PRINCIPAL INVESTIGATOR: Deborah Citrin, MD

STUDY TITLE: Phase I Trial of Image Guided Focally Dose Escalated Prostate SBRT for Locally Recurrent Prostate Cancer after Prior Radiotherapy

STUDY SITE: NIH Clinical Center

Cohort: Affected patient

Consent Version: 05/24/2023

WHO DO YOU CONTACT ABOUT THIS STUDY?

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This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. 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). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Prostate cancer is the second leading cause of cancer death in American men. Radiation of the prostate is an effective therapy for localized prostate cancer. Although most patients are cured of their prostate cancer with radiation treatments, some patients will develop an elevation of PSA in their blood after radiation, which can indicate that the prostate tumor has returned. In this study, we will use prostate cancer imaging studies to detect where the cancer is within the body. If the cancer is limited to the prostate or nearby, we will use this information, along with a special MRI

study and biopsies of the prostate to determine which parts of the prostate have recurrent cancer. We will use this information to target the radiation to the area where the tumor has returned. In this study, we will determine the maximum dose that can be safely delivered to the area of recurrent tumor in the prostate with a highly focused (localized) type of radiation which is given in only 5 treatments, known as stereotactic body radiation therapy (SBRT).

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 recurrent prostate cancer after prior radiation therapy and no evidence of distant metastatic disease.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 46 men will be included in this study.

DESCRIPTION OF RESEARCH STUDY

This study will evaluate the maximum tolerated dose and side effects of focal radiation with stereotactic body radiation therapy (SBRT) in participants with a local recurrence of prostate cancer after prior radiation treatment. All participants included in this study have had radiation of the prostate and now have a rising PSA that means their prostate cancer is growing again. The goal is to develop a treatment for recurrent prostate cancer after radiation that is tolerable and potentially curative.

Participants with evidence of recurrent prostate cancer in the prostate gland on MRI imaging and/or 18F-DCFPyL, a research imaging study, will undergo biopsies to confirm that the prostate cancer has reappeared in the prostate gland. Participants with recurrent prostate cancer in the prostate gland will receive a highly-focused type of radiation, known as stereotactic body radiation therapy (SBRT), that will be given over two weeks. This treatment is given with a special technique that allows the radiation to be focused very carefully so that higher doses can be given with each treatment. The study participants will be divided into two groups (called Cohorts): Cohort 1will include participants that were treated with prior external beam radiation therapy for treatment of their prostate cancer and have developed a rising PSA. Cohort 2 will include participants with prior brachytherapy of the prostate, regardless of whether it was given alone or in combination with external beam irradiation. All participants will receive focal (localized) radiation to the area in the prostate that is found to have cancer on MRI of the prostate and a separate research imaging study known as 18F-DCFPyL. Participants who received prior brachytherapy will also receive a lower dose of focused radiation aimed at the entire prostate gland since the brachytherapy seeds can make it hard to see small tumors on MRI.

WHAT WILL HAPPEN IF YOU TAKE PART IN THIS RESEARCH STUDY?

BEFORE YOU BEGIN THE STUDY

Before you begin the study, screening blood tests requiring about approximately 3 teaspoons of blood for routine tests, and a comprehensive physical exam and medical history will be done. You will be asked to complete imaging studies, such as an MRI of the prostate, to look for tumor in your prostate gland.

We may access data in your medical record that was collected under other protocols and use it for research in this study, so you do not have to repeat procedures/tests. Medical records for assessments performed at outside facilities may be collected.

MRI of the prostate

In order to look carefully at your prostate and identify the area that may have recurrent prostate cancer, you will also undergo a prostate MRI if you have not had one at the NIH very recently. 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. The entire prostate MRI imaging session is expected to take about 1 hour.

You may also be asked to have additional studies, such as a bone scan and a sodium fluoride PET/CT scan, a very sensitive bone scan, to make sure you do not have prostate cancer that has spread outside of the prostate area. Your doctor will review all of the blood tests and x-rays in addition to your previous treatment records to ensure you meet all the criteria before you enter the study. If you are determined to be eligible for this study, and you wish to participate, you will then be scheduled to return for the imaging studies that will help guide the radiation treatment.

Brachytherapy

Brachytherapy is NOT given to participants on this research study, but many of the participants who are eligible to receive treatment on this study will have had brachytherapy in the past for treatment of their prostate cancer. Brachytherapy for prostate cancer is a type of radiation treatment. During a brachytherapy procedure, small radioactive seeds are placed into the prostate gland using needles. These radioactive seeds give off radiation from inside the gland and treat the prostate cancer. Most brachytherapy treatments use permanant seeds, meaning that the radioactive sources stay in the body and are not removed. Over time these radioactive sources use all of their energy and are no longer radioactive.

DURING THE STUDY

Imaging Studies (Scans)

PET/CT Imaging

A special type of PET scan, known as a 18F-DCFPyL PET/CT will be used to help determine the locations of prostate cancer in your body. It is possible that this scan may show us areas that are different or similar to those seen on other imaging studies. It is also possible that your tumor will not be seen with this special scan. When you have this scan, you will receive an IV injection of 18F-DCFPyL over 10-20 seconds. Approximately 1-2 hours after the 18F-DCFPyL injection a PET/CT scan will be done. The scan will last about 50 minutes. During this scanning procedure, you will be asked to lie on your back on the scanner table and a low dose transmission CT scan will be performed. It is important that you remain very still during these scans.

Biopsy and Fiducial marker placement

To receive SBRT to the prostate on this study, small metal seeds, known as fiducials, must be placed into your prostate to provide the most accurate radiation treatment. Fiducials are commonly implanted into the prostate as part of standard radiation treatments. The implanted fiducials are placed in the prostate gland and left permanently. These markers allow the treatment to be given

only when the fiducials are in the correct location, meaning that the prostate is also in the correct location. This is very important because the prostate can move due to breathing, gas in the rectum, filling of the urinary bladder, and movement of stool. Using the fiducial markers allows the amount of tissue treated with radiation to be reduced because the radiation oncologist can be more certain where the tumor is during treatment. When the fiducials are implanted into the prostate, biopsies of the prostate will also be obtained to confirm that the areas in the prostate thought to have tumor on your imaging studies (MRI, 18F-DCFPyL PET/CT) do have tumor, and that areas of the prostate that will not be treated do not have tumor. If you have had fiducials implanted in the past, you will not need to have new ones implanted unless your study doctor considers it necessary. Additional biopsies for research (maximum of three samples from each tumor) will be collected at the same time.

The biopsy will be taken through a needle put through the skin or rectum into your tumor. After the procedure, the nurses will watch your blood pressure and other vital signs. Any biopsy or surgical material obtained from you will undergo routine evaluation by a pathologist. The biopsy specimen will also undergo research evaluation either at NIH or at another site. Your personal information will always be kept confidential and you will only be identified by a code number.

You may receive conscious sedation before undergoing a biopsy, if needed. Conscious sedation is usually given to help someone relax and minimize discomfort. It can be given as a pill, a shot, an IV (intravenous catheter, a small plastic tube that is put into a vein, usually in your arm) or even inhaled. You may have to wait up to an hour to start feel the effects depending on how it is given. Once it takes effect, you will be mostly awake, though relaxed or drowsy. You will be monitored throughout the procedure.

Treatment planning

About one to two weeks after the fiducials have been placed in the prostate gland, you will undergo a radiation treatment planning CT scan in the radiation oncology department, also known as a treatment simulation. During the procedure, you may be asked to use an enema or take special medication to clear your rectum to ensure it is empty. You will also be asked to drink water and to keep your bladder full for the scan. At this time, small marks will be made on your skin with permanent marker that will be used to help set you up for radiation treatments. After the planning CT scan, you will be provided with an appointment to return for your first radiation treatment.

Before your first treatment, you will also be asked to fill out several forms that ask about your urine function, bowel function, erectile function, and aspects of your mood (depression or anxiety). You will fill out these same forms several times while on this study to help us learn how this treatment affects you.

Radiation treatments

You will then receive radiation treatments, using 5 separate doses of highly focused radiation over the span of two weeks. These treatments will be completed as an outpatient. You will drink water, similar to what was done for the planning scan, and you will be lined up very carefully on the table using the marks on your skin and the fiducial markers in your prostate. After each treatment, you are free to go home and continue your normal activities.

If you previously had radioactive seeds used for your radiation treatment, you will receive a lower dose to the entire prostate and a higher dose to the areas that appear to have tumor on imaging and biopsy. The lower dose to the entire prostate gland is used because the radioactive seeds that are left behind can make to harder to see tumor on MRI, which is used to plan the radiation treatments. If you were only treated with external beam radiation therapy during your previous treatment, only areas that have tumor on imaging studies and biopsy will receive the higher dose.

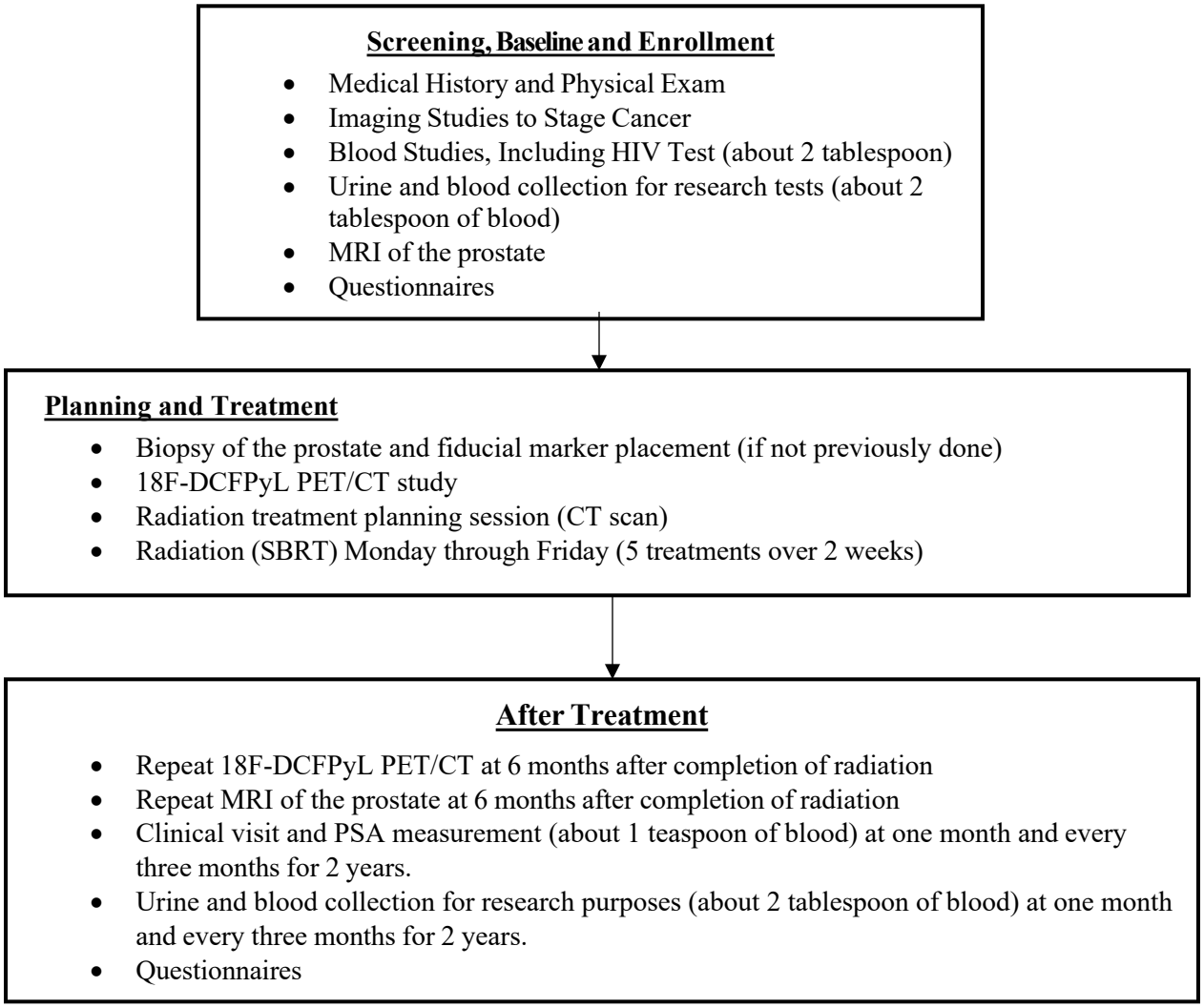
WHEN YOU ARE FINISHED TAKING THE DRUGS (TREATMENT)

After the treatment, you will return to the radiation oncology clinic for visits every three months to make sure that you are doing well and not having side effects. Some of these visits may be done with your local provider if you are unable to return to the NIH. If you have side effects from the treatment, we will try to help relieve them with medications if necessary. You will also fill out the same questionnaires that you filled out before the treatment that ask about your bladder function, bowel function, sexual health, and mood. At these visits, you will also have a physical examination and blood tests (about 2 tablespoon will be collected). Your blood PSA (about 1 teaspoon) will be measured and additional blood (approximately 2 tablespoon) taken for research studies.

At six months after the radiation is completed, we will repeat the 18F-DCFPyL PET/CT and MRI. If your prostate cancer was not visible on the first 18F-DCFPyL PET/CT, this study will not be repeated. This scan is being completed for research purposes, to help us learn if this study can be used as a way to follow prostate cancer that has already been treated. This study will not be used to change your care unless findings are confirmed on other studies (imaging studies, biopsy).

We will continue to see you for routine visits until two years after your treatment is completed. At that time, you will be removed from this protocol, but may be eligible for further care in the Radiation Oncology Branch on other protocols.

STUDY CHART



STANDARD OF CARE TREATMENT

When prostate cancer returns after prior radiation treatment, one option is to not undergo treatment (observation) unless the PSA starts to increase rapidly or there is evidence that the prostate cancer has spread outside the prostate (metastasized).

There are some participants who may be cured with treatment of the prostate after the tumor comes back there, but there is no guarantee that these treatments are effective and they may have significant side effects, usually involving bowel movements, urination, or erectile function. The potentially curative options include having the prostate removed (prostatectomy), although this is not commonly used and only performed at a few institutions in the United States. If the prostate cancer is only in the prostate, some doctors would offer reirradiation with brachytherapy (radioactive seeds). Some participants can also be treated with cryotherapy, where the prostate is frozen. Each of these potentially curative treatments can have lasting side effects and there is no guarantee that they will cure the disease.

Finally, many participants are treated with androgen deprivation therapy (hormones) to reduce rate of growth of the prostate cancer. Hormone treatments (androgen deprivation therapy) can be effective for prolonged periods of time, but are not considered curative.

BIRTH CONTROL

Because radiation can cause damage to sperm, it is advisable to practice careful contraception. If you have a female partner who has the ability to get pregnant, you must agree to use a barrier method of birth control during the study or for at least six months after the radiation treatment (and at least 2 months after the last 18F-DCPyL PET/CT). 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. Pregnant partners may be offered the opportunity to participate in a pregnancy registry protocol to provide data about the outcome of the pregnancy.

Effective forms of birth control include:

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

GENOMIC PROJECT RESULTS

We plan to perform genome and exome sequencing on your tissue samples and link this to your medical history. Your blood and tissue samples contain genes, which are made up of DNA (**d**eoxyribo**n**ucleic **a**cid) which serves as the "instruction book" for the cells that make up our bodies. Sequencing will determine the exact order of the base pairs (chemical letters) in the tumor being studied. Your sample(s), will help us study how genes influence the course of prostate cancer.

The analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing. Changes that we observe unrelated to our research may or may not be valid. Therefore, we do not plan to inform you of the results of testing on your specimens that is performed in our research lab. There may be exceptions to what we share with you and this is described later in this consent form in the section for “Return of research results.”

RISKS OR DISCOMFORTS OF PARTICIPATION

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

Risks of MRI

People are at risk for injury from the MRI magnet if they have some kinds of metal in their body. It may be unsafe for you to have an MRI scan if you have pacemakers or other implanted electrical devices, brain stimulators, some types of dental implants, aneurysm clips (metal clips on the wall of a large artery), metal prostheses (including metal pins and rods, heart valves, and cochlear

implants), permanent eyeliner, tattoos, an implanted delivery pump, or shrapnel fragments. Welders and metal workers may have small metal fragments in the eye. You will be screened for these conditions before having any MRI scan. If you have a question about metal in your body, you should inform the staff. You will be asked to complete an MRI screening form before each MRI scan you have.

In addition, all magnetic objects (like watches, coins, jewelry, and credit cards) must be removed before entering the MRI scan room.

People with fear of confined spaces may become anxious during an MRI. Those with back problems may have back pain or discomfort from lying in the scanner. The noise from the scanner is loud enough to damage hearing, especially in people who already have hearing loss. Everyone having a research MRI scan will be fitted with hearing protection. If the hearing protection comes loose during the scan, you should let us know right away.

There are no known long-term risks of MRI scans.

Risks of MRI Contrast (gadolinium)

The risks of an IV catheter include bleeding, infection, or inflammation of the skin and vein with pain and swelling.

Mild symptoms from gadolinium infusion occur in fewer than 1% of those who receive it and usually go away quickly. Mild symptoms may include coldness in the arm during the injection, a metallic taste, headache, and nausea. In an extremely small number, fewer than one in 300,000 people, more severe symptoms have been reported including shortness of breath, wheezing, hives, and lowering of blood pressure. You should not receive gadolinium if you previously had an allergic reaction to it. You will be asked about such allergic reactions before gadolinium is given.

People with kidney disease are at risk for a serious reaction to gadolinium contrast called "nephrogenic systemic fibrosis (NSF)". This condition always involves the skin and can also involve the muscles, joints and internal organs. NSF has resulted in a very small number of deaths. A blood test of your kidney function may be done within the month before an MRI scan with gadolinium contrast. You will not receive gadolinium for a research MRI scan if your kidney function is below the safe level.

Most of the gadolinium contrast leaves the body in the urine. However, the FDA has issued a safety alert that indicates small amounts of gadolinium may remain in the body for months to years. The long-term effects of the retained gadolinium are unknown. Some types of gadolinium contrast drugs are less likely to remain in the body than others. In this study, we will use the gadolinium contrast drugs that are less likely to remain in the body. We will also give you additional information called a "Medication Guide." Upon request, we will give you individual information about retained gadolinium we see on your studies.

Risks Associated with the 18F-DCFPyL PET Scans

The risks associated with the insertion of the IV include pain at the needle site, bruising, possible dizziness and lowered blood pressure if you stand up quickly, and possible inflammation of the vein or infection at the needle site. Care will be taken to avoid these complications.

Other side effects could include:

- Discomfort from lying on a hard surface for about 90 minutes during the PET scans.
- Infection in the blood
- Leaking of the dose of 18F-DCFPyL into the skin and tissue around the IV possibly causing inflammation at the injection site
- Allergic reaction

Even though we do not anticipate adverse side effects, you should tell the doctors or nurses supervising the scan of any discomfort you may have.

Risks from Radiation

Overall Radiation Risk

During your participation in this research study, your tumor will be exposed to 40 or 42.5 Gy of radiation aimed at the tumor in 5 treatment sessions if you are in arm 1. If you are in arm 2, your prostate will be treated with 30 Gy of radiation in 5 treatment sessions, and at the same time the tumor will receive 40, 42.5 or 45 Gy of radiation (delivered during the same 5 treatments). You will also receive a much smaller amount of radiation from 18F-DCFPyL PET/CT scans used to plan your treatment and measure your progress. The amount of radiation from these scans adds minimal additional risk to the higher radiation doses received in the course of treatment. This radiation has been reviewed by the NIH Radiation Safety Committee and deemed appropriate for this study.

Risks of Radiation Treatments

Radiation can cause both short and long terms side effects. Most of the short-term side effects of radiation resolve within a month or two after treatment. The long-term side effects may go away over time, may improve with treatment, or may be permanent. It is impossible to predict what side effects each participant may experience, but there are some side effects that may be possible based on the part of the body receiving treatment. During or shortly after the radiation treatment, you may have burning with urination, urgent urination, or more frequent urination (even at night). You may also notice hemorrhoidal irritation, more urgent or frequent bowel movements, or loose bowel movements. Some participants also have fatigue during or shortly after the treatment.

Most often, these short- term side effects improve over the first few months after treatment. Months to years after this treatment, there may be a chance of changes in urine or bowel function that could require medications for treatment, such as more frequent or urgent urination, difficulty urinating, and burning with urination. It is also possible to have irritation of the rectum, known as proctitis, that may cause more urgent or frequent bowel movements, or bleeding from the rectum. Other side effects could include a decline in erectile function. Uncommonly, more severe urine or bowel side effects could require a procedure or surgery to correct. Rarely, these treatments could cause severe damage to the bowel, bladder, or urethra that may require a surgery, hospitalization, or a temporary or permanent bag to drain bowel or urine. Other very rare side effects would be an increased risk of fracture in the bones of the pelvis or hip and a risk of a cancer caused by radiation in the area treated.

Risks from CT contrast

Itching, hives or headaches are possible risks associated with contrast agents that may be used during CT imaging. Symptoms of a more serious allergic reaction include shortness of breath and swelling of the throat or other parts of the body. Very rarely, the contrast agents used in CT can cause kidney problems for certain participants, such as those with impaired kidney function.

Risks Associated with the Tumor Biopsy

This procedure usually causes only brief discomfort at the site from which the biopsy is taken. Rarely, infection or bleeding may occur at the needle site. Biopsies are normally performed under the guidance of an imaging technique. Each procedure requires a separate consent prior to the biopsy. The risks may include:

- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.
- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other potentially serious complications from bleeding or organ damage may occur. These might require additional surgical intervention.

Risks Associated with Conscious Sedation

The common side effects of conscious sedation include drowsiness, delayed reflexes, hypotension, headache, and nausea. These are generally mild and last no more than a few hours.

Risks Associated with Blood Collection

Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people faint. The study team member may apply numbing cream to the area so that the needle stick will not hurt as much. It is expected that up to 4 and a half tablespoon of blood will be collected before you begin the study and up to 2 and a half tablespoon may be collected at each subsequent visit.

Risks Associated with Urine Collection

There are no known risks associated with urine collection.

Risks Associated with Questionnaires

The questions asked on the questionnaires may make you feel uncomfortable. You are not required to answer questions that you do not want to answer.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

The goal of this study is to see if using a very focused form of radiation, known as SBRT, can be effective at treating prostate cancer that has come back after radiation. Some small studies have found that 50% to 85% of patients treated with re-irradiation can have their PSA controlled long-term with this approach, which means they do not require additional treatment for their prostate cancer and may avoid chemotherapy or hormonal (androgen deprivation) therapy. We do not know if you will receive personal, medical benefit from taking part in this study. Because there is not much information about using this highly focused form of radiation for recurrent prostate cancer, we do not know if you will benefit from taking part in this study, although the knowledge gained from this study may help others in the future who have cancer.

ALTERNATIVE APPROACHES OR TREATMENTS

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

Instead of being in this study, you have these options:

- Alternatives can include no treatment, which most likely will result in increasing PSA values over time and growth of tumor. Eventually, there may be symptoms in the bowel or bladder relating to growth of the tumor. There may also be symptoms from spread of the prostate cancer to the bones or other organs.
- You may decide to have immediate or delayed treatment with systemic therapy, such as hormone treatment (androgen deprivation therapy), a treatment that lowers your body's production of testosterone, or chemotherapy.
- You may be a candidate for a prostatectomy after radiation. A urologist who routinely performs prostatectomy after radiation treatment can tell you if that is a reasonable option for you.
- You may also be treated with cryotherapy, a procedure in which part of the prostate is frozen to try to kill the tumor.
- You may be a candidate for brachytherapy of the prostate, another type of radiation.
- Each of these treatments may have different side effects depending on where the tumor has come back inside the prostate.
- You are not required to participate in this study and can pursue these other treatments if you would like.
- In addition to these treatments, there are a number of clinical trials testing alternative treatments in participants who have a tumor recurrence after radiation.

Please talk to your doctor about these and other options.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have

learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

In this study, we will use a test that looks at all or most of your genes or DNA. This test may find gene changes that are not related to what is being studied in this research. These are called "secondary findings". Most of the time when we look for these, we do not find anything. If we were to look for them in 100 people, we would expect them in only about 2 to 4 of those people.

If we discover a secondary finding that might be important to you or your family's health, we plan to tell you about this. However, before we can tell you, we may need to do the test again in another laboratory to be sure that the result is correct. To do so, we may need to ask you to submit another sample for testing. Once these results are available, we will invite you to schedule a visit, in person (at our expense) or remote so that you we can give you more information about this result and to help you seek follow-up care outside of the NIH if it is needed. If you are unable to see us, we will provide a referral to a local genetic healthcare provider. The NIH will not generally provide any further follow-up testing or care for this condition for you or your family.

We will not be testing the samples we have collected from you for several years. Because of this, just because you have not heard from us, you should not assume that you do not have any gene changes that might be important for your health.

We also do not know all the gene changes that cause can cause health problems. We could learn later that some gene changes that now we do not think cause health problems are of concern. We will look for gene changes only once and will look for those that are known to cause problems at the time we are looking. We do not plan to look again at a later time for new secondary findings.

It is up to you if you want us to tell you about any secondary findings. At any point you can tell us that you do not want to us to contact you or tell you about any secondary findings.

We can only provide these results to you. If you want us to tell anyone else, then you must provide us with a signed written release of medical information request.

It is very important for you to keep us updated on how to contact you. If we do not have up to date information, we will not be able to get in touch with you to collect an additional sample or tell you about a secondary finding. If your contact information changes, providing us with the new information is your responsibility. To tell us of your new contact information, by reaching out to your study doctor/principal investigator.

If you have questions or concerns about learning this kind of genetic information, please speak with someone from the study team.

Risks of returning secondary genetic findings

- The evaluation for unexpected gene changes is limited and may not be as complete as clinical genetic testing that might be available to you outside of the research study.
- If an unexpected gene change result is confirmed, then that test result will go into your NIH medical record. These documents are confidential, but other NIH investigators can see them.

- Learning about the changes in your genes could mean something about your family members and might cause you or your family distress. Before joining the study, it may be helpful to talk with your family members about whether they want you to share your results with them.
- If a gene change is found, it may reveal whether a particular parent passed on the change to a biological child.
- You may receive a result for an unexpected gene change that turns out not to cause that health condition. This may cause you unnecessary distress or lead to unnecessary medical testing risks and costs.

Benefits of returning secondary genetic findings

An unexpected gene change result may be useful because you may be able to do something about it to protect your health or to help you plan for your future.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

STOPPING THERAPY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease comes back during treatment
- if you have side effects from the treatment that your doctor thinks are too severe
- if new information shows that another treatment would be better for you
- if you lose your ability to provide informed consent

In this case, you will be informed of the reason therapy is being stopped.

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.

CONFLICT OF INTEREST (COI)

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

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

USE OF SPECIMENS AND DATA FOR FUTURE RESEARCH

To advance science, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. A researcher who wants to study the information must apply to the database and be approved. Researchers use specimens and data stored in scientific databases to advance science and learn about health and disease.

We plan to keep some of your specimens and data that we collect and use them for future research and share them with other researchers. We will not contact you to ask about each of these future uses. These specimens and data will be stripped of identifiers such as name, address or account number, so that they may be used for future research on any topic and shared broadly for research purposes. Your specimens and data will be used for research purposes only and will not benefit you. It is also possible that the stored specimens and data may never be used. Results of research done on your specimens and data will not be available to you or your doctor. It might help people who have cancer and other diseases in the future.

If you do not want your stored specimens and data used for future research, please contact us in writing and let us know that you do not want us to use your specimens and/or data. Then any specimens that have not already been used or shared will be destroyed and your data will not be used for future research. However, it may not be possible to withdraw or delete materials or data once they have been shared with other researchers.

Genomic Data Sharing

As part of this research study, we will put your genomic data in a large database for broad sharing with the research community. These databases are commonly called data repositories. The information in this database will include but is not limited to genetic information, race and ethnicity, and sex. If your individual data are placed in one of these repositories, they will be labeled with a code and not with your name or other information that could be used to easily identify you, and only qualified researchers will be able to access them. These researchers must receive prior approval from individuals or committees with authority to determine whether these researchers can access the data.

Summary information about all of the participants included in this study (including you) is being placed in a database and will be available through open access. That means that researchers and non-researchers will be able to access summary information about all the participants included in the study, or summary information combined from multiple studies, without applying for permission. The risk of anyone identifying you with this information is very low.

NIH policies require that genomic data be placed in a repository for sharing. Therefore, we cannot offer you a choice of whether your data will be shared. If you do not wish to have your data placed in a repository, you should not enroll in this study.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will not receive compensation for participation in this study.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

On this study, the NCI will cover the cost for some of your expenses. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. Someone will work with you to provide more information.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- If some tests and procedures are performed outside the NIH Clinical Center, 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 NIH Clinical Center.
- Once you have completed taking part in the study, medical care will no longer be provided by the NIH Clinical Center.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

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 NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- The study Sponsor NIH Clinical Center or their agent(s)

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that,

despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH 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 NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

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, Deborah Citrin, Citrind@mail.nih.gov, 301-496-5457. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

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

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness	Print Name of Witness	Date

NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.