^{68}Ga-RM2 PET/MRI in the Evaluation of Patients with Biochemical Recurrence of Prostate Cancer and Non-Contributory CT Scans

Are you participating in any other research studies? _____ Yes _____No

PURPOSE OF RESEARCH

You were selected as a possible subject in this study because you have been diagnosed with prostate cancer. The purpose of this research study is to see if your tumor can be identified using a special procedure called a positron emission tomography (PET) scan. PET/MRI is used to describe information regarding the function, as well as location and size of a tumor. You will first have a localizer MRI, followed by an injection with a radioactive drug called ^{68}Ga-RM2 that binds to tumor cells that have specific receptors and then have a PET scan. We believe this special PET/MRI scan will be able to see smaller tumors than the standard of care CT or MRI scan. ^{68}Ga-RM2 is considered investigational in the US, which means that it has not been approved by the US Food and Drug Administration (FDA).

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

If you decide to terminate your participation in this study, you should notify the research coordinators at 650-725-4711.

This research study is looking for people diagnosed with prostate cancer that are suspected to have recurrent disease. Stanford University expects to enroll 125 research study participants over 5 years.

DURATION OF STUDY INVOLVEMENT

If you agree to take part in this study, your involvement will include 1 visit (up to 3 hours).

You may have an additional visit for a second ^{68}Ga-RM2 PET/MRI scan. This second scan will happen only if you receive treatment for your tumor, such as chemotherapy or biological therapy. This second ^{68}Ga-RM2 PET/MRI scan is to determine how well your tumor responded.

Each PET/MRI scan will require that you spend up to 3 hours in the Nuclear Medicine and Molecular Imaging Clinic.

PROCEDURES

If you choose to participate, Dr Andrei Iagaru and his research study staff will require the following:

1. Participant will be asked to drink 1 to 2 glasses of water before arrival at the clinic

2. Participants will be weighed and vital signs (heart rate, blood pressure, respiratory rate, pulse oxymetry) will be recorded
3. Participant will be injected IV (intravenously) with 140 MBq of ^{68}Ga-RM2
4. Participant will void immediately prior to the scan
5. Approximately 45 minutes after the ^{68}Ga-RM2 (radiopharmaceutical) is administered through an IV, data acquisition will begin in the pelvic region and move toward the head. First, localizer MRI scans will be performed to define the table positions. After correct positioning of the spatial acquisition windows is ensured, the combined PET/MRI acquisition will be initiated with 3 to 5 table positions at a 4-min acquisition time per table position.
6. Participant will be given a copy of the consent form s/he signed and will be dismissed.
7. Vital signs (heart rate, blood pressure, respiratory rate, pulse oxymetry) will be recorded again at the completion of the study.
8. Participant will be contacted at 24 to 48 hours following the scan in order to capture potential late occurring Adverse Events.

The ^{68}Ga-RM2 PET/MRI may be repeated at the completion of treatment to evaluate response to therapy, if requested by the treating physician at the standard of care, 12 week follow-up time.

You will be asked to lie very still during the scan because movement can interfere with the results. You will be asked to breath normally during the scan. During the scan, you might hear a humming noise but you will not feel anything unusual. You may feel the table move while images are being taken at certain locations on your body. Our technologist will monitor you during the exam.

The MRI scanning procedure is very much like an X-ray CT scan. You may be given an IV contrast injection to enhance the results of your study. If you have had a previous reaction to Gadolinium-based contrast agents or a history of severe allergies, please notify the operator/investigator. If you have kidney problems, please tell the operator. You will be asked to lie on a long narrow couch for about 45 to 60 minutes while the machine gathers data.

During this time you will not be exposed to X-rays, but rather a strong magnetic field and radiofrequency magnetic fields. You will not feel either. You will, however, hear repetitive tapping noises that arise from the MR scanner. We will provide earplugs or headphones that you will be required to wear. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

Your test results will be maintained as part of your Stanford medical record. If you do not have a Stanford medical record, one will be created during this research study.

If you are a man participating in this study and your partner is able to become pregnant, you and your partner must use adequate contraception while you are participating in the study. Your doctor will discuss with you what methods of birth control are considered adequate. You should inform your study doctor if your partner becomes pregnant.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the Protocol Director or research staff if you believe you might be pregnant or gotten your partner pregnant.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

While participating in this research study, you should not take part in any other research project without approval from the Protocol Directors of each study. This is to protect you from possible injury.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If you withdraw from the study, please contact the study staff to let them know of your decision. You will receive a follow up phone call to ask if you had any adverse effects from your participation in the study.

If you decided to withdraw from the study after the tracer is injected and before the scan is done we would like to observe you for any adverse reaction for up to an hour. Once the IV's have been removed it will be safe for you to leave.

The Protocol Director may also withdraw you from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff
- The Protocol Director decides that continuing your participation could be harmful to you
- Pregnancy
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

PET/MRI FOR FUTURE RESEARCH

We would like to save the images and data from your PET/MRI scans for future research projects.

You have the right to refuse to allow us the use of your data for future research. You may withdraw from this study at any time. If you decide later to withdraw from the study, the PHI obtained up until that withdrawal might be used in the study.

Any images that are used in research may result in new products, tests, or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, participants in the study do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests, or discoveries.

Do you agree to allow us to store your data for future research? ☐ Yes ☐ No

Please initial _____

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions. Risks, discomfort and inconveniences include:

- Time involved for the visits to the hospital
- Bruising at the venipuncture/IV site for the radiopharmaceutical injection

PET related risks:

Reasonably foreseeable risks include:

This research study involves exposure to radiation from the PET/MR radioactive compound ^{68}Ga-RM2. This radiation exposure is not necessary for your medical care and is for research purposes only. The additional amount of radiation exposure is about 4.76 mSv, which is approximately equal to 10% of the limit that radiation workers (for example, a hospital x-ray technician) are allowed to receive in one year. This amount of radiation involves minimal risk and is necessary to obtain the research information desired.

- Physical risks – from study medications and procedures (eg, venipuncture, exposure to radiation.
- This procedure may involve risks to you that are currently unforeseeable.

MRI (MAGNETIC RESONANCE IMAGING)

This MRI machine uses a strong magnet and radiofrequency magnetic fields to make images of the body interior.

RISKS of MRI:

Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices.

If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately.

As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed. In addition, watches and credit cards should also be removed as these could be damaged. You will be provided a way to secure these items.

If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator. You should also notify the operator/investigator if you have any tattoos on your body, including eyeliner and other permanent makeup. Tattoos could become warm and irritated during the scan and remain so for several days. If you would prefer not to participate in the MR scan due to the presence of tattoos on your body, please inform a research team member.

There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is expected and should not be painful.

If you have had a previous reaction to Gadolinium-based contrast agents, a history of severe allergies, or a history of kidney disease, please notify the operator/investigator.

Some of the hardware, imaging software and devices being used in your scan are not approved by the FDA, but are similar to counterparts that have been approved by the FDA. There is a small risk of heating from the cables associated with these devices. Please report any heating sensation immediately.

IF YOU FEEL DISCOMFORT AT ANY TIME, NOTIFY THE OPERATOR AND YOU CAN DISCONTINUE THE EXAM AT ANYTIME.

The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. The investigators for this project may not be trained to perform medical diagnosis. The investigators and Stanford are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. When this occurs, a physician will be consulted as to whether the findings merits further investigation, in which case the investigator will contact you and your primary care physician and inform you of the finding. The decision as to whether to proceed with further examination or treatment lies solely with you and your physician. The investigators, the consulting physician, and Stanford are not responsible for any examination or treatment that you undertake based on these findings. Because the images collected in this study

may not comprise a proper clinical MRI scan, these images will not be made available for diagnostic purposes.

Dizziness and nausea may occur if the head is moved rapidly within the bore of the magnet.

POTENTIAL BENEFITS

We don't know if you will benefit from being in this study. We may be able to see more cancer lesions compared to other scans. If you receive a second ^{68}Ga-RM2 PET/MRI scan after treatment, we may be able to determine how much response you had to the treatment. We hope that in the future others will benefit from this study because of knowledge gained in determining whether ^{68}Ga-RM2 PET/MRI scans are more sensitive than the current standard of care scans for detecting prostate cancer and measuring response to treatment. **We cannot and do not guarantee or promise that you will receive any benefits from this study.**

ALTERNATIVES

The alternative is to not participate in this study.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction.

If you decide not to participate, tell the Protocol Director. You will still receive care for your disease and will not lose any benefits to which you would otherwise be entitled.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

CONFIDENTIALITY

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law. However, there is always some risk that even de-identified information might be re-identified.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the safety and effectiveness of ^{68}Ga-RM2; the results may be provided to the Food and Drug Administration, as well as to Piramal Imaging and the Department of Defense.

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

USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

This study will attempt to correlate the results of standard of care scans with ^{68}Ga-RM2 PET/MRI scan, in order to determine the best approach for evaluation of extent of prostate cancer. Your health information related to this study, including but not limited to your medical history, lab results, and imaging results, may be used to correlate with the PET/MRI results. Your health information may be used in scientific publications, but your identity will not be disclosed.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (eg, necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to Dr Andrei Iagaru, 300 Pasteur Drive H2200, MC 5281, Stanford, CA 94305.

What Personal Information Will Be Used or Disclosed?

Your health information related to this study may be used or disclosed in connection with this research study, including, but not limited to, your name, medical record number, medical history, sex, age, diagnosis, results of sans and pathology review, physical examination, lab tests, and imaging tests such as x-rays, CT scans, MRI scans, bone scans, and ultrasounds studies.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- Dr Andrei Iagaru (the Protocol Director) and members of the research team including technicians and research coordinators
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary

Who May Receive / Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the US Department of Health and Human Services
- The Food and Drug Administration (FDA)
- Piramal Imaging
- The Department of Defense (DoD)

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your health information will expire December 31, 2070.

Will access to my medical record be limited during the study?

To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (eg, if included in your official medical record).

_____ _____
Signature of Participant Date & Time

_____
Print Name of Participant

_____ _____
Signature of Legally Authorized Representative (LAR) Date & Time
(eg, parent, guardian or conservator)

_____
Print Name of LAR

_____
LAR's Authority to Act for Participant
(eg, parent, guardian or conservator)

FINANCIAL CONSIDERATIONS

PAYMENT: You will be paid $250 for being in this research study after completion of PET MRI scan. Payments may only be made to US citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

COSTS: If you participate in this study, the study will pay for those services, supplies, procedures, and care associated with the study that are not a part of your routine medical care. However, there may be additional costs to you. These include basic expenses like transportation and the personal time it will take to come to the study visits. You and/or your health insurance must pay for services, supplies, procedures, and care that are required during this study for routine medical care. **You will also be responsible for any co-payments and/or deductibles as required by your insurance.** Participation in this study is not a substitute for health insurance.

Piramal Imaging and the US Department of Defense are providing financial support and/or material for this study.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

- Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this **research study**, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Dr Andrei Iagaru. You may contact him now or later at 650-725-4711.
- Injury Notification: If you feel you have been **hurt by being a part of this study**, please contact the Protocol Director, Dr Andrei Iagaru, at 650-725-4711.
- Alternate Contact: If you cannot reach the Protocol Director, please contact Dr Farshad Moradi, MD, at 650-736-1396.

- Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at 650-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.
- Appointment Contact: If you need to change your appointment, please contact Dr Andrei Iagaru and the research staff at 650-725-4711.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a human subject you have the following rights. These rights include but are not limited to the subject's right to:

- Be informed of the nature and purpose of the experiment;
- Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- Be given a description of any attendant discomforts and risks reasonably to be expected;
- Be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- Be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- Be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- Be given an opportunity to ask questions concerning the experiment or the procedures involved;
- Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- Be given a copy of the signed and dated consent form; and
- Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Adult Participant Date & Time

_____
Print Name of Adult Participant

_____ _____
Signature of Legally Authorized Representative (LAR) Date & Time
(e.g., parent, guardian or conservator)

_____
Print Name of LAR

_____
LAR's Authority to Act for Participant
(e.g., parent, guardian or conservator)

_____ _____
(If available) Signature of Other Parent or Guardian Date & Time

_____
Print Name of Other Parent or Guardian

_____
Authority to Act for Participant

_____ _____
Signature of Person Obtaining Consent Date & Time

_____
Print Name of Person Obtaining Consent

The following witness line is to be signed only if the consent is provided as a summary form and accompanied by a short form foreign language consent.

_____ _____

Signature of Witness Date&Time

_____

Print Name of Witness
(e.g., staff, translator/interpreter, family member)

- *Translated short form must be signed and dated by both the participant (or their LAR) AND the witness.*
- *The English consent form (referred to as the "Summary Form" in the regulations):*
  - *Must be signed by the witness AND the Person Obtaining Consent (POC).*
  - *The non-English speaking participant/LAR does not sign the English consent.*
  - *The non-English speaking participant/LAR should not sign the HIPAA participant line*
  - *If the participant or the LAR is non-English speaking, the Person Obtaining Consent (POC) must ensure that 1) the LAR's Description of Authority is completed and 2) that any questions or options presented by the consent form are documented and initialed by the POC on the Summary Form, per the participant's wishes, as they are understood during the consent process.*