Balloon Cryo-Ablation of Atrial Fibrillation

Aharon Medina, MD
Shaare Zedek Medical Center
Ablate and Pace – Before Ablation
### (AFFIRM) study

**NEJM 2002, Circulation 2004**

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
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<tbody>
<tr>
<td><strong>Age at enrollment</strong></td>
<td>&lt;0.0001 1.06 1.04 1.08</td>
</tr>
<tr>
<td><strong>Coronary artery disease</strong></td>
<td>&lt;0.0001 1.65 1.31 2.07</td>
</tr>
<tr>
<td><strong>Congestive heart failure</strong></td>
<td>&lt;0.0001 1.83 1.45 2.32</td>
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<tr>
<td><strong>Diabetes</strong></td>
<td>&lt;0.0001 1.56 1.22 2.00</td>
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<tr>
<td><strong>Stroke or TIA</strong></td>
<td>&lt;0.0001 1.54 1.17 2.05</td>
</tr>
<tr>
<td><strong>Smoking</strong></td>
<td>&lt;0.0001 1.75 1.29 2.39</td>
</tr>
<tr>
<td><strong>First episode of AFib</strong></td>
<td>0.0067 1.27 1.01 1.58</td>
</tr>
<tr>
<td><strong>Sinus rhythm</strong></td>
<td>&lt;0.0001 0.54 0.42 0.70</td>
</tr>
<tr>
<td><strong>Warfarin use</strong></td>
<td>&lt;0.0001 0.47 0.36 0.61</td>
</tr>
<tr>
<td><strong>Digoxin use</strong></td>
<td>&lt;0.0001 1.50 1.18 1.89</td>
</tr>
<tr>
<td><strong>Rhythm-control drug</strong></td>
<td>0.0005 1.41 1.10 1.83</td>
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The presence of SR but not AAD use is associated with a lower risk of death.

These results suggest that if an effective method for maintaining SR with fewer adverse effects were available, it might improve survival.
• No differences between rhythm-control and rate-control strategies regarding primary endpoints.

• All but one endpoint occurred during AF
Candidates for PV Isolation

- Symptomatic patients with PAF or persistent AF resistant to medical therapy
- No significant heart disease.
- No evidence of LA thrombus or thrombo-embolic phenomena
- Lone AF has best results
“In some patients, especially young individuals with very symptomatic AF, ablation may be preferred over years of drug therapy.”

Atrial Fibrillation Ablation

Ultimate Rhythm Control?
Microscopic Anatomy of Pulmonary Veins

Myocardial sleeve

Focal Atrial Fibrillation - Concept

- Single very fast firing focus initiates chaotic activation of atria
- Proximal pulmonary veins focus location
- Elimination or isolation of pulmonary vein focus can cure Afib.
Pulmonary Vein Isolation (PVI) is the Cornerstone of AF Ablation

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

Each vein should be isolated independently

Complete electrical isolation should be the goal for targeted PVs and entrance and/or exit block should be demonstrated

Cappato et al., Circ Arrhythm Electrophysiol 2010;3;32-38 http://www.HRSonline.org/Policy/ClinicalGuidelines

2007 HRS Consensus Statement
Anatomy of the Pulmonary Veins

- Nuclear magnetic resonance image of the ostia of the right and left superior and inferior PVs and the left atrial appendage

Pulmonary Vein Isolation is Currently the Most Common Ablation Technique Used for Atrial Fibrillation

Principle of Radiofrequency catheter ablation

RF-current: 300-500 kHz
No muscle stimulation
30-60 s delivery
Heating of tissue at cath. tip
Coag. necrosis 8 x 4 x 4 mm
RF Focal Ablation Catheter to Isolate PV and Ablate Atrial Tissue

- Patient anatomy and atrial tissue depth is variable
- Cardiac contractions make maintaining position difficult
- Catheter force varies with position in heart
- Technically challenging
- Good lesions require transmurality
- Successful procedure requires contiguous lesions
Clinical Issues with RF Focal Ablation Catheter

- Risk of perforation
- Uncontrolled energy delivery
- Esophageal damage
- Char/coagulum formation
- Inconsistent results
- Time consuming point-by-point ablation

Ablation Approach for Patients with Persistent Atrial Fibrillation


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CT Image Segmentation
Catheter Cryoablation
Advantages of Cryothermy

- Minimal disruption of endothelium
  - Minimal thrombus production
- Maintenance of extracellular matrix - no collagen denaturation
  - No collagen shrinkage known to occur with thermal injury
  - Advantageous within venous structures - CS or PV’s
Histological Effect on the Connective Tissue Matrix

- Cryoadhesion improves contact and stability
- Preserves the extracellular matrix and endothelial integrity\(^1\)
- Decreases risk of thrombus formation\(^1\)
- Demonstrates well demarcated lesions\(^1\)

Arctic Front® Catheter Design

- Pressurized N₂O delivered through ultrafine injection tube
- Straightforward positioning: over-the-wire, steerable, good visibility
- Several safety mechanisms: double balloon, pressure and flow monitoring, blood detection
- Freezor® MAX operates on similar principles
Cryoablation

Hypothermic Zone

Ablation Zone (sub-zero)
Lesion outline from Arctic Front Catheter 23 mm ablation in swine LA-PV junction (45-day survival). PV is cut open longitudinally and flattened out. Top of image: PV and its branches; Bottom: LA. TTC staining.

- Towards the lungs
- Towards the left atrium
- Pulmonary vein tissue, transition between collagen and muscular sleeve
- Muscular pulmonary veins sleeve distal to the lesion
- Contiguous lesion performed by Arctic Front® Catheter
How the Arctic Front® Cardiac CryoAblation System Works

1. Liquid \( \text{N}_2\text{O} \) is delivered from the CryoConsole through an injection tube to the inner balloon.

2. Inside the balloon the liquid \( \text{N}_2\text{O} \) vaporizes and absorbs heat from the surrounding tissue.

3. The vapor is returned to the console through a lumen maintained under vacuum.

4. The CryoConsole controls safe delivery of \( \text{N}_2\text{O} \) to the catheter and return of the vapor. Numerous safety systems mitigate potential hazards.
Arctic Front PV Isolation
Achieve™ Mapping Catheter

- Achieve is an intracardiac electrophysiology diagnostic catheter which can be deployed through the Arctic Front® guide wire lumen.
- Available in 15 mm and 20 mm loop diameters.
- Both diameters are compatible with 23 mm and 28 mm Arctic Front.
How Arctic Front® Balloon Catheter and Achieve™ Work?

1. Access targeted vein
2. Inflate and position

3. Occlude and ablate
4. Assess PVI
Achieve™ mapping catheter allows for real-time assessment of PV isolation during cryoablation with Arctic Front®.

Arctic Front is positioned against the LIPV ostium, with Achieve positioned to assess PV isolation.

Images: Courtesy of Dr. Schwagten, ZNA Middelheim, Belgium (above) and Dr. Vogt, Herz- und Diabeteszentrum NRW, Germany (right)
CT Image of Pulmonary Veins
Potential Complications of AF Ablation

- Pulmonary vein stenosis -> 5%
- Atrio-esophageal fistula -> 0.5%
- Diaphragmatic palsy -> 10%
CT Analysis of the LA and Esophagus

Solutions?

Ablate within the Left Atrium
Not in the Pulmonary veins!
Pace the Phrenic Nerve
Monitor Esophagial Temperature
Cryo-Ablation of Left Upper PV
Key Inclusion Criteria:

- ≥ 2 documented AF Episodes in the prior 2 months
- Efficacy failure of ≥ 1 AAD (flecainide, propafenone, sotalol)

N = 245 Randomized 2:1 to CRYO* or DRUG

26 centers in US and Canada

* CRYO: Arctic Front® System
STOP AF Trial - Results

CRYO 69.9% (114 / 163)

DRUG 7.3% (6 / 82)

\( p < 0.001 \)
US Continued Access Protocol

- Single-arm, non-randomized study (followed STOP AF)
  - 80 subjects
  - 12 centers
- Purpose to continue evaluating
  - Safety and efficacy of Arctic Front® system
    - Follow-up at 1, 3, 6, 12 months and 2, 3, 4, 5 years post-cryoablation procedure
    - The impact of experience on the learning curve
- The chronic success rate of Cryoballoon ablation increases with experience
  - 12-month efficacy increased from 69.9% to 71%
Phrenic nerve injury risk decreased from 11.2% in STOP AF to 4.8% in CAP AF

Pulmonary vein stenosis decreased from 3.1% to 1.3%

Patient had a second ablation procedure using RF.
Long Term Follow up – Vogt at al
JACC December 2012

• PV isolation was achieved without touch-up in 91.1% of patients, using the smaller balloon in 26.7%, the larger balloon in 25.6%, and both balloons in 47.7% of patients.

• Long-term follow-up data12< months (median 30 months; interquartile range 18 to 48 months) were available for 451 patients.

• 278 patients (61.6%) were free of AF recurrence with no need for repeat procedures after the 3-month blanking period. Rates of freedom from AF after 1, 2, and 3 repeat procedures were 74.9%, 76.2%, and 76.9%, respectively.

• Use of the smaller balloons or both balloons produced the highest rates of long-term freedom from AF. Phrenic nerve palsy occurred in 12 patients (2%), resolving within 3 to 9 months.
Long Term Follow up – Vogt at al

JACC 2012
Shaare Tzedek Experience

• Between July and November 2012, cryo-ablation with a 28 mm balloon was performed in 10 patients (age 59 ± 8, 6 with drug refractory paroxysmal AF, 3 with persistent AF and 1 with left atrial tachycardia.

• 34 of 37 PV’s (91.9%) were successfully isolated. The right inferior PV was not isolated in 3 patients.

• Radiation time was 76 ± 29 min, it is expected to drop with the learning curve.

• Sinus rhythm was maintained in in 80% of patients, however follow up is still too short (108 days, range 24-182).
Shaare Tzedek Experience

- No PV narrowing, right phrenic nerve palsy or atrio-esophagial fistula occurred during cryo-balloon ablation.

- There were no significant complications.

- One patient had a mild to moderate amount of pericardial fluid the day after the procedure, which subsided within 48 hours.
Conclusions

Cryoablation with the Arctic Front® System:

- Effectively treats drug refractory PAF
- Is a safe and efficient procedure
- Has shorter procedure times, compared to RF ablation procedures (European Trials)