**UNIVERSITY OF CALGARY**

**CONSENT TO PARTICIPATE IN RESEARCH**

**Title:** Resynchronization in patients with Ambulatory Heart Failure in Atrial Fibrillation Trial undergoing Pace and atrioventricular node Ablation strategy with Left Bundle Branch Area pacing compared with Biventricular pacing (RAFT-P&A)

**Sponsor/Funder:** The Lawson Institute of Health Research, London, Ontario

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**INTRODUCTION**

Dr. Jacques Rizkallah andassociates from the Cumming School of Medicine at the University of Calgary are conducting a research study. You are invited to participate in this research study because your doctor has determined that you have an irregular rhythm called atrial fibrillation (AF), which has become increasingly challenging to manage with medications alone and will require more permanent intervention to improve your symptoms. AF causes an excessively rapid and irregular heartbeat that can sometimes lead to the inability of the heart to pump efficiently, called heart failure (HF). The fact that your heart is not pumping efficiently and is also irregular may be contributing to some of your symptoms, such as shortness of breath or decreased exercise ability. Your doctor has determined that you may be a suitable candidate to participate in this study, called RAFT-P&A.

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 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.

Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive.

Your doctor has determined that you have periods of difficult to control AF, and that you might benefit from a pacing device followed by ablation of the atrioventricular (AV) node. These procedures electrically disconnect the top of the heart (atria) where the fast impulses start, from the bottom of the heart (ventricles) which pump your blood. The bottom chambers would beat too slowly without a pacemaker.

As part of this study, the pacing device will be one of the following types:

* Cardiac Resynchronization Therapy Device (CRT). CRT is an advanced technique that has been in use for many years to prevent heart failure as it stimulates both ventricles to beat at the same time.
* Left Bundle Branch Area Device (LBBA). LBBA is a relatively new technique which places the wire to stimulate the left ventricle in a different place in your heart. This technique has shown favourable results, but has not been compared directly to CRT.

\*\*If your heart shows a decreased “ejection fraction” (pumping ability) you are considered at higher risk to develop dangerous rhythms and qualify to get a defibrillator to protect you from these dangerous rhythms. If that is the case for you, in addition to receiving one of the above mentioned pacing wires, you will receive another defibrillator wire to allow your device to give you a shock if a life threatening rhythm is seen. This will be done regardless of which arm of the study you are in.\*\*

After the successful implantation of the pacemaker, the AV node will be ablated to prevent it from allowing fast electrical impulses from the atria to reach the ventricles. This procedure is called AV node ablation. The purpose of this study is to determine whether LBBA Pacing compared to CRT-Pacing will improve your symptoms and reduce the number of hospitalizations for HF-related symptoms due to AF.

Either device that you will receive is approved for use by Health Canada. You will receive the most up-to-date device that is currently being used. Any medications you receive as part of your standard care are also approved by Health Canada and will be prescribed by your doctor at the usual doses needed to treat patients with heart failure and atrial fibrillation.

**WHY IS THIS STUDY BEING DONE?**

This study is exploring whether patients such as yourself, with heart failure and AF, will have better results from LBBA pacing when compared with the standard CRT pacing before undergoing an AV node ablation.

**HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY, HOW LONG WILL I PARTICIPATE?**

This study is a multi-center study. A total of 300 patients will participate in this study and will be enrolled in sites across Canada.

Your participation in this study will last approximately 12 months. We hope to enrol 20 patients here at the University of Calgary/Foothills.

**WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?**

Your participation in this study consists of 4 phases; screening/randomization, device implant, AV node ablation procedure and follow-up period. Below are details of each phase.

Screening/Randomization Visits

If you agree to participate in this study, you will sign this consent form. The research team will then consult your medical records and will collect information about your demographics, your medical history, your health, the medications you are taking, and any tests that you have had done. This information will be accessed by the study team through the Alberta NetCare System (a Province wide database containing your health records).

Randomized trials are done when we do not know which way of treating patients is best, and we need to compare new techniques to the current techniques. In this study, you will be randomly assigned by a computer in a 1:1 ratio to one of two study treatment arms, so you have a 50% chance of being assigned to either study group. All patients will receive optimal medical therapy for their heart failure. This means that the usual medications will be prescribed to you, if not done already.

This study will be double-blinded, which means that during the study, you will not know which arm of the study you are in. We do this so that the participant's expectations about the experimental arms do not affect the study's outcomes. The study team will not know which arm of the study you are in except for the study doctor.

***Treatment Arm 1 (Control Group)***

This group will receive a **CRT** before AVNA (Atrioventricular Node Ablation) + medications to control heart failure.

The CRT device and the leads will be implanted during a surgical procedure. As with any medical procedure, a separate surgical standard consent form will be signed, as part of usual care, giving you an opportunity to ask the cardiac specialist any questions you may have prior to the procedure. A small incision will be made in the upper chest region during the implant procedure, and the device will be placed under the skin. You may be awake during the procedure; however, you will be given medication so you will not feel much (if any) discomfort. Through a vein in your upper chest, the leads will be inserted into the right and left lower chamber, one lead for each chamber (also known as ventricles) of your heart and connected to the CRT device. X-ray dye will be injected into a large vein in the left side of your heart, and images will be recorded using x-rays to view the blood vessel anatomy where the left ventricular lead will be placed. This is called a venogram, and it is routinely used during the implant of a CRT system.

Your doctor may decide to test the device by triggering a fast heartbeat and programming the device accordingly.

***Treatment Arm 2 (Experimental Group)***

This group will receive an **LBBA** before AVNA + medications to prevent heart failure. The LBBA device and the lead will be implanted during a surgical procedure. As with any medical procedure, a separate surgical standard consent form will be signed as part of usual care, giving you an opportunity to ask the cardiac specialist any questions you may have prior to the procedure. During the implant procedure, a small incision will be made in the upper chest region, and the device will be placed under the skin. You may be awake during the procedure; however, you will be given medication so you will not feel much (if any) discomfort. The leads will be inserted, through a vein in your upper chest, deep into the wall between the right and left lower chamber (also known as ventricles) of your heart and connected to the LBBA device. The left bundle branch lead may be implanted with the aid of an imaging device (Intra-cardiac Echocardiogram, ICE). In the event the left ventricular lead is not inserted successfully, it will be at your physician’s discretion to discuss options available to you. You may receive a CRT pacing lead despite which arm of the study you are chosen to be in if that approach is more feasible for you.

**Atrioventricular node ablation (AVNA)**

This is considered to be the second step towards controlling the AF for both study groups, and will be scheduled 1 week after your first pacemaker check if there is no concern. During this procedure, the AV node, which electrically connects the right upper (atria) chamber and right lower (ventricle) chamber of the heart, is cauterized to stop electrical signals from being transmitted from the upper to the lower ventricle. This prevents the heart rate in atrial fibrillation from going too fast . This is a permanent treatment. You will be asked to sign a separate surgical consent form for this procedure.

**Follow-Up Visits**

You will be seen in the Device clinic 7-10 days following your device implant procedure, to ensure your device is working well and there are no complications.

You will be seen for study follow-up visits at 6 and 12 months following your AV node ablation procedure. These visits will take approximately 1 hour of your time.

They will include:

* Device check
* Brief physical exam
* Medication review
* Blood test to measure NT-proBNP (indicates the degree of heart failure that you are experiencing. Can be done at your local lab as well)
* ECG
* Questionnaires (you do not have to answer any questions that you are not comfortable with)
* 6-minute walk test (you will be asked to walk the length of a hallway repeatedly for a total of 6 minutes)
* Review of unexpected events and admissions to hospital
* As part of your standard of care, an echocardiogram (heart ultrasound) will be scheduled for you. This echocardiogram will be reviewed at your institute for clinical use but will also be analyzed in a central lab for research purposes.

**WHAT WILL HAPPEN WHEN I AM FINISHED FOLLOW-UP?**

When you have completed the study, you will be followed in the Device clinic as per standard of care every 6 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 study doctor will watch you closely to see if you have side effects.

The specific study risks are related to the implantation of a pacemaker and additional left ventricular lead placement. These include:

* The implantation of an additional lead will require more time and therefore may increase the risk of infection (2%).
* Device pocket erosion resulting from a tight-fitted pocket or longer duration of infection.
* Damage to the wall of the vein used in placement of the left ventricular lead <1% resulting in bleeding on the outside of the heart requiring an additional procedure to evacuate the bleeding.
* With the venogram there is a rare chance of developing an allergy to the contrast. Should this occur, it would be treated immediately with medications.
* Lead dislodging from its original position (1%).
* Lung collapse from obtaining access to your vein from the shoulder. The top aspect of the left lung sits close to the vein and can occasionally be punctured resulting in lung collapse or pneumothorax (1%).
* Radiation exposure - Fluoroscopy is an imaging technique using x-ray technology that allows for real time imaging of the body. The long-term effects of the x-rays used in such a medical procedure are not well defined but the risk of adverse health events is presumed to be low given that you are not routinely being exposed to x-rays during such a procedure.
* With any cardiac procedure there is also the risk of lifethreatening complications such as myocardial infarction, myocardial perforation, stroke, major vascular complication, or death. The combined risk of lifethreatening complications is usually <1%.

**Echocardiogram:**

An echocardiogram is an ultrasound of the heart. It shows moving images of your heart and takes pictures to help your doctor evaluate your heart's health. A technologist uses a gel to slide a microphone-like device over the chest area. This provides a live picture of your heart and valves. No radiation is involved in heart ultrasound. The side effects of this test may be that your chest is irritated by the gel or pads used in this test.

**Blood testing**:

You may experience some temporary discomfort when the blood samples are taken. The main risks of blood tests are discomfort and bruising at the site where the needle goes in. You may experience pain, swelling, bruising, and/or infection as a result of venipuncture or from the adhesive tape used.

This risk is estimated to be small (less than 0.5%)

**Questionnaires:**

You might find the questionnaires tiring. You might not like all of the questions that you are asked. You do not have to answer any questions that make you uncomfortable.

COVID 19 Related Risks

As some of visits for this study must be done in person to allow for procedures, physical examinations, and blood testing, 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.

**ARE THERE ANY REPRODUCTIVE RISKS?**

Being a part of this study while pregnant may expose the unborn child to significant risks related to medications and procedures used during treatment. Therefore, you should not take part in this trial if you are pregnant or intend to become pregnant. Pregnant women will be excluded from the study and all women must agree to try not to become pregnant during this study.

In the event of pregnancy, or suspected pregnancy, you must tell your study doctor or research staff immediately. The study doctor must review your continued participation in the study to avoid unknown risks to the unborn child.

If you are a woman of childbearing age, you will have a pregnancy test done to ensure that you are not pregnant before the study begins.

**ARE THERE ANY POTENTIAL BENEFITS IF I PARTICIPATE?**

You may not receive any direct benefit from your participation in this research. However, your participation will allow the researchers to investigate if the LBBAP device improves survival and reduces hospitalization for heart failure patients with permanent atrial fibrillation compared to whom they have received CRT-P. Due to your cardiac history, your participation may help the Investigators to answer this question and assist in the treatment of heart failure patients in the future.

**WHAT OTHER CHOICES DO I HAVE IF I CHOOSE NOT TO PARTICIPATE?**

If you choose not to participate in this study, you will not be limiting your access to treatments available to manage your heart condition. You have the choice not to participate in this study. If this is the case, your study doctor will discuss other alternatives with you.

**CAN I STOP BEING IN THE STUDY?**

Your participation in this study is completely voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your future care. If you decide not to participate or to withdraw, you will receive the standard medical care and/or surgical care required by your condition. If you decide to withdraw please notify the study team, so that they may discuss any issues involved in leaving the study. If you withdraw from the study, the final assessment visit(s) may need to be completed to ensure your safety and well-being. Withdrawal from this study can be done in any format that you choose, including in writing, or by verbally telling the study team at any time.

Due to the nature with which your study-related personal information is being used, information obtained up until the point of withdrawal will continue to be used or disclosed according to the guidelines set out in this Letter of Information and Consent Form. You may also withdraw your consent to see your study investigator for follow-up visits. At the end of the study, however, the study researcher will want to know if you are alive, whether you have been admitted to the hospital or other health care facilities, have had a stroke, heart attack, or other vascular event. To do so, the study coordinator may try to contact you or a third party, such as your family doctor, for further information related to these events. Whether you withdraw consent or not, your medical records will always be kept confidential.

# **CAN THE RESEARCHERS REMOVE ME FROM THIS STUDY?**

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

* The study intervention does not work for you.
* You are unable to tolerate the study intervention.
* You are unable to complete all required study procedures.
* New information shows that the study intervention is no longer in your best interest.
* The study doctor no longer feels this is the best option for you.
* The research ethics board withdraws permission for this study to continue.
* Your group assignment becomes known to you

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 IF RESEARCHERS DISCOVER SOMETHING ABOUT ME?**

During the study, the researchers may learn something about you that they did not expect. For example, the researchers may find out that you have another medical condition.

If any new clinically important information about your health is obtained as a result of your participation in this study, you will be given the opportunity to decide whether you wish to be made aware of that information. Any medical care and/or referrals will be brought to your attention as clinically applicable.

I consent for the researchers to share findings with me:

❑ YES

❑ NO

# **WITHDRAWAL OF STUDY DATA**

If you decide to stop being in the study, are removed from the study, or the study is stopped, the data collected about you up to that point will remain part of the study because withdrawal of data in clinical trials could bias results.

**CAN I WITHDRAW SAMPLES?**

If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done. You will not be able to participate in this main part of the study if you are unwilling to provides these samples as the results are very important to the study’s goals.

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

You will not be paid for taking part in this study. Parking costs for study specific vistis to the Foothills hospital will be subsidized or reimbursed.

# **WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT CONFIDENTIAL?**

If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study. 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. Only the medical care team and approved research personnel have access to your identifying information. When you enter the study, you will receive a study-specific coded number, which has no information that can identify you. All your data will be “de-identified” and replaced with this code. Any information given to outside agencies will only identify you by the study code. All information collected from you during the study will be disclosed to the coordinating centre of this study, the Clinical Trials Coordinating Centre (CTCC) within the London Health Sciences Centre at the University of Western Ontario and administrated by Lawson Research Informatics. Your information will not be sold to outside agencies. Your privacy will be protected at all times. The hospital and research staff has professional and legal obligations to maintain the privacy of your health information. The CTCC is responsible for overall data management, monitoring and communication among all sites, and general oversight of the conduct of a human research project under the direction of the Lead Investigator.

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.

If you decide to participate in this study, you agree to permit your health care providers and study coordinators to disclose your study-related health information, for audit purposes only, to the representatives of government organizations, to relevant health authorities, to health professionals involved in this clinical study (including their Research Ethics Boards), to other persons who are responsible for watching over the safety and effectiveness of medical therapies and the conduct of research, and as otherwise required by law. If you were to pass away during the study, these parties may still have access to the information required for the study in order to verify it.

Representatives of Western University’s Health Sciences Research Ethics Board may contact you or require access to your study-related records to monitor the conduct of the research.

Results of research studies will be shared, to ensure patients are always provided with the best possible care. Therefore, results from this study will be presented at scientific conferences and/or published in journals but you will not be identifiable in any publications or presentations.

A description of this clinical trial will be available on [[http://www.ClinicalTrials.gov](http://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.

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

Communication via e-mail is not absolutely secure. We do not recommend that you communicate sensitive personal information via e-mail.

This study requires the transfer of identifiable information to Lawson Health Research Institute as part of London Health Sciences Centre for the purposes of data verification and analysis. The following information will be transferred:

* Partial Initials
* Sex
* Gender
* Partial Date of Birth
* Medical Device Identifier
* Admission and Discharge Dates
* Race/Ethnicity

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of the study intervention.

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.

# **HOW LONG WILL INFORMATION FROM THE STUDY BE KEPT?**

This research data will be stored for 15 years by the study staff and the University of Calgary.

**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, appropriate medical treatment will be provided. No compensation will be provided to you by the University of Western Ontario, the London Health Sciences Centre, the University of Calgary, Alberta Health Services or the Researchers. The study doctor and the University of Calgary still have their legal and professional responsibilities. You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

The sponsor of this clinical trial has taken out insurance that covers its civil responsibility for any possible harm and injury that could be inflicted, as well as the study doctors taking part in the study.

# **WHO CAN I CONTACT IF I HAVE QUESTIONS ABOUT THIS STUDY?**

**The Research Team:**

You may contact Dr Rizkallah at 403-210-8498 or 403-210-6047 with any questions or concerns about the research or your participation in this study.

**Conjoint Health Research Ethics Board (CHREB):**

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.

**Public Information about this Study:**

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. This project’s registration number is NCT05428787

# **HOW CAN I FIND OUT ABOUT THE STUDY RESULTS?**

After the completion of the study, you can receive information on the results obtained in the study upon request. Results will also be posted on the above clinicaltrials.gov website.

# **WHAT ARE MY RIGHTS/RESPONSIBILITIES IF I TAKE PART IN THIS STUDY?**

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

You have the right to be informed of the results of this study once the entire study is complete.

The results of this study will be available on the clinical trial registry [[http://www.ClinicalTrials.gov](http://www.clinicaltrials.gov/)].

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

SIGNATURES

By signing this consent form, please ensure that the following statements are correct and accurate.

* All of my questions have been answered,
* I understand the information within this informed consent form
* I allow access to medical records and transfer and related personal health information as explained in this consent form
* I do not give up any legal rights by signing this consent form,
* I understand that my family doctor/health care provider will be informed of study participation
* I agree to take part in this study.

**SIGNATURE OF STUDY PARTICIPANT**

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Name of Participant

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Signature of Participant Date

**SIGNATURE OF THE PERSON OBTAINING CONSENT (Investigator or Delegate)**

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Name of Person Obtaining Consent Contact Number

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Signature of Person obtaining consent Date

**SIGNATURE OF THE WITNESS**

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Name of Witness

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Signature of Witness 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.