related to the Solia S LBB lead that occur through 3 months post-implant, where a Solia S LBB lead includes leads that were implanted or attempted to be implanted in the LBB area. The period of observation starts from the time of the first attempt to implant the Solia S lead in the LBB area through 3 months (90 days) post-implant. Additionally, if an AE meeting primary endpoint 1 criteria is reported after the date of the 3-month follow-up, but on or before 3 months post-implant, this AE will be included in the primary endpoint 1 analysis.

The AE classification, category, resolution and relation to the study device (Solia S LBB lead) for each individual event will be determined by the Clinical Event Committee (CEC) (see Section 9.3).

All SADEs for which the CEC determines the event is causally related or probably related to the Solia S LBB lead will be included in the primary endpoint 1 analysis. In addition, the following serious procedure related events will also be included:

- Pneumothorax directly associated with the Solia S LBB lead or Solia S LLB lead implant procedures
- Cardiac perforation with or without tamponade caused by the Solia S LBB lead or Solia S LLB lead implant procedures

Adverse events with a final CEC adjudicated relation of not related or possible relation will not contribute to or be included in the evaluation of primary endpoint 1.

Finally, subject deaths resulting from a Solia S LBB lead AE will be included in the primary endpoint analysis.

6 Ethics and Regulatory Considerations

6.1 Regulatory Compliance

This study will be conducted according to local legal and regulatory requirements, applicable federal regulations. Adverse events are reported according to ISO 14155 and FDA definitions (refer to Section 5.1).

The study will be conducted in compliance with the international scientific and ethical quality standard for clinical trials known as good clinical practice (ICH GCP). This study will be publicly registered on https://clinicaltrials.gov/.

6.2 Institutional Review Board Approval

Institutional Review Board (IRB) approval is required from each institution prior to participation in this clinical study. Subject enrollment may not begin until both the IRB and BIOTRONIK have granted approval for the study site. IRB approval is also required throughout the duration of this clinical study. If IRB approval is withdrawn, BIOTRONIK must be notified within 5 working days.

6.3 Other Institutions and Physicians

This clinical study is not transferable to other institutions attended by the investigator unless prior approval is obtained from both BIOTRONIK and the appropriate IRB. Only approved investigators are authorized to participate in the study and implant the Solia S lead in the LBB area.

There are certain situations where an investigator might not be immediately available to provide the necessary medical care for a subject enrolled in the clinical study (such as a subject emergency room visit for medical treatment). In these instances, a protocol deviation will not be issued, and all available data will be utilized. In any such situations, the IRB and the investigator must continue to provide oversight for that patient's medical care and rights as a research subject.

6.4 Informed Consent

All subjects must sign and date an IRB approved Informed Consent Form (ICF) prior to enrollment or conducting any protocol related procedures. If a subject is consented and not implanted within 30 days, the subject must be re-consented. Legally authorized representatives are not allowed to consent on a subject's behalf. Informed consent must be obtained in accordance with the FDA regulations (21 CFR Part 50), ISO 14155, ICH GCP Guidelines, the Declaration of Helsinki and any other national or local requirements.

This study does not include vulnerable patient populations. This study does not allow emergency implants of the study device without patient informed consent. The investigator is required to inform BIOTRONIK and the reviewing IRB within 5 working days after the investigational device use occurs if any subject was not appropriately consented to participate in the study. BIOTRONIK is then required to report any failure to obtain subject consent to the FDA within 5 working days of learning of such an event.

The consent process, including discussion of the study, should be documented within the subject's medical record. A copy of the completed signed and dated informed consent form should be given to the subject.

6.5 Investigator Responsibilities

Investigators are responsible for:

- Conducting the investigation in accordance with the agreement, the investigational plan, applicable FDA regulations including 21 CFR Part 50, Part 56 and Part 812, and conditions of approval imposed by the reviewing IRB or FDA;
- Supervising all testing of the device involving human subjects;
- Ensuring that the requirements for obtaining informed consent are met; and
- Providing sufficient accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement as required under 21 CFR Part 54. This includes promptly updating this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.

7 Data Collection

7.1 Electronic Data Capture (EDC)

Mednet Solutions, Inc. (Mednet) is a privately held company that specializes in web-based clinical data management technology. Mednet will host the EDC system and provide a secure environment that is accessible to authorized individuals through the internet (iMednet). BIOTRONIK will implement a study specific configuration using this software to meet the data collection requirements of the protocol. The EDC system is 21 CFR Part 11 compliant and is the platform for electronic case report form (eCRF) data entry, clinical data discrepancy resolution, and access to reports for BIOTRONIK, specified study sites, and any other parties authorized by BIOTRONIK.

7.2 Electronic Case Report Forms (eCRFs)

Each site is responsible for submitting original data in the EDC system via completion of eCRFs and the upload of associated source documentation. The investigator will be required to use an electronic signature to approve the content of the data reported in the eCRFs.

The iMednet EDC system incorporates the ability for sites to upload subjects' unredacted, signed and dated ICFs if permitted by institutional policy or local regulations. BIOTRONIK may request additional documentation for sites not permitting upload of unredacted ICFs in EDC. iMednet is compliant with 21 CFR Part 11 Electronic Records; Electronic signatures. Mednet systems utilize industry standard methods for maintaining confidentiality and integrity of client data, and include (but are not limited to) SSL encryption, digital signatures, and secure technology policies and procedures.

7.3 BIOTRONIK Home Monitoring® Data

Home Monitoring Service Center data from enrolled study subjects will be accessible to the sponsor from implant through the date of subject withdrawal of consent, subject death, or completion of the study. For subjects that are exited for other reasons (including investigator-initiated withdrawal, subject moving, and lost to follow-up) BIOTRONIK Home Monitoring® data may be collected for the proposed study duration (i.e. up to approximately 12 months after implant). BIOTRONIK Home Monitoring® data may be used for evaluation and publication if desired by the sponsor.

All data are transferred to the sponsor in a pseudonymized form. Data includes all information transmitted from the device (e.g. IEGMs, statistics, lead information).

7.4 Data Quality Control

BIOTRONIK will review study data reported in the EDC system. At any time, reports may be generated on data completion and missing data for each study site. The EDC system will be used to track received and expected follow-up data and eCRFs for each participant. This system provides the capability to monitor the status, volume, and

disposition of data. In addition, study data will undergo automatic edit and plausibility checks which provide information to the study sites to help improve and maintain data quality control procedures designed to detect inaccuracies and inconsistencies.

To ensure protocol compliance at all participating study sites, BIOTRONIK monitors will conduct centralized monitoring and/or monitoring visits throughout the course of the study (refer to Section 10).

7.5 Subject Data Confidentiality

All information and data collected concerning subjects or their participation in this investigation will be considered confidential by personnel at BIOTRONIK, BIOTRONIK's parent company, its subsidiaries and affiliates, as well as contracted designees such as the Clinical Events Committee (CEC), Mednet Solutions, Inc. and any other authorized third parties.

Only authorized BIOTRONIK personnel or an authorized BIOTRONIK representative will have access to these confidential files. All data will be handled in accordance with applicable international, national and local laws, including the Health Insurance Portability and Accountability Act (HIPAA) of 1996 and amendments. In order to verify the study data and ensure study integrity, monitors from BIOTRONIK, the FDA, other national regulatory and/or public health authorities and the reviewing IRB, if applicable, may review and/or copy the study records. Source documents supplied to the CEC will have confidential subject identifiers redacted. All data used in the analysis and reporting of this study will not include subject names or other identifiable references.

7.6 Protocol Compliance

The investigator is required to conduct this study in accordance with the signed Investigator Agreement and clinical protocol. The investigator shall notify BIOTRONIK and the reviewing IRB in writing no later than 5 working days after any significant deviation from the clinical protocol to protect the life or physical well-being of a subject in an emergency. Except in such emergency, prior approval by BIOTRONIK is required for significant deviations from the clinical protocol.

The site is responsible for reporting noncompliance via Protocol Noncompliance eCRFs in the EDC system. BIOTRONIK categorizes protocol noncompliance instances as reported in the interim and final clinical progress reports to FDA.

BIOTRONIK will evaluate the noncompliance and issue corrective actions, as necessary, which may include but are not limited to, re-training, discontinuing enrollment at the study site, or closing the study site.

7.7 Protocol Violations

Protocol violations are defined as instances where the protocol requirements and/or regulatory guidelines were not followed and are generally more serious in nature than deviations. Protocol violations are considered to potentially affect the subject's rights, safety, or well-being, and/or the scientific soundness/data reliability, accuracy, or completeness of the primary study endpoint data.

Protocol violations include, but are not limited to:

1. Failure to obtain consent or other instances in which the subject did not provide consent.
2. Subject inclusion/exclusion violations.
3. Protocol requirement violations that affect the primary endpoint(s) of the study design.
4. Unapproved investigator performing the implant procedure using the Solia S lead in the LBB area.
5. Study implant performed at unapproved location.

7.8 Protocol Deviations

Protocol deviations are defined as instances where protocol requirements or regulatory guidelines were not followed but are generally less serious in nature than violations. Protocol deviations generally do not affect the subject's rights, safety, or well-being and/or the completeness, accuracy and reliability of the study primary endpoint data. Instances of noncompliance should be considered a deviation if it does not meet the criteria for being considered a violation.

Protocol deviations include, but are not limited to:

1. Informed Consent documentation issues such as incomplete ICF, missing dates for signature(s), missing initials or illegible information, subject signature date completed by someone other than subject, utilization of an outdated or non-IRB approved ICF, incomplete associated forms required at time of consent, etc. This is not an exclusive list.
2. Procedure not performed within the allowed timeframe.
3. Required data not obtained.

7.9 IRB Reporting of Noncompliance

The investigator must notify the reviewing IRB of all noncompliance issues per the IRB and protocol reporting requirements. At a minimum, all violations and noncompliance issues related to informed consent and informed consent documentation should be reported to the IRB.

In some instances, such as failure to obtain consent, the investigator should also seek guidance from the IRB to ensure the subject received appropriate information to consider their participation in the study.

The site should provide a copy of the IRB protocol noncompliance notification (as applicable) to BIOTRONIK.

7.10 Follow-up Compliance

Sites are expected to ensure follow-up visit compliance over the duration of the study.

The EDC system includes an overview of each subject's follow up schedule, including the windows for each follow-up. BIOTRONIK will provide additional tools to the sites in an effort to minimize the number of subjects that are lost to follow-up.

In addition, BIOTRONIK monitors will review subjects, including those that may be lost to follow-up, to ensure protocol and study visit compliance.

7.11 Audits/Inspections

Study centers may undergo audits or inspections during the course of and after completion of the clinical study by BIOTRONIK or BIOTRONIK designees, the IRB, the FDA, competent authorities, or other applicable regulatory authorities.

The investigator must provide all clinical study documents including the medical records for all enrolled subjects as requested during an audit/inspection.

7.12 Investigational Device Handling

This study will occur under an IDE as the Solia S lead does not currently have labelling for sensing and pacing in the LBB area. All other devices utilized in conjunction with this study are U.S. market approved and prescribed by physicians according to approved indications for use. Since the Solia S lead is a market-released product there will not be investigational device labelling or control of the devices by BIOTRONIK as described in 21 CFR Part 812. BIOTRONIK will maintain a list of physicians who are approved to perform the implant procedure for this study as well as a list of study locations approved by the IRB for investigational procedures.

8 Risk/Benefit Analysis

8.1 Anticipated Clinical Benefits

Subjects who are treated with LLB area pacing may benefit from potential advantages of this implant methodology. As described in Section 1.2, the LBBAP maintains the benefits or physiological pacing, which include narrowing of QRS complexes and improved LVEF, as compared to RVP (Su L et al. 2021). Additionally, LBBAP has demonstrated a reduction in the combined outcomes of heart failure hospitalization, mortality, and upgrade to biventricular pacing as compared to RVP (Sharma P et al. 2021). Additionally, enrolled subjects may benefit from intensified monitoring of the device functionalities during the study period.

Information gained from the conduct of this study may be of benefit to others with the same medical condition. Safety and efficacy data collected on the Solia S lead when implanted in the LBB area will contribute to expand the knowledge of use of conduction system area pacing.

8.2 Anticipated Risks

8.2.1 Risks Associated with Participation in the Study

Subjects participating in this study have an indication for pacemaker therapy and per the inclusion/exclusion criteria are already being considered for LBB area pacing. However, there are specific risks associated with lead implant in the LBB area.

In some cases, implantation of the Solia S lead in the LBB area may not be possible. The physician will determine if the target location for Solia S implant will be changed from LBB to another location, such as the apex of the right ventricle. This decision may be made prior to implant or during implant if attempts to place the lead in the LBB area are unsuccessful or placement does not provide adequate pacing or sensing. Unsuccessful placement of pacing leads in the LBB area occurs in about 3% to 12% of patients (Su L et al. 2021; Padala S et al. 2020; Li X et al. 2021; Vijayaraman P et al. 2019; Wang J et al. 2020; De Pooter J et al. 2020; Li X et al. 2019; Zhang S et al. 2021). Additionally, the duration of implant procedure and fluoroscopy is often longer for LBB area implants. On average, procedure duration is expected to be 26 minutes longer (98 minutes for LBBAP versus 72 minutes for RVP) and fluoroscopy duration is expected to be 7 minutes longer (13 minutes for LBBAP versus 6 minutes for RVP) (Sharma P et al. 2021).

Lead implants in the left bundle branch area also have an increased risk of septal perforation. Published data suggests the risk of perforation of the septum is between 0% and 7.0% (Zhang S et al. 2021; Li X et al. 2021; De Pooter J et al. 2020). In contrast, perforation of the right ventricle is estimated at up to 1.2% (Mahapatra S et al. 2005). Additionally, the risk of coronary artery injury may be increased with

lead bundle branch area pacing. This rare complication has been documented a limited number of times for RVP (Pang BJ et al. 2015) and noted one time as a complication in LBBAP (De Pooter J et al. 2020). The most common post-procedure complications, such as lead dislodgment or threshold increase, occur at a similar rate or slightly lower rate for LBBAP as compared to RVP (Li Y et al. 2021; Sharma P et al. 2021).

8.2.2 Steps to Control or Mitigate the Risks

Overall risks due to prolonged implant procedure, such as increase in surgical site infection, bleeding, and pneumothorax, can be minimized through the utilization of strict aseptic technique, compliance with the device technical manuals, compliance with this clinical investigation plan, adhering to the guidelines for selection of patients, and monitoring of the patient status during implant and follow-up. Risks related to increase in radiation exposure due to longer fluoroscopy are anticipated no higher than those for a CRT-D implant, with reported mean fluoroscopy time of 22 ± 18 minutes (Heist E et al. 2012). Procedures to minimize radiation exposure for the patient, implanting physician, and supportive staff, such as lab awareness programs and plans for use of radioprotection, are standard and compliance with these requirements will minimize exposure.

To further reduce potential risks, participating implanting physicians are selected based on knowledge of conduction system pacing and prior implant experience with Solia S. Additionally, the protocol limits lead placement attempts in the left bundle branch area to no more than five.

Home Monitoring® activation is recommended for study subjects as it enables remote monitoring post-implant. These daily transmissions can be used by site and study personnel to monitor and pro-actively identify any potential post-implant complications or events between follow-up visits.

8.3 Risk-to-Benefit Rationale

As enrolled subjects are already being considered for conduction system pacing, the risk of unsuccessful Solia S lead implant is anticipated to be similar to use of other pacing leads. Similarly, the risk of complications related to use of Solia S in LBB area pacing are expected to occur at a rate comparable to published findings. Given the demonstrated benefits of LBB area pacing and possible benefit to the patient due to increased monitoring, BIOTRONIK believes the potential benefits exceed the potential risks associated with participation in this study.

9 Study Organization

9.1 Sponsor

BIOTRONIK as the study sponsor, has the overall responsibility for the conduct of the study, including ensuring that the study meets and is conducted within the regulatory requirements specified by each reviewing regulatory authority. The sponsor will ensure adherence to the sponsor general duties, selection of study site investigators, monitoring, supplemental applications, maintaining records and submitting reports.

BIOTRONIK's general duties include submitting the application to appropriate regulatory authorities and obtaining overall regulatory approval.

BIOTRONIK is responsible for ensuring informed consent is obtained, proper clinical site monitoring is performed, providing quality data that satisfy regulations, and informing study investigators of UADE and deviations from the protocol, as appropriate.

BIOTRONIK will prepare written reports and a final report as directed. BIOTRONIK Clinical Studies personnel will provide information, assistance, and training needed to conduct the study.

9.2 National Principal Investigator

The National PI is an independent physician familiar with cardiac rhythm management devices and with experience implanting pacing leads in the LBB area. The National PI will assist BIOTRONIK in the planning and conduct of the study and provide scientific and medical expertise.

9.3 Clinical Events Committee

A Clinical Events Committee (CEC) will be established consisting of four independent physicians familiar with cardiac rhythm management devices. All adverse events reported by sites that may be related to 1) the Solia S lead implanted or attempted to be implanted in the LBB area, and/or 2) implant procedures, will be adjudicated by the CEC. The CEC may also evaluate and categorize LBBAP characteristics. Source documents supplied to the CEC will have confidential subject identifiers and site identifiers redacted.

The CEC is charged with the development of specific criteria used for the categorization of clinical events and clinical endpoints in the trial. Explicit rules outlining the minimum amount of data required, and the algorithm followed to classify study endpoint–related clinical events will be established.

10 Monitoring

10.1 Summary

The responsibility of BIOTRONIK as sponsor is to ensure protocol and regulatory compliance through proper monitoring of the clinical study at sites.

BIOTRONIK utilizes a risk-based monitoring strategy consistent with FDA's Guidance for Industry: Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring (2013). Risk-based monitoring starts with performing a study risk assessment of the identified critical data and processes. The resulting monitoring plan focuses on targeted source data verification and trend analyses to improve oversight and data quality, while integrating predefined triggers for additional monitoring visits. The detailed study risk-based monitoring plan developed by BIOTRONIK focuses on a combination of centralized monitoring and monitoring visits.

As BIOTRONIK utilizes risk-based monitoring, the ability to upload unredacted ICFs is one of the factors taken into account when determining the need for a monitoring visit. An unredacted version of the subject's signed and dated ICF allows the centralized monitor to verify that the ICF was signed and dated by the subject prior to study procedures being conducted and that the subject signature and date are legible, complete, and correlate with the subject initials entered into EDC.

Monitors may periodically conduct on-site or remote monitoring visits during the clinical study in accordance with the monitoring plan. On-site monitoring visits are an in-person evaluation carried out at the study site. Remote monitoring visits are a remote evaluation of a study site for those sites providing remote sponsor access to the electronic medical record system. Sites are required to support these monitoring visits and the study monitoring effort, including either direct monitor or site-assisted access to the applicable medical record systems. The principal investigator is encouraged to be available during monitoring visits. Monitoring visits will also provide an assessment of the continued acceptability of the facilities to continue participation in the study.

Centralized monitoring may be conducted throughout the course of the study in accordance with the monitoring plan. Centralized monitoring is conducted via investigator signed electronic case report forms (eCRFs) and/or eCRFs in complete status through the source data verification of source documents uploaded to the eCRF. Some examples of data that may be monitored remotely include: informed consent forms, enrollment, eligibility, implant, study termination, device data, and adverse events reported in the EDC system. Sites are required to support centralized monitoring by providing signed, dated and final source documents to BIOTRONIK in order to source data verify data reported in the EDC system and resolving queries in a timely manner.

The E6(R2) Good Clinical Practice: Integrated Addendum to International Council for Harmonisation (ICH) E6 (R1) Guidance for Industry dated March 2018 outlines the ALCOA-C guidelines for source documentation. All source documentation and study records should meet these ALCOA-C guidelines of attributable, legible,

contemporaneous, original, accurate and complete. This guidance ensures the confidentiality, credibility, accuracy and validation of research records.

Through monitoring visits and/or centralized monitoring, BIOTRONIK will assess the site's performance in the following areas:

- Verification that informed consent was obtained and documented properly
- Adherence to protocol eligibility criteria and requirements
- Conduct and documentation of procedures and assessments related to:
    - Study objectives
    - Protocol required data collection and procedures
    - Evaluating, documenting, and reporting adverse events, unanticipated adverse device effects, and withdrawals, especially when a withdrawal may be related to an adverse event or unanticipated adverse device effect
    - Investigator oversight and delegation of authority to site personnel
    - Verification of study-specific required documentation
    - Procedures essential to trial integrity
    - Adherence to applicable requirements regarding the obligations of the investigator and maintenance of records.

Entries in eCRFs will be reviewed and source data verified by monitors (authorized BIOTRONIK personnel) to ensure that the investigator and the study team conducts the study in accordance with the protocol and applicable FDA and local laws and regulations to ensure adequate protection of the rights, safety and well-being of subjects and the quality and integrity of the resulting data. In addition, BIOTRONIK may require the presence of personnel from BIOTRONIK at implant and/or follow-up visits outlined in this protocol in order to assist the investigator and other site personnel.

If a monitor becomes aware that an investigator is not complying with the signed Investigator Agreement, the study protocol, applicable laws, and FDA and/or local regulations and any conditions of approval imposed by the reviewing IRB, the monitor is obliged to notify BIOTRONIK study management. BIOTRONIK will evaluate the noncompliance and issue corrective actions, as necessary, which may include but are not limited to, re-training, discontinuing enrollment at the study site, or closing the study site.

10.2 Monitors

Monitors are trained, qualified, and designated by BIOTRONIK Clinical Studies Management to oversee the progress of an investigation at the clinical site. Additional monitors may be appointed as necessary.

11 Study Completion or Early Termination

BIOTRONIK will notify the study site upon completion or termination of the clinical study or of the investigator's participation. No formal statistical rule for early termination of the trial due to insufficient effectiveness or safety issues has been defined.

BIOTRONIK reserves the right to discontinue the clinical study at any stage, with suitable written notice to the investigator. Possible reason(s) may include but are not limited to:

- An unanticipated adverse device effect occurs and it presents an unreasonable risk to subjects.
- Further product development is cancelled.
- Sufficient data has been collected to support the endpoint analysis.

Should discontinuation of the trial occur, the investigator shall return all clinical trial materials to the sponsor and provide a written statement to the IRB explaining reasons for premature termination. In the event of a premature termination of the clinical investigation enrolled subjects will be followed up as per the institution's standard of care.

Whenever possible, BIOTRONIK will provide a final report and a copy of the site's eCRFs to each study site as required by FDA regulations. BIOTRONIK will determine and provide details on closure activities to all investigators to ensure the investigator understands any applicable regulatory requirements, including those related to record retention. All participating investigators are required to promptly notify BIOTRONIK if their financial disclosure information has any relevant changes during the course of the study or for one (1) year following completion of the study, in accordance with 21 CFR Part 54.4.

12 Records and Reports

12.1 Investigator Records

Investigators are required to maintain on file the following accurate, complete and current records relating to this investigation:

- All correspondence relating to the study with another investigator, an IRB, BIOTRONIK, a monitor, or any other regulatory agency (e.g., a letter sent from the investigator to the IRB).
- A copy of the clinical study protocol.
- Signed investigator or research agreement.
- Signed Financial Disclosure Form.
- A copy of the IRB approval for the research study.
- A copy of the IRB approved subject Informed Consent Form.
- Records showing use of all investigational devices
- All documentation, including:
    - A copy of all signed Informed Consent Forms.
    - Date and time of exposure to investigational device
    - All supporting documentation for data entered into the EDC system.
    - Records of any adverse events, including supporting documentation.
    - Records pertaining to subject deaths during the study.
    - Documentation and rationale for any deviations from the clinical protocol.
    - Documentation of training.
    - Any other records required by BIOTRONIK.

The investigator must retain records related to the study for a minimum period of 2 years after the investigation is completed consistent with FDA regulations, IRB requirements, and institutional policies. Please ensure that BIOTRONIK is notified of any transfer of records, including changes to your site's address or principal investigator status during the required 2-year period.

12.2 Investigator Reporting Responsibilities

Investigators are required to prepare and submit to BIOTRONIK the following complete, accurate, and timely reports on this investigation as identified in the table below which outlines the responsibilities, including time constraints, for submitting required reports. Additionally, investigators are required to provide any other information upon the request of an IRB, regulatory authority, or BIOTRONIK.

Table 9: Investigator Reporting Responsibilities

Type of Report	Prepared by Investigator for:	Time Constraints of Notification
Unanticipated adverse device effect (UADE) *FDA 21 CFR 812* *ISO 14155:2020*	BIOTRONIK*, IRB	Within 10 working days after notification of the effect
Subject death during investigation	BIOTRONIK*, IRB	BIOTRONIK as soon as possible after notification of the death and as required by reviewing IRB
Withdrawal of IRB approval *FDA 21 CFR 812*	BIOTRONIK	Within 5 working days of receipt of notice of withdrawal of approval
Progress Report(s) *FDA 21 CFR 812*	BIOTRONIK, the monitor, IRB	At regular intervals, but submitted no less than yearly
Significant deviations from study plan *FDA 21 CFR 812*	BIOTRONIK, IRB	Within 5 working days after emergency to protect life or physical well-being of subject, otherwise prior approval by BIOTRONIK is required
Informed consent not obtained *FDA 21 CFR 812*	BIOTRONIK, IRB	Within 5 working days of use of Solia S in the LBB area
Final report *FDA 21 CFR 812*	BIOTRONIK, IRB	Within 3 months after termination or completion of the study or investigator's part of the study

*Documentation of event via EDC eCRF

12.3 Sponsor Records

BIOTRONIK will maintain the following records:

- All correspondence with the investigator(s), IRB(s), and the FDA that pertains to the study
- Investigator agreements, financial disclosures, and curriculum vitae
- Name and address of each investigator and each IRB that is involved with the investigation

- Adverse events
- Adverse device effects
- Complaints
- Electronic Case Report Form data
- Confirmation of completed subject informed consent forms
- Clinical study protocol
- Qualification visit reports
- Monitoring visit reports
- Clinical progress reports

12.4 Sponsor Reporting Responsibilities

BIOTRONIK is responsible for preparing the following reports, when necessary:

Table 10: Sponsor Reporting Responsibilities

Type of Report	Prepared by BIOTRONIK for:	Time Constraints of Notification
Unanticipated adverse device effect (UADE) *FDA 21 CFR 812*	FDA, all reviewing IRBs, and participating investigators	Within 10 working days after notification of effect
Withdrawal of IRB approval *FDA 21 CFR 812*	FDA, all reviewing IRBs and participating investigators	Within 5 working days after receipt of notice of withdrawal of approval
Withdrawal of FDA approval *FDA 21 CFR 812*	All reviewing IRBs and participating investigators	Within 5 working days after receipt of notice of withdrawal of approval
Current investigator list *FDA 21 CFR 812*	FDA	Names and addresses of participating investigators at 6-month intervals
Progress report *FDA 21 CFR 812*	FDA, all reviewing IRBs	Submitted at least annually, unless otherwise specified by FDA
Recalls and device disposition *FDA 21 CFR 812*	FDA, all reviewing IRBs	Within 30 working days and will include reasons for any request that an investigator return, repair or otherwise dispose of any devices

Type of Report	Prepared by BIOTRONIK for:	Time Constraints of Notification
Final report *FDA 21 CFR 812*	FDA, all reviewing IRBs and participating investigators	A final report will be submitted within 6 months after completion or termination of the study.
Informed consent not obtained *FDA 21 CFR 812*	FDA	Within 5 working days of notification of occurrence
Study closure *FDA 21 CFR 812*	FDA, all reviewing IRBs, and participating investigators	Within 30 working days of completion or decision to terminate the study.

13 Insurance

Subjects who participate in this study will be insured against study related injury according to local regulatory requirements.

BIOTRONIK has obtained clinical trial liability insurance with appropriate coverage for the continuation of the entire study.

14 Publication Policy

BIOTRONIK intends to publish the results of this clinical study. As this is a multi-site study, publication or presentation of the results of the study conducted at an institution shall not be made before the first multi-site publication by BIOTRONIK and the Study National Principal Investigator. If there is no multi-site publication within 12 months after the study has been completed or terminated at all study locations, the institution and principal investigator shall have the right to publish and/or present the results of the study generated or collected at the institution. Before publishing, however, the institution and investigator shall submit copies of any manuscript proposed for publication to BIOTRONIK for review at least 30 days in advance of submission for publication or presentation to a publisher or other third party. BIOTRONIK reserves the right to delete any confidential information or other proprietary information (including trade secrets and patent protected materials) that is being utilized and inappropriately released, and to provide input from other investigators in the study regarding the content and conclusions of the publication or presentation. In addition, BIOTRONIK may extend such review period to file patent applications or take other steps to protect its intellectual property interests or to remove from the paper or presentation any language that may impact BIOTRONIK's intellectual property interests.

BIOTRONIK reserves the right to include the report of this clinical study in any regulatory documentation or submission or in any informational materials prepared for the medical profession. The ownership of the data shall at all times be held by BIOTRONIK.

15 Abbreviations and Acronyms

Abbreviation / Acronym	Complete Term
AE	Adverse Event
AF	Atrial Fibrillation
AV	Atrioventricular
AVN	Atrioventricular Node
BiV	Biventricular
CEC	Clinical Events Committee
CPR	Cardiopulmonary Resuscitation
CRT	Cardiac Resynchronization Therapy
CSP	Conduction System Pacing
ECG	Electrocardiogram
eCRF	electronic Case Report Form
EDC	Electronic Data Capture
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HBP	His Bundle Pacing
HF	Heart Failure
HIPAA	Health Insurance Portability and Accountability Act
HMSC	Home Monitoring Service Center
ICF	Informed Consent Form
ICH	International Council for Harmonisation
ICMJE	International Committee of Medical Journal Editors
IEGM	Intracardiac Electrogram
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-To-Treat
LBB	Left Bundle Branch
LBBAP	Left Bundle Branch Area Pacing

Abbreviation / Acronym	Complete Term
LBBB	Left Bundle Branch Block
LOCF	Last Observation Carried Forward
LV	Left Ventricle
LVEF	Left Ventricular Ejection Fraction
NYHA	New York Heart Association
PDF	Portable Document Format
PHI	Protected Health Information
PSA	Pacing System Analyzer
QOL	Quality of Life
QP	Quadripolar
RC	Research Coordinator
RV	Right Ventricle
RVP	Right Ventricular Pacing
SF-36	36-Item Short Form Survey
SMS	Short Messaging System
SR	Sinus Rhythm
SSS	Sick Sinus Syndrome

16 Glossary

Atrial fibrillation – An abnormal heart rhythm characterized by rapid uncoordinated contractions of the atrial chambers of the heart.

Cardiac perforation – Penetration of the lead tip through the myocardium, including micro-perforation, septal perforation, either clinical suspected or confirmed by chest x-ray, fluoroscopy, transthoracic or transesophageal echocardiogram, chest CT, hemodynamic evaluation (i.e. Swan Ganz catheter), intracardiac electrogram, and/or visually.

Hospital admission/Hospitalization – An admission to the hospital that includes a calendar date change.

Implant attempt – Solia S lead coming into contact with subject's ventricular septum with the intent to place the Solia S lead in the LBB area

Lead placement attempt – Extension of the helix of the Solia S lead into the subject's ventricular septum in the LBB area. The Solia S lead tip or screw touching the ventricular septum without intent to implant is not considered a lead placement attempt.

NYHA Classifications

- Class I: Patients with cardiac disease, but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.
- Class II: Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
- Class III: Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
- Class IV: Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Pneumothorax – Air or air and fluid in the pleural space surrounding the lung leading to collapse or partial collapse of the lung.

Prolonged hospitalization – A hospitalization that is extended by one of more calendar dates changes past the initial planned discharge.

Tamponade – Compression of the heart caused by blood accumulation in the space between the myocardium and the pericardium.

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18 Appendix A: Modifications to the Protocol

Protocol Version History

Protocol Version	Summary of Changes since Previous Version
23-Feb-2022	Initial version submitted to sites
10-Aug-2022	Protocol revisions include: • Addition of 12-month Follow-Up Visit • Addition of secondary endpoint 1: Quality of Life (QOL), associated statistical and sample size analyses, QOL data collection at the Enrollment Visit and 3- ,6-, and 12-Month Follow-up Visits, and QOL administration details, and additional data of interest for change in QOL scales from pre-implant baseline to the 3-, 6-, and 12-month follow-up for scale changes not evaluated in secondary endpoint 1 • Addition of collection of implanted system information and implant information, if applicable, at unsuccessful implants • Addition of collection of one 12-lead paced ECG from the time of the 3 or 6-month follow-up visits. Previously, an ECG was optional at follow-ups and collected only 'if available per standard of care'. • The follow-up visit adverse event interview was clarified to allow for either an in-office or phone call interview with subjects. To allow for different visit scenarios, the specific definition of a remote follow-up was removed and device documentation requirements for in-office vs. remote follow-ups were made more general. • Addition of à Sub-group Analysis of the primary and secondary endpoints evaluating subjects ≥65 years of age • Exclusion Criteria "Patient is expected to receive a heart transplant within X months" and "Patient life expectancy is less than X months" were updated from 6 to 12 months • Other minor revisions to improve clarity / streamline protocol

19 Appendix B: SF-36

36-Item Short Form Survey Instrument (SF-36)

RAND 36-Item Health Survey 1.0 Questionnaire Items

Credit - The 36-Item Health Survey was developed at RAND as part of the Medical Outcomes Study.

INSTRUCTIONS

Answer every question. Some questions may seem similar, but each one is different. Please take time to understand each question and the possible responses. Answer each question carefully by putting an "**X**" in the square that best represents your response. If this questionnaire is completed via telephone, please verbalize your response to the study team member. Only one response may be selected for each question.

Choose one option for each questionnaire item.

1. In general, would you say your health is:

   ☐ 1 - Excellent

   ☐ 2 - Very good

   ☐ 3 - Good

   ☐ 4 - Fair

   ☐ 5 - Poor

2. **Compared to one year ago**, how would you rate your health in general **now**?

   ☐ 1 - Much better now than one year ago

   ☐ 2 - Somewhat better now than one year ago

   ☐ 3 - About the same

   ☐ 4 - Somewhat worse now than one year ago

   ☐ 5 - Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
5. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
6. Climbing **several** flights of stairs	☐ 1	☐ 2	☐ 3
7. Climbing **one** flight of stairs	☐ 1	☐ 2	☐ 3
8. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
9. Walking **more than a mile**	☐ 1	☐ 2	☐ 3
10. Walking **several blocks**	☐ 1	☐ 2	☐ 3
11. Walking **one block**	☐ 1	☐ 2	☐ 3
12. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

	Yes	No
13. Cut down the **amount of time** you spent on work or other activities	☐ 1	☐ 2
14. **Accomplished less** than you would like	☐ 1	☐ 2
15. Were limited in the **kind** of work or other activities	☐ 1	☐ 2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	Yes	No
17. Cut down the **amount of time** you spent on work or other activities	☐ 1	☐ 2
18. **Accomplished less** than you would like	☐ 1	☐ 2
19. Didn't do work or other activities as **carefully** as usual	☐ 1	☐ 2

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- ☐ 1 – Not at all
- ☐ 2 – Slightly
- ☐ 3 – Moderately
- ☐ 4 – Quite a bit
- ☐ 5 – Extremely

21. How much **bodily** pain have you had during the **past 4 weeks**?

- ☐ 1 – None
- ☐ 2 – Very mild
- ☐ 3 – Mild
- ☐ 4 – Moderate
- ☐ 5 – Severe
- ☐ 6 – Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- ☐ 1 – Not at all
- ☐ 2 – A little bit
- ☐ 3 – Moderately
- ☐ 4 – Quite a bit
- ☐ 5 – Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
24. Have you been a very nervous person?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
25. Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
26. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
27. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
28. Have you felt downhearted and blue?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
29. Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
30. Have you been a happy person?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
31. Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- ☐ 1 – All of the time
- ☐ 2 – Most of the time
- ☐ 3 – Some of the time
- ☐ 4 – A little of the time
- ☐ 5 – None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
34. I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
35. I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
36. My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5