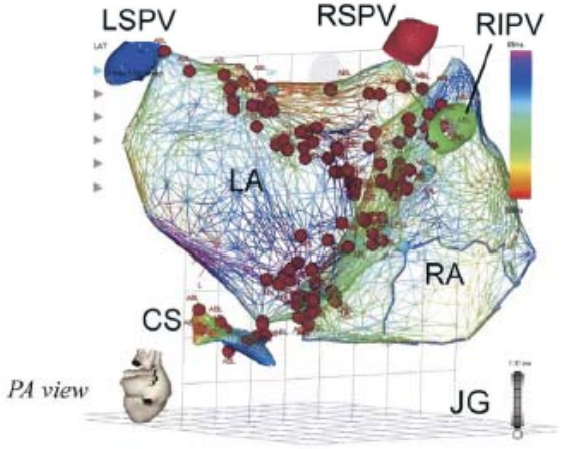
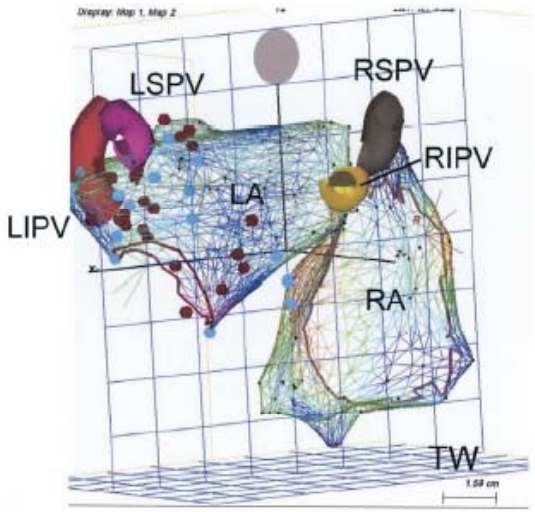
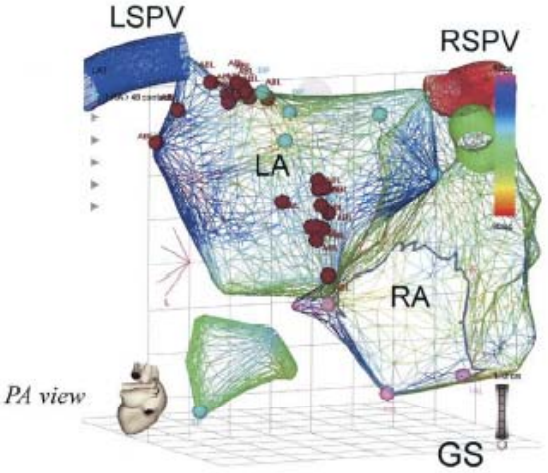
Where are the CFE?









PVs

Roof

Septum

RA

CS

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Nademanee, JACC 2004

- AFCL increased from:
  - 172 ± 26 ms to 237 ± 42 ms
- AF termination during ablation:
  - Paroxysmal – 100% (14% required ibutilide)
  - Chronic – 91% (28% required ibutilide)

- 76% success rate after 1 procedure
- 15% became arrhythmia-free after a second procedure
- At least 5% of these successful patients remained on AAD

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Oral et al, Circulation 2007

- Prospective, non-randomized assessment
- CFE ablation only – no PV isolation
- N=100
- Permanent AF patients only

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Oral et al, Circulation 2007

- Very low acute termination rate of AF during ablation
  - Only 16% terminated acutely
- Long-term success rate of this approach modest
  - 57% AF-free off medications
  - 44% required two procedures
  - Average of 14 months follow-up

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Reproducibility of CFE Results

- Results from other centers not consistent
- Part of the problem stems from definition and understanding of CFE
- Are these targets really spatially and temporally stable?
- Is there a consistent way to define CFE?

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Haissaguerre et al, Heart Rhythm 2006

- "CFE" are dependent on AFCL
- The faster the CL, the more likely it is to see "CFE"
- Since AFCL can be variable, so to can occurrence of "CFE"
- Therefore, "elusive" "transient" target

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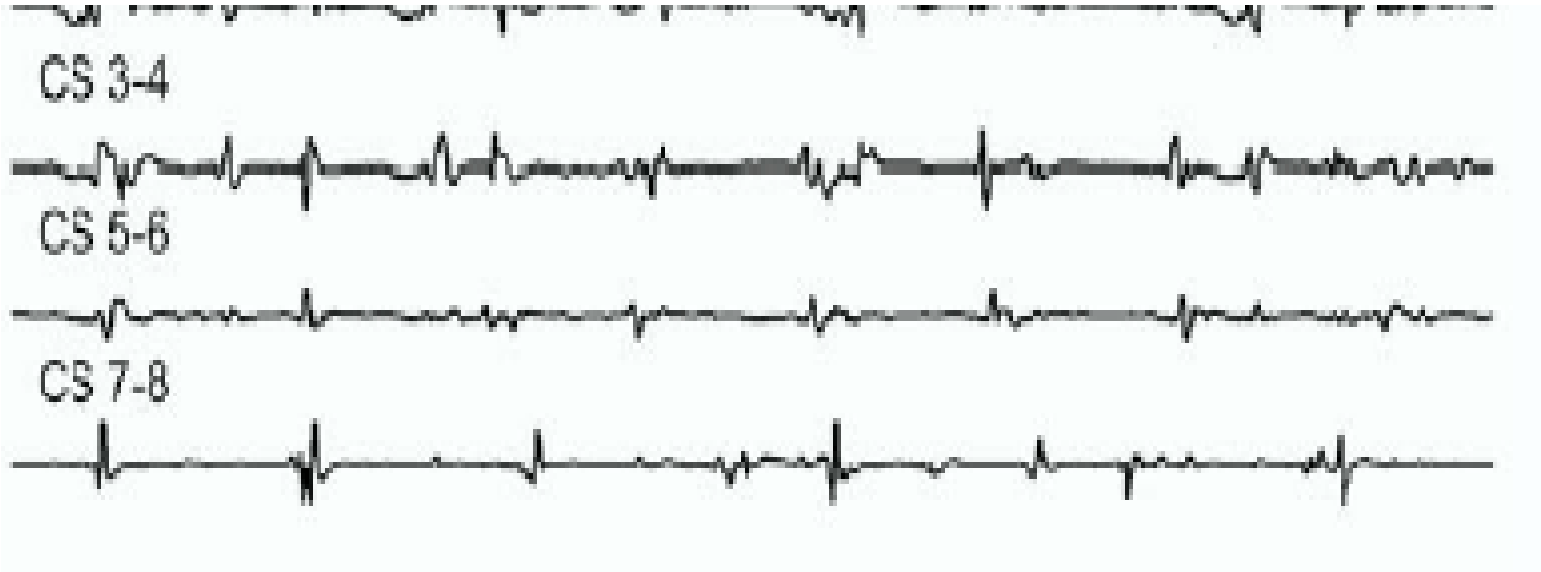
Haissaguerre et al, Heart Rhythm 2006

- Problem: Are these "CFE"?



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Automated CFE Mapping

- Subjectivity of CFE definition still a major limitation
- Automated algorithms are novel tools to standardize CFE definition and mapping
- Averages the signal analysis over 4-8 sec, allowing differentiation from transient vs stable CFE sites

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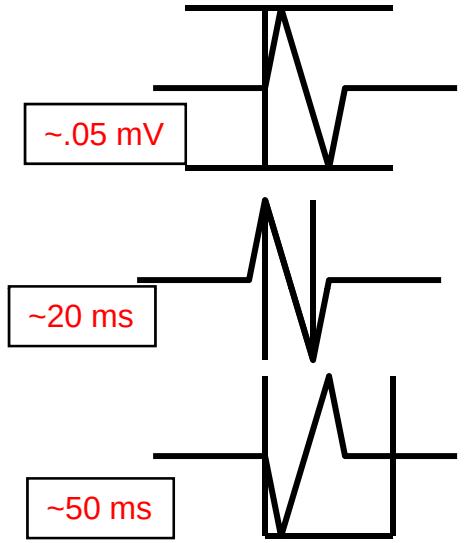
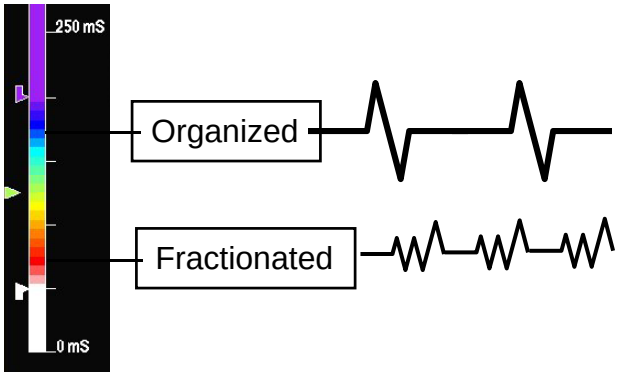
Implementation and Deployment of the CFE Mapping Tool (NAVX)

- Activation Detection Criteria
  - Peak-to-peak voltage threshold
    - > Baseline noise floor
  - Slope threshold
    - Near field vs. far field
  - Refractory setting
    - Avoid double counting



- Map Display Representation
  - Average interval represented with color scale (ms)
    - 1-8 second evaluation length



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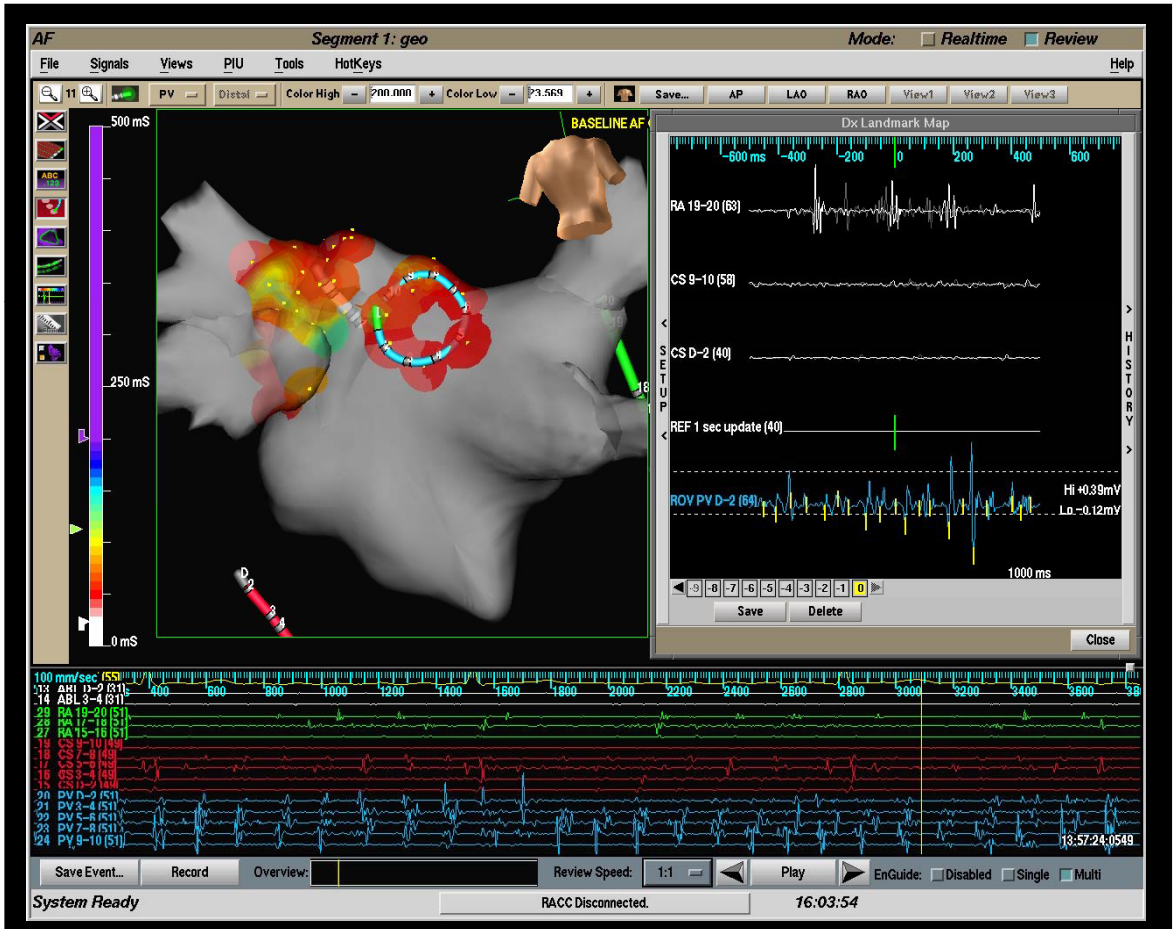
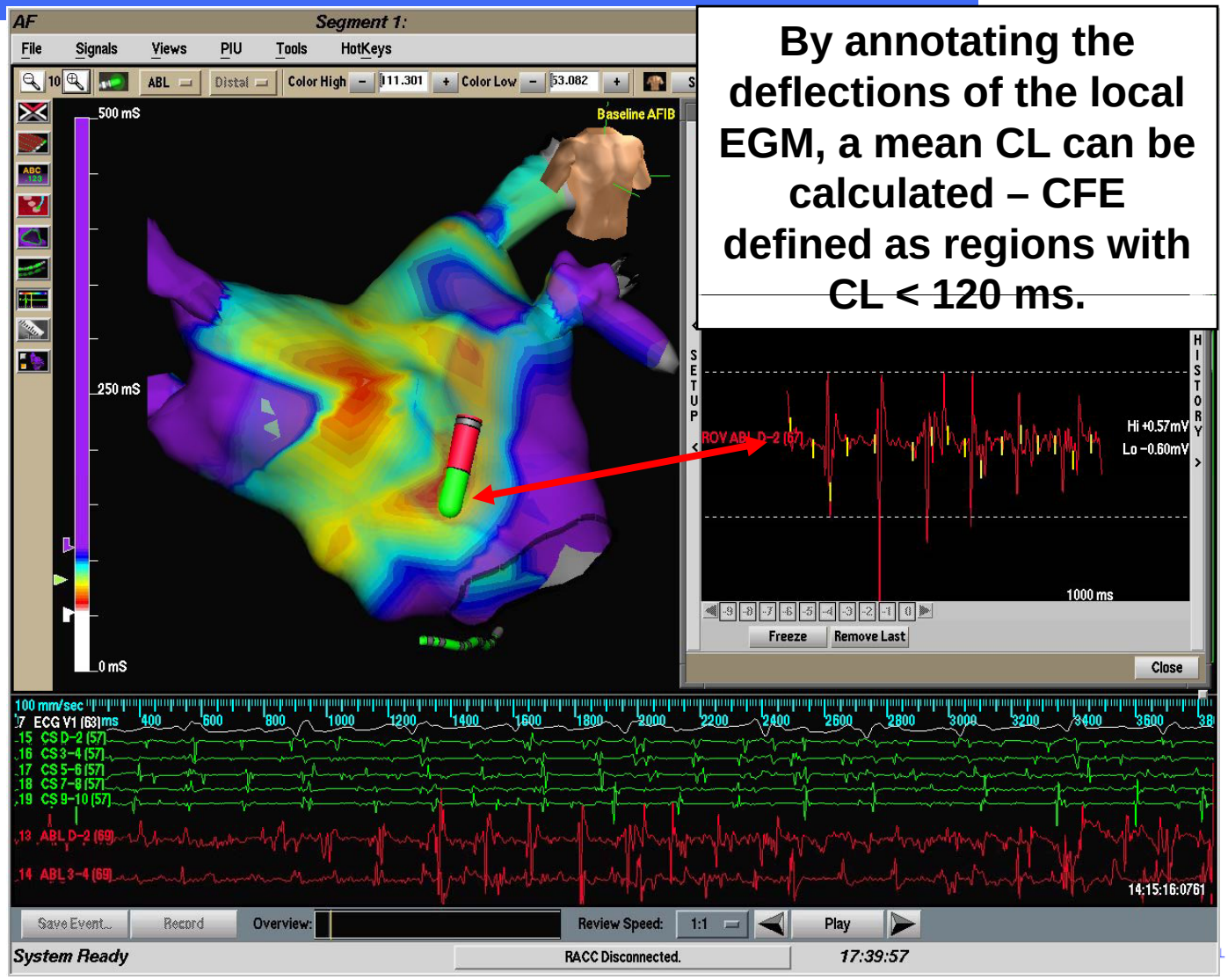
Diagnostic Landmarking: NavX System

- 3D mapping from standard catheters
- Points are collected at electrodes and projected onto map surface
- Using MultiPoint technology, points may be collected from
  - A single electrode
  - A multipolar catheter
  - All catheters in use



MultiPoint DxL mapping of fractionation
Image courtesy of Dr Andrea Natale, CCF

Mapping CFE Regions



By annotating the deflections of the local EGM, a mean CL can be calculated – CFE defined as regions with CL < 120 ms.

Courtesy of Dr. Koonlawee Nademanee, Los Angeles, CA

DxL Map Settings – CFE Mean

Recommended Settings	
Width	10-20 ms (avoid far-field)
Refractory	30-50 ms (avoid double counting)
P-P Sensitivity	0.03-0.05 mV (avoid noise)
Segment Length	4-8 sec
Interpolation	4-10 mm
Internal/External Projection	3-6 mm

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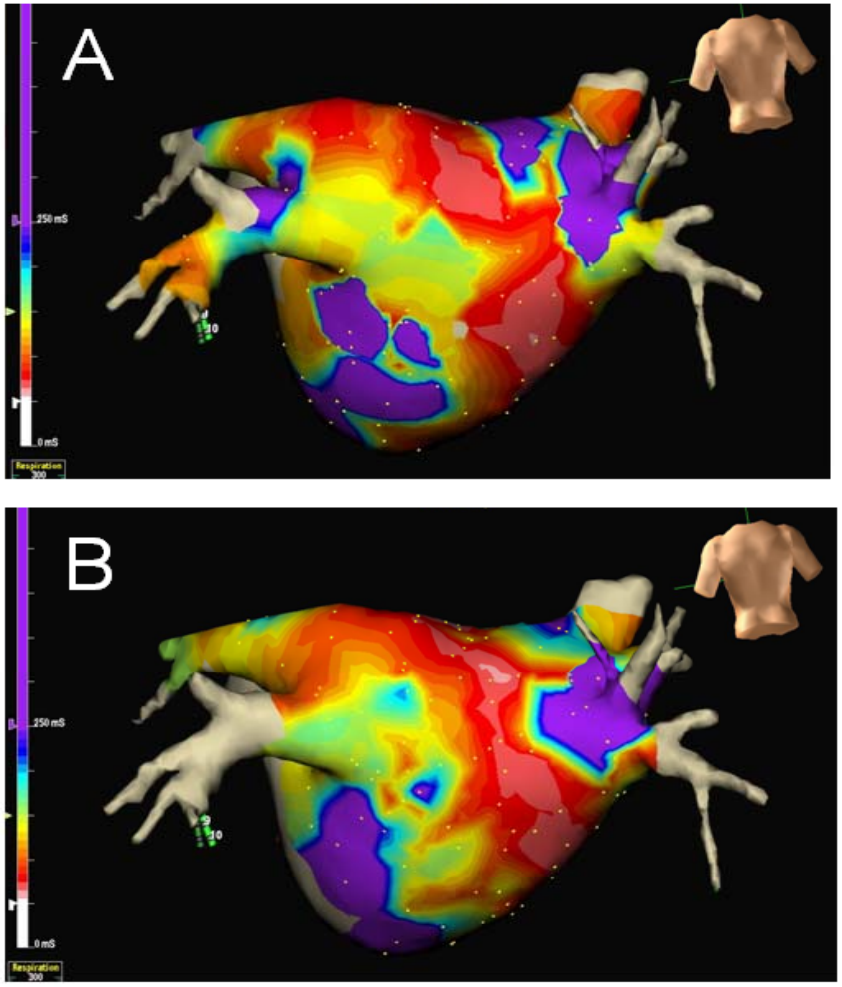
CFE Stability – Verma et al, Heart Rhythm 2008



CFE maps taken at 0 and 20 minutes. Degree of overlap and consistency of CFE areas studied.

CFE definition – regions with local EGM cycle length <120 ms.

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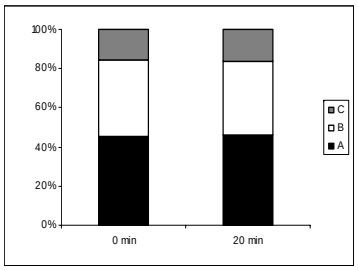
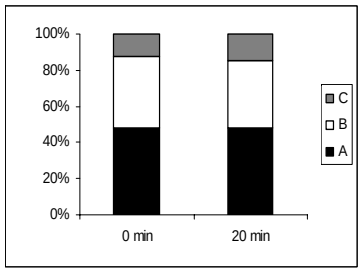
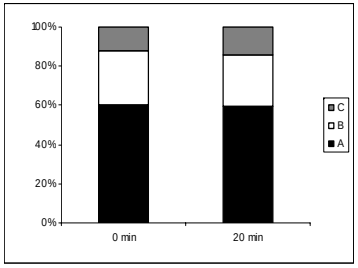
CFE Stability – Verma et al, Heart Rhythm 2008



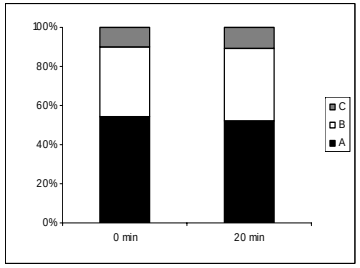
LPV



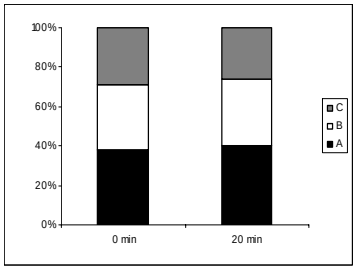
RPV



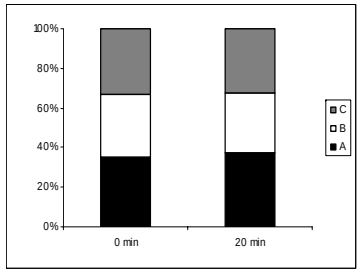
SEPT



PW



RO



FLR

When measured at 0 and 20 minutes, proportion of signals within cycle length ranges are stable.

Black = 50-120 ms

White = 121-200 ms

Grey = >200 ms

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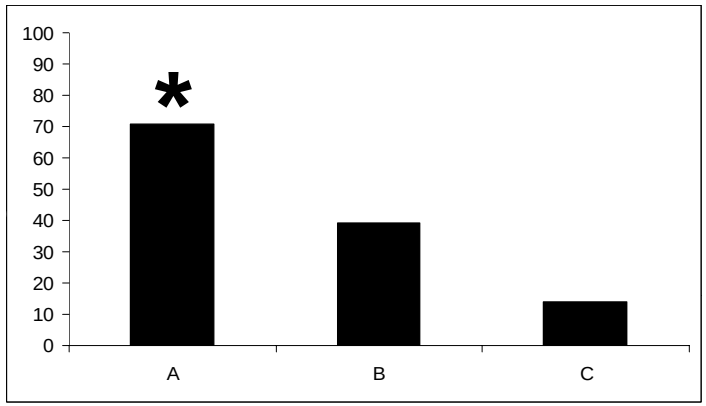
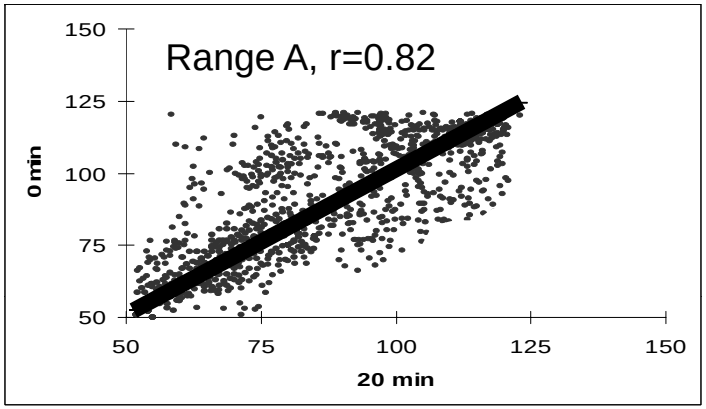
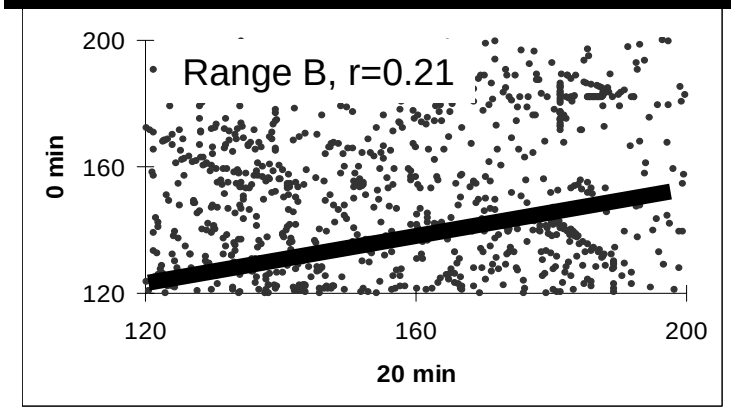
CFE Stability – Verma et al, Heart Rhythm 2008



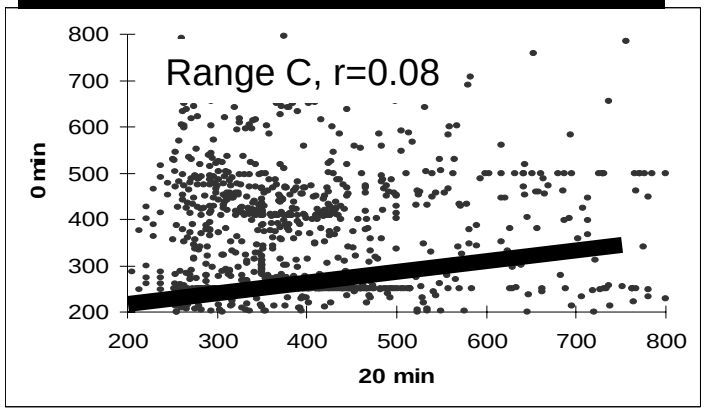
Degree of Overlap 0/20 min



Cycle Length 50-120 ms



Cycle Length 121-200 ms



Cycle Length >200 ms

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Substrate vs Trigger Ablation for Reducing Atrial Fibrillation

A Multicenter, Randomized Trial

Principal Investigator:
Atul Verma, MD FRCPC
Southlake Regional Health Centre, Canada

Presented at Heart Rhythm 2009 – Late Breaking Trials

Study Purpose

- To compare the efficacy of three AF ablation strategies:
  - Targeting the triggers of AF via PV isolation (PVI)
  - Targeting the substrate of AF maintenance via elimination of complex fractionated electrograms (CFE)
  - A hybrid approach of PVI + CFE ablation
- High-burden paroxysmal (65%) and persistent (35%) AF population
- Multicenter, randomized trial

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PVI Strategy

- Wide, circumferential PV antral isolation
- Lesions placed >1-2 cm outside of the PV ostia
- Endpoint of entrance block of all PV antra as documented by a circular mapping catheter

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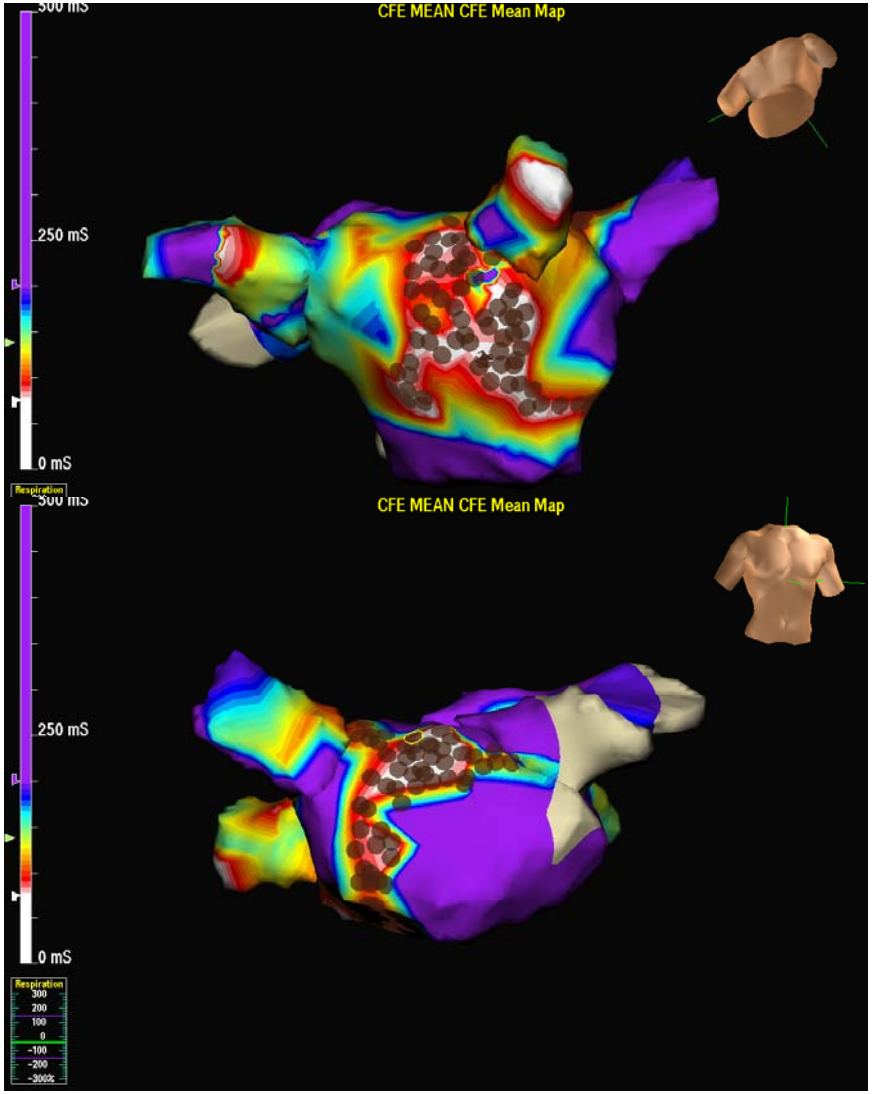
CFE Strategy - I



- Spontaneous or induced AF (must persist >1 min)
- Automated CFE mapping algorithm
- All CFE regions targeted (CL<120 ms)
- Target all CFE regions in LA, then CS, then RA

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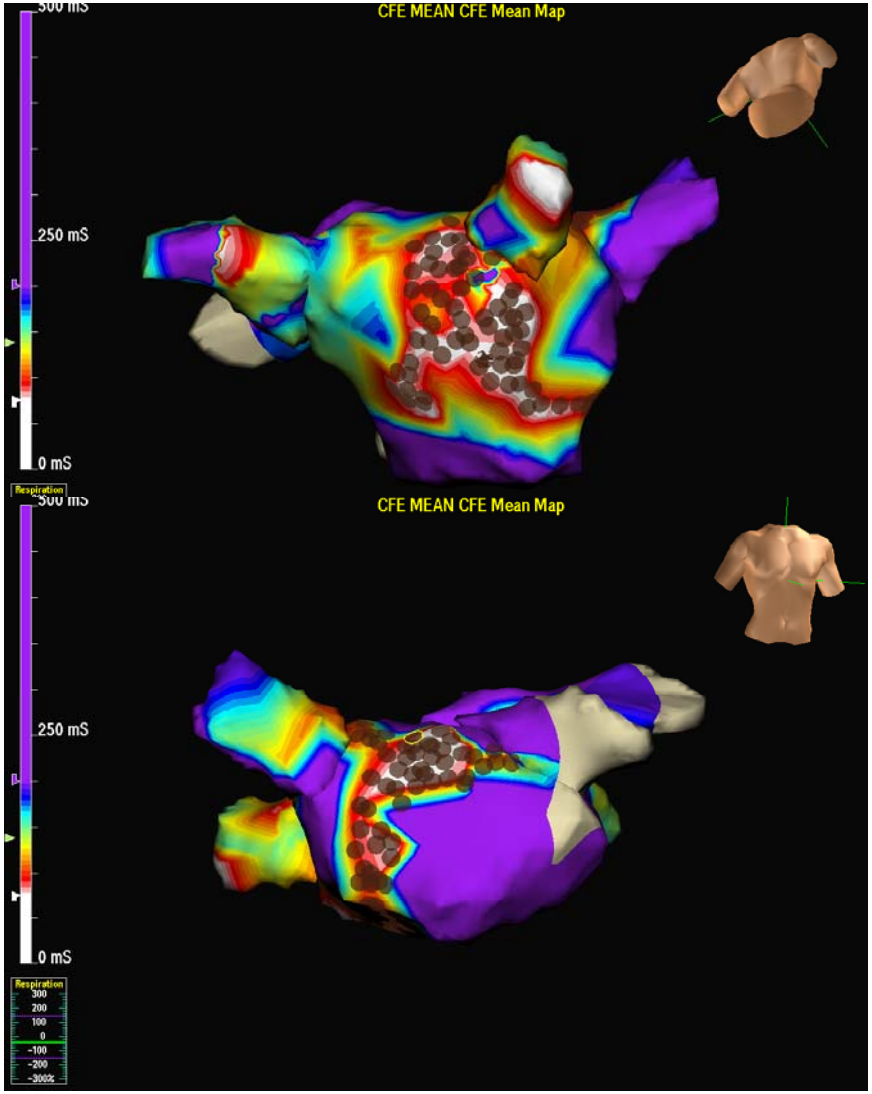
CFE Strategy - II



- Endpoint of elimination of all CFE sites or termination of AF and non-inducibility of AF
- If AF did not terminate after all CFE sites ablated, cardioversion allowed
- If AF terminated to AT or AFL, this was mapped/ ablated when possible
- IV antiarrhythmics not used during ablation

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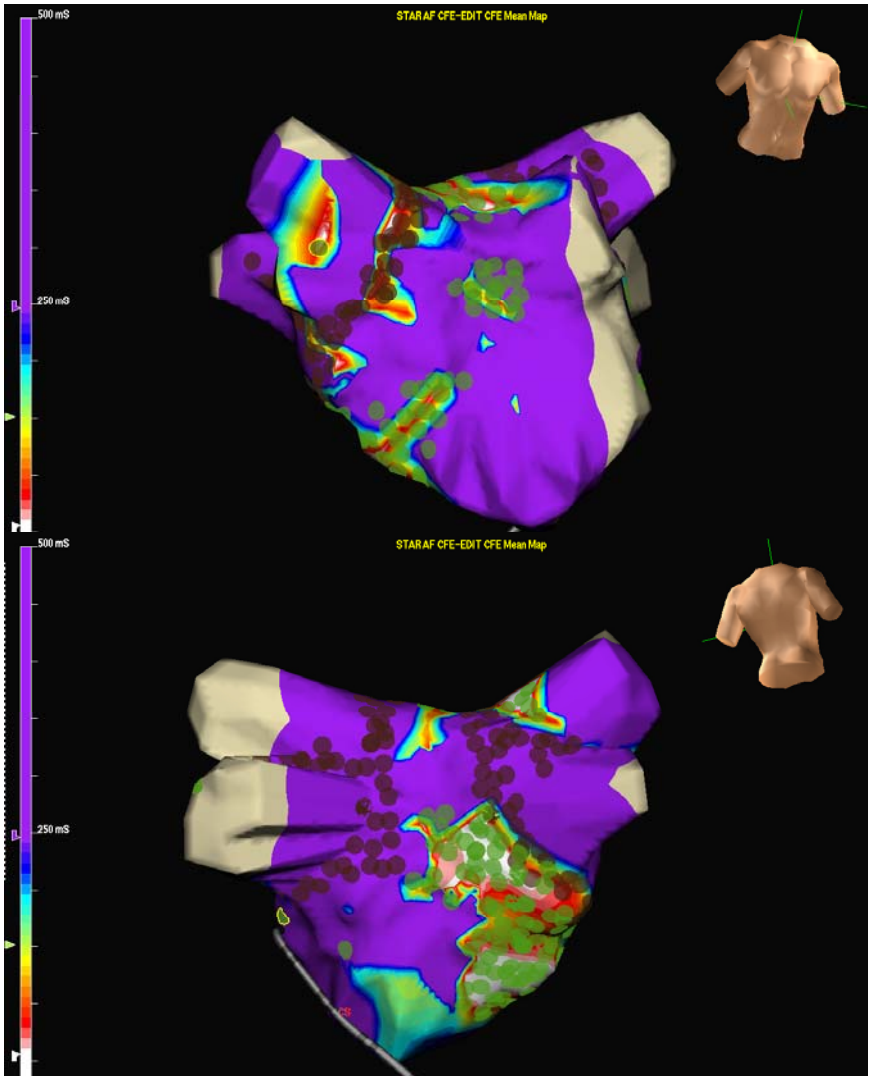
PVI+CFE Strategy



- PVI completed first
- Then, CFE mapped (spontaneous or induced AF) and ablated
- Endpoint of PVI followed by AF termination/ non-inducibility
- If AF not terminated after all CFE ablated, cardioversion allowed

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Procedural Details - II

	CFE	PVI	PVI+CFE	p
Procedure Time (min)	**224 ± 80**	**181 ± 74**	**225 ± 68**	**NS**
Mapping Time (min)	**39 ± 18**	**29 ± 21**	**41 ± 20**	**0.09**
Fluoroscopy Time (min)	**56 ± 28**	**58 ± 27**	**60 ± 34**	**NS**
RF Time (min)	**65 ± 33**	**68 ± 41**	**77 ± 45**	**NS**

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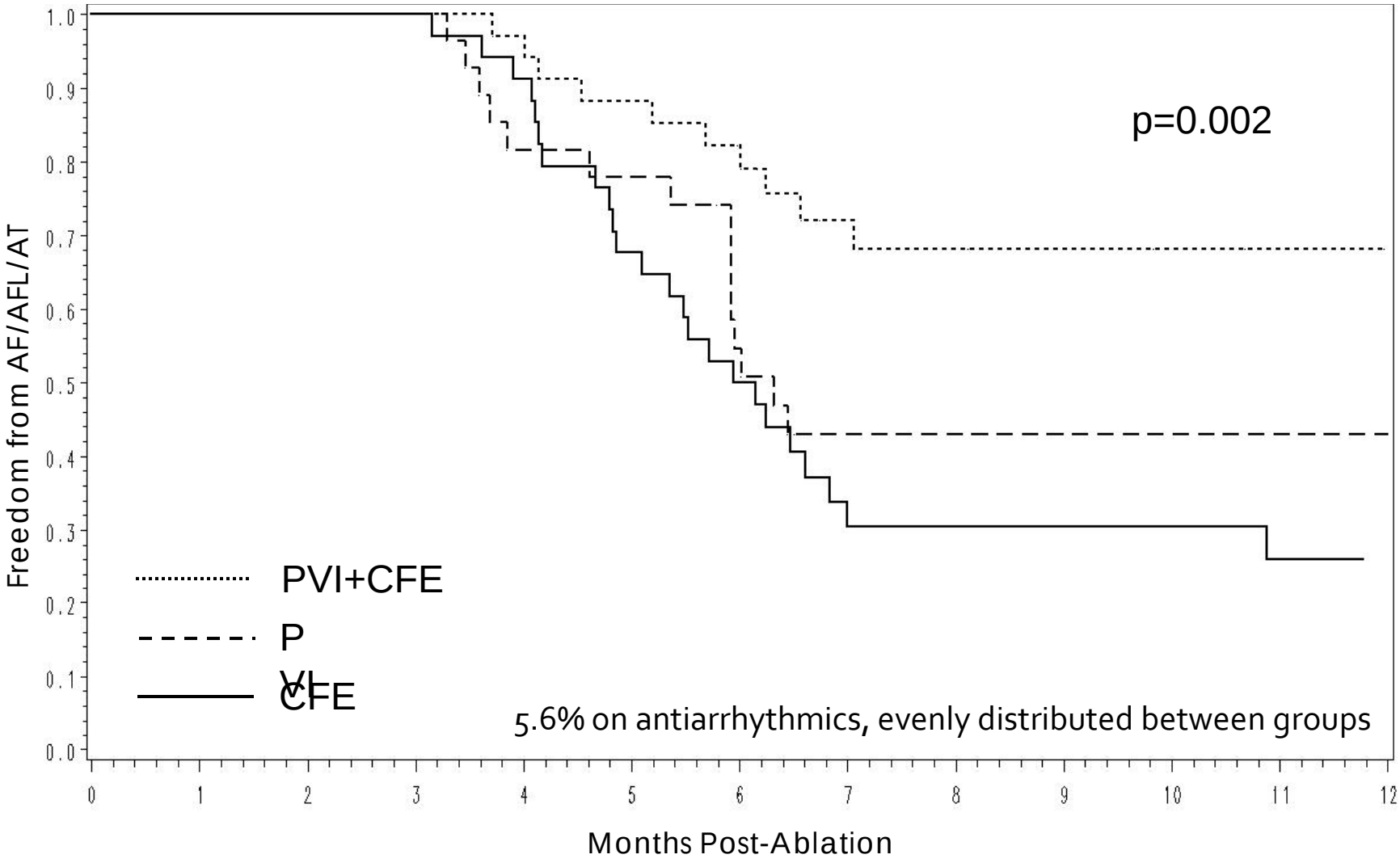
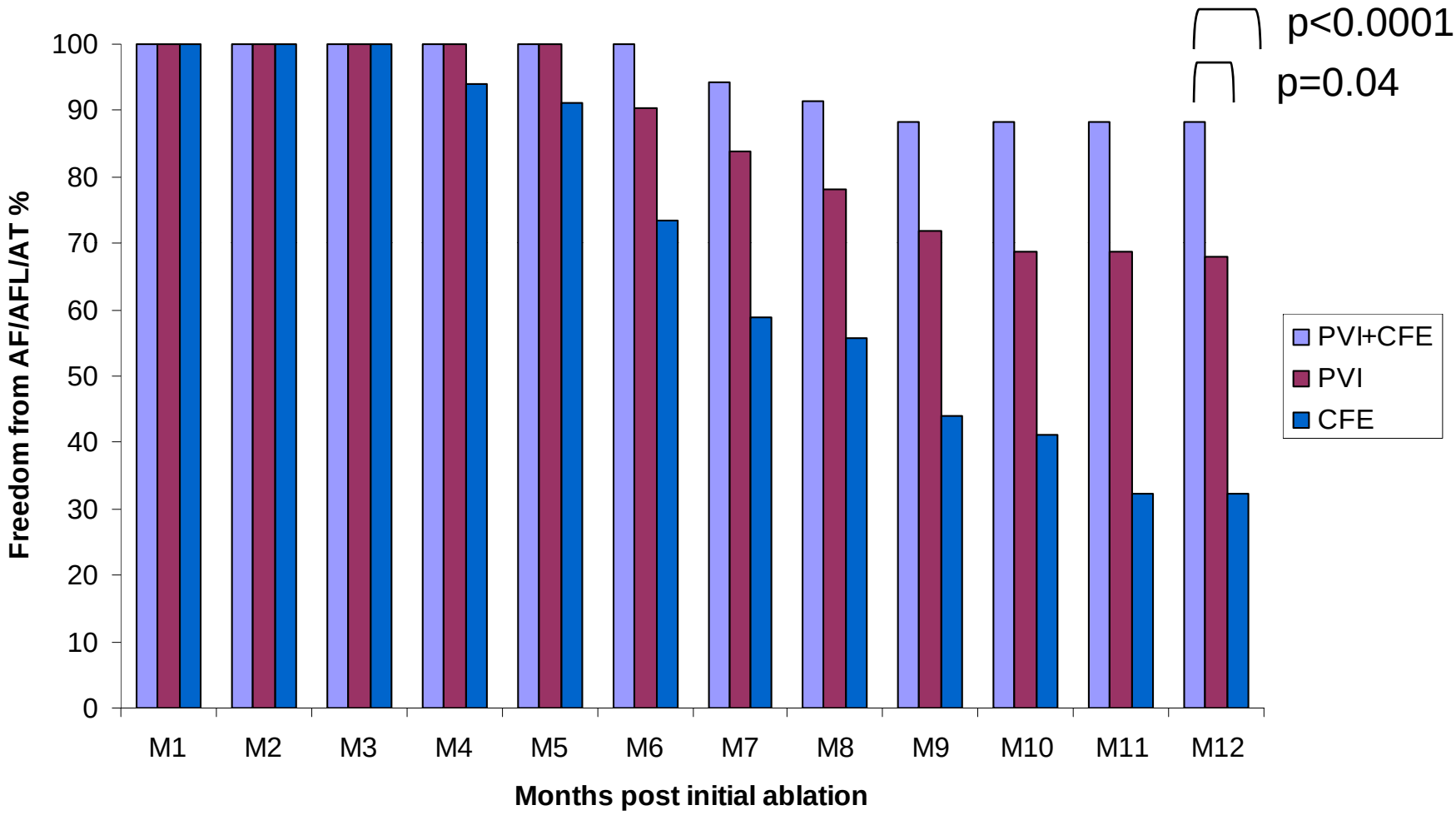
Freedom from AF/AFL/AT

(1 procedure)



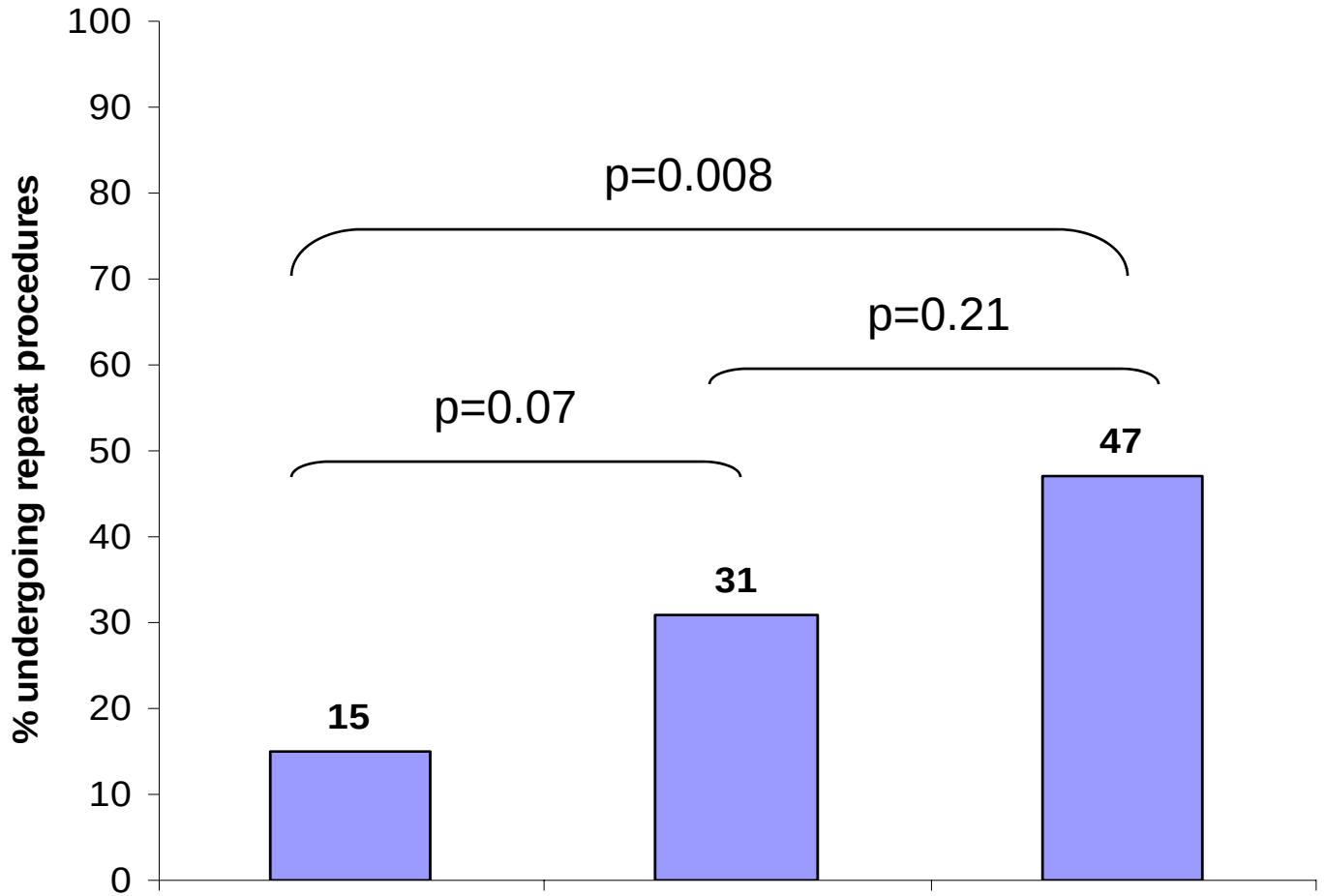
Freedom from AF/AFL/AT

(2 procedures)

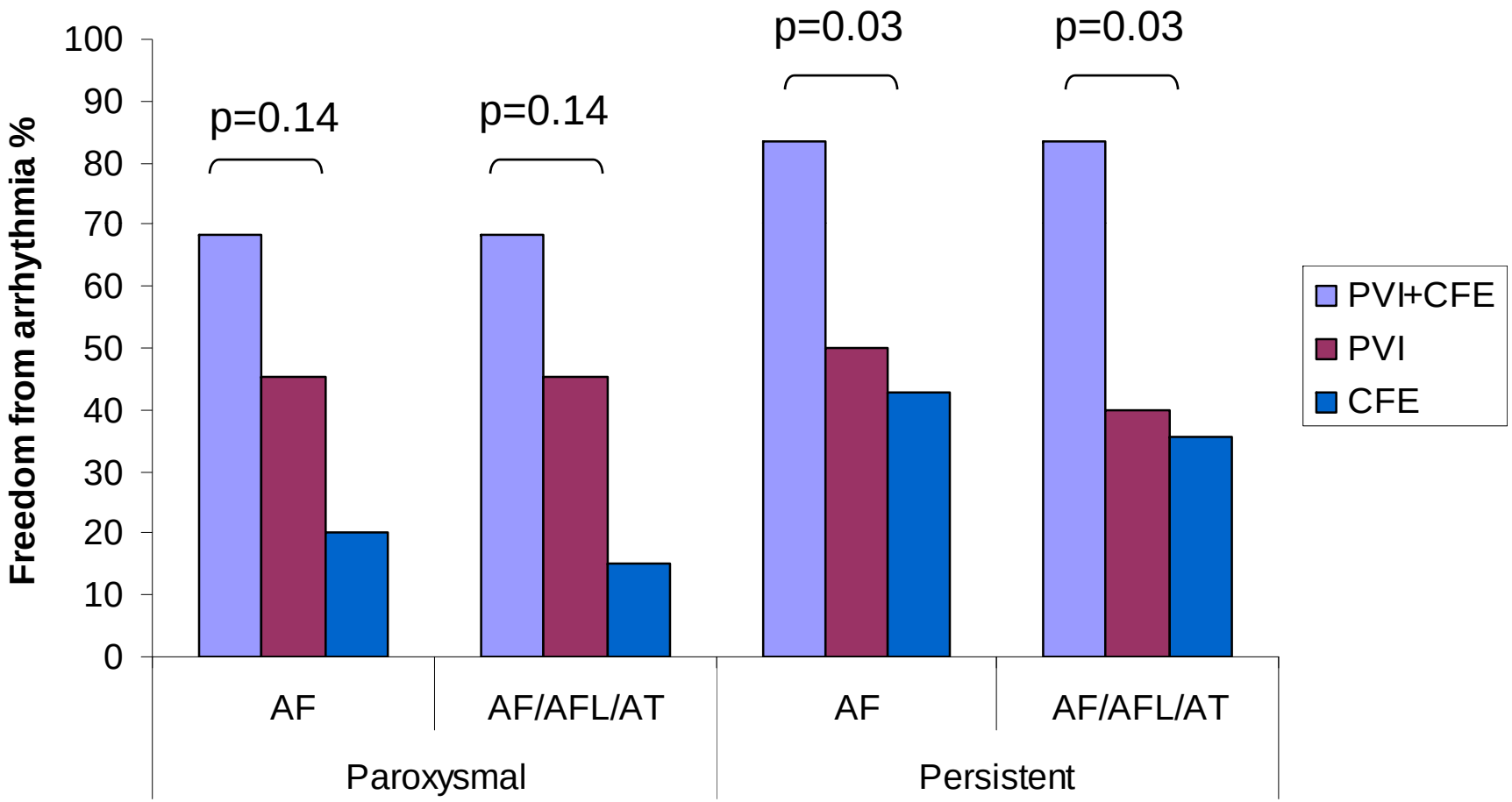


5.6% on antiarrhythmics, evenly distributed between groups

Repeat Procedures



Paroxysmal/Persistent Subgroups



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Conclusions

- In high burden paroxysmal/persistent AF patients, PVI+CFE is associated with the highest freedom from atrial arrhythmia at one year
- PVI+CFE requires fewer repeat procedures compared to either strategy alone
- CFE is associated with the highest recurrence rate and highest number of repeat procedures
- Benefit of PVI+CFE may be more pronounced in persistent AF

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Ganglionated Plexi (GPs)

Ablating Autonomic Inputs

- Evidence from Pappone et al that vagal denervation may be an important reason for AF cure by CARTO-guided approach

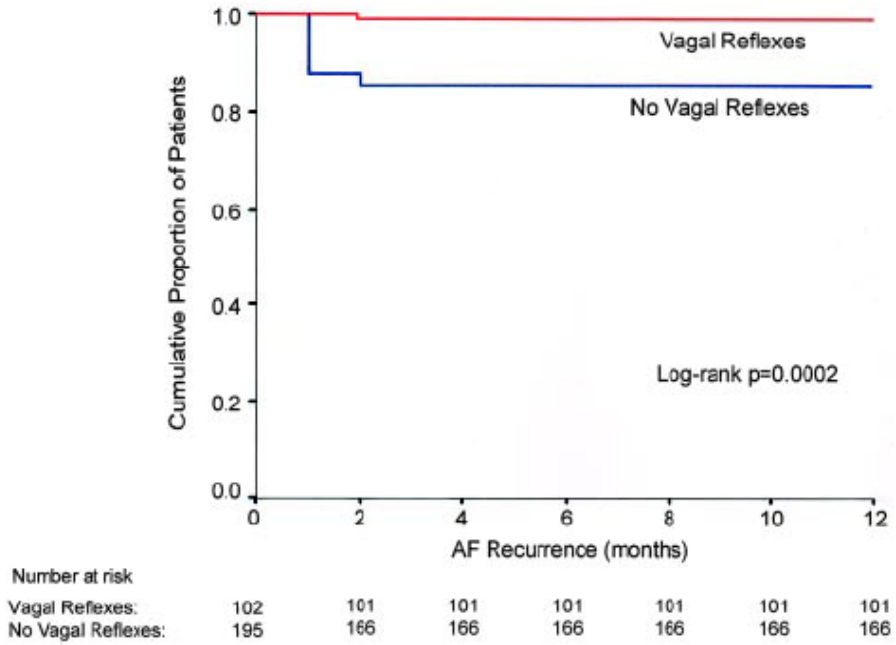

Figure 5. Kaplan-Meier curve of freedom from recurrent AF after CPVA in patients with or without vagal reflexes.

Pappone et al, Circulation 2004

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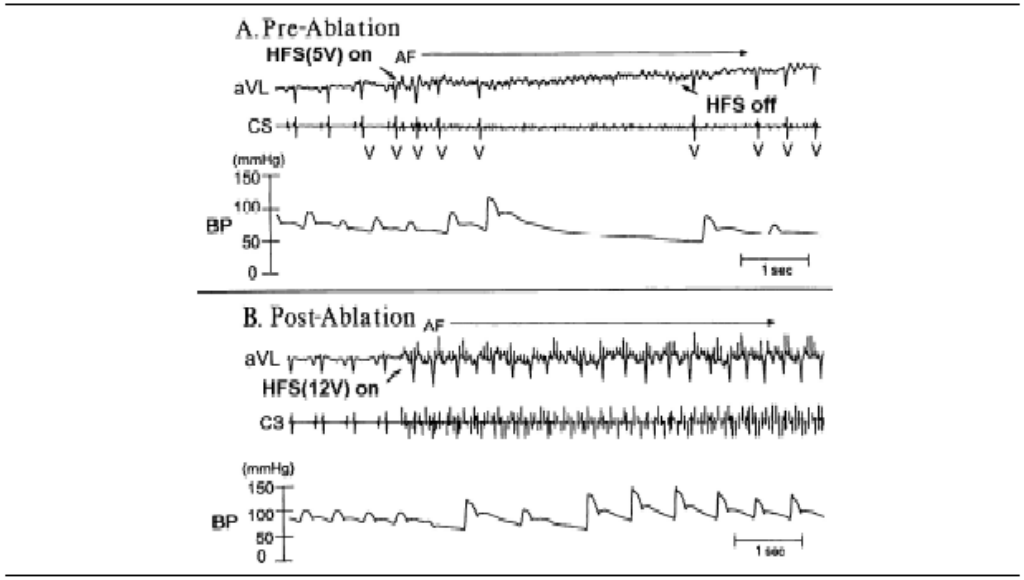
Targeting GP Inputs

- Recently, Sherlag et al, JICE 2005 reported improved success rates with ablation of GPs in addition to PV isolation
  - 90% vs 71% success respectively



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Sherlag et al, JACC 2005

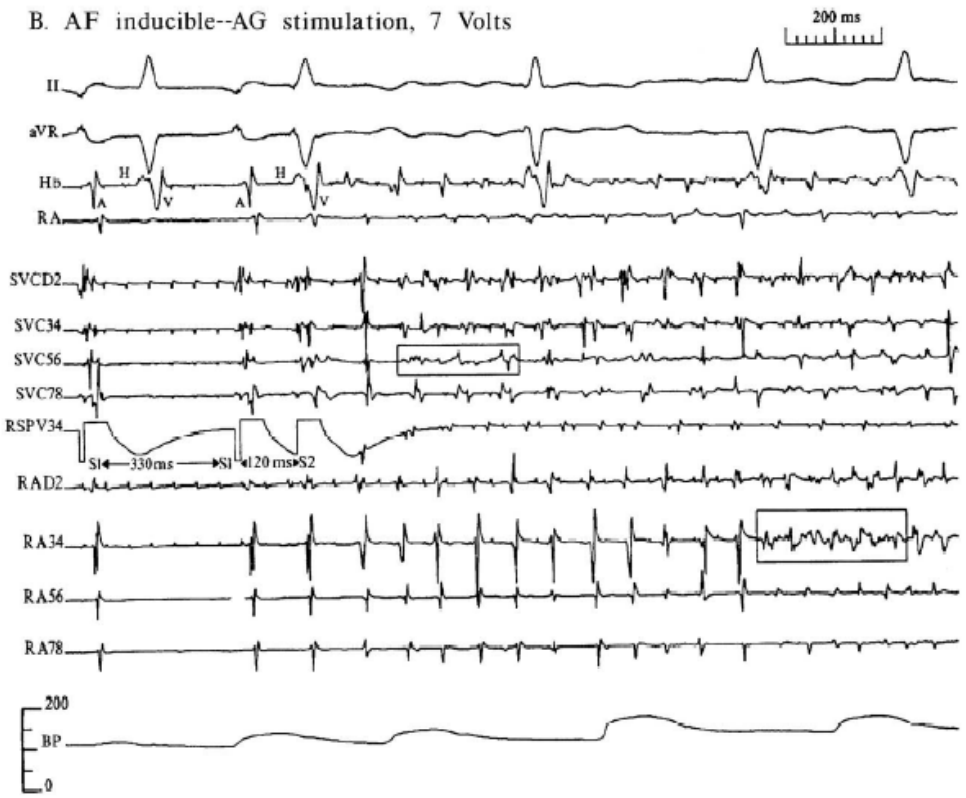

Figure 4 Continued. (B) Initiation and maintenance of AF during AG stimulation by a single APD at the same S_1-S_2 coupling, 120 ms, as in A. Autonomic ganglia stimulation at 7 V induced heart rate slowing from 132 to 81/min (not shown). A single APD S_1-S_2-120 ms now initiated AF, which was associated with complex fractionated electrograms (SVC 5-6; RA 3-4; **boxed areas**). This type of electrogram was seen in all episodes of induced AF at one or more sites. When AG stimulation stopped, the electrograms invariably showed restoration of discrete potentials with isoelectric intervals before termination. Autonomic ganglia stimuli have been reduced in order to clearly differentiate the electrograms from the AG stimulus artifacts. Other abbreviations as in Figures 1 and 2.

GP input may be important in creating a substrate for converting PV firing into AF.

Correlation between CFE and regions of autonomic input.

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Mixed Clinical Results

- Scanavacca et al, Circulation 2006
  - Vagal reflex-guided GP ablation in paroxysmal AF (n=10)
  - 29% success rate after one procedure

- Pokushalov et al, Heart Rhythm 2009
  - Vagal reflex-guided GP ablation vs anatomic ablation of GP sites in paroxysmal AF (n=40)
  - Selective GP ablation success only 43%
  - Anatomic GP ablation success 77%

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Ganglionated Plexi

- Persistent AF population is the next big horizon
- Will not be adequately addressed by the "one size fits all" approach
- New mapping-based targets need to be assessed

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Dominant Frequency (DF)

Dominant Frequency

- May represent specific rotor sites responsible for AF perpetuation
- May be targeted as a lone or combined hybrid strategy

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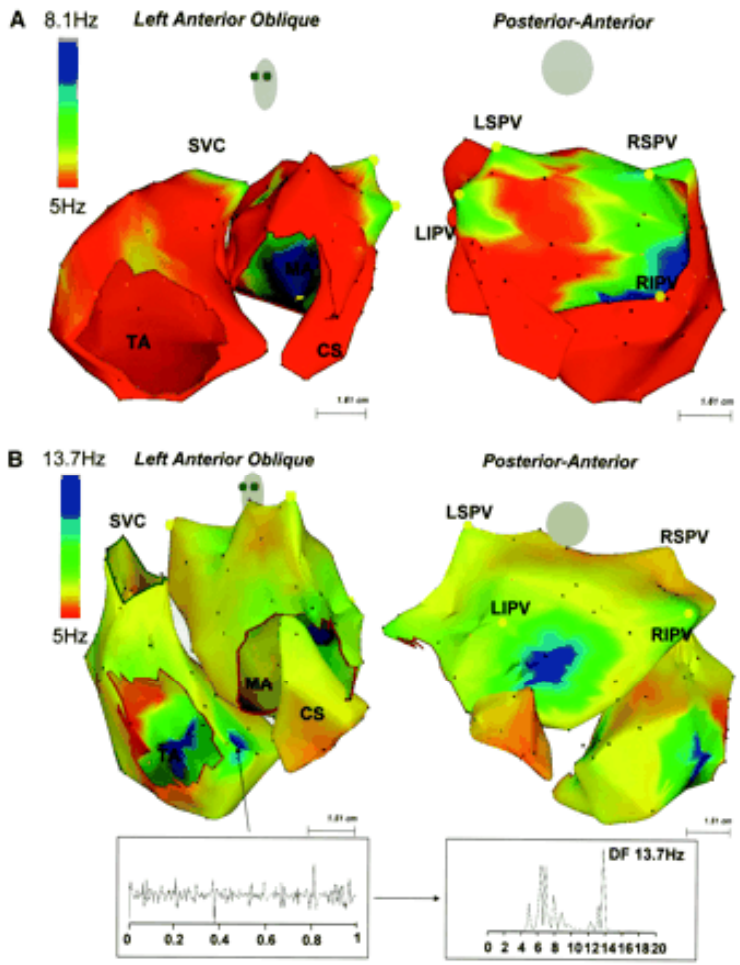
DF Distribution



PAROXYSMAL

CHRONIC

Sanders et al, Circulation 2005

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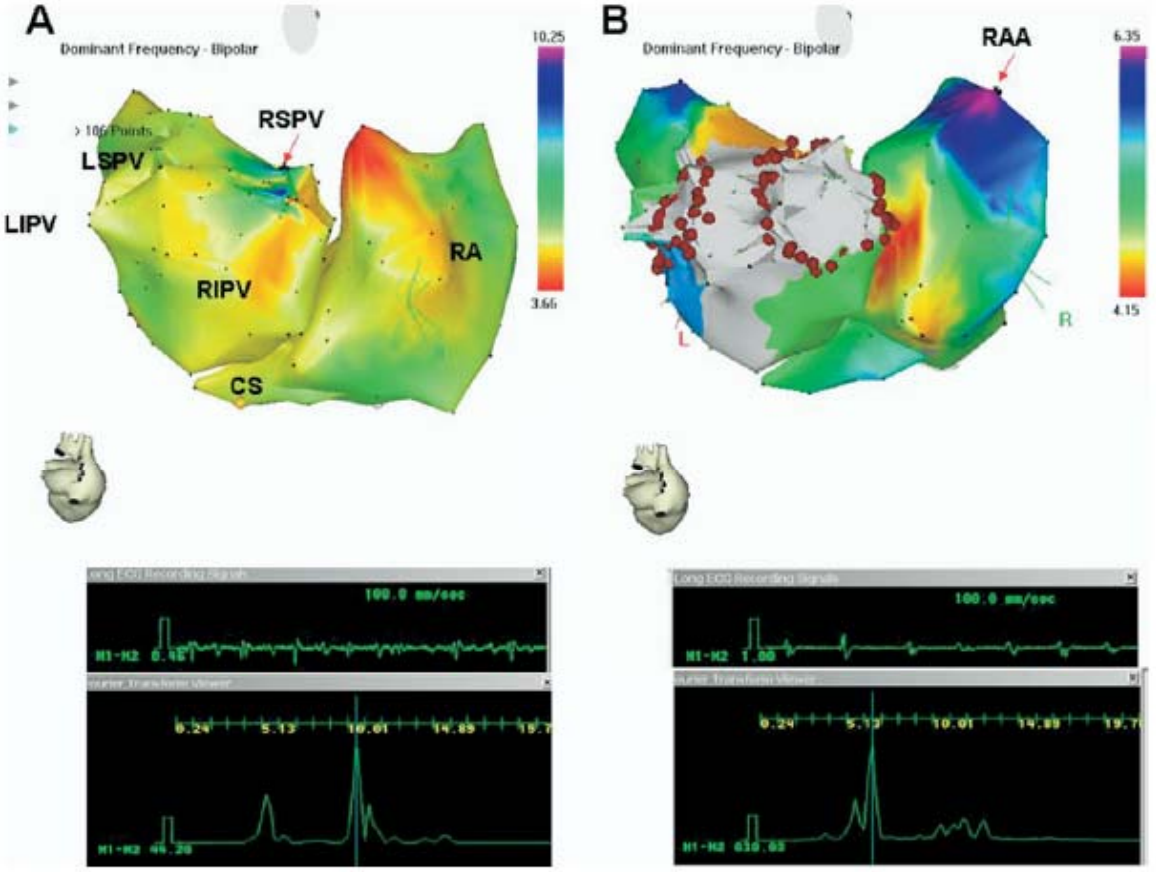
Atienza et al, Heart Rhythm 2009



Acute reduction in DF in all chambers associated with higher freedom from AF long-term.

Ablation of DFmax sites associated with higher freedom from AF (88% vs 30%)

Overall success rate 88% parox and 56% persistent

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Summary

- EGM-guided ablation is a promising avenue for adjuvant ablation in addition to PVI
- May be particularly useful in persistent AF population, but also higher-burden paroxysmals
- CFE offers the most promising target at present, but need for more refined definitions
- GP ablation may overlap a lot with CFE and data still lacking
- DF ablation may be promising, particularly in refining CFE sites

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