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Document Name	Version
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Title	CIP V1.0 07JUL2016 MASS2

APPROVALS

Signed By	Meaning of Signature	Date/Time (UTC)
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Micra Accelerometer Sensor Study 2 (MASS2)

Medtronic **Clinical Investigation Plan**	
Clinical Investigation Plan/Study Title	Micra Accelerometer Sensor Study 2 (MASS2)
Study Product Name	MATS Research System
Sponsor	Medtronic, Inc. 8200 Coral Sea Street NE Mounds View, MN U.S.A. 55112 Phone: +1-800-328-2518
Local Sponsor	Bakken Research Center B.V. Endepolsdomein 5 6229 GW Maastricht The Netherlands Phone: +31-43-35-66-566
Manufacturer	Medtronic, Inc. 710 Medtronic Parkway Minneapolis, MN 55432-5604, USA Tel. +1-763-514-4000 Fax +1-763-514-4879
Document Version	Version 1.0 07/Jul/2016

1. Version History

Version	Summary of Changes	Author(s)/Title
Version 1.0 07/Jul/2016	Not Applicable, New Document (based on 056-F275, Clinical Investigation Plan Template, Version 2.0)	Valentina Amori, Study Manager

2. Investigator Statement

Study product Name	MATS Research System
Sponsor	Medtronic, Inc. 8200 Coral Sea Street NE Mounds View, MN U.S.A. 55112 Phone: +1-800-328-2518
Local Sponsor	Bakken Research Center B.V. Endepolsdomein 5 6229 GW Maastricht The Netherlands Phone: +31-43-35-66-566
Manufacturer	Medtronic, Inc. 710 Medtronic Parkway Minneapolis, MN 55432-5604, USA Tel. +1-763-514-4000 Fax +1-763-514-4879
Version Number/Date	Version 1.0 07/Jul/2016

I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated.

I agree to comply with Declaration of Helsinki, Clinical Investigation Plan, Good Clinical Practice and to the national and local laws, regulations, standards, and requirements. I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic.

I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.

Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

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3. Glossary

Term	***Definition***
MASS	Micra Accelerometer Sensor sub-Study
ECG	Electrocardiogram
MASS2	Micra Accelerometer Sensor Study 2
MATS	Micra Accelerometer and Temperature Sensor
E-CRF	Electronic Case Report Form
EDC	Electronic Data Capture
ICF	Informed Consent Form
EC	Ethics Committee
CIP	Clinical Investigation Plan
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
ISF	Investigator Site File
LVOT	Left Ventricular Outflow Track
VTI	Velocity Time Integral
IC	Informed Consent
AE	Adverse Event
ADE	Adverse Device Effect
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

Term	***Definition***
CEC	Clinical Event Committee
GCP	Good Clinical Practice

4. Synopsis

<table>
<tr><td>Title</td><td>Micra Accelerometer Sensor Study 2 (MASS2)</td></tr>
<tr><td>Clinical Study Type</td><td>Prospective non-randomized, multi-center clinical research study.</td></tr>
<tr><td>Product Name</td><td>MATS Research System</td></tr>
<tr><td>Sponsor</td><td>Medtronic, Inc.
8200 Coral Sea Street NE
Mounds View, MN U.S.A. 55112
Phone: +1-800-328-2518</td></tr>
<tr><td>Local Sponsor</td><td>Bakken Research Center B.V.
Endepolsdomein 5, 6229 GW Maastricht, The Netherlands
Phone: +31-43-35-66-566</td></tr>
<tr><td>Manufacturer</td><td>Medtronic, Inc.
710 Medtronic Parkway
Minneapolis, MN 55432-5604, USA
Tel. +1-763-514-4000
Fax +1-763-514-4879</td></tr>
<tr><td>Investigation Purpose</td><td>The purpose of the MASS2 is to characterize accelerometer signals of Micra implantable device during different postures and activities and to understand the source of the sensed motion, in order to test feasibility for future enhancements in device functionalities.</td></tr>
<tr><td>Product Status</td><td>
<table>
<tr><th>Model Number</th><th>Component (Manufacturer)</th><th>Investigational or Commercially available</th></tr>
<tr><td>MC1VR01</td><td>Micra™ Implantable Device (Medtronic)</td><td>Commercially available in Europe</td></tr>
<tr><td>2090</td><td>Medtronic Carelink Programmer (Medtronic)</td><td>Commercially available in Europe</td></tr>
<tr><td>SW022</td><td>Micra™ Software Version 1.1 (Medtronic)</td><td>Commercially available in Europe</td></tr>
<tr><td>No model number</td><td>MATS Software Version 1.0 (Medtronic)</td><td>Investigational</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><td></td><td>
<table>
<tr><th>Model Number</th><th colspan="2">Component (Manufacturer)</th><th>Investigational or Commercially available</th></tr>
<tr><td rowspan="2">ER220</td><td rowspan="2">Extended Range Holter Monitor System
(Medtronic)</td><td>DR220 Holter (Medtronic)</td><td>Commercially available in Europe</td></tr>
<tr><td>ERX10 Extended range Tel-B antenna cable (Medtronic)</td><td>Investigational</td></tr>
</table>
</td></tr>
<tr><td>Primary Objective</td><td>The primary objective of MASS2 is to collect and characterize the waveform and components of the accelerometer signal from the Micra implantable device during different postures and activities, and to use echocardiography recordings to understand the elements contributing to the accelerometer signal</td></tr>
<tr><td>Study Design</td><td>The MASS2 is designed to extend and advance data collection of its predecessor, the MASS study.

The MASS2 study will be conducted in Europe and may include countries such as Austria, France and Spain. The study is expected to be conducted at approximately four centers.

The target population will consist of subjects aged ≥18 and implanted with a Micra device and not in Atrial Fibrillation. The expected duration of subject participation to the study (from enrollment until the exit of the subject) is approximately 2 hours.

The expected total study duration (from the enrollment of first subject to the exit of last subject) is approximately 6 months, representing the months of enrollments.</td></tr>
<tr><td>Sample Size</td><td>Between 40 and 50 subjects are planned to be enrolled in the MASS2 in order to collect a representative sample of approximately 40 readable datasets. Centers that enroll faster than others will be allowed to do so in order to maintain an adequate enrollment rate, and therefore there is not a minimum or maximum requirement for the number of subjects enrolled at each center.</td></tr>
<tr><td>Inclusion/Exclusion Criteria</td><td>Inclusion Criteria
Subject is ≥ 18 years old
Subject is implanted with a Micra device
Subject or witness (if applicable as per local regulation) is able and willing to provide Informed Consent
Exclusion Criteria
Subject is in atrial fibrillation
Subject is not able to perform study requirements</td></tr>
<tr><td>Study Procedures and Assessments</td><td>After subject enrollment, the investigational MATS software will be downloaded into the implanted Micra device and the subject will be equipped with the Holter for the time of a posture and exercise test. As in MASS, the MATS software will allow telemetry transmission of sensor data from the implanted Micra device to the</td></tr>
</table>

	Holter. After the posture and exercise test, subject will undergo the echo recording with the echo equipment available at the hospital. After the echo recording, the Holter will be removed from the subject and the MATS software will be manually removed from the Micra device. After the software removal, the subject will be exited from the study.
Safety Assessments	Based on the risk assessment of the MATS Research System and results from the previous MASS study, there are no anticipated or foreseeable adverse events expected to be related to MASS2 products or procedures. MASS2 will allow collection of all adverse events and device deficiencies. Medtronic will classify each adverse event according to ISO 14155:2011.
Statistics	Since the study will be exploratory in nature, subjects will be enrolled to collect a representative sample of approximately 40 readable datasets. Study objective is descriptive and therefore no endpoints will be developed.

5. Introduction

5.1. Background

Rate adaptive pacing may improve exercise capacity in subjects with chronotropic incompetence [1-5]. A number of sensors have been used to adjust pacing rate for rate adaptive pacing [6]. Medtronic rate adaptive pacing algorithms use a single axis accelerometer to adjust pacing rate during activity. Micra device is a single chamber ventricular pacemaker implanted in the right ventricle which uses a three-axis accelerometer. The recordings from all three accelerometer vectors may provide information on subject posture and allow for determination of the optimal accelerometer vector to be used for rate adaptive pacing. The accelerometer of Micra device is also capable of sensing heart motion and thus may detect atrial and ventricular contraction. Characterization of the intracardiac accelerometer signal may allow for the development of methods to synchronize ventricular pacing with atrial contractions, and consequently, the ability to provide atrioventricular synchronized pacing. This would potentially broaden the pacemaker indications for which the Micra implantable device may be used.

A previous clinical research study called the Micra Accelerometer Sensor sub-Study (MASS) collected accelerometer data and electrical heart activity of subjects implanted with a Micra device, during various postures and 24 hours of daily living. MASS used electrocardiogram (ECG) data to characterize accelerometer signal as motion associated with the atrial contraction. However, the source of the motion sensed by the accelerometer remains unclear. Understanding the source of the sensed motion may allow for the development of methods to synchronize ventricular pacing with atrial contractions. The recording of cardiac echo data, in addition to ECG data, may help to understand the elements contributing to the sensed activity and consequently may provide the ability to deliver atrioventricular synchronized pacing. This would potentially broaden the pacemaker indications for which the Micra implantable device may be used.

5.2. Purpose

The purpose of the Micra Accelerometer Sensor Study 2 (MASS2) is to characterize accelerometer signals of Micra implantable device during different postures and activities and to understand the source of the sensed motion, in order to test feasibility for future enhancements in device functionalities.

6. Objectives and Endpoints

6.1. Objective

The primary objective of MASS2 is to collect and characterize the waveform and components of the accelerometer signal from the Micra implantable device during different postures and activities, and to use echocardiography recordings to understand the elements contributing to the accelerometer signal.

This objective is descriptive and therefore no endpoints will be developed.

There are no secondary objectives (therefore no secondary endpoints) for MASS2.

7. Study Design

The MASS2 is a prospective non-randomized, multi-center clinical research study, designed to extend and advance data collection of its predecessor, the MASS study.

The study will be conducted in Europe and may include countries such as Austria, France and Spain. The study is expected to be conducted at approximately four centers. Between 40 and 50 subjects are expected to be enrolled in order to collect a representative sample of approximately 40 readable datasets. Since the study will be exploratory in nature, no statistical hypotheses were formulated to calculate the sample size and the number of expected subjects was based on the experience from the previous MASS study.

Centers that enroll faster than others will be allowed to do so in order to maintain an adequate enrollment rate, and therefore there is not a minimum or maximum requirement for the number of subjects enrolled at each center.

The Micra Accelerometer and Temperature Sensor (MATS) Research System was developed in support of the MASS study to allow collection of data from the Micra sensors. MASS2 will use the unchanged MATS Research System for the same purposes of MASS.

MASS2 procedures will be similar to MASS. After subject enrollment, the investigational MATS software will be downloaded into the implanted Micra device and the subject will be equipped with the Holter for the time of the posture and exercise tests. As in MASS, the MATS software will allow telemetry transmission of sensor data from the implanted Micra device to the Holter. The additional procedure introduced in MASS2 compared to MASS is the echocardiography recording. The echo recording will be done after the posture and exercise test using the echo equipment available at the hospital. The collected echo recordings will be used to understand the source of the signals from the intracardiac accelerometer. After the echo recording, the Holter will be removed from the subject and the MATS software will be manually removed from the Micra device. After the software removal, the subject will be exited from the study. The Holter overnight recording, which was optional in MASS, will not be part of MASS2.

Every effort will be undertaken to minimize missing data (e.g. periodic assessment of the accelerometer, ECG and echo data).

7.1. Duration

The expected total study duration (from the enrollment of first subject to the exit of last subject) is approximately 6 months, representing the months of enrollments. The expected duration of subject participation to the study (from enrollment until the exit of the subject) is approximately 2 hours.

7.2. Rationale

The previous MASS study was developed to collect data from the sensors of the Micra device, using the MATS Research System. All pre-clinical testing on the MATS Research System were executed in support of the MASS study and the results showed that all tests have successfully passed. MASS study enrolled 40 subjects. Neither adverse events nor device deficiencies related to MASS system/procedures were reported during the MASS study. Usable recordings were obtained from 32 of the subjects. The continuous accelerometer signal was used to develop a preliminary algorithm to detect atrial contractions using the accelerometer in the right ventricle. The 20 recordings in sinus rhythm were processed and the accuracy of the atrial detection algorithm was assessed. A larger sinus rhythm data set is desired for a wider representation of subjects and for further algorithm development. Therefore, MASS2 is being proposed to record additional subjects to extend the data set, using the unchanged MATS Research System. Furthermore, MASS2 will also collect echocardiography recordings to characterize the source of the accelerometer signal from the intracardiac accelerometer.

With the FDA and CE approval of the Micra device and the resulting launch of closure activities of the Micra Transcatheter Pacing Study (IDE Number: G130245), MASS2 is designed as an independent/stand-alone study.

8. Product Description

8.1. General

MASS2 will use the MATS Research System for the same purposes of MASS. Components of the MATS Research System are detailed in Table 1.

Table 1- MATS Research System components

Model Number	Component (Manufacturer)		Investigational or Commercially available
MC1VR01	Micra™ Implantable Device (Medtronic)		Commercially available in Europe
2090	Medtronic Carelink Programmer (Medtronic)		Commercially available in Europe
SW022	Micra™ Software Version 1.1 (Medtronic)		Commercially available in Europe
No model number	MATS Software Version 1.0 (Medtronic)		Investigational
ER220	Extended Range Holter Monitor System (Medtronic)	DR220 Holter (Medtronic)	Commercially available in Europe
		ERX10 Extended range Tel-B antenna cable (Medtronic)	Investigational

In addition to the MATS Research System, the MASS2 study will use the echocardiography equipment available at the hospital to conduct echo examination.

Instructions for intended use, including indications and contraindications of the components of the MASTS Research System used in this study, as well as medical procedures and information regarding material in contact with tissues or body fluids are provided in their respective manuals and instructions for use.

8.1.1. Micra Implantable Device

The Micra Implantable Device (MC1VR01) is a miniaturized, single chamber pacemaker that provides bipolar sensing and pacing in the right ventricle. The device has an activity sensor that detects the subject's body and heart movement.

The Micra Implantable Device is commercially available in Europe and will be used according to the approved and intended use in the MASS2 study.

8.1.2. Medtronic Carelink Programmer (2090) and Micra Software (SW022)

The Medtronic Carelink Programmer (2090) and Micra Software (SW022) Version1.1 are used to communicate with the Micra device. The use of a programmer head, Medtronic Model 2067 or Model 2067L, based on standard telemetry B, is required for communication between the Micra device and the Medtronic Carelink Programmer.

The Medtronic Carelink Programmer (2090) and Micra Software (SW022) Version1.1 are both commercially available in Europe and will be used according to the approved and intended use in the study.

8.1.3. MATS Software

The Investigational MATS software Version 1.0, created by Medtronic, will be downloaded into the Micra device using the Medtronic Carelink Programmer to enable the telemetry transmission of accelerometer data from the Micra device to the Extended Range Holter Monitor System. The MATS software can be manually removed from the Micra device using the Medtronic Carelink Programmer. In case the software is not manually removed, it automatically deactivates after 48 hours.

To use the MATS Investigational Software with a Medtronic Carelink Programmer, the software must be first installed on the programmer through the Medtronic Software Distribution Network (SDN). When the investigational MATS software is installed on the Medtronic Programmer, the installed Medtronic Programmer will be labeled to indicate that it contains investigational software. The installation only needs to be done once per programmer.
At the beginning of each MASS2 session, the MATS software needs to be activated the programmer, selecting the "MATS Rev 1.0 - For Investigational Use Only" from the list displayed. After the MATS software is activated, an access code is required to communicate with the Micra device. This access code is unique for each device serial number and will be provided by the Study Team.
When the MASS2 study is complete, the software should be uninstalled from the programmers on which it was installed using the Medtronic SDN. Instructions on how to install/uninstall the MATS software on/from the programmer and on/from the Micra device are described in the MATS User Manual (DSN018088 Version 2.0 Initial Release).

8.1.4. Extended Range Holter Monitor System

All subjects in this study will use a customized investigational Extended Range Holter Monitor System (ER220). This ER220 system uses a commercially available Holter (DR220) and an investigational extended range telemetry-B antenna (ERX10) created by Medtronic. The ERX10 antenna is based on a market-released cable that communicates with implanted devices via telemetry; it has been modified to extend its range and increase noise rejection in order to communicate with the Micra device inside the heart.

8.2. Manufacturer

Each of the MATS Research System components is manufactured by Medtronic.

8.3. Packaging

When the investigational MATS software is installed on the Medtronic Programmer, the loaded Medtronic Programmer will be labeled to indicate that it contains investigational software.

The Investigational Holter will be labeled according to the local regulatory requirements.

8.4. Intended Population

The target population will consist of subjects aged ≥18 and implanted with a Micra device and not in Atrial Fibrillation (AF).

8.5. Equipment

In case of technical support and maintenance or calibration of study-specific equipment, the Investigators can contact the appropriate Medtronic study personnel. Medtronic Study Contact list will be provided under a separate cover.

8.6. Product Use

Principles of operation of the Investigational MATS software and ERX10 Extended range Tel-B antenna cable will be provided in the MATS User manual (DSN018088 Version 2.0 Initial Release) and ERX10 Instruction Sheet (DSN011766 Version 2.0 Initial Release), respectively.

8.7. Product Training Requirements

Training on the MATS Research System is required prior to the clinical site's first subject procedure.

8.8. Product Receipt and Tracking

Date when the site receives the installation of the MATS software from the Medtronic SDN will be maintained during and after the clinical investigation. Each programmer loaded with the MATS software will be traced with the programmer serial number.

Date when the site receives the Holters will be maintained during and after the clinical investigation. Each received Holter will be traced with the Holter serial number.

8.9. Product Storage

To use the MATS software installed on the programmer, the software must be first activated. Furthermore, a unique access code is required to communicate with each patient's device serial number. Therefore, the programmer installed with the MATS software can also be used outside the study purposes and there are no storage requirements.

Storage area of ER220 Holters should be locked/secure with access limited only to approved study staff.

8.10. Product Return

The investigational MATS software will be removed from the installed programmers only at the end of the clinical study via the Medtronic SDN.

Holters will be shipped back to Medtronic at the end of the clinical study.

8.11. Product Accountability

Product accountability will be documented in the electronic Case Report Forms (e-CRFs) which will be maintained in the Electronic Data Capture (EDC) system.

The e-CRF will track at least: date of receipt / installation of the investigational product / software from the site, serial number of the product, location of the product, date and reason for return / uninstallation of the product / software.

9. Selection of Subjects

9.1. Study Population

The target population will consist of subjects aged ≥18, implanted with a Micra device and not in AF.

9.2. Subject Enrollment

The subject will be considered enrolled after both the Investigator and the subject have dated and signed the Informed Consent Form (ICF).

9.3. Inclusion Criteria

- Subject is ≥ 18 years old
- Subject is implanted with a Micra device
- Subject or witness (if applicable as per local regulation) is able and willing to provide Informed Consent

9.4. Exclusion Criteria

- Subject is in atrial fibrillation
- Subject is not able to perform study requirements

10. Study preparation

10.1. 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/site is qualified by training, education, and relevant experience appropriate to the use of the product and associated procedures
- Investigator/site expects to have adequate time and resources to conduct the study throughout the duration of the study
- Investigator/site has access to an adequate number of eligible subjects
- Ability to comply with applicable Ethics Committee (EC) and regulatory requirements
- Investigator is not debarred, disqualified, or working under sanctions in applicable regions
- Investigation site has an echo machine available to conduct the echo recording

Qualification visits will be waived for the MASS2 study, since the assessment of the investigator or site will be conducted based on previous experience in conducting clinical studies for Medtronic and more recent visits for similar therapeutic areas.

10.2. Site activation

Before performing study related activities, all requirements shall be fulfilled, including, but not limited to the following:

- EC approval (and voting list, as required by local law) of the current version of the Clinical Investigation Plan (CIP) and ICF.
- Regulatory authority approval or notification (as required per local law)
- Fully executed Clinical Trial Agreement (CTA)
- Curriculum Vitae (CV) of investigators and key members of the investigation site team (as required by local law).
- Documentation of delegated tasks
- Documentation of study training.

Additional requirements imposed by the EC and regulatory authority shall be followed, as appropriate.

Medtronic may distribute pre-populated study-specific Investigator Site File (ISF) and will provide site with documentation of study center/investigator readiness. Evidence of center/investigator readiness must be received prior to subject enrollment and must be filed in the ISF.

11. Study Procedures

Subject may be at the hospital specifically for the MASS2 or for other reasons independent from MASS2, such as routine clinical care. Subject will undergo following study procedures:

- **Informed consent procedure** - The subject will be screened to verify eligibility criteria and willingness to participate to the study. After both subject and investigator sign and date the ICF, the subject is considered enrolled.
- **Baseline, Medical History** – Collect Baseline and Medical History information
- **Micra Implant Procedure History** – Collect information on the previous Micra implant procedure
- **MATS software download** - After subject enrollment, the investigational MATS software will be downloaded into the implanted Micra device.
- **Holter examination** - The subject will be equipped with the investigational ER220 Holter and Holter telemetry will be turned ON. The duration of transmission of Holter telemetry data is recommended to be set at 4 hours and should not exceed 24 hours. The subject will be requested to perform a posture and exercise test. The test consists of a repetition of postures and exercises for each of the three rate response activity vectors (V1, V2 and V3), such as:
  - If the subject is not being paced, temporary overdrive pacing at approximately 10 bpm above the intrinsic heart rate for 30 seconds
  - Supine, right recumbent and left recumbent postures for 1 minute each
  - Sitting and standing for 1 minute each
  - Walking at a normal pace for 2-3 minutes

Subject is allowed to have recovery time during the test as needed. If no recovery is needed, it is possible to move to the next exercise as soon as the subject is ready. In case part of the test cannot be completed, this should not be considered a deviation.

The Holter will allow recording of ECG and accelerometer data during the posture and exercise test, for each of the three rate response activity vectors.

- **Echo examination** - After the posture and exercise test is completed, subject will undergo the echo recording: 4 chamber, left atrial volume, left ventricular outflow track (LVOT) velocity time integral (VTI), pulmonic valve VTI, mitral flow, tricuspid flow. During echo recording, accelerometer data will continue to be recorded on the ER220 Holter. In case the Holter electrodes complicate the echo examination, the electrodes can be moved. After the echo recording, Holter will be removed and Holter telemetry will be set OFF.
- **MATS software removal** - After the echo examination, the Holter will be removed from the subject and the MATS software will be manually removed from the implanted Micra device, using the programmer.
- **Subject exit** – After removal of MATS software, subject will be exited. (Note: in case the MATS software was not manually removed, the subject will be exited after the automatic deactivation of the software).

11.1. Role of the sponsor representatives

Sponsor representatives may provide support as required for the study under supervision of the Principal Investigator, including:

- Study training relevant and pertinent to the involvement of personnel conducting study activities and investigator responsibilities
- Technical support in installing/uninstalling the MATS software into/from the Programmer via the SDN
- Technical support in downloading/removing the MASS2 into/from the implanted Micra device, under the supervision of a study investigator
- Monitoring and auditing activities

No data entry, shall be performed by Medtronic personnel or their representatives at sites

11.2. Schedule of Events

List of study procedures and study events/tests is reported in Table 2. Study procedures will occur all on the same day.

Table 2 – Procedure and events/tests in MASS2

Procedure	Events/Tests
Informed Consent procedure	1. Inclusion/exclusion assessment
	2. Informed Consent Form signature
Baseline, Medical History	3. Collect information on Baseline, Medical History

Procedure	Events/Tests
Micra Implant Procedure History	4. Collect information on the previous Micra implant procedure
MATS software download	5. Initial Device interrogation
	6. MATS software downloaded into Micra device
Holter examination	7. Holter attached and Holter telemetry set to 4 hours
	8. Holter recording during posture and exercise test: V1, V2, V3
Echo examination	9. Echo recording: Use the permanently programmed, chronic vector
	10. Holter removed and Holter telemetry set to OFF
MATS software removed	11. MATS software removed from Micra device
	12. Final Device interrogation
Subject exit	13. Subject exited

11.3. Subject Screening

Pre-screening of potential subjects may be over the telephone or in person (e.g. during a routine clinical care), to determine their initial eligibility and interest in the study.

Final screening of potential subjects needs to be in person on the day of the MASS2 visit, to verify that the subject is not in atrial fibrillation, as per exclusion criterion.

11.4. Prior and Concomitant Medications

There is no restriction about prior or concomitant medication/treatment. Subjects who had already received MATS software in MASS can receive MATS software download again in MASS2.

11.5. Subject Consent

Informed Consent (IC) is defined as a legally effective documented confirmation of a subject's voluntary agreement to participate in a particular clinical study after information has been given to the subject on all aspects of the clinical study that are relevant to the subject's decision to participate. This process includes obtaining an ICF and other privacy language as required by law that has been approved by the study center's EC and signed and dated by the subject. A subject may only consent after information has been given to the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate.

Prior to enrolling subjects, each center's EC will be required to approve the ICF and other privacy language as required by law. The document(s) must be controlled (i.e. versioned and/or dated) to ensure it is clear which version(s) were approved by the EC. Any adaptation of the sample ICF must be reviewed and approved by Medtronic and the EC reviewing the application prior to enrolling subjects.

The investigator must notify the subject of any significant new findings about the study that become available during the course of the study which are pertinent to the safety and well-being of the subject,

as this could impact a subject's willingness to participate in the study. If relevant, approval may be requested from subjects to confirm their continued participation.

ICF templates will be provided under a separate cover.

Prior to initiation of any study-specific procedures, IC must be obtained from the subject. Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize centers to submit subject information to the study sponsor. The IC process must be conducted by the principal investigator or an authorized designee, and the ICF and other privacy language as required by law must be given to the subject in a language he/she is able to read and understand. The process of IC must be conducted without using coercion or undue improper influence on or inducement of the subject to participate by the investigator or other center personnel. The IC process shall not waive or appear to waive subject's legal right. 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 read and understand the ICF, 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.

When the subject decides to participate in the clinical study, the IC must be signed and personally dated by the subject and investigator or authorized designee, as required by the ICF.

If the IC is obtained the same day the subject begins participating in study-related procedures, it must be documented in the subject's case history that consent was obtained prior to participation in any study-related procedures. It is best practice for the IC process to be documented in the subject's case history, regardless of circumstance.

In the event the subject cannot read and/or write and if allowed by local law the IC process shall be obtained through a supervised oral process. An independent witness (if applicable as per local regulation) must be present during this process. The IC and any other information must be read aloud to the prospective subject or his/her legally authorized representative. The witness signs and personally dates the IC attesting that the information was accurately explained and that IC was freely given.

The IC should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study.

The original of the signed ICF must be filed in the hospital/clinical chart and/or with the subject's study documents.

A copy of the ICF and other privacy language as required by law, signed and dated as required by law, must be provided to the subject.

The ICF and other privacy language as required by law and must be available for monitoring and auditing. Any Medtronic Field personnel who support the study procedure must be able to review the subject's signed and dated ICF and verify its completeness prior to proceeding with the study procedure. In the event the Medtronic Field personnel identify IC as being incomplete, the study procedure will not be allowed to occur until the consent of the subject can be adequately and appropriately obtained.

11.6. Randomization and Treatment Assignment

The study is not randomized. There is no comparison to a control group. There will not be statistical comparisons except to describe the study population.

11.7. Treatment Compliance

Subject compliance to the Holter and echo examinations will be monitored with a periodical review of received data.

11.8. Recording Data

Subject data and product accountability data will be collected on the e-CRFs and will be reported to Medtronic via the RDC System, Oracle Clinical.

Device interrogation data will be saved on supported media and will be delivered either electronically via a secure web-based application (Clinical Transfer or BOX) or via mail. Device data are recommended and not mandatory. Missing device interrogation data should not be considered as deviation.

ECG and accelerometer data will be saved on the Holter flashcard and will be delivered either electronically via a secure web-based application (Clinical Transfer or BOX) or via mail.

Echo data will be saved on supported media and will be delivered either electronically via a secure web-based application (Clinical Transfer or BOX) or via mail.

11.9. Deviation Handling

A study deviation is defined as an event within a study that did not occur according to the CIP or the CTA.

Prior approval by Medtronic is expected in situations where the investigator anticipates, contemplates, or makes a conscious decision to deviate. Prior approval is not required when a deviation is necessary to protect the safety, rights or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g. inadvertent loss of data due to computer malfunction, inability to perform required procedures due to subject inability).

For medically justifiable conditions which preempt a subject's ability to complete a study-required procedure, it may be permitted to report only one deviation which will apply to all visits going forward. This may also apply for other unforeseen situations (e.g. the subject permanently refuses to complete a study required procedure and the data will not contribute to the primary end point analysis). However, prior approval from Medtronic is required for such situations.

All study deviations must be reported on the e-CRF regardless of whether medically justifiable, pre-approved by Medtronic, an inadvertent occurrence, or taken to protect the subject in an emergency. Multiple deviations of the same type at the same visit may be reported on one e-CRF.

In the event the deviation involves a failure to obtain a subject's consent, or is made to protect the life or physical well-being of a subject in an emergency, the deviation must be reported to the EC as well as Medtronic. Reporting of all other study deviations should comply with EC policies and/or local laws and must be reported to Medtronic as soon as possible upon the center becoming aware of the deviation. Reporting of deviations must comply with EC policies, local laws, and/or regulatory agency requirements.

The investigator is not allowed to deviate from the CIP, except under emergency circumstances to protect the rights, safety and well-being of human subjects.

Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the CIP, conduct additional training, and terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the investigator and site, and in some cases, necessitate suspending

enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study.

Examples of MASS2 deviations include but are not limited to:

1 Failure to obtain subject IC
2 Inclusion/exclusion criteria not met
3 Missing ECG /accelerometer/echo data

11.10. Subject Withdrawal or Discontinuation

If a subject is withdrawn from the clinical study, the reason for withdrawal will be recorded in the e-CRF and in the subject's hospital record. Possible reasons for withdrawal from the study are:

- Subject withdrew consent;
- Investigator withdrew subject from the study for technical reasons (e.g. unsuccessful software download or Holter telemetry);
- Investigator withdrew subject from the study for medical reasons (e.g. inability to complete posture and exercise test);
- Investigator withdrew subject from the study due to inclusion/exclusion criteria not met.

If withdrawal is because of a safety concern, the subject shall be asked to be followed by the physician for collecting safety data outside the clinical study.

Subjects who are withdrawn before they complete the study can be replaced with new enrollments in order to collect a representative sample of approximately 40 readable datasets.

Since the study procedures will occur all on the same day, lost-to-follow up is not expected to occur.

12. Risks and Benefits

12.1. Potential Risks

Medtronic follows rigorous Quality Assurance and Control procedures throughout the development and clinical study of a product. The formal Hazard/Risk analysis of MATS Research System was done for the MASS study according to ISO 14971 (Medical Device Risk Management) and was used to ensure that the level of risk is acceptable prior to starting the MASS study.

MASS2 will use the same MATS Research System used in MASS (Table 1) and for the same purpose to allow collection of data from the Micra sensors. MASS2 procedures are similar to MASS. The main change in procedures is the addition of the echo examination performed with the echo machine available at the hospital. The echo procedure poses negligible / no risk to the subjects. Therefore, the formal Hazard/Risk analysis of MATS Research System which was done for MASS will not be impacted by MASS2, due to no new or increased risk as an outcome of the study. The comprehensive Hazard Analysis is documented in the MATS Research System Risk Management Report (DSN017848 Version 2.0 Initial Release).

During the course of the MASS2 study, risks will be continuously monitored, assessed and documented by the investigators. The risks are reduced as much as possible, with residual risk being documented within the Risk Management Report and disclosed in the ICF provided to subjects. A list of potential risks, mitigations and risk controls associated with the MASS2 product and procedure is summarized in Table 3 and Table 4.

Any potential risks associated with this study are further minimized by selecting qualified investigators, training study personnel on the Clinical Investigation Plan and User Manual.

Table 3 - Potential product risks and risk minimization

Potential product risk	**Minimization**
Improper MATS software download and manual removal: *Download and manual removal of the MATS software from the Micra device, if done improperly may impact implanted device functionality.*	• Access codes, software version, and software limitation requirements (no other software present in the device RAM) are in place for MATS software download • Programmer user is informed of presence of MATS investigational software on the Micra device on user interface • If the download of the MATS software does not execute correctly, this will be detected by the Micra device and the software will not be activated • The MATS software can be manually removed from the Micra device. The MATS software has an internal timer that automatically deactivates the software 48 hours after download
Interactions of the MATS software with existing Micra device features: *MATS software runs from the device RAM and sends the accelerometer and temperature sensor data via telemetry to the ER220 Holter, potentially causing an unintended interaction.*	• Potential Micra device interactions with the MATS software running with existing Micra device were analyzed. Interactions were limited to the use of telemetry for sensor data uplink and rate response, which were identified to be low risk as no direct therapeutic functionality would be affected. • Verification activities will be performed to ensure no related negative interactions
Missing/ misleading information causing insufficient/ inappropriate medical intervention: *Errors, omissions, or ambiguities in diagnostic data collected/ presented to the user, or corruption of software that influences the user's ability to make an informed medical decision.*	• Misleading information is prevented because MATS temperature sensor data is not viewable by study center personnel and any data not used for diagnosis purposes • Data integrity is controlled via ECC memory checks in the Micra device • Information on MATS supplemental markers on real-time EGM will be provided in training and User Manual • User Manual will instruct investigator to program optimum accelerometer vector in subject' Micra devices prior to leaving the study
Device longevity: *The sensor functionality and telemetry uplink mode will cause a slight current drain on the Micra device.*	• Risk control measures have been implemented to prevent longevity impacts greater than three months by limiting the duration of uplink of sensor data using telemetry to a maximum of 24 hours • The MATS feature set has an internal timer that automatically deactivates the software 48 hours after download • The MATS software download into the Micra Device will be prevented if the device is at pre-RRT (Recommended Replacement Time)

Table 4- Potential procedure risks and risk minimization

Potential procedure risk	Minimization
Excessive exertion from MASS2 Posture and Exercise Test may worsen subject's health conditions.	• Subjects will not be enrolled in the MASS2 if unwilling or not able to perform study requirements • Subject is allowed to have recovery time during the test as needed.
Inappropriate pacing: *The procedure includes steps to set temporary pacing rate approximately 10 bpm above the* subject*'s intrinsic rhythm to collect accelerometer data during pacing*	• Subjects are under the supervision of an experienced Clinician during the protocol steps • Detailed instructions in the MASS2 worksheets instructing overdrive pacing at a rate ~ 10bpm higher than the intrinsic heart rate • Temporary pacing allows immediate cancellation / cessation of pacing if needed due to subject symptom • There are no potential interactions of the MATS software with the temporary parameters of the Micra device

12.2. Potential Benefits

The MASS2 may offer no benefit. It is possible that improved rate response settings may be programmed as a result of the test. Improved rate response may provide improvements for optimal pacing rate.

12.3. Risk-Benefit Rationale

The data collection and procedural steps for MASS2 are assessed to be complete and sound in investigating improvement to rate response using the sensors in the Micra pacemaker, with all risks identified having been reduced to as low as possible for subjects' and investigators' safety.

13. Adverse Event Assessments

13.1. Definitions/Classifications

For the purposes of the clinical report, Medtronic will classify each adverse event according to ISO 14155:2011.

Where the definition indicates "device", it refers to any device used in the study. This might be the device under investigation, or any market released component of the system.

Adverse Event (AE): *(ISO14155:2011 3.2)*

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device

NOTE 1: This definition includes events related to the investigational medical device or the comparator.

NOTE 2: This definition includes events related to the procedures involved.

NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse Device Effect (ADE): *(ISO14155:2011 3.1)*

Adverse event related to the use of an investigational medical device

NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device

Serious Adverse Event (SAE): *(ISO 14155:2011 3.37)*

An adverse event that

a) led to death,
b) led to serious deterioration in the health of the subject, that either resulted in
    1) a life-threatening illness or injury, or
    2) a permanent impairment of a body structure or a body function, or
    3) in- subject or prolonged hospitalization, or
    4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
c) led to fetal distress, fetal death or a congenital abnormality or birth defect.

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE): *(ISO 14155:2011 3.36)*

Adverse device effect that has resulted in any of the consequences characteristic of a Serious Adverse Event.

Unanticipated Serious Adverse Device Effect (USADE): *(ISO 14155:2011 3.42)*

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report

NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

Device deficiency: *(ISO 14155:2011 3.15)*

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance

NOTE: Device deficiencies include malfunctions, use errors, and inadequate labelling.

13.2. Reporting of Adverse Events

All subject adverse events and device deficiencies will be collected starting from time of subject enrollment, until the exit of the subject. The AE e-CRF will be used for collecting event information, including date of event, seriousness, relatedness, resolution. Based on the risk assessment of the MATS

Research System and results from the MASS, there are no anticipated or foreseeable adverse events expected to be related to MASS2 products or procedures.
Adverse Event and device deficiency information will be reported to Medtronic, immediately but no longer than 3 calendar days after the investigator first learns of the event or of new information in relation with an already reported event. Initial reporting may be done by phone, fax, e-mail (Medtronic Study Contact List will be provided on a separate cover) or by completion of the AE e-CRF. In case the investigator requires information from the sponsor in an emergency situation, the investigator can contact study contact personnel (Medtronic Study Contact List will be provided on a separate cover).
In case an adverse event is not completed at the time of the subject exit, the subject shall be asked to be followed by the physician for collecting safety data outside the clinical study.
Medtronic will immediately review any new/modified Adverse Event or Device Deficiency. This review will include the determination whether the Adverse Event meets regulatory reporting requirements (Table 5). Source documents to support adjudication may be requested by Medtronic. The sponsor will ensure timely Adverse Event reporting to meet global regulatory requirements.
Medtronic will immediately report any Adverse Events or Device Deficiencies associated with the procedure or the device to the appropriate Medtronic Complaint Handling Unit. The appropriate Complaint Handling Unit will ensure prompt review, and appropriate reporting.

Table 5 - Adverse Event reporting requirements

Serious Adverse Device Effects (SADE), including Unanticipated Serious Adverse Device Effect (USADE):	
Investigator submit to:	
Medtronic	Immediately after the investigator first learns of the event or of new information in relation with an already reported event.
Regulatory Authority	As per local reporting requirement.
EC/IRB	Submit to EC/IRB per local reporting requirement.
Sponsor submit to:	
Regulatory Authorities	Reporting timeframe as per local requirement.
EC/IRB	Submit to EC/IRB per local reporting requirement.
Serious Adverse Events (SAE)	
Investigator submit to:	
Medtronic	Immediately after the investigator first learns of the event or of new information in relation with an already reported event.
Regulatory Authority	As per local reporting requirement.
EC/IRB	Submit to EC/IRB per local reporting requirement.
Sponsor submit to:	
Regulatory Authorities	Reporting timeframe as per local requirement.
EC/IRB	Submit to EC/IRB per local reporting requirement.
Adverse Device Effects (ADE)	
Investigator submit to:	

Medtronic	Immediately after the investigator first learns of the event.
Regulatory Authority	As per local reporting requirement.
EC/IRB	Submit to EC/IRB per local reporting requirement.
Sponsor submit to:	
Regulatory Authorities	Reporting timeframe as per local requirement
EC/IRB	Submit to EC/IRB per local reporting requirement.
All other AEs	
Investigator submit to:	
Medtronic	Submit in a timely manner after the investigator first learns of the event.
Regulatory Authority	As per local reporting requirement.
EC/IRB	Submit to EC/IRB per local reporting requirement.

13.3. Post Market Surveillance

13.3.1. Definition of 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.

13.3.2. Reporting of product complaints

It is the responsibility of the investigator to report all product complaint(s) associated with a medical device distributed by 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.

Note that although the reporting of product complaints is not part of the clinical study, all potential complaints that are collected as part of this study will be reviewed by Medtronic and, if applicable, reported to the designated complaint handling unit. Medtronic will ensure timely reporting to meet global regulatory requirements.

14. Advisory Committees

An Independent Clinical Event Committee (CEC) will not be installed for MASS2, as there are no anticipated or foreseeable adverse events expected to be related to MASS2 products or procedures.

15. Statistical Design and Methods

Since the study will be exploratory in nature, subjects will be enrolled to collect a representative sample of approximately 40 readable dataset. There is not a minimum or maximum requirement for the number of subjects enrolled at each center.

Data analysis will be performed by a Medtronic statistician and/or scientist.

Every effort will be undertaken to minimize missing data, and no subjects are expected to be lost to follow-up. However, unless otherwise specified, no statistical techniques will be used to impute missing data. The number of subjects included in each analysis will be reported so that the potential impact of missing data can be assessed.

The study endpoint is descriptive and no statistical hypothesis test will be performed.

No interim analysis is planned for this study.

16. Ethics

16.1. Statement(s) of Compliance

The study will be conducted according to the Declaration of Helsinki, Clinical Investigation Plan, Good Clinical Practice (GCP) and in accordance to the national and local laws, regulations, standards, and requirements of the countries/geographies in which the study is conducted. The principles of the Declaration of Helsinki are implemented in this study by means of the informed consent process, EC approval, study training, clinical trial registration, and risk benefit assessment.

Prior to first enrollment at a study center or any study procedures at that study center, approval of the CIP and additional deliverables required needs to be obtained from the study center's country specific regulatory authorities and an EC, as applicable.

EC approval of the clinical study must be received in the form of a letter and provided to Medtronic before commencement of the clinical 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 roster or letter of compliance, to allow verification that the investigator, other investigation site personnel, and/or Medtronic personnel are not members of the EC. If they are members of the EC, written documentation is required stating that he/she did not participate in the approval process. Investigators must inform Medtronic of any change in status of EC approval once the investigation site has started enrollment. If any action is taken by an EC with respect to the investigation, that information will be forwarded to Medtronic by the respective investigator.

Any additional requirements imposed by the EC or regulatory authority shall be followed, if appropriate.

Medtronic Bakken Research Center B.V. is a wholly owned subsidiary of Medtronic plc., 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 local law and custom concerning specific insurance coverage. If required, a study insurance statement/certificate will be provided to the EC and the competent authority.

17. Study Administration

17.1. Monitoring

It is the responsibility of Medtronic to ensure proper monitoring of the study per regulations. Appropriately trained Medtronic personnel or delegates appointed by Medtronic will perform study monitoring at the study center in order to ensure that the study is conducted in accordance with the CIP, the CTA, and applicable regulatory requirements. Medtronic must therefore be allowed to access to the subject's clinic and hospital records when so requested as per the ICF and CTA. Procedures in the CIP require source documentation, which will be maintained at the site. Source documents, which may include subject medical records, device interrogation files, must be created and maintained by the investigational site team. Data which will be directly collected in the e-CRF will not be considered source document, unless there is no other source document and it is authorized by the study-specific monitoring plan for that specific data. Worksheet may be used and will not be considered source document. The investigator will clearly mark clinical record to indicate that the subject is enrolled in this clinical investigation. Where copies of the original source document as well as print outs of original electronic source documents are retained, these shall be signed and dated by a member of the investigation site team with a statement that it is a true reproduction of the original source document. One-hundred percent of ICF will be monitored for this study. More details on monitoring will be documented in the Monitoring Plan.

The principal investigator(s) and his/her delegate(s) shall be accessible to Medtronic field personnel and the Clinical Study Manager. This accessibility is of particular importance for reviewing data in the e-CRF. Direct access to patient medical files for source data verification (if applicable) will need to be granted and prepared prior to any monitoring visits.

A list of participating Investigators and sites and list of Monitors will be provided to the sites on a separate cover.

17.2. Data Management

The e-CRF data reported to Medtronic will be stored in a secure, password-protected database. Data will be reviewed using programmed and manual data checks. Data queries will be made available to centers for resolution. Study management reports may be generated to monitor data quality and study progress. The investigator must ensure accuracy, completeness and timeliness of the data reported in the e-CRFs. Only authorized persons can complete and sign e-CRFs, as specified on the Delegated Tasks List included in the Investigator Site File.

The Device interrogation data, Holter data and Echo data delivered to Medtronic will be downloaded or saved to a secure network drive prior to being processed Direct Access to Source Data/Documents

The sponsor or a regulatory authority may audit or inspect the study center to evaluate the conduct of the study. The clinical investigator(s)/institution(s) shall allow study related monitoring, audits, Ethics Board review and regulatory inspection by providing direct access to source data/documents.

17.3. Confidentiality

All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by Medtronic or a third party designated by Medtronic in a key

coded form, unless it's impossible to make it anonymous, for instance, where the subject's name cannot be removed from the data carrier.

17.4. CIP Amendments

In case the investigator will propose any appropriate modification(s) of the CIP or investigational device or investigational device use, Medtronic will review this proposal and decide whether the modification(s) will be implemented.

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

17.5. Investigator record retention

The investigator is responsible for the preparation and retention of the records cited below. All of the below records, with the exception of case report forms, should be kept in the ISF (i.e., the study binder provided to the investigator) or Subject Study Binder. E-CRFs must be maintained and signed electronically within the electronic data capture system during the study. The following records are subject to inspection and must be retained for a period of two years (or longer as local law or hospital administration requires) after the date on which the investigation is terminated:

- Correspondence with EC, sponsor, monitor, regulatory authority that pertains to the investigation, including required reports
- Signed and dated ICF
- Documentation of the dates and rationale for any deviation from the protocol
- Electronically signed and dated e-CRFs
- List of investigation sites
- Subject screening log & ID log
- All approved versions of the CIP, ICF, and IB
- Signed CTA
- Current signed and dated CV of principal investigators and key members of investigation site team (as required by local law).
- Documentation of delegated tasks.
- EC approval documentation. Written information that the investigator or other study staff, when member of the EC, did not participate in the approval process. Approval documentation must include the EC composition, where required per local law.
- Regulatory authority notification, correspondence and approval, where required per local law.
- Study training records for site staff.
- Insurance certificates
- Any other records that local regulatory agencies require to be maintained (e.g. financial disclosure).

Final Study Report -A copy of the Final Clinical Study Report will be provided by the Investigator to the EC.

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

17.6. Sponsor record retention

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

- All correspondence which pertains to the investigation
- Internal tracking of investigational products
- Signed CTA
- Current signed and dated CV of principal investigator and key members of the investigation site team (as required by local law), delegated task list
- All approved IC Templates
- Copies of all EC approval letters and relevant EC correspondence and EC voting list/roster/letter of assurance
- Names of the institutions in which the clinical study will be conducted
- Regulatory authorities correspondence, notification and approval as required by national legislation
- Insurance certificates
- Final report of the clinical study
- The CIP, Investigator Brochure, and any revision
- Study training records for site personnel and Medtronic personnel involved in the study
- Any other records that local regulatory agencies require to be maintained.

17.7. Publication and Use of Information

Results may be submitted for publication.

The study will be recorded on www.clinicaltrials.gov before the first enrollment.

The following publication policy will have to be adhered to by all participating investigation sites, in case of publications.

Authorship on any publication(s) resulting from this clinical 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. Names of all participating investigators will appear in the Acknowledgment of the paper.

Based on the principle that Medtronic owns the data of this clinical study, a single investigation site may access and use the data provided by itself for scientific publications following prior approval by the Publication Committee.

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 clinical study.

17.8. Suspension or Early Termination

Medtronic or Regulatory Authority may decide to suspend or prematurely terminate the clinical study (e.g. if information becomes available that the risk to study subject is higher than initially indicated). If the clinical study is terminated prematurely or suspended, Medtronic shall promptly inform the clinical investigators of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC and the study subjects or their legal representative.

Medtronic, EC or Regulatory Authority may decide to suspend or prematurely terminate an investigation site (e.g. in case of expiring approval of the reviewing EC, 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 investigator(s) of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC, if required, the study subjects or their legal representative.

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, if applicable. Risks will be continuously monitored, assessed and documented by the Investigators.

In case of early investigation site suspension or termination subjects will be followed-up as per standard of care.

In case of close out, the investigators will be notified and notification/report to Medtronic and Regulatory Authority will be done, if required.

18. References

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