



Arrhythmias & Heart Failure
New Insights & Technological Advances

March 2-3

9th Congress Edition
Novotel PARIS Tour Eiffel

Paroxysmal AF ablation with cryo: index and redo procedures

Olivier THOMAS

CMC Ambroise Paré Neuilly sur Seine

France

Disclosure

.....

I have the following potential conflicts of interest to report:

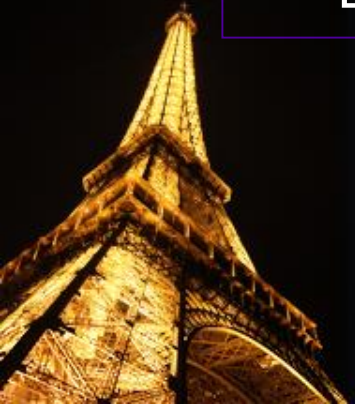
Consulting, lectures, teaching, travel grants:

Boston scientific

Medtronic

Biosense Webster

Livanova



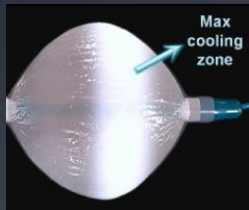
HRS/EHRA/ECAS Expert Consensus Statement

“Ablation strategies which target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures.”

“... point-by-point RF energy and Cryoballoon ablation are the two standard ablation systems used for catheter ablation of AF today . . .”

Cryoablation of AF: a 12 year evolution

Arctic Front™
Cryoballoon



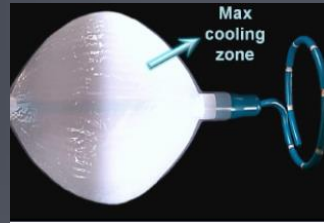
2005

Achieve™ Mapping
Catheter



2011

Arctic Front Advance™
Cryoballoon



2012

FlexCath Advance™
Sheath



2013

Next Generation
Cryoballoon
System



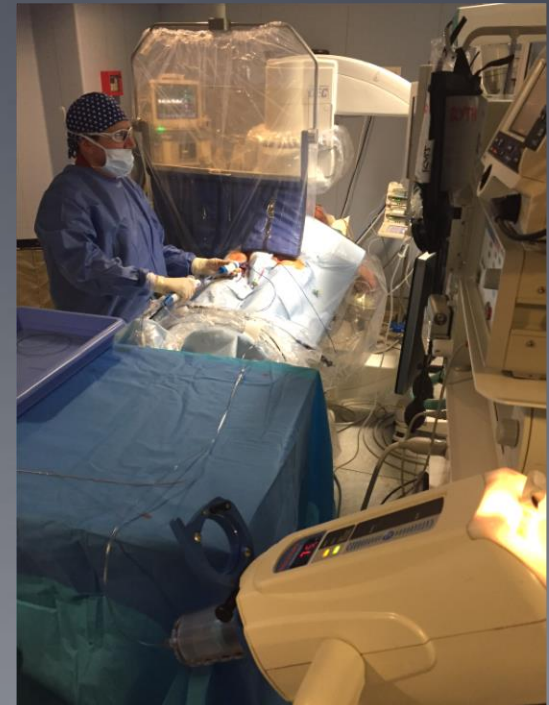
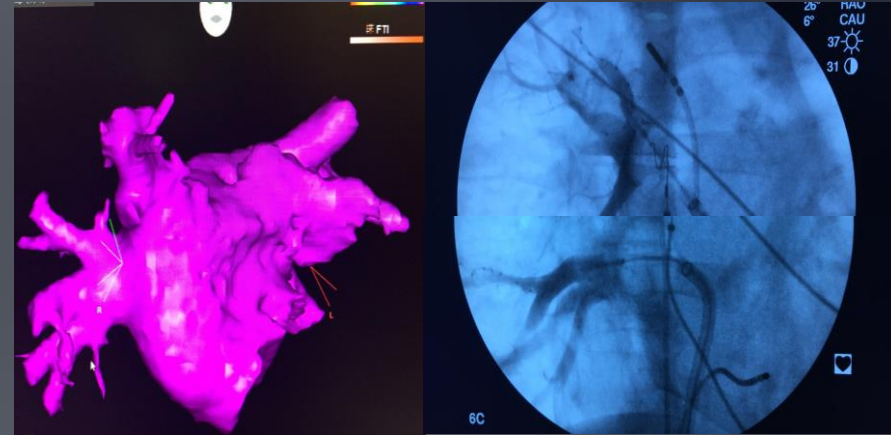
2016

Over 220,000 patients treated with the Arctic Front
Cryoballoon System¹

¹ Medtronic Data on file

AF ablation with cryoballoon: Course of the procedure

- Patients admission the day before.
 - No discontinuation of VKA (INR 2-3). NOAC discontinued
 - CT scan to eliminate thrombus.
- Procedure:
 - 3 D reconstruction of left atria:
Detailed LA anatomy to guide vein access
 - Deep sedation and local anesthesia
 - 2 quadripolar deflectable catheter (CS and His)
 - Heparin 70 to 150UI/kg before transeptal puncture. ACT 300-400 sec.
- One physician performing the ablation with a contrast injector.



AF ablation with cryoballoon: Course of the procedure

1. Access targeted vein



2. Inflate and position



3. Occlude and ablate



4. Assess PVI



The veins are targeted in the following order: LSPV, LIPV, RIPV, RSPV

PAF ablation with cryoballoon: freeze cycle

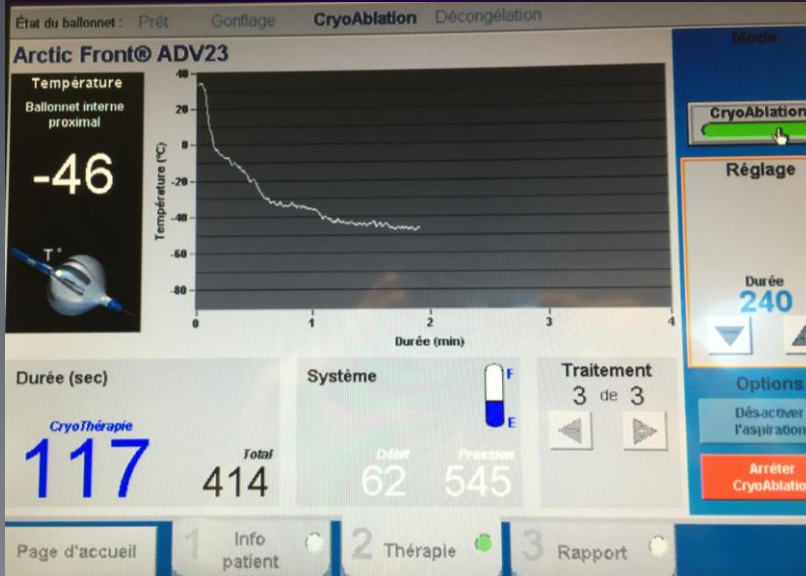
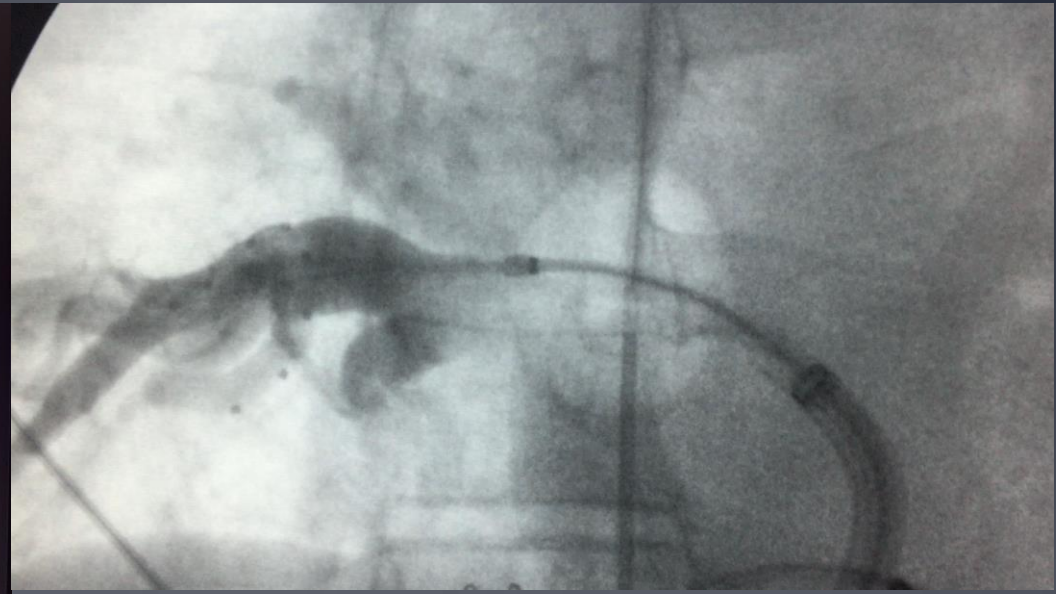
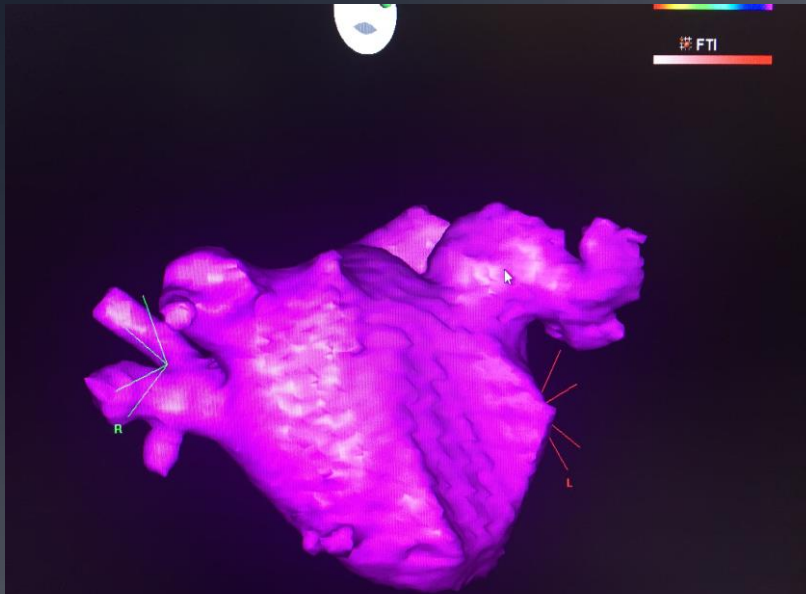
- Phrenic contraction monitoring during right veins isolation.
- A good occlusion of the vein is necessary to obtain a low balloon temperature (at least -40°) and a good efficacy.

- Time To Isolation is monitored



- freeze cycle: 4 min ; optional 3 min bonus freeze cycle according to the TTI and the lowest temperature
- The « pull down » manoeuvre can be useful to improve occlusion

« Pull down » manoeuvre



Post ablation management

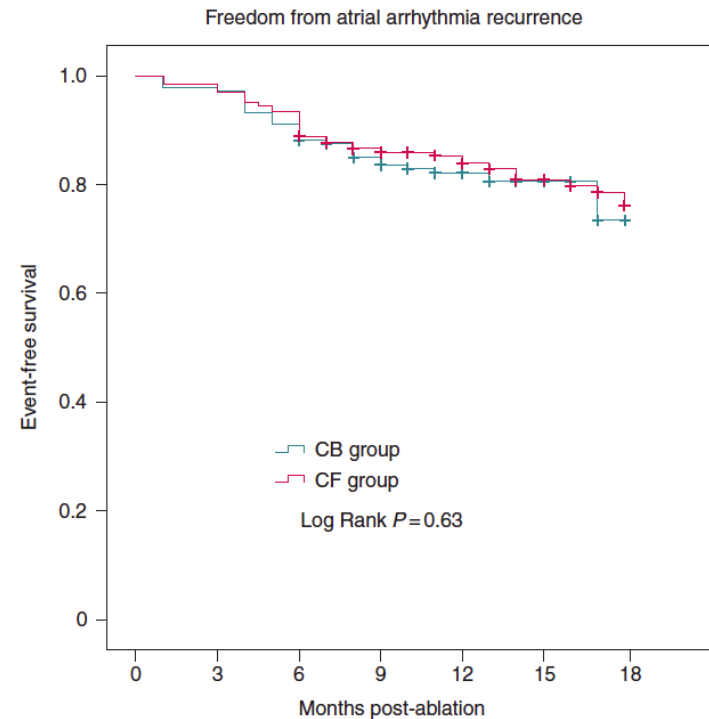
- VP isolation of all veins should be obtained
- Mean procedure time : 75 min \pm 15 min , very reproducible
- Mean fluroscopy time : 4 minutes (pulse mode +low dose)
- Skin closure of the 15 french sheath access
- Patient discharge the day after the ablation
- Anticoagulation for at least 2 months, according to the CHADS₂VASC score
- AAD for 1 month
- PPI for 6 weeks

Comparison between radiofrequency with contact force-sensing and second-generation cryoballoon for paroxysmal atrial fibrillation catheter ablation: a multicentre European evaluation

Fabien Squara^{1,2*}, Alexandre Zhao², Eloi Marijon^{3,4}, Decebal Gabriel Latcu⁵, Rui Providencia³, Giacomo Di Giovanni⁶, Gaël Jauvert², Francois Jourda³, Gian-Battista Chierchia⁶, Carlo De Asmundis⁶, Giuseppe Ciconte⁶, Christine Alonso², Caroline Grimard², Serge Boveda³, Bruno Cauchemez², Nadir Saoudi⁵, Pedro Brugada⁶, Jean-Paul Albenque³, and Olivier Thomas²

Table 1 Patient characteristics

	CF group (n = 198)	CB group (n = 178)	P-Value
Age	61 ± 9	58.4 ± 11.5	0.02
Female gender	45 (12%)	50 (13.3%)	0.24
AF duration, months	57.8 ± 57.9	46.9 ± 53.2	0.08
Hypertension	74 (19.7%)	55 (14.6%)	0.08
Diabetes mellitus	13 (3.5%)	14 (3.7%)	0.76
Cardiopathy (any)	29 (7.7%)	24 (6.4%)	0.60
LA area (cm ²)	21 ± 3.9	19.7 ± 3.2	0.10
LVEF (%)	55.8 ± 9.2	56.6 ± 7.7	0.44
CHADS2 score	0.49 ± 0.63	0.43 ± 0.68	0.42



	Proportion of patients free from arrhythmia recurrence					
	3 months	6 months	9 months	12 months	15 months	18 months
CF group	97%	88.9%	86%	83.9%	80.9%	76%
CB group	97.2%	88.2%	83.6%	82.2%	80.6%	73.3%
	Number of patients at risk					
CF group	192	176	141	117	73	58
CB group	173	157	126	111	42	27

Table 2 Procedural data and complications

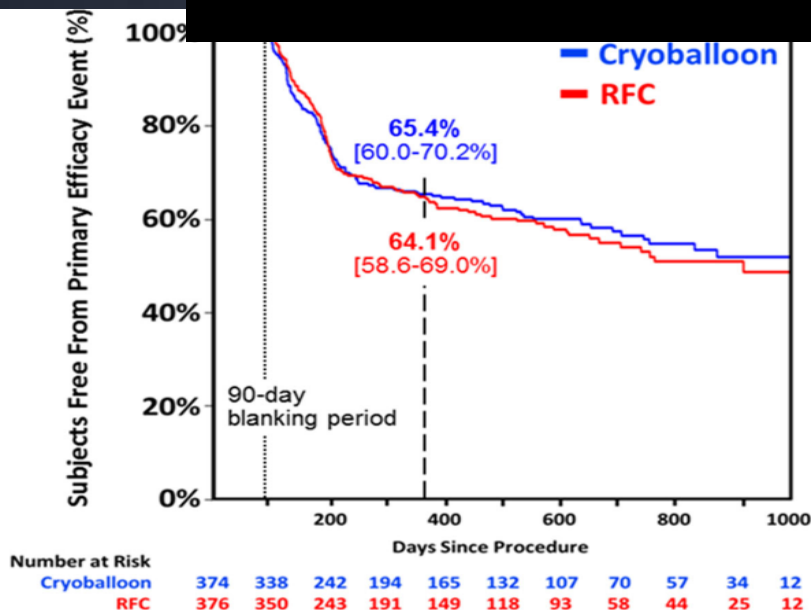
	CF group (n = 198)	CB group (n = 178)	P-Value
Procedural data			
Procedure duration (min)	122.5 ± 40.7	109.6 ± 40	0.003
Fluoroscopy duration (min)	19.3 ± 8.2	17.6 ± 11	0.10
X-ray exposure (cGy cm ²)	4273 ± 2934	4853 ± 5069	0.22
Procedural complications			
Groin haematoma	8 (4%)	3 (1.7%)	0.17
Transient phrenic nerve palsy	0 (0%)	10 (5.6%)	0.001
Severe complications			0.03
Embolic events	2 (1%)	0 (0%)	0.18
Tamponade	2 (1%)	0 (0%)	0.18
Oesophageal complication	1 (0.5%)	0 (0%)	0.34
Periprocedural death	0 (0%)	0 (0%)	NA
Total complications	14 (7.1%)	13 (7.3%)	0.93

Fire and ICE

- Compare the safety and efficacy of PVI by either:
 - **Cryoablation**, n=374 (Arctic Front™ catheters) guided by fluoroscopy OR
 - **RFC ablation**, n=376 (THERMOCOOL® catheters) guided by CARTO® 3D mapping system
- Non inferiority study
- Primary Efficacy Endpoint*: Time to first documented recurrence of AF>30s/AT/AFL, prescription of AAD, or re-ablation
- Primary Safety Endpoint*: Time to first all-cause death, all-cause stroke/TIA or treatment-related serious AEs (e.g. phrenic nerve injury, atrioesophageal fistula, etc.)

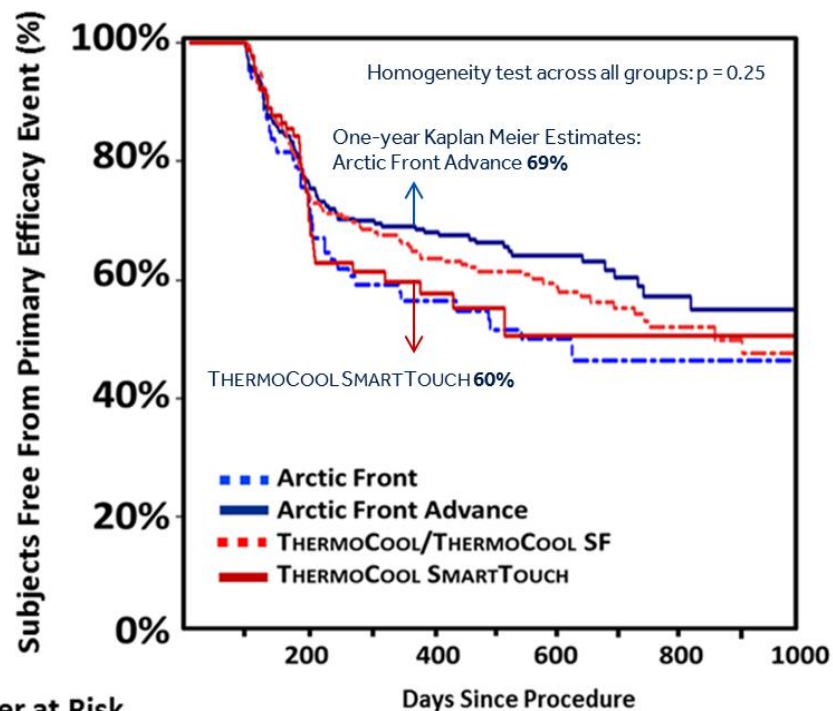
Primary Efficacy Endpoint Met

Primary Efficacy Endpoint



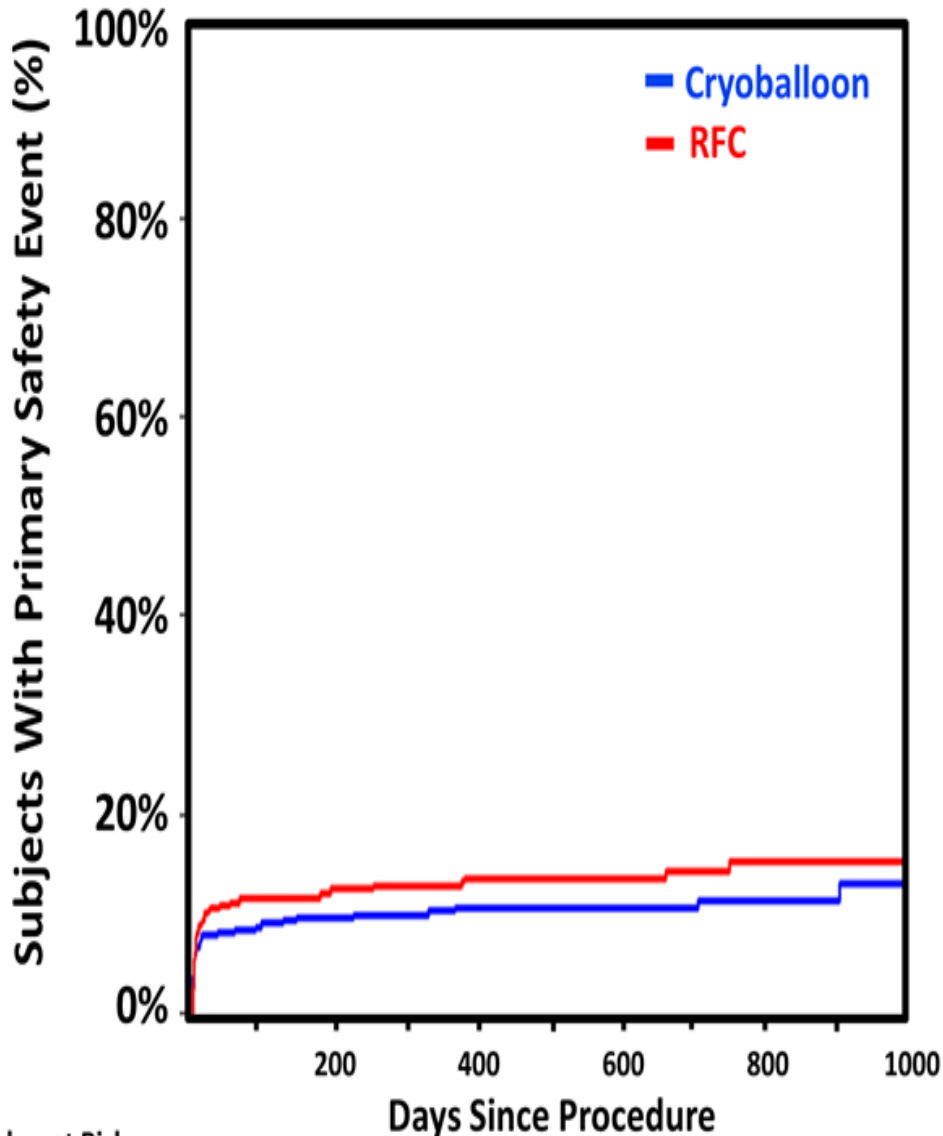
Efficacy End Point Type	Cryo (N=374)	RFC (N=376)
Recurrent atrial arrhythmia	80	87
Antiarrhythmic drug prescription	51	49
Re-ablation	7	7

Primary Efficacy Endpoint By



Days Since Procedure	Arctic Front	Arctic Front Advance	THERMOCOOL/THERMOCOOL SF	THERMOCOOL SMARTTOUCH
0	90	279	284	93
100	83	251	260	90
200	58	183	187	55
300	42	151	151	40
365	36	128	121	28
400	32	99	104	15
500	30	76	84	9
600	24	45	54	4
700	21	35	42	2
800	15	19	23	1
900	8	4	10	1
1000	8	4	10	1

Primary Safety End Point



Number at Risk

	0	100	200	300	400	500	600	700	800	900	1000
Cryoballoon	374	323	298	261	229	189	159	117	94	55	21
RFC	376	315	292	247	215	176	146	110	87	52	27

Modified ITT analysis

▪ HR [95% CI] = 0.78 [0.52-1.18]; p = 0.24

Safety Event Type	RFC (n=376)	Cryoballoon (n=374)
All-cause death*	0	2
All-cause stroke/TIA	2	2
Arrhythmia-related SAE	13	8
Non-arrhythmia-related SAE	36	28
Total	51	40

* Unrelated to treatment/device

Key Treatment-Related Serious Adverse Events

Event (N, %)	RFC (n=376)	Cryoballoon (n=374)
Groin Site Complication*	16 (4.3%)	7 (1.9%)
Atrial Flutter/Atrial Tachycardia**	10 (2.7%)	3 (0.8%)
Phrenic Nerve Injury unresolved at discharge	0	10 (2.7%)***
Unresolved at 3 months	0	2 (0.5%)
Unresolved at > 12 months	0	1 (0.3%)
Cardiac Tamponade/Pericardial Effusion	5 (1.3%)	1 (0.3%)
Stroke/TIA	2 (0.5%)	2 (0.5%)
Atrial Septal Defect	1 (0.3%)	0
Esophageal Ulcer	0	1 (0.3%)
Pericarditis	0	1 (0.3%)
Atrioesophageal Fistula	0	0
Pulmonary Vein Stenosis	0	0

* Includes vascular pseudoaneurysm, AV fistula, device-related infection, hematoma, puncture site hemorrhage, groin pain

** Serious (e.g. hospitalization) and causally related to the therapeutic intervention (e.g. ablation-induced or drug-induced)

*** 8 resolved by 3 month visit, 1 resolved by 6 months visit, 1 unresolved after 12 month visit

Procedural Characteristics

Time Measurement (minutes)	RFC (n=376)*	Cryoballoon (n=374)*	P-value**
Procedure Time***	140.9 ± 54.9	124.4 ± 39.0	<0.0001
LA Dwell Time***	108.6 ± 44.9	92.3 ± 31.4	<0.0001
Fluoroscopy Time	16.6 ± 17.8	21.7 ± 13.9	<0.0001

* Calculations based on mITT

** t-test

*** Protocol required 30-min waiting period after last application to assess PVI

What is the optimal freeze cycle duration?



- Initially: 4 min freeze cycle + 4 min bonus freeze cycle after isolation
- Wissner, Kuck, Europace 2015: A « no bonus » freeze protocol (4 min) resulted in a 82% 1 year clinical success.
- Chierchia, Brugada. JCE 2014: CB ablation is effective in producing PV isolation by using 3 min duration freeze cycle. Freedom from AF in 82% of patients at 6 month follow up.

What is the optimal freeze cycle duration?

- in the majority of targeted PVs, isolation is achieved within the first 60 s of the freeze-cycle and thus a total application time of 4 min might be redundant.
- $TTI > 60$ s independently predicted late PV reconnections and thus, fixed freeze-cycles of r 4 min might be too short for durable PVI in PVs with late isolation

Time To Isolation (TTI): a tool to reduce freeze cycle duration ?

Real-time assessment of pulmonary vein disconnection during cryoablation of atrial fibrillation: can it be 'achieved' in almost all cases?

Serge Boveda^{1*}, Rui Providência¹, Jean-Paul Albenque¹, Nicolas Combes¹, Stéphane Combes¹, Hassiba Hireche¹, Benjamin Casteigt¹, Abdeslam Bouzeman¹, François Jourda¹, Kumar Narayanan², and Eloi Marijon²

- 34 patients, 128 VPs, 28 mm CBA ablation
- Real time assessment of PV disconnection was possible in **97.7%**
 - 36,7% in the standard position (type 1)
 - 49,2 % at a more proximal position (type 2)
 - 11,7% by pacing from the vein (exit block)(type 3)
- Mean TTI : **48,6 ± 33 sec**

- Type 2 : Achiev retracted

Type 3: exit block

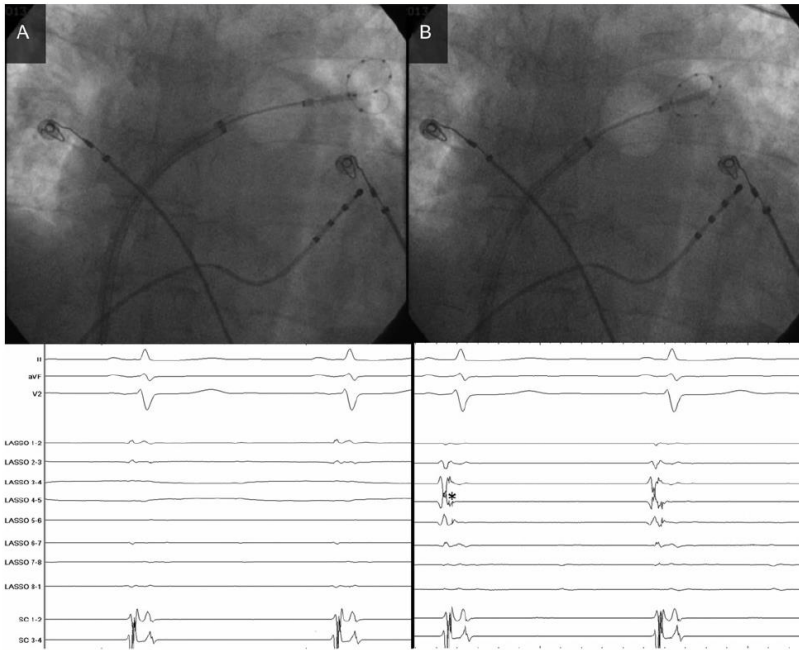
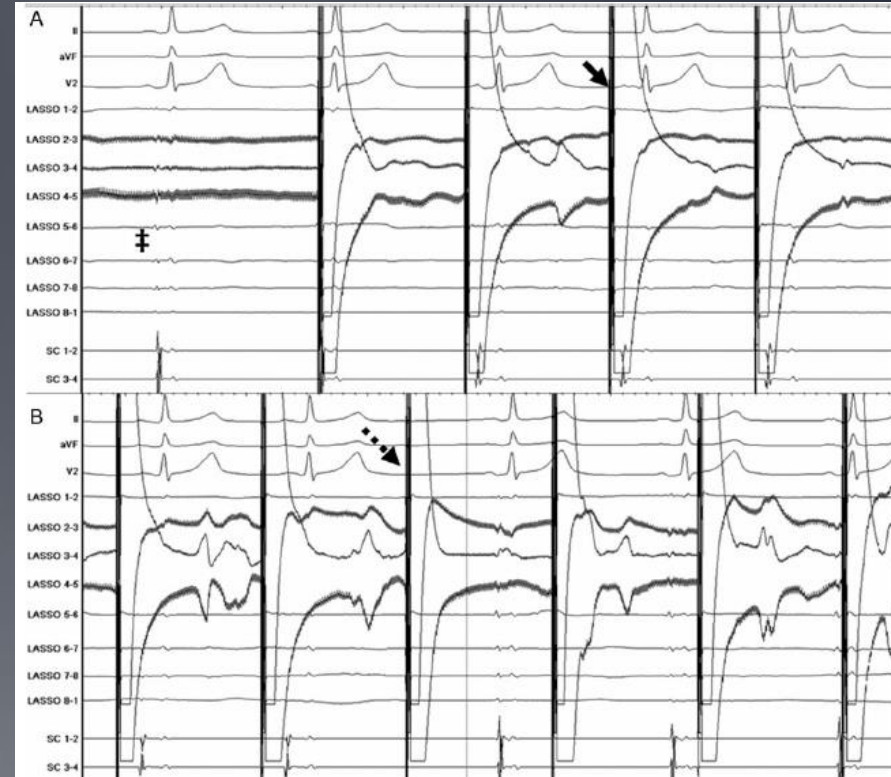


Figure 2 Example of a LSPV where no potentials were found in the conventional AC catheter position (A) and could only be retrieved after a withdrawal and backward displacement manoeuvre (B) (Type 2 PV). Notice that the poles of the AC that are now in close proximity to the balloon and PV antrum, behind the tip of the Artic Front Advance[®] catheter, now display the PV potentials, marked with the *.



TTI to reduce freeze cycle duration

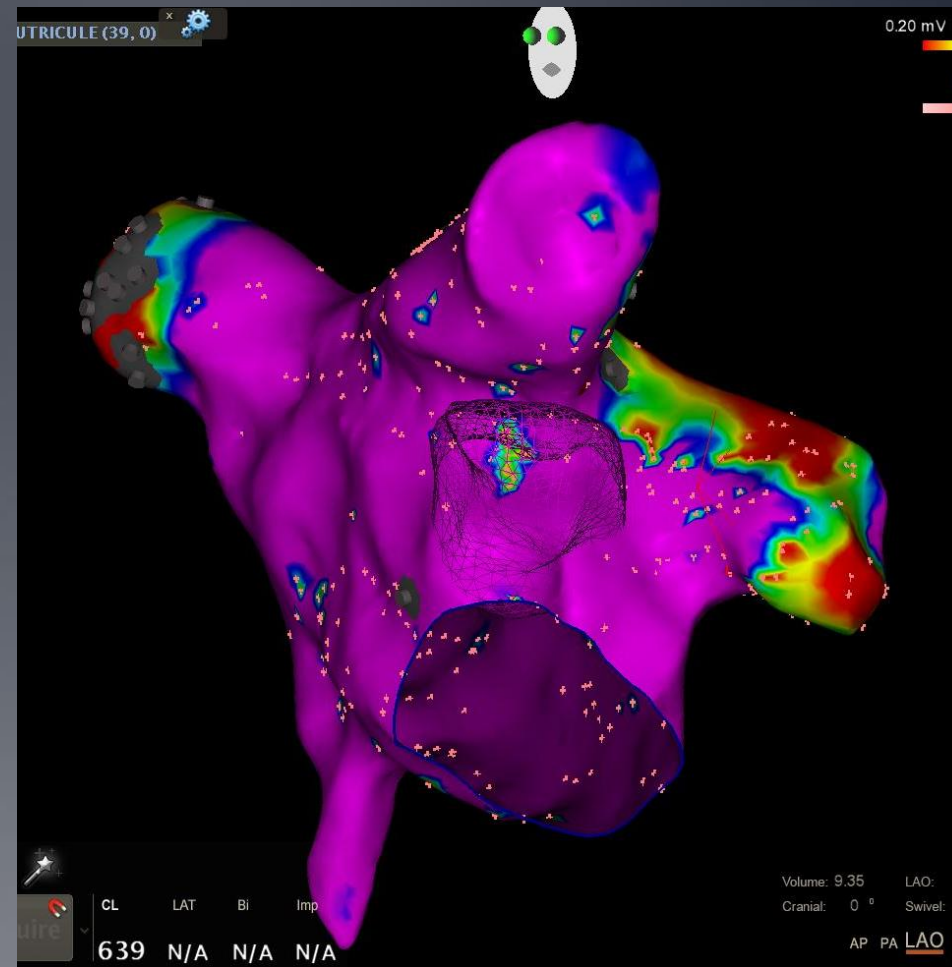
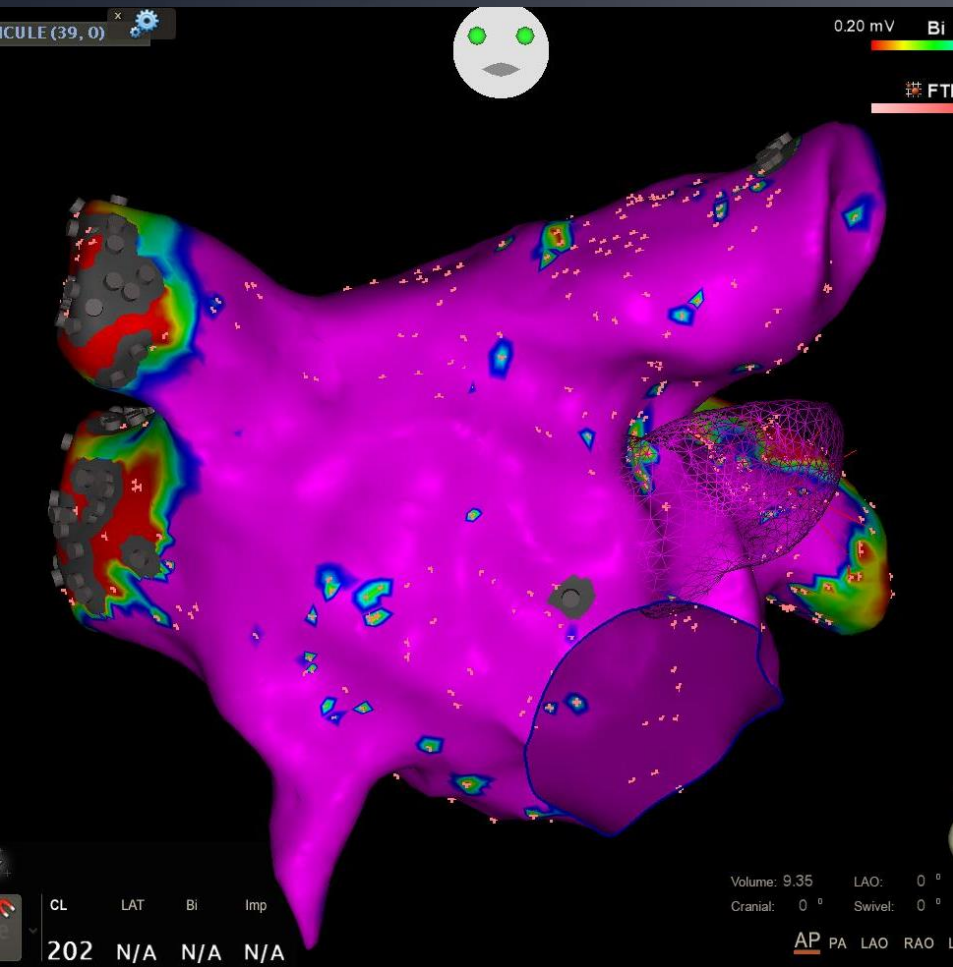


- Reissman, Wissner, Kuck, messner, europace 2016:
 - 60 patients with AF Ablated with CB
 - TTI monitoring
 - If TTI was assessed : **2 min** additional freeze-time after isolation
 - If TTI was not assessed: **fixed 4 min** freeze-time
 - TTI was assessed in **71%** of PVs
 - Mean TTI: **42 ± 32 s**
 - Mean freeze-time duration: **192 ± 41 s**
 - Mean procedure time: **80 ± 24 min**
 - 72 % of patients in sinus rhythm, mean FU > 1 year
 - Advantages of freezing time reduction: decrease the risk of phrenic and oesophageal lesion

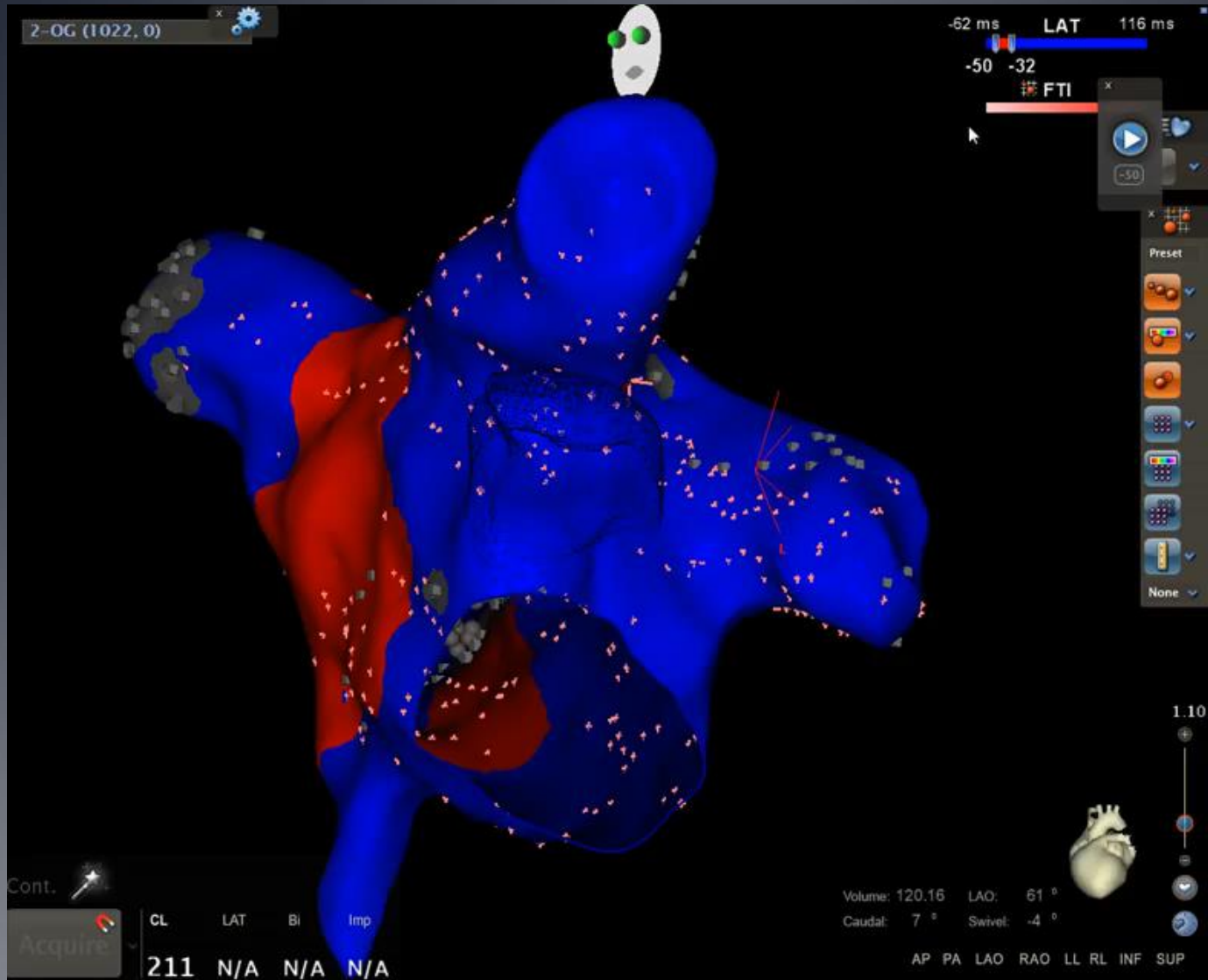
Redo procedure after cryo

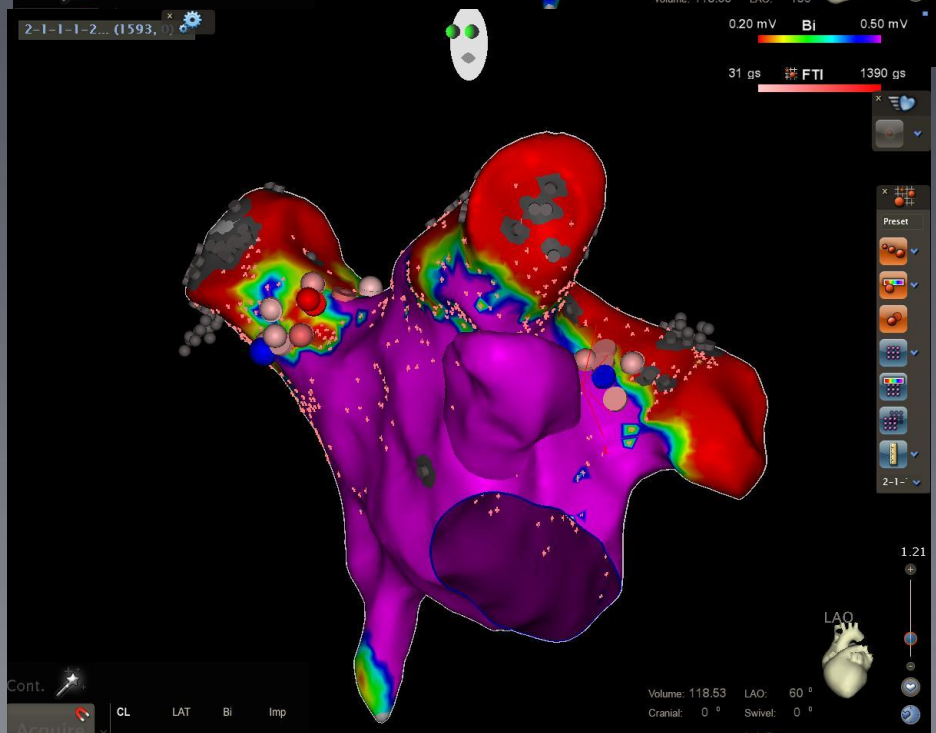
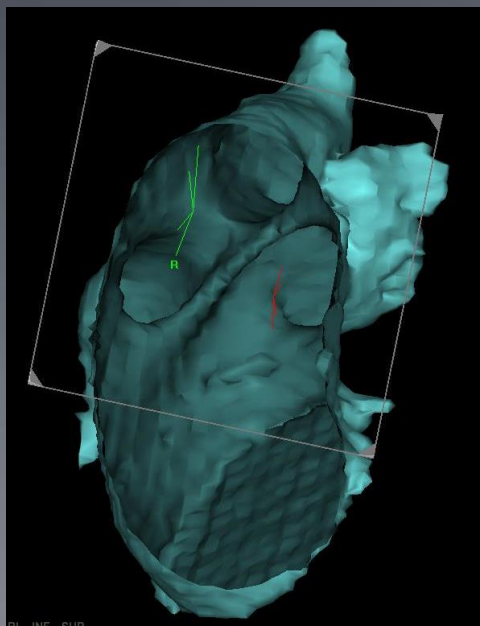
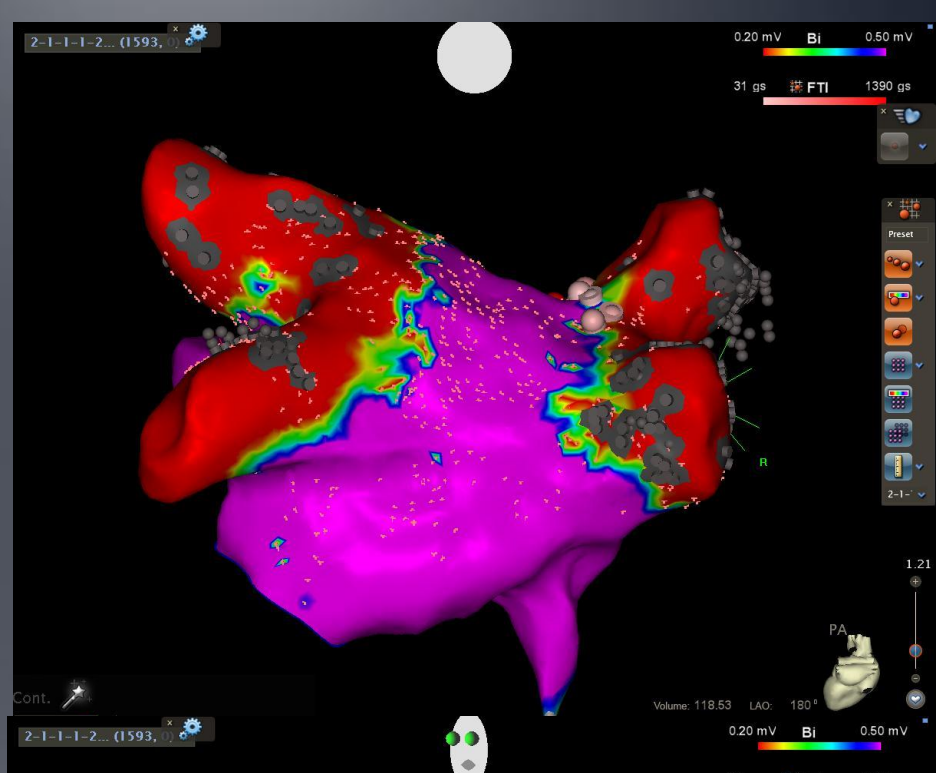
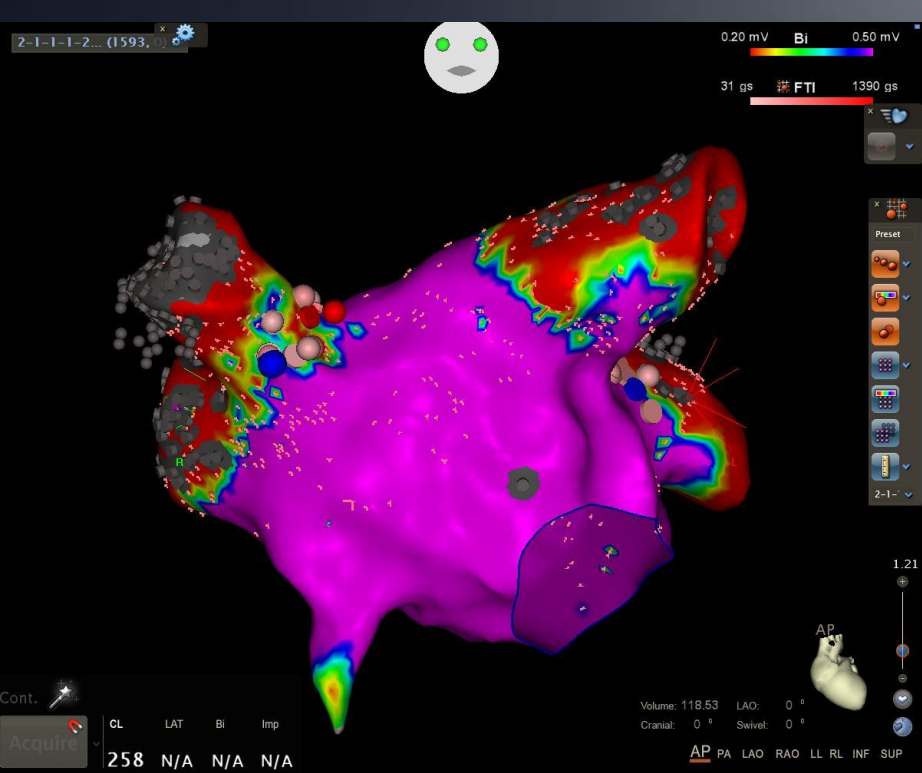
- Contact force RF and 3D mapping system (Carto 3 Biosense)
- Lasso or pentarray catheter
- Voltage map and activation maps of the veins
- Identification of gaps and isolation of reconnected veins
- ATP and isoproterenol to identify dormant reconnection and extra venous foci.

Redo procedure 1 year after cryoablation



Activation mapping of the veins





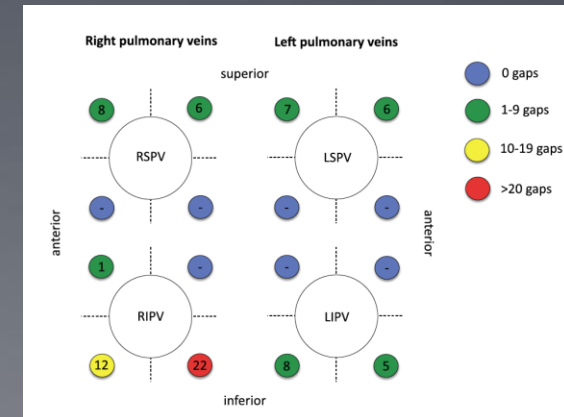
Once Isolated, Always Isolated?

Incidence and Characteristics of Pulmonary Vein Reconnection After Second-Generation Cryoballoon-Based Pulmonary Vein Isolation

Christian-Hendrik Heeger, MD*; Erik Wissner, MD*; Shibu Mathew, MD;
Sebastian Deiss, MD; Christine Lemes, MD; Andreas Rillig, MD; Peter Wohlmuth, PhD;
Bruno Reissmann, MD; Roland Richard Tilz, MD; Feifan Ouyang, MD;
Karl-Heinz Kuck, MD; Andreas Metzner, MD

***Circ Arrhythm Electrophysiol.* 2015;8:1088-1094.**

- 66 patients (16%) with repeat procedure after CBA ablation
- 74% of patients had PV reconnection but 69% of all veins were still disconnected
- Half of PVs demonstrating reconnection had only a single gap
- Most of the gaps are located at the infero posterior segment of RIPV
- No procedural parameters difference between isolated and reconnected veins



2016 personal data

- 23 redo with RF after cryo (14% of the PAF ablation)
- Mean time since first procedure: 450 ± 308 days.

83 % patients with
reconnected VPs

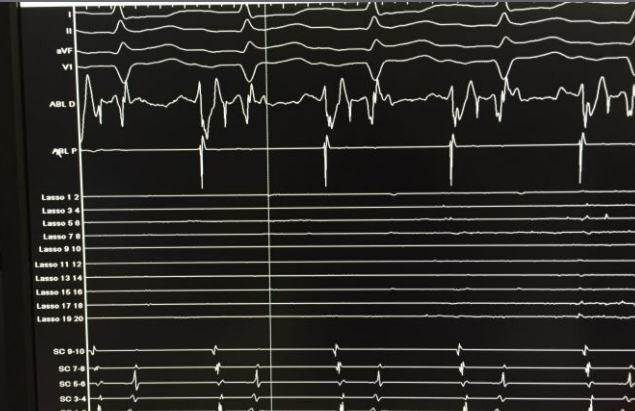
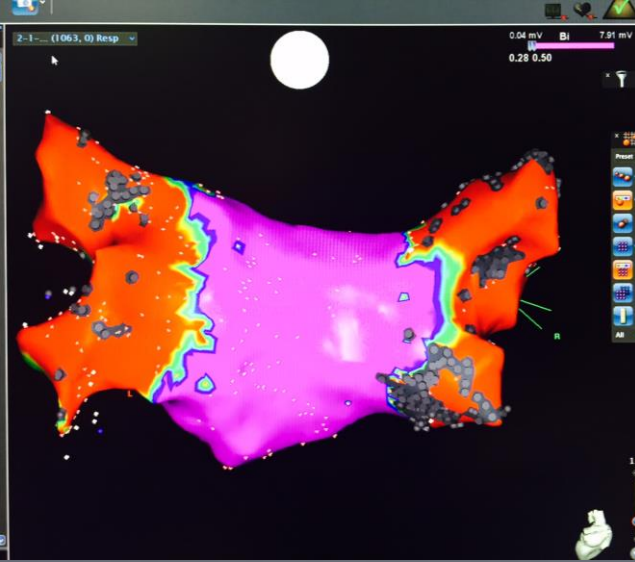
1 PV: 39%
2 PVs: 17%
3 PVs: 22%
4 PVs: 1%

Reconnected veins (43%):

LSPV: 23%
LIPV: 21%
RSPV: 28%
RIPVP: 28%

Redo procedures: what to do when veins are disconnected.

- ATP to search for concealed reconnection.
- Isoproterenol for extra pulmonary foci (LA, RA, superior vena cava).
- Try to induce:
 - Common flutter
 - Left atrial flutter
 - Other tachycardia

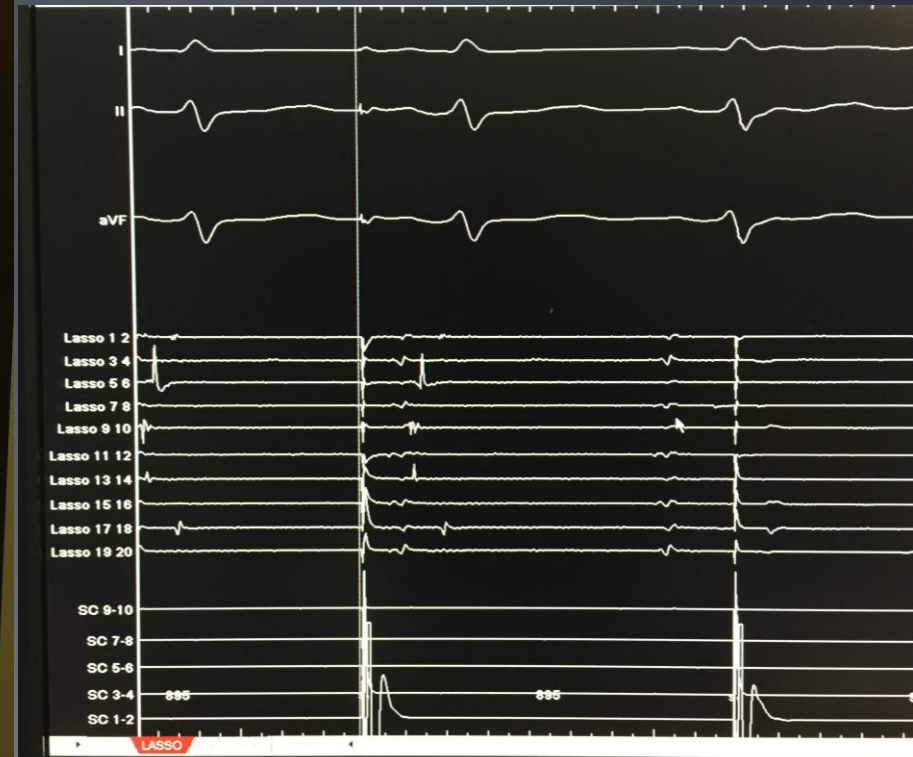
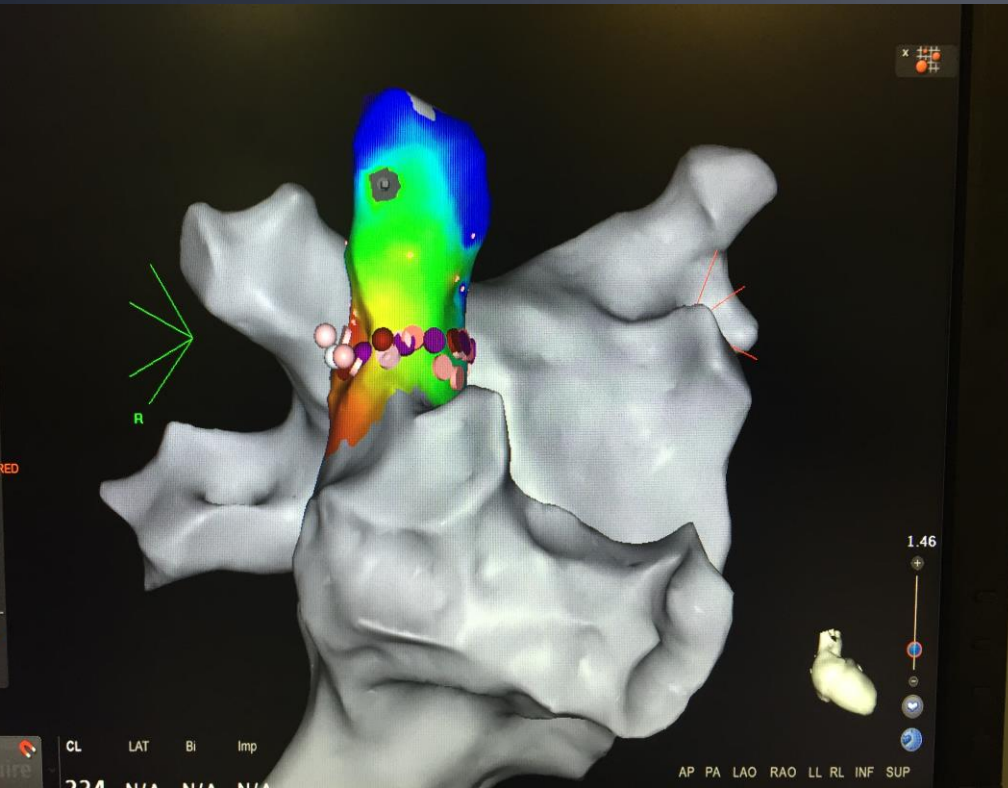


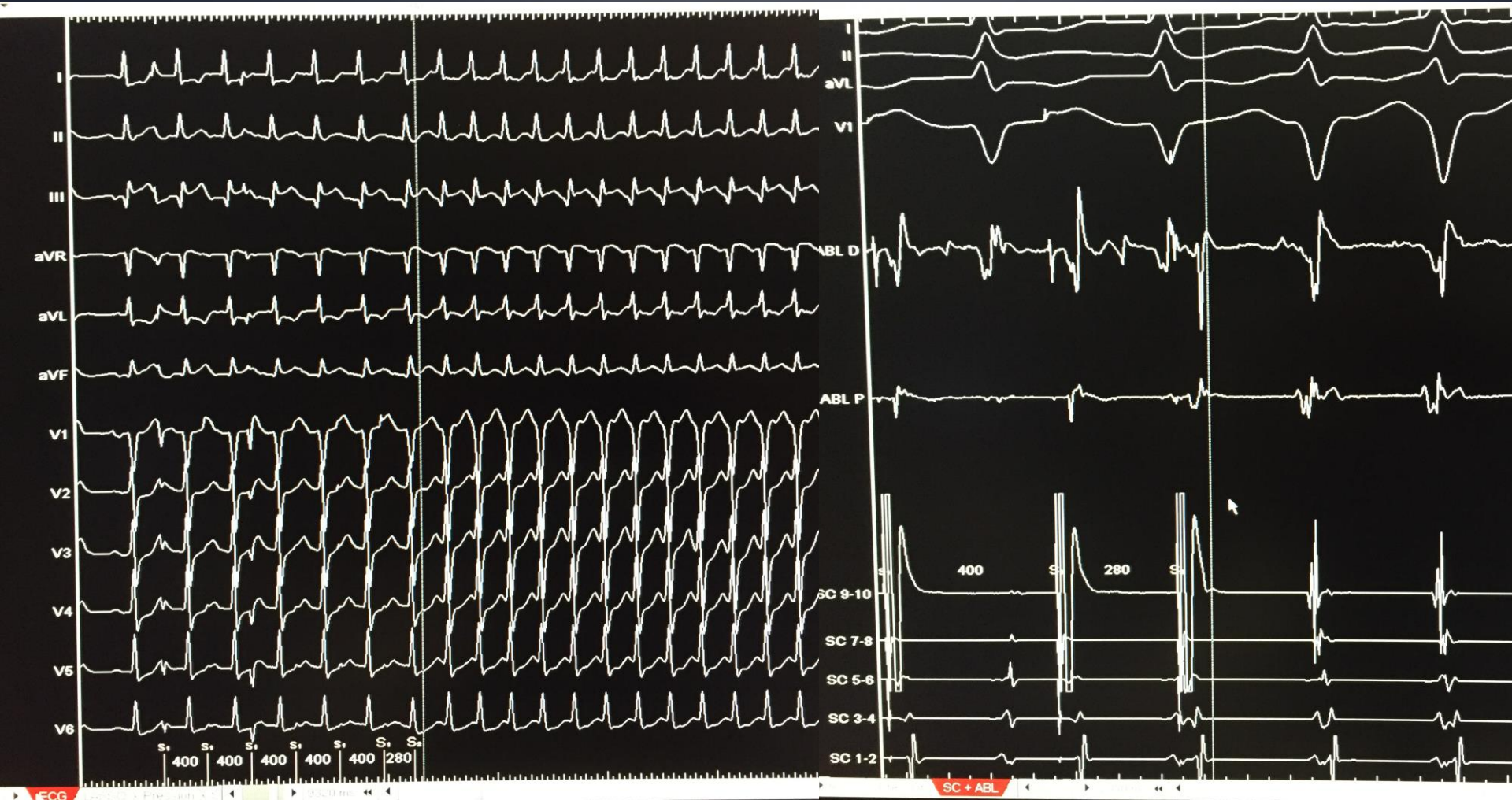
AF recurrence, no reconnection

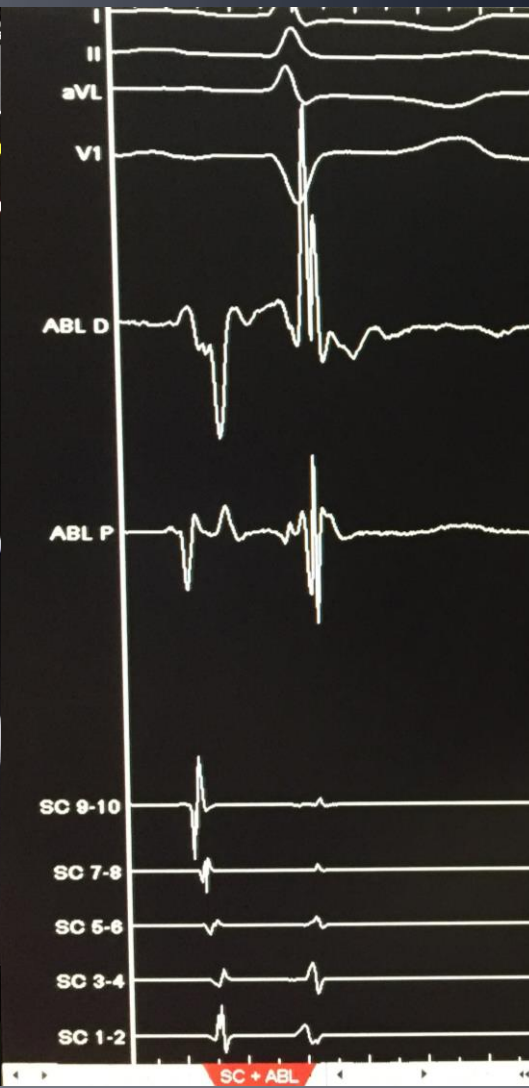


Isoproterenol: ectopy from superior vena cava

Isolation of the superior vena cava





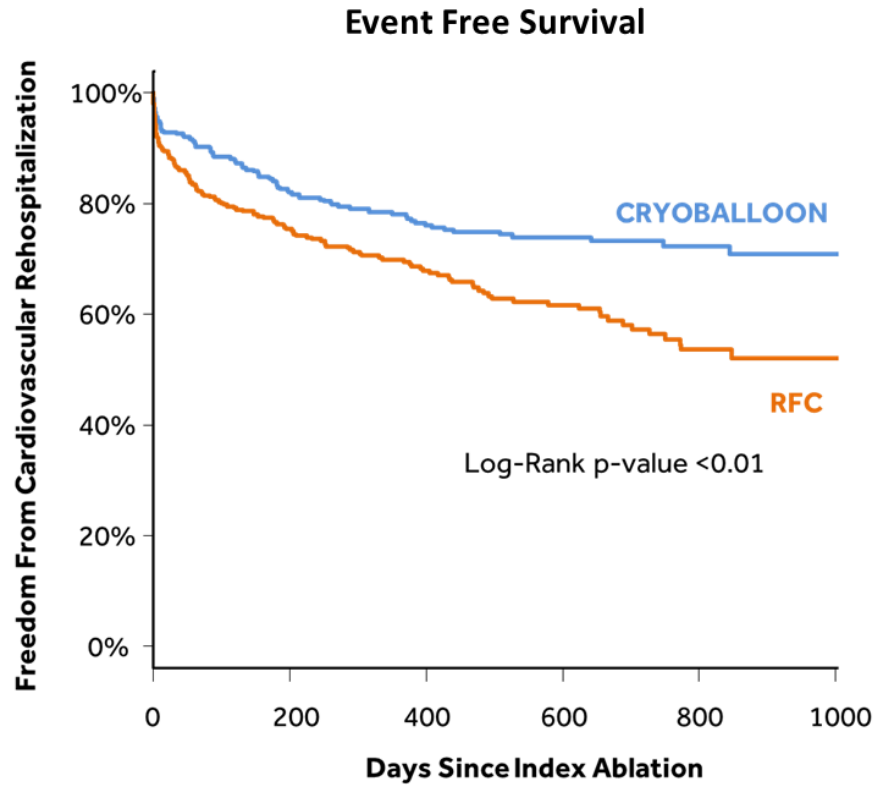


Conclusion

- Cryoablation is as efficient and safe compared to CF RF in paroxysmal AF ablation.
- Procedure duration are shorter than RF and will probably decrease with freezing time reduction (interest of TTI).
- Cryo is painless: anesthesia requirements are lower than RF.
- The procedure is less tiring for the physician , has a faster learning curve, and doesn't need a 3D mapping system.
- Future improvements: reduction of the freezing duration, new ballon with shorter tip, bigger ballons, new Achiev catheter with smaller electrodes...

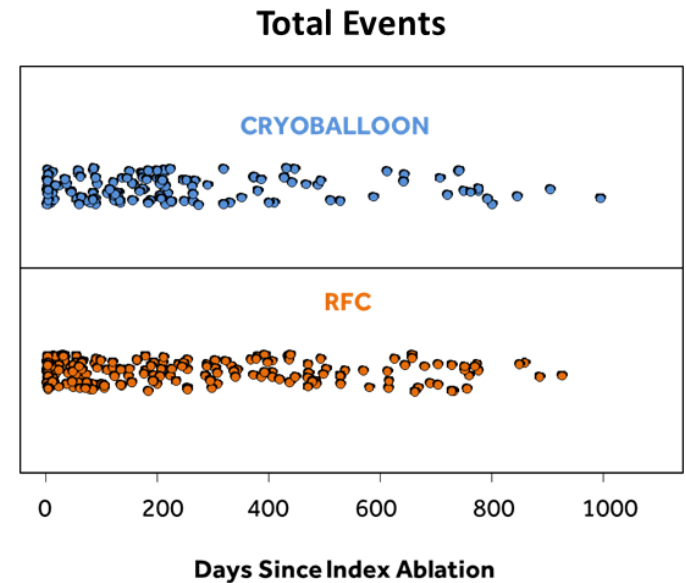
Freedom From Cardiovascular Rehospitalization

34% FEWER CV REHOSPITALIZATIONS IN THE CRYOBALLOON GROUP VS RADIOFREQUENCY GROUP



Number at Risk

CRYOBALLOON	374	271	190	126	68	15
RFC	376	250	167	102	52	14



Cryo: 139 events in 89 subjects
(89/374; **23.8%**)

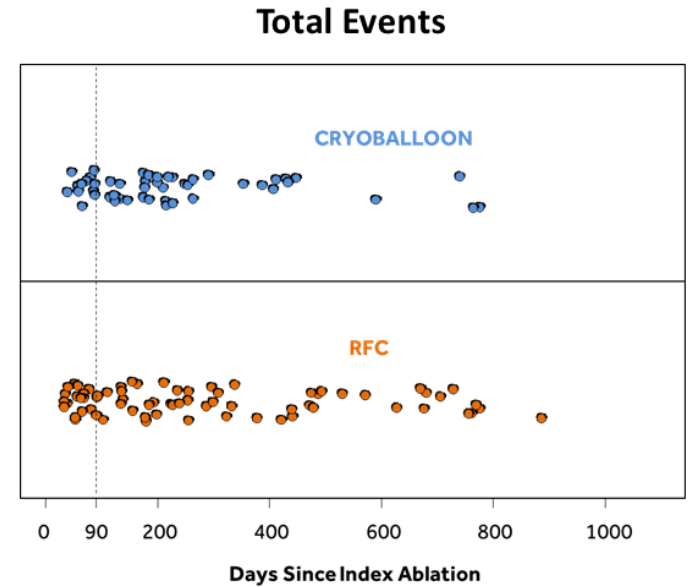
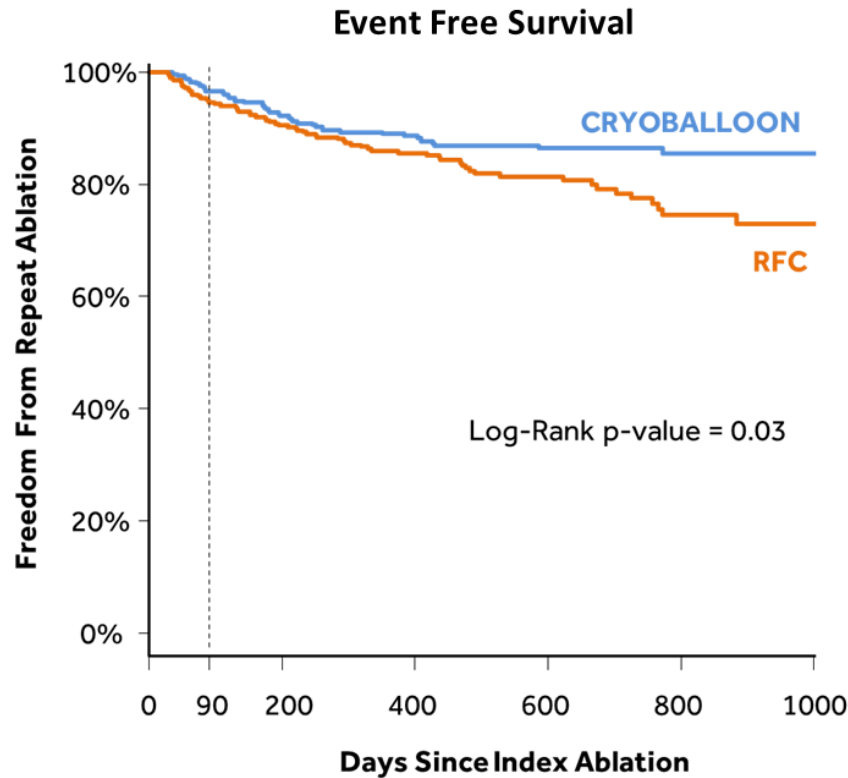
RFC: 203 events in 135 subjects
(135/376; **35.9%**)

Kuck KH, et al. *N Engl J Med.* 2016; 374(23): 2235-45.

Advancements in PVI: Arctic Front Advance™ Cryoballoon

Freedom From Repeat Ablation

33% FEWER REPEAT ABLATIONS IN THE CRYOBALLOON GROUP VS RADIOFREQUENCY GROUP



Number at Risk

	0	90	200	400	600	800	1000
CRYOBALLOON	374	343	301	221	149	84	20
RFC	376	341	302	213	135	72	22

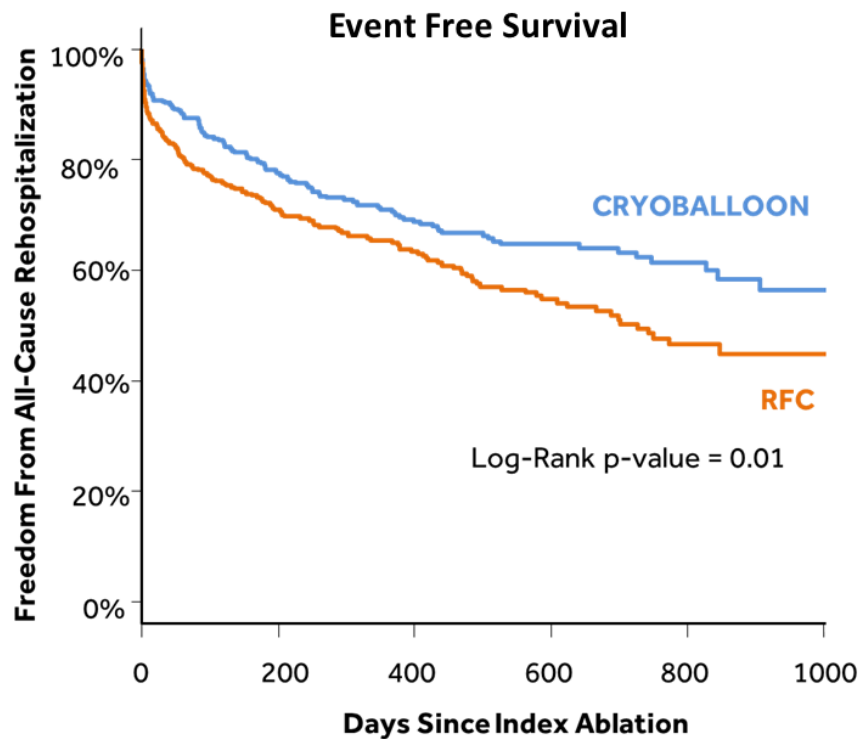
Cryo: 49 events in 44 subjects
(44/374; **11.8%**)

RFC: 70 events in 66 subjects
(66/376; **17.6%**)

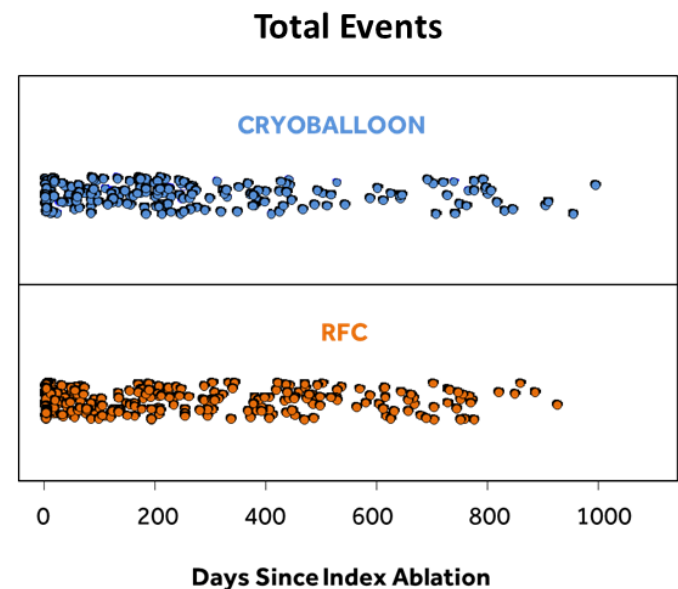
Kuck KH, et al. *N Engl J Med.* 2016; 374(23): 2235-45.

Freedom From All-Cause Hospitalization

21% FEWER ALL-CAUSE HOSPITALIZATIONS IN THE CRYOBALLOON GROUP VS RADIOFREQUENCY GROUP



Number at Risk		Days Since Index Ablation					
		0	200	400	600	800	1000
CRYOBALLOON	374	257	174	113	56	13	
RFC	376	235	157	90	43	10	



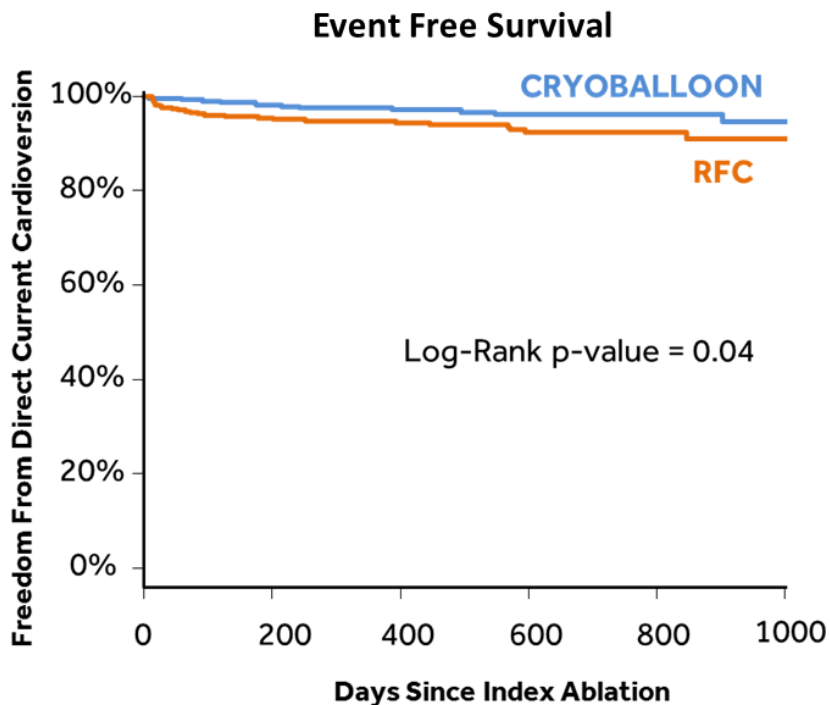
Modified ITT Analysis

Cryo: 210 events in 122 subjects
(122/374; **32.6%**)

RFC: 267 events in 156 subjects
(156/376; **41.5%**)

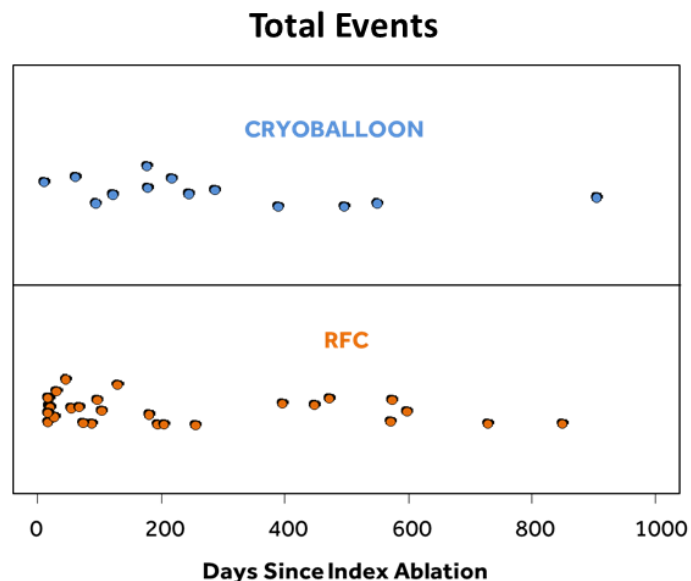
Freedom From DC Cardioversion

50% FEWER DC CARDIOVERSIONS IN THE CRYOBALLOON GROUP VS RADIOFREQUENCY GROUP



Number at Risk

	0	200	400	600	800	1000
CRYOBALLOON	374	321	247	170	100	24
RFC	376	320	235	162	96	30



Modified ITT Analysis

Cryo: 13 events in 12 subjects
(12/374; **3.2%**)

RFC: 28 events in 24 subjects
(24/376; **6.4%**)

Kuck KH, et al. *N Engl J Med.* 2016; 374(23): 2235-45.