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PATIENT INFORMATION SHEET AND INFORMED CONSENT

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

INVESTIGATOR: Local Principal Investigator: Stephen Wilton, M.D. (403-210-7102)

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SPONSOR: Dr. Ratika Parkash, QEII Health Sciences Center, Halifax, NS
Canadian Institutes of Health Research
Abbott Canada

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.

BACKGROUND/INTRODUCTION:

Atrial fibrillation (AF) is an abnormal heart rhythm characterized by irregular and rapid heartbeats of the upper part in of your heart (the atrial chambers). The standard or usual treatment for atrial fibrillation (AF) is medication and/or a procedure called catheter ablation to treat the symptoms of AF. You have been diagnosed with AF, and together with your doctor have decided to treat the condition with a catheter ablation procedure.

Like other heart conditions, AF may be aggravated by a number of common risk factors. These include being overweight, high blood pressure, sleep apnea (difficulties with breathing during sleep), alcohol and tobacco intake, and uncontrolled diabetes. In this project we want to find out if a strategy of aggressively managing these risk factors ***before*** a catheter ablation for AF will improve the success of the procedure.

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

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

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

WHAT IS THE PURPOSE OF THE RESEARCH?

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 aggressive risk factor modification with catheter ablation, versus catheter ablation and the standard of care.

WHAT WOULD I HAVE TO DO?

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.

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.

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.

All patients will have a small cardiac monitoring device (Jot Dx™) inserted around the time of your randomization and removed at the end of the trial (approximately 4 years). The device will be used to wirelessly send information about your heart rhythm to the research team.
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 upper chest. A specialized insertion tool will be used to place the device in the correct position. The incision will then be closed with either surgical tape or a few dissolvable stitches. For most people, the procedure is done in less than 10 minutes with local anesthetic (“freezing” medication).
If the battery in the device becomes depleted, we may need to arrange for you to have a 48 hour holter monitor every 6 months until your last visit.

The data recorded on your implantable cardiac monitoring device will automatically upload to the free MyMerlin.net app on your smartphone using wifi internet and Bluetooth® technology.

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. AHI is a scale from 0-30 that is used to describe the severity of sleep apnea.

Blood samples will be taken by inserting a needle into a vein in your arm at baseline and12 months after your ablation. The amount of blood taken will be less than 2 teaspoons and will be analyzed at your local lab.

The following items will be done at your Baseline and follow-up visits *as* part of this study if they have not been done as part of your usual care:

- Medical history
- Physical examination including non-invasive body composition analysis using a special scale at baseline and 12 month visit. Requires some preparation (fasting)
- Review of medications
- Blood work
- ECG (electrocardiogram) – a non-invasive tracking of your heart's electrical activity
- Exercise stress test – involves walking on a treadmill while connected to an ECG (at baseline, 3, 12 and 24 months)
- Questionnaires regarding how you feel and your activity level
- One Questionnaire regarding the association between your gender, socio-economics, self perception, mental health and your AF risk factors. We estimate 15-30 minutes to complete this.
- Confirmation of the monitoring device uploads
- Holter monitoring (if required) - a small ECG that can be worn for a period of days to collect heart-rhythm data.

If you are assigned to Group 1 (Aggressive, experimental management), the following strategies will be started based on your risk factors (you may have one or more of the following):

- Blood pressure *(BP) management* with the goal to reach a target 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 the Alice NightOne© home sleep testing device followed by any recommended therapy.

- *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

- You will be provided with a *pedometer* that will be used to track your 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 app on your smartphone using wifi internet and Bluetooth® technology.
- 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 for 12 weeks with a phone call once a week from a trained physiotherapist employed by the Ottawa Heart Institute Cardiac

Rehabilitation Program. 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 choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical conditions;
- Tell the doctor about any changes in your health;
- 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 problems you experience that you think might be related to participating in the study.

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

You will be asked to come to the hospital for study related visits/procedures at the following times:

- before or on the date of randomization for insertion of the cardiac monitor,
- The day of your ablation procedure,
- 3 and 6 months after your ablation,
- 12 months after your ablation and every 6 months following that until study end (maximum 48 months)

WHAT ARE THE RISKS?

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.

The catheter ablation procedure may be harmful to a fetus. For this reason, women who are pregnant will not be enrolled in this study. In addition, standard medications used to treat AF may be harmful to a fetus or breastfed child. In the event of pregnancy, or suspected pregnancy, you must tell your study doctor immediately. If you are breastfeeding or planning on breastfeeding, you must tell your study doctor immediately. Your study participation may be stopped in order to avoid unknown risks to you, the fetus or infant.

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 during the implant procedure.

- 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.

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

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

- Dizziness related to low blood pressure if you are treated with medication for high blood pressure.
- Pain, bruising, swelling or infection related to blood sample collection. These discomforts are minimal and brief.

- Exercise training risks to participants are very small, approximately 0.06%. (6 events in 10,000) and may include:
    - a rapid and irregular heartbeat
    - chest pain
    - shortness of breath
    - headache
    - nausea
    - fatigue
    - sudden stop of heart beats

The exercise program was designed for cardiac 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.

<u>COVID 19 Related Risks</u>
As some of visits for this study must be done in person to allow for tests and procedures, there is an added risk of you being exposed to COVID 19 from other people within the facility or by use of public transit to attend your appointment. We have several measures in place to reduce this risk as much as possible including screening each patient who attends our facility, use of PPE for all staff and patients, restrictions on the number of people allowed within the space, enhanced general cleaning procedures and sanitization of any space a patient occupies immediately following their visit.

WILL I BENEFIT IF I TAKE PART?

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

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

DO I HAVE TO PARTICIPATE?

No, you are free to participate in this study or withdraw from it at any time. You may also refuse to answer any specific questions or withdraw your consent to follow-up visits; you will still receive the standard medical care required by your condition.

You can choose to end your participation in this research at any time without having to provide a reason. If you choose to withdraw from the study, please contact the study doctor or study staff:

Dr. Stephen Wilton:

Phone:(403) 210-7102 or (403) 210-6047

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.

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.

WILL I BE PAID FOR PARTICIPATING, OR DO I HAVE TO PAY FOR ANYTHING?

No, you will not be paid to participate in this study. There is no charge for any tests. You may have to pay for medications (depending on your drug plan) such as those prescribed to treat high blood pressure or the purchase/use of a CPAP machine if sleep apnea is identified. Parking costs for follow-up visits at the Foothills Medical Centre or South Health Campus will be paid.

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).

WILL MY RECORDS BE KEPT PRIVATE?

If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study.

A study ID number along with your partial initials will be used to identify you as part of the study. This information will be sent 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 Cardiac Rehabilitation Program. Therefore, for those in Group 1, a member of our research team will provide your name, telephone number and the results from your stress tests and questionnaires to a member of the team at the Ottawa Heart Institute Cardiac Rehabilitation Program, so that they may contact you for these calls. This will be provided to them over the phone to protect your privacy.

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.

All information entered into the MyMerlin.net and pedometer apps will be de-identified and labelled only with your unique study ID number.

Authorized representatives of the following organizations may look at your original (identifiable) medical study records, 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, along with her representatives.
- The University of Calgary and the Conjoint Health Research Ethics Board

The following organizations may also receive study data (which will not include your personal information):

- Research Methods Unit, Nova Scotia Health Authority, Halifax, NS. This is the coordinating centre for the study, where the database is stored and analysis will take place
- Conjoint Health Research Ethics Board at the University of Calgary

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 medical record.
Your family doctor will be informed that you are taking part in this study so that you can be provided with appropriate medical care. If you do not want your family doctor to be informed, please discuss this with the study team.
A description of this clinical trial will be available on www.clinicaltrials.gov. 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.

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 the Nova Scotia Health Authority, the CIHR, the University of Calgary,

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.

SIGNATURES

Your signature on this form indicates that you have read and understood to your satisfaction the information regarding your participation in the research project, that any questions you have about your participation have been addressed by research staff, at that you agree to participate. 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. Stephen Wilton (403) 210-7102

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair, Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990

_____	_____	_____
SUBJECT printed name	Subject Signature	Date
_____	_____	_____
INVESTIGATOR printed name	Investigator Signature	Date
_____	_____	_____
WITNESS printed name	Witness Signature	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.