Informed Consent Cover Page for CT.gov consent posting:

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INFORMED CONSENT TO PARTICIPATE IN RESEARCH

Sponsor / Study Title:	**National Heart, Lung, and Blood Institute (NHLBI), at the National Institutes of Health (NIH)/ "NHLBI DIR Transcatheter Mitral Cerclage Annuloplasty Early Feasibility Study"**
Protocol Number:	**19-H-0088**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

INTRODUCTION

We invite you to take part in a research study. First, we want you to know that taking part in this research is entirely voluntary. You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your study doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone from the research team, or with family, friends or your personal physician or other health professional.

Key Information

This consent form describes the research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study. This section provides the information we believe is most helpful and important to you to in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of this document. Taking part in this research is your choice.

You have heart failure, which means that your heart muscle is weak or stiff. When the heart muscle is weak it is called "heart failure with reduced ejection fraction, HFrEF." When the heart muscle is stiff it is called "heart failure with preserved ejection fraction, HFpEF."

Both cause breathlessness and lack of energy especially when walking or exercising, and hospital admissions for fluid buildup. In your case, the heart chambers (atria or ventricles or both) have expanded enough to cause your mitral valve to leak, which makes the heart failure worse.

Your heart specialists do not believe you should have heart surgery or other standard approaches to repair your heart muscle or leaky mitral valve. A new catheter treatment for leaky mitral valves was recently approved (MitraClip) for some people like you. Your doctors do not believe MitraClip is a good choice for you and will discuss the risks and benefits with you. They believe you may benefit from a new technique with investigational device called "transcatheter mitral valve cerclage annuloplasty" or "cerclage" for short. An investigational device is one that is not approved by the United States Food and Drug Administration (FDA). This is a procedure performed using tubes ("catheters") inserted into your veins, instead of surgery. We are testing, for the first time, study devices implanted (permanently inserted into your body) for the cerclage procedure. The cerclage study device cinches down your heart and mitral valve like a purse-string, which may improve heart function and may make people feel better.

The cerclage procedure is performed at a hospital, where you would stay for one or more days afterwards. To perform cerclage, the study doctors place a wire through veins of the heart, and then cross through a short segment of heart muscle to complete a loop. The study doctors insert a cerclage study device around this loop to compress the mitral valve like a purse-string. The cerclage study device has a special feature that prevents a coronary artery from getting squeezed as part of this purse-string. When the degree of squeezing appears best, the study doctor insert a lock device to maintain the compression. Then the tubes are removed but the cerclage study device is left inside your body.

If you agree to participate you would be among the first subjects in the world using the cerclage study devices. It is not known whether the cerclage procedure, or the cerclage study device permanently placed into your body, are safe or effective.

We hope cerclage study device will improve your heart valve function and your symptoms, but there is too little information available to be sure. In fact you might not benefit from being in this study.

Reasonably foreseeable risks include:

- Heart rhythm disturbance requiring a pacemaker,
- Failure of the procedure,
- Bleeding requiring a blood transfusion,

- Damage to a coronary artery causing chest pain or reduced blood flow to the heart and requiring surgery or stenting,
- Damage to the tricuspid heart valve causing breathlessness,
- A hole in the heart causing bleeding and requiring drainage or surgery,
- Kidney damage from computerized tomography (CT) scan dye, and death.

We believe the main risk is that mitral cerclage may not make you better. At present we believe there is a high chance that you may need a pacemaker because of the cerclage procedure.

After the cerclage procedure we would follow you closely, with standard care after mitral valve repair or surgery. This would involve multiple return trips to this medical center for study doctor visits and to take pictures of your heart using CT scan with contrast dye, and using ultrasound ("echocardiography"). The in-person visits will continue for one year after the cerclage procedure. Then we check on you via telephone, email, mail, and/or through your physicians, if you agree, once a year for a total of five years.

1. Why are we doing this research?
You have heart failure, which means that your heart muscle is weak or stiff.
This causes breathlessness and lack of energy especially when walking or exercising, and hospital admissions for fluid buildup. In your case, the heart chambers (atria or ventricles or both) have expanded enough to cause your mitral valve to leak, which makes the heart failure worse.

Your heart specialists believe you may benefit from a new technique with an investigational device called "transcatheter mitral valve cerclage annuloplasty" or "cerclage" for short. This is a procedure performed using tubes ("catheters") inserted into your veins, instead of surgery.

We are testing, for the first time, study devices implanted (permanently inserted into your body) for the cerclage procedure. These study devices cinch down your mitral valve like a purse-string. You should know there is not enough worldwide experience with cerclage to be certain whether it will succeed. This study will help answer that question. The cerclage study devices are not approved by the Food and Drug Administration (FDA). **The study you are being asked to enroll in is an early feasibility study, which means that you will be among the first subjects in the world using the cerclage study devices. It is not known whether the cerclage procedure, or the cerclage study devices permanently placed into your body, are safe or effective.**

The cerclage procedure is performed at a hospital, where you would stay for one or more days afterwards. To perform cerclage, the study doctor places a wire through veins of the heart, and then cross through a short segment of heart muscle to complete a loop. The study doctor inserts a cerclage study device around this loop to compress the heart and mitral valve like a purse-string. The cerclage study device has a special feature that prevents a coronary artery from getting squeezed as part of this purse-string. When the degree of squeezing appears best,

the study doctors insert a lock device to maintain the compression. Then the tubes are removed but the cerclage study device is left inside your body.

After the research procedure we would follow you closely, with standard care after mitral valve repair or surgery. This would involve multiple return trips to this medical center for study doctor visits and to take pictures of your heart using CT scan with contrast dye, and using ultrasound ("echocardiography").

2. Why are we asking you to be in this study?
We are asking you to be in this study because you have symptoms of congestive heart failure (breathlessness) and mitral valve regurgitation (leakage) caused by diseased heart muscle. Your heart specialists do not believe you should have heart surgery or other approaches (such as MitraClip) to repair your leaky mitral valve because the benefit is not worth the risk. The MitraClip device was recently approved to treat some people like you. Your study doctors will discuss the risks and benefits of MitraClip with you to help you choose the best treatment.

We are asking you to join the study because we are trying to learn whether the study cerclage procedure and study devices are safe and effective to be used in patients in the future.

We also plan to write about the cerclage procedure in medical journals to help take care of other patients, without sharing your identity.

3. How many people will take part in this research study?
30 subjects will undergo attempted transcatheter mitral cerclage annuloplasty.

In total up to 60 people will be screened for this procedure, but only 30 will undergo study treatment with cerclage.

4. How long will you take part in this research study?
Five years.

5. What do we do to decide if you are eligible for this research study?
Before any study-related tests and procedures are performed, you will be asked to read, sign and date this consent document. If you are a woman of childbearing potential you will have a blood sample taken to confirm you are not pregnant. You may have a cardiac CT scan and an echocardiogram done as part of your screening visit.

Your medical care has been discussed in a meeting of the "heart team." The team consists of heart surgeons, interventional cardiologists, imaging experts, and others. The team agrees that you would benefit from a catheter-based, non-surgical, study treatment of your heart and mitral valve. Your doctors, and the heart team believe the standard techniques of surgical mitral valve repair or replacement are not good for you. They also believe that MitraClip is not the best option for you.

These recommendations are based on your medical history and examination, your other medical problems, and results of tests.

6. What procedures, drugs or other treatments are involved in this research study?
If you agree to participate in this study, your study doctors will perform transcatheter mitral cerclage annuloplasty ("cerclage"). This technique was first developed and tested in animals, and so far in a small number of subjects.

The cerclage procedure is performed in the hospital catheterization laboratory. We expect the cerclage procedure will take approximately one to three hours. The procedure is performed with you either completely asleep (general anesthesia) or partially asleep (sedation). After numbing the skin, tubes are placed in the neck vein(s) and groin and/or wrist arteries. In the cerclage procedure the study doctor use catheters (tubes) and wires, while watching using X-rays and ultrasound, to create a purse-string-like loop around your mitral valve. Then they tighten and lock the cerclage study device to try to improve your heart function and reduce your mitral valve leakage (regurgitation). Finally the tubes are removed and the holes in the blood vessels are closed using special devices or by compressing the overlying skin by hand.

You should expect to stay in the hospital overnight if not longer. Afterwards you receive standard medical care for heart failure and mitral valve regurgitation.

You also will undergo a follow-up CT scan before being discharged from the hospital and within the first month and at 6 months, and echocardiograms during follow-up visits in the first year.

Below is a schedule of study activities.

Timing	**Procedure**
Before the procedure	Evaluation of your heart function and mitral valve regurgitation, including a cardiac CT scan you already undergo for medical care, echocardiogram, blood tests, questionnaires, walking tests, and optional stress tests.
Day 0	Transcatheter mitral cerclage annuloplasty procedure.
Pre-discharge or medically necessary	Standard medical care after catheter-based mitral valve repair, including antiplatelet medications, blood tests, questionnaires, echocardiogram. Cardiac CT with contrast before discharge from the hospital.
30-day (±14 days)	Standard medical care after catheter-based mitral valve repair including physical examination, blood tests, questionnaires, echocardiogram, and optional stress tests. Cardiac CT with contrast (which may be performed as late as 90 days) Check for problems ("adverse events")

Timing	**Procedure**
6 months (±30 days)	Standard medical care after catheter-based mitral valve repair including physical examination, blood tests, questionnaires, echocardiogram, and optional stress tests. Cardiac CT scan with contrast Check for problems ("adverse events")
12 months (±30 days)	Standard medical care after catheter-based mitral valve repair including physical examination, antiplatelet medications, blood tests, questionnaires, echocardiogram, and optional stress tests. Cardiac CT scan with contrast Check for problems ("adverse events")
Years 2, 3, 4, and 5 ($\pm$ 1 month)	Research team contacts you or your physician Results of the echocardiogram by your cardiologist are sent to study doctors Check for problems ("adverse events")

In the event of your death, we will request an autopsy. We will also request your heart be removed and sent to the National Institutes of Health for additional analysis. This would help the study doctor understand the effects of the cerclage. Your family and/or your legally authorized representatives have the right to refuse the autopsy, even if you sign and date this consent form.

7. What are the risks and discomforts of this research study?

The risks of the cerclage procedure are not known. We believe the risks may include

- Death
- Heart rhythm disturbance including cardiac arrest
- Cardiopulmonary resuscitation (CPR) in response to heart rhythm disturbance or cardiogenic shock
- Allergic or toxic reaction to anesthesia, medications, or contrast media, or study device materials
- Complications of vascular access (inserting tubes into your blood vessels) including bleeding ("hemorrhage"), fistula (abnormal connection between arteries and veins), dissection, pseudoaneurysm (contained rupture), retroperitoneal hematoma (blood collection behind the organs of the abdomen), pneumothorax (collapsed lung), hemothorax (blood collection between the chest wall and the lung), and catheter-based or surgical repair
- Heart conduction (electrical) system damage requiring cardiopulmonary resuscitation (CPR) or temporary or permanent pacemaker. At present we believe there is a high chance that you may need a pacemaker.
- Compression of your coronary artery (artery supplying blood to your heart) which may cause chest pain, heart attack, or heart rhythm disturbance and that may require catheter-based or surgical treatment

- Dislodging ("embolizing") air, thrombus, or debris to coronary arteries, brain, limbs, or organs causing heart attack, stroke, transient ischemic attack (strokes that last less than a day), or dangerous reduction in blood supply to your organs
- Failure of the investigational Transcatheter Mitral Cerclage Annuloplasty procedure or device, failure to place it in the correct location, or migration/movement of the device requiring surgical retrieval.
- Creating a hole in the heart or a heart vein causing blood to collect around the heart or requiring catheter-based or surgery treatment.
- Bleeding (hemorrhage) caused by the cerclage procedure including blood transfusion
- Bleeding (hemorrhage) caused by placing catheters in blood vessels to implant the cerclage study device, including causing low blood pressure and requiring medications to raise blood pressure or requiring blood transfusion
- Anemia (lack of blood) requiring blood transfusion, including blood loss from the cerclage procedure
- Damage or clotting of the heart veins caused by the cerclage procedure
- Damage to the heart muscle or heart valves causing a heart attack
- Damage or reduced function of the aortic or tricuspid heart valves causing valve regurgitation including requiring surgery
- Damage to the heart muscle or heart valves causing dangerous low blood pressure requiring medicines or artificial heart pumps or surgery
- Damage ("erosion") to the heart muscle over time, causing a hole in the heart or collection of blood which may require catheter or surgery treatment
- Renal (kidney) injury or failure, caused by the cerclage procedure or by contrast dyes used during the procedure, requiring temporary or permanent hemodialysis or medical treatment
- Fluid buildup in your body ("volume overload") or heart failure caused by medicines used during and after the procedure.
- Congestive heart failure, heart muscle damage, low blood pressure, lung failure, or abnormal blood tests caused by the cerclage procedure
- Narrowing the mitral valve too much, causing a condition called mitral valve stenosis. This can result in lung congestion causing shortness of breath, similar to symptoms of leaky (regurgitant) mitral valve.
- Lung failure requiring oxygen or artificial breathing ("mechanical ventilation")
- Infection of the heart valves, blood vessels, or other parts of your body caused by the cerclage study device
- Other infection related to access site or procedure including urinary or pulmonary or sepsis
- Blood clots including deep vein thrombosis, and pulmonary thromboembolism (obstruction of a blood vessel by a blood clot) caused by the cerclage study device or procedure
- Bleeding under the skin ("black and blue marks") and bleeding from the stomach caused by aspirin that you take for the purpose of the study
- Pain including back pain and access site pain and generalized pain

- Low or high blood pressure values, or low or high heart rate values, whether related to anesthesia or not
- Abnormal blood cell tests including platelets and white blood cells
- Abnormal blood chemistries including electrolytes, urea, creatinine, and liver enzymes
- Abnormal blood clotting tests, including PT, PTT, Xa activity
- Emergency surgery on your heart or blood vessels

You will sign and date a separate hospital permission form (informed consent document) for the heart catheterization procedure. This form will outline the risks, benefits and alternative treatments.

Other risks of this study:

- Injury to your kidneys from the CT contrast dye used to take pictures of your heart. This includes pictures during your cerclage procedure and pictures using CT scans afterwards. The contrast dye can cause temporary or permanent kidney damage. It may require temporary or permanent dialysis to live.
- Other complications including allergic or toxic reactions to medicine, anesthesia, contrast dye, or materials in the catheters or the heart valve.
- Complications of radiation necessary for to perform your procedure under X-ray guidance, including long-term damage such as poorly-healing wounds to your skin.
- Drawing blood for tests can cause pain or skin damage.
- IV ("intravenous") tubes for injecting dye or medications can cause pain or damage to skin or veins. This can include vein clotting or infection.
- CT scans require radiation (risks described below), injection of contrast dye (risks described above), and intravenous tubes (risks described above).
- Echocardiography, also known as cardiac ultrasound, involves pushing a probe against your bare chest or inserting an echocardiography tube into your esophagus (swallowing tube). These are performed mainly for your medical care. Rarely your esophagus (swallowing tube) can be scraped by the echocardiography tube causing bleeding or serious infection, or your tooth can be damaged.
- Exercise testing is optional in this study. During bicycle or treadmill exercise you may become tired and breathless.

Since the study device is investigational, there may be other risks that are unknown.

Risks Related to Radiation

Exposure to radiation is necessary for implanting the cerclage study device and to determine its safety of after it is implanted.

We estimate you will be exposed to approximately 3.2 REM from the four CT scans and 36 mSv from approximately 30-50 minutes of fluoroscopy during performance of Transcatheter Mitral Cerclage Annuloplasty. 5 REM is the annual limit for occupational exposure.

Risks related to pregnancy
You are not eligible to participate in this study if you are pregnant. You should not become pregnant while on this study. You may discuss this risk further with the study doctor if it concerns you.

If you are capable of becoming pregnant, we will ask you about pregnancy and perform a pregnancy test before exposing you to radiation.

If you become pregnant during this study, please notify the research team. You should not undergo research CT scans if you are pregnant.

Risks to privacy
Your medical records and medical images from ultrasound and CT scans will be sent to NIH and stored securely. There is a chance your records and identifying information will be disclosed by accident. However, we think that this risk is small.

Some of the information from your medical care, such as CT scans and echocardiograms, will be sent to the National Heart Lung and Blood Institute (NHLBI) CT core laboratory for analysis. Your name and other identifying information will be included in these pictures and in your medical records.

Other scientists at Universities or medical device companies may receive some of this information also. The information will be coded to protect your identity.

8. Are there any benefits to you if you take part in this research study?
You might not benefit from being in this study.

We hope cerclage will improve your heart valve function and your symptoms, but there is too little information available to be sure.

Your participation in this study may result in advances in the medical care of future patients with mitral valve regurgitation.

9. What other choices do you have?
Before you decide whether or not to be in this study, we will discuss the other options that are available to you. Instead of being in this study, you could:

- Request your doctors re-consider the possibility of performing open heart surgery to repair or replace your leaking mitral valve
- Request your doctors re-consider the possibility of performing non-surgical catheter-based repair of your leaking mitral valve, such as *MitraClip*
- Continue treatment of your heart and mitral valve with medications alone

10. What happens if you do not want to participate in the study?
You may choose not to participate in this study.

In that case, it is not possible for you to undergo the cerclage procedure. However you can consider the options described above ("9. What other choices do you have?"). You can ask your doctors to consider standard open heart surgery or catheter-based repair of your mitral valve. Or you can continue standard drug treatment of heart failure (weak or stiff heart) and mitral regurgitation (leaky valve).

11. Are there reasons that your research participation may end early?
You may withdraw from this research study at any time. To do so, please contact the study doctor at the telephone number listed on the first page of this consent document. The study doctor or the sponsor can stop your participation at any time without your consent

12. What will happen when the research study is over?
After the research study is over, you will receive standard medical care for your heart disease.

13. Will your clinical and test results be shared with you?
Details of your medical care during and after cerclage will be shared with the physicians that you designate. If you request the results, they will be provided to you. Any new important information that is discovered during the study and which may influence your willingness to continue participation in the study will be provided to you.

14. Will the results of this research study be shared with you?
If you request the results of this research study, we will send you a summary of the results and what they mean. You may not receive the individual results.

15. Who will have access to your study data?
We will do our best to make sure that the personal health information in your medical record will be kept private. However, we cannot guarantee total privacy. The following organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis. These records and scans will contain your name.

- The National Heart Lung and Blood Institute and other government agencies, like the Food and Drug Administration (FDA) and the Office for Human Research Protections, which are involved in keeping research safe for people.
- Institutional Review Boards at Advarra IRB and at National Institutes of Health
- The manufacturer of the cerclage research device, Transmural Systems, Andover, Massachusetts.
- Qualified representatives at the study site where your cerclage procedure is performed, as well as from National Heart Lung and Blood Institute, who will examine your medical records and research records to make sure they are accurate
- The NHLBI CT CORE Laboratory

16. Will any of your blood, tissue or other samples be stored and used for research in the future?
No

17. Compensation and Charges

17a. Will you receive any compensation (money or other) for taking part in this research study?
You will not receive any monetary compensation or reimbursement for your participation in this study.

17b. Will you be charged for taking part in this research study?
Yes. You and your insurance company are responsible for the costs of medical care involved in heart catheterization and taking pictures of your heart. The study device used in the study will be provided by Transmural Systems, LLC without charge.

18. Do any of the researchers or the NIH have a financial interest related to this research study?
The National Institutes of Health and the research team for this study have developed the cerclage study devices being used in this study. This means it is possible that the results of this study could lead to payments to NIH. By law, the government is required to share such payments with the employee inventors. You will not receive any money from the development of Transmural Systems, LLC, Transcatheter Mitral Cerclage Annuloplasty system.

No NIH employee involved in this study receives any payment or other benefits from Transmural Systems, LLC.

No NIH study staff involved in this study receives payments or other benefits from any company whose device is being tested. However, there are some research partners not associated with the NIH working on this study who may receive payments or benefits, limited by the rules of their workplace.

Some of the non-NIH study doctors do receive payments from heart valve or catheter companies. They do this to perform research, to give advice, or to teach physicians.

OTHER IMPORTANT INFORMATION

1. Confidentiality.
Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. The Investigator (study doctor), the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and the Institutional Review Board (IRB) will be able to inspect and copy confidential study-related records which identify you by name. This means that absolute confidentiality cannot be guaranteed. When

results of this research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified.

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

The Health Insurance Portability and Accountability Act (HIPAA) protects the confidentiality of your medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries.

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you are injured from procedures done for the purpose of this study, the sponsor will not pay for those medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third party coverage. You will not lose any of your legal rights or release the sponsor, the Investigator (study doctor), the study staff, or study site from liability for mistakes by signing this consent document.

3. Whom To Contact About This Study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study doctor at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Participant Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Participant Adviser: Pro00032500.

4. Consent Document. Please keep a copy of this signed and dated document in case you want to read it again.

SIGNATURE OF SUBJECT

I have read (or someone has read to me) the information provided above. I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. I have been given a copy of this consent form.

BY SIGNING AND DATING THIS FORM, I WILLINGLY AGREE TO PARTICIPATE IN THE RESEARCH IT DESCRIBES.

_____

Print Name of Subject

_____

Signature of Subject Date

SIGNATURE OF INVESTIGATOR

I have explained the research to the participant and answered all of his/her questions. I believe that he/she understands the information described in this document and freely consents to participate.

_____

Name of Investigator

_____ _____

Signature of Investigator Date (must be the same participants)