Permission to Take Part in a Human Research Study

Study Title: Utility of Esophageal Temperature Management for the Prevention of Thermal Injury During Cryoballoon Ablation for Atrial Fibrillation

Investigator: Nishant Verma, MD

Supported By: This research is funded by Attune Medical

Financial Interest Disclosure: The following disclosure is made to give you an opportunity to decide if this relationship will affect your willingness to participate in this research study:

If your doctor is also the person responsible for this research study, please note that he is interested in both your clinical care and the conduct of this research study. You have the right to discuss this study with another person who is not part of the research team before deciding whether to participate in the research.

Key Information:
The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?
We are asking you to take part in this research study you have an irregular heart rhythm called atrial fibrillation (AF) and you are scheduled for a first-time AF ablation procedure to treat your AF.

What should I know about a research study?
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?
Atrial fibrillation (AF) is a type of irregular heartbeat and is caused by abnormal electrical signals in the upper chambers of the heart, called the atria, which cause them to beat rapidly and irregularly. When the atria beat rapidly and irregularly they do not pump blood effectively. Patients with AF may experience palpitations, chronic fatigue and weakness, shortness of breath and may also have a higher risk of having a stroke.

AF ablation is a procedure to treat atrial fibrillation. The doctor uses a long thin tube (catheter) to destroy tissue using cryoablation that may be causing the heart to beat out of rhythm. Cryoablation is a process in which cold and freezing causes the heart muscle cells to die in the area involved in the irregular heart rhythm. This creates scar tissue, often called a lesion, inside your heart's chambers that disrupt or eliminate the faulty electrical signals and allows your heart to beat normally. Part of the standard AF ablation procedure involves performing ablation on a part of the heart next to the esophagus (the tube that connect the mouth to the stomach). Sometimes the ablation in this area can also cause damage to the esophagus. Fortunately, complications from ablation are rare.

Current techniques used during AF ablation procedures to try and reduce potential damage to the esophagus during ablation are limited. The purpose of this study is to determine if esophageal warming using the Attune Medical Esophageal Heat Transfer Device (ensoETM) limits the injury to the esophagus during atrial fibrillation ablation procedures. The ensoETM is an FDA approved device used for temperature management, but is not routinely used during atrial fibrillation ablation procedures.

How long will the research last and what will I need to do?
We expect that you will be in this research study for approximately 2 months. In addition, research staff will collect data from your clinical visits for up to 1 year after your AF ablation.

Half of the participants will have the ensoETM device placed prior to the ablation procedure and the other half will have a routine device placed. All patients will be asked to have a scope of their esophagus (known as an EGD) the day after the procedure. No additional study related visits will be required after hospital discharge.

More detailed information about the study procedures can be found under the section **What happens if I say "Yes, I want to be in this research"?**

Is there any way being in this study could be bad for me?
It is possible that placement of the ensoETM device can result in or worsen esophageal tissue damage and injury. The EGD procedure may cause bleeding and there is a small risk of having a reaction to the medications used during the procedure.

More detailed information about the risks of this study can be found under **"Is there any way being in this study could be bad for me? (Detailed Risks)"**

Will being in this study help me anyway?
We cannot promise any benefits to you or others from your taking part in this research. However, a possible benefit may include less damage to your esophagus during the ablation procedure. The knowledge gained by participation in this study may benefit society as a whole in the future and potentially lead to additional studies.

What happens if I do not want to be in this research?
Participation in research is completely voluntary. You decide whether or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled.

Your alternative to participating in this research study is to not participate and receive the standard ablation procedure without use of the ensoETM.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

Whom can I talk to?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at (312) 926-4000. Nishant Verma, M.D. is the person in charge of this research study. You can call him at 312-926-9641, Monday through Friday, from 9am to 5pm. For problems arising evenings or weekends, you may call the on-call Cardiologist at 312-695-0008.

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be studied?
We expect about 40 people here will be in this research.

What happens if I say "Yes, I want to be in this research"?
Before any tests or procedures are performed, you will be asked to review and sign this consent form. If you agree to participate, research personnel will ask you questions and perform tests to see if you qualify for the study. Copies of your records may be placed in your research record as part of this study.

If it is determined that you are eligible to participate in the study, you will return to the hospital for your ablation procedure as planned. Your doctor will discuss the ablation procedure in detail and a separate hospital informed consent form will be presented to you for review and signature after the procedure has been explained to you.

On the day of your procedure you will be randomly assigned to one of two treatment groups by chance (like the flip of a coin); neither you nor the study doctor will be able to decide to which group you are assigned. You will have an equal chance of being given either treatment. Of the 40 participants in the study, half (20) will receive the study specific warming device, EnsoETM, during the catheter ablation procedure and one half (20) will receive the standard of care (standard temperature probe monitoring) during the catheter ablation procedure. Insertion of the study device will be in place of the standard temperature probe and will not add any additional time to the AF ablation procedure. The device will be used according to FDA indications (for warming) and temperature measures will be collected during the clinical ablation procedure.

Both the temperature probe and the EnsoETM will be removed after the procedure ends and before you wake up. The ablation procedure is otherwise not altered from standard clinical practice.

Prior to Discharge
After the ablation you will be monitored in the hospital for 1-3 days as determined by your physician and you will receive standard medical therapy and care that would normally be given. Additionally, the following procedures will be performed for the purposes of this study:

- Results of physical exam, including a review of any complications you experienced during your hospital stay, will be collected
- A review of all medications you have taken while in the hospital prior to discharge
- All patients, regardless of the assigned group, will undergo an esophagogastroduodenoscopy (EGD) procedure, commonly known as an upper endoscopy, which is a test routinely used to examine the lining of the esophagus and stomach. This procedure usually takes about 20 minutes and will be done 1-2 days following the catheter ablation. You will not be able to eat or drink anything for at least 6 hours prior to the procedure. The EGD will be performed under "conscious sedation", meaning you will be given a combination of intravenous medications, which make you very relaxed and sleepy during the procedure. A local anesthetic (with a bitter taste) will be sprayed into your mouth to make it numb and reduce gagging. Monitoring devices will be placed on your skin to measure blood pressure, heart rate, and blood oxygen during the procedure. After you are sleepy, a physician will pass a small flexible camera through the mouth and into the esophagus to evaluate the esophagus following the ablation procedure. This will be performed by a physician that specializes in gastroenterology.

Follow-up
Follow up data will be collected from your medical record for one year after your ablation procedure at 3 time points (2-3 months, 6 months and 12 months). These are standard of care visits following an ablation procedure and participation in this study will not require any additional visits beyond what is recommended clinically by your physician. You will be informed which group you were assigned to at your 2-3 month follow-up visit.

If you need more than one ablation to treat your AF, data from the additional ablations will be collected. In addition, results of other routine tests and images used to monitor your heart rhythm may be collected for this study including, but not limited to, CT scan, MRA scan, MRI Scan, echocardiograms and EGC. Your name and personal information will be removed from these tests/images.

If you do not return for any of these routine visits research personnel will contact you to see how you are doing and if you have had any heart procedures or events.

What happens if I say "Yes", but I change my mind later?
You can leave the research at any time; it will not be held against you.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Detailed Risks: Is there any way being in this study could be bad for me?
This research may hurt you in the following ways:

This study occurs during a routine ablation procedure that your doctor has scheduled as part of your standard of care. Your doctor will discuss the details of the ablation procedure and all of its associated risks with you when you review and sign the clinical consent form separate from this study.

For subjects randomized to the control group, all procedures conducted during the ablation are standard of care and should not pose additional risks. However, for participants assigned to use of the ensoETM device there may be additional risks. All subjects in this study will be asked to undergo an endoscopy for research purposes and there may be additional risks posed by this procedure. The risks are described below.

Risks of EnsoETM (subjects assigned to the device treatment group)
Placement of the ensoETM device can result in or worsen esophageal tissue damage and injury, particularly in patients with known esophageal deformity (esophagus is not formed properly) or evidence of esophageal trauma. In very long procedures (i.e., longer than 8 hours), there is a risk that the device may cause minor injuries to the skin if it is left in one place. We will minimize this risk by regularly repositioning the ensoETM during your procedure. The ensoETM has been used safely in thousands of patients for various temperature management needs (cooling or warming patients in the intensive care unit, emergency department, or operating room). The ensoETM will be removed immediately following your ablation procedure.

These risks are similar to those whom receive the standard of care temperature monitor probes inserted into the esophagus during routine ablation procedures.

Risks of EGD Procedure (all participants)
This procedure is being done as part of this research study and is not standard of care for patients undergoing a cardiac ablation procedure.

In general, diagnostic upper endoscopy procedure is a very safe test, but does have some risks associated with the procedure and with the anesthesia. The risks associated with the procedure range from minor discomforts to significant medical problems.

Minor risks include:

- Sore throat lasting less than 24 hours
- Bloating and gas

Major risks include:

- Bleeding (less than 3/10,000}
- Tearing or perforation of the GI tract (less than 1/1,000)
- Aspiration or inhaling stomach contents (less than 1/1,000)

The risks associated with conscious sedation include:

- Allergic reaction (such as hives, wheezing, anaphylaxis)
- Problems with cardiac and pulmonary function (irregular heartbeat and slowed breathing)

Although the overall risks to the procedure are quite small, occurring in less than 2/1,000 patients, there have been reports of serious, unpredicted complications that include death. You will be monitored closely during the procedure and there are medications that will reverse some of the adverse effects of those medications used during the procedure if necessary.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: **"What happens to the information collected for the research?".**

What do I need to know about reproductive health and/or sexual activity if I am in this study?
Per standard practice a pregnancy test is performed prior to any ablation procedure in females of childbearing potential. Any female determined to be pregnant will not undergo the ablation procedure and therefore not be able to participate in this study.

Will it cost me anything to participate in this research study?
There will be tests and procedures that are done only for this study and other tests and procedures that are part of your regular medical care (not part of the research).

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay, including cost of the ablation procedure, hospitalization and follow-up care for your condition. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay. If your health insurance or Medicare requires any co-payment, co-insurance, or deductible, you will be responsible for making that payment.

You or your insurance will not be charged for the tests or procedures required only for the study. Any procedures that were not done as part of your standard care will be paid for by the study. The EGD done after the procedure will be paid for by the study. In addition, the ensoETM probe is provide at no cost.

What happens to the information collected for the research?
Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution.

The company funding this project, auditors, the IRB, the Northwestern University Office for Research Integrity, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), and the US Food and Drug Administration (FDA) may be granted direct access to

your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at 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.

Data Sharing
De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Can I be removed from the research without my OK?
The person in charge of the research study or the company funding the study can remove you from the research study without your approval. Possible reasons for removal include:

- The study doctor feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study doctor or the funding agency has decided to stop the study.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?
If you become ill or are injured as a result of this study devices or procedures, you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The hospital [university, researchers] will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you agree to take part in this research study and complete the EGD procedure, we will pay you $75.00 for your time and effort. A check will be mailed to you 4 to 6 weeks after discharge. If you do not complete the EGD, you will not receive compensation.

The Accounting Services at Northwestern University will be given your name, address, and Social Security Number in order to issue a check for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are $600 or more in a calendar year.

HIPAA Authorization
We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- Results of physical examinations
- Medical history
- Lab tests, or certain health information indicating or relating to heart disease/atrial fibrillation

- Device model or serial number of the warming device used for ablation
- Results from a physical exams includes blood pressure, heart rate, breathing rate and temperature
- Tests such as echocardiogram (transesophageal and transthoracic), CT scan/MRI or other clinical imaging will be collected if they have been performed for standard clinical care
- Data and results from the ablation procedure
- Billing information

During this study, you may be coming to a Northwestern Memorial Healthcare Corporation entity (for example, Northwestern Memorial Hospital, Prentice Women's Hospital) for research appointments or to get clinical services, such as lab tests, needed for the study. When that happens, you will be scheduled for these services through the NMHC computer system. When a clinical exam or lab is done by NMHC or one of its employees for the purpose of this research study, that information will be kept in both NMHC's clinical records and in the study records.

The following clinical providers may give the researchers information about you: all current and previous health care providers, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH).

Once we have the health information listed above, we may share some of this information with the following offices or entities outside of Northwestern University and its clinical partners (or affiliates): the Northwestern University Institutional Review Board Office and Office for Research Integrity; the US Office of Research Integrity; the US Office for Human Research Protections; the US Food and Drug Administration.

Any research information shared with outside entities will not contain your name, address, telephone or social security number or any other personal identifier unless disclosure of the identifier is necessary for review by such parties or is required by law or University policy [except that such information may be viewed by the company funding this project and its partners or contractors at the Principal Investigator's office].

The following entities may receive your health information:

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board.
- Clinical affiliates, including but not limited to the Shirley Ryan AbilityLab (SRALAB), Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), Northwestern Lake Forest Hospital (NLFH), and the Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's). Your participation in this clinical trial may be tracked in an electronic database and may be seen by investigators running other trials that you are enrolled in and by your healthcare providers.
- Clinical affiliates, including but not limited to Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH), for purposes including, but not limited to, the affiliate's provision of care to you and/or the affiliate's scheduling of appointments and/or billing activities.
- Other University research centers and University contractors who are also working on the study
- Attune Medical who is providing funding to support the study, and that company's contractors and partners.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will not expire.

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

PI's Name: Nishant Verma, MD
Institution: Northwestern Medicine
Department: Medicine
Address: 251 E. Huron, Feinberg Pavilion, Suite 8-500; Chicago, IL 60611

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

A copy of this signed consent document, information about this study, and the results of any test or procedure done may be included in your medical records and may be seen by your insurance company.

Signature Block for Capable Adult:

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

_____ _____
Signature of Participant Date

_____
Printed Name of Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Printed Name of Person Obtaining Consent