

Room GAC82, HRIC Building, 3280 Hospital Drive NW

Calgary, AB, Canada T2N 4Z6

**STUDY: Risk Estimation Following Infarction, Non-invasive Evaluation ICD efficacy (REFINE ICD).**

SPONSORS: Canadian Institutes of Health Research, Cardiac Arrhythmia Network of Canada (CANet), Alberta Health Services (AHS), Alberta Advanced Education and Technology, Western Economic Diversification and GE Healthcare.

**INVESTIGATORS:** Katherine Kavanagh MD, Derek Exner MD, Andrew Howarth MD, Aaron Low MD, James White MD.

**INTRODUCTION**

This consent form is only part of the process of informed consent. It should give you the basic idea of what the research is about and what your participation will involve. If you would like more detail about something mentioned here or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

Your doctor has determined that you have had a heart attack. After heart attacks, some people develop dangerous and irregular fast heart rhythms. Why these irregularities occur and why they happen to some people but not to others is only poorly understood. It has been shown that changes in the heart’s electrical system may indicate a higher risk of these dangerous irregular heart rhythms. These changes in the heart’s electrical system can be identified using a portable 24-hour heart monitor or Holter monitor.

**STUDY PURPOSE**

This is a research study. Your study doctor will explain the study to you. You are being asked to consider participating in this study because you have had a heart attack. This document, known as the informed consent, will provide you with an explanation of the research study and what your participation may involve. Please take the time to read this document carefully and to review any accompanying information. You should ask your study doctor about anything pertaining to the research study or your participation that you do not understand.

The sponsor of the study in Canada is the University of Calgary located in Calgary, Alberta. The Canadian Institutes of Health Research (CIHR), Alberta Health Services (AHS), Alberta Advanced Education and Technology, Western Economic Diversification, GE Healthcare and the Cardiac Arrhythmia Network of Canada (CANet) are providing financial support for the study. Dr. Derek Exner at the University of Calgary is the overall principal investigator for this study.

The purpose of the REFINE ICD study is to test whether an implantable cardioverter defibrillator (ICD) can increase the likelihood of survival in patients at risk of heart irregularities, as determined from a 24-hour heart monitor that is performed at least 2 months after a heart attack.

An ICD is a device that is implanted under the skin, typically below the collarbone, and contains the battery and circuitry of the system. One or two insulated metal wires (leads) are passed from the veins in the shoulder region to the heart and carry the electrical energy from the device to the heart. The ICD monitors the heart rhythm using these leads. If your heart is beating too fast, the ICD may first use small painless electrical signals to correct your heart rate. If potentially life-threatening heart rate continues, the ICD will deliver a necessary life-saving shock and restore your heart to a more normal rate. If your heart is beating too slowly, the implantable defibrillator acts as a pacemaker to return your heart to a normal rhythm. The Medtronic ICD and leads that will be used in this study have been approved by Health Canada and other International regulatory agencies for use in people who have very weak heart muscles.

Approximately 2,100 patients will sign a consent form and be enrolled in the study. Of these 2,100 patients, it is estimated that testing will identify approximately 700 patients eligible to be randomized. Of the 700 patients eligible to be randomized, half (~350) will be assigned to receive an ICD.

The study will include patients from up to 50 sites worldwide. Your participation in the study is expected to last an average of 10 years or a maximum of up to 14 years depending on when you are enrolled in the study. We anticipate that up to 360 patients will be enrolled over the entire duration of the study at the Calgary site. Of these, approximately 120 patients will be eligible for randomization.

**STUDY PROCEDURES**

Your participation in this study may involve 3 phases: Screening, Randomization and Follow-up.

**Screening**. You will be asked to undergo an electrocardiogram (ECG) and wear a 24-hour heart monitor. If these tests show you are not eligible to be randomized, your participation will continue through yearly telephone contact to inquire about your health. Your study doctor will let you know if you are eligible to participate in the randomized phase, based on your heart monitor results. If the heart monitor results are not clear, you may be asked to retake this test.

**Randomization**. If the 24-hour heart monitor indicates that you are eligible for randomization, you will be asked to return to your study doctor’s office within a week to undergo a brief medical history, physical exam and complete Quality of Life surveys. None of these procedures are investigational. Once this information has been collected, you will be assigned or randomized to one of two groups. You will have an equal chance of being assigned to receive usual medical (Usual Care Group) or to receive an ICD (ICD Group). Neither you nor the study doctor will be able to select your group assignment.

If you are assigned to the ICD Group, your doctor will schedule a date for you to have an approved ICD and lead system implanted. The implant must take place within 30 days after randomization. The surgical procedures for implanting the ICD system in this study are the same as the implant procedures used for any patient that receives an ICD. This will require an overnight stay in the hospital. A separate document will be provided to you to explain the implant procedure. Your ICD will be programmed to correct only very slow (< 40 beats per minute) or very fast (> 181 beats per minute) heart rhythms. The ICD will not increase your heart rate as your activity level increases (rate response “off”). These programming parameters have been intentionally chosen for the REFINE ICD study so that only potentially life-threatening heart rhythm problems are treated. It is very important that you contact the study doctor or their team if any changes are made to your ICD by non-study related personnel (other clinics, emergency room, etc…) so that they can find out what changes were made (either through sending this information from your ICD over an analog telephone line or checking it directly in their clinic.

**Follow-Up.** All patients, both the Usual Care Group and the ICD Group, are required to return for follow-up visits as outlined in the **Follow-Up Visits section** on the following pages.

**Study-Related Testing**

**Heart Pumping Measurement**. You will need to have your heart’s pumping function measured if this has not been done at least 40 days after your heart attack. This is being done, generally, as per usual clinical practice to see if you are eligible for this study.

The heart's pumping function can be measured by a common heart test (i.e., echocardiogram, a MUGA scan or Cardiac MRI. During an echocardiogram sound waves called ultrasound are used to produce images of your heart that show the size and shape of your heart. A MUGA scan is a Nuclear Medicine Scan. Trace amounts of radioactive material are injected into your bloodstream. Special cameras then detect those tracers in your blood as it flows through your heart and lungs. A Cardiac Magnetic Resonance test uses magnetic field and radio waves to create images of your heart.

**ECG, Heart Monitor and Walk Test**. If the results of the heart pumping test show that you are a potential candidate for this study, then you will be asked to have an ECG and wear a 24-hour heart monitor. The ECG is the same as a routine clinical ECG. For the 24-hour heart monitor you will have patches placed on your chest and attached to the monitor. While wearing the monitor you will be asked to rest for 10-20 minutes, and then walk as far and as quickly as possible for six minutes. This will help measure how much exercise you can perform. You will then be asked to lie still for 20-30 minutes. You will also be asked to continue wearing the monitor for 24 hours, during your usual activities. Showering, bathing and swimming are not permitted during this time. After 24 hours you will be required to return the monitor to the study doctor.

**Quality of Life Surveys**. These surveys ask questions about how you are feeling and what you can or cannot do. They will take approximately 30 minutes to complete.

**Heart Magnetic Resonance Test**. It is thought that the amount of scarring in the heart after a heart attack may predict the risk of serious heart rhythm problems and death. However, this is not proven. A heart MRI test requires you to lie still in a magnetic resonance imaging (MRI) machine (tube) for 60-65 minutes. You will need to have an IV placed for this test. This test uses magnetic pulses to make a detailed picture of the heart. There are no known risks of an MRI test in people who are eligible. People with implanted medical devices, metal fragments, or certain types of heart valve and artificial joints are not eligible. If you are eligible you will receive a small amount of a contrast agent to allow precise measurement of the amount of scarring in your heart. This carries a very small (0.001%) risk of a serious skin reaction. This reaction mainly occurs in people with advanced kidney disease. People with severe claustrophobia may find it difficult to lie in the MRI tube and you will be offered a relaxing pill (sedative) if you have problems with claustrophobia. Please indicate (checkmark) whether or not you are willing to undergo a heart Magnetic Resonance test:

I agree to have a heart Magnetic Resonance test if I am eligible: Yes\_\_ No\_\_

**Echocardiogram Test**. If you have had a cardiac echocardiogram, also called a heart ultrasound, or will have one in the next six months we are requesting that you allow this study to be sent to the University of Calgary for analysis. You do not need to have an echo performed for the purpose of this aspect of the study. If you agree to have your echo study sent for analysis, it will be stored at the University of Calgary using only your study identification number.

I wish to allow my echocardiogram study to be sent to the University of Calgary. Yes\_\_ No\_\_

**Follow-Up Visits**. If you are eligible for the randomized part of this study you will be required to come back for a follow-up visit in 2-8 weeks and 6 months after your randomization visit. You will also be required to have yearly visits for up to 14 years. At each visit you will have a physical exam and your study doctor will review any heart related problems you have had since your last visit. If you have an ICD it will be checked and that information collected for the study.

You will also be asked to complete the Quality of Life surveys at the 6-month visit and the yearly visits.

**Telephone Visits**. If you are eligible for the randomized part of this study you will be contacted by telephone between the yearly visits (18, 30, 42 months, etc…) by your study doctor or someone from their staff and asked about your health.

**CareLink Visits**. If you are in the ICD group, you will be required to use the Medtronic CareLink system to send information from your device to the study doctor at least once per year. This system allows you to send information from your device over a standard (analog) telephone line to the study doctor’s office from any location in Canada or the United States. Separate instructions with more information about how to use the CareLink system will be provided to you.

**Additional Information**. Because we need to know the details of your health during the study, you may be asked to help us get information from doctors or any hospital or clinic that you visit while you are in this study. If we cannot contact you directly we will contact your family members in order to obtain this information. We will ask your doctor questions about your health, the use of heart procedures, the results of these and other tests and whether any changes were made to your medications.

**POTENTIAL RISKS**

**The following section is applicable to all study participants**

**Heart Pumping Measurement:**

Echocardiogram: There are no known risks associated with the use of a heart echocardiogram.

MUGA: A heart scan exposes you to a small amount of radiation (similar to a chest x-ray), and possible, bruising or bleeding at the site of injection of the tracer. The amount of radiation used is roughly equivalent to that which you receive from natural background radiation in about 24 months.

MRI: There are no known risks from Magnetic Resonance tests and few, if any, side effects. If you have any type of metal implants from previous surgeries or metal fragments from injuries, or certain types of heart valve and artificial joints, you may not be able to receive this test because it uses magnets.

**ECG, 24-hour Heart Monitor and Walk Test**: There is a possible risk that you may experience skin irritation from the ECG electrodes or monitor patches. You will not be able to swim, bathe or shower while wearing the 24-hour heart monitor. There is also a small risk that you may experience chest pain, shortness of breath, or other symptoms during the walk test. If any significant symptoms develop you will be asked to stop walking and to rest. Prior studies have found that the information being collected from these tests is useful in identifying groups of patients who may or may not develop heart related problems. However, these tests are not perfect. It is not known if they truly identify people likely to benefit from an ICD or other therapy. That is the reason for performing this study.

**The following sectionS applY to study participants RANDOMIZED TO AN ICD**

**ICD Implant**: There are risks associated with an ICD implant that will be explained to you by your doctor. You will be required to sign a separate consent for the implant procedure

Common risks include swelling or bruising (2-3%) at your incision or movement of the lead from its original location (2-4%), which may require the lead be replaced or repositioned in your heart.

Uncommon risks (<1%) include puncture or damage to your heart muscle, vein, heart sac, or lung space, damage to the nerves in the arm, a blood clot in your vein, air entering your vein which can lead to blood clot formation, infection of your incision or heart, heart muscle irritation, heart muscle inflammation, heart valve damage, or death.

Lead damage or breakage resulting in loss of function or inappropriate function, changes in heartbeat, or the system stimulating muscles other than the heart muscle can also occur. If this occurs it may require that the lead or system be replaced or moved to another position. The long-term effects of the x-rays used are unknown today but are estimated to be small (less than 0.5% increase in cancers).

The risk percentages described in this section are based on published literature. If you are female and become pregnant, there may be unknown risks to you or to the embryo or fetus.

**ICD Settings**. The ICD settings being used in this study may result in a small (< 1%) higher risk of fainting if a fast heart rhythm problem develops. These settings are being used because they greatly reduce the risk of getting a shock from the ICD (by > 8.0% reduced risk of non-essential ICD shocks).

**CareLink Remote Monitoring.** If you receive an ICD you will need to be enrolled in the Medtronic CareLink Network. Malfunction of the Medtronic CareLink Network or CareLink Monitor may result in the loss of transmitted data; however device data will be kept in your implanted device.

**The REMAINDER OF THIS DOCUMENT is applicable to ALL study participants**

**Women of Childbearing Potential.** Candidates who are pregnant cannot be enrolled in this study. If you suspect that you are pregnant, you must notify the study doctor promptly. A pregnancy test is required prior to randomization and / or ICD surgery if you suspect that you are or may be pregnant.

There may be additional risks related to study participation that are unknown at this time.

**BENEFITS**

There may be no direct benefit to you by your participation in this research study. However, the knowledge gained from your participation may benefit other people with your type of heart disorder in the future

**ALTERNATIVES**

If you choose not to participate in this study it will not limit your access to established therapies that are available to manage your heart condition. You may choose not to participate in this study. If you do not wish to participate in this study, the study doctor will discuss other treatment options for heart disease that may include additional medications and exercise and nutritional programs.

**INFORMATION THAT WILL BE COLLECTED DURING THE STUDY**

**Device Recovery**. For those assigned to an ICD, in the event of your death, the study doctor or their representatives will seek copies of your medical records regarding your death from your primary care physicians or heart specialists. This may include emergency room records, records from office or clinic visits and hospital records. This information will be used for research purposes and will be kept with the other information collected for the study. It is important that we understand how your device works. Your family will be asked to allow us to collect information from the device or to allow the removal of the device and the leads. The devices, leads, and information will be sent to Medtronic as part of the other health information collected for the study. Your family will not be charged for the device explant procedure. If your family objects to the removal, they will be asked if information can be collected from the device. This information may help determine the cause of death. Your family's wishes will be honored.

**USE OF STUDY DATA AND HEALTH INFORMATION**

The University of Calgary and its representatives and GE Healthcare will keep your health information confidential in accordance with all applicable laws and regulations. The University of Calgary and its representatives and GE Healthcare may use your health information to conduct this research. GE Healthcare may use your health information for additional purposes such as overseeing and improving the performance of their devices, new medical research and proposals for developing new medical products or procedures, and other business purposes. Any reports or publications about the study or any other research will not include your name or a description of you. Information received during the study will not be used to market you; your name will not be placed on anymailing lists or sold to anyone for marketing purposes. The University of Calgary and its representatives, and GE Healthcare may disclose your health information to Health Canada, as well as to other regulatory agencies responsible for assuring the safety of medical devices. The University of Calgary and its representatives and GE Healthcare also may disclose your health information to institutional review boards and other persons who are required to watch over the safety and effectiveness of medical products and therapies and the conduct of research.

De-identified data will be shared securely with the CANet Heart-SIGN system for future linkage with related CANet studies and analysis.

**PRIVACY OF RECORDS**

If you decide to participate in the study, you agree to permit the study doctor and the research staff, the University of Calgary and its representatives and GE Healthcare, and their representatives, to collect, use and disclose your health information among themselves and with other researchers participating in the study for purposes of conducting the study and for other purposes described in this informed consent.

You agree to allow access to and use of your health information, as well as disclosure to the University of Calgary, GE Healthcare, and their representatives.

You also agree to permit the study doctor and research staff to disclose your health information as required by law and to representatives of government organizations, research review boards, and other persons who are responsible for watching over the safety and effectiveness of medical products and therapies and the conduct of research. Health Canada and other regulatory agencies may inspect the study records and your health information to ensure its quality and accuracy.

Authorized representatives from the University of Calgary and the Conjoint Health Research Ethics Board may look at your identifiable medical/clinical study records held at this site for quality assurance purposes.

**Loss of Privacy**. Reasonable efforts will be used to protect the privacy of your study records, but absolute confidentiality cannot be guaranteed as persons other than the study investigator(s) may view your study records, whether in connection with this study, in the delivery of healthcare to you, in your potential participation in other research projects (based on permission you have given in this Consent Form or in other studies) or if required by law to be disclosed. If you are in the ICD group, Medtronic takes steps to protect the privacy of the health information sent to the secure Medtronic server that is viewed by the study staff on the Internet. However, Medtronic cannot guarantee the health information is protected against unauthorized interception.

**VOLUNTARY PARTICIPATION / WITHDRAWAL**

Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

There may be circumstances under which the study or your participation in the study may be suspended or terminated by the study doctor, including health and safety concerns and non-compliance with the study protocol. The study doctor may decide to withdraw you from the study at any time without your consent. If this happens, you will be notified and the reasons will be explained.

If you decide to leave the study please contact your doctor. If you are randomized and choose to stop participating you will be encouraged to see your study doctor for one more visit so that we can obtain final information for study related purposes. Because there are risks involved in removing the ICD system, your study doctor may decide to leave in all or parts of the system. The decision to remove the ICD system will be made by you and your study doctor.

In the event that you withdraw from the study, any data you have contributed will be destroyed at your request, wherever possible, and will not be used in any research dissemination from that point forward.

If, during the course of the study, your study doctor becomes aware of new findings that relate to this study that may affect your willingness to continue participating in the study, your study doctor will promptly notify you of such findings so that you can decide whether or not you wish to continue participating. Following completion of the study, you can find out the overall study results of the study by contacting your study doctor.

**COMPENSATION FOR PARTICIPATING AND MEDICAL COSTS**

You will not be paid to be part of this research study. All testing and services performed only because of the study will be provided at no cost to you.

**IF I SUFFER A RESEARCH-RELATED INJURY, WILL I BE COMPENSATED?**

In the event that you suffer injury as a result of participating in this research, no compensation will be provided to you by GE Healthcare, the University of Calgary, the Alberta Health Services, or the Researchers.You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

**FINANCIAL DISCLOSURE**

GE Healthcare is compensating the University of Calgary for work related to analyzing the 24-hour heart monitor tests The University is paying sites in Canada for work involved in collecting study data. The other financial supporters listed above are providing funding to the University of Calgary to conduct the study. Information collected during this study may contribute to the development of commercial products from which GE Healthcare may receive an economic benefit.

**WILL THIS CLINICAL TRIAL BE REGISTERED?**

A description of this clinical trial is available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

## SIGNATURES

## Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a subject. In no way does this waive your legal rights nor release the investigators, or involved institutions from their legal and professional responsibilities. You are free to withdraw from the study at any time without jeopardizing your health care.

## If you have further questions concerning matters related to this research, please contact Dr. Katherine Kavanagh at 403-210-6152, or if you are in the Lethbridge Region, Dr. Aaron Low at 403-388-6032.

## If you have any questions concerning your rights as a possible participant in this research, please contact Wei Qi, Research Coordinator, University of Calgary, at 403-210-7395.

## If you feel you have suffered an injury as a result of your participation in the study, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

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| Participant’s Name or Name of subject’s legally authorized representative |  | Signature and Date |
|  |  |  |
| Investigator/Delegate’s Name |  | Signature and Date |

**The University of Calgary Conjoint Health Research Ethics Board has approved this research study.**

**A signed copy of this consent form has been given to you to keep for your records and reference.**