

**UNIVERSITY OF PENNSYLVANIA
RESEARCH SUBJECT
COMBINED INFORMED CONSENT FORM AND HIPAA AUTHORIZATION**

Protocol Title: Pilot cohort study of Rb-82 Myocardial PET Imaging to Evaluate Coronary Microvascular Dysfunction in Men with Prostate Cancer Receiving Androgen-Deprivation Therapy

Funding Source: American Cancer Society Institutional Research Grant

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Emergency Contact: 24 Hour Emergency – Call 215-662-4000
Ask for Oncologist On-Call

Why am I being asked to volunteer?

You are being asked to participate in this research study because your physician has recommended androgen-deprivation therapy (ADT) along with radiation therapy for the treatment of prostate cancer. Your participation is voluntary, which means you can choose whether or not you want to participate. If you choose not to participate, your clinical care will not be affected. Before agreeing to participate in this research study, it is important that you read the following explanation of the proposed procedures and how long you will be in the study. This document describes the purpose, procedures, benefits, risks, discomforts and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time.

Please take time to read the following information carefully. You may wish to discuss it with your family, friends, and your personal doctor (i.e., your family doctor or primary care doctor). If you have any questions, you may ask your study doctor and/or the research team for more information. Take time to decide whether or not you wish to take part. If you decide to participate, you will be asked to sign this form. If you decide to participate, you can change your mind at any time and withdraw from the study without giving a reason.

What is the purpose of this research study? What does this study involve?

This study is being done because we are trying to develop better methods for detecting and managing cardiovascular risk when men receive androgen-deprivation therapy (ADT) for the treatment of prostate cancer. The main purpose of this study is to determine the feasibility and usefulness of performing heart (myocardial) positron emission tomography/computed tomography (PET/CT) imaging stress tests in men with prostate cancer who are planned for treatment with ADT. Heart PET/CT imaging stress tests are frequently used in the general population to assess a patient's cardiac risk by determining if there are abnormalities in blood flow to the heart muscle. However, heart PET/CT imaging is not routinely performed in men with prostate cancer.

This present research study will evaluate the use of heart PET/CT imaging stress tests specifically in men with prostate cancer who are planned for treatment with ADT. This study will involve undergoing two heart PET/CT imaging tests (one test at the beginning of your ADT, and one test after 6 months of ADT). In this study, we will test whether there are changes in heart PET/CT imaging over the course of your prostate cancer treatment. We hope to use the results of this research to improve the detection and prevention of cardiac injury due to ADT in the future.

About 20 people will be enrolled in this study.

Who is sponsoring this study?

Vivek Narayan, MD the Principal Investigator, is also the sponsor. An American Cancer Society Institutional Research Grant will cover some of the research costs, such as the collection of medical information associated with the conduct of the study.

How long will I be in the study?

Your active participation in this study will be for approximately 7 months. In addition, your medical records will be reviewed for up to 3 years after you initiate treatment with ADT.

During this time, you will continue to receive your usual medical care as determined by your oncology providers.

What am I being asked to do?

If you meet all of the criteria for being in the study, you will be registered to participate.

Screening Procedures:

You will need to have the following exams or tests performed to find out if you can be in the study. Some of these exams or tests are part of routine cancer care, and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor, and this will be discussed with you.

These tests/exams will be performed during the screening visit. Before these tests/exams are performed, you will first be asked to sign this consent form.

- Review of your medical history, including any other medical problems you may have, any medications that you are taking, and your prior use of cigarette/tobacco products.
 - You should let your study doctor know about any medications you have taken recently or are currently taking. This includes prescription and over-the-counter drugs, illegal drugs, vitamins, and health food supplements. You should also let your doctor know about any changes in your medication throughout your participation in this study.
- Review of your vital signs (including heart rate, blood pressure, height and weight).
- Blood tests – about 2 tablespoons of blood will be drawn to check blood cholesterol levels (lipid panel test).
 - This would not typically be done as a part of your standard of care treatment.

Study Tests/Procedures

The study visits will coincide with regularly scheduled clinic visits with your prostate cancer doctor. You will be asked to complete the following tests/exams during the course of this study at the time points noted below (Study Calendar).

A heart PET/CT imaging test will be performed at Study Visit 1 and Study Visit 2. Each heart PET/CT test will be performed within 3 weeks of your routine scheduled clinical visit and treatment with your prostate cancer doctor. While this test is frequently performed as a medical test to evaluate cardiac risk, it is not routinely performed specifically in men with prostate cancer without a current cardiac medical issue. The

purpose of this test is to determine if abnormalities in blood flow to the heart muscle can be detected by nuclear imaging with a tracer labeled with a radioactive particle (called rubidium (Rb) 82) after the IV administration of dipyridamole, a drug that increases the work of the heart similar to exercise. As this is a clinical test that is performed in routine cardiac evaluations (outside of typical prostate cancer medical care), you will sign a separate clinical consent form prior to undergoing each heart PET/CT imaging stress test.

Shortly after your arrival for the heart PET/CT imaging stress test and consent has been obtained, you will be given a dose of the radiolabelled tracer through a small IV catheter placed in a vein in your arm. After approximately an hour in the waiting room, which allows time for the isotope to circulate, your heart will be imaged while you are lying down for 15 minutes. These are the resting images. After that, you will be taken into a stress room and electrodes will be applied for the stress portion of the test. dipyridamole will then be given through your IV line for approximately 4-5 minutes. The infusion will be stopped sooner if you become distressed in any way or if the monitor reveals the development of abnormalities, which the physician considers significant. In addition, you may ask to have the test stopped at any time. During the dipyridamole infusion, your heart will be continuously monitored with an EKG (electrocardiogram) and your blood pressure will be monitored at periodic intervals. Two minutes after the dipyridamole infusion, the radiopharmaceutical isotope will be injected again through your IV line. An hour after the stress portion of the test has been completed, additional images of your heart will be taken for 15 minutes. These are the stress images.

Each visit for the heart PET/CT test will take approximately 90 minutes to complete.

As heart PET/CT imaging is a standard clinical test, you will receive the results of the heart PET/CT imaging stress test from your physician. If there are abnormalities noted on the heart PET/CT imaging stress test, you will have the option to be referred to a cardiologist (heart doctor) for clinical consultation, discussion of the results, and further evaluation and counseling.

Visit Number:	1	2
Timing:	Beginning of ADT	After 6 months of ADT
Vital signs and weight		X
Waist circumference measurement	X	X
Review current medications		X
Blood sample for blood cholesterol level testing (lipid panel) ¹		X
Blood sample for blood sugar level testing (Hgb A1c) ¹	X	X
Clinical heart PET/CT stress imaging ^{1,2}	X	X
¹ This would not typically be done as a part of your standard of care treatment.		
² A separate clinical consent will be obtained in the Division of Cardiovascular Medicine prior to each clinical heart PET/CT imaging test that is obtained as part of this study.		

Follow-up Procedures:

After you complete your study participation, we would like to continue to follow you to see how you are doing. This study follow-up will occur through periodic review of your medical chart in the Electronic Health Record. Information regarding your health status, including any cardiovascular disease events or medications, will also be collected. This will allow us to understand how the research findings might be related to your cardiovascular health in the future. Finally, we are also requesting your permission to re-contact you in the future for new studies or questions that may develop as we perform this research.

What are the possible risks or discomforts?

While on the study, you are at risk for the following side effects. Some of these side effects may be potentially serious or life-threatening, and may include death. You should discuss these with the study

doctor. There also may be other side effects that are not known and other very rare side effects that are known but not included in this list.

Risks of Blood Draws

Blood samples will be taken at screening and both of the study visits. The amount of blood to be taken by these blood draws is very small (about 2 tablespoons at each visit), and may be associated with discomfort and/or bruising at the site where the needle is inserted; and less commonly, fainting, the formation of a small blood clot or swelling of the vein and surrounding tissue, bleeding, and infection.

Risks of PET/CT Tests

This study involves the use of two planned heart PET/CT imaging stress test, as described above. There are no known side effects associated with the radiopharmaceutical isotope. There are some potential risks associated with the dipyridamole infusion. These risks include inflammation of the vein (phlebitis), infection, a local abscess, bleeding, the development of a blood clot, episodes of dizziness, fainting, chest discomfort, or leg cramps. There is a small risk of stroke, an air bubble (air embolism) in your vein, heart attack, or sudden death. There is a slight chance that the dipyridamole infusion will cause a minor heart beat irregularity. If this irregularity results in symptoms the test will be stopped. Other potential side effects from the dipyridamole infusion include but are not limited to chest pain, shortness of breath, low blood pressure, nausea, lightheadedness, headache, tremors, palpitations, anxiety, and chills. Most of the side effects of dipyridamole promptly resolve when the infusion is stopped. If necessary, medications to reverse the side effects of the dipyridamole can be given.

Since this is a radiological test, this research study involves exposure to radiation from the heart PET/CT imaging stress test. Therefore, you will receive a radiation dose. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is very likely that you will see no effects at all.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. If we discover new information about the study that could affect your decision to stay in the study, you will be notified in a timely manner. You will be able to ask questions about this new information and can discuss it with your family, friends, or doctor.

What are the possible benefits of the study?

This study may result in the discovery of better ways to diagnose, predict, and manage cardiovascular risk for prostate cancer patients on androgen-deprivation therapy.

What other choices do I have if I do not participate?

Your participation in this study is entirely voluntary. If you choose not to participate in this study, you would proceed with normal clinical care as discussed with your doctor. Talk to your doctor about your choices before you decide if you will take part in this study.

Will I be paid for being in this study?

You will not be paid for taking part in this study. However, your hospital parking lot fees will be reimbursed during visits for the 2 heart PET/CT stress imaging tests.

Will I have to pay for anything?

You and/or your insurance provider will be responsible for the costs of any standard tests, exams or procedures that would be done for your routine clinical care (i.e. done even if you were not in this study).. Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your

type of insurance. There will be no charge to you for those laboratory tests and other procedures that are being done only for the purposes of this research study (the blood draws and the heart PET/CT stress imaging tests).

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Website at: <http://cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Website.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured or hurt during the study?

If you have a medical emergency during your participation on this study, you should go to the nearest emergency room. You should contact the Principal Investigator or Emergency contact listed on page one of this form. You may also contact your own doctor, or seek treatment outside of the University of Pennsylvania. Be sure to tell the doctor or his/her staff that you are in a research study being conducted at the University of Pennsylvania. Ask them to call the telephone numbers on the first page of this consent form for further instructions or information about your care.

The University of Pennsylvania will offer you the care needed to treat side effects and/or injuries that occur while you are taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury.

Financial compensation for such things as traveling, lost wages, disability or discomfort due to injury is not routinely available.

You will not lose any of your legal rights when you sign this form.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected.

You may stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first. You can also choose to leave the study at any time without giving a reason. Leaving the study will not affect your future medical care.

The doctor may stop you from taking part in this study at any time if he/she believes that it is in your best interest, if you do not follow the study rules, or if the study is stopped. If new information becomes available that might affect your choice to stay in the study, your study doctor will notify you as soon as possible.

This study may also be stopped at any time without your consent because:

- The Principal Investigator feels that it is in your best interest to discontinue the study. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions
- The Principal Investigator has decided to stop the study due to new information regarding side effects.
- For any other reason that is not known at this time

If you are removed from the research study, your study doctor will explain to you why you were removed. The study doctor and study team will help arrange for your continued care.

Who can see or use my information? How will my personal information be protected?

If you decide to participate in this study, the study doctor and staff will collect medical and personal information about you as part of completing the study. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. Please refer to the information below which explains more specifically how your personal information will be protected. If you do not want to allow these uses, you should not participate in this study. Information identifying you will be kept confidential as described below.

What personal health information is collected and used in this study, and might also be disclosed?

The following personal health information will be collected and used for the purposes of this study.

- Name, address, telephone number, gender, date of birth
- The history and diagnosis of your disease
- Specific information about the therapy you received, including previous treatment(s) you may have had
- Information about other medical conditions that may affect your care
- Medical data including laboratory test results, PET/CT scan results, pathology results, etc
- Information on side effects (adverse events) you may experience, and how these were treated
- Long-term information about your general health status and the status of your disease. This may include information from other health care providers.
- Data that may be related to tissue samples that may be collected from you
- Numbers or codes that will identify you, such as your medical record number
- Information related to study visits and other tests/procedures performed while you are participating on this study.

While collected as part of this study by your study doctor and study team, identifying information (including your name, address, telephone number, medical record number, or any number/codes that will directly identify you) will be kept as confidential as possible and will not be routinely disclosed outside of the University of Pennsylvania.

You will be assigned a unique subject registration number upon enrollment. This number and your initials will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the University of Pennsylvania study team will have access to this code. However, some of the study data (e.g. date of birth) could be used in combination with other information, in order to identify you. If you have questions about the specific information that will be released, you should ask your study doctor.

Why is my personal health information being used?

Your personal contact information is important for the research team to contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study, and will be used to conduct and oversee this research study, and to help guide your medical care.

Which personnel may use or disclose my personal health information?

The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team

- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide care as part of this study or as part of your routine care, to manage accounting or billing matters, etc.). This includes members of the Institutional Review Board (IRB), an Ethics Committee at the University of Pennsylvania who are responsible for reviewing and overseeing research studies to ensure that they are safe and being well managed.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who, outside of UPHS and the School of Medicine, might receive my personal health information?

As part of the study, the Principal Investigator, the study team and others listed above, may disclose your study-related records, including the results of the research study tests and procedures, to those listed below. This study data may be processed and transmitted using secure computer systems. In all disclosures outside of the University of Pennsylvania Health System and School of Medicine, you will not be identified by name, medical record number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. In records and information disclosed outside of the University of Pennsylvania Health System and School of Medicine, you will be assigned a unique code number.

Your original medical records also may be reviewed by the Institutional Review Board overseeing this study, and any of the regulatory or safety oversight organizations outlined below. They may review these records for the purpose of checking data collected for the study, to make sure the study is being done properly, and to analyze the results of the study.

Individuals or organizations responsible for administering the study:

- Vivek Narayan, MD (the sponsor of this study) and his study team.

Regulatory and safety oversight organizations

- Regulatory agencies and/or their designated representatives (such as the Office of Human Research Protections), including international agencies
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law

Once your personal health information is disclosed to others outside of UPHS or the School of Medicine, it may no longer be covered by United States federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may UPHS and the School of Medicine be able to use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. If you sign this form, we will collect your health information until the end of the research study. We may collect some information from your medical records even after you finish taking part in this study or after your death. We will keep all of the information forever in case we need to look at it again. We will protect this information and keep it confidential.

Your information may be held in a research database. However, UPHS and the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so

- The University of Pennsylvania's Institutional Review Board grants permission after ensuring that appropriate privacy safeguards are in place
- As permitted by law

The data from this study may be published or used for teaching purposes, however you will not be personally identified in any publication. Your identity will remain confidential unless disclosure is required by law.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

Can I change my mind?

You have the right to withdraw your permission for the use of your personal health information, but if you do so, you must stop taking part in this study. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study and no new information will be collected. However, even if you do withdraw your permission to use the data about you, we are required by national regulatory authorities to record anything that relates to the safety of the investigational procedure under study.

Will I be able to access my research records?

You have the right to see and get a copy of your medical records kept by the University of Pennsylvania. However, you will not be able to review or receive some of your records related to the study until after the entire study has been completed. When the study is over, you may write to the study doctor to ask to see or copy all of your medical information that was collected during the study. You also have the right to say how your medical information may be used, and to have any incorrect data about yourself updated or corrected.

By signing this document you are permitting the UPHS and the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

What is an electronic medical record and/or a clinical trial management system?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

A clinical trial management system (CTMS) is used to register your information as a participant in a study and to allow for your research data to be entered/stored for the purposes of data analysis and any other required activity for the purpose of the conduct of the research.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, information related to your participation in the research (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS. Information related to your participation in clinical research will also be contained in the CTMS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance

you have). Information related to your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR or in the CTMS, your information may be accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc.).

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study you should speak with the Principal Investigator listed on page one of this form. If you have any questions about your rights as a research subject, you may contact the Office of Regulatory Affairs at the University of Pennsylvania with any questions, concerns or complaints by calling (215) 898-2614.

Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). You may also visit the NCI website at <http://cancer.gov/>. For NCI's clinical trials information, go to <http://cancer.gov/clinicaltrials/>. For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo>.

Making Your Decision

Please circle "yes" or "no" below and initial next to your choice:

Someone may contact me in the future to participate in other research studies:

Yes

No

Initials: _____

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, the study has been explained to you, your questions have been answered, you have had time to make your decision, and you have decided to volunteer to participate. You have been given the names of study staff that you can contact if you need assistance or if you have any additional questions or concerns. You agree to follow all of the instructions of your study doctor to the best of your ability, and report any changes in your health that may occur during the study.

Your signature also means that you are permitting the University of Pennsylvania Health System and the School of Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania Health System and the School of Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

You agree that your primary care physician can be informed about your participation in this clinical trial.

A copy of this signed and dated consent form will be given to you.

Name of Subject (Print)

Signature of Subject

Date

Name of Person Obtaining
Authorization (Print)

Signature of Person Obtaining
Authorization

Date