Project ID: 12/0399

Version: 2.4

Date: 8th April 2013

**PATIENT INFORMATION SHEET**

**FOCAL THERAPY FOR LOCALISED PROSTATE CANCER USING IRREVERSIBLE ELECTROPORATION (‘NANOKNIFE’)**

**Short name: NEAT - Nanoknife Electroporation Ablation Trial**

**Part 1**

You are being invited to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Talk to others about the study if you wish.

* Part 1 tells you the purpose of this study and what will happen to you if you take part.
* Part 2 gives you more detailed information about the conduct of the study.

Do ask us if there is anything that is not clear or if you would like more information. Please take your time to decide whether or not you wish to participate.

**1. What is the purpose of the study?**

Main Aim of the Project

We are testing a new way of treating only the part of the prostate gland containing clinically important prostate cancer. This is called **focal therapy**. It is being investigated as a new way of treating prostate cancer. The cancer areas in your prostate requiring treatment will already have been located using a scan called Magnetic Resonance Imaging (MRI) and a special type of prostate biopsy called Transperineal Prostate Mapping Biopsy (TPM). Focal therapy to the clinically important cancer will be carried out using irreversible electroporation, using a device called the NANOKNIFE. The term ‘irreversible’ refers to the effect that this type of treatment has on the cells. In other words, the effect on the cells is permanent. Although the NANOKNIFE treatment has been used to treat other types of cancer, we will be investigating its effects on the prostate.

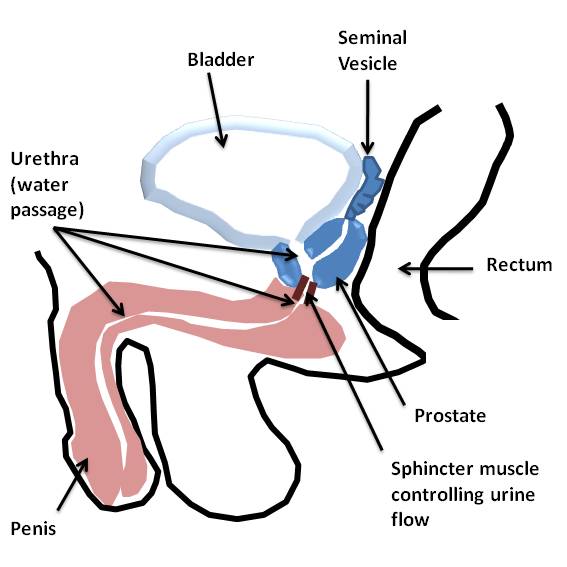
NANOKNIFE is a new type of device which uses electrical current to disrupt cells which in turn destroys the tissue. The treatment is delivered through needles placed in the prostate through the skin in front of the back passage (rectum), under general anaesthetic. Early studies have shown that NANOKNIFE seems to be accurate, can cause destruction of small areas of tissue, but causes little harm to other surrounding structures, such as nerves and vessels. We are doing this study for two reasons. Firstly, to find out what side-effects men get when NANOKNIFE is used to treat prostate cancer areas, and how safe the procedure is. Secondly, to find out how effective it is in controlling the cancer in the short term. If successful, this could lead to larger trials across the NHS to see how good NANOKNIFE is in the medium and long term in controlling cancer.

Why is this trial needed?

Men who have prostate cancer that has not spread outside the prostate gland can choose to have a number of treatments. These include radiotherapy or surgery to treat the whole gland. In many men, active surveillance can be carried out instead, as prostate cancer does not always need to be treated unless it gets worse.

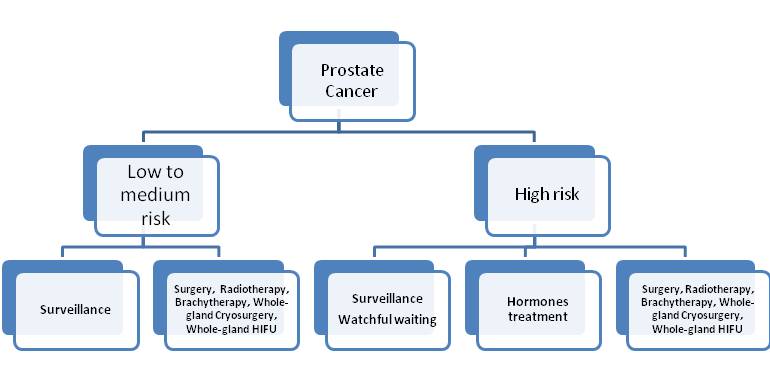
Men who have treatment to the whole prostate (surgery or radiotherapy) have more certainty that all of the cancer is treated. However, treatment to the whole prostate frequently affects sexual function (poor erections), urine control (urine leakage requiring pads) and can cause back passage problems (bleeding, diarrhoea or pain). This is because the nerves, muscles and back passage are very close to the prostate and can get damaged. On average, 1 in 2 men suffer with erection problems (insufficient for penetrative sex), 1-2 in 10 has leakage of urine requiring pads and 1-2 in 20 has back passage problems. In those men who do have return of their erections and in whom control of urine flow is good, have to wait between 12 and 18 months for such recovery of their function. The diagram below illustrates the prostate and how close these different structures are.

Side View of the Prostate and Surrounding Structures



Some men are not suitable for whole-gland surgery or radiotherapy or do not want to have the symptoms of these treatments. For these men active surveillance can be an option. Active surveillance involves watching the disease carefully and if it shows any signs of getting worse, one of the many treatment options is given.

The following diagram gives an overview of the treatment options that are available to men with prostate cancer. It is important you discuss which options are available and suitable for you with your doctors. This study will involve the treatment of men with low and medium risk prostate cancer only:



The difference between active surveillance and whole-gland treatment in terms of reducing cancer-related deaths is very small. A recent large study comparing a group of men having surgery to another group of men having surveillance, showed no survival benefit from having surgery over 10 years of follow-up. These results were in men with all types of prostate cancer (some aggressive, some not). However, the study did show that surgery seemed to benefit men with more aggressive forms of prostate cancer, but this effect was small.

One possible solution to reduce side-effects of treatment whilst keeping the small benefit of treating prostate cancer may be to treat only the area of the prostate that contains cancer. This is called focal therapy. Early results from previous small trials show that the risk of side effects is low following focal therapy. In men who have good erections and urine function before focal therapy, the side-effects after focal therapy are: 1 in 10-20 men suffer erection problems, 1 in 100 has a urine leak requiring pads, and back passage problems are rare. These early results have shown that men have a return to what their sexual and urine function was like before treatment after about 6 months following treatment.

Focal therapy can involve treating all areas of cancer if there is only a small amount in the prostate. Focal therapy can also involve treating only the biggest area of cancer and leaving the smaller lower risk cancer areas alone, so that less damage is caused. This can be done because we now think that large cancer areas are responsible for progression (cancers getting worse) and spread. The untreated areas would then be watched carefully to check for changes which suggest that new cancers or small cancer areas are getting worse.

In this trial we aim to destroy cancer areas that we can see on MRI and that are clinically important (likely to progress), and not treat those areas that have no cancer, or clinically unimportant cancer (unlikely to progress). Evidence has shown that cancers below a certain size have a low risk of getting worse if left alone. We cannot be absolutely certain that these small cancer areas will remain clinically unimportant after we treat only the large area of cancer but the evidence is now very strong that for this. Nonetheless, we will carefully follow men after this treatment to make sure we can see any change in untreated areas of the prostate.

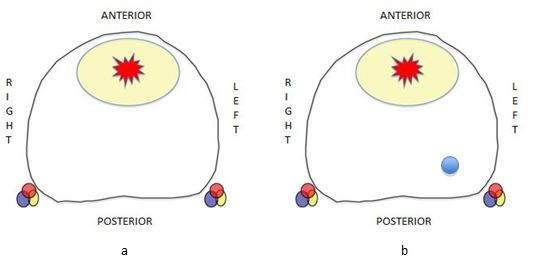
**2. What is Irreversible Electroporation?**

In this study, we are aiming to treat clinically important tumours at the front, or ‘anterior’, part of the prostate. This area is often difficult to treat using other types of focal therapy. However, NANOKNIFE can access this part of the prostate more easily, and therefore, this treatment may allow some men to have focal therapy who would not have been offered this option before. Also, the anterior part of the prostate is far away from the back passage area, so the risk of harm to the back passage should be lower than focal therapies currently used (although the risk of back-passage damage for any treatment is rare).

The types of treatments that will be done in this trial are shown below. The type of treatment that you will receive if you agree to take part in the study will depend on the results of your MRI and TPM biopsies. In this study, low risk cancers that cannot be seen on MRI, and are very low volume on biopsy, are considered clinically unimportant and therefore will not be treated. Medium and high-risk areas will be treated.

Each of the diagram below represents a ‘slice’ of a prostate as you were looking at it. The areas of ‘clinically unimportant’ and ‘clinically important’ cancer, the location of nerve and vessel bundles surrounding the prostate, and the treatment area are illustrated (see legend below). Since the treatment is in the anterior part of the prostate, and because the back passage is close to the posterior part, the possibility to undergo injury to the back passage is unlikely.

In the example ‘a’, all cancer is treated (clinically important cancer in front of the prostate). In the example ‘b’, clinically important cancer is treated, but clinically unimportant cancer is left untreated for surveillance.



This is what the areas mean in the diagram:

Low-risk, ‘clinically unimportant’ area of cancer

Medium or high-risk, ‘clinically important’ area of cancer

Nerve and vessel bundles surrounding the prostate

Treatment zone

This trial will look at treating 20 men in this way at University College Hospital London. The prostate will be treated with a new technology called Irreversible Electroporation (NANOKNIFE). This uses electrical current to permanently disrupt cells by making holes in their linings (the cell membranes). We think it can do this very discretely, so that a small area of tissue is destroyed. We will test how well it can do this in this trial. NANOKNIFE is not the only energy source that can be used to treat focal areas of the prostate. Other energy sources are high-intensity focused ultrasound (sound-waves), cryosurgery (freezing), photodynamic therapy (light activated drug), brachytherapy (radioactive seeds inserted into the prostate) and photothermal therapy (laser heat).

We are aiming to find out whether the encouraging results in focal therapy trials using any of the treatments described above, can be repeated using the NANOKNIFE. If the treatment is well tolerated and does not cause significant side effects, then this trial may be used to plan and justify a larger trial, with longer follow-up.

NANOKNIFE has been used to treat prostate cancer in a few men already. However, it is still new, and we need to find out more about whether it is well tolerated, what types of side effects it may cause, and how effective it is at treating prostate cancer. This is best done in a clinical trial. We have chosen to use NANOKNIFE in this trial because it has the following **potential** benefits:

1. It seems to be very precise so could be used to treat a small area of tissue
2. **The surrounding healthy tissue and structures (e.g. nerves, blood vessels) may not be effected**
3. The treatment does not take a long time (about 60 minutes in total) so can be done as a day-case procedure
4. It can reach difficult areas of the prostate that some other treatments cannot using the insertion of small needles into the prostate (no cuts) through the skin behind your scrotum.

This is an experimental form of treatment that is not standard practice. Your doctors will discuss other options with you in detail so that you can make a decision about whether to take part in this clinical trial.

NANOKNIFE has been used to treat other types of cancer elsewhere in the body, such as the liver, pancreas, and lung. It appears to be safe, can cause effective tumour treatment, and with minimal side-effects in these other organs.

Am I eligible for NANOKNIFE treatment in this study?

As NANOKNIFE treatment is in an early stage of treating prostate cancer, patients are carefully selected. This requires the research team to apply certain criteria in order to be eligible to participate.

We look at the following characteristics of your individual case before making a decision about whether IRE is suitable for you:

i. You have localised prostate cancer with a Gleason grade of 7 (3+4 or 4+3) or less

ii. Your PSA is 15ng/ml or less

iii. You have cancer that can be seen on MRI, and can be accessed using this treatment type

iv. You have clinically important cancer in only the front (anterior) area of the prostate

v. You have cancer that has been assessed as localised to the prostate using imaging

vi. Using an ultrasound scan, we may need to assess if the gland has fluid-filled areas (cysts) that will interfere with the treatment.

1. You must be at least 40 years old and have a life expectancy of at least 10 years
2. You must be able to read, understand and sign a consent form.
3. You must agree to take part in study visits, tests, questionnaires and treatments

In addition, patients with the following criteria will not eligible for this study:

i. Men who have had radiation therapy, prostatectomy, High Intensity Focused Ultrasound (HIFU) or cryosurgery for prostate cancer

ii. Men who have had hormone treatment within the previous 12 months

iii. Men with evidence of disease that has spread outside of the prostate to local lymph nodes and/or beyond (metastases)

iv. If you have a cancer that cannot be seen on the MRI scan.

v. If you have a narrowing in your water passage (urethral stricture) or have any metal implants or stents in the urethra.

vi. Men who have had previous prostate surgery for symptoms (including TURP, Thermal or Microwave therapy within 6 months of the trial screening date)

vii. Men with an inability to tolerate a transrectal ultrasound probe

x. Men who have undergone previous back passage surgery that makes the NANOKNIFE treatment high risk (this depends on the type of surgery and an individual decision will be made).

# xi. If you have a pacemaker, metal implants, prostheses, clips, or renal failure that prevents you from having an MRI scan of the prostate.

xii. Men who are not fit for a general anaesthetic as decided by a Consultant Anaesthetist.

**3. Why have I been invited?**

You have been invited to consider this trial because you have had a diagnosis of prostate cancer. The cancer seems not to have spread outside the prostate and the area of tumour may be suitable for NANOKNIFE focal treatment. The research team, after looking at your results, think that you may be suitable for the trial, which aims to destroy the important or dominant areas of cancer and leave non-cancer and unimportant areas of cancer alone. However, there are other treatments that are standard practice and which you may be suitable for. Your doctors will have explored these other treatments with you so that you can make a decision whether you wish to take part in this experimental form of treatment.

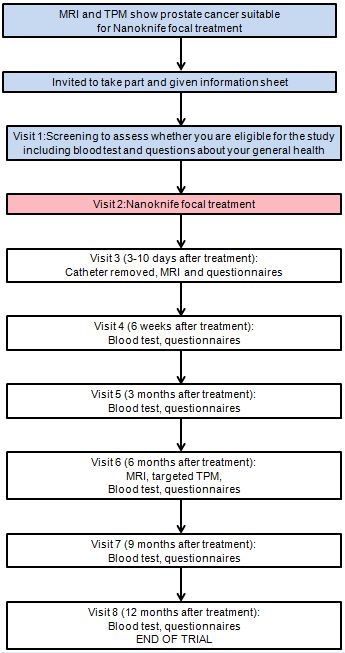
**4. Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. 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.

**5. What will happen to me if I take part?**

If you decide to take part in the trial, you will be asked to attend study visits over the course of the next year. The precise commitment this will involve is laid out below. After this period, your care will continue in the same way as if you had not taken part in the study. Your progress and condition will be monitored by your doctors in the urology or oncology clinic in the same way that it would have been if you had decided against taking part in the trial.

The flowchart below gives a summary of what this study involves.



TPM = Transperineal prostate mapping biopsies

We would like to carry out some of these visits via telephone consultation (with a member of the trial team). We would also like to assess completion of an electronic (computerized) version of the patient questionnaires for patients attending the clinic for consultation. The computer (e-tablet) that will be necessary for obtaining and completing the questionnaires will be loaned to you by the team in the trial clinic when you attend, for use during the clinic only. We also want to test how acceptable online completion of questionnaires outside of the hospital. There is a separate patient information sheet and consent form for these parts of the study. This means you can have normal clinic visits in person if you prefer.

**6. What happens exactly at each visit is outlined below**

Screening Visit

Your research doctor will see you as an outpatient, explain the procedure to you, and answer any further questions that you might have. You will be asked to sign a consent form before we carry out anything further as part of the study. By this stage, you will have had an MRI and TPM biopsies that suggest you are eligible for the trial. Arrangements will be made for your NANOKNIFE treatment at this visit.

We will ask for the following things as well:

- Questionnaires to complete. These will include questions of a personal nature relating to erectile/sexual function, urinary flow/continence and your quality of life. You will be free to complete these in privacy.

- Blood PSA tests if necessary (if you have not had one done within 60 days of the trial visit). The amount of blood taken will be 5mls. This is about the same as a teaspoon of blood.

NANOKNIFE Focal Ablation Treatment

- You will be asked to not eat anything for at least 6 hours before the procedure. You should NOT drink anything for at least 4 hours before the procedure. On the morning of the procedure you may be given an enema to clear your rectum. Alternatively, you may be given a glycerine suppository to take the night before in order to clear the back passage.

- An anaesthetist will explain the anaesthetic options available to you and make sure that your preferred option is both appropriate and safe. The anaesthetic will have to be a general anaesthetic (which puts you into a deep sleep during which you cannot feel anything and cannot move). The NANOKNIFE focal ablation will use a probe, like the one used when you had your prostate biopsies taken, which is placed into the rectum. Needles will then be inserted into the cancer area through the skin in front of your back passage. The treatment will be delivered using these probes. The treatment normally takes around 5 minutes. However, you will be asleep for around 60 to 90 minutes because of the time needed to set up the procedure.

- Before starting the treatment, a urinary catheter (a tube that drains urine from the bladder) is placed in the bladder. This tube can feel uncomfortable and unusual to pass urine through. This may be placed either through the skin directly into the bladder (called a suprapubic catheter), or via your penis (called a urethral catheter). A suprapubic catheter will require a 1cm cut in the skin for the tube to be placed.

- Once the NANOKNIFE treatment is complete your anaesthetist will wake you up. Most men will be able to have their treatment and go home about four to five hours later, provided there is someone to escort them and stay with them overnight. Occasionally, there will be the need for an overnight stay after treatment if your medical team think it is safer.

- You will be taught all about your catheter and how to look after it. Mild pain killers and a 7 day course of antibiotics will be provided. In addition, laxatives will be prescribed for a total of one week after the treatment. A contact number will be given if you have any problems at home.

Removal of Catheter (3-10 days) and MRI scan (3-10 days) after NANOKNIFE Treatment

The MRI scan will allow us to see how successful the destruction of prostate tissue was, and make sure that no harm was caused to the surrounding structures. However, the scan will not tell us how effective the treatment was at this stage i.e. whether the tumour has been fully treated. You will also be asked to complete some questionnaires at this visit.

Your catheter will be removed and the nurse will check that you are passing urine successfully.

We will try to organise the catheter removal and MRI scan on the same day if possible, but sometimes they have to be done on two separate occasions. You may have the removal of the catheter locally if you live far and if a practice nurse or your local urology department nurse is happy to do this. The catheter removal is a simple procedure that is not painful although it may be uncomfortable.

In some cases, the catheter will need to be put back in (under local anaesthetic) for a few more days if you cannot pass urine well enough yet. Alternatively, we may have to teach you the technique of Clean Intermittent Self Catheterisation (CISC) if we think the catheter should be removed but you may have problems with emptying your bladder properly. Although this may sound difficult to perform, most people learn it very quickly. It involves you passing a small slippery soft plastic tube (the catheter) into the bladder to empty it and then removing the catheter once the bladder is empty. You would only do this when you needed to. With time your bladder would start to work again and your need for CISC would become less and less.

If you cannot re-establish normal bladder emptying a cystoscopy (using a telescope to look into the bladder) will be carried out to investigate the cause. Some men, about 1 in 50, may need this to be done. At the same time a small procedure may be performed in order to improve normal bladder emptying. This might involve releasing some scar tissue in the prostate (formed as a result of the NANOKNIFE therapy) or cutting through a tight bladder neck in order to allow more of the bladder to empty. Very occasionally some dead tissue or debris within the prostate would have to be removed. These procedures can be done using a telescope and should require no more than a one-night stay in hospital. If you need these procedures, they will be explained to you in detail at the time and your consent will be required.

6 weeks after focal NANOKNIFE treatment

- Blood test to measure PSA. Other blood tests or urine test may be necessary but are not always required.

- You will be asked about any symptoms that you experienced following the therapy.

- Complete the same questionnaires that you completed prior to the NANOKNIFE therapy.

- You will be asked about any new treatments that you have undergone or started since we last saw you

3 months after focal NANOKNIFE treatment

- Blood test to measure PSA. Other blood tests or urine test may be necessary but are not always required.

- You will be asked about any symptoms that you experienced following the therapy.

- Complete the same questionnaires that you completed prior to the NANOKNIFE therapy.

- You will be asked about any new treatments that you have undergone or started since we last saw you

6 months after focal NANOKNIFE treatment

At this visit we will ask you to have another MRI scan to assess the success of the treatment. Biopsies will also be taken under local anaesthetic with sedation or general anaesthetic if you choose, in the same way as the biopsies you have already had prior to the NANOKNIFE treatment. In other words, transperineal prostate biopsies. The main difference is that fewer biopsies will be taken, and most or all of these will be targeted to the area of the prostate where you had NANOKNIFE treatment. This is to ensure that there is no significant cancer tissue left in the treated area. The biopsies will be taken with you asleep, or sedated, and using a template on the skin and an ultrasound probe in the back passage. The biopsies will be taken through the skin around the back passage area. You should not need to stay in hospital overnight. This visit will also involve blood tests and questionnaires.

9 months after focal NANOKNIFE treatment

- Blood test to measure PSA. Other blood tests or urine test may be necessary but are not always required.

- You will be asked about any symptoms that you experienced following the therapy.

- Complete the same questionnaires that you completed prior to the NANOKNIFE therapy.

- You will be asked about any new treatments that you have undergone or started since we last saw you

12 months after focal NANOKNIFE treatment

- Blood test to measure PSA. Other blood tests or urine test may be necessary but are not always required

- You will be asked about any symptoms that you experienced following the therapy.

- Complete the same questionnaires that you completed prior to the NANOKNIFE therapy.

- You will be asked about any new treatments that you have undergone or started since we last saw you

Arrangements for your continued follow-up with the appropriate urology team will be discussed at this final visit.

**7. What will happen once the trial finishes?**

Longer-term follow up will be carried out in the form of routine clinical appointments. This would be similar to the follow-up that you would expect to receive if you had chosen active surveillance at the outset.

**8. What will happen to me if the treatment fails?**

The focal therapy outlined here may fail if side-effects such as urine incontinence or poor erections occur. The NANOKNIFE therapy can also fail locally because the treatment was not effective in destroying the area of cancer fully. This will be shown by the MRI scans after treatment and the biopsies carried out at six months. Rises in PSA blood tests may also occur if the treatment has failed within the prostate. Rises in PSA are less reliable because most of the prostate gland is left untreated and this tissue still secretes PSA into the blood. Non-cancerous prostate tissue can continue to grow as you age and the PSA can rise slowly after treatment.

When treating in a focal manner with other types of devices, we have found that 1 in 4 men on average may need a further focal treatment to the area that has been treated. Should this be the case, we will discuss the options for focal re-treatment. This may include further NANOKNIFE treatment, or an alternative treatment type, such as high-intensity focused ultrasound (HIFU) or cryosurgery. You may choose to not have this, and other treatment options will be discussed which might include: whole-gland treatments (surgery, radiotherapy, cryotherapy, HIFU), hormonal treatment, or active surveillance/watchful waiting. You will be given detailed information on this.

Focal therapy can also fail if the disease has spread outside the prostate. This can be shown up by a positive bone-scan or by the MRI scan or by a rising PSA. This can cause side-effects of widespread disease including bone pain, weight loss, tiredness/lethargy and fractures of bone. If this occurs, further treatment options will be discussed with you and might include watchful waiting or hormonal treatment.

**9. What data will be collected?**

All clinic visit information including questionnaires, scans, biopsy results and blood results will be kept in study records so that we can analyse how NANOKNIFE treatment has performed. We will hold information about you without anything that could identify you to that data. You will be given a study number and this will be used on all your study records. The code for this number will be known to Professor Mark Emberton, Mr Hashim Ahmed, Miss Louise Dickinson, Mr Massimo Valerio, and another nominated trial person at the trial centre. By using a study number, the link between your name and the data we hold on you is not completely broken.

**10. What do I have to do?**

You may continue to take your regular medication or other prescribed over-the-counter drugs. You should not be involved in any other studies that involve the prostate gland. Normally, you should not be involved in any other type of study using drugs or medical devices. Please discuss this with your research doctors and they will advise you. It is important that you attend all visits, undergo all study investigations and agree to fill in all questionnaires before and after the treatment. If you think that this may not be possible, then you should discuss this with your doctor before agreeing to participate. If you hold private medical insurance, you should inform your insurance company that you intend to take part in the study.

**11. What is the device or procedure that is being tested?**

The procedure we are testing is destruction of only the area of the prostate that contains either clinically important cancer. This treatment will be carried out with a device NANOKNIFE which uses an electrical current to disrupt cell membranes and destroy small areas of tissue. The treatment is delivered using needles put into the prostate through the skin in front of the back passage. This study will help us to find out just how safe and well-tolerated NANOKNIFE is in destroying only the cancer areas of the prostate.

**12. What are the alternatives for treatment?**

At the time of diagnosis, prostate cancer may be confined to the prostate itself, or may have spread to other sites within the body. If prostate cancer is confined to the prostate and is amenable to curative therapies then there are a number of treatments available. The types of treatment that aim to destroy the whole prostate include surgery (radical prostatectomy), external beam radiotherapy, brachytherapy (small implanted radioactive seeds), cryosurgery (freezing) or HIFU. Active surveillance is also possible if the cancer is low risk. This means watching the cancer and giving treatment if the disease shows signs of progressing. The men who are suitable for this trial will all have low and medium risk disease, which is most often suitable for curative treatment. Your doctors will explain which standard treatments are suitable for you.

There are also other types of focal therapy that can be given – these are also usually part of a clinical trial.

The treatment outlined in this information sheet is experimental and is not standard practice.

**13. What are the side effects of any treatment received when taking part?**

One of the main aims from this trial is to find out how many side-effects this type of treatment causes. However, there is some evidence from small groups of men who have already been treated with NANOKNIFE and other focal therapy devices (such as HIFU and cryosurgery) that give us some indication of the rate of side-effects. These are only estimates and if you take part in this trial, you will help us to find out what the rate of side-effects could be.

Complications from NANOKNIFE

Complications from the treatment may occur from use of the device. Since use of NANOKNIFE treatment within the prostate is very limited, the side-effect risks are not yet fully known. However, the manufacturers of the NANOKNIFE have acknowledged the following possible complications:

Muscle contraction

Burn

Electrical shock

Temporary heart rhythm abnormalities (very short term, not requiring treatment)

Heart rhythm abnormalities (requiring treatment)

Heart attack

Slowed heart rate

Infection/Sepsis

Unintended tissue gets treated

Stroke

Death

Within the first clinical trials using NANOKNIFE, short-term heart rhythm problems have been described in a very small number of patients. Muscle contraction can occur more commonly, but muscle relaxant medication can be given during the general anaesthetic to reduce this risk. The other risks are thought to be rare.

Complications of the NANOKNIFE treatment may occur from treatment of the prostate in the form of ‘focal therapy’. We know more about the rate of these side-effects from treating men with focal therapy using other techniques, such as HIFU and cryosurgery.

Most patients report temporary urinary symptoms (frequency, urgency, difficulty in urination) during the first 1-2 months after focal treatment. Other complications are listed with the chances of them happening in brackets. These rates of side-effects are only guides because they are taken from other focal therapy studies:

- Urinary tract infection (1 in 20)

- Urethral stricture (narrowing in the urine passage) (1 in 50)

- No semen produced during ejaculation (dry climax) (1 in 2)

- Reduced amount and quality of semen during ejaculation in those men who do have wet ejaculation

- Reduced fertility even if semen is produced

- Epididymitis (infection of the tubes surrounding the testicles) (1 in 100)

- Urinary retention requiring surgery (1 in 100)

- Impotence (1 in 10-20)

- Urinary incontinence (leakage requiring pads) (1 in 100)

- Recto-urethral fistula (an abnormal connection between the rectum and urinary passage (1 in 500)

We believe that using NANOKNIFE, instead of other therapies like HIFU, to treat only part of the gland may mean fewer complications, because it is precise and may cause less surrounding tissue damage. However, we will only know the true extent of complications and the effectiveness of destroying the cancer cells after the study results have been analysed. If you have a repeat focal therapy treatment, or a different form of treatment afterwards, then the side-effect rates are likely to be higher. We do not know exactly by how much as there is not much experience in this.

**14. What are the other possible disadvantages and risks of taking part?**

Complications from the Contrast-agent Gadolinium during the MRI Scan

Gadolinium contrast is a solution injected into the vein to make cancers appear more clearly on the MRI. The use of gadolinium is very safe and widely used in clinical practice and not just for this study. Some complications occur and include:

- nausea and vomiting (less than 1 in 2,000)

- mild allergic reaction (e.g., rash, itching) (less than 1 in 250)

- moderate allergic reaction (less than 1 in 2,000)

- severe allergic reactions (breathing problems, face swelling) (less than 1 in 10,000)

## Complications from General Anaesthetic

## There are risks associated with undergoing any anaesthetic procedure.

- Nausea/vomiting after anaesthetic (less than 1 in 10).

- Most men will have a dry cough for an hour or two and may experience a sore throat for 24 hours. This occurs because a mask and/or tube are placed in the throat during the anaesthetic.

- Minor bruises from intravenous catheters (drips) are common.

- Occasionally extensive bruising, temporary hardening of the vein (phlebitis) or infection can occur from intravenous catheters (1 in 20).

- The known risk of death under anaesthesia in the UK is 1 in 150,000 anaesthetics. To put this in perspective, if we anaesthetised a volunteer every day for 400 years there would be one death.

Complications from Transperineal Prostate Mapping biopsiesThese include:

- Bloody urine for up to 48 hours (most men)

- Bloody semen for up to 3-4 months (most men)

- Bloody urine requiring admission to hospital with catheter tube drainage and washout of the bladder (1 in 50)

- Retention of urine requiring a temporary catheter (1 in 20)

- Prostatitis (inflammation or infection of the prostate, less than 1 in 100)

- Temporary pain/discomfort in the anal area (most)

- Temporary problems with erections for up to 6-8 weeks (most men)

- Infection requiring admission and intravenous antibiotics (rare)

Complications of having a Catheter (Suprapubic or Urethral)

These include:

- Discomfort (most)

- Infection of the wound site (1 in 100)

- Pain around the wound site (1 in 20 to 1 in 50)

- Urine leakage through the wound during or after the suprapubic catheter is removed (1 in 20)

- Injury to bowel requiring an open operation (rare)

If, during the course of this trial, we were to discover a condition of which you were unaware, we will inform you, and if necessary refer you to the relevant medical practitioner. If you have private medical insurance you should check with the company, before agreeing to take part in the trial, whether participation is considered a ‘material fact’ that should be reported. You will need to do this to ensure that your participation will not affect the medical insurance cover.

Please share this information with your partner if it is appropriate: it is not known if the study device will affect sperm or semen. It is possible that the sperm quality could be affected by participation in the study.  You should not assume that you will be infertile as the majority will not be affected. We think that ejaculation will be maintained but the study will help us find out.

**15. What are the possible benefits of taking part?**

The possible benefits from this treatment are that we may be able to treat only the part of the prostate that contains significant areas of cancer and therefore eliminate any active cancer tissue and reduce the risk of disease progression with fewer side-effects. We hope that you will personally benefit from NANOKNIFE therapy. However, this cannot be guaranteed. There may be a number of disadvantages to you by taking part in the trial, which are explained in section 8. The treatment may not treat all of the cancer, or you may have recurrence of the cancer later requiring further treatment.

The information provided in this information sheet should help you to decide whether you wish to undergo this experimental form of treatment.

**16. What happens when the research study stops?**

When the research study is completed, the results will be analysed. If the treatment has been shown to be safe and tolerable, the next step would be to run a larger trial in order to find out more about whether focal prostate cancer treatment with NANOKNIFE is effective over a longer follow-up period and whether the technique and results can be reproduced by other doctors. After this, we would compare the longer-term results of focal treatment with other standard treatments such as radiotherapy, surgical removal of the prostate or active surveillance in a large clinical trial.

**17. 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 have suffered will be addressed. The detailed information on this is given in Part 2.

**18. Will my taking part in the 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.

**19. Contact Details**

In the first instance, for further information or any concerns specifically about the study, please contact

Mr Massimo Valerio (Trial Doctor, University College Hospital London)

Tel: 0203 447 9194 (via Professor Emberton’s secretary)

E mail: Massimo.Valerio@uclh.nhs.uk

OR

Mr Neil McCartan (Trial Manager, University College Hospital London)

Tel: 0203 447 9404

E mail: [Neil.McCartan@uclh.nhs.uk](mailto:Neil.McCartan@uclh.nhs.uk)

You may also contact Professor Emberton (Urology Consultant) or Mr Hashim Ahmed via their office. The details will be given to you.

In an emergency it is best to contact your local GP or go to your local Casualty department or dial 999 for an ambulance. It is important that your GP and local hospital know whom they should contact for further information. Therefore, if possible in such a situation please take the above contact details with you.

For general enquiries or concerns about your care at University College Hospital London, please contact:

Patient Advice and Liaison Service (PALS)

Tel: Via hospital switchboard (0845 155 5000)

E mail: pals@uclh.nhs.uk

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.

**Part 2**

**20. What if relevant 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 research doctor will tell you about it and discuss whether you want to or should continue in the study. If you decide not to carry on, your research 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.

Also, on receiving new information your research 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.

**21. What will happen if I don’t want to carry on with the study?**

Your participation in the trial is entirely voluntary. You are free to decline to enter or to withdraw from the study any time without having to give a reason. If you choose not to enter the trial, or to withdraw once entered, this will in no way affect your future medical care. All information regarding your medical records will be treated as strictly confidential and will only be used for medical purposes. Your medical records may be inspected by competent authorities and properly authorised persons, but if any information is released this will be done in a coded form so that confidentiality is strictly maintained. Participation in this study will in no way affect your legal rights.

22. What if there is a problem?

Every care will be taken in the course of the study. However, in the unlikely event that you are injured by taking part, compensation may be available. If you suspect that the injury is the result of the Sponsor’s (University College London) or the hospital’s negligence then you may be able to claim compensation. After discussing with the research doctor, please make the claim in writing to Professor Mark Emberton who is the Chief Investigator for the research, and is based at University College Hospital London. The Chief Investigator will then pass the claim to the Sponsor’s Insurers, via the Sponsor’s office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

Regardless of this, if you wish to complain, or have concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced during your participation in the research, the normal National Health Service complaints mechanisms are available to you. Please ask your research doctor if you would like more information on this. Details can also be obtained from the Department of Health website: <http://www.dh.gov.uk>.

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

Our procedures for handling, processing, storage and destruction of their data are compliant with the Data Protection Act 1998.

Your data will be collected at each visit. Blood and biopsy results will be collected from UCLH NHS Trust computer database and your medical notes. The data will be held in both paper form and on secured laptop computers at University College Hospital London.

The data will be stored securely, in a coded manner so that no information that could identify you is held in study records. The controller for this data is University College Hospital NHS Trust. The custodian of this data who is responsible for the safety and security of the data is Professor Mark Emberton (Chief Investigator).

The data will be analysed and any results may be published in medical journals. The data will also help us plan larger trials using this form of treatment if it is successful. If the data is to be used in any other way in future studies then approval will be sought from the local Research Ethics Committee.

The following persons will have authority to view identifiable data:

- Professor Mark Emberton and Mr Hashim Ahmed (Chief Investigators)

- Miss Louise Dickinson and Mr Massimo Valerio (Trial Co-ordinators and Co-investigators)

- The trial specialist nurse and trial manager

The data will be retained for at least 10 years after the end of the study. All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital/surgery will have your name and address removed so that you cannot be recognised from it.

24. Involvement of your General Practitioner/Family doctor (GP)/Other Doctors

With your consent, your GP and other doctors not involved in the research but looking after you in this or another hospital will be notified of your participation in this study. If you will not consent for this then we cannot enter you into the trial as it is important that these doctors are aware of what treatment you have had for the prostate.

25. What will happen to any samples I give?

The trial PSA blood samples will be processed in the hospital laboratories as part of routine anaesthetic work-up or for follow-up after treatment. Samples are not kept for more than 2 days in the laboratory and no further tests are carried out on them. All these blood tests would occur if you were to undergo surgery or radiotherapy and are not extra samples taken just for this study.

The prostate biopsies you have taken will be processed and reported by the Department of Histopathology at University College Hospital London. After the biopsies are reported by a Consultant Histopathologist, no further test or studies will be carried out on the samples. Biopsy samples are normally stored following analysis according to Histopathology standard operating procedures in the NHS.

26. Will any genetic tests be done?

No genetic studies will be carried out as part of this study.

**27. What will happen to the results of the research study?**

The results of the study will be analysed and presented as publications for medical journals and at scientific meetings around the world. There will be no identifiable data in these publications. A summary of these results will be available for you and copies of full publications will also be available if you wish to have them.

**28. Who is organising and funding the research?**

University College London is sponsoring the study and is responsible for making sure it runs according to best research practice and relevant laws of the United Kingdom. The funding for this trial is being supported by a charity called Prostate Cancer UK, and by a commercial company called AngioDynamics. Funding is available only for the costs of the NANOKNIFE treatment, and to fund other trial support costs. Funding is not available for patient travel expenses unfortunately. The involvement of a commercial group will have no impact on your care and will be exactly the same as the trial is fully sponsored by a public body.

**29. Who has reviewed the study?**

The study has been reviewed by independent peers, who are doctors and researchers familiar with this type of treatment. Their suggestions have been included in the study plan. Ethics approval for the study has been sought and a favourable outcome given by the NRES Committee - Dulwich.

A copy of this Information Sheet will be given to you and if you decide to participate, a copy of the signed consent form will also be given. Please feel free to ask any questions to the Research Staff.

**Many thanks for taking the time to read this Information Sheet and considering taking part in our Study.**

Contact Details

Mr Massimo Valerio

Clinical Research Fellow / Trial Co-ordinator

Tel: 0203 447 9194 (via Professor Emberton’s secretary)

E-mail: Massimo.Valerio@uclh.nhs.uk

Professor Mark Emberton

Consultant Urological Surgeon/ Trial Chief Investigator

Tel: 0203 447 9194 (secretary)

Mr Hashim U. Ahmed

MRC Clinician Scientist/Trial Chief Investigator

Tel: 0203 447 9194 (secretary)