AF Ablation Targeting Rotors

Venice Arrhythmias, 2015

Paul J. Wang, MD
Stanford University

Disclosures: None

Computational Mapping for AF

- [x] Clinical Challenges. Need for Advanced Mapping
- [ ] Current Mapping Approaches – Mechanisms
- [ ] FIRM
- [ ] ECG Imaging; Other approaches
- [ ] Clinical outcomes; Future directions

Why is Functional AF Mapping Required?

Current AF Ablation Suboptimal – Paroxysmal and Persistent

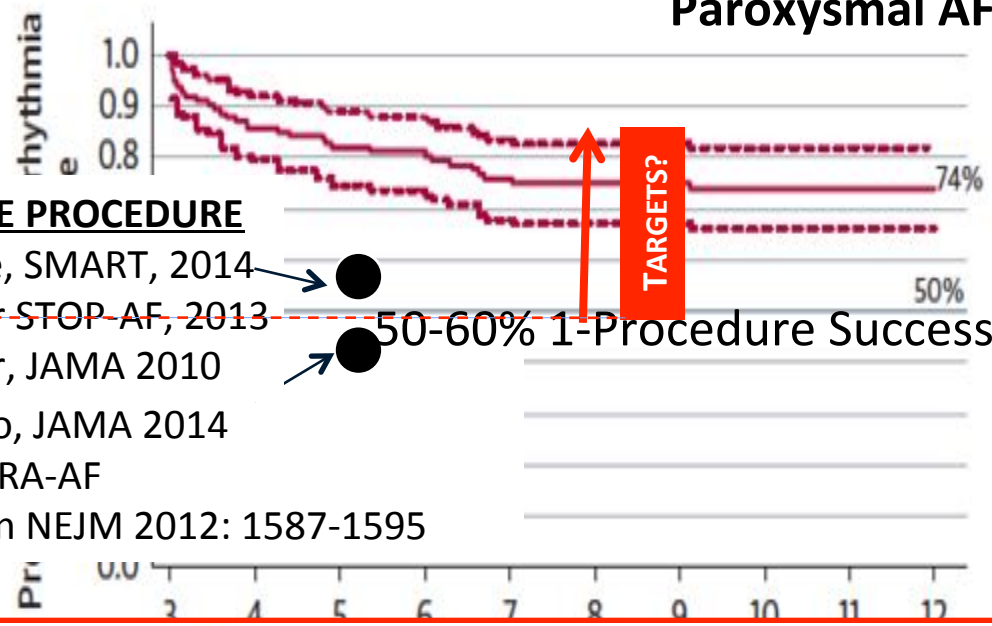
Many targets (even PAF)

Thermocool™AF 2010
- Linear 22.3%
- SVC 16.5%
- Other RA/LA 16.5%
- (CTI, 35.9%)

RAAFT-2 (PAF), 2014
- CFAE 17%
- Roof 21.3%
- ?GP, other
- (CTI 18.7%)

SMART-Touch (PAF), '14
- Linear 41.2%
- Lines+foci 6.9%
- Foci 1.9%
- (CTI 19.4%)

Paroxysmal AF



SINGLE PROCEDURE

Natale, SMART, 2014

Packer STOP-AF, 2013

Wilber, JAMA 2010

Morillo, JAMA 2014

MANTRA-AF

Nielsen NEJM 2012: 1587-1595

50-60% 1-Procedure Success

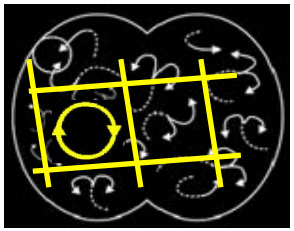
Randomized, Controlled Trial of the Safety and Effectiveness of a Contact Force–Sensing Irrigated Catheter for Ablation of Paroxysmal Atrial Fibrillation

Results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) Study

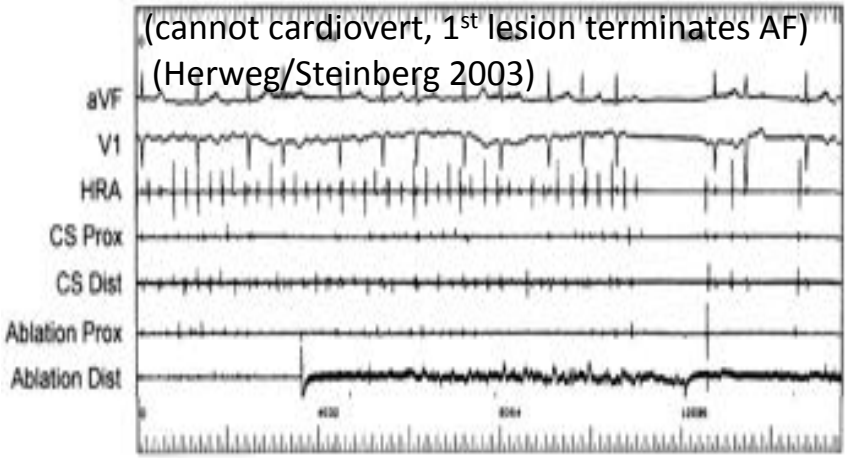
Vivek Y. Reddy, MD; Srinivas R. Dukkipati, MD; Petr Neuzil, MD; Andrea Natale, MD; Jean-Paul Albenque, MD; Josef Kautzner, MD; Dipen Shah, MD; Gregory Michaud, MD; Marcus Wharton, MD; David Harari, BS; Srijoy Mahapatra, MD; Hendrik Lambert, PhD; Moussa Mansour, MD

Wilber et al., JAMA 2010; Packer et al., STOP-AF. JACC 2013; Morillo et al., RAAFT-2, JAMA 2014
Natale et al. SMART-Touch, JACC 2014; Ganesan, J. Am Heart Association 2013; 2:e004549
Arbelo, Brugada, Hindricks et al, Eur H J 2014; 25: 1466-1478
Reddy et al., Circulation 2015; Toccastar

Patient-Specific Ablation – Sources Rationalize Many Dichotomies



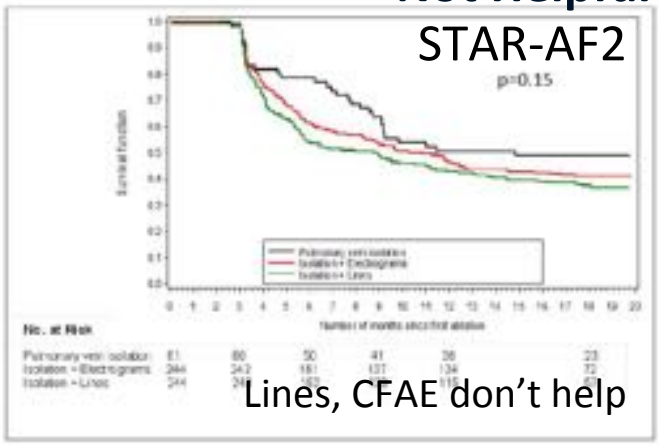
1. Localized Therapy Modulates/Terminates AF



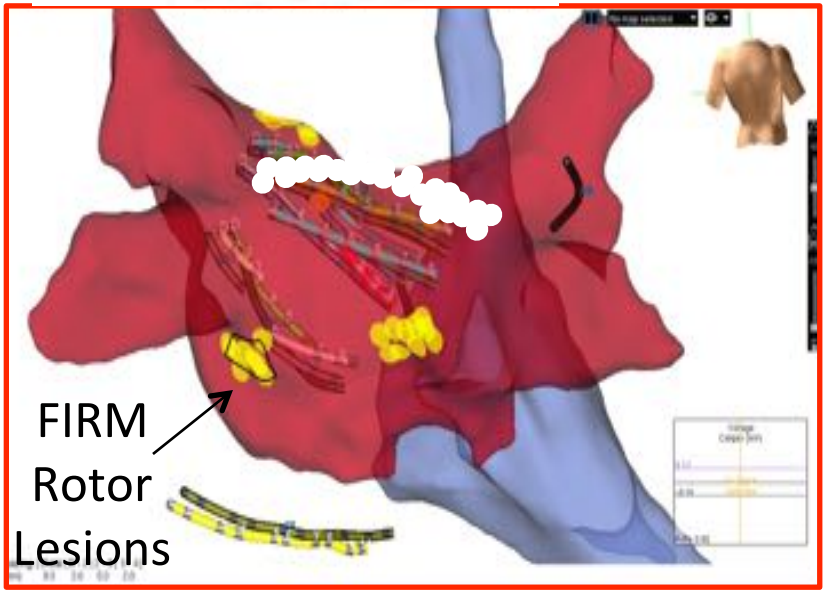
Haystack

Yet Including successful AF Rx by any non-Maze therapy

2. Extensive ablation – Not Helpful



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



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Calkins et al., HRS/ESC position paper Heart Rhythm 2012; Rensma, Circ Res 1988: 395-410.; Narayan, Circ 2002; 1968-1973
Forclaz, A., S. M. Narayan, et al. (2011). "Early temporal and spatial regularization of persistent AF predicts arrhythmia-free outcome." Heart Rhythm **8(9): 1374-1382.**

Advanced 3D Mapping for AF

- [x] Clinical Challenges. Need for Advanced Mapping
- [x] Current Mapping Approaches – Mechanisms
- [ ] FIRM
- [ ] ECG Imaging; Other approaches
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Why the Debate on AF Mechanisms?

"Nonhierarchical" Disorganization

Rotors – Sources

Cause multiwavelet disorganization

Traditional Electrograms vs Optical Mapping

- Mo
  - Va
- Sheep
  - Gray, Nature 1998; Skanes Circ 1998 [1,2]
- Canine
  - Chou, J Am Coll Cardiol 2011
- C
  - Bhimani, Heart Rhythm 2014
- Human
  - De Groot, Circulation 2010
- No localized sources

- Human AF: Optical – Stable Rotors
  - Hansen et al, Eur H J 2015
  - Fedorov et al., Circulation A/E 2015

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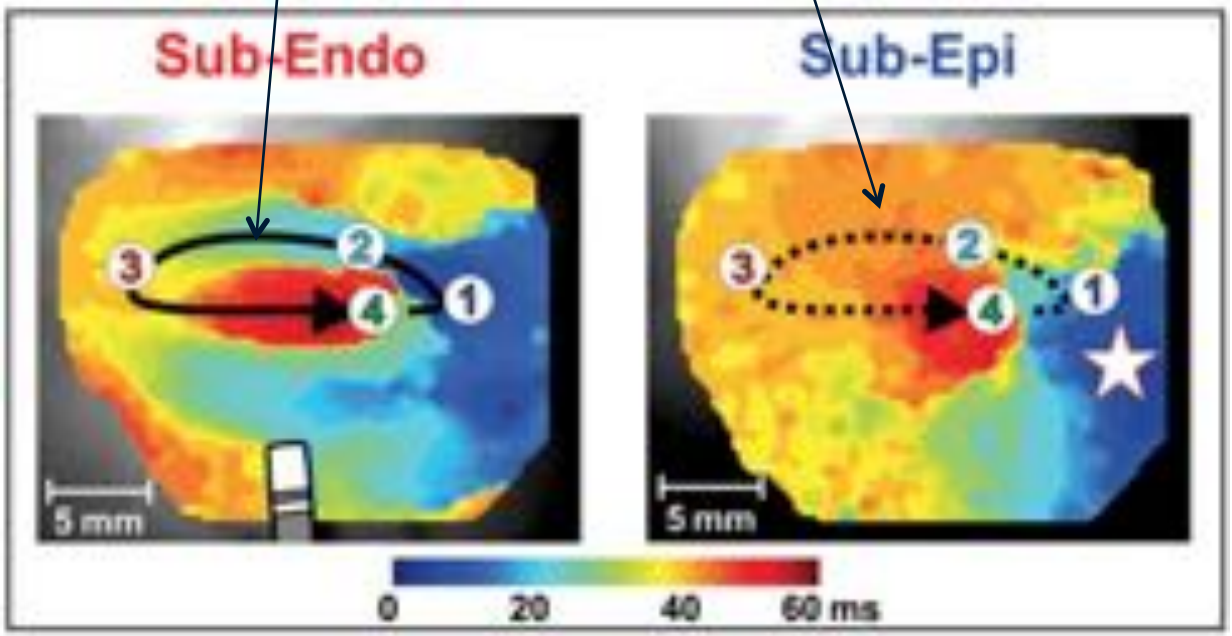
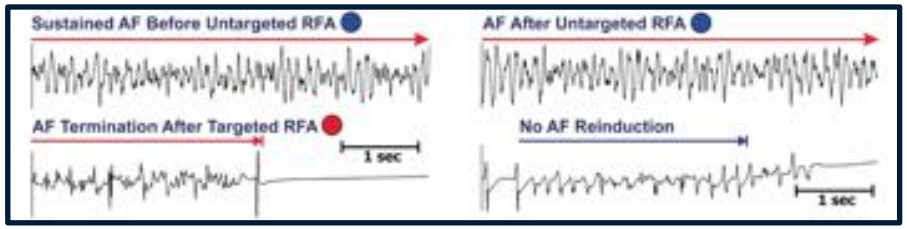
(1) Vaquero/Jalife Heart Rhythm 2008;872-879; (2) Skanes Circulation 1998; 1236-48; (3) Ryu, Stambler JCE 2005; 16: 1348-1358; (4) Lin Circ 2005; 112:1692-700; (5) Cuculich, Rudy. Circ 2010; 1364-1372; (6) Allessie Circ EP 2010; 1674-1682; (7) Narayan, Miller et al, J Am Coll Cardiol 2012; 60(7): 628-636

Human AF Optical Maps

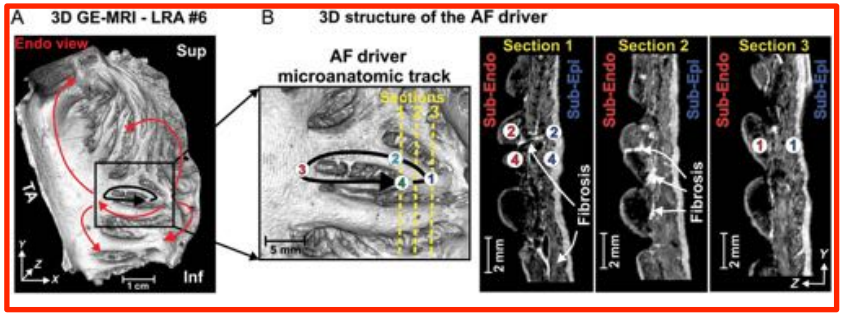
Stable Endocardial Rotation Sources (>1 cm^2 domain), Ablatable, with a Fibrillatory "Wake" on the Epicardium



- Diseased human RA (1) and LA (2)
- **Endocardial stability related to fiber tracts (≈1.5 x 0.5 cm), fibrosis**
- Fibrillatory "wake" in epicardium, elsewhere



Endocardial Ablation terminates AF



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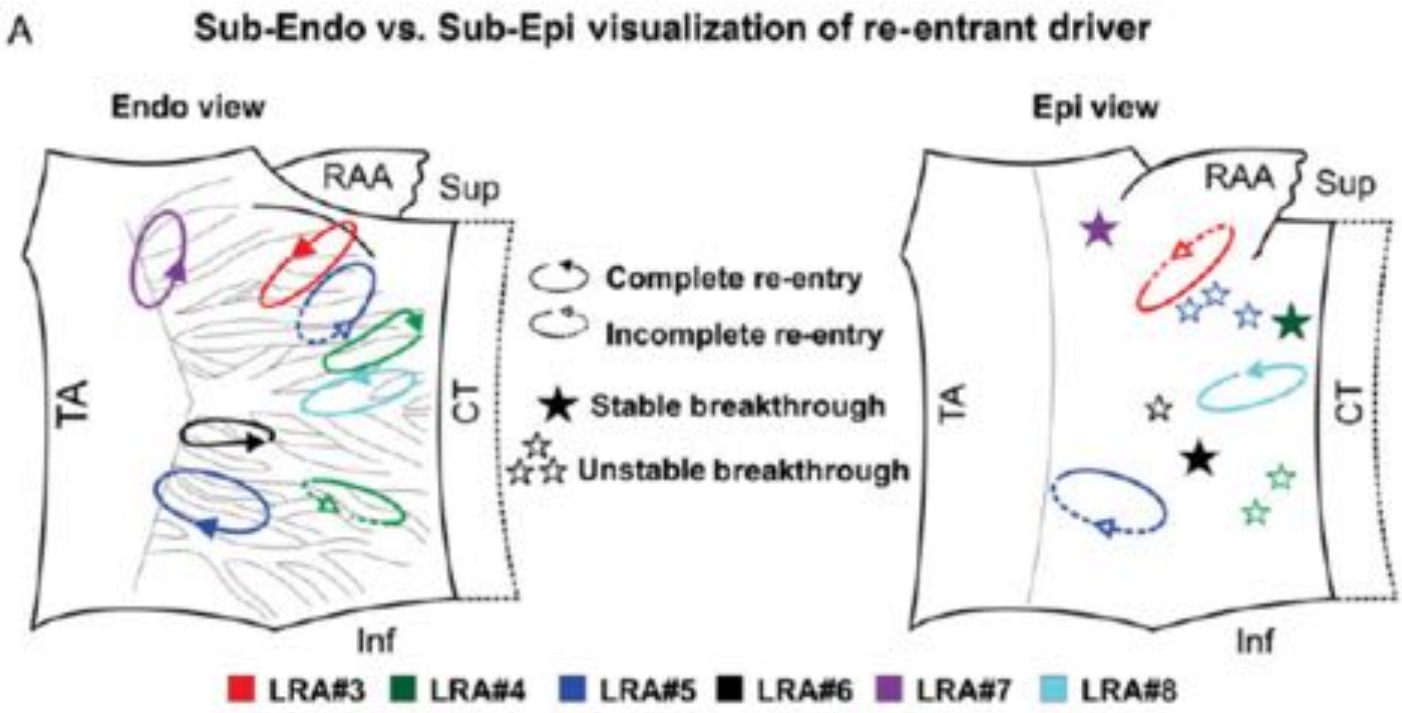
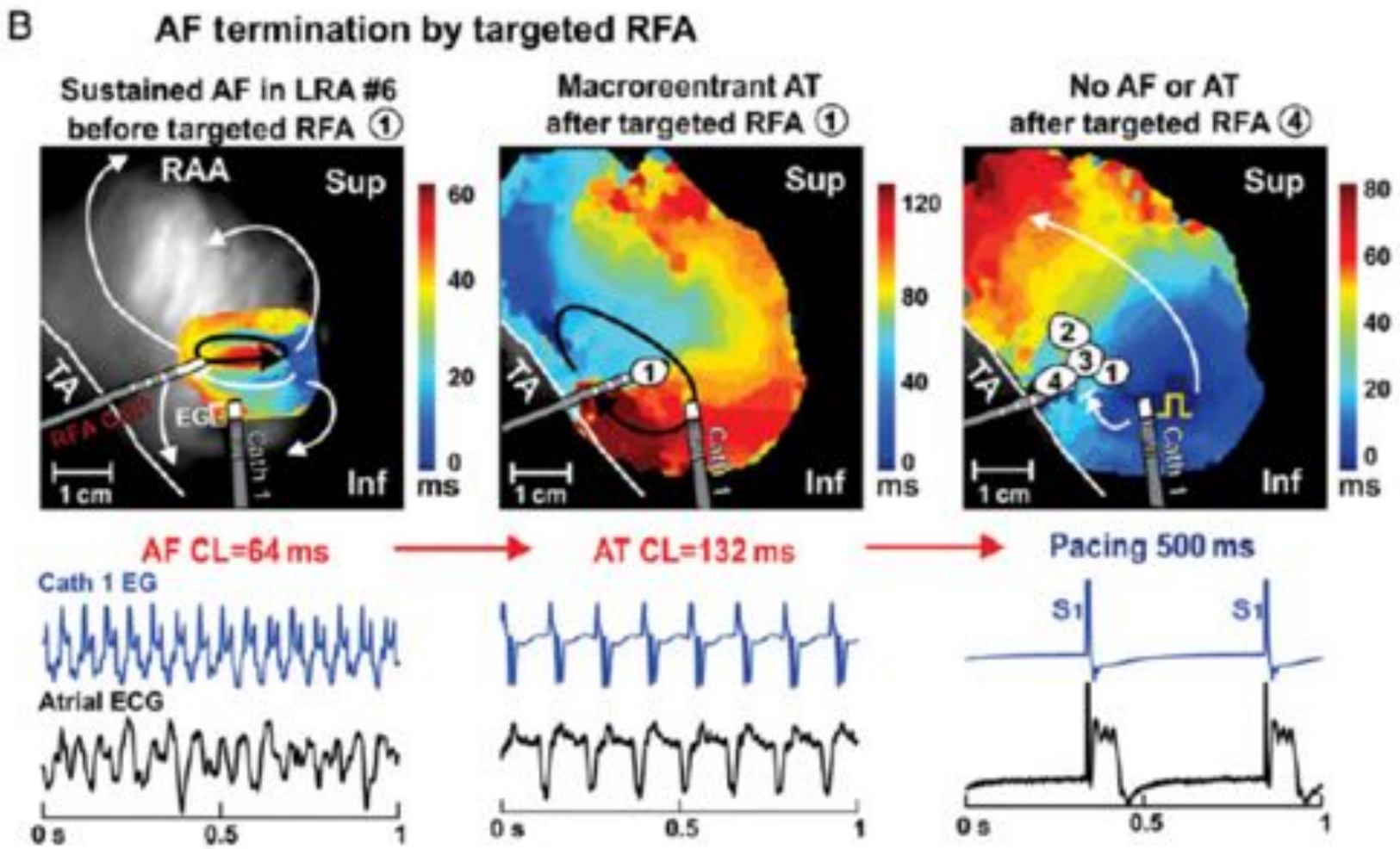
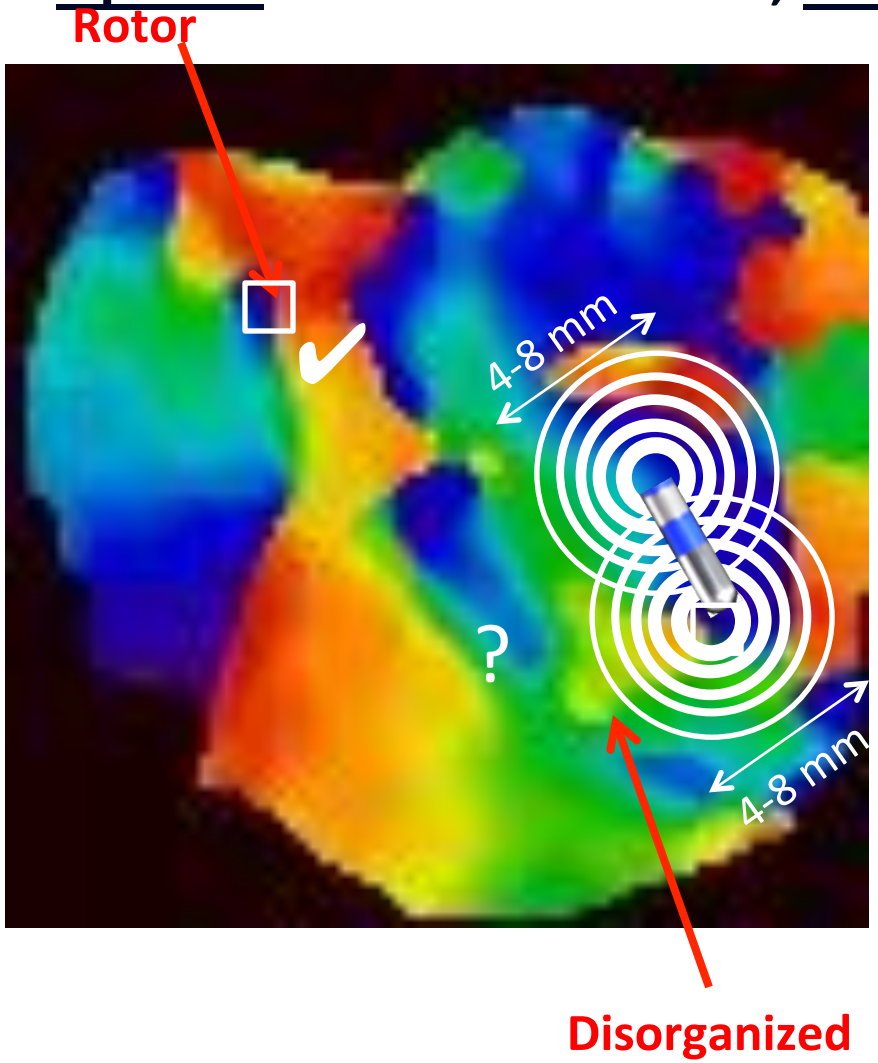
1. Hansen, Fedorov et al. AF driven by micro-anatomic intramural re-entry revealed by simultaneous sub-epicardial and sub-endocardial optical mapping in explanted human hearts. *Eur Heart J. 2015. epub*
2. Zhao, Fedorov et al. Two Localized AF Rotors in Human Left Atrium. *Circulation A/E 2015; epub*


A
Sub-Endo vs. Sub-Epi visualization of re-entrant driver
Endo view
Epi view
RAA
Sup
TA
CT
Inf
Complete re-entry
Incomplete re-entry
Stable breakthrough
Unstable breakthrough
LRA#3
LRA#4
LRA#5
LRA#6
LRA#7
LRA#8


B
AF termination by targeted RFA
Sustained AF in LRA #6
before targeted RFA ①
Macroreentrant AT
after targeted RFA ①
No AF or AT
after targeted RFA ④
RAA
Sup
Inf
TA
EGM
Cath 1
1 cm
60
40
20
0
ms
120
80
40
0
ms
80
60
40
20
0
ms
AF CL=64 ms
AT CL=132 ms
Pacing 500 ms
Cath 1 EG
Atrial ECG
S1
S1
0 s
0.5
1

Patient Specific Mapping: Optical versus Electrograms

Optical: Minimal Cross talk; EGM: Integrate Undefined Volumes



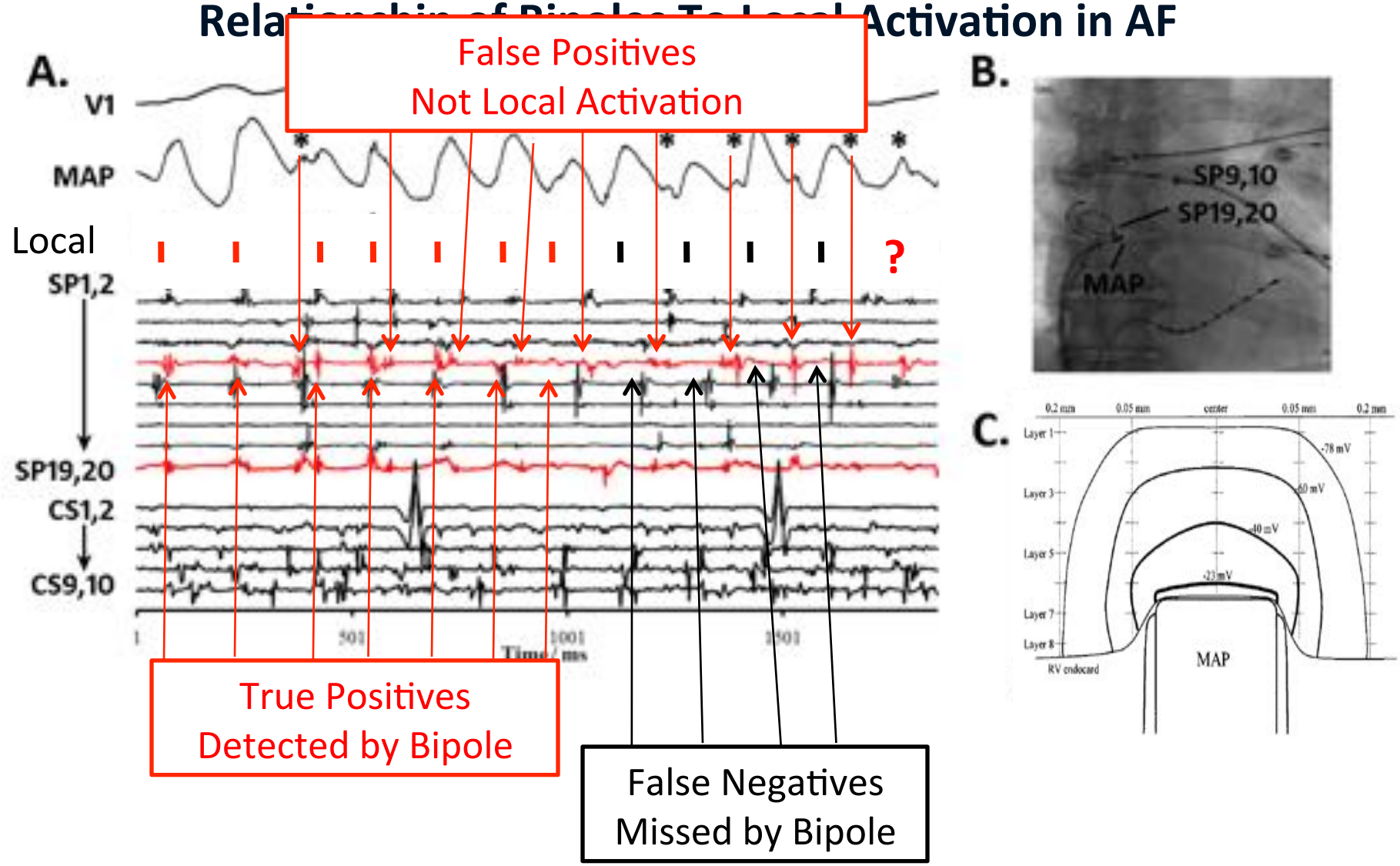
- "Gold standard"
- Preclinical[1,2]: Toxicity, motion, blood absorption.
- Phase singularity: surrounded by all activation stages ("head-meets-tail" rotor) [2]
- **Minimizes cross-talk from far-field regions [1,2]**

Q: How Bad is Intrachamber Cross-Talk in AF Electrograms ?

1.Narayan SM, Santori E, Toga AW, Cerebral Cortex 1994; 4(2): 194-204
2. Kalifa et al., Circulation 2003; 108:668-671

Rhythm Specific Mapping

Relationship of Bipoles To Local Activation in AF



Narayan, Franz et al, PACE 2006; 29:1209-1218; Narayan, Wright, Hocini et al. *Heart Rhythm. 2011;8:244-253*
Knollmann, Franz JCE 2002;13:1246-1252; Verma and Narayan, JACC: Clinical EP 2015; 1(1): 25-28

Advanced 3D Mapping for AF

- [x] Clinical Challenges. Need for Advanced Mapping
- [x] Current Mapping Approaches – Mechanisms
- [x] FIRM
- [ ] ECG Imaging; Other approaches
- [ ] Clinical outcomes; Future directions

"A 54 year old man with Persistent AF"

- 54 YO man with persistent AF x 6 Years. Five Cardioversions, failed flecainide, dofetilide.
- Past medical history: Obstructive sleep apnea, treated hyperthyroidism (AF despite treatment), No Prior Ablations.

- $CHA_2DS_2VASc=0$; LA 50 mm TTE (55 mm ICE), LVEF 65%. BMI 28.3 kg/m2. TSH 0.78 uIU/ml

- Medications: Rivaroxaban; intermittent beta-blockers; Levothyroxine.

- Social History: Under stress as he is about to take his internet company public. No alcohol, no tobacco, no recreational drugs.

1. Map Human AF Widely in the Human Atria

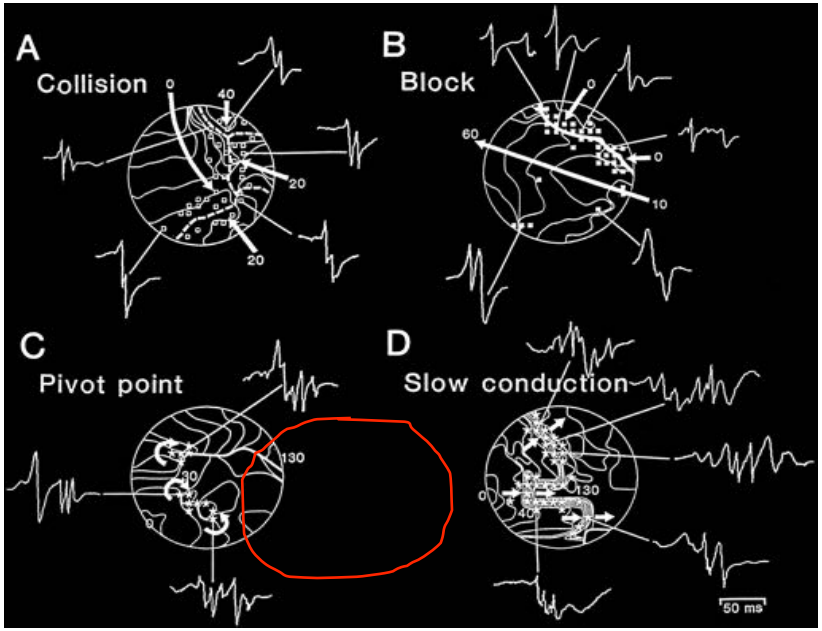
Right Atrium, 134 msec

Disorder!

≈10 cm^2

vs LA area >100 cm^2

(Jadidi et al., JACC 2013)



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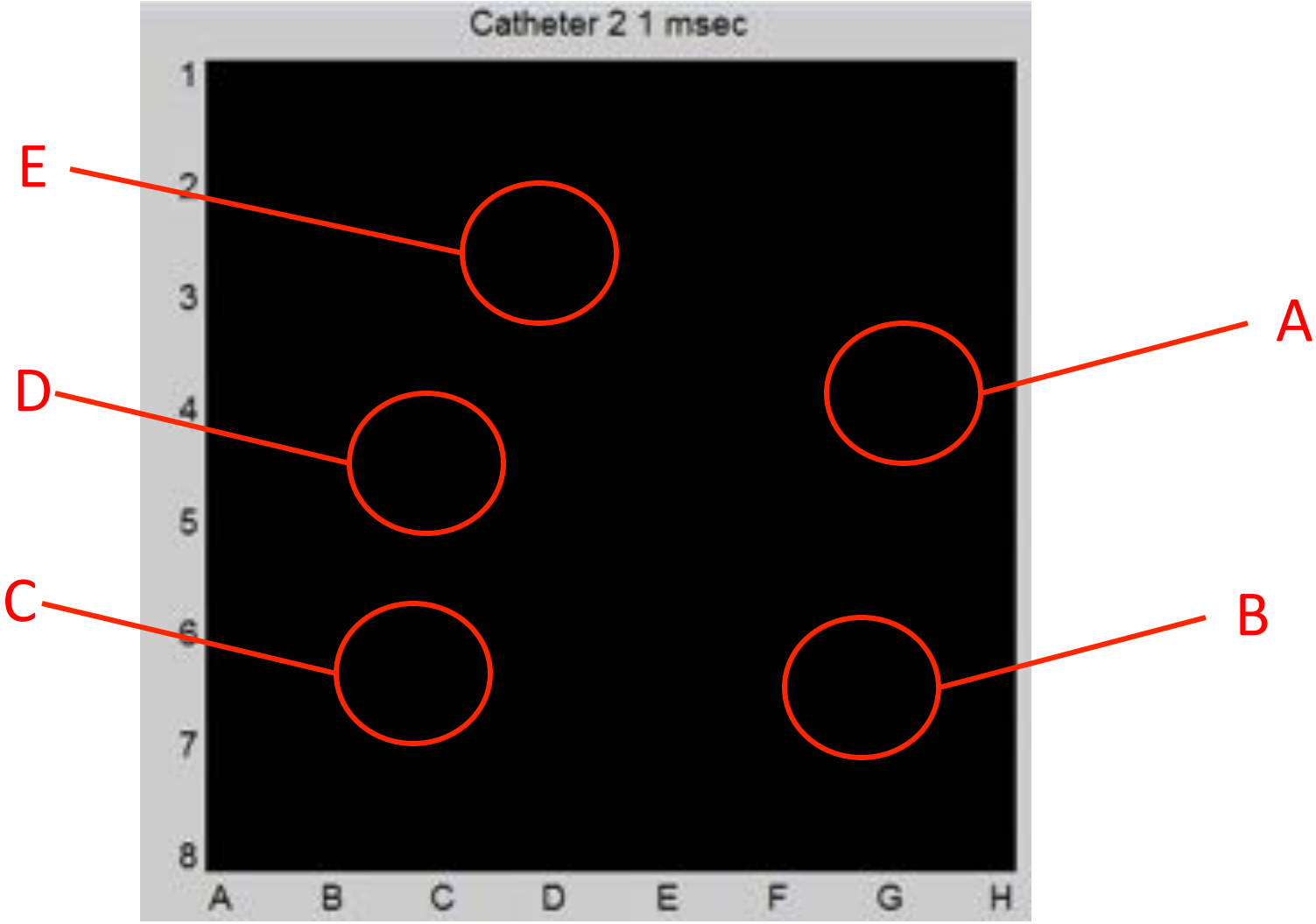
[1]Konings, Circulation 1997;95:1231-1241; [2]Allessie et al., Circulation A/E 2010;3:606-15
[3]Walters and Kalman, JACC: Clinical EP 2015; 1(1): 18-25. **Stable patterns in >62% of epochs**

Audience Response Question 1. In RA FIRM Map

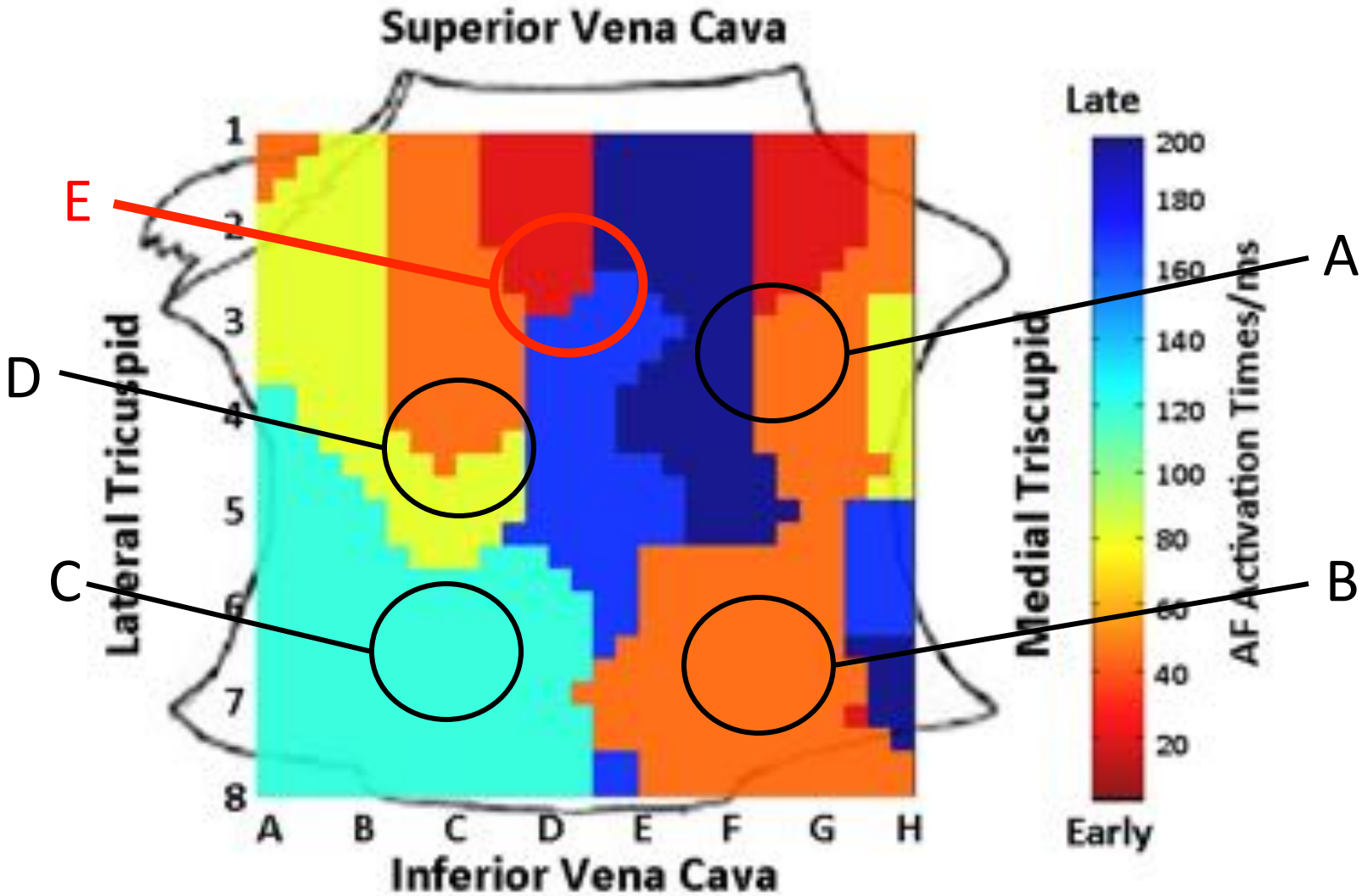
Where is the ablation target?



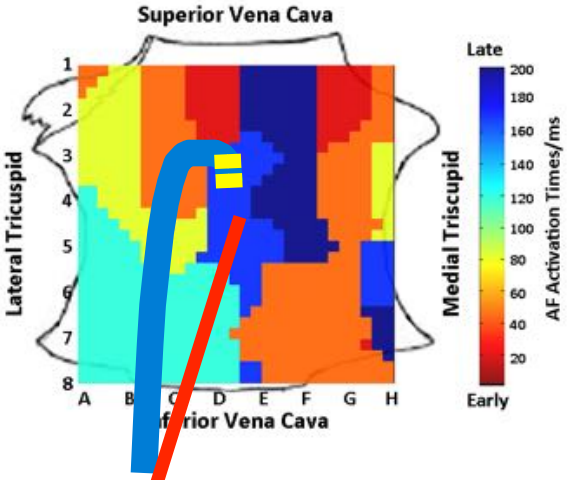
(Only 18 consecutive cycles shown for brevity)

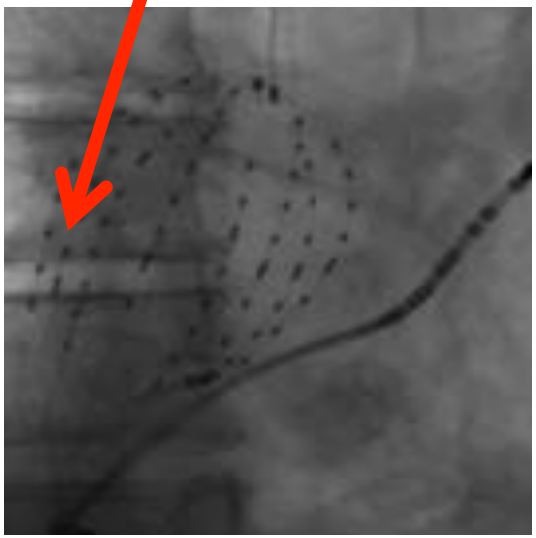
Answer 1. In Right Atrial FIRM Map

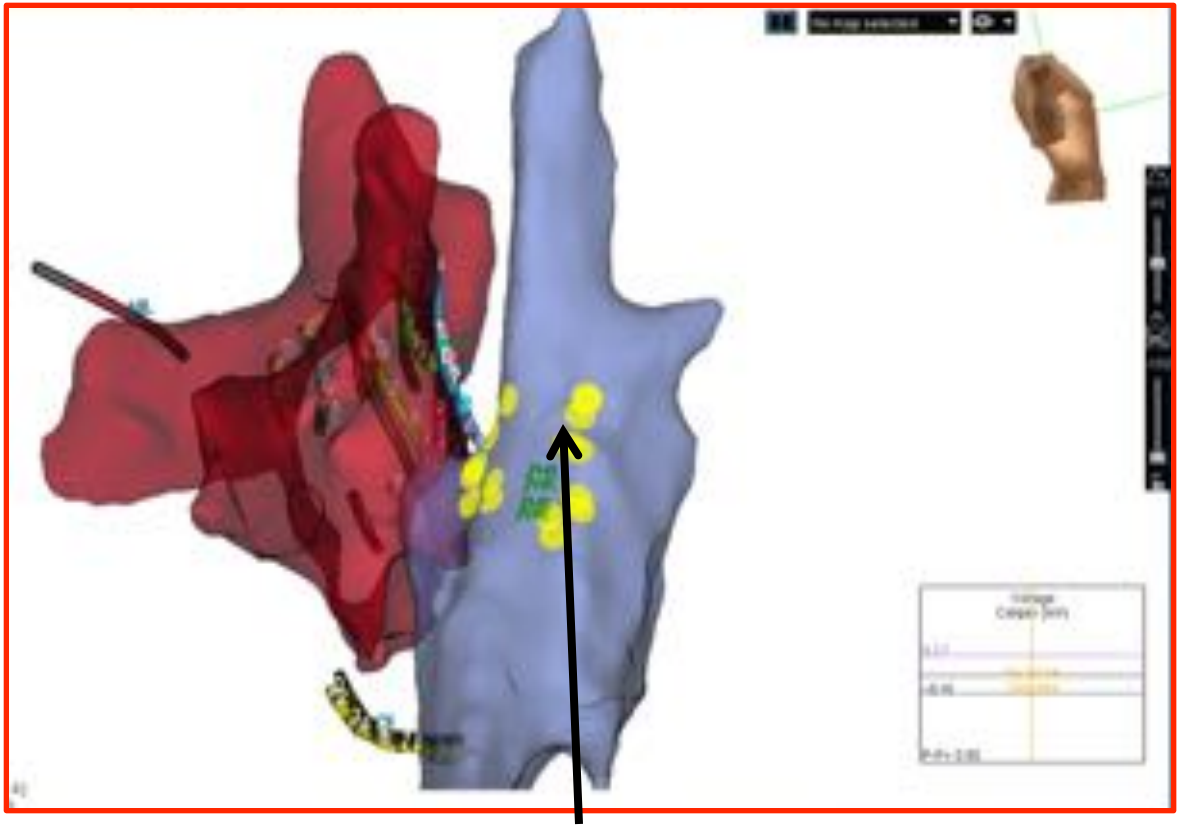
Ablation target is E



Step 2. 3D Maps of RA Rotor Locations

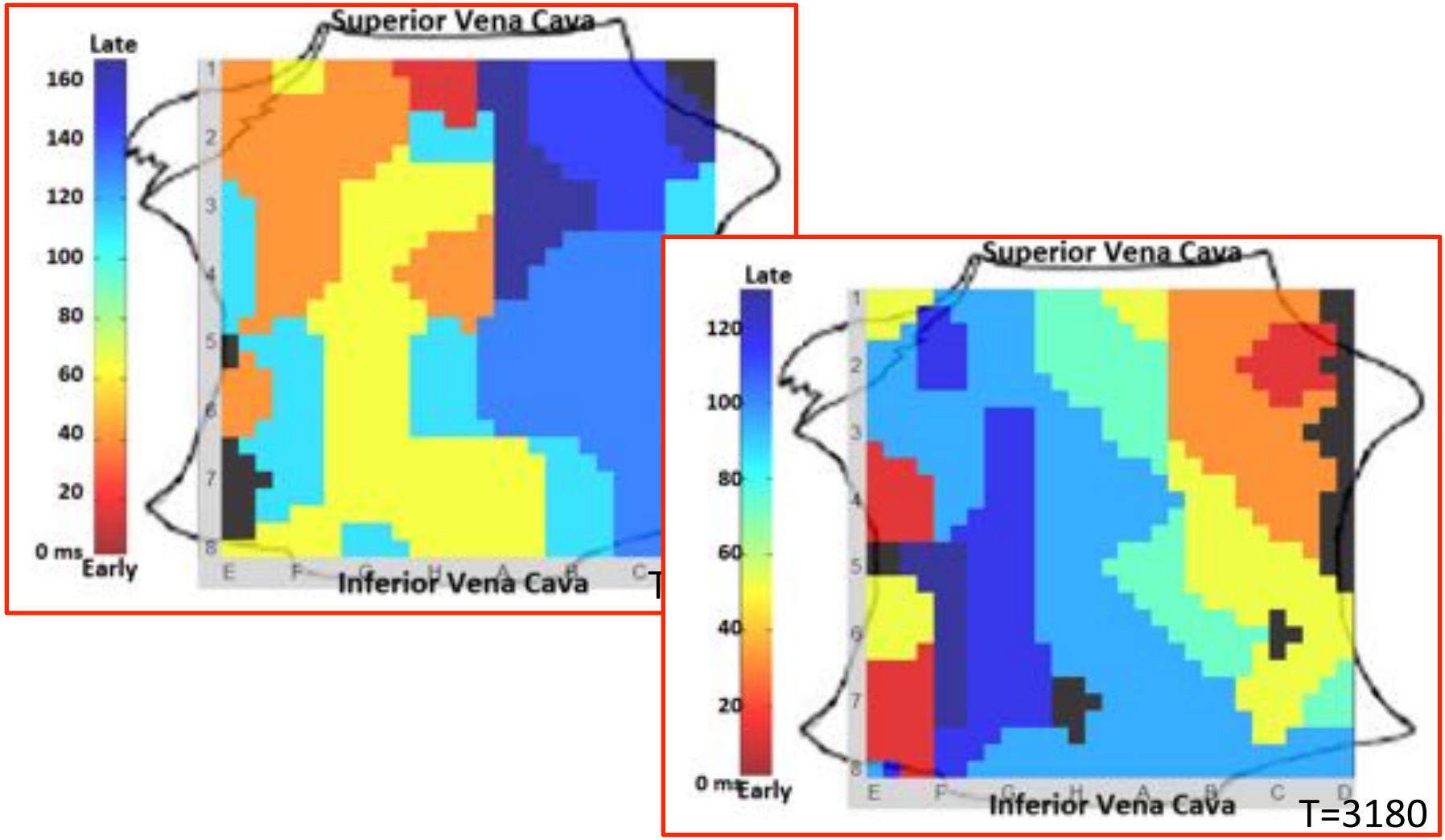






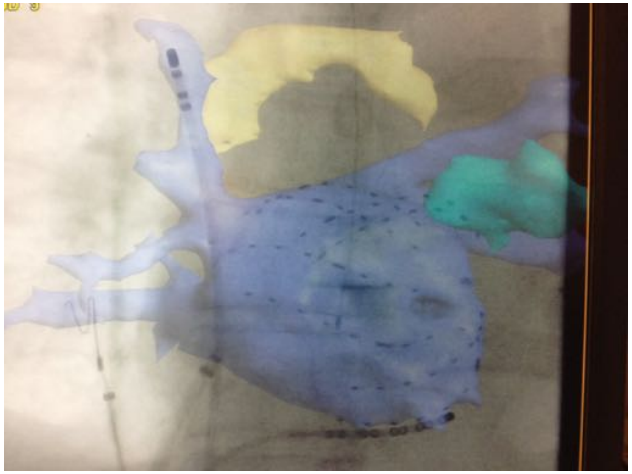
Phrenic Area NOT ablated
(i.e. maintain all usual safety precautions)

Step 3. RA Rotor Eliminated on FIRM Remap



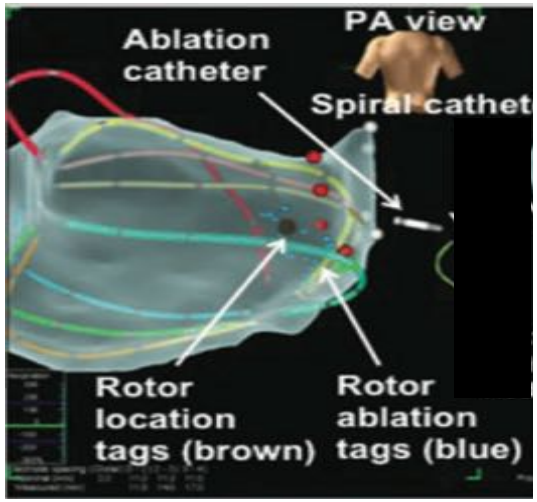
"Cleaned Up" Map; No Consistent Rotors

Step 4: Place Basket in LA. Optimize Positioning …

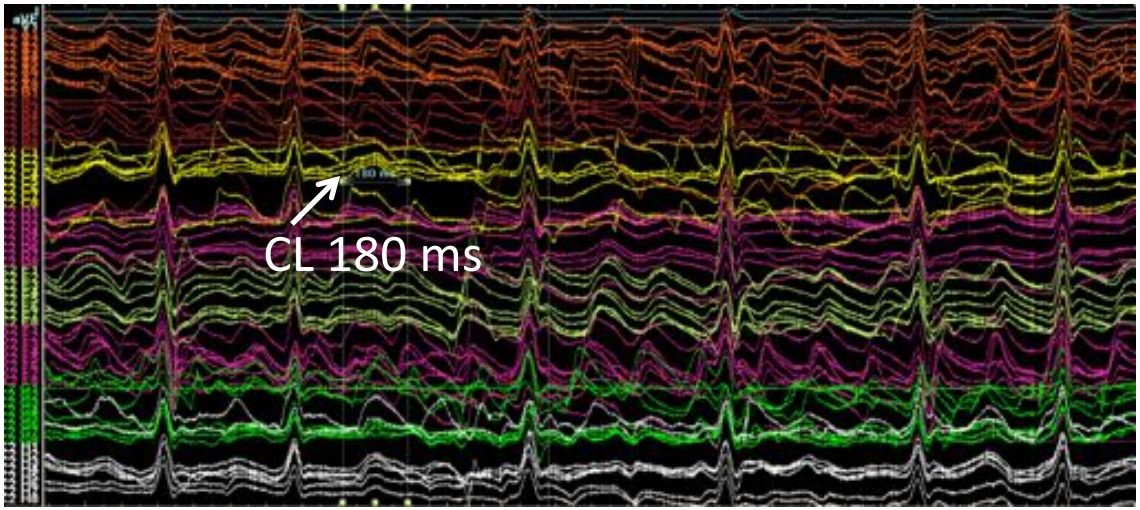


M. Orlov JICE 2014

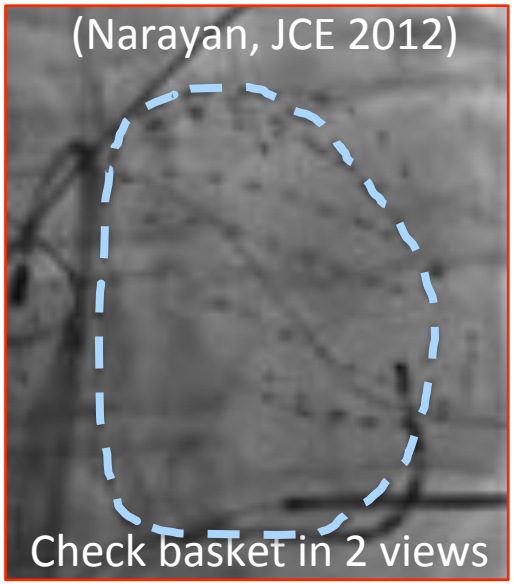
Tilz, Kuck et al. Eur Heart J. 2014

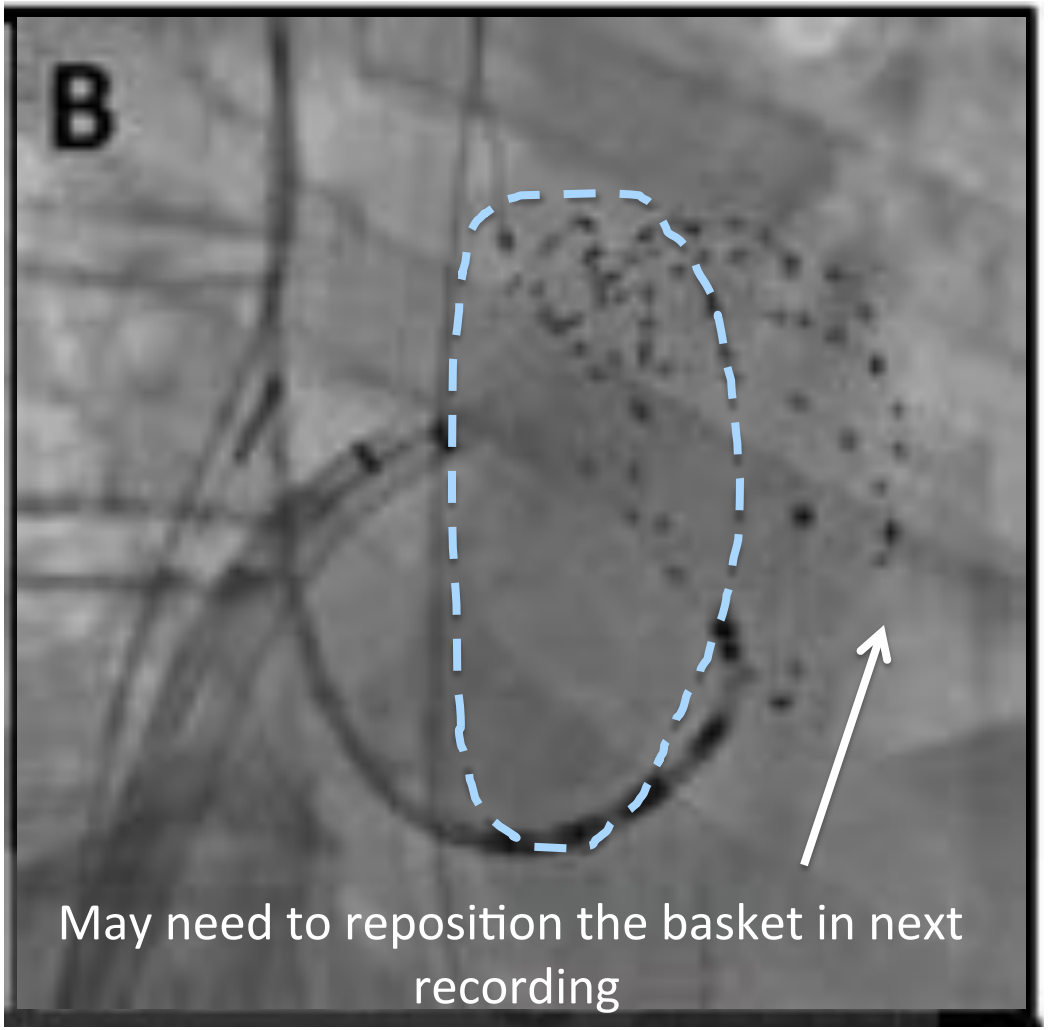


Many (8+) existing/ proposed basket solutions for 3D mapping of AF



Learning Curve for Placing Baskets





Narayan et al., J Cardiovasc Electrophysiol 2012; 23:447-454
Benharash, Shivkumar et al., Circulation A/E 2015; 8:554-61

Advanced 3D Mapping for AF

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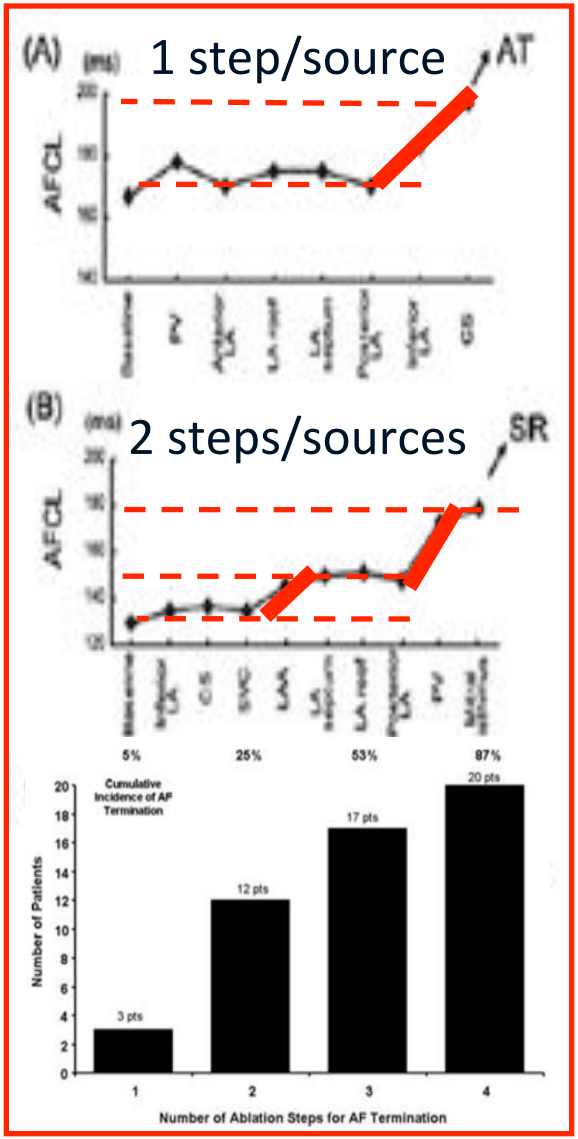
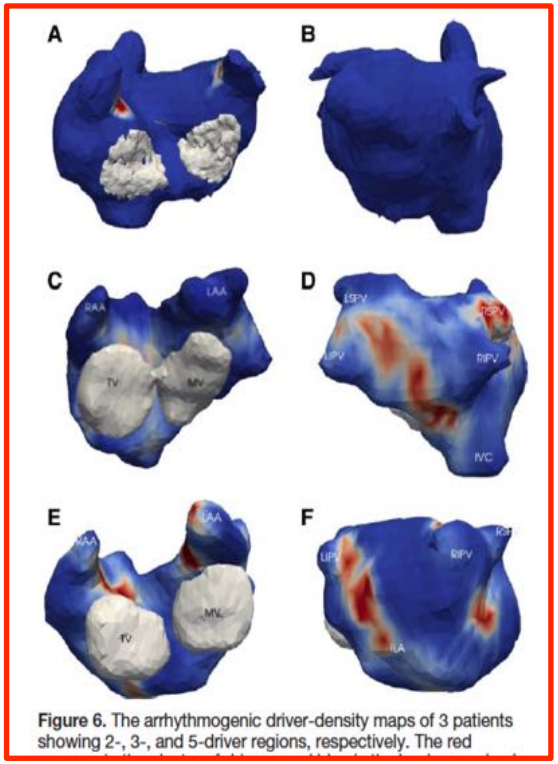
Personalized Ablation: Other Methods to Show AF Sources

ECGI: Less stable; Epicardium? Technical differences?

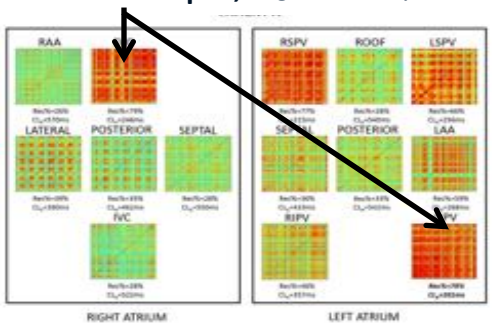




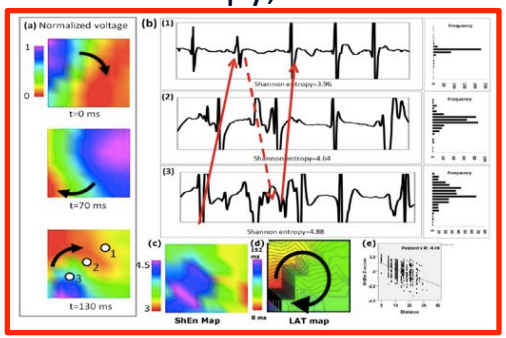
Haïssaguerre, Circulation 2014

- Sources in same region for days….
- ECGI: Projection amplifies Meander Rodrigo, Heart Rhythm 2014;11:1584-91.

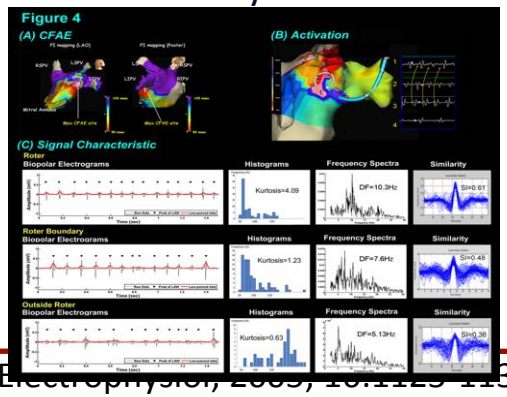
Stable Shape, Ng Heart Rhythm 2014



Stable Entropy, Ganesan Circ AE 2013



Wave Similarity. Lin Circ AE 2013



Haissaguerre et al., J Cardiovasc Electrophysiol, 2003; 14:1125-1137
Haissaguerre et al. Driver Domains in Persistent AF. Circulation 2014;130:530-8

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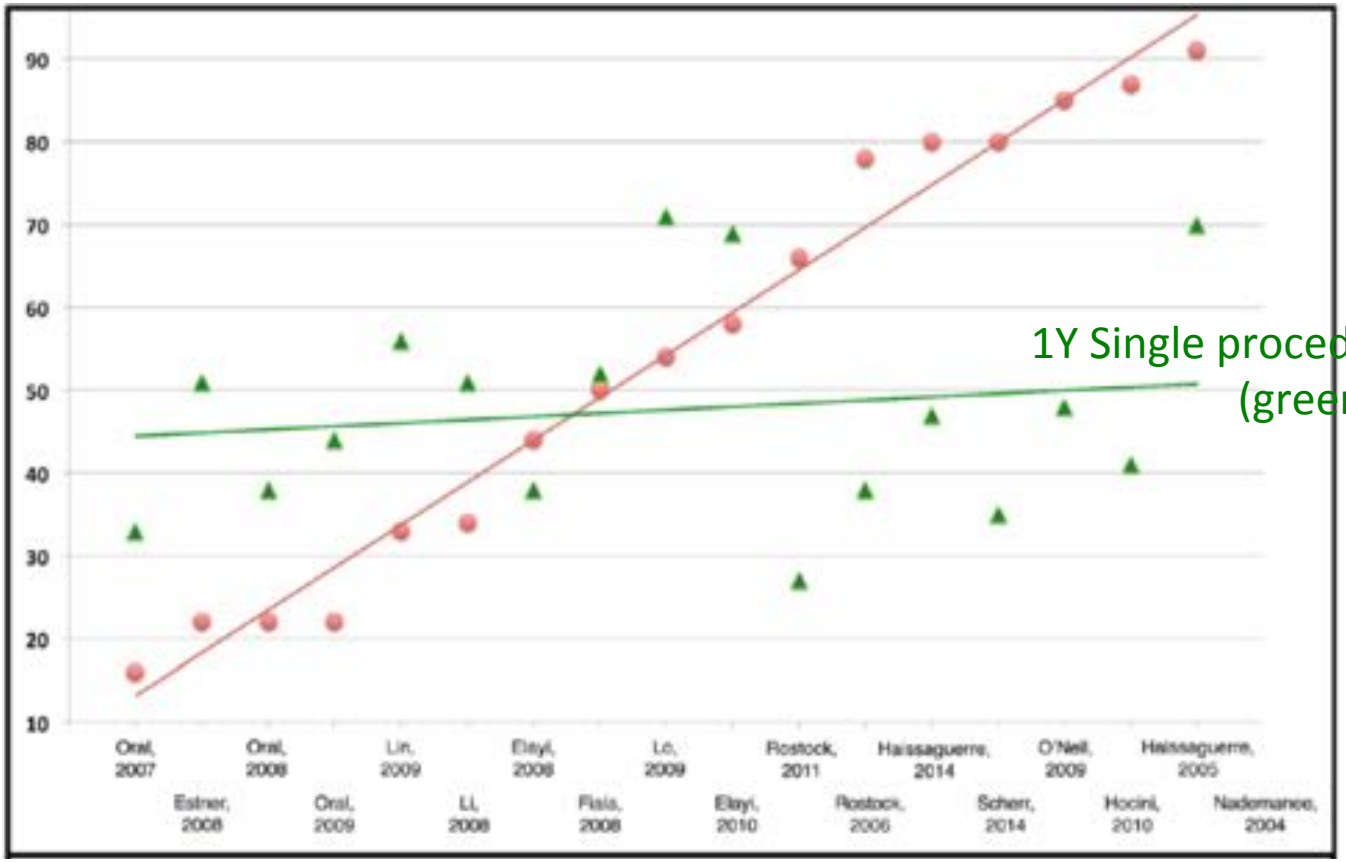
Does Acute AF termination matter clinically?

Relationship to Long-Term Outcomes in Published Studies

AF termination Rate (red)

%

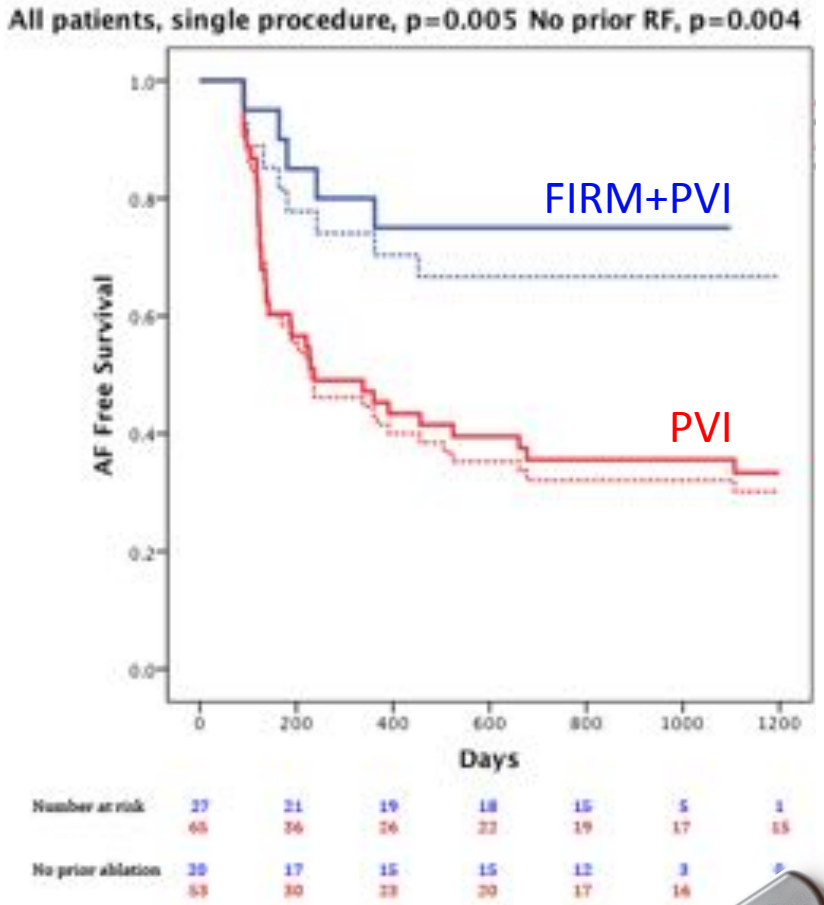


1Y Single procedure success (green)

Studies

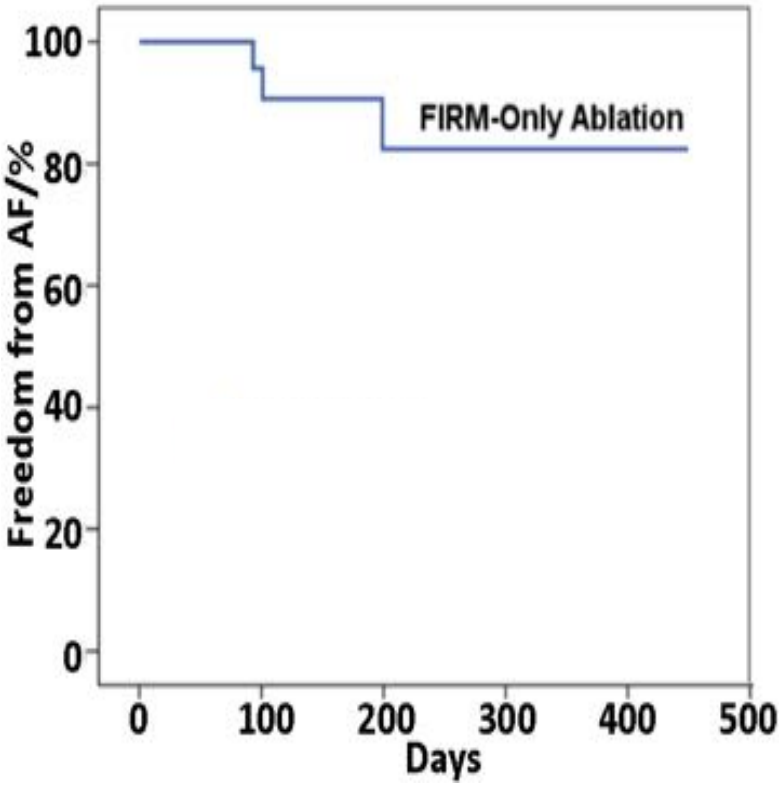
FIRM-Guided Ablation: Single Procedure Results

Very Long-Term Follow-Up In CONFIRM
Median 890 days



85.2% ILR in FIRM-Guided Group

Paroxysmal AF: FIRM-Only
PRECISE Trial (5 Centers)



(64.5%)

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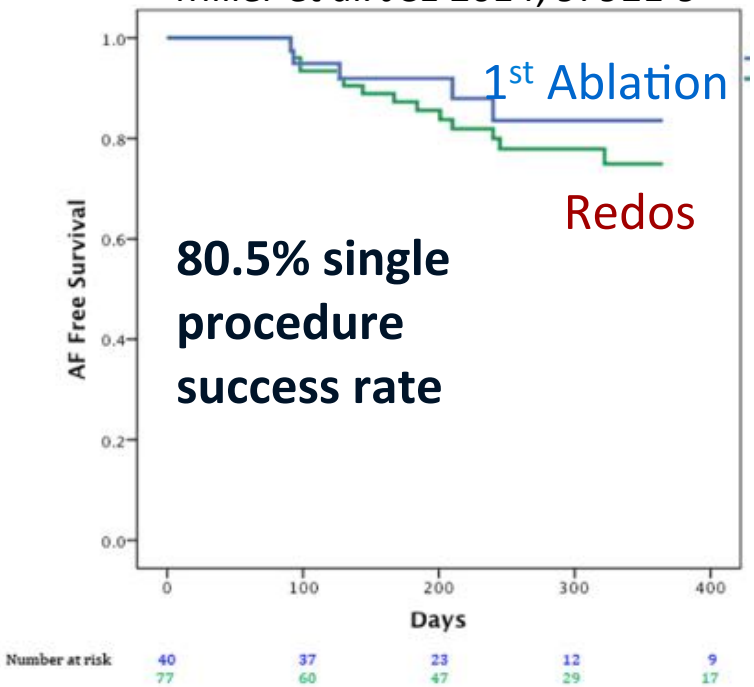
Narayan, Miller, Krummen et al., JACC 2014; 63:1761-8
Narayan, Swarup, Miller et al. PRECISE-PAF. Heart Rhythm. 2013 LBCT; *In review*

Multicenter FIRM Studies

Single Procedure Success Rates

Miller et al. JCE 2014; 9: 921-9



John Hummel/OHSU

•74% single proc 2Y AF freedom (75% PeAF)

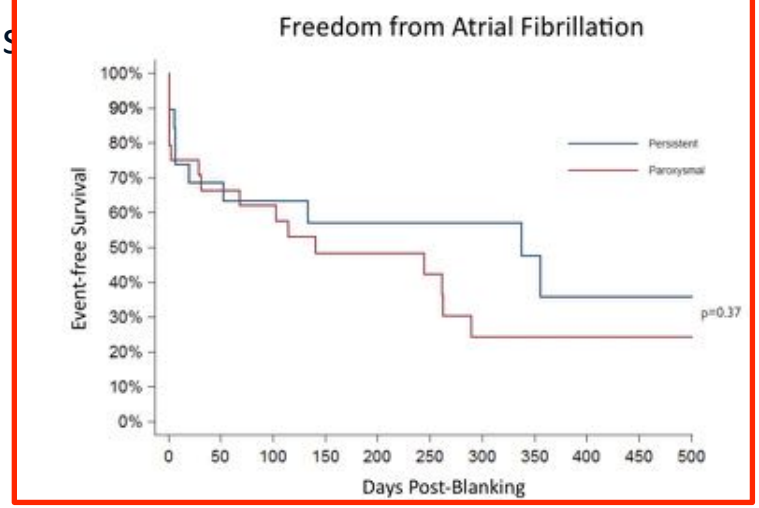
Foreman/Prystowsky:

•75% single proc AF freedom (n=175; 60% PeAF >6 mo)

Wilber

•Rotors/fibrosis

Share, Shivkumar et al. HRS 2015 n=43



Tilz/Kuck

•80% single 1Y proc freedom from AF (n=25)

Tomassoni

•76% single proc 2Y AF freedom (n=80; 65% PeAF)

Summary

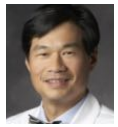
- **Electrogram analyses of AF <u>often differ</u> from optical maps of local action potentials**

- **Vast majority of optical studies, FIRM and possibly other clinical methods show AF sources in localized regions of RA and LA. Mostly rotors – a minority of focal sources.**

- **Early studies (non-randomized) show that mapping AF substrates improves ablation success**

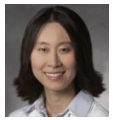
- **Future studies:**
  - Clinical – randomized controlled trials (pending)
  - Mechanistic – more optical studies, how do rotors cause disorder, other targets? (all pending)

Stanford Complex Arrhythmia Program/Funding

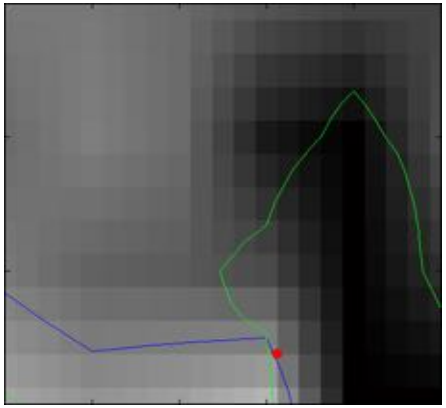
EP Clinical/ Physiology






Narayan
NIH HL83359 (2014-2019)
NIH HL103800 (2015-2020)

Tina Baykaner
HRS Fellowship (2015-6)



Computer Modeling


Wouter Rappel/Narayan
NIH HL122384 (2014-2019)

Junaid Zaman
Fulbright Scholar 2015-6
British Heart Found 2014-5
AHA Young Invest. 2015


Imaging

Philip Yang, Mike McConnell
NIH HL103800 (2015-2020)
Several other grants

AJ Rogers
Resident

George Leef
Resident

Trials/ Outcomes


Mintu Turakhia, Kenneth Mahaffey (Bob Harrington)
Narayan: NIH HL103800 (2015-2020)
Pending Funds

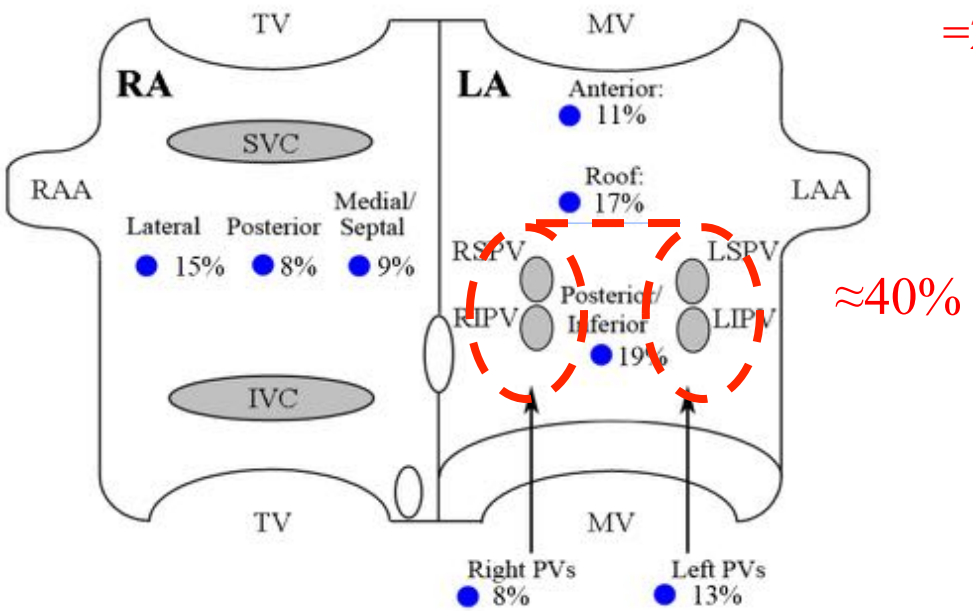
Ongoing Clinical Trials

Europe
US

Narayan Complex Arrhythmia Program: NIH (2001-2020), AHA, ACC, HRS, Fulbright, BHF)

Rotor/Focal Source Locations

Diverse. Can Avoid Posterior Wall etc



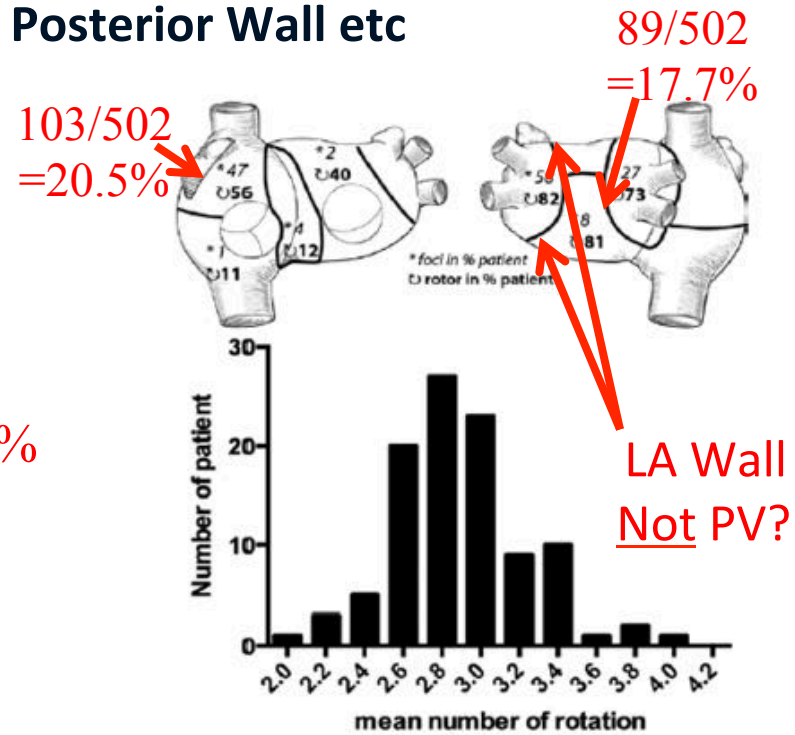


Figure 2. Top, Distribution of drivers (focal breakthroughs, asterisk; reentry events, curved arrows) in 7 regions is reported as the percentage of patients. For example, 82% of the 103 patients had repetitive reentries, and 58% had repetitive focal breakthroughs in left pulmonary vein-appendage region. **Bottom,** The bar diagram shows the distribution of the mean number of rotations in 103 patients.

N (>1000)	Centers	PI
101	UCSD	Narayan (CONFIRM), 2012
78	10	Miller (FIRM Registry), 2014
260	6	Swarup, Miller, 2014
	~30	Multiple

N	Centers	PI
103	Bordeaux	Haissaguerre, 2014
		Others