THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Bayesian Phase I Trial of Proton Image-guided Radiation Assignment for Therapeutic Escalation via high risk patient Selection
2019-0467

Study Chair: Clifton D. Fuller

_____ _____
Participant's Name Medical Record Number

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this clinical research study is to test a new radiation schedule that administers more radiation to the tumor tissue using image guided proton therapy for patients that have a high risk of having a tumor recurrence (the tumor comes back after treatment).

The additional dose that you will receive may increase the side effects and the severity of these side effects that you can have.

This is an investigational study. Proton image-guided radiation in this study is delivered using FDA-approved and commercially available methods. It is considered investigational to increase the frequency of radiation administration.

The change in dose radiation frequency and dose investigated in this study may help to better control the tumor and prevent it from coming back or growing. Future patients may benefit from what is learned. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side

effects, potential expenses, and time commitment. You may choose to not take part in this study because of claustrophobia related to MR-scanners or inability to stop tobacco or alcohol use during and after treatment.

You can read a full list of potential side effects below in the Possible Risks section of this consent.

Your overall participation on the study will be over after about 5 years.

You and/or your insurance provider will be responsible for the cost of conventional radiation therapy.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive the standard radiation therapy, which could be photon IMRT or proton IMPT treatment. You may choose to receive other investigational therapy, if available. You may choose not to have treatment for cancer at all. In all cases, you will receive appropriate medical care, including treatment for pain and other symptoms of cancer.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean you will be able to take part in this study. Within 2 weeks before you start radiation therapy, you will have screening tests to help the doctor decide if are eligible to take part in this study. The following tests and procedures will be performed:

- You will have a physical exam.
- You will be asked to complete a questionnaire to learn if you are able to have an MRI. This should take about 10 minutes to complete.
- You will have a CT, PET/CT, and MRI scan (if needed) to check the status of the disease.
- Blood (about 3 teaspoons) will be drawn for routine tests.
- Urine will be collected to test for signs of tobacco/alcohol use. For you own safety, you will no longer be able to take part in this study if the tobacco/alcohol tests during and after treatment are positive. Use of alcohol/tobacco while receiving treatment as part of this study may increase your risk of side effects, which may be fatal.
- Leftover tumor tissue may be used to check for signs of tumor cell growth and tumor marker testing. Tumor cells can be used to test the tumor response to radiation. Tumor markers may be related to the radiation response of the disease.
- If you can become pregnant, you will have a urine pregnancy test. To take part in this study, you must not be pregnant.

The doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in this study, you will not be enrolled. Other options will be discussed with you.

Up to 18 participants will be enrolled in this study. All will take part at MD Anderson.

Baseline Visit (Your first radiation therapy visit)
The following tests and procedures will be performed as a standard of care within the first 2 weeks of your radiation treatment:

- You will have a hearing test.
- You will have a dental exam. During this exam, your saliva flow will be measured and you will be checked for lockjaw.
- Photos of the inside of your mouth will be taken to check for mouth sores.
- You will have a video-strobe procedure to check your vocal cords. To perform a video-strobe procedure, a small camera will be inserted into the throat through your nose or mouth. You will be awake for this procedure and the study staff will give you the option of receiving a numbing spray for your nose and/or throat.
- Your swallowing function will be tested with a special type of x-ray called a modified barium swallow (MBS). During the test, you will eat and drink foods and liquids mixed with a "contrast" chemical called barium that will make your throat more visible in the x-rays. A special x-ray tube will be connected to a television screen to allow the doctor to watch the foods and liquids pass from your mouth and down your throat.

If you are found to be eligible to take part in this study and agree, you will have the following additional tests as part of this study:

- You will complete a questionnaire about swallowing that should take about 5 minutes to complete.
- You will fill out questionnaires about your quality of life, work status, medical history, smoking status, and any symptoms you may have. Completing these questionnaires should take about 10-15 minutes.

Treatment Planning and Schedule
You will receive a standard CT simulation which will cover your head and neck for treatment planning. You will also have a PET-CT and MRI to check the status of the disease and for treatment planning purposes.

All patients will receive radiation therapy 1 time each day for the first 18 days, 5 days a week (Monday through Friday), followed by 2 times each day for 15 days. The overall treatment time will be 33 days (about 6½ weeks).

Study Visits
Every week while you are receiving radiation therapy:

- You will have a physical exam.
- Blood (about 1-2 tablespoons) will be drawn for routine tests.
- You will fill out the same questionnaires as before.

- You will have an MRI to check that the dose of radiation is being administered accurately.
- You will meet with a nutritionist who will advise you on your diet in order to not lose weight and keep your nutrition levels up.

At **Weeks 1 and 3**, urine will be collected for an alcohol/tobacco test.

At **Weeks 3 and 6**:

- Photos of the inside of your mouth will be taken to check for mouth sores.
- You will have a dental exam.

Six (6) weeks after finishing radiation therapy, you will complete the same questionnaires as before.

Within 8-12 weeks after finishing radiation therapy:

- Photos of the inside of your mouth will be taken to check for mouth sores.
- Urine will be collected for an alcohol/tobacco test.
- You will have a hearing test.
- You will have standard MRI to check the status of the disease.

Six (6) months, 1 year, and 2 years after finishing radiation therapy:

- Photos of the inside of your mouth will be taken to check for mouth sores.
- You will fill out the same questionnaires as before.
- You will have a standard of care mouth exam to check your swallowing function.
- You will have a standard of care video-strobe procedure to check your vocal cords.
- At 6 months and 2 years only, you will have a dental exam and an MBS exam to test your swallowing function.
- At 1 year and 2 years only, you will also have a hearing test.
- At 6 months and 1 year only, urine will be collected for an alcohol/tobacco test.

Five (5) years after finishing radiation therapy, you will have an MBS exam to test your swallowing function and will complete the same questionnaires as before.

If the doctor thinks it is needed during follow-up, you will have a tumor biopsy for tumor marker testing and a CT scan, MRI scan, and/or PET/CT scan to check the status of the disease. Tumor markers may be related to the status of the disease.

Follow-Up Calls

During the 8-12 weeks while you are recovering from treatment, you will be called or emailed by an automated system every 2 weeks.

This will be to remind you to complete a web-based form that asks about any side effects you may have had. Completing the form should take about 10-15 minutes each time.

Other Instructions

If you decide to stop taking part in this study the study doctor will tell you how to stop safely. It is important to tell the study doctor if you are thinking about stopping so any side effects from the treatment can be looked at by your doctor and you can discuss what follow-up care and testing could be most helpful for you.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after treatment is stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effect you may have, even if you do not think they are related to the study procedures.

Radiation Therapy Side Effects

Common side effects of head and neck radiotherapy	Rare side effects of head and neck radiotherapy	General chemo-radiation side effects (rare)
• swelling • skin changes (possible dryness, itching, peeling, and/or blistering) • hair loss at the treatment site • mouth problems • trouble swallowing	• hearing loss • tube feeding dependency • slow working thyroid gland	• urinary and/or bladder changes • sexual changes • inability to produce children • joint problems • secondary cancers • swelling of the arms or torso • vomiting • nausea • diarrhea

If you have head and neck cancer, you may be more likely to develop certain side effects listed in the above table.

Radiation therapy may cause you to develop another type of cancer. Side effects may not occur for up to 6 months after radiation therapy is over. Side effects will vary depending on what part of the body is receiving radiation therapy.

Other Risks

During the **MRI**, you may feel mild vibrations throughout your body. The machine will produce a loud knocking noise. This is normal. You will be given earplugs to protect your ears. Some people, especially those who tend to feel uncomfortable in small or closed spaces, may feel “closed in” and become anxious while in the scanner. The scanner has an intercom, which will allow you to speak to the staff during the procedure. If you feel ill or anxious during scanning, tell the MRI staff and the scanning will be stopped if you wish.

The magnetic field used in MRI scanning may harm you if you have certain types of metal in your body (as might be found in pacemakers, neurostimulators, or certain clips). It may cause problems with devices, such as pacemakers. If you have metal in your body or devices such as a pacemaker, you should discuss this with the study doctor.

Contrast drugs may cause a feeling of warmth or pain at the injection site. They may cause nausea, vomiting, headache, dizziness, and/or heart and kidney complications. They may cause hypersensitivity reactions which may cause breathing and/or skin problems (rash, redness, blisters, itching, and/or local swellings) and may appear either immediately or up to a few days after the injection. It may cause water to collect in the lungs and/or anaphylactic shock (a severe allergic reaction that can cause breathing difficulty and/or a drop in blood pressure). It may cause changes in the way you move or changes in your senses.

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Having **biopsies** performed may cause pain, bruising, bleeding, redness, low blood pressure, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

Drinking the contrast agent for the **modified barium swallow** (MBS) may cause constipation. You can avoid constipation by drinking plenty of water (or putting water through your feeding tube if you cannot drink by mouth) after the procedure.
The **xrays** taken during the modified barium swallow send a small amount of radiation though the body. The radiation during this procedure is equal to the amount of radiation that an average individual experiences from background radiation (around

the house, for example) in about 1 month. All radiation adds up over a lifetime and may increase the risk of a new cancer forming.

Laryngoscopy/videostroboscopy may cause bleeding and/or bruise or puncture the lining of the throat and/or nose. It may also cause sore throat.

Hearing tests and dental exams do not present any risks to you. They are screening procedures done to establish a baseline of your oral and audiological health prior to starting treatment. If there is a concern resulting from the hearing test or dental exam these concerns will be discussed and addressed by your physician.

Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study. Only the study doctor and designated staff will have access to study data.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks
Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant, breastfeed a baby, or father a child while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: Please ask your study doctor about acceptable methods of birth control to use while taking part in this study.

Males: Tell the doctor right away if your partner becomes pregnant or suspects pregnancy.

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However,

your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

You will receive no compensation for taking part in this study.

Additional Information

4. You may ask the study chair (Dr. Clifton Fuller, at 713-563-2300) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you decide you want to stop taking part in the study, it is recommended for your safety that you first talk to your doctor, as it may be dangerous to suddenly stop taking study drug. If you withdraw from this study, you can still choose to be treated at MD Anderson. The study staff may ask if they can continue collecting the results of routine care from your medical record.

6. This study or your participation in it may be changed or stopped without your consent at any time by the study chair, the U.S. Food and Drug Administration (FDA), the Office for Human Research Protections (OHRP), or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study, and you may be asked to sign another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

Future Research

Data
Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and/or shared with other researchers and/or institutions for use in future research.

Samples
Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover material that is stored at MD Anderson in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research
Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you. The same level of data protection that covers your individual data does not apply to summary results (when data from the whole study is combined).

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.

- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this federal law prohibit discrimination based on an already known genetic disease or disorder.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - Any future sponsors/supporters of the study
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible (according to state and federal law). However, in some situations, the FDA could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under Protocol 2019-0467.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for vulnerable adult participants. If witnessing the assent of a pediatric participant, leave this line blank and sign on the witness to assent page instead.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____ _____ _____
NAME OF TRANSLATOR SIGNATURE OF TRANSLATOR DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line below.)

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL TRANSLATION DATE
(OTHER THAN TRANSLATOR, PARENT/GUARDIAN,
OR STUDY CHAIR)

_____
PRINTED NAME OF WITNESS TO THE VERBAL TRANSLATION