

Very Long-Term Outcome of Cryoballoon Ablation in AF patients: 10 Years FU from real world Italian Multicenter Experience

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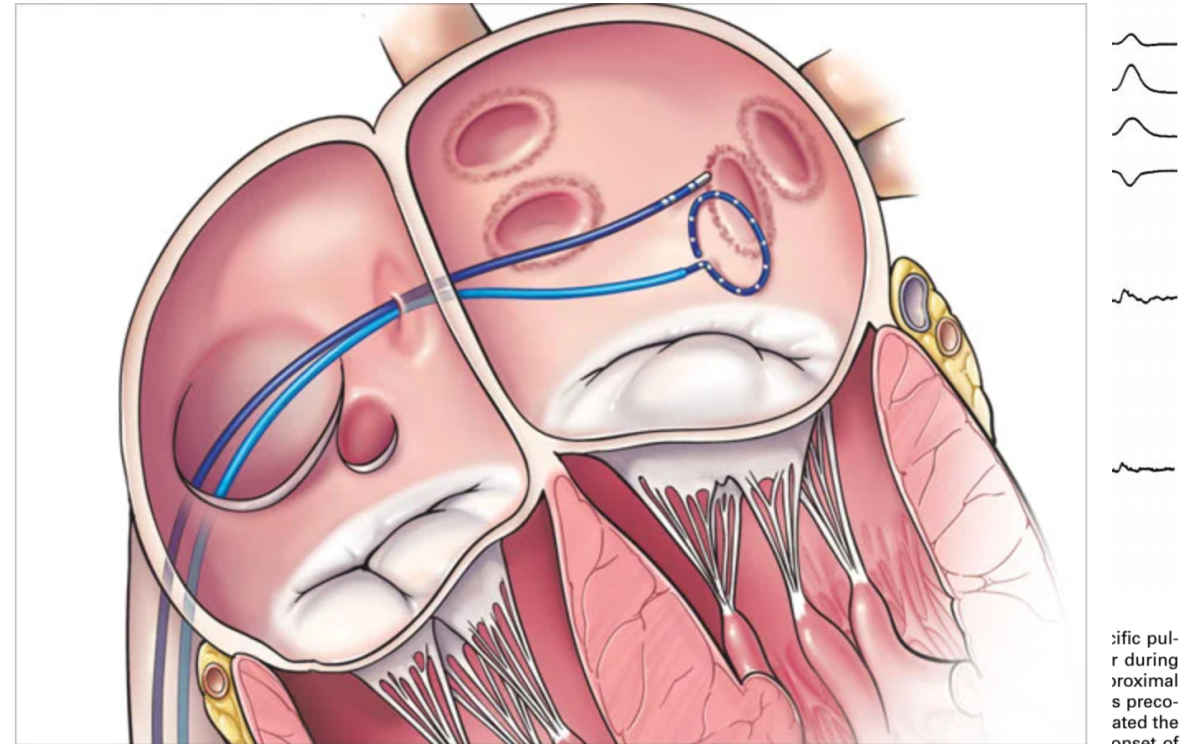
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Disclosures

- *Recipient lectures' fee from Abbott Medical, Boston Scientific, Haemonetics*
- *Recipient tutoring, proctoring fees from Abbott Medical, Medtronic Inc, Biosense&Webster, Boston Scientific*
- *Member of Advisory Board of Abbott Medical, Medtronic, Boston Scientific*

AF ablation, from RF.

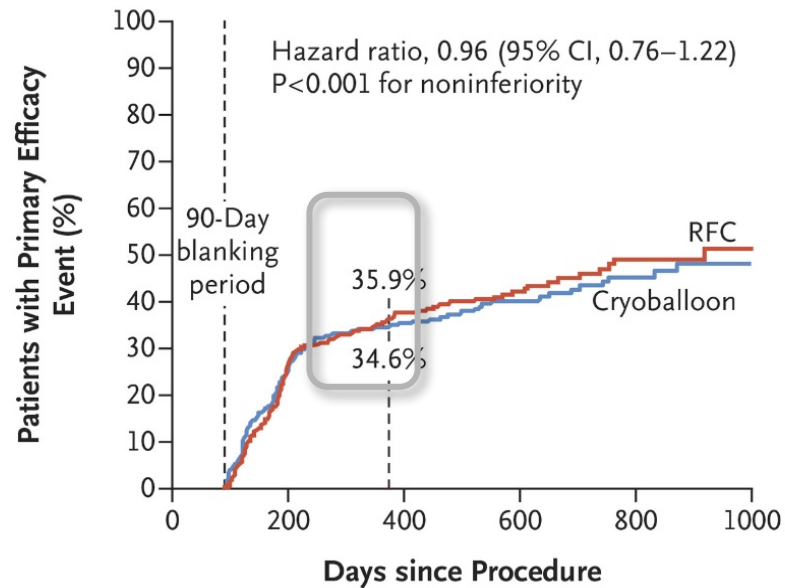
- Radiofrequency (RF) represent the traditional form of energy delivered during catheter-based pulmonary vein isolation (PVI) for atrial fibrillation (AFib) ablation.
- First described for the treatment of focal AFib triggers in **1998**
- RF ablation is now used to achieve PVI with continuous, point-by-point application of thermal injury around the antrum of each PV (or PV pair)
- However, this approach has been viewed by many electrophysiologists as time-consuming, high-risk for procedural complications, and suboptimal for achieving durable PVI.



near-field atrial activity. The radiograph (center panel) shows the position of electrographic recordings inside the pulmonary vein at the source and exit.

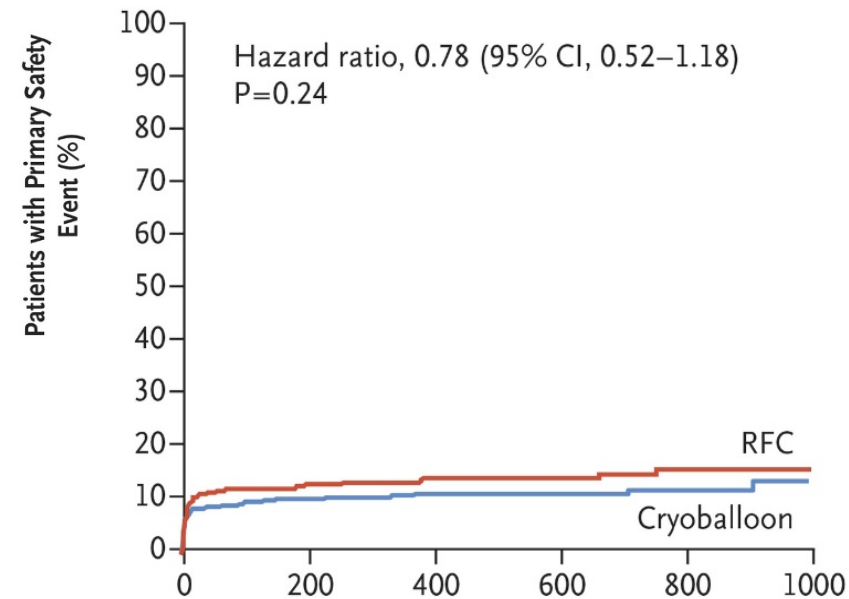
FIRE AND ICE Clinical Study

Similar 1-yr atrial arrhythmia recurrence rates



374	338	242	194	165	132	107	70	57	34	12
376	350	243	191	149	118	93	58	44	25	12

No significant differences with regards to overall safety



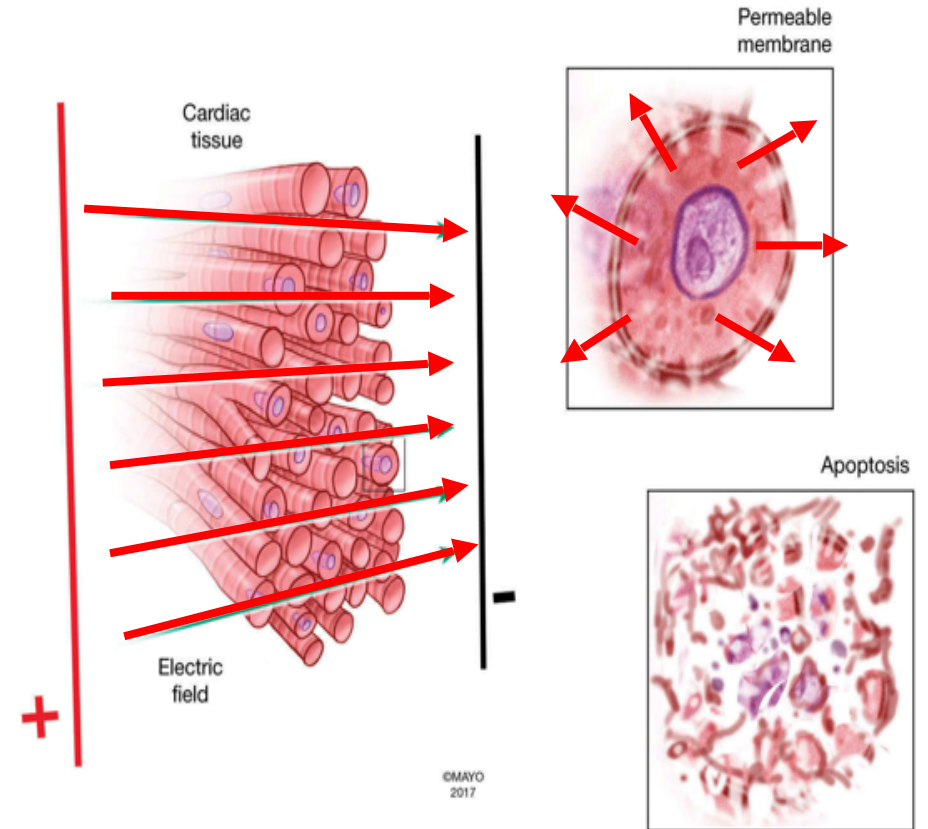
Cryoballoon ablation was non-inferior to RF ablation for the treatment of patients with drug-refractory PAF

To electroporation!

- Ultra-short, high-voltage electrical impulses
- Large increase in the electric field across cell membrane - accumulated transmembrane potential exceeds a critical value
 - Nanoscale pores
- Permanent nanopores - Cell death (Irreversible Electroporation)
- Transient nanopore- Cell recovery (Reversible Electroporation)

Irreversible electroporation (IRE) leads to:

- Electro-conformational protein denaturation, osmotic imbalance, flush in/out of ions
- Depletion of adenosine triphosphate (ATP), uptake of toxic/foreign molecules



Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation

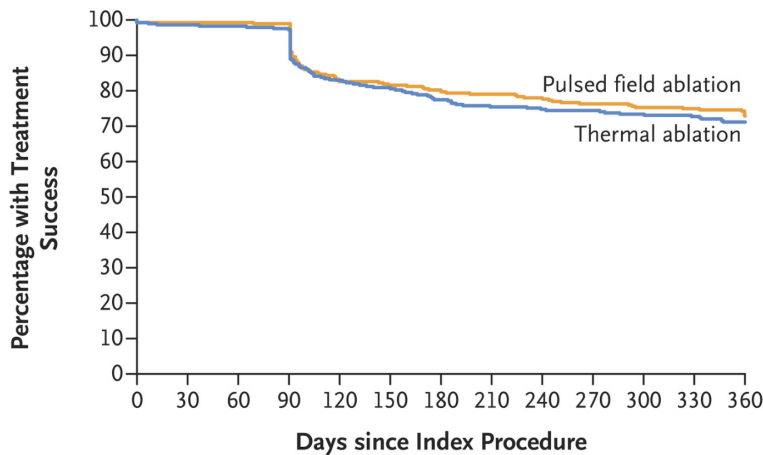
Authors: Vivek Y. Reddy, M.D., Edward P. Gerstenfeld, M.D., Andrea Natale, M.D., William Whang, M.D., Frank A. Cuoco, M.D., Chinmay Patel, M.D., Stavros E. Mountantonakis, M.D.,

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687 patients were randomized to pulsed field ablation (305 patients) or conventional thermal ablation (167=RF – 135=cryoballoon ablation).



No. at Risk					
Pulsed field ablation	301	298	238	228	176
Thermal ablation	296	292	228	219	150
Treatment Success (%)					
Pulsed field ablation	99.3	99.0	79.7	76.4	73.1
Thermal ablation	98.7	97.3	77.5	74.5	71.3

Table 3. Serious and Nonserious Adverse Events.*

Event	Serious Adverse Events†		Serious or Nonserious Adverse Events‡	
	Pulsed Field Ablation (N=305)	Thermal Ablation (N=302)	Pulsed Field Ablation (N=305)	Thermal Ablation (N=302)
	number of patients (percent)			
Any event	6 (2.0)§	4 (1.3)	7 (2.3)§	6 (2.0)
Death	1 (0.3)	0	1 (0.3)	0
Myocardial infarction	0	0	0	0
Persistent phrenic-nerve palsy	0	0	0	2 (0.7)
Stroke	0	1 (0.3)	0	1 (0.3)
TIA	1 (0.3)	0	1 (0.3)	0
Systemic thromboembolism	0	0	0	0
Cardiac tamponade or perforation	2 (0.7)	0	2 (0.7)	0
Pericarditis	1 (0.3)	0	2 (0.7)	0
Pulmonary edema	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)
Vascular-access complication	1 (0.3)	2 (0.7)	1 (0.3)	2 (0.7)

PFA was faster but no differences in terms of procedural outcomes in PVI-only procedures in paroxysmal AF patients were found.

Circulation: Arrhythmia and Electrophysiology

ORIGINAL ARTICLE

Very Long-Term Follow-Up of Pulmonary Vein Isolation Using Cryoballoon for Catheter Ablation for Atrial Fibrillation: An 8-Year Multicenter Experience

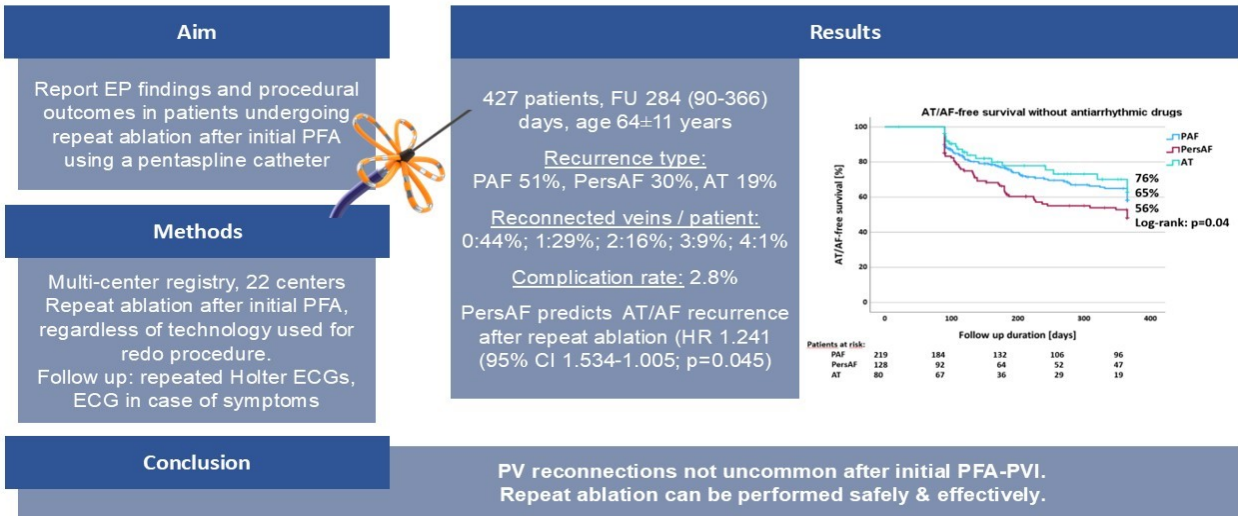
Marco Schiavone^{ID}, MD, PhD*; Giulio Molon^{ID}, MD*; Paolo Pieragnoli, MD; Giuseppe Arena^{ID}, MD; Saverio Iacopino^{ID}, MD; Giovanni Battista Perego^{ID}, MD; Enrico Chieffo^{ID}, MD; Emanuele Bertaglia^{ID}, MD; Giuseppe Stabile^{ID}, MD; Massimiliano Manfrin, MD; Roberto Verlato^{ID}, MD; Umberto Startari, MD; Roberto Rordorf^{ID}, MD; Massimiliano Marini^{ID}, MD; Gaetano Fassini^{ID}, MD; Alessandro Costa^{ID}, MD; Chiara Bartoli, MD; Jacopo Colella, MD; Giulia Girardengo^{ID}, MD; Cinzia Dossena^{ID}, MD; Francesco Rivezzi, MD; Assunta Iuliano, MD; Enrico Baldi^{ID}, MD; Claudio Tondo^{ID}, MD, PhD

Repeat procedures after pulsed field ablation for atrial fibrillation: MANIFEST-REDO study

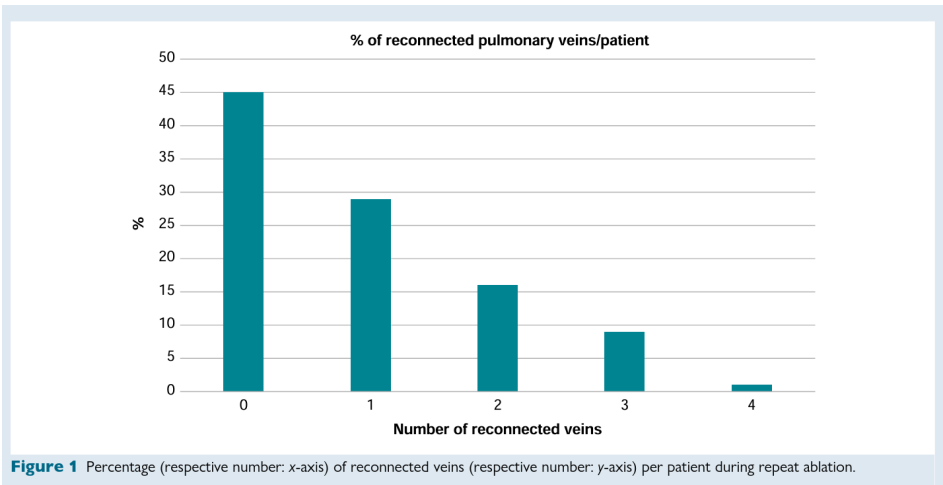
Daniel Scherr ^{1*}, Mohit K. Turagam ², Philippe Maury ^{3,4}, Yuri Blaauw⁵,

CLINICAL DATA!

Central Figure: Repeat Procedures After Pulsed Field Ablation for Atrial Fibrillation: MANIFEST-REDO Study



- The durability of lesions in patients undergoing a repeat procedure after PFA is limited in real-world clinical practice and may contribute to recurrent AF.
- At the time of the repeat procedure, only 45% of patients with recurrences exhibited complete PV isolation.
- Persistent AF as the recurrent arrhythmia is an independent predictor of lower procedural success during follow-up.



- *Data from consecutive patients treated with CB-PVI for symptomatic AF between 2012 and 2018 in 13 institutions were analyzed.*
- *1330 patients were enrolled (28.4% female, mean age was 60.1 ± 10.5 years).*
- *Paroxysmal AF patients were 73.1%, median AF duration was 36.0 (13.0-75.0) months.*

Table 1. Baseline Characteristics of the Study Cohort

	Patients undergoing CB-PVI with at least 5-year follow-up (n=1330)
Age, y; mean $\pm$ SD	60.1 $\pm$ 10.5
Female sex, n (%)	378 (28.4)
Body mass index, median (IQR)	26.3 (24.1–29.0)
Diabetes, n (%)	67 (5.7)
Hypertension, n(%)	604 (46.6)
Hypertensive cardiomyopathy, n (%)	136 (10.6)
Ischemic cardiomyopathy, n (%)	78 (6.1)
Nonischemic cardiomyopathy, n (%)	33 (2.6)
Heart failure, n (%)	26 (2.0)
Valvular heart disease (more than moderate), n (%)	48 (3.7)
Mitral valve, n (%)	37 (2.9)
Aortic valve, n (%)	14 (1.1)
Tricuspid valve, n (%)	6 (0.5)
Chronic kidney disease, n (%)	29 (2.3)
Previous stroke/TIA, n (%)	56 (4.4)
Atrial fibrillation type	
Paroxysmal, n (%)	972 (73.1)
Persistent, n (%)	317 (23.8)
Long-standing persistent, n (%)	41 (3.1)
History of atrial fibrillation (duration in months), median (IQR)	36.0 (13.0–75.0)
History of atrial flutter/ATA, n (%)	185 (17.0)

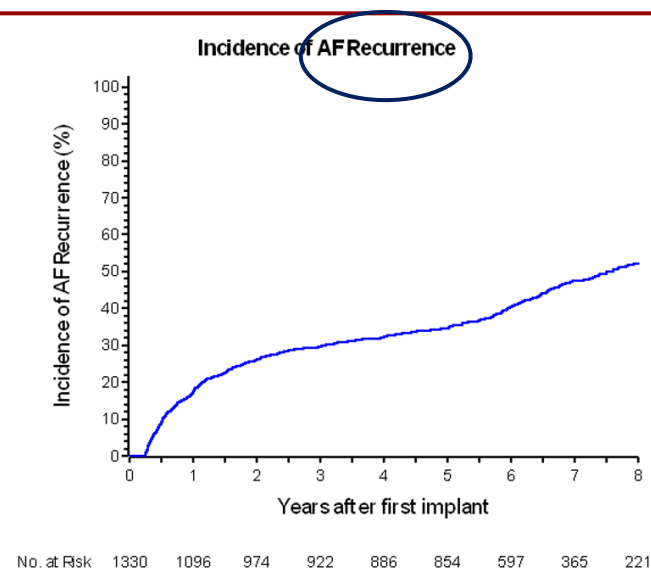
Any symptom, n (%)	1088 (81.8)
Palpitations, n (%)	996 (74.9)
Symptoms other than palpitations, n (%)	1061 (79.8)
EHRA score, median (IQR)	2.0 (1.0–2.0)
I, n (%)	218 (34.5)
II, n (%)	323 (51.2)
III, n (%)	88 (13.9)
IV, n (%)	2 (0.3)
More than 2 antiarrhythmic drugs tested, n (%)	386 (37.3)
OAC contraindications, n (%)	18 (1.4)
CHA2DS2-VASc, median (IQR)	1.0 (0.0–2.0)
0, n (%)	300 (26.4)
1, n (%)	366 (32.2)
2, n (%)	247 (21.7)
3, n (%)	158 (13.9)
4, n (%)	52 (4.6)
≥ 5 , n(%)	14 (1.2)

- *45.9% experienced at least 1 AF / AT / AFL recurrence*
- *A low incidence of progression to permanent AF was seen in the entire cohort (7.0%).*
- *Importantly, 16.3% patients underwent a redo ablation for AF during follow-up.*
- *Among those, in 45.9% of cases all PVs were isolated; the median number of PVs isolated after the index procedure was 3 [1-4] veins.*
- *Very low rate of late adverse events.*

Table 3. Long-Term Outcomes

	n=1330
Median follow-up duration, mo; median (IQR)	81.1 (70.5–98.0)
Patients with at least 1 AF/ATA/AFL recurrence, n (%)	611 (45.9)
Patients with at least 1 redo ablation during follow-up, n (%)	218 (16.3)
Redo ablation for AF, n (%)	209 (95.9)
Redo ablation for left AT/AFL, n (%)	4 (1.8)
Redo ablation for typical AFL, n (%)	2 (0.9)
Redo ablation for focal AT, n (%)	2 (0.9)
Redo ablation for AVNRT, n (%)	1 (0.4)
Findings at redo procedure for AF recurrence, n (%)	209 (100)
All veins isolated, n (%)	96 (45.9)
No. of PV isolated, median (IQR)	3 (1–4)
Three veins isolated, n (%)	27 (12.9)
Two veins isolated, n (%)	29 (13.8)
One vein isolated, n (%)	22 (10.5)
All veins reconnected, n (%)	35 (16.7)
Late adverse events, n (%)	22 (1.7)
Stroke, n (%)	4 (0.3)
TIA, n (%)	2 (0.2)
Major bleedings, n (%)	4 (0.3)
Admissions for acute heart failure, n (%)	2 (0.2)
Acute myocardial infarction, n (%)	4 (0.3)
Pacemaker implantation, n (%)	2 (0.2)
Cardiovascular mortality, n (%)	24 (1.8)

Long-term data about cryo

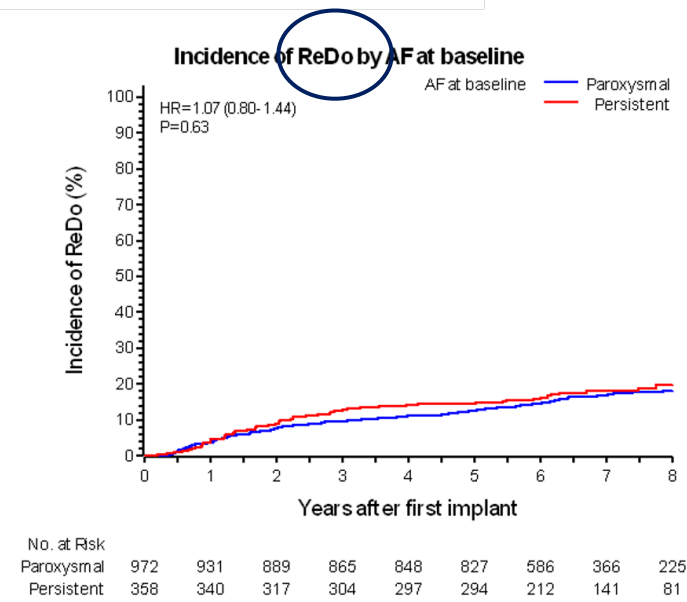


Supplementary Table 1A: Time to first AF relapse

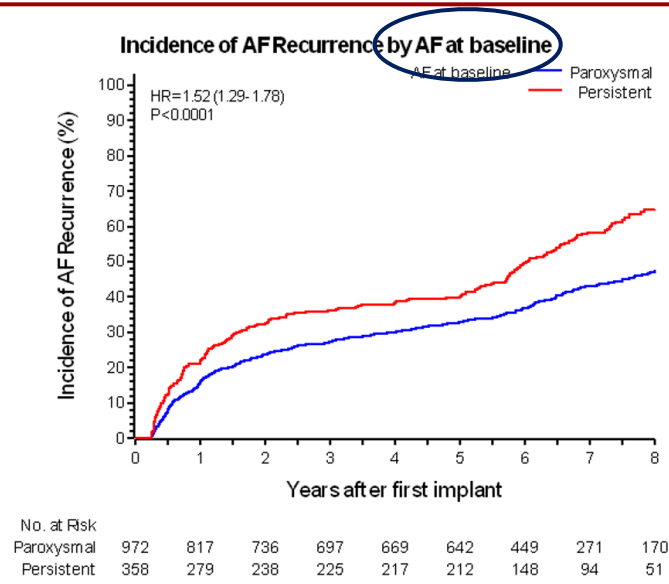
Years after ablation	Number of patients at risk	Cumulative Number of events	Event rate (%) (95% CI)
0	1330	0	0.0% (0.0% - 0.0%)
1	1096	227	17.1% (15.2% - 19.3%)
2	974	345	26.1% (23.8% - 28.5%)
3	922	393	29.7% (27.3% - 32.3%)
4	886	427	32.3% (29.9% - 34.9%)
5	854	458	34.7% (32.2% - 37.3%)
6	597	523	40.4% (37.7% - 43.1%)
7	365	582	47.4% (44.5% - 50.4%)
8	221	611	52.5% (49.4% - 55.8%)

Supplementary Table 1B: Time to first redo ablation

Years after ablation	Number of patients at risk	Cumulative Number of events	Event rate (%) (95% CI)
0	1330	0	0.0% (0.0% - 0.0%)
1	1271	49	96.3% (95.1% - 97.2%)
2	1206	106	92.0% (90.4% - 93.3%)
3	1169	138	89.5% (87.7% - 91.1%)
4	1145	157	88.1% (86.2% - 89.7%)
5	1121	173	86.8% (84.9% - 88.5%)
6	798	194	84.9% (82.8% - 86.8%)
7	507	211	82.8% (80.6% - 84.9%)
8	306	218	81.5% (79.0% - 83.7%)

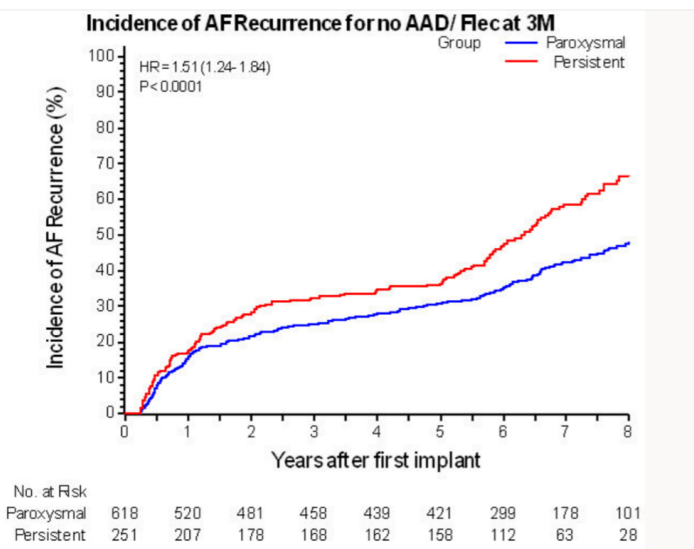


Long-term data about cryo



Supplementary Table 2A: Time to first AF relapse per AF type

Years after ablation	Paroxysmal AF			Persistent AF		
	Pts at risk	Cum. no. of events	Event rate (%) (95% CI)	Pts at risk	Cum. no. of events	Event rate (%) (95% CI)
0	972	0	0.0% (0.0% - 0.0%)	358	0	0.0% (0.0% - 0.0%)
1	817	150	15.5% (13.4% - 17.9%)	279	77	21.6% (17.7% - 26.3%)
2	736	229	23.7% (21.1% - 26.5%)	238	116	32.6% (28.0% - 37.7%)
3	697	264	27.3% (24.6% - 30.2%)	225	129	36.3% (31.5% - 41.5%)
4	669	290	30.0% (27.2% - 33.0%)	217	137	38.5% (33.7% - 43.8%)
5	642	316	32.7% (29.9% - 35.8%)	212	142	40.0% (35.1% - 45.3%)
6	449	350	36.9% (33.9% - 40.0%)	148	173	49.8% (44.6% - 55.2%)
7	271	387	43.1% (39.8% - 46.6%)	94	195	58.2% (52.8% - 63.8%)
8	170	404	47.5% (43.9% - 51.3%)	51	207	64.8% (59.0% - 70.5%)



The rate of AF/atrial tachycardia recurrences progressively increased over time, with an event rate of 52.5% (49.4%–55.8%) at 8-year follow-up, and 78.3% off AADs at the last available follow-up.

Persistent atrial fibrillation and chronic kidney disease were the strongest predictors of late arrhythmia recurrence, highlighting the need for tailored patient selection and long-term monitoring.

Various hypotheses have been proposed to explain the link between CKD and the increased incidence of AF:

- *Neurohormonal activation leading to heightened sympathetic activity*
- *Chronic inflammation*
- *Shared underlying risk factors*

Table 4. ATAs Recurrence Predictors

Variable	Univariate results			Multivariable-adjusted results		
	HR	95% CI	P value	HR	95% CI	P value
Age, y (continuous)	1.01	(1.00–1.01)	0.152	1.00	(0.99–1.01)	0.661
Male sex	0.88	(0.75–1.04)	0.134	0.98	(0.80–1.15)	0.638
Hypertension	1.10	(0.94–1.28)	0.224			
Body mass index	1.00	(0.98–1.02)	0.882			
Diabetes	1.10	(0.79–1.52)	0.579			
Chronic kidney disease	1.72	(1.11–2.65)	0.015	1.77	(1.12–2.82)	0.016
Heart failure	1.27	(0.79–2.06)	0.327			
Persistent atrial fibrillation	1.34	(1.22–1.43)	<0.001	1.36	(1.14–1.62)	<0.001
History of Stroke/TIA	1.06	(0.74–1.53)	0.751			
Ischemic cardiomyopathy	0.82	(0.59–1.14)	0.235			
AF during Blanking Period of 90 d	2.68	(2.12–3.39)	<0.001	3.46	(2.75–4.35)	<0.001
AF during Blanking Period of 60 d	2.34	(1.74–3.14)	<0.001			

Bold indicates statistically significant values. AF indicates atrial fibrillation; ATA, atrial tachyarrhythmia; HR, hazard ratio; and TIA, transient ischemic attack.

*This study has several **limitations**.*

- *Being observational, it inherently carries limitations related to data collection.*
- *During follow-up, Holter ECGs were collected annually or in the case of symptoms, which may have underestimated arrhythmia recurrence when compared with other studies evaluating outcomes of different ablation techniques with implantable loop recorders.*
- *Most patients were treated with the Arctic Front Advance CB, which has some technical differences compared with more recent CB devices.*



CB with PVI as the index procedure for AF ablation resulted in a favorable long-term outcome in patients with symptomatic AF, with limited progression towards permanent AF during follow-up.

Nearly half of the patients undergoing redo AF ablation procedures had all PVs isolated after the initial procedure, and PeAF was the strongest predictor of recurrences at long-term follow-up.

