Informed Consent Form

RAD2156-11: Phase 1 Dose Escalation Trial of Hypofractionated Radiosurgery for Large Brain Metastases

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You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: Phase 1 Dose Escalation Trial of Hypofractionated Radiosurgery for Large Brain Metastases

Principal Investigator: Bree Eaton, MD

Introduction

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?

Standard treatment options for the treatment of brain metastases with radiation therapy include whole brain radiation and stereotactic radiosurgery (SRS). Whole brain radiation therapy is when small doses of radiation are delivered to the whole brain every day, Monday through Friday, for a period of 2-3 weeks. SRS is when one large dose of radiation is delivered to the tumor only in one single treatment. Many patients and physicians like to use SRS to treat brain metastasis because it treats the tumor and not the whole brain. This controls growth of the brain tumor but does not prevent the growth of tumors in other parts of the brain. For patients with large brain metastasis, it is considered unsafe to use one large dose of radiation in a single treatment as in SRS and so instead, hypofractionated radiosurgery can be used. Hypofractionated radiosurgery involves 2-5 medium size doses of radiation therapy delivered to the tumor only and not the whole brain, with 2-3 treatments received each week.

The purpose of this study is to define the best radiation dose for treating large metastatic brain tumors, or areas of the brain where metastatic brain tumors have been removed by surgery. The radiation will be delivered in a total of 5 treatments. We give radiation therapy to try to keep the tumor from growing further or coming back in that location. We think higher radiation doses will work better in keeping tumors from growing but higher doses also can have more side effects. In this study, the radiation doses will be increased slowly, from patient to patient, in order see how safe each dose is. The dose of radiation that you will receive will be determined before you enroll and will not change during

your 5 treatments. Radiation doses and side effects can vary with the size of the tumor treated and so it is important to conduct this study for tumors of large size. The best dose will be defined as the highest dose that is okay for patients and causes minimal side effects. This study is important because it will help radiation oncologists know what is the highest, safe dose of radiation, that can be delivered to brain tumors greater than 3cm in size over a short course of five treatments. We will enroll a total of 24 patients in this study.

Procedures

Radiotherapy will consist of a total of 5 treatments with 2-3 treatments delivered per week. Your treatment will finish in 2-3 weeks from the day you start. Treatments take thirty to forty minutes at the clinic each day. Prior to beginning radiotherapy, the radiation therapy fields will be planned in a session called simulation. During this procedure a head cast will be made to help keep the head still during treatment. A CT scan will be done to help identify the critical normal structures in the brain so that the best treatment may be planned by your radiation oncologist. When the scan is complete, you will remain on the table for approximately 10 minutes longer while your doctor sets up the fields for your treatment. When the planning is complete, ink marks will be placed on the head cast to mark where the radiation should go. Lastly, the cast will be removed and you will receive an appointment time to start radiation. Your radiation treatment will start approximately 3-5 business days later. When you come back for radiation you will put in the same position wearing the head mask made during your simulation. The treatment will take about 15 minutes, during which time you will have to lay very still. You will not see or feel anything but you may hear the machine moving around you. You will be able to talk to the therapist outside the room at any time, and they will always be able to see and hear you. After the treatment you will go home and come back at your next scheduled treatment. After all treatments are over, you will come back for a follow-up appointment with your doctor in one month and will have a repeat MRI of the brain at that time. After that first appointment, you will see your doctor every 3 month for additional appointments and you will also have an MRI before each of these appointments as well. Your first 3 follow-up appointments are the most important for participation in this trial, but we would like you to continue to follow-up with your doctor throughout the remainder of your life.

Who owns my study information?

If you join this study, you will be donating your study information. You will not receive any compensation if your information is used to make a new product. If you withdraw from the study, data that was already collected may be still be used for this study.

Risks and Discomforts

There may be side effects from the study drug that are not known at this time. Your condition may not get better, and it may even get worse, as a result of your being in this study. These are some side effects which are possible from the treatment.

The **most common** risks and discomforts expected in this study are:

Right away (during treatment or up to 1-2 months afterwards):

- Fatigue
- Skin irritation or tanning
- Swelling in the tumor
- Temporary hair thinning or hair loss,
- Headache

Months to years after treatment:

- Increased risk of cataract development

The **less common** risks and discomforts expected in this study are:

Right away (during treatment or up to 1-2 months afterwards) :

- Nausea or vomiting
- Nasal congestion
- Eye irritation
- Ear fullness

Months to years after treatment:

- Radiation necrosis or dead tissue from treating the tumor built up in the brain
- Short-term memory loss

Rare but possible risks include:
Right away (during treatment or up to 1-2 months afterwards):
- Seizure
- Bleeding in the tumor
- Stroke like symptoms from bleed into tumor

Months to years after treatment:
- Neurologic damage
- Vision loss
- Stroke like symptoms
- Increased risk of a second malignancy

If you are a woman: to protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

If you are a man: the effect of radiation on sperm is not known. To protect against possible side effects, if you are a man you should not get a sexual partner pregnant while receiving radiation and for 6 months after the last dose. You and the study doctor should agree on a method of birth control to use throughout the study.

In addition to the radiation therapy you will receive additional radiation from the CT scans used to plan you treatment. Although the risk for radiation-induced cancer is cumulative, this additional radiation dose in not expected to adversely affect your condition of treatment.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Benefits

This study is not designed to benefit you directly. Your condition may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about radiation doses. The study results may be used to help other patients in the future.

Payment for Participation

You will not be offered payment for being in this study.

Other Treatment Outside this Study

If you decide not to enter this study, there is care available to you outside of research. The study doctor will discuss these options with you. One option is for you could receive radiation therapy to the whole brain, in daily treatments, five days a week for 2-3 weeks. Other options include partial brain radiation therapy to the tumor/resection cavity only delivered with fractionated radiosurgery. The study doctor will discuss alternative treatment options with you. You do not have to be in this study to be treated for your metastatic brain tumor.

You are free to choose not to take part in this study.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Medical Record

If you have been an Emory and Saint Joseph's Hospital patient before, then you already have an Emory and Saint Joseph's Hospital medical record. If you have never been an Emory and Saint Joseph's Hospital patient, you do not have one. An Emory and Saint Joseph's Hospital medical record will be made for you if an Emory and Saint Joseph's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory and Saint Joseph's Hospital medical record you have now or any time during the study.

Emory and Saint Joseph's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory and Saint Joseph's Hospital medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include: None.

Tests and procedures done at non-Emory and Saint Joseph's Hospital places may not become part of your Emory and Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory and Saint Joseph's Hospital will help you get medical treatment. Emory, Saint Joseph's and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory, Saint Joseph's or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Bree Eaton at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

Costs

Emory and Saint Joseph's Hospital will pay for the pregnancy test that is required to see if you are eligible for this study.

You will have to pay for the other items or services for which we do not pay. The study will not pay for your regular medical care. If you have insurance, Emory and Saint Joseph's Hospital will submit claims to your insurance for items and services that Emory and Saint Joseph's Hospital does not cover. Emory and Saint

Joseph's Hospital will send in only those claims for items and services that it reasonably believes your insurance will pay and that the study has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and Saint Joseph's Hospital will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory and Saint Joseph's Hospital will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study

You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that Will be Used/Disclosed:

The PHI that we will use or share for the main research study includes: any medical record information that is related to your brain metastases including surgical records, chemotherapy records, radiation therapy records, radiology records, medication records and/or any records including Emergency department visits or inpatient hospitalization records related to your diagnosis of cancer or occurring at any time point after your enrollment in this trial and before the trial is closed.

Purposes for Which Your PHI Will be Used/Disclosed:

We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors,

contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory and Saint Joseph's Hospital may use and disclose your PHI to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory and Saint Joseph's Hospital offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Office for Human Research Protections; Food and Drug Administration
    - Public health agencies
    - Research monitors and reviewer
    - Accreditation agencies
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Dr. Bree Eaton
Department of Radiation Oncology
The Emory Clinic

1365 Clifton Rd. NE, Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information
Contact Dr. Bree Eaton at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____

Name of Subject

_____ _____ ____:____ am / pm

Signature of Subject (18 or older and able to consent) **Date** **Time (please circle)**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____

Name of Person Conducting Informed Consent Discussion

_____ _____ ____:____ am / pm

Signature of Person Conducting Informed Consent Discussion **Date** **Time (please circle)**

Study Coordinator (initial if applicable):

_____***I attest that I participated in the informed consent discussion with the subject***

_____***I attest that I was present when the subject gave informed consent***

_____ _____

Signature of Study Coordinator **Date**