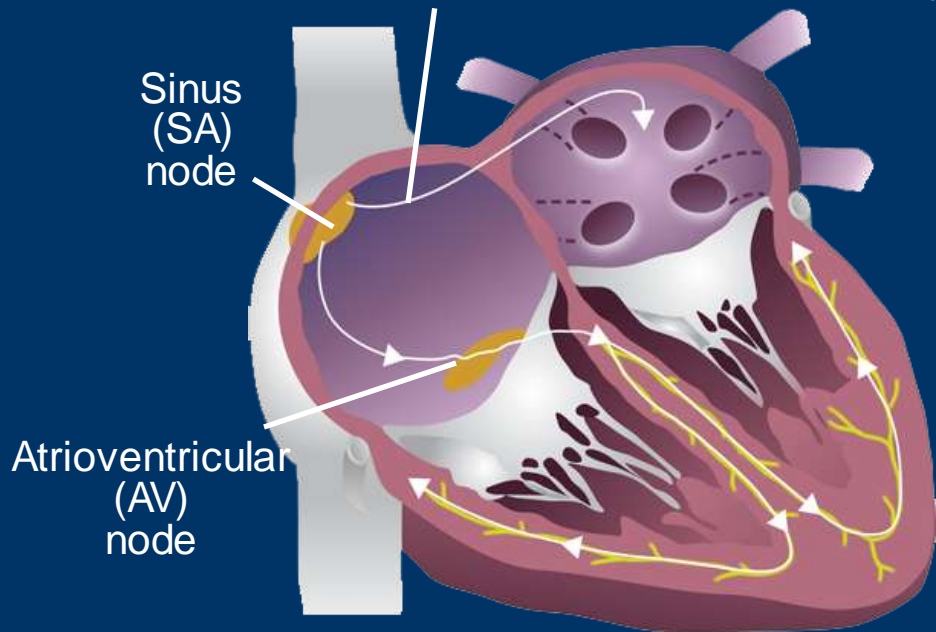


Avancées dans le Traitement de la Fibrillation Atriale CRYOABLATION PAR BALLON

Dr Najib GARTI
Clinique du Val d'Anfa Casablanca

Fibrillation Atriale: Fibrillation des muscles des Oreillettes

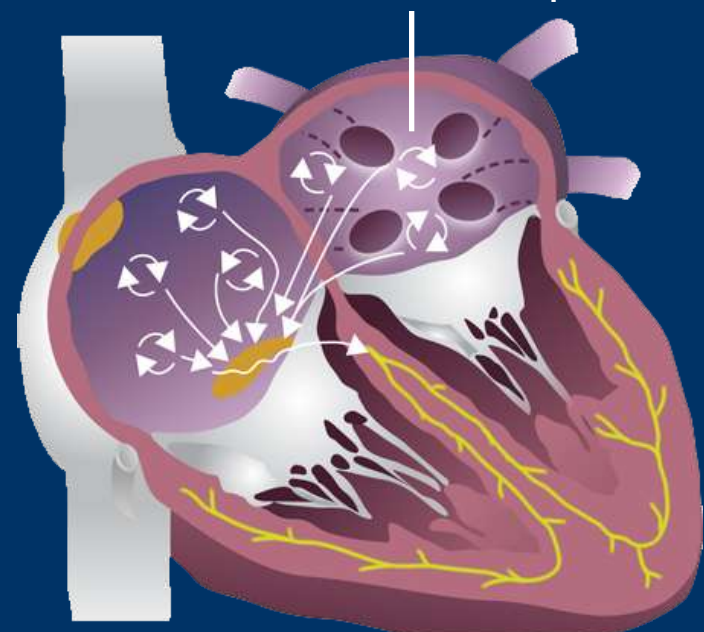
Normal electrical pathways



Normal sinus rhythm



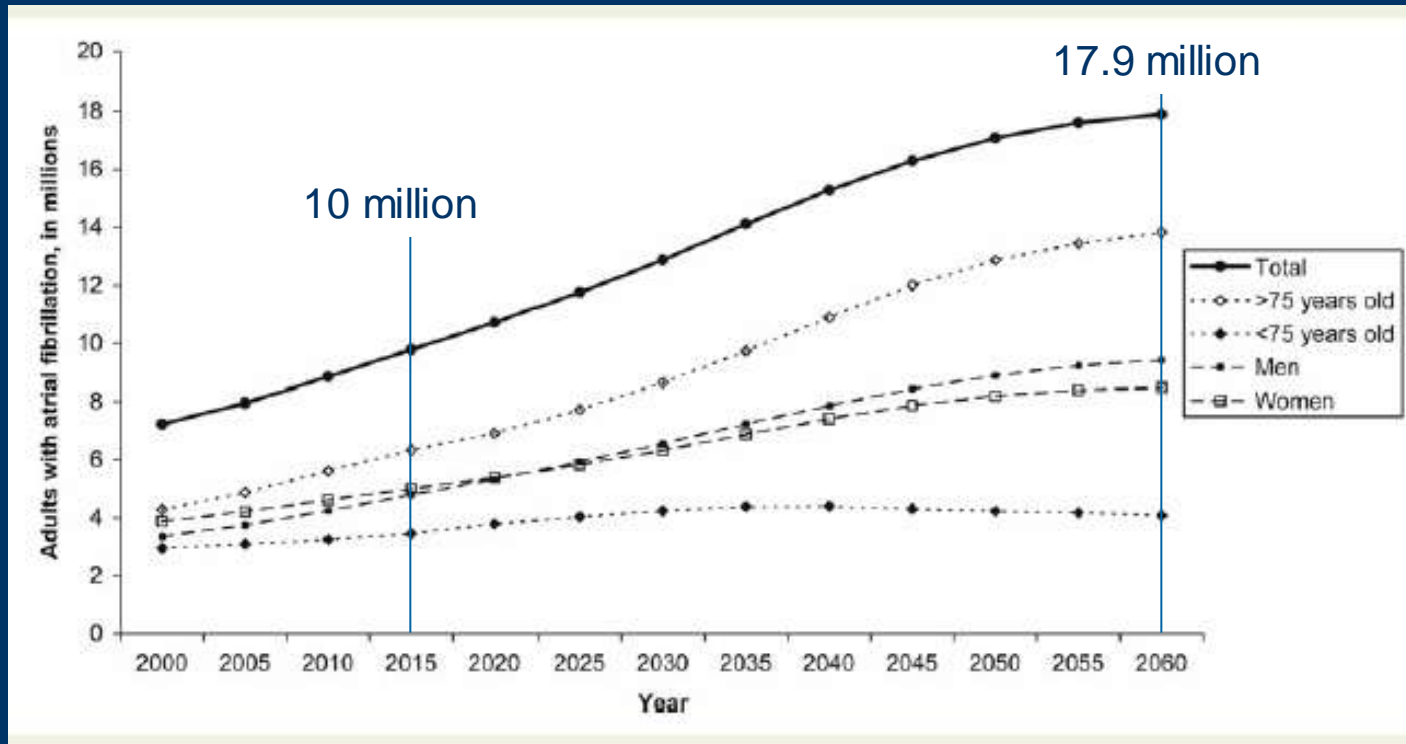
Abnormal electrical pathways



Atrial fibrillation



L'Incidence et la Prévalence de la FA est Large et en Augmentation en Europe



- EU AF Prevalence is estimated at 10 million today and is predicted to double by 2060.^{1,2}
- Age-adjusted AF incidence is predicted to grow as a result of a growing elderly population and increased risk factors – obesity, hypertension, diabetes, and cardiovascular disease^{2,3}

¹ B.P. Krijthe et al. *Euro Heart J* 2013 Sep;34(35):2746-51.

² Zoni-Berisso, et al. *Clinical Epidemiology* 2014;6:213–220.

³ Miyasaka Y, et al. *Circulation*. 2006;114:119-125.

Fibrillation Atriale

Risks et Coûts

- Impact négatif sur la qualité de la vie
- Cause majeure d'AVC: X risque par 5
- Augmente le risque d'insuffisance cardiaque
- Augmente les coûts de santé : hospitalisations, interventions & médicaments

¹ Singh SN, et al. *J Am Coll Cardiol*. 2006;48:721-730.

² Kang Y. *HeartLung*. 2006;35:170-177.

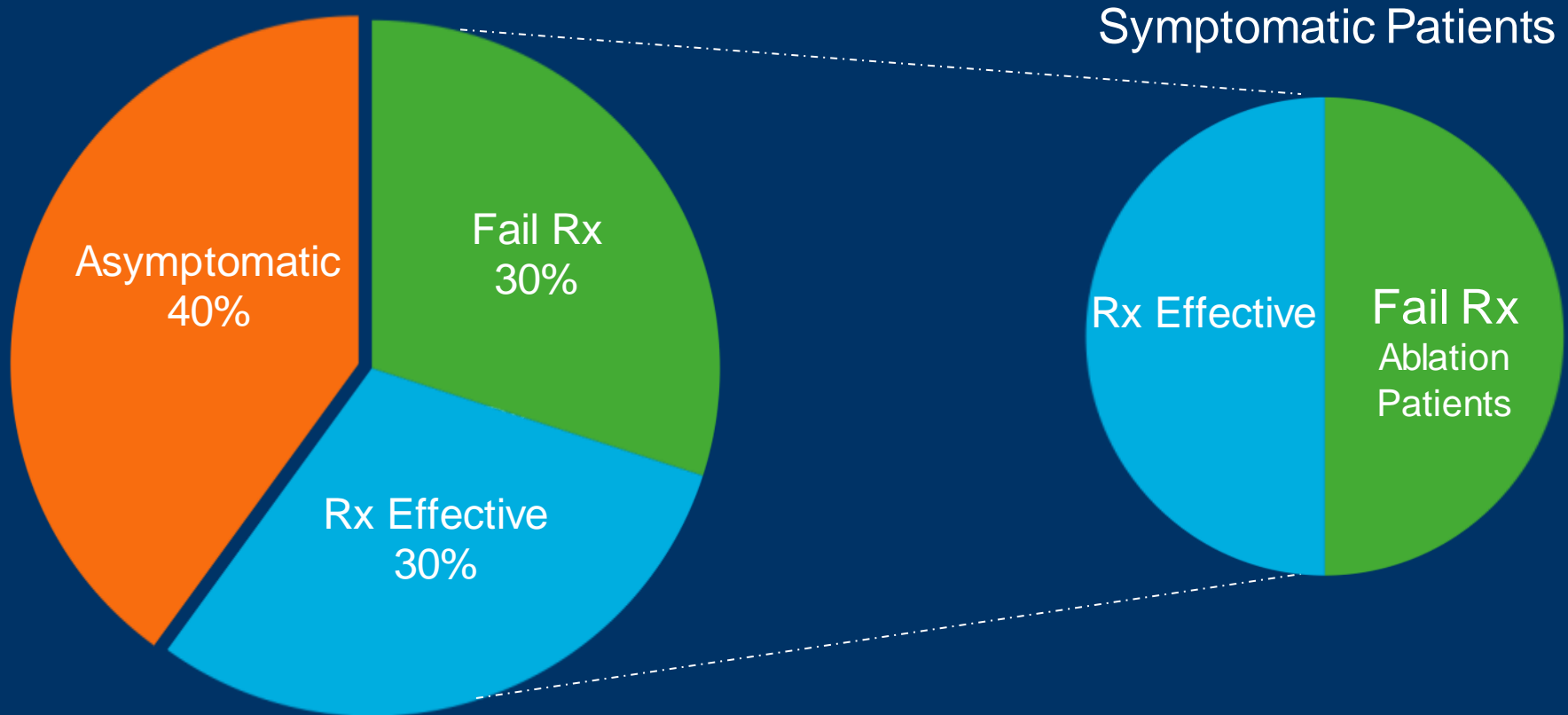
³ Wolf PA, et al. *Stroke*. 1991;22:983-988.

⁴ White PD: Heart disease. New York, NY, The McMillan Co, 1937.

⁵ Kim MH, et al. *Adv. Ther.* 2009;26:847-857.

⁶ Zoni-Berisso, et al. *Clinical Epidemiology* 2014;6:213–220.

La moitié des patients avec FA symptomatique ne répondent pas au traitement médical

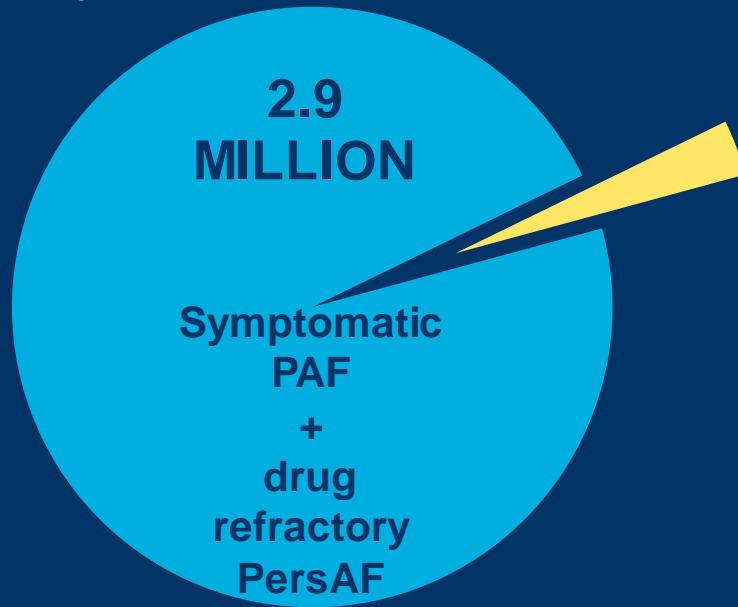


Medtronic internal estimates

Les Candidats à l'ablation sont sous traités

6 Patients Européens symptomatiques 6 millions

- Patients cherchent la disparition des symptômes
- Ablation pour patient FAP symptomatiques + FA Perst résistante au traitement
- L'Ablation par Catheter est sous utilisée



~3%³ Annual ablation rate

(EU ablation volume >90,000)

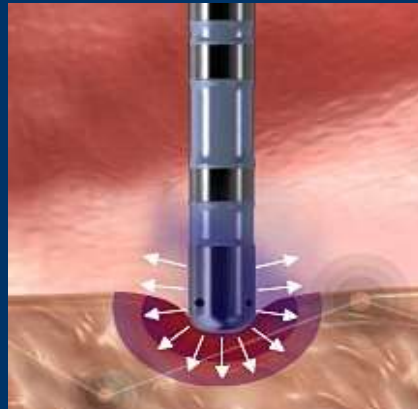
¹ B.P. Krijthe et al. Euro Heart J 2013 Sep;34(35):2746-51.

² Zoni-Berisso, et al. Clinical Epidemiology 2014;6 213-220

³ Medtronic internal estimates taking into account of clinical and economic exclusion.

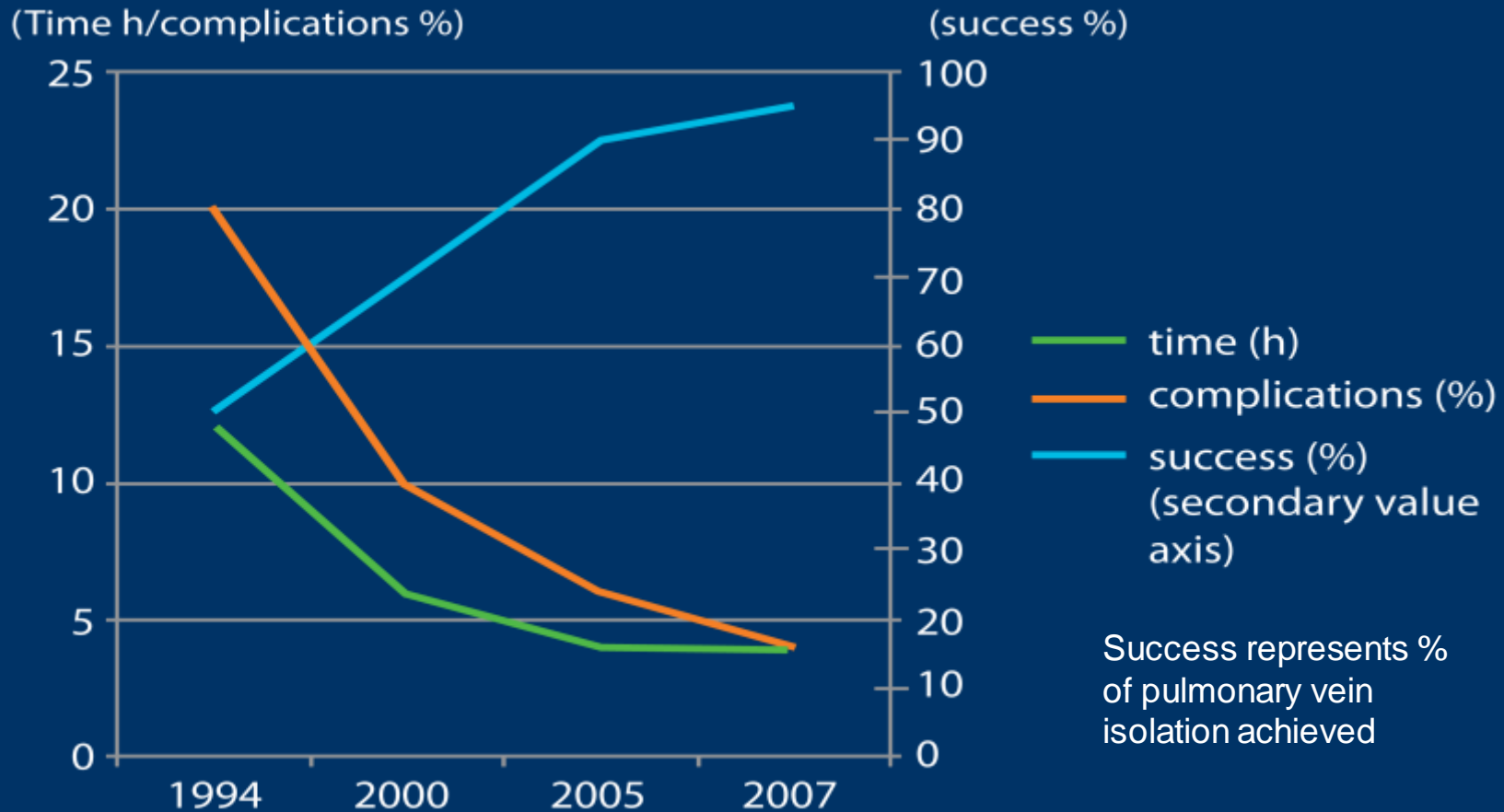
Options Thérapeutiques

- Thérapies pharmacologiques
- Cardioversion
- Thérapies chirurgicales
- Ablation par cathéter
 - Radiofréquence
 - Cryoablation



Amélioration de l'Ablation de la FA

Succès, Sécurité et Rapidité



Catheter Ablation est indiquée pour les Patients Symptomatiques après Echec de Un médicament Antiarrhythmique *Class IA Level Evidence*

HRS/EHRA/ECAS AF Ablation Guidelines^{1,2}

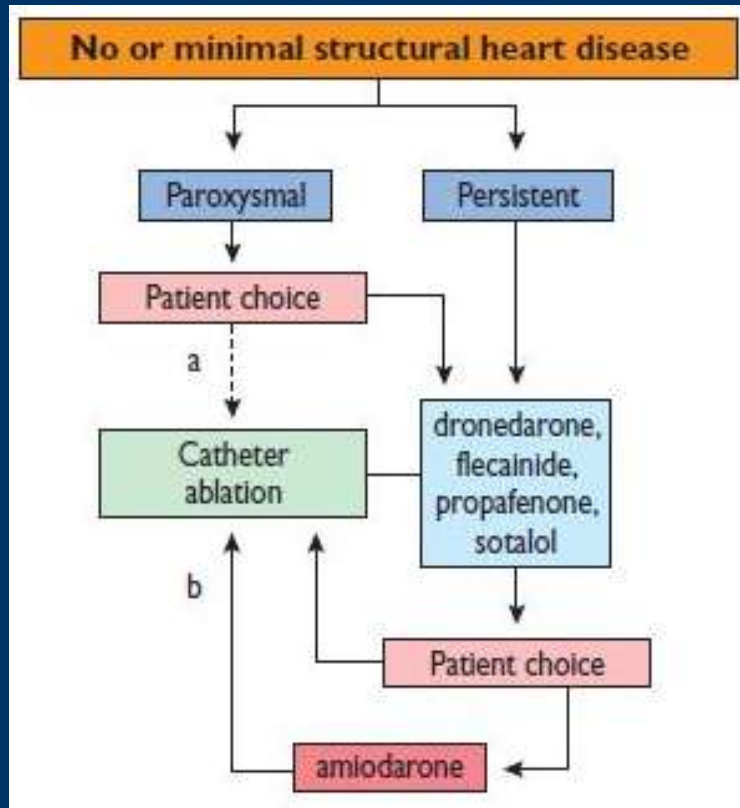
Indications for catheter ablation of AF	Class	Level
Symptomatic AF refractory or intolerant to at least one Class 1 or 3 antiarrhythmic medication		
Paroxysmal: Catheter ablation is recommended*	I	A
Persistent: Catheter ablation is reasonable	IIa	B
Longstanding Persistent: Catheter ablation may be considered	IIb	B
Symptomatic AF prior to initiation of antiarrhythmic drug therapy with a Class 1 or 3 antiarrhythmic agent		
Paroxysmal: Catheter ablation is reasonable	IIa	B
Persistent: Catheter ablation may be considered	IIb	C
Longstanding Persistent: Catheter ablation may be considered	IIb	C

*Catheter ablation of symptomatic paroxysmal AF is considered a Class 1 indication only when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced center.

¹ Calkins H, et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation:

² Camm A.J, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation published in the *European Heart Journal*. (2012) 33, 2719–2747.

Le choix du patient joue un rôle primordial. HRS/EHRA/ECAS AF Ablation Guidelines^{1,2}



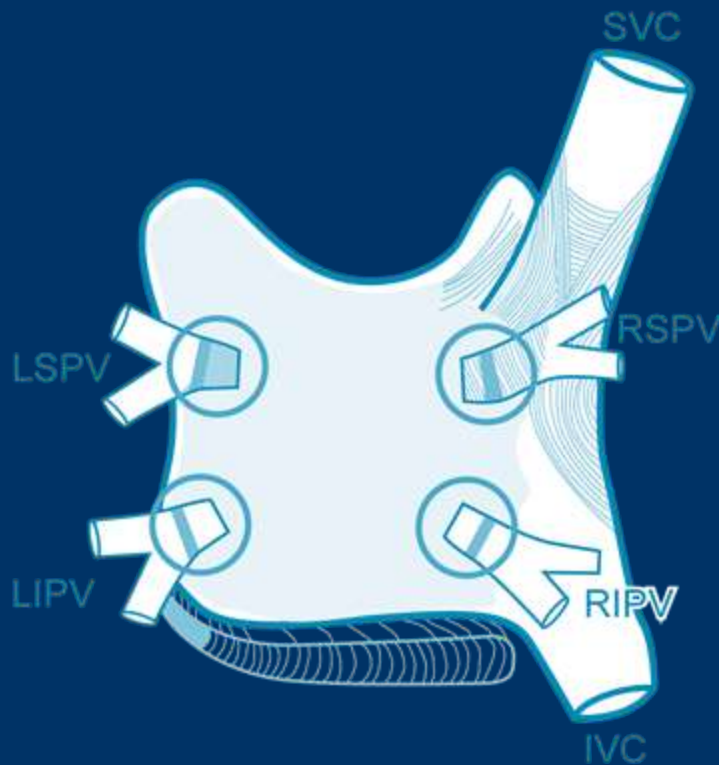
- Traitement de première intention (avant les Antiarythmiques) est une indication raisonnable pour les patients avec FA paroxystique.

¹ Calkins H, et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation:

² Camm A.J, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation published in the *European Heart Journal*. (2012) 33, 2719–2747.

L'Isolation des Veines Pulmonaires (PVI) est le pivot de toutes les thérapies Ablatives

“The recognition of the crucial role of pulmonary vein myocardial sleeves for the initiation of atrial fibrillation is regarded as one of the greatest discoveries of the last decades in cardiac electrophysiology.”^{2,3,4,5}



2012 HRS Consensus Statement

“Ablation strategies which target the PVs and/or PV antrum are the cornerstone for most AF ablation procedures.”¹

1 Calkins H, et al. Heart Rhythm. April 2012;9(4):632-696

2 Nathan H, et al. The junction between the left atrium and the pulmonary veins: an anatomic study of human hearts. Circulation. 1966; 34:412-422.

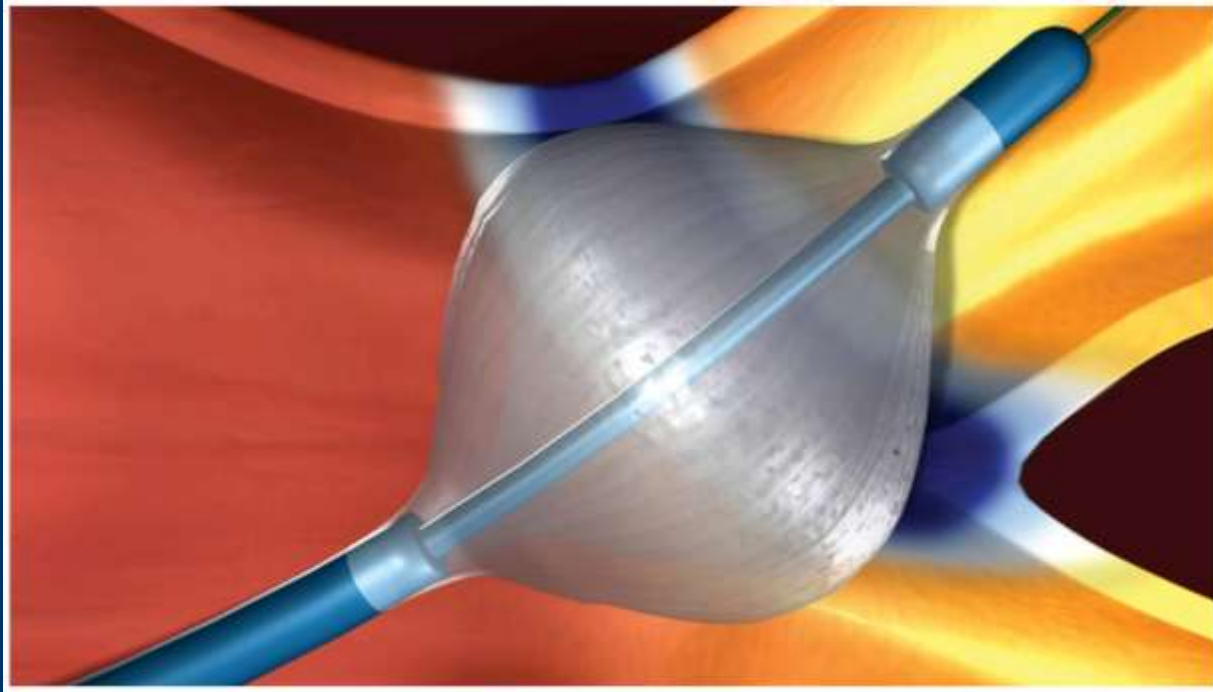
3 Ho SY, et al. Architecture of the pulmonary veins: relevance to radiofrequency ablation. Heart. 2001;86:265-270.

4 Haïssaguerre M, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998;339:659-666.

5 Ammar S, et al. Selective Versus Total Pulmonary Vein Isolation In Atrial Fibrillation Ablation. JAFib 2014 June/July.

Cryoablation pour le Traitement de la FA

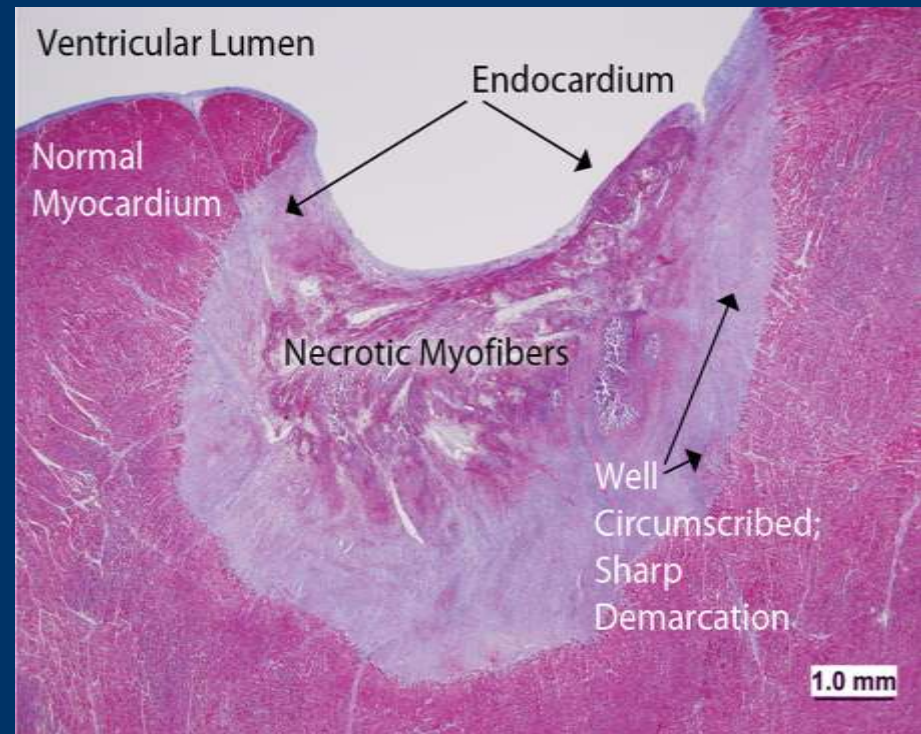
Propriétés de la Cryoablation



- Retir la chaleur des tissus
- Ablate les tissus au contact avec le ballon

Avantages de la Cryoablation sur le Tissu connectif

- Cryoadhesion améliore contact et la stabilité, minimisant le besoin de la fluoroscopie
- Préserve la matrice extracellulaire et intégrité endothéliale
- Diminue le risque de formation de thrombus
- Donne des lésions bien démarquées



Histological View

¹ Sarabanda AV, et al. *J Am Coll Cardiol.* 2005;46:1902-1912.

Approche Simplifiée de l' Isolation des VP

Comment le système de Cryo marche



1. Accès à la Veine



2. Inflation du Cryoballon

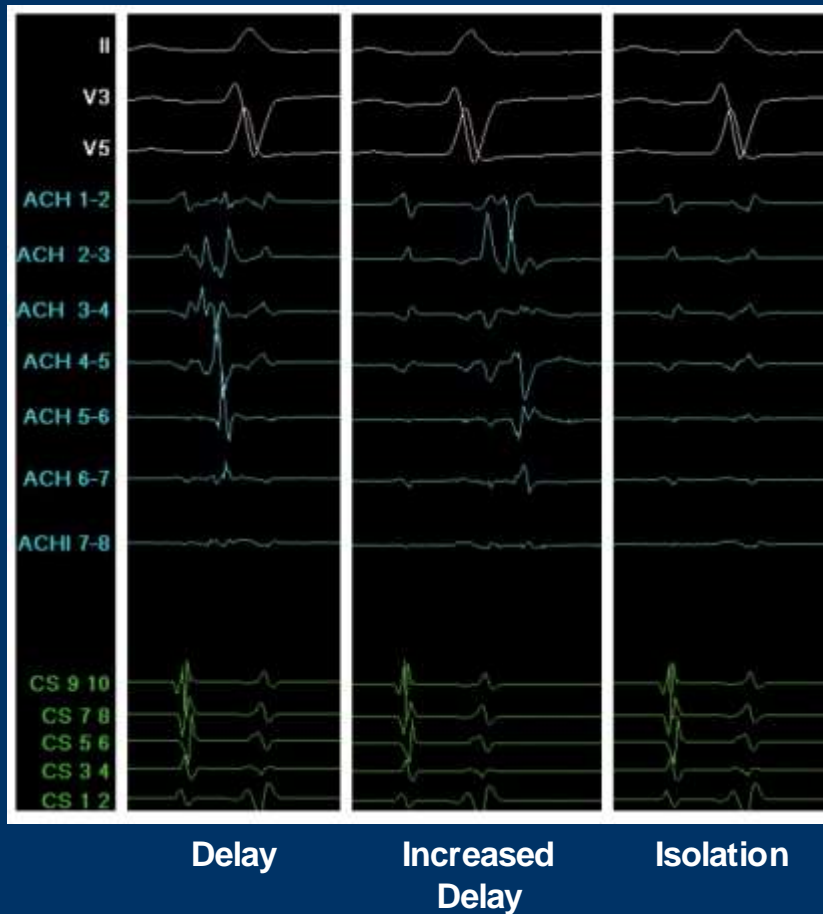


3. Position pour Occlure et Refroidir



4. Evaluer PV Isolation

Catheter Mapping Achieve permet l'évaluation en temps réel de l'isolation Veines Pulmonaires pendant cryoablation



Arctic Front is positioned here against the LIPV ostium, with Achieve Mapping Catheter inside to read signals at the same time.

Les progrès de la Technologie Cryo

2001



Premier produit
cryoablation percutané
en Europe
(Freezor catheters)

2005



Premier Cryoballoon
en Europe
(Arctic Front)

2010



Arctic Front
Approuvé aux USA

2011



Premier **catheter EP** :
Achieve Mapping
Catheter

2012



Arctic Front Advance
Approuvé
Encore le seul **Cryoballoon**
indiqué pour FA

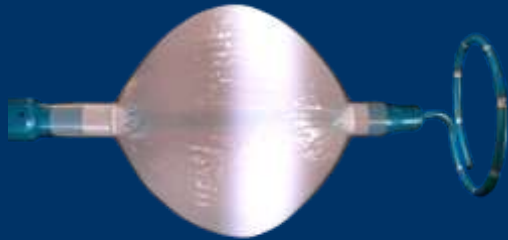
2013



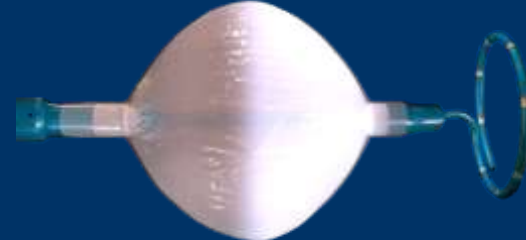
FlexCath Advance
Sheath orientable

2ème Generation Cryoballoon adaptée pour Ablater les bords des Veines Pulmonaires

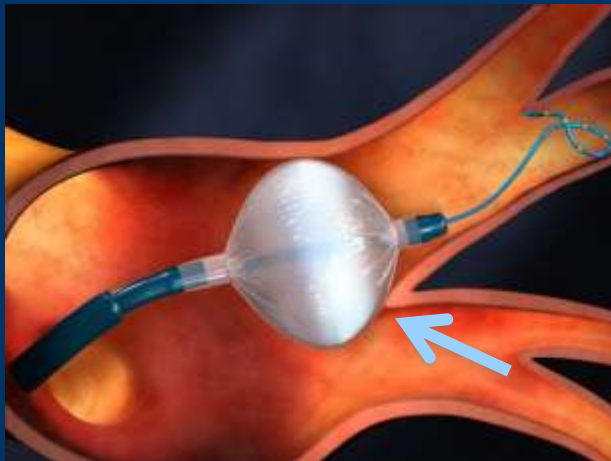
Featuring EvenCool™
Cryo Technology



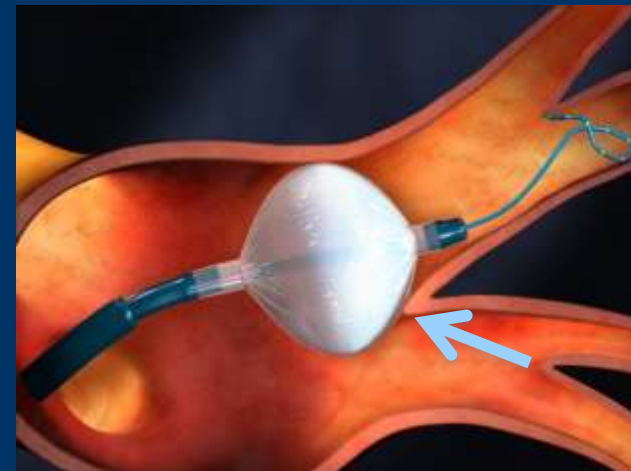
Arctic Front®



Arctic Front Advance®



Anular equatorial cooling zone. Co-axial alignment of the balloon with the PV may be difficult in some vein anatomies.



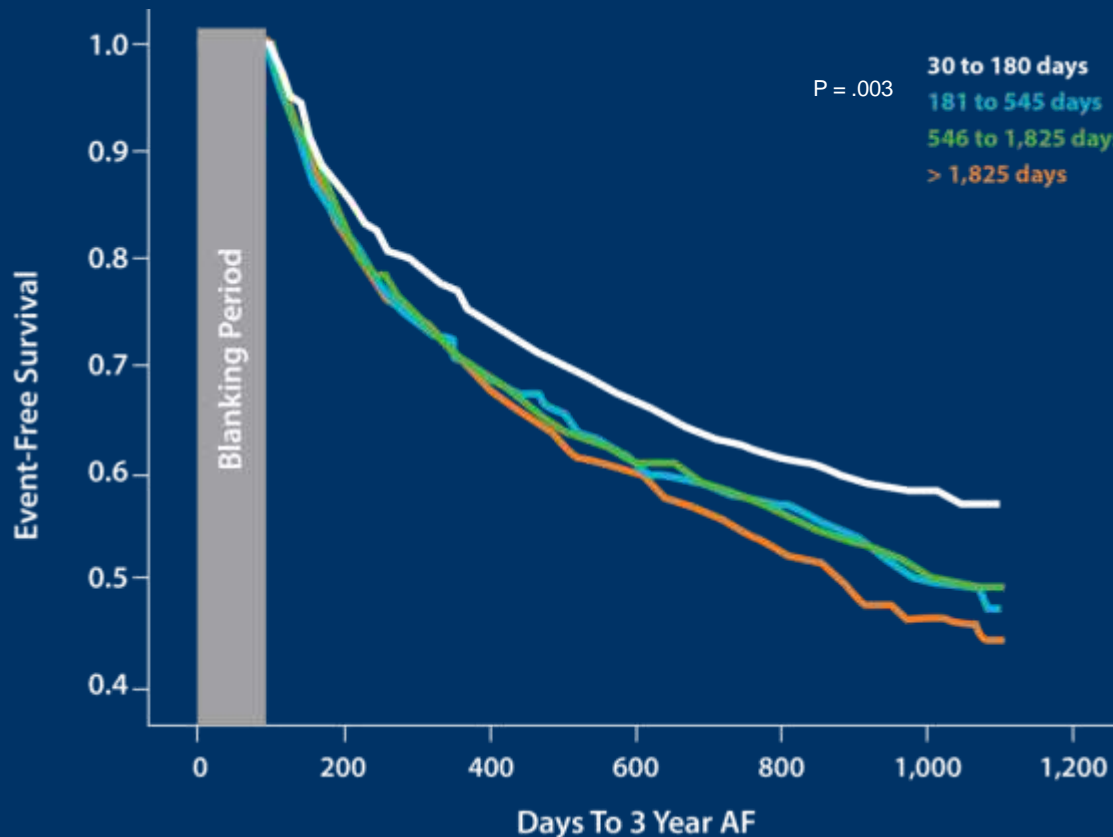
Second generation has homogeneous cooling of the complete northern balloon-hemisphere which allows more flexibility and simplicity in balloon positioning.

Ablation par Catheter et Cryoablation: Efficacité et Sécurité

Le traitement précoce par Catheter Ablation diminue les récurrences

Retrospective analysis of 4,535 consecutive AF patients

Event-Free Survival

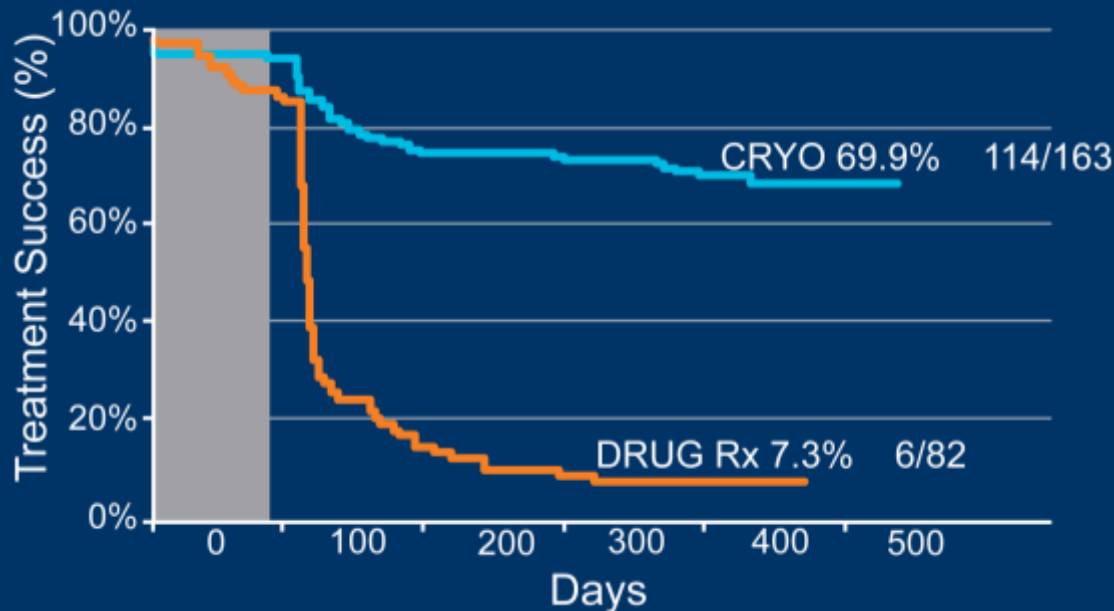


Results

- Patients who underwent earlier treatment had improved 3-year survival free of AF (log rank $P = .003$)
- Delays in catheter ablation treatment led to higher 1-year AF recurrence post ablation for entire population (P trend = .02)
- No difference in stroke rate demonstrated

Cryoablation 10 Fois mieux que le traitement médical pour traiter la FA paroxystique

STOP AF trial: 245 patients were prospectively randomized to either 1st generation Cryoballoon ablation or drug therapy.



OR = 29.5 (12.0 – 72.2) p < 0.001

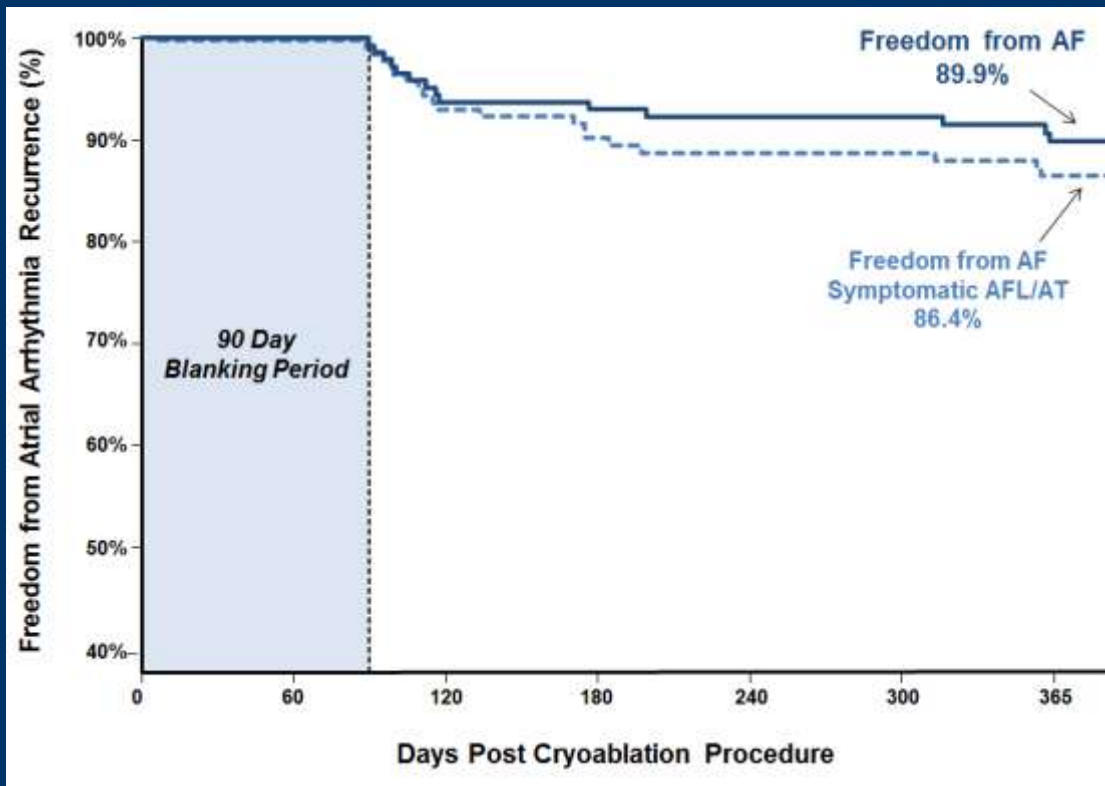
RESULTS

- **98.2%** acute procedural success
- **69.9%** reached primary endpoint of freedom from AF
- **62.2%** of patients were treatment successes without any AF drugs at 12 months
- **60.1%** single procedure success rate

Cryoballoon de 2ème Génération :

Environ 90% de Succés

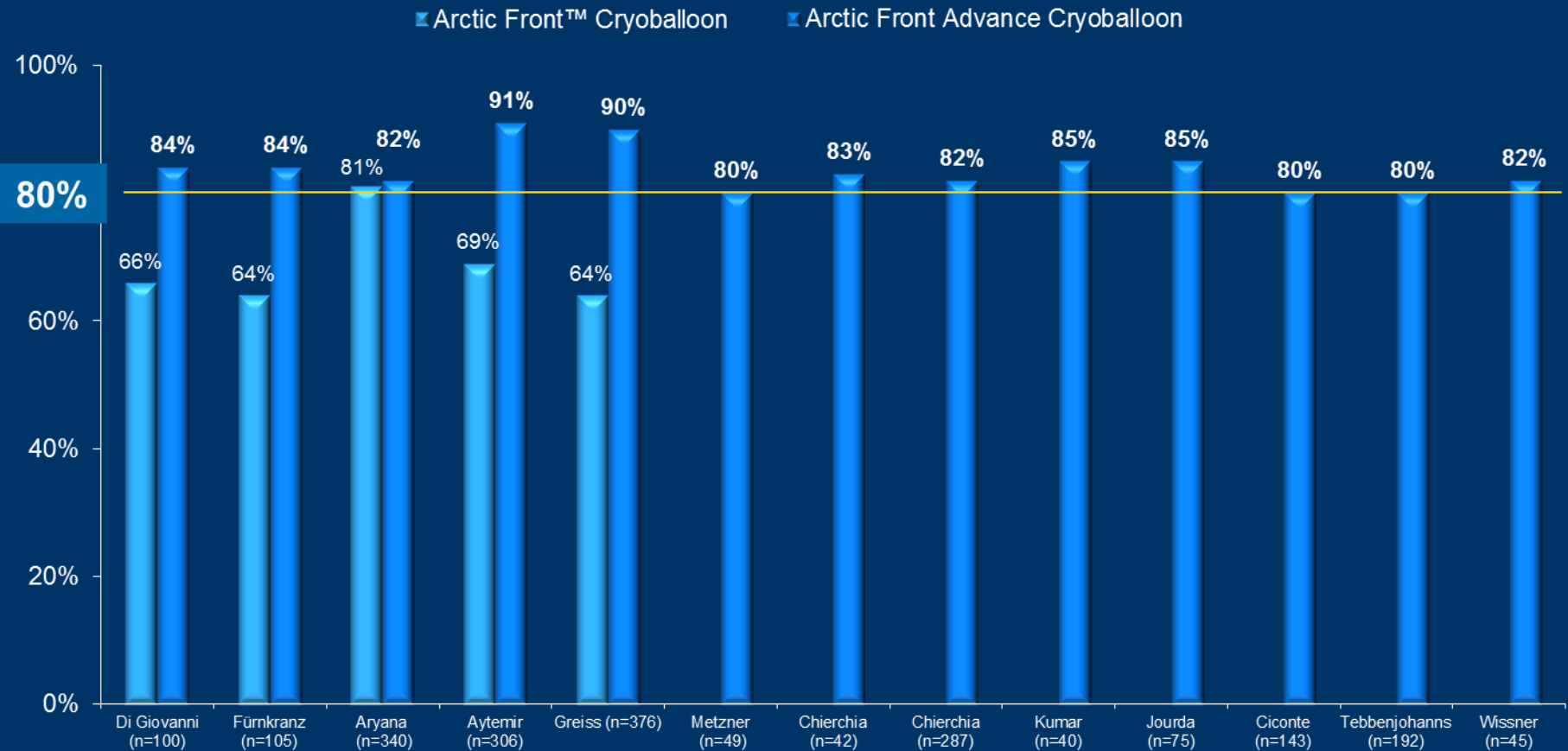
STOP AF PAS:



Results:

- Nearly **90%** freedom from AF at 12 months (n=146)
- 12 month freedom for AF and symptomatic AFL/AT was **86.4%** (n=146)
- **5.9%** (20/146) adverse event rate
- **2.9%** (10/341) repeat ablation rate during the 90 day blanking period

Plus de 80% de disparition de la AF avec Cryoballon 2ème Génération (13 single center studies)



Arrhythmia monitoring methods and definition of procedure success (Freedom from AF Only or AF/AT/AFL) varied between studies.

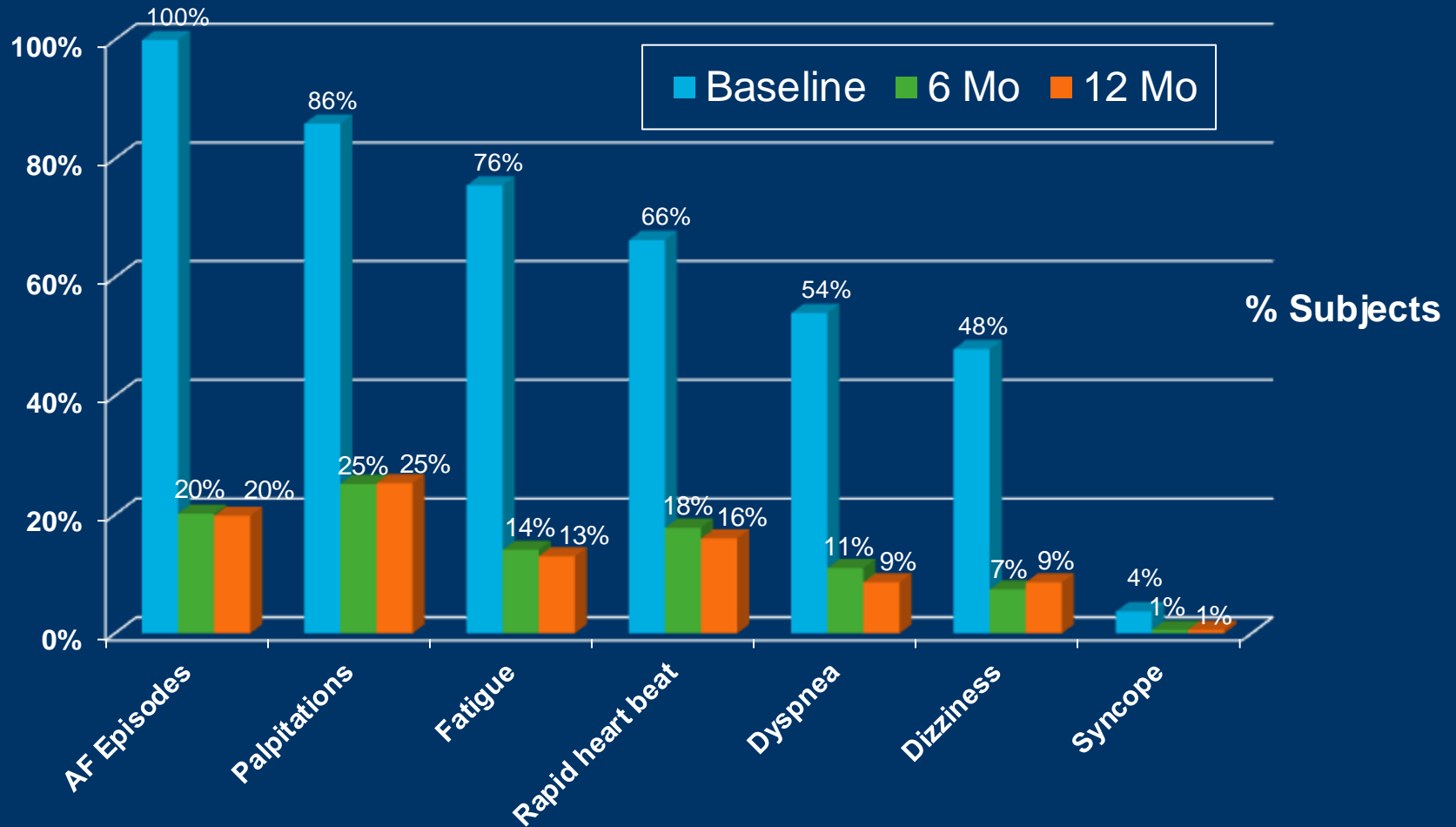
Di Giovanni, et al. *J Cardiovasc Electrophysiol.* 2014; 25(8):834-9; Fürnkranz, et al. *Journal of Cardiovascular Electrophysiology.* 2014; 25(8):840-4; Aryana, et al. *J Interv Card Electrophysiol.* 2014; 41(2):177-186; Aytemir, et al. *Europace.* 2015; 17(3):379-87; Greiss, et al. *PACE.* 2015 Jul; 38(7):815-24; Metzner, et al. *Circ Arrhythm Electrophysiol.* 2014; 7(2):288-292; Chierchia, et al. *Europace.* 2014; Chierchia, et al. *J Cardiovasc Electrophysiol.* 2015; In Press; 16(5):639-644; Kumar et al. *J Interv Card Electrophysiol.* 2014; 41(1):91-7; Jourda, et al. *Europace.* 2015; 17(2):225-31; Ciconte, et al. *Heart Rhythm.* 2015; 12(4):673-80; Tebbenjohanns, et al. *Europace.* 2015; Wissner, et al. *Europace.* 2015 Aug; 17(8):1236-40

Ablation par Cryoballon Démontre une Amélioration Significative de Qualité de Vie



STOP AF Changes in SF-36

Cryoablation Diminue les Symptomes



Self-Reported Symptom Relief Results from STOP AF trial

Sécurité de Ablation par Cathéter

Meta-analysis Montre 5% d'effets secondaires

Safety Outcomes for Patients with AF Undergoing Catheter Ablation

Outcomes	t	n/N	%
Mortality			
Death overall	65	42/5781	0.7
Procedure-related	64	0/5192	0.0
Vascular access complications			
Arteriovenous fistula	32	1/2885	0.0
Bleeding	33	1/2960	0.0
Hematoma	38	17/3719	0.5
Pneumothorax	34	0/2974	0.0
Femoral artery pseudoaneurysm	34	15/3032	0.5
Periprocedure events			
Stroke, ischemic	62	17/5665	0.3
TIA	60	13/5467	0.2
Cardiac Tamponade	63	45/5723	0.8
PE	60	3/5496	0.1
DVT	56	1/4758	0.0
Other embolism	57	10/5347	0.2
LA-esophageal fistula	60	0/5496	0.0
Other fistula	58	3/5407	0.1
Pericardial effusion	64	36/5719	0.6
PV stenosis*	65	91/5831	1.6
AV block	60	1/5496	0.0
CHF exacerbation	60	0/5496	0.0
Need for a pacemaker	46	4/3902	0.1
Total No. of patients with events	28	97/1964	4.9

t indicates No. of treatment groups; n, No. of patients with this adverse event; N, No. of patients evaluated in studies reporting this adverse event; %, percent of patients with adverse event of interest; TIA, transient ischemic accident; PE, pulmonary embolism; DVT, deep vein thrombosis; LA, left atrial; PV, pulmonary vein; AV, atrioventricular; CHF, congestive heart failure.

* > 70% Stenosis (early, < 7 days after ablation; late, < 7 days after ablation).

- Most common complication is symptomatic or asymptomatic pulmonary vein stenosis (1.6%)
- Cardiac tamponade (0.8%)
- Pericardial effusion (0.6%)
- Periprocedural stroke (0.3%)
- No procedure-related deaths reported among the studies meeting inclusion criteria

Sécurité du Cryoballon vs RF Ablation dans FA Paroxystique : Resultat du Registre Ablation Allemand

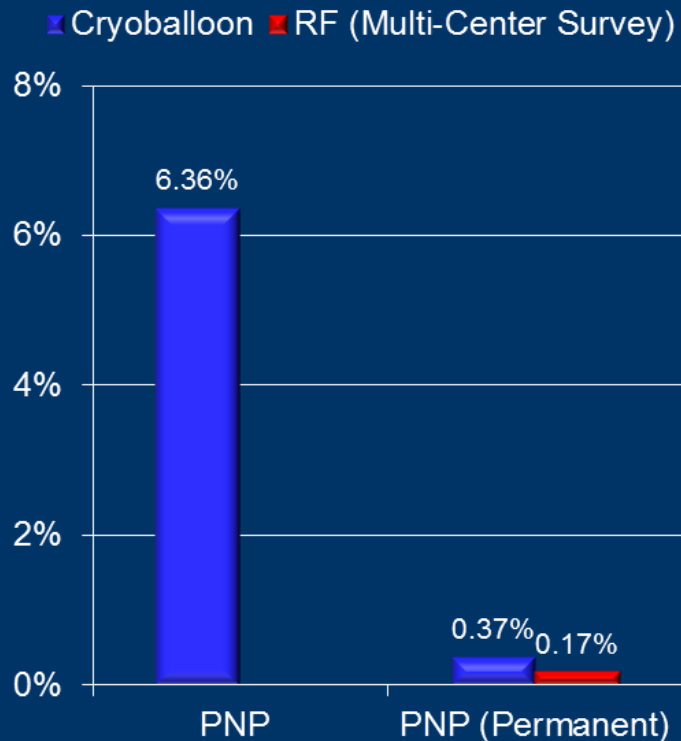
- Le premier et le plus large cryoballon / RF registre publié (n=3,775)
- Taux de complications majeures similaire (4.6% pour les 2 groups)
- Paralysie du Nerf Phrenique environ la moitié des complications de Cryoballon (2.1%)

TABLE 5
Procedural Complications

Complication	RF Ablation (n = 2,870)	Cryoballoon (n = 905)	P Value
Death	0	0	
Myocardial infarction	0	1 (0.1%)	0.40
Stroke/TIA	9 (0.3%)	3 (0.3%)	0.83
Major bleeding	30 (1.1%)	5 (0.6%)	0.16
PV stenosis	0	0	
Atrial-esophageal fistula	0	0	
Aneurysma spurium/AV fistula	33 (1.1%)	7 (0.8%)	0.33
Tamponades	37 (1.4%)	7 (0.8%)	0.17
Pneumothorax	8 (0.3%)	0	0.10
Hemothorax	6 (0.2%)	0	0.16
Sepsis	1 (0.0%)	0	0.57
Pulmonary embolism	1 (0.0%)	0	0.57
Surgical accident	3 (0.1%)	0	0.32
AV block III	0	1 (0.1%)	0.08
Phrenic nerve palsy	1 (0.0%)	18 (2.1%)	<0.001
Total	132 (4.6%)	42 (4.6%)	1.00

AV block III = atrioventricular block grade III; AV fistula = arteriovenous fistula; PV stenosis = pulmonary vein stenosis; RF ablation = radiofrequency ablation; TIA = transient ischemic attack.

Meta-analyse après Cryoablation montre une faible incidence de Paralyse Phrénique permanente



539 Arctic Front articles screened, 23 were retained for the final analysis (1309 patients):

- PNP overall incidence of **6.38%**
 - **4.73%** of PNP persisted after the ablation procedure
 - **0.37%** of patients experiencing PNP that persisted beyond 1 year.

Large Essai Randomisé montre PVI suffisante pour la FA Persistante

“The results of the STAR AF 2 trial will likely change practice by shifting the focus to shorter and more effective PVI alone without the addition of other ablation. Our results have important implications for procedural safety and duration. Experts will need to reconsider current ablation guidelines to reflect these findings in patients with persistent AF.”²

Atul Verma, MD, STAR AF 2 Principal Investigator

STAR AF 2 Trial Design - Largest randomized trial to examine outcomes of catheter ablation in persistent AF with 589 patients recruited from 48 experienced ablation centers in 12 countries.

Conclusions:

- PVI alone achieved freedom from recurrence in about 50% of patients – comparable to published success rates from randomized, multicenter trials in PersAF
- Additional CFAE or linear ablation increase procedural time which may increase risk

Freedom from AF at 18 month FU

- **59% for PVI alone**
 - **48% for PVI + CFAE**
 - **44% for PVI + lines**
- } (p=0.15)

Freedom from AF after 2 procedures

- **72% for PVI alone**
 - **60% for PVI + CFAE**
 - **58% for PVI + lines**
- } (p=0.18)

¹ Verma A et al. N Engl J Med 2015;372:1812-1822

² Verma, ESC press release (<http://www.escardio.org/about/press/press-releases/esc14-barcelona/Pages/hotline-three-star-af-2.aspx>).

Conclusions

- L'ablation par Catheter est sûre et efficace pour les patients en FA
- L'ablation par Cryoballon ablation est un traitement innovant qui a des avantages par rapport à l'ablation par radiofréquence
- [La clinique du Val d'Anfa] utilise la dernière technologie (CRYO) qui offre aux patients des traitements efficaces de la FA