[To be printed on hospital headed paper]

The PACE trial: Image-guided conventional radiotherapy (8 weeks) 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 is 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 doctor will discuss all options which are suitable for you.

The purpose of this research is to investigate whether radiotherapy (X-Ray treatment) is best given over 8 weeks (conventional image-guided radiotherapy) or over 1-2 weeks using stereotactic body radiotherapy (SBRT). We know that image-guided conventional radiotherapy is a very good treatment for early prostate cancer. SBRT is a new way of delivering radiotherapy (X-Ray treatment) using a radiotherapy machine which can accurately target the prostate. We believe that both treatments are likely to cure your prostate cancer, but we don't know if one is slightly better than the other. Also, we know that the side effects may be different, but we don't know to what extent and which treatment results in the best chance of cancer cure with the fewest side effects.

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 men across Europe and North America. Because the difference between the treatments is likely to be small, we need over a thousand men to enter in order to prove whether there is any difference between the treatments or not. 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 are going to compare people who have SBRT with those people who have conventional radiotherapy. 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 over 1-2 weeks and half of the patients will receive conventional radiotherapy over 8 weeks. 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.

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).

Method for targeting the prostate

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 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 happens during conventional radiotherapy?
Conventional (standard) radiotherapy is given every day, Monday to Friday, over 8 weeks, which makes a total of 39 treatment visits. Each treatment session lasts around 15 minutes and the radiotherapy procedure is completely painless. We will ask you to stay as still as possible on the treatment bed.

What happens after my treatment has finished?
We will review you in clinic or by telephone at 2 weeks, 4 weeks, 8 weeks and 12 weeks after starting 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.

At each clinic visit we will ask you about any symptoms you may have, and at some clinic visits we will ask you to fill in the quality of life questionnaire again.

What are the side effects?

The risks and side effects of conventional radiotherapy are well known 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 conventional radiotherapy or SBRT:

Common side effects during and immediately after treatment (most patients (>50%) 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)

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 (around 30% risk)
Small amounts of blood in urine

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.

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. If you decide not to take part, you will be offered conventional radiotherapy.

What are 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 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 doctor will tell you about it and ask whether you would like to continue with the study. If you decide to withdraw, your 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 have conventional radiotherapy, 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 like you with prostate cancer. We cannot however 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 conventional radiotherapy. 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 GP if you decide to participate 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 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 this information 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.

Data sharing

The organisers of this study would like to have your permission to combine information they collect about patients in this study with information collected from other studies. In the future, this may advance our knowledge of treatment for cancer. If these projects occur, information about you may be passed to other legitimate researchers, but they would not be able to identify you from the information provided. You can choose whether to give your permission for this on the consent form.

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 doctor, you will be offered the treatment felt to be best for you at that time.

Your 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 doctors 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 general practitioner 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 consultant:

Local Consultants name (Site PI)
Address
Telephone

Contact Number