The ROYAL MARSDEN
NHS Foundation Trust

[To be printed on hospital headed paper]

The PACE trial: Prostatectomy vs stereotactic radiotherapy

Dear Sir

We would like to invite you to take part in a research study. Before you decide whether to take part, it is important to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Take your time to decide whether or not you would like to take part, and please do ask us if there is anything that is not clear, or if you would like more information.

What is the purpose of the study?

You have been invited to join this trial because you have early (localised) prostate cancer. There are several options for treatment of prostate cancer, including surveillance (no active treatment) in some cases, brachytherapy, surgery and external radiotherapy. Your hospital doctor will discuss all options which are suitable for you.

The purpose of this research is to investigate whether there are differences between the quality of life of patients who receive surgery or radiotherapy (X-Ray treatment) using stereotactic body radiotherapy (SBRT). SBRT uses a radiotherapy machine which can accurately target the prostate. The type of surgical technique (also called prostatectomy) that you will undergo will be discussed with you depending on the standard practice in your hospital. We know that the side effects may be different, but we don't know to what extent. As part of this trial we will also collect data on how well the surgery or radiotherapy treated your prostate cancer.

Why have I been chosen?

You have been diagnosed with prostate cancer and a team of prostate cancer specialists feel that you would be suitable for both treatments in this study. This study is hoping to recruit approximately 234 men across the UK. You have been approached because your hospital doctor feels that you are suitable to take part.

What will happen to me if I agree to take part?

In this study we need to compare people who have SBRT with those people who have surgery. The best way to compare the treatments is to have similar groups of patients receiving either treatment. We can then be sure that if one group fares better than the other group, it is because of the treatment, and not because the patients in the groups are different from each other in some way. Everyone who agrees to take part in this research study will be allocated to one of two groups of patients. Half of the patients will receive SBRT and half of the patients will receive surgery. The only way to make sure that the groups of patients are as similar as

possible is to have your treatment decided upon by chance: a process called randomisation. This process ensures that the treatments are compared fully and fairly. If you agree to take part, your hospital doctor or nurse will contact the research centre. The centre will then record your details and tell your specialist your treatment, which will be selected by chance, meaning you will have an equal chance of having either of the treatments. Whichever group you are in, you will be treated with the best possible care and will be monitored closely.

The main aim of this study is to assess the Quality of Life of prostate cancer patients receiving surgery or radiotherapy. We will ask you to fill in a questionnaire before you are randomised, at weeks 2, 4, 8, 12 and months 6, 9 and 12 after the end of treatment and yearly after that until year 5. There are 12 questionnaires in total. There is more information about these questionnaires in Part 2 of the patient information sheet. If you are unable to complete the questionnaires, then unfortunately, you will not be able to take part in the trial.

What do I have to do before treatment?

Before starting your treatment all patients will have some checks to make sure that all options are suitable treatments for you. This will consist of a complete review of your medical history, a physical examination and some blood tests. We will also assess how advanced your prostate cancer is using a rectal examination or ultrasound scan or MRI scan. We will also ask you to fill in some detailed questionnaires about your current symptoms and your quality of life (further information regarding these questionnaires is given in Part 2 of this information sheet).

Patients receiving surgery

If you have surgery, you will have an assessment appointment (called "pre-assessment") to check that you are ready to go ahead with the operation and will have the chance to discuss any questions with your hospital doctor. Surgery will involve a general anaesthetic and a stay in hospital for a few days. You will have a tube put into your bladder (catheter) for a few days after the operation.

Patients receiving SBRT

The radiotherapy machine must be able to target the prostate, so 3 or 4 small markers are inserted into the prostate so that we can monitor its position during each radiotherapy treatment. These markers are either inserted during a procedure similar to the prostate biopsy you had (using a probe in the back passage to guide the placement of the markers) or in some hospitals they are put in via the skin in between the legs.

This procedure usually takes about 20 minutes and you can go home straight afterwards. Most patients experience some bleeding after the procedure, in the stools, urine or semen. There is also a small risk of infection. Because of this we may give you some antibiotic tablets to take before and after the procedure and also an antibiotic suppository just before the procedure. The procedure may be painful or uncomfortable for a day or so.

The markers stay in the prostate forever, and do not cause any problems in the long term.

Within 7-10 days after placement of the markers, you will have a CT scan of pelvis and you may have an MRI scan, both on the same day. The images obtained during the scans will be used to plan the radiotherapy and to make it specific for you.

An alternative to marker insertion for monitoring of prostate position, is to do a CT scan at each treatment session (cone beam CT). This allows the position of the prostate to be monitored without marker insertion. Some hospitals may choose to use this method (you will be informed of which method will be used by your hospital doctor).

What happens during SBRT?
SBRT consists of 5 treatment sessions spread over 1-2 weeks. Each treatment session lasts between 30 and 60 minutes. The radiotherapy procedure is completely painless. We will ask you to stay as still as possible on the treatment bed, and the machine will move around you without touching you.

What if I have surgery?
If you have surgery, you will be in hospital for a day or two and then will need a period of recuperation.

What do I have to do after treatment?
Whether you receive SBRT or surgery we will review you in clinic or by telephone at 2 weeks, 4 weeks, 8 weeks and 12 weeks after finishing treatment. After that, clinic appointments will be every 3 months for the first 2 years then 6 monthly until 5 years and then yearly until 10 years post treatment. This long follow-up is needed to be absolutely sure about the effectiveness and side effects of the treatment.

What are the side effects?
The surgery that patients will receive in this trial is just the same as surgery would be outside the trial. Risks and side effects of the treatment are therefore no different in and out of the trial setting and will be explained as part of the informed consent process. SBRT is not usually standard of care in the UK at the present time and as this is a relatively new treatment, there may be some side effects which are more or less common than usual radiotherapy.

Possible side effects of surgery:
Common side effects (affect >20% patients)
Pain – usually well controlled with painkillers
Infertility (100% risk i.e. a certainty)
Impotence (50% risk)
Temporary incontinence (25% risk). Almost all men (85%) are continent by one year post surgery, and most of the rest have only occasional incontinence. Severe incontinence is rare (2% to 3%) and can be treated with another intervention to tighten up the urinary tube.

Rare side effects (<25% patients)
Bladder spasms leading to a strong sensation of needing to pass urine – usually lasts several hours and occurs in around 10% of patients.

Wound infection
Mild abdominal/penis pain, bruising of the scrotum
Burning sensation after catheter removal – this will be temporary
Blood in urine for a few days
Temporary urine leak from the new joint between the tubes (urethra) and bladder
Difficulty in passing urine after your catheter has been removed needing re-catheterisation or further surgery
Passing small plastic surgical clips in the urine weeks/months after the operation - this may need a small procedure to remove clips

Very rare side effects (<1%)
Risk of hernia around the scar (<1%)
Severe bleeding requiring additional surgery (<1%)
Injury to nerves which control the muscles on the inside of the thigh (<1%)
Bowel injury needing a temporary stoma bag (<1%)
Damage to the tubes leading to the kidneys (<1%)
Also, there is a risk that the cancer may be more advanced than anticipated at surgery and further treatment, such as radiotherapy may be needed in the future.
Severe blood clots affecting the legs or lungs

Possible side effects of SBRT:
Common side effects during and immediately after treatment (at least half (>50%) of patients will experience one or more of these)
Tiredness
Loose bowel motions or diarrhoea
Discomfort in the back passage
Needing to pass water more frequently
Discomfort on passing water
Skin redness
Temporary loss of pubic hair
Small risk of needing a urinary catheter (1-2% risk)
Small amounts of blood in urine

Common side effects in the long term (months-years after treatment)
Impotence or change in sexual experience (about 50% risk)
Infertility (almost 100% risk)
Minor change in bowel habit (about 30% risk)

Rare side effects (likely to affect less than 1 in 10 patients) occurring in the months and years after treatment
Narrowing of the urethra (tube to the bladder) causing problems passing water (<5%)
Permanent change in bowel habit (<10% risk)
Bleeding from the back passage needing surgical treatment (<5%)
Bowel or bladder incontinence (<1%)
Possible small increase in the risk of rectal (bowel) cancer

Severe bleeding upon urination (<1%)

The radiotherapy and associated imaging that you will receive is part of your routine care. It is the current state of the art image guided radiotherapy. If you take part in this study you will not undergo any additional exposure to radiation over and above standard practice. These procedures use ionising radiation (x-rays) to form images of your body, to ensure targeted treatment delivery and associated higher energy radiation provides your radiotherapy treatment.

Radiotherapy treatments use ionising radiation. If you take part in this study you will not undergo any additional exposures to ionising radiation. Ionising radiation can alter the way cells work, which may lead to a small increase in the risk of developing a further cancer in the years or decades after radiotherapy. There is always a chance of this occurring with any radiotherapy treatment (whether this is part of a study or not).

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What are the possible disadvantages and risks of taking part?

You may have side effects associated with this treatment. Most of these are listed above, but there may be others that we cannot predict. Side effects will vary from person to person in terms of severity and type, so you are encouraged to report anything you notice to your hospital doctor.

Because you may receive radiotherapy, which can cause damage to developing cells, you must take full contraceptive precautions if there is any possibility that you may father children.

If you have private medical insurance, please ensure that your insurers are aware that you are considering joining the trial and that it does not adversely affect any claim you may have.

What if new information becomes available?

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

What are the expected benefits?

Taking part in this trial may mean that you benefit from a new treatment which delivers a high dose of radiation to the prostate with relative sparing of surrounding healthy tissue. If you receive surgery, we know that this is an excellent treatment for prostate cancer.

In addition, this study will allow scientists and the medical community to increase their knowledge concerning the best treatment for men with prostate cancer. Unfortunately, we cannot guarantee or promise that you will receive any benefit from this clinical study.

What are the alternatives for treatment?

If you decide not to participate in this trial, you will be offered surgical treatment. It is important that you only enter this trial if you are prepared to accept either of the treatments.

What if there is a problem?

Any complaint about the way you have been dealt with during this study or any possible harm you might suffer will be addressed. Detailed information on this is given in Part 2.

Will my taking part in this study be kept confidential?

Yes. All the information about your participation in this study will be kept confidential. The details are included in Part 2. We will inform your General Practitioner (GP) if you decide to take part in this study.

Who to contact should you have questions or problems

For any questions regarding your care in the context of this study your hospital doctor may be contacted as follows:

Dr ……..
Address: …….
Tel: ……..

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

PATIENT INFORMATION SHEET - PART 2 (additional information)

Will my participation in the study be kept confidential?

If you consent to take part in the research, all the information that is collected about you will be kept strictly confidential. The patient information, kept on a web based database held by a third party, will not include your name. The information collected will be primarily to do with the treatment you receive, the side effects you may or may not have whilst receiving treatment, the period for which the cancer remains under control and your survival. Your date of birth and NHS number (or equivalent) will be recorded on this database but no other personal information (i.e. name, address etc). In order to check that the information on the database is accurate, the research Sponsors, the clinical trials unit at the Institute of Cancer research or those individuals acting in its name may wish to access the data. The appropriate regulatory authorities may also look at your records, to check that the study is being carried out correctly. You have a right to access all your medical data at any stage during this study and this can be done through your research study team. Your GP will be informed by letter of your participation in this trial.

We will contact your hospital over the years to find out how you are getting on. Ideally we would like to do this for life, but patients often change address and/or GP or lose touch with their hospital. If this happens we would like to use national records which are kept on everyone's health status to find out how you are. We will need to give them enough information to identify you. This is usually your name, date of birth and NHS number (or Community Health Index and/or hospital number in Scotland). Any details we receive from any source are confidential and will only be used for the purposes of the PACE study. Please initial the consent form to show that we have your permission to do this.

Confidentiality

The Royal Marsden NHS Foundation Trust is the sponsor for this study based in the UK, and The Institute of Cancer Research, also based in the UK, is the clinical trials unit working with the sponsor. The Institute of Cancer Research will be using information from you and/or your medical records in order to undertake the study and will act as the data controller for the study. This means that we are responsible for looking after your information and using it properly. The Institute of Cancer Research will keep identifiable information about you for at least 5 years after the study has finished, in line with local policies and legal requirements.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information at www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/transparency.

[NHS site – details to add] will collect information from you and/or your medical records for this research study in accordance with our instructions.

[NHS site – details to add] will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from The Institute of Cancer Research and regulatory organisations may look at your medical and research records to check the accuracy of the research study. [NHS site] will pass these details to The Institute of Cancer Research along with the information collected from you and/or your medical records. The only people in The Institute of Cancer Research who will have access to information that identifies you will be people who need to contact you to send a Quality of Life booklet by post or audit the data collection process.

[NHS site – details to add] will keep identifiable information about you from this study for 5 years after the study has finished.

You will be given a unique registration number, which will be used together with your initials and date of birth on forms that the research staff send to the Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU). All information about you will be treated as strictly confidential and nothing that might identify you will be revealed to any third party. Only members of the research teams at your hospital and the ICR-CTSU will have access to the information that could allow this trial ID number to be linked to you.

We will be contacting your hospital from time to time to find out how you are getting on. Ideally we would like to do this for a long time, but patients sometimes change address and/or GP or lose touch with their hospital. If this happens we would like to use national records which are kept on everyone's medical history to find out how you are and to collect some basic information about your health. We will need to give the organisations that hold these records enough information to identify you. This is usually your name, date of birth and NHS number (or Community Health Index and/or hospital number in Scotland). Any details we receive from any source are confidential and will only be used for the purposes of the study. Please initial the consent form to show that we have your permission to do this.
If you decide to take part in this study your General Practitioner (GP) will be informed.

As you may be receiving radiotherapy in this study a copy of the scans (such as CT and MRI) used to design your treatment plan will be sent to the national Radiotherapy Quality Assurance team. The data is sent electronically by a secure file transfer system and your name will not be included in any of the files sent. We need to send this information to the Quality Assurance team to make sure that radiotherapy given to patients is consistent across the different hospitals taking part.

Data sharing

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other

organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research.

Your information could be used for research in any aspect of health or care, and could be combined with information about you from other sources held by researchers, the NHS or government.

Where this information could identify you, the information will be held securely with strict arrangements about who can access the information. The information will only be used for the purpose of health and care research, or to contact you about future opportunities to participate in research. It will not be used to make decisions about future services available to you, such as insurance.

Where there is a risk that you can be identified your data will only be used in research that has been independently reviewed by an ethics committee.

Quality of life Study

We would also like to look at how the different types of treatment affect your life and general well being ('Quality of Life'). We will ask you to fill in a short questionnaire before you find out which treatment group you are allocated to and then at weeks 2, 4, 8, 12 and months 6, 9 and 12 after the end of treatment and yearly after that until year 5. You will receive all these questionnaires at your hospital visits.

The questionnaire will ask about your general health, side effects of treatment, and the way you feel, both physically and emotionally. Some of the questions may seem a little repetitive, but since these are standard questionnaires, we would ask you to be patient and complete all the sections as best as you can.

The questionnaires do include some questions that may make you feel uncomfortable or upset, especially those regarding sexual function and continence. Whilst we don't want to make you feel uncomfortable or embarrassed, these questions address important areas of men's health that we aim to investigate as part of the study outcomes. If you do feel upset by any of the questions, or any aspect of your disease, Macmillan Cancer Support is a registered charity offering their support to you. The contact details are found in the "further information" section of this leaflet.

Tissue donation

Additionally, we would like to collect the tissue samples taken at the time of your prostate cancer diagnosis (biopsy). These samples are routinely stored (in a block of paraffin wax) in the pathology department of your hospital, even after it has been examined to give the diagnosis. You will not need to undergo any more surgery for this – we are just aiming to use what has already been taken. We would like you to agree to the donation of some of this stored tissue for future research into the effects of radiotherapy on tumour tissue. If you agree, the

identification number of the sample and the hospital at which it is stored will be recorded. It is expected that future studies may collect a small amount of the sample for use in research. This research will not benefit you directly, but may help doctors give a more personalised approach to future patients with prostate cancer. This donation is optional, and your treatment will not be affected if you choose not to give these samples as a gift.

What if something goes wrong?

Any complaint about the way you have been dealt with during this study, or any possible harm you might suffer, will be addressed. Your progress will be watched closely and you will be offered whatever help is available to cope with any side effects. Occasionally some patients need a short stay in hospital for side effects to be treated, and on rare occasions these can be serious. If this were to happen, full details of what has happened will be reviewed carefully by the Doctor who has overall responsibility for the PACE trial. It is unlikely that anything will go wrong with your treatment or care, but if you wish to complain about any aspect of the way you have been approached or treated during the course of the study you can do so using the normal NHS complaints procedure. Concerns should be raised by speaking to a member of staff at your hospital or by talking to the local Patient Advice and Liaison Service (PALS) which has been established in every NHS Trust.

NHS bodies are liable for clinical negligence and other negligent harm to individuals covered by their duty of care. In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the NHS Trust but you may have to pay your legal costs. Alternative indemnity arrangements apply to private clinics.

What happens if I decide to withdraw from the study?

You may decide to stop and withdraw from the study at any time without giving a reason. A decision to withdraw at any time will not affect the standard of care you receive. After discussion with your hospital doctor, you will be offered the treatment felt to be best for you at that time

Your hospital doctor may also withdraw you from the study without your consent if they believe that another treatment would be better for you, or for other unanticipated reasons.

What will happen to the results of the research study

It will take approximately 10 years to complete the study but some data may be available sooner. It is intended that the results will be written up and published in scientific journals. Your doctor will be informed when the results are available and you can ask him/her about the progress of the study. These results will also be available on the Cancer Research UK's patient website http://www.cancerresearchuk.org/cancer-help/trials/. No individual patient will be identified in any report or publication.

Who is organizing and funding the research?

The sponsor of this study is the Royal Marsden NHS foundation trust. The trial has also been financially supported by Accuray, the company who manufacture the Cyberknife machines,

which is one of the ways SBRT can be delivered. The trial has been endorsed by Cancer research UK and is part of the National Cancer Research Network portfolio.
There is no payment for your participation in this study including lost earnings, your time or travel expenses. None of the medical staff involved in your care receive payment from this trial.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, well-being and dignity. This research has been reviewed and given a favourable opinion by the NRES Committee London – Chelsea.

Your GP will be notified of your participation in this study as well as possible side effects and recommendations for monitoring and surveillance.

What do I have to do now?
You will have some time to think about the study and make your decision. You may wish to discuss it with your family or friends. Please keep this information sheet and copies of the signed consent form. If, at any time, you have any questions about the study you should contact your hospital doctor.

Further information

Macmillan Cancer support is a registered charity and helps with all the things that people affected by cancer want and need, from specialist health care and information to practical, emotional and financial support (www.macmillan.org.uk). You can learn more about clinical trials on the Cancer Research UK's patient website http://www.cancerresearchuk.org/cancer-help/trials/

Thank you for interest in our research.

Contact Details
If, at any time, you have any questions about the study you should contact the following doctor at your hospital (site Principal Investigator):

Name:
Address
Telephone

Contact Number