INSTITUTE: National Cancer Institute

STUDY NUMBER: 05-C-0241 PRINCIPAL INVESTIGATOR: Aradhana Kaushal, M.D.

STUDY TITLE: A Pilot Study of Image Guided Prostate and Pelvic Nodal Irradiation with Intensity Modulated Radiation Therapy (IMRT)

Continuing Review Approved by the IRB on 02/28/11
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Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Description of Research Study

You are being asked to take part in this study because you have cancer of the prostate and will be receiving radiation therapy. The purpose of this study is to deliver radiation just to prostate and the lymph nodes around your prostate that have the cancer. To do this we will use an MRI scan (Magnetic Resonance Imaging) that can better detect and localize cancer within your prostate gland. We may also perform a special MRI scan, called Dynamic Contrast Enhanced MRI (DCE-MRI), a medicine is injected into your veins and the MRI can measure how the medicine flows through your prostate gland. These measurements can tell us about the blood vessels in your prostate gland, which can also provide information about the cancer. In this study, you will undergo a procedure where needle biopsies from different parts of your prostate gland will be obtained during the MRI. The biopsy results will then be compared with the measurements from the MRI. This information will tell us where in the prostate gland your cancer is located. We will use this information to plan and deliver your radiation therapy. About 28 men will take part in this study.

Before you can start this procedure, we will do an evaluation to see if you are eligible to participate in this study. This will include a physical examination and blood laboratory and questionnaires that will assess your bowel, urinary and sexual functioning. The questionnaires will take approximately 15 minutes to complete and you may chose not to answer the questions that make you feel uncomfortable. The day before the procedure you will take an antibiotic, called Levofloxacin. Some antacids or other drugs may interfere with this antibiotic; please discuss this with your doctor. The morning of the procedure, you will have another dose of antibiotic and a small enema. We will place a needle in a vein in your arm to inject the MRI medicine.

The doctor will give you some local anesthetic into the area around the prostate to numb the tissues in that area and decrease any discomfort from the procedure. This may be done just before, or at the beginning the MRI procedure before the biopsies are obtained from your prostate. You will be taken to the MRI scanner and an antenna shaped like a tube will be placed in your rectum. The antenna provides a channel to take needle biopsies and obtain better pictures of your prostate gland. During the procedure you will need to lie very still on your stomach while MRI images are taken. During the scan, you may be asked to breathe carbogen air through a tube placed in your mouth. Carbogen contains high concentrations of both oxygen and carbon dioxide compared to room air. The doctor will use these scans to decide where to take the biopsies. For each of the biopsies, a needle will be placed through your rectum into your prostate gland while you lie in the MRI. Once the needle is in place, a small biopsy will be taken through the needle. This procedure will be repeated until 4-10 biopsies are taken. You will be lying still on your stomach for approximately one hour. The equipment has been specially made for this procedure and has been tested for safety. We will also observe you for any problems you might be having and will ask you to report any symptoms.

It is possible that up to four gold markers may be placed in the prostate gland during this procedure. These markers are about 1mm in diameter and are harmless and no longer painful after they are left in place. The markers will help us target the radiation treatments better and also will help us know where the biopsies were taken from if the prostate is removed.

When you are finished, you will be moved to a stretcher and transferred to a bed to recover. You will be able to get up in about 30 – 60 minutes and will be able to walk and urinate as your medication wears off. We will observe you for any problems you might have and you will be asked to report any symptoms. You will be able to go home the same day of the procedure, and may need acetaminophen, such as Tylenol or ibuprophen, such as Motrin if you have any pain. You will need to take another dose of antibiotic the day after the procedure.

Some patients may choose to repeat this biopsy procedure in the MRI during or after their treatment for prostate cancer. This step will help us find out whether the MRI test is still helpful after treatment.

Radiation therapy is usually given once a day, Monday through Friday, except for holidays. You will be lying on your back and each treatment takes about 10 minutes. You will then receive an 8 and half-week course of standard external beam radiation therapy using a newer form of radiation delivery called "intensity modulated radiation therapy" (IMRT). More radiation dose has been shown to be better when treating cancer localized to the prostate gland. Before IMRT, it was not possible to give more dose to the lymph nodes without giving the bowel so much dose that it caused severe symptoms. The use of IMRT will allow your doctor to increase the dose of radiation just to the areas of the lymph nodes around your prostate that appear on MRI and/or biopsy to have the cancer. During the course of this study the amount of radiation dose to these lymph nodes will be increased and it is possible that some lymph nodes may be receiving more radiation than is usually given as a standard dose. However, dose to the bowel will remain at standard levels. We will be closely

monitoring you for any side effects that may tell us if this is harming your normal tissues and you will be asked to report any bowel symptoms and to fill out questionnaires. Each week of your radiation treatment, we will also take an x- ray to check the position of the prostate and fiducial markers.

In all patients, before the start of radiation, a CT scan is done as a standard part of radiation treatment planning. In addition to this standard CT scan, the first 10 patients on this study will also have an additional 5 scans performed during the course of treatment. These additional scans are safe. These additional scans will allow us to make sure that it is safe to give higher doses to the patients in the second part of this study.

Once your radiation treatment is completed, you will return to the Radiation Oncology Clinic for follow-up visits after your radiation treatment at 2, 4 8, and 12 weeks and then at 6, 9, 12,18 and every 6 months for up to 36 months. At these times you will have a PSA blood test, a physical examination and will also be asked to report any bowel symptoms and to fill out questionnaires. The questionnaires will assess your bowel, urinary and sexual functioning and should take approximately 15 minutes to complete. You may choose not to answer any questions you are uncomfortable with.You will be removed from this study after 3 years. It is possible, but not guaranteed that you may be eligible for other protocols in the future. Your physician will discuss this with you.

Alternative Approaches or Treatments

You may choose to not participate in this study. Alternatives to this study include receiving the appropriate standard treatment for your prostate cancer. Standard treatments for your condition may include the following: 1) external beam radiation, 2) brachytherapy, 3) surgery, or 4) hormones. These treatments could be given either alone or in combination with each other. You may also choose to be treated at another facility.

Risks or Discomforts of Participation

Treatments often have side effects. It is possible that you may experience some, all, or none of the side effects described below. It is also possible that this combination treatment may cause some side effects that we cannot anticipate. For that reason, you will be watched closely while you are receiving treatment for any signs of unexpected side effects. The risks and discomforts of this research protocol are related to the normally expected risks associated with external radiation therapy for prostate cancer, and those expected for the placement of needles into the prostate through the rectum.

Biopsies can cause pain and bleeding. There is also a small risk (<0.5%) of developing an infection or complication requiring hospitalization although you will be receiving an antibiotic to prevent this.

Local Anesthesia for the procedure is provided with Bupivacaine, which is a medicine that is used routinely for prostate biopsies and rarely causes adverse reactions. At much higher doses this drug can cause restlessness, anxiety, dizziness, hearing changes, blurred vision and tremors, convulsions, seizures, decreased cardiac output, heart block, low blood pressure, heart arrhythmias, and cardiac arrest. You will have a chance to discuss these risks with your doctor.

MRI scans cannot be done on people who have a cardiac pacemaker, neural pacemaker, surgical metal clips in the brain or on blood vessels, cochlear implants, or foreign metal objects within the eye. At the time of your MRI, you will be asked about these things. When you are in the scanning machine, a feeling of claustrophobia may come over you, and there will be a repetitive thumping noise. Cool air will surround you, and the room is lit so you will not feel like you are in a cave or underground. It is important to remain still during the MRI scan. You may have some discomfort or feeling of heat from the tube placed in the rectum. If you are very claustrophobic in MRI scanners you may ask your physician for a mild sedative for the procedure. If you do this you will not be discharged until the sedation has sufficiently resolved and/or someone else is available to drive. You can notify the MRI technologist of any discomfort you feel. The medicine that is used for the injection may rarely (1:2000) cause an allergic reaction such as hives, shortness of breath, or low blood pressure. The medical personnel in the MRI room are prepared to treat you for this kind of reaction. If you participate in carbogen breathing during the MRI scan, a tube will be placed in your mouth that contains high concentrations of oxygen, called carbogen, and a clamp will be placed over your nose. Because the oxygen-risk gas (carbogen) contains carbon dioxide some people may feel short of breath while they breathe it. They are actually getting much more oxygen than is usually present in room air. We will monitor the blood oxygen with "pulse oximetry," which is a small device that clips over your finger, to make sure you are getting enough oxygen. If you feel you cannot tolerate breathing the gas you can simply spit out the mouthpiece and begin breathing room air. The feeling of shortness of breath will stop in a few seconds. The MRI study will be stopped any time you request.

Antibiotic therapy with Levofloxacin can cause nausea, diarrhea, vomiting, and abdominal pain. Bad taste in the mouth, restlessness, rash, sensitivity to sunlight and seizures are other possible side effects. If you are known to be allergic to this antibiotic or if you have a reaction to it, please let us know and a different one, such as Bactrim, will be prescribed.

Blood drawing may include pain, swelling, or bruising at the needle puncture site. These are expected and temporary. In addition, there is a very small risk of fainting or of infection at the needle entry site.

Fiducial Maker Placement can cause pain and bleeding. There is also a small risk of developing an infection although you will be receiving an antibiotic to prevent this.

Radiation Therapy can cause tiredness, skin reddening, and inflammation. The most common side effects of radiation to the prostate are cystitis (an inflammation of the urine system or bladder) causing frequent, painful, or urgent urination, and proctitis (an inflammation of the rectum) causing diarrhea, painful bowel movements, bleeding or increased gas. These side effects can be treated with medications and comfort measures if they occur and usually resolve over time after the radiation therapy is finished.

Long-term or chronic side effects from radiation for prostate cancer do not usually occur, but they may include: increased gas, frequent urination, difficulty urinating, impotence, and infertility. Less common long term side effects can include discomfort in the prostate area, bleeding from the rectum or bladder, leakage of urine or bowel movements. Rare or extremely rare long-term side effects can include swelling of the legs and genital organs, injury to the hips or other bones, or new tumors caused by radiation.

The side effects listed above are the same as those for standard external beam radiation therapy for prostate cancer. However, because we will be using larger doses to the lymph nodes that actually have cancer, it is possible that the side effects listed here may occur more frequently or be worse than they would be with standard external beam therapy.

Potential Benefits of Participation

If you agree to take part in this study there may or may not be direct medical benefit to you, but you will be receiving treatment for your prostate cancer. By placing the fiducial markers into your prostate gland, we hope that the radiation can be better aimed at your prostate. In addition, the information learned from this study may benefit other patients with prostate cancer in the future.

Research Subject's Rights

Participation in this research study is voluntary and you can withdraw at any time. We encourage you to ask questions so you can make the most informed decisions during your participation in this study. Refusal to participate will not result in penalty or less benefits to which you are otherwise entitled.

It is important to stress that being in this protocol does not promise long-term medical care here at the NIH Clinical Center. If there is no further research study that is suitable for you and your state of disease, or if you are not currently on another research study, you will be returned to the care of your referring doctor or institution, or alternative sources of care closer to your home. If you have any questions about your treatment at NIH, you can contact the Principal Investigator, Dr Aradhana Kaushal (301-496-5457), the study chairpersons, Dr. Peter Pinto (301-496-6353) or the patient care representative (301-496-2626).

All possible attempts will be made to maintain confidentiality of information concerning participants on this research study. Names of participants or material identifying participants will not be released without permission except as required by law. Patient medical records related to this research may be reviewed by qualified representatives of the National Cancer Institute or the Food and Drug Administration. Information regarding the safety and efficacy of the results of this study may also be published in scientific journals. It will not be possible to identify you specifically in any publication that results from this study.

Associate Investigators of the research team have developed the device being used in this research and hold a patent on it. This means that it is possible that the results of this study could lead to payments to an NIH or non- NIH scientist involved in the research. By law, government scientists are required to receive such payments for their inventions. You will not receive any money from development of the device.

Optional Studies:

We would like to keep some of the biopsy specimen(s) that is collected for future research. These specimen(s) will be identified by a number and not your name. The use of your specimen(s) will be for research purposes only and will not benefit you. It is also possible that the stored specimen(s) may never be used. Results of research done on your specimen(s) will not be available to you or your doctor. It might help people who have cancer or other diseases in the future.

If you decide now that your biopsy specimen(s) can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your specimen(s). Then any biopsy specimen(s) that remain will be destroyed.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial each answer that is right for you. No matter what you decide to do, it will not affect your care.

1. My biopsy specimen(s) may be kept for use in research to learn about, prevent, or treat cancer.

_____Initials Yes No

2. My biopsy specimen(s) may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease or heart disease).

_____Initials Yes No

3. Someone may contact me in the future to ask permission to use my biopsy specimen(s) in new research not included in this consent.

_____Initials Yes No

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator Aradhana Kaushal, M.D., Building 10 CRC, Room B23500, Bethesda, MD 20892, telephone (301) 496-5457 If you have any questions about the use of your tissue for future research studies, you may also contact the Office of the Clinical Director, telephone: 301-496-4251.

You may also call the Clinical Center Patient Representative at (301) 496-2626.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM FEBRUARY 28, 2011 THROUGH FEBRUARY 27, 2012.

Signature of Investigator _____ Date _____ Signature of Witness _____ Date _____

Print Name _____ Print Name _____