Alleviating Pain · Restoring Health · Extending Life

Therapy coil Electrogram Collection Study (TEC Study)

Clinical Investigation Plan

Version 2.0

27 AUG 2014

Sponsor
Bakken Research Center BV, Medtronic Endepolsdomein 5, 6229 GW Maastricht, The Netherlands

Approval sheet

Author:

Carolina Moltó Puigmartí (name) | Scientist (functional role)

(signature) | (date)

Author:

Bruce Gunderson (name) | Sr. Prin Scientist (functional role)

(signature) | (date)

Clinical Management:

Rogier Receveur (name) | Sr. Engineering Manager, Research and Technology (functional role)

(signature) | (date)

Regulatory Affairs:

Evelien Scheepers (name) | Regulatory Affairs Specialist, Regulatory Affairs International West (functional role)

(signature) | (date)

Statistician:

James Johnson (name) | Sr Prin Statistician (functional role)

(signature) | (date)

Change History record

CIP Change History		
Version	**Summary of Changes**	**Author**
1.0	Initial Release	Teena Bonizzi
2.0	• Any reference to the inclusion criterion ”less than full energy shock delivered” replaced with “less than 50% of programmed shock energy delivered”. • Any reference to the inclusion criterion ”Abrupt high voltage impedance change (75% increase or 25% decrease from baseline)” replaced with ”Abrupt high voltage impedance change (more than 75% increase or more than 25% decrease from baseline)”. • Section C.8: names of investigators have been removed to be provided under separate cover. • Section E.5: memory cards provided with Holters have been mentioned. • Section E.5: clarification made on the way of storing and tracking Holters and flashcards. • Section F.3: mention to “pre-paid postage bags” removed. • Section G.3.2: added requirement for the investigator to assess whether or not to continue the study at the respective investigation site. • Section I.3.2: mention to submission of AE and death forms has been removed as no AE and death forms will be used for this study. • Section I.3.2: added that Investigator will submit final report to EC/IRB if required. • Table 3 on section I.3.4: reference to the correct section (F.6.2) regarding Vigilance Reporting has been given. • Appendices: list of abbreviations updated. • Appendices: List of participating investigation sites and investigators has been removed from appendix and will be provided under separate cover. • Appendices: Case Report Forms section in the appendix has been added, with mention that Case Report Forms will be provided under separate cover. • Appendices: Patient Informed Consent Master version has been removed from appendix and will be provided under separate cover.	Carolina Moltó Puigmartí

TABLE OF CONTENTS

A SYNOPSIS

Title

Therapy coil Electrogram Collection (TEC) Study.

Purpose

Collect electrograms (EGM) from patients at risk of a suspected insulation failure to the high voltage portion of the defibrillator lead and evaluate the electrograms for unique noise characteristics.

Design

Prospective non-randomized, multicentre, post market release study.

Medical device

Patients previously implanted with a commercially released Medtronic defibrillator device (ICD or CRT-D) connected to a market released St. Jude Medical Riata or Durata lead within indicated use.

Objectives and endpoints

The primary objective is to report the number of patients with a unique noise characteristic (e.g. high frequency spike) on their Far-field EGM (RV coil to SVC coil or RV coil to Can) and a high voltage lead failure within 1 month.

The secondary objectives of this study are to:

- Compare the proportion of patients with a unique noise characteristic (e.g. high frequency spike) on their Far-field EGM (RV coil to SVC coil) and a high voltage lead failure within 1 month to those patients with a high frequency spike and no lead failure within 1 month.
- Identify additional characteristics in the Far-field EGM (e.g. RV coil to SVC coil) that may help identify patients at risk of a high voltage ICD lead failure.

The clinical endpoint is an abnormal EGM noise signature, one instance of a noise spike during the 24 hour recording will be sufficient to classify the noise signature as present.

Subject population

It is expected only two centers will participate in this study as the population of interest is rare. During routine follow up, if a patient is suspected to be at risk for a high voltage lead failure they will be invited to participate in the study. It is estimated that approximately 50 patients will meet these criteria over 2 years and be enrolled in the study.

Treatment

All patients will have been previously implanted with an ICD or CRT-D and be attending a routine follow up visit. As part of the study patients will be asked to wear a 24 hour Holter. All treatment decisions will be at the discretion of the physician in accordance with local practice.

Inclusion criteria

- Subject is willing to sign and date the study Informed Consent form
- Subject is at least 18 years of age (or older, if required by local law)
- Subject is willing and able to wear a Holter monitor for up to 24-hours.

- Subject has a Medtronic ICD or CRT-D device connected to a St Jude Medical Riata or Durata lead AND

  One of the following events occurs:

  1) Externalized conductor with normal pacing and sensing electrical characteristics; or

  2) ICD or CRT-D change out with St Jude lead and normal pacing and sensing electrical characteristics; or

  3) Abnormal device diagnostic for high voltage portion of lead including

     - Abrupt high voltage impedance change (more than 75% increase or more than 25% decrease from baseline)
     - Non-physiologic noise on a high voltage EGM
     - Less than 50% of programmed shock energy delivered

Exclusion criteria

Subjects who meet any of the following exclusion criteria are not eligible to participate in the study:

- Subject has medical conditions that would limit study participation (per physician discretion)
- Subject is enrolled in one or more concurrent studies that would confound the study results of this study as determined by Medtronic

B GENERAL INFORMATION

B.1 Introduction

Lead problems can manifest themselves in multiple ways, including out-of-range impedance, failure to defibrillate, oversensing and loss of capture. Currently, there are limited means for identifying situations due to an insulation breach. The current method monitors for an abnormal high voltage impedance value which in many cases does not occur. There is a clinical need for detecting insulation concerns involving the therapy coil conductors.

ICD lead failures involving the insulation of the high voltage portion of the lead may cause an electrical short when delivering a high voltage shock. Anecdotal data has been reported which shows that the St Jude Medical Riata lead can short and fail to deliver the full programmed shock energy [1-3]. In other reports, the far-field electrogram including the shocking electrogram shows unique noise spikes [3,4]. Since this electrogram is rarely used for sensing and detection, the noise is rarely observed. It is hypothesized that a far-field electrogram, specifically the RVcoil to SVCcoil or RVcoil to Can, has a high probability of showing noise for an insulation break.

A Holter monitor (DR220, Northeast Monitoring, Inc, Maynard, MA) has the capability to continuously record multiple electrograms from a Medtronic device. The goal is to acquire electrogram recordings from patients who may be at risk for a high voltage lead failure. The probability of a high voltage lead failure is low with literature containing only anecdotal cases of high voltage conductor failure. Because of this we will be studying a specific population (Medtronic defibrillator device connected to a St. Jude Medical Riata or Durata lead) to enrich

the sample population. In December 2010, St Jude Medical issued an advisory regarding lead abrasion failures in the Riata leads (Kneller, 2012).

Because these failures are difficult to predict and may not show early electrical warning signs, the patients that will be invited to participate will be those with the unique device and lead configuration and have an increased probability of a lead failure. The Far-field EGMs (see RVcoil to SVCcoil EGMs in Figure 1) and the lead status at 1 month will be used to evaluate the feasibility of differentiating between a lead failure and intact lead.

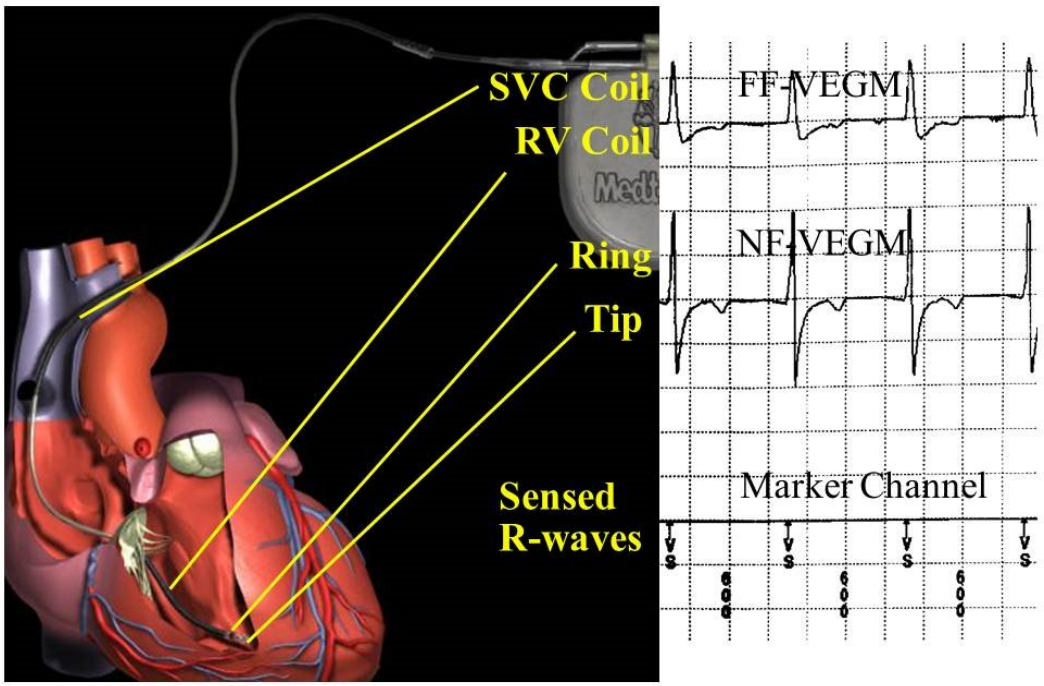

Figure 1. Schematic of Far-field and Near-field EGMs

B.2 Device information

The study will be conducted in subjects previously implanted with a currently commercially available Medtronic ICD or CRT-D device. The components of these devices consist of:

- Market-released Medtronic ICD or CRT-D device

- Market-released Medtronic Model 2090 Series programmer - The Medtronic Programmer (Model 2090 with FullView software or later Medtronic releases) is used to program the devices to detect and treat arrhythmias with various pre-specified characteristics. In addition, the programmer allows the physician to view, save, and print the records currently held within the devices.

Instructions for use of the devices are provided in their respective manuals of use. Labeling is available in local language.

Subjects will also be wearing a St Jude Medical Riata or Durata high voltage lead which is market-released.

B.3 Digital Holter

The digital Holter model DR220 with market-release, manufactured by NorthEast monitoring, Inc. is an external, battery-powered, ambulatory recorder designed to record ECG and telemetered data from an implanted Medtronic device. Digital Holter monitor recordings allow an extensive evaluation of rhythm variations by storing continuous electrogram (EGM), electrocardiogram (ECG) and extended marker channel information. Data from the Holter will be downloaded into a chronologically readable format and analyzed off-line. Only one ECG signal (using 3 electrodes) will be used.

C STUDY PLAN

C.1 Study objectives

The purpose of this study is to collect electrograms from patients at risk of a suspected insulation failure to the high voltage portion of the defibrillator lead and evaluate the electrograms for unique noise characteristics.

C.1.1 Primary objective

The primary objective is to report the number of patients with a unique noise characteristic (e.g. high frequency spike) on their Far-field EGM (RV coil to SVC coil or RV coil to Can) and a high voltage lead failure within 1 month.

C.1.2 Secondary objectives

The secondary objectives of this study are to:

- Compare the proportion of patients with a unique noise characteristic (e.g. high frequency spike) on their Far-field EGM (RV coil to SVC coil) and a high voltage lead failure within 1 month to those patients with a high frequency spike and no lead failure within 1 month.
- Identify additional characteristics in the Far-field EGM (e.g. RV coil to SVC coil) that may help identify patients at risk of a high voltage ICD lead failure.

C.2 Clinical endpoints

The clinical endpoint is an abnormal EGM noise signature. Abnormal noise is defined as an inflection from the standard R-wave, T-wave, and isoelectric line of a Far Field-EGM. The Far Field-EGM is susceptible to low amplitude myopotentials which would be considered normal. An example of abnormal noise is in Figure 2 below with asterisks showing the positive noise spike during the normally flat isoelectric line of the RVcoil to SVC EGM signal. This is one example and it is unknown whether all lead failures exhibit this same signature. The noise signature will be considered present if one instance is observed during the 24 hour recording.

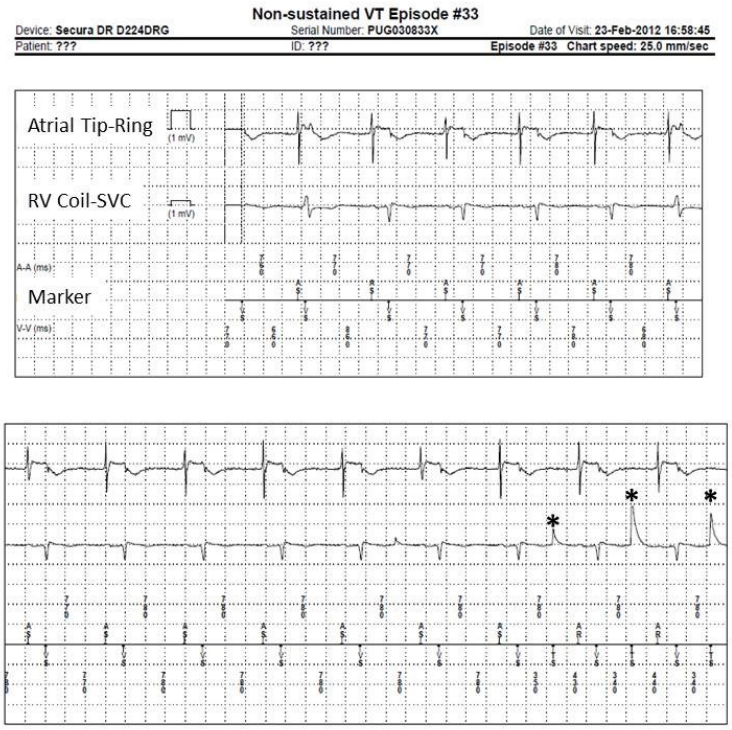

Figure 2. Example of the positive noise spike during the normally flat isoelectric line of the RVcoil to SVC EGM signal.

C.3 Study hypothesis

The study hypothesis is that 10 out of the 50 patients will have a high voltage lead failure, of which 5 of these will also have an abnormal noise, manifesting as a high frequency spike.

C.4 Study population

Patients with a Medtronic ICD or CRT-D and St. Jude Riata or Durata lead will be identified during pre-screening. The study population of interest are those patients that satisfy one of 3 inclusion criteria (abnormal device diagnostic such as abnormal impedance, abnormal fluoroscopic image, or ICD/CRT-D change out).

C.5 Study design

Prospective, non-randomized, multicentre, post market release study. The study will take place in Slovakia at two investigation sites.

C.6 Randomization and blinding

This is an observational study, no randomization will be used in this study. Evaluation of the EGM signals will be done centrally at Medtronic and the scientist determining the clinical endpoint (i.e. an abnormal EGM noise signature) will be blinded from the lead status during evaluation of the EGMs Additionally the physician will be blinded from the scientist's evaluation of the Holter EGM during the study.

C.7 Sample size

It is estimated that a population of 300 patients with the required combination of device and lead exist in Europe. Over a two year period, we expect approximately 50 patients to fulfill the inclusion criteria and provide analyzable Holter data. In the unlikely situation that Holter data from a patient is not analyzable due to signal quality they will be replaced by another patient.

With data from these 50 patients we estimate 10 patients will have a high voltage lead failure of which 5 will have the unique high frequency spike. In the 40 patients without a high voltage lead failure we estimate 1 may also have the unique high frequency spike.

Using a Fisher's exact test, assuming a two-sided alpha of 0.5 we will be able to detect differences with power greater than 80%.

Additionally with an estimated proportion of patients with the unique noise characteristic and a high voltage lead failure of 10%, 50 patients will provide a precision of +/- 7% with a confidence interval of 90%.

C.8 Number of investigation sites and study duration

It is anticipated that two sites will participate in this study. The first site will be the National Institute of Cardiovascular Diseases, Department of Arrhythmias and Cardiac Pacing, Bratislava, Slovakia. The second site will be the Middle Slovakia Institute of Cardiovascular Disease, SUSCCH a.s, Banska Bystrica, Slovakia. These sites were chosen because they have a unique, large pool of patients with Medtronic devices connected to St. Jude Riata leads. A list of investigators will be kept under separate cover.

There will be no upper limit of subject enrollment for each investigator. Once 50 patients with analyzable data have been enrolled the study will stop. There will be no minimum limit that each investigator must enroll, however it is expected that sites will have at least 100 suitable patients (i.e. patients with a Medtronic ICD or CRT-D and St Jude lead) in their referring area.

We estimate that at least 200 patients will need to be screened to identify at least 50 patients who fulfill the inclusion criteria. Assuming approximately 2 patients presenting per month the study is expected to last 2 years. This estimate will be evaluated after 6 months and modifications to the study may be made if assumptions are inaccurate.

Once patients have fulfilled the inclusion criteria they will be invited to participate in the study. Participation will involve wearing a Holter monitor for 24 hours. A 24 hour Holter is required to allow a sufficient amount of time for an abnormality to be observed on the EGM. One month after the return of the Holter the physician will be asked to complete a study exit form, this form will collect the current status of the lead and information from any additional tests that were performed. The patient is not required to be present when the physician completes the study exit form.

D SUBJECT SELECTION

D.1 Inclusion criteria

- Subject is willing to sign and date the study Informed Consent form
- Subject is at least 18 years of age (or older, if required by local law)
- Subject is willing and able to wear a Holter monitor for up to 24-hours.
- Subject has been implanted with a Medtronic ICD or CRT-D device and a St. Jude Medical Riata or Durata lead and satisfy one of three conditions:

1. Externalized conductor with normal P/S electrical characteristics, or
2. ICD/CRT-D change out and normal P/S electrical characteristics, or
3. Abnormal device diagnostics for high voltage portion of lead
    - Abrupt HV impedance change (more than 75% increase or more than 25% decrease from baseline)
    - Non-physiologic noise on HV EGM
    - Less than 50% of programmed shock energy delivered

D.2 Exclusion criteria

Subjects who meet any of the following exclusion criteria are not eligible to participate in the study:

- Subject has medical conditions that would limit study participation (per physician discretion)
- Subject is enrolled in one or more concurrent studies that would confound the study results of this study as determined by Medtronic

E STUDY PREPARATION PROCEDURES

E.1 Investigator / Investigation site selection

An investigator/investigation site may be included in the investigation if the investigator/investigation site complies with the following requirements:

- Investigator has education / experience in the field of the research (implantable cardiac rhythm devices and cardiac rhythm disturbances)
- The center has adequate resources, facilities and equipment at the center to meet the expected enrollment rate. Calibration and maintenance of equipment will be performed as per hospital practice and the responsibility of the investigator.
- A quiet room suitable for attaching the Holter to the subject.
- The investigator/center has at least 100 patients with the combination of Medtronic ICD or CRT-D and St Jude Medical Riata or Durata in their referring area.
- Investigator has experience in conducting clinical research trials.

E.1.1 Clinical Investigation Agreement

A Clinical Investigation Agreement shall be entered into effect by the participating investigation site and/or the principal clinical investigator at each investigation site as per the local legal requirements, and returned to Medtronic prior to the commencement of any study activities. The investigator is indicating approval of the Clinical Investigation Plan and subsequent amendments, by signing and dating the agreement. Amendments to this Clinical Investigation Plan shall be agreed upon between Medtronic and clinical investigator(s) and be recorded with a justification for the amendments.

E.1.2 Curriculum Vitae

Recent signed and dated curriculum vitae from each investigator, including co-investigators participating in this study, evidencing the required qualifications, including the year and where obtained, and shall include their current position at the investigation site. The signature on the CV must be dated within 3 years prior to the date of activation of the site.

E.2 Ethics

E.2.1 EC/IRB approval

Prior to enrolling subjects in this study, each investigation site's EC/IRB must have approved the current study clinical investigation plan, the Patient Information and Informed Consent form, any other written information to be provided to the subjects and if applicable the Investigator's Brochure and materials used to recruit subjects. EC/IRB approval, or documentation confirming that committee review is not required of the clinical study must be received in the form of a letter and provided to Medtronic before commencement of the study at an investigation site. The approval letter must contain enough information to identify the version or date of the documents approved. If this information is not contained in the approval letter, it must be retrievable from the corresponding submission letter. In addition the approval letter needs to be accompanied by an EC/IRB roster or letter of compliance, to allow verification that the investigator, other center study staff, and/or Medtronic personnel are not members of the EC/IRB. If they are members of the EC/IRB, written documentation is required stating that he/she did not participate in the approval process. If the EC/IRB imposes any additional requirements (e.g. safety reports, progress reports etc.), Medtronic will prepare the required documents and send them to the investigator for reporting to the EC/IRB. Investigators must inform Medtronic of any change in status of EC/IRB approval once the investigation site has started enrolment. If any action is taken by an EC/IRB with respect to the investigation, that information will be forwarded to Medtronic by the respective investigator.

E.2.2 Informed consent process

The investigator or authorized designee must obtain written informed consent prior to subjecting the subject to any study related activity.

Well in advance of the consent discussion, the subject should receive the EC/IRB approved Patient Information and Informed Consent Form. During the consent discussion the investigator or his/her designee must fully inform the subject of all pertinent aspects of the study including the approval of the EC/IRB of the written Patient Information. If a subject is illiterate, an impartial witness must be present during the entire informed consent discussion and the patient information sheet and consent form shall be read aloud to the subject. All items discussed in the Patient Information and the Informed Consent Form must be explained. The language used shall be as non-technical as possible and must be understandable to the subject and the impartial witness, where applicable.

The subject must have ample time and opportunity to inquire about details of the study, and to decide whether or not to participate in the clinical study. All questions about the study should be answered to the satisfaction of the subject.

Neither the investigator, nor the investigation site staff shall coerce or unduly influence a subject to participate or to continue to participate in the clinical study. The informed consent process shall not appear to waive the subject's rights.

When the subject decides to participate in the clinical study, the Informed Consent Form must be signed and personally dated by the subject and investigator.

If applicable, the witness shall also sign and personally date the consent form to attest that the information in the Patient Information and Informed Consent Form was accurately explained and clearly understood by the subject, and that informed consent was freely given. When possible the subject should also sign the Informed Consent Form.

After all persons have signed and dated the Informed Consent Form the investigator must provide the subject with a copy of the Patient Information and the signed and dated Informed Consent Form.

E.2.3 Revisions in Patient Information and Informed Consent Form

Medtronic will inform the investigators whenever information becomes available that may be relevant to the subject's confirmed participation in the study. The investigator or his/her designee should inform the subject in a timely manner.

Medtronic will revise the written Patient Information and Informed Consent Form whenever new information becomes available that may be relevant to the subject's confirmed participation in the study. The revised information will be sent to the investigator for approval by the EC/IRB. After approval by the EC/IRB, a copy of this information must be provided to the participating subjects, and the informed consent process as described above needs to be repeated.

E.2.4 Regulatory notification / approval

In countries where submission to the regulatory authority is required per local law, no patients will be enrolled in the study until the particular regulatory authority has approved the current study clinical investigation plan and other documents as required according to the local requirements.

E.3 Regulatory compliance

This study will be conducted in compliance with the latest version of the Declaration of Helsinki, laws and regulations of the country in which the study is conducted, including data protection laws, the clinical investigation agreement and the Clinical Investigation Plan.

The principles of the Declaration of Helsinki have all been implemented in this study by means of the patient informed consent process, EC/IRB approval, study training, clinical trial registration, preclinical testing, risk benefit assessment, publication policy, etc.

If the regulatory authority imposes any additional requirements (e.g. safety reports, progress reports etc.), Medtronic will prepare the required documents and send them to the respective authority.

E.4 Training requirements

Prior to investigation site activation or subsequent involvement in study activities, Medtronic will provide study training relevant and pertinent to the involvement of personnel conducting study activities and investigator responsibilities. Training will be given on the CIP, the informed Consent (IC) process, the use of the data collection tools and any applicable regulatory requirements.

E.5 Study materials and study-specific equipment

Each investigational site will be provided with study materials (e.g. Investigator Site File and paper case report forms (CRF)).

The Holters (including memory cards) will be distributed to a center only when Medtronic has received all required documentation and has notified the center of center readiness. Distribution of the Holters to study centers during the clinical study will be managed by Medtronic.

It is the responsibility of the investigator to correctly handle, store, and track the allocation of Holters to patients. The method of storage shall prevent the use of the Holter for other applications than mentioned in this Clinical Investigation Plan. Tracking will be done via entering the Holter serial number and flashcard ID number in the patient CRF.

The Holter monitor and the recorded data on the flashcard from the Holter must be returned to Medtronic. Medtronic will facilitate Holter maintenance and retrieval.

F STUDY METHODS

This section explains the study visits that are required, when they should occur and what study procedures should be performed during the visit.

F.1 Screening

Patients with a Medtronic ICD or CRT-D and a St. Jude Medical Riata or Durata lead will be pre-screened from medical charts for potential enrollment in the clinical investigation. A log will be maintained in the investigational site file

F.2 Point of enrollment

Patients will be enrolled in the study once they have provided written informed consent. At this point, the patient will be assigned a subject number and is considered a subject in the investigation.

The investigator will maintain a log of all subjects enrolled in the clinical investigation, assigning an identification code linked to their names, alternative subject identification or contact information.

The investigator will clearly mark clinical records to indicate that the subject is enrolled in this clinical study.

F.3 Evaluation Visit

During the patients routine scheduled ICD or CRT-D device follow up one of the following events will be required for enrollment:

1) Externalized conductor with normal pacing and sensing electrical characteristics has been found; or

2) The decision is made to schedule an ICD or CRT-D change out with St Jude lead and pacing and sensing electrical characteristics are normal; or

3) Abnormal device diagnostic for high voltage portion of lead including

- Abrupt high voltage impedance change (more than 75% increase or more than 25% decrease from baseline)
- Non-physiologic noise on a high voltage EGM
- Less than 50% of programmed shock energy delivered

If any one of these three criteria are observed the subject will be invited to participate in the study.

A “Save To Disk” procedure will be performed to store the initial parameter settings and device memory.

The following collection settings will be programmed:

2 EGM devices Single and Dual Coil Leads	4 EGM devices Single Coil Lead	4 EGM Devices Dual Coil Lead
Select Parameters>Data Collection Setup> EGM 1: RVtip to RVring EGM 2: Can to RVcoil Press “OK” Press “PROGRAM”	Select Parameters>Data Collection Setup> LECG: RVcoil to Aring EGM 1: RVtip to RVring EGM 2: Can to RVcoil EGM 3: RVtip to RVcoil Press “OK” Press “PROGRAM”	Parameters>Data Collection Setup> LECG: Can to SVC EGM 1: RVtip to RVring EGM 2: RVcoil to SVC EGM 3: Can to RVcoil Press “OK” Press “PROGRAM”

The Holter Telemetry will be turned on for 24 hours

Select Parameters>Data Collection Setup>Select Holter telemetry [24 hours]

Press “PROGRAM”

Note: For wireless telemetry ICD devices select <find patient> then uncheck “Allow Wireless Communication”

The Holter monitor will be attached to the subjects and they will be asked to continue wearing the Holter monitor to record rhythm data for up to 24 hours.

The Holter monitor and the recorded data on the flashcard from the Holter must be returned to the study center. Medtronic will facilitate Holter retrieval for each study participant and this is the end of the study involvement for the patients.

The SD Disks will be sent to Medtronic within 7 working days and at the end of the study the Holters must be returned to Medtronic. Medtronic will facilitate Holter retrieval from the centers.

F.4 Lead Status and Study Exit Form

One month after the evaluation visit, the physician will be asked to complete a study exit form, this form will collect the current status of the lead and information from any additional tests that were performed during routine clinical practice to determine the status of the lead.

The status of the lead will be classified as intact or failed based on the physician’s assessment of the lead with supporting data. The supporting data includes the results of a full output test shock (if performed), returned product analysis (full lead needs to be returned of intact, partial lead can be returned for failure), or device diagnostics (e.g. abnormal high voltage impedance, less than 50% of programmed shock energy delivered for detected episodes).

F.5 Data collection requirements

	Screening	Enrollment	Evaluation Visit	Study Exit
Device and lead Criteria	✓			
Inclusion/Exclusion Criteria		✓		
Subject Informed Consent		✓		
Demographics, device history			✓	
Save-to-disk			✓	
Device Data Collection Settings programmed			✓	
Holter Attached			✓	
Lead Status				✓
Exit				✓

F.6 Post Market Surveillance

F.6.1 Definition/classification

Product Complaint:

Any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a medical device that has been placed on the market.

F.6.2 Reporting of product complaints

All devices used in this study are marked released. Therefore, Post Market Surveillance is applicable.

The reporting of product complaints is not part of the clinical study. It is the responsibility of the investigator to report all product complaint(s) associated with a medical device (Medtronic or non-Medtronic) regardless whether they are related to intended use, misuse or abuse of the product. Reporting must be done immediately and via the regular channels for market released products.

Medtronic will notify the Regulatory Authority of the following incidents immediately on learning of them:

- Any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or instructions for use which led or might have led to the death or serious deterioration in the state of health of a patient, user, or other person.
- Any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.

A serious deterioration in the state of heath includes:

- Life-threatening illness or injury
- Permanent impairment of a body function or permanent damage to a body structure
- A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

F.7 Subject accountability

Study Exit is defined as the moment when a subject officially stops participating in the study. If a subject is withdrawn from the study before the one month lead status evaluation/study exit visit, the reason for withdrawal shall be recorded on the study exit CRF and in the subject's hospital record. If discontinuation is because of safety or performance issues of the Medtronic defibrillator device (ICD or CRT-D), normal vigilance reporting will be applicable. .

Reasons subject may be exited form the study include, but are not limited to:

- Study completion
- Subject did not provide consent
- Subject did not meet inclusion/exclusion criteria
- Subject chooses to withdraw (e.g., consent withdrawals, relocation to another geographic location)
- Investigator deems withdrawal necessary (e.g., medically justified, inclusion/exclusion criteria not met, failure of subject to maintain adequate study compliance)
- Subject death

If the Holter recording fails i.e. the file becomes corrupted or the signal quality is poor, an additional patient may be enrolled to ensure there is at least 50 readable Holter recordings are available for analysis.

F.8 Study deviations and CIP changes

A study deviation is an event where the investigator or site personnel did not conduct the study according to the Clinical Investigational Plan or Clinical Investigation Agreement. The investigator is not allowed to deviate from the above mentioned documents except with prior approval and under emergency circumstances. All deviations shall be documented and explained, regardless the reason for the deviation.

Medtronic will assess the significance of all deviations and evaluate the need to amend the Clinical Investigation Plan or to early terminate the investigation, in accordance with Medtronic SOPs.

F.8.1 Request for approval of study deviations

The investigator shall obtain documented approval from Medtronic and if required EC/IRB and regulatory authority, before implementation, for any change in or deviation from the Clinical Investigation Plan. The investigator shall timely contact the Clinical Research Specialist / study manager for review of the proposed change/deviation.

Prior approval is not always realistic in situations where unforeseen circumstances are beyond the investigator's control. However, also in these cases the event is considered a deviation, and shall be reported.

In any emergency situation the investigator shall exercise his/her judgment to safeguard the subject's interest. Such deviations from the Clinical Investigation Plan do not require the prior approval of Medtronic. The investigator shall report the deviation as soon as possible to Medtronic and the reviewing EC/IRB, if applicable. Medtronic will inform the regulatory authorities, if required.

F.8.2 Reporting requirements for study deviations

Study deviations directly related to a subject, including informed consent violations, will be documented in the subject's case history record and recorded on the Deviation CRF. Medtronic will be responsible for analyzing the documented deviations, assessing their significance, and identifying any necessary corrective and/or preventive action. Reporting of deviations must comply with Ethics Board policies, local laws, and or regulatory agency requirements. It is the investigator's obligation to report deviations to IRB/MEC, as required.

F.8.3 Amendments to the Clinical Investigation Plan

Medtronic will submit any significant amendment to the Clinical Investigation Plan, including a justification for this amendment, to the appropriate regulatory authorities and to the investigators to obtain approval from their EC/IRB, if applicable. Administrative amendments to the Clinical Investigation Plan will be submitted to the EC/IRB and appropriate regulatory authorities for notification, if applicable.

G QUALITY CONTROL PROCEDURES

G.1 Procedures for data management

G.1.1 Data collection

The investigator must ensure accuracy, completeness, legibility and timeliness of the data reported in the CRFs and in all other required reports. Data reported on the CRFs which are derived from source documents (e.g. hospital records, laboratory notes or fluoroscopic images) must be consistent with the source documents or the discrepancies need to be justified in a documented rationale, signed and dated by the (principal) investigator, to be filed in the patient medical file.

Only authorized persons can complete CRFs. CRFs shall be signed by investigators (physician) as specified on the Delegated Tasks List included in the Investigator Site File.

In order to maintain an audit trail, changes or corrections in CRFs are made by making a single strike-through on the wrong data and an addition of the correct data. The change in the CRF must be signed, dated, and explained (if necessary) by the person that made the change. If a person only authorized to complete CRFs made changes to an already signed CRF, the investigator shall re-sign this CRF.

Beside the data on the Case Report Forms, save to disk files, Holter files and fluoroscopic images (if available), will also be collected.

All data shall be secured against unauthorized access. The privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data.

Additional details regarding data management will be described in the Data Management Plan.

G.1.2 Source data to be directly recorded on the Case Report Forms

For all data collected on the CRF the source data will be the hospital chart, except for the serial number of the Holter SD disk which will be handled as source data.

The Holter recordings and (if available) fluoroscopic images will be collected additionally to the CRF and handled as source data. Details of source data verification will be contained in the study monitoring plan. Time windows for completion and submission of Case Report Forms

It is anticipated that CRFs will be completed and submitted to Medtronic in a timely manner.

G.1.3 Data review and processing

Data management will be done according to Medtronic SOPs and the Data Management Plan for this study. These documents will be made available on request.

All collected data will be reviewed for completeness, correctness and consistency. In case of issues, queries will be sent to the investigator to complete, correct or comment the data.

G.2 Monitoring procedures

It is the responsibility of the study sponsor to ensure that proper monitoring of this clinical investigation is conducted. The Investigator Site File will be verified during the first visit by Medtronic personnel, which is most likely to be at time of the site initiation visit and at the end of the study. No additional monitoring visits are anticipated. Should additional monitoring visits be required the principal investigators, his delegate(s) and the study coordinator(s) shall be accessible to Medtronic representative. Details will be contained in the study monitoring plan.

Appropriately trained personnel appointed by Medtronic will conduct monitoring activities, as needed, to check if the investigation is conducted in accordance with:

- The signed Investigator Agreement
- The Clinical Investigational Plan
- Applicable local laws
- Any conditions of approval imposed by the reviewing IRB/MEC

Center activation and study closure will occur on-site or via telephone/email.

G.2.1 Accessibility of investigation site staff and study materials

The principal investigator(s), his/her delegate(s) and the study coordinator(s) shall be accessible to Medtronic field personnel and the Clinical Research Specialist/Study Manager. This accessibility is of particular importance for reviewing data in the Case Report Form (CRF). Direct access to patient medical files that pertain to the clinical study for source data verification will need to be granted and prepared prior to the monitoring visits, taking into account any restrictions due to local law.

G.2.2 Audits and investigation site inspections

Medtronic may conduct audits at participating investigation sites. The purpose of an audit is to verify the adequate performance of the study related activities. Independent of the employees involved in the study. Regulatory authorities may also perform inspections at participating investigation sites. Any regulatory authority inspection announcements shall be forwarded immediately to the Medtronic study contact person.

The investigator and/or institution shall permit Medtronic and regulatory bodies direct access to source data and documents that pertain to the clinical study, taking into account any restrictions due to local law, to perform study-related monitoring, audits, EC/IRB review, and regulatory inspections.

G.3 Study suspension or early termination

G.3.1 Study suspension or early termination

Medtronic or Regulatory Authority may decide to suspend or prematurely terminate the study (e.g. if information becomes available that the risk to study subject is higher than initially indicated). If the study is terminated prematurely or suspended, Medtronic shall promptly inform the clinical investigators and the regulatory authority where applicable of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC/IRB, if required and the study subjects and general practitioner. If the study is terminated, study exit forms will be completed for each patient and the patients will no longer be followed.

G.3.2 Investigation site suspension or early termination

Medtronic, EC/IRB or Regulatory Authority may decide to suspend or prematurely terminate an investigation site (e.g. in case of expiring approval of the reviewing EC/IRB, non-compliance to the Clinical Investigation Plan or lack of enrollment). If an investigation site is suspended or prematurely terminated, Medtronic shall promptly inform the clinical investigator(s) of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC/IRB, if required (please check the regulatory affairs website), and the study subjects and general practitioner. If the EC/IRB decides to suspend or terminate the site the investigator must inform Medtronic immediately.

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definite outcomes, investigators must assess whether to continue, modify or immediately stop the clinical study in the respective investigation site and immediately inform the sponsor and EC/IRB, if applicable.

G.4 Study close out

Study closure is defined as closure of a clinical study that occurs when Medtronic and/or regulatory requirements have been satisfied per the Clinical Investigational Plan and/or by a decision by Medtronic or EC/IRB, whichever occurs first. Study Closure is a process initiated by distribution of a study closure letter. Ethics Board approval renewals are required until the study closure process is complete at the center and the final report submitted. Where applicable, regulator authorities will be notified upon study closure.

H DATA ANALYSIS AND REPORTING

Any deviations from this section will be described and justified in the Final Report/ publication.

H.1 Analysis of clinical data

Each Holter recording will be reviewed for the presence of an abnormal signal (e.g. noise) on the far-field (e.g. RVcoil to SVC) EGM. Only one instance of abnormal noise (e.g. spike) will be needed to classify the recording as abnormal.

The lead from each patient will be adjudicated as a lead failure or intact lead by the physician using routine current practice methods of assessing an ICD lead and recorded on the study exit CRF form. The proportion of Holter recordings with abnormal noise in the lead failure group will be compared with the control group with intact leads. Fisher's exact test will be used to compare the proportions of the 2 independent groups.

Only patients with a good quality Holter recording (minimum 12 hours of telemetry) and a documented assessment of the lead status by the physician will be used in the analysis. Other Holter recordings will not be used.

H.2 Publication Policy

Publications and presentations referring to Therapy coil Electrogram Collection Study will be coordinated by Medtronic to allow the use of all available data. The following publication policy will have to be adhered to by all participating investigation sites:

Medtronic intends to publish the results of the study in a manner that is sensitive to the commercial application of the results. It is likely publication will be delayed until closer to the potential release of a device feature.

Authorship on any publication(s) resulting from this study will be assigned according to substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content and final approval of the version to be published. This is in accordance with the Vancouver principles (The Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, ICMJE, October 2008), as agreed upon by the editors of all major medical journals.

The number of authors will be dependent on the regulations of the concerning journal with a maximum of 10 authors. Names of all participating investigators will appear in the Acknowledgment of the paper.

There are no plans to form a publication committee. Publication activities will be assessed after the study is completed and any collaboration with the investigators will be determined at that time.

Based on the principle that Medtronic owns the data of the Therapy coil Electrogram Collection Study a single investigation site may access and use the data provided by itself for scientific publications following prior approval by Medtronic.

Pooling data from several investigation sites for publication purposes, national projects and international projects all require prior approval from Medtronic.

Medtronic as the owner of the data can use the data and/or any results derived from the data or publications based on that data for marketing purposes, further research and development of devices or educational use.

The study sponsor will collect data in such way that no subject can be identified, and monitor study records.

Participating subjects will not be identified by name in any published reports about the study.

I STUDY MANAGEMENT

I.1 Study staff

A list of the sponsor's study staff will be kept under separate cover.

I.2 Advisory committees

I.2.1 Data Monitoring Committee

No Data Monitoring Committee will be installed for this clinical study as no interventions intended to prolong life or reduce risk of a major adverse health outcome (e.g., cardiovascular events) are evaluated, for which favorable or unfavorable study results suggest study

termination. Nor are there safety concerns suggesting the need for a Data Monitoring Committee.

I.3 Records and reports

I.3.1 Investigator records

The investigator is responsible for the preparation (review and signature) and/or retention of the records cited below. All study related information and records are subject to inspection and must be retained for a period of two years after study termination or closure or longer if required by local or hospital regulations, e.g:

- All key correspondence that pertains to the investigation
- Subject's case history records, including: completed CRFs, copy of data collected during study visit, signed and dated subject informed consent form, all relevant observations, observations of serious adverse events, records of reported adverse events, medical history, and documentation of the dates and rationale for any deviation from the Clinical Investigational Plan or Investigator Agreement
- Subject identification and screening log
- Sponsor contact information
- List of participating sites
- The approved Clinical Investigational Plan and any amendments
- Sample patient information and informed consent form
- Insurance certificates
- Signed and dated Investigator Agreement and compensation records
- IRB/MEC approval documents and documentation that the investigator did not participate in the approval process
- Training documentation, current, signed and dated (co-)investigator curriculum vitae, delegated task list and final report
- Any other records that local regulatory agencies require to be maintained

I.3.2 Investigator reporting responsibilities

The investigator is responsible for the preparation (review and signature) and submission to Medtronic of all case report forms and deviations from the clinical investigational plan. If any action is taken by an IRB/MEC with respect to the investigation, the information must be forwarded to Medtronic immediately. Reports are subject to inspection and to the retention requirements as described above for investigator records. The investigator shall prepare and submit in a complete, accurate and timely manner the reports listed in Table 2.

Table 2: Investigator Reports

Report	Submit To	Description / Constraints
Withdrawal of IRB/MEC approval	Medtronic	report as required by local law
Study Deviations	Medtronic, IRB/MEC	Any deviation from the CIP shall be recorded together with an explanation for the deviation. Deviations shall be reported to the sponsor who is responsible for analyzing them and assessing their significance. Note: When relevant, Ethics Boards, competent authorities or the appropriate regulatory bodies should be informed.
Failure to obtain informed consent	Medtronic, IRB/MEC	Notification within five working days.
Progress Reports and final report (if required)	Medtronic, IRB/MEC	Provide if required by local law or Ethics Board

I.3.3 Sponsor records

Medtronic shall maintain the following accurate, complete, and current records e.g.:

- All correspondence which pertains to the investigation
- Signed and dated Investigator Agreement, current signed and dated (Co-) investigator curriculum and delegated tasks list
- All case report forms submitted by investigator and samples of consent forms
- Copies of all IRB/MEC approval letters, voting list and relevant IRB/MEC correspondence
- Name of the institutions in which the clinical investigation will be conducted
- Correspondence with authorities as required by national legislation
- Statistical analyses and underlying supporting data
- Device shipment records
- Final report of the clinical investigation
- All approved versions of the Clinical Investigation Plan and study related reports
- Study training records for site personnel and Medtronic personnel involved in the study
- Insurance certificates
- Monitoring visit reports
- Any other records that local regulatory agencies require to be maintained

I.3.4 Sponsor reporting responsibilities

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in the Table 3 below. In addition to the reports listed below, Medtronic shall, upon request of reviewing IRB/MEC or regulatory agency, provide accurate, complete and current information about any aspect of the investigation.

Table 3: Sponsor Reports

Report	Submit To	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators, IRB/ MEC, Regulatory Authority	Provide prompt notification of termination or suspension and reason(s).
Withdrawal of MEC approval	Investigators, Regulatory Authority	Medtronic will be notified.
Progress Reports	Regulatory Authority	This will be submitted to the only if required
Final Report	Investigators, IRB/MEC	The investigator shall have the opportunity to review and comment on the final report. If a clinical investigator does not agree with the final report, his/her comments shall be communicated to the other investigator(s). The principal clinical investigator at the centers shall sign the report.
Study deviation	Investigators	Ensure that all deviations from the Clinical Investigation Plan are reviewed with the appropriate clinical investigator(s), are reported on the case report forms and the final report of the clinical investigation.
Vigilance Reporting	Regulatory Authorities	Report incidents. Refer to section F.6.2 for details
Significant New Evidence	Investigator, IRB/ MEC, Regulatory Authorities	Ensure that IRB/MEC and Regulatory Authorities are informed of significant new information about the clinical investigation. Investigator to inform patients.

Electronic versions of Medtronic records and reports will be kept on a password-protected document management system during the course of the study. After closure of the study, all records and reports will be archived indefinitely.

I.3.5 Record retention

The investigator must retain the Investigator Site File, patient medical files and CRFs in accordance with local law and regulations.

The investigator should take measures to prevent accidental or early destruction of the study related materials.

I.4 Miscellaneous

I.4.1 Insurance

The Bakken Research Center B.V. is a wholly owned subsidiary of Medtronic Inc., which as the parent company of such entity maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable law and custom concerning specific insurance coverage. If required, a Clinical Trial Insurance statement/certificate will be provided to the EC/IRB.

I.4.2 Subject confidentiality

Participating subjects will not be identified by name in any published reports about the study.

J RISKS AND BENEFITS

J.1 Anticipated Clinical Benefits

The objective of this study is to collect data from the subjects' device with no direct clinical benefit to the subject. The benefit is for future patients that may have improved lead monitoring diagnostics.

J.2 Risks

Subjects are treated according to general clinical practice, no extra tests and follow-ups are required other than the wearing of a Holter for 24 hours.

There is a foreseeable inconvenience to the patient having to wear the Holter monitor for 24 hours and there could also be irritation to the skin from the ECG electrodes. The irritation has been minimized by using only 3 ECG electrodes instead of the standard 7 ECG electrodes.

K REFERENCES

1. Shah P, Singh G, Chandra S, Schuger CD. Failure to Deliver Therapy by a Riata Lead with Internal Wire Externalization and Normal Electrical Parameters During Routine Interrogation. JCE 2013:24:94-6.

2. Leong DP, Van Erven L. Unrecognized Failure of a Narrow Caliber Defibrillation Lead: The Role of Defibrillation Threshold Testing in Identifying an Unprotected Individual. PACE 2012;1-2.

3. Goldstein MA, Badri M, Kocovic D, Kowey PR. Electrical Failure of an ICD Lead due to a Presumed Insulation Defect Only Diagnosed by a Maximum Output Shock. PACE 2013.

4. Sharma, Gunderson BD. Data on file.

L APPENDICES

L.1 Names and addresses

A complete list of participating sites and investigators will be provided under separate cover

L.2 Abbreviations

CIP	Clinical Investigation Plan
CRF	Case Report Form
CRT-D	Cardiac Resynchronization Therapy Defibrillator
DMC	Data Monitoring Committee
EC	Ethical Committee
ECG	Electrocardiogram
EGM	Electrogram
ICD	Implantable Cardioverter Defibrillator
IRB	Institutional Review Board
MEC	Medical Ethics Committee
RV	Right Ventricle
SOP	Standard operating procedure
SVC	Superior Vena Cava

L.3 Case Report Forms

Case Report Forms for this study will be provided under separate cover

L.4 Patient Informed Consent Master version

Patient Informed Consent for this study will be provided under separate cover