

## PATIENT INFORMATION SHEET

### BIOPROP20: Biologically optimised IMRT for Prostate Radiotherapy

#### Hypofractionated radiotherapy with intra-prostatic boosts to tumour nodules in men with intermediate and high risk prostate cancer

You have been invited to take part in a research study. Before you decide, it is important that you 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.

- **Part One** tells you the purpose of the study and what will happen to you if you take part.
- **Part Two** gives you more detailed information about the conduct of the study.

The clinical team in charge of your care will go through the details with you, but please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

#### Part One

#### What is the purpose of the study?

High dose radiotherapy is a very effective treatment for prostate cancer. However, there is an increased risk of side effects compared to lower dose radiotherapy. This study will investigate the use of dose painting radiotherapy. Dose painting radiotherapy administers a high dose of radiotherapy to areas of cancer inside the prostate and a lower (standard) dose to the rest of the prostate. This may improve control of the cancer without increasing the side effects. The radiotherapy is given in 20 doses, called fractions.

External radiotherapy uses beams of high energy x-rays to destroy cancer cells in the area of the body it is aimed at. Ideally, a very high dose of radiotherapy needs to be given to the tumour, to kill all of the tumour cells. However, it is not possible to treat the *whole* prostate

with a very high dose, as it would result in an unacceptable risk of side effects. Radiotherapy can damage healthy cells, in organs near the prostate such as in the bladder and bowel

There is a new technique (dose painting) available which increases the radiotherapy dose to the area in the prostate containing the cancer in a way that is designed not to increase the side effects. A MRI (magnetic resonance imaging) or PET-CT (positron emission tomography) scan are the best ways to identify the areas of cancer in the prostate. Once the areas of prostate are known, a radiotherapy plan specifically designed for these nodules is created; we call this Intensity Modulated Radiation Therapy (IMRT) 'dose painting radiotherapy'.

Dose painting radiotherapy is administered in treatment doses called fractions. The BIOPROP20 trial uses a schedule of treatment called 'hypofractionated' treatment. Hypofractionated treatment means giving the patient's total radiotherapy treatment over fewer fractions (20) and a shorter time. The national standard is currently 32-37 fractions over 7-8 weeks. Recent research has shown that hypofractionated schedules are safe and effective for the treatment of prostate cancer.

### **Why am I being invited to take part?**

You have been diagnosed with a type of prostate cancer (localised) that can be treated with radiotherapy. Your doctor feels that you are suitable for treatment in this study. We plan to recruit 50 patients in total.

### **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do you will be asked to sign a consent form but you are 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 will happen to me if I take part?**

Your doctor will have already completed several tests (screening tests) to assess whether you are suitable for radiotherapy treatment. If the functional MRI and bone scan were not completed, or were completed more than 3 months before you enter the study, they will need to be repeated.

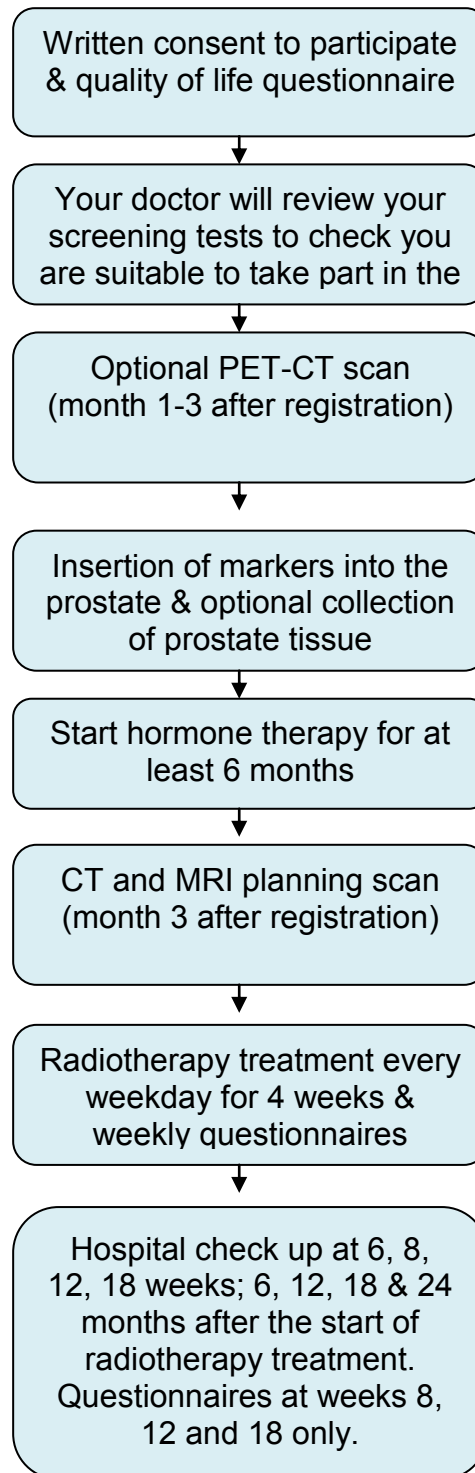
If you choose to take part in this study, written consent will be taken from you and your doctor will double check that the tests confirm that you are suitable to take part in this study.

At this time you will also be asked to complete a questionnaire as part of this study, which you would not normally complete.

If you choose to take part, you will be involved in the study for approximately 2 years and 3 months. The frequency of your visits to see your doctor will change. After your radiotherapy treatment has completed, you will not need to see your doctor as often.

The summary of visits you will need to attend is shown in the diagram on the next page.

## Schedule of tests, planning and treatment.



**Blood tests**

Routine blood tests will be done to check you are suitable for radiotherapy treatment. You will also have a routine blood test for a prostate cancer marker (PSA) 18 weeks after you start treatment, and then at 6-monthly intervals for 5 years. We will only collect data from this blood test for the study up to 2 years after you started radiotherapy treatment.

**Optional tests**

The quality of life questionnaires will help us to assess the effect of dose painting radiotherapy. We have found PET CT scans and targeted prostate biopsies useful to design dose painting radiotherapy. These tests are optional and you and your doctor will decide whether you will have them.

*Quality of Life Questionnaires (optional)*

You will be asked to complete a maximum of 8 questionnaires about your quality of life throughout the study. If you don't want to complete questionnaires, you still can take part in the study.

The questionnaires ask for your views on your general health as well as more specific questions about bladder, bowel and sexual functioning.

The other questionnaires will need to be filled out each time you attend the hospital for your radiotherapy treatment and at some visits afterwards:

- During your screening tests
- Weekly during your radiotherapy treatment (4 weeks)
- 8 weeks after your radiotherapy treatment started
- 12 weeks after your radiotherapy treatment started
- 18 weeks after your radiotherapy treatment started

These questionnaires will help us to understand more about the side effects of this radiotherapy treatment and may be of benefit to patients undergoing radiotherapy treatment for cancer of the prostate in the future.

*PET CT scan (optional)*

PET CT scans are particularly useful if the MRI is difficult to read. Your study team will explain whether this is the case. You will have a PET CT scan at the beginning of the study (in the first 3 months). This is to help your doctor check the size and location of the tumour in your prostate.

You may need to have this scan at a different hospital to the one you receive your treatment at.

You will be asked to avoid choline rich food for several days before the scan. Your appointment card should give you details of about what to do. You will then have an injection of a very small amount of a radioactive form of choline (radiotracer). The amount of radiation is very small and only stays in the body for a few hours. In addition to the

injection the CT part of the scan exposes you to a small amount of radiation in the form of X-rays.

Following the injection you will lay on a scanning table as the scanner passes around you. We will repeat the scan at 60 and 90 minutes.

#### *Collection of prostate biopsies & extra blood test (optional)*

This is an optional procedure and will only be completed if you provide consent.

If your doctor thinks you will benefit from collecting tissue from your prostate specifically for this study, a maximum of 12 biopsies will be taken under general anaesthetic. At the end of the biopsy, we insert the 3 gold markers. These are required to focus the radiotherapy accurately (see below).

The biopsies will be used to check the results of your MRI scan and PET CT scan. This is because sometimes scans show abnormal areas, which are not cancerous. For the type of radiotherapy treatment you will have it is important to know exactly where the cancer cells are in the prostate.

With your permission, we would like to store any leftover tissue to use in future research. We would also like to collect any leftover tissue from the biopsy taken to diagnose your cancer.

With your permission, we will also take an extra blood test (around 21ml or 4 teaspoons) on the same day as we take the extra biopsies for future research.

#### **Mandatory tests**

The functional MRI and the procedures below are required to deliver dose painting radiotherapy safely and effectively.

#### *Gold marker insertion*

If you did not have the extra biopsies, we will insert 3 tiny gold markers into the prostate approximately 2 weeks before your scan used to plan your radiotherapy. We will use local anaesthetic. The markers show up very clearly on both x-rays and CT scans and therefore help us to check accurately the position of your prostate. This is so we can plan your radiotherapy treatment accurately. You would normally have insertion of the 3 gold markers as part of your routine care.

#### *Hormone therapy*

Before radiotherapy starts, the majority of patients will be treated with a course of hormonal therapy. This is the standard treatment. Please discuss your questions with the doctor looking after you. You can read about it in the information leaflets available at your hospital.

#### *Radiotherapy planning*

Your doctor will need to plan where to give your radiotherapy treatment. This requires a planning CT and MRI scan. This helps us to locate the prostate and the boost areas accurately.

We use a preparation protocol for planning. We ask you to empty your bowels with a mini-enema and will drink 3 cups of water. After 20 minutes, we will insert a urinary catheter in the bladder. You have a CT scan of your pelvis. After this, you will go to the MRI scanner. You will have an MRI scan of the prostate only, which does not take as long as the other scans. After the MRI scan, we remove the catheter. The CT scan and the bladder / bowel preparation is the standard protocol, the MRI and the catheter are done only for dose painting planning.

After the scans you will get a list with your treatment dates on from the research team and you can go home. You will start your radiotherapy treatment about 3-4 weeks later.

Your doctor will use information from your CT and MRI scan and your biopsies (if taken) and PET-CT scan (if completed) to plan radiotherapy treatment specifically for you.

### *Radiotherapy Treatment*

Your radiotherapy treatment will be given in 20 sessions, every weekday for four weeks. Each treatment session will take 10-15 minutes. This may be less treatment sessions than is usually given at your hospital (the national standard is 32 – 37).

Before you have your radiotherapy, we will ask you to empty your bowels beforehand, just like for your radiotherapy planning. You will drink 3 cups of water. After this the radiographer will position you on the couch and ensure that you are comfortable ready for your treatment.

The radiotherapy treatment only takes a few minutes, but you will need to lie still for approximately 10 minutes whilst we check the prostate position and the machine moves to deliver the treatment from different angles. You will not feel anything - it is similar to having an x-ray. During radiotherapy treatment you will be seen by your doctor and/or nurse every week to manage and record any side effects you may be experiencing.

### *Check ups after your radiotherapy treatment*

You will be seen regularly by your doctor and/or nurse after treatment so that any side effects you may be experiencing can be measured as well as any benefits of the treatment.

After your course of radiotherapy treatment has been completed, you will be seen at 6, 8, 12, 18 weeks after you began your treatment.

You will also be seen at 6, 12, 18 and 24 months after you began your treatment. At these visits your doctor will manage and record any side effects.

### **What do I have to do?**

You will have to visit the hospital to receive your treatment and other tests. You may have to visit a different hospital to have your PET-CT scan, if you have one. If you wish, you are welcome to bring a friend or relative to the visits. You will also have to see your doctor for follow-up visits after trial treatment has been stopped, at 6, 8, 12, 18 weeks; 6, 12, 18 & 24

months after the start of radiotherapy treatment. At some of the visits, you will be asked to complete quality of life questionnaires, which should take about 15 minutes to complete.

### *Contraception*

During treatment and for one year after treatment, your sperm may not be formed normally, if they are produced at all. If appropriate, you or your partner should use effective contraception during this period, i.e. two forms of contraception, one of which must be a condom. If your partner should become pregnant during the course of the study, you must tell your study doctor *immediately*.

If you are taking any other medicines please discuss this with your doctor and nursing staff.

### **What are the alternatives for treatment?**

Alternatives to radiotherapy include standard treatment with surgery, radioactive implants, or close observation with later treatment if necessary. You should discuss these options with your doctor before deciding to take part in this study.

### **What are the side effects of the treatment I will receive when taking part?**

Radiotherapy treatment can cause side effects because of the healthy tissue around the cancer being exposed to the radiation. This means that radiotherapy to the prostate can produce side effects on the surrounding organs such as the bowel and bladder. Radiotherapy can also cause you to feel more tired than normal.

No one can predict whether you will have some, all or none of the side effects, or how severe they will be. We have carefully chosen the dose of the radiation you will receive to reduce the risk of causing major symptoms.

It is important that you tell your study doctor or nurse about any problems you have at each hospital visit, so that appropriate action can be taken. You can telephone your doctor nurse or Cancer Specialist between visits if you are concerned. Their numbers are on page 9 of this information sheet.

### *Bowel side effects*

During radiotherapy there may be an increase in the frequency and urgency of bowel movements with passing of mucus. Bleeding is uncommon during radiotherapy. After treatment, symptoms are expected to substantially settle within 4-12 weeks but some degree of urgency and looseness can persist. Rectal bleeding is usually slight but may occur in approximately one man out of 10 treated. Bleeding most commonly occurs 18-24 months after radiotherapy; it is less common later on. The cause of any bleeding needs to be determined by viewing your bowel using a telescope. The majority of men do not need any treatment for bleeding. In addition, rectal or lower abdominal discomfort can occur in fewer than 2 out of 10 men during and after radiotherapy treatment.

### *Bladder side effects*

It is quite common for patients to urinate more frequently and/or urgently during radiotherapy, sometimes with discomfort. These side effects usually subside within 4-12 weeks of treatment finishing, and commonly any remaining symptoms are less than those



reported before radiotherapy started. However, a small proportion of men continue to have frequency or urgency. Urinary incontinence is rare. In addition, fewer than 2 out of 10 men will experience slight blood loss whilst urinating during and after radiotherapy.

### Sexual impotence and Fertility

We expect men to become infertile after radiotherapy treatment. Sexual activity is likely to be significantly impaired during hormone and radiotherapy treatment but may recover in about 60% men after radiotherapy. Older men have more difficulties than younger patients. However we strongly recommend that you or your partner should use effective contraception during this period. See section 'what do I have to do'.

## **What are the possible disadvantages and risks of taking part?**

By participating in this study, you may have some extra tests. These are:

### **Optional Tests**

#### *Completion of questionnaires (optional)*

During the study we will ask you to complete 8 questionnaires. Each one will take about 15 minutes to complete which may be inconvenient. However we will give you these questionnaires to complete during your hospital visit whilst you are waiting to see the doctor/nurse

#### *PET-CT scan (optional)*

You will have to visit a different hospital to the one you are attending for treatment for your PET-CT scan. You will not have anything to eat for several hours before the scan although you can drink plain water. The amount of radiation is very small and only stays in the body for a few hours. In addition to the injection the CT part of the scan exposes you to a small amount of radiation in the form of X-rays.

#### *Collection of tissue from your prostate (optional)*

The type of prostate biopsies that will be taken (known as targeted biopsies) have a small risk (<2%) urinary retention due to fluid retention in the prostate (oedema). As there will be a maximum of 12 biopsies taken, the risks are much lower than for systematic template biopsies. The tissue will be collected using a method that has only a minimal risk of infection compared to standard trans-rectal biopsies.

#### *Collection of an extra blood sample (optional)*

If you give permission, we will take some extra blood from you at the same time that you have your markers inserted.

### **Mandatory Tests**

#### *Receiving a higher dose than normal in some areas of your prostate*

We have developed this program at the Clatterbridge Cancer Centre over the last 2 years. We have undertaken extensive tests and evaluation to discover any potential problems with it. So far, we have treated successful 20 patients using this method. Elsewhere (mainly London and the Netherlands) many more patients received dose painting radiotherapy. If



you receive a higher dose to a small part of the prostate, there is a slightly increased risk of side effects. We have so far not observed a problem, but it could happen.

If we don't think it is possible to produce a good plan for treating you in this way, we will treat you with a standard treatment plan. We will tell you before you start the treatment whether we had any problems designing the plan or not.

### **What are the possible benefits of taking part?**

We hope that the treatments will help you and give you a better chance to get rid of the cancer. However, this cannot be guaranteed. The information we get from this study may help us to improve the future treatment of patients with prostate cancer.

### **What happens when the research study stops?**

If you choose to stop taking part in this study, or if it finishes earlier than expected, you will receive standard medical care.

### **What if there is a problem?**

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

### **Will my taking part in this study be kept confidential?**

Yes. All the confidential information about your participation in this study will be kept confidential. The detailed information on this is given in Part 2.

### **Contact for Further Information**

Should you have any further queries regarding this study or about any of the treatments described above,

#### **Please contact:**

#### **Appropriate job title:**

#### **Dr Isabel Syndikus:**

Clatterbridge Cancer Centre NHS Foundation Trust

Clatterbridge Road

Bebington

Wirral

CH63 4JY

#### **Contact Number is:**

0151 334 1155

**This completes Part One of the Information Sheet. If the information in Part One has interested you and you are considering participation, please continue to read the additional information in Part Two before making any decision.**

## **Part Two**

### **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 discuss with you whether you want to or should continue in the study. If you decide to withdraw your doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

On receiving new information your doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason you will be told why and your continuing care will be arranged.

### **What will happen if I don't want to carry on with the study?**

You are free to withdraw from the study at any time. You do not have to give a reason and your future treatment will not be affected. Your doctor will discuss your treatment with you and will offer the most suitable treatment available. However, if you were to withdraw, we will ask for your permission to continue to collect information on your progress that is routinely recorded in your medical records. If you do not wish for this to happen please speak to your doctor.

If you withdraw your consent we will remove and dispose of your blood and tumour tissue samples. If consent is withdrawn several months after donation it is possible some of the samples may have already been issued to researchers. The University of Liverpool will alert the relevant researchers and request the immediate return of any unused tissue for disposal. If tissue samples have been used by researchers no further action can be taken. If any research has already been performed, then the results of the research will not be destroyed. In this case only sample and any DNA extracted will be destroyed.

### **What if there is a problem?**

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the normal NHS Complaints Procedure. Details can be obtained from the hospital.

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence, then you may have grounds for a legal action for compensation against the NHS Trust where you are being treated, but you may have to pay for your legal costs. The normal National Health Service complaints mechanisms should be available to you (if appropriate).

In the event of defective equipment then you may have grounds for a legal action for compensation against the manufacturer, but you may have to pay for your legal costs.

**In case of emergencies, please contact the hospital on 0151 334 1155 and ask for Triage on Bleep 5555.**

### **Will my taking part in this study be kept confidential?**

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from Cancer Research UK or their collaborators who are also involved in organising this research project and may be used in a number of research projects and/or for research related to the development of pharmaceutical products, diagnostics or medical aids by other scientists and research organisations within and outside the European Economic Area, in universities, the NHS or commercial companies involved in medical research worldwide which may also involve discussions with regulatory authorities. Patients' safety data may be reviewed outside the EU but no one will be able to identify you. Data may also be looked at by representatives of regulatory authorities and by authorised people from the Trust, other NHS bodies or the commercial companies referred to above to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant.

A copy of your completed consent form will be sent to the Liverpool Cancer Trial Unit to allow them to check you have agreed to the trial. This will be kept in a secure location away from all the study data.

Data collected during the study may be transferred for the purpose of analysis/registration within or outside the European Economic Area. Some countries outside Europe may not have laws which protect privacy to the same extent as the Data Protection Act in the UK or European law. We will take all reasonable steps to protect your privacy, and any confidential information (such as your name, address and GP details) will be removed before being shared.

### **Involvement of the General Practitioner/Family Doctor (GP)**

With your consent, your GP will be informed of your involvement in the trial. Any other medical practitioners who treat you, e.g. should you be admitted to hospital for any reason, will also be informed.

### **What will happen to any samples I give?**

Your routine blood samples will be analysed at your hospital for the purpose of your treatment.

As discussed in part 1, if you consent we will transfer the extra blood sample and any stored or new tumour tissue samples to the University of Liverpool for storage. The University of Liverpool is approved by the Human Tissue Authority to store Human samples for use in research. The blood and tumour tissue samples will be used for this project and may be used in a number of research projects and/or for research related to the development of pharmaceutical products, diagnostics or medical aids by other scientists and research organisations within and outside the European Economic Area, in universities, the NHS or commercial companies involved in medical research worldwide which may also involve discussions with regulatory authorities

The samples will be kept in a secure place until we need them.

We will allocate your samples a unique identifying number and we store this within secure databases, nobody outside of the study will have access to **any** confidential information that

you give to us. Confidential details (such as your name, address and GP details) will be kept locally and not made available to collaborators.

Researchers carrying out tests on the samples will only be given the information they need to carry out the tests and analyse the results.

### **Will any genetic tests be done?**

There are cells, chemicals, and proteins in the blood stream and we would like to use the blood samples and the tumour tissue to look at. We will look at the genes from the cells and to analyse the proteins. We may perform other analyses relevant to prostate cancer. We hope these scientific studies will help us to understand prostate cancer better and hopefully help us to find new treatments in the future.

### **What will happen to the results of the research study?**

It is intended that once the study is complete a report will be written and the results will be published to make them available to the public. They may also be used to design future research. You will not be named or identified in any publication.

### **What rights do I have to the results of the research?**

Any information derived directly or indirectly from this research, as well as any patents, diagnostic tests, drugs, or biological products developed directly or indirectly as a result of this research may be used for commercial purposes. You have no right to this property or to any share of the profits that may be earned directly or indirectly as a result of this research. However, in signing this form and donating tissue samples for this research, you do not give up any rights that you would otherwise have as a participant in research.

### **Who is organising and funding the research?**

This study is funded by The Clatterbridge Cancer Centre charitable funds. The study is being managed by the Cancer Research UK Liverpool Cancer Trials Unit which is based at the University of Liverpool and funded by Clatterbridge Cancer Centre.

### **Your doctor will not receive any payment for including you in this study.**

Your doctor will not receive any payment if you take part. You will not be paid for taking part in this study.

### **Who has reviewed the study?**

The study has been reviewed for scientific content by members of the NRES Committee North West - Cheshire has reviewed the study for ethical considerations.

Thank you for taking the time to read and consider this information sheet. Should you decide to take part in the study, you will be given a copy of the information sheet and a signed consent form to keep.