London Heart Rhythm Program

London Health Sciences Centre, University Hospital, 339 Windermere Road, London, ON N6A 5A5
Tel: (519) 663-3746 Web Site: www.londoncardiac.ca Fax: (519) 663-3782

Informed Consent Form for Participation in a Research Study

Study Title: Reversal of atrial substrate to prevent atrial fibrillation (RASTA-AF)

Study Doctor: Dr. Allan Skanes, 339 Windermere Road, London, ON, Canada N6A 5A5

Sponsor/Funder(s): Dr. Ratika Parkash, QEII Health Sciences Center, Halifax, NS
Canadian Institutes of Health Research
Abbott Canada

Emergency Contact: You should proceed to your local Emergency Department.

INTRODUCTION

You are being invited to participate in a clinical trial (a type of study that involves research). You have been asked to participate in this trial because you have an abnormal heart rhythm coming from the upper chambers of your heart called atrial fibrillation (AF), the most common type of abnormal heart rhythm. AF causes the heart to beat in an irregular and sometimes rapid fashion. This consent form provides you with information to help you make an informed choice about your participation. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study.

Please take your time in making your decision. You may find it helpful to discuss it with your friends and family.

Taking part in this study is voluntary. Deciding not to take part or deciding to leave the study later will not result in any penalty or affect current or future health care.

The study doctor is receiving financial reimbursement from the Sponsor/Funder to cover the cost of conducting this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

The standard or usual treatment for atrial fibrillation (AF) is medication and/or a procedure called catheter ablation to treat the symptoms of AF.

In this trial we want to find out if aggressive management of risk factors is useful for people with your type of heart rhythm problem. This study involves managing risk factors associated with AF such as: high blood pressure (hypertension), diabetes, obesity, tobacco use, alcohol intake and sleep apnea (difficulties with breathing during sleep) ***before*** your ablation procedure, and whether this strategy could prevent your abnormal heart rhythm from returning after the procedure.

WHY IS THIS STUDY BEING DONE?

The purpose of this study, called a randomized control trial, is to find out if patients with risk factors for AF will benefit from a treatment strategy that combines risk factor modification with catheter ablation, versus catheter ablation only.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study in order to receive treatment or care. Other options (in addition to the standard or usual treatment described above) may include, but are not limited to:

- other research studies may be available if you do not take part in this study

Please talk to your usual doctor or the study doctor about the known benefits and risks of these other options before you decide to take part in this study. Your usual doctor or the study doctor can also discuss with you what will happen if you decide not to undertake any treatment at this time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

It is anticipated that about 670 people will take part in this study, from research sites located in 15 Canadian centers and one site in the Netherlands.

This study should take 4 years to complete and the results should be known in about 4.5 years.

WHAT WILL HAPPEN DURING THIS STUDY?

If you decide to participate then you will be "randomized" into one of the groups described below. Randomization means that you are put into a group by chance (like flipping a coin). There is no way to predict which group you will be assigned to. You have a 50:50 chance to be in either of the two groups. Neither you, the study staff, nor the study doctors can choose what group you will be in. You will be told which group you are in.

If you participate in this study, you will still receive your usual care by your physician. Data that is collected for study purposes will not be part of your usual care.

This study involves the use of downloaded smartphone applications (apps). In order to participate in this study, you will be required to have regular daily access to a smartphone and wifi (wireless internet) connection. If you have access to a wifi connection but not a smartphone, a study-specific phone will be provided for the duration of the study. The phone will have limited functions, and will only be used to house the apps necessary to communicate with the study-specific devices

WHAT IS THE STUDY INTERVENTION?

Group 1: Aggressive Risk Factor Management – your risk factors will be managed by the study team, which could include blood pressure control, diabetes control, sleep apnea therapy, smoking cessation, increased activity, dietary and alcohol intake counseling.

Group 2: Standard of Care Group – your risk factors will continue to be managed by your Family Physician and/or Heart Specialist.

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WHAT ARE THE STUDY PROCEDURES?

Non-Experimental Procedures

The following tests will be done as part of this study. Some of these tests may be done as part of your standard care, in which case the results may be used. Some of these tests may be done more frequently than if you were not taking part in this study and some may be done only for the purpose of the study. If the results show that you are not able to continue participating, the study doctor(s) will let you know.

- Medical history
- Physical examination
- Blood work
- ECG (electrocardiogram) – a non-invasive tracing of your hearts electrical activity
- Exercise stress test – involves walking on a treadmill while connected to an ECG
- Holter monitoring (if required) - a small electrocardiogram that can be worn for a period of days to collect heart-rhythm data.

All patients will have a small cardiac monitoring device inserted around the time of your randomization, and removed 2 years later. The device will be used to wirelessly send information about your heart rhythm to the research team via a free MyMerlin.net app which will be downloaded on your smartphone.

The monitor is about the size of a small, thin eraser (49mm x 9.4mm x 3.2mm) and is inserted just below the skin. To insert the monitor your doctor will create a small incision in the pectoral region (upper chest), use an insertion tool to place the device in the correct position, and then close the incision. For most people, the procedure is done in less than 10 minutes with local anesthetic around the incision area.

All patients who haven't undergone recent sleep apnea screening, will be provided (on loan) with a home sleep testing (HST) device.

Participant Diaries

Patients using sleep apnea therapy (i.e., a CPAP device) will be asked to record information about their apnea-hypopnea index (AHI) as recorded on their device (if available). AHI is a scale from 0-30 that is used to describe the severity of sleep apnea.

Experimental Procedures

If you are assigned to the experimental group, the following risk factor management strategies will be started based on your presenting risk factors (you may have several of the following requiring further management):

- Blood pressure (BP) management with the goal to reach a target systolic blood pressure of <120/80mmHg. Management of your blood pressure will be under the direction of the study team and supervised by a study investigator.
- Sleep apnea screening (using a home sleep testing device) and therapy. All patients who haven't undergone recent sleep apnea screening, will be provided (on loan) with a home sleep testing (HST) device
- Alcohol reduction to 2 drinks/day for men, 1 drink/day for women, binge drinking (>5 drinks at one setting) will be discouraged.
- Smoking cessation – if you are a smoker, you will be referred to a smoking cessation program

- Diabetes management, with the aim to achieve a blood sugar level (hemoglobin A_1C) less than 7.1%. Recommendations will be made to your family physician and you may be referred to a diabetes clinic, as clinically indicated.

If randomized to the experimental group you will participate in a 10-14 week structured, home-based exercise program and nutritional counseling, which will be tailored to your level of fitness. You will be provided with an exercise and diet plan and followed with phone calls once a week from a trained physiotherapist employed by either the Ottawa Heart Institute Cardiac Rehabilitation Program (English) or Institut universitaire de cardiologie et de pneumologie de Québec - Université Lava (French). You will be asked to track the details of your exercise activities using a paper log, and to share the details of the log during your weekly phone call. Following your ablation, a member of the research team will check in with you monthly, for one year, to ask about your physical activity.

If you are randomized to the experimental group you will also be provided with a pedometer that will be used to track physical activity for 12-months. The pedometer clips on to your waistband and is able to provide feedback to you, and the research team. The results from your pedometer will upload to a free VIRTUES Step-app on your smartphone using wifi internet and Bluetooth® technology. The VIRTUES Step-App has been developed by the Cardiac Arrhythmia Network of Canada (CANet) to allow pedometer data to be shared with the study team. The app does not require a login and only transfers de-identified information regarding steps and minutes of activity.

Participants in both groups will complete visits at baseline, then every three months for the first year, and every 6 months after that. Some visits can be completed remotely over the phone, but for the following you will be asked to come to the hospital:

- Visit 1: before or on the date of randomization for insertion of the cardiac monitor,
- Visit 2: 3 months after being randomized (ideally this will be the day of your ablation procedure, if the procedure is significantly delayed, your follow-up visits will be scheduled according to the date you were randomized)
- Visit 3: ~ 3 months after your ablation procedure,
- Visit 5: ~ one year after your ablation procedure
- Visit 7: ~24 months after your ablation
- 2 years following insertion of the cardiac monitor for removal of the device.

At each research-related visit, the following will be done/asked of you:

- Physical exam
- ECG
- Exercise stress test (only at baseline, 3, 12 and 24 month visits)
- Quality of Life questionnaires
- Physical activity questionnaire
- Bloodwork where applicable.
- 3-day Holter monitoring (only if your implanted cardiac device runs out of batter and you haven't experienced a symptomatic episode of AF lasting ≥ 24 hours, visit the emergency department due to AF, or been hospitalized for an AF-related reason).

Each of these follow-up visits will take approximately 30-45 min. Every effort will be made to schedule follow-up research appointments on the same day as your clinical follow-up post ablation.

<u>Blood Collection</u>

Blood samples will be taken by inserting a needle into a vein in your arm. These will be taken at the same time as your study related tests whenever possible, at the first visit and 12 months after your ablation. The amount of blood taken will be less than 2 teaspoons and will be analyzed at your local hospital.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical conditions;
- Tell the study doctor about all prescription and non-prescription medications and supplements, including vitamins and herbals, and check with the study doctor before starting, stopping or changing any of these. This is for your safety as these may interact with the intervention you receive on this study.
- Tell the study doctor if you are thinking about participating in another research study
- Complete and return any diaries that you take home.
- Tell the doctor about any changes in your health;

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The study will follow you for a minimum of 24 months after your ablation procedure, and may continue you until the end of the study (maximum of 48 months).

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff.

You may withdraw your permission to use information that was collected about you for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early, and without your consent, for reasons such as:

- New information shows that the study intervention is no longer in your best interest
- The Sponsor decides to stop the study
- The Regulatory Authority/ies (for example, Health Canada) or research ethics board withdraw permission for this study to continue

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form.

If you are removed from this study, the study doctor will discuss the reasons with you and plans will be made for your continued care outside of the study.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be other side effects that are not expected. You should discuss these with the study doctor.

There are risks and side effects related to the implant of the insertable cardiac monitor. A small percentage of patients may develop complications including:

- Bleeding.
- Infection.
- A reaction to the device or a drug used.
- Internal tissue damage.
- Scarring at the incision site and a small bump where the implanted device rests in your chest. If you are concerned about this, your doctor may be able to place your device in a place that is less noticeable.

Risks and side effects related to the experimental intervention (risk factor management) we are studying may include:

- If you are being treated for high blood pressure with blood pressure medication, you may experience symptoms related to low blood pressure, such as dizziness.
- There is a possibility of pain, bruising, swelling or infection related to giving blood. These discomforts are minimal and brief.
- The effects or discomforts of tests/procedures that are part of this study but are part of your normal clinical care will be reviewed by your family or treating doctor.
- The risks from exercise training to participants are small. These risks may include a very rapid and irregular heartbeat, chest pain, shortness of breath, headache, nausea, and fatigue. There is a small risk of cardiac events such as severe chest pain, abnormal heart rate, and sudden stop of heart beats. Approximately 6 cardiac events may happen for every 10,000 exercise sessions, which is 0.06%. The exercise program was designed for a cardiac rehab patients. It will be delivered by an expert in exercise training and based on your fitness level.
- There is always the possibility of a privacy breach, although your privacy and confidentiality will be protected to the best of our ability.

There is a possible risk that you may experience skin irritation from the ECG or Holter monitor electrodes (patches). You will not be able to swim, bathe or shower while wearing the Holter monitor.

The risks and side effects of the standard or usual treatment will be explained to you as part of your standard care. These risks are not included in this consent form.

Risk of Insurability: We will take all reasonable steps to keep your research information confidential. Should someone not involved in the research find out that you took part in the study, or if you choose to share your results (if they are provided to you), there is a possibility that this could affect your insurability under certain policies of insurance, depending on the exclusions in such policies.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

There are no medical benefits to you for taking part in this study. If you agree to take part in this study, the experimental intervention may or may not be of direct benefit to you.

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We hope the information learned from this study will help other people with atrial fibrillation in the future.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

This institution and affiliated sites has direct access to participant medical/clinical study records. If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study, such as your:

- Name, address, and telephone number;
- Age or month/year of birth;
- Responses the study questionnaires;
- New and existing medical records; or
- The types, dates and results of various test and procedures.

Any study data about you that is sent outside of this institution and affiliated sites will be de-identified, meaning it will have a code made up of your study ID number along with your partial initials. Your initials are being used as a second measure to ensure that the correct patient is being referenced. This de-identified information will be sent off site to the centre coordinating the study in Halifax, NS.

As mentioned above, if you are randomized to Group 1 (Aggressive Risk Factor Management), you will receive weekly telephone calls regarding the exercise and diet plan from a physiotherapist at the Ottawa Heart Institute (OHI) Cardiac Rehabilitation Program or Institut universitaire de cardiologie et de pneumologie de Québec - Université Laval. Therefore, a member of our research team will provide the cardiac rehabilitation staff with the following identifiable information so that they can contact you and design a personalized cardiac rehabilitation program:

- Name and telephone number,
- Results from your most recent stress rest,
- Baseline questionnaire responses.

Your name and phone number will be provided to them over the phone to protect your privacy. Your questionnaire and stress tests results will be labeled with your study ID number and sent via secure email.

No identifiable information will be required to use any devices or smartphone apps associated with this study. The apps are used to move coded data to the study team. Data from the VIRTUES pedometer app may be accessed by the members of the VIRTUES app development team. Only the rehabilitation mentors and study coordinators will be able to match study ID's with patient names.

Records identifying you at this centre will be kept confidential and, to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines.

- Dr. Ratika Parkash, the Sponsor of this study
- Representatives of Clinical Trials Ontario, a not-for-profit organization, may see study data that is sent to the research ethics board for this study.

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- The research ethics board who oversees the ethical conduct of this study in Ontario. This institution and affiliated sites, to oversee the conduct of research at this location
- The Quality Assurance and Education Officers from Lawson Health Research Institute (Lawson) may audit this research study for quality assurance purpose

The following organizations may also receive study data:

- Research Methods Unit, Nova Scotia Health Authority, Halifax, NS. This is the coordinating centre for the study – it is where the database is setup and data analysis will take place

It is expected the results of this study will be published; however, your identity will remain confidential. Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

A copy of the consent form that you sign to enter the study may be included in your health record/hospital chart.

WILL FAMILY DOCTORS/HEALTH CARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your family doctor/health care provider will be informed that you are taking part in a study so that you can be provided with appropriate medical care. If you do not want your family doctor/health care provider to be informed, please discuss this with the study team.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE ONLINE?

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*. This website will not include information that can identify you. You can search this website at any time.

WHAT IS THE COST TO PARTICIPANTS?

You will not be paid to be in the study. There is no charge for any tests. You may have to pay for other medications (depending on your drug plan) such as those prescribed to treat high blood pressure. The costs of your medical treatment will be paid for by your provincial medical plan to the extent that such coverage is available.

Smartphone applications used in this study are provided free through the Apple iOS or Android app store. Data can be transmitted via Bluetooth and wifi internet connection and you should not incur any additional cell phone charges. Your study coordinator can assist you in setting up the applications to make sure they will not transmit data when you are not connected to the internet (i.e., via your data plan).

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

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You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of the results of this study, please contact the study doctor.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the study doctor, sponsor or involved institutions for compensation, nor does this form relieve the study doctor, sponsor or their agents of their legal and professional responsibilities.

You will be given a copy of this signed and dated consent form prior to participating in this study.

CONFLICT OF INTEREST

If you would like additional information about the funding for this study, or about the role of the doctor in charge of this study, please speak to the study staff or the Patient Relations Office at LHSC at (519) 685-8500 ext. 52036 or access the online form at: https://apps.lhsc.on.ca/?q=forms/patient-relations-contact-form

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor who is in charge of the study at this institution. That person is: Dr. Allan Skanes, Study Doctor, London Health Sciences Centre, 519-663-3746

If you have any questions about your rights as a research participant or the conduct of this study, you may contact the Patient Relations Office at LHSC at (519) 685-8500 ext. 52036 or access the online form at: https://apps.lhsc.on.ca/?q=forms/patientrelations-contact-form

If you have any questions about your rights as a research participant or the conduct of this study, you may contact the Office of Human Research Ethics at Western University by *phone at: 519.661.3036* or email: ethics@uwo.ca

Informed Consent Form for RASTA-AF

SIGNATURES

- All of my questions have been answered,
- I understand the information within this informed consent form,
- I allow access to my medical records as explained in this consent form,
- I do not give up any of my legal rights by signing this consent form,
- I understand that my family doctor/health care provider will be informed of my participation in this study
- I have read, or someone has read to me, each page of this Participant Informed Consent Form.

_____	_____	_____
Signature of Participant	PRINTED NAME	Date

I have carefully explained the study to the study participant. To the best of my knowledge, the participant understands the nature, demands, risks and benefits involved in taking part in this study.

_____	_____	_____
Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date

Complete the following section only if the participant is unable to read or requires an oral translation:

- The informed consent form was accurately explained to, and apparently understood by, the participant and
- Informed consent was freely given by the participant

_____	_____	_____
Signature of Impartial Witness/Translator *(If participant were unable to read/required an oral translation)*	PRINTED NAME	Date