MODULAR ATP Clinical Study

Effectiveness of the EMPOWER™ Modular Pacing System and EMBLEM™ Subcutaneous ICD to Communicate Antitachycardia Pacing

C1907

CLINICAL INVESTIGATION PLAN

[redacted]

NCT#: NCT04798768

Sponsored By

Boston Scientific Corporation

4100 Hamline Avenue North

St. Paul, MN 55112, USA

And

Boston Scientific International SA

Le Val Saint-Quentin,

2 rue René Caudron, 78960

Voisins le Bretonneux, France

And

Guidant Europe NV

Lambroekstraat 5D

1831 Diegem, Belgium

[redacted]

Contact Information

Role	Contact	
Clinical Contact	**United States and Canada Contact:** [redacted]	
	Europe Contact: [redacted]	
	US and Canada Technical Services: Tel: 1.800.CARDIAC/ 1.800.227.3422 [redacted]	
Coordinating Principal Investigators	**US** [redacted]	**Europe** [redacted]

	[redacted]	[redacted]

Original Version: A, 26 June 2018

Current Version: I, 29 April 2022

Revision History

Revision Version	Protocol Date	Template number and version	Protocol Section Modified	Existing Text as Written in Protocol, Version	Revised/New Text as Written in Protocol, Version	Justification for Modification
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Revision History

Revision Version	Protocol Date	Template number and version	Protocol Section Modified	Existing Text as Written in Protocol, Version	Revised/New Text as Written in Protocol, Version	Justification for Modification
			[redacted]			
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

2 Protocol Synopsis

MODULAR ATP Clinical Study Effectiveness of the EMPOWER™ Modular Pacing System and EMBLEM™ Subcutaneous ICD to Communicate Antitachycardia Pacing	
Study Objectives	To demonstrate the safety, performance and effectiveness of the EMPOWER™ Modular Pacing System (MPS), as well as the EMPOWER and EMBLEM™ Subcutaneous ICD Coordinated System. Additionally, data from this study may be used to support pre-market and post-market approval requirements for the EMPOWER MPS.
Planned Indication(s) for Use	The mCRM Modular Therapy System is intended to provide: • Defibrillation (tachyarrhythmia) therapy from the S-ICD, which is used to treat rhythms associated with sudden cardiac death (SCD), such as VT and VF • Anti-tachycardia pacing (ATP) therapy, commanded from the S-ICD and provided from the EMPOWER System for the treatment of MVT • Anti-bradycardia pacing from the EMPOWER System to detect and treat bradyarrhythmias and to provide pacing support after defibrillation therapy
Test Device	The implantable portion of the investigational system comprises three component devices that are collectively referred to as the *mCRM Modular Therapy System*. The three component devices of the mCRM Modular Therapy System are: • (EMBLEM/ EMBLEM MRI) S-ICD Pulse Generator, Models A209/A219 or future BSC S-ICD, with mCRM clinical firmware, • (EMBLEM) S-ICD Electrode, Model 3400/ 3401, Model 3501 or future BSC S-ICD Electrode • EMPOWER MPS Pulse Generator and Delivery Catheter, Model B170
Study Design	A prospective, non-randomized, multi-site study, single-arm, global study utilizing performance goals to demonstrate safety, performance, and effectiveness of the EMPOWER System and mCRM Modular Therapy System.
Planned Number of Subjects	Enrollment of up to 300 patients at up to 60 sites will be allowed to ensure all necessary data are collected [redacted]

MODULAR ATP Clinical Study Effectiveness of the EMPOWER™ Modular Pacing System and EMBLEM™ Subcutaneous ICD to Communicate Antitachycardia Pacing	
Planned Number of Investigational Sites/ Countries	Up to 60 sites in North America, the United Kingdom, and Europe.
Safety Endpoint 1	Major EMPOWER MPS System- and Procedure-related Complication-Free Rate from Implant through 6 Months Post-Implant
Safety Endpoint 2	Major EMPOWER MPS System- and Procedure-related Complication-Free Rate from Implant through 12 Months Post-Implant
Secondary Safety Endpoint	All-Cause Survival from Implant through 2 Years Post-Implant
Primary Effectiveness Endpoint 1	Communication Success between the S-ICD and EMPOWER PG at the 6 Month Visit
Primary Effectiveness Endpoint 2	Proportion of subjects with adequate Pacing Capture Threshold (PCT) (defined as ≤ 2 V@0.4 ms) at the 6 Month Visit
Secondary Effectiveness Endpoint 1	Mean Metabolic-Chronotropic Relation (MCR) slope from the Kay-Wilkoff model at the 3 Month Visit

Additional Objectives	• Summary of the mCRM Therapy System implant procedure characteristics:
	  ○ Initial implant success rate of the EMPOWER PG
	  ○ Initial implant success rate of the S-ICD (de novo Implants)
	• Summary of pacing impedance and sensing amplitude at protocol-required follow ups
	• Summary of ventricular tachycardia (VT)/ ventricular fibrillation (VF) conversion and sensing interaction testing
	• Summary of Communication Threshold Test at Implant, Pre-Discharge, 1-Month Visit and available Semi-Annual visits
	• Summary of incidence and threshold for Communication Muscle Stimulation at Implant

MODULAR ATP Clinical Study Effectiveness of the EMPOWER™ Modular Pacing System and EMBLEM™ Subcutaneous ICD to Communicate Antitachycardia Pacing	
	• Summary of EMPOWER PG Pacing Capture Thresholds (PCT) at protocol-required follow ups • Summary of spontaneous treated VT/VF episodes • Incidence of syncope related to treated and untreated spontaneous episodes of VT/VF above the lowest programmed rate cutoff • Incidence and appropriateness of post-shock demand pacing by the EMPOWER PG • Summary of Inappropriate Therapy • Summary of Major EMPOWER MPS System- and Procedure-related Complications through both 6 and 12 months after the implant procedure • Summary of mCRM Therapy System-related complications through both 6 and 12 months after the implant procedure* • Summary of EMPOWER PG performance from Holter Monitor recording • Summary of EMPOWER PG battery charge remaining to End of Service (EOS) at protocol-required follow ups • Summary of S-ICD PG remaining battery to Elective Replacement Indicator (ERI) per protocol-required follow ups (baseline adjusted to time of enrollment for S-ICD PGs implanted prior to enrollment in MODULAR ATP) *S-ICD PG replacement due to normal battery depletion will not be included in this analysis
Follow-up Schedule	Follow up will be required at the following time points: • Pre-Discharge, • 1 month, • 3 months (for subjects participating in the Rate Response Substudy only), • 6 months, • 12 months, • 18 months, and • 24 months after the mCRM Coordinated System is implanted. [redacted]

MODULAR ATP Clinical Study Effectiveness of the EMPOWER™ Modular Pacing System and EMBLEM™ Subcutaneous ICD to Communicate Antitachycardia Pacing	
	Evaluation of communication between S-ICD and EMPOWER will be required at Implant, Pre-Discharge, and all protocol-required follow-ups post mCRM Coordinated System implant, including any Additional Visits due to adverse events related to communication of the Coordinated System. Communication testing requires an in-clinic visit.
Study Duration	The MODULAR ATP Clinical Study is expected to start in Q4 2021 and last for approximately 5 years.
Inclusion Criteria	• Patient who meets Class I, IIa, or IIb guideline ICD indications[1,2], or who has an existing TV-ICD* or S-ICD** • Patient who is deemed to be at risk for MVT based on at least ONE of the following: o History of Non-Sustained MVT with LVEF ≤ 50% o History of sustained VT/VF (secondary prevention) with LVEF ≤ 50% or significant cardiac scar*** o History of syncope deemed to be arrhythmic in origin o History of ischemic cardiomyopathy with LVEF ≤35% o History of non-ischemic cardiomyopathy with LVEF ≤35% and significant scar*** • Patient is willing and capable of providing informed consent (which is not to include the use of a legally authorized representative (LAR) for documentation of informed consent) and participating in all testing associated with this investigation at an approved study site and at the intervals defined by this protocol • Patient is age 18 years or above, or of legal age to give informed consent specific to state and national law

[1] Al-Khatib, et al. 2017 AHA/ACC/HRS Guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. (2018); 138:e272-e391.

[2] 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). *European Heart Journal* (2015) 36, 2793–2867.

MODULAR ATP Clinical Study Effectiveness of the EMPOWER™ Modular Pacing System and EMBLEM™ Subcutaneous ICD to Communicate Antitachycardia Pacing	
	*TV-ICD system is expected to be fully explanted during or prior to full Coordinated System implant **Potential subjects with a Model 1010 S-ICD Pulse Generator are only eligible for MODULAR ATP if they are getting upgraded to Model A209, A219 or future BSC S-ICD Pulse Generator **Patients with an existing S-ICD PG subject to the electrical overstress field action are only eligible for MODULAR ATP if they are getting a new BSC Model A209 or A219, or future BSC S-ICD Pulse Generator ***Significant cardiac scar is defined as a scar involving at least one ventricular myocardial segment (i.e., basal infero-septum) as identified in the official findings of a cMRI, or nuclear viability study, or echo report by the interpreting radiologist/ cardiologist who is not affiliated with the study
Exclusion Criteria	• Patient with an ongoing complication due to Cardiac Implantable Electronic Device (CIED) infection or CIED explant • Transvenous lead remnants within the heart from a previously implanted CIED (Note: transvenous lead remnants outside the heart (e.g., in the SVC) are allowed) • Patient with a known LA thrombus • Patient with a ventricular arrhythmia due to a reversible cause • Patient indicated for implantation of a dual chamber pacemaker or cardiac resynchronization therapy (CRT) • Patient with another implanted medical device that could interfere with implant of the leadless pacemaker, such as an implanted inferior vena cava filter or mechanical tricuspid heart valve • Patient requires rate-responsive pacing therapy • Patient is entirely pacemaker-dependent (defined as escape rhythm ≤ 30 bpm) • Patient with Acute Coronary Syndrome (i.e. Acute Myocardial Infarction, Unstable Angina) within 40 days • Inability to access femoral vein with a 21-French or larger inner diameter introducer sheath due to known anatomy condition, recent surgery, and/ or other relevant condition • Patient who has an active implanted electronic medical device intended for chronic use concomitantly with the study system, such as a left ventricular assist device (LVAD). Note that a temporary pacing wire is allowed. • Patient with known or suspected sensitivity to Dexamethasone Acetate (DXA) • Patient with a known cardiovascular anatomy that precludes implant in the right ventricle • Patient with a known allergy to any system components

MODULAR ATP Clinical Study Effectiveness of the EMPOWER™ Modular Pacing System and EMBLEM™ Subcutaneous ICD to Communicate Antitachycardia Pacing	
	• Patient with a known or suspected intolerance to S-ICD conversion testing, based on physician discretion • Patient is not likely to have meaningful survival[1] for at least 12 months (documented or per investigator's discretion) • Patient is enrolled in any other concurrent study. Co-enrollment into other studies such as observational studies/registries needs prior written approval by BSC. Local mandatory governmental registries are accepted for co-enrollment without approval by BSC • Patient who is a woman of childbearing potential who is known to be pregnant at the time of study enrollment (method of assessment upon investigator's discretion) [1] meaningful survival means that a patient has a reasonable quality of life and functional status.

Statistical Methods

	Assessment	Expected Value	Performance Goal	Statistical Test	Alpha Level	Power Level	Number of Subjects	Assumed Attrition	Number of Subjects with Assumed Attrition
Safety 1	Major EMPOWER MPS System- and Procedure-related Complication-Free Rate from Implant through 6 Months Post-Implant	93%	86%	Kaplan-Meier	2.5% (Overall) 1.2% (Interim) 1.9% (Final)	90%	134 (Interim) 223 (Final)	25%	179 (Interim) 298 (Final)
Safety 2	Major EMPOWER System and Procedure-related Complication-free Rate from Implant through 12 Months Post-Implant	92%	81%	Kaplan-Meier	2.5%	90%	112	30%	160
Primary Effectiveness 1	Communication Success between the S-ICD and EMPOWER PG at 6 Month Visit	95%	88%	One-Sided Lower Pointwise Confidence Limit	2.5%	80%	152 tests/ 38 subjects	30%	220 tests/55 subjects
Primary Effectiveness 2	The percent of subjects with an adequate EMPOWER pacemaker PCT measurement.	95%	80%	One-Sided Lower Confidence Limit	2.5%	90%	57	30%	82

3 Table of Contents

[redacted]

[redacted]

Table of Figures

Table of Tables

[redacted]

4 Introduction

4.1 Background

Despite technological advances in pacing and defibrillation, the overwhelming majority of acute and chronic complications are related to incisional access for device pockets connected to indwelling transvenous leads. Over 600,000 patients implanted yearly worldwide are faced[2] with adverse events due to the pulse generator (e.g., hematoma, skin erosion, pocket infections) or transvenous lead placement (e.g., pneumothorax, cardiac perforation, lead dislodgement)[3].

Advancements in electronic circuitry and battery technology enable manufacturers to develop pacemakers that can be completely implanted inside the right ventricle of the patient's heart while keeping battery durability and longevity with communication to an entirely extravascular (subcutaneous) defibrillation system.

The EMPOWER™ Modular Pacing System (EMPOWER MPS, comprised of the EMPOWER pacemaker and delivery catheter) and EMPOWER MPS accessories used for delivery and retrieval of the EMPOWER pacemaker build on Boston Scientific's (BSC's) decades of experience designing and manufacturing conventional transvenous pacemakers, as well as new key technologies within the rhythm management industry, such as circuit miniaturization, catheter technology, and new materials (e.g., innovative alloys). The EMPOWER pacemaker is placed directly into the right ventricle using a newly designed steerable, atraumatic delivery catheter system that enters the vasculature via the femoral vein. Leadless cardiac therapy eliminates the need for a transvenous pacing lead, as well as the subcutaneous pocket required for a conventional pulse generator; thereby, eliminating a larger proportion of complications common to transvenous pacemaker systems.

The potential hazards and risks associated with the EMPOWER System throughout the product life cycle were identified by means of an exhaustive risk assessment. These risks were then compared to those of existing transvenous single-chamber pacemakers. The assessment and comparison identified many similarities between conventional transvenous single-chamber pacemakers and the EMPOWER pacemaker; however, the EMPOWER pacemaker decreases or eliminates several risks associated with transvenous pacemakers mainly due to the lack of a device pocket and/or use of a transvenous lead. While there are limited novel risks associated with the use of the EMPOWER System, the outcomes of the pre-clinical testing validate that the benefits of the EMPOWER System likely outweigh the possible risks. It is therefore considered safe and justified to continue evaluating the EMPOWER pacemaker by implanting it in human subjects.

The subcutaneous implantable cardioverter defibrillator system (S-ICD System) was developed in part to address complications associated with traditional transvenous implantable cardioverter defibrillator (TV-ICD) leads. The nature of the transvenous system with the need for leads to be permanently dwelling in the venous circulation and cardiac chambers for very long term, increases the likelihood of certain types of lead failure like conductor fracture, insulation break and dislodgement that can compromise the system's performance. Furthermore, when a system infection occurs, it usually

represents a severe complication and requires lead extraction with its own risks. Analyses of multiple large patient claims databases have evaluated transvenous device and lead complications.[3,4,5] When TV-ICD leads are specifically considered, it is noted that the mechanical complication rate is 5% by 3 years post implant and continues to rise to 23.9% for those patients who reach 10 years of follow-up[7]. Therefore, these complications have substantial implications for patient outcomes and health care system costs. According to an analysis of U.S. claims data[6], these complications will affect 1 in 6 patients by 3 years, which has substantial implications for patient outcomes and health care system costs.

The S-ICD System does not require a lead to be placed either in (endocardium) or on (epicardium) the heart, which may be advantageous in reducing:

- Implant-associated risks related to central venous access or endocardial lead positioning and fixation.
- Exposure of the lead to stresses induced by repeated cardiac pulsations
- Serious infections with a direct pathway to the blood stream and endocardium
- Complications related to lead extraction

Because the S-ICD System lacks a transvenous lead in the heart, it has no ability to provide bradycardia pacing or antitachycardia pacing (ATP). This limitation restricts the ICD-indicated patient population that can benefit from the S-ICD system. The approved indication for the S-ICD System reflects this restriction by specifically identifying S-ICD candidates as ICD-indicated patients *who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with anti-tachycardia pacing*.[6]

These restrictions limit the patients who receive an S-ICD based on their initial indication and the clinical likelihood of requiring the therapies not provided by this system in the future. However, some S-ICD candidates have or eventually develop symptomatic bradycardia or ventricular tachycardias that can be terminated with ATP. For S-ICD patients who develop bradycardia, published reports indicate that a concomitant

---

[3] Ranasinghe I, Parzynski CS, Freeman JV, et al. Long-Term Risk for Device-Related Complications and Reoperations After Implantable Cardioverter-Defibrillator Implantation: An Observational Study. *Ann Intern Med*. 2016 Jul 5; 165(1):20-29.

[4] Cantillon DJ, Exner DV, Badie N, et al. Complications and Health Care Costs Associated with Transvenous Cardiac Pacemakers in a Nationwide Assessment *JACC: Clin Electrophysiology*. 2017 Nov; 3 (11) 1296-1305; DOI: 10.1016/j.jacep.2017.05.007

[5] Koneru JN, Jones PW, Hammill EF, et al. Risk Factors and Temporal Trends of Complications Associated With Transvenous Implantable Cardiac Defibrillator Leads. *J Am Heart Assoc*. 2018;7(10):e007691. Published 2018 May 10.

[6] EMBLEM S-ICD Pulse Generator Instructions for Use.

pacemaker may be implanted without adversely affecting the S-ICD function.[7,8,9,10] Unlike these S-ICD patients, those who need ATP do not currently have a concomitant device option as the implanted pacemaker and the S-ICD perform as individual systems and don't communicate to one another. Options for patients who develop incessant or frequently recurring ventricular tachycardia (VT) include VT ablation or replacement of the S-ICD with a TV-ICD.

The MODULAR ATP Clinical Study will evaluate another option for patients who may benefit from ATP: the investigational mCRM Modular Therapy System. The mCRM Modular Therapy System combines an S-ICD System with a specially designed leadless pacemaker (EMPOWER PG)) that can receive communication signals from the S-ICD System to provide ATP prior to (or as an alternative to) an S-ICD shock. The intended indication for the mCRM Modular Therapy System will be *to provide defibrillation therapy and anti-tachycardia pacing (ATP) therapy for the treatment of life threatening ventricular tachyarrhythmias.* The EMPOWER PG can also be programmed to provide bradycardia backup pacing when required. For the purpose of the MODULAR ATP Clinical Study, the devices included in the mCRM Modular Therapy System (S-ICD System and the EMPOWER PG) will be called the mCRM Coordinated System.

Boston Scientific conducted extensive testing to determine that the EMPOWER MPS System and the coordination of the EMBLEM S-ICD System and EMPOWER MPS System elements of the mCRM System functions safely and effectively per the design intent. Boston Scientific performed safety risk management, nonclinical bench testing, and animal studies to support the project. These activities were performed in accordance with established national and international industry standards, Good Laboratory Practices (GLPs), product specifications, and internal Boston Scientific procedures. All testing demonstrated that the investigational EMPOWER MPS System and the coordination of the EMBLEM S-ICD System and EMPOWER MPS System elements of the mCRM System performed as intended and met all electrical and mechanical performance specifications.

Note: Acronyms and terms used in this protocol are defined in **Sections 25.1** and **25.2**, respectively.

---

[7] Huang J, Patton KK, Prutkin JM. Concomitant Use of the Subcutaneous Implantable Cardioverter Defibrillator and a Permanent Pacemaker. *PACE* 2016 Nov; 38(11):1240-1245

[8] Ahmed FZ, Cunnington C, Motwani M, Zaidi AM.Totally Leadless Dual-Device Implantation for Combined Spontaneous Ventricular Tachycardia Defibrillation and Pacemaker Function: A First Report.*Can J Cardiol* 2017 Aug;33(8):1066

[9] Ljungstrom, E., Brandt, J., Mortsell, D., Borgquist, R., & Wang, L. (2019). Combination of a leadless pacemaker and subcutaneous defibrillator with nine effective shock treatments during follow-up of 18months. *Journal of Electrocardiology*, 56, 1-3. doi:10.1016/j.jelectrocard.2019.06.001

[10] Ito R, Kondo Y, Winter J, et al. Combination of a leadless pacemaker and subcutaneous implantable cardioverter defibrillator therapy for a Japanese patient with prosthetic valve endocarditis. *J Arrhythm*. 2019;35(2):311-313. Published 2019 Jan 16. doi:10.1002/joa3.12152

5 Device Description

[redacted]

5.1 mCRM Coordinated System

The mCRM Coordinated System has both implantable and non-implantable components that are being evaluated in this study. A number of other market-released accessories are listed below that may be used with the system, but are neither investigational nor under direct study in the MODULAR ATP Clinical Study.

5.2 Implantable Study Devices

The implantable portion of the system comprises three component devices that comprise the mCRM Coordinated System. The three component devices of the mCRM Coordinated System are:

- (EMBLEM/ EMBLEM MRI) S-ICD Pulse Generator, Models A209/A219 or future BSC S-ICD Pulse Generator, with Coordinated System clinical firmware. (This, along with the S-ICD Electrode is referred to in this protocol as the "S-ICD System")
- S-ICD Electrode, Model 3400/3401, Model 3501 or future BSC S-ICD Electrode[11]
- EMPOWER MPS Pulse Generator and Delivery Catheter[12], Model B170

Patients with an indication for rate-responsive pacing therapy are excluded from the MODULAR ATP Clinical Study. However, patients enrolled in the study may develop a need for this therapy during the course of the clinical study. Rate-responsive pacing may be programmed 'on' based on Section 10.3.4.6.

5.3 Non-Implantable Study Devices

The non-implantable portion of the mCRM Coordinated System includes accessories associated with both the EMPOWER MPS and the S-ICD System.[13]

5.3.1 Non-Implantable Study Devices Associated with the EMPOWER System

The EMPOWER MPS and associated retrieval accessories consist of both investigational and market-approved devices. The non-implantable EMPOWER System accessories that may be used during the implant and/or retrieval procedures at clinical sites include:

- Delivery Catheter portion of the EMPOWER MPS, Model B170 (refer to **Section 26.2.1.1**).
- EMPOWER MPS Introducer Sheath, Model 8782

Note: Another compatible introducer sheath may be used that is not part of the EMPOWER System accessories. Refer to **Table 26-1** and the EMPOWER Modular Pacing System Physician's Technical Manual and Label Supplement, as well as the

---

[11] Note that Cameron Health Q-Trak Electrode Model 3010 is the same as BSC Models 3400/3401, and is also allowable.

[12] Note that the Delivery Catheter is a non-implantable device; however, it is an integral part of Model B170.

[13] Subjects may be enrolled with an existing S-ICD System. In such subjects, information on the non-implantable implant accessories will NOT be collected from the original procedure.

EMPOWER Retrieval System Physician's Technical Manual and Label Supplement for more information.

- Amplatz Super Stiff™ Guidewire Model M001465010, or equivalent stiff 0.035" (0.89mm) Guidewire
    - A 5-pack of Amplatz Super Stiff™ Guidewires carries Model Number M00146511, where each individual guidewire in that pack includes Model Number M00146510
- EMPOWER MPS Retrieval System, (refer to **Section 26.2.1.2**):
    - Retrieval Catheter, Model 8780
    - Single-loop Snare, Model 8784
    - Tri-loop Snare, Model 8785
- Surface ECG Cable, Model 3153 or equivalent
- LATITUDE™ Programming System, Model 3300, using Programmer Software Application, Model 3870 and associated Firmware
- Physical media containing the Programmer Software Application, such as a pen drive, Model 6226 (see **Section 5.3.2**)
- LATITUDE Programming System – Feature Key, Model 6252
- Sterile Tray Cable, Model 6157
- Conducted Telemetry Cable (non-sterile and re-usable), Model 6396

5.3.2 Model 3870 Programmer Software Application and Associated Firmware

Investigational firmware for the Model 3300 LATITUDE Programming System is bundled with the Model 3870 Programmer Software Application installer. This firmware allows the use of the conducted telemetry hardware within the Model 3300 LATITUDE Programming System.

The Model 3870 Programmer Software Application is used to support the communication with the EMPOWER PG.

Note: the version of the 3870 software application may be updated during the study. If this occurs, study sites will be notified of the new software version(s) and a BSC representative will update the software on the PRM*.

[redacted]

[redacted]

5.3.3 Non-implantable Study Devices Associated with the S-ICD System

The non-implantable S-ICD System accessories that may be used during the implant procedure at clinical sites include:

- S-ICD Programmer, Model 3200, using Programmer Software Application, Model 2877*
- LATITUDE Programming System, Model 3300, using Programmer Software Application, Model 3877 (when available, per geography)
- S-ICD Subcutaneous Electrode Insertion Tools (EIT), Model 4711
- S-ICD Electrode Delivery System (EDS), Model 4712

*The S-ICD Programmer, Model 3200 will be used in the MODULAR ATP Clinical Study until the LATITUDE Programming System, Model 3300 is available per geography

[redacted]

5.4 Accessories

Non-study accessories associated with the EMPOWER MPS include:

- ECG patches for conductive communication (commercially available)

Non-study accessories associated with the S-ICD System include:

- EMBLEM S-ICD Patient Screening Tool, Model 4744
- EMBLEM S-ICD Automatic Screening Tool (AST), Model 2889 (Used in conjunction with the ZOOM LATITUDE PRM, Model 3120 for ECG screening only; will not interrogate an S-ICD device)
- EMBLEM S-ICD Automatic Screening Tool (AST), Model 3889 (Used in conjunction with the LATITUDE Programming System, Model 3300 for ECG screening only; will not interrogate an S-ICD device (when available, per geography)

5.5 Additional Equipment

A commercially approved Holter monitor and its accessories will be provided to select study sites to conduct the 16-24 hour Holter Substudy. The equipment and monitoring service will be provided by an independent core lab. Refer to **Section 10.5.5** for a description of the Holter Substudy.

Equipment needed to perform required testing in subjects participating in the Rate Response Substudy (**Section 10.6**) include:

- Treadmill (provided by the selected study site),
- Laser Tachometer, Advent Model A2103/LSR/K
- Tachometer-to-Programmer Cable, BSC equipment number E90017-100,
- LATITUDE Programming System – Feature Key (Model 6252)

6 Study Objectives and Endpoints

Refer to **Table 6-1** and **Table 6-2** for a summary of the primary and secondary objectives and endpoints for the MODULAR ATP Clinical Study. Further justification for the study design is included in **Section 7.2**.

Table 6-1: Primary Objectives and Endpoints

Objective	Endpoint	Justification
Assess safety of the EMPOWER Modular Pacing System (MPS)	Safety Endpoint 1: Freedom from Major EMPOWER MPS System and Procedure-Related Complications through 6 months Post-Implant > 86%	Similar endpoints have been used for transvenous and leadless pacing system
	Safety Endpoint 2: Freedom from Major EMPOWER System- and Procedure-related Complications through 12 months Post-Implant > 81%	Similar endpoints have been used for historical pacing systems and similar market-released devices
Assess effective communication between the S-ICD and EMPOWER MPS	Primary Effectiveness Endpoint 1: The proportion of communication attempts between the S-ICD and EMPOWER MPS that are successful at the 6 Month Visit > 88%	Communication between the devices was chosen as a measure of effectiveness as it is the novel part of the Coordinated System and ATP effectiveness has already been proven.
Assess effectiveness of the EMPOWER MPS	Primary Effectiveness Endpoint 2: Proportion of subjects with adequate PCT (defined as ≤ 2 V@0.4 ms) collected at the 6 Month Visit > 80%	Similar endpoints have been used for historical pacing systems and similar market-released devices[12, 13]

Table 6-2: Secondary Objectives and Endpoints

Objective	Endpoint	Justification
Assess safety of the EMPOWER Modular Pacing System (MPS)	Secondary Safety Endpoint: All-Cause Survival through 2 years Post-Implant > 85%	Similar endpoints have been used for similar market release devices
Assess the Rate Response function of the EMPOWER PG	Secondary Effectiveness Endpoint 1: Mean Metabolic-Chronotropic Relation (MCR) slope from the Kay-Wilkoff model is between 0.65 and 1.35 at the 3 Month Visit	Similar endpoints have been used for historical pacing systems and similar market-released devices[14]

6.1 Study Objectives

The objective of the MODULAR ATP Clinical Study is to demonstrate the safety, performance and effectiveness of the EMPOWER™ Modular Pacing System (MPS), as well as the EMPOWER and EMBLEM™ Subcutaneous ICD Coordinated System. [redacted]

6.2 Study Endpoints

The following endpoints will be evaluated to establish the safety, performance and effectiveness of the Coordinated System to satisfy global regulatory requirements. Refer to **Section 11.1** for details on each endpoint.

6.3 Safety Endpoints

- Safety Endpoint 1: Major EMPOWER MPS System- and Procedure-related Complication-Free Rate from Implant through 6 Months Post-Implant
- Safety Endpoint 2: Major EMPOWER MPS System- and Procedure-related CFR from Implant through 12 Months Post-Implant
- Secondary Safety Endpoint: All-Cause Survival from Implant through 2 Years Post-Implant

6.4 Effectiveness Endpoints

- Primary Effectiveness Endpoint 1: Communication Success between the S-ICD and EMPOWER PG at the 6 Month Visit
- Primary Effectiveness Endpoint 2: Proportion of Subjects with Adequate Pacing Capture Threshold (defined as ≤2 V @ 0.4 ms) at the 6 Month Visit

---

[14] Reynolds D, Duray GZ, Omar R, Soejima K, Neuzil P, Zhang S, Narasimhan C, Steinwender C, Brugada J, Lloyd M, Roberts PR, Sagi V, Hummel J, Bongiorni MG, Knops RE, Ellis CR, Gornick CC, Bernabei MA, Laager V, Stromberg K, Williams ER, Hudnall JH and Ritter P. A Leadless Intracardiac Transcatheter Pacing System. *N Engl J Med*. 2016;374:533-41.

- Secondary Effectiveness Endpoint: Mean Metabolic Chronotropic Relation (MCR) Slope from the Kay-Wilkoff Model at the 3 Month Visit

6.5 Ancillary Objectives

Further data will be collected in the MODULAR ATP Clinical Study and summarized. Refer to **Section 11.2** for more information.

6.6 Study Rationale

Patients may benefit from ventricular arrhythmia termination with ATP because it can avoid a shock that is often painful and consumes battery energy. The effectiveness of ATP therapy in terminating VT is well established[15] and recognized by international guideline recommendations for ICD programming.[16,17] Therefore, ATP therapy effectiveness is not the primary focus of the study. Instead, the MODULAR ATP Clinical Study will focus on the novel aspects of the mCRM Coordinated System for the delivery of ATP.

The MODULAR ATP Clinical Study evaluates the safety and effectiveness of the EMPOWER MPS and the unique aspect of the mCRM Coordinated System, which is the unidirectional transmission of conductive communication signals from the S-ICD System to the EMPOWER PG. The EMPOWER PG is designed to recognize communication signals sent from the S-ICD coil towards the S-ICD PG, creating a communicating vector. Because this communication can be affected by the orientation of the devices relative to each other, the primary effectiveness endpoint will demonstrate communication success in varied orientations by altering body postures of subjects. Communication is tested by commanding a communication signal from the S-ICD that results in EMPOWER pacing for 10 beats above the subject's intrinsic rate.

Additionally, communication success will be demonstrated during spontaneous ventricular tachyarrhythmia episodes.

The effectiveness of the EMPOWER PG will be assessed by measuring adequate Pacing Capture Threshold (PCT) during follow-up visits post-implant. PCT has been shown to be affected by multiple factors, including the method and stability of fixation. The EMPOWER PG is designed to deploy using 4 active-fixation nitinol talons, as compared to the conventional active-fixation screw or passive-fixation tine engagement used in a transvenous lead system. The MICRA leadless pacemaker uses a similar mechanism consisting of 4 active-fixation nitinol tines, but the NANOSTIM leadless pacemaker uses a different mechanism consisting of an active-fixation fixed screw. Results from other

---

[15] Wathen M. Implantable cardioverter defibrillator shock reduction using new antitachycardia pacing therapies. *Am Heart J*. 2007 Apr;153(4 Suppl):44-52.

[16] Wilkoff BL, Fauchier L, Stiles MK, et al. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Europace*. 2016 Feb;18(2):159-83.

[17] Martin K. Stiles, MBChB, PhD, FHRS (Chair), Laurent Fauchier, MD, PhD, Carlos A. Morillo, MD, FHRS, Bruce L. Wilkoff, MD, FHRS, CCDS. 2019 HRS/EHRA/APHRS/LAHRS focused update to 2015 expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Heart Rhythm* 2019;17:220–228.

leadless pacemaker clinical trials showed that dislodgment was higher for the NANOSTIM leadless pacemaker as compared to the MICRA leadless pacemaker. In the LEADLESS trial[5] studying the NANOSTIM leadless pacemaker, no device dislodgements were identified. However, there were six device dislodgements in the LEADLESS II trial[18]. In comparison, there were no dislodgements in the MICRA IDE trial[19] and only one occurred in the MICRA Post-Approval Study[20]. The difference in dislodgement rate could be related to the difference in the fixation mechanism design between the two leadless devices. The fixation mechanism of the EMPOWER devices warrants evaluation in the pre-market clinical study.

The EMPOWER pacemaker uses a motion-based accelerometer to generate an electronic signal, which can be translated to a rate increase in proportion to the activity level of the patient. The rate response function will be evaluated during the trial due to the differences in the location of the accelerometer of an EMPOWER pacemaker, which resides inside of the heart chamber, compared to a transvenous pacemaker, which resides outside of the heart, usually in the infraclavicular or abdominal region.

Modern VVI(R) transvenous pacemakers are proven to be reliable in providing adequate pacing support. The reliability of the EMPOWER leadless pacemaker in providing appropriate pacing must be demonstrated before using it in pacemaker-dependent patients. Therefore, the MODULAR ATP Clinical Study protocol is designed to obtain data using Holter monitoring to support use of the EMPOWER PG in future pacemaker dependent patients.

Demonstration of the safety and effectiveness of the EMPOWER System in this study is required to obtain global market approval for commercial release. In addition, safety data collected may be used to support future post-market approval conditions mandated by global regulatory agencies.

The data from this study will be used to support global regulatory approvals.

7 Study Design

The MODULAR ATP Clinical Study is a prospective, non-randomized, multi-site study, single-arm, global study utilizing performance goals to demonstrate safety, performance, and effectiveness of the EMPOWER MPS and mCRM Coordinated System.

---

[18] Reddy VY, Exner DV, Cantillon DJ, Doshi R, Bunch TJ, Tomassoni GF, Friedman PA, Estes NA, 3rd, Ip J, Niazi I, Plunkitt K, Banker R, Porterfield J, Ip JE and Dukkipati SR. Percutaneous Implantation of an Entirely Intracardiac Leadless Pacemaker. N Engl J Med. 2015;373:1125-35.

[19] Dwight Reynolds, M.D., Gabor Z. Duray, M.D., Ph.D., Razali Omar, M.D. A Leadless Intracardiac Transcatheter Pacing System. N Engl J Med 2016; 374:533-541.

[20] El-Chami et al. Updated performance of the Micra transcatheter pacemaker in the real-world setting: A comparison to the investigational study and a transvenous historical control. Heart Rhythm 2018; 15:1800-1807.

7.1 Scale and Duration

The MODULAR ATP Clinical Study will enroll up to 300 subjects at approximately 60 sites in North America, the United Kingdom, and Europe. Other geographies may be added over the course of the study. [redacted] Therefore, subjects will continue to be followed every 6 months until [redacted], all subjects have been followed for at least 24 months, and BSC communicates study closure.

Figure 7-1 shows the follow-up plan for the MODULAR ATP Clinical Study. Subjects will be followed in the MODULAR ATP Clinical Study based on the date of their mCRM Coordinated System (both S-ICD and EMPOWER MPS) implant (i.e., the date on which the latter device was implanted.

Follow up in the MODULAR ATP Clinical Study is required at Pre-Discharge, 1 month, 3 months (only for subjects participating in the Rate Response Substudy), 6 months, 12 months, 18 months, and 24 months after the full mCRM Coordinated System is implanted. Subjects will continue to be followed every 6 months until BSC notifies sites that follow up is complete. Please note S-ICD labeling suggests patients be followed every 3 months. Therefore, subjects may be seen more often than the follow ups required for this clinical study. Refer to **Section 10.9** for reporting requirements of Additional Visits.

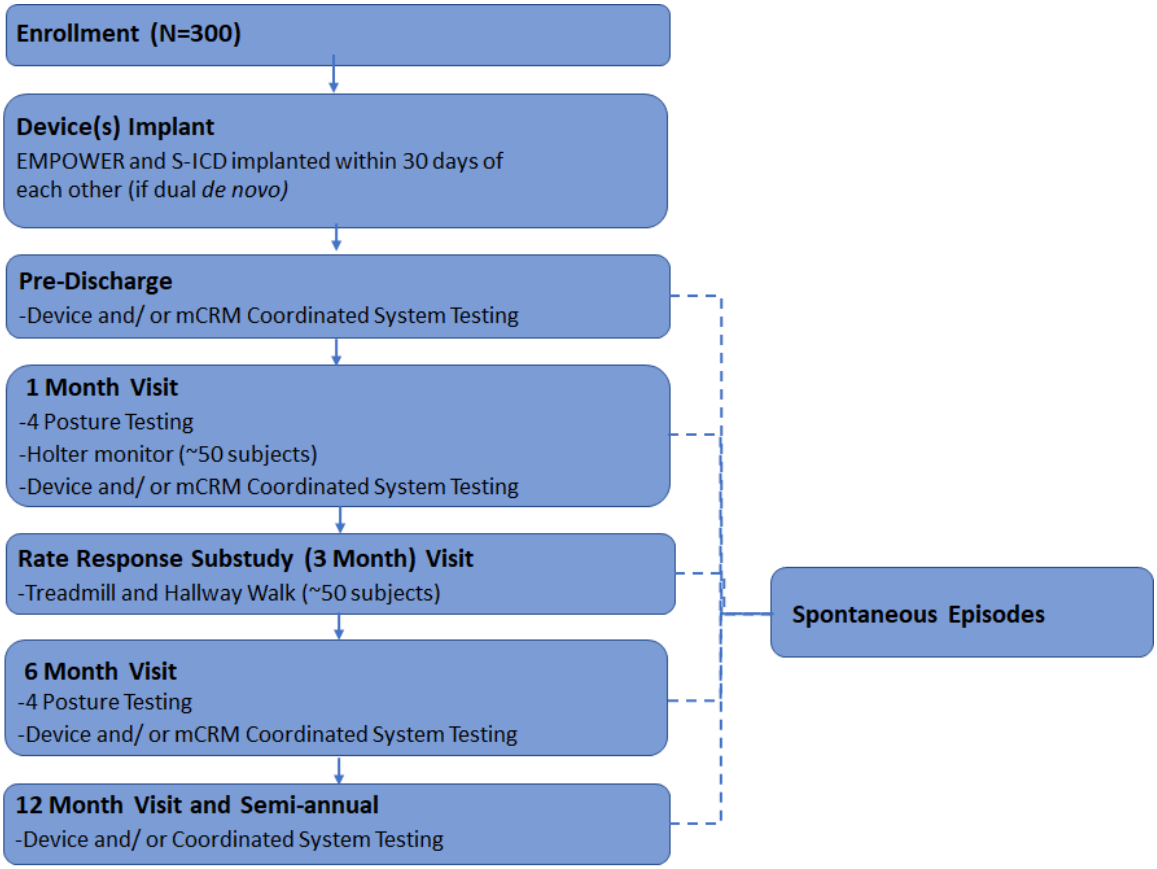


Figure 7-1: MODULAR ATP Clinical Study Design

7.2 Justification for the Study Design

[redacted]

The EMPOWER PG was developed and built on historic experience of comparable devices. Therefore, the Safety Endpoint 1 of the MODULAR ATP Clinical Study aims to establish the clinical safety profile of the EMPOWER PG at 6 months post-implant. Subjects are also required to complete 12-month, 18-month, and 24-month follow-ups, serving as a longer-term assessment of the mCRM Coordinated System, including the EMPOWER PG within the scope of the pre-market clinical study.

The effectiveness of the EMPOWER PG will be assessed by measuring adequate Pacing Capture Threshold (PCT) during follow-up visits post-implant. PCT has been shown to be impacted by multiple factors, including the method and stability of fixation. The EMPOWER PG is designed to deploy using 4 active fixation nitinol talons, as compared to the conventional active fixation screw and passive tine engagement used in a transvenous lead system.

The EMPOWER PG uses a motion-based accelerometer to generate an electronic signal, which can be translated to a rate increase in proportion to the activity level of the patient.

The rate response function will be evaluated during the MODULAR ATP Clinical Study to gather data in support of the differences in the location of the accelerometer of an EMPOWER pacemaker, which resides inside of the heart chamber, compared to a transvenous pacemaker, which resides in the subcutaneous infraclavicular region of the patient.

Modern VVI(R) transvenous pacemakers are proven to be reliable in providing adequate pacing support. The reliability of the EMPOWER leadless pacemaker in providing appropriate pacing must be demonstrated before using it in pacemaker-dependent patients.

The mCRM System was designed as an evolution to the stand-alone EMBLEM S-ICD System such that it integrates wireless intrabody communication between an EMBLEM S-ICD and a co-implanted EMPOWER pacemaker; thereby, allowing the coordination of ATP therapy.

As such, the mCRM System is intended to address the following patient needs, in addition to the therapy provided by the EMBLEM S-ICD alone:

- ATP therapy to reduce shocks for patients who have or develop recurring monomorphic ventricular tachycardia (VT)
- Ventricular bradycardia pacing therapy for EMBLEM S-ICD patients who could benefit from VVI(R) pacing

The MODULAR ATP Clinical Study represents a scientifically and statistically-based study to evaluate the safety and effectiveness of both the EMPOWER System and mCRM System, while maintaining focus on a patient population with a unique and heretofore unmet clinical need: patients with an existing EMBLEM S-ICD or patients deemed candidates for an EMBLEM S-ICD device who also have a need for ATP.

[redacted]

8 Subject Selection

8.1 Study Population and Eligibility

Subjects included in the MODULAR ATP Clinical Study should be selected among those with a standard ICD indication applying international practice guidelines, as well as those who already have an implanted S-ICD System and satisfy the inclusion criteria for this study, while not meeting any exclusion criteria. [redacted]

The investigator is responsible for screening all potential subjects and selecting those who meet the eligibility criteria for the study as described in **Sections 8.2** and **8.3**.

8.2 Inclusion Criteria

Subjects who meet all of the following criteria (**Table 8-1**) may be given consideration for inclusion in the MODULAR ATP Clinical Study, provided none of the exclusion criteria (refer to **Section 8.3**) are met.

Table 8-1: Inclusion Criteria

Inclusion Criteria	• Patient who meets Class I, IIa, or IIb guideline ICD indications[21,22], or who has an existing TV-ICD* or S-ICD**
	• Patient who is deemed to be at risk for MVT based on at least ONE of the following:
	  ○ History of Non-Sustained MVT with LVEF ≤ 50%
	  ○ History of sustained VT/VF (secondary prevention) with LVEF ≤ 50% or significant cardiac scar***
	  ○ History of syncope deemed to be arrhythmic in origin
	  ○ History of ischemic cardiomyopathy with LVEF ≤35%
	  ○ History of non-ischemic cardiomyopathy with LVEF ≤35% and significant scar***
	• Patient who is willing and capable of providing informed consent (which is not to include the use of a legally authorized representative (LAR) for documentation of informed consent) and participating in all testing associated with this investigation at an approved study site and at the intervals defined by this protocol
	• Patient who is age 18 years or above, or of legal age to give informed consent specific to state and national law

*TV-ICD system is expected to be fully explanted during or prior to full Coordinated System implant

**Patients with a Model 1010 S-ICD Pulse Generator are only eligible for MODULAR ATP if they are getting upgraded to BSC Model A209 or A219, or future BSC S-ICD Pulse Generator

**Patients with an existing S-ICD PG subject to the electrical overstress field action are only eligible for MODULAR ATP if they are getting a new BSC Model A209 or A219, or future BSC S-ICD Pulse Generator

***Significant cardiac scar is defined as a scar involving at least one ventricular myocardial segment (i.e., basal infero-septum) as identified in the official findings of a cMRI, or nuclear viability study, or Echo report by the interpreting radiologist/ cardiologist who is not affiliated with the study

Abbreviations: ECG = Electrocardiogram; **ICD** = Implantable Cardioverter-Defibrillator; **LAR** = Legally Authorized Representative; **MRI** = Magnetic Resonance Imaging; **cMRI** = cardiac Magnetic Resonance Imaging; **LVEF** = Left Ventricular Ejection Fraction; **MI** = Myocardial Infarction; **MVT** = Monomorphic Ventricular Tachycardia; **S-ICD** =

[21] Al-Khatib, et al. 2017 AHA/ACC/HRS Guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. (2018); 138:e272-e391.

[22] 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). *European Heart Journal* (2015) 36, 2793–2867.

Subcutaneous Implantable Cardioverter-Defibrillator; **TV-ICD** = Transvenous Implantable Cardioverter-Defibrillator; **VF** = Ventricular Fibrillation; **VT** = Ventricular Tachycardia

8.3 Exclusion Criteria

Patients who meet any one of the following criteria (**Table 8-2***)* will be excluded from this clinical study.

Table 8-2: Exclusion Criteria

Exclusion Criteria	• Patient with an ongoing complication due to Cardiac Implantable Electronic Device (CIED) infection or CIED explant • Transvenous lead remnants within the heart from a previously implanted CIED (**Note**: transvenous lead remnants outside the heart (e.g., in the SVC) are allowed) • Patient with a known LA thrombus • Patient with a ventricular arrhythmia due to a reversible cause • Patient indicated for implantation of a dual chamber pacemaker or cardiac resynchronization therapy (CRT) • Patient with another implanted medical device that could interfere with implant of the leadless pacemaker, such as an implanted inferior vena cava filter or mechanical tricuspid heart valve • Patient requires rate-responsive pacing therapy • Patient is entirely pacemaker-dependent (defined as escape rhythm ≤ 30 bpm) • Patient with Acute Coronary Syndrome (i.e. Acute Myocardial Infarction, Unstable Angina) within 40 days • Inability to access femoral vein with a 21-French or larger inner diameter introducer sheath due to known anatomy condition, recent surgery, and/ or other relevant condition • Patient who has an active implanted electronic medical device intended for chronic use concomitantly with the study system, such as a left ventricular assist device (LVAD). Note that a temporary pacing wire is allowed. • Patient with known or suspected sensitivity to Dexamethasone Acetate (DXA) • Patient with a known cardiovascular anatomy that precludes implant in the right ventricle • Patient with a known allergy to any system components • Patient with a known or suspected intolerance to S-ICD conversion testing, based on physician discretion • Patient is not likely to have meaningful survival[1] for at least 12 months (documented or per investigator's discretion) • Patient is enrolled in any other concurrent study. Co-enrollment into other studies such as observational studies/ registries needs prior written approval by BSC. Local mandatory governmental registries are accepted for co-enrollment without approval by BSC.

	• Patient who is a woman of childbearing potential who is known to be pregnant at the time of study enrollment (method of assessment upon investigator's discretion) [1] meaningful survival means that a patient has a reasonable quality of life and functional status.

9 Subject Accountability

9.1 Point of Enrollment

Subjects will be considered enrolled into the MODULAR ATP Clinical Study at the time of Informed Consent Form (ICF) execution. All subject enrollments will be counted against the enrollment ceiling for the study.

9.2 Subject Status and Classification

9.2.1 Intent

Intent - refers to a subject who has been enrolled in the MODULAR ATP Clinical Study, but then does not have anesthesia administered in preparation for an EMPOWER PG and/ or S-ICD implant procedure. The original ICF and enrollment documentation for intent subjects should be maintained in the study site's files and an End of Study Form completed in eDC. There are no follow-up requirements for intent subjects; intent subjects must be withdrawn from the study.

9.2.2 Attempt

Attempt - refers to a subject who 1) has been enrolled in the MODULAR ATP Clinical Study, 2) has had anesthesia administered in preparation for the surgical implant procedure of an EMPOWER PG and/or S-ICD, but 3) is not successfully implanted with the EMPOWER PG and/or S-ICD.

Attempt subjects must be followed at least 30 days (either in-clinic or phone contact) post-attempted EMPOWER PG and/or S-ICD device implant to assure there are no associated adverse events or to assure the resolution of any adverse events associated with the attempted S-ICD and/or EMPOWER PG device implants. Attempt subjects will be included in the data analysis for the implant success rate. Attempt subjects must be withdrawn from the study after satisfying the follow-up of at least 30 days from attempted device implant.

9.2.3 Partial Implant

Partial Implant - refers to a subject who 1) has been enrolled in the MODULAR ATP Clinical Study, 2) has had either the S-ICD System introduced into their subcutaneous space or the EMPOWER MPS introduced into their vasculature, 3) is successfully implanted with either the S-ICD System or EMPOWER PG device, **but not both**, AND 4) is unable to or for whom there is no intention to implant the full mCRM Coordinated System.

Subjects classified as a Partial Implant that are implanted with an EMPOWER PG must be followed according to this protocol, with all relevant EMPOWER PG device data and

testing collected. Time 0 for the purpose of determining timing of follow ups for these subjects is the day it is determined the S-ICD will not be implanted.

Note that subjects implanted with an S-ICD System (prior to upgrading with clinical firmware in the MODULAR ATP Clinical Study) who are not implanted with an EMPOWER PG may be withdrawn from the MODULAR ATP Clinical Study after satisfying the follow-up of at least 30 days from S-ICD device implant.

9.2.4 Implant

Implant - refers to a subject who has been enrolled in the MODULAR ATP Clinical Study and is successfully implanted with the S-ICD **and** EMPOWER PG device per the study protocol (this includes those subjects previously implanted with an S-ICD System). Implant subjects are followed in accordance with the follow-up schedule included in this protocol and included in analyses of safety, effectiveness, and performance based on provisions discussed in **Section 11**.

9.3 Access to EMPOWER MPS Programmer Software and S-ICD System mCRM Programming

If a subject classified as either "Partial Implant" (those with the EMPOWER PG implanted, but not an S-ICD system) or "Implant" seeks routine or emergency care in a facility or from a physician who is not a study investigator, there may be a delay in:

- accessing the EMPOWER PG's data due to the need to secure access to the Programmer Software Application Model 3870, or
- accessing programmable mCRM parameters of the S-ICD device due to the need to provide a device-specific PIN, which is only available to trained study personnel with authorized access as part of the MODULAR ATP Clinical Study
    - **Note:** Non-investigational S-ICD parameters continue to be accessible at all times.

Trained study personnel (ie, BSC personnel or trained site personnel) are required to be present to access the Programmer Software Application Model 3870 and investigational features of the S-ICD (mCRM parameters) and report their use in these circumstances.

9.4 Strategies for Recruitment and Retention

The MODULAR ATP Clinical Study will include subjects deemed at risk for monomorphic ventricular tachycardia (MVT), SCD, and who are indicated for an ICD (**Section 8.2**). The incidence of SCD increases markedly with age regardless of sex or race: Accordingly, the SCD rate is estimated to range from 1.40 per 100,000 person-years in women to 6.68 per 100,000 person-years in men. SCD in younger individuals has an estimated incidence of 0.46–3.7 events per 100,000 person-years, corresponding to a rough estimate of 1100–9000 deaths in Europe and 800–6200 deaths in the USA every year. The inclusion and exclusion criteria are not expected to have a negative effect on recruitment or retention of said populations. In the United States, the subjects eligible for inclusion in this study are likely to be a mixture of private payer and Medicare patients due to their expected age and the results of this study are likely to be generalizable to a Medicare population.

9.5 Withdrawal

All subjects enrolled in the clinical study (including those withdrawn) shall be accounted for and documented. If a subject withdraws from the clinical study, the reason(s) shall be reported. [redacted]

Reasons for withdrawal include, but are not limited to:

- Subject who does not receive either device for the purpose of supporting the study (EMPOWER PG **or** S-ICD). This includes subjects classified as "Intent", and those classified as "Attempt", according to the definitions in **Section 9.2**.
- Subject found to be ineligible to participate in the study prior to implant of the S-ICD and/ or EMPOWER PG (refer to **Section 9.2** for further information on follow up requirements)
- Physician discretion
- Subject choice to withdraw consent
- Explant of the investigational device(s) (EMPOWER PG and/ or S-ICD converted with clinical firmware) *; subjects should be followed at least 30 days (either in-clinic or phone contact) post-explant of the mCRM Coordinated System to assure there are no associated adverse events or to assure the resolution of any adverse events associated with the explanted mCRM Coordinated System.
    - ***Note**: this provision includes explant of the EMPOWER PG in all subjects, and the S-ICD in the case where the device has had clinical firmware uploaded.
- Lost to follow-up
- Death

While study withdrawal is discouraged, subjects may withdraw from the MODULAR ATP Clinical Study at any time, with or without reason, and without prejudice to further treatment. In cases of study withdrawal where the EMPOWER PG remains actively implanted, the subject should be informed that he/she will need to continue to have the EMPOWER PG evaluated per BSC's recommended follow-up (1, 3, 6 months and every 6 months) at a MODULAR ATP Clinical Study site where there is access to the investigational software (Model 3870) to interrogate the EMPOWER PG.

[redacted]

All applicable case report forms up to the point of subject withdrawal and an End of Study Form must be completed in eDC.

Additional study data may no longer be collected after the point at which a subject has been withdrawn from the study or withdraws his/her consent, for whatever reason. All open adverse events should be closed or documented as chronic. Data collected up to the point of subject withdrawal may be used.

9.6 Lost-to-Follow-up

Subjects who are "lost-to-follow-up" should have three documented attempts to contact them prior to completion of the End of Study Form in eDC. **Note**: the end-of-study date should be on or after the last documented contact attempt.

9.7 End-of-Study Definition

A clinical study is considered completed when participants are no longer being examined or the last participant's final study visit has occurred.

[redacted] Upon completion of participation in the study, subjects will be followed per the normal standard of care.

9.8 End of Study Action Plan

BSC reserves the right to terminate the study, discontinue implanting the EMPOWER PG, or discontinue allowing conversion of the S-ICD with clinical firmware at any stage of the study. BSC intends to exercise this right only for valid scientific or administrative reasons and reasons related to protection of subjects. In the event of any of these occurrences, BSC will communicate to the investigators of the MODULAR ATP Clinical Study. The investigators will be responsible for communicating any information necessary to the subjects. BSC will support the investigators by providing recommendations for ensuring the safety of the subjects and the handling of the implantable investigational devices (EMPOWER PG and S-ICD converted with clinical firmware) which may include, but are not limited to:

- Standard-of-care procedures
- More frequent follow ups of the subject and the EMPOWER PG device and/or S-ICD converted with clinical firmware than per standard procedures
- Longer-term follow-up (beyond length of initial consent)
- Explant of EMPOWER PG and/or S-ICD converted with clinical firmware upon careful risk-benefit analysis
- Other possible actions

[redacted]

10 Study Methods

10.1 Data Collection

Data will be collected from each subject at Enrollment, Implant, Pre-discharge, 1 Month, 3 Months (only for subjects participating in the Rate Response Substudy), 6 Months, and follow-up visits every 6 months thereafter until BSC notifies study sites that follow up is complete, as defined in **Section 9.7**. Additional follow-up visits must be collected as defined in **Section 10.9**. All study-related visit windows are calculated from the date of both devices (EMPOWER PG and S-ICD converted with clinical firmware) being implanted (exceptions for those not implanted with both devices is included in **Section 9.2.3**).

The data collection schedule is shown in **Table 10-1.**

Table 10-1: MODULAR ATP Clinical Study Data Collection Schedule

Procedure/ Assessment	Enrollment	EMPOWER PG Implant	S-ICD Implant	mCRM Coordinated System		Follow-up In-Office Visits				Additional Visit
				System Testing	Pre-Discharge	1 Month	3 Month (treadmill only)	6 Month	Semi Annual	
Time Frame	≤30 days prior to EMPOWER PG and/ or S-ICD implant	--	--	Time 0	Prior to hospital discharge with mCRM Coordinated System	10d -42d	90±15d	180 ± 30d	12 Mo: 360 ± 45d 18 Mo: 540 ± 45d 24 Mo: 720 ± 45d 30 Mo: 900 ± 45d 36 Mo: 1080 ± 45d Etc.	--
Informed consent	**X**	--	--	--	--	--	--	--	--	--
Demographics	**X**	--	--	--	--	--	--	--	--	--
Physical assessment	**X**	--	--	--	--	--	--	--	--	--
Medical history	**X**	--	--	--	--	--	--	--	--	--
Cardiac disease history	**X**	--	--	--	--	--	--	--	--	--
Arrhythmia history	**X**	--	--	--	--	--	--	--	--	--
Cardiovascular medications	**X**	--	--	--	--	--	--	--	--	--
S-ICD screening ECG	**X**[23]	--	--	--	--	--	--	--	--	--
Implant details	--	**X**	**X**[23]	--	--	--	--	--	--	--
Product information	--	**X**	**X**	--	--	--	--	--	--	--
Fluoro/ Cine image	--	**X**	--	**X**	--	--	--	--	--	--
Chest X-Ray	--	--	--	**X (Either/ or)**		--	--	--	----	
Pace Morphology Sensing Test (PMST)	--	--	--	**X**	**X**	--	**O**	--	--	**O**
Communication Test/ Communication Threshold Test	--	--	--	**X****	**X****	**X****	--	**X****	**X****	**X****
Muscle stimulation testing	--	--	--	**X**	--	--	--	--	--	--
S-ICD conversion and sensing interaction testing	--	--	--	**X (Either/ or)**		**O**	**O**	**O**	**O**	**O**
EMPOWER MPS Evaluation	--	**X**	--	**X**	**X**	**X**	--	**X**	**X**	**X***

[23] Only needed if *de novo* S-ICD

Procedure/ Assessment	Enrollment	EMPOWER PG Implant	S-ICD Implant	mCRM Coordinated System		Follow-up In-Office Visits				Additional Visit
				System Testing	Pre-Discharge	1 Month	3 Month (treadmill only)	6 Month	Semi Annual	
S-ICD Evaluation	--	--	--	**X**	**X**	**X**	--	**X**	**X**	**X***
Holter Monitor data recording (~ 50 subjects)	--	--	--	--	--	**X***	--	--	--	--
Rate Response testing (~ 50 subjects)	--	--	--	--	--	--	**X***	--	--	--
Adverse events assessment	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X***

Legend: X = Required; **X*** = Required, if applicable; **** = See further information on Communication Threshold Test/ Communication Test in **Table 10-6**; **O** = Optional; **--** = Not required/ Not applicable; **d** = days; **yr** = years; **add'l** = additional

10.2 Enrollment Visit

10.2.1 Informed Consent

Subjects who meet all of the inclusion criteria and none of the exclusion criteria and agree to participate in the MODULAR ATP Clinical Study must give written informed consent approved by the regional regulatory body and the study site's IRB, EC, or REB prior to study participation and use of any investigational device testing/ data collection. The Investigator is responsible for ensuring that informed consent is obtained prior to any study-required procedure and/or testing, or data collection.

A subject is considered enrolled in the MODULAR ATP Clinical Study at the time the subject signs and dates the ICF.

10.2.2 Enrollment Data

All enrolled subjects must have a physical assessment for the study that includes height, weight, and vital signs. Also, women of child-bearing potential must have an assessment of pregnancy where the method of assessment is the investigator's discretion. Other baseline data to be included at enrollment for all subjects includes:

- Demographics
- Medical History
- Arrhythmia History
- Cardiac Disease History, and
- Cardiovascular Medications

For enrolled subjects who are not already implanted with an S-ICD System, an S-ICD Screening ECG must be obtained. The screening assessment may be performed with either method described in the S-ICD User's Manual, (i.e., Patient Screening Tool or S-ICD Automated Screening Tool (AST)). The method and results of the S-ICD Screening ECG will be collected. As stated in the S-ICD User's Manual, "Special circumstances may present in which the physician elects to proceed with the implantation of the S-ICD System despite failing the screening process. In this case, careful attention should be

applied to the device setup process of the S-ICD System as the risk of poor sensing and/or inappropriate shock is increased. Rationale for proceeding with S-ICD implantation in the event of a failed screening will be collected.

A subject deemed unsuitable for an S-ICD according to the discretion of the investigator, will be classified as an "Intent" subject and withdrawn from the study (refer to **Section 9.2**). The screening assessment pertains only to S-ICD sensing of intrinsic rhythms and cannot predict whether the S-ICD will be able to appropriately sense paced rhythms. The Paced Morphology Sensing Test (PMST) described in **Section 10.3.4.6** is used to assess appropriate S-ICD sensing of EMPOWER PG pacing and can only be performed after both the EMPOWER PG and S-ICD System have been implanted.

For enrolled subjects who are already implanted with an S-ICD System, including those subjects getting an upgraded S-ICD/ changeout, an S-ICD Screening ECG is not required, and may proceed with the study. Baseline data will be collected from these subjects as included in **Table 10-2**.

10.2.3 Enrollment Visit Source Documentation Requirements

Enrollment data and source documentation requirements are listed in **Table 10-2**.

Table 10-2: Enrollment Data and Source Documentation

Data Collection	Retention of Original Source Documentation
Informed consent documentation	Study site
Assessment of pregnancy for women of childbearing potential (method of assessment upon investigator's discretion)	Study site
Results of S-ICD Screening: • Report and ECGs (appropriately annotated) when using the Patient Screening tool • AST Report and associated ECGs (this requirement is only for subjects not previously implanted with an S-ICD System)	Study site
Baseline data: • Demographics • Physical Assessment • Medical History • Arrhythmia History • Cardiac Disease History • Cardiovascular Medications	Study site

10.3 Implant

Subjects who do not already have a compatible S-ICD PG, Model A209 or A219, will undergo two implant procedures: one for the EMPOWER PG and one for the S-ICD System.

For those subjects, it is recommended to implant the EMPOWER PG first and the S-ICD System second. The implant procedures may, but are not required, to occur on the same day; however, it is strongly recommended that both implant procedures be complete within 30 days of enrollment.

Required data collection is outlined separately for each implantable device system in **Section 10.3.1** and **Section 10.3.2**. Additionally, there are data requirements associated with the complete mCRM Coordinated System, which are outlined in **Section 10.3.4**.

10.3.1 Implant of the EMPOWER PG

The EMPOWER PG should be implanted in accordance with the implant procedure described in the EMPOWER MPS Physician's Technical Manual (PTM) labeling. For a subject with an existing S-ICD System, an S-ICD Programmer must be available during the procedure. There are no protocol requirements for S-ICD programming during the EMPOWER PG implant. Ultimately, the two devices will be tested together as a coordinated system, as described in **Section 10.3.2**.

For a subject without an existing S-ICD System, there are special considerations for the implantation of an EMPOWER PG and S-ICD during a single procedure. This includes the appropriate preparation and pre-placement of external defibrillation patches, EMPOWER PG conducted communication patches, and surface ECG patches. Investigators should adhere to the implant technique described in the mCRM Modular Therapy System PTM labeling.

The hospital's standard implantation practices should be followed (e.g., maintenance of sterile technique, administration of anesthesia, external defibrillation, etc.), and in accordance with the EMPOWER MPS PTM for the implantation of the EMPOWER PG. The implant must be performed by an investigator who has completed the BSC standardized EMPOWER Training Program that covers the procedure to implant and the procedure to retrieve the EMPOWER PG.

10.3.1.1 Procedure Medications

There are no protocol requirements regarding procedure-related medications, however, data will be collected for management of anesthesia/sedatives, anticoagulants, antiplatelets, and antibiotics.

10.3.1.2 Product Information

Product identification information (e.g., model, serial, or lot number, as applicable) will be recorded, at minimum, for the following EMPOWER system devices:

- EMPOWER MPS, consisting of a pacemaker and delivery catheter system
- EMPOWER Retrieval System, including retrieval catheter and snares (if used)
- EMPOWER Introducer Sheath

Note: Another compatible introducer sheath may be used that is not part of the EMPOWER System accessories. Refer to **Table 26-1** and the EMPOWER Modular Pacing System Physician's Technical Manual and Label Supplement, as well as the EMPOWER Retrieval System Physician's Technical Manual and Label Supplement for more information.

- Sterile Tray Cable, Model 6157
- Conducted Telemetry Cable, Model 6396

10.3.1.3 EMPOWER PG Implant Procedure Duration

Total procedure time of the EMPOWER PG implant will be derived from the following time points.

- time of first venous access in preparation for the introducer sheath
- time of the introducer sheath insertion
- time of EMPOWER delivery catheter insertion
- time of EMPOWER delivery catheter removal
- time of introducer sheath removal
- time of introducer sheath site closure

- total fluoroscopy time

10.3.1.4 Fluoroscopy Imaging

Fluoroscopy or cine images are required to be collected to document the final position of the EMPOWER PG once it is released from the tether and the delivery catheter has been retracted. A minimum of two orthogonal fluoroscopy/cine views approximately 90° apart are strongly recommended:

- LAO 30°/45° and
- RAO 30°/45°

Note: It is also recommended to review the angle of the EMPOWER PG with respect to the sternum from LAO/RAO views, or from a separate fluoro/cine in AP view (to ensure the LCP is not implanted in a parallel orientation relative to the sternum)

Save the images in an appropriate electronic format. These recorded images are kept at the study site and provided to BSC upon request.

10.3.1.5 Device Position

The position of the EMPOWER PG within the right ventricular chamber is required to be recorded. Investigators should follow recommendations provided in the EMPOWER MPS PTM regarding positioning of the EMPOWER PG.

10.3.1.6 Implant Success Criteria

There are no protocol requirements for the final position of the EMPOWER PG. Investigators should follow all labeling recommendations regarding the final implanted location within the right ventricle.

Sensing, capture thresholds and impedance measurements should be considered in the acceptance of a final position, but any measurements made prior to full deployment are not collected as study data. **Table 10-3** includes recommended measurements for optimal position of the EMPOWER PG. If the device stability and/or the electrical performance are inadequate, reposition the pulse generator as described in the EMPOWER MPS PTM. It is recommended to limit the number of times the active fixation talons are engaged to 5 attempts. Note that the wound closure technique for the EMPOWER PG implant will be collected.

Table 10-3: Recommended Measures for Optimal EMPOWER PG Position

Programming Parameter	Recommended Range of Value
Pacing Capture Threshold	≤ 1.0 V @ 0.4ms
Pacing Impedance	≥ 400 Ω to ≤ 1500 Ω
R-Wave Amplitude	≥ 5.0 mV

10.3.1.7 EMPOWER PG Evaluation

Once the EMPOWER PG is released from the tether, perform the final implant device evaluation, including sensing amplitude, PCT and pacing impedance measurements must be recorded.

It is required that the PCT measurement be collected using the *Temp Brady* programming screen in the following fashion:

- Confirm connection of/ connect the Surface ECG Cable, Model 3153 or equivalent to the subject and the EMPOWER programmer
- Assure that the surface electrogram is displayed on the programmer
- The PCT test(s) shall be conducted at 0.4 ms pulse width
- The starting voltage is discretionary and may be predetermined before documenting the PCT
    - **Note:** it is strongly recommended that the starting voltage to be at least 2 programmable voltage steps above the highest pre-determined loss of capture
- Start the real-time recording on the programmer as the means of documenting the PCT
- Initiate temporary pacing at the desired voltage that consistently captures then stop temporary pacing and step down the voltage by one programmable value (0.1 V or 0.5 V, as appropriate) and restart pacing. Continue in this manner until loss of capture is noted
- Stop the real-time recording
- The threshold is defined as one voltage level above the level where a single Loss of Capture (LOC) is noted.

It is required to retain the "Real-time Log Report" from the programmer, documenting at a minimum the LOC portion of the threshold testing (i.e., the lowest voltage setting demonstrating capture and the highest voltage that fails to capture). This documentation will be retained at the study site.

If more than one set of electrical measurements are recorded, the final set must be used for the study.

Note: Additional testing is required once the S-ICD System is implanted and both devices can be tested as a system, as described in **Section 10.3.4**.

10.3.1.8 EMPOWER PG Programming

EMPOWER PG programming is left to physician discretion until mCRM Coordinated System testing is completed, as described in **Section 10.3.4**.

10.3.1.9 EMPOWER PG Implant Data and Source Documentation

EMPOWER PG implant data and source documentation requirements are summarized in **Table 10-4**.

Table 10-4: EMPOWER MPS Implant Source Documentation

Data Collection	Retention of Original Source Documentation
Implant details: - Procedural medications (e.g., anesthesia, anticoagulants, antiplatelets, antibiotics) - EMPOWER implant procedure duration (all times listed in **Section 10.3.1.3**) - Fluoro or cine images of EMPOWER PG final position	Study site
Product information: - EMPOWER MPS details (model/serial, etc.) - Guidewire used to introduce introducer sheath (model/ lot, etc)	Study site
EMPOWER PG Combined Follow-up Report	Study site
EMPOWER PG Real-time Log Report (to document loss of capture)	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.3.1.10 Unsuccessful EMPOWER PG Implant

Subjects who are not successfully implanted with the EMPOWER PG (i.e., classified as "Attempt" subjects, as defined in **Section 9.2**) are to be withdrawn from the study after a minimum of 30 days from the implant procedure, including a required follow up either by phone or an in-clinic visit as included in **Section 9.2**. Attempted EMPOWER PG devices used in the implant procedure, but not implanted, must be reported on the appropriate *Device Tracking* Form in the database and returned to BSC.

Subjects who are not implanted with the EMPOWER PG, but who are implanted with an S-ICD System as part of the MODULAR ATP Clinical Study, are classified as "Partial Implant" subjects. Refer to **Section 9.2** for more information and follow-up requirements.

10.3.2 Implant of the S-ICD

This section pertains only to subjects who are receiving a new S-ICD System implant (*de novo* or changeout from TV-ICD or S-ICD). Note that product information data will be collected on those S-ICD systems that were implanted previously and intended to remain implanted.

Implantation of the S-ICD System should be performed using the standard-of-care methods established by the study site. The EMBLEM S-ICD System User's Manual

provides detailed instructions regarding the implantation and use of the S-ICD System, including the determination of the appropriate sensing vector.

For a subject with an existing EMPOWER PG implanted, a Model 3300 Programmer must be available during the procedure, with **Programmer Software Model 3870, as well as Conducted Telemetry Cables, Model 6396.** Affix conducted telemetry patches to the subject and connect the conducted telemetry cable to the EMPOWER programmer.

There are no protocol requirements for EMPOWER PG programming during the S-ICD System implant. Ultimately, the two devices will be tested together as a coordinated system, as described in **Section 10.3.4**.

For a subject without an existing EMPOWER PG implanted, there are special considerations for the implantation of an S-ICD System and EMPOWER PG during a single procedure. This includes the appropriate preparation and pre-placement of external defibrillation patches and EMPOWER PG communication patches. Investigators should adhere to the implant technique described in the mCRM (Modular Cardiac Rhythm Management) Therapy System PTM.

10.3.2.1 S-ICD Implant Procedure

Implantation of the S-ICD System should be performed using the standard-of-care methods established by the study site, in conjunction with the S-ICD System User's Manual. The S-ICD System User's Manual provides detailed instructions regarding the implantation and use of the S-ICD System.

10.3.2.2 Procedure Medications

There are no protocol requirements regarding procedure-related medications; however, data will be collected for management of anesthesia/ sedatives, anticoagulants, antiplatelets, and antibiotics.

10.3.2.3 Product Information

Product identification information (e.g., model and serial number, or model and lot number) will be recorded, at minimum, for the following S-ICD system devices:

- EMBLEM S-ICD PG
- S-ICD Electrode
- S-ICD Electrode Insertion Tool (EIT)
- S-ICD Electrode Delivery Tool (EDS)

10.3.2.4 S-ICD Implant Procedure Duration

Total procedure time must be documented, specifically first incision to last incision closure for the S-ICD System implant.

10.3.2.5 S-ICD Programming

S-ICD programming is left to physician discretion until mCRM Coordinated System testing is completed, as described in **Section 10.3.4**.

Note: Until the Paced Morphology Sensing Test (PMST) has been completed (and passed), the EMPOWER LRL should be programmed to <1/3 of the lowest S-ICD detection limit per the mCRM PTM. Refer to **Section 10.3.4.6**.

10.3.2.6 S-ICD Implant Data and Source Documentation

S-ICD implant data and source documentation requirements are summarized in **Table 10-5.**

Table 10-5: S-ICD Implant Source Documentation

Data Collection	Retention of Original Source Documentation
Implant details: - Procedural medications (e.g., anesthesia, anticoagulants, antiplatelets, antibiotics) - S-ICD implant procedure duration	Study site
Product Information: - S-ICD and electrode details (model/serial, etc.) - EIT or EDS details (model/ lot)	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.3.2.7 Unsuccessful S-ICD Implant

In the event of an unsuccessful S-ICD System implant, those subjects who are not already implanted with the EMPOWER PG (i.e., classified as "Attempt" subjects, refer to **Section 9.2**), are to be withdrawn from the study after a minimum of 30 days from the attempted implant procedure including the required follow up either by phone or an in-clinic visit as included in **Section 9.2**. Pulse Generators and electrodes used in the S-ICD System implant procedure, but not implanted, must be reported in the database and should be returned to BSC.

Those subjects already implanted with an EMPOWER PG are classified as "Partial Implant" subjects. Refer to **Section 9.2** for more information and follow-up requirements.

10.3.3 S-ICD Firmware Update

Firmware on the S-ICD needs to be updated with mCRM clinical firmware to enable communication with the EMPOWER PG. This conversion takes about 4-8 minutes to complete. If telemetry is interrupted, the update ceases and the S-ICD reverts to the existing firmware.

[redacted]

[redacted]

10.3.4 mCRM Coordinated System Imaging and Testing

mCRM Coordinated System testing occurs once both the S-ICD System and EMPOWER PG are implanted, the S-ICD clinical firmware update has been completed, and mCRM features are activated.

Note that study-required follow ups will be determined based on the date that the mCRM Coordinated System is implanted (successful implant of both the S-ICD System, with clinical firmware, and EMPOWER PG). This date is referred to as "Time 0".

10.3.4.1 Communication Evaluation in the MODULAR ATP Clinical Study

Communication is evaluated by one of two methods:

The first method is a *Communication Threshold Test*. This method determines the minimum S-ICD PG Telemetry Setting value that achieves two successful communication tests, regardless of sequence. The Communication Threshold Test is required at Implant, Pre-Discharge, and the 1-Month Follow-up for all subjects in the study with an mCRM Coordinated System implanted. Further details are included in each follow up.

The second method of communication testing is a *Communication Test,* which tests communication only at the initial programmed S-ICD PG Telemetry Setting and is recorded as a pass or fail at that single Telemetry Setting. A Communication Test is required at the 6-Month, Semi-Annual (Refer to **Sections 10.7** and **10.8**) and Additional Visits (if applicable, refer to **Section 10.9**). Note that if the Communication Test ends in unsuccessful communication, a Communication Threshold Test is required.

Refer to **Section 10.3.4.2** for information on setting up the EMPOWER PG and S-ICD for Communication testing.

Note: During the Communication Test, the S-ICD will request the EMPOWER PG to pace for up to 10 beats slightly faster than the intrinsic rhythm. The subject should be judged medically able to tolerate this pacing before testing is conducted.

Note: If intrinsic rhythm is not present, ATP pacing pulses in response to a communication request will not be delivered because a sensed beat is required. If the

S-ICD S-ECG Report indicates that a single paced beat follows the ATP request signal (denoted by an "A" marker; [redacted]), this may have been the case. If this occurs, the Communication Test may be repeated using the same parameters, and the results from the repeated test can be considered the official results.

Requirements for communication testing in the study are included in **Table 10-6,** with more detail in each individual timepoint section. Medical discretion should be used to determine if testing beyond the stated requirement is warranted.

Table 10-6: Communication Testing in the MODULAR ATP Clinical Study

Test/ Visit Timepoint	(Coordinated System) Implant	Pre-Discharge	1-Month	6-Month	Semi-Annual	Additional Visit
Communication Threshold	**X**	**X** (Upright Posture Only)	**X** 4 postures as described in **Section 10.5.3.1**	*	*	*
Communication Test	--	--	--	**X** 4 postures as described in **Section 10.7.3.1**	**X** (One Posture Only)	**X** (One Posture Only, if applicable)
X= Required; **--** = Not required, *Required in the event of a *Communication Test* failure; see applicable visit section						

10.3.4.2 EMPOWER and S-ICD Setup for Communication Testing

Both the EMPOWER PG and S-ICD PG need to be set up for communication testing. Refer to the mCRM PTM for full instructions.

10.3.4.2.1 EMPOWER Communication Testing Setup

- Program "mCRM Communication" On
- Configure the backup pacing mode for the Communication Test (or Communication Threshold)

[redacted]

- Confirm the EMPOWER PG is ready for Communciation testing by verifying with the mCRM Communication Test pop-up screen. This screen should remain on the EMPOWER programmer during S-ICD programming.

10.3.4.2.2 S-ICD Communication testing Setup:

- Program “mCRM Communication” On
- Assure the subject’s specific EMPOWER PG information is entered in the mCRM Configuration screens on the S-ICD programmer
- Conduct the Communication Test (or Communication Threshold Test) based on **Section 10.3.4.4** and **Section 10.3.4.5**, respectively

10.3.4.3 Communication Muscle Stimulation Testing

Test for muscle stimulation by palpating around the location of the electrode shocking coil while performing a communication test at the maximum communication Telemetry Setting of 7. If stimulation is noted at 7, step down incrementally until loss of stimulation is noted and record the value where muscle stimulation is no longer perceived.

Note: mCRM Communication for the EMPOWER PG does not need to be programmed to On for this testing to occur.

10.3.4.4 Communication Test

A Communication Test is required at the 6 Month Visit, all Semi-Annual Visits, as well as at Additional Visits (as applicable). See **Section 10.7**, **Section 10.8**, and **Section 10.9** respectively, for specifics related to each visit.

Refer to the mCRM PTM, as well as **Section 10.3.4.2** to prepare for a Communication Test. Source documentation for the Communication Test is included in **Section 10.7**, **Section 10.8, and Section 10.9**.

- Conduct the Communication Test.
- Determine success of the communication test and record in EDC

[redacted]

10.3.4.5 Communication Threshold Test

Assure the EMPOWER PG and S-ICD PG are set up for communication testing as described in **Section 10.3.4.2.**

There are no requirements for the Telemetry Setting value used to start this test. Choose a Telemetry Setting value to start the Communication Threshold Test. If successful, then step down incrementally by 0.5, and repeat the test. Continue stepping down by 0.5 and

repeating the test until an unsuccessful test occurs. After having a single unsuccessful test, step up by 0.5 and repeat the test as needed until success is achieved. The communication threshold is recorded as the minimum value that achieves two successful tests, regardless of sequence.

It is required to retain the "Communication Test S-ECGs" documenting the maximum Telemetry Setting value demonstrating loss of communication, as well as the minimum Telemetry Setting value that achieves two successful tests. This documentation will be retained at the study site.

Program the communication Telemetry Setting value 1 unit above the highest communication threshold value among all tested postures as applicable, with a minimum Telemetry Setting of 4. For example, if the threshold is 5, program the output to 6.

[redacted]

Note: If intrinsic rhythm is not present, pacing pulses in response to a communication request will not be delivered because a sensed beat is required.

10.3.4.6 Paced Morphology Sensing Test (PMST)

PMST is important to complete to determine appropriate S-ICD settings to avoid oversensing for subjects receiving pacing from the EMPOWER PG. A sensing vector that appropriately senses both the paced and intrinsic rhythms avoids S-ICD oversensing of the evoked response and the possibility of delivering inappropriate shock therapy [redacted].

- Program the S-ICD to Therapy Off.

Set the subject's EMPOWER PG:

- mode to VVI,
- pacing output to ensure capture, and
- LRL to 10-20 ppm above their intrinsic rate (with a maximum of 120 ppm) to promote pacing.

Use the 'Capture All Sense Vectors' feature of the S-ICD programmer to collect and retain S-ECG snapshots in the supine posture for each S-ICD sensing vector.

Note: a deviation shall not be assessed for subjects who cannot tolerate this testing due to high-rate pacing.

Document any oversensing, e.g., double counting, on the associated Form in EDC, and collect the "Captured S-ECG Reports" generated from the Manual Setup feature on the S-ICD programmer.

If there is an S-ICD vector that demonstrates appropriate sensing for both intrinsic and paced rhythms, this vector should be used, which will minimize the risk of oversensing and inappropriate shocks. If there is not an S-ICD vector that demonstrates appropriate sensing for both intrinsic and paced rhythms, a vector that demonstrates appropriate

sensing of intrinsic rhythms should be used, and the EMPOWER PG's LRL should be programmed to <1/3 of the lowest programmed S-ICD tachy detection zone.

[redacted]

When the PMST is complete, program the S-ICD to Therapy On.

10.3.4.7 S-ICD Conversion and Sensing Interaction Testing

S-ICD Conversion and Sensing Interaction Testing is important to complete since the detection of LCP pulses by the S-ICD may alter S-ICD sensitivity, resulting in failure of the S-ICD to sense a tachyarrhythmia and failure to deliver therapy in the presence of pacing by the LCP.

Conduct an S-ICD Conversion and Sensing Interaction Test to determine the appropriate S-ICD tachyarrhythmia sensing while the LCP is pacing [redacted]

Note: It is recommended to conduct the S-ICD Conversion and Sensing Interaction Test at implant. However, if the subject is not able to tolerate the test at implant, this testing may also be conducted prior to hospital discharge.

During S-ICD Conversion and Sensing Interaction Testing, it is required that S-ICD therapy be programmed on and the EMPOWER PG be programmed to pace in VOO mode during the induction. It is recommended that the EMPOWER PG be programmed to the intended programmed LRL and 5.0 V @ 1.0 ms pulse width. More information is available in the mCRM Modular Therapy System PTM labeling. Following induction of a ventricular arrhythmia via the S-ICD, at least one S-ICD shock should be delivered at 65J. In the event there is a failure of the S-ICD to detect or convert the arrhythmia, professional medical judgment should be used to determine the appropriate course of action.

Induction S-ECG Reports or external ECGs strips are to be retained at the study site, as well as uploaded to the EDC System for each induction that results in a shock by the S-ICD or external defibrillator. Induced episodes that spontaneously convert prior to an S-ICD shock do not require documentation.

Shock polarity, shock energy, shock impedance, and conversion outcome must be included on the appropriate Technical Source Form or annotated directly on the "Induction S-ECG Report".

Note that Conversion Testing may also be performed at other times during the study at the discretion of the investigator (e.g., following system revision, S-ICD PG changeout). It is not required to repeat S-ICD Conversion and Sensing Interaction Tests after the Pre-Discharge Visit.

10.3.4.8 Fluoro Imaging of Final Placement for the mCRM Coordinated System

Once the mCRM Coordinated System is fully implanted, final implant position must be documented with a minimum of one recorded fluoroscopy cine/ image in A/P view, with

a minimum of the S-ICD electrode and EMPOWER PG in view. Additional images may be desirable to document system position and are allowed, but are not required.

10.3.4.9 mCRM Coordinated System Chest X-Ray

It is required to document final mCRM Coordinated System position via chest X-ray in Posterior/ Anterior and Lateral views. Please note that the S-ICD System and EMPOWER PG must be visible in the image. This X-ray may be collected at Implant or Pre-Discharge.

10.3.5 S-ICD Evaluation

10.3.5.1 S-ICD Summary Report

It is required to retain the "S-ICD Summary Report" from the programmer, documenting initial and final parameter settings, episode counters, etc.

10.3.5.2 Spontaneous Episodes

All available "Full S-ECG Report(s)" and "Full S-ECG Report(s) Untreated" (AF diagnostic episodes labeled "Full S-ECG Report AF" are not required) not previously reported must be obtained and uploaded to BSC via the EDC System. Documentation of any symptomatic episodes associated with a spontaneous event will be collected, specifically any syncope.

Note: any spontaneous stored episodes that occurred prior to enrollment should not be reported. Justification shall be provided for any missing episodes.

10.3.6 S-ICD System Programming Considerations

There are no device programming requirements for the S-ICD or EMPOWER PG at implant. Final programming from both devices will be documented in the database.

10.3.7 mCRM Coordinated System Data and Source Documentation Requirements

mCRM Coordinated System data and source documentation requirements are listed in **Table 10-7**.

Table 10-7: mCRM Coordinated System Implant Source Document Requirements

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - Interim EMPOWER Combined Follow-up Report for S-ICD Conversion and Sensing Interaction Testing - EMPOWER Real-Time Log Report (to document LOC) - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - S-ICD Summary Report from the end of the visit - Captured S-ECG Reports from 'Capture All Sense Vectors' on S-ICD programmer for Paced Morphology Sensing Test - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable - S-ICD Induction S-ECG Report for S-ICD Conversion and Sensing Interaction Testing, if performed - Shock polarity, shock energy, shock impedance, and conversion outcome documented on the Technical Source Form or annotated directly on the "Induction S-ECG Report"	Study site; upload copy to BSC via study EDC System
Communication Test S-ECG Report(s)	Study site
At least one fluoroscopy/ cine image in A/P view to document mCRM Coordinated System placement	Study site, available upon request
Chest x-ray (P/A and Lateral), to document mCRM Coordinated System placement, if performed at this visit	Study site, available upon request
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.4 Pre-Discharge Visit

The Pre-Discharge Visit is to occur after the mCRM Coordinated System is fully implanted and prior to the subject's discharge from the hospital. **Note**: It is strongly recommended the subject be able to sit upright for testing at this visit, which may include back support.

10.4.1 EMPOWER PG Evaluation

PCT, Pacing Impedance, and R-wave Amplitude are required to be measured. Collect PCT measurements according to **Section 10.3.1.7**.

It is required to retain the "Real-Time Log Report" from the programmer, documenting at a minimum the LOC portion of the threshold testing (i.e., the lowest voltage setting demonstrating capture and the highest voltage setting that fails to capture). This documentation will be retained at the study site.

If more than one set of electrical measurements are recorded, the final set must be used for the study.

It is required to document the following:

- "%V paced" from the "Combined Follow up Report",
- "Time remaining to EOS" from the "Combined Follow up Report",
- "Charge remaining to EOS" documented on the TSF.

10.4.2 S-ICD Evaluation

10.4.2.1 S-ICD Sensing Configuration Setup

Conduct sensing configureation setup as described in the EMBLEM S-ICD/ EMBLEM MRI S-ICD User's Manual. The method of selecting the sensing vector (Automatic Setup or manual), as well as the result will be collected on the Pre-Discharge TSF.

10.4.2.2 S-ICD Summary Report

It is required to retain the "S-ICD Summary Report" from the programmer, documenting initial and final parameter settings, episode counters, battery status, etc.

10.4.2.3 Spontaneous Episodes

All available "Full S-ECG Report(s)" and "Full S-ECG Report(s) Untreated" (AF diagnostic episodes labeled "Full S-ECG Report AF" are not required) not previously reported must be obtained and uploaded to BSC via the EDC System. Documentation of any symptomatic episodes associated with a spontaneous event will be collected, specifically any syncope.

Note: any spontaneous stored episodes that occurred prior to enrollment should not be reported. Justification shall be provided for any missing episodes.

10.4.3 mCRM Coordinated System Testing

10.4.3.1 Communication Threshold Test

Communication Threshold Testing is required at Pre-Discharge with the subject in an upright position.

Refer to the mCRM PTM, as well as **Section 10.3.4.2** to prepare for a Communication Threshold Test. Follow Communication Threshold Test methodology in **Section 10.3.4.5**.

Program the communication telemetry output 1 unit above the highest communication threshold value from the tested posture, with a minimum *Telemetry Setting* of *4*. For example, if the threshold is 5, program the output to 6.

[redacted]

10.4.3.2 Paced Morphology Sensing Test (PMST)

Perform a PMST as described in **Section 10.3.4.6**, [redacted].

10.4.3.3 S-ICD Conversion and Sensing Interaction Testing

If not performed at Implant, S-ICD Conversion and Sensing Interaction Testing is required to be performed at Pre-Discharge. Refer to **Section 10.3.4.7**.

10.4.3.4 mCRM Coordinated System Chest X-Ray

It is required to document final mCRM Coordinated System position via chest X-ray in Posterior/ Anterior and Lateral views. Please note that the S-ICD System and EMPOWER PG must be visible in the image. This X-ray may be collected at Implant or Pre-Discharge.

10.4.4 mCRM Coordinated System Programming

Programming parameters for the EMPOWER PG and S-ICD are included in the sections below.

10.4.4.1 EMPOWER PG Programming

Refer to **Table 10-8** for recommended programming of the EMPOWER PG. Pacing pulses must be delivered at an adequate safety margin above the PCT. A minimum 2X voltage safety margin is recommended based on the PCT. The investigator should refer to the Projected Service Life information for the EMPOWER PG in the EMPOWER MPS PTM and determine the optimal Pacing Amplitude to meet the needs of the subject while maintaining an adequate safety margin.

Note: Rate responsive pacing modes should not be programmed in the EMPOWER PG unless appropriate sensing of both paced and intrinsic beats is observed; refer to **Section 10.4.3.3**.

Print out a copy of the final "Combined Follow-up Report" and a copy of the "S-ICD Summary Report". Once all study activities are completed at the end of the visit, reset the EMPOWER PG brady counters/ histograms and tachy counters.

Table 10-8: EMPOWER PG Programming

EMPOWER PG Programming (all Recommended programming, except where noted with *)	
Parameter	**Programming**
Safety Margin	2X PCT voltage
Pacing Mode	VVI*
Lower Rate Limit	LRL should be programmed <1/3 of the lower bound of the conditional shock zone i.e., if Conditional Shock Zone = 180, Program LRL <60
mCRM Communication	On
ATP Type	Burst or Scan
ATP Coupling Interval	88%[24,25] (Primary Prevention; no specific recommendation for Secondary Prevention)
Pulses per Burst	Per physician discretion, programmable at 5, 6, 8, or 10 (10 is nominal)
*** The EMPOWER PG should not be programmed to the VVIR brady mode unless appropriate S-ICD sensing of both paced and intrinsic beats is observed; refer to Section 10.4.3.3**	

10.4.4.2 S-ICD Programming

Therapy zone and ATP settings are recommended to be programmed per **Table 10-9** for primary prevention subjects and **Table 10-10** for secondary prevention subjects. All other programming parameters (e.g., sensing vector, gain) are left to the discretion of the investigator. Rationale for not following the recommended programming parameters will be collected.

Table 10-9: S-ICD Programming for Primary Prevention Subjects

S-ICD Programming for Primary Prevention Subjects (all Recommended programming, except where noted)		
Therapy Zone	**Rate**	**ATP Parameters**
Conditional Shock Zone	180-230 bpm[26]	At least 1 ATP request **Required**; up to 3 acceptable (ATP scheme is per physician discretion)
Shock Zone	>230 bpm	Quick Convert ATP ON

[24] Stiles, Martin K., et. al 2019 HRS/EHRA/APHRS/LAHRS focused update to 2015 expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Heart Rhythm* 2019;17:220–228)

[25] Wilkoff BL, Fauchier L, Stiles MK, et al. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Europace*. 2016 Feb;18(2):159-83

[26] Lower bound of the conditional shock zone should be >3x the Lower Rate Limit (LRL) of EMPOWER

Table 10-10: S-ICD Programming for Secondary Prevention Subjects

S-ICD Programming for Secondary Prevention Subjects (all Recommended programming, except where noted)		
Therapy Zone	**Rate**	**ATP**
Conditional Shock Zone	Physician Discretion[27]	At least 1 ATP request **Required**; up to 3 acceptable (ATP scheme is per physician discretion)
Shock Zone	Physician Discretion	Quick Convert ATP ON

Note: As stated in the mCRM PTM, post-shock pacing interaction with LCP pacing could generate a ventricular arrhythmia. Do not program post-shock pacing On in the S-ICD if the LCP is programmed to a pacing mode.

10.4.5 Pre-Discharge Source Documentation Requirements

Pre-discharge data and source documentation requirements are listed in **Table 10-11**.

[27] Lower bound of the conditional shock zone should be >3x the Lower Rate Limit (LRL) of EMPOWER

Table 10-11: Pre-Discharge Source Document Requirements

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - Interim EMPOWER Combined Follow-up Report for S-ICD Conversion and Sensing Interaction Testing, if performed - EMPOWER Real-Time Log Report (to document loss of capture) - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - S-ICD Summary Report from the end of the visit - Captured S-ECG Reports from 'Capture All Sense Vectors' on S-ICD programmer for Paced Morphology Sensing Test - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable - S-ICD Induction S-ECG Report for S-ICD Conversion and Sensing Interaction Testing, if performed - Shock polarity, shock energy, shock impedance, and conversion outcome documented on the Technical Source Form or annotated directly on the "Induction S-ECG Report"	Study site; upload copy to BSC via study EDC System
Communication (Threshold) Test S-ECG Report(s)	Study site
Chest x-ray (P/A and Lateral), to document mCRM Coordinated System placement, if performed at this visit	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.5 1 Month Visit: (10 days – 42 days post-Coordinated System Implant)

The 1 Month Visit must be performed as a clinic visit between 10 and 42 days after the mCRM Coordinated System is implanted.

10.5.1 EMPOWER PG Evaluation

PCT, Pacing Impedance, and R-wave Amplitude are required to be measured. Collect PCT measurements according to **Section 10.3.1.7**.

It is required to retain the "Real-Time Log Report" from the EMPOWER programmer, documenting at a minimum the LOC portion of the threshold testing (i.e., the lowest voltage setting demonstrating capture and the highest voltage setting that fails to capture). This documentation will be retained at the study site.

If more than one set of electrical measurements are recorded, the final set must be used for the study.

It is required to document the following:

- "%V paced" from the "Combined Follow up Report",
- "Time remaining to EOS" from the "Combined Follow up Report",
- "Charge remaining to EOS" documented on the TSF.

10.5.2 S-ICD Evaluation

10.5.2.1 S-ICD Summary Report

It is required to retain the "S-ICD Summary Report" from the programmer, documenting initial and final parameter settings, episode counters, battery status, etc. Note whether MRI Protection Mode was programmed "On" since the Pre-Discharge Visit; if it was, report this in eDC in the Medically Necessary MRI Scan page.

Any changes to the sensing vector will be documented in EDC. The method by which the change was determined will be documented on the visit-specific TSF.

10.5.2.2 Spontaneous episodes

All available "Full S-ECG Report(s)" and "Full S-ECG Report(s) Untreated" (AF diagnostic episodes labeled "Full S-ECG Report AF" are not required) not previously reported must be obtained and uploaded to BSC via the EDC System. Documentation of any symptomatic episodes associated with a spontaneous event will be collected, specifically any syncope.

[redacted]

10.5.3 mCRM Coordinated System Testing

10.5.3.1 Four-Posture Communication Threshold Test

Perform Communication Threshold Testing in each of the 4 postures included in **Figure 10-1**. It is recommended to test postures in the order presented in **Figure 10-1**. Document the order of postures on the appropriate Technical Source Form.

Figure 10-1: Recommended Order of Postures for Four-Posture Communication Threshold Test

10.5.3.2 Communication Threshold Test

Communication Threshold Testing is required at the 1 Month Visit with the subject in each posture noted in **Figure 10-1**.

Refer to the mCRM PTM, as well as **Section 10.3.4.2** to prepare for a Communication Threshold Test. Follow Communication Threshold Test methodology in **Section 10.3.4.5**. All required testing should be completed in the selected posture before changing to another posture.

Program the communication telemetry output 1 unit above the highest communication threshold value among all tested posture(s), with a minimum *Telemetry Setting* of *4*. For example, if the threshold is 5, program the output to 6.

[redacted]

Note: If intrinsic rhythm is not present, pacing pulses in response to a communication request will not be delivered because a sensed beat is required.

Note: Since pacing has the potential to interfere with communication, it is recommended to select Off for the mCRM Communication Test backup pacing setting. However, if the subject is pacemaker dependent, configure the backup pacing mode at the lowest pacing rate needed for the subject, preferably 50 ppm or lower, for the duration of the Communication Test.

10.5.4 mCRM Coordinated System Programming

Recommended programming parameters for the EMPOWER PG and S-ICD are included in **Sections 10.4.4.1** and **10.4.4.2**, respectively.

Print out a copy of the final "Combined Follow-up Report" and a copy of the "S-ICD Summary Report". Once all study activities are completed at the end of the visit, reset the EMPOWER PG brady counters/ histograms and tachy counters.

10.5.5 Holter Substudy

To demonstrate adequate performance of the EMPOWER PG, a subset of subjects enrolled in the MODULAR ATP Clinical Study (approximately the first 50 subjects enrolled in the study, at select sites) will undergo Holter monitoring. This will include up

to 30 minutes of pacing prior to continuing to wear the Holter monitor to provide an ECG recording ranging from 16 to 24 hours. The investigator should enroll subjects sequentially from the start of the clinical study but should use medical discretion in selecting subjects for participation in the Holter monitoring. Therefore, it is not a protocol deviation if the Holter monitoring is not performed on consecutive subjects.

Holter monitoring equipment capable of recording continuously for 24 hours will be provided to select study sites participating in this substudy. Participating subjects will be provided with Holter monitoring equipment and instructions on their use, as well as instruction on returning the Holter monitor. A summary report of the EMPOWER PG performance and Holter data findings (e.g., pause, inappropriate sensing, LOC) will be provided by the core lab to the study site and to BSC within a mutually established timeframe.

10.5.5.1 25-35 Minute Pacing

Subjects in the MODULAR ATP Clinical Study are not expected to need a high level of pacing. Therefore, participating subjects will have a 30±5-minute pacing period prior to finalizing the 1-month follow-up.

After the Holter is applied, and prior to the end of the visit, 30±5 minutes of pacing will be collected. Determine the subject's intrinsic rate, and program LRL to approximately 5-10ppm above the intrinsic rate, with EMPOWER in VVI. Investigator discretion and/or the subject's tolerance of pacing should be considered when choosing the LRL or adjusting it after pacing has started. The subject should be instructed to sit calmly for 30±5 minutes. Document the time of programming the higher LRL, and time of programming the LRL back to the intended programmed value. The investigator has the discretion to stop the pacing early due to subject condition; the rationale for early stopping will be collected.

10.5.5.2 16 to 24 Hour Holter Monitoring

Complete data recording consisting of at least 16 hours of usable data from a minimum of 25 subjects are required, and it is expected that an enrollment of 50 subjects will be sufficient to provide the minimum number of datasets required. Once BSC determines that the requirement of 25 usable datasets is met, Holter substudy sites will be notified that the Holter monitoring is no longer needed for any additional subjects and the Holter monitoring part of the clinical study will be completed.

10.5.6 1 Month Visit Source Documentation Requirements

The 1 Month Visit data and source documentation requirements are listed in **Table 10-12**.

Table 10-12: 1 Month Visit Source Document Requirements

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - EMPOWER Real-Time Log Report (to document loss of capture) - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - S-ICD Summary Report from the end of the visit - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable[28]	Study site; upload copy to BSC via study EDC system
- Communication (Threshold) Test S-ECG Reports - Order of postures tested documented on TSF	Study site
Holter Substudy: - (Clock) Time of programming to LRL +5-10ppm above intrinsic - (Clock) Time of programming to intended LRL - Information regarding the Holter monitor distribution, and return - Information regarding submission to the core lab	Study site
Holter monitoring report and ECG strips	Core lab; a report copy is sent to BSC
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.6 Rate Response Substudy (3 Month Visit (90±15 Days Post-implant))

The 3 Month Visit is only for those in the Rate Response Substudy and must be performed as a clinic visit between 90±15 days after the mCRM Coordinated System is implanted.

A subset of enrolled subjects (up to 59 subjects enrolled earlier in the trial, and preferably sequential enrollments at selected sites) at approximately 15-20 selected study sites with treadmill equipment and facility will complete an assessment of the Rate Response function of the EMPOWER PG. The investigator will review physical capabilities and clinical condition of enrolled subjects, as well as their willingness to perform and complete the Treadmill Walk protocol. This must include an evaluation of any clinical condition that predisposes the subject to higher risk of developing symptoms during the Treadmill Walk. A list of potential risks is described in **Section 18.5**. It is not a deviation if participation is from non-consecutive subjects at the selected Rate Response Substudy site.

Usable datasets from 35 subjects are required to support Secondary Effectiveness Endpoint 2, and it is expected that an enrollment up to 59 subjects will be sufficient to provide the minimum number of datasets required. BSC will notify participating study sites once a sufficient number of datasets are obtained and additional Rate Response testing subjects are no longer needed.

The Rate Response Substudy may consist of some or all of the following:

- Tachometer Functionality Test
- Initial Response Factor Set-up and Selection
- Treadmill Walk
- Hall Walk

Specific information about each of these steps is included in the Rate Response Substudy strategy document (Document 92614291, provided separately).

10.6.1 Paced Morphology Sensing Test (PMST)

If the patient is to be programmed to VVIR after testing, consider performing a PMST as described in **Section 10.3.4.6**[redacted].

10.6.2 Rate Response Substudy Source Documentation Requirements

Refer to **Table 10-13** for a list source documentation for the Rate Response Substudy and retention requirements.

[28] Note that AF diagnostic episodes labelled “Full S-ECG Report AF” are NOT required.

Table 10-13: Rate Response Substudy Source Data

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - EMPOWER Real-Time Log Report from PCT (to document loss of capture) - Interim Combined Follow-up Report(s) as described in Doc# 92614291 to document sequential programming changes - Captured S-ECG Reports from 'Capture All Sense Vectors' on S-ICD programmer for Paced Morphology Sensing Test, if performed - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - Initial Summary Report - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable[29] - Interim Summary Reports as described in Doc 92614291 as needed to document sequential programming changes - Final Summary Report	Study site
Rate Response Testing: - Rate Response testing data recorded on the TSF including but not limited to handlebar usage and timing of blood pressure measurements - Reports from EMPOWER Programmer, as required, which may include Real-time Log, Combined Follow-up, and Sensor Trending saved on USB following the: - Tachometer Functionality Test - Initial Response Factor Set-up - Treadmill Walk - Hall Walk	Study site: - TSF - Copy of USB files BSC: -USB with associated files
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

[29] Note that AF diagnostic episodes labelled "Full S-ECG Report AF" are NOT required.

10.7 6 Month Visit (180 days ± 30 days Post-system Implant)

The 6 Month Visit must be performed as a clinic visit between 180 ± 30 days after the mCRM Coordinated System is implanted.

10.7.1 EMPOWER PG Evaluation

PCT, Pacing Impedance, and R-wave Amplitude are required to be measured. Collect PCT measurements according to **Section 10.3.1.7**.

It is required to retain the "Real-Time Log Report" from the programmer, documenting at a minimum the LOC portion of the threshold testing (i.e., the lowest voltage setting demonstrating capture and the highest voltage setting that fails to capture). This documentation will be retained at the study site.

If more than one set of electrical measurements are recorded, the final set must be used for the study.

It is required to document the following:

- "%V paced" from the "Combined Follow up Report",
- "Time remaining to EOS" from the "Combined Follow up Report",
- "Charge remaining to EOS" documented on the TSF.

10.7.2 S-ICD Evaluation

10.7.2.1 S-ICD Summary Report

It is required to retain the "S-ICD Summary Report" from the programmer, documenting initial and final parameter settings, episode counters, battery status, etc. Note whether MRI Protection Mode was programmed "On" since the previous protocol-required visit; if it was, report this in EDC in the Medically Necessary MRI Scan page.

10.7.2.2 Spontaneous Episodes

All available "Full S-ECG Report(s)" and "Full S-ECG Report(s) Untreated" (AF diagnostic episodes labeled "Full S-ECG Report AF" are not required) not previously reported must be obtained and uploaded to BSC via the EDC System. Documentation of any symptomatic episodes associated with a spontaneous event will be collected, specifically any syncope. Justification shall be provided for any missing episodes.

10.7.3 mCRM Coordinated System Testing

10.7.3.1 Four-Posture Communication Test

Perform communication testing in each of the 4 postures included in **Figure 10-2,** It is recommended to test postures in the order presented in **Figure 10-2**. Document the order of postures on the appropriate Technical Source Form.

Figure 10-2: Recommended Order of Postures for Four-Posture Communication Test

10.7.3.2 Communication Test

A single Communication Test is required to be performed at the initial programmed Telemetry Setting in each of the four postures noted in **Figure 10-2**. In the event that multiple communication tests are performed within a posture, only the first Communication Test S-ECG Report obtained at the initial programmed Telemetry Setting will serve as the source document for the endpoint. All required testing should be completed in the selected posture before changing to another posture.

In the event of a communication failure in one or more of the four postures during the single test, perform a Communication Threshold Test (described in **Section 10.3.4.5**) in the posture(s) of communication failure. Use the highest value to program the Telemetry Setting output 1 unit above threshold among all tested posture(s). For example, if the threshold is 5, program the output to 6.

[redacted]

[redacted]

10.7.4 mCRM Coordinated System Programming

Recommended programming parameters for the EMPOWER PG and S-ICD are included in **Sections 10.4.4.1** and **10.4.4.2**, respectively.

Print out a copy of the final "Combined Follow-up Report" and a copy of the "S-ICD Summary Report". Once all study activities are completed at the end of the visit, reset the EMPOWER PG brady counters/ histograms and tachy counters.

10.7.5 6 Month Visit Source Documentation Requirements

6 Month Visit data and source documentation requirements are listed in **Table 10-14**.

Table 10-14: 6 Month Visit Data Collection Requirements

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - EMPOWER Real-Time Log Report (to document LOC) - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - S-ICD Summary Report from the end of the visit - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable[30]	Study site; upload copy to BSC via study EDC system
- Communication Test S-ECG Reports, including Communication Test (Threshold) S-ECG Reports, if conducted - Order of postures tested documented on TSF	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.8 Semi-Annual Visits

Semi-Annual Visits are required to be conducted as clinic visits for MODULAR ATP subjects, starting at 12 months post mCRM Coordinated System implant and continuing until study closure. Note subjects are required to be followed until the last enrolled subject is followed for at least 24 months post mCRM Coordinated System implant. Timing of the Semi-Annual Visits is based on the date the mCRM Coordinated System was fully implanted:

- 12 Month: 360±45d
- 18 Month: 540±45d
- 24 Month: 720±45d
- 30 Month: 900±45d
- 36 Month: 1080±45d
- Etc, until BSC notification of follow-up completion

[30] Note that AF diagnostic episodes labelled "Full S-ECG Report AF" are NOT required.

10.8.1 EMPOWER PG Evaluation

PCT, Pacing Impedance, and R-wave Amplitude are required to be measured. Collect PCT measurements according to **Section 10.3.1.7**.

It is required to retain the "Real-Time Log Report" from the programmer, documenting at a minimum the LOC portion of the threshold testing (i.e., the lowest voltage setting demonstrating capture and the highest voltage setting that fails to capture). This documentation will be retained at the study site.

If more than one set of electrical measurements are recorded, the final set must be used for the study.

It is required to document the following:

- "%V paced" from the "Combined Follow up Report",
- "Time remaining to EOS" from the "Combined Follow up Report",
- "Charge remaining to EOS" documented on the TSF.

10.8.2 S-ICD Evaluation

10.8.2.1 S-ICD Summary Report

It is required to retain the "S-ICD Summary Report" from the programmer, documenting initial and final parameter settings, episode counters, battery status, etc. Note whether MRI Protection Mode was programmed "On" since the previous protocol-required visit; if it was, report this in eDC in the MRI Scan page.

10.8.2.2 Spontaneous Episodes

All available "Full S-ECG Report(s)" and "Full S-ECG Report(s) Untreated" (AF diagnostic episodes labeled "Full S-ECG Report AF" are not required) not previously reported must be obtained and uploaded to BSC via the EDC System. Documentation of any symptomatic episodes associated with a spontaneous event will be collected, specifically any syncope. Justification shall be provided for any missing episodes.

10.8.3 Communication Test in One Posture

A single Communication Test is required to be performed at the initial programmed telemetry value with the subject in one selected posture. The upright posture shown in **Figure 10-2** is recommended, but the posture to be used is at the physician's discretion. For example, a different posture might be appropriate for subjects in which the highest mCRM communication threshold has been observed for a different posture or for subjects that have experienced ambulatory VT events in another posture. The actual posture tested must be recorded. In the event that multiple communication tests are performed within the selected posture, only the first "Communication Test S-ECG Report" obtained at the initial programmed Telemetry Setting value will serve as the source document for the test. Refer to the mCRM PTM, as well as **Section 10.3.4.2** to prepare for a Communication Test. Follow Communication Test methodology in **Section 10.3.4.4**.

In the event of a communication failure in the selected posture during the single test, perform a Communication Threshold Test in the selected posture; refer to **Section**

10.3.4.5. Use the resulting value from that test to program the Telemetry Setting output 1 unit above threshold. For example, if the threshold is 5, program the output to 6.

10.8.4 mCRM Coordinated System Programming

Therapy zone and ATP settings are to be programmed per **Table 10-9** for primary prevention subjects and **Table 10-10** for secondary prevention subjects. All other programming parameters (e.g., sensing vector, gain) are left to the discretion of the investigator. Rationale for not following the recommended programming parameters will be collected.

Recommended Programming Parameters for the EMPOWER PG and S-ICD are included in **Sections 10.4.4.1** and **10.4.4.2**, respectively.

Print out a copy of the final "Combined Follow-up Report" and a copy of the "S-ICD Summary Report". Once all study activities are completed at the end of the visit, reset the EMPOWER PG brady counters/ histograms and tachy counters.

10.8.5 Semi-Annual Visit Source Documentation Requirements

Semi-Annual Visit data and source documentation requirements are listed in **Table 10-15.**

Table 10-15: Semi-Annual Visit Data Collection Requirements

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - EMPOWER Real-Time Log Report (to document loss of capture) - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - S-ICD Summary Report from the end of the visit - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable[31]	Study site; upload copy to BSC via study EDC system
Communication Test S-ECG Report(s), including Communication Test (Threshold) S-ECG Reports, if conducted	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.9 Additional Visits

Additional Visits must be collected if they are associated with a reportable adverse event,[32] spontaneous episode, or device deficiency. Routinely scheduled office visits for purposes other than these events, do not require Additional Visit forms to be completed.

In the event of an adverse event related to communication of the mCRM Coordinated System, a Communication Test, and possibly a Communication Threshold Test (as described in **Section 10.8.3**) is required. In the event of an adverse event related to the EMPOWER device, an evaluation of that device is required as described in **Section 10.3.1.7**.

10.9.1 EMPOWER PG Evaluation

Device evaluation is optional at these visits. If performed, collect PCT measurements according to **Section 10.3.1.7**, except that a pulse width of 0.4 ms is recommended.

It is required to document the following:

[31] Note that AF diagnostic episodes labelled "Full S-ECG Report AF" are NOT required.

[32] Refer to **Section 25.2** for definition of reportable adverse event

- "%V paced" from the "Combined Follow up Report",
- "Time remaining to EOS" from the "Combined Follow up Report",
- "Charge remaining to EOS" documented on the TSF.

10.9.2 S-ICD Evaluation

10.9.2.1 S-ICD Summary Report

It is required to retain the "S-ICD Summary Report" from the programmer, documenting initial and final parameter settings, episode counters, battery status, etc. Note whether MRI Protection Mode was programmed "On" since the previous protocol-required visit; if it was, report this in eDC in the MRI Scan page.

10.9.2.2 Spontaneous Episodes

All available "Full S-ECG Report(s)" and "Full S-ECG Report(s) Untreated" (AF diagnostic episodes labeled "Full S-ECG Report AF" are not required) not previously reported must be obtained and uploaded to BSC via the EDC System. Documentation of any symptomatic episodes associated with a spontaneous event will be collected, specifically any syncope.

Note: any spontaneous stored episodes that occurred prior to enrollment should not be reported. Justification shall be provided for any missing episodes.

Print out a copy of the final "Combined Follow-up Report" and a copy of the "S-ICD Summary Report". Once all study activities are completed at the end of the visit, reset the EMPOWER PG brady counters/ histograms and tachy counters.

10.9.3 Additional Visit Source Documentation Requirements

Additional Visit data and source documentation requirements are listed in **Table 10-16.**

Table 10-16: Additional Visit Data Collection Requirements

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - EMPOWER Real-Time Log Report (to document loss of capture), if applicable - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - S-ICD Summary Report - FULL S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable[33]	Study site; upload copy to BSC via study EDC system
Communication Test S-ECG Report(s), if applicable, including Communication Test (Threshold) S-ECG Reports, if conducted	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.10 Medically Necessary MRI Scans

During the MODULAR ATP Clinical Study, if a subject requires a medically necessary MRI scan, BSC recommends the subject be directed to have the scan at the study site.

The investigational EMPOWER PG is MR Conditional during the course of the clinical study, as is the mCRM System. Labeled recommendations for device testing included in relevant PTMs will be collected in the MODULAR ATP Clinical Study, as well as any adverse events that may occur. Refer to "mCRM and EMPOWER MRI Tech Guide" for the Conditions of Use for the mCRM System, and programming recommendations for the EMPOWER PG. Refer to the S-ICD MRI Tech Guide for programming guidance for the S-ICD during the scan.

Based on the PTMs listed above, collect the following data prior to and after the MRI Scan:

- PCT (refer to **Section 10.3.1.7**), pace impedance, and sensed amplitude from the EMPOWER PG

[33] Note that AF diagnostic episodes labelled "Full S-ECG Report AF" are NOT required.

- Communication Test in a single posture (refer to **Section 10.3.4.2** and **Section 10.3.4.4**). It is recommended to use the same posture for the pre- and post-MRI scan Communication Test.
- PMST (refer to **Section 10.3.4.6**)

[redacted]

10.10.1 Medically Necessary MRI Scan Source Documentation Requirements

Data and source documentation requirements for medically necessary MRI scans are listed in **Table 10-17**.

Table 10-17: Medically Necessary MRI Scan Visit Data Collection and Source Documentation Requirements

Data Collection	Retention of Original Source Documentation
EMPOWER Programmer Reports: - Initial EMPOWER Combined Follow-up Report - Interim Combined Follow-up Report with MRI settings documented (based on the mCRM and EMPOWER MRI Tech Guide) - EMPOWER Real-Time Log Report (to document LOC prior to and after MRI scan) - Final EMPOWER Combined Follow-up Report	Study site
S-ICD Programmer Reports: - S-ICD Summary Report showing MRI Protection Mode programming - S-ICD Summary Report After the MRI Scan - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable[34]	Study site; upload copy to BSC via study EDC system
Communication Test S-ECG Reports	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.11 LATITUDE Monitoring

Subjects may be followed using the LATITUDE™ NXT Patient Management System from the time they are implanted with the S-ICD System. Note that LATITUDE surveillance of the EMPOWER PG will not be available during the study.

Spontaneous episodes can be collected via the LATITUDE NXT System, if applicable, but this does not replace the Semi-Annual in-clinic visits, nor does it replace the requirement to upload all device episodes in the study database. Required MODULAR ATP Clinical Study follow ups cannot be substituted with a LATITUDE remote follow up.

[34] Note that AF diagnostic episodes labelled "Full S-ECG Report AF" are NOT required.

10.12 Revisions, Replacements and Explants

If the S-ICD electrode, S-ICD PG, and/or EMPOWER PG are surgically revised, explanted, or removed from service after the initial implant procedure, or the S-ICD PG, EMPOWER PG is permanently programmed off, or disabled, the associated Device Tracking Form is used to record changes to the system, including rationale for the change.

Subjects with the EMPOWER PG or S-ICD with clinical firmware implanted will continue to be followed in the study. Subjects undergoing explant of the mCRM Coordinated System must be followed at least 30 days post-explant (either in-clinic or phone contact) to assure there are no associated adverse events, or to assure the resolution of any adverse events associated with the explant. These subjects must be withdrawn from the study after satisfying the follow-up period of at least 30 days; refer to **Section 9.5** for more information on study withdrawal.

If the EMPOWER PG is retrieved, procedure times of the device retrieval including fluoroscopy time, sheath in/out times, and retrieval catheter in/out times, as well as the outcome of the retrieval procedure will be collected. The explanted EMPOWER PG must be returned to BSC for returned product analysis. A copy of the Combined Follow-up Report from the programmer before the EMPOWER PG is taken out of service or explanted should be obtained. If the S-ICD with clinical firmware is explanted, it must be returned to BSC for returned product analysis. A copy of the S-ICD Summary Report before the S-ICD is taken out of service or explanted should be obtained. **Table 10-18** lists the data required for system revisions.

Document any subsequent implant of another EMPOWER PG or S-ICD, regardless whether the previous EMPOWER PG is explanted or not, on the appropriate eCRF. These subjects should continue with the original follow-up schedule established using the initial Time 0.

Regardless of which device is revised or replaced, collect the following data.

10.12.1 EMPOWER PG Evaluation

PCT, Pacing Impedance, and R-wave Amplitude are required to be measured. Collect PCT measurements according to **Section 10.3.1.7**.

It is required to retain the “Real-Time Log Report” from the EMPOWER PG programmer, documenting at a minimum the LOC portion of the threshold testing (i.e., the lowest voltage setting demonstrating capture and the highest voltage setting that fails to capture). This documentation will be retained at the study site.

If more than one set of electrical measurements are recorded, the final set must be used for the study.

10.12.2 S-ICD Evaluation

It is required to retain the “S-ICD Summary Report” from the programmer, documenting initial and final parameter settings, episode counters, etc.

10.12.3 mCRM Coordinated System Programming

Recommended programming parameters for the EMPOWER PG and S-ICD are included in **Sections 10.4.4.1** and **10.4.4.2**, respectively.

Print out a copy of the final "Combined Follow-up Report" and a copy of the "S-ICD Summary Report". Once all study activities are completed at the end of the visit, reset the EMPOWER PG brady counters/ histograms and tachy counters.

10.12.4 Revisions, Replacements, and Explants Data and Source Documentation Requirements

Data and source documentation requirements for revisions, replacements, and explants are listed in **Table 10-18**.

Table 10-18: Revisions, Replacements, and Explants Data and Source Documentation Requirements

Data Collection	Retention of Original Source Documentation
- Newly implanted product and accessories utilized for S-ICD System (model/serial/lot/batch/etc.), if applicable - Newly implanted product and accessories utilized for the EMPOWER MPS (model/serial/lot/batch/etc.), if applicable	Study site
S-ICD Programmer Printouts: - S-ICD Summary Report - Full S-ECG Report(s) Treated, if applicable - Full S-ECG Report(s) Untreated, if applicable[35]	Study site; upload copy to BSC via study EDC System
- Chest x-ray (P/A and Lateral), to document mCRM Coordinated System placement - Fluoro or cine images of EMPOWER PG final position	Study site
Reportable Adverse Events, Device Deficiencies, and Protocol Deviations, if applicable	Study site
Data items that do not have an original source document will be collected on a TSF	Study site

10.13 Study Completion

All subjects enrolled in the MODULAR ATP Clinical Study will be followed per the defined follow-up schedule until they withdraw from the study or until BSC notifies study sites of follow-up completion for the study. Subjects will receive standard of care by their

[35] Note that AF diagnostic episodes labelled "Full S-ECG Report AF" are NOT required.

physician after their study participation is completed. Refer to **Section 9.8** for more information.

10.14 Source Documents

It is preferable that original source documents are maintained, when available. In lieu of original source documents, certified copies are required to be maintained. A certified copy is a copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.

11 Statistical Considerations

11.1 MODULAR ATP Clinical Study Endpoints

Each MODULAR ATP Clinical Study endpoint will describe which subjects are eligible for inclusion in the analysis of that endpoint.

11.1.1 Safety Endpoint 1: Major EMPOWER MPS System- and Procedure-related Complication-Free Rate from Implant through 6 Months Post-Implant

Safety Endpoint 1 will be assessed for subjects who undergo any portion of the EMPOWER PG implant procedure. Safety will be confirmed by evaluating the Major EMPOWER MPS-related Complication-free rate (CFR) between the EMPOWER PG implant procedure date and 180 days (6 months) post-implant procedure date. For the purpose of this endpoint, a major EMPOWER MPS-related complication will be defined as those complications that are related to the EMPOWER MPS (pacemaker and/or delivery catheter), or its implant procedure and that are identified as major complications. Major complications are defined as those adverse events resulting in:

- Death
- Permanent loss of device (EMPOWER PG) function due to mechanical or electrical dysfunction of the device (e.g., pacing function disabled, leaving device abandoned electrically)
- Hospitalization[36]
- Prolonged Hospitalization by at least 48 hours[37]
- System revision (reposition, replacement, explant).

At a minimum all complications that the study site reports as EMPOWER MPS-related will be adjudicated by an external committee to identify events that will meet the endpoint definition. Major complications that are determined to be related to the EMPOWER PG or its implant procedure by the external committee will be considered

[36] Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event or Major complication.

[37] Hospitalization is extended by ≥48 hours beyond expected hospital discharge (from implant or hospital admission for another cause)

major EMPOWER MPS-related complications and will count against this endpoint. For the purpose of this endpoint, the adjudication of the CEC will be used.

11.1.1.1 Hypotheses

The following hypotheses will be used to evaluate Safety Endpoint 1 from implant through 6 months post implant:

H_0: The Major EMPOWER MPS System- and Procedure-related complication-free rate through 6 months is ≤ 86%

H_A: The Major EMPOWER MPS System- and Procedure -related complication-free rate through 6 months is > 86%.

11.1.1.2 Sample Size

A group sequential design based on the z test of a binomial proportion will be used to assess the Safety Endpoint 1. The assumptions and parameters pertaining to this endpoint are as follows:

[redacted]

- Performance Goal: 86% Major EMPOWER MPS System- and Procedure-related CFR through 6 months post-implant
- Attrition: 25% of enrolled subjects through the 6-month visit
- Power = 90%
- Alpha < 2.5% (1-sided)
- Alpha boundary determination: A power error spending function will be used with ρ=1.5

[redacted]

- Number of analyses: 2
- Timing of analyses: The single interim endpoint analysis will occur after a minimum of 134 subjects who have undergone any portion of the EMPOWER PG implant procedure have been followed for 6-months (based on a required 0.6 Information Fraction for the interim analysis). The final analysis of this endpoint may occur when 223 subjects who have undergone any portion of the EMPOWER PG implant procedure have been followed for 6-months if the null hypothesis of Safety Endpoint 1 is not rejected at the interim analysis.

[redacted] Based on these assumptions and parameters, a sample size of 134 subjects is required for the interim analysis with an alpha of 1.2%. If the null hypothesis is not rejected at the interim analysis, a sample size of 223 subjects is required for the final analysis with an alpha of 1.9%.

[redacted]

[redacted]

11.1.1.3 Statistical Methods

Endpoint analysis will be performed on data from subjects that have undergone any portion of the EMPOWER PG implant procedure, including subjects that do not have the EMPOWER PG successfully implanted. The major EMPOWER MPS System and Procedure-related CFR from the date of the EMPOWER PG implant procedure through 6 months (180 days) post-implant will be calculated using Kaplan-Meier methodology.

The interim analysis will be conducted once 134 subjects have undergone the EMPOWER PG implant procedure and have been followed for 6 months (180 days). Using the allocated alpha level of 1.2% for the interim analysis, the 98.8% one-sided lower pointwise confidence limit of the Major CFR will be calculated via log-log methodology and compared to the performance goal of 86%. If the lower confidence limit exceeds 86%, the null hypothesis will be rejected.

If the interim analysis does not result in the rejection of the null hypothesis, the final analysis will be conducted once 223 subjects have undergone the EMPOWER PG implant procedure and have been followed for 6 months (180 days). Using the allocated alpha level of 1.9% for the final analysis, the 98.1% one-sided lower pointwise confidence limit of the Major CFR will be calculated via log-log methodology and compared to the performance goal of 86%. If the lower confidence limit exceeds 86%, the null hypothesis will be rejected.

The Kaplan-Meier methodology was chosen for this endpoint to utilize all available data for each subject. To assess the robustness of this analysis method and the potential impact missing data could have had on the analysis results, a tipping point analysis will be conducted that will include subjects that have undergone any portion of the EMPOWER PG implant procedure, including subjects that do not have the EMPOWER PG successfully implanted. The tipping point analysis will assign each subject with missing data as either having or not having a Major EMPOWER MPS System- and Procedure-related complication. All possible combinations of these subjects' data will be evaluated along with the actual observed data to find the point, if any, at which the endpoint is failed.

11.1.2 Safety Endpoint 2: Major EMPOWER MPS System- and Procedure-related Complication-free Rate from Implant through 12 Months Post-Implant

Safety Endpoint 2 will be assessed for subjects who undergo any portion of the EMPOWER PG implant procedure. Safety will be confirmed by evaluating the Major EMPOWER MPS System- and Procedure-related CFR between the EMPOWER PG implant procedure date and 365 days (12 months) post-implant procedure date. The same definition of Major EMPOWER System- and Procedure-related Complication that was used for Safety Endpoint 1 (refer to **Section 11.1.1**) will also be used for Safety Endpoint

2. This endpoint will support both the CE Mark and FDA's requirements for Post Market 1 submissions.

11.1.2.1 Hypotheses

The following hypotheses will be used to evaluate Safety Endpoint 2 from implant through 12 months post-implant:

H_0: The Major EMPOWER MPS System- and Procedure-related CFR through 12 months is ≤ 81%

H_A: The Major EMPOWER MPS System- and Procedure-related CFR through 12 months is > 81%

The performance goal was selected to be consistent with the initial recommendations for study of leadless cardiac pacemaker therapy, written by the Medicines & Healthcare Products Regulatory Agency (MHRA) Expert Advisory Group[38].

11.1.2.2 Sample Size – CE Mark Cohort

Endpoint analysis will be performed on subjects that undergo an EMPOWER PG implant procedure, including subjects that do not have an EMPOWER PG successfully implanted. The CE Mark cohort analysis must include at least 112 subjects that underwent an EMPOWER PG implant procedure with data at 12 months to be sufficiently powered. Sample size estimates were obtained using the normal approximation to the binomial and verified through simulations based on Kaplan-Meier methodology using SAS 9.4; Kaplan-Meier methodology will be used for the analyses.

Sample size was calculated using the following assumptions:

- Performance goal = 81%[37]
- [redacted]
- One-sided significance level = 2.5%
- Power = 90%

The sample size for this study was not determined by this endpoint.

11.1.2.3 Sample Size – Post-Market 1 Cohort[39]

The Post-Market 1 cohort analysis will be done on the full subject enrollment (n=300). Given a 30% attrition rate, it is expected that 210 subjects will be followed through 1 year. Using the normal approximation to the binomial method and the assumptions outlined below, the Post-Market 1 analysis will be powered at 99.8%.

- Performance goal = 81%
- [redacted]

[38] Leadless cardiac pacemaker therapy: design of pre- and post-market clinical studies. Recommendations from MHRA Expert Advisory Group. October 2018.

[39] DCD / IEDB Improved Submission Paradigm for Leadless Cardiac Pacemakers (2015)

- One-sided significance level = 2.5%
- Attrition Rate = 30%

11.1.2.4 Statistical Methods

Endpoint analysis will be performed on subjects that undergo an EMPOWER PG implant procedure, including subjects that do not have the EMPOWER PG successfully implanted (i.e., both implant and attempt subjects), using two different cohorts. The CE Mark cohort will consist of the minimum number of subjects required to evaluate this endpoint - 112 subjects who undergo an EMPOWER PG implant procedure and have been followed for 12 months. The FDA Post-Market 1 cohort will consist of all subject enrollments who undergo an EMPOWER PG implant procedure and are followed for 12 months.

The Major EMPOWER MPS System- and Procedure-related CFR from the date of the EMPOWER PG implant procedure through 365 days post implant will be calculated using Kaplan-Meier methodology.

The 97.5% one-sided lower pointwise confidence limit of the Major EMPOWER MPS System- and Procedure-related CFR will be calculated via log-log methodology and compared to the performance goal of 81%. If the lower confidence limit exceeds 81%, the null hypothesis will be rejected.

The Kaplan-Meier methodology was chosen for this endpoint to utilize all available data for each subject. To assess the robustness of this analysis method and the potential impact missing data could have had on the analysis results, a tipping point analysis will be conducted that will include subjects with the EMPOWER PG implanted and the attempted subjects. The tipping point analysis will assign each subject with missing data as either having or not having a Major EMPOWER MPS System- and Procedure-related Complication. All possible combinations of these subjects' data will be evaluated along with the actual observed data to find the point, if any, at which the endpoint is failed.

11.1.3 Secondary Safety Endpoint: All-Cause Survival from Implant through 2 Years Post-Implant

The Secondary Safety Endpoint will be assessed for all implant subjects. Safety will be confirmed by evaluating the 2-Year all-cause survival rate post implant. Deaths due to any reason will count against this endpoint. Data from this endpoint will be used to evaluate the longer-term safety of the EMPOWER PG for the purposes of obtaining CMS approval and Medicare reimbursement. This analysis will be performed when all implanted subjects have been followed for a minimum of 730 days. In order to control the overall study Type I error rate, this endpoint will only be evaluated if Safety Endpoint 1,the primary effectiveness endpoints, and the Secondary Effectiveness endpoint are successful.

11.1.3.1 Hypotheses

The following hypotheses will be used to evaluate the Secondary Safety Endpoint:

H_0: The all-cause survival rate through 2 years post-implant ≤ 85%

H_A: The all-cause survival rate through 2 years post-implant > 85%.

11.1.3.2 Sample Size

A sample size of 123 implanted subjects followed for 2 years is required to evaluate the Secondary Safety Endpoint. This sample size was calculated based on a one-sided normal approximation for a single binomial proportion, using SAS Version 9.4 with the following assumptions:

- Performance goal = 85%
- [redacted]
- Significance level = 2.5% one-sided
- Power = 80%

Given an expected attrition rate of 40%, 275 subjects are needed, which is less than the 300 enrolled subjects. This means that the overall study sample size is not being driven by this endpoint.

11.1.3.3 Statistical Methods

Endpoint analysis will be performed on all implanted subjects.

The survival rate from the implant through 730 days post-implant will be calculated using Kaplan-Meier methodology. Deaths for any reason will count as an event for this endpoint. The 5% one-sided lower pointwise confidence limit of the survival rate will be calculated via log-log methodology and compared to the performance goal of 85%. If the lower confidence limit exceeds 85%, the null hypothesis will be rejected.

11.1.4 Primary Effectiveness Endpoint 1: Communication Success between the S-ICD and EMPOWER PG at the 6 Month Visit

Primary Effectiveness Endpoint 1 will be assessed at the time of the interim analysis of Safety Endpoint 1 if its null hypothesis is rejected, or at the final analysis if its null hypothesis is not rejected at the interim analysis (refer to **Section 11.3**). The assessment will include subjects who are successfully implanted with both the EMPOWER PG and S-ICD. Effectiveness will be confirmed by evaluating the communication between S-ICD and the EMPOWER PG in four postures: upright, supine, and right and left side. The test unit for this endpoint will be the result from each posture. Communication success will be defined as any evidence of a paced beat during communication testing in a given posture at the initial programmed communication Programmed Telemetry Setting.

11.1.4.1 Hypotheses

The following hypotheses will be used to evaluate Primary Effectiveness Endpoint 1 at the 6 Month Visit:

H_0: The communication success rate is ≤ 88%

H_A: The communication success rate is > 88%.

11.1.4.2 Sample Size

The sample size estimates were obtained using the normal approximation to the binomial and verified through simulations. The required sample size of 152 tests from a minimum of 38 subjects (220 tests including attrition) was calculated using the following assumptions:

- Performance goal = 88%
[redacted]
- One-sided significance level = 2.5%
- Power = 80%
- Attrition = 30%

The sample size for this study was not determined by this endpoint.

11.1.4.3 Statistical Methods

The analysis for this endpoint will be performed once, either in conjunction with the interim analysis of Safety Endpoint 1, if the analysis of Safety Endpoint 1 is successful in rejecting the null hypothesis, or at the time of the final analysis of Safety Endpoint 1. The analysis for this endpoint will use the communication results taken at the 6 Month Visit and the communication success rate will be calculated using the data from all postures.

A repeated measure logistic regression will be fit with an indicator of communication success of each posture test as the response and subject as the repeated measure in an intercept only model to calculated the adjusted communication success rate and the 97.5% one-sided lower pointwise confidence limit. An unstructured correlation matrix will be used, unless a different structure is found to be more appropriate. The adjusted communication success rate and the 97.5% one-sided lower pointwise confidence limit by converting the intercept estimate and 97.5% one-sided upper pointwise conficence limit from the model previously described into an event rate and corresponding confidence limit. This adjusted 97.5% one-sided lower pointwise confidence limit of the communication success rate will compared to the performance goal of 88%. If the lower confidence limit exceeds 88%, the null hypothesis will be rejected. Please see the Statistical Analysis Plan (SAP) for more specifics. The unadjusted rate and 97.5% one-sided lower pointwise confindence limit calculated using the one-sided Score methodology will also be presented as sensitivity analysis.

A subject-level evalution of the communication success rate across the four postures is being analyzed as an ancillary objective. See **Section 11.2**.

Missing posture testing data due to missed 6 Month Visits or a missing posture of the 4 tested will be considered missing data. To assess the potential impact missing data could have had on the analysis results, a tipping point analysis will be conducted. The tipping point analysis will assign each missing posture test as either a failure or success. All possible combinations of these posture tests' data will be evaluated along with the actual observed data to find the point, if any, at which the endpoint is failed.

The poolability of the communication success rate will be assessed across postures. As part of this analysis the communication success rate will be presented for each posture, and the poolability will be assessed as outlined in pooling analysis in **Section 11.7.3**.

11.1.5 Primary Effectiveness Endpoint 2: Proportion of Subjects with Adequate PCT at the 6 Month Visit

Primary Effectiveness Endpoint 2 will be assessed at the time of either the interim analysis of Safety Endpoint 1, if its null hypothesis is rejected, or at the final analysis, if its null hypothesis is not rejected at the interim analysis (refer to **Section 11.3**). Effectiveness will be confirmed by evaluating the percentage of subjects considered to be a Pacing Capture Threshold (PCT) Responder, defined as a subject with a PCT measurement of ≤ 2.0 V @ 0.4 ms pulse width.

11.1.5.1 Hypotheses

H_0: PCT Responders at 6-Month Visit is ≤ 80%

H_A: PCT Responders at 6-Month Visit is > 80%,

11.1.5.2 Sample Size

A total of 57 measurements (6-month PCT @ 0.4 ms) are required to sufficiently power the Primary Effectiveness Endpoint 2. The following assumptions were used to calculate the sample size:

- Performance goal = 80%
- [redacted]
- One-sided significance level = 2.5%
- Power = 90%

The sample size for this study was not determined by this endpoint.

11.1.5.3 Statistical Methods

The analysis for this endpoint will be performed once, either in conjunction with the interim analysis of Safety Endpoint 1, if the analysis of Safety Endpoint 1 is successful in rejecting the null hypothesis, or at the time of the final analysis of Safety Endpoint 1. Two groups of subjects will be included in the endpoint evaluation: (1) PMA Sample cohort subjects with an EMPOWER PG PCT measurement taken at the 6 Month Visit (with a 0.4 ms pulse width), and (2) PMA Sample cohort subjects with a Major EMPOWER MPS System- and Procedure-related Complication between implant and 6 months due to an elevated threshold. The number of responders (PCT at 6 Month Visit ≤ 2.0 V @ 0.4 ms) divided by the total number of subjects included in the endpoint evaluation will be calculated. The one-sided 2.5% binomial exact lower confidence limit will be calculated and compared to the performance goal of 80%. If the lower confidence limit exceeds 80%, the null hypothesis will be rejected.

To assess the potential impact missing data could have had on the analysis results, a tipping point analysis will be conducted that will include subjects with the EMPOWER PG implanted. The tipping point analysis will assign each subject with missing data as

either being a PCT responder or a PCT non-responder. All possible combinations of these subjects' data will be evaluated along with the actual observed data to find the point, if any, at which the endpoint is failed.

11.1.6 Secondary Effectiveness Endpoint: Mean Metabolic-Chronotropic Relation (MCR) Slope from the Kay-Wilkoff Model at the 3 Month Visit

The Secondary Effectiveness Endpoint evaluates the adequacy of the EMPOWER PG Rate Response feature using the Metabolic-Chronotropic Relation Slope (MCR Slope). Data for this endpoint will be obtained from the subset of subjects who performed treadmill testing at 3 months. Using the Kay-Wilkoff model, the Secondary Effectiveness Endpoint will evaluate the proportionality of the EMPOWER PG's sensor-indicated rate to the subject's workload during the treadmill test. In order to control the overall study Type I error rate, this endpoint will only be evaluated if Safety Endpoint 1 and the primary effectiveness endpoints are successful.

11.1.6.1 Hypotheses

The following set of hypotheses will be used to evaluate the Secondary Effectiveness Endpoint:

H_0: Mean slope < 0.65 or Mean slope > 1.35

H_A: 0.65 ≤ Mean slope ≤ 1.35,

where the mean slope is calculated from the Kay-Wilkoff model.

11.1.6.2 Sample Size

A minimum of 35 usable datasets is required to sufficiently power the Secondary Effectiveness Endpoint. A usable dataset is defined as one for which the subject completes at least treadmill Stage 4 without continuous use of the treadmill handlebars in either treadmill Stage 3 or Stage 4, as described further in Document 92614291 (provided separately).

Sample size estimates were obtained using two one-sided t-tests (TOST).

The sample size of 35 usable datasets was calculated using the following assumptions:

- Performance goals = mean slope between 0.65 and 1.35
- [redacted]
- Expected standard deviation = 0.35
- One-sided significance level = 2.5%
- Power = 90%

Assuming that 40% of subjects will not have usable datasets, at least 59 subjects will be included in the treadmill test in order to obtain at least 35 usable datasets.

The sample size for this study was not determined by this endpoint.

11.1.6.3 Statistical Methods

All datasets from treadmill tests at 3 months with at least 4 stages of data will be included in the endpoint evaluation. Normalized sensor-indicated rate and normalized workload (METS) will be used for evaluation; the range of values for each normalized value will be between 0 and 1. The normalized rates will be calculated as follows:

$$Normalized\ sensor\ rate = \frac{(sensor\ rate_{stage} - sensor\ rate_{rest})}{(sensor\ rate_{max} - sensor\ rate_{rest})}$$

$$where\ sensor\ rate_{rest} = Programmed\ LRL\ during\ treadmill\ test$$

$$Normalized\ workload = \frac{(METS_{stage} - 1)}{(METS_{max} - 1)}$$

Subject-specific slopes from each test will be calculated by performing a general linear model with normalized sensor rate as the outcome and normalized workload as the predictor. These subject-specific slopes will be used in a TOST using an alpha of 2.5% for each test. If the lower limit of the 95% confidence interval is greater than 0.65 and the upper limit of the 95% confidence interval is less than 1.35, then the null hypothesis will be rejected. Each comparison represents a one-sided 2.5% test. Per Union-Intersection Test methodology, the overall alpha is maintained at 2.5%.

11.2 Ancillary Objectives

The following data will be collected in the MODULAR ATP Clinical Study and summarized at the time of endpoint analysis for all subjects, where applicable, and the data are available. Additional information regarding the ancillary objectives can be found in the MODULAR ATP SAP.

- Summary of the mCRM Therapy System implant procedure characteristics
    - Initial implant success rate of the EMPOWER PG
    - Initial implant success rate of the S-ICD (*de novo* Implants)
- Summary of pacing impedance and sensing amplitude at protocol-required follow ups
- Summary of ventricular tachycardia (VT)/ ventricular fibrillation (VF) conversion and sensing interaction testing
- Summary of Communication Threshold Test at Implant, Pre-Discharge, 1 Month Visit and available Semi-Annual visits
- Summary of Communication Test results at available Semi-Annual visits
- Summary of incidence and threshold for Communication Muscle Stimulation at Implant
- Summary of number of postures with a successful Communication Test at the 6 Month Visit
- Summary of EMPOWER PG PCT at protocol-required follow ups
- Summary of spontaneous treated VT/ VF episodes
- Incidence of syncope related to treated and untreated spontaneous episodes of VT/ VF above the lowest programmed rate cutoff
- Incidence and appropriateness of post-shock demand pacing by the EMPOWER PG

- Summary of Inappropriate Therapy
- Summary of Major EMPOWER MPS System- and Procedure-related Complications through both 6 and 12 months after the implant procedure
- Summary of mCRM Therapy System-related complications through both 6 and 12 months after the implant procedure*
- Summary of the EMPOWER PG performance from Holter Monitor recording
- Summary of EMPOWER PG battery charge remaining to End of Service (EOS) at protocol-required follow ups
- Summary of S-ICD PG remaining battery to Elective Replacement Indicator (ERI) per protocol-required follow ups (baseline adjusted to time of enrollment for S-ICD PGs implanted prior to enrollment in MODULAR ATP)

[redacted]

11.4 Sample Size Summary

The study will enroll up to 300 subjects, which is approximately what is required for the sample size of the final analysis of Safety Endpoint 1, 223 subjects followed for 6 months or 298 subjects enrolled and accounting for an estimated 25% attrition rate (223 ≈ 298 × 75%).

11.5 General Statistical Methods

11.5.1 Study Success Criteria and Control of Type I Error

The study will be considered successful if Safety Endpoint 1 and all primary effectiveness endpoints are passed.

Safety Endpoint 1 and the primary effectiveness endpoints can be tested at the significance level of 2.5% while still maintaining the overall type I error level at no greater than 2.5%. This follows the methodology of the Intersection-Union Test (IUT). Additionally, in order to control the overall type I error level a gating approach will be employed. The Secondary Effectiveness Endpoint and Secondary Safety Endpoint will only be evaluated if Safety Endpoint 1 and the primary effectiveness endpoints are successful. The secondary endpoints will be tested in the following order:

- Secondary Effectiveness Endpoint
- Secondary Safety Endpoint, which will only be tested if Seconardy Effectiveness Endpoint is successful.

11.5.2 Control of Systematic Error/Bias

Selection of patients will be made from the Investigator's usual patient population. All patients meeting the eligibility criteria and having signed the ICF will be eligible for enrollment in the study. To control for inter-observer variability among sites, an independent CEC will determine the EMPOWER MPS System- and Procedure-related complications to be used in the analysis of Safety Endpoint 1.Number of Subjects per Study Site

To avoid any study site effect and bias, no study site will be authorized to implant or attempt more than 20% of the maximum number of subjects without approval from BSC. A minimum of 50% of total enrollments from North America will be maintained.

11.6 Data Analyses

11.6.1 Interim Analyses

[redacted]

11.6.1.2 Endpoints

As stated in **Section 11.3** the single interim endpoint analysis will occur after a minimum of 134 subjects who have undergone an EMPOWER PG implant procedure have been followed for 6 months. The final analysis of this endpoint may occur when 223 subjects who have undergone an EMPOWER PG implant procedure have been followed for 6 months if the null hypothesis of Safety Endpoint 1 is not rejected at the interim analysis. The hypothesis test for Primary Effectiveness Endpoints 1 and 2 and the Secondary Effectiveness Endpoint will be performed in conjunction with either the interim analysis of Safety Endpoint 1 if the null hypothesis is successfully rejected or at the time of final analysis if it is necessary.

11.6.2 Subgroup Analyses

Analyses will be performed for each endpoint to determine whether significant differences exist in endpoint results between subgroups. The list of subgroups (with applicable definitions in parentheses) includes, but is not necessarily limited to:

- Sex (Female vs. Male),
- BMI (Obese – BMI ≥ 30 vs. Non-Obese – BMI < 30) for effectiveness endpoints only,
- Geography (North America vs. Other Countries),
- Age (< 65 years vs. ≥ 65 years),
- Race (Black or African heritage vs. other races)

The subgroup variable will be added to a logistic regression model. A test for significance at the 15% level will be performed. For each subgroup variable in which a significant difference exists, the results for each subgroup will be presented separately. BSC does not plan to seek labeling for these subgroups based on these analyses.

11.6.3 Pooling Analyses

11.6.3.1 Assessment of Pooling Across Communication Test Postures

The poolability of the Primary Effectiveness Endpoint 1 data by communication test postures will be performed to determine whether there are differences among the four postures: upright, supine, and right and left side.

Communication test posture heterogeneity will be assessed by performing fixed effects logistic regression analyses. Communication test posture will be added into the model as a fixed effect. Postures will be deemed to be heterogeneous if the variance of the fixed posture effect is found to significantly differ from zero. A significance level of 15% will be used for the test.

11.6.3.2 Assessment of Pooling Across Geographies and Study Sites

The poolability of data by geography and investigational study site will be performed to determine whether there are differences between the US and international geographies, and from study site-to-study site.

Study site-to-study site heterogeneity will be assessed for each endpoint by performing random effects logistic regression analyses. Study sites enrolling 5 subjects or fewer will be combined within region (North America versus other countries) into pooled sites of 6 or more subjects for this pooling analysis.

Study site will be added into the model as a random effect. Study sites will be deemed to be heterogeneous if the variance of the random study site effect is found to significantly differ from zero. A significance level of 15% will be used for each test.

11.6.3.3 Assessment of Pooling Across Introducer Sheaths

The poolability of data by introducer sheath will be performed to determine whether there are differences between the EMPOWER Introducer Sheath and any commercially available introducer sheaths. The poolabilty of introducer sheaths will only be assessed for safety endpoints.

Introducer sheath heterogeneity will be assessed by performing random effects logistic regression analyses. Introducer sheath will be added into the model as a random effect. Introducer sheaths will be deemed to be heterogeneous if the variance of the random introducer sheath effect is found to significantly differ from zero. A significance level of 15% will be used for the test.

11.6.4 Multivariable Analyses

Univariable analyses of various baseline covariates and their relationship to each endpoint are outlined in **Section 11.7.2**. For each endpoint, all baseline characteristics found to be significantly associated with the outcome will be included as covariates in a multivariable regression model. The impact of each baseline characteristic's subgroups will be presented along with the multivariable model results.

11.7 Changes to Planned Analyses

Any changes to the planned statistical analyses made prior to performing the analyses will be documented in a SAP approved prior to performing the analyses. Changes from the planned statistical methods after performing the analyses will be documented in the clinical study report along with a reason for the deviation.

[redacted]

[redacted]

13 Data Management

13.1 Data Collection, Processing, and Review

Subject data will be recorded in a limited access secure electronic data capture (EDC) system.

The clinical database will reside on a production server hosted by [redacted]. All changes made to the clinical data will be captured in an electronic audit trail and available for review by the sponsor or its representative. The associated [redacted] software and database have been designed to meet regulatory compliance for deployment as part of a validated system compliant with laws and regulations applicable to the conduct of clinical studies pertaining to the use of electronic records and signatures. Database backups are performed regularly.

The Investigator provides his/her electronic signature on the appropriate electronic case report forms (eCRFs) in compliance with local regulations. A written signature on printouts of the eCRFs must also be provided if required by local regulations. Changes to data previously submitted to the sponsor require a new electronic signature by the Investigator acknowledging and approving the changes.

Visual and/or electronic data review will be performed to identify possible data discrepancies. Manual and/or automatic queries will be created in the [redacted] EDC

system and will be issued to the site for appropriate response. Site staff will be responsible for resolving all queries in the database.

Boston Scientific will provide all participating study sites eCRF Completion Guidelines along with training on completion of the eCRFs for the MODULAR ATP Clinical Study.

All access to the clinical database will be changed to "Read only" after all data is either "Hard Locked" or "Entry Locked". Once acceptance of the final report or finalization of publications (as applicable) is received, final database storage and archiving activities can begin. Once all of the closeout activities are completed a request to IT is submitted to have the "Database Locked" and all database access revoked.

13.2 Data Retention

The Principal Investigator, his/her designee, or study site will maintain all essential study documents and source documentation that support the data collected on the study subjects in compliance with applicable regulatory requirements.

The Principal Investigator or his/her designee will take measures to prevent accidental or premature destruction of these documents. If for any reason the Principal Investigator or his/her designee withdraws responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility and BSC must receive written notification of this custodial change. Sites are required to inform BSC in writing where paper or electronic files are maintained in case files are stored off site and are not readily available.

13.3 Technical Source Forms

A Technical Source Form (TSF) is developed by BSC or by the investigational site to capture protocol required data elements that are not duplicated in any other source documents. These forms are to be used by the study sites as a source document. A BSC representative may complete the TSF at the request of the Principal Investigator. The TSF will be reviewed and signed for approval by the Principal Investigator or his/her designee at the end of each procedure.

13.4 Core Laboratory

A Holter core lab will be used to provide Holter Monitoring equipment and Holter data analysis for subjects enrolled in this portion of the trial. Details are provided in **Section 10.5.5** and separate study instructions may be provided to the participating sites.

14 Deviations

An Investigator must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. An investigator shall notify the sponsor and the reviewing IRB/EC/REB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency, and those deviations which affect the scientific integrity of the clinical investigation. Such notice shall be given as soon as possible, but no later than 5 working days after the emergency occurred, or per prevailing local requirements, if sooner than 5 working days.

All deviations from the investigational plan, with the reason for the deviation and the date of occurrence, must be documented and reported to the sponsor using the EDC system. Sites may also be required to report deviations to the IRB/EC/REB, per local guidelines and government regulations.

Deviations will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective and preventive actions, notification, site re-training, or site discontinuation/termination will be put into place by the sponsor.

15 Device Accountability

Items labeled as Investigational shall be securely controlled, managed and used only as authorized by the Sponsor.

The Sponsor shall keep records documenting the location of items labeled as Investigational from shipment/transference to the study sites until disposal at site or return from the site to the Sponsor or designee.

The principal investigator or an authorized designee shall document the receipt, disposition, return and disposal of all consigned items labeled as Investigational, as directed by the Sponsor. At minimum, this shall include the following:

- Date of receipt and by whom
- Identification (and quantity) of each item (batch number or unique code)
- Date or dates of use (or other disposition) and by whom
- Date of return (and number) of items, as applicable.

The principal investigator or an authorized designee shall keep records documenting the assignment/usage of study-related devices as per the Sponsor's data collection requirements (see protocol **Section 16.2**). Study-related devices designated for data collection, may or may not be labeled as investigational.

16 Compliance

16.1 Statement of Compliance

This study will be conducted in accordance with 21 CFR 814.20, part 56, part 50 and part 812, European Medical Device Regulation, EN ISO 14155 Clinical Investigation of Medical Devices for Human Subjects, relevant parts of the ICH Guidelines for Good Clinical Practice, ethical principles that have their origins in the Declaration of Helsinki, and pertinent individual country laws and regulations. The study shall not begin until the required approval/favorable opinion from the IRB/EC/REB and/or regulatory authority has been obtained, if appropriate. Also, the study shall not begin prior to issuance of the site Authorization to Enroll, as provided by the sponsor. Any additional requirements imposed by the IRB/EC/REB or regulatory authority shall be followed, if appropriate.

16.2 Investigator Responsibilities

The Principal Investigator of a study site is responsible for ensuring that the study is conducted in accordance with the Clinical Study Agreement, the clinical investigation

plan, ISO 14155, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing IRB/EC/REB, and prevailing local and/or country laws and/or regulations, whichever affords the greater protection to the subject.

The Principal Investigator's responsibilities include, but are not limited to, the following.

- Prior to beginning the study, sign the Clinical Study Agreement and comply with the Investigator responsibilities as described in such Agreement.
- Prior to beginning the study, sign the Investigator Brochure Signature Page and Protocol Signature page documenting his/her agreement to conduct the study in accordance with the protocol.
- Provide his/her qualifications and experience to assume responsibility for the proper conduct of the study and that of key members of the site team through up-to-date curriculum vitae or other relevant documentation and disclose potential conflicts of interest, including financial, that may interfere with the conduct of the clinical study or interpretation of results.
- Make no changes in or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency; document and explain any deviation from the approved protocol that occurred during the clinical investigation.
- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical-investigation-related records are retained per requirements.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Record, report, and assess (seriousness and relationship to the device/procedure) every adverse event as applicable per the protocol and observed device deficiency.
- Report to sponsor, per the protocol requirements, all SAEs and device deficiencies that could have led to a SADE and potential/USADE or UADE.
- Report to the IRB/EC/REB and regulatory authorities any SAEs and device deficiencies that could have led to a SADE and potential/USADE or UADE, if required by applicable laws or regulations or this protocol or by the IRB/EC/REB, and supply BSC with any additional requested information related to the safety reporting of a particular event.
- Maintain the device accountability records and control of the device, ensuring that the investigational device is used only by authorized/designated users and in accordance with this protocol and instructions/directions for use.
- Allow the sponsor to perform monitoring and auditing activities, be accessible to the clinical research monitor or auditor, and respond to questions during monitoring visits or audit(s).
- Allow and support regulatory authorities and the IRB/EC/REB when performing auditing activities.
- Ensure that informed consent is obtained in accordance with applicable laws, this protocol and local IRB/EC/REB requirements.
- Provide adequate medical care to a subject during and after a subject's participation in a clinical study in the case of adverse events, as described in the ICF.

- Inform the subject of the nature and possible cause of any adverse events experienced.
- As applicable, provide the subject with necessary instructions on proper use, handling, storage, and return of the investigational device when it is used/operated by the subject.
- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Ensure that, if appropriate, subjects enrolled in the clinical investigation are provided with some means of showing their participation in the clinical investigation, together with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided).
- Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.
- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical investigation while fully respecting the subject's rights.
- Ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation.

16.3 Delegation of Responsibility

When specific tasks are delegated by the Principal Investigator, including but not limited to, conducting the informed consent process, the Principal Investigator is responsible for providing appropriate training, assessing that the delegate(s) is/ are competent to perform the tasks they have been delegated, and providing adequate supervision of those to whom tasks are delegated. Where there is a sub-investigator at a site, the sub-investigator should not be delegated the primary supervisory responsibility for the site. The Principal Investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

16.4 Institutional Review Board/ Ethics Committee/ Research Ethics Board

The study site will obtain the written and dated approval/favorable opinion of the IRB/EC/REB for the clinical study before recruiting subjects and implementing all subsequent amendments, if required.

A copy of the written IRB/EC/REB and/or competent authority approval of the protocol (or permission to conduct the study) and ICF, must be received by the sponsor before recruitment of subjects into the study and shipment of investigational product/equipment. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Any amendment to the protocol will require review and approval by the IRB/EC/REB before the changes are implemented to the study. All changes to the ICF will be

IRB/EC/REB approved; a determination will be made regarding whether a new ICF needs to be obtained from participants who provided consent, using a previously approved ICF. Annual IRB/EC/REB approval and renewals will be obtained throughout the duration of the study as required by applicable local/ country laws or regulations or IRB/EC/REB requirements. Copies of the study reports and the IRB/EC/REB continuance of approval must be provided to the sponsor.

16.5 Sponsor Responsibilities

All information and data sent to BSC concerning subjects or their participation in this study will be considered confidential by BSC and will be kept confidential in accordance with all applicable laws and regulations. Only authorized BSC personnel or a BSC representative including, but not limited to Contract Research Organization (CRO) will have access to this information. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study. Study data collected during this study may be used by BSC for the purposes of this study, publication, and to support future research and/or other business purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products and procedures. All data used in the analysis and reporting of this study or shared with a third-party researcher will be without identifiable reference to specific subjects

Information received during the study will not be used to market to subjects; subject names will not be placed on any mailing lists or sold to anyone for marketing purposes.

16.6 Role of Boston Scientific Representatives

Boston Scientific personnel can provide technical support to the investigator and other health care personnel (collectively HCP) as needed during implant, testing required by the protocol, and follow-ups. Support may include HCP training, addressing HCP questions, or providing clarifications to HCPs concerning the operation of BSC equipment/devices (including programmers, analyzers, and other support equipment).

At the request of the investigator and while under investigator supervision, BSC personnel may operate equipment during implant or follow-up, assist with the conduct of testing specified in the protocol, and interact with the subject to accomplish requested activities.

Typical tasks may include the following:

- Interrogating the device or programming device parameters to investigator-requested settings as well as operating investigational equipment
- Performing device diagnostic testing using a programmer to obtain pacing, sensing, and impedance measurements
- Clarifying device behavior, operation or diagnostic output as requested by the investigator or other health care personnel
- Assisting with the collection of study data from programmers, and other equipment
- Entering technical data on a Technical Source Form if the responsible investigator verifies and signs the completed form

- Obtain programming reports directly from the programmer and provide original reports to the clinical site as source documentation
- Provide technical expertise/support to subjects during office visits and/or during teleconference calls/electronic communications with the principal investigator or their delegated site staff and the subject.

In addition, BSC personnel may perform certain activities to ensure study quality. These activities may include the following.

- Observing testing or medical procedures to provide information relevant to protocol compliance
- Use of Remote Case Support Technology to establish a tele-mentoring communication stream/live stream to perform R&D technical support and physician mentoring. The streaming will be in a secure and encrypted high-definition format which has been proven and is robust. The streaming will not be recorded. The use of remote case support will be in compliance with applicable regulations governing patient privacy. The BSC personnel on the live stream will not have any direct contact with the subject and in no instance will the subject be shown on video.
- Reviewing collected data and study documentation for completeness and accuracy
- Reporting the use of programmer application software Model 3870 or investigational features of Model 2877 and/or Model 3877 software for medically necessary patient care at facilities not participating in the clinical study.

Boston Scientific personnel will not do the following:

- Practice medicine
- Provide medical diagnosis or treatment to subjects
- Discuss a subject's condition or treatment with a subject
- Independently collect critical study data (defined as primary or secondary endpoint data)
- Enter data in electronic data capture systems or on paper case report forms (with the exception of reporting the use of programmer application software Model 3870 or investigational features of Model 2877 and/or Model 3877 software for medically necessary patient care at facilities not participating in the clinical study)

16.7 Insurance

Where required by local/country regulation, proof and type of insurance coverage, by BSC for subjects in the study will be obtained.

17 Monitoring

Monitoring will be performed during the study to assess continued compliance with the protocol and applicable regulations. In addition, the clinical research monitor verifies that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Principal Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively.

The Principal Investigator/ institution guarantees direct access to original source documents by BSC personnel, their designees, and appropriate regulatory authorities.

The sponsor will put a plan in place to document the specific monitoring requirements.

The study may also be subject to a quality assurance audit by BSC or its designees, as well as inspection by appropriate regulatory authorities. It is important that the Principal Investigator and relevant study personnel are available during on-site and/or remote monitoring visits or audits and that sufficient time is devoted to the process.

18 Potential Risks and Benefits

Refer to **Sections 18.1** and **18.2** for Potential Adverse Events relating to implant and operation of the EMPOWER PG, and the mCRM Coordinated System, respectively. **Section 18.4** includes Potential Adverse Events related to retrieval of the EMPOWER PG, in the event it is necessary. The Potential Adverse Events listed in **18.2** are in addition to the established risks for the S-ICD Pulse Generator and S-ICD Electrode (including subcutaneous Electrode Insertion Tool and the Electrode Delivery System) included in the respective users manuals.

Refer to **Section 18.3** for Potential Adverse Events related to performing an MRI scan of subjects with the mCRM Coordinated System or those in the study that are "Partial Implant" subjects and are implanted only with the EMPOWER PG.

18.1 Risks Associated with the EMPOWER MPS

Potential adverse events and risks related to the EMPOWER MPS and the implantation of the EMPOWER PG may include, but are not limited to, the following[40]:

- Aneurysm or pseudoaneurysm
- Allergic reaction
- Arterial injury
- Arteriovenous (AV) fistula
- Bleeding
- Bradycardia
- Breakage/ failure of instruments
- Cardiac arrest
- Cardiac injury, such as rupture, tear, or perforation, possibly resulting in pericardial effusion or cardiac tamponade
- Cerebrovascular accident
- Complications due to prolonged fluoroscopic radiation, such as skin burn
- Component failure

[40] EMPOWER™ MODULAR PACING SYSTEM Leadless Cardiac Pacemaker with Delivery Catheter Physician's Technical Manual

- Damage to cardiac structures, such as tissue damage, valve damage, or coronary arterial constriction
- Death
- Device embolism
- Disabling device unintentionally
- Electrolyte imbalance/dehydration
- Elevated thresholds
- Embolism, such as pulmonary embolism
- Extracardiac (muscle/nerve) stimulation
- Fixation deformation and/ or breakage
- Fluid accumulation
- Foreign body reaction/ rejection phenomena
- Heart failure following chronic RV apical pacing
- Heart failure, worsening
- Hematoma or seroma
- Inability to communicate with device, including inability to reprogram
- Inappropriate or ineffective rate response
- Incision site complications, such as excessive fibrotic tissue growth
- Induction or acceleration of arrhythmia
- Infection, including endocarditis
- Local tissue reaction
- Loss of capture
- Nerve damage
- Oversensing/undersensing leading to loss of pacing or inappropriate pacing
- Pacemaker syndrome
- Pain
- Pericardial rub, effusion, or pericarditis
- Pulse generator dislodgment or migration
- Renal failure from contrast media
- Surgery for early replacement or implantation of a new device, such as due to premature battery depletion
- Syncope
- Thrombosis, such as deep vein thrombosis
- Tissue necrosis, such as myocardial infarction (MI)
- Toxicity
- Valve damage
- Vasovagal response
- Venous occlusion

- Venous trauma, such as perforation, dissection, or erosion
- Vessel spasm

Patients may develop psychological intolerance to a pulse generator and may experience the following:

- Dependency
- Depression
- Fear of premature battery depletion
- Fear of device malfunction

18.2 Risks Associated with the mCRM Coordinated System

Potential adverse events and risks related to the mCRM Coordinated System may include, but are not limited to, the following[41]:

- Bleeding
- Bradycardia
- Cardiac arrest
- Change in amount of energy required to convert arrhythmia due to the presence of the LCP
- Communication failure between the S-ICD and the LCP
- Death
- Delayed therapy delivery
- Extracardiac (muscle/nerve) stimulation
- Failure to convert arrhythmia
- Failure to deliver therapy
- Hematoma or seroma
- Inability to defibrillate or pace
- Inappropriate therapy (e.g., shocks and antitachycardia pacing [ATP] where applicable, pacing)
- Induction or acceleration of arrhythmia
- LCP damaged by a shock from S-ICD
- Oversensing/undersensing
- Stroke
- Surgical revision or replacement of the mCRM System
- Syncope
- Thromoboemboli

[41]mCRM™ Modular Cardiac Rhythm Management System Model A209/ A219 (EMBLEM™), B170 (EMPOWER™) Physician's Technical Manual

Patients may develop psychological intolerance to a pulse generator system and may develop psychological disorders that include, but are not limited to, the following:

- Anxiety
- Depression
- Fear of device malfunction
- Fear of shocks

18.3 Risks Associated with MRI Scans

Potential adverse events differ depending on whether the MRI Conditions of Use are met. Refer to "MR Conditional mCRM™ Modular Cardiac Rhythm Management System (EMBLEM™ S-ICD and EMPOWER™ Leadless Cardiac Pacemaker) or MR Conditional Standalone EMPOWER™ Leadless Cardiac Pacemaker (LCP) MRI Technical Guide" for information on Conditions of use for the mCRM System, or standalone EMPOWER PG.

18.3.1 mCRM System Conditions of Use MET

- arrhythmia induction
- bradycardia
- damage to mCRM System component(s)
- muscle stimulation
- patient death
- patient discomfort due to slight movement and/or heating of mCRM System component(s)
- side effects of asynchronous pacing at elevated fixed rate and increased output including reduced exercise capacity, acceleration of heart failure, and competitive pacing/arrhythmia induction
- syncope
- worsening heart failure

18.3.2 mCRM System Conditions of Use NOT MET

- arrhythmia induction
- bradycardia
- damage to mCRM System component(s)
- defibrillation therapy not available
- erratic LCP and/or S-ICD behavior
- inappropriate pacing, inhibition of pacing, failure to pace
- inappropriate shock
- increased rate of LCP migration or dislodgement (within six weeks of LCP implant or revision)
- irregular or intermittent capture or pacing
- muscle stimulation
- pacing threshold changes

- patient death
- patient discomfort due to movement and/or heating of mCRM System component(s)
- physical movement of LCP
- sensing changes
- syncope
- worsening heart failure

18.3.3 EMPOWER-only Conditions of Use MET

- arrhythmia induction
- bradycardia
- patient death
- patient discomfort due to slight movement and/or heating of the LCP
- side effects of asynchronous pacing at elevated fixed rate and increased output including reduced exercise capacity, acceleration of heart failure, and competitive pacing/arrhythmia induction
- syncope
- worsening heart failure

18.3.4 EMPOWER-only Conditions of Use NOT MET

- arrhythmia induction
- bradycardia
- damage to the LCP
- erratic LCP behavior
- inappropriate pacing, inhibition of pacing, failure to pace
- increased rate of LCP migration or dislodgement (within six weeks of LCP implant or revision)
- irregular or intermittent capture or pacing
- pacing threshold changes
- patient death
- patient discomfort due to movement and/or heating of the LCP
- physical movement of LCP
- sensing changes
- syncope
- worsening heart failure

18.4 Risks Associated with Retrieval of the EMPOWER PG

Potential adverse events and risks related to retrieval of the EMPOWER PG may include, but are not limited to, the following[42]:

[42]EMPOWER™ Retrieval System Physician's Technical Manual

- Aneurysm or pseudoaneurysm
- Allergic reaction
- Arterial injury
- Arteriovenous (AV) fistula
- Bleeding
- Bradycardia
- Breakage/ failure of instruments
- Cardiac arrest
- Cardiac injury, such as rupture, tear, or perforation, possibly resulting in pericardial effusion or cardiac tamponade
- Cerebrovascular accident
- Complications due to prolonged fluoroscopic radiation, such as skin burn
- Component failure
- Damage to cardiac structures, such as tissue damage, valve damage, or coronary arterial constriction
- Death
- Device embolism
- Disabling device unintentionally
- Electrolyte imbalance/dehydration
- Embolism, such as pulmonary embolism
- Extracardiac (muscle/nerve) stimulation
- Fixation deformation and/ or breakage
- Fluid accumulation
- Foreign body reaction/ rejection phenomena
- Heart failure, worsening
- Hematoma or seroma
- Inability to communicate with device, including inability to reprogram
- Incision site complications, such as excessive fibrotic tissue growth
- Induction or acceleration of arrhythmia
- Infection, including endocarditis
- Local tissue reaction
- Nerve damage
- Pain
- Pericardial rub, effusion, or pericarditis
- Pulse generator dislodgment or migration
- Renal failure from contrast media
- Surgery for device removal
- Syncope

- Thrombosis, such as deep vein thrombosis
- Tissue necrosis, such as myocardial infarction (MI)
- Valve damage
- Vasovagal response
- Venous occlusion
- Venous trauma, such as perforation, dissection, or erosion
- Vessel spasm

18.5 Other Risks Associated with Participation in the Clinical Study

Treadmill walks and Holter monitoring are commercially approved procedures frequently used in patients, like those enrolled in the MODULAR ATP Clinical Study, with cardiovascular conditions and who receive CIEDs. However, they are not mandatory when a patient receives an S-ICD or a leadless pacemaker. Therefore, the potential risks of these procedures are considered to be related to the clinical study when required per protocol.

Subjects participating in the Rate Response Substudy portion of the MODULAR ATP Clinical Study will have added risks associated with the Treadmill Walk which may include, but are not limited to, the following:

- Arrhythmias
- Chest pain or discomfort
- Dyspnea
- Hypotension or hypertension
- Muscular or joint pain
- Myocardial infarction
- Pre-syncope or syncope
- Skin irritation or allergic reaction resulting from applications of adhesive patches
- Trauma from falling off the treadmill

Subjects participating in the Holter Monitor Substudy will have an added risk associated with the use of the Holter Monitor, which may include, but is not limited to, the following:

- Skin irritation or allergic reaction resulting from prolonged applications of the adhesive patches

There may also be additional risks which are unknown at this time.

18.6 Risk Minimization Actions

Additional risks may exist. Risks can be minimized through compliance with this protocol, performing procedures in the appropriate hospital environment, adherence to subject selection criteria, close monitoring of the subject's physiologic status during research procedures and/or follow-ups and by promptly supplying BSC with all pertinent information required by this protocol.

18.7 Anticipated Benefits

Anticipated benefits of the Coordinated System include the potential avoidance of shocks for monomorphic ventricular tachycardias that can be safely terminated with ATP. This could also positively impact the overall number of shocks that a given patient will receive during the device's life and their associated morbidity. As with the traditional transvenous ICD, the Coordinated System provides ATP and shock therapy while limiting the exposure to the risks frequently associated with long-term intravascular lead implantation. This is of particular importance for patients with challenging vascular access or high risk of infection who might not be candidates for transvenous ICD and whose arrhythmias might be successfully converted by ATP.

An additional anticipated benefit of the Coordinated System is the option to implant a leadless pacemaker in a patient with an existing S-ICD System who has developed a new indication for single-chamber right ventricular pacing. The alternative to this option would be the explant or inactivation of the S-ICD System and the implantation of a traditional transvenous ICD system, which would expose the patients to the risks frequently associated with long-term intravascular lead implantation.

18.8 Risk to Benefit Rationale

The implantation of an S-ICD has proven to be a successful/effective therapy to reduce sudden cardiac death without the complications associated with having leads in the vasculature and the heart. As such, it may be the only option for patients at high risk of sudden cardiac death with challenging or no venous access or complex congenital heart disease. For patients at risk of sudden cardiac death who do not require pacing or cardiac resynchronization therapy and are at high risk of infection, or have inadequate vascular access, implantation of an S-ICD is a Class I or Class IIb recommendation based on 2017 AHA/ACC/HRS and 2015 ESC guidelines, respectively. Furthermore, contemporary guidelines suggest that the advantages of the system compared to TV-ICDs make S-ICD implant beneficial in the broad population of patients at risk for sudden cardiac arrest if they do not have an indication for pacing or cardiac resynchronization therapy (Class I recommendation in the 2017 AHA/ACC/HRS guidelines, Class IIa recommendation in the 2015 ESC guidelines). According to the published data of the 2-year results from a pooled analysis of the S-ICD IDE Study and the EFFORTLESS registry[43], the S-ICD terminated spontaneous ventricular tachyarrhythmias in 90.1% of events with the first shock and in 98.2% of events within the 5 available shocks. Data from the UNTOUCHED Study revealed first shock conversion rate is 92.2%, and final shock conversion rate is 98.4%[44]. The addition of the EMPOWER PG, which can communicate with the S-ICD (Coordinated System), will provide the option of delivering ATP, which may reduce the number of unnecessary shocks and improve patients' quality of life and

---

[43] Burke MC, Gold MR, Knight BP, et al. Safety and Efficacy of the Totally Subcutaneous Implantable Defibrillator: 2-Year Results From a Pooled Analysis of the IDE Study and EFFORTLESS Registry. *J Am Coll Cardiol*. 2015 Apr 28;65(16):1605-1615.

[44] Gold MR, Lambiase PD, El-Chami MF, et al. Understanding Outcomes with the S-ICD in Primary Prevention Patients with Low Ejection Fraction (UNTOUCHED) Trial Primary Results. *Heart Rhythm Society*. Presented by Michael Gold, *Heart Rhythm*, D-LBCT02-05, 2020.

device longevity[45]. The incremental benefits related with providing ATP through the communication between S-ICD and the EMPOWER PG are expected to be greater than the risks related to implanting both systems. The benefit might be significantly greater for those patients who are not candidates to receive a TV-ICD for the reasons outlined above.

19 Safety Reporting

19.1 Reportable Events by Study Sites to Boston Scientific

Only events as described below are reportable in the MODULAR ATP Clinical Study. For this study, the mCRM Coordinated System will be referred to as the study device. Reporting starts from the date of informed consent. Refer to **Sections 18.1**, **18.2**, **18.3,** and **18.4** of this protocol, as well as the EMPOWER MPS PTM, mCRM PTM, and S-ICD User's Manual, for the known risks associated with the study devices.

ISO 14155, MDCG 2020-10/1, and 21 CFR Part 812 define various types of safety events. [redacted]. For this study, a subset of those events is reportable to the sponsor.

19.2 Reportable Adverse Events for this Study

Reportable adverse events for this study include those defined as a serious adverse event (SAE), adverse device effect (ADE), serious adverse device effect (SADE), unanticipated adverse device effect (UADE), and unanticipated serious adverse device effect (USADE). Refer to **Table 26-3** for definitions of each of these event types.

Specifically, adverse events to be reported in the MODULAR ATP Clinical Study include any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, if they meet any one of the following criteria:

- Led to death,
- Led to serious deterioration in the health of the subject as defined by either:
    - a life-threatening illness or injury, or
    - a permanent impairment of a body structure or a body function, or
    - in-patient hospitalization or prolongation of existing hospitalization (excluding planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without a serious deterioration in health), or

[45] Wathen MS, DeGroot PJ, Sweeney MO, et al. Prospective Randomized Multicenter Trial of Empirical Antitachycardia Pacing Versus Shocks for Spontaneous Rapid Ventricular Tachycardia in Patients With Implantable Cardioverter-Defibrillators: Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (PainFREE Rx II) Trial Results. Circulation. 2004;110:2591–2596.

- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function

- Led to fetal distress, fetal death, or a congenital abnormality or birth defect,
- Are related to the investigational medical device, procedure or protocol,
  - This includes events resulting from insufficiencies or inadequacies in the instructions for use, use error, or intentional abnormal use of the investigational medical device.
- Are unanticipated in nature, severity, or degree of incidence in the investigational plan, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
- Any reportable event experienced by the study subject after informed consent and once considered enrolled in the study (as defined in study subject classification **Section 9.2**), whether prior to, during, or subsequent to the study implant procedure, must be recorded in the eCRF.
- Underlying diseases and chronic conditions are not reported as AEs unless there is an increase in severity or frequency during the course of the investigation. Death should not be recorded as an AE, but should only be reflected as an outcome of one (1) specific SAE (refer to **Table 26-3**).

Note: S-ICD replacement due to normal battery depletion is not considered an adverse event for the MODULAR ATP Clinical Study and does not need to be reported.

19.3 Reportable Device Deficiencies

Reportable Device Deficiencies include any inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance. This may include malfunctions, use error, or inadequacy in the information supplied by the manufacturer.

19.4 Subject Death Reporting

A subject death during the study should be reported to BSC as soon as possible and, in any event, within three (3) calendar days of site notification. The site's IRB/EC/REB must be notified of any deaths in accordance with that site's IRB/EC/REB policies and procedures.

Notification of death must include a detailed narrative (death letter) that provides detailed information describing the circumstances surrounding the death **and is signed and dated by the Principal Investigator or authorized sub-Investigator**. **A death narrative in the local language is acceptable, and will be translated to English by BSC (signed by an authorized translator).** The details listed below must be addressed in the death narrative, for BSC to understand the circumstances surrounding the death:

- Date and time of death
- Place death occurred
- Immediate cause of death
- Cardiac rhythm at the time of death, if known (include any available documentation)

- Whether the death was related to the S-ICD System and/ or the EMPOWER System, clinical investigation, procedure, or patient condition
- Whether or not the death was witnessed
- S-ICD System and/ or the EMPOWER PG status and/or activity at the time of death (device recipients only – pacing, ATP, and defibrillation: active or inactive)
- Whether the patient had worsening heart failure
- Any other circumstances surrounding the death
- Approximate time interval from the initiating event to death (temporal course); items to consider include, but are not limited to: information regarding last time subject was seen by investigator, last office visit, etc.
- Investigator or sub-investigator signature and date

Also submit the following documentation:

- If the patient expired in the hospital:
    - A copy of the medical records for that admission (e.g., H & P, consults, test results, operative reports, and/or progress notes from the hospital chart)
    - Death certificate (if available)
    - Autopsy report (if applicable)
- If the patient expired outside of the hospital (e.g., at home):
    - A copy of the most recent clinic visit (if not already submitted to BSC)
    - Death certificate (if available)
    - Autopsy report (if applicable)

Whenever possible, the Coordinated System should be interrogated. The investigational Coordinated System (both S-ICD System and EMPOWER PG) should be removed intact and returned promptly to BSC for analysis, if possible. In the event of a death during the implant and/ or retrieval procedure, the EMPOWER delivery catheter, introducer sheath, and snare(s), and/or retrieval catheter must be returned to BSC for analysis.

The Clinical Events Committee (CEC) must review information regarding subject deaths, refer to **Section 21.2**.

19.5 Investigator Reporting Requirements

The communication requirements for reporting to BSC are as shown in **Table 19-1**. Only events as described in **Section 19.2** are reportable in the MODULAR ATP Clinical Study.

Adverse events should always be reported through the EDC system for the MODULAR ATP Clinical Study. However, in case of any issues where an alternative method of reporting is necessary (i.e. the EDC is not available), please report the adverse event to BSC by sending the AE Notification Form via email to the following email address:

[redacted]

Source documentation for UADE/USADE, SAE/SADE and BSC requested AE's can either be uploaded in the EDC system or sent via email, with the accompanying source document checklist to the following email address:

[redacted]

The Investigator must assess the relationship of the reportable AE to the study device, therapy/stimulation or procedure. See criteria in **Table 19-1**.

Table 19-1: Investigator Reporting Requirements

Event Classification	**Communication Method**	**Communication Timeline Pre-Market Studies*** (21 CFR 812; MDCG 2020-10/1:
Serious Health Threat	Complete applicable eCRF/paper form with all available new and updated information	• Within 1 business day of first becoming aware of the event • Reporting required through the end of the study
	Provide all relevant source documentation (deidentified/pseudonymized for reported event	• Upon request of sponsor
Unanticipated Adverse Device Effect / Unanticipated Serious Adverse Device Effect	Complete AE eCRF page with all available new and updated information	• Within 1 business day of first becoming aware of the event • Reporting required through the end of the study
	Provide all relevant source documentation (deidentified/ pseudonymized) for reported event	• Upon request of sponsor
Serious Adverse Event	Complete AE eCRF page with all available new and updated information	• Immediately, but not later than 3 calendar days of first becoming aware of the event or as per local/regional regulations • Reporting required through the end of the study
	Provide all relevant source documentation (deidentified/ pseudonymized) for reported event	• Upon request of sponsor
Serious Adverse Device Effects	Complete AE eCRF page with all available new and updated information	• Immediately, but not later than 3 calendar days of first becoming aware of the event or as per local/regional regulations • Reporting required through the end of the study

Table 19-1: Investigator Reporting Requirements

Event Classification	**Communication Method**	**Communication Timeline Pre-Market Studies*** (21 CFR 812; MDCG 2020-10/1:
	Provide all relevant source documentation (deidentified/ pseudonymized) for reported event	• When documentation is available
		• Upon request of sponsor
Device Deficiencies (including but not limited to malfunctions, use errors, and inadequacy in information supplied by the manufacturer, including labeling) Note: Any Device Deficiency that might have led to a serious adverse event if anappropriate action had not been taken, intervention had not occurred, circumstances had been less fortunate is considered a reportable event	Complete Device Deficiency section of the AE eCRF with all available new and updated information	• Immediately, but not later than 3 calendar days of first becoming aware of the event • Reporting required through the end of the study
	Provide all relevant source documentation (deidentified/ pseudonymized) for reported event	• Upon request of sponsor
Adverse Event including Adverse Device Effects	Complete AE eCRF page, which contains such information as date of AE, treatment of AE resolution, assessment of seriousness and relationship to the device	• In a timely manner (e.g., recommend within 10 business days) after becoming aware of the information • Reporting required through the end of the study • Upon request of sponsor
	Provide all relevant source documentation (deidentified/pseudonymized) for reported event as requested by the sponsor	

Table 19-1: Investigator Reporting Requirements

Event Classification	Communication Method	Communication Timeline Pre-Market Studies* (21 CFR 812; MDCG 2020-10/1:

* Please note that pre-market studies are clinical studies with investigational devices or with medical devices that bear the regulatory approval and are not being used for the same approved indications.

19.6 Sponsor and CEC Definitions and Classification

Events reported to BSC during the study will be reviewed and reported to comply with applicable regulations (relevant parts of ISO 14155 and/or 21 CFR Part 812). Investigators will be asked to classify whether an adverse event is considered serious or non-serious, whether it is anticipated or unanticipated (meets USADE/ UADE definition) as defined in **Table 26-3** [redacted] and whether it is considered device or procedure related, as defined in **Table 26-4**. Any event that is determined to be an unanticipated serious adverse device effect (USADE; ISO 14155) will also be considered an unanticipated adverse device effect (UADE; CFR Part 812), as defined in **Table 26-3**.

Death should not be recorded as an adverse event. Death should be recorded as an outcome of only one serious adverse event.

[redacted]

20 Informed Consent

Subject participation in this clinical study is voluntary. Informed Consent is required from each subject. The Investigator is responsible for ensuring that Informed Consent is obtained prior to the use of any investigational devices, study-required procedures and/or testing, or data collection.

The obtaining and documentation of Informed Consent must be in accordance with the principles of the Declaration of Helsinki, ISO 14155, any applicable national regulations, and local Ethics Committee and/or Regulatory authority, as applicable. The ICF must be accepted by BSC or its delegate (e.g., CRO), and approved by the site's IRB/EC/REB, or central IRB, if applicable.

Boston Scientific will provide a study-specific template of the ICF to investigators participating in this study. The ICF template may be modified to meet the requirements of the investigative site's IRB/EC/REB. Any modification requires acceptance from BSC prior to use of the form. The ICF must be in a language understandable to the subject and if needed, BSC will assist the site in obtaining a written consent translation. Translated

consent forms must also have IRB/EC/REB approval prior to their use. Privacy language shall be included in the body of the form or as a separate form as applicable.

The process of obtaining Informed Consent shall at a minimum include the following steps, as well as any other steps required by applicable laws, rules, regulations and guidelines:

- be conducted by the Principal Investigator or designee authorized to conduct the process,
- include a description of all aspects of the clinical study that are relevant to the subject's decision to participate throughout the clinical study,
- avoid any coercion of or undue influence of subjects to participate,
- not waive or appear to waive subject's legal rights,
- use native language that is non-technical and understandable to the subject or his/her legal representative,
- provide ample time for the subject to consider participation and ask questions if necessary,
- ensure important new information is provided to new and existing subjects throughout the clinical study.

The ICF shall always be signed and personally dated by the subject competent to sign the ICF under the applicable laws, rules, regulations and guidelines and by the investigator and/or an authorized designee responsible for conducting the informed consent process. The original signed ICF will be retained by the site and a copy of the signed and dated document and any other written information must be given to the person signing the form.

Failure to obtain subject consent will be reported by BSC to the applicable regulatory authority according to their requirements (e.g., FDA requirement is within 5 working days of learning of such an event). Any violations of the informed consent process must be reported as deviations to the sponsor and local regulatory authorities (e.g., IRB/EC/REB), as appropriate.

If new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the affected subject(s) in written form via a revised ICF or, in some situations, enrolled subjects may be requested to sign and date an addendum to the ICF. In addition to new significant information during the course of a study, other situations may necessitate revision of the ICF, such as if there are amendments to the applicable laws, protocol, a change in Principal Investigator, administrative changes, or following annual review by the IRB/EC/REB. The new version of the ICF must be approved by the IRB/EC/REB. Acceptance by Boston Scientific is required if changes to the revised ICF are requested by the site's IRB/EC/REB. The IRB/EC/REB will determine the subject population to be re-consented.

21 Committees

21.1 Data Monitoring Committee

The Data Monitoring Committee (DMC) is responsible for the oversight review of all AEs. The DMC will include leading experts in cardiology, and biostatistics who are not participating in the study and who have no affiliation with BSC. During the course of the study, the DMC will review accumulating safety data to monitor the incidence of CEC events and other trends that would warrant modification or termination of the study. Responsibilities, qualifications, membership, and committee procedures are outlined in the DMC Charter.

Any DMC recommendations for study modification or termination because of concerns over subject safety or issues relating to data monitoring or quality control will be submitted in writing to BSC for consideration and final decision. However, if the DMC at any time determines that a potentially serious risk exists to subjects in this study, the DMC chairman will immediately notify both BSC and the Principal Investigators.

21.2 Clinical Events Committee

A Clinical Events Committee (CEC) is an independent group of individuals with pertinent expertise that reviews and adjudicates all treated spontaneous episodes with available source documentation, relevant AEs, and all subject deaths reported by study investigators. Relevant AEs are those deemed to be attributed to either/ both of the PGs in the mCRM Coordinated System, the S-ICD electrode, or the procedure to implant the EMPOWER PG. The CEC will review a safety event dossier for each submitted AE or death, which may include copies of subject source documents provided by study sites, BSC reserves the right to submit other AEs as well, if deemed necessary.

Committee membership will include practitioners of cardiology, as well as other experts with the necessary therapeutic and subject matter expertise to adjudicate the event categories outlined above. CEC responsibilities, qualifications, membership, and committee procedures are outlined in the CEC charter.

22 Suspension or Termination

22.1 Premature Termination of the Study

Boston Scientific reserves the right to terminate the study at any stage but intends to exercise this right only for valid scientific or business reasons and reasons related to protection of subjects. Investigators, associated IRBs/ECs/REBs, and regulatory authorities, as applicable, will be notified in writing in the event of study termination.

22.2 Criteria for Premature Termination of the Study

Possible reasons for premature study termination include, but are not limited to, the following.

- The occurrence of unanticipated adverse device effects that present a significant or unreasonable risk to subjects enrolled in the study.
- An enrollment rate far below expectation that prejudices the conclusion of the study.

- A decision on the part of Boston Scientific to suspend or discontinue development of the device.

22.3 Termination of Study Participation by the Investigator or Withdrawal of IRB/ EC/ REB Approval

Any investigator, or associated IRB/EC/REB, or regulatory authority may discontinue participation in the study or withdraw approval of the study, respectively, with suitable written notice to Boston Scientific. Investigators, associated IRBs/ECs/REBs, and regulatory authorities, as applicable, will be notified in writing in the event of these occurrences.

22.4 Requirements for Documentation and Subject Follow-up

In the event of premature study termination, a written statement as to why the premature termination has occurred will be provided to all participating sites by BSC. The IRB/EC/REB and regulatory authorities, as applicable, will be notified. Detailed information on how enrolled subjects will be managed thereafter will be provided.

In the event an IRB, REB or EC terminates participation in the study, participating investigators, associated IRBs/ECs/REBs, and regulatory authorities, as applicable, will be notified in writing. Detailed information on how enrolled subjects will be managed thereafter will be provided by BSC.

In the event a Principal Investigator terminates participation in the study, study responsibility will be transferred to another investigator, if possible. In the event there are no opportunities to transfer Principal Investigator responsibility; detailed information on how enrolled subjects will be managed thereafter will be provided by BSC.

The Principal Investigator or his/her designee must return all study-related documents and investigational product, including the PRM software pen drive, to BSC, unless this action would jeopardize the rights, safety, or welfare of the subjects.

22.5 Criteria for Suspending/ Terminating a Study Site

Boston Scientific reserves the right to stop the inclusion of subjects at a study site at any time after the study initiation visit if no subjects have been enrolled for a period beyond 3 months after site initiation, or if the site has multiple or severe protocol violations/noncompliance without justification and/or fails to follow remedial actions.

In the event of termination of site participation, all study devices and testing equipment, as applicable, will be returned to BSC unless this action would jeopardize the rights, safety or well-being of the subjects. The IRB/EC/REB and regulatory authorities, as applicable, will be notified. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

23 Study Registration and Results

23.1 Study Registration

To comply with applicable laws and regulations, the study will be registered on a publicly accessible database.

23.2 Clinical Investigation Report

Study results will be made available in accordance with the legal requirements and the recognized ethical principles, in accordance with the Boston Scientific Policy. A Clinical Investigation Report will be made available to all investigators, IRB/EC/REB and regulatory authorities, as applicable in accordance with the Boston Scientific Policy and local requirements. As applicable an abbreviated Clinical Investigation Report will be made available on a publicly accessible database.

23.3 Publication Policy

BSC requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to a BSC study or its results. BSC will submit study results for publication (regardless of study outcome) following the conclusion or termination of the study. The study results submitted will include the number of subjects that enroll into the study, as well as the number of subjects that complete the study, a summary of results for primary and secondary outcome measures, statistical analyses, and adverse events.

Boston Scientific adheres to the Contributorship Criteria set forth in the Uniform Requirements of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org). In order to ensure the public disclosure of study results in a timely manner, while maintaining an unbiased presentation of study outcomes, BSC personnel may assist authors and investigators in publication preparation provided the following guidelines are followed:

- All authorship and contributorship requirements as described above must be followed.
- BSC involvement in the publication preparation and the BSC Publication Policy should be discussed with the Coordinating Principal Investigator(s) and/or Executive/Steering Committee at the onset of the project.
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

The data, analytic methods, and study materials for this clinical trial may be made available to other researchers in accordance with the Boston Scientific Data Sharing Policy (https://www.bostonscientific.com/)[redacted]

[redacted]

25 Abbreviations and Definitions

25.1 Abbreviations

Abbreviations are shown in **Table 25-1**.

Table 25-1: Abbreviations

Abbreviation/Acronym	Term
ADE	Adverse Device Effect
AE	Adverse Event
A/P	Anterior/ Posterior
AST	Automated Screening Tool
ATP	Anti-tachycardia Pacing
BSC	Boston Scientific
CA	Competent Authority
CEC	Clinical Events Committee
CFR (within stats sections)	Complication-free Rate
CFR	Code of Federal Regulations
CIED	Cardiac Implantable Electronic Device
CMS	Center for Medicare and Medicaid Services
CRF	Case Report Form
CRM	Cardiac Rhythm Management
DMC/ DSMB	Data Monitoring Committee/ Data and Safety Monitoring Board
DXA	Dexamethasone Acetate
EC	Ethics Committee
ECG	Electrocardiogram
EDS	Electrode Delivery System (for S-ICD)
EIT	Electrode Insertion Tools (for S-ICD)
EMPOWER MPS	EMPOWER Modular Pacing System; consists of the EMPOWER PG and implant delivery catheter
EMPOWER PG	EMPOWER Pulse Generator
EOS	End of Service (pertaining to EMPOWER PG battery)
ERI	Elective Replacement Indicator (pertaining to S-ICD PG battery)
Fr	French, a measurement system commonly used to measure the size of a catheter
FDA	Food and Drug Administration
ICD	Implantable Cardioverter Defibrillator
ICF	Informed Consent Form
IDE	Investigational Device Exemption
IRB	Institutional Review Board
ISO	International Standard Organization

Table 25-1: Abbreviations

Abbreviation/Acronym	Term
J	Joules
LAO	Left Anterior Oblique views
LCP	Leadless Cardiac Pacemaker
LOC	Loss of Capture
LRL	Lower Rate Limit
LVAD	Left Ventricular Assist Device
MCR	Metabolic-Chronotropic Relation
MPS	Modular Pacing System
MVT	Monomorphic Ventricular Tachycardia
P/A	Posterior/ Anterior
PCT	Pacing Capture Threshold
PG	Pulse Generator
PMDA	Pharmaceuticals and Medical Devices Agency
PMST	Paced Morphology Sensing Test
PRM	Programmer/ Recorder/ Monitor
PTM	Physician's Technical Manual
REB	Research Ethics Board
RV	Right Ventricle
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SCD	Sudden Cardiac Death
S-ECG	Subcutaneous electrocardiogram
S-ICD	Subcutaneous ICD
TSF	Technical Source Form
TV-ICD	Transvenous ICD
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
VF	Ventricular Fibrillation
VOO	Asynchronous pacing mode
VT	Ventricular Tachycardia

25.2 Definitions

Terms used in this protocol are defined in **Table 25-2**.

Table 25-2: Definitions

Term	Definition
S-ICD System	(EMBLEM/ EMBLEM MRI) S-ICD Pulse Generator, Models A209/ A219 or future BSC S-ICD Pulse Generator + (EMBLEM) S-ICD Electrode Model 3400/3401, Model 3501 or future BSC S-ICD Electrode[46]
EMPOWER MPS	EMPOWER Modular Pacing System, Model B170, which consists of the EMPOWER leadless pacemaker and the delivery catheter
EMPOWER PG	EMPOWER Pulse Generator: the leadless pacemaker

EMPOWER System	• EMPOWER MPS (EMPOWER pacemaker and Delivery Catheter) and Luer Cap (Model B170)
	• EMPOWER MPS accessories:
	  ○ EMPOWER Retrieval Catheter, Snare Catheter Lock, Luer Caps, and Hemostasis Valve (Model 8780)
	  ○ EMPOWER Introducer Sheath (Model 8782)[47]
	  ○ EMPOWER Conducted Telemetry Cable (Model 6396)
	  ○ EMPOWER Sterile Tray Cable (Model 6157)
	  ○ EMPOWER Single-loop Snare (Model 8784) or EMPOWER Tri-loop Snare (Model 8785)
	• LATITUDE Programming System (Model 3300)
	• Programmer Application Software (Model 3870) and associated Programmer Firmware
	• Guidewire
	• Electrocardiogram electrodes (supplied by clinical center)

Communication Success	Any evidence of a paced beat during communication testing in a given posture at the initial programmed communication Programmed Telemetry Setting
Communication Threshold Test	This is a communication test that results in determining the minimum Telemetry Value that achieves two successful communication tests, regardless of sequence. A Communication Threshold test is required at

[46] Note that Cameron Health Q-Trak Electrode Model 3010 is the same as BSC Models 3400/3401, and is also allowable.

[47] Note: Another compatible introducer sheath may be used that is not part of the EMPOWER System accessories. Refer to Table 26-1 and the EMPOWER Modular Pacing System Physician's Technical Manual and Label Supplement, as well as the EMPOWER Retrieval System Physician's Technical Manual and Label Supplement for more information.

Table 25-2: Definitions

Term	Definition
	Implant, Pre-Discharge, and the 1-Month Follow-up in one or more postures, as described in the specific follow-up section. A Communication Threshold test is required at any other protocol-required follow-up in the event of a failed Communication Test.
Communication Test	This is a communication test that is initiated at the initial programmed Telemetry Setting. A Communication Test is required at the 6-Month, and Semi-Annual Visits, as well as any Additional Visits which are conducted due to an adverse event related to communication of the mCRM Coordinated System. Note that if the Communication Test ends in unsuccessful communication, a Communication Threshold Test is required.
Coordinated System/ mCRM Coordinated System/ mCRM Therapy System	(EMBLEM) S-ICD System + EMPOWER PG
Major complication related to EMPOWER MPS	Major complications are those adverse events resulting in: • Death • Permanent loss of device function due to mechanical or electrical dysfunction of the device • Hospitalization • Prolonged Hospitalization by at least 48 hours* • System revision, including reposition, replacement, and explant. *Hospitalization is extended by ≥48 hours beyond expected hospital discharge (from implant or hospital admission for another cause)
mCRM Programmable Parameters	The S-ICD parameters listed below are not accessible without the PIN. These parameters are all related to ATP. • mCRM (On/Off) • Number of ATP Requests in Conditional Shock Zone (0, 1, 2, 3) • QUICK CONVERT™ ATP in Shock Zone (On/Off) • Telemetry Setting (1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7)
Normal battery depletion	A pulse generator that is not associated with a complaint and has reached its elective replacement indicator(s) with implant time that meets or exceeds the nominal (50th percentile) predicted longevity at default (labeled) programmable settings OR with implant time exceeding 75% of the expected longevity using the longevity calculation tool available at time of product introduction, calculated using the device's actual use conditions and programmable settings

Table 25-2: Definitions

Term	Definition
Permanent Loss of Device Function	Refers to: 1) the permanent loss of shock therapy and/or post shock pacing (S-ICD only); 2) permanent loss of appropriate sensing in all available sensing configurations (oversensing that results in persistent inappropriate shocks or undersensing that could lead to undetected arrhythmias) (S-ICD only). Loss of device function includes programming the PG permanently off or temporarily off in advance of an explant/revision (applies to both EMPOWER and S-ICD.
Patient/ Potential Subject	A person who is a potential candidate for the MODULAR ATP Clinical Study
Subject	A person who has been enrolled into the MODULAR ATP Clinical Study
Spontaneous episode	Any arrhythmia that is stored by the S-ICD pulse generator. For the purpose of the MODULAR ATP Clinical Study, only ventricular arrhythmias will be collected.
Time 0	Timing of study-required follow ups will be determined based on the date that the mCRM Coordinated System is implanted (successful implant of both the S-ICD System, with clinical firmware, and EMPOWER PG) **Note:** Subjects classified as a Partial Implant that are implanted with an EMPOWER PG must be followed according to this protocol, with all relevant EMPOWER PG device data and testing collected. Time 0 for the purpose of determining timing of follow ups for these subjects is the day it is determined the S-ICD will not be implanted.
Time to therapy for inductions	Time to therapy for induced episodes is defined as the interval starting 2000ms after the last induction artifact (the time of the post induction refractory) and ending at the onset of the shock deflection on the S-ECG recording.
Time to therapy for spontaneous episodes	Time to therapy for spontaneous episodes is defined as the interval starting when the cycle length of the patient's rhythm is greater or equal to the lowest programmed zone cutoff and measured until the start of delivery of ATP pulses or the shock marker.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

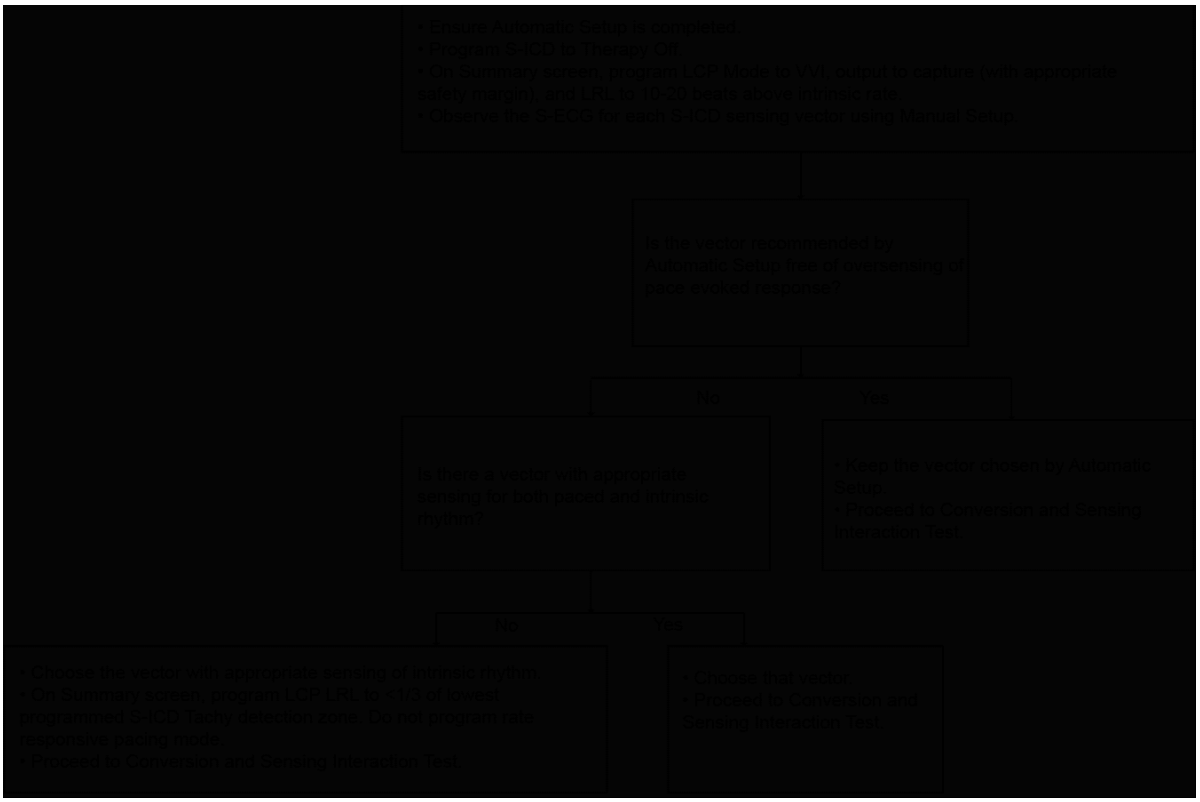
[redacted]

[redacted]

[redacted]

[redacted]

[redacted]


• Ensure Automatic Setup is completed.
• Program S-ICD to Therapy Off.
• On Summary screen, program LCP Mode to VVI, output to capture (with appropriate safety margin), and LRL to 10-20 beats above intrinsic rate.
• Observe the S-ECG for each S-ICD sensing vector using Manual Setup.
Is the vector recommended by Automatic Setup free of oversensing of pace evoked response?
No
Yes
Is there a vector with appropriate sensing for both paced and intrinsic rhythm?
• Keep the vector chosen by Automatic Setup.
• Proceed to Conversion and Sensing Interaction Test.
No
Yes
• Choose the vector with appropriate sensing of intrinsic rhythm.
• On Summary screen, program LCP LRL to <1/3 of lowest programmed S-ICD Tachy detection zone. Do not program rate responsive pacing mode.
• Proceed to Conversion and Sensing Interaction Test.
• Choose that vector.
• Proceed to Conversion and Sensing Interaction Test.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]	[redacted]
	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]
		[redacted]
	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]
		[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	
	[redacted]	
	[redacted]	

[redacted]	[redacted]	[redacted]
	[redacted]	
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]
	[redacted]	

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]
	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]
	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	
[redacted]	[redacted]	[redacted]
	[redacted]	
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	
[redacted]	[redacted]	[redacted]
	[redacted]	
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]
	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]	[redacted]	[redacted]
		[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]