FROzEN-AF US IDE clinical trial results

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OBJECTIVE

- Evaluate the safety and effectiveness of the Boston Scientific **POLARx™ Cryoablation System** for treatment of symptomatic, drug refractory, recurrent, paroxysmal atrial fibrillation (PAF).

FROzEN-AF TRIAL DESIGN[1]

- Global, prospective, non-randomized, single-arm study (NCT04133168)
- 385 patients (325 primary, 60 roll-in subjects) across 44 sites in 10 countries
- **POLARx™ FIT** extension arm[2]
  - 50 patients were treated to collect safety and effectiveness data on the **POLARx FIT** expandable (28 mm and 31 mm) cryoballoon (CB) catheter

PROCEDURAL CHARACTERISTICS

- The FROzEN-AF and extension study procedural characteristics are shown in **Table 1**
- The LA dwell time was 8 minutes shorter and fluoroscopy time was 6 minutes shorter in the FIT extension arm
- There was an increase in grade 4 occlusion and single-shot success with the 31 mm CB

Table 1 : Procedural Characteristics

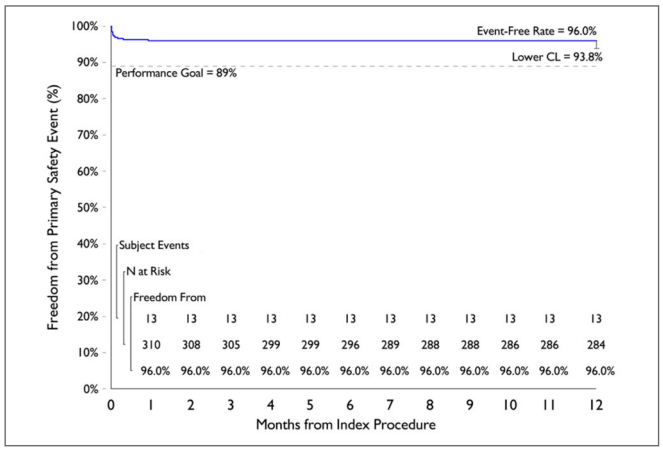
	FROzEN-AF (28 mm balloon)	POLARx FIT extension Arm (28 mm/ 31 mm balloon)
General Anesthesia (%)	78.5%	100%
Conscious Sedation/MAC (%)	21.5%	-
Procedure Time (min)	91 min	101 min
LA Dwell Time (min)	59 min	51 min
Fluoroscopy Time (min)	13 min	7 min
Grade 3-4 Occlusion* (%)	95.9% (69.9% – Grade 4)	97.7% (66.4% / 77.6% – Grade 4)
Single Shot Success* (%)	55.9%	35.3% / 62.1%

Mean ± SD
*Only ablations with duration >60S included in ablation counts

PROCEDURAL AND LONG-TERM SAFETY

- The primary safety event-free rate was 96.0%‡ for the FROzEN-AF (12-month) **(Figure 1)** and 100% for the FIT extension arm (12-month)
- There were no reports of moderate or severe PV stenosis, persistent phrenic nerve palsy, or esophageal fistulas in both patient cohorts

Figure 1 : Procedural and Long-term Safety



No reported:
- PV stenosis
- Persistent phrenic nerve palsy
- Esophageal fistulas

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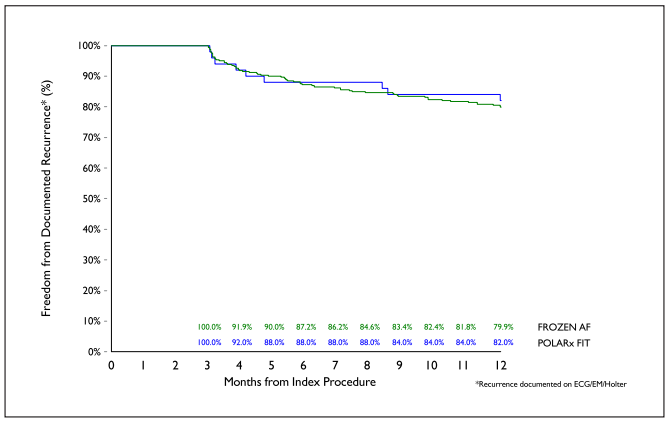
EFFICACY

- The 12-month freedom from documented atrial arrhythmias was 79.9% (AF 82.7%, AFL 96.5%, AT 98.1%) **(Figure 2)**
- The FIT extension arm 12-month freedom from documented atrial arrhythmias was 82.0% (AF 84%, AFL 94%, AT 100%)
- Electroanatomic mapping was used in 184/325 cases; examination of recurrence in these patients revealed a trend (p=0.08) toward higher freedom from recurrence (83.7%) when EAM was used, compared to 75.9% when not

Figure 2. Freedom from Documented Recurrence of Atrial Arrhythmias



FROzEN (n = 325)
12-Month
79.9%

FIT Extension (n = 50)
12-Month
82.0%

POLARx™ FIT voltage single-center experience[3]

- A single-center characterized lesions with high-density voltage maps on 14 patients (8 ablated with the 31 mm CB and 6 with the 28 mm CB)
- Voltage maps revealed wide antral lesions around all veins (100%)
- Lesion assessment of atrial scar burden revealed a statistically significant difference in the fractional antral scar, 68% (31 mm) vs. 60.5% (28 mm) (p = 0.048) indicating a significantly larger lesion being created by the 31 mm CB **(Figure 3)**

Figure 3. High Density Maps of Atrial Scar Burden of the 28 mm and 31 mm CB

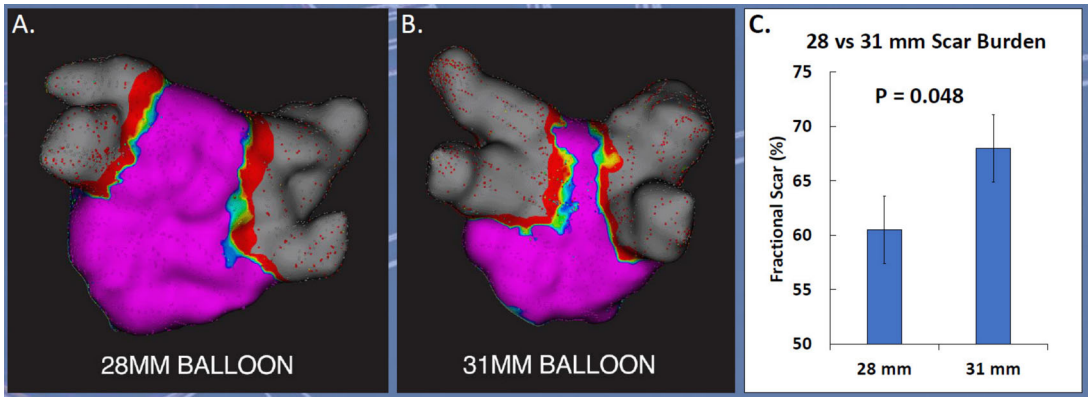


Figure Legend. High density voltage maps from 28 mm (A) and 31 mm (B). C. scar burden analysis.

CONCLUSION

- The choice of balloon sizes (31 and 28 mm) with **POLARx FIT** may assist in overcoming challenges related to variability in patient PV size and geometry with the 31 mm CB achieving high-grade 3-4 vein occlusion, lowering the LA dwell and fluoroscopy times and increasing the single-shot isolation rate
- The primary safety event-free rate was 96.0%‡ (FROzEN-AF) and 100% (FIT extension arm) with no reported PV stenosis, persistent phrenic nerve palsy, or esophageal fistulas
- The documented atrial arrhythmia recurrence rate was low with 20.1% (FROzEN-AF) and 18% (FIT extension) at 12-months
- In the single-center experience, **POLARx FIT** produced significantly larger, more antral lesions and the 31 mm balloon and sheath maneuverability allowed greater control of balloon occlusion and lesion placement

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

POLARx™ FIT Cryoablation Balloon Catheter

INTENDED USE
The Boston Scientific Cardiac Cryoablation System is intended for cryoablation and electrical mapping of the pulmonary veins for pulmonary vein isolation (PVI) in the ablation treatment of paroxysmal atrial fibrillation. The POLARx FIT Cryoablation Balloon Catheter is a single use, flexible, over-the-wire balloon catheter intended to ablate cardiac tissue.

INDICATIONS FOR USE
The Boston Scientific Cardiac Cryoablation System using the POLARx FIT Cryoablation Balloon Catheter is indicated for the treatment of patients with drug refractory, recurrent symptomatic paroxysmal atrial fibrillation (PAF).

CONTRAINDICATIONS
Use of the POLARx FIT Catheter is contraindicated as follows: In patients with an active systemic infection as this may increase the risk for endocarditis and sepsis. In patients with a myxoma or an intracardiac thrombus as the catheter could precipitate an embolic event. In patients with a prosthetic heart valve (mechanical or tissue). In the ventricle of the heart where the device may become entrapped in a valve or chordae structures. In patients with a recent ventriculotomy or atriotomy as this may increase the risk of cardiac perforation or embolic event. In patients with pulmonary vein stents as the POLARx FIT Catheter may dislodge or damage the stent. In patients with cryoglobulinemia as the cryoablation application may lead to vascular injury. In conditions where insertion into or manipulation in the atrium is unsafe as this may increase the risk of perforation or systemic embolic event. In patients with intra-atrial septal patch or any other surgical intervention in or adjacent to the intra-atrial septum. In patients with an interatrial baffle or path as the transseptal puncture could fail to close. In patients with hypercoagulopathy or an inability to tolerate anticoagulation therapy during an electrophysiology procedure. In patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe. In patients previously implanted with a percutaneous Left Atrial Appendage Occlusion device.

WARNINGS
Introducing catheters and sheaths into the circulatory system increases the risk of air emboli. Always advance/ retract components slowly and use proper flushing techniques to minimize risk of air embolism. Avoid proximity to all heart valves whenever possible. Manipulation of the POLARx FIT Catheter across a heart valve structure may result in entanglement and damage to the valve. Use of N2 O as a refrigerant during the cryoablation procedure increases the risk of a gas embolism if the integrity of the POLARx FIT Catheter balloon is disrupted. Replace the POLARx FIT Catheter if there is any concern the POLARx FIT Catheter balloon has been damaged. Do not use the POLARx FIT Catheter without a POLARMAP Mapping Catheter fully inserted into the guidewire lumen, past the POLARx FIT Catheter balloon. An absent or partially inserted POLARMAP Mapping Catheter may not provide sufficient mechanical support for POLARx FIT Catheter balloon inflation and cryoablation operations and may result in POLARx FIT Catheter damage and N2 O leakage. Administer appropriate peri-procedural anticoagulation therapy per standard of care for patients undergoing cardiac cryoablation procedures. Administer anticoagulation therapy during and post-procedure according to local institution standards to minimize bleeding and thrombotic complications. Electrophysiology procedures, including ablation, may introduce arrhythmias. Always deflate the POLARx FIT Catheter and retract into the POLARSHEATH Sheath before pulling back across the septum. Crossing the septum with the POLARx FIT Catheter balloon exposed, inflated or inflating within the septum may cause endocardial damage. Do not use the POLARx FIT Catheter if it is not working properly. A POLARx FIT Catheter failing to function properly should be removed and replaced before continuing with the procedure. Do not inflate the balloon while housed in the POLARSHEATH Sheath. Always verify that the POLARx FIT Catheter balloon is outside the POLARSHEATH Sheath before inflation to prevent POLARx FIT Catheter damage. Do not inflate the balloon while the POLARx FIT Catheter is positioned inside the PV. Always inflate the POLARx FIT Catheter balloon while the POLARx FIT Catheter is positioned in the LA and then position it in the PV ostium. Inflating the POLARx FIT Catheter balloon in the PV may result in vascular injury. Always deflate and extend the POLARx FIT Catheter balloon prior to retraction of the balloon back into the POLARSHEATH Sheath. Do not use the POLARx FIT Catheter if any part of the POLARx FIT Catheter shaft appears to be kinked or damaged. If the POLARx FIT Catheter shaft appears kinked while in the body, remove the POLARx FIT Catheter and replace with a new POLARx FIT Catheter before continuing with the procedure. When using the POLARx FIT Catheter, catheter manipulation must be carefully performed in order to avoid cardiac damage, perforation, or tamponade. Do not advance the POLARx FIT Catheter with an exposed lumen; always advance the POLARx FIT Catheter over the POLARMAP Mapping Catheter, with the POLARMAP Mapping Catheter distal to the POLARx FIT Catheter balloon. Do not use excessive force to advance or withdraw the POLARx FIT Catheter when resistance is encountered. The steerability feature of the POLARx FIT Catheter is designed to operate in a single plane of motion. Attempts to deflect the distal section in other planes (e.g. perpendicular to normal steering plane, etc.) may result in damage to the steering mechanism and impaired ability to position the POLARx FIT Catheter as desired by the operator. Do not pull or move the POLARx FIT Catheter, POLARSHEATH Sheath, attached cables, or SMARTFREEZE Console while the POLARx FIT Catheter balloon is frozen as this may lead to tissue damage. Catheter ablation procedures near or in the PV may cause narrowing or stenosis. Avoid ablation in the tubular portion of the PV. Implantable pacemaker (PM) and cardioverter/defibrillator (ICDs) leads may be displaced during an EP procedure. See PM/ICD technical manual for additional instructions.5 Black (K) ΔE ≤5.0 BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324F), eIFU, MB, POLARx FIT, US, 51594697-01A. To prevent occlusion of the refrigerant line, over-pressurization and potential POLARx FIT Catheter failure when using the POLARx FIT Catheter in combination with the POLARSHEATH Sheath, avoid applying simultaneous high torque (twisting) and tensile stress (pulling) on the POLARx FIT Catheter while the catheter is engaged in the POLARSHEATH Sheath and the POLARx FIT Catheter is deflected. Cryoablations may cause collateral injury to the esophagus and in rare instances atrio-esophageal fistulas. Temperature monitoring with a probe placed within the esophagus may mitigate this risk. Cryoablations may cause collateral phrenic nerve injury. Stop cryoablation immediately if phrenic nerve impairment is observed. Continuous phrenic nerve pacing, and diaphragm movement monitoring should be performed to mitigate this risk. The POLARx FIT Catheter contains pressurized gas during operation. Failure of the POLARx FIT Catheter balloon to operate properly may result in a release of gas into the circulatory system and potential gas emboli. Use caution when manipulating the POLARx FIT Catheter around other intracardiac devices. Entanglement may prevent removing the devices from the cardiac chamber and require surgical intervention. Significant x-ray exposure during an electrophysiology procedure may result in acute radiation injury as well as increased risk for somatic and genetic effects, to both patients and laboratory staff. Catheter ablation should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure and steps taken to minimize this exposure.

PRECAUTIONS
Use only isolated equipment (IEC 60601-1 Type CF equipment, or equivalent) with the POLARx FIT Catheter and SMARTFREEZE Console. The POLARx FIT Catheter shall only be used with the SMARTFREEZE Console. Use only the POLARMAP Mapping Catheter with the POLARx FIT Catheter. Use only the POLARSHEATH Sheath with the POLARx FIT Catheter. If necessary, use only 0.081 cm (0.032 in.) or 0.089 cm (0.035 in.) guidewires with the POLARx FIT Catheter. Use of other guidewire sizes may damage the POLARx FIT Catheter. It is the user's responsibility to ensure that the equipment used with the POLARx FIT Catheter meets all local applicable electrical safety requirements. Perform cryoablation procedures only within environmental parameters as outlined in Section 11.8, Specifications. Do not immerse the POLARx FIT Catheter handle or Cryo-Cable in fluids; electrical performance could be affected. Do not change the equipment configuration or modify the equipment or applied parts in any way. Doing so may cause the system to behave unreliably and affect the patient adversely. Always straighten the POLARx FIT Catheter prior to insertion or withdrawal from the body. Flush the guidewire lumen initially and then frequently throughout the cryoablation procedure to prevent coagulum formation. If contrast is used, flush the lumen thoroughly after each contrast injection. Do not physically scrub or twist the POLARx FIT Catheter balloon surface as damage to the POLARx FIT Catheter balloon may impact balloon shape or integrity. Do not apply excessive torque to the POLARx FIT Catheter during the procedure as it may adversely affect the cryoablation function. Do not apply excessive torque to the steering lever as doing so may damage the POLARx FIT Catheter deflection mechanism. Do not apply excessive force to the POLARx FIT Catheter extension slider switch (slider switch) during cryoablation or while the POLARx FIT Catheter balloon temperature is below freezing as doing so may damage the catheter. Properly scavenge and dispose of the N2 O with appropriate hospital systems. Do not outgas in the operating room. Dispose of the POLARx FIT Catheter per local regulatory and biohazard standards.

ADVERSE EVENTS
Potential adverse events associated with manipulation of the POLARx FIT Catheter within the left atrium and pulmonary veins may include the following conditions: Arrhythmia (new or exacerbated), Conduction pathway injury, Cardiac arrest, Cardiac trauma, for example: Cardiac perforation/tamponade/effusion, Valvular damage, Stiff left atrial syndrome. Death, Edema/heart failure/pleural effusion, GI disorders, Hypertension, Hypotension, Infection/inflammation/exposure to biohazardous material, Injury related to tissue damage and/or adjacent structures, for example: Esophageal injury, Pulmonary injury, Catheter entrapment, Physical trauma. Injury due to embolism/thromboembolism/air embolism/ foreign body embolism: CVA/stroke, TIA, MI. Neurological impairment, and its symptoms, for example: Cognitive changes, Visual disturbances, Headache, Motor impairment, Sensory impairment, Speech impairment, Pulmonary embolism, Asymptomatic cerebral embolism, Nerve injury, for example: Phrenic nerve injury. Vagal nerve Injury, Pain or discomfort, for example: Angina, Chest pain, Non-cardiovascular pain7 Black (K) ΔE ≤5.0. Procedural related side effects, for example: Allergic reaction (including anaphylaxis), GU complications, Side effects related to medication or anesthesia, Radiation injury/tissue burn, Renal failure/insufficiency. Vasovagal response, PV Stenosis and its symptoms, for example: Cough, SOB, Fatigue, Hemoptysis. Respiratory distress/insufficiency/dyspnea. Surgical and access complications, for example: Hematoma/seroma, AV Fistula, Bleeding, Pseudoaneurysm, Pneumothorax, Residual atrial septal defect. Thrombus/thrombosis, Vessel Trauma, including: Perforation, Dissection, Coronary artery injury, Vasospasm, Occlusion, Hemothorax. 97085860 (Rev. A)

‡Updated analysis with corrected data

1. Ellenbogen KA, Mittal S, Varma N, et al. One-year outcomes of pulmonary vein isolation with a novel cryoballoon: Primary results of the FROZEN AF trial. J Cardiovasc Electrophysiol. 2024 March 6. doi.org/10.1111/jce.16220.
2. Su, et al. Clinical application of a novel 31 mm cryoballoon for pulmonary vein isolation for paroxysmal atrial fibrillation: procedural data from the FIT arm of FROzEN-AF. Presented at: Heart Rhythm Society 2023; May 19-21, 2023; New Orleans, LA, USA.
3. Makati, et al. Voltage mapping of a novel 31 mm cryoballoon for pulmonary vein isolation to manage paroxysmal atrial fibrillation: a single center experience. Presented at: AF Symposium 2023; Feb. 2-4, 2023; Boston, MA, USA.

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