INSTITUTE: National Cancer Institute

STUDY NUMBER: 14-C-0140 PRINCIPAL INVESTIGATOR: Maria Liza Lindenberg, M.D.

STUDY TITLE: A Pilot Study of ^{18}F-DCFBC PET/CT in Prostate Cancer

Continuing Review Approved by the IRB on 04/25/16
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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.

Why is this study being done?

Prostate cancer is the second leading cause of cancer deaths in American men. Currently there are not many options available to image this type of cancer. In this study we will use an experimental radiotracer called, ^{18}F-DCFBC, to see if it can identify sites of prostate cancer in you.

Why are you being asked to take part in this study?
You are being invited to take part in this research study because you have prostate cancer that has been newly diagnosed, relapsed, or has spread outside the prostate gland.

How many people will take part in this study?
Up to 125 men will be included in this study.

Description of Research Study

This research will determine if the experimental radiotracer, ^{18}F-DCFBC, can identify sites of prostate cancer in the body. The study participants will be divided into 3 groups. The first group will be patients with cancer only in the prostate. The second group will be patients who have had their prostate removed or had radiation therapy and now have a rising PSA without other evidence for disease. The third group will be those patients with verified metastatic disease. All patients will be imaged with ^{18}F-DCFBC. Subjects in the first group of patients will have a MRI performed. If you are in the third group of patients you will also be imaged with ^{18}F-NaF for evaluation of bone disease.

What will happen if you take part in this research study?

Before you begin the study, screening labs requiring about 3 teaspoons of blood, and a limited physical exam and medical history will be done. Your doctor will review all the eligibility requirements to ensure you meet all the criteria before you enter the study. If you are determined to be eligible for this study, you will then be scheduled to return for the study injection and imaging scans.

Imaging Studies (Scans)

For subjects in group 1 only:

MRI Imaging

An MRI scan will be performed on a 3 Tesla magnet in the Molecular Imaging Clinic. "Tesla" is the unit of magnetic field strength. There are no known health effects from MRI scanning at any field strength including 3 Tesla, which is the highest strength magnetic currently in routine clinical use. MRI does not use any ionizing radiation (such as x-rays). In order to better see your prostate with MRI, a tube, known as an endorectal coil, will be placed in your rectum. Additional coils may be wrapped around the outside of your pelvis to further improve the quality of the scan. The MRI scan usually takes 75-90 minutes. You will need to lie still on the scanning table during that time. An intravenous line will be started and a contrast agent called Gadolinium chelate will be injected. This provides additional information about your prostate. Gadolinium chelate is FDA approved and is routinely used in MRI exams with very few side effects. You will receive more information about your MRI scan when you visit the Molecular Imaging Clinic and you may ask questions at any time. In addition, you should ask your doctor any questions you have concerning this study**.**

PET/CT Imaging

For subjects in group 1 & group 2:

You will receive an IV injection of ^{18}F-DCFBC over 10-20 seconds. A dynamic PET/CT will be performed immediately after the ^{18}F-DCFBC injection. This scan will last about 45 minutes. About an hour from the 18F-DCFBC injection, a whole body PET/CT will be performed. This scan will last about 50 minutes. Approximately 2 hours from the ^{18}F-DCFBC injection the last whole body PET/CT scan will be done. The scan will also last about 50 minutes.

For subjects in group 3 only:

You will receive an IV injection of ^{18}F DCFBC over 10-20 seconds**.** A whole body PET/CT will be performed about 1 hour after the ^{18}F-DCFBC injection. This scan will last about 50 minutes. Another whole body PET/CT will be done approximately 2 hours from the ^{18}F-DCFBC injection. This scan will also last about 50 minutes.

For subjects in group 2 only who have had their prostate gland removed:

A urinary catheter will be inserted into your bladder if needed, to improve our ability to view your bladder and the nearby anatomy during PET/CT imaging. The catheter will be attached to an irrigation system that allows for continuous rinsing and drainage of your bladder.

The urinary catheter is a thin hollow tube that is placed into the bladder to drain urine from your bladder. This tube has 3 separated channels within it. One channel allows for the urine to drain from the bladder into a fluid collection bag. The second channel has a valve on the outside end and connects to a balloon at the tip of the catheter. The balloon is inflated with sterile water to keep the catheter in place. The third channel allows for fluids to be put into your bladder. If you cannot tolerate this type of urinary catheter, we will use a catheter with 2 separate channels that only allows for drainage of urine from bladder. If you are not able to tolerate catheter placement, you will be asked to urinate frequently during the procedure.

The male urethra is long compared to the female urethra. A catheter is placed while lying down. The urethra and the surrounding areas are cleaned with a cotton-ball dipped in antiseptic solution. Beginning at the urethra, the cleansing is performed in a circular motion, moving outward to the surrounding areas. The urinary catheter, lubricated with water-soluble jelly, is inserted into the bladder through the urethra. Once the catheter is passed, the balloon is in the bladder. It is then slowly inflated with about 10cc of air using a syringe. Inflating the balloon should not be painful. At this time, urine, if present in the bladder, should flow back through the catheter and into the sterile drainage bag.

For subjects in group 3 only:

For patients in group 3 with known metastasis, an additional PET/CT scan with **^{18}**F-NaF will be performed to evaluate bone disease within 21 days of the ^{18}F-DCFBC PET/CT.

Patients in group 3 will also be asked to repeat the ^{18}F-NaF PET/CT and ^{18}F-DCFBC PET/CT. These will scans will be performed 4-6 months after the initial scans.

PET/CT Imaging Session:

During this scanning procedure, you will be asked to lie on your back on the scanner table and a low dose transmission CT scanner will be performed. It is important that you remain very still during these scans. The entire imaging session is expected to take not more than 3 hours and breaks will be permitted as needed. Interval monitoring of vital signs and for possible adverse events will be performed through the study.

When you are finished with each imaging scan, a member of the study team will contact you within 1-3 days for follow-up.

PET/MRI Imaging Session:

During this scanning procedure, you will be asked to lie on your back on the PET/MRI scanner table and PET/MRI imaging of your whole body will be performed simultaneously. It is important that you remain very still during these scans. In order to better see your prostate with MRI, a tube, known as an endorectal coil, may be placed in your rectum. Additional coils may be wrapped around the outside of your pelvis to further improve the quality of the scan. The entire imaging session is expected to take about 1 hour.

Prostatectomy: (group 1 only)

If you are in group 1 you may have surgery (a procedure called a prostatectomy) to remove your prostate gland or a biopsy to remove some prostate tissue. This procedure will be standard of care and is not a part of this protocol. Tissue collected during your surgery to remove your prostate will be evaluated at NIH just as it would be if you were not participating in this trial.

Birth Control

Due to the unknown effects on sperm or the fetus, it is advisable to practice careful contraception. If you are a male with a female partner who has the ability to get pregnant, you must agree to use a barrier method of birth control during the study and 2 months following the injection of the study agent. Your partner must also agree to use another method of birth control while you are on the study.

If you think that your partner is pregnant, you should tell your study doctor or nurse at once.

Effective forms of birth control include:

- Abstinence
- Intrauterine device (IUD)
- Hormonal [birth control pills, injections, or implants]
- Tubal ligation
- Vasectomy

Alternative Approaches or Treatments

There are no alternative approaches or treatments. You are not required to participate in this study. If you decide not to participate, it will not alter your planned treatment.

What other choices do I have if I do not take part in this study?

You are not obligated to participate in this study. If you decide not to participate, it will not alter your planned treatment**.**

Risks or Discomforts of Participation

What side effects or risks can I expect from being in this study?

Risks of MRI (For subjects in group 1 only)

Having an MRI requires that you lie still with part of you or all of you inside a tube shaped machine for about 45 minutes to an hour. Even with the ear plugs we give you it can be noisy with loud clicking and thumping sounds, which bothers some people. Some people may feel 'closed in' or 'trapped' (even though they are being closely watched and are quite safe). This is called claustrophobia. Cool air will surround you, and the room is large and brightly lit to help avoid claustrophobia. You may ask your physician for a mild sedative for the procedure if you think it will help. If you take a sedative you must not drive a vehicle until it wears off after the MRI.

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.

Risks from Gadolinium

Gadolinium has been generally safe when given to people as a contrast agent for MRI scans. Side effects from Gadolinium may occur in this trial. If they do happen it is usually right around the time of injection, which is why you will be closely watched at that time, and promptly treated if necessary. These effects include:

- coolness in the arm during injection
- whole body allergic reactions, which can range from mild to serious or life threatening (this is called anaphylaxis),
- low blood pressure, which can lead to becoming unconscious (fainting, passing-out)
- feeling hot, nausea, headache

Potential discomforts from the IV and injection of the radiotracer include

- Mild pain and possible bruising at the injection site,
- Discomfort from lying on a hard surface for about 90 minutes.
- Infection at the IV site or infection in the blood
- Leaking of the dose of ^{18}F-DCFBC into the skin and tissue around the IV
- Allergic reaction
- Vasovagal reaction, a lowered blood pressure and heart rate during the IV insertion

Risks of Urinary Catheter Insertion

- The balloon can break while the catheter is being inserted. In this case, the catheter and all of the balloon fragments are removed.
- The balloon does not inflate after it is in place. The balloon inflation is checked before inserting the catheter into the urethra and if it does not inflate after its placement into the bladder, it is removed and another urinary catheter is inserted.
- Urine stops flowing into the bag. This is usually corrected by adjusting the positioning of the catheter and bag to allow urine flow within the catheter tube.
- The urethra begins to bleed. A small amount of bleeding can be caused by irritation. This will be monitored
- The urinary catheter may introduce an infection into the bladder. The risk of infection in the urine increases with the number of days the catheter is in place.
- If the balloon is opened before the urinary catheter is completely inserted into the bladder, bleeding, and damage to the urethra can occur. To avoid this, the balloon is not inflated until the catheter is in the bladder.
- Bladder spasms can occur when a catheter is placed. This is a sudden intense urge to urinate and can be painful. Often, urine will leak around the outside of the catheter when a spasm occurs. Medication can be prescribed for bladder spasms.

Radiation Exposure:

You will receive a small amount of radiation exposure that you would not otherwise receive. Radiation exposure is **not** necessary for your medical care and is for research purposes only.

Using the standard way of describing radiation dose, from participating in this study subjects in groups one and two will receive one ^{18}F-DCFBC PET/CT imaging session. The activity of F18 FDCFBC is 8 mCi. Subjects in group one and two will receive up to 2.4 rem of radiation per year. Subjects in group three with known prostate cancer metastasis will undergo up to two ^{18}F DCFBC PET/CTs and two ^{18}F NaF PET/CTs. The activity of F18 NaF is 3 mCi. The subjects in

this group will receive 5.9 rem of radiation per year which exceeds the NIH Radiation Safety Committee's guidelines of 5.0 rem per year for adults.

This calculated value is known as the "effective dose" and is used to relate the dose received by each organ to a single value. For comparison, the average person in the United States receives a radiation exposure of 0.3 rem per year from natural background sources, such as from the sun, outer space, and from radioactive materials that are found naturally in the Earth's air and soil.

The effects of radiation exposure on humans have been studied for over 60 years. In fact, these studies are the most extensive ever done of any potentially harmful agent that could affect humans. In all these studies, no harmful effects were ever observed from the levels of radiation you will receive by taking part in this research study. However, scientists disagree on whether radiation doses at these levels are harmful. Even though no effects have been observed, some scientists believe that radiation can be harmful at any dose - even low doses such as those received during this research.

If you would like more information about radiation and examples of exposure levels from other sources, please ask the investigator for a copy of the pamphlet called, An Introduction to Radiation for NIH Research Subjects. Please tell your doctor if you have taken part in other research studies or received any medical care at the NIH or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. Consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body.

Results from the ^{18}F-DCFBC PET/CT will be discussed with your NIH physician but is not intended for management decisions in your care. The ability of this agent to image the prostate in humans is not known and the scan may show findings that are different from the MRI.

One Year Follow-up Period

We will collect information related to your prostate cancer for one year after the completion of your last DCFBC PET/CT scan. We will contact you and/or your treating physician to collect PSA levels and prostate cancer related medical history, biopsy results, and imaging study results (reports and CD copies of the imaging studies).

Potential Benefits of Participation

Are there benefits to taking part in this study?

Since this an imaging study and NOT a treatment protocol, there are no direct benefits, although the knowledge gained from this study may help others in the future who have cancer.

Research Subject's Rights

What are the costs of taking part in this study?

If you choose to take part in the study, the following will apply, in keeping with the NIH policy:

- You will receive study treatment at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- Medicines that are not part of the study treatment will not be provided or paid for by the Clinical Center, NIH.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Cancer Institute Institutional Review Board
- The study Sponsor, the NCI, or their agent(s).

A description of this clinical trial will be available on http://www.Clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most the Web site will include a summary of the results. You can search this Web site at any time.

Stopping Rules

Your doctor may decide to remove you from this study for the following reasons:

- if he/she believes that it is in your best interest
- if you have side effects from the imaging agent that your doctor thinks are too severe

In this case, you will be informed of the reason why you are being taken off this study.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to NCI or designated representatives. If you withdraw your consent and leave the trial, any samples of yours that have been obtained for the study and stored at the NCI can be destroyed upon request. However, any samples and data generated from the samples that have already been distributed to other researchers or placed in the research databases cannot be recalled and destroyed.

Conflict of Interest

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a Protocol Review Guide. You may ask your research team for a copy of the Protocol Review Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines but they do not need to report their personal finances to the NIH.

Members of the research team working on this study may have up to $15,000 of stock in the companies that make products used in this study. This is allowed under federal rules and is not a conflict of interest.

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, Maria Liza Lindenberg, M.D., Building 10, Room B3B402, Telephone: 301- 443-0604. 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 APRIL 25, 2016 THROUGH APRIL 24, 2017. _____ _____ _____ _____ Signature of Investigator Date Signature of Witness Date _____ _____ Print Name Print Name	