DOCUMENT APPROVAL PAGE

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Title: Ambulatory Remote Patient Monitoring using the µCor Heart Failure and Arrhythmia Management System (PATCH) Feasibility Study: Protocol NCT04512703

Author: Ramu Perumal, PhD **Date:** 9-February-2018

Approvals

("☒" indicates approval signature required)

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DOCUMENT REVISION HISTORY PAGE

Document Number:	Rev:	Page:
90D0167	C	2 of 32

Title: Ambulatory Remote Patient Monitoring using the µCor Heart Failure and Arrhythmia Management System (PATCH)Feasibility Study: Protocol

Revision History Of Document

Rev	CO Number	Description of Change	Author	Effective Date
FI	NA	First version	RP	7/17/17
A	NA	Changed the device name from Continuous Mobile Cardiac Telemetry System to uCor Heart Failure and Arrhythmia Management System.	RP	8/22/17
B	NA	The following changes were made: 1. Removed CE-mark reference for the device 2. Subjects no longer have to send photographs of the skin and device placement. Instead, they will note their skin condition and device location on the subject diary 3. Study coordinators will collect subject diaries once a week 4. Removed the requirement that phase II of the study can start only after completion of phase I 5. Updated the adverse event section per MEDDEV guidelines 6. Edits to improve the study implementation	RP	10/16/17
C	NA	The following changes were made: 1. First monitoring report to be sent within 24 hours rather than 2 hours. 2. Devices that are worn for only the first 7 days will now be sent to the sponsor 3. End of use study visit will occur at 90 days or when subject decides to end the study. 4. In the Subject Diary, replaced AM/PM with the 24-hour clock numbers 5. In the Subject Diary, subjects now will record when they replace the patch	RP	2/19/18

REMOTE PATIENT MONITORING USING THE μCOR HEART FAILURE AND ARRHYTHMIA MANAGEMENT SYSTEM (PATCH) FEASIBILITY STUDY

Short Title: PATCH Feasibility Study

Principal Investigator(s):

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Study Device: ZOLL μCor Heart Failure and Arrhythmia Management System (μCor System)

Protocol Number: 90D0167

Version: **C**

I have read and understand the information in the protocol and I understand my requirements for executing the protocol based on sound knowledge of GCP and ICH Guideline for Good Clinical Practice (E6).

PRINTED NAME OF INVESTIGATOR	SITE NUMBER
INVESTIGATOR SIGNATURE	DATE
SPONSOR	DATE

Table of Contents

Study Summary

Title	Ambulatory remote patient monitoring with the µCor Heart Failure and Arrhythmia Management System (PATCH) feasibility study.
Short Title	PATCH Feasibility Study
ZOLL Protocol Number	90D0167
Study Design	Prospective, non-interventional, feasibility study.
Study Duration	8 months, from start of screening to finishing the study.
Study Center(s)	Multi-center study, with a maximum of 8 centers in Europe.
Primary Objective(s)	To observe the feasibility of remotely monitoring patients with the novel µCor Heart Failure and Arrhythmia Management System (µCor system) that non-invasively captures thoracic fluid content, electrocardiogram, heart rate, respiratory rate, activity, and body posture.
Study Population	Health adult volunteers (21 years or older) and adult patients with a clinical indication for ambulatory outpatient cardiac monitoring.
Intervention	The study will consist of two phases. Phase I of the study will enroll 6 healthy volunteers, who have no indication for remote cardiac monitoring. Subjects are required to participate in the study for 30 days. Phase II of the study will enroll up to 44 patients indicated for outpatient cardiac monitoring and will participate in the study for up to 90 days. All subjects will wear the device in two locations, one along the left midaxillary line and the other along the left midclavicular line for the first seven days. Thereafter, for the remainder of the study, half the enrolled subjects will only wear the device in the left midclavicular position and the other half will wear the device in the left midaxillary position. Subjects will use a diary to keep a daily log their activities of daily living (phase I) or a log of any symptoms related to heart rhythm abnormalities and heart failure (phase II). Data will be acquired with the µCor system and wirelessly transmitted daily to a remote server for processing, generating thoracic fluid content, ECG, heart rate, respiration rate, activity, and posture measurements. Investigators will have access only to ECG data. Study staff will make weekly phone calls to subjects and record any new clinically actionable events. Patients will have monthly office visits. At the end of 30 days (phase I) or 90 days (phase II), patients will end wear and will complete the study follow-up questionnaire.
Study Size	The study will enroll a maximum of 50 subjects. Six healthy volunteers will be enrolled for phase I of the study. Remaining 44 subjects will be enrolled for phase II and will have an indication of outpatient cardiac monitoring.

1 Introduction

This document is a protocol for a human research study. This study is to be conducted according to US and international standards of Good Clinical Practice (International Conference on Harmonization ICHE6).

1.1 Background

Mobile cardiac telemetry (MCT) allows for ambulatory monitoring of electrocardiograph (ECG) signal continuously.[1] When a cardiac event occurs, the MCT system instantaneously transmits the data to a monitoring center, where the data is analyzed live and a report is sent to the patient's physician for diagnosis and therapy management.[1,2] Previous studies have shown that use of MCT, instead of a Holter or event monitor, leads to better outcomes with regard to diagnostic yield, management of arrhythmias through the use antiarrhythmic drugs, and cost savings in the hospital for cardiac procedures.[2–4]

Given the patient management capabilities of the MCT system, ZOLL has developed a novel radiofrequency (RF) based µCor Heart Failure and Arrhythmia Management System (µCor system). The system records ECG and heart rate through 2 electrodes and respiration rate, activity, and posture through a tri-axial accelerometer. Thoracic impedance, a measure of lung fluid, is estimated using low-power electromagnetic pulses at radio frequencies of 0.5-2.5GHz. The µCor system continuously records and transmits ECG and accelerometer data to the monitoring center. RF data are recorded periodically according to a predefined schedule. Physiological parameters such as thoracic impedance, heart rate, respiration rate, activity, and posture are extracted from the recorded data by dedicated software at the monitoring center. Certified technicians at the monitoring center review received data and prepare clinical reports to the prescribing physician. Because the µCor system has not yet been tested in a real-world setting, the purpose of this study is to observe the feasibility of the novel µCor system to remotely monitor patients in a real-world, ambulatory setting.

1.2 Preclinical Data

NA

1.3 Clinical Data to Date

NA

1.4 Study Device

1.4.1 System Components

The µCor System consists of the following components:

A) Patch
B) Sensor
C) Charger
D) Data transmission device (Gateway)
E) Server

Once activated, the wearable Sensor automatically acquires ECG, thoracic impedance, Heart Rate, Respiration Rate, Activity, and Posture measurements. Patients can also activate a patient trigger when they experience symptoms such as palpitations, shortness

of breath, or lightheadedness by double tapping the Sensor when it is on the body. Data are automatically transmitted from the Sensor to the Data transmission device, and from there to the Server for analysis (see Fig. 1). Certified technicians at the Monitoring Center review the data generated by the Server and prepare reports according to the pre-defined criteria as requested by the prescribing physician. Data provided in the report will aid the prescribing physicians in the diagnosis and identification of various clinical conditions, events and/or trends. The µCor System is designed for use in outpatient clinic and home settings.

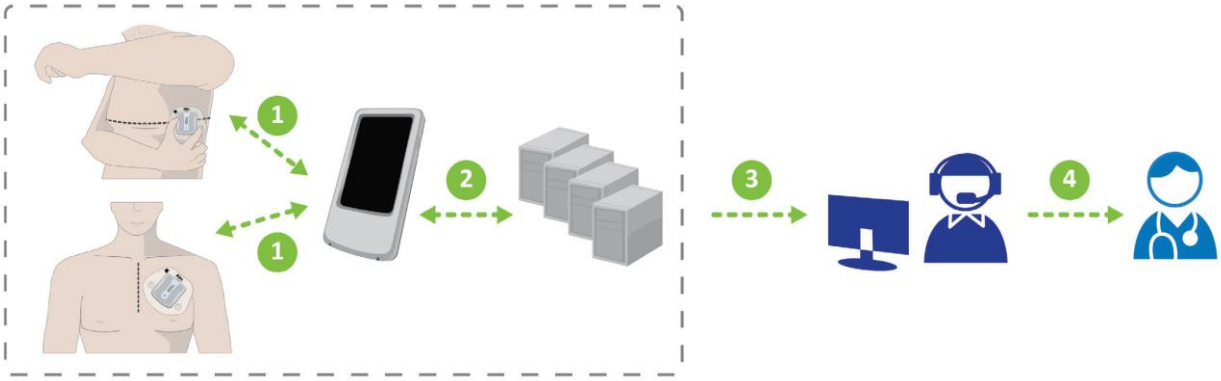


Figure 1: Data transmission of the µCor System

1.4.2 Patch

The Patch (Fig. 2) consists of a plastic frame intended for housing the Sensor, and two ECG electrodes on each side of the frame. It is applied to your body.
The Patch is a single-use, disposable item. At the end of 5 days, it should be replaced with a new Patch.

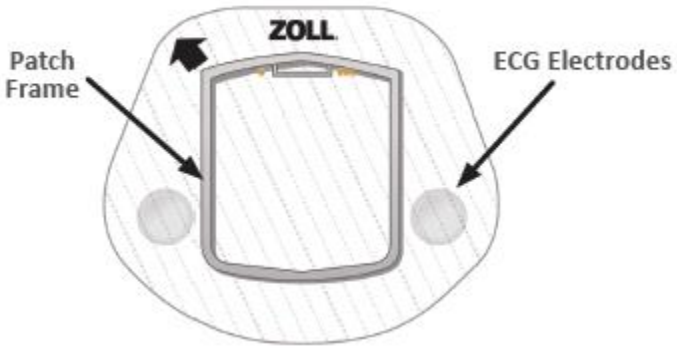


Figure 2: Patch

1.4.3 Sensor

The Sensor (Fig. 3) is a battery powered unit that acquires data. The Sensor connects to the Patch via the snap-in clip and positioning tabs. Through the adhesive backing on the Patch, the device becomes wearable. The Sensor is not disposable and needs to be returned to ZOLL upon the completion of the prescription. A light indicator is located close to the center and serves to communicate the Sensor's status at different points of use. Note that the light indicator is visible only when lit.

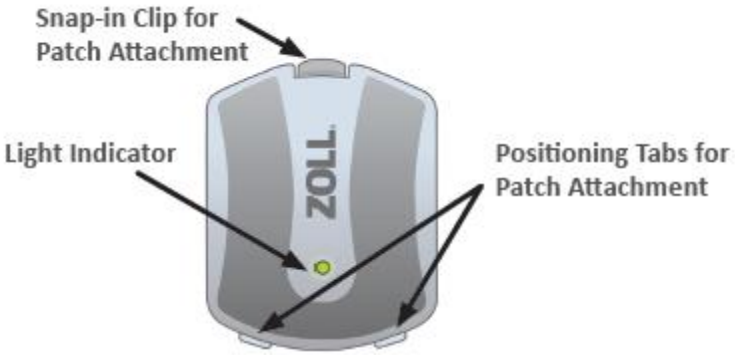


Figure 2: Sensor's front view

1.4.4 Charger

A dedicated Charger (Fig 4) is supplied with the µCor System for recharging the Sensor and the Data Transmission Device. A blue light appears when the Charger is connected to an AC outlet.

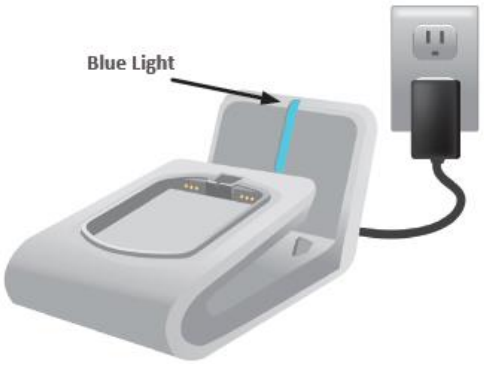


Figure 4: Charger

1.4.5 Data transmission device (Gateway)

A Data Transmission Device or Gateway is responsible for sending data from the Sensor to the Server for data analysis. When the screen display is on, the gateway battery status is visible on the screen. Once the battery status is under a certain level, a short beeping sound will be made every few minutes until the battery is depleted or the Gateway is placed in the Charger.

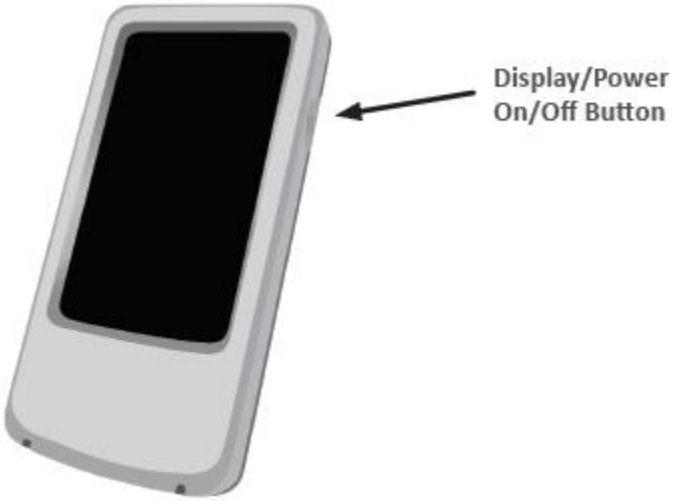


Figure 5: Gateway

1.4.6 Server

The Server refers to the hardware and the processing software and resides in a remote cyber-secure location. The software analyzes the data received from the Sensor via the Gateway and processes the data into clinical values for presentation to your healthcare provider after review by certified technicians at the Monitoring Center.

1.4.7 Device (Sensor +Patch) Placement Location

There are two locations for device (Sensor + Patch) placement: (1) along the left midaxillary line in line with the nipple (side location) and (2) along the left midclavicular line, above the nipple and below clavicle.

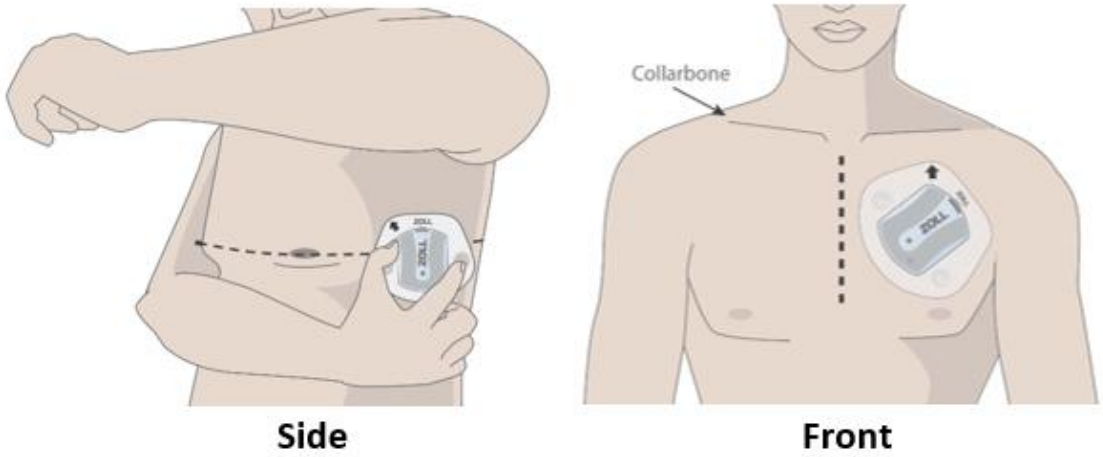


Figure 6: Device (Sensor + Patch) placement location

2 Study Objectives

2.1 Primary Objective(s)

The primary objective of this study is to observe the feasibility of the novel µCor system to remotely monitor patients. Feasibility will be assessed in terms of:

2.1.1 Logistics of equipping patients with the µCor system in the physician's office. This will include verifying that the system is able to transmit data to a remote server and that a monitoring report is received by the physician's office.

2.1.2 Subject's ability to wear the device for the specified time period of up to 90 days.

2.1.3 Subject's ability to place the device in the correct anatomical position during every reapplication, as described in the patient instructions for use. Device placement case report forms and daily device data signal quality will be used to track the accuracy of device placement and repeatability.

2.1.4 Ability of the system to transmit data daily to the remote servers for processing.

2.1.5 Ability to provide a timely arrhythmia monitoring (daily, episodic, and end of monitoring) reports to physicians.

2.1.6 Documenting the following clinically actionable events in an outpatient setting via weekly phone calls to the subject:

2.1.6.1 Emergency room visits

2.1.6.2 Unplanned physician visits

2.1.6.3 New arrhythmia and heart failure (HF) symptoms

2.1.6.4 All-cause and HF hospitalizations

2.1.6.5 Alterations and additions in HF and cardiac medications

2.1.6.6 All-cause and cardiovascular mortality at 90 days

2.2 *Secondary Objective(s)*

A number of **secondary objectives** will be evaluated and these will include:

2.2.1 Equivalency of data recorded by the device placed along the left midaxillary line versus the data recoded by the device placed along the left midclavicular line.

2.2.2 Correlation between detected heart rhythm abnormalities and any clinically actionable events.

2.2.3 Correlation between detected thoracic fluid content changes and any clinically actionable events.

2.2.4 Correlation between changes in thoracic fluid content and/or detected heart rhythm abnormalities with all-cause and cardiovascular mortality.

2.2.5 Short term (days), mid-term (weeks), and long-term (months) stability of the device recorded data in the same patient.

2.2.6 Stability of the device recorded data with multiple reapplications of the µCor system.

2.3 Safety Objective(s)

To document the number and severity of serious adverse events and adverse events related to use of the µCor system.

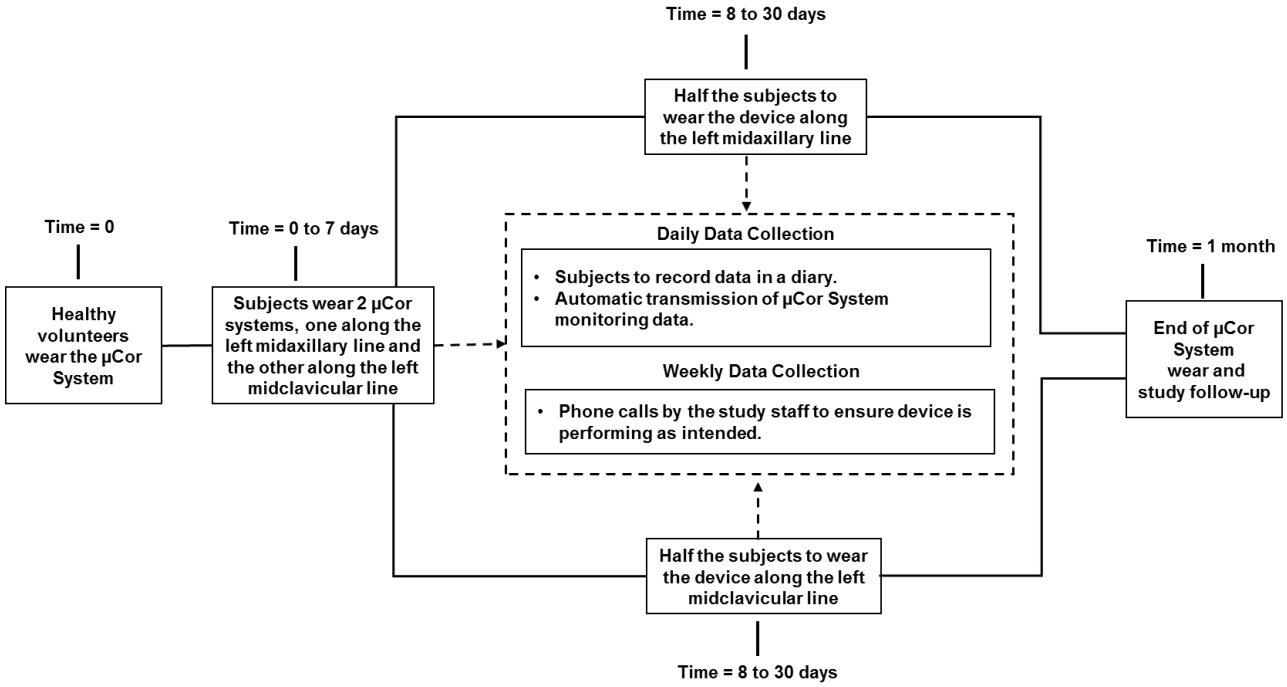
2.4 Additional Objective(s)

NA

3 Study Design

3.1 General Design

A) Phase I



B) Phase II

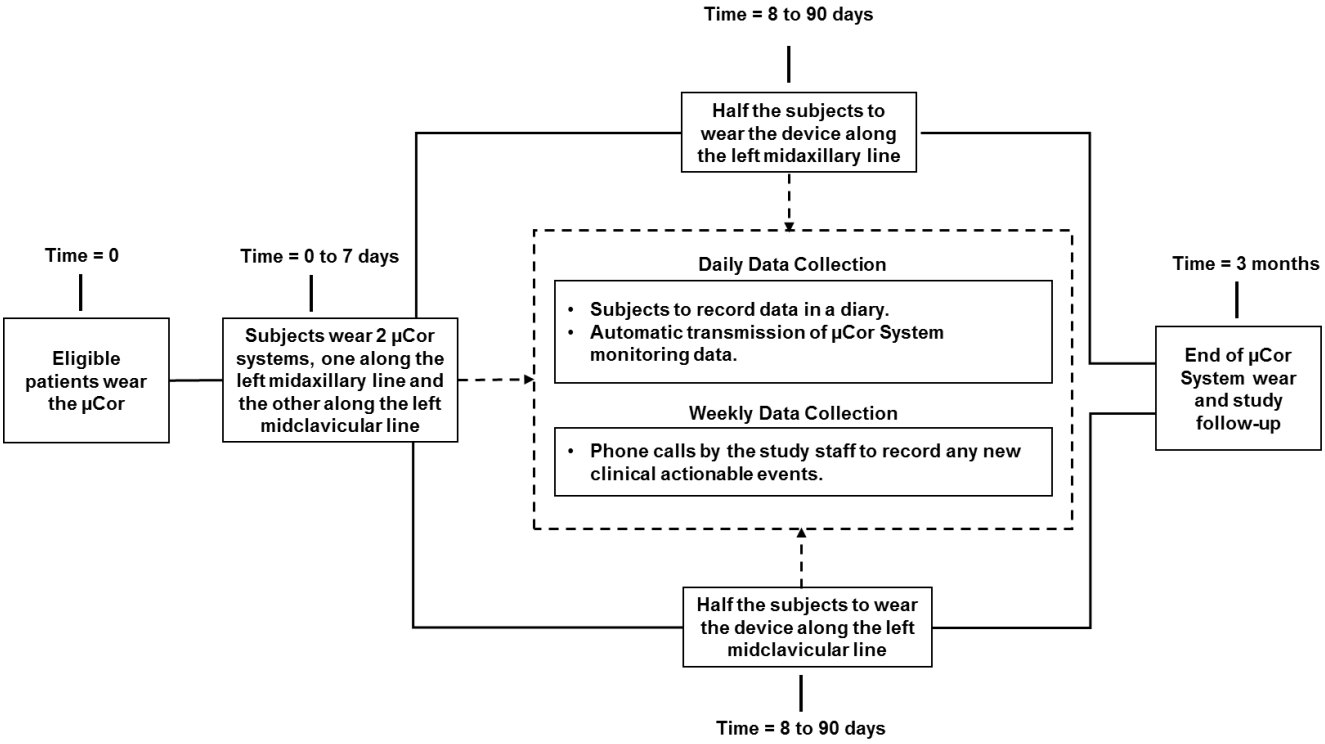


Figure 2: Schematic of trial design with various phases of the study.

This is a multicenter, prospective, non-interventional, feasibility study. A maximum of 8 centers in Europe will participate in the study. Phase I of the study will enroll 6 healthy volunteers, who have no indication for remote monitoring. Subjects are required to participate in the study for 30 days. For the first seven days, all subjects will wear the µCor system in two locations, one along the left midaxillary line and the other along the left midclavicular line. Thereafter, for the remainder of the study period (23 days), 3 subjects will wear the device in the midclavicular position and the remaining 3 subjects will wear the device in the midaxillary position. Data will be acquired with the µCor system and wirelessly transmitted daily to a remote server for processing. Subjects will keep a diary to record their daily activities of living, their skin condition due to use of the µCor device/s, and placement location of the device/s. (Appendix A). In addition, the subjects will receive weekly phone calls to ensure that the device is performing as intended. Furthermore, the study staff will ask the subject send their diaries after each week of wear to the study coordinator. At the end of 30 days, these subjects will end wear and will complete study follow-up questionnaire.

For phase II of the study, up to 44 patients eligible for remote monitoring will receive a µCor system after they are enrolled in the study. Subjects must be willing to wear the µCor system continuously for 90 days. In case of adverse skin reaction to the µCor adhesive and/or electrodes, on the discretion of physician, subjects may discontinue wearing the device for up to 72 hours. All subjects will wear the device in two locations, one along the left midaxillary line and the other along the left midclavicular line for the first seven days. Thereafter, for the remainder of the study, half the enrolled subjects will only wear the device in the left midclavicular position and the other half will wear the device in the left midaxillary

position. Subjects will use a diary to keep a daily log of their daily activities of living, any symptoms related to heart rhythm abnormalities and heart failure, their skin condition due to use of the µCor device/s, and the placement location of the device/s (Appendix A). Data will be acquired with the µCor system and wirelessly transmitted daily to a remote server for processing, generating thoracic fluid content, ECG, heart rate, respiration rate, activity, and posture measurements. Investigators will have access only to ECG data. Study staff will make weekly phone calls to subjects and record any new clinical actionable events. Furthermore, the study staff will ask the subject send their diaries after each week of wear to the study coordinator. Patients will have monthly office visits. At the end of the participation period (anticipated 90 days), patients will end wear and will complete the study follow-up questionnaire.

3.2 Primary Study Endpoints

Only observational data will be collected to assess the feasibility of implementing the µCor system to monitor patients in an outpatient setting. There are no target objectives associated with these data; however, these endpoints will be assessed:

3.2.1 Logistics that captures device placement, subject training, device data transmission, and monitoring report receipt during the initial device fitting at the physician's office.

3.2.2 Total number of days the device is worn and wear time per day.

3.2.3 Accuracy and repeatability of device placement during the anticipated 90 day wear period.

3.2.4 Number of data transmissions from the device to the remote severs during the study period.

3.2.5 Timing of the monitoring reports to physicians.

3.2.6 Weekly documentation of skin condition.

3.2.7 Timely documentation of clinically actionable events.

3.3 Secondary Study Endpoints

Various secondary endpoints that will be evaluated for the study are detailed in Section 2.2.

3.4 Safety Endpoints

Adverse events related to the use of the µCor system and all serious adverse events will be used to assess safety during the study.

4 Study Subject

4.1 Inclusion Criteria

The following criteria will be used to include subjects in **phase I** portion of the study:

4.1.1 Healthy male and female volunteers.

4.1.2 Subjects older than 21 years of age.

4.1.3 Subjects willing to wear the µCor device for up to 30 days.

4.1.4 Subjects willing to answer weekly phone calls from the study staff.

The following criteria will be used to include subjects in **phase II** portion of the study:

4.1.5 Patients with a clinical indication for outpatient cardiac monitoring.

4.1.6 Patients older than 21 years of age.

4.1.7 Patients willing to wear the µCor device for up to 90 days.

4.1.8 Patients willing to make monthly (30-, 60-, and 90-day) office visits during the study period.

4.1.9 Patients willing to answer weekly phone calls regarding their health status.

4.2 Exclusion Criteria

The following criteria will be used to exclude subjects from **phases I** and **II** portions of the study:

4.2.1 Subjects reporting or planning to be pregnant.

4.2.2 Subjects with any cardiac implantable electronic devices, including loop recorders.

4.2.3 Subjects with a wearable cardioverter defibrillator.

4.2.4 Subjects with Holter monitors, wearable event recorders, and other mobile cardiac telemetry devices.

4.2.5 Subjects with any skin condition that would prevent them from wearing the µCor system.

4.2.6 Subjects who are non-ambulatory.

4.2.7 Subjects without adequate cellular transmission access that would prevent data download from the µCor device.

4.2.8 Subjects participating in another clinical study.

4.2.9 Subjects unable to give informed consent.

4.2.10 Employees of ZOLL or their family members.

4.2.11 Subjects traveling during the study participation period that prevents planned office visits and weekly phone calls from the study coordinator.

4.2.12 Subjects expected to undergo a planned MRI exam during the participation period.

5 Study Enrollment Plan

5.1 Enrollment Strategy

Physicians with clinical research capabilities and willing to use the µCor system will be identified as potential investigators for the study. Study related educational training may be provided to study coordinators and clinicians to increase awareness about the trial. In addition, study brochure describing the potential benefits and risks of the study may be provided to likely candidates for the study.

5.2 Study Size

The study will enroll a maximum of 50 subjects. Six healthy volunteers will be enrolled for phase I of the study. Remaining 44 subjects will be enrolled for phase II and will have an indication of outpatient monitoring. Subjects will be enrolled from a maximum of 8 sites. All sites will be located in Europe.

5.3 Enrollment Period

The anticipated total enrollment period will be 5 months. All subjects are anticipated to complete the µCor wear period at 8 months from start of the study.

5.4 Early Withdrawal of Subjects

5.4.1 When and How to Withdraw Subjects

Subjects may voluntarily withdraw participation at point during the study period. In addition, subjects will be withdrawn from the study prior to study completion under following scenarios:

5.4.1.1 Skin irritation and/or rash due to use of the µCor device that prevents subjects from wearing the device for longer than 72 hours.

5.4.1.2 Any life-threatening condition that prevents subjects from participating in the study for longer than 7 days.

5.4.1.3 Subjects no longer meeting the inclusion/exclusion criteria.

5.4.2 Data Collection and Follow-up for Withdrawn Subjects

All data from withdrawn subjects will be retained. Reasonable attempts should be made to obtain the end of study follow-up data. At minimum, the end of study follow-up data should include survival data.

6 Study Procedures

6.1 Subject Recruitment and Screening

6.1.1 **Subject recruitment**

Subjects will be identified from investigator sites. The investigator or the designated study coordinator will approach potential subjects to discuss the details of the clinical study, including benefits and risks of participating in the study.

6.1.2 **Subject screening**

Screening of subjects will be take place based on the inclusion/exclusion criteria. For phase I of the study, healthy volunteers will be screened. For phase II, only subjects with a documented clinical indication for outpatient cardiac monitoring will be screened for the study.

6.2 Scheduled Visits

6.2.1 **Visit 1: Screening and fitting of the µCor system**

6.2.1.1 For phase I of the study, healthy volunteers will be screened. For phase II, a chart review of patients will be used to evaluate patients for enrollment. A screening log will be maintained.

6.2.1.2 Informed consent will be obtained on eligible patients who wish to participate in the study.

6.2.1.3 The initial clinical and demographic data will be recorded. This may be done by chart review.

6.2.1.4 Subjects will be trained on care and use of the µCor system per the Instructions for Use manual.

6.2.1.5 Each site will sequentially assign a number to each subject as they are enrolled, starting at 001.

6.2.1.6 Subjects will be then fitted, per the Instructions for Use manual, with two µCor systems, one along the left midaxillary line and the other along the left midclavicular line. Subjects will wear the two devices for first seven days. After that, subjects with an odd number will be assigned to wear the device only

along the midaxillary line and those with an even number will wear the device only along midclavicular line.

6.2.1.7 A confirmation e-mail will be sent to the designated study staff within 1 hour of fitting and activating the devices that the µCor system is able to transmit data to a remote server.

6.2.1.8 First monitoring report will be sent the physician-investigator or designated study staff within 24 hours of fitting and activating the devices.

6.2.2 **Visit 2: Wear period from 0 to 7 days**

Subjects will wear two µCor devices for the first 7 days. All subjects will keep a diary to record their daily activities of living, their skin condition due to use of the µCor device/s, and the placement location of the device (Appendix A). For subjects participating in phase II of the study they will keep a dairy to record any symptoms related to heart rhythm abnormalities and heart failure (Appendix A). Symptoms associated with transient arrhythmias include syncope, near syncope, dizziness, palpitation, shortness of breath, chest discomfort, weakness, and diaphoresis. Symptoms of heart failure include: dyspnea, fatigue and weakness, edema, persistent coughing or wheezing, lack of appetite and nausea, confusion and impaired thinking, and increased heart rate. Arrhythmia monitoring reports will be provided to the physician when an actionable arrhythmia is detected per the notification specified by the physician-investigator. On day 7, the study coordinator will call the subjects to record any clinical actionable events and check on status of the device. During the call, subjects will be requested to send to send their dairy every week to the study coordinator. In addition, the study coordinator will remind the subjects to remove one of the devices, midaxillary or midclavicular, depending on whether the subjects are assigned an odd or even number. Subjects will also be instructed on how to send one of the study devices back to the sponsor.

6.2.3 **Visit 3: Wear period from 8 to 30 days**

Study coordinators will make weekly phone calls to record any clinical actionable events and ask subjects to send their weekly diaries. During this phone call, study coordinators will answer any device related questions, and if possible help with troubleshooting per the µCor Instruction for Use manual. All subjects will continue recording the requested information in their diary (Appendix A) and send their diaries to the study coordinator once a week. Arrhythmia monitoring reports will be provided to the physician when an actionable arrhythmia is detected per the notification specified by the physician-investigator. At day 30, all subjects will perform an office visit. During this visit, the study coordinator will collect subject diaries, answer questions related to the study and the device. In addition, subjects participating in phase I of the study will return all their study devices and study related material.

6.2.4 **Visit 4 and 5: Wear period from 31 to 90 days**

Only subjects participating in phase II of the study will wear the device up to 90 days. All subjects will continue recording the requested information in their diary (Appendix A) and send their diaries to the study coordinator once a week. Study coordinators will make weekly phone calls to record any clinical actionable events. During this phone call, study coordinators will ask the subjects to send their diary, answer any device related questions, and if possible help with troubleshooting per the µCor Instruction for Use manual. Arrhythmia monitoring reports will be provided to the physician when an actionable

arrhythmia is detected per the notification specified by the physician-investigator. At day 60 and 90, subjects will perform an office visit. During this visit, study coordinator will collect the subject diaries, and answer questions related to study and the device.

6.2.5 **Visit 5: End of study follow-up**

End of study follow-up will take place at the 90 day office visit or when the subject decides to end the study. Study coordinators will be responsible for collecting the subject diaries, any adverse events, and the study device.

6.3 Unscheduled Visits

Based on the physician-investigator discretion, subjects can be seen at any time during the study period.

6.4 Long-term Clinical Outcome Assessment

NA

6.5 Study Procedures Flowchart (or Table)

Summary of the activities and procedures to be followed at each visit is as detailed below (Table I)

Table I

	Visit 1 (Day 0)	**Visit 2 (Day 7)**	**Visit 3 (Day 30)**	**Visit 4 (Day 60)**	**Visit 5 (Day 90 / End of Study)**
Eligibility	X				
Consent	X				
Subject number assignment	X				
Clinical and demographic data	X				
Device training	X				
Device fitting	X				
Data transmission confirmation	X				
Monitoring report	X				
Collection of subject diary		X	X	X	X
Weekly phone calls		X	X	X	X
Subject diaries		X	X	X	X
Office visit			X	X	X
Filling of case report forms	X	X	X	X	X
Return of device 1		X			
Return of device 2			X (for phase I subjects)		X
Survival information		X	X	X	X

6.6 Blinding and Unblinding of Study

Investigator-physicians and study staff will not be blinded to the ECG data. They will be blinded to the thoracic impedance, respiration rate, activity, and posture data. Furthermore, all patients will be blinded to all device data.

7 Study Device Management

7.1 Subject Compliance Monitoring

7.1.1 **µCor wear time**

µCor wear time will assessed throughout the study period. Wear time will be monitored by the sponsor based on the daily data transmissions from the µCor device. It is anticipated that the wear time with µCor system will be over 70% through the study period. For subjects who show early signs of non-compliance, the sponsor will inform the study coordinators, who will then make phone-calls to encourage subjects to continue wear the µCor system. In addition, the study coordinators with the support of sponsor's technical support will try to trouble shoot and alleviate the reasons for subject's non-compliance.

7.2 Dispensing, Storage and Return

7.2.1 **Dispensing of Study Device**

The sponsor will ship sufficient µCor devices and other study-related supplies to each site. The site will be responsible for safe storage of the devices. The Investigator will be responsible for recording the receipt of the µCor system in an appropriate device log. Similarly, devices fitted on subjects will also be logged in an appropriate device log.

7.2.2 **Return of Study Device**

The Investigator will be responsible for ensuring all study devices are returned back to the site by the subjects in a timely manner. During the study, the study coordinator must ship these returned devices to the sponsor within 10 working days. In addition, at the end of the study all unused devices must be returned to the sponsor.

7.3 Device Malfunction or Defect

In case of device malfunction or defect, subjects will call the study coordinator to help debug the issue with the help of sponsor. In case the defect or malfunction cannot be resolved, new equipment will be provided to the subject.

8 Statistical Plan

8.1 Sample Size and Power Calculation

No sample size estimates or power calculations were performed for this feasibility study. The number of subjects for this study was determined by convenience sampling, where a maximum of 50 subjects are anticipated to participate in the study.

8.2 Randomization Scheme

NA

8.3 Endpoint Assessment

Study endpoints will be assessed in this feasibility study without predefined acceptance criteria.

8.4 Statistical Methods

Data from all subjects in the study will be analyzed. Descriptive statistics and qualitative analysis will be used to analyze the primary, secondary, and safety endpoints.

8.5 Additional Statistical Analysis

NA

8.6 Handling Missing Data

NA

8.7 Futility Analysis

NA

9 Health Economic Evaluation

NA

10 Safety and Adverse Events

10.1 Definitions

Adverse event are any untoward medical occurrence, unintended disease or injury or any untoward clinical signs in subjects, users, or other persons whether or not related to the study device. Serious adverse events (SAEs) are adverse events that:

- led to a death, injury or permanent impairment to a body structure or a body function
- led to a serious deterioration in health of the subject, that either resulted in a life-threatening illness or injury, a permanent impairment of a body structure or a body

function, in-patient hospitalization or prolongation of existing hospitalization, or in medical or surgical intervention to prevent life threatening illness
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

Adverse device effects (ADEs) are events related to of study device. An unanticipated ADE is any adverse effect not identified by nature, severity, or frequency prior to the study. Serious device effect are adverse device effect that has resulted in any of the consequence characteristics of a serious adverse event. Unanticipated serious adverse device effects are serious ADEs that by its nature, incidence, severity or outcome has not been identified prior to the study.

10.1.1 **Common Anticipated Device Effects with µCor Study Device**

Anticipated events include, but are not limited to:

10.1.1.1 Discomfort from wearing the device.

10.1.1.2 Skin irritation, redness, itching, or rash.

10.1.1.3 Tearing of the skin if the adhesive patch is not removed carefully.

10.1.1.4 Allergic reaction to the hydrogel and/or Patch adhesive

10.2 Recording and Reporting of Adverse Events

10.2.1 **Investigator Recording**

Investigators must assess the seriousness of all adverse events. All serious adverse events must be recorded in the pertinent case report form (CRF). The investigator must also record if the serious adverse event is related to the study device and assess whether it is anticipated. For non-serious adverse events, the Investigators are responsible for only recording the adverse device effects and whether the ADE is anticipated or unanticipated in the pertinent case report form (CRF).

The clinical course of each event should be followed until resolution, stabilization, or until it has been determined that the study treatment or participation is not the cause. Serious adverse device effects that are still ongoing at the end of the study period must be followed up to determine the final outcome. Any serious adverse device effects that occur after the study period should be recorded.

The minimum initial information to be captured in the subject's source document concerning the adverse device effect includes:

- Study identifier
- Study Center
- Subject number
- Device model and serial number
- A description of the event
- Date of onset
- Investigator assessment of the association between the event and study treatment
- Current status
- Whether study treatment was discontinued
- Whether the event is serious and reason for classification as serious

10.2.2 **Reporting of Adverse Events**

The following events are considered as reportable events per MEDDEV 2.7/3 revision 3 guidelines:

- any serious adverse event,
- any device deficiency that might have led to a serious adverse event if:
    1. suitable action had not been taken or
    2. intervention had not been made or
    3. if circumstances had been less fortunate
- new findings/updates in relation to already reported events

Investigators are to report all reportable events to the sponsor immediately, but no later than 3 calendar days after the investigational site study personnel's awareness of the event.

Reportable event are to be reported by the sponsor of the clinical investigation to all the National Competent Authorities (NCAs) where the clinical investigation has commenced. The sponsor must report to the NCAs:

- immediately, but no later than 2 calendar days of becoming aware of all reportable events that indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for subjects
- immediately, but no later than 7 calendar days of becoming aware of other reportable events or new findings or updates to it.

10.3 Protocol Deviations

Deviations from the protocol must receive both Sponsor and the investigator's Ethics Committee approval before they are initiated. Any protocol deviations initiated without Sponsor and the investigator's Ethics Committee approval that may affect the scientific soundness of the study, or affect the rights, safety, or welfare of study subjects, must be reported to the Sponsor and to the investigator's Ethics Committee as soon as a possible.

11 Administrative Responsibilities

11.1 Sponsor

ZOLL Services LLC, the Sponsor, is responsible for study administration as well as providing devices and related materials for the study. The Sponsor will select appropriate investigators, assure collection of investigator agreements, assure IRB approval of the protocol, and monitor informed consent records.

The Sponsor will designate appropriately trained and qualified individuals to monitor the investigation. These individuals will verify the adherence to procedures specified in the protocol, and verify maintenance of required subject and data records.

11.2 Investigators

The Investigators are responsible for obtaining and maintaining ethics approval of the study protocol. The Investigators are responsible for obtaining patient consent, and maintaining Informed Consent Forms and Case Report Forms for each subject. All forms must be signed by the Investigator or by the Investigator's designee. If the Investigators designate an individual to sign these forms, written notification must be provided to the Sponsor. The Investigators are responsible for maintaining records of study protocol deviations and amendments and all correspondence relating to the study. The Sponsor will provide an Investigator Notebook to serve as a study reference and regulatory binder. At the conclusion of the study, the Investigators will provide a summary report to the Sponsor and the reviewing Ethics Committee.

11.3 Data Coordination Center (DCC)

ZOLL Services LLC, the Sponsor, will be the acting DCC. The DCC has the responsibility for clinical data coordination.

11.4 Steering Committee

There is no steering committee for this study.

11.5 Data Safety Monitoring Board (DSMB)

The study will not be monitored by an independent Data Safety Monitoring Board (DSMB). ZOLL Services LLC, the Sponsor, will be the acting DSMB. They will periodically review all aspects of the trial, including all adverse events, to ensure the safety of the participants.

12 Data Collection and Management Plan

12.1 Data Collection

The following data points will be collected during the study:

- Patient demographics
- Clinical history, including comorbidities
- Medication and dosage
- Device placement, subject training, device data transmission, and monitoring report receipt during the initial device fitting at the physician's office
- Wear time data
- Accuracy and repeatability of device placement
- Skin condition
- Number of data transmissions from device to remote servers
- Timing of monitoring reports to physicians
- Emergency room visits
- Physician visits
- New arrhythmia and HF symptoms
- All-cause and HF hospitalizations

- Survival information

12.2 Data Coordinating Center (DCC)

NA

12.3 Data Handling and Record Keeping

12.3.1 **Case Report Forms (CRFs)**

Data will be collected at the investigational sites using the electronic data capture (EDC) system Clindex*LIVE* (Fortress Medical Systems, LLC, Hopkins, MN). Electronic Case Report Forms (eCRFs) will be implemented within Clindex*LIVE* by ZOLL's Clinical Data Manager. Data will be entered at the investigational sites by trained staff. Entered data will be reviewed by the site investigator, who will affirm its accuracy and completeness by electronic sign-off. The capability of the Clindex*LIVE* system to implement edit checks during the data entry process (front end edit checks) will be utilized to generate queries automatically at the time of data entry when malformed, out-of-bounds or missing required data are detected. All data queries, whether automatically or manually generated, will be communicated to and cleared by investigational site staff via Clindex*LIVE*, which provides a full featured query handling capability. Center staff will either correct or affirm all data that generates queries, which keeps all data processing in the hands of the investigational sites, not ZOLL. ZOLL's Clinical Data Manager and Clinical Scientist will review all cleared queries for appropriateness. A final comprehensive review of all of the data will occur at the conclusion of the trial. All queries will be resolved and all eCRFs will be electronically signed by appropriate center investigators prior to database lock.

Paper CRFs will be available for recording patient data in the event that the data entry system becomes unavailable because of a technical failure. All paper CRFs will be completed by the same trained personnel who would otherwise use the EDC system. Appropriately completed and signed paper CRFs may become the source data, and will be retained by the individual centers. Once the EDC system again becomes available, the patient data will be transcribed from the paper form into the EDC system by the same person who completed the paper form.

The paper CRFs for this study are documented under 90D0167_CRF.

12.3.2 **Source Documents**

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.

12.3.3 **Electronic Data Capture (EDC) System**

The Clindex*LIVE* software system was selected for use for this clinical trial because of its full-featured capability, security features, and wide acceptance within the clinical trial industry. ZOLL's Clinical Data Manager, in consultation with ZOLL's Clinical Scientist, will implement the set of eCRFs in Clindex LIVE, and develop a set of test data. User acceptance testing at ZOLL will demonstrate accurate and complete functioning of all data and edit check elements prior to rollout of the EDC system to the investigational sites. The clinical database will be hosted at Fortress Medical Systems, LLC, using redundant on- and off-site resources, throughout the data collection process. Data access (both entry and review) will be controlled by user ID and password restricted user authentication. Only users who have been appropriately trained will be permitted to perform data entry. Once entered by site personnel, data will be reviewed by the site investigator who will have eCRF signature authority. The Clindex*LIVE* system features a fully documented audit trail on all CRF data modified after first pass entry and automatic audit trail on all data changes. Individual report level security allows for a customized report environment for individual users and sites, so that users and sites may access only the data which they have entered into the system. The Clindex*LIVE* system has been independently certified to be 21 CFR Part 11 compliant.

12.4 Data Transmission from Sponsor

NA

12.5 Study Monitoring Plan

Monitoring activities will be conducted according to ZOLL's Monitoring of Clinical Studies Standard Operating Procedure (ZOLL 90D0013) and will be documented.

13 Risks and Benefits

The µCor system is a non-significant risk, noninvasive medical monitoring device. The potential risks from wearing the device may include discomfort, skin irritation, itching, rash, contact dermatitis, or breaching of skin if the patch adhesive is the removed too quickly. The µCor system has not been tested for compatibility with magnetic resonance imaging machines and external defibrillators.

No benefits to participation in this study are anticipated for subjects participating in phase I portion of the study. For subjects participating in phase II portion of the study, the µCor system may help to detect abnormal heart rhythms in a timely manner and thus prompting a suitable treatment.

14 Ethical Considerations

This study is to be conducted according to US and international standards of Good Clinical Practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent Ethics Committee (EC) or Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the EC/IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study. The investigator should provide a list of EC/IRB members and their affiliate to the sponsor.

14.1 Subject Consent and Confidentiality

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. See Documents 90D0167_ICD for a copy of the Subject Informed Consent Form. This consent form will be submitted with the protocol for review and approval by the EC/IRB for the study. The formal consent of a subject, using the EC/IRB-approved consent form, must be obtained before that subject undergoes any study procedure. The consent form must be signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

Each subject will receive a unique subject identification number. The subject's name and identity will be known to the local principal investigator and the Sponsor, as necessary for device use and study conduct, but will be kept confidential. Authorized personnel from the IRB and regulatory authorities may have access to original subject records.

At the end of the data collection period, a fully de-identified, HIPAA-compliant dataset will be created using all variables available from the Case Report Forms and device data contained within LifeVest network. This dataset will be used for analysis and publication purposes.

In the event that a subject revokes authorization to collect or use Protected Health Information (PHI), the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

14.2 Subject Financial Responsibility and Stipends

There is no cost to the patient to participate in this research study. The sponsor will cover the cost of the device. The cost of a subject’s ongoing medical care will remain the responsibility of his/her insurance.

15 Publication Plan

15.1 Authorship

The publication committee will consist of the following members:

1. The sponsor’s Vice President of Medical and Clinical Affairs and/ or their representatives, up to three individuals in total.
2. A minimum of 3 physician investigators will be chosen by the sponsor using the following criteria:

A. Contribution to study design
B. Contribution to patient enrollment
C. Contribution to data analysis
D. Contribution to manuscript preparation

The publication committee will then chose authors based on the above criteria. The publication committee will decide on the publication strategy, including all sub-studies and other presentations. Physicians on the publication committee can serve as authors. No employees of the sponsor will serve as authors. The authors agree that any proposed publication relating to the research conducted under this protocol will be submitted to the sponsor for review at least forty five (45) days prior to submission for publication. Upon notice by the sponsor during this period that any of sponsor's confidential information is contained in the publication(s) and/or intellectual property considerations apply, the publication may be delayed for an additional period of up to ninety (90) days (for intellectual property considerations) or until all confidential information has been eliminated from the publication(s) and sponsor has approved the publication. It may be determined by the sponsor that no data from this study will be published.

15.2 Data ownership

Data resulting from this study are the property of the sponsor, with each site having co-ownership with sponsor of the data generated within their site. The sponsor may make copies of all documents and reports related to the study at sponsor's expense, and all sites will maintain and retain study records for a period of ten (10) years following the termination of the study. The sponsor shall have access to all such records during this period with adequate prior notice and during normal business hours.

16 List of Abbreviations

ECG – Electrocardiograph
HF – Heart Failure
MCT – Mobile Cardiac Telemetry
RF – Radio Frequency

17 Bibliography

1. Joshi AK, Kowey PR, Prystowsky EN, et al. Telemetry (MCOT) System for the Diagnosis and Management of Cardiac Arrhythmia. 2005;95:878-881.

2. Rothman SA, Laughlin JC, Seltzer J, et al. The diagnosis of cardiac arrhythmias: a prospective multi-center randomized study comparing mobile cardiac outpatient telemetry versus standard loop event monitoring. *J Cardiovasc Electrophysiol*. 2007;18(3):241-247.

3. Tsang J-P, Mohan S. Benefits of monitoring patients with mobile cardiac telemetry (MCT) compared with the Event or Holter monitors. *Med Devices Evid Res*. 2014;7:1-5.

4. Zimetbaum P, Goldman A. Ambulatory Arrhythmia Monitoring Choosing the Right Device. 2010:1629-1636.

18 Appendix A

Subject Diary

DATE________________________________ **Sun Mon Tue Wed Thu Fri Sat**

Daily activities

Please circle the level of activity for each time slot. If applicable, you should add additional detail. For example: "I watched television from 10:30 am - 11:30 am" or "I walked around the mall from 01:45 pm - 02:30 pm"

morning

Circle your activity level.

00:00 – 02:00	Active Sitting Sleeping Details:
02:00 – 04:00	Active Sitting Sleeping Details:
04:00 – 06:00	Active Sitting Sleeping Details:
06:00 – 08:00	Active Sitting Sleeping Details:
08:00 –10:00	Active Sitting Sleeping Details:
10:00 –12:00	Active Sitting Sleeping Details:

evening

Circle your activity level.

12:00 – 14:00	Active Sitting Sleeping Details:
14:00 – 16:00	Active Sitting Sleeping Details:
16:00 – 18:00	Active Sitting Sleeping Details:
18:00 – 20:00	Active Sitting Sleeping Details:
20:00 – 22:00	Active Sitting Sleeping Details:
22:00 – 24:00	Active Sitting Sleeping Details:

Symptoms

Please circle any of the following symptoms that you are experiencing. If possible, note the time when the symptoms started and duration.

Racing heartbeat Slow heartbeat Flutter in your chest Chest pain Shortness of breath Lightheadedness or dizziness Sweating Near fainting Fatigue Swelling of feet, ankles, legs, or abdomen Other:____________________	Time:____________________ Duration:________________
Racing heartbeat Slow heartbeat Flutter in your chest Chest pain Shortness of breath Lightheadedness or dizziness Sweating Near fainting Fatigue Swelling of feet, ankles, legs, or abdomen Other:____________________	Time:____________________ Duration:________________
Racing heartbeat Slow heartbeat Flutter in your chest Chest pain Shortness of breath Lightheadedness or dizziness Sweating Near fainting Fatigue Swelling of feet, ankles, legs, or abdomen Other:____________________	Time:____________________ Duration:________________

DATE_____ **Sun Mon Tue Wed Thu Fri Sat**

Skin Condition

Please rate the skin condition under the µCor patch adhesive. Do this before reapplying the new patch. Provide the skin condition rating for each device (front and side location) that you are wearing.

Front Location

Date and Time of patch replacement: _____

Please rate the skin condition in the following manner:

1. Grade 0 (None): No redness, rash, irritation, or itchiness ☐
2. Grade 1 (Mild): Redness ☐
   Rash ☐
   Irritation ☐
   Itchiness ☐
3. Grade 2 (Moderate): Rash that breaks skin, hard or soft pimples or light peeling/scaling ☐
4. Grade 3 (Severe): Blistering, open ulcers, wet peeling, serious rash over a large area ☐

Side Location

Date and Time of patch replacement: _____

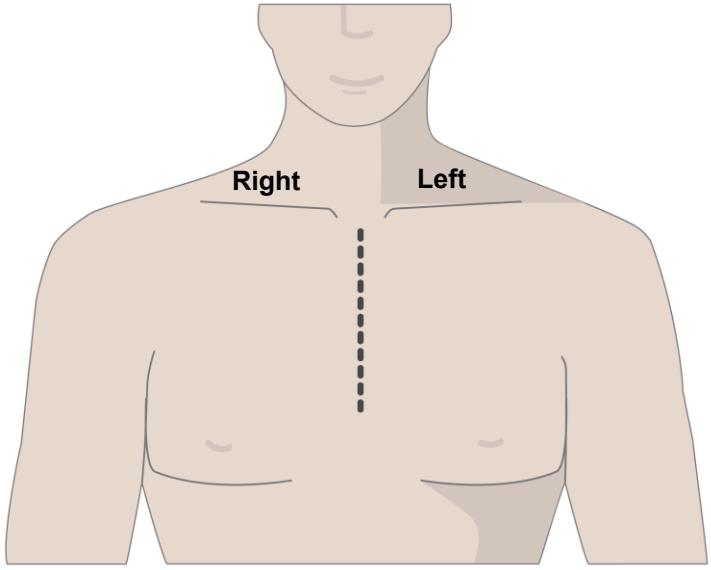
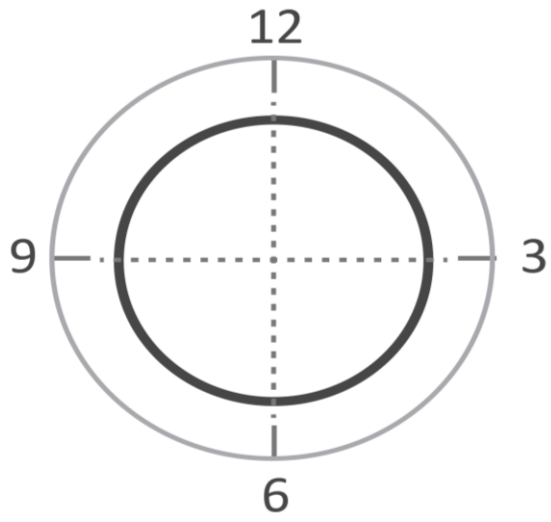
Please rate the skin condition in the following manner:

1. Grade 0 (None): No redness, rash, irritation, or itchiness ☐
5. Grade 1 (Mild): Redness ☐
   Rash ☐
   Irritation ☐
   Itchiness ☐
2. Grade 2 (Moderate): Rash that breaks skin, hard or soft pimples or light peeling/scaling ☐
3. Grade 3 (Severe): Blistering, open ulcers, wet peeling, serious rash over a large area ☐

Patch Location

Please outline the µCor patch location for each device that you are wearing.

Front Location

Outline the approximate location of the patch.	Mark location of the arrow in the clock diagram
	

Side Location

Outline the approximate location of the patch.	Mark location of the arrow in the clock diagram