Supplementary Appendix

Table S1. Enrollment summary by center

Country	City	Investigator	Center	Enrolled Subjects	Randomized Subjects
Argentina	Buenos Aires	F. Scazzuso	Instituto Cardiovascular de Buenos Aires (ICBA)	1	1
Australia	Clayton	S. Healy	Monash Medical Center	15	15
Belgium	Brussel	GB. Chierchia	Vrije Universiteit Brussel	25	25
Croatia	Zagreb	N. Pavlovic	Sestre Milosrdnice University Hospital Centre,	37	37
Croatia	Zagreb	V. Velagic	University Hospital Centre Zagreb	30	30
France	Tours	C. Loose	Clinique Saint-Gatien	2	2
France	Rouen	F. Anselme	CHU de Rouen	5	5
France	Amiens	JS. Hermida	Centre Hospitalier Universitaire d'Amiens-Picardie	21	20
France	Paris	N. Badenco	AP-HP Sorbonne Université, Hopital Pitié-Salpétrière	10	10
France	Grenoble	P. Defaye	Centre Hospitalier Universitaire de Grenoble-Alpes	1	1
Germany	Kaiserslautern	B. Schumacher	Westpfalz-Klinikum	0	0
Germany	Hamburg	C. Meyer	University Heart Center	10	10
Germany	Frankfurt	K.R. Julian Chun	Cardioangiologisches Centrum Bethanien (CCB)	1	1
Germany	Bad Nauheim	M. Kuniss	Kerckhoff Heart Center	31	31
Germany	München	U. Dorwarth	Klinik Bogenhausen	2	2
Italy	Massa Carrara	G. Arena	Ospedale Apuane	13	13
Italy	Cotignola	S. Iacopino	Maria Cecilia Hospital	7	6
Netherlands	Eindhoven	L. Dekker	Catharina Ziekenhuis	2	2
Netherlands	Rotterdam	T. Szili-Torok	Erasmus Medisch Centrum	0	0
Norway	Bergen	J. Chen	Haukeland University Hospital	7	7

Table S2. General procedural characteristics in patients undergoing ablation in the cryoballoon arm

Procedural Characteristics	Cryoballoon CA (N = 107)
Number of patients who received Cryo-Ablation	96 (89.7%)
Procedure duration (min)	83.8±28.6
Fluoroscopy time (RAO+LAO) (min)	16.4±13.7
Length of catheter exposure time in left atrium (min)	60.7±44.1
Adjunctive mapping or visualization device used	3 (2.8%)

1 **Table S3. Procedural characteristics by vein in patients undergoing ablation in the cryoballoon arm**

Procedure Characteristic	Vein					
	LSPV	LIPV	LCPV	RSPV	RIPV	RMPV
Patients without vein present	11 (10.3%)	11 (10.3%)	85 (79.4%)	0 (0.0%)	0 (0.0%)	88 (82.2%)
28 mm cryoballoon used	84 (78.5%)	83 (77.6%)	11 (10.3%)	95 (88.8%)	96 (89.7%)	8 (7.5%)
23 mm cryoballoon used	1 (0.9%)	2 (1.9%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)
Max grade of occlusion:						
I	1 (0.9%)	1 (0.9%)	1 (0.9%)	1 (0.9%)	1 (0.9%)	1 (0.9%)
II	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (4.7%)	0 (0.0%)
III	5 (4.7%)	10 (9.3%)	4 (3.7%)	5 (4.7%)	15 (14.0%)	3 (2.8%)
IV	79 (73.8%)	74 (69.2%)	7 (6.5%)	88 (82.2%)	75 (70.1%)	3 (2.8%)
Focal cryo catheter used?	2 (1.9%)	2 (1.9%)	0 (0.0%)	1 (0.9%)	4 (3.7%)	2 (1.9%)
Number of cryo-applications	1.4±0.6	1.4±0.6	2.4±1.5	1.4±0.6	1.4±0.8	1.3±0.5
Number of bonus freezes performed	0.7±0.6	0.7±0.6	1.3±0.8	0.7±0.7	0.7±0.6	0.5±0.7
Minimum temperature (degrees Celsius)	46.7±11.6	44.8±7.2	49.4±6.5	49.8±6.0	46.8±6.7	43.3±9.5
Achieve mapping catheter utilized?						
No	3 (2.8%)	4 (3.7%)	0 (0.0%)	6 (5.6%)	3 (2.8%)	0 (0.0%)
Yes, 15 mm	8 (7.5%)	8 (7.5%)	1 (0.9%)	10 (9.3%)	8 (7.5%)	2 (1.9%)
Yes, 20 mm	74 (69.2%)	73 (68.2%)	10 (9.3%)	80 (74.8%)	85 (79.4%)	6 (5.6%)
Achieve mapping catheter online signal:						
No	16 (15.0%)	30 (28.0%)	7 (6.5%)	28 (26.2%)	33 (30.8%)	3 (2.8%)
Yes	63 (58.9%)	48 (44.9%)	4 (3.7%)	61 (57.0%)	56 (52.3%)	4 (3.7%)
If yes, time to effect (seconds)	54.8±37.8	34.6±18.4	46.6±25.8	44.0±45.9	49.1±32.0	70.3±73.6
If premature freeze interruption, reason						
No premature freeze interruption	74 (69.2%)	72 (67.3%)	9 (8.4%)	76 (71.0%)	81 (75.7%)	8 (7.5%)

Technical reason	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Patient discomfort	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Phrenic nerve palsy	1 (0.9%)	0 (0.0%)	0 (0.0%)	4 (3.7%)	1 (0.9%)	0 (0.0%)
Dislocation	1 (0.9%)	2 (1.9%)	0 (0.0%)	1 (0.9%)	1 (0.9%)	0 (0.0%)
Other	2 (1.9%)	0 (0.0%)	1 (0.9%)	5 (4.7%)	5 (4.7%)	0 (0.0%)

1 Values are n (%) or mean ± standard deviation. LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; LCPV,
2 left common pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; RMPV, right middle
3 pulmonary vein.

4

Table S4. Atrial fibrillation detection and percent of time in atrial fibrillation during 7-day Holter monitoring at each follow-up visit amongst patients in the intention-to-treat cohort.

	Cryoballoon CA	AAD
Baseline		
Number of subjects with measure available, N (%)	84 (100.0%)	88 (100.0%)
AF burden amongst all subjects, Mean (StD)	1.9 (7.7)	2.3 (10.3)
Number of subjects with AF detected, N (%)	15 (17.9%)	17 (19.3%)
AF burden amongst subjects with AF detected, Mean (StD)	10.9 (15.6)	11.7 (21.6)
1 Month FUP		
Number of subjects with measure available, N (%)	81 (98.8%)	85 (100.0%)
AF burden amongst all subjects, Mean (StD)	0.6 (4.5)	1.6 (5.8)
Number of subjects with AF detected, N (%)	4 (4.9%)	17 (20.0%)
AF burden amongst subjects with AF detected, Mean (StD)	12.5 (18.5)	7.9 (11.0)
3 Month FUP		
Number of subjects with measure available, N (%)	88 (100.0%)	96 (100.0%)
AF burden amongst all subjects, Mean (StD)	0.3 (2.0)	1.1 (7.6)
Number of subjects with AF detected, N (%)	3 (3.4%)	10 (10.4%)
AF burden amongst subjects with AF detected, Mean (StD)	9.3 (6.7)	10.9 (22.3)
6 Month FUP		
Number of subjects with measure available, N (%)	86 (100.0%)	86 (100.0%)
AF burden amongst all subjects, Mean (StD)	0.0 (0.2)	2.3 (11.6)
Number of subjects with AF detected, N (%)	2 (2.3%)	9 (10.5%)
AF burden amongst subjects with AF detected, Mean (StD)	1.0 (0.0)	21.6 (30.9)
9 Month FUP		
Number of subjects with measure available, N (%)	78 (100.0%)	82 (98.8%)
AF burden amongst all subjects, Mean (StD)	0.8 (6.3)	1.1 (5.1)
Number of subjects with AF detected, N (%)	5 (6.4%)	9 (10.8%)
AF burden amongst subjects with AF detected, Mean (StD)	12.8 (23.7)	9.9 (12.8)
12 Month FUP		
Number of subjects with measure available, N (%)	78 (98.7%)	75 (98.7%)
AF burden amongst all subjects, Mean (StD)	0.0 (0.2)	1.7 (8.8)
Number of subjects with AF detected, N (%)	1 (1.3%)	7 (9.2%)
AF burden amongst subjects with AF detected, Mean (StD)	2.0 ( )	18.3 (24.5)

The presence of atrial fibrillation and the estimated percent of time in atrial fibrillation was classified by the Holter core lab.

Figure S1. Boxplot showing the estimated percent of time in atrial fibrillation during 7-day Holter monitoring at each follow-up visit amongst patients in the intention-to-treat cohort. The presence of atrial fibrillation and the estimated percent of time in atrial fibrillation was classified by the Holter core lab.