THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

A Phase III Trial of Pre-Operative Stereotactic Radiosurgery (SRS) versus Post-Operative SRS for Brain Metastases
2018-0552

Study Chair: Debra N. Yeboa

_____ _____
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

Currently, it is standard practice to give stereotactic radiosurgery (SRS) to patients after surgery. SRS is the delivery of focused, high-dose radiation given in a single session to the tumors, with a minimal dose given to uninvolved areas of the brain.

The goal of this clinical research study is to compare the effects of giving SRS before surgery to the current standard practice to learn which method will decrease the spread of brain cancer cells through the brain and/or spine (leptomeningeal disease) in patients with brain tumors.

This is an investigational study. SRS in this study is being delivered using FDA approved and commercially available methods. It is considered investigational to learn if SRS is more effective when given before or after surgery. The study doctor can explain in more detail how SRS is designed to work.

The study treatments may help to control the disease and the spread of cancer cells in the brain and/or spine. 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 should also talk to the study doctor about what it means to be randomized (randomly assigned) to a study group and how that may impact your participation in this study.

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

Your active participation on the study will last about 24 months, or 2 years. If you are diagnosed in the future with concern for spread to tumor in the brain, it may last up to 36 months or 3 years.

You and/or your insurance provider will be responsible for the cost of SRS.

You may choose not to take part in this study. Instead of taking part in this study, you may choose to receive standard brain radiation after surgery outside of this study. You may choose to have surgical removal of brain tumors. You may choose to receive other investigational treatment, if available. The study doctor will discuss with you the possible risks and benefits of these treatments. You may choose to have no treatment 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 that you will be able to take part in this study. You will have the following screening tests to help the doctor decide if you are eligible to take part in this study:

- You will have a physical exam
- You will have a neurological exam (tests to check the functioning of your nerves).
- You will have an MRI of the brain to check the status of the disease. If needed, you may also have an MRI of the spine.
- Blood (about 1 tablespoon) will be drawn for routine tests and to check the status of the disease. This routine test will include a blood/urine pregnancy test if you can become pregnant. To take part in this study, you must not be pregnant.
- If you have surgery as part of your standard care and leftover tissue is available, it will be collected for research testing that may help researchers understand your response to SRS.
- If blood or cerebral spinal fluid (CSF) is being collected as part of your standard care and/or if there is blood/CSF fluid leftover from a previous

procedure, it will be collected to check for conditions related to the disease (such as brain metastases and/or leptomeningeal disease [LMD]. The study doctor can explain this to you in more detail.

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

Study Groups

If you are found to be eligible to take part in this study, you will be randomly assigned (as in the flip of a coin) to receive SRS either before or after your scheduled surgery.

This is done because no one knows if one group is better, the same, or worse than the other. Neither you nor the study doctor can choose which group you will be in. You will have an equal chance (50/50) of being assigned to either group.

Up to 180 participants will be enrolled at MD Anderson and other participating sites.

Study Procedure

Up to 30 days either before or after surgery, you will receive SRS. If the disease returns after treatment, you may receive additional SRS, depending on what the doctor thinks is in your best interest. Your treatment options will be discussed with you.

You will sign a separate consent form for SRS and surgery that will explain the procedure and risks in detail.

You will no longer be able to take part in the study if the disease gets worse, if intolerable side effects occur, or if you are unable to follow study directions.

Study Follow-Up Visits

At **1½, 4, 6, 9, 12, 15, 18, 21 and 24 months (+/- 30 days)** after your surgery:

- You will have a physical exam, including a neurological exam (when applicable, depending on if telemedicine is available with your provider).
- You will have an MRI to check the status of the disease.
- You will be asked about any drugs you may be taking

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. These side effects will vary from person to person. 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.
Because the study treatments are standard of care, it is not anticipated that the risks on this study would be greater than standard treatment. Data on this will still be collected and monitored. Tell the study staff about any side effects you may have, even if you do not think they are related to the study treatment.

If you receive **stereotactic radiosurgery** (SRS), you may be at risk for new tumors developing at previously untreated sites in the brain. Radiosurgery may cause nausea, vomiting, and/or increased swelling and/or bleeding in the brain. It may also cause destruction of brain tissue, requiring high-dose steroids or even surgery.

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 MRI will require a catheter to be inserted into one of your veins in order to inject the MRI contrast agent. This may cause skin irritation, bleeding, and/or infection. You may have an allergic reaction to the contrast agent.

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.

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.

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).

Spinal taps may be done if needed as part of your standard of care consistent with best medical care practices (i.e., spinal taps are not done for research only). Spinal taps may cause headaches, sensitivity of the eyes to light, nausea, vomiting, confusion, drowsiness and/or pain at the injection site. They may cause fever, infection, and/or bleeding. Spinal taps may cause inflammation/bleeding around the brain and/or the covering of the spinal cord, which can lead to nerve damage. In rare instances, spinal taps may cause seizures, leakage of spinal fluid, and/or blockage of spinal fluid, which can lead to brain swelling. Severe infections of the spinal fluid or

bleeding within the brain can result in coma and/or death. If a standard of care spinal tap is done, fluid obtained may be used for research if/when available.

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.

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: If you can become pregnant or father a child, you must use birth control while you are on study. Acceptable forms of birth control include birth control pills, barrier methods (such as condoms or diaphragms), or sterilization.

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.

OPTIONAL PROCEDURES FOR THE STUDY

Optional Procedure #1: If you agree, blood (about 2 tablespoons) will be collected for genetic and biomarker testing before SRS/surgery and at study visits at 1 ½, 6 and 12 months or if you have future progression of disease. If during a standard of care procedure, including surgery or spinal tap, fluid residual is available, about 2 tablespoon may be collected at that time. Biomarkers are found in the blood/tissue and may be related to your reaction to the study treatment.

Optional Procedure #2: If you agree, leftover blood and/or fluids collected as part of this study will be collected and stored at MD Anderson for genetic and biomarker testing and future research related to cancer.

Before your samples can be used for research, the people doing the research must get specific approval from the Institutional Review Board (IRB) of MD Anderson. The IRB is a committee made up of doctors, researchers, and members of the community. The IRB is responsible for protecting the participants involved in research studies and making sure all research is done in a safe and ethical manner. All research done at MD Anderson, including research involving your samples from this bank, must first be approved by the IRB.

Your samples will be given a code number. No identifying information will be directly linked to your samples. Only the researcher in charge of the bank will have access to the code numbers and be able to link the samples to you. This is to allow medical data related to the samples to be updated as needed. Other researchers using your samples will not be able to link this data to you.

Optional Procedure #3: If you agree, you will complete 3 cognitive function research tests at screening, 1 ½, 6 and 12 months. These tests will be used to check your attention span, your memory, and your thinking speed.

Optional Procedure #4: If you agree, you will complete 2 research questionnaires at screening, 1 ½, 6 and 12 months about your quality of life and any symptoms you may be having. It should take about 45 minutes total to complete the cognitive function tests and questionnaires.

You do not have to agree to the optional procedures in order to take part in this study. There are no benefits to you for taking part in the optional procedures. Future patients may benefit from what is learned. You may stop taking part at any time. There will be no cost to you for taking part in the optional procedures.

Optional Procedure Risks:

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).

Spinal taps may be done if required as part of your standard of care if there is already a potential medical concern by your doctor for work up of leptomeningeal disease consistent with best care practices (not for research only). They may cause headaches, sensitivity of the eyes to light, nausea, vomiting, confusion, drowsiness and/or pain at the injection site. They may cause fever, infection, and/or bleeding. Spinal taps may cause inflammation/bleeding around the brain and/or the covering of the spinal cord, which can lead to nerve damage. In rare instances, spinal taps may cause seizures, leakage of spinal fluid, and/or blockage of spinal fluid, which can lead to brain swelling. Severe infections of the spinal fluid or bleeding within the brain can result in coma and/or death. Repeated spinal taps may result in learning or memory difficulties.

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.

MD Anderson and others can learn about cancer and other diseases from your **banked samples**. In the future, people who may do research with these samples may need to know more information about your health. This information may be collected from your medical record. MD Anderson will make reasonable efforts to preserve your privacy, but cannot guarantee complete privacy. Sometimes your

samples may be used for genetic research about diseases that are passed on in families. **Genetic research** may result in the development of beneficial treatments, devices, new drugs, or patentable procedures. There are no plans to provide you compensation from such developments. MD Anderson will not be able to give you, your family, or your doctor the reports about the research done with these samples, and these reports will not be put in your medical record. If this information were released, it could be misused. Such misuse could be distressing, and it could cause you or your family members to have difficulty obtaining insurance coverage and/or a job.

If you withdraw your consent to the storage of leftover blood or bodily fluid in the tissue bank, then the leftover materials will no longer be collected for storage. Any of your blood or bodily fluid that remains in the tissue bank will no longer be used for research and will be removed from the tissue bank and destroyed.

However, if any of your de-identified blood or bodily fluid was already released for research purposes before you withdrew consent, MD Anderson will not be able to destroy it.

CONSENT/PERMISSION/AUTHORIZATION FOR OPTIONAL PROCEDURES

Circle your choice of "yes" or "no" for each of the following optional procedures:

Optional Procedure #1: Do you agree to allow extra blood or spinal fluid to be collected for genetic and biomarker testing?

YES NO

Optional Procedure #2: Do you agree to allow leftover blood and/or fluid to be stored at MD Anderson for use in future research related to cancer?

YES NO

Optional Procedure #3: Do you agree to complete cognitive function tests?

YES NO

Optional Procedure #4: Do you agree to complete questionnaires?

YES NO

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. Debra N. Yeboa, 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 who can then decide if you need to have any visits or tests to check on your health. If you withdraw from this study, you can still choose to be treated at MD Anderson.

   If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data

from your routine medical care. If you agree, this data will be handled the same as research data.

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

Participation in future research is not required. You can still take part in the main study even if you do not want your data or samples used for future research. If you do not want your data or samples used for future research as described below, please tell the study doctor.

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.

You do not have to allow your data to be used in future research to take part in the main study. If you do not want your data to be used for future research, tell the research study doctor. However, the data already collected will be kept and may be used.

Samples

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

If you do not want your samples to be used for future research, tell the study doctor. You may withdraw your samples at any time by telling your study team. If you decide to withdraw your samples, they will be returned to the lab they came from or destroyed. However, the data and test results already collected from your samples will be kept and may be used.

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 will 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
- Study monitors and auditors who verify the accuracy of the information
- Individuals who put all the study information together in report form

The results of this research may be published. However, your name and other identifying information will be kept confidential. Your information will be protected from disclosure to others to the extent required by law. Complete privacy cannot be promised.

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

LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

The following signature line should only be filled out when the participant does not have the capacity to legally consent to take part in the study and/or sign this document on his or her own behalf.

_____ _____
SIGNATURE OF LAR DATE

_____
PRINTED NAME and RELATIONSHIP TO PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

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

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
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