ST VINCENT'S HOSPITAL
SYDNEY
A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

Participant Information Sheet/Consent Form

Title	Metastasis assessment with Gallium-68 PSMA and Nanoparticle Imaging Fusion International
Short Title	Magnifi Trial
Project Sponsor	The Garvan Institute of Medical Research
Principal Investigators	Prof Phillip Stricker and A/Prof Louise Emmett
Location	St Vincent's Hospital, Sydney
HREC Approval Ref No.	HREC/15/SVH/402

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you have prostate cancer and have been referred to prostate cancer surgery with lymph node dissection. The research project is to determine the value of "Combidex" Nanoparticle-Magnetic Resonance Lymphography (Nano MRL) and 68Ga-PSMA positron emission tomography (PET) for the detection of cancer in lymph nodes.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

In some cases of prostate cancer, the cancer cells can spread out of the prostate and into the lymph nodes. As part of the surgical procedure, the surgeon may decide whether or not to remove the lymph nodes at the same time that the prostate is removed. The lymph nodes are then sent for histopathological review where they are examined under a microscope to see whether they do contain cancer cells. This is considered as the current "gold" standard in determining whether the cancer cells have spread outside of the prostate.

There are two new imaging techniques that may improve the detection of cancer cells in the lymph nodes prior to the surgery. This would assist the surgeon in determining whether the lymph nodes need to be removed as well as which lymph nodes needs to be removed. The first is 68-Gallium Prostate Specific Membrane Antigen (68Ga-PSMA) PET scan. PSMA is a protein that is found on the surface of the prostate cells. When cancer develops, the level of PSMA increases and sites where the cancer is located can be detected when seen under a PET scan with the addition of 68-Gallium.Currently, we perform a 68Ga-PSMA PET scan in every patient diagnosed with prostate cancer before the surgeon will remove the pelvic lymph node as standard of care.

The second new technology is "Combidex" Nanoparticle-Magnetic Resonance Lymphography (Nano-MRL). Nano-MRL uses dextran coated small iron particles for the detection of metastatic lymph nodes, that can been seen with the use of Magnetic Resonance Imaging (MRI). Nano-MRL is an experimental treatment. This means that it is not an approved for detecting metastatic lymph nodes in Australia. The results obtained from Nano-MRL scans will not be used to influence clinical decision making processes, and will not be reported back to the treating surgeon until after the operative procedures are completed and the information has been analysed.

The aim of this study is to determine whether 68Ga-PSMA PET and Nano-MRL are able to detect cancer in the lymph nodes when compared to histopathological review. If one or both are able to do so, it will better assist the surgeon in deciding whether the removal of the lymph nodes is required and if so how many lymph nodes to remove. This would reduce unnecessary surgery if cancer cells are not found in the lymph nodes, reduce side effects associated with the surgery and consequently reduce the health care costs.

This research has been initiated by the study doctors, Prof Phillip Stricker and A/Prof Louise Emmett at St Vincent's Hospital, Sydney/The Garvan Institute of Medical Research and Prof Jelle Barentsz at Radboud University Nijmegen, the Netherlands. It is sponsored by the Garvan Institute of Medical Research through a grant from the Paul Ramsay Foundation.

3 What does participation in this research involve?

This consent form must be signed before any study assessment is performed.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

If you agree to participate in the research, the study will provide you with the 68Ga-PSMA PET and Nano-MRL free of charge. You will still need to pay for the cost of the surgery and other surgery related costs (standard care) and, you will not be paid to participate in the study. The 68Ga-PSMA PET scan will be part of your standard of care and will assist your doctor plan for your surgery. Nano-MRL is being trialled and is not part of the standard of care. It will be compared with the 68Ga-PSMA PET scan and histology findings following your surgery to evaluate it can better detect cancer in the lymph nodes.

68Ga-PSMA PET/CT Scan You will be referred to the St Vincent's Nuclear Medicine Department (Level 2, Xavier Building, St Vincent's Hospital) for a 68Ga-PSMA PET scan. This will involve a needle inserted into your arm and you will be injected with a small volume of 68Ga-PSMA. You will be placed under the PET scanner, and some pictures will be taken of your whole body about 45 minutes after injection. The scan will take 30 minutes.

The tracer (the substance that is used to detect the cancer cells in your body) has not had any significant side effects documented (you should have no symptoms). The test does involve a small dose of radiation which is similar to that of other PET scans used in the diagnosis of cancer (from a 68Ga-PSMA, you will receive less than half the radiation dose you would normally get from a routine CT scan of the chest, abdomen and pelvis). Your body excretes the 68Ga-PSMA very rapidly in the urine.

You will then be requested to make a return visit to the St Vincent's Nuclear Medicine Department for the "Combidex" Nano-MRL.

"Combidex" Nano-MRL

This visit will involve a catheter inserted into your arm and you will be infused with the imaging contrasting agent, ferumoxtran-10 (Combidex) over 30 minutes. You will be closely monitored at all times and will remain in hospital for at least one hour before being allowed to return home. Arrangements will then be made for you to attend Medscan Barangaroo two to three days following the infusion. At Medscan Barangaroo, you will undergo a magnetic resonance imaging (MRI). You will be asked to lie under a MRI scanner for approximately 60 to 75 minutes so that the imaging can take place. Arrangements will be made to send you home.

After you have undergone both 68Ga-PSMA PET and Nano-MRL scans, you will then undergo the radical prostatectomy and lymph node dissection as planned. The prostate and the lymph nodes will be sent to histopathology where they will be reviewed for cancer. The pathology report will be sent to your surgeon as well as the research team to compare with the results of the 68Ga-PSMA PET and Nano-MRL scans.

If the results from either or both of the 68Ga-PSMA PET and Nano-MRL scans show signs of cancer, while the histopathology did not, we may ask you to undergo the 68Ga-PSMA PET and Nano-MRL scans again. This is to see whether the cancer containing lymph nodes was removed during the surgery.

Your surgeon as part of your normal clinical management will arrange follow up visits with you to check on your well being following your surgery. These will occur approximately at 6 weeks, 3 months, 12 months and 24 months following your surgery.

This study will also look at your quality of life before and after you had surgery. We would like to collect information on how the removal of the prostate and the lymph nodes with the use of 68Ga-PSMA PET and Nano-MRL scans effects your physical, emotional and psychological outcomes. You will be asked to complete the Expanded Prostate Cancer Index Composite (EPIC) survey prior to your surgery, at 6 weeks, 3 months, 12 months and then yearly for a maximum of 5 years following your surgery. The information collected will also be included in the NSW Cancer Institute Prostate Clinical Registry (NSW PCCR). This registry has been designed to collect the data on men across NSW who have been diagnosed with prostate cancer.

4 Other relevant information about the research project

This study involves researchers from a number of organisations working in collaboration. St Vincent's Hospital Sydney and the St Vincent's Prostate Cancer Centre will be selecting participants for the project. The Garvan Institute of Medical Research will be managing the data and operations for the project. The Radboud University Nijmegen in the Netherlands will be providing the Combidex contrasting agent as well as teaching staff in Australia on how to administer it.

5 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with St Vincent's Hospital, Sydney, St Vincent's Prostate Cancer Centre, the Garvan Institute of Medical Research or Radboud University Nijmegen, the Netherlands.

6 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. Other options are available. Your doctor will discuss a range of other treatment options available to treat your cancer and symptoms, or you may choose not to have treatment.

7 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research. However, you will be provided with 68Ga-PSMA PET and Nano-MRL scans free of charge. The results obtained from this study have the potential to help the treatment of future patients undergoing prostate cancer surgery.

8 What are the possible risks and disadvantages of taking part?

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

Medical imaging may cause side effects. You may have none, some or all of the effects mentioned below, and they may be mild, moderate or severe. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

Risks of 68GAa PSMA PET/CT

Prostate specific membrane antigen (PSMA) concentrates in the body at sites of prostate cancer. In fact, it concentrates 1000 times higher in prostate cancer cells then in normal prostate cells. When it is bound to 68Ga, it becomes a radiochemical compound that can be followed through your body with a PET scanner, and we are able to identify sites of prostate cancer in the body from the images we take. There is no special preparation for the study.

Several preclinical and clinical studies have shown the safety of ^{68}Ga-PSMA. The whole body radiation dose is less than half that of a routine CT abdomen / pelvis, and is well below the radiation limit recommended by the United States Food and Drug Administration (FDA). The FDA is the peak government agency responsible for reviewing and regulating the use of prescription drugs, electromagnetic radiation emitting devices and other medical devices in the United States. Their decisions are well regarded worldwide. No adverse effects due to intravenous administration of ^{68}Ga-PSMA for imaging have been reported in the published literature. The level of risk from radiation exposure as a result of your participation in this study is likely to fall into the low risk category.

Risks of "Combidex" Nano-MRL

To date over 200 patients have undergone Combidex scanning at Radboud University Nijmegen, with only 2 patients experiencing any issues. Most of the issues occur at the time of the Combidex infusion and can relieved by stopping the infusion for several minutes. If you experience hypersensitivity, an allergic reaction, dizziness or light headiness at the time of the infusion, you must immediately inform the treating doctor who will stop the infusion. If you develop any other symptoms at the site of injection at a later stage, you must inform the treating doctor.

There has been only one reported death associated with the infusion of Combidex in more than 1000 different patients worldwide. This was due to the patient having a pre-existing heart condition and the infusion rate was too fast for this patient. Since that death, precautionary measures have been taken to screen patients who might be at risk if they undergo the procedure. Those who will be responsible for the administration of Combidex have been instructed on the correct infusion procedure and will ask you about any pre-existing conditions that you may have.

The effects of 68Ga-PSMA PET and Nano-MRL scans on the unborn child and on the newborn baby are not known. If your partner is considering falling pregnant within six months following the treatment, then you need to speak with the study doctor. If your partner does fall pregnant within the six months, you must tell the study doctor immediately. The study doctor may ask for information about the pregnancy and the birth of the baby. The study doctor may share this information with the sponsor, and the Human Research Ethics Committee.

9 What will happen to my results?

Your results will be entered onto a secure database together with other clinical and demographic information. Your information will be assigned to a unique study number and this study number will be used in place of any identifiable information.

You will also be contacted by the research team prior to your surgery and at 6 weeks, 3 months, 12 months and the yearly for a maximum of 5 years following your surgery as ask to complete the EPIC quality of life survey. This survey will collect information about how you are prior to and after your surgery. The information will also be entered onto a database using a unique study number in place of any identifiable information. Information from the Quality of Life survey will also be included in the NSW Cancer Institute Prostate Clinical Registry (NSW PCCR).

The New South Wales Prostate Cancer Clinical Registry (NSW PCCR)

The Cancer Institute New South Wales (CINSW) has established the NSW Prostate Cancer Clinical Registry (NSW PCCR) in partnership with the Agency for Clinical Innovation. The NSW PCCR is the NSW arm of the Prostate Cancer Outcomes Registry – Australia & New Zealand (PCOR-ANZ), an initiative funded by Movember to improve the health outcomes of men living with prostate cancer. The aim of the NSW PCCR is to improve the quality of care provided to men with prostate cancer. Information from the registry will be used to monitor care provided, including treatment, complications and both short and long term outcomes of care. Your contribution will help towards better understanding and managing prostate cancer disease and ensure men are receiving the best possible healthcare service both within the state and in comparison to the rest of the nation and New Zealand. The Registry has been approved by the NSW Population and Health Services Research Ethics Committee (NSWCI Ref: 2015/02/578).

The Registry uses the same EPIC questionnaire as this study and to avoid asking you to complete the questionnaire twice, we would like to transfer information provided in the study to the Registry. The information to be transferred include your name, age, address, clinical information related to condition and treatment and your responses to the EPIC questionnaire prior to your surgery, 12 months and 24 months following surgery. There will be no other requirement from you for participating in the Registry.

The information will be sent to the NSW PCCR electronically and will be password protected using secure file sharing system. The information collected will be combined with data collected from other men diagnosed with prostate cancer who are participating in the Registry. Data within the Registry will be identifiable. Identifiable data refers to your name, date of birth and address. This information is required to enable the Registry to collect data about your care from participating hospitals and clinicians and to enable accurate linkage to the NSW Cancer Registry and the PCOR-ANZ. It will be safeguarded by CINSW policies and procedures, state laws and guidelines governing privacy and confidentiality laws. Information will be stored securely, with access restricted only to Registry staff. Reports and publications arising from the Registry will only be based on grouped data and no personal information about you or any other individuals will be published.

If you wish not be involved in the NSW PCCR, you can elect to do so in the consent form. The information collection will only be used for the purposes of this study and will not be forwarded to the NSW PCCR.

10 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

11 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

12 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. Should you decide to withdraw, your relationship with the hospital and your treating doctor is not affected.

13 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The treatment being shown not to be effective
- The treatment being shown to work and not need further testing

14 What happens when the research project ends?

We will keep your information for an indefinite period of time as part of the requirements for conducting this type of research. We will be able to provide you with any publications arising from this research if you wish us to do so.

Part 2 How is the research project being conducted?

15 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. Your information will be identified with a unique study number.

Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the study team accessing health records if they are relevant to your participation in this research project.

Information about your participation in this research project may be recorded in your health records.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. Confidentiality will be maintained through the use of your unique study number.

Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

16 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

17 Who is organising and funding the research?

This research project is being conducted by Professor Phillip Stricker and A/Prof Louise Emmett and a number of co-investigators at St Vincent's Hospital, Sydney. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages). The study is being funded by the St Vincent's Prostate Cancer Centre, through donations made directly for prostate cancer research.

18 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of St Vincent's Hospital, Sydney (HREC Reference No: HREC/15/SVH/402).

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

19 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on 02 8382 2621 or any of the following people:

Clinical contact person

Name	A/Prof Louise Emmett
Position	Principal Co-Investigator
Telephone	02 8382 2621
Email	louise.emmett@svha.org.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Research Office Manager
Telephone	02 8382 2075
Email	SVHS.Research@svha.org.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC name	St Vincent's Hospital, Sydney, HREC
HREC Executive Officer	HREC Executive Officer
Telephone	02 8382 2075
Email	SVHS.Research@svha.org.au

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Consent Form

Title	Metastasis assessment with Gallium-68 PSMA and Nanoparticle Imaging Fusion International
Short Title	Magnifi Trial
Project Sponsor	The Garvan Institute of Medical Research
Principal Investigators	Prof Phillip Stricker and A/Prof Louise Emmett
Location	St Vincent's Hospital, Sydney
HREC Approval Ref No.	HREC/15/SVH/402

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to St Vincent's Hospital, Sydney concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I understand that my participation in this study will also include my participation in the NSW Prostate Clinical Cancer Registry. My participation will only involve the transfer of specified data collected as part of this study to the Registry and I will not be required to provide any further information.

I can elect not to have my information sent to the NSW PCCR by ticking this box ☐.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) _____

Signature _____ Date _____

Under certain circumstances (see Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 at 4.8.9*) a witness* to informed consent is required.*

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

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Form for Withdrawal of Participation

Title	Metastasis assessment with Gallium-68 PSMA and Nanoparticle Imaging Fusion International
Short Title	Magnifi Trial
Project Sponsor	The Garvan Institute of Medical Research
Principal Investigators	Prof Phillip Stricker and A/Prof Louise Emmett
Location	St Vincent's Hospital, Sydney
HREC Approval Ref No.	HREC/15/SVH/402

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with St Vincent's Hospital, Sydney.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.