Patient I.D. Plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: Occult Small Vessel Cerebrovascular Disease in High Risk Families

Application No.: NA_00002856

Sponsor: NINDS

Principal Investigator: Paul Nyquist, MD

1. What you should know about this study:

- You are being asked to join a research study.
- This consent form explains the research study and your part in the study.
- Please read it carefully and take as much time as you need.
- Please ask questions at any time about anything you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. You can decide not to take part or you can quit at any time. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to be in the study.
- Ask your study doctor or the study team to explain any words or information in this informed consent that you do not understand.
- For clinical trials, a description of the research will be available at www.ClinicalTrials.gov. This website will not include information that can identify you. You can search the website at any time.

2. Why is this research being done?

This research is being done to find out if brothers and sisters or adult offspring of people who have coronary heart disease at a young age are at increased risk for future stroke.

The research will look at patterns that can be seen in the brain using imaging techniques that show silent processes that have happened in the brain, Silent process are ones that have no symptoms.

The study will also try to find out whether these silent processes in the brain are related to high blood pressure, smoking, body weight, blood sugar, and blood markers of inflammation.

People from the Johns Hopkins Sibling and Family Heart Study who are now 30-75 years of age and who have never had a stroke or heart attack themselves are being asked to join the study.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following: 1. undergo a cardiovascular history and physical examination by a physician, 2. complete questionnaires about your health, 3. do some testing that tests your memory and ways in which you process information, 4. have an MRI of your head to look for signs of silent stroke or small vessel disease of the brain, 5. perform an exercise test with scanning of your heart for silent coronary heart disease, 6. have blood drawn for risk factors like cholesterol, diabetes, and some markers of other processes that may affect your health, like markers of inflammation. We may call you back a second time for a second blood draw at a later date. We will describe each procedure for you.

If you agree, there is also another aspect of the study involving some additional scans of your coronary artery using a CT of your chest, but that is not part of this main study of silent stroke. You do not have to participate in that if you would prefer not. Later in the consent form you will be given a chance to indicate if you wish to do this.

EXERCISE TESTING AND SESTAMIBI SCAN OF YOUR HEART

In order to determine if you have silent coronary artery disease, an exercise treadmill test will be performed with a Technetium-99m sestamibi scan to look at blood flow in your heart. This part of the testing will take about 2 hours. The exercise heart scan is done in our usual research unit, the MIRU where you were seen for the other stress tests we have done. You will get an IV inserted and electrocardiogram leads will be placed on your chest so your electrocardiogram can be checked frequently during the test. You will be asked to perform a standard exercise test where you exercise at increasing levels on a treadmill until you feel like you have to stop because of shortness of breath, fatigue, or other symptoms. A radioactive tracer called technetium-99m sestamibi (also known as Cardiolite) will be given twice through the intravenous line, once while you are at rest, and a second time at the end of the exercise test. After each injection you will lie down under a special camera to obtain a picture of the blood flow to your heart. Each of the two scans will take about 30 minutes and you will have to lie still with your arms above your head while the camera rotates around your chest. The entire test will be supervised by a cardiologist and a nurse.

BLOOD TESTS

You will also have blood drawn for measurement of your cholesterol, blood sugar, and the inflammatory markers. This will be done at the same time you have the needle inserted for your heart scan. If you are eligible some blood may used to look at the activity of white cells in your blood. We may call you at a later date to drawn 17ml (or 5 teaspoons) of blood.

MAGNETIC RESONANCE IMAGING EXAM (MRI)

MRI can detect tiny areas of brain tissue abnormalities that may indicate small strokes that you have not been aware of. Many people have these patterns, and in some cases they are large enough to be related to a higher risk for a more serious stroke in the future.

As part of your participation in this research study, you will have a Magnetic Resonance Imaging (MRI) exam. MRI uses magnets and radio signals to make pictures of the part of your body we are scanning. The MRI exam will take approximately 35 minutes. Prior to your exam, you will be asked to complete a standard questionnaire. The purpose of this questionnaire is to ensure that you are able to safely enter the MRI area. If you have a history of metal in your head or eyes or are unsure about exposure to metal, you will not be allowed to take part in this study. An orbital X-ray may be offered to you if you have a history of exposure to metal fragments. If the orbital x-ray is offered and you consent to do it will detect

any retained metal fragments that might exist unknown to you in your eyes. If the Orbital X-ray is clear, you will be allowed to have the MRI regardless of any history of exposure to metal.

To start your MRI test, you will lie on a padded table. The table you are laying on will be moved to the center of a large magnet, which looks like a long narrow tube. The tube is open on both ends but some people feel confined in small places. If this bothers you, please notify the MRI staff right away. You may end your participation in this study at any time by telling the MRI staff. When MRI pictures are taken, it is normal for the MRI machine to make loud, banging, and clicking noises. You will wear headphones for your comfort during the MRI exam.

During the exam, the MRI staff is able to see and hear you via microphone in the machine. You will be able to hear the MRI staff. The MRI staff will be talking to you throughout your MRI exam and may give you simple instructions. You will generally lie perfectly still throughout the exam.

A Neuroradiologist experienced in MRI, will analyze the brain images and send a signed report with an interpretation to the Principal Investigator, Dr. Nyquist. Dr. Nyquist is a neurologist who is a specialist in strokes. You will receive a letter about your results, including any major findings, like significant silent strokes, or any other finding that the neuroradiologist indicates is important. If you have any unusual findings, your results will be reviewed by a monitoring board consisting of a Johns Hopkins radiologist, and 2 other neurologists and recommendations will be made based on their review. With your permission, your results will also be sent to your own doctor. There is more information about sending results to your own doctor in the next section.

Incidental Findings

The MRI you are having as part of this research study will be reviewed by a qualified person just as it would be if you were having the MRI as part of your routine medical care.

There is a possibility that while reviewing your MRI we may see an abnormality that we did not expect to see in this study. 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, someone may go to your home.

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 doctor or we will refer you to an appropriate doctor 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.

4. What are the risks or discomforts of the study?

MAGNETIC RESONANCE IMAGING (MRI)

The effects of magnetic fields in an MRI scanner have been extensively studied, and the risks with an MRI exam are low, particularly if you qualify for the testing based upon the screening questions. You may, however, be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the procedure. You will be asked to wear ear plugs or earphones while in the magnet. You may not participate in this study if you have a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices such as braces on your teeth. It is important for you to advise the MRI staff if you have had brain surgery for a cerebral aneurysm, implanted medical or metallic devices, shrapnel, or other metal, such as metal in your eye. The Orbital X-ray is associated with a small dose of radiation, less than .01 REM, and is thought to have no impact on your health.

It is possible that you may have unanticipated findings on your scan. These may include those that require no follow-up or referral (minimal sinus disease for example), or that may require referral for a follow-up scan or specialist (a mass that is uncommon or larger than normally seen that may indicate a tumor). Incidental findings that require referral occur in about 1-2% of people.

EXERCISE STRESS TEST WITH TECHNETIUM-99m

The risks of the screening are low. The exercise test can fairly frequently produce minor problems such as pain in the muscles or joints, anxiety, dizziness or loss of balance, or heart rhythm disturbances. These occasionally may result in the test being stopped. Major problems such as heart attack, stroke, or death occur in 1 in 10,000 people with symptoms of heart disease and less often in people who are apparently healthy. Your test will be supervised by a licensed health professional and your electrocardiogram will be watched carefully throughout the test to maximize your safety.

A radioactive tracer, Technetium-99m sestamibi will be injected at rest before the treadmill scan, and then again at a higher dose during the treadmill test. The main risk associated with technetium-99m sestamibi is from radiation exposure (see below). Other associated side-effects to this drug are extremely rare (<1%), including been few reports of mild to severe allergic reaction, headache, upset stomach. Pregnant women and any woman who may be pregnant at the time of the visit will not be tested. Women should have experienced menopause or be practicing effective birth control, be within 10 days of their last menstrual period, and have a negative pregnancy test.

RADIATION

This research study includes exposure to radiation from x-rays or gamma rays. This radiation exposure is for research purposes only and is not part of your medical care. X-rays and gamma rays from natural or medical sources can damage the genetic material (DNA) in your cells. At low doses, the body is usually able to repair the damage.

The radiation exposure that you will get in this research study is 1.2 rem for the Sestambi scan (a rem is a unit of absorbed radiation). Should you undergo the CT scan you will have an additional radiation exposure of 1 rem for a total of 2.2 rem. This is more than the 0.3 rem that the average person in the United States gets each year from natural sources like the sun, outer space, air, food and soil. It is less than the 5 rems of radiation that is allowed each year for people who are exposed to radiation in their jobs.

The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other tests outside of this study that are a part of your medical care. If you have questions about the total amount of radiation you will be receiving, you should ask your doctor.

SHARING THIS INFORMATION WITH YOUR DOCTOR:
You should be aware that we may discover some new things about your health that may affect your subsequent care and that sharing the information with your doctor may result in better care for you. You should also be aware that sometimes new information about the presence of a finding on your MRI or exercise test may also influence your insurance eligibility and other factors based on your health. Once any information is sent to your doctor, it is then part of your record and can be seen by others who MIGHT request your medical records from your doctor. In all cases, we will send results to you and let you know if there are problems that should be followed up by your doctor. Thus, if you would prefer that we not send informaiton to your doctor, please check the box below that relates to this.

☐ Yes, I want to have results sent to my doctor.

☐ No, I do not want results sent to my doctor.

5. Are there benefits to being in the study?
There is no direct benefit to you from taking part in this study. If you take part in this study, you may help others in the future. The information may help us to understand what causes strokes and disease in blood vessels in people with a family history of heart disease or stroke.

6. What are your options if you do not want to be in the study?
You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

7. Will it cost you anything to be in this study?
No.

8. Will you be paid if you join this study?
If you participate in this study you will be reimbursed $100 for travel and parking.

9. Can you leave the study early?
- You can agree to be in the study now and change your mind later.
- If you wish to stop the testing at any time, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care or affect your continued participation in The Johns Hopkins Sibling and Family Heart Study or GeneSTAR.

10. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it already has if the information is needed for this study or any follow-up activities**.**

11. How will your privacy be protected?

Johns Hopkins has rules to protect information about you. Federal and state laws also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

Generally, only people on the research team will know that you are in the research study and will see your information. However, there are a few exceptions that are listed later in this section of the consent form.

The people working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may collect other information including your name, address, date of birth, and other details.

The research team will need to see your information. Sometimes other people at Johns Hopkins may see or give out your information. These include people who review the research studies, their staff, lawyers, or other Johns Hopkins staff.

People outside of Johns Hopkins may need to see your information for this study. Examples include government groups (such as the Food and Drug Administration), safety monitors, other hospitals in the study and companies that sponsor the study.

We cannot do this study without your permission to use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Hopkins who receive your information may not be covered by this promise. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee this.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by contacting the Principal Investigator of this study. The Principal Investigator can be reached by phone at 410 955 2611 or by sending a letter to:

Paul Nyquist, Associate professor of Neurology, Anesthesia/Critical Care Medicine, Neurosurgery, and Internal Medicine, Meyer 8-140, 600 N Wolfe St, Baltimore MD, 21287, phone **410 955 2611 fax 410614 7903**

You also may choose the option of contacting the Johns Hopkins Privacy Officer. The Johns Hopkins Privacy Officer can be reached by phone at 410-735-6509 or by sending a letter to**:**

Johns Hopkins Privacy Officer
5801 Smith Avenue
McAuley Hall, Suite 310
Baltimore, MD 21209
Fax: 410 735-6521

If you send a letter, please be sure to include the study number and your contact information.

If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

12. Will the study require any of your other health care providers to share your health Information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers.

We will ask these other health care providers to give us ANY information about your health status or your health care.

13. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

- If you have health insurance: The costs for any treatment or hospital care you receive as the result of a study-related injury will be billed to your health insurer. Any costs that are not paid for by your health insurer will be billed to you.

- If you do not have health insurance: You will be billed for the costs of any treatment or hospital care you receive as the result of a study-related injury.

14. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- People from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

b. What do you do if you have questions about the study?
Call the principal investigator, **Dr. Paul Nyquist at (410) 955 2611.** If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?
Call **Dr. Paul Nyquist at 410 955 2611** if you have an urgent medical problem related to your taking part in this study.

Call the principal investigator of this study, Dr. Paul Nyquist, at **410 955 2611**, if you think you are injured or ill because of this study.

d. What happens to Data and Blood that are collected in the study?
Scientists at Johns Hopkins work to find the causes and cures of disease. The data and blood collected from you during this study are important to both this study and to future research.

If you join this study:

- You will not own the data given by you to the investigators for this research.
- Both Johns Hopkins and any sponsor of this research may study your data and the blood collected from you.
- If data or blood are in a form that identifies you, Johns Hopkins may use them for future research only with your consent or IRB approval.
- You will not own any product or idea created by the researchers working on this study.
- You will not receive any financial benefit from the creation, use or sale of such a product or idea.

e. What are the Organizations that are part of Johns Hopkins?
Johns Hopkins includes the following:

- The Johns Hopkins University
- The Johns Hopkins Hospital
- Johns Hopkins Bayview Medical Center
- Howard County General Hospital
- Johns Hopkins Community Physicians.
- Suburban Hospital
- Sibley Memorial Hospital

Approved October 27, 2011

ADDITIONAL STUDY USING A HEART SCAN

There is 2nd related research study available on the same day with the same team. The purpose of the second study is to find out more about silent coronary artery disease in people with a family history of coronary heart disease at a young age. A scan of your coronary arteries involves a dye with x-ray pictures of your heart. This scan can be taken from the outside of your body. The scans assist in identifying how much disease people have in their coronary arteries. The study may provide more information to help identify silent coronary heart disease.

It is not necessary for you to participate in this second study. If you do, we will explain this to you in more detail and ask you to consider that study using another consent form. The 2nd study will be done today following the silent stroke study if you agree.

If you agree after having the 2nd study described to you, you will sign another consent form for the 2nd study. Please indicate below whether you would consider joining the second study. This does not mean you agree to the 2nd study, but it gives us your permission to discuss it with you.

If you are willing to discuss and consider the second study with us, we will review that with you fully prior to your participation. Please indicate your preference for considering this by placing your initials in the appropriate box below.

☐ Yes, I am willing to consider the second study and will be asked to sign a different consent for it. I understand that I do not have to participate in the second coronary heart study if I prefer not to. It will not influence my participation in the silent stroke study.

☐ No, I would prefer not to consider the second study.

Approved October 27, 2011

15. What does your signature on this consent form mean?

Your signature on this form means that:

- you understand the information given to you in this form
- you accept the provisions in the form
- you agree to join the study

You will not give up any legal rights by signing this consent form.

_____

Signature of Participant Date/Time

_____

Signature of Person Obtaining Consent Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; AND, IF APPROPRIATE A COPY OF THE CONSENT FORM MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD.

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED FOR CONSENTING RESEARCH PARTICIPANTS. IF THIS CONSENT FORM DOES NOT HAVE A JOHNS HOPKINS MEDICINE LOGO, DO NOT USE IT TO CONSENT RESEARCH PARTICIPANTS.