SECONDARY ANALYSES
Secondary analyses from the FIRE AND ICE trial demonstrated significant improvements that favor the Cryoballoon group over the RFC group for clinically meaningful outcomes.

STUDY DESIGN
Randomized non-inferiority study design with the Cryoballoon meeting the primary endpoints

The FIRE AND ICE Trial included 762 patients randomized 1:1 at 16 sites in 8 countries

Relative to RFC, Cryoballoon Demonstrated:

- **21%** Fewer All-cause Hospitalizations
- **33%** Fewer Repeat Ablations*
- **34%** Fewer Cardiovascular Hospitalizations* (including AF hospitalization†)
- **50%** Fewer Direct Current Cardioversions

*Predefined secondary analyses
†Not predefined but included in analyses

Arctic Front Advance™ Cryoballoon

Medtronic
### Study Design/ Objectives
Multicenter, prospective, 1:1 randomized, non-inferiority, parallel group, open, blinded-endpoint study comparing the efficacy and safety of pulmonary vein isolation using Arctic Front™ catheters versus ThermoCool® point-by-point radiofrequency catheters with CARTO® 3D mapping system in patients with paroxysmal atrial fibrillation.

### Enrollment Criteria
- Key Inclusion Criteria:
  - Symptomatic paroxysmal atrial fibrillation (PAF)
  - Prior failure of ≥ 1 antiarrhythmic drug (class I or III AAD)
  - ≥ 18 and ≤ 75 years of age

### Primary Endpoints
- **Primary Efficacy Endpoint:** Time to first documented recurrence of atrial fibrillation (AF) > 30 sec/atrial tachycardia (AT)/atrial flutter (AFL), prescription of AAD, or repeat ablation (a blanking period of 3 months was maintained after the index procedure)
- **Primary Safety Endpoint:** Time to first all-cause death, all-cause stroke/TIA or treatment-related serious AEs

### Primary Outcomes
The Cryoballoon met the primary safety and efficacy endpoints of non-inferiority.

### Secondary Analyses
Sites reported time to first and number of all-cause hospitalizations, including:
- Cardiovascular-related hospitalizations (including AF hospitalization)
- In-patient stay not concurrent with index procedure of ≥ 1 calendar day
- Quality of life was assessed every 6 months using the SF-12 and EQ-5D-3L

### Secondary Outcomes
- **All-cause hospitalizations:**
  - RFC: 267 events in 156 patients (156/376; 41.5%)
  - Cryo: 210 events in 122 patients (122/374; 32.6%)
  - Kaplan Meier Log-Rank p-value = 0.01
- **Cardiovascular hospitalizations:**
  - RFC: 203 events in 135 patients (135/376; 35.9%)
  - Cryo: 139 events in 89 patients (89/374; 23.8%)
  - Kaplan Meier Log-Rank p-value < 0.01
- **Repeat ablation:**
  - RFC: 70 events in 66 patients (66/376; 17.6%)
  - Cryo: 49 events in 44 patients (44/374; 11.8%)
  - Kaplan Meier Log-Rank p-value = 0.03
- **Direct Current Cardioversion:**
  - RFC: 28 DCCVs in 24 patients (24/376; 6.4%)
  - Cryo: 13 DCCVs in 12 patients (12/374; 3.2%)
  - Kaplan Meier Log-Rank p-value = 0.04

### References

### Brief Statement
**Arctic Front™ and Arctic Front Advance™ Cardiac CryoAblation Catheter Systems**
- Indications: The Arctic Front Advance™ Cardiac CryoAblation Catheter catheter is indicated for the treatment of patients with atrial fibrillation (AF).
- Contraindications: Use of either Arctic Front or Arctic Front Advance cryoballoons is contraindicated:
  - In the ventricle because of the danger of catheter entrapment in the chordae tendinae,
  - In patients with one or more pulmonary vein stents,
  - In patients with cryoglobulinemia,
  - In patients with active systemic infections,
  - In conditions where the manipulation of the catheter within the heart would be unsafe (e.g., intracardiac mural thrombus).
- **Brief Statement:** Refer to the device technical manual for detailed information regarding the procedure, indications, contraindications, warnings, precautions, and potential complications/adverse events. For further information, please contact your Medtronic Sales Representative and/or consult Medtronic’s website at www.medtronic.eu.