NRG ONCOLOGY

NRG-BR002

(ClinicalTrials.gov NCT #: **02364557***)*

A PHASE IIR/III TRIAL OF STANDARD OF CARE THERAPY WITH OR WITHOUT STEROTACTIC BODY RADIOTHERAPY (SBRT) AND/OR SURGICAL ABLATION FOR NEWLY OLIGOMETASTATIC BREAST CANCER

Amendment 6: August 12, 2021

NRG-BR002 Consent Form

Study Title for Study Participants: Testing whether treating breast cancer metastases with surgery or high-dose radiation improves survival

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:

NRG-BR002

A Phase IIR/III Trial of Standard of Care Therapy with or without Stereotactic Body Radiotherapy (SBRT) and/or Surgical Ablation for Newly Oligometastatic Breast Cancer (12-AUG-2021)

What is the usual approach to my breast cancer? (14-JUN-2018)

You are being asked to take part in this research study because you were treated for breast cancer in the past and now have breast cancer that has spread (metastasized) to up to 4 locations in your body. Your doctors have confirmed this by a biopsy. The usual treatment (when not participating in a study) when breast cancer has spread (metastasized) to another part of the body, is oral or intravenous (through a vein) medications (chemotherapy, hormonal therapy, biologic therapy and others) to help stop the cancer sites from getting larger and the spread of the cancer to additional body sites. Treatment can be given to a specific metastatic breast cancer site when it causes a symptom (such as pain) or is at risk for causing injury that is not controlled with medication alone. In this case, other therapies (surgery, radiation, and others) are directed at a specific body site to relieve (palliate) the symptom or potential injury the metastatic breast cancer is causing. In general, less than 50% of metastatic breast cancer patients will require palliative radiotherapy to a metastatic body site to relieve a symptom. Even if you participate in this study, you will continue to receive the usual medications and other therapies as needed as determined by your doctor to treat your cancer if it progresses.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have the usual approach to treatment with the oral or intravenous (IV) medications described above that involves hormonal therapy, chemotherapy, biologic and other therapy; and may also include other palliative therapies such as surgery, radiation or other therapy to relieve breast cancer symptoms. Taking part in this study will NOT limit those choices.
- you may choose to take part in a different study, if one is available.
- or you may choose not to be treated for your metastases, but you may want to receive comfort care (palliation) to relieve symptoms caused by the breast cancer metastases with medication, radiation therapy, surgery or other palliative method.

Why is this study being done? (14-JUN-2018)

The purpose of this study is to compare any good or bad effects of delivering ablative local therapy to ALL known metastatic tumor sites, (even those that are not causing symptoms); in addition to the usual approach of intravenous or oral medications for treatment of breast cancer that has spread to up to 4 body sites. **Ablative** means that the **intention** of the local treatment is to put an end to the cancer at that metastatic site. The ablative local therapy can be either very focused, intensive radiotherapy called Stereotactic Body Radiotherapy (SBRT)

or surgical resection. Both SBRT and surgical resection have been tested for safety, but are not part of the usual approach. The addition of ablative local therapy to all known metastatic sites to the usual approach of oral and intravenous medications could prevent your breast cancer from progressing; that means preventing it from returning to the treated site and from spreading to new sites in your body - but it could also cause side effects. This study will allow researchers to know whether this different approach that includes ablative local therapy to all metastatic sites is better, the same or worse than the usual approach. To be better, ablative local therapy to all known metastatic sites should increase life without cancer progressing by 9 months or more compared to the usual approach. There will be about 128 metastatic breast cancer patients taking part in this part of the study. If this different approach increases life without cancer progressing by 9 months, then about 232 more patients with breast cancer that has spread to up to 4 body sites will take part in the study to compare if delivering ablative local therapy to all known metastatic sites in addition to usual therapy can improve the number of breast cancer patients living at 5 years. There will be about 360 total patients taking part in the entire study.

What are the study groups?

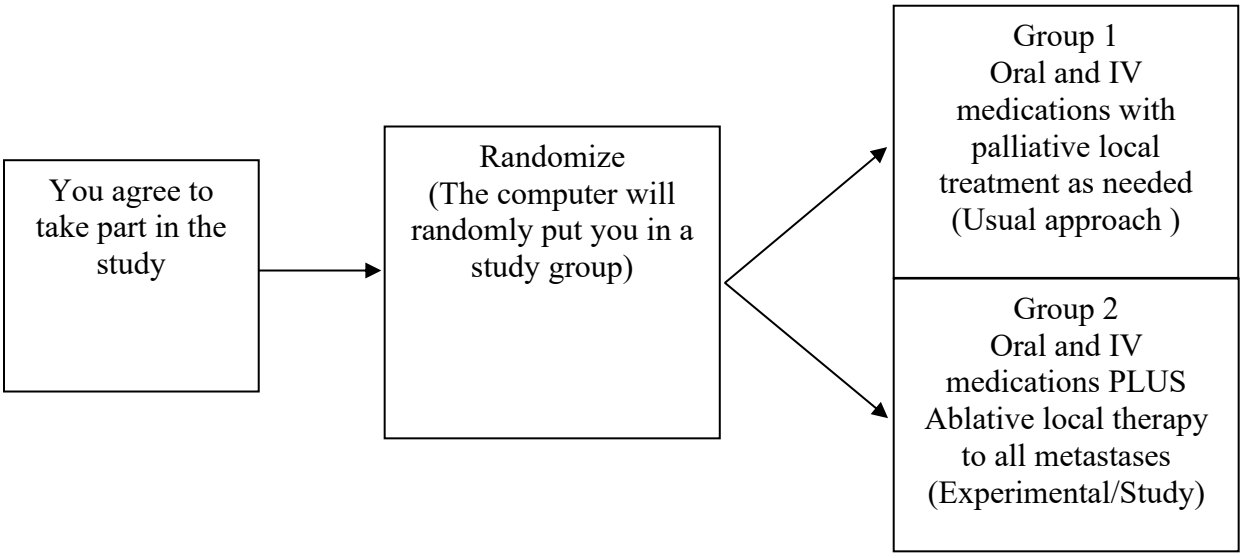
A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the others.

This study has two study groups:

- Group 1 will get the usual treatment for metastatic breast cancer which is oral or intravenous (IV) medications (hormonal therapy, chemotherapy, biologic and other therapy) as directed by your doctor; and may also include palliative local therapies such as surgery, radiation or other methods if necessary to help relieve uncontrolled symptoms at your known site of metastasis.
- Group 2 will get the usual treatment for metastatic breast cancer which is oral or intravenous medications (hormonal therapy, chemotherapy, biologic and other therapy) as directed by your doctor, **plus** ablative local therapy to all known metastatic sites. Ablative local therapy can be with SBRT or surgical resection. Which ablative local therapy to be used will be decided by you and your doctor.

If SBRT or surgery is used, it will be performed with established methods and in a way other patients, similar to yourself, have been treated in the past. It is also possible that one tumor will have radiation and another surgery depending on where it is located in your body and the judgements of the doctors caring for you.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

If you receive the SBRT for ablative local therapy, your radiation therapy will take approximately 1-3 weeks and if you receive surgery for ablative local therapy your operation will be done within 6 weeks. After you finish ablative local therapy (Group 2) or if you are receiving the usual approach (Group 1) your doctor will continue to watch you with visits to the office for follow-up exams for side effects and follow your breast cancer condition for at least two years. Your doctor will continue to watch you for side effects and follow your condition for *up to 10 years or more.* Keeping in touch with you and checking on your condition helps us to look at the long-term effects of the study therapy.

What extra tests and procedures will I have if I take part in this study?

All exams, tests, and procedures in this study are part of the usual approach for the treatment of metastatic breast cancer, or when ablative local therapy with SBRT or surgical resection is used.

What possible risks can I expect from taking part in this study? **(9/16/16)**

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual;
- You may be asked sensitive or private questions which you normally do not discuss.
- The study treatment of ablative local therapy with SBRT or Surgery for all metastases may not be better, and could possibly be worse, than the usual approach for your metastatic breast cancer.
- The study treatment of ablative local therapy with SBRT or Surgery may affect how different parts of your body work such as your liver, kidneys, heart, and blood. Your doctor will be monitoring your condition with regular office visits including testing your blood and will let you know if changes occur that may affect your health.
- You and your doctor will decide what Usual Therapy, oral or intravenous medications(chemotherapy, hormone therapy, biologic therapy, etc) you will receive and palliative therapy when necessary for treatment of your metastatic breast cancer. The risks of your Usual Therapy depends on the specific type of therapy delivered. Your doctor will explain the risks associated with your therapy
- Chemotherapy, hormone therapy, biologic therapy or other medications that will be used to treat your metastatic breast for usual care and the study group all have associated potential side effects. Your doctor will explain the known risks specific to the oral or IV medication used to treat your cancer.

- Palliative therapy with radiation, surgery, or other method that is sometimes used during usual care has associated potential side effects. Your doctor will explain the known risks specific to whichever palliative therapy is recommended.

Here are important points 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 interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may discontinue or adjust the radiation treatment or abort a surgery to try to reduce side effects.

The tables below show the most common and the most serious side effects of **the local ablative therapy with SBRT or surgery used in Group 2** that researchers know about. There might be other side effects that researchers do not yet know about. If new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of SBRT Radiation Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, more than 20 and up to 100 may have:
• Reddening, tanning, or peeling of the skin in the treatment area • Mild pain • Hair loss • Tiredness • Diarrhea, nausea, decreased appetite • Anemia, which may require blood transfusion • Infection, especially when white blood cell count is low • Frequent urination

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, from 4 to 20 may have:
• Thickening and numbness of the skin in the treatment area • Sores or ulcers on the skin or near the cancer location • Permanent hair loss • Bleeding from the skin • Sores in mouth which may cause difficulty swallowing • Cough • Shortness of breath • Pain in your ribs • Belly pain • Sexual dysfunction which may include pain during intercourse.

You may also experience the additional risks specific to the area of the body where you receive the radiation.

Possible Side Effects of SBRT Radiation Therapy to the **LUNG, NECK OR CHEST**

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the **LUNG, NECK OR CHEST**, more than 20 and up to 100 may have:
• A common effect of this treatment in previous studies was scarring of the lung tissue that can lead to cough, thick mucus (phlegm), difficulty breathing, and other symptoms of pneumonia. There can also be permanent scarring of a portion of the lung or ribs. Efforts will be made to reduce this risk and limit its effect. However, it is possible that you will have shortness of breath at rest or during exercise, may need to receive oxygen, and/or may have chest wall pain. A few patients may need oxygen therapy permanently. In rare cases, this can be life threatening. • Tiredness, which is temporary • The skin in the treatment area may become reddened and/or dry, and chest hair in the treatment area may fall out and may not grow back.

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the **LUNG, NECK OR CHEST**, from 4 to 20 may have:

- Cough
- Difficulty breathing
- Chest radiotherapy can cause changes in normal lungs. These changes can be as unimportant as small amounts of "scarring" seen on x-rays that does not cause symptoms. Sometimes chest radiotherapy can cause lung damage that leads to symptoms such as chest pain, shortness of breath, cough, or fever. Rarely, these symptoms can be severe or life threatening. Treatment for this lung damage involves pain medicines, anti-inflammatory medicines (corticosteroids), and rarely, oxygen therapy, which may be permanent. You should tell your doctors immediately if you have any of these symptoms.
- Irritation of the esophagus, which may result in heartburn or pain on swallowing
- Fever
- Chest wall discomfort or pain
- Rib fracture, which may cause pain

RARE, AND SERIOUS

In 100 people receiving radiation therapy to the **LUNG, NECK OR CHEST**, 3 or fewer may have:

- Irritation of the lining around the heart, which can cause chest pain, shortness of breath, and irregular or rapid heartbeat; rarely, this can require surgery to correct.
- Irritation and/or damage to the heart muscle; rarely, this can cause a heart attack, heart failure, and/or death.
- Irritation and/or damage to the spinal cord (the major nerve within the spine), which can lead to weakness, tingling or numbness of the lower body and legs; very rarely, this can lead to inability to move or control the lower half of the body.
- Damage or scarring of nerves in the chest, which may result in a hoarse voice or a tingling “pins and needles” sensation, or pain in the chest and rib area, depending on the nerve affected.
- Damage or scarring of nerves at the top of the lungs, which may result in a tingling “pins and needles” sensation or pain or weakness of the muscles of the arm and hand, since these nerves provide sensation and muscle control for the arm and hand.
- Narrowing of the esophagus (tube to the stomach), which can result in swallowing difficulty.
- Thinning of the wall of the esophagus; rarely, this can cause a hole in the esophagus and/or a hole in your lung which could result in difficulty with eating and breathing.
- Irritation of the large blood vessels surrounding the heart; rarely, this can cause bleeding (coughing up blood) and/or death.
- Irritation of the voice box which can cause hoarseness and/or pain.
- Damage to the blood vessels in the neck.

Possible Side Effects of SBRT Radiation Therapy to the **LIVER OR ABDOMEN (BELLY)**

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the LIVER OR ABDOMEN (BELLY), more than 20 and up to 100 may have:
• Fatigue, which generally goes away after the radiation therapy is completed • Skin irritation, redness, sunburn or ulcer in the skin of upper abdomen and chest wall, itchiness, and discomfort • Temporary changes in blood work (decrease in blood counts, increase in liver enzymes), without symptoms.

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the LIVER OR ABDOMEN (BELLY), from 4 to 20 may have:
• Nausea, vomiting (during therapy): more common if stomach or gastrointestinal tract receives radiation • Stomach, esophagus, small or large intestine irritation/ulceration, bleeding, obstruction, changes in bowel habits, or a tear or hole that may require medications or surgery. • Chest wall pain requiring medications, rib fracture • Temporary bleeding due to low platelet count

RARE, AND SERIOUS In 100 people receiving radiation therapy to the LIVER OR ABDOMEN (BELLY), 3 or fewer may have:
• Liver damage that can cause swelling of your abdomen (belly) and pain in the liver and spleen (right and left upper abdomen) within 3 months of completing therapy. • A decline in liver function within 12 weeks from start of therapy. This can cause similar symptoms to those above, plus fatigue, confusion, itchiness and/or change in skin color. This can lead to liver toxicity that can lead to death. There is an increased risk of liver toxicity in patients with large tumors and in patients with pre-existing liver disease. • Permanent low platelets which may lead to bleeding. • Kidney injury which may lead to a need for medication.

Possible Side Effects of SBRT Radiation Therapy to the **SPINE**

COMMON, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the **SPINE**, more than 20 and up to 100 may have:

- Inflammation of the lining of the mouth, throat and esophagus (passageway from mouth to stomach), which can result in difficulty swallowing, and if you cannot swallow water, dehydration can occur (the state in which your body does not have as much water and fluids as it should).
- Inflammation of the part of the airway that includes the vocal cords, which can result in hoarseness or loss of voice.

OCCASIONAL, SOME MAY BE SERIOUS

In 100 people receiving radiation therapy to the **SPINE**, from 4 to 20 may have:

- Inflammation of the lungs due to radiation treatment, which can result in cough, phlegm (thick mucus), difficulty breathing, and/or pneumonia.
- Fracture or compression of the treated bones of the spine, which can result in pain and which may need nonsurgical or surgical treatment.
- Discomfort or anxiety due to 60-90 minutes lying in a specific position, possibly within a frame device, for the planning session and 60 minutes for treatment; your doctor may give you medicine to decrease the discomfort and/or anxiety.

RARE, AND SERIOUS

In 100 people receiving radiation therapy to the **SPINE**, 3 or fewer may have:

- Esophageal fistula (abnormal opening in the passageway from mouth to belly).
- Scarring of the small or large bowel, which can result in a blockage in the bowel that would require treatment.
- Temporary or permanent damage to the spinal cord, which can result in:
    - Skin sensations, such as burning, prickling, itching, or tingling
    - Muscle weakness causing inability to walk (paralysis)

Possible Side Effects of SBRT Radiation Therapy to the **BONE**

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the **BONE**, more than 20 and up to 100 may have:
• Skin irritation in the treatment area • Hair loss • Reddening, rash or peeling of the skin in the treatment area.

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy to the **BONE**, from 4 to 20 may have:
• Pain

RARE, AND SERIOUS In 100 people receiving radiation therapy to the **BONE**, 3 or fewer may have:
• Weakening of your bone(s), potentially resulting in a fracture.

SURGERY:
As part of this study (in both treatment groups), surgery may be an option to remove metastatic tumor in some parts of the body. Possible sites for surgery include: lung, liver, abdomen, lymph nodes and bone. Common side effects of surgery include (but are not limited to) pain, bleeding, infection, wound healing difficulties, and injury to surrounding areas. The table below lists some of the common side effects of surgery depending on the type and location of your surgery. Prior to your surgery, you will need to sign a surgical consent form that is separate from this trial and is specific to the type of surgery you will undergo. The surgical consent will include risks specific to the type and location of your surgery. When you sign the surgical consent and during discussions with your surgeon, you should ask your surgeon about those risks.

COMMON, SOME MAY BE SERIOUS In 100 people undergoing surgery, more than 20 and up to 100 may have:
• Nausea, anorexia • Pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people undergoing surgery, from 4 to 20 may have:
• Surgery to the liver may result in liver damage that can causes yellowing of the skin and eyes, bleeding/bruising, fluid in the abdominal, tiredness, confusion, and itching • Bleeding • Infection • Wound healing difficulties • Swelling of the body • Injury to the nerves causing numbness

RARE, AND SERIOUS In 100 people undergoing surgery, 3 or fewer may have:
• Prolonged need to be on a breathing machine with a breathing tube in place, and/or prolonged need to have a tube in the chest because of damage to the lung • Injury to the areas near the site of abdominal surgery: ▪ Injury to the bowels resulting in the need for a "bag" so that the bowels drain outside of the body ▪ Kidney damage ▪ Pancreas injury

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant or breastfeed while in this study. If you are able to become pregnant, you will have a pregnancy test prior to starting this study. Radiation delivered either in Group 2 or Group 1 could be very damaging to an unborn baby. Additionally some medical therapies for breast cancer could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study approach is better than the usual approach, so this study may or may not help you. This study may help researchers learn things that may help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The 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.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest;
- If new information becomes available;
- If you do not follow the study rules;
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or the Food and Drug Administration (FDA).

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

You and/or your health plan/insurance company will need to pay for the radiation and/or surgery and all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

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

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors *will not* offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information? (14-JUN-2018)

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 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:

- The study sponsor: NRG Oncology;
- The 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 (FDA) and the National Cancer Institute (NCI) in the U.S., and similar ones if other countries are involved in the study.

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.

Who can answer my questions about this study?

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 the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION
This section is about optional studies 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. You will not get health benefits from any of these studies. The researchers leading this optional study 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.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the 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 Laboratory Studies and/or Biobanking for Possible Future Studies (14-JUN-2018)

1. Optional Sample Collections for Laboratory Studies:

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

We will ask to draw blood to look for the presence of circulating breast cancer tumor cells (CTC). The number of cells may provide information about what type treatment to use for breast cancer and who may respond best to a treatment. About 50% of patients may have these cells in their blood. This study will help determine whether this test is useful for other patients. Some of the blood will be stored for future research.

We will also look at levels of circulating tumor DNA (ctDNA). ctDNA levels may give more information about response to treatment and longterm outcomes than CTCs. The number of cells may provide information about what type treatment to use for breast cancer and who may respond best to a treatment. This study will help determine whether this test is useful for other patients. Some of the blood will be stored for future research.

We will ask to draw blood for CTC and ctDNA levels before you start treatment, about 4 weeks after surgery or radiation, and if your disease progresses we will collect another sample at that time to determine whether the treatment eliminated any tumor cells from the blood. If you are in the standard medical treatment group, we will draw blood before you start treatment, at 3 months of treatment, and if your disease progresses.

Group 1

Assessment	Timepoint		
	Before start of treatment	At 3 months	Disease progression
CTC and ctDNA Blood Collection	X	X	X

Group 2

Assessment	Timepoint		
	Before start of treatment	25-35 days after SBRT	Disease progression
CTC and ctDNA Blood Collection	X	X	X

2. Optional Sample Collections for Biobanking for Future Research Studies:

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part in this study, tissue (as blocks and/or slides) from your primary and metastatic tumor that were collected previously and stored by your hospital will be requested for research. If your disease progresses and your doctor recommends a new biopsy, tissue from this biopsy stored by your hospital will also be requested for research. Also, a sample of blood will be collected before you start treatment. The researchers ask your permission to store and use your samples and health information for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called “biobanking”. The Biobank is being run by *NRG Oncology* and supported by the National Cancer Institute.

WHAT IS INVOLVED? (9/16/16)

If you agree to take part, here is what will happen next:

1) For the optional laboratory study about *2* tablespoons of blood will be collected from a vein in your arm before you start treatment, once after that, and if your disease gets worse.
2) For the optional biobanking for future studies, about 2 tablespoons of blood will be collected from a vein in your arm before you start treatment. Previously collected tissues from your primary and metastatic tumor(s) will be sent to the NRG Oncology Biobank before you start treatment. Also, another sample of tissue from your metastatic tumor if obtained when your disease progresses will be sent to the Biobank.
3) Your sample and some related information will be sent to a researcher for use in the laboratory study described above. Remaining samples may be stored in the Biobank, along with samples from other people who take part. The samples will be kept until they are used up.
4) *For future unspecified research:* Your sample and some related information may be stored in the Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up.
5) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.

6) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
7) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. *(For non-US participants, please verify existence of such laws before including the following text.)* There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

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

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and *NRG Oncology* staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom *NRG Oncology* sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

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?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no

longer be used. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS? (12-AUG-2021)

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your answer to show whether or not you would like to take part in each option (*include only applicable questions)*:

SAMPLES FOR THE LABORATORY STUDIES:

I agree to have my specimen collected and I agree that my specimen sample(s) and related information may be used for the laboratory study(ies) described above.

YES NO

SAMPLES FOR FUTURE RESEARCH STUDIES:

My samples and related information may be kept in a Biobank for use in future health research.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My Signature Agreeing to Take Part in the Main 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 copy of this form. I agree to take part in the main study and any additional studies where I circled "yes."

Participant's signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____