

**SEVEN YEARS OF CRYO-BALLOON CATHETER  
ABLATION. FOLLOW-UP ANALYSIS, RESULTS,  
RECURRENCES, COMPLICATIONS AND SIDE EFFECTS IN  
PATIENTS TREATED FOR PAROXYSMAL ATRIAL  
FIBRILLATION, WITH A PROSPECTIVE PROTOCOL  
GUIDED BY COMPLETE BIDIRECTIONAL LEFT ATRIUM-  
PULMONARY VEINS DISCONNECTION AFTER  
ADENOSINE AS MAIN TARGET END POINT. A SINGLE  
CENTER REPORT.**

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# INTRODUCTION

Complete pulmonary veins isolation (PVI)  
from the **left atrium (LA)** is **CRUCIAL** to cure  
patients with Atrial Fibrillation.

# INTRODUCTION

**PVI with Cryo-Balloon (CB) has demonstrated its effectiveness for the treatment of Paroxysmal Atrial Fibrillation (PAF).**

However, Cryo-Energy **CB** application **doesn't produce a homogeneous circumferential lesion** (\*) in all **PV**, which is related to their anatomical shape and size.

(\*) Paylos J.M. et.al. "Gadolinium Delayed-Enhancement MRI to assess the extension of residual cryo-balloon catheter induced lesion at the Left-Atrium-PV-Junction level in patients treated for Paroxysmal Atrial Fibrillation". *Heart Rhythm* Vol. 7. No.5 May Supplement 2010.

# INTRODUCTION

And a better quantification of the **Cryo-ablation zone** and the anatomical extent of pulmonar vein have been better clarify in recent years(\*).

(\*) Chierchia G.B. et.al. "Anatomical extent of pulmonary vein isolation after cryoballoon ablation for atrial Fibrillation: Comparison between the 23 and 28mm balloons". J. Cardiovasc Med (Hagerstown) 2011 ; 12:840-84.

(\*) Kenigsberg D.N. et. al . "Quantification of the cryoablation zone demarcated by pre- and postprocedural electroanatomic mapping in patients with atrial fibrillation using the 28-mm second-generation cryoballoon" .Heart Rhythm. 2015;12 No2: 282-290

# INTRODUCTION

**Incomplete lesions with dormant tissue** (despite a “perfect” occlusion) can occur leading to a **residual conduction (RC) gaps** causing (or responsible) for PV reconnection which is the principal cause of **RECURRENCE**.

# INTRODUCTION

- **Adenosine (AD)** has been used to “unmask” **RC** in apparently isolated **PV** with Radiofrequency (**RF**).
- Routine use of **AD** after acute **CB-PVI** allows to identify incomplete lesions with **dormant tissue** not evident in basal conditions.
- **Focal/ Freeze/RF** applications eliminates such **RC**.

# INTRODUCTION

The Only “**No Evidence**” of PV/Electrical activity on the “circular-mapping-catheter” at the **LA-PV Junction** level after **CB-PVI** is “**Not Enough**” to assure “complete **acute PVI**”, and checking for **Entry** and **Exit** Block is Mandatory to **confirm it**.



# INTRODUCTION

We analyzed our **seven years** follow-up experience of our patients, initially treated with **CB** for **PAF**, with demonstration of complete bidirectional electrical isolation (**CBEI**) of the pulmonary veins (**PV**) from the left atrium (**LA**) after **AD** as the main target end point to achieve, in all cases.

# INTRODUCTION

## (Protocol)

- **Exit** block
  - By pacing **PV** from all 20 poles of the circular catheter at high amplitude voltage with consistent 1:1 **PV** capture and **no evidence at all** of **Any atrial** response.
- **Entry** block
  - By pacing **LA** from the CS-Catheter at three different cycle lengths (600, 500, 400 mS) with consistent 1:1 **LA** capture and **no evidence at all** of **Any PV** electrical activity in **any** of the 20 poles of circular-catheter mapping placed into the vein at the **LA-PV Junction** level.

- **With this approach:**
  - Checking for **Entry** and **Exit** / Block.
  - After Basal / Acute **PVI**, and **repeating** / After **AD**.
  - Elimination of “Residual **gaps**” by **Freeze/Focal RF** / Applications.
- **Since November 2008 to July 2015:**

**114 Patients**

- **Highly symptomatic, suffering from recurrent PAF, refractory to medical treatment, were treated with the “CB” and Followed-Up**

# METHODS

- **114 Patients** (mean age  $56 \pm 13$  years).
  - **86 Male (75.4%)** – mean age  $53 \pm 13$
  - **28 Female (24.6%)** – mean age  $61 \pm 10$
- ✓ **Mean / Years / PAF:**  $5 \pm 5$  (1-25)
- ✓ **Folow-up time / Days:**  $1693 \pm 653$  (90-2520)
- ✓ **Mean / Episodes PAF / Year:**  $58 \pm 66$  (2-200)
- ✓ **None Structural Heart Disease.**

**Mean LVEF:**  $67 \pm 5$  %.

# METHODS

- All patients previously treated with antiarrhythmic:
  - ✓  $\beta\beta$  (87%)
  - ✓ Class III (1.7%)
  - ✓ Class 1C (89.5%)
  - ✓  $\beta\beta$  + 1C (76.3%).

Morphological and structural data:

LA Diameters (mm)	LA/ AREA (cm <sup>2</sup> )	PV(mm) 434	CT 22	LVEF
AP:37±6 (21-50)	22±4 (11-32)	AP:18±5 (8-32)	AP: 26±6 (18-35)	67±5% (59-79)
LAT: 47±7 (35-61)		SI:20±4 (10-28)	SI: 26±5 (17-31)	
SI: 54±7 (40-75)				

# METHODS

- ❑ First-Generation Cryoballoon:  
**74 Patients.**

- 28 mm: 73 patients
- 23 mm: 1 Patient

- ❑ Second-Generation Cryoballoon:  
**\*40 Patients**

- 28 mm: 37 Patients
- 23 mm: 4 Patients

\* In 1 patient 28mm CB was used (Proximal application) & 23mm CB (Distal application).

## PV CARTOGRAPHY / MAPPING

- **Circular** Duodecapolar 7 French with adjustable diameter catheter. (Saint Jude Reflexion Spiral).

Grade(\*) of **CB** / Application / **Occlusion** / for **PVI**

**III**  
( 12.9 % )  
**143**  
Applications

**IV**  
( 80 % )  
**885**  
Applications

(\*) Neumann T, et. al. "Circumferential pulmonary vein isolation with the cryoballoon technique results from a prospective 3-center study". J Am Coll Cardiol. 2008;52:273-8.



## Cryo-Ablation (Mean Temperature Reached)

Occlusion  
Grade **III** :

Temperature: **42±5 °C**

Nº Occlusions: **2±1**

Occlusion  
Grade **IV** :

Temperature: **- 51±8 °C**

Nº Occlusions: **2±1**

## Adenosine / Protocol

- **Bolus** administration of increasing doses (12-18-24... mgrs).
- **Pacing** PV / LA (600, 500, 400 mS CL).
- **WHEN**  
↓- **A-V** Conduction **Block** Ocurrent.

## Freeze/ RF protocol

- Residual Conduction **gaps** (RC)
  - Basal
  - After checking (Basal) for **Entry** and **Exit** Block
  - After checking (**Adenosine**) for **Entry** and **Exit** Block

Were eliminated by Freeze/**Focal** RF Applications.

- Only the most Extensive **RC** required  $\geq 2$  **RF Focal** Applications to **Abolished**.

- **RC** >2 Pair / Electrode / Circular Catheter



**Repeated**

- **New CB / Application (Occlusion)**

# RESULTS

A total of **434 PV** and **22 Common Trunks (CT)** were treated with **CB**

CBEI demonstrated in **392 (90.3%)**.

Acute reconnection post CB showed **42 (9%) PV**.

**14 (3,2%)**  
Residual  
Conduction  
(gap).

**16 (3,5%) /392 PV**  
Reconnection  
after Adenosine.

**10**  
patients

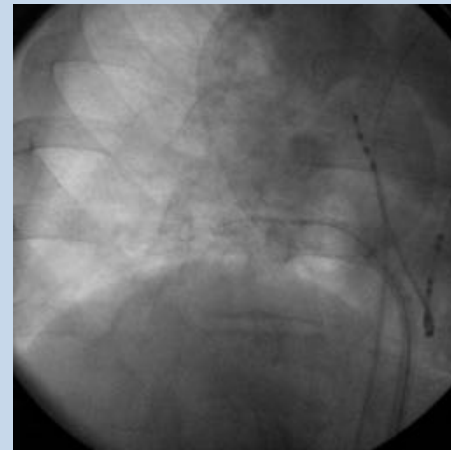
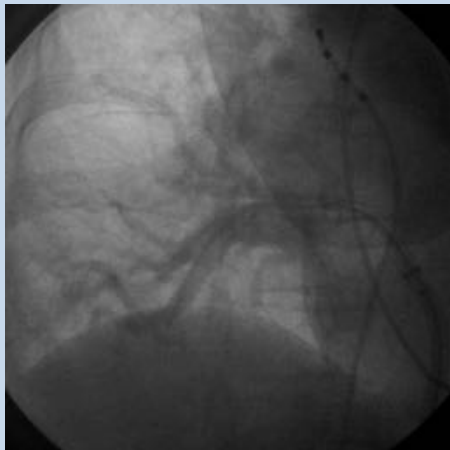
**12 (2,7%)**  
Extrapulmonary  
Muscular  
Connections  
(EMC)(\*)

**9**  
patients

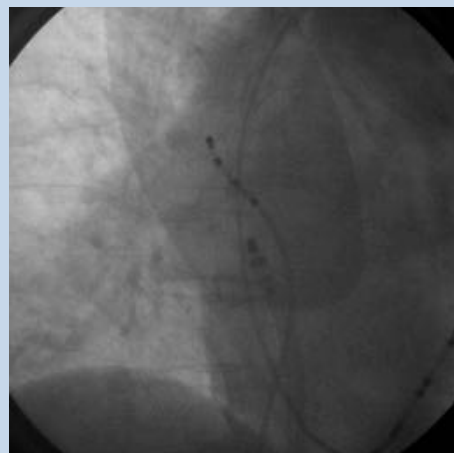
(\*) Cabrera J.A, Ho S.Y., Climent V. et al, "Morphological evidence of muscular connections between contiguous pulmonary venous orifices: Relevance of the interpulmonary isthmus for Catheter ablation in Atrial Fibrillation" Heart Rhythm 2009;6:1192-1198

(\*) Squara F., Liuba I., Chik W. et al. "Electrical connection between ipsilateral pulmonary veins: Prevalence and implications for ablation and adenosine testing" Heart Rhythm 2015;12:275-282.

## Oclusionion Degree III with contrast / Leakage



RF / RSPV **gap**

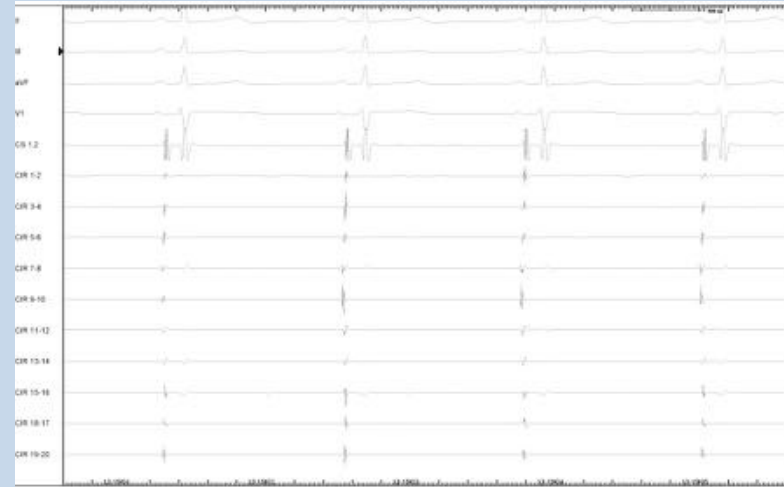


**gap** After Adenosine

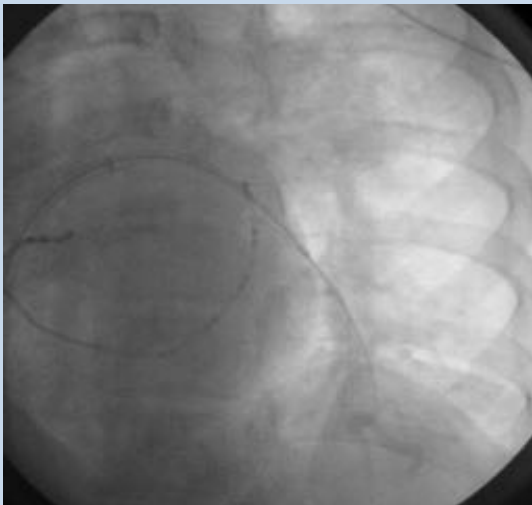


# METHODS

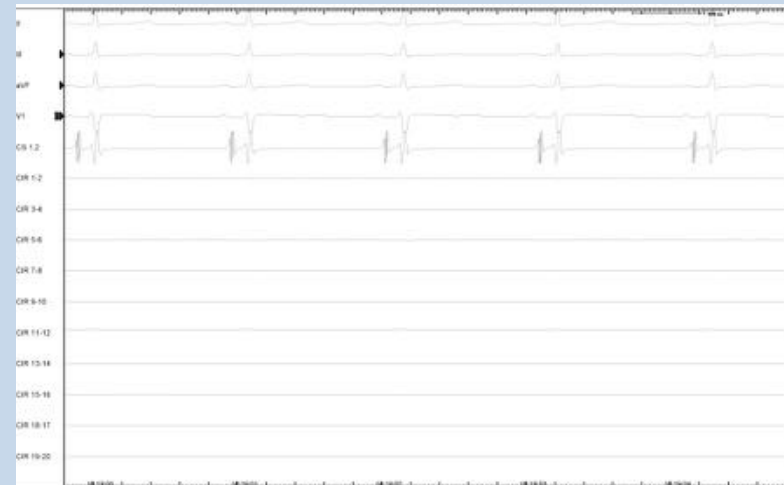
LIPV / Basal



Oclusion Degree IV / LIPV

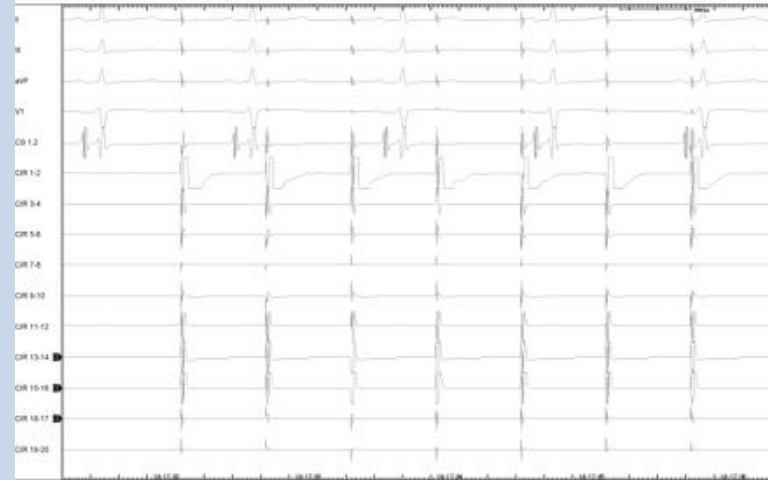


LIPV Post-Crio

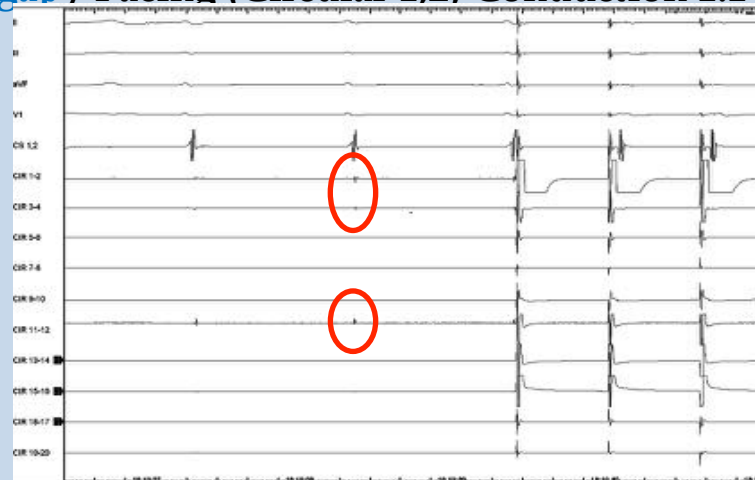


# METHODS

Pacing (Circular 1,2) PV  
Exit Block



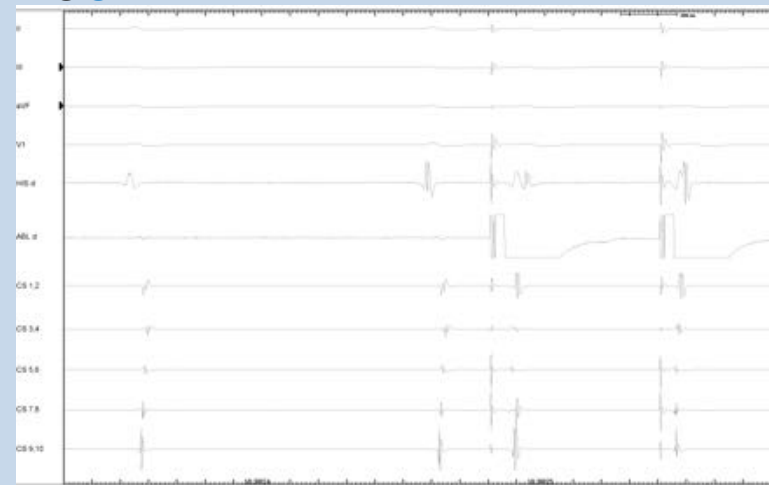
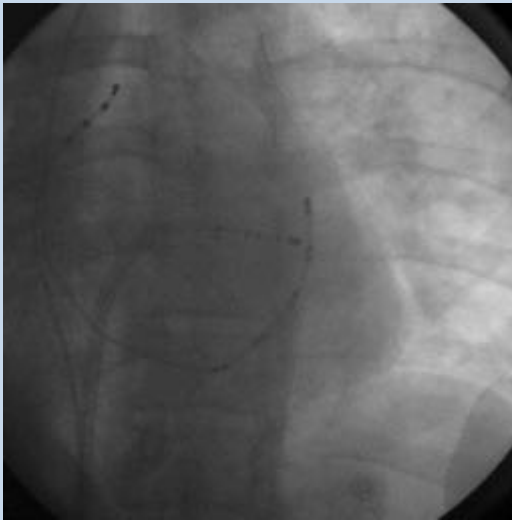
Adenosine 12 mg. i.v.  
RC / **gap** / Pacing (Circular 1,2) Conduction 1:1 PV/LA



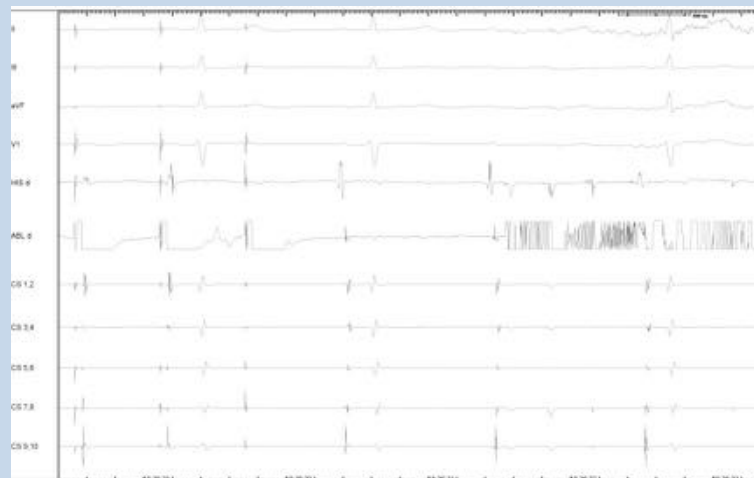
# METHODS

RF / Residual Potential / **gap**

Adenosine 12 mg. i.v.  
Pacing **gap** / RF Catheter Conduction 1:1 PV/LA



RF / Residual Potential / **gap**





# RESULTS

- BB after Adenosine 422/434 PV

96.5 %

- The Remaining 12/434 PV

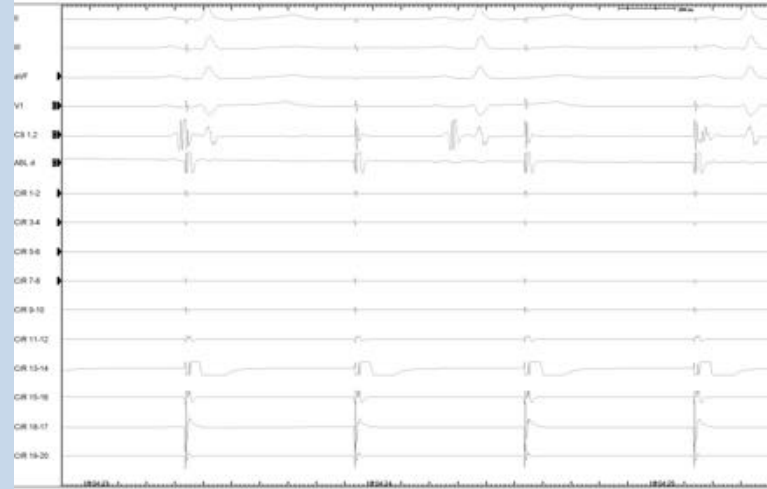
Extrapulmonary Muscular Connection

Were Demonstrated  
and

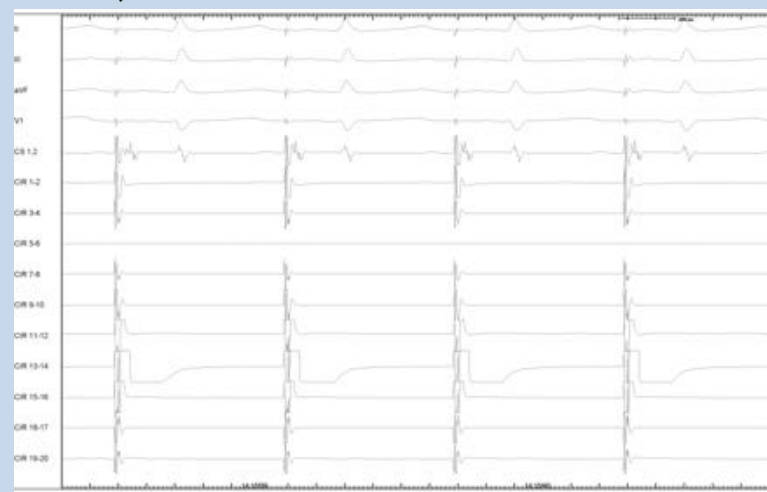
All finally abolished by Focal RF applications distal into the vein.

## EXTRAPULMONARY MUSCULAR CONNECTION

### Pacing Proximal Antrum (Circular 13-14) Exit Block

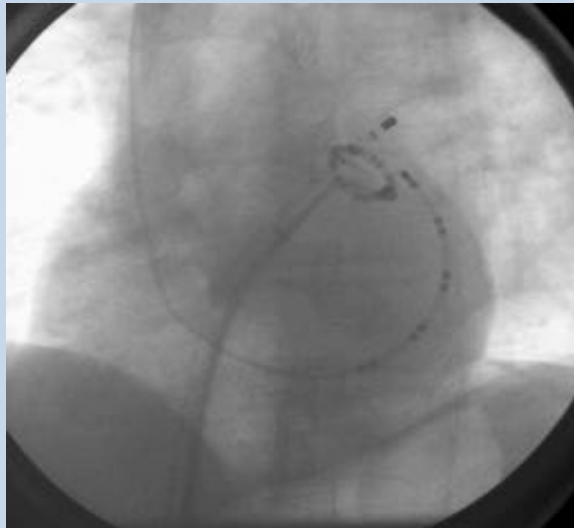


### Pacing Distal Vein (Circular 13-14) Conduction 1:1 PV/LA

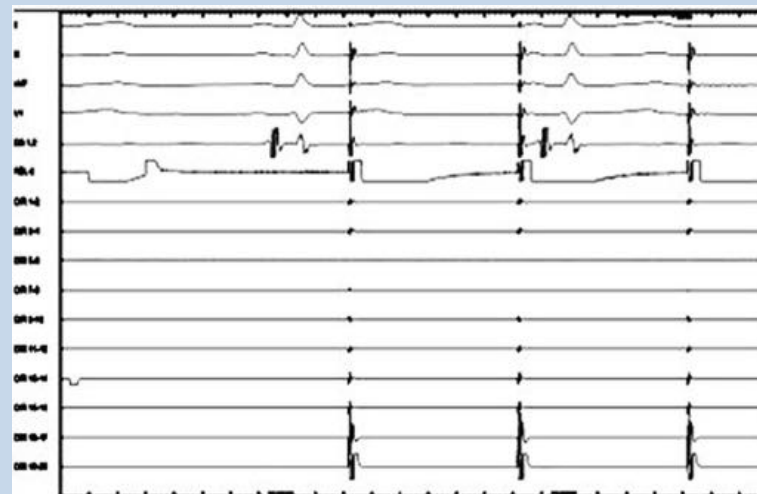
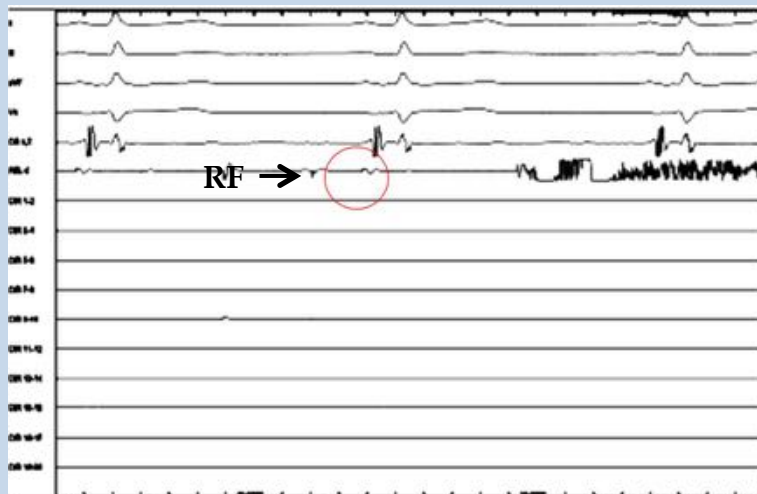


## EXTRAPULMONARY MUSCULAR CONNECTION

Pacing **gap** Distal Vein / RF Catheter Conduction 1:1 PV/LA



Pacing Distal / Post Focal RF  
**Exit Block**



- First / 3 months / after CB / ablation
- All patients were under medical treatment, including:
  - Flecainide
  - Atenolol
  - Oral Anticoagulation (Dicumarine)
- And completely / stopped and discontinued / After this period.



Follow-Up  
 $1693 \pm 653$  / days  
( $3 \pm 84$  months)

14 pts. (12.3%) had clinical recurrence.



• 12 M ( $52 \pm 8$ )  
years



• 2 F ( $63 \pm 13$ )  
years

### Early Recurrences.

- Occurred when medication stopped after three months blanking-period in 9 male.

### Late Recurrences.

- Presented 3 male at 24, 27 and 60 months and 2 female at 7 and 40 months respectively.

# RESULTS

## FOLLOW-UP

## RECURRENCES

- 14 Patients out of 114 RECURRED.

**12.3 %**

- Second procedure (REDO)

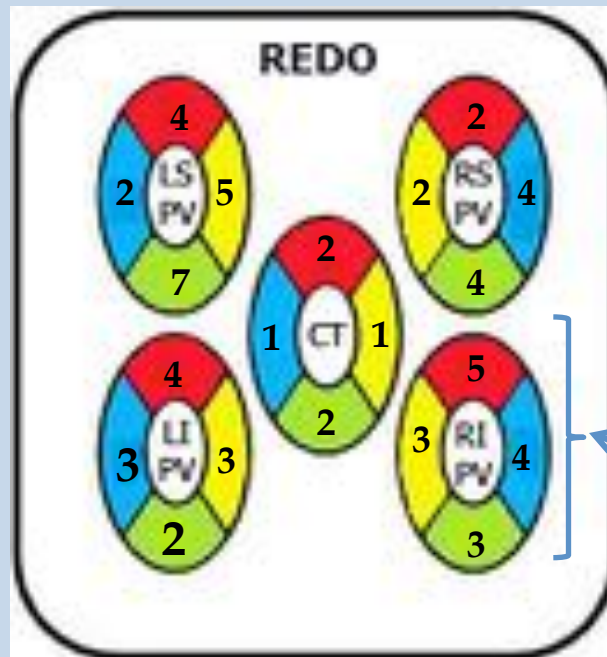
**14** /14 (100%)

# RESULTS

## RECURRENCES

- **REDO Cases (Second Procedure)**  
14 patients with 54 PV. Including 2 CT.

**54 PV** → **29** (53,7%) Reconstructed



## SEGMENTS

SUPERIOR

INFERIOR

ANTERIOR

POSTERIOR

Same Patient

# RESULTS

## RECURRENCES

**14 PATIENTS**

(REDO)

SEGMENT/ LOCATION

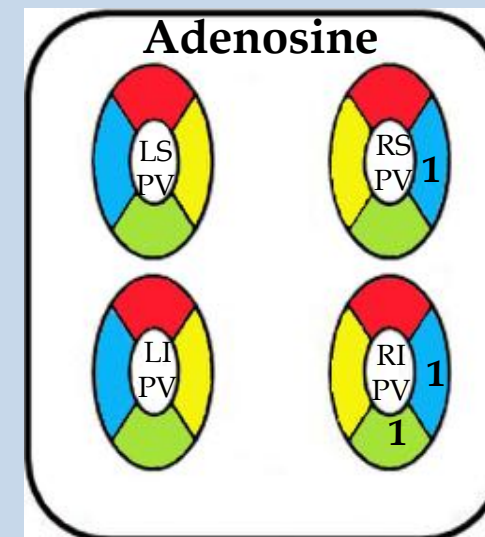
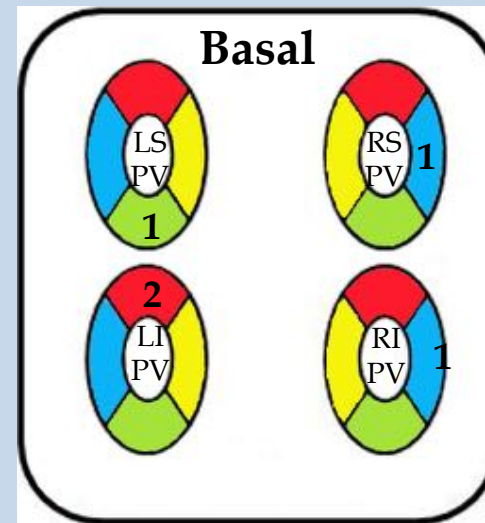
1<sup>st</sup>. Procedure

**6 PATIENTS**

**9 PV**

**TOTAL: 9 Segments**

(Different segment location  
First/Second Procedure)



**SEGMENTS**

**SUPERIOR**

**INFERIOR**

**ANTERIOR**

**POSTERIOR**



- We have not done any protocol to rule out **Non PV-Foci** (as a potential cause of Arrhythmia recurrence)\*, because all recurrences were **REDO**, and **PV-LA reconnection** demonstrated in **all cases**.

(\*) Hayashi K, An Y, Nagashima M. et. al. "Importance of nonpulmonary vein foci in catheter ablation for paroxysmal atrial fibrillation". Heart Rhythm 2015;12:1918-1924

# RESULTS

In a **REDO** follow-up ( $40 \pm 14$  months) All **14** pts remain in **Sinus Rhythm** with not medication.

- The **REMAINING 100** Patients  
Follow-up  $1693 \pm 653$  days (3-84 months)

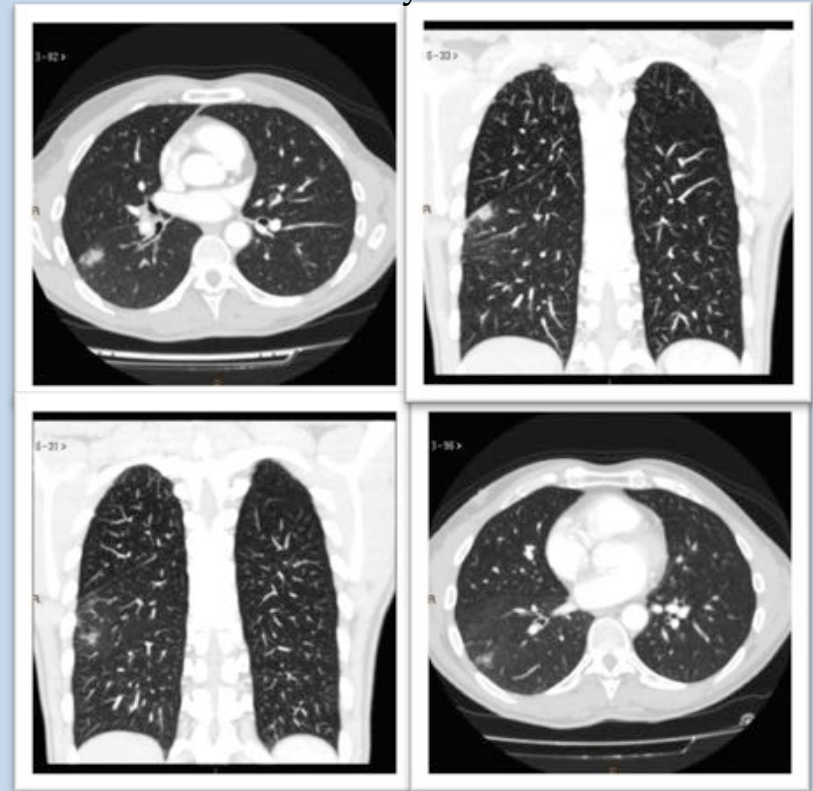
**87.7 %**

- Are Asymptomatic, Free of Drugs, in **Sinus Rhythm**.

## •SIDE EFFECTS AND COMPLICATIONS:

- ✓ Aphonia(\*): 6 pts (5.7%).
- ✓ Phrenic paresia(\*\*): 7 (6.7%).
- ✓ Phrenic palsy(\*\*): 2 (1.9%).
- ✓ Pulmonary infiltrates\*: 5 (4.8%).
- ✓ Dyspepsia: 2 (1.9%).
- ✓ Bronchospasm: 2 (1.9%).
- ✓ Intra-nodal reentry: 2 (1.9%).
- ✓ In-hospital arrhythmia: 1 (0.9%).

\* Pulmonary infiltrates



(\*) Cabrera J.A., Murillo M, Climent V. et. al. "Relationship between the left Recurrent Laryngeal nerve and left atrium: A postmortem study in patients with and without Atrial Fibrillation". Heart Rhythm. 2011;S413: PO5-152.

(\*\*) Mugnai G. De Asmundis C, Ciconte G. et. al. "Incidence and Characteristics of complications in the setting of second-generation cryoballoon ablation: A large single-center study of 500 consecutive patients". Heart Rhythm. 2015;12:1476-1482..

## SIDE EFFECTS AND COMPLICATIONS

### RSPV –CB application.

#### TRANSIENT PHRENIC NERVE PARESIA

	T °C	Seconds	CB mm.	CB Generation
1	-68	122	28	FIRST
2	-73	222	28	FIRST
3	-55	89	28	SECOND
4	-56	165	23	SECOND
5	-60	115	28	SECOND
6	-68	100	28	SECOND
7	-65	190	28	SECOND

#### PERMANENT PHRENIC NERVE PALSY

1	-70	100	28	FIRST
2	-68	156	28	FIRST

**78%**  
Mean T.°C≥

**-60°C**

# RESULTS

## SIDE EFFECTS AND COMPLICATIONS

Follow-up.

- **Aphonia:** Lasting  $\leq 72$  hours.
- **Permanent Phrenic Nerve Palsy:** Chest X-Ray (1-3 years)
- **Pulmonary Infiltrates:** (No Symptoms). Showed at first month CT-Scan control . No evidence at 3 months CT-Scan control .
- **Dyspepsia:** Quick complete resolution  $\leq 72$  hours (Omeprazol).

# RESULTS

## SIDE EFFECTS AND COMPLICATIONS

**Mortality** 0

**Atrioesophageal fistula** 0

**PV Stenosis** 0

1. Cryo-Energy PV application **doesn't produce a homogeneous circumferential lesion in all PV.**
2. Checking for **BB** and **Adenosine** protocol allow to identify **19%** of patients with potential substrate for **PV/LA** Reconduction and possibly recurrence of the Arrhythmia.
3. **Routine use of AD** after acute **CB-PVI** allows to identify incomplete lesions with **dormant tissue**, and eliminate them by **freeze** or **focal RF** applications, **Improves** the long-term rate of the “**possible**” definitive cure of patients suffering **PAF**.

4. CB technique **alone** is very **effective** and **safe** for the definitive treatment of PAF, with **68.7%** success rate, increasing up to **87.7%** when this protocol is applied, remaining Patients in sinus rhythm, **free of arrhythmia**, without medication, in a very **long-term follow-up**.



# CONCLUSIONS

5. However, **Late Recurrences**, generates some concern about a greater increase number of patients with recurrent arrhythmia in a longer term, **specially in the future patients who don't feel symptoms of the arrhythmia**

# CONCLUSIONS

**“To the best of our Knowledge... This serie includes  
the largest follow-up described, so far”.**

