PRINCIPAL INVESTIGATOR: Deborah Citrin, M.D.

STUDY TITLE: A Pilot Study of High Dose Rate Brachytherapy in the Radiation Oncology Branch

STUDY SITE: NIH Clinical Center

Cohort: Standard

Consent Version: 12/09/2020

WHO DO YOU CONTACT ABOUT THIS STUDY?

Principal Investigator:
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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?

The staff of the Radiation Oncology Branch Clinic and their collaborators are conducting a study in which people with cancer can receive a form of radiation therapy, called brachytherapy, which allows a more focused area of treatment. A more focused area of treatment should allow us to better direct the radiation to give more of the dose of radiation directly to the site of your cancer or cancer removal and less of the dose to the normal healthy tissue surrounding these sites. This is done by placing hollow implant device(s) into the area to be treated and then moving a radiation source into each. The type of device depends on your type of cancer and the site to be treated. These devices can range from hollow applicators, needles or balloon-like equipment. Brachytherapy is available as a non-investigational treatment at other radiation oncology facilities,

and enrolling in this study is not necessary to receive brachytherapy treatment. The purpose of this study is to determine the quality of the brachytherapy procedure here in the Radiation Oncology Branch.

WHY ARE YOU BEING ASKED TO TAKE PART IN THIS STUDY?

You are being asked to take part in this study because you have a cancer that can be treated with radiation. One of the standard ways of giving radiation is to combine external beam treatments with internal "brachytherapy" treatments. Brachytherapy means short-range radiation therapy and it is a way to give a high dose of radiation directly to your cancer or to the area where your cancer was removed.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 112 subjects will be enrolled in this study, which will be conducted at this site.

DESCRIPTION OF RESEARCH STUDY

Your participation in this study will require communication with your primary doctor. Before you begin the study, we need to establish that you have a primary medical or surgical oncologist in the community or at NCI who is willing to collaborate with the Radiation Oncology Branch staff in your clinical care while you are on this protocol.

Before you begin this study, you will need to have standard clinical exams and tests to make sure you are eligible for this study. We will need to have access to all of your medical records about your cancer, including pathology reports, prior treatments and radiographic imaging studies. You may need a CT scan for staging studies, depending on the site of your cancer. Then, we will do an evaluation to see if you are eligible to participate in this study. This will include a physical examination, blood laboratory studies, and a urine pregnancy test for women.

The standard therapy for your type of cancer may include chemotherapy with a combination of external beam irradiation and brachytherapy. You may receive chemotherapy and external beam irradiation from your primary oncologist in the community or at NCI. However, your brachytherapy implants will occur here at the Radiation Oncology Branch. Due to the individual needs and requirements of each type of cancer and each participant treated with brachytherapy on this protocol, the number of external beam days and brachytherapy treatments will vary. These slight differences will be discussed with you prior to the beginning of therapy and if necessary during therapy as well. You will also be asked to sign a separate procedure consent form for the radiation therapy that specifies your cancer type and details your treatment and side effects.

If you require external beam radiation treatment, it may be given at a cancer center closer to your home, provided arrangements can be agreed upon between your NCI doctors and your local radiation oncologist. In addition, precertification may be necessary for your insurance to cover this treatment and this is your responsibility to obtain. The NCI will not provide reimbursement for radiation therapy administered outside of the Clinical Center. To plan your course of external radiation treatment, you will have standard CT and/or MRI scans of your cancer site. 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 up to 30 minutes.

For each brachytherapy treatment, you will arrive in the Radiation Oncology clinic. If your hollow implant device was not already placed, for example during a prior surgical procedure, we will need

to insert it/ them before you can receive the brachytherapy. We may give you some medicines to relax you and to decrease any discomfort you may feel, or you may require anesthesia to prevent pain from the procedure. Your skin and/or the area to be treated will be cleansed with a solution to help kill any bacteria that may be present. We will then place the hollow implant device(s). Once the implant device(s) is/are in place, we may need to place some gauze or other material to hold them still and to help prevent movement. In some cases, additional studies may be needed to plan the brachytherapy treatment. If this is the case, you will then be transferred to the CT scanner on a stretcher. The CT scan is obtained in order to check placement of the catheters and to plan your brachytherapy treatment. If you are receiving prostate brachytherapy, an additional CT scan will usually not be required and an ultrasound will be performed instead.

We will then need to calculate the proper dose to deliver to your tumor, which may take a few hours. During that time you will remain on a stretcher in the radiation oncology clinic. When the calculations are finished, you will receive the radiation. The implant device(s) that were placed around your tumor or tumor removal site will be connected to a radiation machine called an "afterloader". Once you are connected to the afterloader, a thin wire that has the radioactive "source" material on its tip is inserted into each applicator and withdrawn a little at a time. This is when you are actually receiving the radiation treatment. The "source" is the actual radioactive material; in this case, it is a substance called Iridium. The treatment will take about 10-30 minutes. When you are finished you will not have any radioactive material in your body, nor will you be radioactive. You will then be disconnected from the afterloader. The applicators and gauze will be removed. We will monitor you for comfort as your medication wears off. This may take an hour or two. You should be able to leave for home from the clinic. However, if you have received anesthesia, you may be kept for an overnight stay in the hospital.

You will return to the Radiation Oncology Clinic for follow-up visits after your radiation treatment at 1, 3, 6, 9 and 12 months after the completion of radiation therapy. Follow- up evaluations will include: a history and physical examination, assessment of any side effects of radiation therapy you may be experiencing. In some cases, we will also repeat any imaging (i.e., CT, MRI, x- ray) that was done at baseline to follow your tumor response. In general, for prostate cancer, imaging is not required after brachytherapy because we can better follow the cancer with a blood test (PSA).

BIRTH CONTROL

If you are a woman who is breast feeding or pregnant, you may not take part in the study because we don't know how this medicine would affect your baby or your unborn child. If you are a woman who can become pregnant, or are the partner of a woman who can become pregnant, you will need to practice an effective form of birth control before starting study treatment, during study treatment. If you think that you or 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

RISKS OR DISCOMFORTS OF PARTICIPATION

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

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 treatment in combination with others you may be receiving may cause some side effects that we cannot anticipate. For that reason, you will be watched closely 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 and high dose rate brachytherapy.

Radiation Therapy, including Brachytherapy

The side effects of radiation therapy depend on the site that is treated. Because the side effects vary by the site receiving treatment, a separate consent will be signed that describes the particular side effects that you may experience from the treatment you receive.

In general, radiation can cause the following side effects regardless of the site that is being treated. These side effects tend to go away after the radiation therapy is completed. However, there are some long-term or chronic side effects that primarily affect the small bowel, liver, kidneys, and spinal cord. Many of these side effects take months to years to develop.

Likely

- Tiredness
- Lowered blood counts
- Skin reddening
- Mild ache at the site that received radiation

Rarely

- Treatment with radiation may also lead to developing other types of cancer, usually years after receiving the treatment.
- Depending on the sites receiving treatment, bleeding and damage of the treated tissue or surrounding tissue are possible.

If you are receiving chemotherapy or are scheduled to receive chemotherapy, it is important that you discuss this with the radiation oncologist. Certain chemotherapy drugs may increase the side effects that you experience from radiation. You should not receive certain chemotherapy drugs within two weeks before you receive the radiation or within four weeks after receiving the radiation. The principal investigator or a member of the research team will discuss this with your medical oncologist to determine if this would interfere with your care. If not giving chemotherapy would be inappropriate, alternative therapies including standard radiation treatments will be discussed with you.

Overall Radiation Risk

During a year in this research study, your tumor may be exposed to up to 15 Gy of radiation from High Dose Rate Brachytherapy. You will also receive a much smaller amount of radiation from scans used to plan your treatment and measure your progress. The total scans include up to 4 CT

scans. 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.

Hollow Implant Device

You may feel pain and discomfort from the implant and/or implant procedure.

Blood tests

Likely

- Sharp pricking pain at the needle puncture site.

Rarely

- A bruise may form at the needle puncture site. This will generally go away on its own without any treatment.
- There is a small risk of infection, fainting, or lightheadedness with this procedure.

Scans

MRI and CT, PET and Nuclear Medicine Scans are common standard imaging tests used in the diagnosis of cancer.

Likely

Discomfort is associated with the length of time you must lie still during a scan.

Occasionally, you may become uncomfortable with the closed space of the machines, particularly the MRI. If this occurs, your doctor can order a medicine to help you relax during this scan.

CT contrast

If a contrast agent (the special dye) is given with the scan there is a small risk of having a reaction to the contrast which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock or rarely, death. Common symptoms are nausea, pain in the vein where the contrast was given, a metallic or bitter taste in the mouth, and a warm or flushing feeling that lasts from 1-3 minutes. Rarely do these common symptoms require any treatment. In very rare cases, people have had severe reactions that affect their breathing and heart rhythm. If you have had a reaction in the past, be sure to tell your doctor or nurse about it. The study doctors will do a blood test prior to the to confirm that it is safe you to receive the contrast.

MRI scan contrast: Gadolinium

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 not 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.

Anesthesia

During the brachytherapy procedures, anesthesia can cause the following side effects. You will have a chance to discuss these risks with your anesthesia specialist and will sign a separate consent for the anesthesia.

Likely

- Nausea,
- Vomiting,
- Headache,
- Backache

Less likely but serious

- Blood pressure problems,
- Heart rhythm problems, breathing changes, drug reactions, paralysis, heart attack, stroke, or death.

POTENTIAL BENEFITS OF PARTICIPATION

Are there benefits to taking part in this study?

There are no direct medical benefits to you from taking part in this study. We hope the information learned from this study will benefit participants in the future.

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**:**

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly. Instead, it tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Please talk to your doctor about these and other options.

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 are no longer able to provide 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.

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 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 can**not** 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.

USE OF 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.

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. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides 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

Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your sample and health information. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you.

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 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, M.D, citrind@mail.nih.gov, 240-760-6206. 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 to the oral short-form consent process only:

Witness:

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: _____.