Permission to Take Part in a Human Research Study

Title of Research Study: ***HeartShare Deep Phenotyping Study***

Principal Investigator: Sanjiv J. Shah, MD

Supported By: This research is supported by National Institutes of Health (NIH)

Financial Interest Disclosure: None

If your doctor is also the person responsible for this research study, please note that s/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 because you have been diagnosed with and/or receive treatment for heart failure or may be at risk for heart failure. Alternatively, you may have no risk factors at all. Our research team is working to better characterize why people develop heart failure and how people feel when living with heart failure. Many people living with heart failure have significant symptoms that limit their ability to perform daily activities. If we are better able to identify early abnormalities that may be present, we may be able to minimize the risk for heart failure or improve quality of life and outcomes once people develop heart failure.

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?

This research is being done to learn more about what causes heart failure, which is a medical condition in which the heart does not keep up to the demands of the body, resulting in shortness of breath and swelling. People who have early-stage heart failure or are at risk for heart failure may not know that they have heart failure because they feel well. Some people who have heart failure may experience many symptoms and some experience very few symptoms. HeartShare is studying why some people develop heart failure while others do not. In addition, HeartShare aims to better categorize heart failure into subtypes that can be targeted with specific treatments. In order to learn this information, the study team is recruiting people who do and or do not have heart failure. For this research, the study team will perform a variety of tests (explained below) to evaluate your health. The study team will also send you information on participating in additional study opportunities. You will be able to choose to participate in these additional opportunities or not as they arise.

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How long will the research last and what will I need to do?

We expect that you will be in this research study for 5-7 hours per day for two days for the baseline examination with follow-up in-person visits occurring annually lasting up to 5 years. You also will be contacted by phone or via an online survey in the Eureka app periodically to ask you about your health since the last contact.

The examination will include measurements of your height, weight, waist, hips, blood pressure, and pulse; interview of your health; collection of blood, urine, stool, and saliva samples; walking test; electrocardiogram ("EKG", a test that measures electrical signals from your heart to determine heart rhythm); echocardiogram (ultrasound of the heart and blood vessels); cardiopulmonary exercise test (a bicycle exercise test where we measure oxygen and carbon dioxide in your breath while you are exercising); peripheral arterial tonometry (a test to measure your blood flow at your fingertips); and arterial stiffness applanation tonometry measurement (a test to measure your pulse in your neck and thigh). The examination will also include CT ("CAT scan") of the chest, abdomen, and thigh, which is a test where you lay flat in a scanner so we can obtain images of your internal organs; MRI of the heart and liver (a test where you lay flat so we can take detailed pictures of your heart and liver); and a lung function test, in which you breathe in and out of a tube so we can measure how your lungs are working. We will also include an optional assessment of fat and muscle tissue with a small biopsy.

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?

All of the tests performed here are performed for research purposes and may have some risks. More detailed information about the risks of this study can be found under **"Detailed Risks: Is there any way being in this study could be bad for me?"**

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include a comprehensive assessment of your health in this study. You may also find it rewarding to contribute to scientific discoveries about heart failure.

You will receive results from some tests at no cost to you or your insurance provider. (These tests, like the entire study, are paid for by the National Institutes of Health). Information from the tests will be given to you and your health care provider, if you want. However, please keep in mind that these tests are being performed for research purposes and not to diagnose any specific medical conditions. Also, HeartShare is not intended to provide medical care or interfere with your relationship with your own health care provider. If you do not have your own health care provider, you can be referred to one if you would like.

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.

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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) 503-2515.

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irbcompliance@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?
Up to 2000 participants will be enrolled in this study.

What happens if I say "Yes, I want to be in this research study"?
All procedures for this study are research-related and not part of your routine clinical care. Some of this information may be useful to you or your doctor, and we will share results with you. If you decide to take part in the examination, you will be asked to undergo several procedures at the baseline and follow-up visits.

The baseline examination will be split into two days. Each visit may be scheduled as shorter visits over more than two days according to availability of testing equipment and personnel, and/or for your convenience. The baseline visits will include the following procedures:

1. Measurements of your blood pressure, height, weight, waist and hip size, and pulse oximetry. Pulse oximetry uses a sensor placed on your finger to painlessly measure the amount of oxygen in your blood. If you usually use supplemental oxygen, you will remove it for about 10 minutes for this test. These procedures will take about 15 minutes.

2. Interviews about previous illnesses, hospitalizations, physical activity and function, symptoms and risk factors, urinary incontinence, smoking, and use of alcohol and medications. We will also use the Montreal Cognitive Assessment Test (MoCA) to assess cognitive function. It will take about 30 minutes to complete the questionnaires, and 15 minutes to complete the MoCA test.

3. Collection of a blood sample (up to 6 tablespoons (70 mL) for the main blood draw, and up to 1 tablespoon (15 mL) on the second visit day if needed for the MRI) after an overnight fast (no food and only water, black coffee or tea to drink) to measure blood sugar, blood fats (including cholesterol), and other substances that may be related to the risk of disease. Samples will also be frozen and stored indefinitely for future analysis. The blood draw will take about 10 minutes, including preparation.

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4. Collection of a urine sample (approximately 1 cup) to be frozen and stored for future analyses. The urine sample collection will take about 5 minutes.

5. Collection of stool and saliva sample: We would also like to have you collect a stool sample at home using a kit we provide. The kit includes everything you need to collect the sample easily and safely and to package the sample up for shipment. We will provide a similar kit for saliva. You will collect these samples at home on a day that is convenient for you. You will send the sample to the mailing address provided via a pre-stamped mailer (USPS/United States Postal Service or post office). We estimate that these study activities will take no more than 15 minutes of your time.

6. A walking test to determine how far you can walk in six minutes. If you use oxygen when you walk, you will use it for this test. This test will take about 15 minutes.

7. A test to measure your strength and balance called the Short Physical Performance Battery (SPPB). This test consists of everyday movements like standing up from a chair or standing for 10 seconds with your feet side by side or one slightly in front of the other. If you use oxygen when you walk, you will use it for this test. This test takes about 10 minutes.

8. Electrocardiogram: An electrocardiogram (EKG) is a test that gives us a measure of the heart's electrical activity. You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on the body. This test takes about 10 minutes.

9. Echocardiography, which is an ultrasound imaging test that uses sound waves to show how well your heart muscle and valves are working. A transducer (a device that looks like a microphone) is placed on your chest and is used to bounce sound waves off of your heart. These waves are harmless and painless. A computer changes the sound waves into images that are seen on a video screen. We may also place the device on your neck and groin. Additionally, we will estimate the pressure in your heart during exercise with the echocardiogram. An echocardiogram involves putting an ultrasound probe on your chest during exercise. The echocardiography probe will be used at several points during the exercise period (for example, before exercise, during exercise, and during recovery). The whole echocardiogram study will take about 45 minutes.

10. Exercise Echocardiography: Echocardiography will be performed during exercise during the cardiopulmonary exercise test described below.

11. Cardiopulmonary exercise test: We will ask you to perform a bicycle exercise test where you will be lying partially reclined but in a seated position. This test will be used to assess your overall exercise capacity. The test will begin with a low level of resistance that will then increase every 3 minutes. We would like you to exercise for as long as you possibly can, as the goal is to push yourself to your peak. We will be monitoring you throughout this period and will stop you if we see anything unsafe. When you stop exercising, we will ask you to remain lying in the same position for about 6 minutes while we continue to collect information about your recovery. The total length of this bicycle exercise test will depend on you. During bicycle exercise testing you will breathe through

a mouthpiece that is connected to a machine that monitors that air that you breathe in and out. Specifically, the machine tells us about how much oxygen you are using, and how much carbon dioxide your body is making during exercise. We will also continuously monitor your heart rate and rhythm, and we will be checking your blood pressure frequently during the study. We will also monitor the oxygen levels in your blood using a finger probe. This information will allow us to determine how much oxygen your body is using during exercise. The length of the exercise test will vary based on how long you can exercise for, but we want you to exercise for as long as you safely can while we monitor you the entire time. This exercise testing protocol is considered safe. Rarely, people have an adverse event during exercise. The risk of this happening is the same in our lab as it would be if you exerted yourself elsewhere. You will be closely monitored throughout the exercise period by individuals who are trained to respond to situations that might develop during exercise. It is expected that you will become tired and short of breath during this exercise test, as we do ask that you push yourself to the most that you can possibly do. The whole test including setting up and observing you after exercise will usually takes about 45 minutes.

12. Arterial stiffness applanation tonometry: This measurement is a brief, painless test designed to measure the stiffness of your arteries and how your heart interacts with your arteries. It uses a sensitive pen-like device placed on the skin, on top of the arteries in your wrist, groin and neck to record pulse waves in your arteries. We will also measure your blood pressure using a cuff on your arm and will use sticker electrodes to record a limited electrocardiogram during the test to detect and record pulse waves in your arteries. The arterial pulse in your neck may also be checked. This measurement will take about 20 minutes.

13. EndoPAT™ (Endothelial function Peripheral Arterial Tonometry): The EndoPAT™ is a non-invasive test assessing endothelial function (the endothelium is the inner lining of the blood vessels where cardiovascular disease starts and progresses) by measuring the pressure and pulse in your fingertips through probes (one on each hand). The test takes approximately 30 minutes and is performed resting lying on a bed. Measurements will be obtained before, during, and after 5 minutes inflation of a blood pressure cuff applied to the forearm, which can cause some mild discomfort.

14. Spirometry: This lung tests how your lungs work by measuring how much and how fast air moves out of your lungs. You will wear a nose clip and forcefully blow into a tube hooked to a machine. You will be asked to take a deep breath in and blow your breath out as hard and fast as you can into a machine for at least 6 seconds. The machine measures the amount of air you can blow out and how fast you can blow it out. We have you do this 3 or more times so we can get an accurate measure of your lung function. This test will take about 30 minutes.

15. Computed Tomography (CT) scan: This is a special type of x-ray examination that will be done to examine your lungs, abdomen, and thighs. You will be asked to lie on a table with just the upper part of your body inside the CT scanner. You will need to remain still and, at times, hold your breath for about 10 seconds during the test. The CT scan will take about 15-30 minutes.

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16. Heart MRI: This study uses magnetic resonance imaging (MRI) to look at the heart. Heart MRI is a type of scan that uses magnetic fields and radio waves to make a picture of the heart to measure the size of your heart, how well your heart is pumping, and how well the blood flows in your heart. We will also make some measurements in the liver, including the amount of liver fat.

In order to make sure the MRI procedure will be safe, you will be asked to fill out a screening form before starting the study. It is important that you tell the researchers in this study if you have any history of:

- Metal fragments in your eyes or face.
- Implantation of any electronic devices such as (but not limited to) cardiac pacemakers, cardiac defibrillators, cochlea implants or nerve stimulators.
- Surgery on the blood vessels of your brain or the valves of the heart
- Claustrophobia (fear of enclosed places)
- Body piercing or tattoos

You will be given instructions outside the MRI scanner about the scanning. Next, you will be asked to lie still on the MRI patient table and your head will be placed in a specially-designed head holder. Your head will be cushioned by a firm foam pillow. The table will then slide into the enclosed space of the MRI scanner. Some people feel tired, uncomfortable, or claustrophobic (afraid of small spaces) in the MRI scanner. The MRI scanning session will take 60 minutes to complete once you are in the scanner.

You will be encouraged to hold as still as possible, and to let the investigators know if you are uncomfortable in any way as soon as possible after the imaging session begins.

The MRI scanner makes loud banging noises while taking a measurement, so either ear plugs or specially designed headphones will be used to reduce the noise. The researchers will be in communication with you through an intercom system to tell you how the study is going. The earplugs or headphones should not get in the way of communicating with the researchers.

During the MRI, we plan to inject a contrast agent (dye) into your veins. You will feel a slight pin prick when the needle is inserted into your vein. You may have a warm, flushed sensation during the injection of the contrast materials and a metallic taste in your mouth that lasts for a few minutes. Occasionally, a patient will develop itching and hives, which can be relieved with medication. If you become light-headed or experience difficulty breathing, you should notify the technologist or nurse, as it may indicate a more severe allergic reaction.

The contrast agent to be used contains gadolinium and is called Gadavist. It is approved for use by the Food and Drug Administration (FDA) for its use in this study. The dose to be given is 0.1mg/kg and is within FDA approved guidelines.

Before we give you this contrast agent, we will ask you about any history of kidney problems or liver transplant. Also, within 24 hours of the MRI, we will test the health of your kidneys by laboratory tests. If your medical history suggests a recent significant change in kidney function and/or the result of this blood test shows that you currently have significantly reduced kidney function, you will not be eligible to participate in the

part of the study that uses gadolinium contrast, and we will do the heart MRI without giving contrast.

17. Genetic and Related Chemical Research: The researchers involved in this study want to learn about the role of genes (or inherited traits) in health and disease. Genetic research may discover genes, find out how genes work, or help researchers learn how to use what we know about genes to treat or prevent disease. In this study, with your permission, we will be collecting samples to be part of a genetic biobank. A genetic biobank is a collection of blood-based samples, such as DNA and RNA, and health information. These samples and health information may be used to learn more about the roles genes and chemicals the genes determine to provide better understanding of why heart failure develops and how it can be better treated.

    Samples will be collected for:

    - DNA (deoxyribonucleid acid) which stores information that helps determine traits, such as eye color, height, or disease risk that is passed on from a parent to child.
    - RNA (ribonucleic acid) is a genetic material that has a major role in making proteins. Proteins are the building blocks of your body, cells and organs.

DNA and RNA are both composed of sequences of nucleotides. Sequences of nucleotides in your DNA comprise genes. Genes are transcribed into RNA which is then translated into proteins. Changes in your DNA sequence, known as genetic variants, may have no effect, alter the product of the gene or even prevent the gene from functioning completely. Researchers will be looking at your genetic code for heart disease and related conditions. We would also like to make your data and samples available for other research studies that may be done in the future. The research may be about similar diseases or conditions to this study. However, research could also be about unrelated diseases, conditions, or other types of research. These studies may be done by researchers at this institution or other institutions, including commercial entities. Our goal is to make more research possible. We plan to keep your data and samples indefinitely. Your data and samples may be shared with researchers around the world. Your name and identifying information will be removed from any data and samples you provide before they are shared with other researchers. Researchers cannot easily link your identifying information to the data and biospecimens. For more information, see the section called “What will you do with my data and samples?”

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18. At-home Measures. The researchers involved in this study want to learn about how some of the measures change at home and over time.
    - Ambulatory blood pressure monitoring: You will receive an upper arm blood pressure monitor to wear for 24 hours. Afterwards, you will return it in a pre-paid, pre-addressed mailer to the study center.
    - AliveCor Kardia 6-lead ECG: This is a handheld portable device that will perform an electrocardiogram. A member of the study team will teach you how to use the Kardia device and you will receive written instructions about its use. We will ask you to take a recording once a month. You will keep this device for the duration of your enrollment in the study.

    We may also ask you to use other at-home monitors or wearable devices as part of this study that we would provide for your use. These might include smartwatches, smart-rings, activity monitors, ECG patches, and sleep monitors. These devices will be provided to you by the study free of charge and we will explain those to you as they become available.

19. We will get some information from other places to be sure we get a complete picture of your health.
    - Electronic health records
      If you have electronic health records, we will get certain information from your medical records from places where you receive health care. We will get information from past health records from 2006 until now. We will see data about your health problems, test results, medical procedures, images (such as X-rays), and medicines you take. Health records can contain sensitive data. For example, they may tell us about your mental health, genetic conditions, or use of alcohol or drugs. They may contain sexual or infection data, including HIV status. In some cases, we might need you to sign an extra form saying it is okay for us to get the information we need for the study. The information from your health record will be recorded and sent along other the other information you provide us as described in the "What will you do with my data and samples?" section below.
    - Data about your health from other sources
      We will add data from other sources to the data you give us. For example, environmental data and pharmacy records. This will give researchers more data about factors that might affect your health. There are two ways we will add data from other sources to your HeartShare record:
      - Based on where you live and work

      We will add data about your area based on where you live and work. For example, we may add data about the number of people in your area. We may add pollution data. We may add data like how close you live to the nearest grocery store or park.
      - Based on data that identifies you

      We will use data that identifies you, like your name and date of birth, to add data that is specific to you. For example, we may add data from pharmacy records or health insurance records.

These other sources can contain sensitive data. For example, they may tell us about your mental health, or use of alcohol or drugs. They may contain sexual or infection data, including HIV status. Because of this, we will ask the HeartShare safety monitoring board to review and approve each data source before we add it.

20. Additional Procedures: In addition, you may be asked to undergo the following

procedures:

Muscle tissue biopsy: We will also obtain a small sample of muscle. This procedure is used to obtain muscle cells from the thigh. After cleaning the skin on the front of your thigh with iodine, a local anesthetic (numbing medicine similar to what a dentist uses) will be injected under the skin to numb the area. The doctor or a trained/certified designee will make a small incision in the skin and insert a needle into the muscle above the knee to remove muscle cells. Approximately 600 milligrams (a little more than the weight of pencil eraser) of muscle will be removed. The needle may be inserted through the incision up to 5 times to obtain adequate/enough muscle tissue. After the sample is removed, the skin will be held closed with sterile adhesive strips and a bandage. Of note, you will not be allowed to swim or soak in a bathtub/whirlpool/hot tub for 72 hours after this procedure.

Fat tissue biopsy: We may also obtain a small amount of fat. This procedure is used to sample fat cells from the abdomen (belly). After cleaning the skin on the front of your abdomen with iodine, a local anesthetic will be injected under the skin. The doctor or a trained/certified designee will make a small incision in the skin of your abdomen and inject additional lidocaine and some saline (salt water solution) that allows for easier removal of the fat cells using a needle with a suction device. The needle may be inserted through the incision up to 3 times to obtain adequate/enough fat. Suction will continue for several minutes if necessary. About 3 grams (approximately 1 teaspoon size) of fat will be removed. After the fat sample is completed, the skin will be held closed with sterile adhesive strips and a bandage. Of note, you will not be allowed to swim or soak in a bathtub/whirlpool/hot tub for 72 hours after this procedure.

During the procedures described above (1-19) we may also ask you to wear additional sensors to validate their readings. These will not significantly change the nature of the test or the duration of the test.

Clinical follow up: During follow-up visits, we will ask you to share information about your health and participation in the study information by phone, online, and in-person and will include the following:

We will contact you by phone or via an online survey in the Eureka app every month and ask you about your health since the last contact. If you are unable to answer questions yourself, we may contact a person you have named who could answer questions for you. If you are hospitalized or admitted to a rehabilitation facility or nursing home, we will ask that institution for your records. We will review the records to determine the reason for your admission and your diagnosis. We may request records from your doctor for certain office or clinic visits to determine if you have been diagnosed with one of the diseases that HeartShare is studying. We may also request Medicare records. We would also want to access information about the cause of death, if anything unfortunate should happen during the study. We may request death certificates or coroner's reports from the local department of health. If you should lose contact with the HeartShare study, we may attempt to contact your relatives or friends. We may also use the Internet or a commercial locator service to find your current address and telephone number.

Follow-up in-person visits will occur annually (every 12 months) for 5 years. At these visits, a clinical exam, electrocardiogram, walking test, and blood (3 tablespoons) and urine collection (approximately 1 cup) will occur.

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.

Detailed Risks: Is there any way being in this study could be bad for me?

This research may hurt you in the following ways related to study procedures:

Moderate Risk Procedures:

- **Echocardiogram with and without exercise:** Some individuals may experience some mild pressure, discomfort, and/or irritation from the transducer on the chest. During the portion of the test with exercise, you may feel muscle soreness or fatigue, shortness of breath, abnormal blood pressure, or fainting (all common). Rarely, exercise tests can cause irregular heart rhythms, heart attack, stroke, or sudden cardiac death. The exercise will be stopped if you want it to be stopped or if the amount of oxygen in your blood falls below 80%. This will be measured using a pulse oximeter, which is a small device that attaches to your index finger.

- **Cardiopulmonary exercise test:** During exercise test, you may feel muscle soreness or fatigue, shortness of breath, abnormal blood pressure, or fainting (all common). Rarely exercise can cause irregular heart rhythms, heart attack, stroke, or sudden cardiac death.

- **CT of the lung, abdomen and thigh:** The CT scan uses x-rays to make pictures. This test involves a small amount of radiation. Background radiation is present on Earth (soil, air, water, food) and also includes cosmic radiation. Exposure to radiation from natural sources is a feature of everyday life. Your participation in this study will involve additional exposure to radiation. The radiation dose received for one chest/abdomen/pelvis/thigh CT scan is approximately equal to 4.3 years of background radiation.

- **Cardiac MRI:** Some people cannot have an MRI because they have some type of metal in their body. For instance, if you have a heart pacemaker, artificial heart valves, metal implants such as metal ear implants, bullet pieces, chemotherapy or insulin pumps or any other metal such as metal clips or rings, you may not be able to have an MRI. During the MRI test, you will lie in a small, closed area inside a large magnetic tube. Some people are scared or anxious in small places (claustrophobic). The MRI scanner makes loud banging noises while taking a measurement, so either ear plugs or specially designed headphones will be used to reduce the noise. The use of gadolinium-based contrast agents in patients who already have severely reduced kidney function or who have had a recent (within 4 weeks) kidney or liver transplant is uncommonly (less than 1%) associated with a possibly fatal disease involving the skin, muscle and internal organs. This disorder is called nephrogenic systemic fibrosis (NSF). As stated in the earlier sections of the consent form, you will have blood drawn to test your kidney function and will be asked if you have any history of kidney problems or have had a kidney and/or liver transplant. Deposits of gadolinium remain in the brain of some patients who have undergone MRI scans with gadolinium for a prolonged time after the last administration. Deposits of gadolinium have also been reported in skin and bone. The FDA determined that there is no evidence of long-term safety risk.

  The dose and frequency of the contrast agent we are giving you is standard. We do not expect any additional risk to be posed to you beyond those already described above. You should avoid receiving additional gadolinium within 24 hours before or after the dose given in this research study.

- **Genetic research:** Risks from Genetic Research. We will be collecting samples from you so we can study your DNA. We will do everything we can to maintain your confidentiality and privacy, but a risk of genetic research is that your DNA may allow someone to identify you. We believe the chances of this are very small, but they are not zero. If released, you may be worried that genetic information could be used to discriminate against you. A law was passed in 2008 by the Federal Government (“GINA” or Genetic Information Nondiscrimination Act) that prevents many forms of discrimination based on genetic information. More details about this can be found under the section, **“What else do I need to know?”**

- **Fat and muscle biopsies (optional procedures):** The biopsy may cause some pain and discomfort. It is possible, but not likely that you could get an infection. In very rare

cases, people might have an allergic reaction to the numbing medicine. The allergic reaction could include rash/hive, flushing of the face, itching, wheezing, and tightness in the throat. There will be a small scar from the biopsy. You may be asked to stop or reduce your blood thinner(s) if you take them (for example, anti-platelet therapy or anti-coagulation therapy) during the week leading up to a study muscle biopsy procedure. Stopping or reducing your anti-platelet therapy or anti-coagulation therapy during this week may increase your risk of a heart attack or stroke.

Low Risk Procedures:

- **Clinic exam:** The procedures used in this study are considered to be low risk.
- **Cognitive testing:** Questions that you will be asked may cause mental or emotional discomfort.
- **Blood draw:** Risks of drawing a blood sample are discomfort at the site of needle insertion, bruising (black and blue discoloration) or inflammation at the site, and rarely, faintness. Bruising, if it occurs, is usually painless and disappears within a few days.
- **Ambulatory blood pressure monitoring:** This is considered to be low risk. You may feel some pressure when the blood pressure cuff inflates while you are wearing it.
- **Urine, stool, and saliva collections:** These are considered to be low risk.
- **Six-Minute Walk Test:** Risks of this test include shortness of breath and chest tightness, and rarely, faintness or heart problems. We will guard against these by asking you questions before the test to determine whether it is safe for you to have this test. You will also be monitored closely by study staff during the test.

  Short Physical Performance Battery (SPPB): Risks of this test include shortness of breath and rarely, faintness or loss of balance. We will guard against these by asking you questions before the test to determine whether it is safe for you to have this test. You will also be monitored closely by study staff during the test.
- **Electrocardiogram:** The test may cause some redness or itching where the pads are placed.
- **Arterial applanation tonometry (arterial stiffness measurement):** There is a risk that inflation of the blood pressure cuff will feel temporarily uncomfortable. We will make every effort to make you feel comfortable during the procedure.
- **EndoPAT™ (Endothelial function Peripheral Arterial Tonometry):** During the 5 minutes when the blood pressure cuff is inflated, you may feel some discomfort. We will make every effort to make you comfortable during the procedure.

- **Spirometry:** This lung test may make you cough or feel lightheaded. This will go away shortly after the test is finished.

Incidental findings: The CT, MRI, and echocardiogram scan you are having as part of this research study is not the same as a clinical exam. It is designed to answer specific research questions. The exam will be reviewed by a qualified person and read to an appropriate standard. The research studies are not a replacement for clinical studies and are often less comprehensive. There is a possibility that while reviewing your CT, MRI, or echocardiography scan that we may see a finding that we did not expect to see in this study. If this finding might be significant to your immediate health, we will report this to you. This is what is called an "incidental finding." We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by mail or by phone. In the case of a potential serious emergency, we will make every effort to contact you in a timely manner. A qualified person (usually a member of the research team) will talk to you if there is an incidental finding. You do not have an option to decline information about an incidental finding.

If you want, we will give information about this incidental finding to your primary health care provider or we will refer you to an appropriate health care provider for further evaluation.

- An incidental finding may cause you to feel anxious.
- Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance.
- The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

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 will you do with my data and samples?"

What do I need to know about reproductive health and/or sexual activity if I am in this study?

Some of the procedures (CT scan) in this research are known to harm a pregnancy or fetus. Therefore, only people who are not pregnant will complete the CT scan. Any birthing individuals who are premenopausal will complete a urine pregnancy test before completing this portion of the research study.

Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you or your insurer for medical procedures.

Will being in this study help me in any way?

You and your doctor will receive results from some tests at no cost. (These tests, like the entire study, are paid for by the National Institutes of Health). However, please keep in mind that these tests are being performed for research purposes and not for diagnosing any specific medical conditions. In addition, HeartShare is not intended to provide medical care or interfere with your

relationship with your own health care provider. If you do not have your own health care provider, you can be referred to one if you would like.

What will you do with my data and samples?

We will store your data and samples securely, along with the data and samples from all the other people who take part in HeartShare. Researchers will use the data and samples to make discoveries.

1. We will study your data and samples, including your DNA
   DNA is in your blood and other samples. All human beings share more than 99% of their DNA with each other. The tiny bit that is different is part of what makes each of us unique. Things like our hair color and eye color depend on the bits of DNA that are different between human beings. We call these our DNA changes. These DNA changes can also tell you about your health and how your body works. They can tell you about where your ancestors may be from. We are still learning about what role DNA plays in many parts of our lives.

   We will use many methods to study your samples. For example, we might study your DNA using whole genome sequencing. Whole genome sequencing is a way of studying nearly all of a person's DNA. Every person's whole genome sequence is different. It is unique to them, like a fingerprint.

   Because HeartShare will last for five or more years, some of the methods we use to study your data and samples may not even be invented yet.

2. We will create a scientific database
   The scientific database will have individual-level data and samples. This includes your DNA data. Access to this database will be controlled. Researchers will have to be approved by HeartShare to use this database. They will have to have special training before they can be approved. Their research may be on nearly any topic. They may look for patterns in DNA. This may help them discover different ways that DNA affects people. These researchers may be from anywhere in the world. They may work for commercial companies, like drug companies.

3. Researchers can also ask to study your samples or DNA directly
   We may send them a small amount of your samples or DNA so that they can do this. Before we send researchers your samples or DNA, they will have to take special training and sign a contract stating that they will not try to find out who you are. They will have to tell us what they want to study. HeartShare will have to approve it.
   Researchers will use many methods to study your samples and DNA. Because HeartShare will last for five or more years, some of the methods may not even be invented yet. The data researchers get from studying your samples and DNA may be added to the HeartShare scientific database.

4. 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, and:

   - Authorized members of the workforce at the study site, who may need to see your information, such as administrative staff members from the Office for Research and the Office for Research Integrity, and members of the Institutional Review Board (a

committee responsible for the ethical oversight of the study)

- Representatives of our study sponsor, the National Institutes of Health and the National Heart, Lung, and Blood Institute, the Office for Human Research Protections (OHRP), and other researchers (the Principal Investigators of the HeartShare Clinical Centers study at the Massachusetts General Hospital/Brigham and Women's Hospital, Mayo Clinic, University of Pennsylvania, University of California-Davis, and Wake Forest University, the staff of the HeartShare Data Translation Center and other HeartShare staff involved with this study).

Your information will be transmitted and stored using very secure systems, including the National Heart, Lung, and Blood Institute BioData Catalyst, a secure, encrypted, web-based "cloud" that is a repository for research-related data. All data in BioData Catalyst will be de-identified. The network servers where your data are stored sit behind firewalls that do not allow unauthorized access and are physically located in a secure server room that can only be accessed by critical staff members. You are participating in a research project supported by the Eureka Research Platform, which maintains a Privacy Policy and Data Security Measures. You will be notified of any changes in this policy. Here is the Policy:

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate does not stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate cannot be used to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate does not stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also does not prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

Permission to Take Part in a Human Research Study

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.

Will I find out the results of the research?

Results explain or interpret data. In HeartShare, we will study lots of things about your data and samples. We might tell you if there are results about you from what HeartShare studies. Some of the results we give you may tell you about your health, and others may not.

1. Results that may tell you about your health

These are results that could be used by a healthcare provider to take better care of you. For example, if any of your physical measurements are outside of what we would expect, we will tell you so you can follow up with your healthcare provider. You will have to pay for the cost of follow-up care with your own health care provider.

2. Results that would not tell you about your health

These results might be interesting to you, but a health care provider probably would not use them to take better care of you. For example, these results might come from tests that are still experimental.

We will not tell you or your health care provider results from genetic research, such as whole genome sequencing.

What else do I need to know?

If you become ill or are injured as a result of this study (medications, 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.

Commercial use of data and samples:

Researchers from private companies, such as those that develop diagnostic lab tests or treatments for diseases, may request access to your study information or samples. However, these researchers will not have access to personal information that identifies you, such as your name, date of birth, social security number, address, etc.

Your samples will not be sold to any person, institution, or company and will not be used for human cloning (creating body organs, tissues, fluids, or human beings from your genetic material).

HeartShare data may lead to inventions or patents in which private companies or the universities conducting HeartShare may participate and may benefit.

Neither you nor your family would benefit financially from discoveries made using the information and/or specimens that you provide.

Very detailed information about your collected DNA will be stored centrally at the National

Permission to Take Part in a Human Research Study

Institutes of Health, where it will be shared with other investigators for research. This information, along with all of your other clinical data, will be used by researchers to look for genes/related chemicals that affect the risk of developing diseases and may lead to better methods for prevention and treatment of disease. The stored information is de-identified, which means that identifying information such as your name, date of birth, social security number, address, etc., is removed.

Access to this stored information is controlled by the National Institutes of Health. The National Institutes of Health is committed to protecting the confidentiality of all the information it receives, but will also comply with relevant laws, which might include Freedom of Information Act (FOIA) requests for de-identified information. This is explained on the following website: http://www.nih.gov/icd/od/foia/efoia.htm

HeartShare takes extensive efforts to protect your identity and privacy. Yet, because of the large amount of information collected about you, we cannot absolutely guarantee that

information about you or your blood relatives will never become known. This is partly because of the possibility of matching your DNA sample with other DNA collections (such as those kept by law enforcement agencies). However, researchers are strictly prohibited from attempting to identify you.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

If you agree to take part in this research study, we will pay you $250 per day ($500 total) at the completion of study procedures for your time and effort. We will pay you an additional $125 each for the optional biopsies (i.e., $125 for 1 biopsy, $250 for both biopsies). You may also be eligible for reimbursement of travel and lodging expenses, which will be determined by your local enrolling site.

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 a particular condition as well diaries and questionnaires
- Records about study medication or drugs
- Records about study devices
- Billing information

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During this study, you may be coming to a Northwestern Memorial HealthCare/Northwestern Medicine entity 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) and Northwestern Memorial HealthCare/Northwestern Medicine entities and its current and future affiliates.

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 Study sponsor 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 Memorial HealthCare, 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 Memorial HealthCare, 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,
- Other researchers who are approved members of the study team
- Study monitors and auditors who make sure that the study is being done properly,
- The National Institutes of Health who are funding the study
- 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.

Permission to Take Part in a Human Research Study

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: Sanjiv Shah, MD
Institution: Northwestern University Feinberg School of Medicine
Department: Medicine
Address: 676 N. St. Clair, Chicago, IL 60611

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.

Optional Elements:

If you agree to participate in the HeartShare Deep Phenotyping study, you will be asked to consent to participate in optional research activities, meaning that you do not have to agree to them in order to participate in the research study. You will indicate your willingness to participate in these optional activities immediately following your response to participating in this study.

Signature Block for Adult Capable of Providing Consent:

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