



Persistent AF: when and why using the Cryo Technology

Cesare Storti

Electrophysiology and Cardiac Pacing Unit
Istituto di Cura Città di Pavia, Pavia, Italy

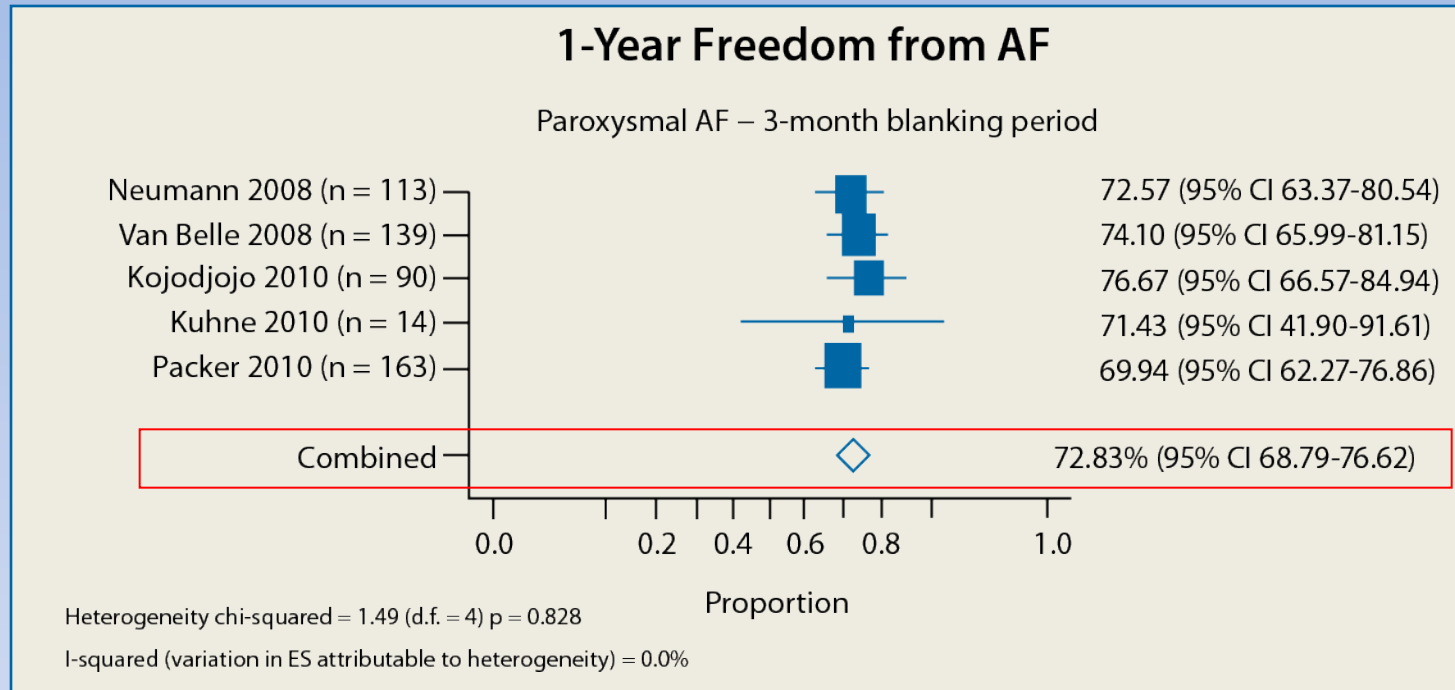
Persistent AF: when and why using the Cryo Technology

- For many years, symptomatic atrial fibrillation has been successfully treated via radiofrequency catheter ablation in which pulmonary vein isolation formed the cornerstone of treatment.
- More recently, cryoablation with the Arctic Front CryoAblation balloon catheter is another method besides RF ablation to treat symptomatic drug-refractory atrial fibrillation.
- Cryo balloon PV isolation is now proven to be an effective and safe technology for the isolation of PVs and the treatment of paroxysmal AF with a large body of clinical evidence.

Arctic Front Cryoballoon (1st Generation) PVI in paroxysmal AF patients

Author	Study Size	Freedom from AF	Follow-Up method	Complications
Andrade 2011 Meta-analysis	1221	73%	12 months	6.4 PNP 0.37% lasted > 1 year 0.1 PV stenosis requiring intervention 0.57% thromboembolic events
Packer STOP AF 2010	245	69.9%	12 months 24h Holter at 3, 6, 12 months	3.1 PV stenosis 11.2 PNP 3.1% cryoablation procedure events
Kojodjojo 2010	90	77%	13 months 24h Holter at 1,3,6,12 months	1.6% transient PNP 0.8% pericardial effusion
Chun 2009	27	70%	12 months	11.1 PNP
Klein 2008	21	86%	6 months	14.3%PNP
Neumann 2008	293	74%	12 months 24h Holter	2.8% PNP 5.7% pericardial effusion 0.7% hematomopneumothorax

Arctic Front[®] efficacy - Meta Analysis



Andrade, et al: 539 articles evaluated, 23 considered for the final analysis

Results:

- Acute success rate 98%
- 1-year Freedom from AF: 73%
- Results at 6 months and one year comparable with the conventional technique with RF

Arctic Front Cryoballoon (1st Generation) PVI in paroxysmal and persistent AF patients

Author	Study Size	Paroxysmal Freedom from AF	Persistent Freedom from AF	Follow-Up method
Neumann 2008	293+53	74%	42%	12 months 24h Holter
Kojodjojo 2010	90+34	77%	44%	13 months 24h Holter at 1,3,6,12 months
Nadji 2011	85+33	75%	51%	18 months
Aytemir 2013	188+48	80%	50%	18 months

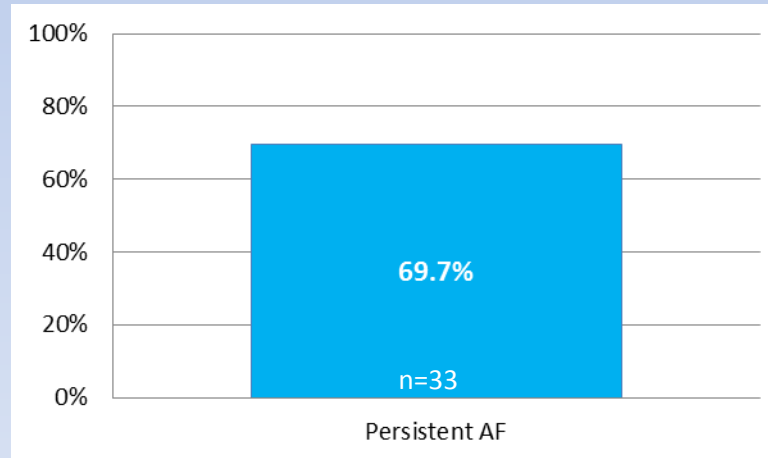
Schmidt et al: Dual cryoballoon strategy in persistent atrial fibrillation: a pilot study

Study Details

- Study with 1st generation cryoballoon, Arctic Front; PVI only.
- 33 persistent AF patients.
- Median follow-up 15 months (range 12 – 18).
- The study sought to investigate clinical efficacy of PVI and antral substrate modification with 23mm and 28mm cryoballoon catheter.

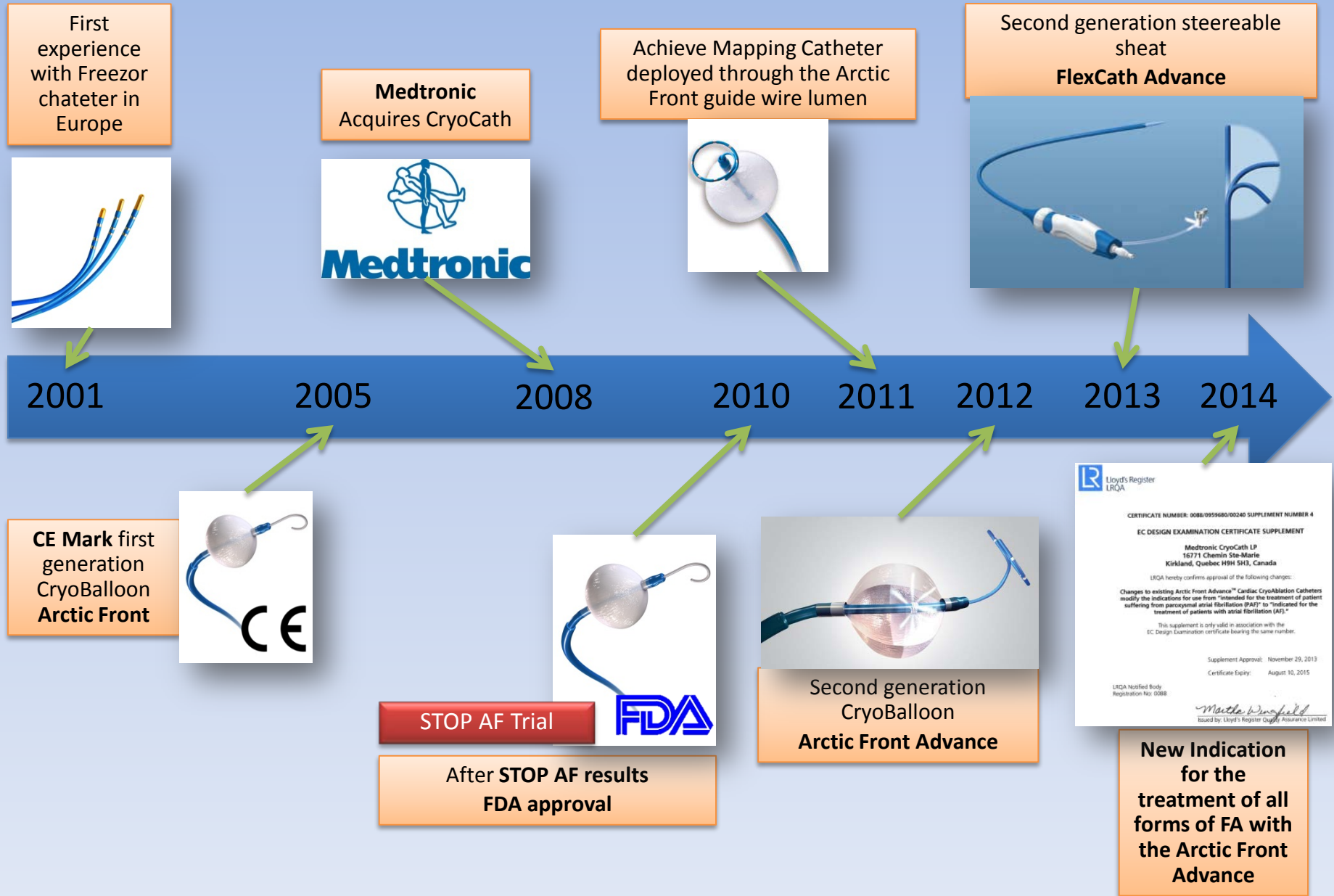
Results

Single-Procedure Freedom From Persistent AF



- No major peri-procedural complications.

New Advancement in Pulmonary Vein Isolation



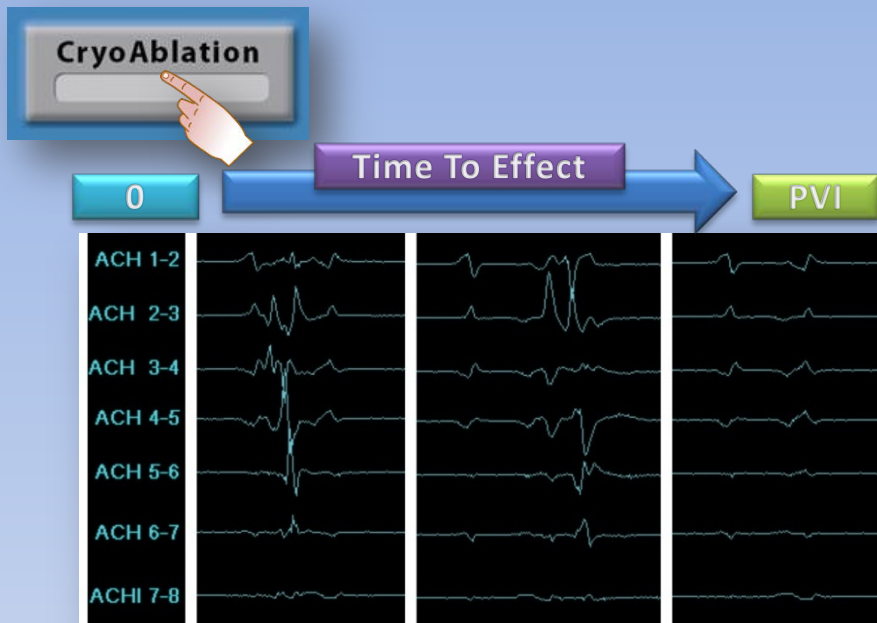
Achieve™ Mapping Catheter

The Achieve Mapping Catheter allows for the assessment of pulmonary vein isolation during the cryoablation procedure with Arctic Front.

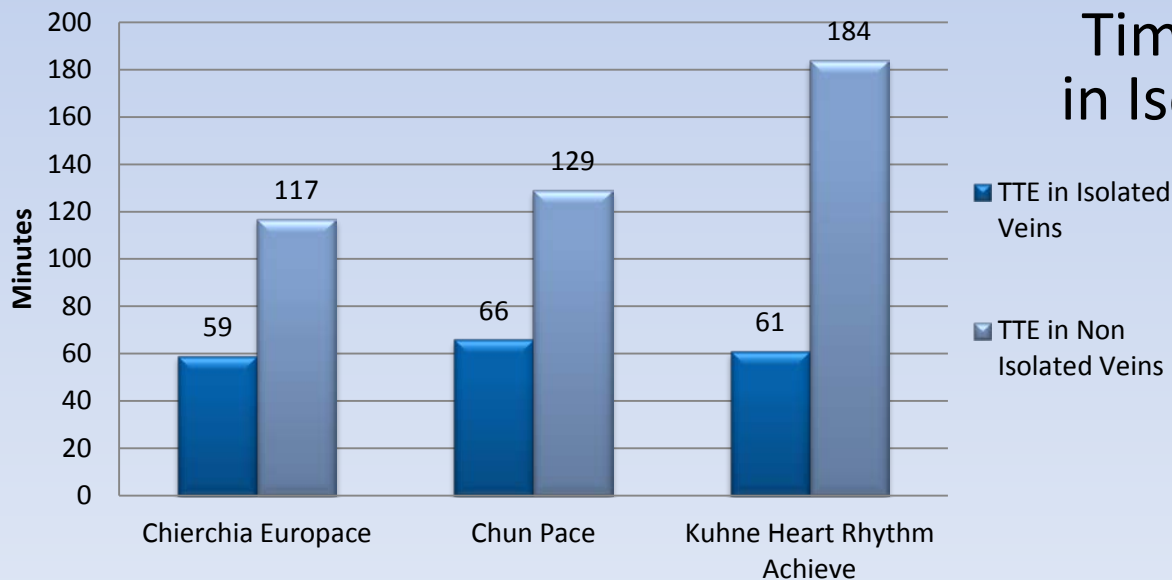
Achieve is deployed through the Arctic Front guide wire lumen, minimizing the number of catheter exchanges and allowing the procedure to be performed using a single transseptal puncture. Achieve may also provide recording of real-time PV potentials during cryoablation with Arctic Front.

The distal mapping section of the Achieve Mapping Catheter is a circular loop with eight evenly spaced electrodes for mapping electrical conduction between the left atrium and pulmonary veins. The catheter may also be used for cardiac stimulation during electrophysiology studies.





TTE PVI Observations



Time to Effect (TTE)



The Time to Effect (TTE) is the time (in seconds) elapsed between the start of the ablation and the disappearance of the potential of Pulmonary Vein

Some recent clinical studies have shown that the Pulmonary Veins that are isolated in time, showed a TTE <60 seconds

Time to Effect (TTE) Lower in Isolated vs. Non-Isolated Veins

1. Chierchia GB, et al. *Europace*. 2012 Mar 11.
2. Chun KJ. *Pacing Clin Electrophysiol*. 2012 Aug 6. doi: 10.1111/j.1540-8159.2012.03475.x. [Epub ahead of print]
3. Kühne M, et al. *Heart Rhythm*. <http://dx.doi.org/10.1016/j.hrthm.2012.10.009>

New Advancement in Pulmonary Vein Isolation

Arctic Front Advance™ Cryoballoon



The world's leading balloon therapy for the treatment of patients with AF

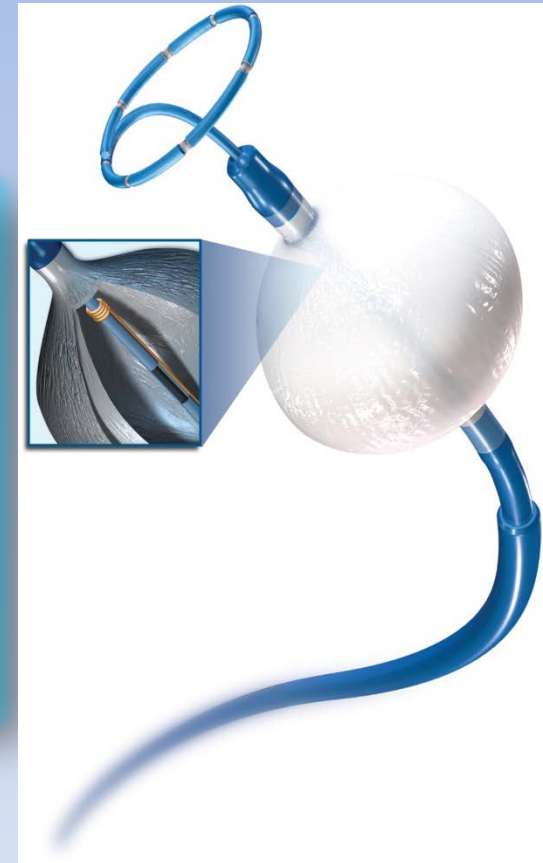
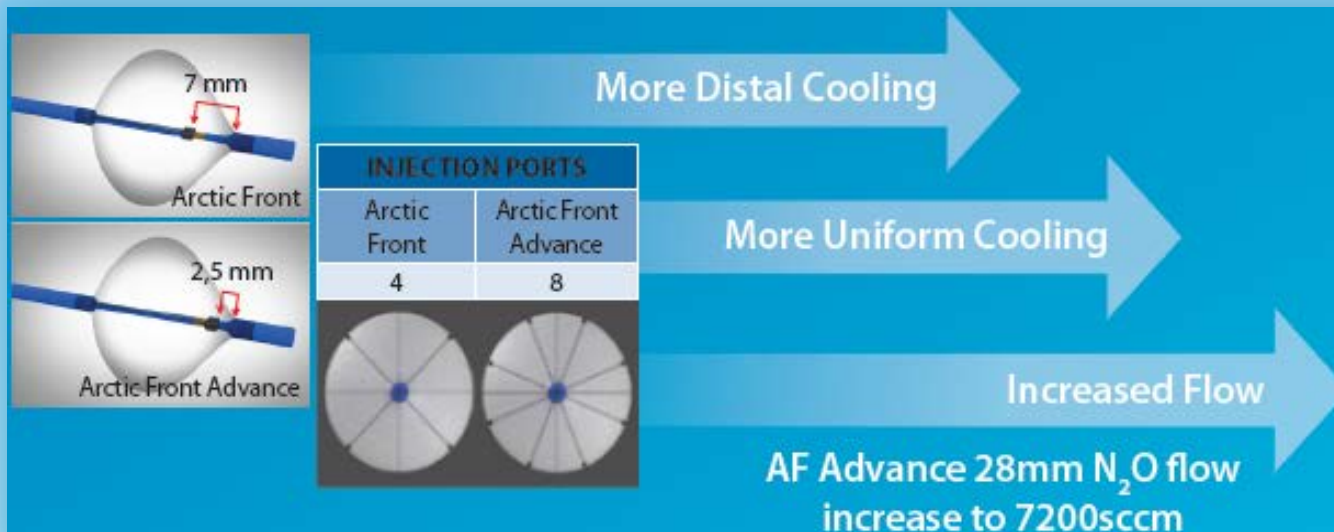
Enhancing what has already changed the PVI landscape

EvenCool™ Cryo Technology provides an improved cooling uniformity

Designed to provide a more contiguous lesion and treat a broader range of pulmonary vein anatomies with less effort

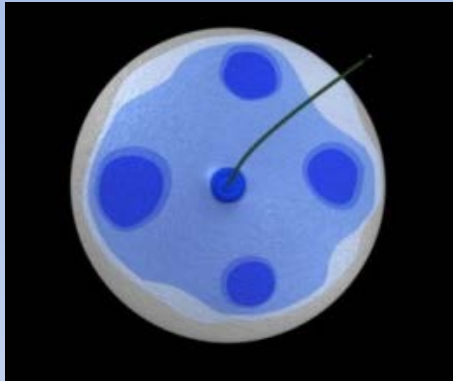
How Is More Uniform Cooling Achieved?

Arctic Front Advance™

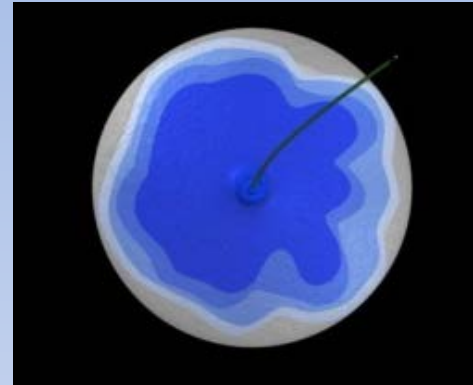


Second Generation CrioBalloon Arctic Front **Advance**

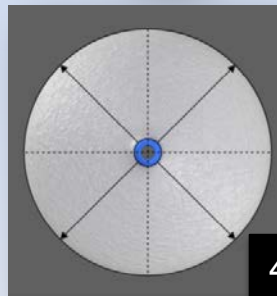
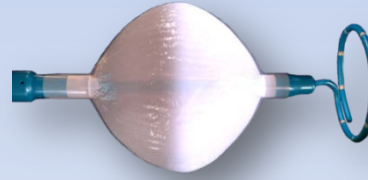
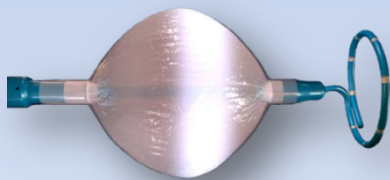
Improved Temperature Uniformity



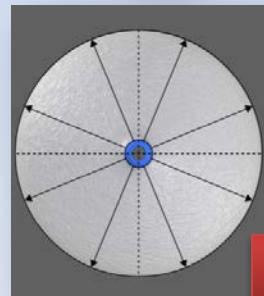
Refrigerant distribution near equator of balloon with four jets.



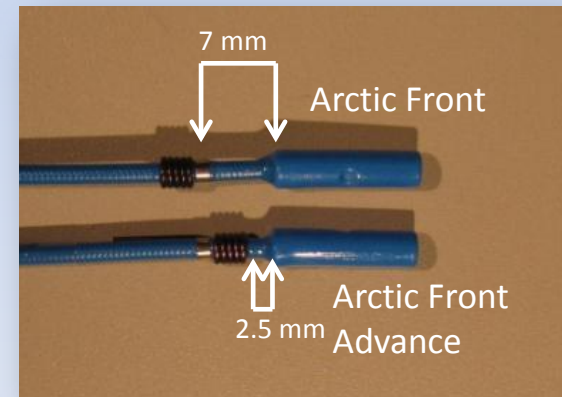
Improved surface temperature gradient



4 injectors



8 injectors



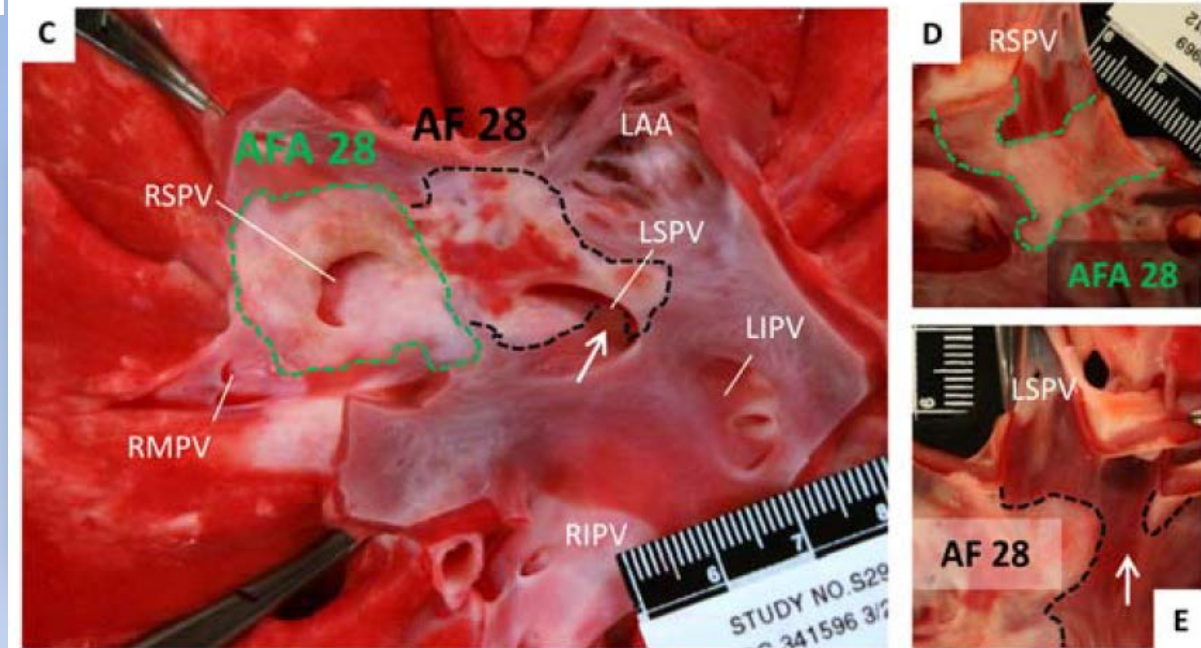
Arctic Front Advance

In the first generation CryoBalloon, the coldest area is located at the equator.

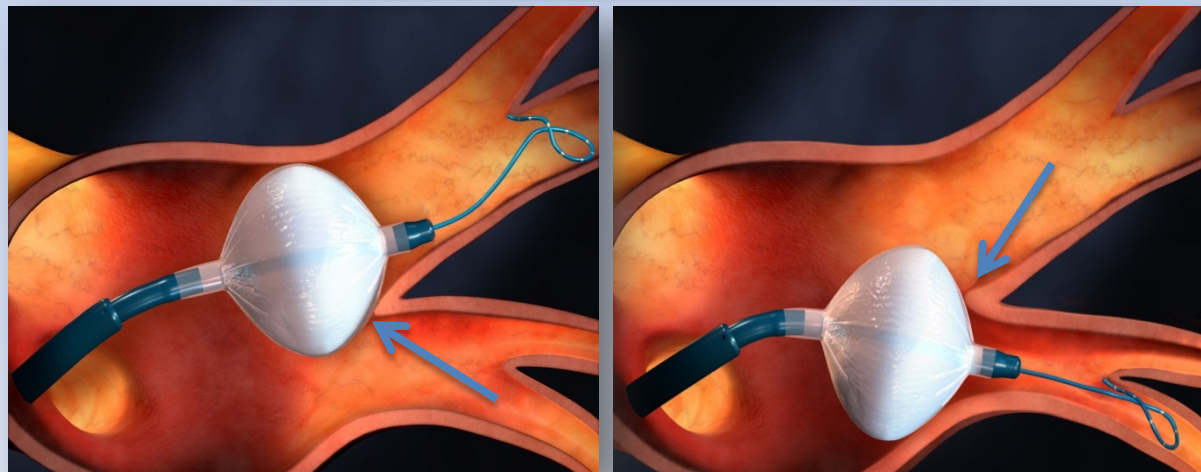
It is very important to place the CryoBalloon coaxially to the vein, as well as choose the right diameter.

The Arctic Front Advance, with the EvenCool™ technology, cools an area larger and more homogeneous. This means less dependence on the position of the balloon with respect to the vein and size.

The Arctic Front Advance allows to treat a wider variety of Pulmonary Veins, with less effort.

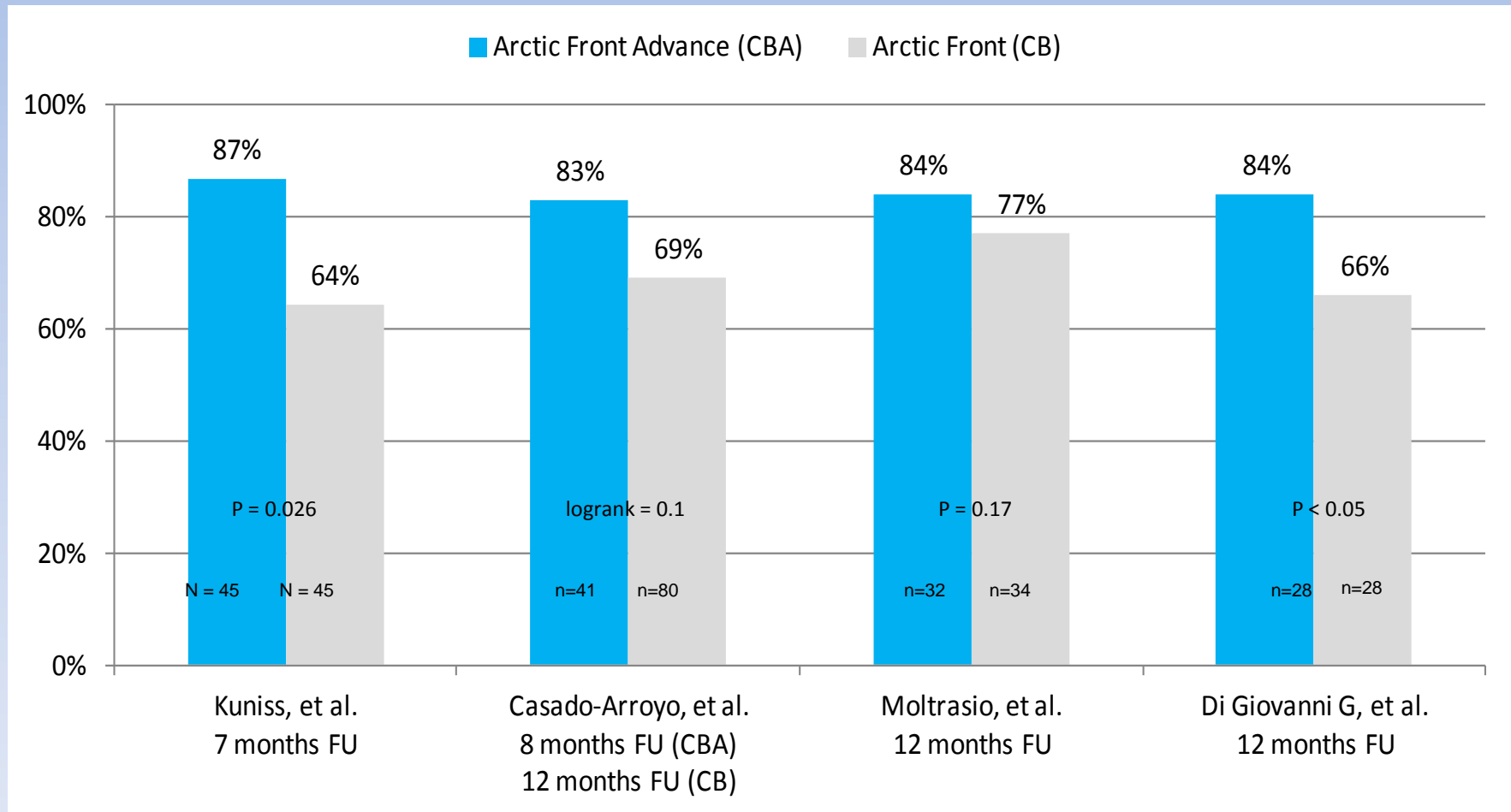


ARCTIC FRONT ADVANCE®



Arctic Front Advance is Effective for Pulmonary Vein Isolation in PAF Patients

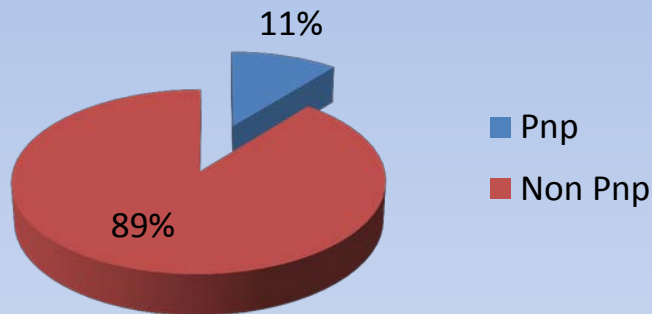
% Free from AF after a Single Procedure



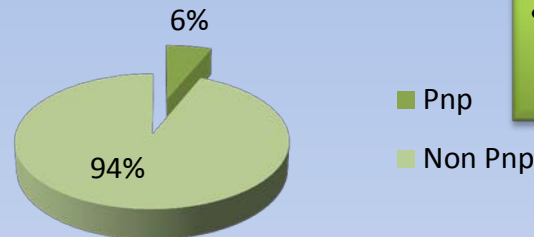
Arctic Front Advance™ Clinical Experience

Phrenic nerve paralysis during cryoballoon ablation for atrial fibrillation: A comparison between the first- and second-generation balloon

Pnp Incidence Overall

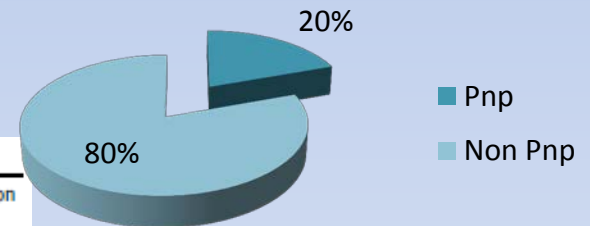


Pnp Incidence AF



- 100% resolved before discharge

Pnp Incidence AFA



- 5/8 resolved before discharge
- 2/8 resolved in 2 months
- 1/8 persistent at 7 Months FU

Table 3 Patients with PNP during cryoballoon application

Patient ID no.	Group	Sex: 1 woman, 2 man	Age (y)	PNP in RSPV = 1, RIPV = 2	Temperature at PNP (°C)	Time to PNP (XX)	Resolution of PNP
1	1	2	63	1	-52	224	Yes
2	1	2	57	1	-49	218	Yes
3	1	2	65	1	-46	213	Yes
4	1	2	67	1	-57	198	Yes
5	1	1	54	1	-56	115	Yes
6	2	1	58	1	-59	107	Yes
7	2	2	54	1	-57	103	Yes
8	2	1	55	1	-58	111	Yes
9	2	2	57	2	-58	138	Yes
10	2	2	62	1	-59	187	No
11	2	2	57	2	-57	80	Yes
12	2	1	54	1	-59	121	Yes
13	2	2	58	1	-48	145	Yes

Fürnkranz et al: Improved Procedural Efficacy of Pulmonary Vein Isolation (PVI) with Arctic Front Advance

Study Details

- A total of 60 patients were enrolled consecutively using Cryoballoon PVI (CB-PVI) and Achieve, with 30 in each of Arctic Front Advance (CBA) and Arctic Front (CB) groups.
- The Study sought to investigate the impact of the novel design on the procedural efficacy of CB-PVI.

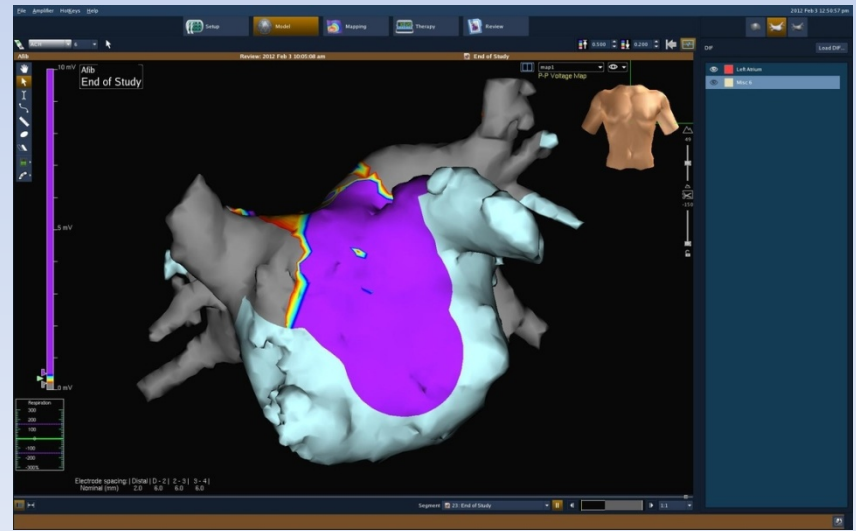
Results

Procedural Efficacy Measure	CBA	CB	P-value
Procedure Time	98 ± 30 min	128 ± 27 min	P < 0.001
Fluoro Time	13.4 ± 5.3 min	19.5 ± 7.4 min	P = 0.001
Frequency of PVI after 1 st freeze	84%	51%	P < 0.001
Time to PVI	52 ± 36 sec	79 ± 60	P = 0.049

- Safety results showed comparable procedure-related complications (2 in AF group; 1 in AFA group: left-sided PN palsy)

II generation CryoBalloon and persistent AF

- Reduced procedural time and good safety profile.
- High rate of PVI with a lower incidence of reconnections.
- Wide antral ablation, leading to a potential substrate modification of these regions which are involved in the persistency of the arrhythmia.



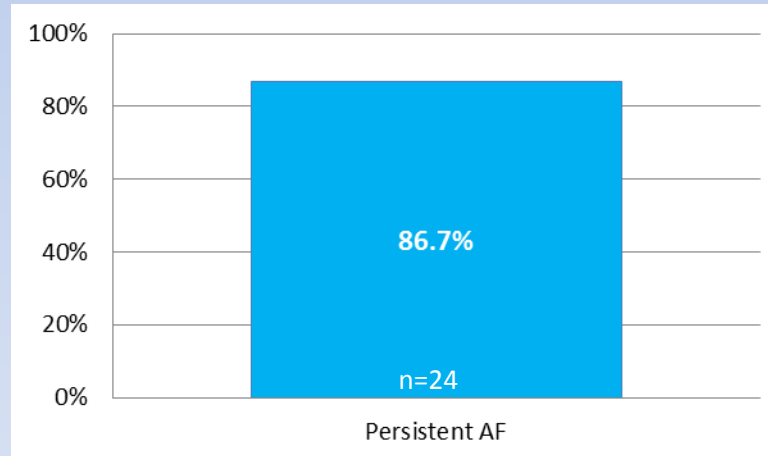
Brala et al: Arctic Front Advance Cryoballoon mid-term efficacy in complex PV anatomies and persistent AF

Study Details

- Study with 1st (CB) and 2nd generation cryoballoon (CBA); PVI only.
- 61 AF patients (37 paroxysmal and 24 persistent).
- 15 (63%) patients presented with persistent AF in the CBA group.
- Follow-up 6 months.
- The study sought to investigate mid-term freedom of persistent AF.

Results

Single-Procedure Freedom From Persistent AF



- No major complications occurred.
- Incidence of PNP was up to 7%.



Pulmonary Vein Isolation as Index Procedure for Persistent Atrial Fibrillation: One-Year Clinical Outcome After Ablation Using The Second-Generation Cryoballoon

Giuseppe Ciconte MD, Luca Ottaviano MD, Carlo de Asmundis MD PhD, Giannis Baltogiannis MD, Giulio Conte MD, Juan Sieira MD, Giacomo Di Giovanni MD, Yukio Saitoh MD, Ghazala Irfan MD, Giacomo Mugnai MD, Cesare Storti MD, Annibale Sandro Montenero MD PhD, Gian-Battista Chierchia MD PhD, Pedro Brugada MD PhD.

Heart Rhythm, Article in press:

<http://dx.doi.org/10.1016/j.hrthm.2014.09.063>

Study population baseline clinical characteristics

63 Patients

- Mean age, years 62.7 ± 9.7
- Male gender, n (%) 45 (71.4)
- LA dimension, mm 47.1 ± 7.9
- Ejection Fraction, % 57.4 ± 3.5
- Hypertension, n (%) 31 (49.2)
- Diabetes, n (%) 7 (11.1)
- Heart Failure, n (%) 2 (3.2)
- Coronary Artery Disease, n (%) 6 (9.5)
- AF duration, months 32.4 ± 34.6
- AF persistency, months 7.2 ± 2.1
- Number of previous AADs, n 1.7 ± 0.6
- Number of previous electrical cardioversions, n 1.8 ± 1.1
- AF presenting rhythm at the procedure, n 26 (41.3)

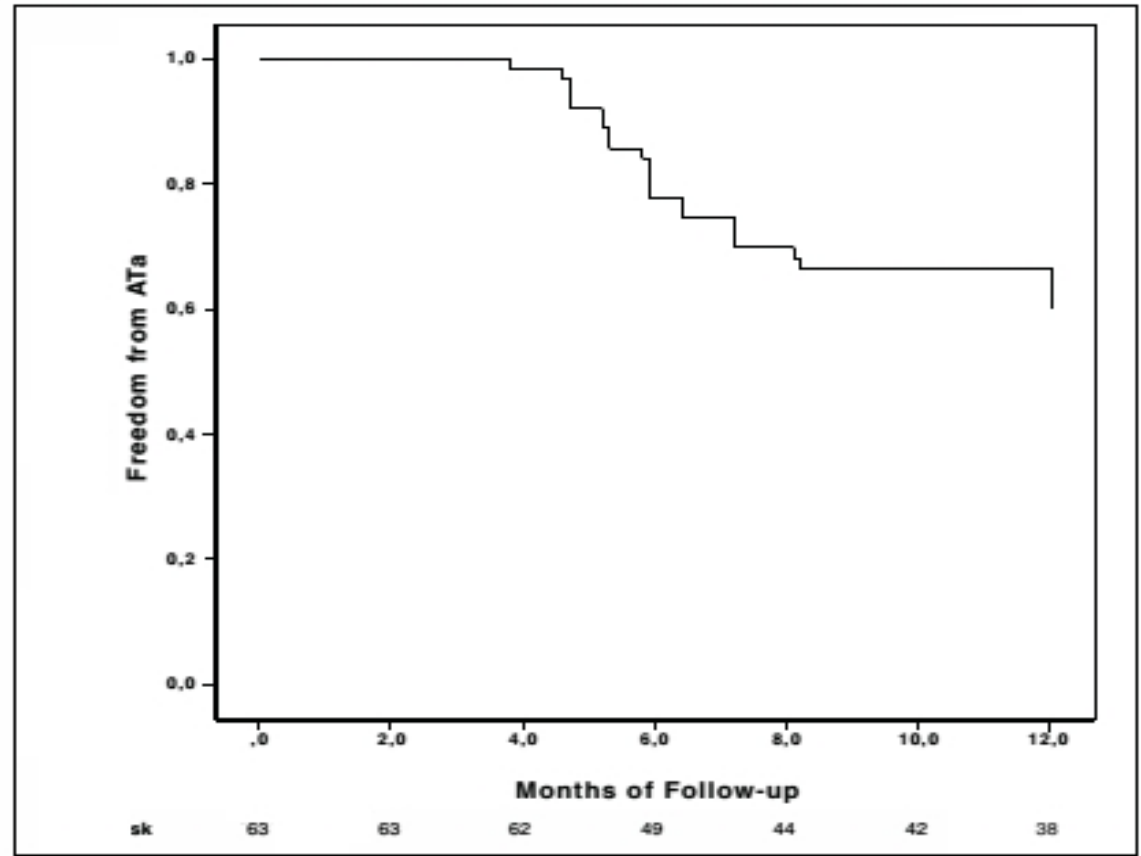
Results and complications

One-year follow-up:

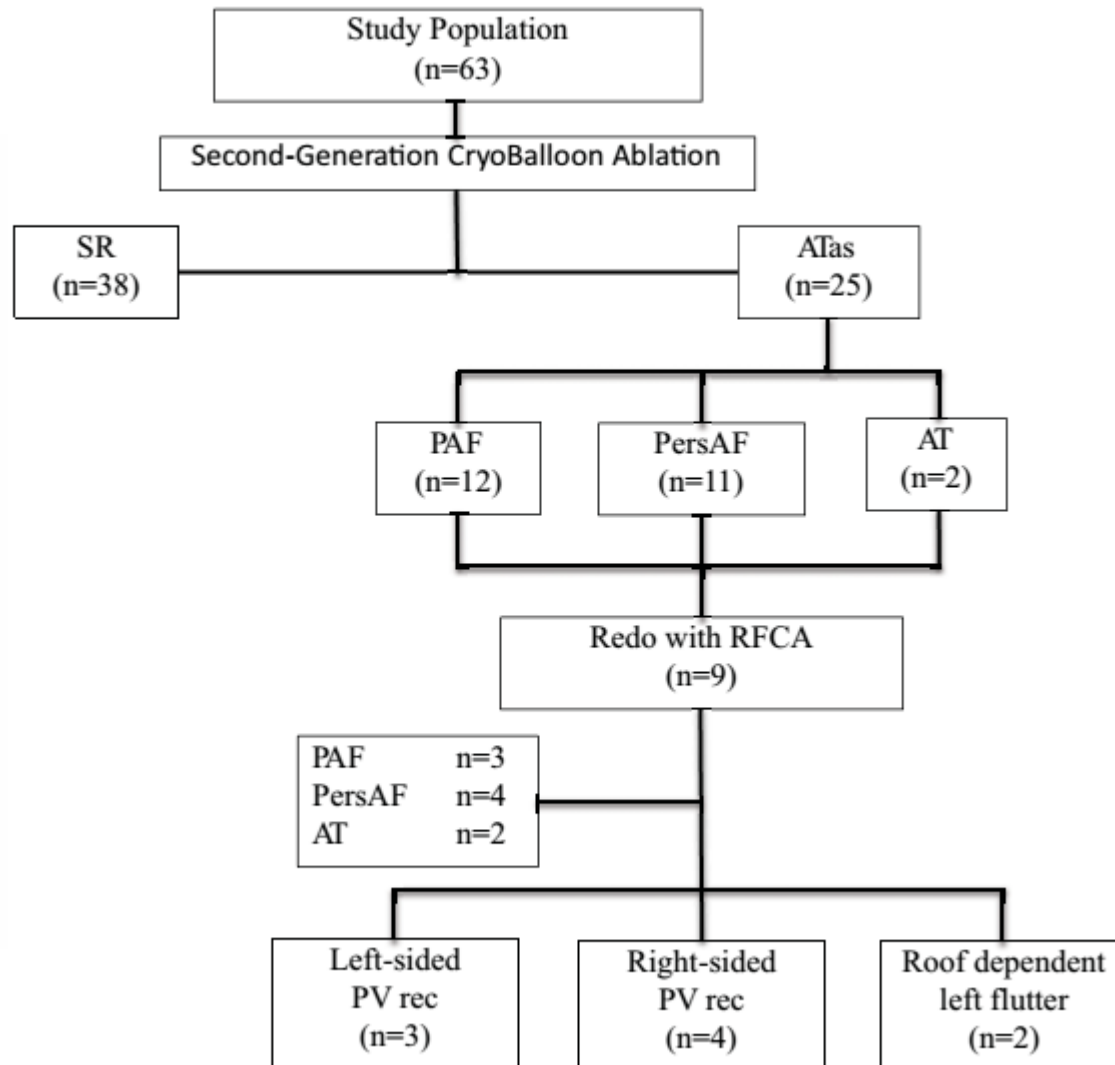
- Freedom From Persistent AF
38/63 pts (60%)

Complications:

- Femoral pseudoaneurysm
2/63 pts (3.2%)
- PNP 4/63 (6.4%)



One-year follow-up results



Clinical predictors of arrhythmia recurrence

Variables	β Coefficient	Hazard Ratio (95% CI)	p value
Univariate analysis			
Age, yrs	0.02	1.00 (0.96-1.05)	0.93
Male gender	0.55	1.65 (0.56-4.87)	0.37
Hypertension	0.38	0.73 (0.34-1.54)	0.40
AF duration	0.01	1.00 (0.99-1.01)	0.57
LA dimension	0.02	1.08 (1.03-1.13)	<0.01
BP recurrences	0.38	5.07 (2.39-10.76)	<0.01
AF persistency	0.09	1.40 (1.18-1.67)	<0.01
Multivariate analysis			
BP recurrences	0.88	2.43 (1.03-5.75)	0.04
AF persistency	0.27	1.31 (1.06-1.62)	0.01

The hazard ratio for persistent AF duration considers every month increase.
The hazard ratio for LA dimension considers every millimeter increase.
Abbreviations: AF atrial fibrillation, BP blanking period, LA left atrium.

Clinical predictor of arrhythmia recurrence

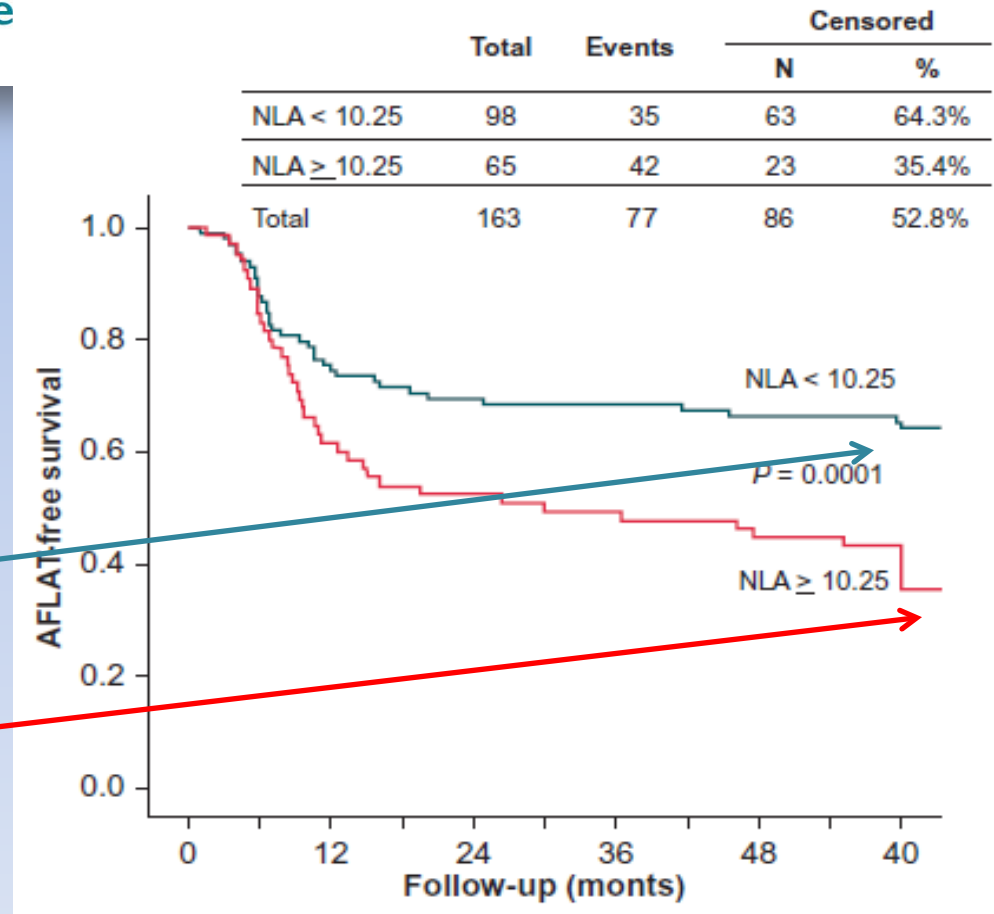
Cryoballoon ablation of paroxysmal atrial fibrillation: 5-year outcome after single procedure and predictors of success

Results:

64,3% success rate after single CB ablation without AAD after 5 year follow-up, **normal LA**

Not Enlarged LA:
64,3%

Enlarged LA:
35,4%



Conclusions

The II generation CryoBalloon Catheter has allowed to increase the success rate in paroxysmal atrial fibrillation and also it can be used effectively in the persistent form while maintaining a good safety profile.

A selection of the patients in an earlier stage of persistent atrial fibrillation, also on the left atrium, may allow a higher success rate.

BUT....

In patient
modification
time of the
long-term

“Less May be More”

Atul Verma

Barcelona, september 2014

substrate
and at the
prove the

Optimal Method and Outcomes of Catheter Ablation of Persistent AF: The STAR AF 2 Trial

**Atul Verma, Jiang Chen-yang, Tim Betts, John Radcliffe, Jian Chen,
Isabel Deisenhofer, Roberto Mantovan, Laurent Macle,
Carlos Morillo, Prashanthan Sanders
on behalf of the STAR AF 2 Investigators**

ClinicalTrials.gov NCT01203748

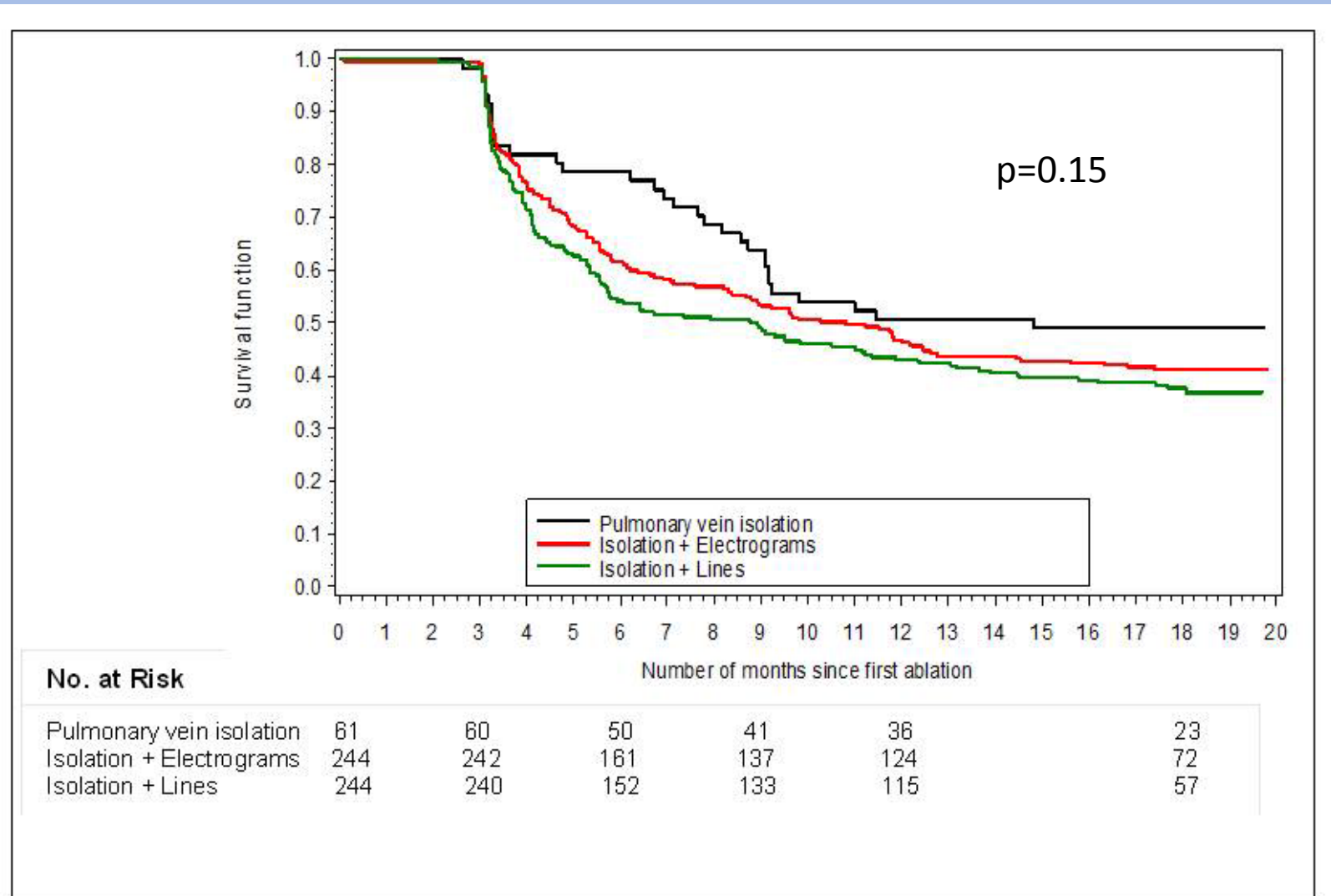
The STAR AF 2 trial was funded by St Jude Medical Inc.

Purpose

- To compare the efficacy of three different AF ablation strategies in patients with persistent AF targeting:
 - (1) Only the triggers of AF via PVI alone versus
 - (2) A combination of the triggers plus the substrate of AF as defined by complex fractionated electrograms (PVI+CFE) versus
 - (3) A combination of the triggers plus the substrate of AF by empiric linear ablation (PVI+Lines).

Primary Outcome

589 pts from 48 ablation centers in 12 countries



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

Complications

Category	PVI (n=64)	PVI+CFE (n=254)	PVI+Lines (n=250)	Total (n=568)
Access site hematoma	2	0	3	5
Access site arteriovenous fistula or pseudoaneurysm	0	3	3	6
Pericarditis	0	1	2	3
Fluid overload	0	1	3	4
Sedation related complication	0	3	5	8
Skin burn	1	0	0	1
Cardiac tamponade	1	0	2	3
Transient ischemic attack or Stroke	0	2	1	3
Atrial esophageal fistula - procedural death	0	1	0	1

Conclusions

- Largest randomized trial to examine outcomes of catheter ablation in persistent AF
- Additional CFE or Lines ablation increased procedural time (may increase risk)
- No benefit in AF reduction when additional substrate ablation (CFE or Lines) was performed on top of PVI
- PVI alone achieved freedom from recurrence in about 50% of patients – comparable to published success rates from randomized, multicenter trials in paroxysmal AF