Experience with Cryoablation

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Disclosures

- Consultant: Biosense-Webster and Medtronic
- Research support: Abbott, Biosense-Webster, Boston Scientific, and Medtronic
Cryoballoon Ablation of Atrial Fibrillation

- EU approval of Arctic Front cryo-balloon in July 2005
- FDA approval in US
  - Dec 2010 for Arctic Front
  - Aug 2012 for Arctic Front Advance
  - Nov 2018 for Arctic Front Advance ST Pro
FIRE AND ICE

A Primary Efficacy End Point

Hazard ratio, 0.96 (95% CI, 0.76–1.22)
P<0.001 for noninferiority

90-Day blanking period
35.9%
34.6%

Days since Procedure

Patients with Primary Efficacy Event (%)

No. at Risk
Cryoballoon 374 338 242 194 165 132 107 70 57 34 12
RFC 376 350 243 191 149 118 93 58 44 25 12

FIRE AND ICE

B Comparison of Catheters

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>First-generation cryoballoon</th>
<th>Second-generation cryoballoon</th>
<th>First-generation RFC</th>
<th>Advanced-generation RFC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>90</td>
<td>83</td>
<td>58</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>279</td>
<td>251</td>
<td>183</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>284</td>
<td>260</td>
<td>187</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>93</td>
<td>90</td>
<td>55</td>
<td>40</td>
</tr>
</tbody>
</table>

The CIRCA-DOSE Study: A Randomized Clinical Trial of Cryoballoon vs. Irrigated Radiofrequency Catheter Ablation for Atrial Fibrillation

Objectives

- To evaluate the safety and efficacy of:
  - Second-generation Cryoballoon vs. Contact-force Irrigated Radiofrequency Catheter Ablation for AF (CIRCA)
  - Double Short (2-minute) vs. Standard (4-minute) cryoapplication Exposure (DOSE)

- Using continuous cardiac monitoring
The CIRCA-DOSE Study: A Randomized Clinical Trial of Cryoballoon vs. Irrigated Radiofrequency Catheter Ablation for Atrial Fibrillation

Primary Outcome – freedom from any atrial tachyarrhythmia (AF/AFL/AT) after a single ablation procedure

Continuous cardiac monitoring using a ILR

Event-free survival (%)
The CIRCA-DOSE Study: A Randomized Clinical Trial of Cryoballoon vs. Irrigated Radiofrequency Catheter Ablation for Atrial Fibrillation

Secondary Outcome – freedom from symptomatic tachyarrhythmia (AF/AFL/AT) after a single ablation procedure

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Event-Free Survival (%)</th>
<th>0</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF-RF</td>
<td>79.1%</td>
<td>115</td>
<td>100</td>
<td>95</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>CRYO-4</td>
<td>79.1%</td>
<td>116</td>
<td>99</td>
<td>89</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>CRYO-2</td>
<td>73.3%</td>
<td>115</td>
<td>106</td>
<td>96</td>
<td>66</td>
<td></td>
</tr>
</tbody>
</table>

P-values:
- P = 0.96 for CRYO-4 vs. CF-RF
- P = 0.26 for CRYO-2 vs. CF-RF
- P = 0.25 for CRYO-4 vs. CRYO-2

Andrade et al; EHRA 2019
The CIRCA-DOSE Study: A Randomized Clinical Trial of Cryoballoon vs. Irrigated Radiofrequency Catheter Ablation for Atrial Fibrillation

**Secondary Outcome** – Median atrial fibrillation burden (percentage time in AF) pre and post ablation

<table>
<thead>
<tr>
<th></th>
<th>CF-RF</th>
<th>CRYO-4</th>
<th>CRYO-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF Burden</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>1.57 (0.08, 16.09)</td>
<td>3.71 (0.22, 13.78)</td>
<td>1.46 (0.09, 9.17)</td>
</tr>
<tr>
<td>Post</td>
<td>0.00 (0.00, 0.11)</td>
<td>0.00 (0.00, 0.24)</td>
<td>0.01 (0.00, 0.34)</td>
</tr>
</tbody>
</table>

P=0.55 CRYO-4 vs. CF-RF
P=0.52 CRYO-2 vs. CF-RF
P=0.16 CRYO-4 vs. CRYO-2

What is your efficacy?
Cryo-balloon is a great equalizer!!!
Parameters for Durable PV Isolation

Good occlusion of the PV is critical.

LIPV Occlusion
RIPV 
Occlusion
Parameters for Durable PV Isolation

Duration of ablation:
- 4 min x 2
- 3 min x 2
- 3 min x 1 or TTI + 2 min if TTI is less than 60 seconds
- 3 min + 2 min
- 2 min x 2

Longer ablation is more likely to cause collateral damages such as AE fistula, phrenic nerve injury and bronchial injury.
Real time assessment of PV Isolation
Real time assessment of PV Isolation
Acute PVI using a TTI of < 60 sec.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of subjects</th>
<th>Repeat ablation</th>
<th>TTI &lt;60 s predicts durable PVI</th>
<th>TTI in durable PVI (s)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciconte et al</td>
<td>29</td>
<td></td>
<td></td>
<td>42.3 ± 27.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Aryana et al</td>
<td>71</td>
<td></td>
<td></td>
<td>39.1 ± 11.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Ciconte et al</td>
<td>26</td>
<td></td>
<td></td>
<td>50.2 ± 32.9</td>
<td>.030</td>
</tr>
</tbody>
</table>

PV = pulmonary vein; PVI = pulmonary vein isolation.

Cryo-DOSING Study

First Cryoapplication

TT-PVI ≤60 sec

TT-PVI >60 sec

But ≤90 sec

TT-PVI >90 sec

TT-PVI Cannot be Measured

Stop

Reposi

Cryob

Assess PV exit/entrance block

TT-PVI + 2 min

TT-PVI + 2 min

2-min Second Cryoapplication

Assess PV exit/entrance block

Route 1

Route 2

Freedom from atrial arrhythmia (%)

0 10 20 30 40 50 60 70 80 90 100

0 3 6 9 12

Time (months)

Number at Risk

Cryo-AF_{Dosing} 355 355 331 316 299

Cryo-AF_{Conventional} 400 400 363 329 326

90-Day Blanking Period

Log-rank P=0.13

Heart Rhythm 2017 14, 1319-1325DOI: (10.1016/j.hrthm.2017.06.020)
## Cryo-DOSING Study

### Table 2
Procedural characteristics and adverse events between the 2 groups

<table>
<thead>
<tr>
<th>Variable or outcome</th>
<th>Cryo-AF&lt;sub&gt;Dosing&lt;/sub&gt; (n = 355)</th>
<th>Cryo-AF&lt;sub&gt;Conventional&lt;/sub&gt; (n = 400)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ablation variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TT-PVI (s)</td>
<td>48 ± 16</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>TT-PVI recorded</td>
<td>1,145 (81%)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Total cryoapplications/PV (n)</td>
<td>1.7 ± 0.8</td>
<td>2.9 ± 0.8</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Cryoapplication duration (s)</td>
<td>149 ± 34</td>
<td>226 ± 46</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Cryoballoon nadir temperature (°C)</td>
<td>-47 ± 8</td>
<td>-48 ± 6</td>
<td>.41</td>
</tr>
<tr>
<td>Cryoballoon thaw time (s)</td>
<td>43 ± 27</td>
<td>45 ± 19</td>
<td>0.009</td>
</tr>
<tr>
<td>Total cryoablation time (min)</td>
<td>16 ± 5</td>
<td>40 ± 14</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>RF ablation</td>
<td>53 (15%)</td>
<td>76 (19%)</td>
<td>.14</td>
</tr>
<tr>
<td>Total RF ablation time (min)</td>
<td>20 ± 17</td>
<td>19 ± 17</td>
<td>.79</td>
</tr>
<tr>
<td><strong>Procedural variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left atrial dwell time (min)</td>
<td>51 ± 14</td>
<td>118 ± 25</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Fluoroscopy time (min)</td>
<td>13 ± 6</td>
<td>29 ± 13</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Total procedure time (min)</td>
<td>84 ± 23</td>
<td>145 ± 49</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Groin vascular complications</td>
<td>3 (0.8%)</td>
<td>2 (0.5%)</td>
<td>.56</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>2 (0.6%)</td>
<td>4 (1.0%)</td>
<td>.50</td>
</tr>
<tr>
<td>Persistent phrenic nerve palsy</td>
<td>2 (0.6%)</td>
<td>5 (1.2%)</td>
<td>.33</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD or n (%), unless otherwise indicated.

Cryo-AF = cryoablation of atrial fibrillation; N/A = not available; PV = pulmonary vein; RF = radiofrequency; TT-PVI = time-to-pulmonary vein isolation.

*Significant P value.
Parameters for Durable PV Isolation

• Review prestudy imaging
• Assess PV signals at baseline
• Good seal or consider segmental delivery

Before Ablation

During Ablation

TTI < 60 sec: TTI+ 2 min x1 freeze
TTI > 60 <90 sec or cannot assess: 3 min x 2 freezes

After Ablation

Thaw time to 0 deg > 10 sec.
Entrance and exit block
Post ablation voltage map

Scar Map Following PVI with Cryoballoon
**AVATAR–AF**

**Hypothesis**

*A streamlined AF ablation procedure done without PV mapping as a daycase is more effective than anti-arrhythmic drugs at reducing all hospital episodes related to treatment for recurrent atrial arrhythmias.*

Patients were randomised to 3 arms
1) AVATAR-protocol AF ablation (treatment arm)
2) Medical therapy (control arm)
3) Conventional Cryoablation (control arm)
AVATAR Protocol

- Anticoagulation according to HRS/ESC/ECAS guidelines using CHA2DS2-VASC score
- Sedation or general anaesthetic.
- Transeptal puncture by TOE, ICE, CS catheter or aortic pigtail guidance
  - coronary sinus catheter inserted without electrograms.
- Balloon occlusion to achieve Grade 3/4 and deliver 2 x 3 min cryoablations vein.
- Phrenic nerve monitoring by temporary transvenous pacing wire
- No specialist EP catheters and no formal assessment of PVI is done
Endpoints

• **Primary Endpoint:** All hospital episodes (Emergency Room or patient request for OPD) related to treatment for atrial arrhythmia

• **Secondary Endpoints:**
  • Stroke and Death from any cause
  • Any complications caused by the procedure or the anti-arrhythmic drug
  • All hospital episodes which results in a change in therapy for atrial arrhythmia
AVATAR-AF

AVATAR vs Anti-Arrhythmics

Time to all hospital episodes related to treatment for atrial arrhythmia
With Number of Subjects at Risk

Censored
Log-Rank Test: P < .0001

Event Total

<table>
<thead>
<tr>
<th>Group</th>
<th>AVATAR-AF</th>
<th>Anti-Arr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVATAR-AF</td>
<td>23 103</td>
<td>76 100</td>
</tr>
</tbody>
</table>

Probability of Survival Free of Hospital Episode

Days of Follow-up

#EHRA2019
AVATAR vs Conventional Cryoballoon

Time to all hospital episodes related to treatment for atrial arrhythmia
With Number of Subjects at Risk

Event Total
AVATAR-AF 23 109
Conventional 19 109

Group
- AVATAR-AF
- Conventional

Days of Follow up
Probability of Sinus node Free of Hosp. Episode

0 50 100 150 200 250 300 350 400

www.escardio.org/EHRA-Congress #EHRA2019
NON-PV Ablations using a Cryoballoon

- LA roof ablation (posterior wall)
- LAA isolation
LA posterior wall (Dome) ablation:
Scar Mapping Following PVI with Cryoballoon
Cryo PVI and posterior wall
Posterior wall isolation using the cryoballoon in persistent atrial fibrillation: a non-randomized study

Aryana et. al. Heart rhythm 2018;15:1121-1129
**DURABLE PWI AT ‘REPEAT’ PROCEDURE**

Mean number of points collected: $1,232 \pm 425$

Durable PWI encountered in 61 pts (88.4%)
Cryo PVI and posterior wall + RF
Cryo PVI and posterior wall + RF
Left Atrial Appendage Isolation with a cryoballon
Phrenic nerve injury with cryoballoon

- PN palsy is an important and serious complication of AF ablation
- Observed with all technologies of AF ablation, but more common with a balloon based technologies
- Mechanisms
  - Wedging or exerting force to direct the balloon into the RPV for complete PV occlusion can distort the anatomy and decrease the distance between the RPV and the right PN
  - Smaller balloon increases the risk.
- Balloon position, duration of cryo, number of deliveries and nadir temperatures are important controllable factors.
PVI with Cryoballoon Ablation

- Cryoballoon ablation allows pulmonary vein isolation with a continuous lesion rather than multiple, discontinuous energy deliveries.
- Similar efficacy to RFA for both paroxysmal and persistent atrial fibrillation
- Reduce the complexity
- Shorter learning curve
- Similar overall safety profiles except for more phrenic nerve injury
- Less cardiac tamponade
Summary

- PVI is the cornerstone of atrial fibrillation ablation.
- PVI can be done safely and efficiently using a cryo-balloon technology with similar efficacy as RFA.
- Good seal and TTI are important for durable lesions.
- Permanent phrenic nerve palsy is uncommon, but can be devastating. Careful real-time monitoring of phrenic nerve injury is essential to minimize phrenic nerve injury.
- Extra PV ablations using cryo-balloon are feasible and may improve efficacy in pts with persistent afib.