ADVANCING IN CRYOABLATION OF ATRIAL FIBRILLATION AFTER 10 YEARS OF EXPERIENCE: STATE OF THE ART AND WHAT'S COMING

Roberto Verlato

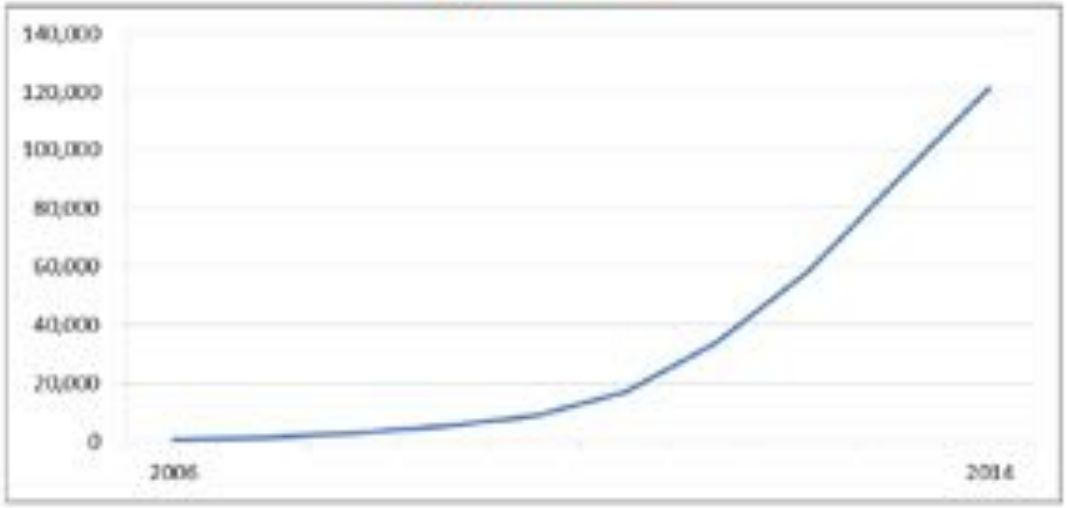
U.O.A. Cardiologia, Camposampiero, Padova

Venice Arrhythmias 2015

Extensive Worldwide Adoption and Clinical Experience

- 250 peer-reviewed articles and numerous abstracts
- 9 years of clinical experience
- Used in over 50 countries worldwide

Worldwide Cumulative Growth of Arctic Front Cryoballoon



1 Medtronic, Inc. data on file.

2005: FIRST ANIMAL EXPERIENCE IN 8 DOGS

Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 46, No. 10, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.07.046

Efficacy and Safety of Circumferential Pulmonary Vein Isolation Using a Novel Cryothermal Balloon Ablation System

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Rochester, Minnesota; and Ribeirão Preto, Brazil

OBJECTIVES We sought to evaluate the efficacy and safety of a novel cryothermal balloon ablation system in creating pulmonary vein (PV) isolation.

BACKGROUND Pulmonary vein isolation using standard radiofrequency ablation techniques is limited by procedure-related complications, such as thrombus formation and PV stenosis. Cryothermal ablation may reduce the risk of such complications.

METHODS Eight dogs underwent circumferential ablation of both superior PVs for either 4 or 8 min using a cryothermal balloon catheter (CryoCath Technologies Inc., Kirkland, Canada). Both fluoroscopy and intracardiac ultrasound (ICE)-guided balloon and Lasso catheter positioning at the PV ostia assessed short-term PV integrity. In six additional dogs, long-term PV integrity was assessed by computed tomography at 16 weeks after ablation.

RESULTS Successful electrical isolation was achieved acutely in 14 of 16 (87.5%) PVs and was confirmed in one-week survival studies in 10 of 12 (83%) PVs. Successful isolation was higher in the absence of any peri-balloon flow leak as seen by ICE ($p = 0.015$), and with balloon temperatures $\leq -80°C$ ($p = 0.015$). Cryolesions were located at the veno-atrial junction and were homogeneous, with intact endothelium and free of thrombus formation. Although limited angiographic PV narrowing was noted in the early follow-up period, no significant PV narrowing was seen long-term. Right phrenic nerve injury was seen in 50% of the animals studied at one week.

CONCLUSIONS This novel cryothermal balloon ablation system is effective for isolating PVs, but injury to the right phrenic nerve was noted in this early experience. Further studies are needed to assess the long-term efficacy and safety of this technique. (J Am Coll Cardiol 2005;46:1902–12)

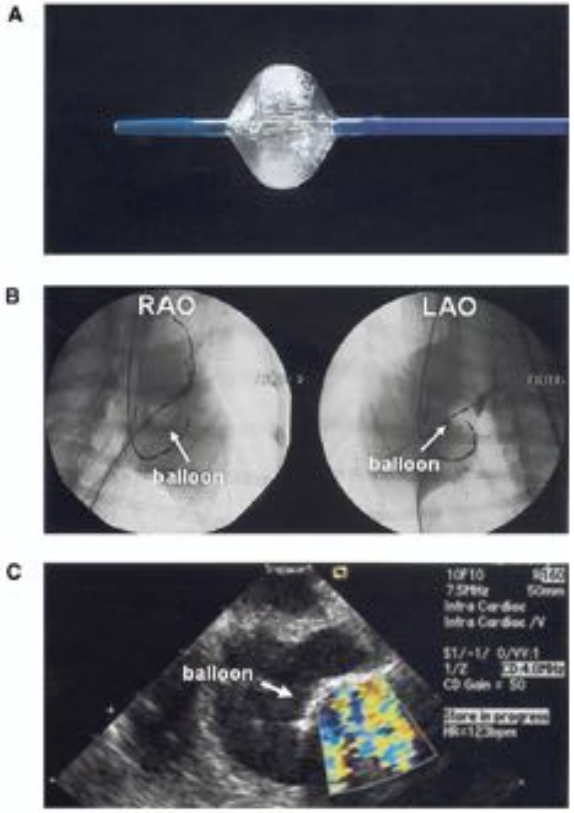


Figure 1. (A) Photograph of the cryothermal balloon catheter. (B) Fluoroscopic image of the inflated balloon engaged at the left superior pulmonary vein (LSPV) orifice (**arrows**). (C) Intracardiac echocardiographic image of the inflated balloon positioned at the orifice of the LSPV (**arrow**), illustrating an example of an unsuccessful occlusion of the pulmonary vein orifice, with a peri-balloon flow leak as seen by color Doppler flow. LAO = left anterior oblique projection; RAO = right anterior oblique projection.

SARABANDA, JACC 2005

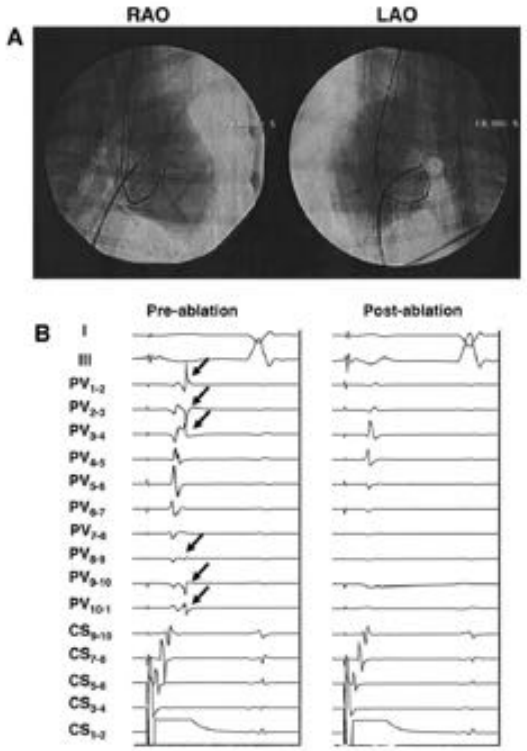
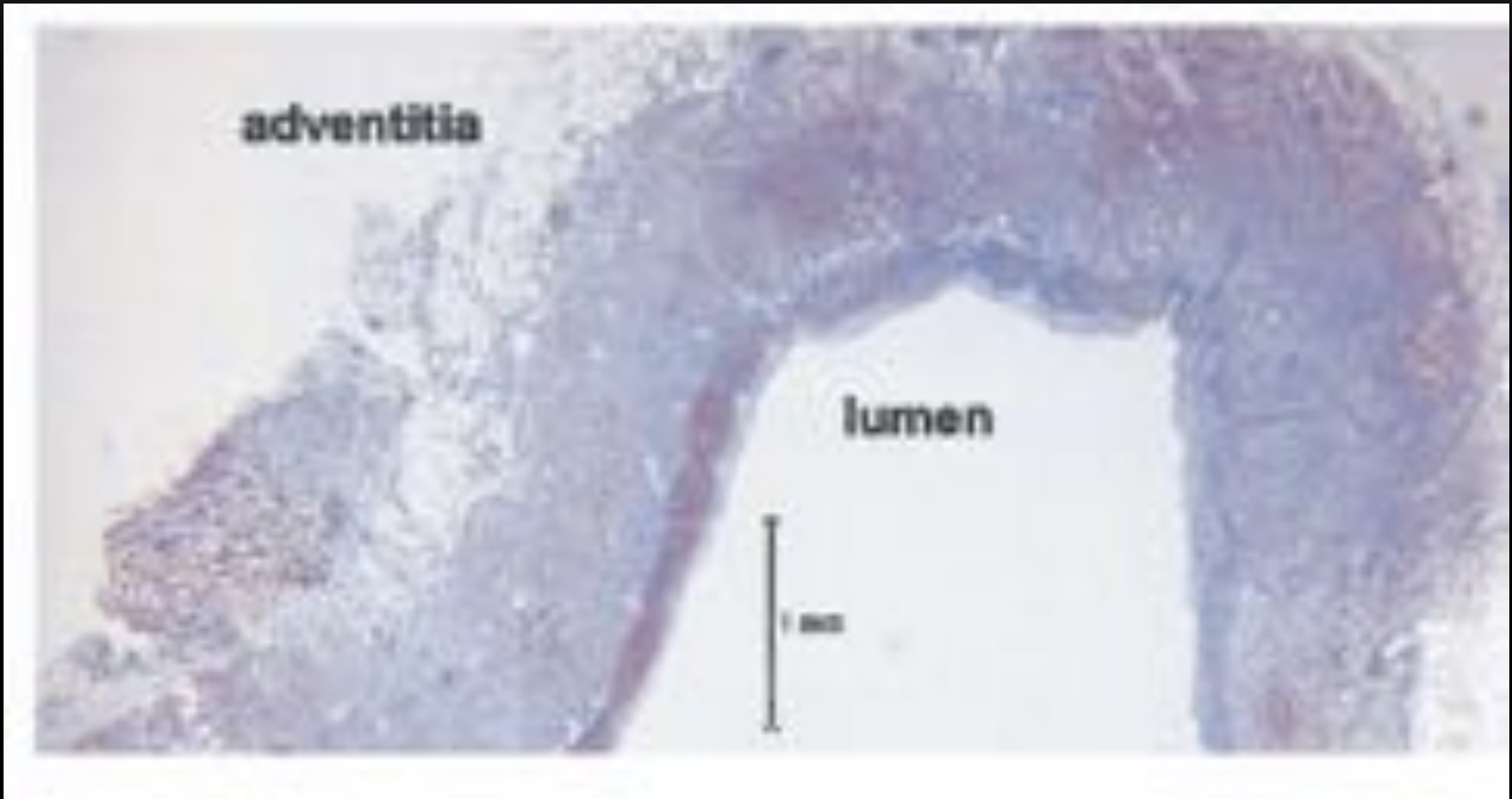


Figure 2. Successful circumferential cryoablation of the left superior pulmonary vein. (A) Fluoroscopic image of the Lasso catheter positioned at the pulmonary vein (PV) ostium. (B) Tracings of the surface electrocardiographic leads I and III and PV ostial electrograms as seen by the Lasso catheter (PV_{1-2}

COMPLETE CIRCUMFERENTIAL AND TRANSMURAL LESION AT THE VENO-ATRIAL JUNCTION



Complete circumferential and transmural lesion at the veno-atrial junction of the left superior pulmonary vein (LSPV)

Sarabanda, Jacc 2005

2007-2011
23 PUBBLICATIONS
FOUR EUROPEAN STUDIES, NON-RANDOMIZED
AND THE STOP-AF TRIAL

Neumann T, Bad Nauhaim, Germany, 346 pts
Circumferential pulmonary vein isolation with the cryoballoon technique: results from a prospective 3-center study. JACC 2008; 52: 273-278

Van Belle Y, Rotterdam, The Nederland, 138 pts
One-year follow-up after cryoballoon isolation of pulmonary veins in patients with paroxysmal atrila fibrillation. EUROPACE 2008; 10: 1271-1276

Malmborg H, Uppsala, Sweden 40 pts
Acute and clinical effects of cryoballoon pulmonary vein isolation in patients with symptomatic paroxysmal and persistent atrial fibrillation. EUROPACE 2008: 10: 1277-1280

Dorwarth U, Munich, Germany, 146 pts: < 83 seconds time to PVI = stable PVI
Pilmonary vein electrophysiology during cryoablation as a predictor for procedural success. J Interv Card Electrophysiol 2011: 32: 205-211

EARLY EUROPEAN EXPERIENCES SHOWED ACCEPTABLE SUCCESS RATE AND LOW ADVERSE EVENT RATES, MOSTLY RIGHT PHRENIC NERVE PALSY

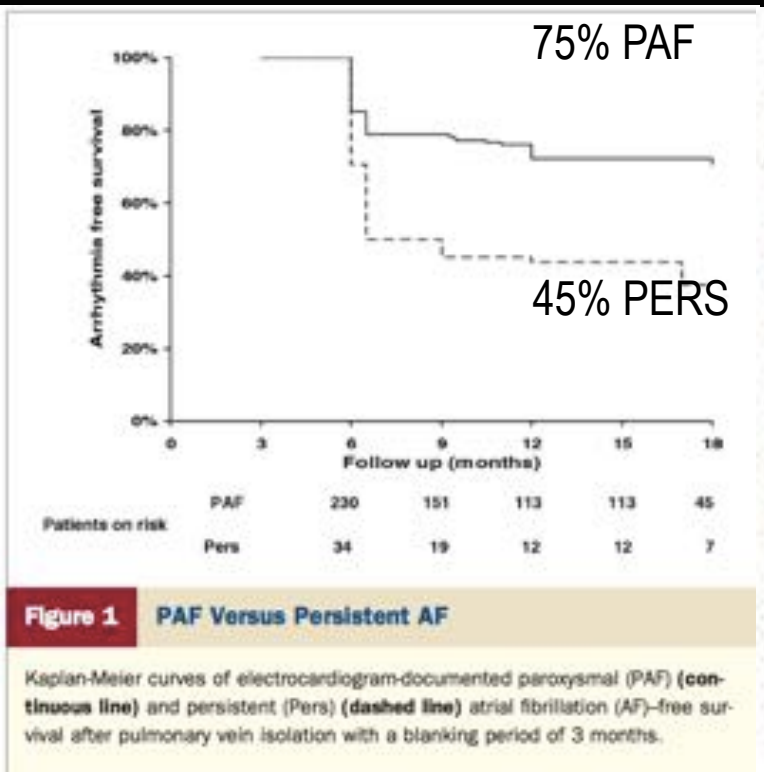


Figure 1 **PAF Versus Persistent AF**

Kaplan-Meier curves of electrocardiogram-documented paroxysmal (PAF) **(continuous line)** and persistent (Pers) **(dashed line)** atrial fibrillation (AF)–free survival after pulmonary vein isolation with a blanking period of 3 months.

Procedural characteristics. The median total procedure time was 170 (interquartile range 25/75 = 140 to 195) min. The median fluoroscopy time was 40 (30 to 57) min. Total cryoablation time was 46 (26 to 60) min/patient. Time of applications per freeze was 300 (range 28 to 480) s with a median number of applications 11 (9 to 13). The median number of cryoballoon applications per PV was 2.8 (2.3 to 3.4). Early discontinuation of an application was mainly due to right phrenic nerve palsy (PNP) detected by deep breathing or stimulation of the right phrenic nerve during ablation of the right superior PV.

97% of PVs disconnected, 5 minutes x 2-3 freezing cycles / vein

Neumann T, Bad Nauhaim, Germany

Circumferential pulmonary vein isolation with the cryoballoon technique: results from a prospective 3-center study. JACC 2008; 52: 273-278

Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 61, No. 14, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.11.064

Cryoballoon Ablation of Pulmonary Veins for Paroxysmal Atrial Fibrillation

First Results of the North American Arctic Front (STOP AF) Pivotal Trial

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Rochester, Minnesota; Dallas, Texas; Tampa, Florida; Quebec, Canada; New York, New York; Minneapolis, Minnesota; and Wayland and Boston, Massachusetts

Objectives This study sought to assess the safety and effectiveness of a novel cryoballoon ablation technology designed to achieve single-delivery pulmonary vein (PV) isolation.

Background Standard radiofrequency ablation is effective in eliminating atrial fibrillation (AF) but requires multiple lesion delivery at the risk of significant complications.

Methods Patients with documented symptomatic paroxysmal AF and previously failed therapy with ≥1 membrane active antiarrhythmic drug underwent 2:1 randomization to either cryoballoon ablation (n = 163) or drug therapy (n = 82). A 90-day blanking period allowed for optimization of antiarrhythmic drug therapy and reablation if necessary. Effectiveness of the cryoablation procedure versus drug therapy was determined at 12 months.

Results Patients had highly symptomatic AF (78% paroxysmal, 22% early persistent) and experienced failure of at least one antiarrhythmic drug. Cryoablation produced acute isolation of three or more PVs in 98.2% and all four PVs in 97.6% of patients. PVs isolation was achieved with the balloon catheter alone in 83%. At 12 months, treatment success was 69.9% (114 of 163) of cryoblation patients compared with 7.3% of antiarrhythmic drug patients (absolute difference, 62.6% [p < 0.001]). Sixty-five (79%) drug-treated patients crossed over to cryoablation during 12 months of study follow-up due to recurrent, symptomatic AF, constituting drug treatment failure. There were 7 of the resulting 226 cryoablated patients (3.1%) with a >75% reduction in PV area during 12 months of follow-up. Twenty-nine of 259 procedures (11.2%) were associated with phrenic nerve palsy as determined by radiographic screening; 25 of these had resolved by 12 months. Cryoablation patients had significantly improved symptoms at 12 months.

Conclusions The STOP AF trial demonstrated that cryoballoon ablation is a safe and effective alternative to antiarrhythmic medication for the treatment of patients with symptomatic paroxysmal AF, for whom at least one antiarrhythmic drug has failed, with risks within accepted standards for ablation therapy. (A Clinical Study of the Arctic Front Cryoablation Balloon for the Treatment of Paroxysmal Atrial Fibrillation [Stop AF]; NCT00259978) (J Am Coll Cardiol 2013;61:1713–23) © 2013 by the American College of Cardiology Foundation

FIRST PROSPECTIVE RANDOMIZED TRIAL

Cryo vs drugs,

2:1 randomization
Cryo in 163 pts

PAF

245 pts

STOP-AF RESULTS: 63-69% FREE FROM ANY T.A.

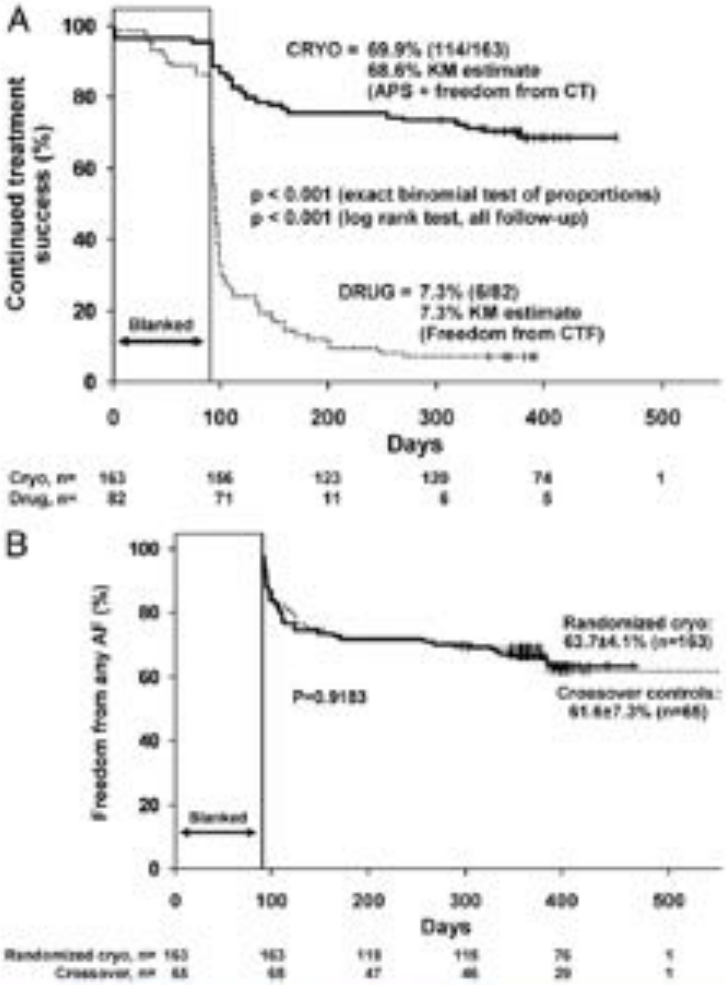


Figure 3 Procedural Success Given as Freedom From CTF as a Function of Time

(A) Intention-to-treat primary effectiveness endpoint for freedom from chronic treatment failure (CTF) between patients treated with cryoablation and those treated with drugs. (B) Freedom from any AF between the on-treatment cryoablation and drug-treated patients. KM = Kaplan-Meier estimates; OR = odds ratio.

PVI: 91%

23 and 28 mm CB-I

CONTEMPORARY REVIEW

Efficacy and safety of cryoballoon ablation for atrial fibrillation: A systematic review of published studies

Jason G. Andrade, MD,* Paul Khairy, MD, PhD,* Peter G. Guerra, MD,* Marc W. Deyell, MD, MSc,† Lena Rivard, MD,* Laurent Macle, MD,* Bernard Thibault, MD, FHRS,* Mario Talajic, MD, FHRS,* Denis Roy, MD, FHRS,* Marc Dubuc, MD, FHRS*

*From the *Electrophysiology Service, Department of Cardiology, Montreal Heart Institute, Université de Montréal, Montreal, Quebec, Canada, and †Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.*

Introduction

Catheter ablation for atrial fibrillation (AF) is centered on electrical isolation of pulmonary veins (PVs) through circumferential lesions around PV ostia. Focal point-by-point radiofrequency (RF) ablation has shown considerable success in treating paroxysmal AF.[1,2] However, major complications include cardiac perforation with pericardial tamponade, injury to adjacent structures (esophagus, phrenic nerve, and aorta), and pulmonary vein stenosis (PVS).[1–5] Furthermore, the procedure is complex, time consuming, and highly dependent on operator competency given the difficulties associated with creating contiguous curvilinear lesions with focal ablation. As such, considerable effort has been directed toward deriving more effective and safer approaches.

Balloon-based ablation systems potentially offer a simpler and faster means of achieving pulmonary vein isolation (PVI) that, theoretically, is less reliant on operator dexterity. Concurrently, cryothermal energy offers advantages over RF energy, including increased catheter stability, less endothelial disruption with lower thromboembolic risk, and minimal tissue contraction with healing, an observation thought to result in less esophageal damage and PVS.[6–11] The objective of this study was to systematically review the available literature to more precisely define the efficacy and safety of cryoballoon ablation for paroxysmal and persistent AF.

Methods

This systematic review was performed using a predetermined protocol and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[12]

Search strategy

To identify and retrieve all potentially relevant literature describing the outcomes of cryoballoon ablation for AF, we conducted a literature search with the assistance of reference librarians and investigators trained in systematic review procedures in MEDLINE, Embase, and BIOSIS. Search terms included "atrial fibrillation" [MeSH and All Fields], "Cryosurgery" [MeSH], and "(cryo: or cryosurg" or cryoballoon).mp". The search was limited to Humans, Adults (19+ years), and publication date between January 2000 and January 2011. The language was not restricted to English.

In addition, secondary source documents were identified by manual review of reference lists, review articles, editorials, and guidelines, and by contacting experts in the field. A manual review of the Science Citation Index was undertaken for articles selected for inclusion.

Study selection

Identified abstracts were retained if they made specific reference to cryoballoon for AF ablation. Articles identified from abstract screening underwent full-text review to determine eligibility for data extraction based on the following criteria: (1) original data in humans reported (animal and in vitro studies were excluded); (2) study design consisting of a case series, case-control study, cohort study, or controlled trial (abstracts, case reports, letters, comments, reviews, and meta-analyses were excluded); and (3) absolute numbers for study endpoints were reported or could be derived from available data.

KEYWORDS Atrial fibrillation; Catheter ablation; Cryoablation

ABBREVIATIONS **AAD** = antiarrhythmic drug; **AF** = atrial fibrillation; **CI** = confidence interval; **PNP** = phrenic nerve palsy; **PRISMA** = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **PV** = pulmonary vein; **PVI** = pulmonary vein isolation; **PVS** = pulmonary vein stenosis; **RF** = radiofrequency; **RIPV** = right inferior pulmonary vein; **RSPV** = right superior pulmonary vein (Heart Rhythm 2011;8:1444–1451)

Dr. Khairy is supported by a Canada Research Chair in Electrophysiology and Adult Congenital Heart Disease. Dr. Dubuc is a consultant for Medtronic (Medtronic CryoCath LP). **Address reprint requests and correspondence:** Dr. Marc Dubuc, Electrophysiology Service, Montreal Heart Institute, 5000 Belanger Street East, Montreal, QC, Canada, H1T 1C8. E-mail address: marc.dubuc@hellbent.ca. (Received February 5, 2011; accepted March 22, 2011.)

HEART RHYTHM 2011 8:1444-1451

ANDRADE META-ANALYSIS: 19 studies, 974 pts
98.8% THE ACUTE PROCEDURAL SUCCESS

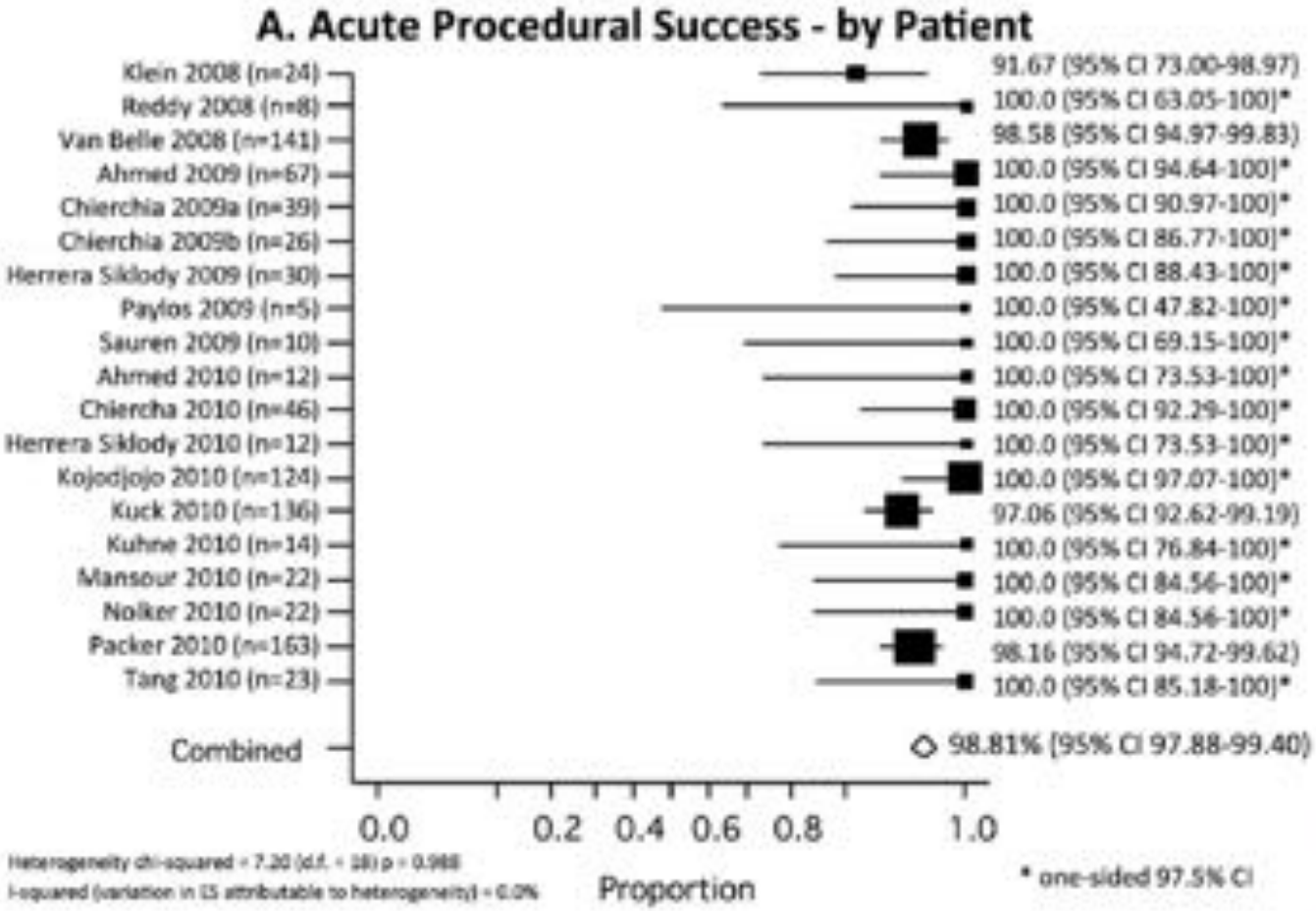


Figure 2 Acute procedural success as defined by complete isolation of all targeted pulmonary veins. A: Per patient

A: PAF + 3-Month blanking

B: PAF w/o 3-Month blanking

C: Persistent AF + 3-Month blanking

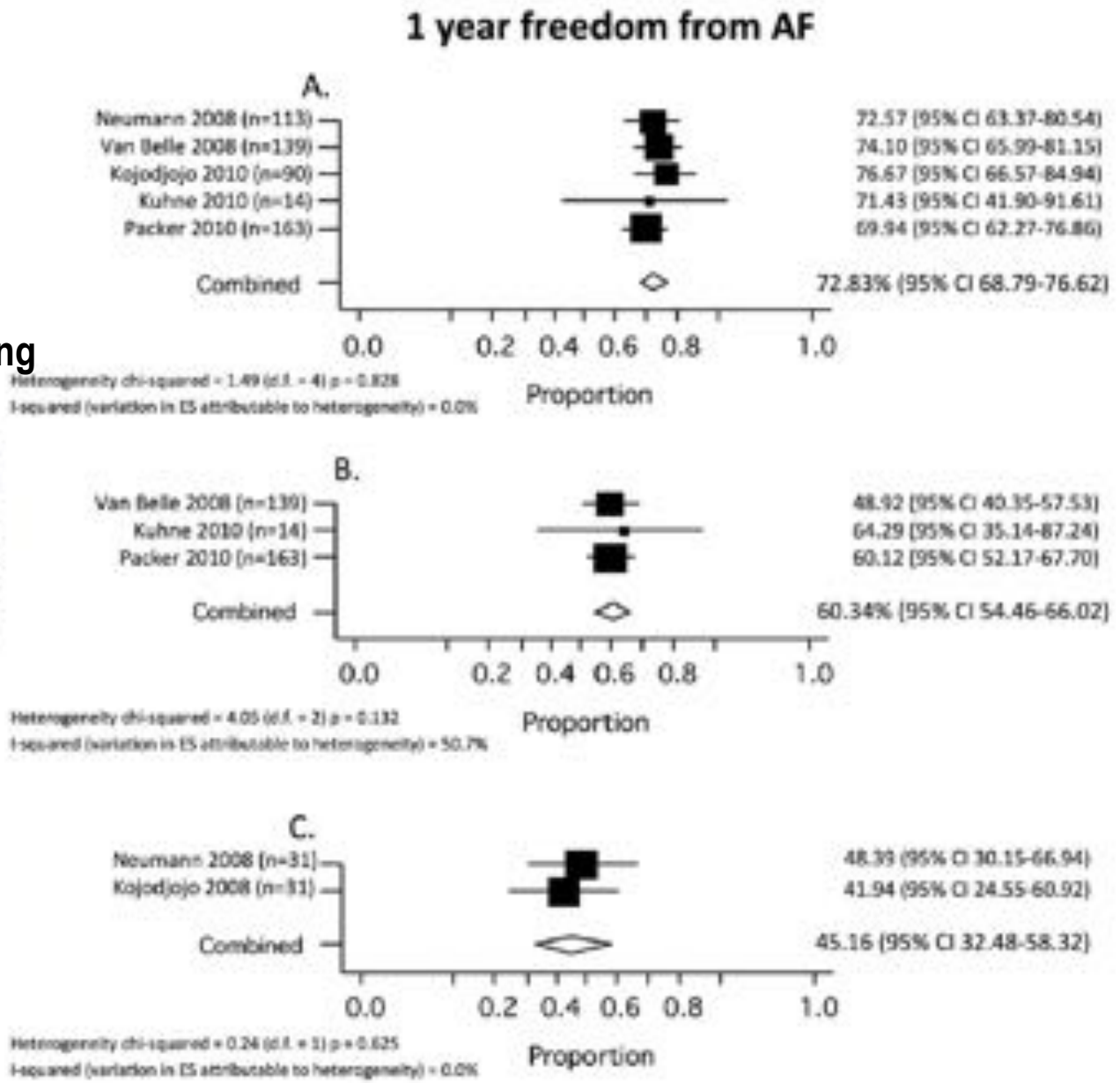


Figure 3 One-year freedom from recurrent atrial fibrillation (AF). A: Patients with paroxysmal AF after a 3-month blanking period. B: Patients with paroxysmal AF without a 3-month blanking period. C: Patients with persistent AF after a 3-month blanking period. CI = confidence interval; ES = effect size.

MORE PNP, LESS TAMPONADE, PVS, LA-ESO FISTULA, STROKE-

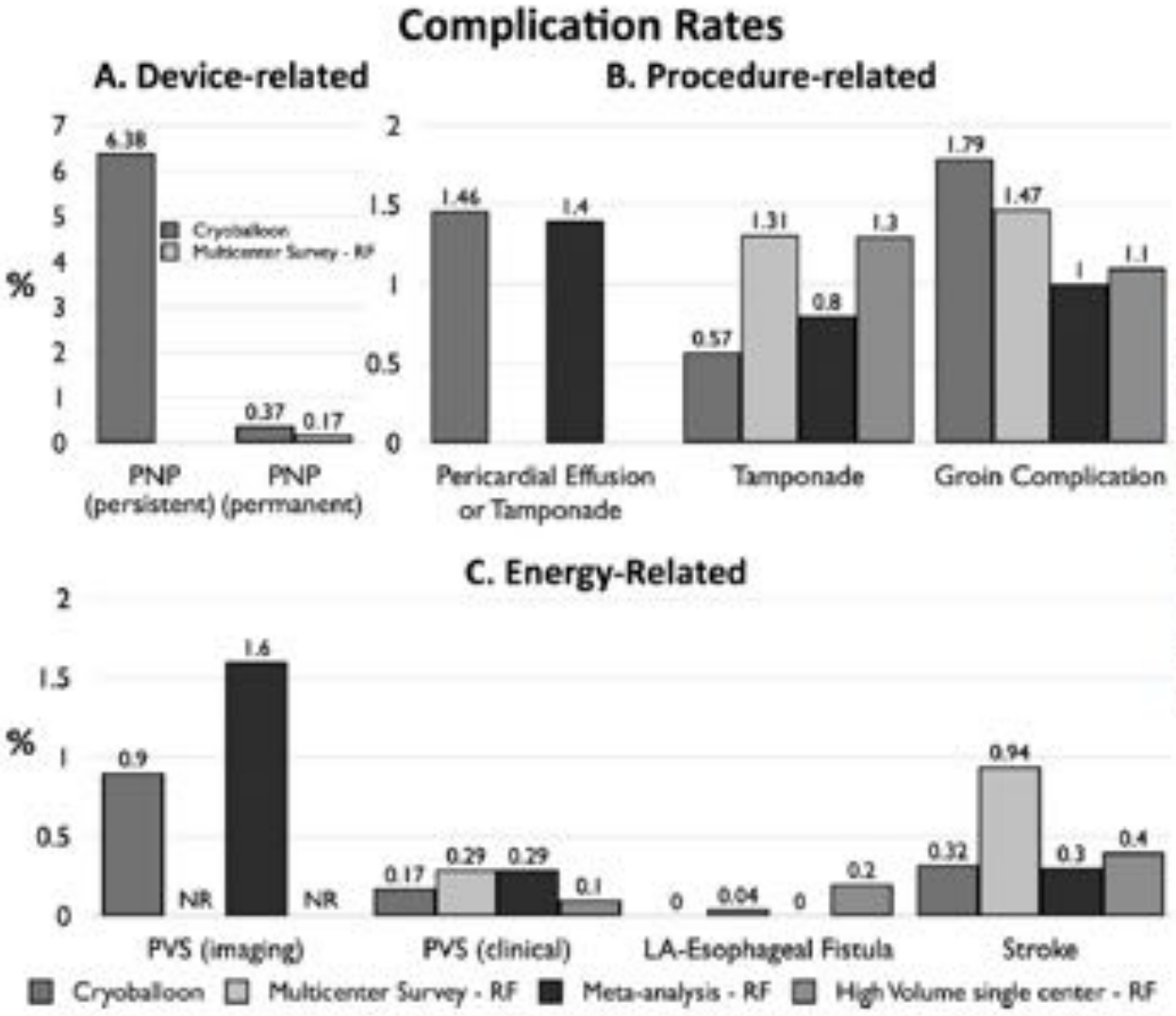


Figure 4 Complication rates for cryoballoon atrial fibrillation ablation. A: Device-related complications. B: Procedure-related complications. C: Energy-related complications. For comparison, three studies reporting complications with radiofrequency (RF) ablation are depicted: a multicenter survey,[4] a meta-analysis,[2] and a high-volume single center.[5] LA = left atrium; NR = not reported; PNP = phrenic nerve palsy; PVS = pulmonary vein stenosis.

Cryoballoon Therapy Now a Standard Treatment for AF Ablation

2012 HRS Consensus Statement

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

Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Patient Selection, Procedural Techniques, Patient Management and Follow-up, Definitions, Endpoints, and Research Trial Design. *Heart Rhythm.* April 2012;9(4):632-696.

IN 2012 CB-1 EVOLVED , CB-ARCTIC FRONT II BECAME AVAILABLE, MAKING IMMEDIATELY OBSOLETE THE CB-I TECH

THE CORE DIFFERENCE BETWEEN CB-1 AND -2: EQUATORIAL ONLY COOLING ZONE VS THE ENTIRE DISTAL HALF OF BALLOON

Arash Aryana
Received: 5 April 2014 / Accepted: 29 July 2014

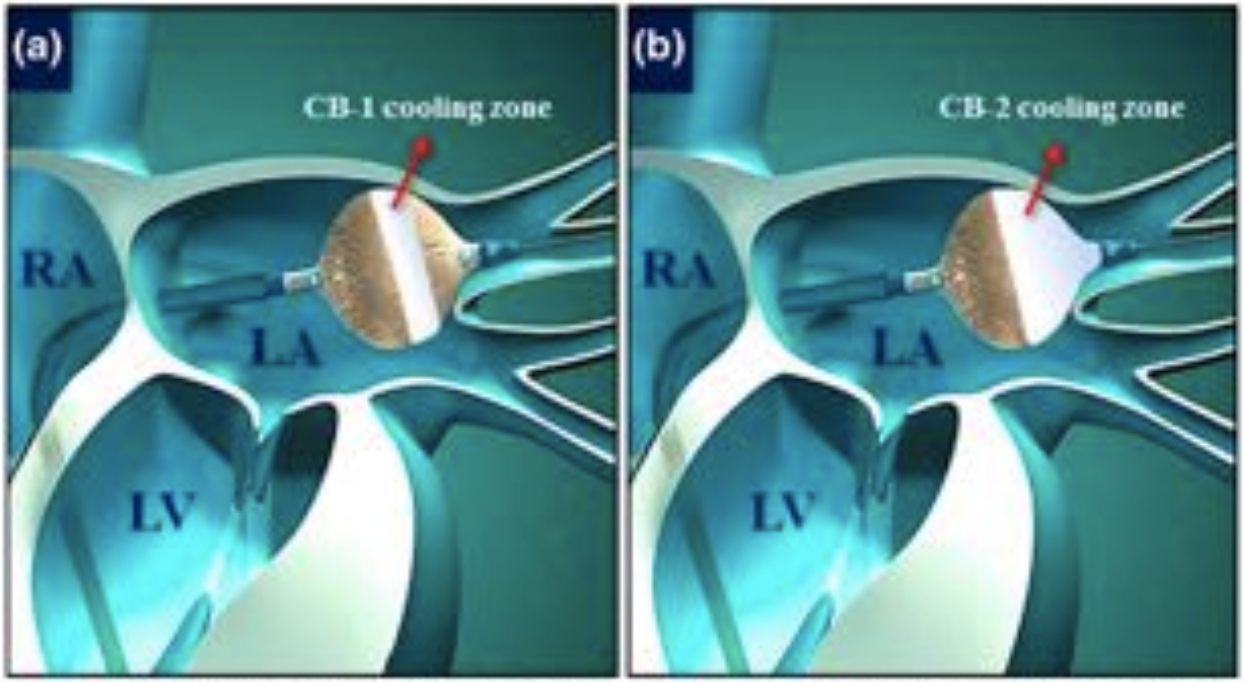
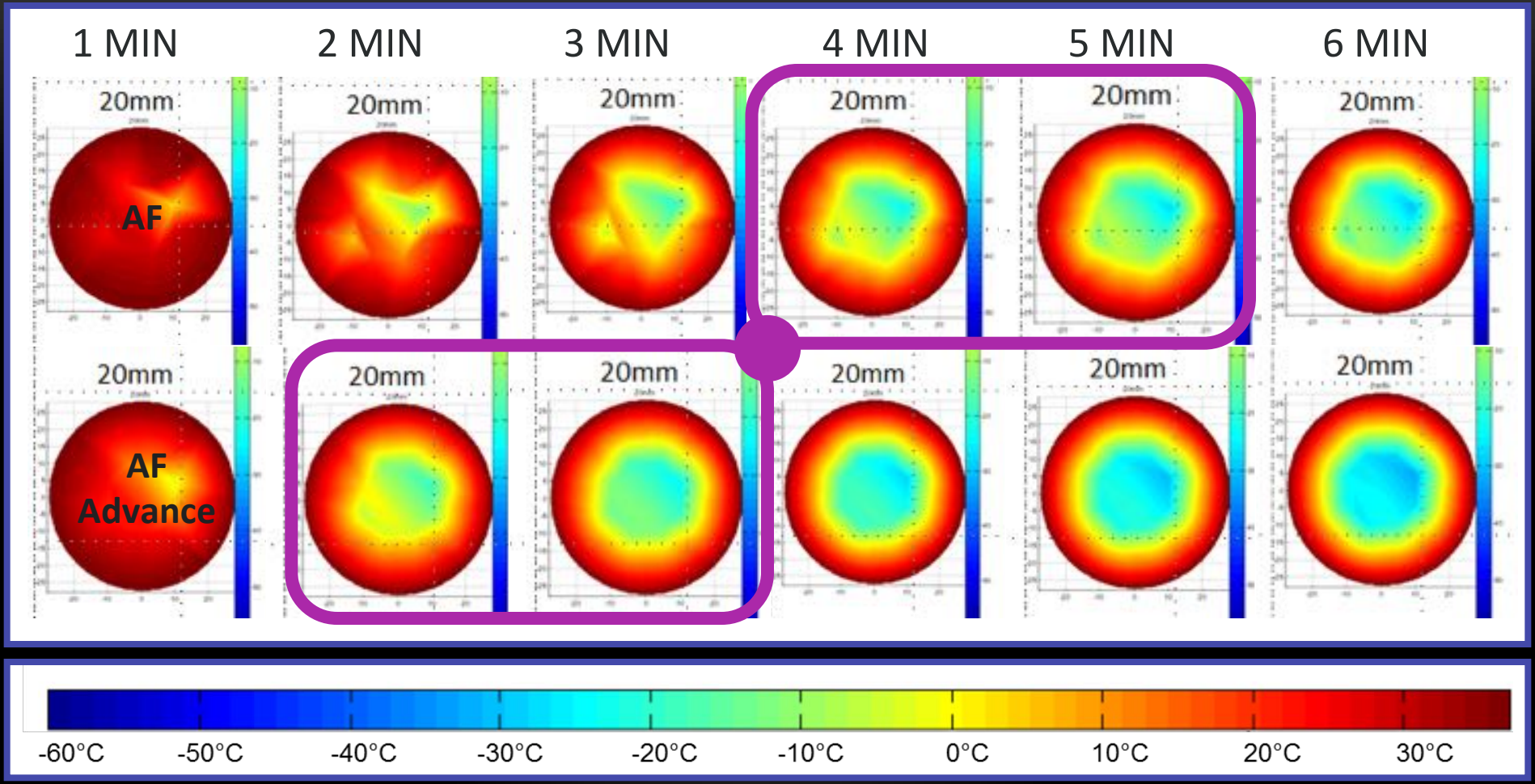
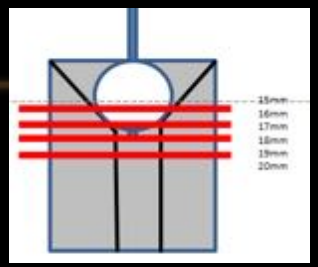


Fig. 1 The design of CB-1 and CB-2. a In CB-1, the cooling zone consists of a central equatorial band. Accordingly, optimal balloon positioning is key to ensure circumferential contact between PV antral tissue and the balloon cooling zone. In this illustration, the inferior segment of the left superior PV antrum is not in direct contact with the balloon cooling zone. Ablation in this orientation will likely lead to incomplete PV isolation. b On the other hand, the CB-2 cooling zone spans over the entire distal half of its surface. This design modification offers a larger cooling surface area, minimizing the impact of balloon orientation on optimal tissue contact. *LA* left atrium, *LV* left ventricle, *RA* right atrium

28mm Balloon - Thermocouple Gel Model Isotherms
Progression of Temperature Change at 20mm Depth By Minute



240 seconds on Arctic Front was roughly equivalent to 120 – 180 seconds with Arctic Front Advance as observed in the thermocouple gel model.



Medtronic data on file

Does not necessarily reflect PV tissue temperatures

ABLATION WITH THE CB- AF ADVANCE II
WHAT WE KNOW FROM A LARGE NUMBER OF REPORTS

1. Highly effective in achieving PVI
2. Significant improvements in procedural and clinical outcomes vs first generation CB (complications, efficacy)
3. Long-term results better than, at worst comparable with RF ablation for both paroxysmal and early persistent AF
4. Right Prenic nerve palsy more common in CB-Adv II vs RF ablation but severe complications might be less frequent

Improved Procedural Efficacy of Pulmonary Vein Isolation Using the Novel Second-Generation Cryoballoon

ALEXANDER FÜRNKRANZ, M.D.,* STEFANO BORDIGNON, M.D.,* BORIS SCHMIDT, M.D.,* MELANIE GUNAWARDENE,* BRITTA SCHULTE-HAHN, M.D.,* VERENA URBAN, M.D.,* FRANK BODE, M.D.,† BERND NOWAK, M.D.,* and JULIAN K. R. CHUN, M.D.*

From the *Cardioangiologisches Centrum Bethanien, Medizinische Klinik III, Markus Krankenhaus, Frankfurt am Maim; and †Universitätsklinikum Medizinische Klinik II, Lübeck, Germany

Improved Procedural Efficacy in all Parameters

JCE 2012

	CB-1G	CB-2G	P value
Balloon applications per vein (excluding bonus)	1,8±1,2	1,3±0,8	< 0,001
Distance to Achieve proximal electrode (mm)	18±8	12±5	< 0,001
T_{PVI} (seconds)	79±60	52±36	0,049
Procedure duration (minutes)	128±27	98±30	< 0,001
Fluoroscopy exposure (minutes)	19,5±7,4	13,4±5,3	0,001
Contrast medium (ml)	134±33	120±34	n.s.

CB-II IS HIGHLY EFFECTIVE AND MORE EFFECTIVE THAN CB-I

Higher Frequency (Overall) of PVI Observed after the First Freeze and Real-Time PVI Visualization

	Single-shot PVI		P	Real-time PVI visualization		P
	CB-1G	CB-2G		CB-1G	CB-2G	
LSPV	60%	77%	n.s.	57%	81%	0,054
LIPV	60%	100%	< 0,001	57%	81%	0,054
LCPV	-	75%	-	-	25%	-
RSPV	37%	80%	0,001	53%	90%	0,002
RIPV	47%	80%	0,007	30%	60%	0,02
Overall	51%	84%	< 0,001	49%	76%	< 0,001

Improved procedural efficacy of pulmonary vein isolation using the novel second-generation cryoballoon. Alexander Fürnkranz MD, Stefano Bordignon MD, Boris Schmidt MD, Melanie Gunawardene, Britta Schulte-Hahn MD, Verena Urban MD, Frank Bode MD, Bernd Nowak MD and Julian KR Chun MD. Journal of Cardiovascular Electrophysiology, doi: 10.1111/jce.12082

*Single shot PVI: PVI observed after the first freeze
**CB-1G = first-generation cryoballoon or Arctic Front
***CB-2G = second-generation cryoballoon or Arctic Front Advanc
****n.s.: non-significant

CB-ADV II IS HIGHLY EFFECTIVE TO ACHIEVE PVI

- 99% (240 + 180 sec bonus freeze), Metzner 2014 *(Circ Arrhythmia, march 2014)*, 28 mm CB
- 94% (180 sec, ONE freeze), Ciconte 2015, *(Heart Rhythm 2015)*, 28 mm CB

Metzner 2014

Table 2. Acute ablation results

	RSPV	RIPV	LSPV	LIPV	LCPV
No. of PVs (n)	50	50	42	42	8
Isolated PVs, n (%)	50/50 (100)	49/50 (98)	42/42 (100)	42/42 (100)	8/8 (100)
Isolation during first cryo-appl. n (%)	46/50 (92)	41/50 (82)	37/42 (88)	42/42 (100)	4/8 (50)
No. of cryoapplications until PVI, mean±SD	1.1±0.5	1.3±0.6	1.1±0.3	1.0±0	1.5±0.5

PV = Pulmonary Vein; PVI = PV Isolation; RSPV = Right Superior PV; RIPV = Right Inferior PV; LSPV = Left Superior PV; LIPV = Left Inferior PV; LCPV = Left Common PV

Ciconte, 2015

Table 2. Study population procedural and ablation parameters.

	Overall (n=143)
Total Procedure Time, minutes	95.2±16.3
Fluoroscopy time, minutes	13.5±8.1
LSPV	
Time to isolation, seconds	43.3±24.4
Temperature at isolation, °C	-29.0±23.6
Nadir temperature, °C	-52.6±5.3
Mean number of freeze, n	1.1±0.3
LIPV	
Time to isolation, seconds	34.3±15.9
Temperature at isolation, °C	-30.8±9.1
Nadir temperature, °C	-48.6±6.8
Mean number of freeze, n	1.1±0.4
RSPV	
Time to isolation, seconds	32.5±19.5
Temperature at isolation, °C	-29.9±11.1
Nadir temperature, °C	-51.1±11.5
Mean number of freeze, n	1.2±0.4
RIPV	
Time to isolation, seconds	48.6±27.8
Temperature at isolation, °C	-32.5±10.4
Nadir temperature, °C	-48.6±6.8
Mean number of freeze, n	1.1±0.3

Data are expressed in mean±1 standard deviation

ONE-SHOT PVI WITH 28 mm CRYOBALOON (AF II): LSPV, 43 SEC TTI
PROCEDURE PERFORMED IN A COMMUNITY HOSPITAL

12-MONTH EFFICACY: Arctic Front I

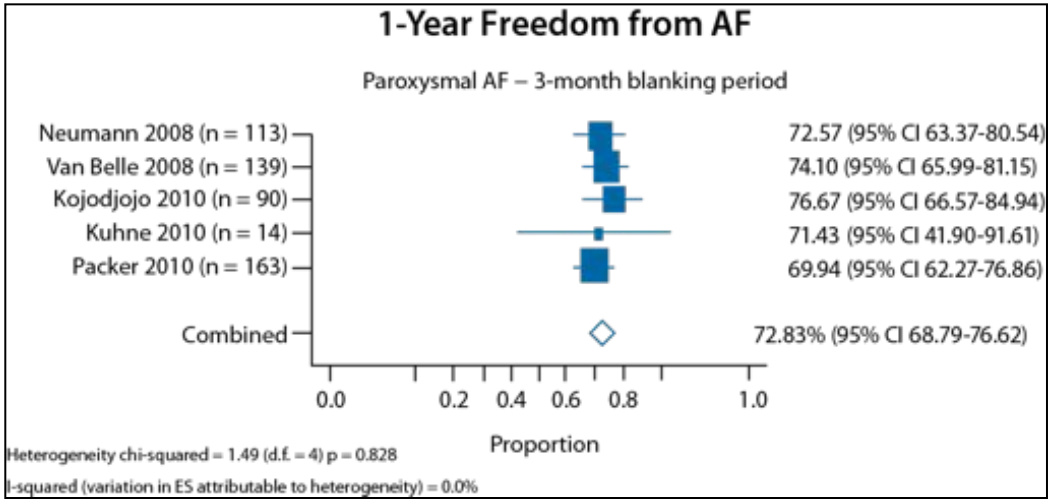
Efficacy and safety of cryoballoon ablation for atrial fibrillation: A systematic review of published studies

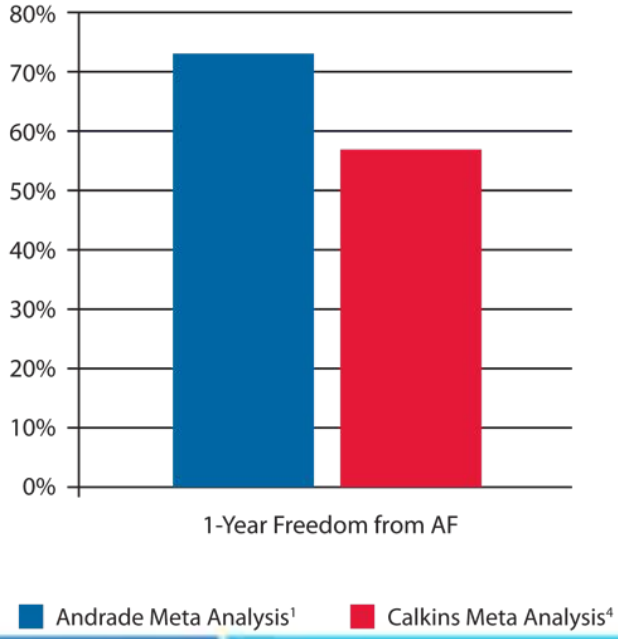
Jason G. Andrade, MD,* Paul Khairy, MD, PhD,* Peter G. Guerra, MD,* Marc W. Deyell, MD, MSc,† Lena Rivard, MD,* Laurent Macle, MD,* Bernard Thibault, MD, FHRS,* Mario Talajic, MD, FHRS,* Denis Roy, MD, FHRS,* Marc Dubuc, MD, FHRS*

Successo a 12 Mesi

Nella Metanalisi del 2011 viene riportato un successo a 12 mesi mediamente del 73% per l'Arctic Front.

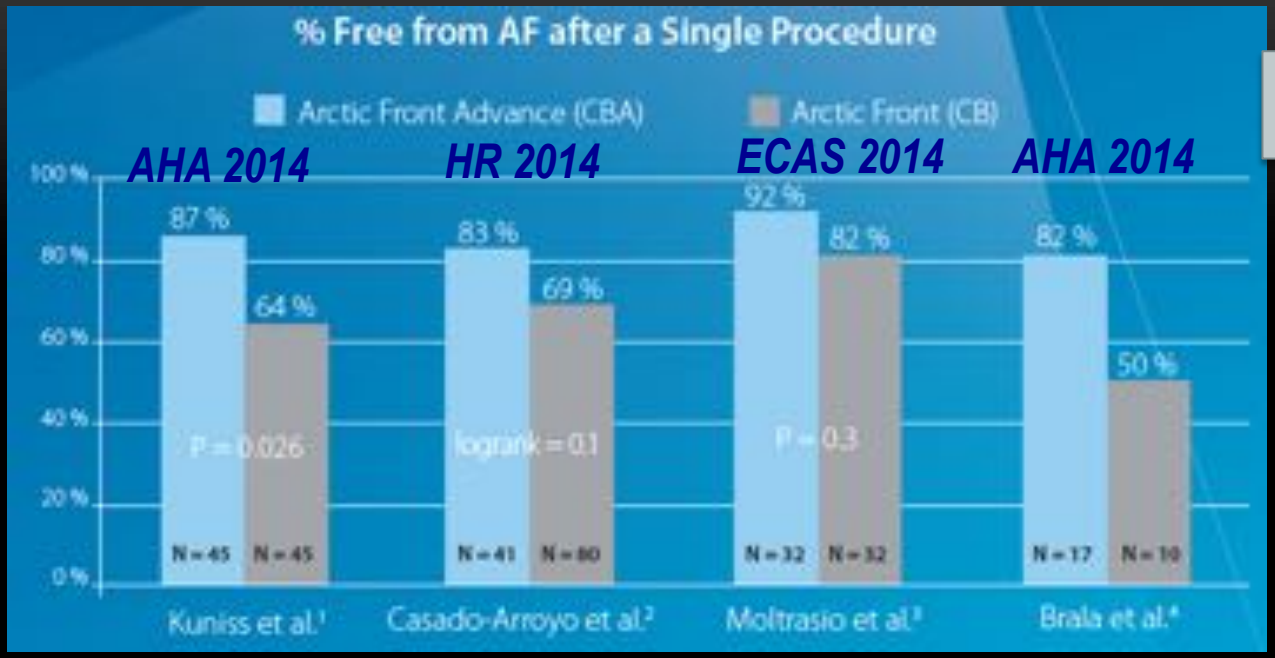
La metenalisi di Calkins relvativa alla RF riporta un successo complessivo inferiore al 60%.





Andrade JG, Khairy P, Guerra PG, et al. Efficacy and Safety of Cryoballoon Ablation for Atrial Fibrillation – A Systematic Review of Published Studies. Heart Rhythm. 2011.

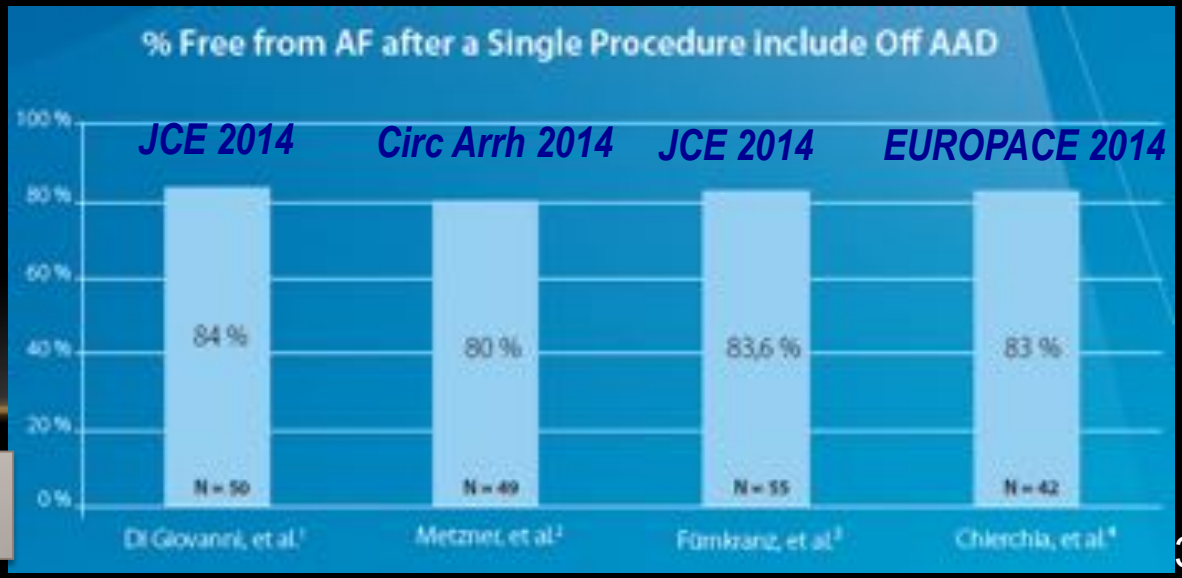
Second generation vs first generation CB PV ablation



FU 6-12 MONTHS

Munchen
Bruxelles
Milan
Berlin

Bruxelles
Hamburg
Frankfurt
Bruxelles



FU 12 MONTHS

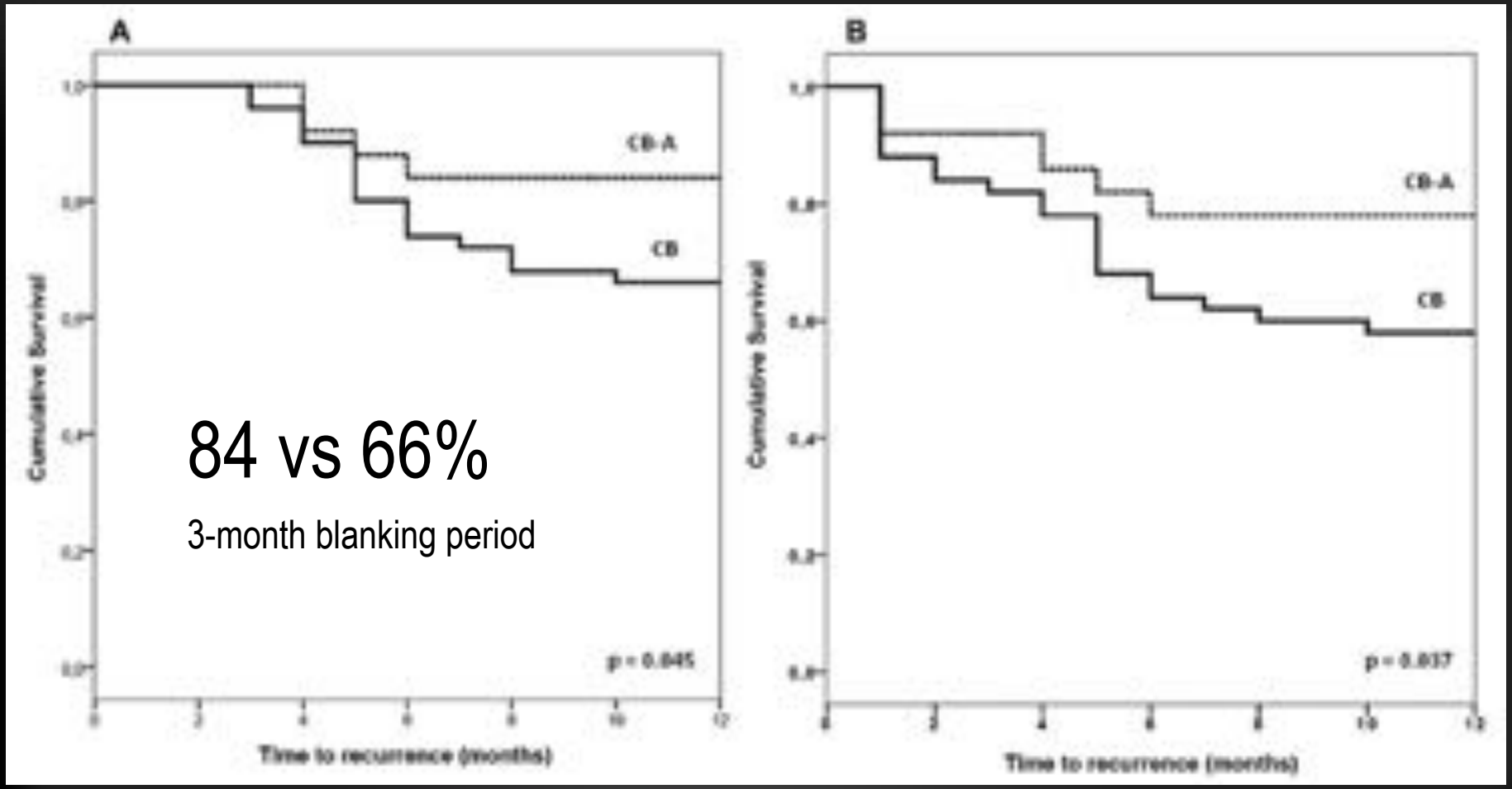
Freedom from AF in 128 consecutive pts,

Camposampiero hospital

Ce *hoort Report*

At 10 months FU **80%** of patients free from AF, *after 3 months of blanking period*

Comparison between first and second generation cryoballoons: 84 vs 66 % after 3-month blanking, off-drugs



84 vs 66%

3-month blanking period

One-Year Follow-Up After Single Procedure Cryoballoon Ablation: A Comparison Between the First and Second Generation Balloon

GIACOMO DI GIOVANNI, M.D., KRISTEL WAUTERS, M.D., GIAN-BATTISTA CHIERCHIA, M.D., PH.D., JUAN SIEIRA, M.D., MOISES LEVINSTEIN, M.D., GIULIO CONTE, M.D., CARLO DE ASMUNDIS, M.D., PH.D., GIANNIS BALTOGIANNIS, M.D., PH.D., YUKIO SAITOH, M.D., GIUSEPPE CICONTE, M.D., JUSTO JULIA, M.D., GIACOMO MUGNAI, M.D., GHAZALA IRFAN, M.D., and PEDRO BRUGADA, M.D., PH.D.

From the Heart Rhythm Management Center, Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel, Brussels, Belgium

Di Giovanni et al, JCE 2014

Improved 1-Year Clinical Success Rate of Pulmonary Vein Isolation with the Second-Generation Cryoballoon in Patients with Paroxysmal Atrial Fibrillation

ALEXANDER FÜRNKRANZ, M.D., STEFANO BORDIGNON, M.D., DANIELA DUGO, M.D., LAURA PEROTTA, M.D., MELANIE GUNAWARDENE, M.D., BRITTA SCHULTE-HAHN, M.D. BERND NOWAK, M.D., BORIS SCHMIDT, M.D., and JULIAN K.R. CHUN, M.D.

From the Cardioangiologisches Centrum Bethanien, Medizinische Klinik III, Markus Krankenhaus, Frankfurt, Germany

Improved Efficacy of Second-Generation Cryoballoon. *Background:* **The second-generation cryoballoon (CB2) has recently been introduced featuring improved surface cooling. Increased procedural efficacy of pulmonary vein isolation (PVI) when compared to the first-generation balloon (CB1) has been reported. The aim of the study was to investigate the clinical outcome of cryoballoon PVI after 1 year using the CB2 as compared to the CB1.**

Methods and Results: **A total of 105 consecutive patients with paroxysmal atrial fibrillation (AF) were studied. Cryoballoon PVI (28 mm) was performed in 50 patients using the CB1, and in 55 patients using the CB2. Patients were scheduled for 72-hour Holter ECG recording at 3, 6, 9, and 12 months and every 6 months thereafter. The study endpoint was defined as recurrent AF or atrial tachycardia >30 seconds documented after a blanking period of 90 days after the procedure. Complete PVI was achieved in 49/50 (98%) and 55/55 (100%) patients in the CB1 and CB2 group, respectively. After a mean follow-up of 416 ± 75 days, 21 (CB1 group) and 10 (CB2 group) patients reached the study endpoint. Kaplan–Meier estimates of arrhythmia-free survival after a single procedure without AAD therapy after 1 year were 63.9% versus 83.6% (P = 0.008) in the CB1 and CB2 group, respectively. Persistent phrenic nerve palsy with delayed healing occurred in 2 (CB1 group) and 3 (CB2 group) patients.**

Conclusion: **Clinical outcome of PVI using the CB2 was significantly improved when compared to the CB1.** *(J Cardiovasc Electrophysiol, Vol. 25, pp. 840-844, August 2014)*

atrial fibrillation, catheter ablation, cryoballoon, phrenic nerve palsy, pulmonary vein isolation

Improved 1-Year Clinical Success Rate of Pulmonary Vein Isolation with the Second-Generation Cryoballoon in Patients with Paroxysmal Atrial Fibrillation

ALEXANDER FÜRNKRANZ, M.D., STEFANO BORDIGNON, M.D., DANIELA DUGO, M.D., LAURA PEROTTA, M.D., MELANIE GUNAWARDENE, M.D., BRITTA SCHULTE-HAHN, M.D., BERND NOWAK, M.D., BORIS SCHMIDT, M.D., and JULIAN K.R. CHUN, M.D.

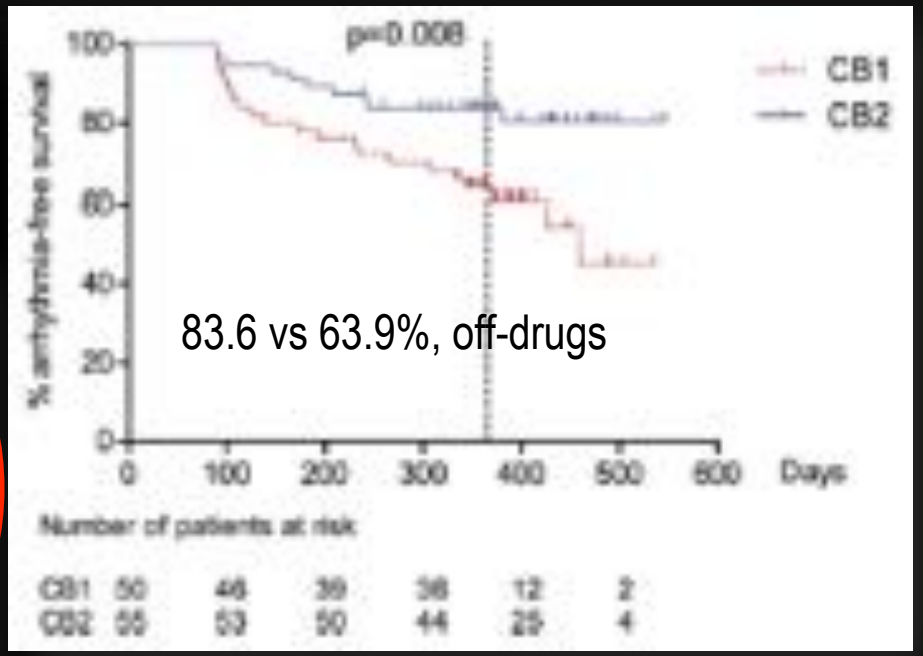
JCE 2014

- 105 Pts (50 CB1, 55 CB2)

Procedural Data

	Group 1 (CB1) n = 50	Group 2 (CB2) n = 55	P Value
Complete PVI (%)	98	100	0.48
Duration (min)	137 ± 33	94 ± 24	< 0.001
Fluoro exposure (min)	21.5 ± 9.5	12.9 ± 4.5	< 0.001
Balloon applications/patient	10.4 ± 2.0	8.3 ± 1.3	< 0.001
Isolation with the first application (% PVs)	53	89	< 0.001

CB1 = first-generation cryoballoon; CB2 = second-generation cryoballoon; PVI = pulmonary vein isolation; PVs = pulmonary veins.



83.6 vs 63.9%, off-drugs

Conclusion

Clinical outcome of PVI using the CB2 was significantly improved when compared to the CB1. After 1 year, 83.6% (CB2) versus 63.9% (CB1) of patients were free of recurrent AF/AT without AAD therapy.

One-Year Clinical Outcome After Pulmonary Vein Isolation Using the Second-Generation 28-mm Cryoballoon

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

Background—The use of second-generation cryoballoon for pulmonary vein isolation in patients with paroxysmal atrial fibrillation has demonstrated encouraging acute and mid-term results. Long-term outcome data are not yet available.

Methods and Results—Fifty patients (18 women; mean age, 61±11 years; mean left atrial diameter, 43±5 mm) with paroxysmal (36 of 50 patients; 72%) or short-standing (<3-month duration) persistent atrial fibrillation (14 of 50 patients; 28%) underwent cryoballoon-based pulmonary vein isolation. Freeze cycle duration was 240 seconds. After successful pulmonary vein isolation, a bonus freeze was applied. Follow-up was based on outpatient clinic visits at 3, 6, and 12 months including Holter-ECGs and telephonic interviews. Recurrence was defined as a symptomatic or documented arrhythmia episode >30 seconds excluding a 3-month blanking period. A total of 192 pulmonary veins were identified, and 191 of 192 (99%) pulmonary veins were successfully isolated. Phrenic nerve palsy occurred in 1 of 50 (2%) patients. Follow-up was available for 49 of 50 (98%) patients with a mean follow-up duration of 440±39 days. Thirty-nine of 49 (80%) patients remained in stable sinus rhythm. Of 8 of 10 patients with arrhythmia recurrence, a second procedure using radiofrequency ablation demonstrated left atrial to pulmonary vein reconduction.

Conclusions—The use of second-generation 28-mm cryoballoon for pulmonary vein isolation results in an 80% 1-year success rate. (*Circ Arrhythm Electrophysiol.* 2014;7:288-292.)

Key Words: ablation ■ atrial fibrillation ■ follow-up studies

One-year follow-up after CB Advance II PVI, off drugs
80% IN STABLE SINUS RHYTHM

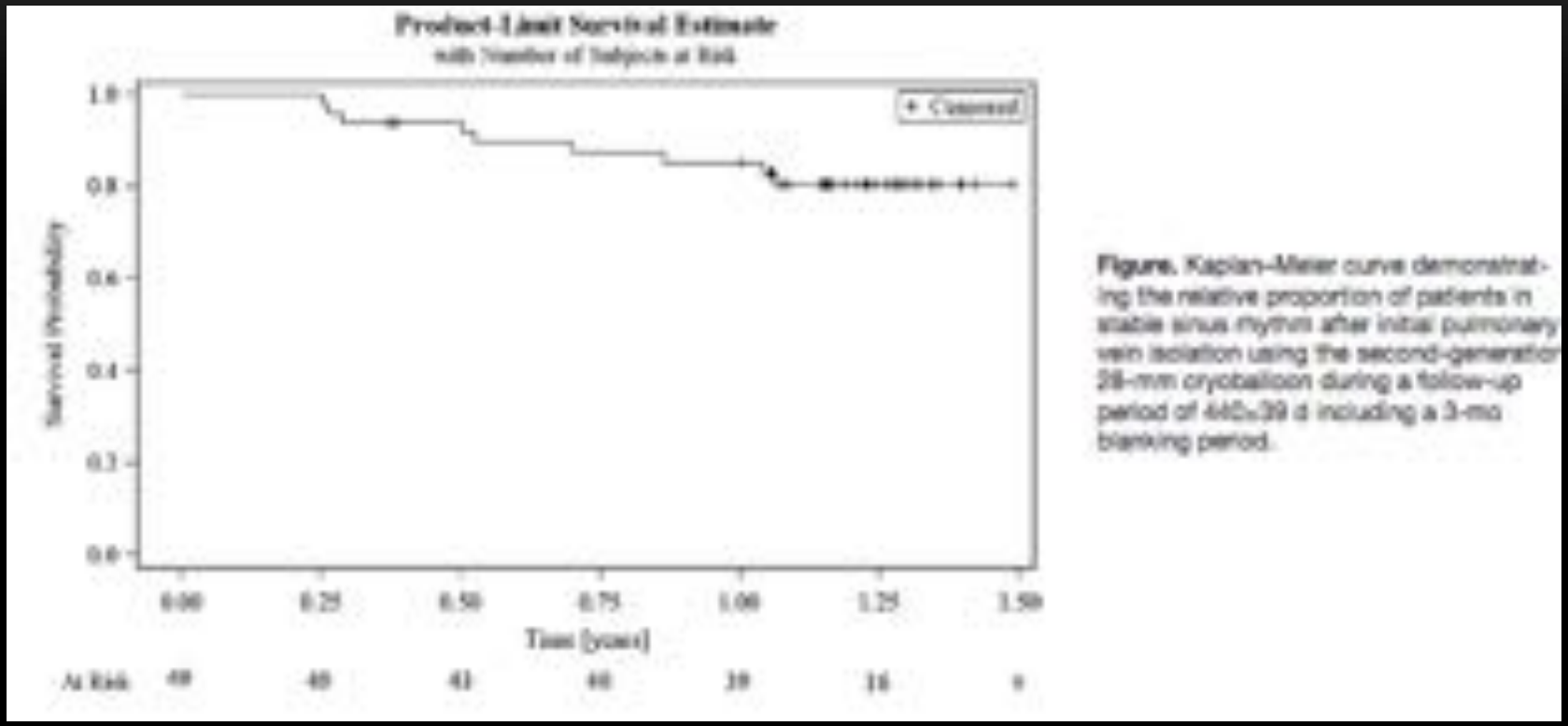


Figure. Kaplan–Meier curve demonstrating the relative proportion of patients in stable sinus rhythm after initial pulmonary vein isolation using the second-generation 28-mm cryoballoon during a follow-up period of 445±39 d including a 3-mo blanking period.

Complications

As the only complication, PN palsy occurred in 1 of 50 (2%) patients during cryoablation along the RSPV. PN palsy was persistent throughout the hospital stay and during fluoroscopic reevaluation at 3 and 6 months postablation. However, PN palsy completely resolved 10 months postablation.

Metzner, Circ Arrhyth 2014

SINGLE 3-MINUTES FREEZE WITH THE CB-ADVANCE II

Author's Accepted Manuscript

Single Three-Minutes Freeze for Second-Generation Cryoballoon Ablation: One-Year Follow-Up Following Pulmonary Vein Isolation

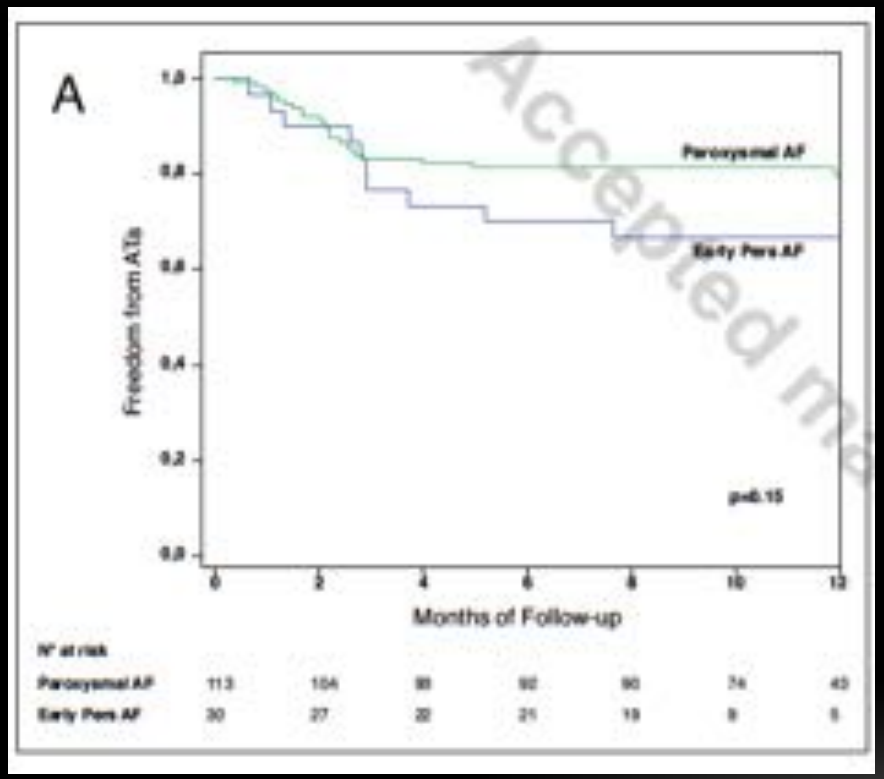
Giuseppe Ciconte MD, Carlo de Asmundis MD Ph.D. FHRS, Juan Sieira MD, Giulio Conte MD, Giacomo Di Giovanni MD, Giacomo Mugnai MD, Yukio Saitoh MD, Giannis Baltogiannis MD Ph.D., Ghazala Irfan MD, Hugo Enrique Coutiño-Moreno MD, Burak Hunuk MD, Vedran Velagić MD, Pedro Brugada MD Ph.D., Gian-Battista Chierchia MD Ph.D.

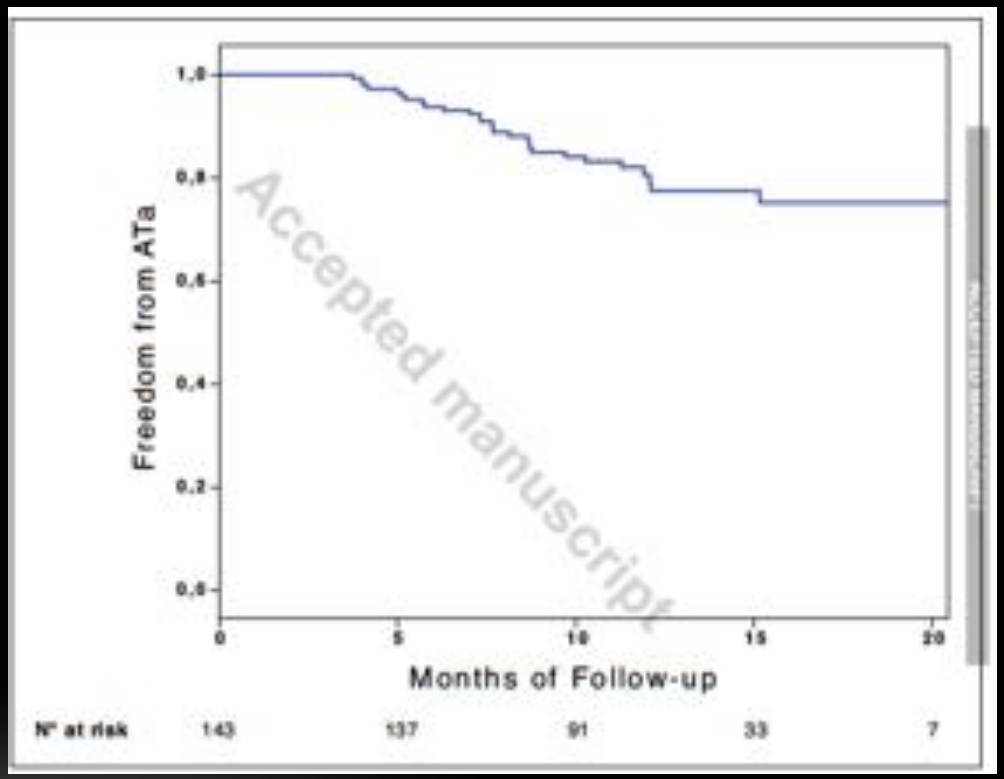
Heart rhythm 2015; 12:673-80

PII: S1547-5271(14)01544-6
DOI: http://dx.doi.org/10.1016/j.hrthm.2014.12.026
Reference: HRTHM6062

To appear in: *Heart Rhythm*

ONE-YEAR FREEDOM FROM ATRIAL TACHYARRHYTHMIAS
82.3% IN PAROXYSMAL AF
73.3% IN EARLY PERSISTENT AF





Ciconte et al, Hearth Rhythm 2015

Time-to-Isolation a Reported Predictor of AF Recurrence

Ciconte, et al. reported:

- < 40 seconds time-to-isolation was associated with no clinical recurrence with 90% sensitivity and 81% specificity
- For every 10sec in additional time-to-isolation, the risk of arrhythmia recurrence increased 1.3 times (CI 1.21-1.34, p<0.01)

Study Details:

- N=143 patients
- Arctic Front Advance Cryoballoon
- 180s application time
- No bonus freeze beyond PVI

Additional Study Results:

- 94% (538/572) of PVs isolated on first freeze
- All PVs were isolated with a mean of 1.1 ± 0.4 freezes
- 1-year freedom from atrial tachyarrhythmias off AADs after a single procedure was 80.4% (115/143)

[1] Ciconte, et al. Heart Rhythm. 2014 Dec 23. doi: 10.1016/j.hrthm.2014.12.026. e-pub ahead of print.

LONG-TERM RESULTS BETTER THAN, AT WORST COMPARABLE WITH RF ABLATION FOR BOTH PAROXYSMAL AND EARLY PERSISTENT AF

Europace Advance Access published April 2, 2015

Europace
doi:10.1093/europace/euv060

CLINICAL RESEARCH

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 Zhao[2], Eloi Marijon[3,4], Decebal Gabriel Latcu[5], Rui Providencia[3], Giacomo Di Giovanni[6], Gaël Jauvert[2], Francois Jourda[3], Gian-Battista Chierchia[6], Carlo De Asmundis[6], Giuseppe Ciconte[6], Christine Alonso[2], Caroline Grimard[2], Serge Boveda[3], Bruno Cauchemez[2], Nadir Saoudi[5], Pedro Brugada[6], Jean-Paul Albenque[3], and Olivier Thomas[2]

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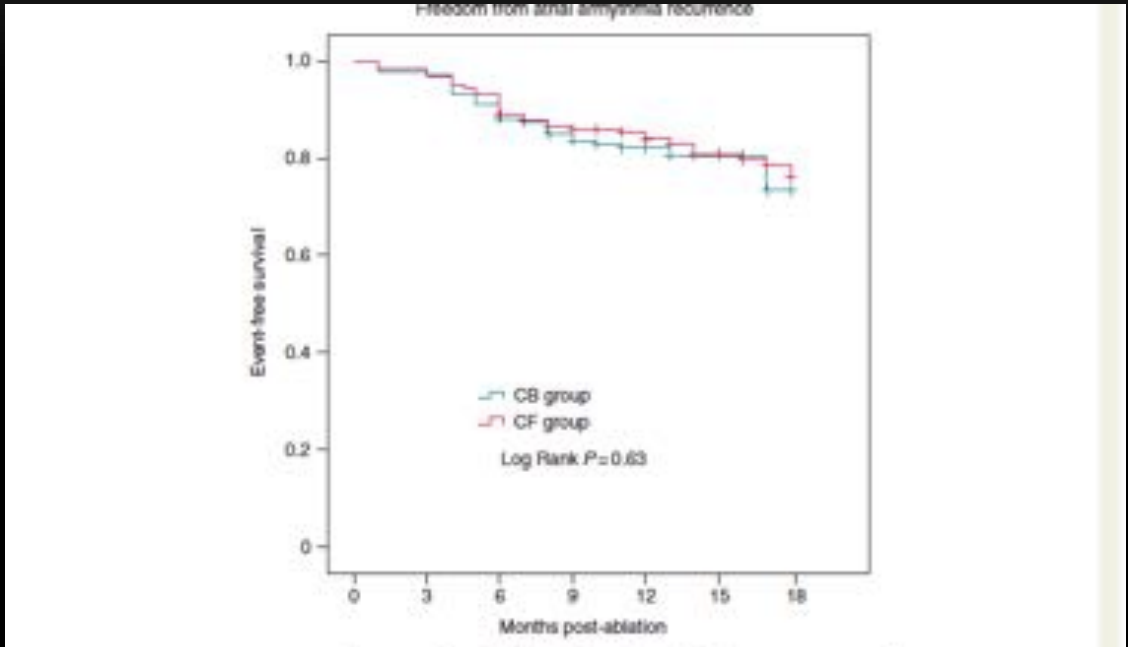
Received 28 November 2014; accepted after revision 10 February 2015

Aims Whether pulmonary vein isolation (PVI) for paroxysmal atrial fibrillation (PAF) using contact force (CF)-guided radiofrequency (RF) or second-generation cryoballoon (CB) present similar efficacy and safety remains uncertain.

Methods We performed a multicentre study comparing procedural safety and arrhythmia recurrence after standardized PVI cath-

RESULTS: FREEDOM FROM ANY ATRIAL ARRHYTHMIA, OFF-DRUGS NO DIFFERENCE (76 VS 73% AT 18 MONTHS) *(NON-RANDOMIZED)*



	Proportion of patients free from arrhythmia recurrance					
	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%	73.9%
	Number of patients at risk					
CF group	192	176	141	117	73	58
CB group	173	157	126	111	42	27

Figure 2 Cumulative freedom from atrial arrhythmia recurrence after a single ablation procedure, using the Kaplan–Meier survival analysis (blanking period 1 month).

F. Squara *et al.* **Europace Advance Access published April 2, 2015**

DATI PROCEDURALI E COMPLICANZE: CB SIGNIFICANT SHORTER SEVERE NON-LETHAL COMPLICATIONS IN CF ONLY (2.5% VS 0%)

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

F. Squara *et al.* | **Europace Advance Access published April 2, 2015**

FIRE AND ICE PROSPECTIVE TRIAL

Principal Investigators and Steering Committee

Principal Investigator	Prof. Dr. Karl-Heinz Kuck, Hamburg, Germany
Co-chair	Prof. Dr. Josep Brugada, Barcelona, Spain
Steering Committee Members	•Dr. Jean-Paul Albenque, Toulouse, France •Prof. Dr. Josep Brugada, Barcelona, Spain •Dr. David Wyn Davies, London, UK •Prof. Dr. Karl-Heinz Kuck, Hamburg, Germany •Prof. Dr. Claudio Tondo, Milan, Italy
Current Participating Countries (# of Sites)	•Belgium (2) •Czech Republic (1) •France (5) •Germany (4) •Hungary (1) •Italy (2) •Netherlands (1) •Spain (4) •Switzerland (1) •UK (1)

Arctic Front Advance ST Cryoballoon

40% Shorter Tip

- **World's leading Cryoballoon therapy** for the treatment of drug refractory recurrent symptomatic paroxysmal AF.
- Designed to help **improve Achieve Mapping Catheter's ability to measure time-to-isolation** by bringing the electrodes anatomically close to the veins' muscular sleeves[1]
- Continues to **provide stability and support to maintain occlusion** while Achieve Mapping Catheter is proximally positioned near balloon tip
- Shortened tip may allow **additional catheter maneuverability in some PV anatomies**

[1]Medtronic Data on File

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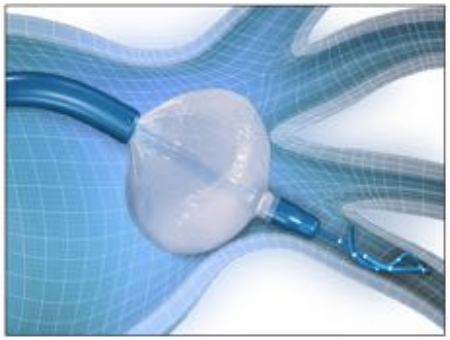
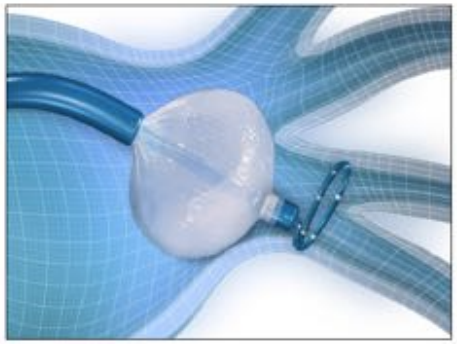
PV Anatomies Potentially Benefitting Shorter Tip: *Early PV Branching*

Arctic Front Advance Cryoballoon



Using the Arctic Front Advance Cryoballoon, in order to cannulate the inferior branch of this PV, the Achieve Mapping Catheter needs to be placed in a prolapsed position, potentially limiting ability to visualize time to isolation

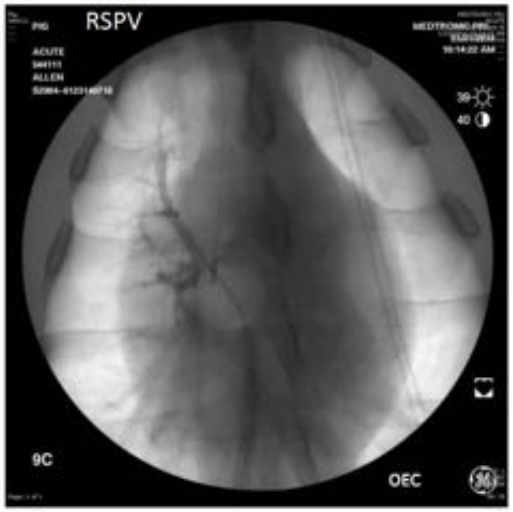
Arctic Front Advance ST Cryoballoon



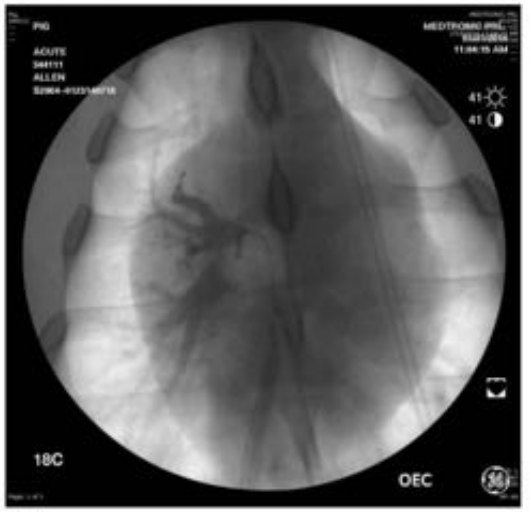
Using the Arctic Front Advance ST Cryoballoon, the shorter tip allows more electrodes of the Achieve Mapping Catheter to be positioned closer to the PV ostia, potentially increasing the likelihood of visualizing electrograms during the freeze.

PV Anatomies Potentially Benefitting Shorter Tip: *Early PV Branching*

Arctic Front Advance Cryoballoon



Arctic Front Advance ST Cryoballoon



On the left, the Arctic Front Advance Cryoballoon's longer tip requires wiring of an upper branch of this RSPV, whereas the shorter tip of Arctic Front Advance ST Cryoballoon (right image) allows for more flexibility in choosing which branch to wire

WHAT CAN WE EXPECT FROM THIS RAPIDLY EVOLVING CRYOABLATION TECHNOLOGY

- Shorter procedure duration (≈ 60 minutes)
- Shorter Fluoroscopy-time (≈ 10 minutes)
- >90% of PVs isolation with a single 3-minute application
- Further reduction of complications (less LA time, and less freeze- cycles)
- PVs isolation applied early in AF history