ISRCTN11165621 https://doi.org/10.1186/ISRCTN11165621

Investigating whether ultrasound stimulation can be used to reset or regulate the heart's rhythm in patients with heart failure

Submission date
21/12/2018

Recruitment status
No longer recruiting

Registration date
08/03/2019

Overall study status
Completed

Last Edited
12/08/2021

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Heart failure is an illness in which the heart does not pump enough blood to meet the body's needs. A normal heart has four chambers in which blood flows. These chambers contract one after another in a regular and synchronized way. In heart failure patients, these chambers can beat out of sync, which causes a decrease in the flow of blood being pumped by the heart. To restore synchronicity to the heart chambers, doctors can implant a medical device called a Cardiac Resynchronization Therapy (CRT) device (a type of pacemaker) into the chest that makes the chambers beat at a normal rate using electrical impulses (pacing the heart). However, CRT therapy fails in about 3 in 10 implanted patients for unknown reasons. The purpose of the PACE-US study is to find out if it is possible to use ultrasound (sound waves) to pace the heart without inserting anything into the body, and to find out what the effects of this kind of pacing are for participants whose heart chambers beat out of sync. The study's findings will help doctors and researchers understand if pacing the heart with ultrasound can help predict a patient's response to CRT therapy before implanting a device in the patient's body.

Who can participate?
Adults over the age of 18 who are not pregnant and whose doctor recommends that they get a cardiac resynchronization device.

What does the study involve?
Study participants will be divided into two groups. Those in the first group will undergo an examination that uses ultrasound to record the heart and the organs around it (echocardiogram or echo/ECG) and an initial blood draw but will not receive ultrasound stimulation (Control group). Those in the second group will undergo an echo examination and an initial blood draw and will then receive ultrasound stimulation (Procedure group). Ultrasound stimulation may happen on the same day, or another day up to a month after the echo exam, and up to a month before CRT device implantation. During the ultrasound stimulation visit, participants will be fitted with a vest to record electrical signals coming from their heart. They will then undergo a Computed Tomography (CT) scan, which uses X-rays to make pictures of their heart. Next, participants will receive several injections into a vein of a substance called 'contrast agent' that

will make it easier to stimulate the heart using ultrasound. After each injection, the doctor will administer a dose of ultrasound energy to their heart from the surface of their chest. These two last steps will be repeated several times. Finally, participant will undergo one or two additional blood draws up to two days after the initial blood draw.

What are the possible benefits and risks of participating?
There will be no direct benefit to those taking part in the PACE-US study. There could be benefits for future patients with heart failure because the results of this study may influence how cardiac resynchronization therapy is performed in the future. The main risk of participating in the study is the pain from the blood draws. Moreover, for participants in the Procedure group, the main risks are the pain and possible bruising from having the contrast agent injected into a vein. A rare (up to 1 in 500 patients) risk of the contrast agent is to have a serious allergic reaction to it. Therefore, the study team will follow routine safety procedures to minimize the risks related to the blood draw and the injection of the contrast agent. Finally, a risk of receiving ultrasound stimulation comes from the fact that the study equipment will make the heart beat using ultrasound (sound waves) rather than electrical impulses, which is how the heart beats naturally. Therefore, there is a risk of injury to the heart muscle and changes in the way that the heart beats. The study team will minimize the risk from the ultrasound by following safety measures when using the equipment, and by selecting participants who are at low risk for injury. There may be other risks related to this study that are not yet known.

Where is the study run from?
The PACE-US study will be run from the Heart and Vascular Center at the University of Virginia (UVA), USA.

When is the study starting and how long is it expected to run for?
March 2018 to May 2021

Who is funding the study?
Medtronic, a company that develops and sells medical devices

Who is the main contact?
Joy Aso (updated 23/04/2020, previously: Jessica Lukken)
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MDT18016

Study information

Scientific Title
Feasibility of ultrasound as a temporary pacing or resynchronization technique, an acute clinical evaluation

Acronym
PACE-US

Study objectives
This study uses non-invasive ultrasound to assess the feasibility of temporary cardiac pacing or resynchronization; and characterizes troponin I level before and after non-invasive ultrasound stimulation.
This feasibility study is not powered to formally test a hypothesis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/06/2019, University of Virginia IRB for Health Sciences Research (IRB-HSR) (One Morton Drive Suite 400, Box 5, Charlottesville, VA 22903), ref: 00000447

Study design
Prospective non-randomized multicenter feasibility study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available.

Health condition(s) or problem(s) studied
Cardiac Resynchronization Therapy (CRT) in patients with heart failure

Interventions
Standard demographic and medical history will be colected at a baseline visit. The subjects will be assigned to either a Procedure cohort or Control cohort at the baseline visit, based on several criteria to be evaluated by the Investigator.
The study Procedure testing will precede the subject’s planned indicated CRT procedure. Subjects assigned to the Control cohort will undergo a blood draw for troponin measurement prior to their standard indicated CRT procedure. Patients assigned to the Procedure Cohort will undergo several non-invasive study testings, which are expected to add approximately 40 minutes to the patient's planned indicated CRT procedure.
Patients assigned to the Procedure Cohort will be fitted with a disposable CardioInsight™ Mapping Vest that can gather electrophysiological data from the body surface and will undergo a cardiac CT scan. They will then be injected with ultrasound contrast agent intravenously and will receive a series of non-invasive stimulation bursts targeted at their heart from an ultrasound probe placed on their chest. The position and orientation of the ultrasound probe will be changed during the Ultrasound Stimulation Procedure in order to find a pacing location where cardiac capture can be achieved. The ultrasound bursts will be triggered by atrial activation (i.e., the P-wave) and delivered with a variable time delay for each ultrasound probe position in an attempt to resynchronize the heart. Surface ECG signals will be acquired continuously to assess the occurrence of ultrasonically captured beats. Chest ECG data from the CardioInsight™ Mapping Vest will be acquired to assess the electrical activation map with and without Ultrasound Stimulation.Ultrasound pacing and resynchronization data will be programmed and collected during the Procedure visit for the Procedure cohort subjects by an investigational study system. Also blood measurement, medication and CT scan will be collected for the Procedure cohort subjects prior to their planned indicated CRT procedure.
Subjects will be followed through their routine pre-hospital discharge visit to collect two blood draws prior to hospital discharge. After their standard hospital discharge visit the subjects will have completed their study participation and will continue to receive their standard of care. In case of any ongoing adverse events related to the study procedure or system, all efforts will be made to follow-up the subject until the adverse event is resolved or until 30 days after their CRT procedure visit.
During this study following data will also be collected, as they occur: adverse event, device deficiencies, study deviations, study exit, and death.

Intervention Type
Device

Phase
Not Applicable

Primary outcome measure
Proportion of subjects who achieve successful pacing, defined as heart capture observed on the ECG for at least three consecutive beats after ultrasonic pacing stimuli are delivered to at least one pacing location. Descriptive statistics will be used to summarize the number of captured beats. The number and percent of subjects with a successful pacing outcome will be reported. All Procedure cohort subjects who complete enrollment and for whom at least one acoustic window is found will be included in the analysis.

Secondary outcome measures
1. Successful resynchronization event, defined as normalization of the QRS duration and electrical dyssynchrony index assessed using CardioInsight electrical activation maps at any time point during Ultrasound Stimulation testing
2. Cardiac Troponin I level in blood at baseline and at 4-8hrs or 24-48hrs after Ultrasound Stimulation testing for the subjects assigned to the Procedure cohort or at baseline and at 4-8hrs or 24-48hrs after baseline for the subjects assigned to the Control cohort

Overall study start date
01/03/2018

Completion date
03/05/2021

Eligibility

Key inclusion criteria
1. Meets standard criteria for implantation of a CRT-P or CRT-D device according to local guidelines
2. Subject (or legally authorized representative) has signed and dated the Informed Consent Form
3. Aged 18 years or older

Participant type(s)
Patient

Age group
Mixed

Lower age limit
18 Years

Sex
Both

Target number of participants

30

Total final enrolment
20

Key exclusion criteria
1. Confirmed myocardial damage, cardiac or chest surgery, or coronary procedure within the previous 30 days
2. Enrolled in a concurrent study that may confound the results of this study, without documented pre-approval from a Medtronic study manager
3. Pregnant, or of childbearing potential and not on a reliable form of birth control. Women of childbearing potential are required to have a negative pregnancy test within 7 days prior to the PACE-US Procedure visit.
4. Meets exclusion criteria required by local law (e.g. age, etc.)
5. Has any medical condition that would limit study participation per physician discretion

Date of first enrolment
25/09/2018

Date of final enrolment
28/05/2021

Locations

Countries of recruitment
United States of America

Study participating centre
University of Virginia Medical Center
1001 North Emmet Street
Charlottesville
United States of America
22903

Sponsor information

Organisation
Medtronic, Inc.

Sponsor details
Cardiac Rhythm and Heart Failure Clinical Research
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Sponsor type
Industry

Website
https://www.medtronic.com/us-en/index.html

ROR
https://ror.org/00grd1h17

Funder(s)

Funder type
Industry

Funder Name
Medtronic

Alternative Name(s)
Medtronic Inc.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/11/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available because datasets are considered Medtronic-confidential. Analysed data will be available in the results publication.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		12/08/2021	12/08/2021	No	No