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AF ablation guided by spatio temporal dispersion of EGM

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www.rhythmcongress.com

Disclosure

Speaker name: Dr Clément BARS

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I have the following potential conflicts of interest to report:

Consulting: Abbott, Biosense Webster

Shareholder of a healthcare company: Volta Medical

Visual appraisal of the sequence and morphology of intracardiac electrograms is sufficient to guide ablation of most arrhythmias, Atrial fibrillation is an exception to this paradigm so far.

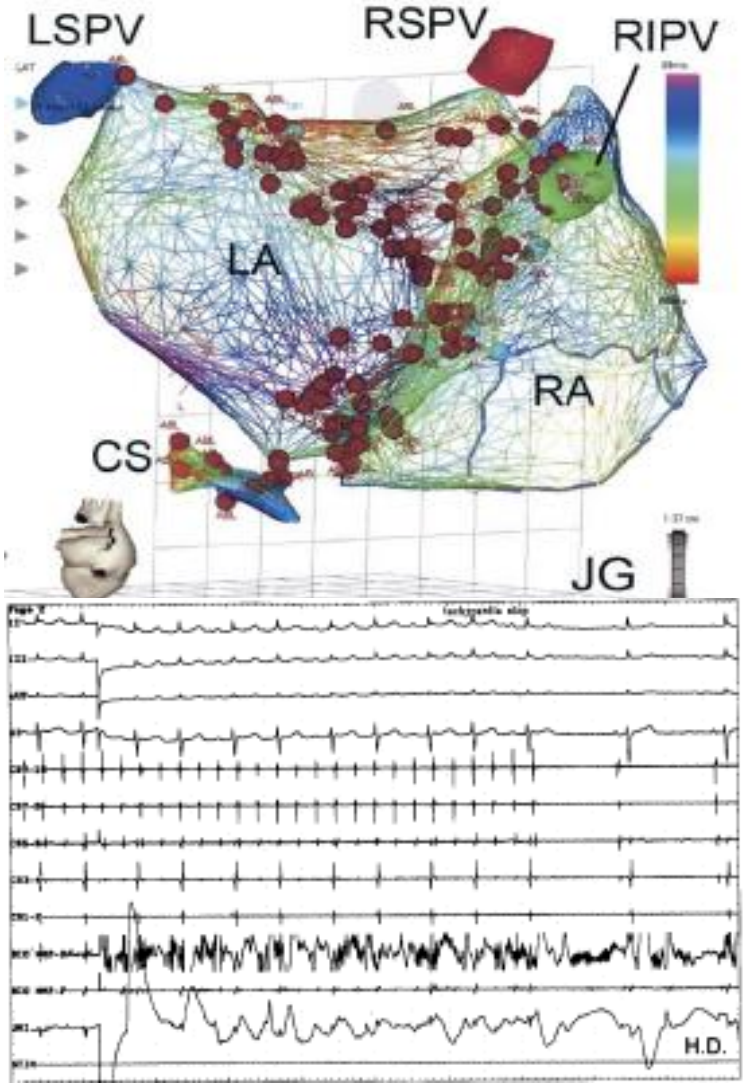
EGM-based ablation

121 pts (47 parox, 64 Persist.)
CFAE ablation only (no PVI)

<u>Endpoints:</u>
- CFAE elimininination
- AF termination
- non inducibility (Parox.)

- AF termination:
100% Parox, 91% Persist.
- Redo: 50%

Outcome: 91% success (1 year), 81% (28 months)

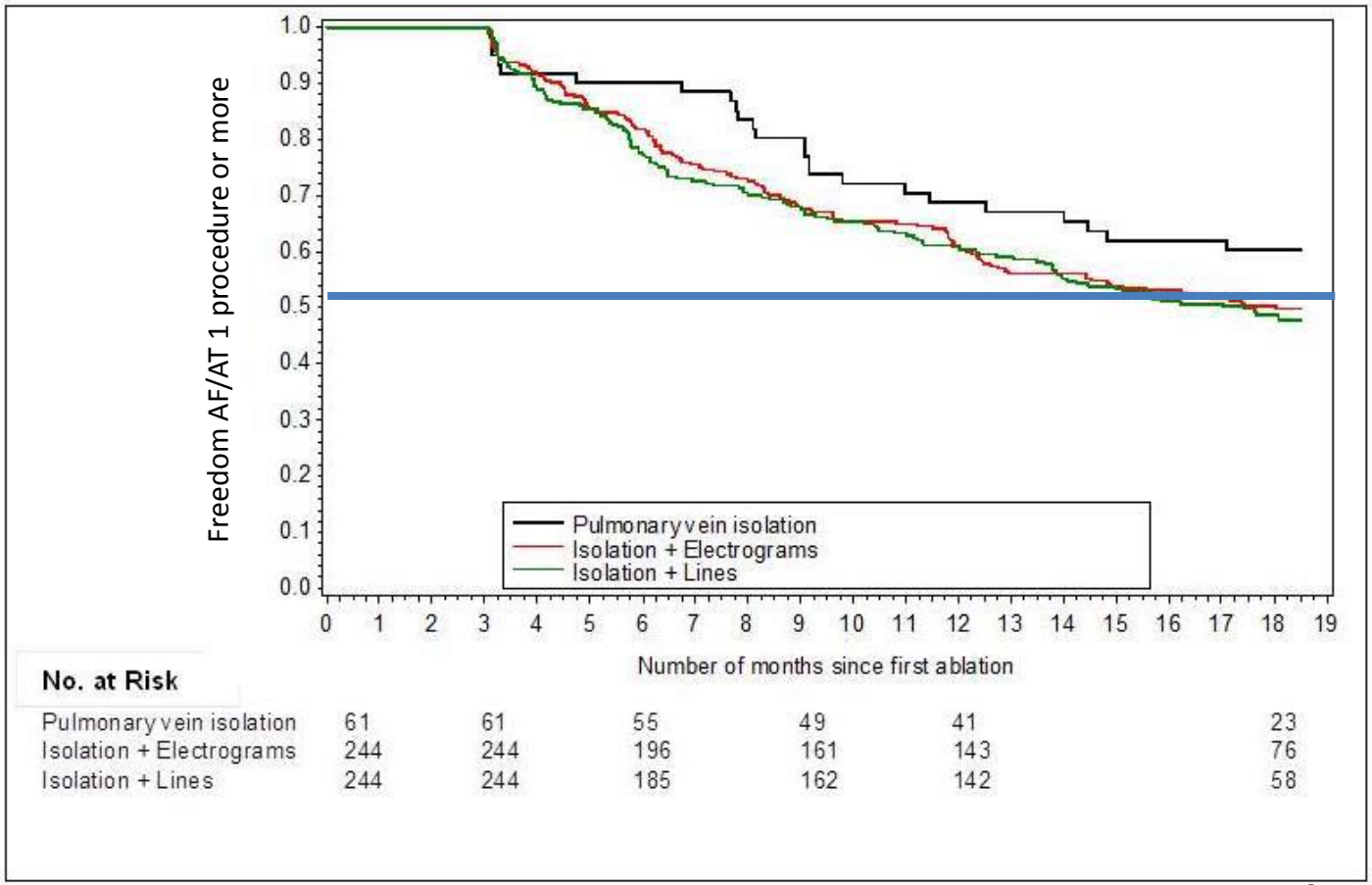


Nademanee et al. J Am Coll Cardiol. 2004

PVI for persitent & LS-persistent AF:

~ 50% Freedom from AF/AT after multiple procedures with or without AA drugs

Averaged results (589 patients , no statistical difference between techniques):

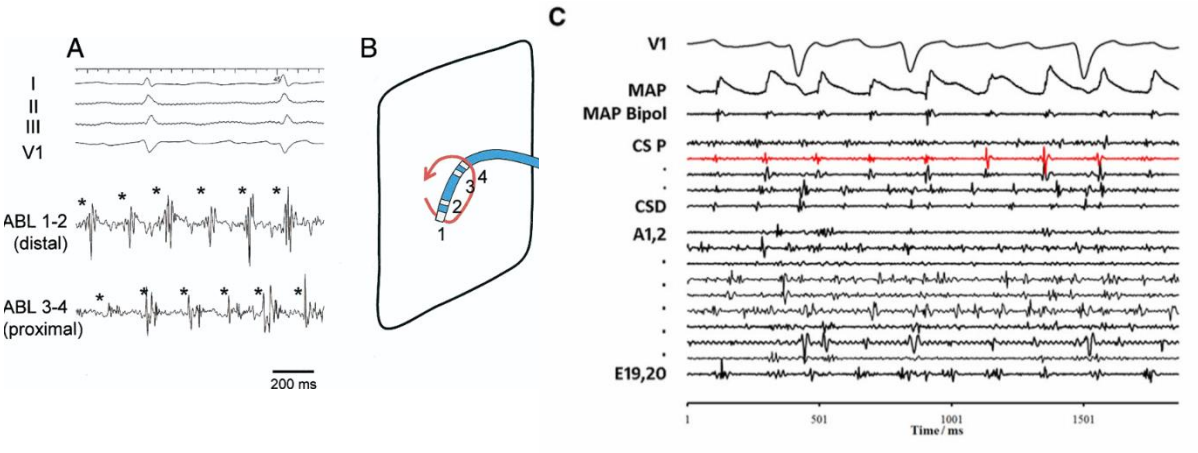


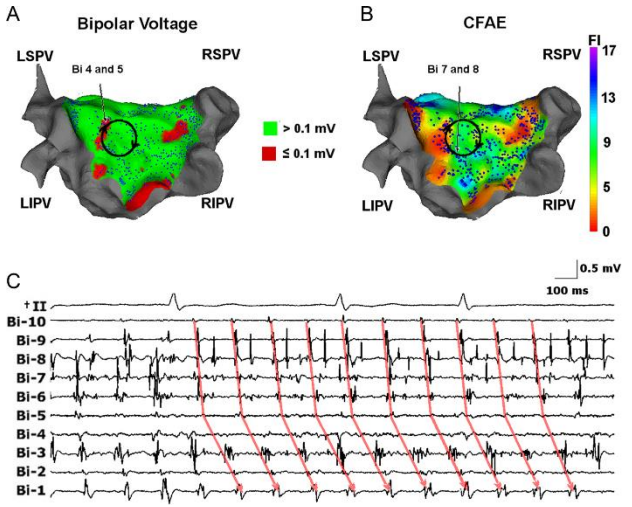
~ 50 %

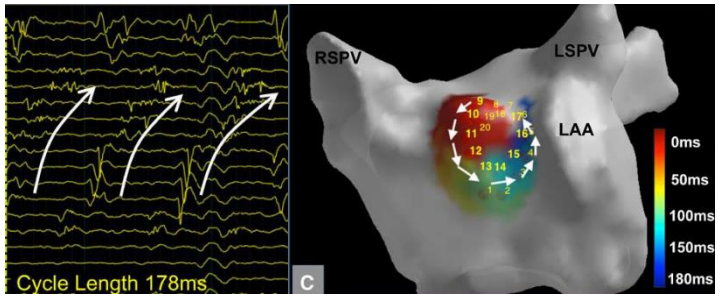
Verma et al. NEJM 2015

Multipolar mapping of AF

Several authors have specifically pointed out that fractionation occurring in a non-simultaneous fashion at neighboring electrode locations (time dispersion) and organized in well-defined clusters (spatial dispersion) may indicate the presence of an underlying source of AF.







Jaïs P, Haïssaguerre et al. PACE 1996;19:1998–2003.

Rostock et al. Heart Rhythm Soc. 2006;3:27–34

Takahashi , O'Neill et al. JACC. Vol. 51, No. 10, 2008

Haïssaguerre, Hocini et al. Circulation 2006;113:616–625.

Narayan et al. Heart Rhythm Soc. 2011;8:244–253.

Ganesan, Ghoraani et al. Heart Rhythm december 2013

Jadidi, Arentz et al. Circ. Arrhythm.Electrophysiol. 2016;9:e002962. *2016*

- How extensive are these regions of STD in patients in Afib?

- What would happen should we ablate the STD areas

JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Wholly Patient-tailored Ablation of Atrial Fibrillation Guided by Spatio-Temporal Dispersion of Electrograms in the Absence of Pulmonary Veins Isolation

Julien Seitz*, MD; Clément Bars*ʸ, MD; Guillaume Théodoreᶻ, MD; Sylvain Beurtheret*, MD; Nicolas Lellouchéˣ, MD, PHD; Michel Bremondy*, MD; Ange Ferracci*, MD; Jacques Faure*; Guillaume Penarandaʲʲ; Masatoshi Yamazakiᵗ; Uma Mahesh R. Avulaᵗ, MD; Laurence Curel*, MS; Sabrina Siame* Omer Berenfeldᵗ, PHD; André Pisapia*, MD; Jérôme Kalifaᵗ, MD, PHD.

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GROUPE HOSPITALIER HENRI MONDOR

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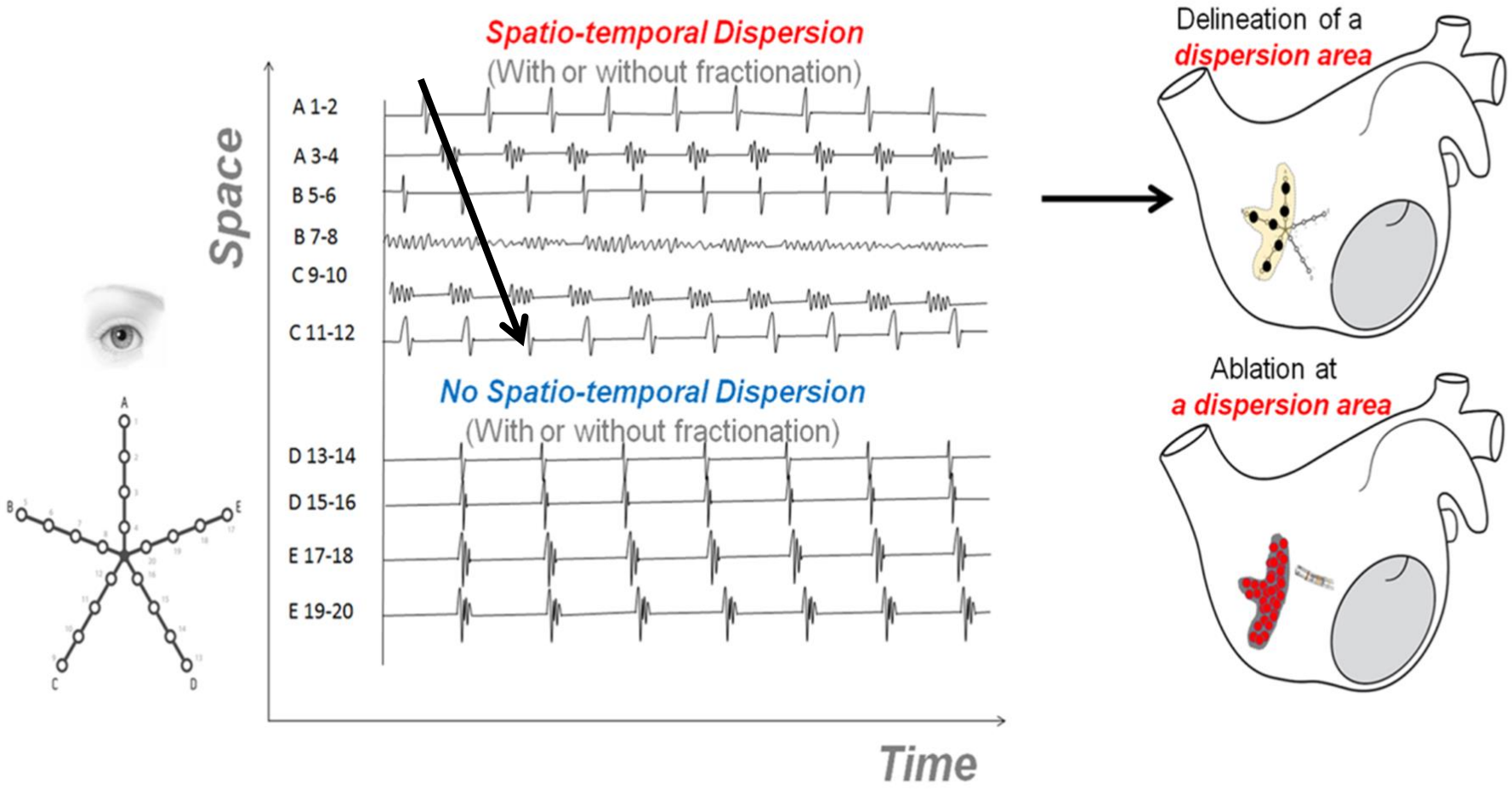
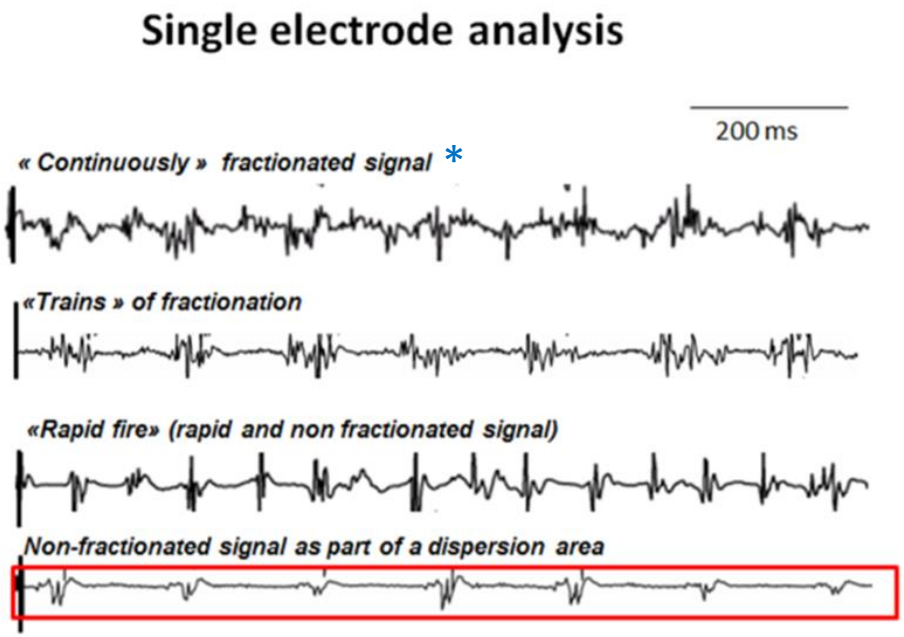
Spatio-temporal dispersion



"Dispersion areas were defined as **clusters of electrograms, either fractionated or non-fractionated,** that displayed inter-electrode time and space dispersion at a minimum of three adjacent bipoles such that **activation spread over all the AF cycle length**"

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Example of EGMs from dispersion regions



*: Nademanee et al. JACC 2004

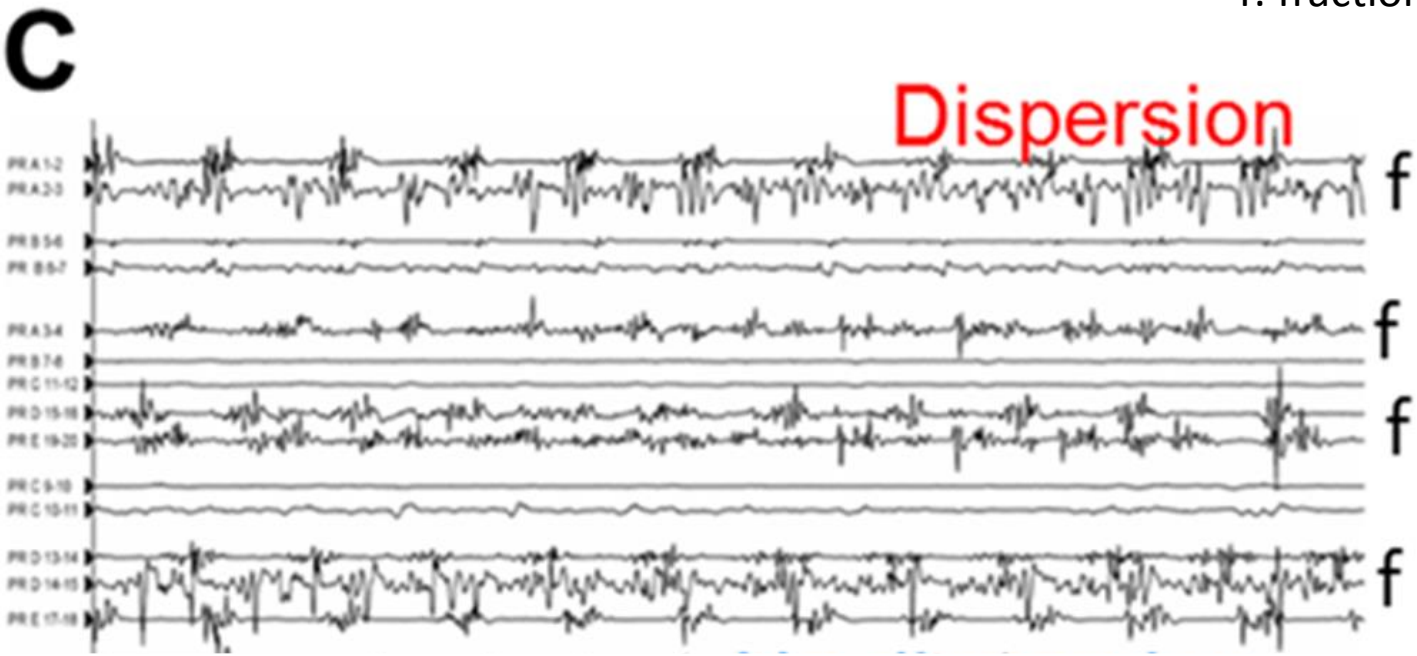
Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

You may find non fractionated EGMs within dispersion regions and to the oposite fractionated EGMs within non dispersion regions

f: fractionated EGM

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

f: fractionated EGM



Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

f: fractionated EGM

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

HOPITAL SAINT JOSEPH MARSEILLE

University of Michigan Health System

Substrate HD

Clinical study

L'INSTITUT MUTUALISTE MONTSOURIS GHMF

GROUPE HOSPITALIER HENRI MONDOR

Centre Hospitalier Universitaire de Nice

Objectives

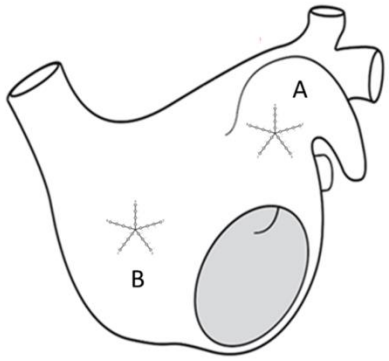
- Determine whether spatio temporal dispersion morphologies may enable the identification of AF drivers regions.
- Demonstrate that spatio temporal dispersion regions are effective target sites for AF ablation.

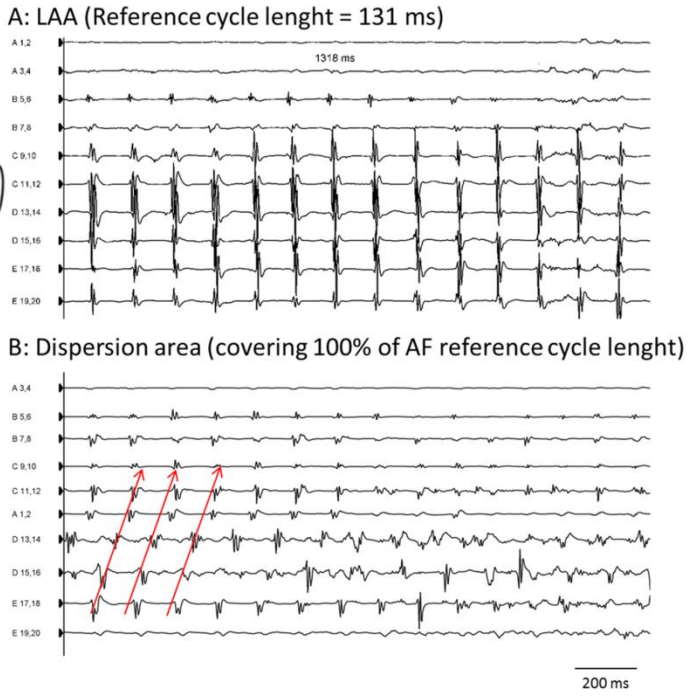
Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Clinical Study

- **Prospective enrollment of 105 patients** in 3 centers for AF ablation (7 ablationists)
- **AF sequential mapping in both atria** with the 20-pole catheter PentaRay in all regions.
- **Visual selection of Electrode locations that display Spatio temporal dispersion**

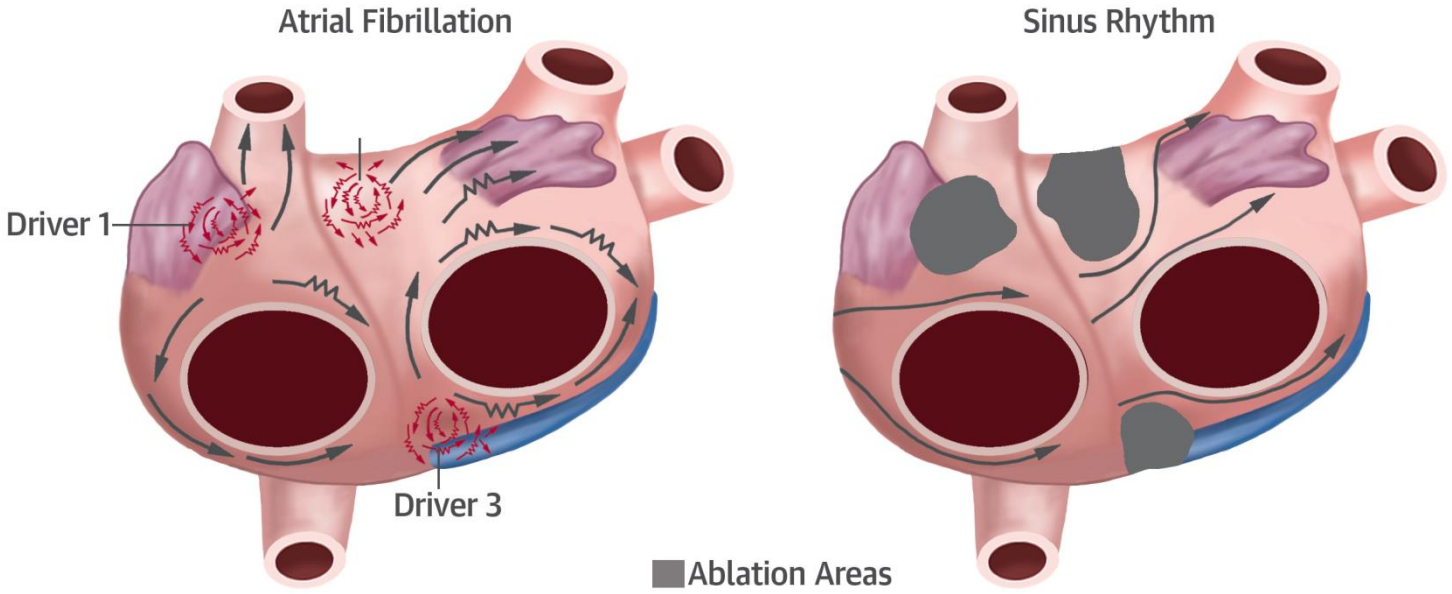
Highest density of points needed to delineate driver regions frontiers accurately





Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Atrial Fibrillation Ablation Method Guided by Spatio-Temporal Dispersion of Electrograms



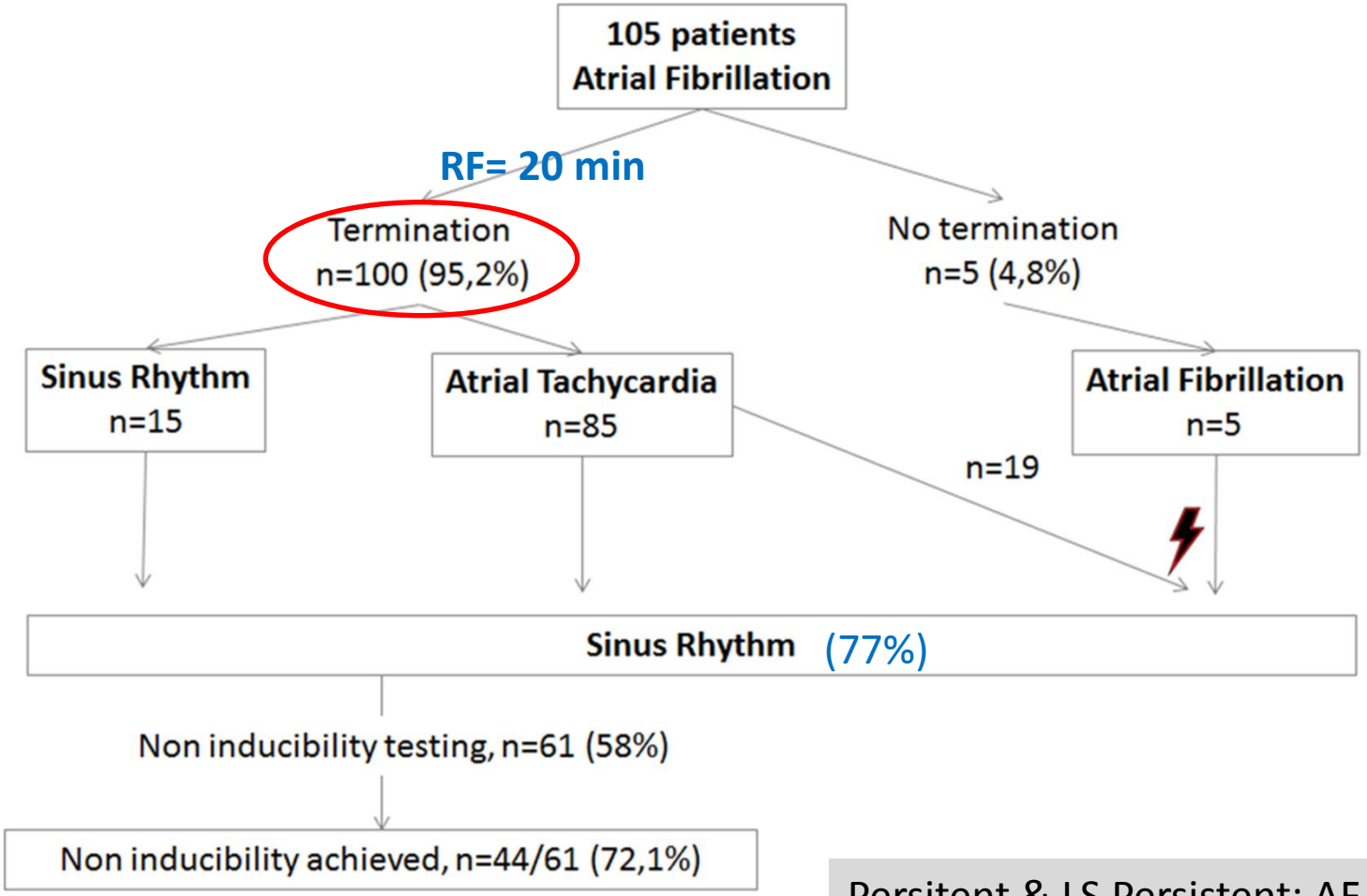
Biatrial Dipersion map

- **Ablation at dispersion regions (10-45W).**
- If two ablated areas were very close (<1cm) they were connected by RF applications.
- **No probabilistic ablation (no PVI or lines)**
- **Ablation endpoints** : AF termination, SR conversion acutely, and freedom from AF/AT (after 18 mo-follow-up with or without AA drugs).
- **Same approach for redo**

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

	Study population (n=105)	Validation set (n=47)	p
Age (years), mean ± SD	63 ±11	58±11	0.0046
Male, n (%)	80 (76.2%)	35 (74%)	0.8191
AF type			
Paroxysmal AF, n (%)	24 (22.8%)	9 (19,2%)	0,6
Non-paroxysmal AF, n (%)	81 (77,2%) **LS-Pers. = 30**	38(80,8%)	0,6
Maximum sustained AF duration (months), mean + SD	12.2 ± 20 **Pers+LS pers=14 ±21 LS pers=33 ±27**	19.4±31.6	0.2457
Structural heart disease, n(%)	38 (36%)	14 (35%)	0.4665
Hypertension, %	48(45,7%)	20 (42,5%)	0.5217
Diabetes, %	13(12.4%)	5(10,6%)	0,5995
LA diameter (mm),mean ± SD	45,6± 7,6	42,4±12,4	0,09
LVEF (%), median mean ± SD	52 ± 11	54 ± 12	0,2082
Amiodarone before ablation, %	32%	NA	
Spontaneous AF at the beginning of procedure (persistent and longstanding persistent AF only), n	65 (80,2% of the non PAF)	NA	
Prior AF ablation	0	0	
LAA CL (ms)	182[164-203] non PAF: 174[157-200]	NA	

Procedural outcome



RF time = 49±21 minutes

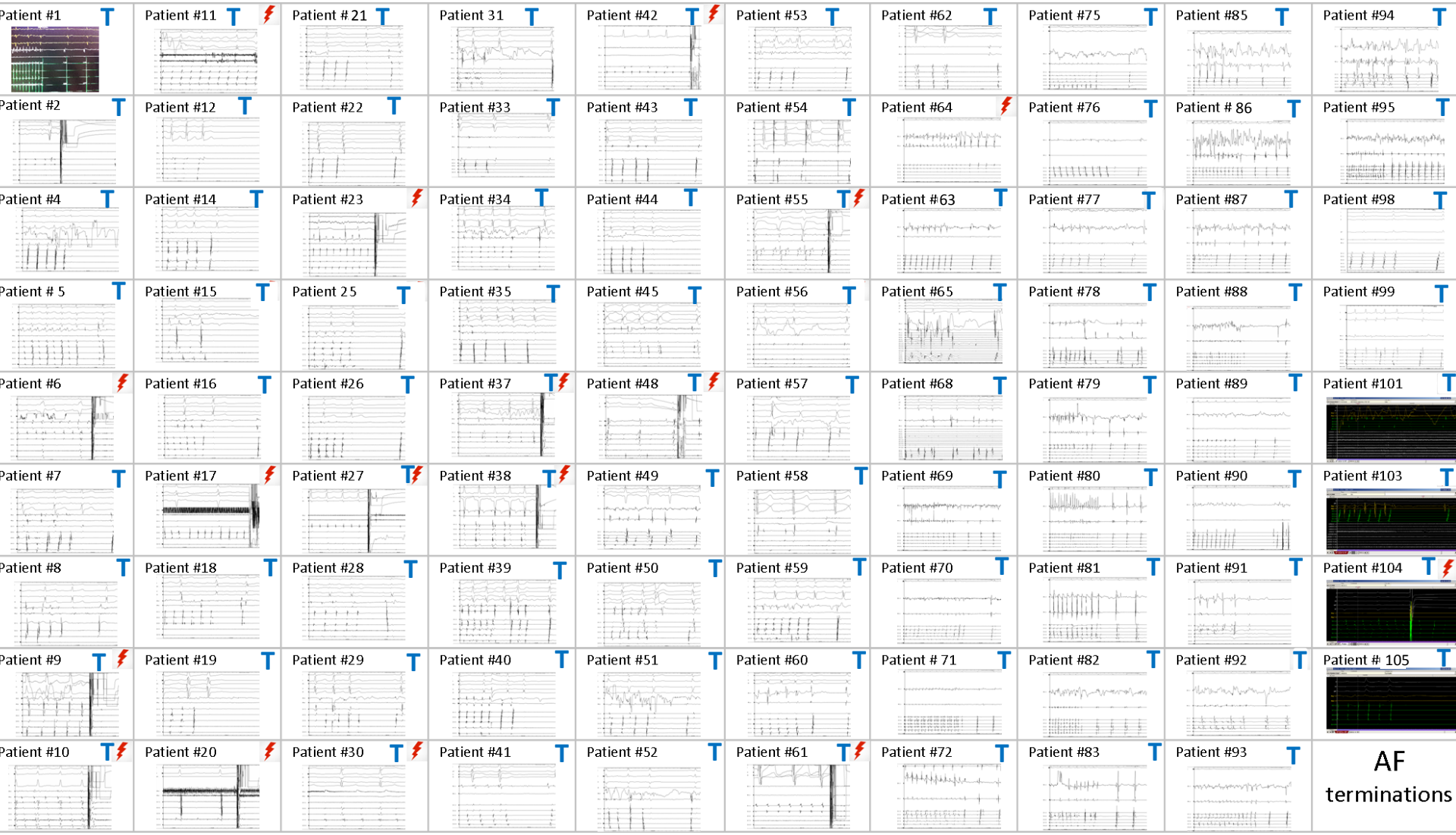
Non extensive ablation: Ablated surface= 17±10% LA surface and 10±5 % biatrial surface

Persitent & LS Persistent: AF termination = 95% & SR conversion = 72%

LS persistrent: AF termination = 90%, SR conversion = 53%

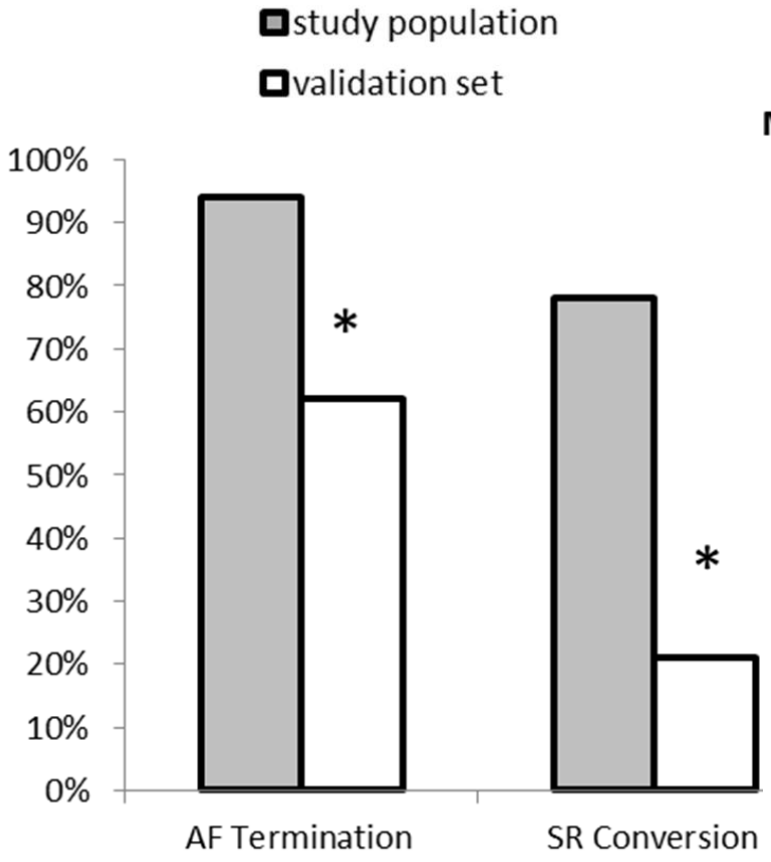
Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

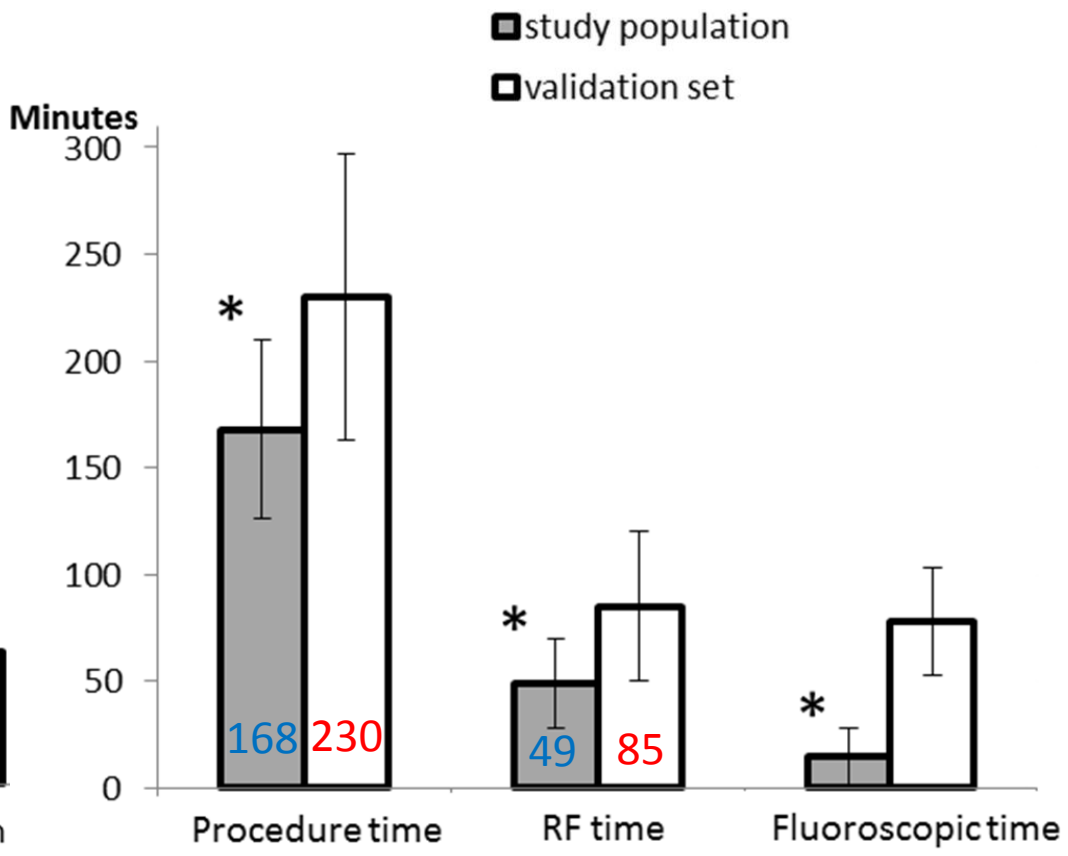
AF terminations (T) from the Substrate HD study



Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Better acute efficacy with shorter and less extensive ablation





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Each patient is unique

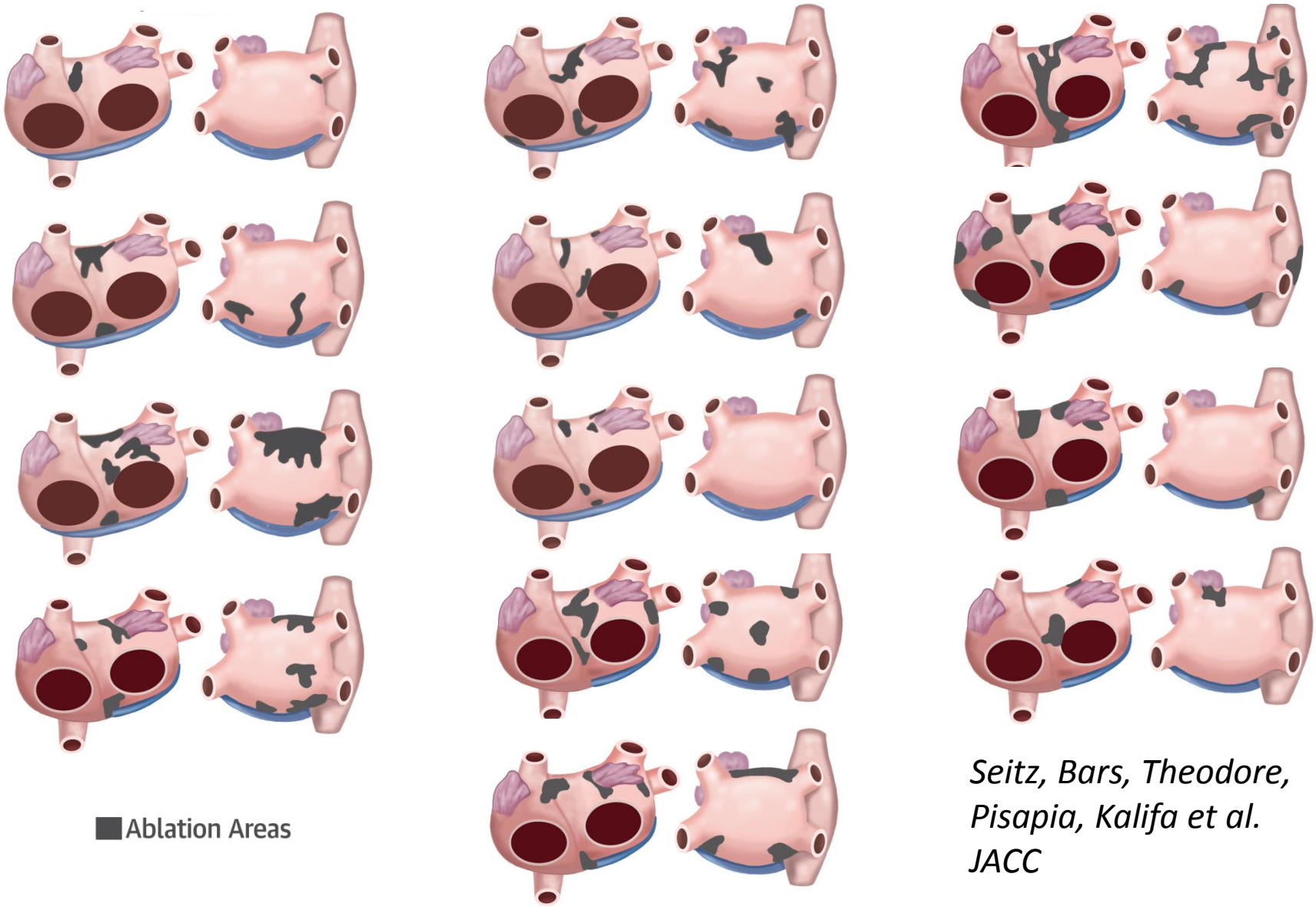

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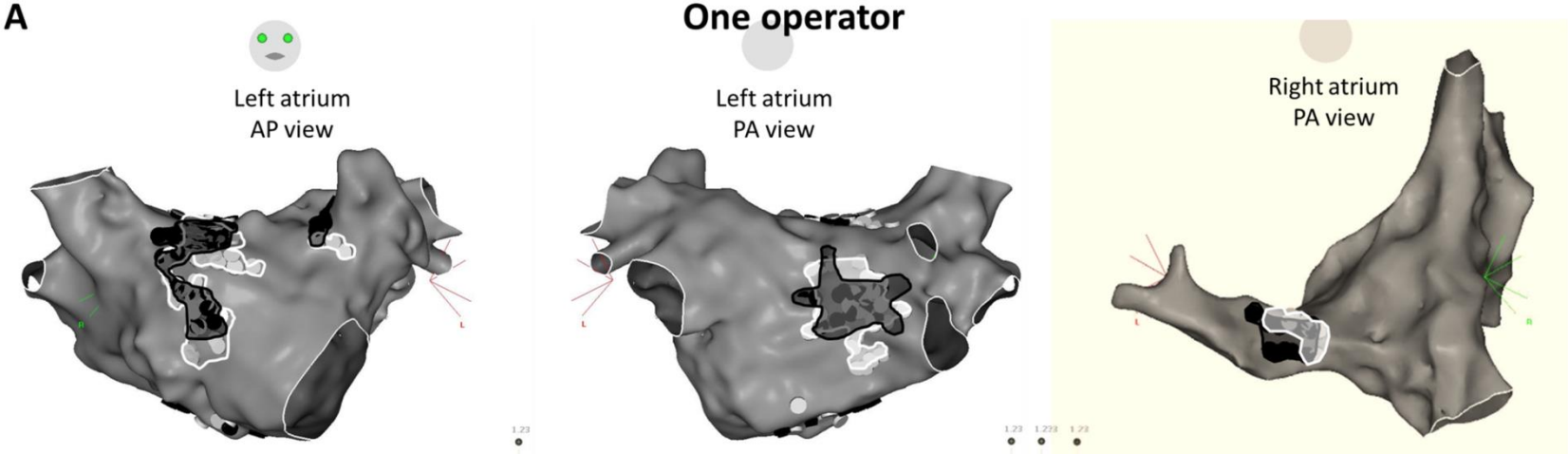
TABLE 2 Surface Area

	All Patients (N ¼ 43)	Paroxysmal (n ¼ 15)	Persistent (n ¼ 17)	LS Persistent (n ¼ 11)	p Value
Dispersion areas					
Total dispersion area surface, cm^2					
Mean ± SD	22.5 ± 13.5	18 ± 10	17 ± 9	41 ± 12	<0.0001
Median (IQR)	19 (12.5–33)	17 (13–22)	15 (11–19)	40 (32–50)	
Mean dispersion area surface, cm^2					
Mean ± SD	5 ± 2	5 ± 2	4 ± 1.5	6 ± 2	0.0025
Median (IQR)	4.5 (3–6)	4.5 (3.4–6.0)	3.2 (2.9–5.6)	6.0 (4.9–8.2)	
Number of dispersion areas					
Mean ± SD	5 ± 1.5	4 ± 1.7	5 ± 1.2	6 ± 1	0.02
Median (IQR)	5 (4–6)	4 (3–5)	5 (4–5)	6 (5–7)	
Ablation in the LA					
LA ablated surface, cm^2					
Mean ± SD	25.5 ± 15.7	20.5 ± 10.5	16.5 ± 6	46 ± 13.5	<0.0001
Median (IQR)	20.6 (15–35.5)	19 (14–27)	17 (11–21)	40 (36–56)	
LA total surface, cm^2					
Mean ± SD	157 ± 47	139 ± 44	167 ± 53	165.5 ± 35	0.18
Median (IQR)	156 (135–171)	153 (114–164)	156 (135–172)	165 (152–175)	
Percent of LA ablated surface					
Mean ± SD	17 ± 10	15.8 ± 8.8	10.1 ± 4.0	29 ± 9.7	<0.0001
Ablation in both atria					
Biatrial total surface, cm^2					
Mean ± SD	302 ± 85	266 ± 97.5	296 ± 53	361 ± 82.5	0.06
Median (IQR)	312 (257–350)	288 (207–331)	293 (273–322)	340 (320–398)	
Bi-atrial total ablated surface, cm^2					
Mean ± SD	31 ± 19	25 ± 12	21 ± 7.0	55 ± 17.5	<0.0001
Median (IQR)	24.5 (18–39.5)	21 (17–39)	20 (16–23)	50 (42–74)	
Percent of biatrial ablated surface, cm^2					
Mean ± SD	10 ± 5	10 ± 4	7.5 ± 2.5	15 ± 4	0.0005

A

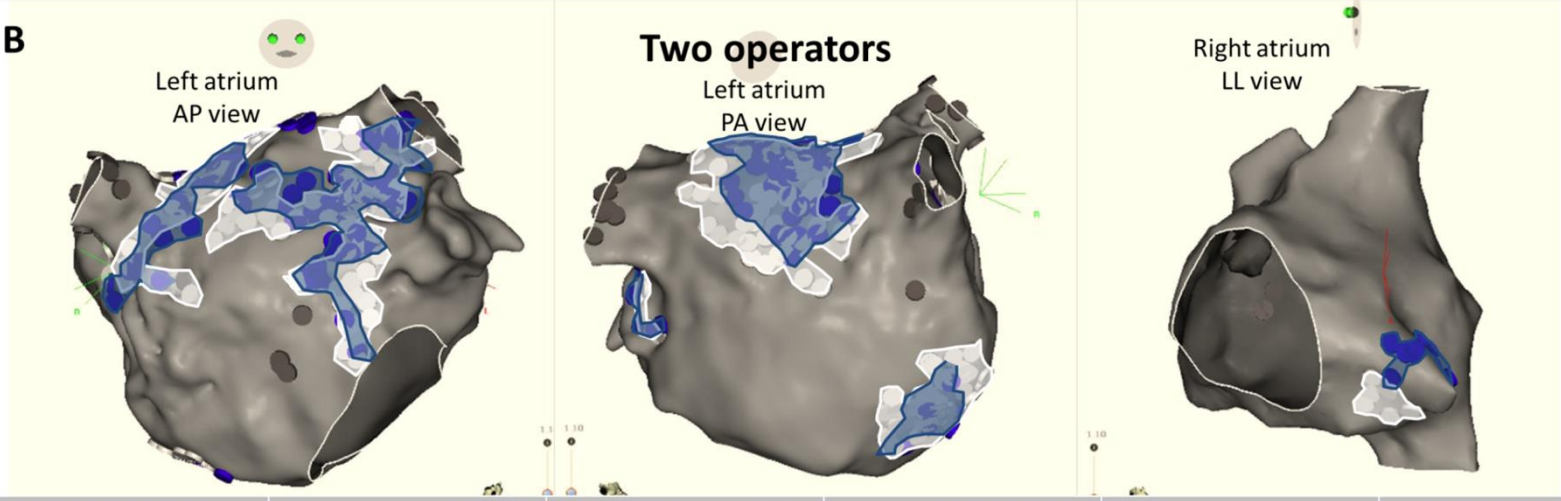
One operator



N=13 patients	Mapping 1	Mapping2	Match mapping 1 & 2	Mismatch mapping 1	Mismatch mapping 2
Involved areas	5,6±0,9	5,3±1	5,2±0,9	0,4±0,6	0,07±0,3
Mapping surface (cm2)	30±12	28±12	26±13	4±3	2±2
% biatrial surface	14±8	13±9	12±9	2±1	1±1

B

Two operators



N=7 patients	operator 1	operator 2	Match operator 1 & 2	Mismatch operator 1	Mismatch operator 2
Involved areas	6±0,8	6,3±0,7	6±0,8	0	0,3±0,5
Mapping surface (cm2)	32±11	29±8	23±7	12±3	7±4
% biatrial surface	11±4	10±3	8±2	4±1	2±1

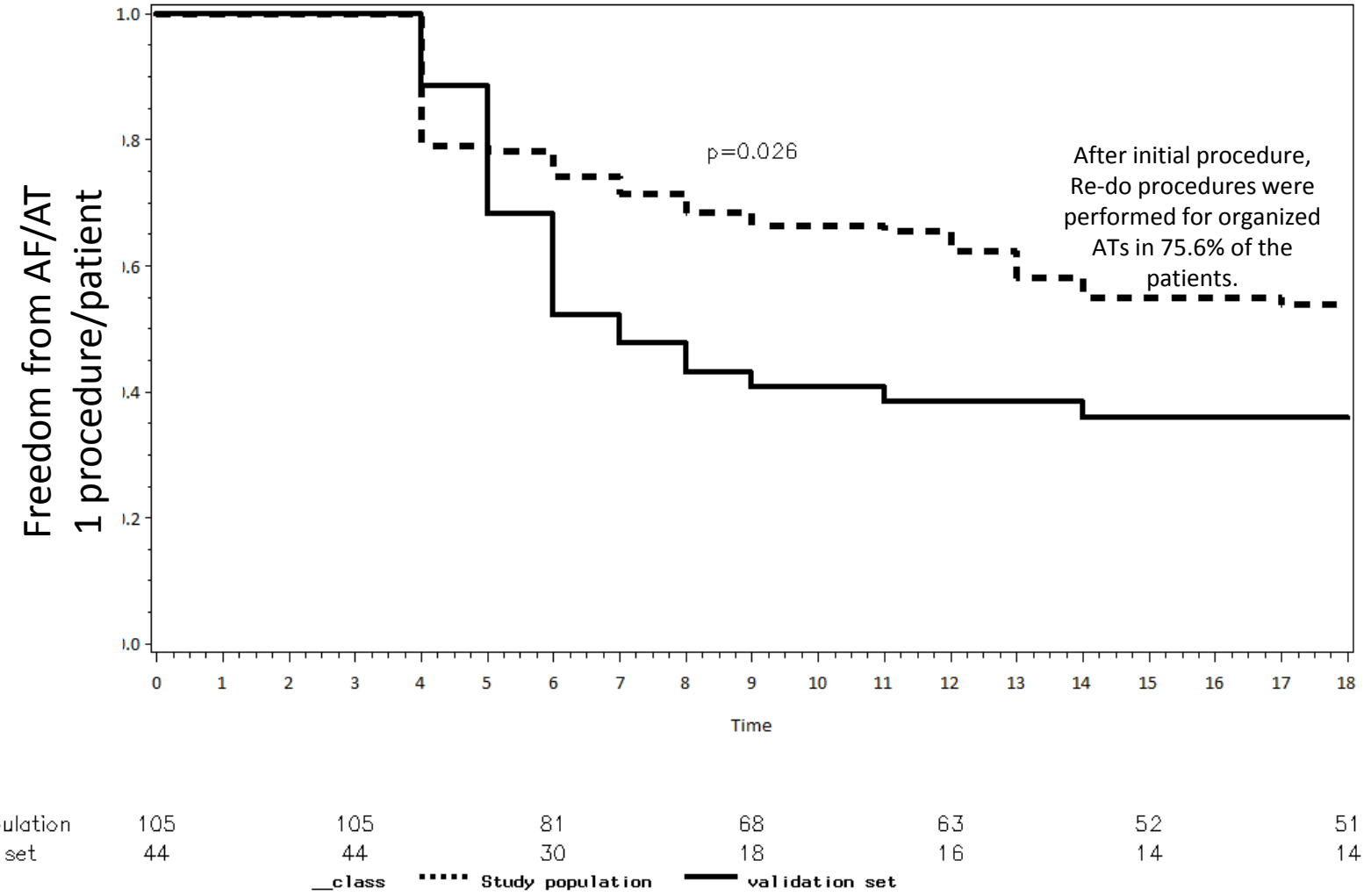
18 month-follow up

Completed in 91% of the patients: follow-up visits and 24-hour Holter ,
7days holter-monitor/ PM-ICD memories in 20 pts

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

18 month-FU: 55% free from AF/AT after 1 procedure

with or without AA drugs



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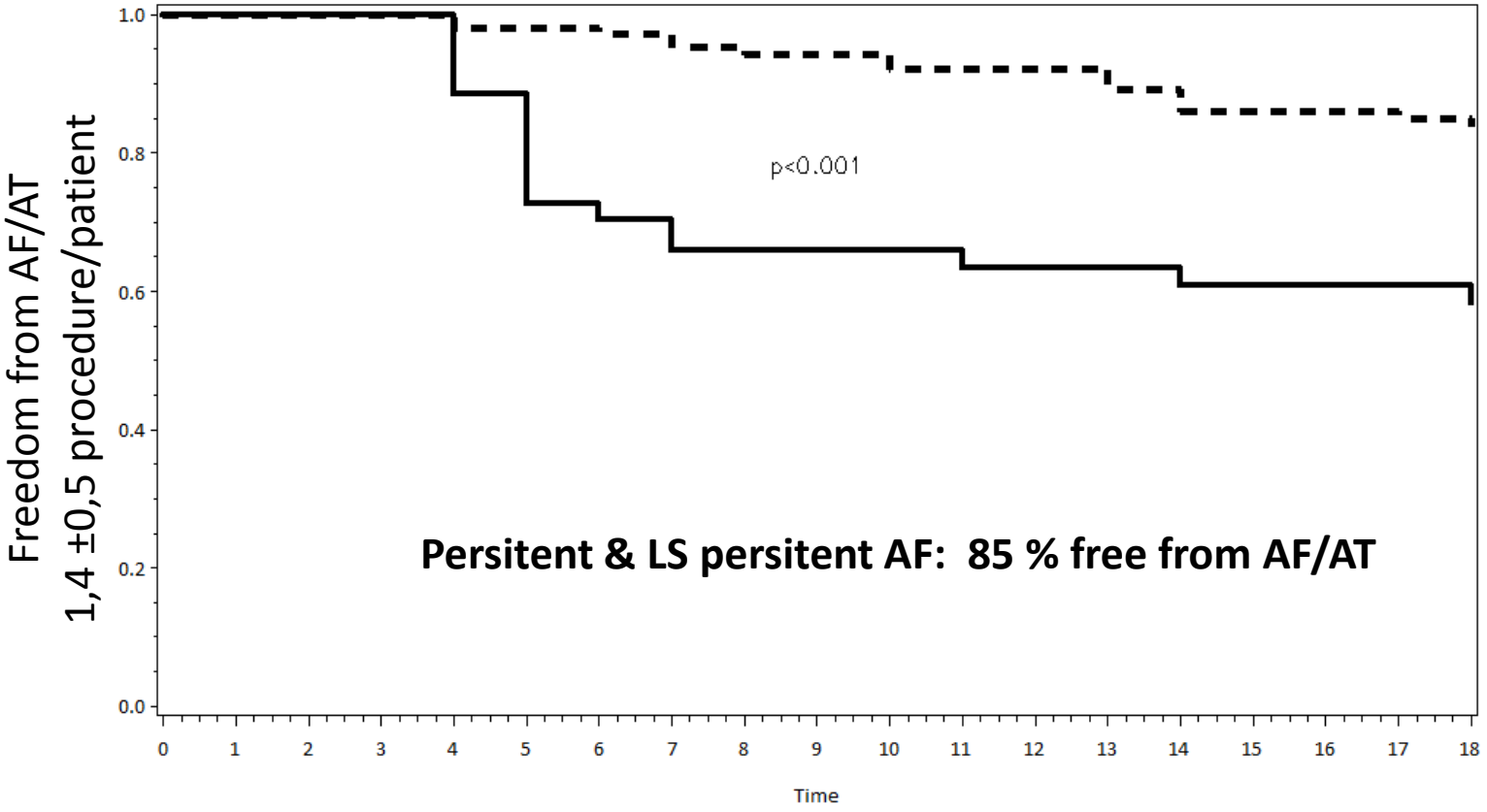
18 month-FU: 85% free from AF/AT after 1,4 procedure/patient

with or without AA drugs



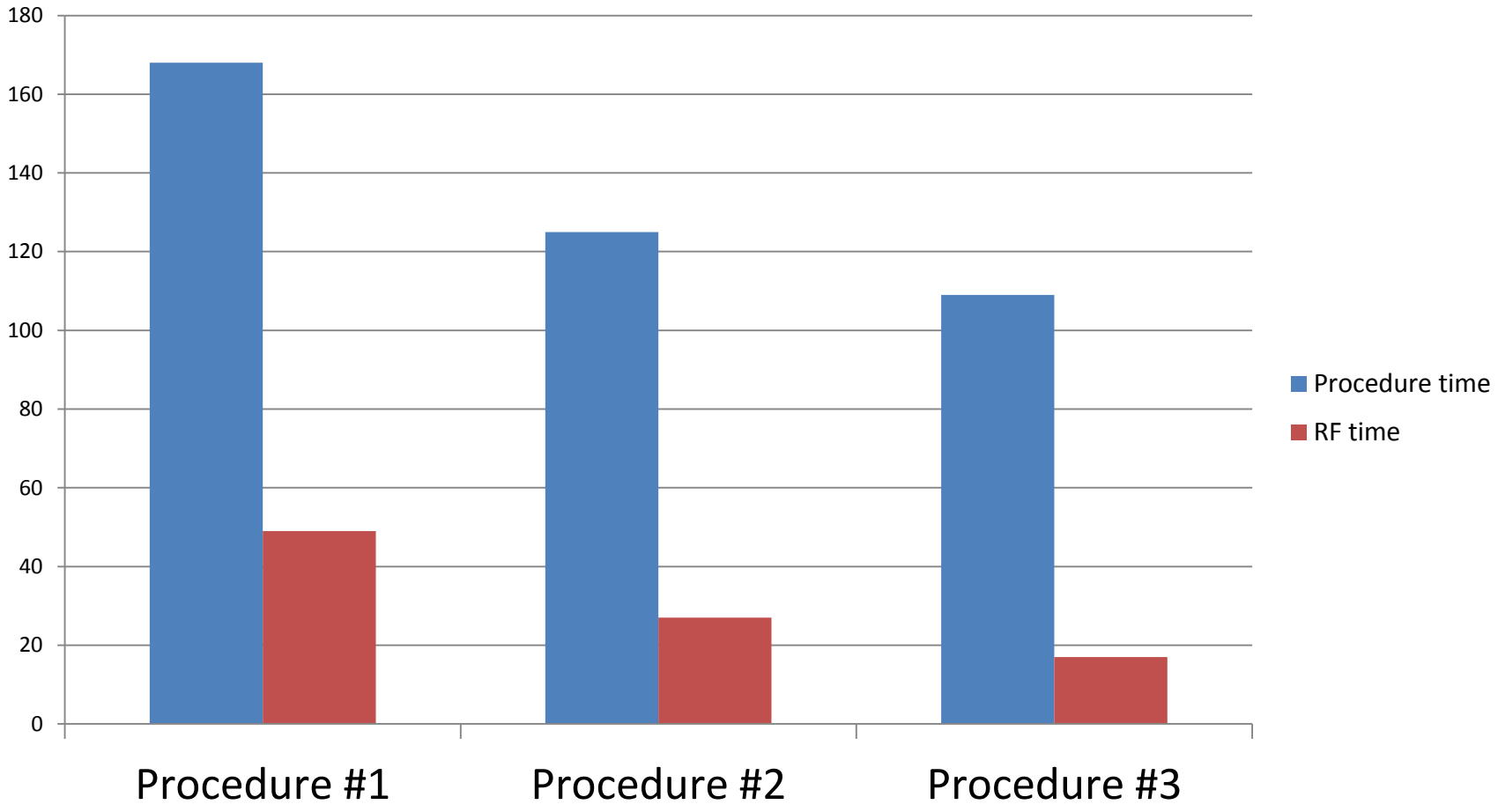
Study population	105	105	102	95	91	83	81
validation set	44	44	32	28	26	23	23

__class ····· Study population ——— validation set

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

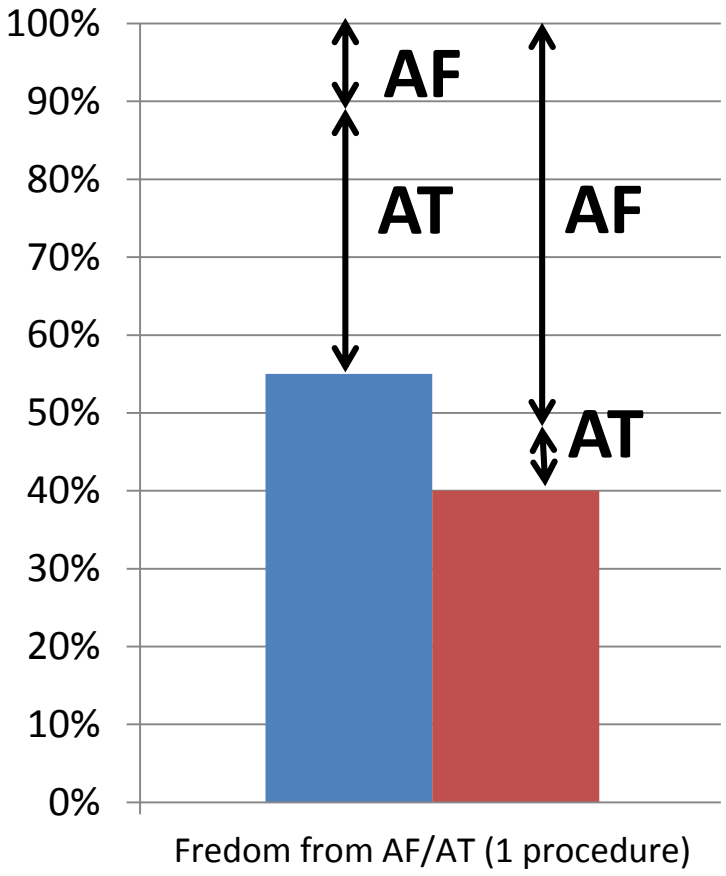
Atrial fibrillation
&
Atrial tachycardias….

ATs are much easier to ablate than AF



Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Substrate HD vs STAR AF2*



* average results of the comparable 3 groups (PVI, PVI+cfe, PVI+lines)

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Conclusion

- The clustering of intra-cardiac electrograms exhibiting spatio-temporal dispersion may guide a wholly patient-tailored ablation for AF especially for persistent AF.
- AF termination =95% within ~ 20 min of RF.

- Using this approach, Redo procedure are mostly performed for Atrial tachycardias recurrences that are much easier to ablate than AF what led to promising long term results. Freedom from AF/AT at 18 mo-FU =85% (1,4 procedure /pt)

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Perspective

- Very high density maps would improve dispersion regions frontiers
- MRI scar distribution, voltage and dispersion regions
- The use of drugs during procedure may help in driver vizualization (Ibutilide/Flecainide ?)
- Better Lesion creation & assesment (Ablation index? unipolar?)
- These preliminary results must be confirmed by a randomized trial

THANK YOU!


200 ms
V1
ABL d
ABL p
PR A 1-2
PR A 2-3
PR B 5-6
PR B 6-7
PR A 3-4
PR B 7-8
PR C 11-12
PR D 15-16
PR E 19-20
PR C 9-10
PR C 10-11
PR D 13-14
PR D 14-15
PR E 17-18
CS 1,2
CS 3,4
CS 5,6
CS 7,8
CS 9,10
Stim Carto
10:20:50

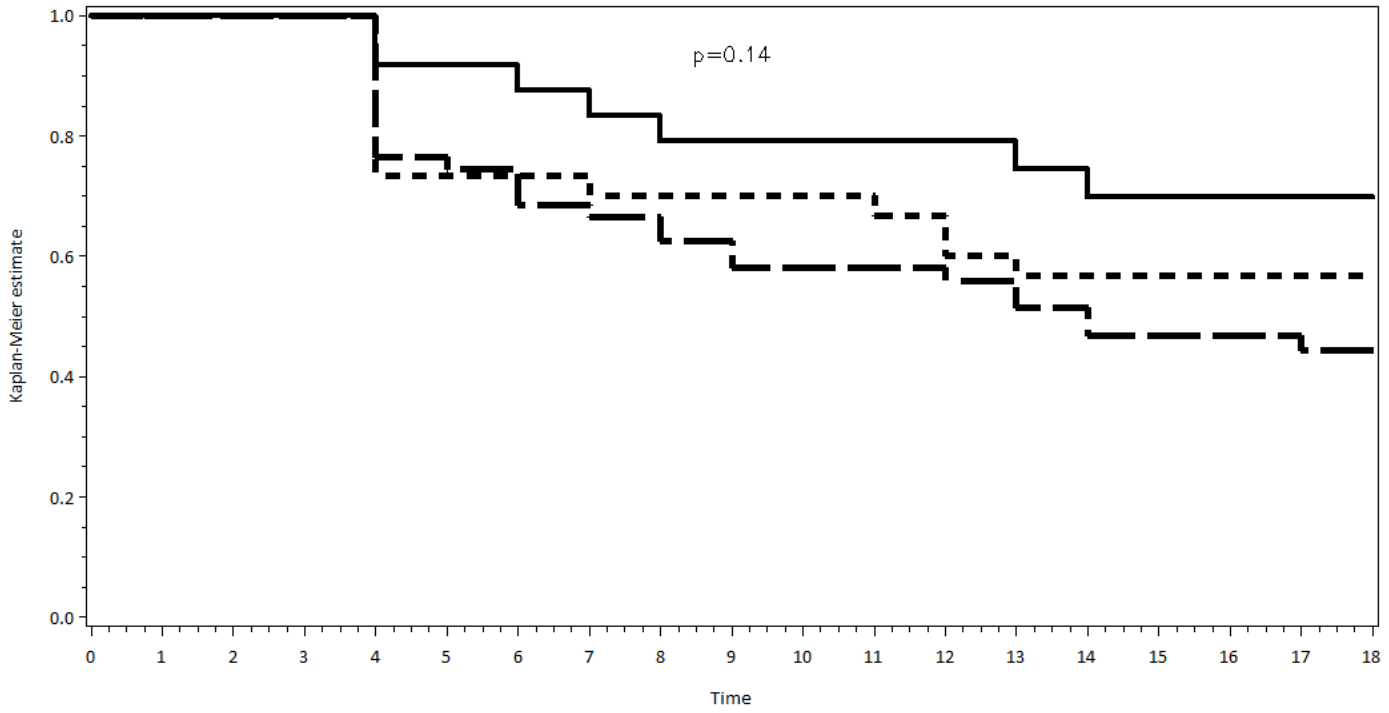
	LAA CL	Driver CL	Non driver CL	Continuous CFE in driver regions	Global voltage <0,5 mV in driver regions	Majority of AF CL In driver regions
Takayashi et al. *JACC 2008*	167 ms	166 ms*	182 ms	yes	yes	yes
Haissaguerre et al. *Circ 2014*	NA	185 ms	189 ms	yes	No (0,8 mV)	yes
Jadidi et al. *Circ ep 2016*	168 ms	NA	NA	yes	yes	yes
Seitz et al. *JACC 2017* (PAF excluded)	174 ms	165 ms*	190 ms	yes	yes	yes

*: CL significantly shorter than in non driver regions

AA drugs before ablation

	AA drugs before ablation	Pts presenting in SR	Prior AF ablation
Rostock et al. Circ ep 2008	41%	0%	0%
O'Neill et al, EHJ 2009	25%	0%	0%
Narayan et al. JACC 2012	0%	30%	42%
Haissaguerre et al. Circ 2014	43%	25%	20,3% (PVI)
Verma et al. (STAR AF2, PVI grp) NEJM 2015	0%	NA	0%
Jadidi et al. Circ ep 2016	NA	31%	22% (PVI)
Seitz et al. (present study)	32%	38% (non PAF=20%)	0%

Freedom from AF/AT 1 procedure

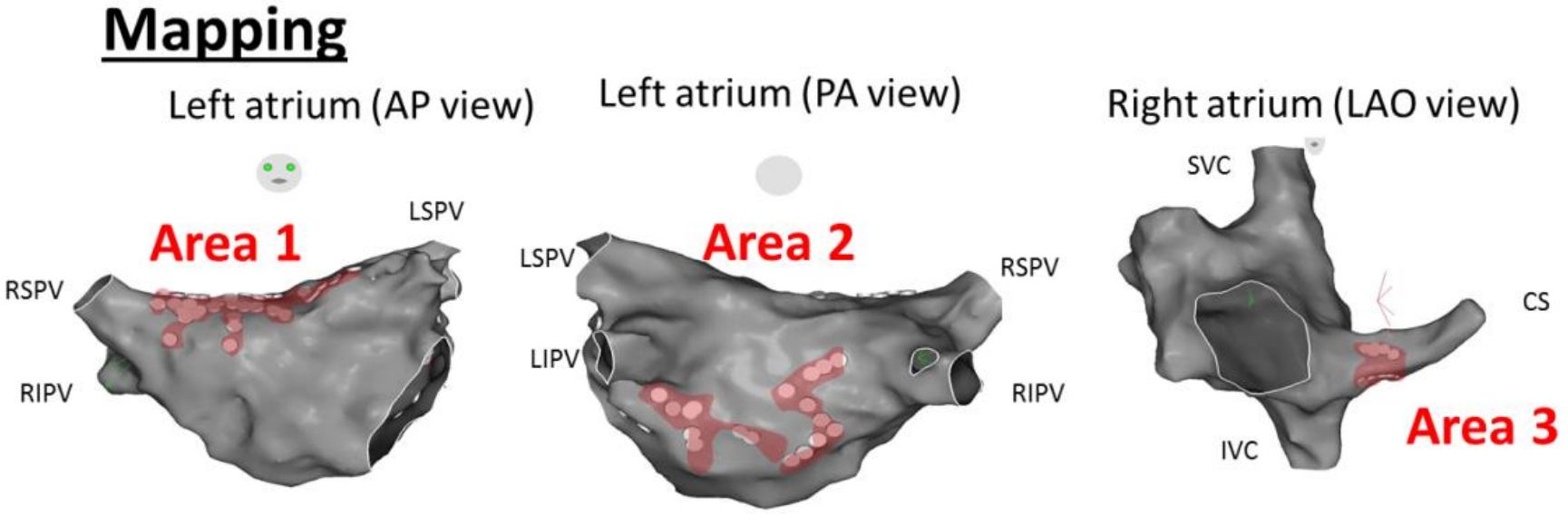


LS−persist	30	30	22	21	20	17	17
Paroxysmal	24	24	22	18	17	15	15
Persistent	51	51	37	29	26	20	19

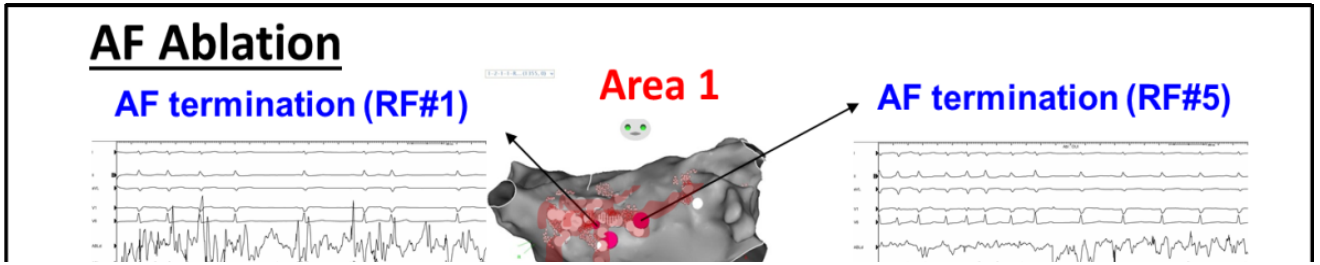
__class LS-persist Paroxysmal Persistent

	AA drugs before ablation	Pts presenting in SR	Prior AF ablation	Sustained AF duration (months)	Long-standing persistent	Paroxysmal	LA diameter	structural Heart disease	AF terminati on	LAA CL
Rostock et al. Circ ep 2008	41%	0%	0%	median: 12 (range:3-264)	NR	0%	50 ±7 mm	64%	77%	155 ms
O'Neill et al, EHJ 2009	25%	0%	0%	21.8+33.2, median: 12 (range:1-240)	54%	0%	47 ± 9 mm	48%	85%	151+21 ms
Narayan et al. JACC 2012	0%	30%	42%	NR	NR	19%	43 ± 6 mm	NR (>28%)	56%	NR
Haissaguerre et al. Circ 2014	43%	25%	20,3% (PVI)	NR	20%	0%	48 ± 7 mm	61%	80%	NR (local driver CL ~185 ms)
Verma et al. (STAR AF2, PVI grp) NEJM 2015	0%	NR	0%	NR (78% > 6 months)	NR	0%	44 ± 6 mm	NR (>7,5%)	8%	NR
Jadidi et al. Circ ep 2016	NR	31%	22% (PVI)	NR	0%	0%	44 ± 5 mm	14%	73%	168±27 ms
Seitz et al. (present study)	32%	38% (non PAF=20%)	0%	12.2 ± 20	29%	22,80%	45,6 ± 7,6 mm	36%	95%	182[164-203] ms, non pAF=174[157-200]

Mechanism of AT and its relationship with the original AF



Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC



Analysis in 21 patients:
44 ATs, 22 macroreentries & 22 localized AT (88,6% in non- ablated areas).

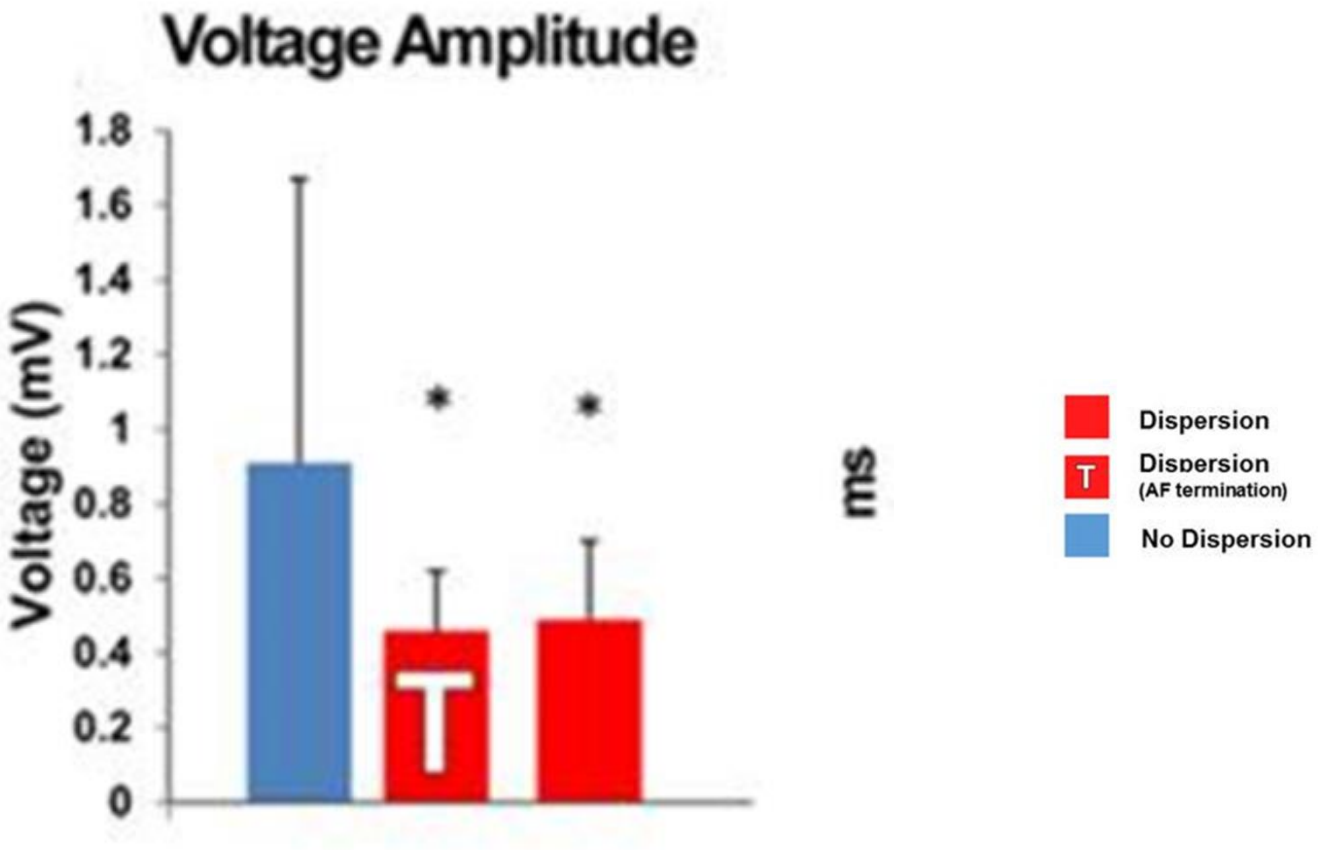
Importantly 17/22 (77,3%) localized ATs arose from dispersion regions that were not previously ablated!

The 2 ATs were located in dipersion areas non already ablated

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC

Since the majority of ATs arise from the dispersion regions that were not previously ablated, it implies that such ATs may be part of AF substrate and were unmasked after the areas of fibrillatory conductions had been ablated…

Global lower voltage in dipersion regions



Dispersion and Low voltage maps

- Biatrial Voltage maps (<0,5 mv) compared to dispersion maps in 43 patients:

- low voltage regions = 92,6 +/- 83,4 cm2
- Dispersion regions = 22,5 +/- 13,5 cm2
- 21 % of the dispersion regions exhibited low voltage
- 3,8% of the low voltage area exhibited dispersion

ATs that occurred during the follow-up or any re-do procedure:

- We analyzed the long-term AT recurrences after the index AF ablation procedure.
- We focused our analysis on determining whether the AT that occurred arose from the dispersion regions that were targeted during the index procedure (dispersion-index regions) or from non-dispersion regions (non-dispersion-index regions), which were not ablated.
- During the 1 year follow-up period, 11 AT ablation procedures were conducted. In total, 18 distinct recurrent ATs were analyzed.

 11/18 ATs (61%) originated from non-dispersion-index regions as follows: six macro-reentries previously ablated at non-dispersion regions such as the mitral isthmus or the roof relapsed presumably because of conduction recovery of ablation lines; four macro-reentries which were not present during the index case. Finally, one focal tachycardia arose from a non-dispersion-index region.

 3/18 (16.6%) ATs originated from within a dispersion-index region.

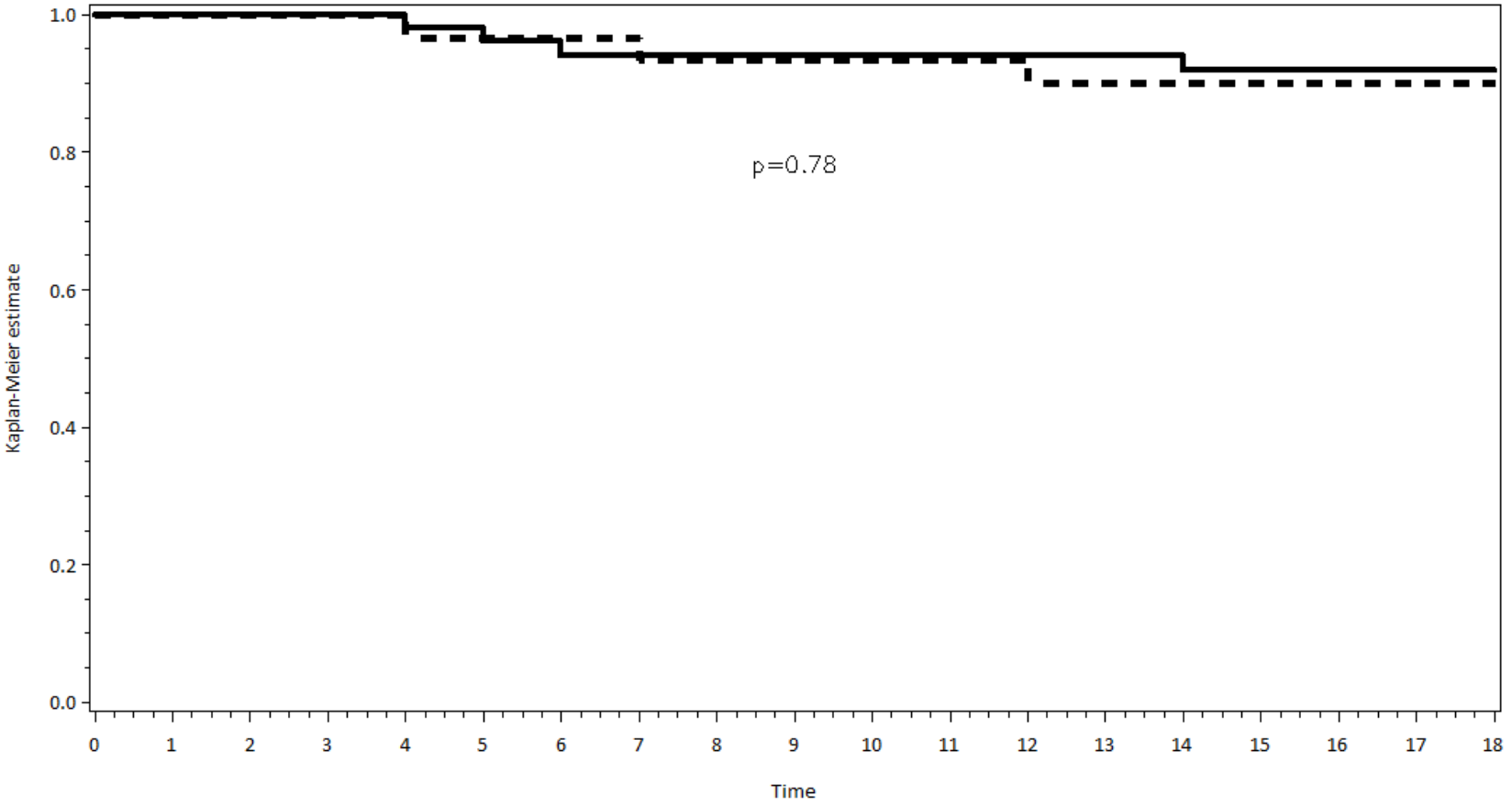
4/18 (22%) were found in close vicinity of a dispersion-index-region (<1 cm).

Study	*PVI ablation time*	*Time to AF termination or AF cycle length prolongation (Narayan et al.)*	*AT ablation time*	*Total Ablation time*
Narayan et al. JACC 2012 (FIRM group)	~39.3 min	18.5 (7.9–24.5) min.	Not reported.	57.8 ± 22.8 min. **(32% patient-tailored)**
Jadidi et al. 2016	28±11 min.	11±9 min.	12±9 min	44±19 min. **(52% patient-tailored)**
Seitz et al. 2016 (present work)	No PVI	20 [10-37] min.	~30 min	49±21min. **(~100% patient-tailored)**

Patient-tailored
Non-Patient-tailored

Persistent & LS-persistent:

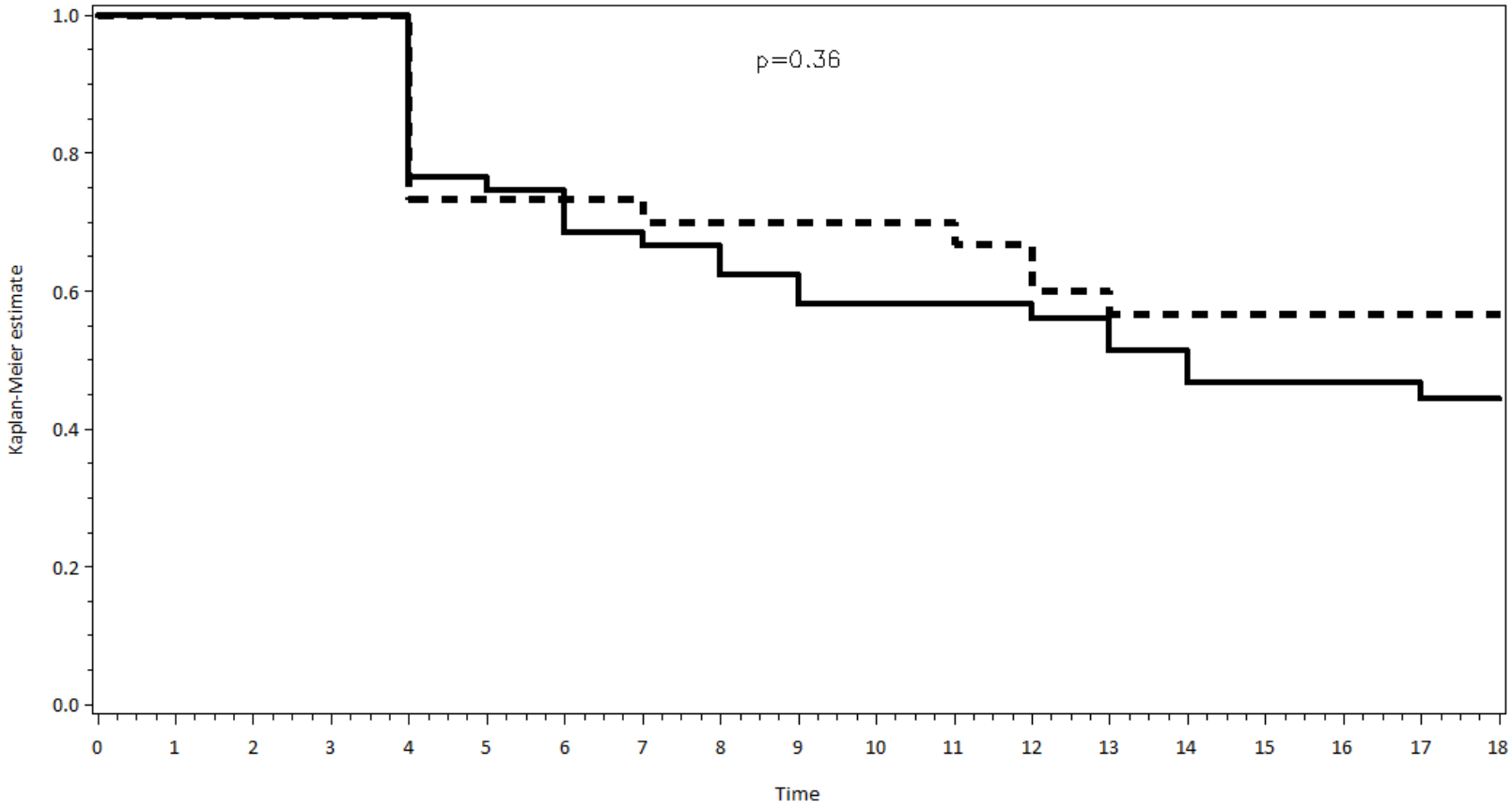
85% free from AF/AT (1,4 procedures) with or without AA drugs (18 month-FU)



LS−persist	30	30	29	28	28	27	27
Persistent	51	51	48	45	44	42	42

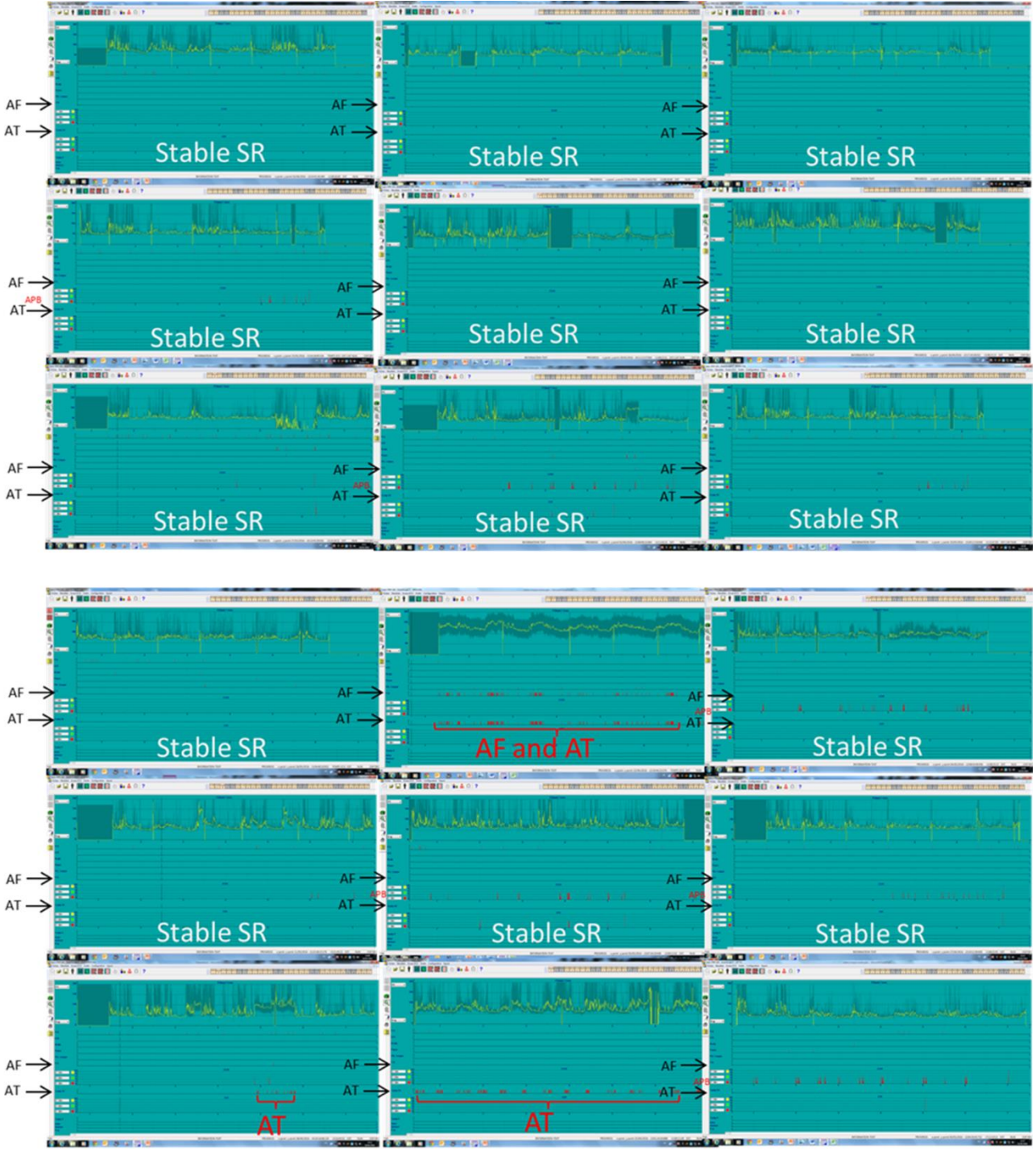
__class LS-persist Persistent

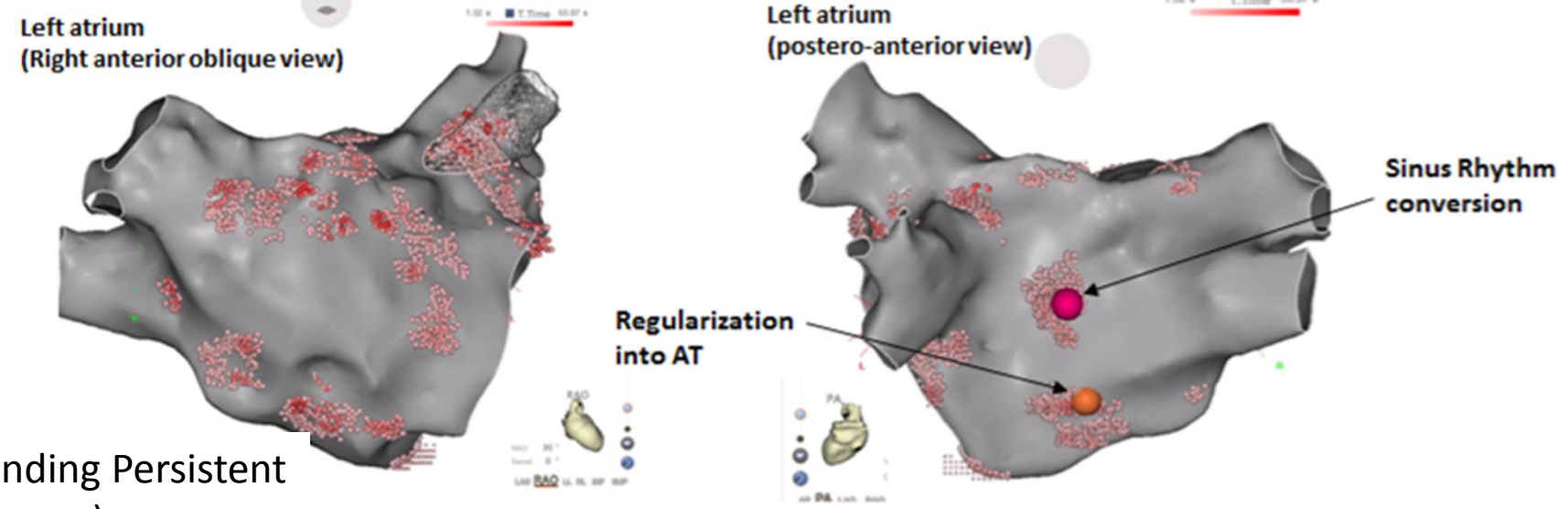
Freedom AF/AT 18 month-FU (1 procedure)



LS−persist	30	30	22	21	20	17	17
Persistent	51	51	37	29	26	20	19

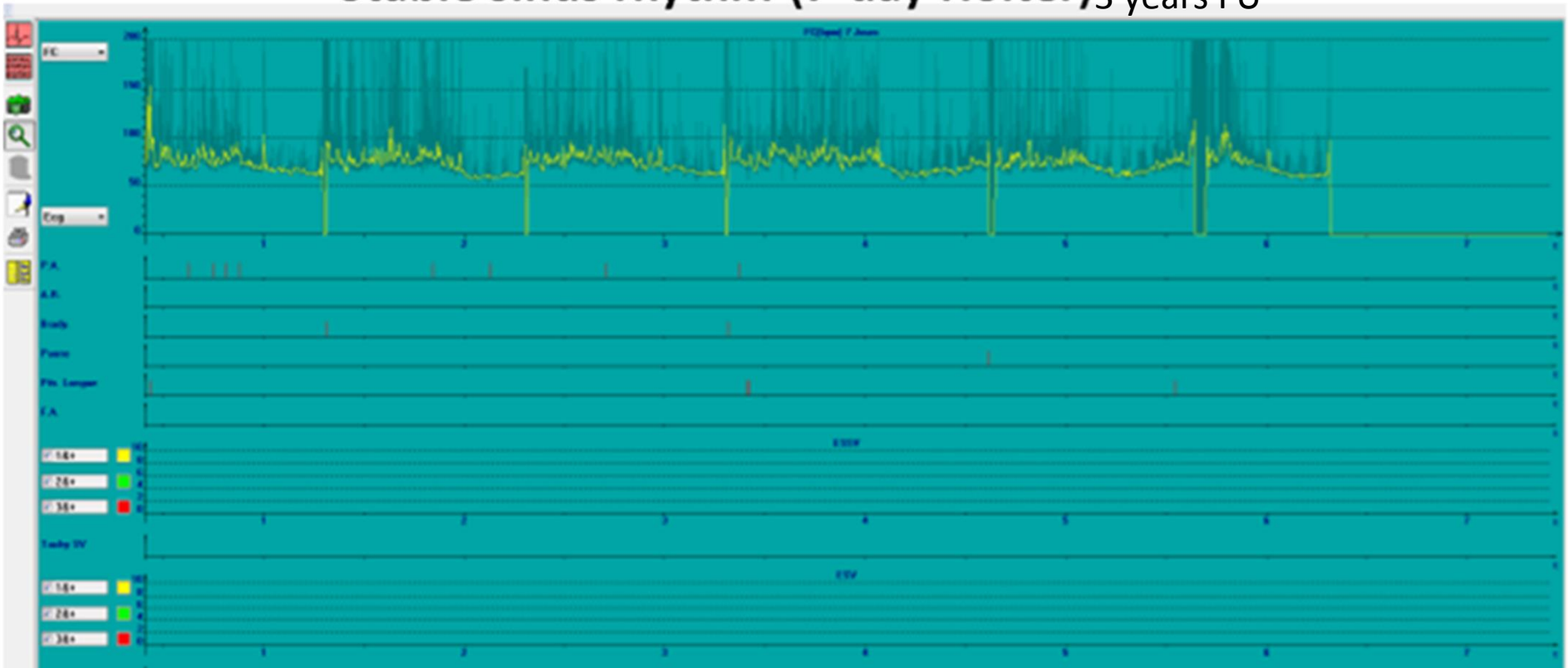
__class LS-persist Persistent


AF
AT
APB
Stable SR
AF and AT
AT

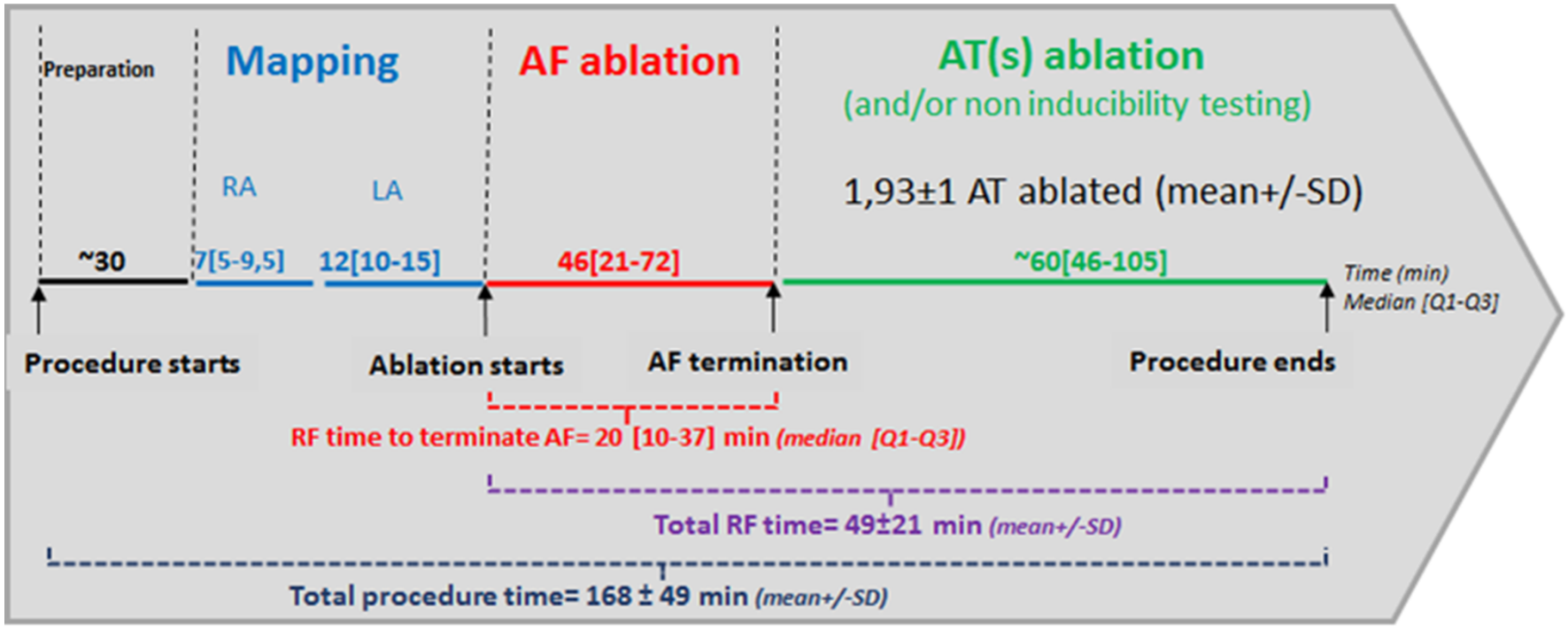


Longstanding Persistent
AF (2,5 years)

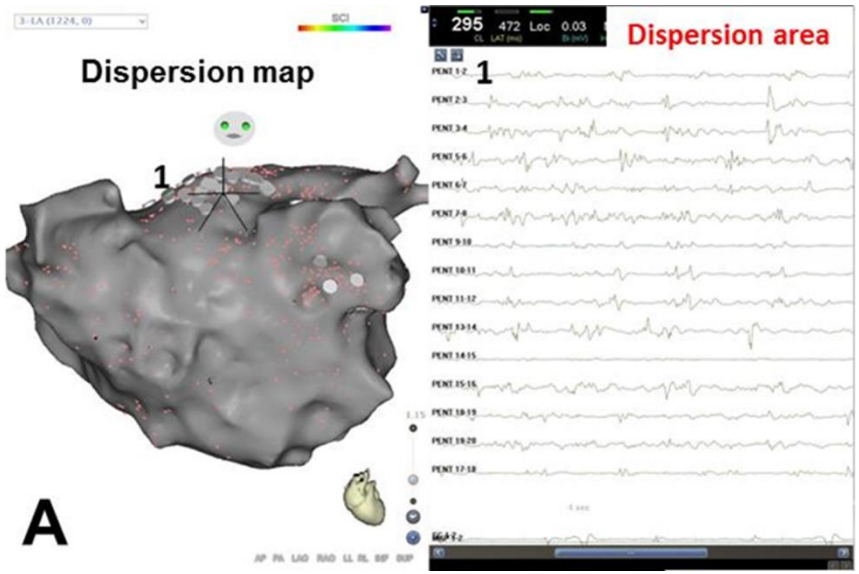
Stable sinus rhythm (7-day Holter) 3 years FU

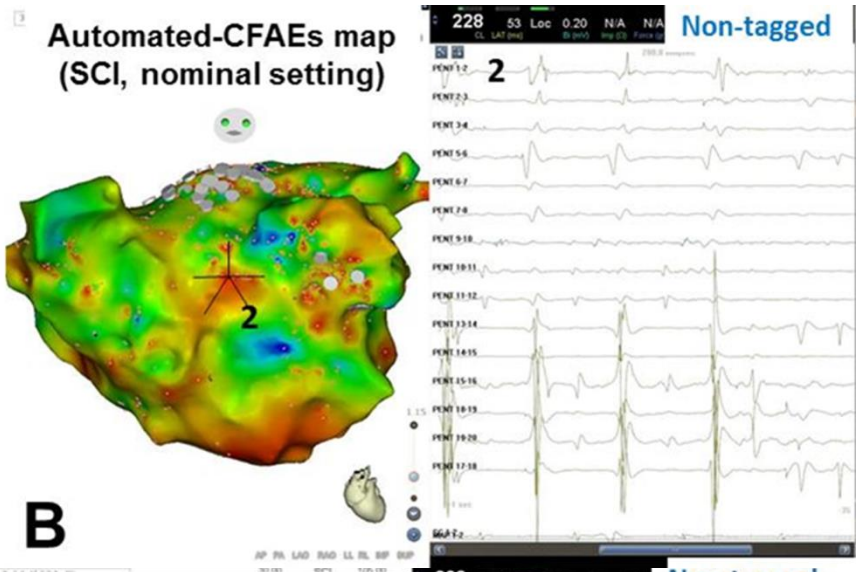


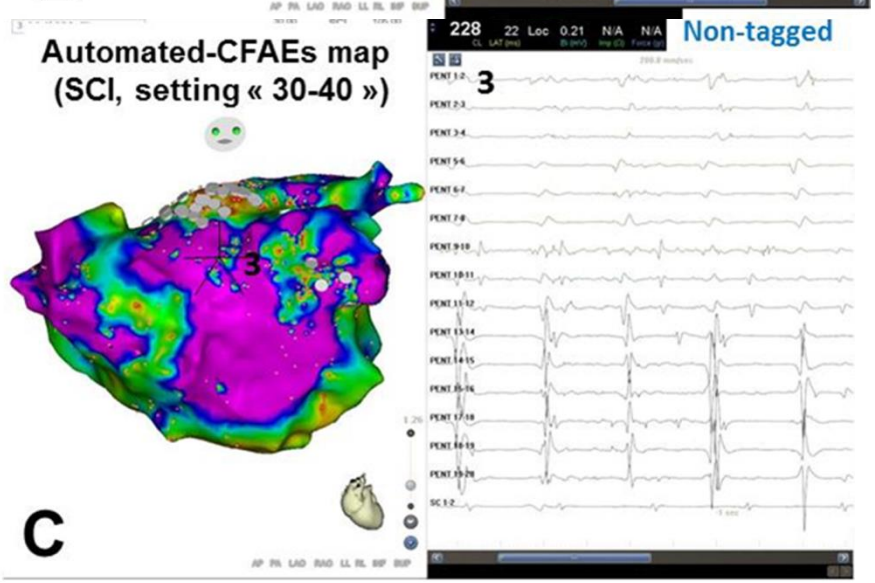
Procedure time line



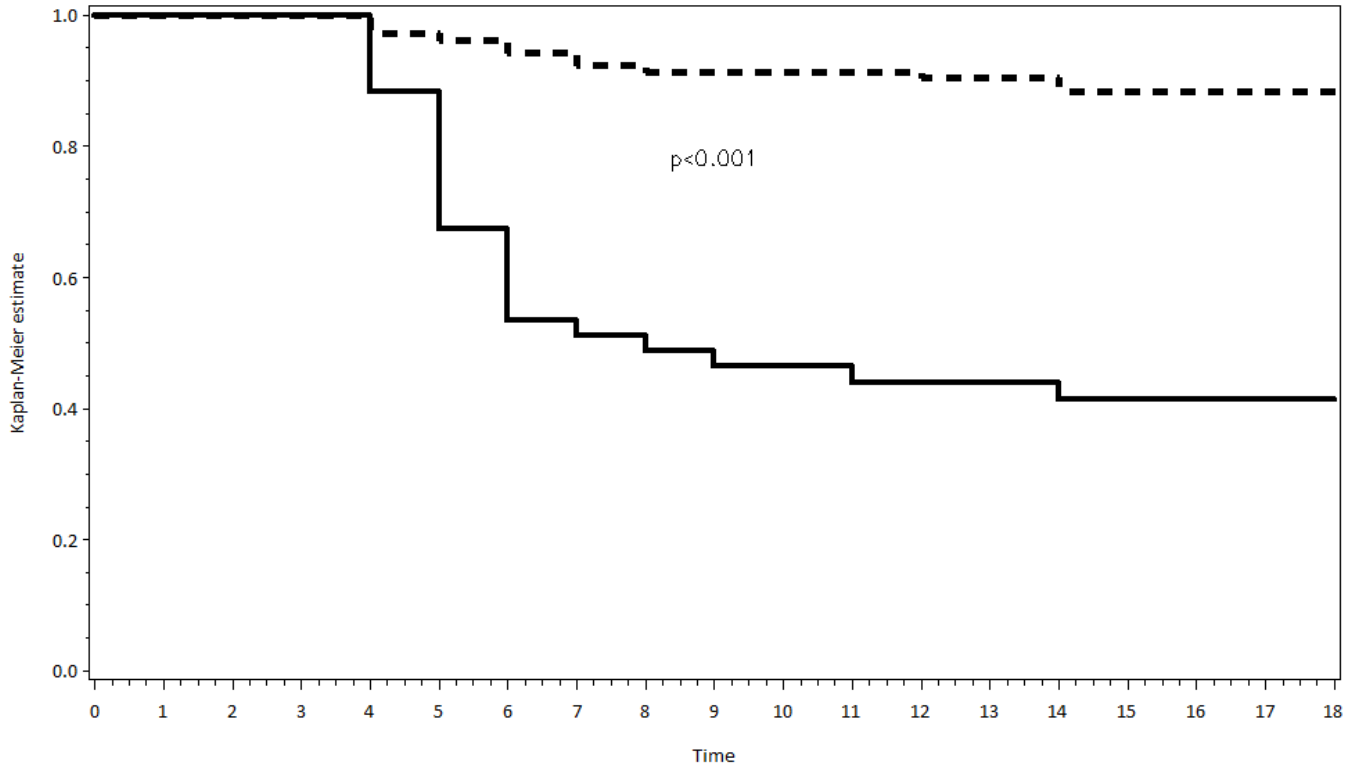
Dispersion maps & CFAE maps







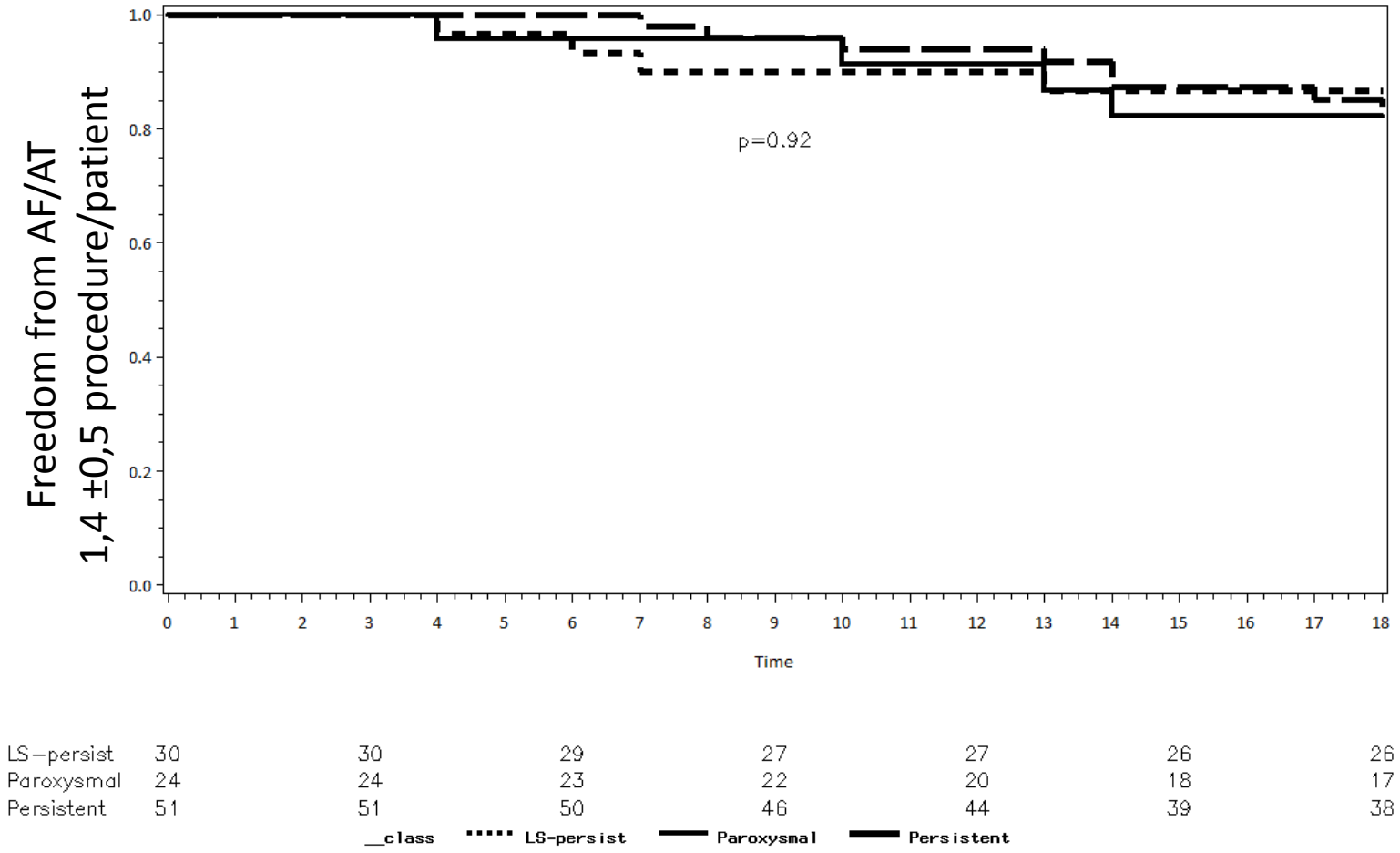
Freedom from AF 1 procedure



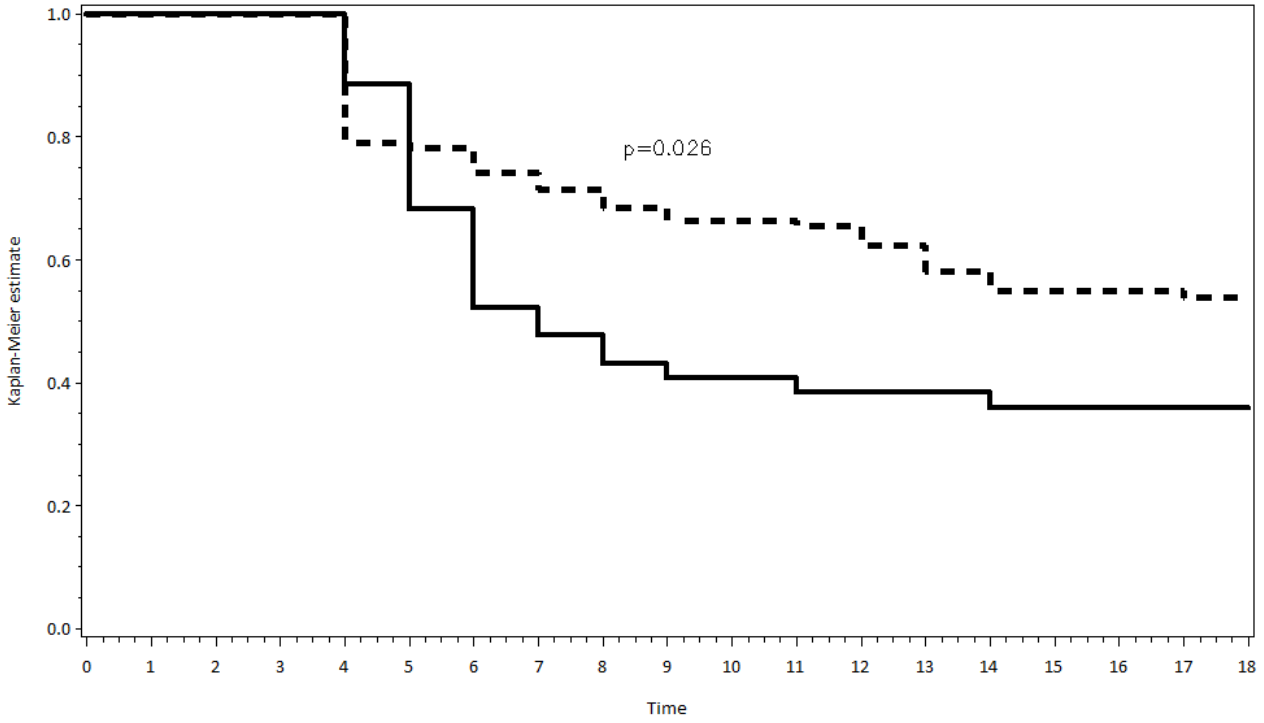
Study population	105	105	100	92	90	86	85
validation set	43	43	29	20	18	16	16

__class Study population validation set

18 month-FU: 85% of stable sinus Rhythm whatever the type of AF



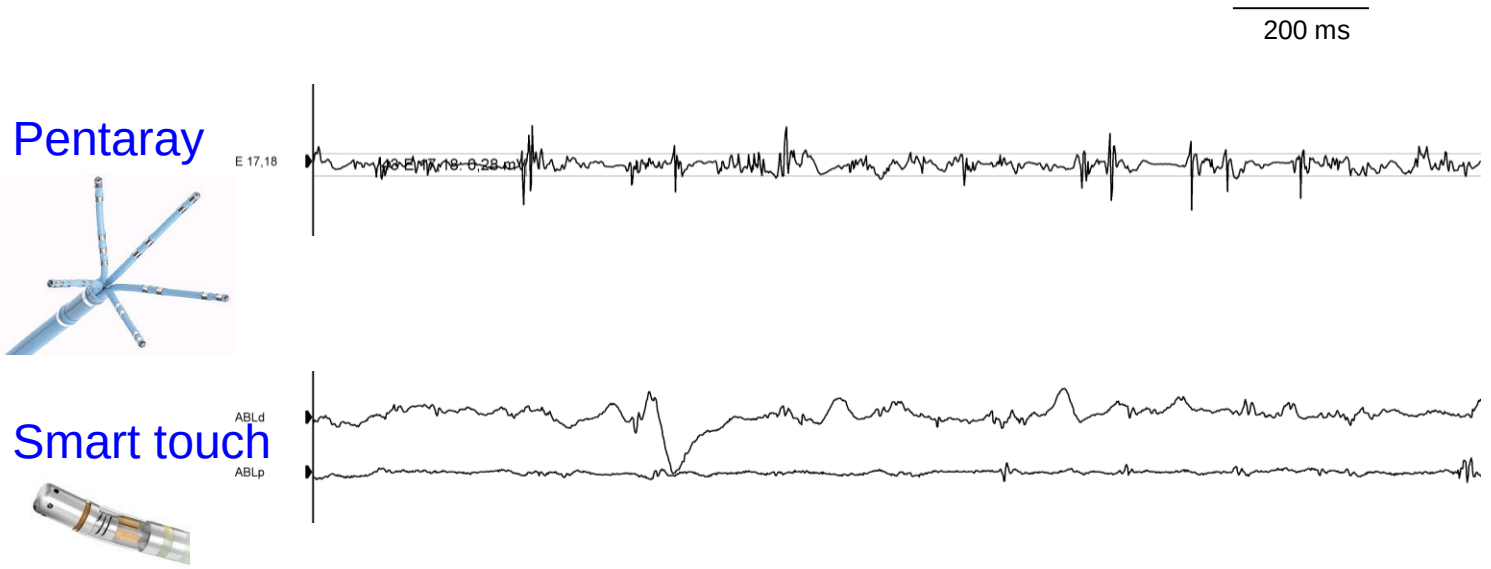
Freedom AF/AT 1 procedure



Study population	105	105	81	68	63	52	51
validation set	44	44	30	18	16	14	14

__class Study population validation set

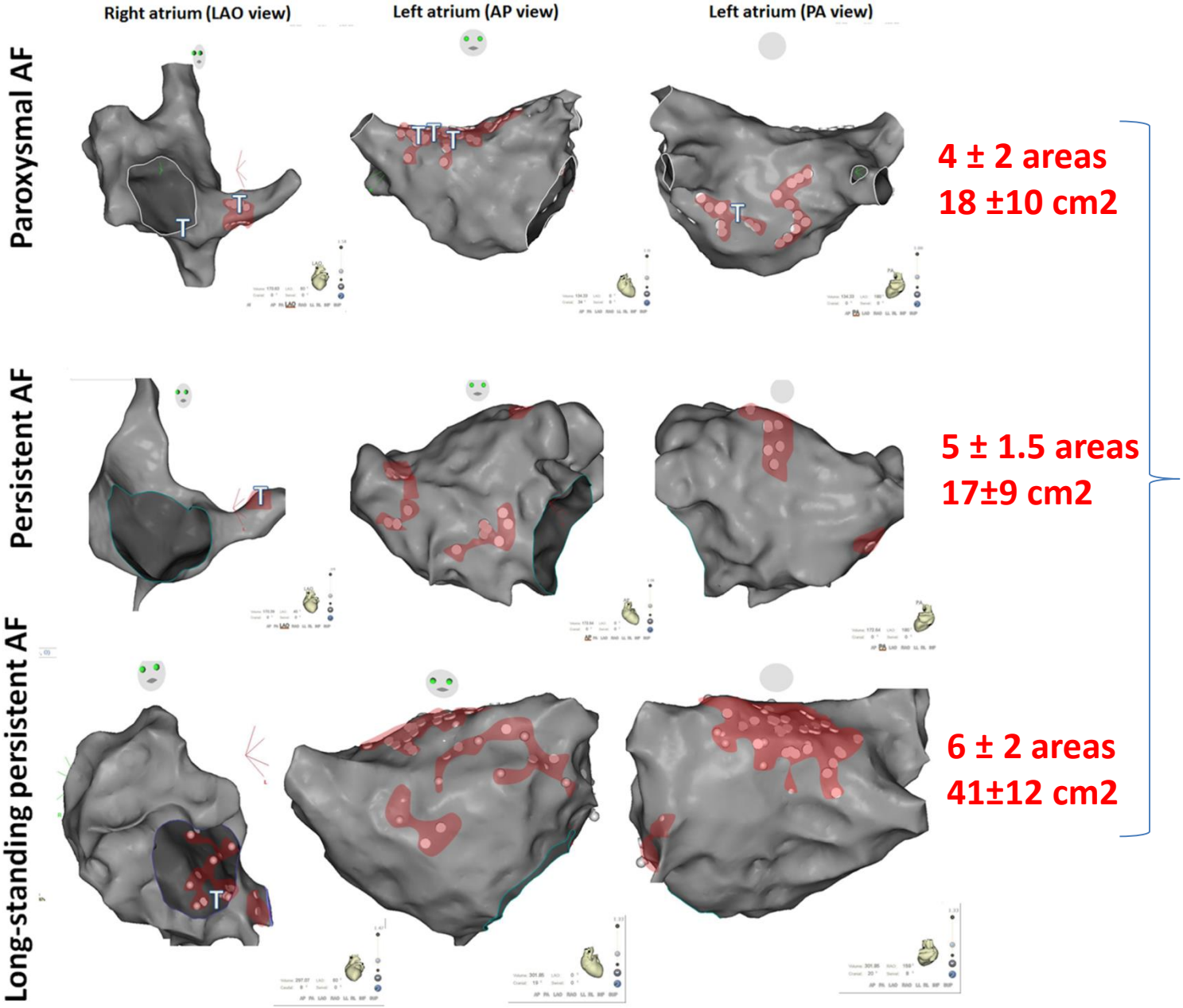
EGM recorded by Pentaray have a better quality signal than with 3.5mm ablation catheter



Primary target are often low voltage EGMs.
The size of electrodes and the space between electrodes provides a high quality recorded signal which is essential in detecting AF substrate.

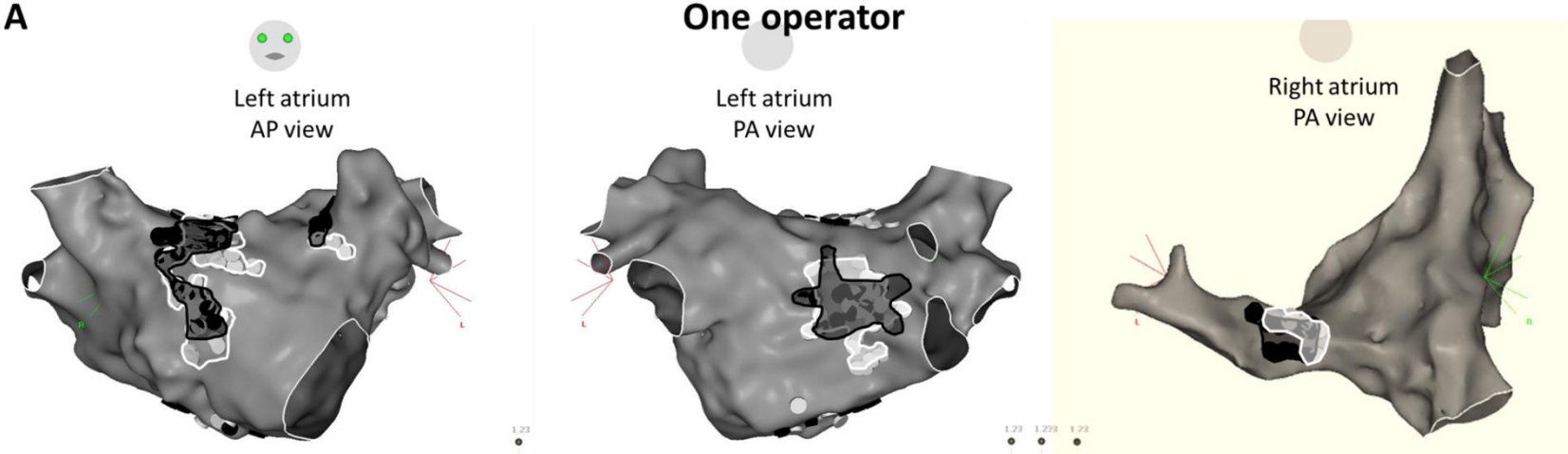
	AA drugs before ablation	Pts presenting in SR	Prior AF ablation	Sustained AF duration (months)	Long-standing persistent	Paroxysmal	LA diamet
ck et al. Circ ep 2008	41%	0%	0%	median: 12 (range:3-264)	NA	0%	50 ±7 m
leill et al, EHJ 2009	25%	0%	0%	21.8+33.2, median: 12 (range:1-240)	54%	0%	47 ± 9 m
yan et al. JACC 2012	0%	30%	42%	NA	NA	19%	43 ± 6 m
guerre et al. Circ 2014	43%	25%	20,3% (PVI)	NA	20%	0%	48 ± 7 m
Verma et al. R AF2, PVI grp) NEJM 2015	0%	NA	0%	NR (78% > 6 months)	NA	0%	44 ± 6 m
di et al. Circ ep 2016	NA	31%	22% (PVI)	NA	0%	0%	44 ± 5 m
et al. (present study)	32%	38% (non PAF=20%)	0%	12.2 ± 20	29%	22,80%	45,6 ± mm

Dispersion regions characteristics



A

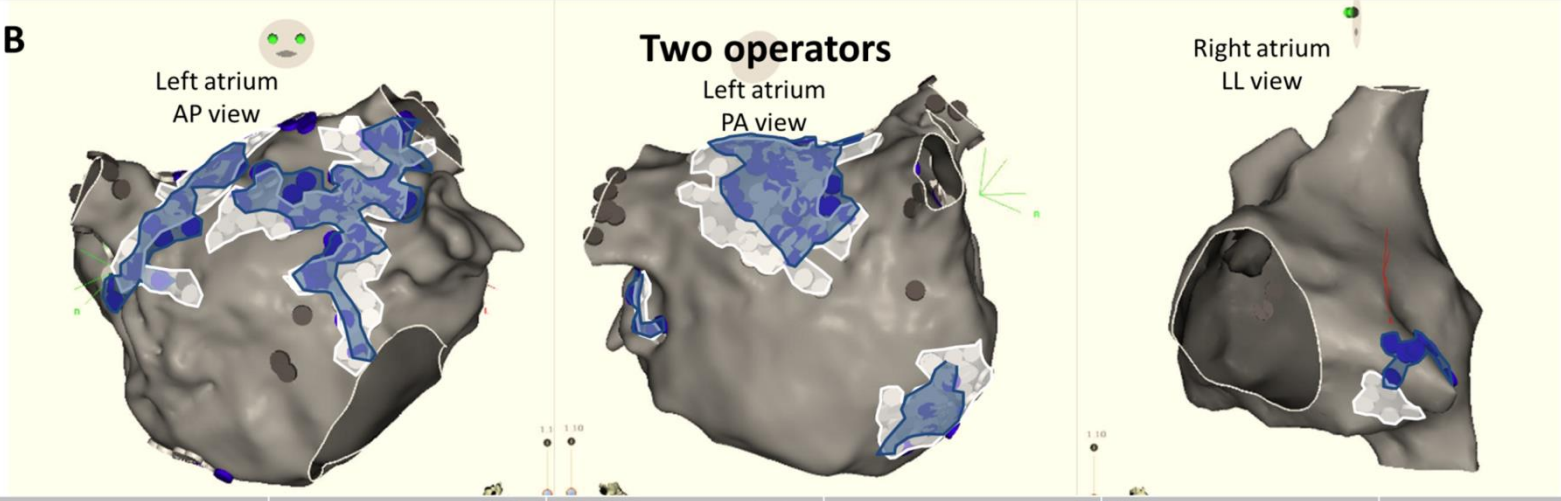
One operator



N=13 patients	Mapping 1	Mapping2	Match mapping 1 & 2	Mismatch mapping 1	Mismatch mapping 2
Involved areas	5,6±0,9	5,3±1	5,2±0,9	0,4±0,6	0,07±0,3
Mapping surface (cm2)	30±12	28±12	26±13	4±3	2±2
% biatrial surface	14±8	13±9	12±9	2±1	1±1

B

Two operators



N=7 patients	operator 1	operator 2	Match operator 1 & 2	Mismatch operator 1	Mismatch operator 2
Involved areas	6±0,8	6,3±0,7	6±0,8	0	0,3±0,5
Mapping surface (cm2)	32±11	29±8	23±7	12±3	7±4
% biatrial surface	11±4	10±3	8±2	4±1	2±1

HOPITAL SAINT JOSEPH MARSEILLE

University of Michigan Health System

Substrate HD

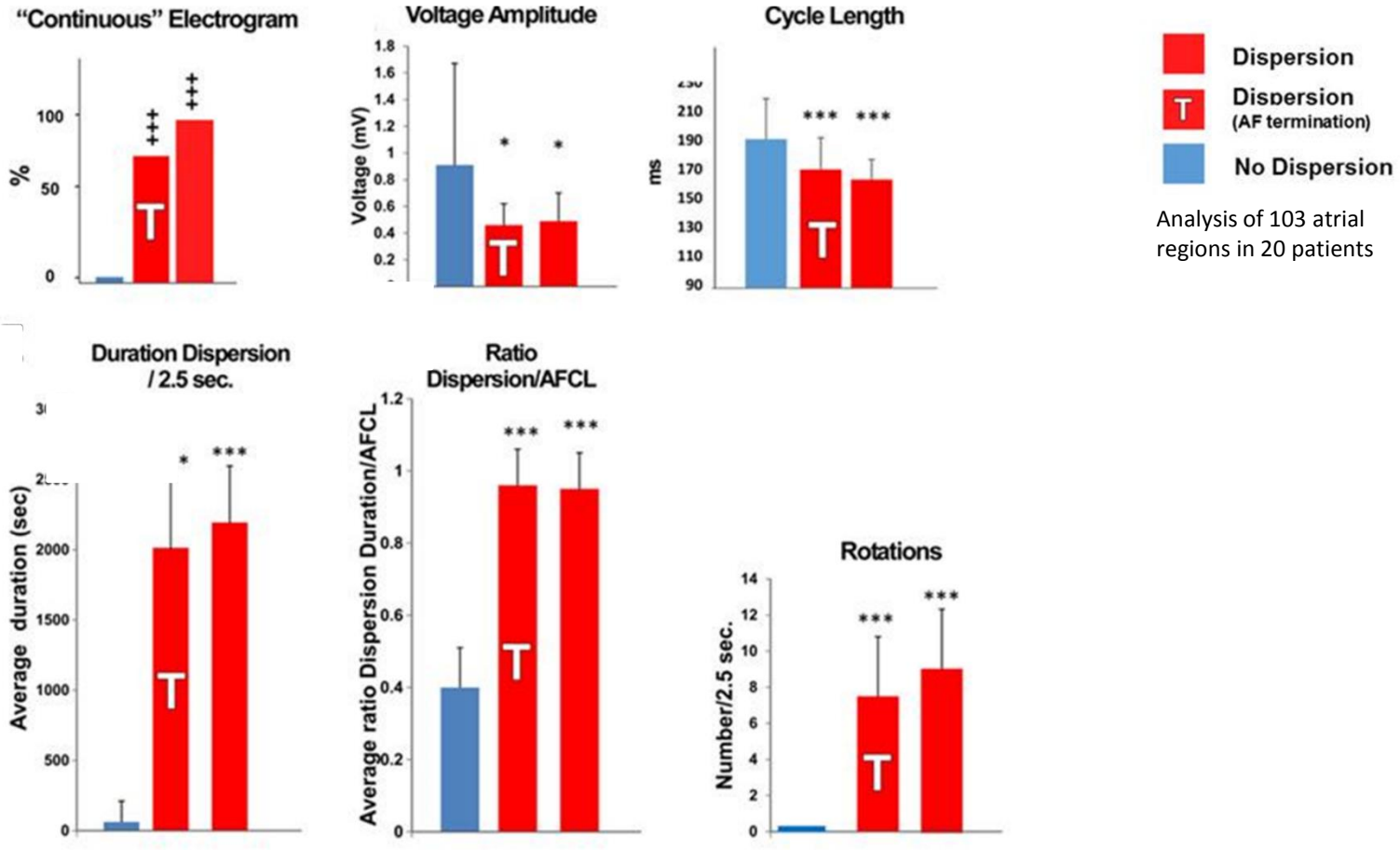
Mechanistic study

L'INSTITUT MUTUALISTE MONTSOURIS GHMF

GROUPE HOSPITALIER HENRI MONDOR

Centre Hospitalier Universitaire de Nice

Electrograms characteristics in dispersion regions



Dispersion area abnormal electrograms exhibited a higher occurrence of **single-bipole fractionated continuous signals**, a **reduced voltage** & a significantly **shorter cycle length**. **Dispersion was stable** (2,5 sec window) and spanned ~**100% AFCL**.

Seitz, Bars, Theodore, Pisapia, Kalifa et al. JACC (In press)