CRYO4PERSISTENT AF CLINICAL TRIAL

STUDY DESIGN\textsuperscript{1,2}

First prospective, multi-center, single arm study designed to assess the single procedure outcomes of pulmonary vein isolation (PVI)-only using Arctic Front Advance™ Cryoballoon in patients with symptomatic persistent AF. The CRYO4PERSISTENT AF trial included 101 patients at 11 sites in Europe (France, Germany, and Greece).

60.7%

Freedom from all atrial arrhythmias (AF/AT/AFL) at 12 months\textsuperscript{1}

- Single procedure - all repeat ablations were failures, inclusive of blanking period
- PVI-only Cryoballoon ablation (no additional empirical lesions and/or complex fractionated electrogram ablations)
- 3 patients in sinus rhythm on AAD at 12 months

4%

Major procedure or device-related events occurred in 4/101\textsuperscript{1}

- No device or procedure related AE fistulae, PV stenosis, or death
- No clinical sequela
- 2 (2%) vascular pseudoaneurysm
- 1 (1%) transient ST segment elevation
- 1 (1%) pericardial effusion

53 min

Short and predictable procedure time\textsuperscript{1,3}

- Lab occupancy time: 133.1 ± 51.3 min
- Procedure time: 53.2 ± 22.2 min
- Fluoroscopy time: 17.7 ±11.5 min
### Study Design/ Objectives

Prospective, multi-center, non-randomized, single arm study. Designed to assess the single procedure outcomes of PVI using Arctic Front Advance™ Cryoballoon in patients with symptomatic persistent AF. 11 sites in Europe (France, Germany, and Greece). 101 patients met inclusion/exclusion criteria, demonstrated 100% AF burden, were treated per protocol, and included in the primary analysis.

### Inclusion Criteria

Key Inclusion Criteria:
- Diagnosis of symptomatic persistent AF ≤12 months
- 100% AF burden of 7-180 days documented on ECG recording and/or AF requiring cardioversion
- 18-Hour Holter Monitor at baseline
- 18-80 years of age
- Prior AAD failure or refusal

### Objective Measures

- Freedom from all arrhythmias (AF/AT/AFL) at 12 months
- Core lab adjudicated recurrence of AF/AT/AFL ≥30sec and/or DCCV (outside of 3-month blanking period)
- Repeat ablation post-index-procedure (inclusive of 3-month blanking period)

Only use of Arctic Front Advance™ Cryoballoon is allowed to obtain PVI
- No additional left atrial empirical lesions and/or complex fractionated electrogram ablations

### Primary Outcomes

In this cohort of persistent AF patients, Cryoballoon ablation is an effective treatment with freedom from all atrial arrhythmias of 60.7% at 12 months with predictable procedure times.

### Secondary Outcomes

Cryoballoon ablation demonstrated a low device and procedure related complication rate of 4% with no long term clinical sequela and no patients experiencing PNI at hospital discharge. Patients treated with the Cryoballoon demonstrated a clinically significant improvement in arrhythmia-related symptoms and QOL from baseline to 12 months post-ablation.

### SYMPTOMS REDUCTION:

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness</td>
<td>14%</td>
<td>66%</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Palpitations</td>
<td>2%</td>
<td>8%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Rapid Heart Beat</td>
<td>8%</td>
<td>27%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>5%</td>
<td>6%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>6%</td>
<td>4%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Δ 12% p<0.01 for all arrhythmic symptoms, excluding syncope (2% to 0%)

### QUALITY OF LIFE (QOL):

<table>
<thead>
<tr>
<th>SF36 Qol Improvement</th>
<th>Baseline</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>46.9%</td>
<td>53.9%</td>
</tr>
<tr>
<td>Mental</td>
<td>47.3%</td>
<td>50.6%</td>
</tr>
</tbody>
</table>

Δ 7.1 p=0.0001
Δ 3.3 p=0.008

### References:

2. Metzner A. Presented LBCT at DGG: Mannheim April 6, 2018; Mannheim, Germany.

### Brief Statement

See the device manual for detailed information regarding the instructions for use, indications, contraindications, warnings, precautions, and potential adverse events. For further information, contact your local Medtronic representative. Medtronic and the Medtronic logo are trademarks of Medtronic.

### Indications

The Arctic Front Advance™ Cardiac Cryoablation Catheter system is indicated for the treatment of patients with atrial fibrillation.

### Contraindications

1) In the ventricle because of the danger of catheter entrapment in the chordae tendineae.
2) In patients with one or more pulmonary vein stents.
3) In patients with cryoglobulinemia.
4) In patients with active systemic infections, and
5) In conditions where the manipulation of the catheter within the heart would be unsafe (e.g., intracardiac mural thrombus).