Official Title:	Radiation Enhancement of Local and Systemic Anti-Prostate Cancer Immune Responses
NCT number:	NCT03649841
Document Type:	Informed Consent Form
Date of the Document:	2/8/2021

University Of Washington
Seattle Cancer Care Alliance

Consent to take part in a research study:

RADIATION ENHANCEMENT OF LOCAL AND SYSTEMIC ANTI-PROSTATE CANCER IMMUNE RESPONSES

Principal Investigator: Jing Zeng, MD University of Washington; Fred Hutchinson Cancer Research Center. 206-598-4100

Emergency number (24 hours): 206-598-6190

Ask for the Radiation Oncologist on-call.

Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to study the effects of neutron radiation therapy on your immune system and whether it helps stimulate body's own immune system to help fight prostate cancer.

People who agree to join the study will be asked to attend 3-4 clinic visits over 6 months. The study involves physical exam, blood draw, optional tumor biopsy, routine blood test for prostate specific antigen (PSA) and CT scan.

We do not know if neutron radiation therapy would help stimulate a larger immune response inside the body in castration sensitive prostate cancer (CSPC) condition, and it could even make your condition/disease worse. Neutron radiation therapy could cause side effects such as fatigue, itchy skin, diarrhea, urinary irritation, rectal irritation, inability to have children etc. as described below in this form.

You do not have to join this study. You can choose to receive standard methods to treat CSPC instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

We invite you to join this research study.

We invite you to join this research study because you have CSPC. Up to 30 people will join this study.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in the study. You are free to say "yes" or "no", or to drop out after joining. If you say "no," you would have no penalty or loss of benefits. Whatever you decide, your regular medical care would not change.

Why are we doing this study?

We are doing this study to examine the effects of neutron radiation therapy on your immune system. Adding a short course of high intensity radiation early in the treatment course may improve the anti-tumor environment by acting as a "vaccine". Neutron radiation treatment has a higher relative biological effectiveness (RBE) compared to standard photon radiation, which essentially means the neutron radiation is more damaging than the standard radiation. Neutron radiation treatment is the experimental aspect of this research study. We want to know whether the radiation can help improve your treatment. Patients with metastatic prostate cancer often receive radiation for a variety of reasons, most commonly-

1) To help relieve a symptom caused by a tumor (such as a tumor in a bone causing pain); or
2) To help prevent a future problem that will be caused by a tumor (such as a tumor in a bone that can cause a bone fracture); or
3) To potentially help control the cancer by helping kill as many cancer cells as possible when there are only a limited number of metastatic sites in the body.

Therefore, it is currently clinical acceptable to both give radiation to patients with metastatic prostate cancer and to just give androgen deprivation therapy (ADT).

ADT is a standard treatment for CSPC. Your prostate cancer cells grow because of male hormones (androgens), so reducing levels of androgens would help combat and slow the spread of prostate cancer cells. Recent studies have shown that the addition of abiraterone (Zytiga®), a pill that blocks an enzyme your body requires to make testosterone, can improve survival compared to ADT alone. A steroid, called prednisone, must be taken with the abiraterone to reduce its side-effects. Not much is known about the immune system effects of abiraterone plus prednisone, but there is data that suggests abiraterone may create an immune response against prostate cancer.

There are 2 groups of participants in this study. We will give different treatments to different groups, and compare the results. This is how we hope to find out if radiation is helpful.

In this study, we use a computer program to decide which treatment to give. If you join this study, you would not be allowed to choose the treatment. You would have a 1-in-1 chance of receiving radiation.

What research tests, procedures, and treatments are done in this study?

- Group 1 participants would receive- ADT + abiraterone + prednisone
- Group 2 participants would receive- ADT + abiraterone + prednisone+ Radiation

Participants in both Group 1 and Group 2 would receive the following tests and procedures at specified time points-

- **Medical History and Physical Exam-** Before you begin abiraterone + prednisone, 1 and 4 months after start of abiraterone + prednisone
- **Review your performance status-** Before you begin abiraterone + prednisone, 1 and 4 months after start of abiraterone + prednisone
- **CT scans or MRI or PET/CT –** CT scan is preferable but MRI or PET/CT is also acceptable. Required only before you begin abiraterone + prednisone treatment.
- **PSA (prostate specific antigen) level-** Before you begin abiraterone + prednisone, 1 and 4 months after start of abiraterone + prednisone and every 4 weeks until 6 months after start of abiraterone.
- **Research Blood draw-** We will be collecting your blood at specific time-points for us to study changes in your body's immune response. We will make attempts to collect blood during the times you would normally get blood drawn (to check for your blood counts and PSA) to minimize the amount of needle pricks you receive.

  3 Collection Time-points:

  - Before you begin abiraterone + prednisone treatment
  - 1 month after you start abiraterone + prednisone treatment
  - 4 months after you start abiraterone + prednisone treatment

  We will collect 9 tubes of blood, or about 5-6 tablespoons each collection. If we are not able to combine a research blood draw with a clinical blood draw, arrangements will have to be made to return to SCCA or UWMC for the research blood collection. Each blood draw visit would be 10 minutes or less. We will make every attempt to make this convenient for you.

Neutron Radiation Treatment (Group 2)

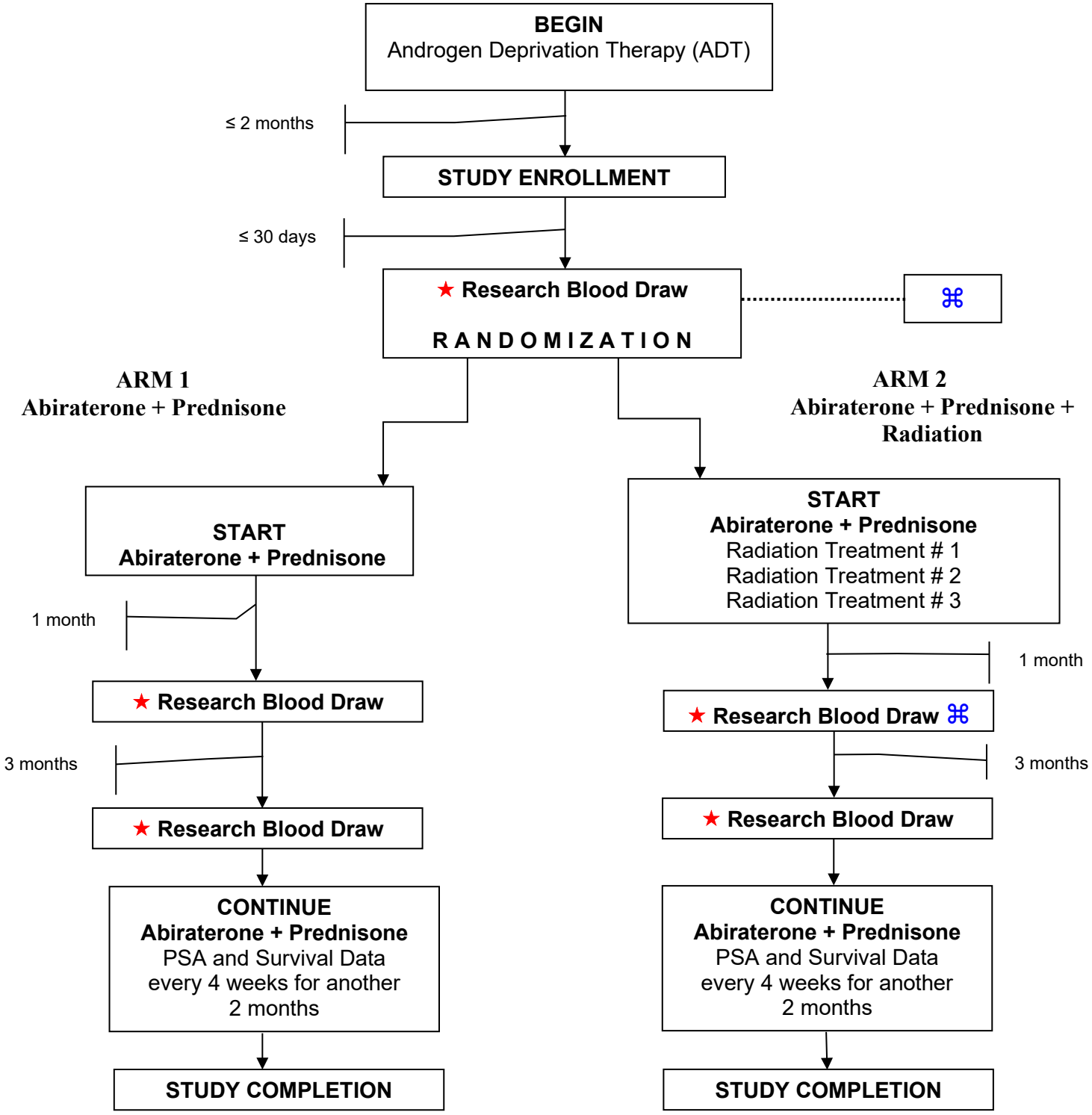
If you are randomized to the Abiraterone + Prednisone + Radiation Arm, you will start radiation treatment around the time you start abiraterone + prednisone. You can have up to 3 lesions, or cancerous spots, radiated at the same time. Being on this treatment arm would require extra visits to accommodate the radiation treatment.

Visits

- CT-based simulation for radiation treatment planning
- 1st dose of radiation
- 2nd dose of radiation
- 3rd dose of radiation

Your radiation oncologist may spread out your treatment doses to 5 doses if he/she is concerned for any side-effects you may experience. The total dose of neutron radiation you will receive will range between 6-10 gray units (radiation dose is measured in terms of how your tissue absorbs energy). Each radiation treatment will be a visit that is 30 minutes or less. Neutron radiation is FDA approved for treating cancers, and has been in use at the University Of Washington Medical Center for over 40 years. It is covered by Medicare and many other insurance plans.

Another way to find out what will happen to you during the study is to read the chart below.



Symbol Key

★ 9 tubes of blood for research purposes

⌘ Optional research biopsy of a non-radiated tumor

How long would you stay in this study?

If you join this study, you would stay in this study for about 6 months after starting abiraterone + prednisone regimen.

Doctors could take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are not able or willing to follow study procedures.
- The whole study is stopped.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

What are the side effects (risks)?

In this part of the consent form, we describe the side effects we expect from the tests and treatments in this study. Neutron radiation treatment could cause side effects we do not know about yet. We carefully watch everyone in the study for side effects.

If you join this study, we would tell you if we discover new side effects that could affect you.

On both Group 1 and Group 2 of the study, the treatment of ADT plus Abiraterone + Prednisone you receive is not experimental and is the care that you would normally receive, regardless of being enrolled on this trial.

Side effects may be mild or very serious. Medicines could be given to help lessen side effects. Many side effects go away soon after you stop receiving neutron radiation. In some cases, side effects can last a long time or never go away.

Research blood collection

- Bruising or minor swelling at the site of needle injection
- Light headedness or dizziness
- Pressure from the tourniquet (rubber band around your upper arm to increase blood flow)

Drug risks

- Abiraterone Acetate
    - Likely side effects of abiraterone acetate are (≥5% of patients):
        - joint swelling or discomfort

        - hypokalemia
        - edema
        - muscle discomfort
        - hot flush
        - diarrhea
        - urinary tract infection
        - cough
        - hypertension
        - arrhythmia
        - urinary frequency
        - nocturia
        - dyspepsia
        - upper respiratory tract infection
    - Less likely side effects of abiraterone acetate are (<1% of patients):
        - aspartate aminotransferase increased
        - alanine aminotransferase increased
        - urosepsis
        - cardiac failure
- Prednisone
    - Likely side effects of prednisone are:
        - fluid retention
        - alteration in glucose tolerance
        - elevation in blood pressure
        - behavioral and mood changes
        - increased appetite
        - weight gain

Prednisone is given as a low dose medication in combination with abiraterone acetate in order to manage the potential side effects of abiraterone, such as low potassium or high blood pressure.

Radiation risks

If you are randomized to Group 2 (ADT plus Abiraterone + Prednisone + Radiation), then you will receive neutron radiation treatment, which is the experimental aspect of this research study. The amount of radiation is equivalent to what you would receive with standard photon radiation. Exact toxicity depends on the site of treatment and your radiation oncologist will discuss this with you.

- General
    - Fatigue
    - Itchy Skin
    - Hair loss inside radiation field
- Head and neck treatment
    - Dry mouth
    - Inflammation of membranes
    - Difficulty swallowing
    - Nausea
    - Tooth decay
- Chest treatment
    - Difficulty swallowing
    - Nausea
    - Lung damage causing shortness of breath, cough, or fever
- Abdomen treatment
    - Nausea/vomiting
    - Diarrhea
- Pelvis treatment
    - Diarrhea
    - Urinary irritation
    - Rectal irritation causing bleeding or urgency

Reproductive risks

Inability to have children - The effects of neutron radiation treatment on fathering a child is also unknown. Men who join this study must also agree to use one or more forms of

effective and acceptable birth control from the time this form is signed until at least 4 months after the last dose of neutron radiation treatment.

CT scans

CT scans in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called "background radiation". This radiation is natural and comes from space, air, water, soil, and the food you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. For comparison, the estimated radiation dose from each of these scans is listed below. This does not include the dose to subjects who will receive neutron therapy. The risk to your health from this level of radiation exposure is too low to be detectable and may be nonexistent.

- CT Chest: 7 mSv
- CT Abdomen: 8 mSv
- CT Pelvis: 6 mSv

Non-physical risks

If you join this study, non-physical risks are:

- You might not be able to work.

What are the benefits?

We do not know if this study would help you. We are trying to compare abiraterone + prednisone alone versus abiraterone + prednisone + radiation to see its effects on people with CSPC. You might get better if you receive neutron radiation treatment, but your condition could stay the same or even get worse. We do not know which treatment is more effective for advanced CSPC. We hope the information from this study will help other people with CSPC in the future.

You have other choices besides this study.

You do not have to join this study. You are free to say "yes" or "no". Your regular medical care would not change if you decide to say "no".

You have other choices for treatment. Each of these choices has risks and benefits. You should talk to your doctor or healthcare provider about these choices.

Other choices include: Standard Treatment; If your doctor recommends abiraterone + prednisone and/or neutron radiation, you can still receive those treatments as part of your regular care without being on this clinical trial.

Enrollment in this study may exclude you from other research studies.

Protecting Privacy as an Individual and the Confidentiality of Personal Information

If you join this study, some people or organizations might need to look at your medical records and research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Research Center, University of Washington, Seattle Children's, and Seattle Cancer Care Alliance.
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

We will do our best to keep personal information confidential. But we cannot guarantee total confidentiality. Personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

If you join this study, information about your participation would be made part of your permanent medical record. This information would include a copy of this consent form. If an insurance company or employer or anyone else were authorized to see your medical record, they would see a copy of this consent form.

Would we pay you if you join this study?

There is no payment for being in this study.

Would you have extra costs if you join this study?

Under normal circumstances you would have physician appointments and undergo similar lab and scan procedures as you would on this study. If you join this study, you or your insurance company would have to pay for the costs of standard treatment in this study. While on study you will be responsible for meeting your insurance plan co-pay/deductible requirements. If you are randomized to Group 2 of the study, you or your insurance company would have to pay for the costs to receive neutron radiation treatment.

You would **not** be billed for:

- Up to 3 Research blood collection (if not done during standard blood draws) and supplies
- Up to 2 Optional research biopies

You may incur additional medical care costs associated with the medical management of side effects experienced while you are receiving abiraterone + prednisone and/or radiation.

What if you get sick or hurt after you join this study?

For a life threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

For all other medical problems or illness related to this research, immediately contact 206-598-6190 Radiation Oncologist on-call. They will treat you or refer you for treatment. You or your health insurance will have to pay for the treatment. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family. State or national law may give you rights to seek payment for some of these expenses. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

You would not lose any legal right to seek payment for treatment if you sign this form.

What will my information and/or tissue samples be used for?

Your information and tissue samples (such as blood and tumor cells) will be used for the purposes of this study.

Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

During this study, if the researchers learn new information that may be important to your general health or to your disease or condition, they will share that information with you.

In addition, be aware that by agreeing to participate in this study, your information or tissue samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. These future research studies will be reviewed by an oversight group known as an institutional review board if required by law. The information that identifies you will first be removed from your information or tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Your rights

- You do not have to join this study. You are free to say “yes” or “no”.
- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we might learn new information that you need to know. For example, some information may affect your health or well-being. Other information might make you change your mind about being in this study. If we learn these kinds of information, we would tell you.
- If you join this study, you would not have to stay in it. You could stop at any time (even before you start). Your regular medical care would not change. You would have no penalty for stopping, but it would be better not to join the study if you think that you would change your mind later.
- If you decide to drop out, we would want you to tell the study doctor. The doctor could tell you about the effects of stopping neutron radiation treatment. You and the doctor could talk about the follow-up care and testing that would help the most.
- Before you leave the study, the doctor might ask you to obtain permission to record treatment related data up to 6 months post-treatment.

  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.

Your responsibilities

If you join this study, you would have some responsibilities.

- Follow the schedule of study visits and procedures.
- Take study medications as directed.
- Prevent pregnancy.
- Tell us about side effects.

For more information

If you have questions or concerns about this study, you can talk to your doctor anytime. Other people you could talk to are listed below.

If you have questions about:	**Call:**
This study (including complaints and requests for information)	206-598-4100 (Dr. Jing Zeng) 206-598-8239 (Priya Vissamraju, Research Coordinator)
If you get sick or hurt in this study	206-598-4100 (Dr. Jing Zeng)
Your rights as a research participant	206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Research Center) 206-543-0098 (Human Subjects Division, University of Washington)
Your bills and health insurance coverage	206-606-6226 Seattle Cancer Care Alliance Financial Services 206-598-1950 UW Medical Center Financial Services

Emergency number (24 hours): **(206) 598-6190**

Tumor Biopsy (Optional)

The additional research biopsy part of this study is completely optional. You can still participate in the main part of this study without undergoing the research biopsy. This will only apply to patients randomized to the radiation arm (Group 2), although that determination will be made after obtaining your willingness to undergo the biopsy. There are two tumor biopsies for patients who consent, pre-radiation treatment and post-radiation treatment (2-4 weeks after radiation). Biopsied tissue of an untreated site after radiation therapy for castration sensitive prostate cancer has never been studied in this setting. It is important to understand that the results of this research biopsy are not designed specifically to help you. This is an opportunity for us to generate more information regarding your type of cancer. Information from this research will not be included in your medical record. For those who give permission for the research tumor biopsy, the biopsy will be scheduled prior to radiation treatment and within 4-weeks after your radiation treatment.

There will be a separate procedure consent form that will outline the risks associated with the area planned for biopsy. You and your insurance company will not be charged for this research procedure.

Read each question and think about your choice. When you decide on each question, please circle **YES** or **NO**.

Do you agree to donate your tissue to study cancer? (Circle one) **YES** **NO**

Signatures

Please sign below if you:

- have read this form (or had it read to you);
- had the opportunity to ask any questions you have;
- had the opportunity to discuss the research with the person obtaining consent; and
- agree to participate in this study.

Participant (age 14+):

Printed Name	Signature	Date

If you served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

Printed Name	Signature	Date

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

Printed Name	Signature	Date

Protocol: CC9938
Current consent version date: 8/31/19
Previous consent version date:
Copies to:

FHCRC IRB Approval
02/08/2021
Document Released Date