Clinical Trial: CCTG CE.7

This is a cover page for a consent form for a clinical trial. This cover page provides the contact information for your physician and research staff.

This consent form contains important information to help you decide whether to participate in this clinical trial. Your physician and research staff will explain this trial to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about and discuss with family or friends.

- Being in a clinical trial is voluntary – your choice.
- If you join this clinical, you can still stop at any time.
- No one can promise that a clinical trial will help you.
- Do not join this clinical trial unless all of your questions are answered.

After reading and discussing the information in this consent form you should know:

- Why this clinical trial is being done;
- What will happen during the clinical trial;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this clinical trial;
- How your personal health information will be treated during the clinical trial and after the trial is over;
- Whether being in this clinical trial could involve any cost to you; and
- What to do if you have problems or questions about this clinical trial.

Some of the hospitals that are members of Montana Cancer Consortium are Catholic health institutions and therefore uphold the Ethical and Religious Directives for Catholic Health Care Services that do not promote or condone artificial/ medically induced pregnancy prevention methods. The attached consent may contain language that is not consistent with this religious directive.

Please read this consent form carefully.

You should talk to your doctor or research coordinator about any questions or concerns you have about this study. Their contact information is listed below.

Physician Name & Phone Number: _____

Research Coordinator Name & Phone Number: _____

Cancer Center Address: _____

You may also contact Montana Cancer Consortium
2132 Broadwater Ave, Suite A1, Billings, MT 59102
Phone: 406-969-6060, Fax: 406-969-6070

Acknowledgement of Consent Cover Page

Participant Signature Date

Research Study Informed Consent Document

Study Title for Study Participants: A study comparing stereotactic radiosurgery to whole brain radiotherapy (using a technique that avoids the hippocampus) with memantine in people with cancer that has spread to the brain.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Protocol CCTG CE.7, A Phase III Trial of Stereotactic Radiosurgery Compared with Hippocampal-Avoidant Whole Brain Radiotherapy (HA-WBRT) Plus Memantine for 5 or More Brain Metastases

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. This study has public funding from the National Cancer Institute (NCI), part of the National Institutes of Health (NIH) in the United States Department of Health and Human Services. We do research studies to try to answer questions about how to prevent, diagnose, and treat diseases like cancer. We are asking you to take part in this research study because you have cancer somewhere else in your body that has spread to your brain.

Taking part in this study is your choice.

You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered. See the "Where can I get more information?" section for resources for more clinical trials and general cancer information.

Why is this study being done?

This study is being done to answer the following question: Can we reduce your symptoms and lower the chance of the cancer growing or getting worse by using stereotactic radiosurgery, compared to the usual radiotherapy? Stereotactic radiosurgery or SRS is a commonly used treatment for brain tumors. It is a one-day (or in some cases two day), out-patient procedure

during which a high dose of radiation is delivered to small spots in the brain while excluding the surrounding normal brain.

We are doing this study because we want to find out if this approach is better or worse than the usual approach for your type of cancer. The usual approach is defined as care most people get for cancer that has spread to the brain.

What is the usual approach to my type of cancer?

The usual approach for patients who are not in a study is treatment with whole brain radiation therapy using a technique called hippocampus avoidance (HA-WBRT). The hippocampus is a brain structure that is important for memory. Hippocampus avoidance during HA-WBRT decreases the amount of radiation that is delivered to this area. This treatment can reduce symptoms and may stop the cancer from growing for several months or longer.

Memantine is also often given with whole brain radiotherapy. It is an oral tablet given during and after radiation therapy that can decrease the risk of cognitive side effects after radiation therapy to the brain. Memantine is already FDA-approved for use in patients with dementia and is commonly used off-label (that is, for a purpose for which it is not FDA approved) for patients receiving whole-brain radiation therapy for cancer that has spread to the brain.

What are my choices if I decide not to take part in this study?

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- you may choose not to be treated for cancer, but you may want to receive comfort care to relieve symptoms
- you may choose a different approach for treatment, including but not limited to radiotherapy, surgery, chemotherapy, or a combination of these approaches.

What will happen if I decide to take part in this study?

If you decide to take part in this study, you will either get whole brain radiation therapy with the hippocampus avoidance technique (HA-WBRT) for about 2 weeks, or you will get stereotactic radiosurgery (SRS). SRS is usually given as a single treatment, but can sometimes be given over two days. If you get HA-WBRT, you will also receive the drug memantine to help prevent symptoms of HA-WBRT. After you finish treatment, your doctor will continue to watch you for side effects and follow your condition for up to 5 years.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks
We want to make sure you know about a few key risks right now. We give you more information in the "What risks can I expect from taking part in this study?" section.

If you choose to take part in this study, there is a risk that the study approach may not be as good as the usual approach at reducing symptoms or stopping tumor growth. There is also a risk that you could have side effects from the study treatment. These side effects may be worse and may be different than you would get with the usual approach for your cancer.

There is also a risk that you could have side effects from the SRS, HA-WBRT, or from memantine. These side effects may be worse and may be different than you would get with the usual approach for your cancer that has spread to the brain.

Some of the most common side effects that the study doctors know about are:

Stereotactic radiosurgery

- temporary (short-term) pain from with the head frame placement (if a head frame is used)
- swelling of the brain in the treated area which may require treatment with steroids
- severe local damage to or death of normal brain tissue, which may require surgery to remove

Whole brain radiation therapy with hippocampus avoidance

- hair loss, which may be permanent
- temporary scalp redness and drying
- fatigue (tiredness)
- memory loss
- the development of cancer in or near the hippocampus

Memantine

- fatigue or drowsiness
- indigestion

There may be some risks that the study doctors do not yet know about.

Benefits
There is evidence that this stereotactic radiosurgery is effective in controlling your type of cancer. It is not possible to know now if the study approach will extend your life compared to the usual approach. This study will help the study doctors learn things that will help people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time. If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The study doctor may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- For women: You become pregnant while on the study.
- The study is stopped by the National Cancer Institute (NCI), Institutional Review Board (IRB), Food and Drug Administration (FDA), Health Canada or study sponsor (Canadian Cancer Trials Group). The study sponsor is the organization who oversees the study.

This is the end of the Overview and Key Information section

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

What is the purpose of this study?

The purpose of this study is to compare the usual treatment of whole brain radiation therapy with hippocampus avoidance (HA-WBRT) plus a drug called memantine, to stereotactic radiosurgery (SRS). Receiving SRS could control your cancer that has spread to your brain. But, it could also cause side effects, which are described in the risks section below.

This study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach. To decide if it is better, the study doctors will be looking to see if the stereotactic radiosurgery (SRS) helps to either slow the growth of your cancer or stop it from coming back, compared to the usual approach. Doctors will also look to see if this new approach increases the life span of patients with this type of cancer, and if it helps with your quality of life and cancer related symptoms. The researchers hope that SRS will show better results for patients at 6 months after treatment, when compared to the usual approach.

There will be about 206 people from Canada and the United States taking part in this study.

What are the study groups?

This study has 2 study groups. You will be told which group you are in.

- **Group 1**
  If you are in this group, you will get the usual type of radiation therapy, called whole brain radiation therapy with hippocampus avoidance (HA-WBRT), to treat this type of cancer. The hippocampus is a brain structure that is important for memory. Hippocampus avoidance during HA-WBRT decreases the amount of radiation that is delivered to this area. All efforts will be made to decrease in the amount of radiation to the hippocampus with HA-WBRT, however, radiation decrease depends on how far from hippocampus the cancer requiring radiation treatment is located, and despite the best efforts radiation to hippocampus may not be completely eliminated. HA-WBRT will be given to you as an outpatient for 5 days a week for about 2 weeks (about 10 treatments). The treatments last about 10 to 20 minutes, including the set-up. You will also be given a drug called memantine to help prevent symptoms of HA-WBRT. Memantine will be taken by mouth once or twice daily with water, with or without food. Memantine will be taken for up to 24 weeks.

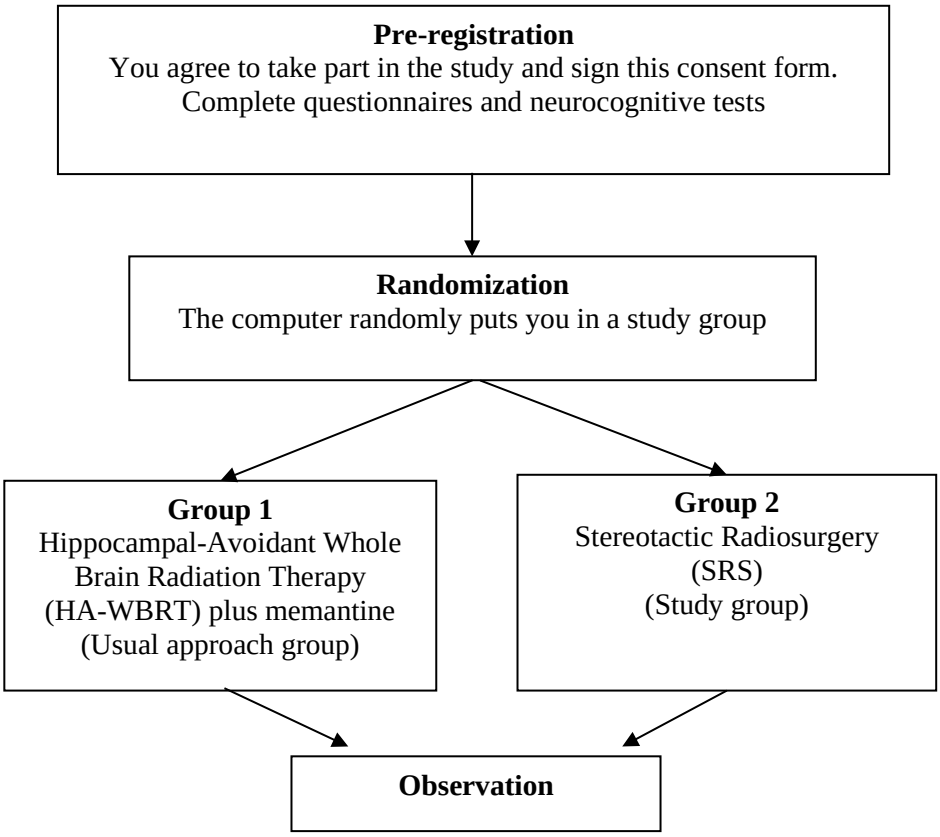
  There will be about 103 people in this group.

- **Group 2**
  If you are in this group, you will receive a type of combined radiation and surgery treatment called stereotactic radiosurgery (SRS). SRS is a one-day (or in some cases two day), out-patient procedure, during which a high dose of radiation is delivered to small spots in the brain while excluding the surrounding normal brain. For most patients, the usual time on the radiosurgery treatment machine is 30 to 90 minutes, but the entire procedure can take up to 4-6 hours including preparation time.

  There will be about 103 people in this group.

We will use a computer to assign you to one of the study groups. This process is called "randomization." It means that your doctor will not choose and you cannot choose which study group you are in. You will be put into a group by chance. You will have an equal chance of being in Group 1 or Group 2.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the top and read down to the bottom, following the lines and arrows.



What exams, tests, and procedures are involved in this study?

Before you begin the study, your doctor will review the results of your exams, tests, and procedures. This helps your doctor decide if it is safe for you to take part in the study. If you join the study, you will have more exams, tests, and procedures to closely monitor your safety and health. Most of these are included in the usual care you would get even if you were not in a study.

Some exams, tests, and procedures are a necessary part of the research study, but would not be included in usual care. Listed below are procedures that will be done for research purposes only.

Before you begin the study
You may need to have the following extra tests to find out if you can be in the study:

- A urine or blood pregnancy test for women of child bearing potential.

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra tests described below. They may not be part of the usual approach for your type of cancer.

During the study
You will be asked to visit your study doctor for follow-up visits after your study treatment is completed. These follow-up visits will be at 8 weeks, 4 months, 6 months, 9 months, 12 months, 16 months, and 24 months after you began treatment. These visits may include the following extra tests:

- A medical history, an interview including questions about your past and current health, medications and current symptoms.
- A neurologic history and examination.

After that, you will be followed every 12 months for up to 5 years. For these visits, you will be asked for information about any medications and current symptoms.

In the event of a public health emergency, the timing of these planned procedures or visits may change. Some visits may happen over the phone or video conference or with your family doctor. Some of the tests that you undergo may be missed, rescheduled or done at other hospitals or laboratories, or may not be done. There may also be changes to your treatment schedule as well as where and how you receive your study drug/treatment. We may also collect information about screening you may have in a public health emergency.

The study team will let you know if changes are required and will make changes if it is safe to do so.

Mandatory Specimen Collection for Research Purposes Only
You will need to have blood and urine samples collected for the study. Samples will be taken six times during the study: after you are pre-registered to the study, but before treatment, right after your treatment, and then at 8 weeks, 4 months, 6 months, and 12 months after you have finished treatment. At each time point, about 3 tablespoons of blood will be drawn and a single urine sample will be taken.

The researchers doing this study need to do tests on samples to better understand the nature of your cancer, and to see how patients respond to treatment. You and your doctor will not get the results of this testing.

The samples will be sent to the CCTG's Biorepository at Queen's University in Kingston, Ontario. If planned testing cannot be done at Queen's University, it may be done in another laboratory in Canada or a laboratory outside of Canada with the specific expertise needed but only under the direction of the Canadian Cancer Trials Group. Samples sent to another laboratory will only include a unique tumour bank code that is assigned upon receipt at the lab at Queen's University. The samples will not include participant study ID or initials and will be used completely, destroyed or returned to Queen's University. Personal information about you will not be sent with the samples and all results will be returned to the Canadian Cancer Trials Group.

Questionnaires and Neurological Examinations
If you choose to take part in this study, you will be asked to fill out a form with questions about daily activities, and mental, physical and emotional symptoms, etc. Researchers will use this information to understand how your treatment and illness affects your quality of life. You will also asked to complete a brief cognitive test, with a series of mental function tasks given by an examiner. Researchers will use this information to understand how your treatment and illness affects your mental function.

Since these forms are being used for research, the responses you provide will not be shared with your study doctor. If you have any serious health issues or other concerns, please talk with your doctor or nurse right away.

You will be asked to fill out the form with questions and complete the cognitive test before starting this study and at each follow up visit after your treatment. The form with questions takes about 15 minutes to complete and the cognitive test takes 20 to 30 minutes to complete.

You will also be asked to fill out a form with questions about health care resources used in your care. Researchers will use this to learn more about the costs of this new treatment (SRS) compared to the standard treatment (HA-WBRT). This form will take about 5 minutes to complete. You will be asked to fill out this form before starting this study, and at each follow up visit after your treatment.

Central Radiology Imaging Review
Copies of your magnetic resonance imaging (MRI) scans will be collected as part of this study. This is required for quality assurance and data management. The scan copies will be uploaded to the American College of Radiology (ACR) Transmission of Imaging and Data (TRIAD) system. They will then be sent to the Imaging and Radiation Oncology Core (IROC) Quality Assurance Centre in Houston, Texas and in Rhode Island.

They will be kept there until the end of the study monitoring period. After that, they will be sent to Queens University in Kingston, Ontario for storage and review. To protect your identity, the information that will be on your MRI will be limited to your participant code. This may also include your initials.

Drug Diary
If you are randomized to Group 1 (HA-WBRT + Memantine), you will be asked to keep a diary of when you take your memantine tablets. You should return the diary to the clinic at each visit during the time when you are taking memantine. While it is not mandatory to complete this diary, you are highly encouraged to do so in order to ensure that you are taking the pills as directed and to track the exact number of memantine tablets you have taken during the study.

What risks can I expect from taking part in this study?

General Risks
If you choose to take part in this study, there is a risk that the stereotactic radiation therapy may not be as good as the usual approach with whole brain radiation at controlling your cancer or preserving your quality of life.

You also may have the following discomforts:
- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

The memantine used in this study could be very harmful to an unborn or newborn baby. There may be some risks that doctors do not yet know about. It is very important that you check with your study doctor about what types of birth control or pregnancy prevention to use during the study and for 90 days after the last dose of memantine.

Your safety is our first priority, and in the event of a public health emergency, your study doctor will discuss any additional risks or changes to your treatment with you.

Side Effect Risks
The stereotactic radiation therapy used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will test your blood and let you know if changes occur that may affect your health.

There is also a risk that you could have other side effects from the study treatment.

Here are important things to know about side effects:
- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:
- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects

Drug Risks
The tables below show the most common and most serious side effects doctors know about. Keep in mind that there might be other side effects doctors do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Study Group 1 - Whole Brain Radiation Therapy with hippocampus avoidance is the usual approach for treating cancer that has spread to the brain. Memantine is given to help reduce the symptoms of HA-WBRT.

Possible Side Effects of Hippocampal-Avoidant Whole Brain Radiation Therapy (HA-WBRT)

COMMON, SOME MAY BE SERIOUS In 100 people receiving HA-WBRT, more than 20 and up to 100 may have:
• hair loss, which may be permanent • temporary scalp redness and drying • fatigue (tiredness) • memory loss, which can occur in the first few months after whole brain radiotherapy and may be permanent

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving HA-WBRT, from 4 to 20 may have:
• nausea • cataract formation • dry mouth • taste changes • temporary ear and ear canal redness, plugging or drainage • headaches • increased sleepiness (occurring four to ten weeks after radiation therapy is complete and lasting for several days up to two weeks) • the development of cancer in or near the hippocampus

RARE, AND SERIOUS In 100 people receiving HA-WBRT, 3 or fewer may have:
• decreased brain function such as motor function (coordination/movement) • severe local damage to or death of normal brain tissue, which may require surgery to remove • hardening of the arteries in the brain which rarely may lead to strokes many years after whole brain radiotherapy • a second new cancer caused by radiation, in the brain or nearby organs which rarely may occur many years after whole brain radiotherapy • eye damage with the possibility of permanent blindness

Possible Side Effects of Memantine

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Memantine, from 4 to 20 may have:
• dizziness, fainting • depression • tremor • inability to speak or to understand speech • sore throat, runny nose • changes in motor activity which may cause trouble moving • restlessness • leg pain • swelling of the joints • pain and weakness of the muscles • shortness of breath • tiredness/fatigue • difficulty sleeping • loss of appetite, decreased weight • indigestion • buildup of fluid in the body causing swelling • changes in frequency of urination which may be painful and sometimes urine leakage • inability to control bowel movements • swelling of the veins around the rectum (hemorrhoids) • problems with teeth • rash, blisters which maybe severe and can involve the inside of the mouth and other parts of the body and may cause the top layer of your skin to peel from all over your body and can cause severe infections • changes in the levels of minerals and enzyme in the blood as seen on blood tests. you may not have symptoms.

RARE, AND SERIOUS In 100 people receiving Memantine, 3 or fewer may have:
• pain including back, joints, belly • increased levels of sugar (glucose) in the blood which may make you feel thirsty, need to urinate more often, headaches, trouble concentrating and tired • headache • flu-like symptoms including body aches, fever, chills, tiredness, loss of appetite, cough • constipation • nausea • diarrhea • vomiting

RARE, AND SERIOUS In 100 people receiving Memantine, 3 or fewer may have:
• anxiety or nervousness, and other changes in behaviour • abnormal changes in the brain including a sudden loss of blood flow that may last a few minutes to an hour but has no lasting effects. symptoms may include confusion, dizziness, loss of balance • hallucinations (strange visions or sounds) • sleepiness • coughing • inflammation in the lungs that can cause coughing, wheezing and shortness of breath and may cause chest discomfort • infections • allergic reactions that may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat and may be life-threatening • abnormal gait (movement/walking) which may lead to falling • heart problems. signs and symptoms may include: hypertension (increased blood pressure), shortness of breath, cough, tiredness, abnormal heartbeat, chest pain, swelling of the ankles • blood clots in your veins, which can include blot clots in your lungs • seizure • problems with the eyes including changes in vision

Study Group 2 - Stereotactic Radiosurgery is the study approach.

Possible Side Effects of Stereotactic Radiosurgery (SRS)

COMMON, SOME MAY BE SERIOUS In 100 people receiving SRS, more than 20 and up to 100 may have:
• temporary (short-term) pain from with the head frame placement (if a head frame is used)

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving SRS, from 4 to 20 may have:
• headache • localized hair loss which may be permanent • nausea • vomiting • allergic reaction to the local anesthesia (rash, itching, nausea, or difficulty breathing) • bleeding and/or infection around the head frame (if a head frame is used) • swelling of the brain in the treated area which may require treatment with steroids

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving SRS, from 4 to 20 may have:
• severe local damage to or death of normal brain tissue, which may require surgery to remove

RARE, AND SERIOUS In 100 people receiving SRS, 3 or fewer may have:
• decreased brain function such as motor function (coordination/movement) • hardening of the arteries in the brain which rarely may lead to strokes many years after stereotactic radiosurgery • a second new cancer caused by radiation, in the brain or nearby organs which rarely may occur many years after stereotactic radiosurgery • damage to vision tracts (eye damage) with the possibility of permanent blindness

Long term effects of the radiation or radiosurgery used in this study include an increased risk of developing other cancers.

What are my responsibilities in this study?

If you choose to take part in this study you will need to:
- Keep your study appointments.
- Tell your doctor about:
    - all medications and supplements you are taking
    - any side effects
    - any doctors' visits or hospital stays outside of this study
    - if you have been or are currently in another research study.

For women: Do not get pregnant or breastfeed while taking part in this study. **For men:** Do not father a baby while taking part in this study. **For all:** Tell your study doctor right away if you think that you or your partner have become pregnant during the study or within 90 days after your last dose of memantine.

What are the costs of taking part in this study?

You and/or your insurance plan will need to pay for the costs of medical care you get as part of the study, just as you would if you were getting the usual care for your cancer. This includes:
- the costs of tests, exams, procedures, and drugs that you get during the study to monitor your safety, and prevent and treat side effects.
- the cost of giving the whole brain radiation therapy, which is considered usual care for your cancer
- the cost of giving the stereotactic radiosurgery (SRS)
- the cost of the memantine given as part of this study
- your insurance co-pays and deductibles.

Talk to your insurance provider and make sure that you understand what your insurance pays for and what it doesn't pay for if you take part in this clinical trial. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study. These include:

- The 6 extra blood and urine samples collected during the study.
- The questionnaires and neurological examinations given as part of this study

Taking part in this study may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your cancer. You may:

- Have more travel costs.
- Need to take more time off work.
- Have other additional personal costs.

You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What happens if I am injured because I took part in this study?

If you are injured as a result of taking part in this study and need medical treatment, please talk with your study doctor right away about your treatment options. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for a study-related injury. Ask them if they will pay. If you do not have insurance, then you would need to pay for these medical costs.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in the study, you have the legal right to seek payment, even though you are in a study. Agreeing to take part in this study does not mean you give up these rights.

No funds have been set aside to compensate you in the event of injury.

Who will see my medical information?

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should

happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at or receive copies of some of the information in your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group.
Some of these organizations are:

- Montana Cancer Consortium
- The study sponsors supporting the study (Canadian Cancer Trials Group, Alliance for Clinical Trials in Oncology, and NRG Oncology Foundation Inc.) now or in the future
- The NCI Central Institutional Review Board, IRB, which is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration, Health Canada and the groups they work with to review research.
- The NCI and the groups it works with to review research.
- The NCI's National Clinical Trials Network and the groups it works with to conduct research, including the Imaging and Radiation Oncology Core (IROC) Quality Assurance Centre

In addition to storing data in the study database, data from studies that are publicly funded may also be shared broadly for future research with protections for your privacy. The goal of this data sharing is to make more research possible that may improve people's health. Your study records may be stored and shared for future use in public databases. However, your name and other personal information will not be used.

Some types of future research may include looking at your information and information from other patients to see who had side effects across many studies or comparing new study data with older study data. However, right now, we don't know what research may be done in the future using your information. This means that:

- You will not be asked if you agree to take part in the specific future research studies using your health information.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your information.

Where can I get more information?

You may visit the NCI web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, call the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

Optional studies that you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. They are separate from the main study described above. These optional studies will not benefit your health. The researchers leading these optional studies hope the results will help other people with cancer in the future. The results will not be added to your medical records and you or your study doctor will not know the results.

Taking part in these optional studies is your choice. You can still take part in the main study even if you say "no" to any or all of these studies. There is no penalty for saying "no." You and your insurance company will not be billed for these optional studies. If you sign up for, but cannot complete any of these studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional sample collections for known laboratory studies and/or storage for possible future studies

Researchers are trying to learn more about cancer and other health problems using blood and tissue samples from people who take part in clinical trials. By studying these samples, researchers hope to find new ways to prevent, detect, treat, or cure diseases.

Some of these studies may be about how genes affect health and disease. Other studies may look at how genes affect a person's response to treatment. Genes carry information about traits that are found in you and your family. Examples of traits are the color of your eyes, having curly or

straight hair, and certain health conditions that are passed down in families. Some of the studies may lead to new products, such as drugs or tests for diseases.

Known future studies
If you choose to take part in this optional study, researchers will use blood that is leftover from the main study for research on genes (DNA) found in your blood. Urine that is leftover from the main study will be stored for research on radiotherapy related changes in genes (DNA).

Unknown future studies
If you choose to take part in this optional study, blood will be collected and stored. Any urine leftover from the known future studies will also be stored, so additional urine samples are not required for this purpose. Storing samples for future studies is called "biobanking." The biobank is being run by the Canadian Cancer Trials Group. This is a publicly funded study. Samples from publicly funded studies are required to be shared as broadly as possible. However, we will protect your privacy. The goal of this is to make more research possible that may improve people's health. Any health-related information, such as your response to cancer treatment, results of study tests, and medicines you took, will be stored for future use.

The biobank is a public research resource. It has controlled access. This means that researchers who want to get samples and data from it must submit a specific research request. The request identifies who they are and what their planned research project is. Before getting the samples and data, the researchers must agree to keep the data private, only use it for their planned research project, and never use it to try to identify you.

Right now, we don't know what research may be done in the future using your blood or urine samples. This means that:

- You will not be asked if you agree to take part in the future research studies.
- You and your study doctor will not be told when or what type of research will be done.
- You will not get reports or other information about any research that is done using your samples.

Unknown future research studies may include sequencing of all or part of your DNA. This is called genomic sequencing. Sequencing allows researchers to identify your genetic code. Changes in your genetic code may be passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

What is involved in this optional sample collection?
If you agree to take part, here is what will happen next:

1. About 4 teaspoons of blood will be collected from a vein in your arm each time. Samples will be taken after you are pre-registered to the study, but before treatment, right after your treatment, and then at 8 weeks, 4 months, 6 months, and 12 months after you have finished treatment.Whenever possible, these samples will be taken at the same time as

your study related tests. Urine samples that are leftover from the main study will be sent to the biobank

2. Your samples will be stored in the biobank. There is no limit on the length of time we will keep your samples and research information. The samples will be kept until they are used for research or destroyed.
3. Researchers can only get samples from the biobank after their research has been approved by experts. Researchers will not be given your name or contact information.
4. Some of your genetic and health information may be placed in central databases for researchers to use. The databases will not include your name or contact information.

What are the risks in this optional sample collection?

- The most common risks related to drawing blood from your arm are brief pain and maybe a bruise.
- Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. Researchers believe the chance that someone could access and misuse your information is very small. However, the risk may increase in the future as people find new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job and get or keep health insurance. There are laws against the misuse of genetic information, but they may not give full protection. For more information about the laws that protect you, ask your study doctor or visit: https://www.genome.gov/10002328/

How will information about me be kept private?

Your privacy is very important to the study researchers and biobank. They will make every effort to protect it. Here are just a few of the steps they will take:

1. They will remove identifiers, such as your initials, from your sample and information. They will replace them with a code number. There will be a master list linking the code numbers to names, but they will keep it separate from the samples and information.
2. Researchers who study your sample and information will not know who you are. They also must agree that they will not try to find out who you are.
3. Your personal information will not be given to anyone unless it is required by law.
4. If research results are published, your name and other personal information will not be used.

What are the benefits to taking part in this optional sample collection?

You will not benefit from taking part. The researchers, using the samples from you and others, might make discoveries that could help people in the future.

Are there any costs or payments to this optional sample collection?

There are no costs to you or your insurance. You will not be paid for taking part in this study. The research may lead to new tests, drugs, or other products for sale. If it does, you will not get any payment.

What if I change my mind about this optional sample collection?
If you decide you no longer want your samples to be used, you can call the study doctor, Dr. David Roberge at 514-890-8254, who will let the biobank know. Then, any sample that remains in the biobank will be destroyed or returned to your study doctor. This will not apply to any samples or related health information that have already been given to or used by researchers.

What if I have questions about this optional sample collection?
If you have questions about the use of your samples for research, contact the study doctor, Dr. David Roberge at 514-890-8254.

Please circle your answer below to show if you would or would not like to take part in each optional study:

Samples for known future studies:

I agree that my blood and urine samples leftover from the main study, and related health information, may be used for the laboratory study described above.

YES NO

Samples for unknown future studies:

I agree that my fresh blood and leftover urine samples and related health information may be kept in a biobank for use in future health research.

YES NO

This is the end of the section about optional studies.

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed and dated copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)

Consent Acknowledgement Form

By signing this form I, _____ am acknowledging the following:

- I have been given adequate time to review the consent form for Clinical Trial CCTG CE.7.
- My physician has answered my questions to my satisfaction at this point.
- If I have any study-related questions in the future, I will talk with my doctor, nurse, or research coordinator.
- I understand that participation in this clinical trial is optional, and that I may withdraw from the trial at any time.
- No matter what I decide to do, and whether or not I decide to participate in this study, my decision will not harm the care that I receive or my relationship with my doctor, nurses, or other healthcare provider.
- No study procedures specific for this clinical trial were performed prior to my signing this consent form.
- I have reviewed with my doctor all medications that I am currently taking, including nonprescription medications, vitamins, herbal supplements, and naturopathic preparations, to avoid possible drug interactions.
- I have been informed of the potential reproductive risks associated with treatment on this clinical trial and understand precautions must be taken to avoid pregnancy while undergoing treatment and for a period of time after the conclusion of treatment.
- While abstinence is the most effective way of preventing a pregnancy, we understand that you may consider other pregnancy prevention methods. You are encouraged to ask your study doctor or research nurse for more information about reproductive risks and pregnancy prevention methods.
- If I become pregnant or have reason to believe I might be pregnant or fathered a child while receiving treatment on this clinical trial, I will notify my doctor immediately.
- Once I am no longer receiving treatment on this clinical trial, I may discuss with my doctor when it may be safe to become pregnant or father a child.
- I have received a signed copy of the consent form for the above named clinical trial.

_____ _____
Patient Signature Date

_____ _____
Person Obtaining Consent Signature Date

Montana Cancer Consortium
Authorization (Permission) to Use or Disclose (Release) Identifiable Health Information for Research

Participant's Name: _____

Birth Date: _____

1. What is the purpose of this form?

The CCTG, is an organization that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your health information for research. This information may include data that identifies you. Please carefully review the information below. If you agree that researchers can use your personal health information, you must sign and date this form to give them your permission.

2. What personal health information do the researchers want to use?

The researchers want to copy and use the portions of your medical record that they will need for their research. If you enter a CCTG research study, information that will be used and/or released may include the following:

- the history and diagnosis of your disease;
- specific information about the treatments you received, including previous treatment(s) you may have had;
- information about other medical conditions that may affect your treatment;
- medical data, including laboratory test results, tumor measurements, CT scans, MRIs, x-rays, and pathology results;
- information on side effects (adverse events) you may experience, and how these were treated;
- long-term information about your general health status and the status of your disease;
- data that may be related to tissue and/or blood samples that may be collected from you; and
- numbers or codes that will identify you, such as your social security number, medical record number, initials, and date of birth.

You may request a blank copy of the CCTG data forms from Montana Cancer Consortium to learn what information will be shared.

3. Why do the researchers want my personal health information?

Montana Cancer Consortium will collect your health information and share it with CCTG if you enter a cooperative group research study, or to evaluate your eligibility for a study. CCTG will use your information in the following cancer research study:

CCTG CE.7: A Phase III Trial of Stereotactic Radiosurgery Compared with Hippocampal-Avoidant Whole Brain Radiotherapy (HA-WBRT) Plus Memantine for 5-15 Brain Metastases

4. Who will be able to use my personal health information?

Montana Cancer Consortium will use your health information for research. As part of this research, they may give your information to the following groups taking part in the research. Montana Cancer Consortium may also permit the following groups to come in to review your original records that are kept by Montana Cancer Consortium so that they can monitor their research study**:**

- National Cancer Institute (NCI) Central Institutional Review Board (CIRB)
- the CCTG Operations Center;
- the CCTG Biostatistical Center;
- the Cancer Trials Support Unit (CTSU) or designees, a research group sponsored by the National Cancer Institute to provide greater access to cancer studies;
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law;
- other people or organizations assisting with CCTG research efforts. This may include drug manufacturers, drug companies that may provide partial support for the study, drug distributors, and/or their designees; and
- central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed in the bullets above.

5. How will information about me be kept private?

CCTG will keep all patient information private to the extent possible, even though they and other federal research groups are not subject to the same federal privacy laws governing clinical centers. CCTG will not release identifiable health information about you to others except as authorized by this form, or required by law. If your identifiable health information must be shared with other organizations, the privacy laws that govern those organizations would apply.

6. What happens if I do not sign this permission form?

If you do not sign this permission form, you will not be able to take part in the research study for which you are being considered.

7. If I sign this form, will I automatically be entered into the research study?

No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a separate research consent form.

8. What happens if I want to withdraw my permission?

You can change your mind at any time and withdraw your permission to allow your personal health information to be used in the research. If this happens, you must withdraw your permission in writing. Beginning on the date you withdraw your permission, no new personal health information will be used for research. However, researchers may continue to use the health information that was provided before you withdrew your permission.

If you sign this form and enter the research study, but later change your mind and withdraw your permission, you will be removed from the research study at that time.

To withdraw your permission, please contact the institution below. They will make sure your written request to withdraw your permission is processed correctly.

Montana Cancer Consortium
2132 Broadwater Ave, Suite A1
Billings, MT 59102
406-969-6060
Fax: 406-969-6070

9. How long will this permission last?

If you agree by signing this form that researchers can use your personal health information, this permission has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

10. What are my rights regarding access to my personal health information?

You have the right to refuse to sign this permission form. You have the right to review and/or copy records of your personal health information kept by Montana Cancer Consortium. You do not have the right to review and/or copy records kept by CCTG or other researchers associated with the research study.

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Signatures

I agree that my personal health information may be used for the research purposes described in this form.

Signature of Patient: _____Date: _____

Signature of Person Obtaining Permission: _____Date: _____

Printed Name of Person Obtaining Permission: _____