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.
PVI with Cryo-Balloon (CB) has demonstrated it’s 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.

INTRODUCTION

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

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

• 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**

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

• **114 Patients** (mean age 56±13 years).
  – **86 Male** (75.4%) – mean age 53 ± 13
  – **28 Female** (24.6%) – mean age 61 ±10

✓ **Mean / Years / PAF**: 5 ±5 (1-25)

✓ **Follow-up time / Days**: 1693 ±653 (90-2520)

✓ **Mean / Episodes PAF / Year**: 58±66 (2-200)

✓ **None Structural Heart Disease.**

**Mean LVEF**: 67 ±5 %. 
• All patients previously treated with antiarrhythmic:
  ✓ ββ (87%)
  ✓ Class III (1.7%)
  ✓ Class 1C (89.5%)
  ✓ ββ + 1C (76.3%).
**METHODS**

Morphological and structural data:

<table>
<thead>
<tr>
<th>LA Diameters (mm)</th>
<th>LA/ AREA (cm²)</th>
<th>PV (mm)</th>
<th>CT</th>
<th>LVEF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AP</strong>: 37±6</td>
<td></td>
<td>AP:18±5</td>
<td>AP:26±6</td>
<td>67±5%</td>
</tr>
<tr>
<td><strong>LAT</strong>: 47±7</td>
<td>22±4</td>
<td>SI:20±4</td>
<td>SI:26±5</td>
<td></td>
</tr>
<tr>
<td>(35-61)</td>
<td>(11-32)</td>
<td>(10-28)</td>
<td>(17-31)</td>
<td></td>
</tr>
<tr>
<td><strong>SI</strong>: 54±7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(40-75)</td>
<td></td>
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</tr>
</tbody>
</table>
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).
METHODS

PV CARTOGRAPHY / MAPPING

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

Grade(*) of **CB** / Application / **Oclusion** / for **PVI**

<table>
<thead>
<tr>
<th>III (12.9 %)</th>
<th>IV (80 %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>143 Applications</td>
<td>885 Applications</td>
</tr>
</tbody>
</table>

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
METHODS

Adenosine / Protocol

• **Bolus** administration of increasing doses (12-18-24… mgrs).

• **Pacing PV / LA** (600, 500, 400 mS CL).

• **WHEN**

  • **A-V Conduction Block** Ocurred.
METHODS

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 ≥2 RF Focal Applications to Abolished.

- RC >2 Pair / Electrode / Circular Catheter
  - Repeated
- New CB / Application (Occlusion)
A total of 434 PV and 22 Common Trunks (CT) were treated with CB

CBEI demonstrated in 392 (90.3%).
Acute reconduction post CB showed 42 (9%) PV.

14 (3.2%) Residual Conduction (gap).
16 (3.5%) /392 PV Reconduction after Adenosine.
12 (2.7%) Extrapulmonary Muscular Connections (EMC)(*)

METHODS

Oclussion 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

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

RF / Residual Potential / gap

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.
METHODS

EXTRAPULMONARY MUSCULAR CONNECTION

Pacing Proximal Antrum (Circular 13-14) Exit Block

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

EXTRAPULMONARY MUSCULAR CONNECTION

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

Pacing Distal / Post Focal RF Exit Block
RESULTS

FOLLOW-UP

- 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 ± 653 / days
(3 ±84 months)
14 pts. (12.3%) had clinical recurrence.

- 12 M (52 ± 8) years
- 2 F (63 ±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
RECURRENTS

• 14 Patients out of 114 RECURRED.

12.3 %

• Second procedure (REDO)

14 /14 (100%)
RESULTS

RECURRANCES

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

54 PV → 29 (53.7%) Reconduted

SEGMENTS
- SUPERIOR
- INFERIOR
- ANTERIOR
- POSTERIOR

Same Patient
RESULTS

14 PATIENTS
(REDO)

SEGMENT/LOCATION
1\textsuperscript{st} Procedure

6 PATIENTS

9 PV

TOTAL: 9 Segments

(Different segment location
First/Second Procedure)
• 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 reconduction demonstrated in all cases.

RESULTS

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

- The REMAINING 100 Patients
  Follow-up 1693±653 days (3-84 months)

  87.7 %

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

• 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%).

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

## SIDE EFFECTS AND COMPLICATIONS

RSPV – CB application.

<table>
<thead>
<tr>
<th></th>
<th>T °C</th>
<th>Seconds</th>
<th>CB mm.</th>
<th>CB Generation</th>
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<tbody>
<tr>
<td><strong>TRANSIENT PHRENIC NERVE PARESIA</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-68</td>
<td>122</td>
<td>28</td>
<td>FIRST</td>
</tr>
<tr>
<td>2</td>
<td>-73</td>
<td>222</td>
<td>28</td>
<td>FIRST</td>
</tr>
<tr>
<td>3</td>
<td>-55</td>
<td>89</td>
<td>28</td>
<td>SECOND</td>
</tr>
<tr>
<td>4</td>
<td>-56</td>
<td>165</td>
<td>23</td>
<td>SECOND</td>
</tr>
<tr>
<td>5</td>
<td>-60</td>
<td>115</td>
<td>28</td>
<td>SECOND</td>
</tr>
<tr>
<td>6</td>
<td>-68</td>
<td>100</td>
<td>28</td>
<td>SECOND</td>
</tr>
<tr>
<td>7</td>
<td>-65</td>
<td>190</td>
<td>28</td>
<td>SECOND</td>
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</table>

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<thead>
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<th>Seconds</th>
<th>CB mm.</th>
<th>CB Generation</th>
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<tbody>
<tr>
<td><strong>PERMANENT PHRENIC NERVE PALSY</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>1</td>
<td>-70</td>
<td>100</td>
<td>28</td>
<td>FIRST</td>
</tr>
<tr>
<td>2</td>
<td>-68</td>
<td>156</td>
<td>28</td>
<td>FIRST</td>
</tr>
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</table>
RESULTS

SIDE EFFECTS AND COMPLICATIONS

Follow-up.

- **Aphonia**: Lasting ≤ 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 ≤ 72 hours (Omeprazol).
## RESULTS

### SIDE EFFECTS AND COMPLICATIONS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>0</td>
</tr>
<tr>
<td>Atrioesophageal fistula</td>
<td>0</td>
</tr>
<tr>
<td>PV Stenosis</td>
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</table>
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.
5. However, **Late Recurrences**, generates some concern about a greater increase number of patients with recurrent arrhythmia in a longer term, specifically in the future patients who don’t feel symptoms of the arrhythmia
"To the best of our Knowledge... This serie includes the largest follow-up described, so far".