The Ohio State University Consent to Participate in Research

Study Title:	**Feasibility of Assessing Radiation Response with MRI/CT Directed Preoperative Accelerated Partial Breast Irradiation in the Prone Position for Hormone Responsive Early Stage Breast Cancer**
Principal Investigator:	**Sasha Beyer, MD PhD**
Sponsor:	**Susan G. Komen for the Cure**

This is a clinical trial (a type of research study). Clinical trials include only patients who choose to take part. Please take your time to make your decision. Discuss it with your friends and family. The National Cancer Institute (NCI) booklet, "Taking Part in Clinical Trials: What Cancer Patients Need To Know," is available from your doctor.

You are being asked to take part in this study because you have breast cancer and are planning to receive breast conserving treatment with lumpectomy and breast radiotherapy.

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

1. Why is this study being done?

You are being asked to participate in this study because you have early stage breast cancer and are undergoing breast conserving therapy, which involves lumpectomy (removal of the tumor, saving the breast) and breast radiation. The breast conservation approach to therapy is established and recommended instead of mastectomy (removal of the entire breast) for early stage breast cancer patients because both approaches have the same effect on survival and the chance of cancer coming back (recurrence).

This is a pilot study to establish the feasibility of using a specific method of radiation. Advances in radiation technology have rapidly improved breast cancer treatment over the last decade, reducing both the length of treatment and the size of the area that must be treated. While radiation of the whole breast was previously the typical treatment choice after lumpectomy, recent research supports the use of accelerated partial breast irradiation (APBI) as an equally effective method of treating early stage breast cancer. APBI is an approach that reduces the area of breast tissue receiving radiation by only targeting the area around where the tumor was removed, rather than treating the entire breast. As a result, patients experience fewer side effects with APBI than with whole breast radiation. APBI also shortens the length of treatment, while still maintaining the same low rates of recurrence and survival as whole breast irradiation.

Accelerated partial breast irradiation (APBI) is currently delivered after surgery. However, there have been two recent research studies that have treated patients with APBI *before* surgery i.e. *pre-operatively*. In these studies, magnetic resonance imaging (MRI: a way to visualize the tumor) of the breast was used to guide radiation treatment by providing more precise identification of the tumor. Scientists believe that this approach can help to increase the accuracy in targeting the breast tumor with radiation, potentially further reducing the chance of the cancer coming back and reducing the amount of breast tissue that is irradiated. Additionally, the preliminary results from the APBI approach before surgery have also had better cosmetic outcomes (the appearance of the breast) for patients than radiation after surgery.

The two studies that have tested APBI treatment before surgery have both performed the MRI (imaging) with the patient lying face-down and the radiation with the patient face-up. The investigators of this study believe that it will be easier to target the radiation to the correct location around the tumor if patients are in the same position (face down) for both the imaging and the radiation.

The purpose of this study is to test the safety and feasibility of treating your early stage breast cancer with accelerated partial breast irradiation (APBI) before your lumpectomy is performed. This study will also examine whether toxicity (side effects) of the radiation is reduced both shortly after your radiation therapy, and in the years following the surgery. Also, the study will collect information about recurrence (whether the cancer comes back) and survival, as well as the cosmetic appearance of your breasts in the years following radiation. The researchers will also study how the radiation effects the breast cancer stem cells found in your breast tissue and biomarkers found in your blood.

2. How many people will take part in this study?

A total of 33 participants will take part in this study, which consists of 3 participants for optimizing the imaging method (Cohort 1), and 30 participants in the treatment (Cohort 2).

3. What will happen if I take part in this study?

Before you begin the study:

You will need to have the following tests and exams to find out if you can be in the study. Most of these tests and exams are part of regular cancer care and may be done even if you do not join the study. If some of these tests were done recently, they may not need to be repeated.

- History & physical exam (including weight)
- Breast exam
- Discussion with your provider about toxicity (side effects) related to radiation therapy
- Blood test to check your blood counts
- Research blood draw to check for biomarkers (molecules circulating in the blood that can indicate a normal or abnormal process within the body, and may also be used to assess the body's response to treatment)
- Request of tissue biopsy slides from diagnosis for research purpose
- Bra cup size
- Breast MRI (magnetic resonance imaging – a way to image the tumor)
- Breast CT (computed tomography) scan for planning the radiation therapy
- Axillary Ultrasound (examines the concentration of lymph nodes in your armpit)
- If there is a medical reason to do so, other imaging may be done. These tests could include the following: CT scan of chest and/or abdomen, a chest x-ray, and a bone scan
- Mammogram (on both breasts)
- Patient and doctor will both complete a questionnaire about breast appearance (cosmesis)
- Complete a questionnaire about your breast appearance, arm function, and pain
- Digital images (photos) of your breasts will be taken by the physician

During the study:

If you qualify for the study and choose to participate, you will undergo the procedures described below. Some of these procedures and tests would be performed even if you were not part of a research study. The history and physical exam, blood work, x-rays, scans and other testing may be performed more frequently if your physician feels that it is best.

Radiation therapy:
You will receive accelerated partial breast irradiation (APBI). This will require radiation treatment twice per day (separated by at least 6 hours), given on 5 treatment days within a 10 day period. To receive the radiation, you will lie face down with your arms extended above your head.

After radiation therapy:
At the end of your radiation therapy, you will have the following tests and exams:

- History & physical exam (including weight)
- Breast exam
- Research blood draw to check for biomarkers
- Discussion with your provider about toxicity (side effects) related to radiation therapy

Four weeks after radiation therapy and before your surgery, you will have the following tests and exams:

- History & physical exam (including weight)
- Breast exam
- Research blood draw to check for biomarkers
- Discussion with your provider about toxicity (side effects) related to radiation therapy
- Breast MRI. The MRI will last approximately 45 minutes.
- Breast CT scan
- Complete a questionnaire about your breast appearance, function, and pain
- Digital images (photos) of your breasts will be taken by study staff or clinic nurses.

Lumpectomy:
Between 4 and 6 weeks after radiation, you will have surgery to remove the tumor from your breast and a sentinel node biopsy to study the lymph nodes in your armpit. The research team will request the biopsy slides for research purposes.

Chemotherapy:
Chemotherapy may be given if your physician feels you should receive it. If you do receive chemotherapy, it will begin after your radiation therapy and lumpectomy.

Following surgery:
Approximately 1 month after surgery, you will have the following test:

- Research blood draw to check for biomarkers

6 months and 12 months after surgery, you will have the following tests and exams:

- History & physical exam (including weight)

- Breast exam
- Discussion with your provider about toxicity (side effects) related to radiation therapy
- Blood test to check your blood counts if your physician feels that it is necessary.
- Bra cup size
- Mammogram (on both breasts)
- Patient and doctor will both complete a questionnaire about breast appearance (cosmesis)
- Complete a questionnaire about your breast appearance, function, and pain
- Digital images (photos) of your breasts will be taken by the physician

12 months after surgery, you will have the following additional tests and exams:

- Breast MRI (magnetic resonance imaging – a way to image your breast)

Every 6 months, for years 2-5 after surgery, you will have the following tests and exams:

- History & physical exam (including weight)
- Breast exam
- Discussion with your provider about toxicity (side effects) related to radiation therapy
- Bra cup size

Every 12 months, for years 2-3 after surgery, you will have the following tests and exams:

- History & physical exam (including weight)
- Mammogram (on both breasts)
- Patient and doctor will both complete a questionnaire about breast appearance (cosmesis) (years 3 only)
- Complete a questionnaire about your breast appearance, function, and pain
- Digital images (photos) of your breasts will be taken by the physician (years 3 only)

4. How long will I be in the study?

You will undergo study visits for 5 years after your surgery.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

You may have side effects while on the study. Most of these are listed here, but there may be other side effects that we cannot predict. Side effects will vary from person to person.

Everyone taking part in the study will be watched carefully for any side effects. However, doctors do not know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop radiation therapy. In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to radiation therapy:

During this study, you will receive accelerated partial breast irradiation (APBI) prior to your lumpectomy. This radiation will be administered on five separate treatment days with two fractions per day, and each of the two fractions will be administered at least 6 hours apart. Each of these fractions will be 3.85 Gy, which amounts to a total radiation therapy dosage of 38.5 Gy after all 10 doses have been administered. This radiation is for research purposes only.

Prone positioning is similar to standard of care radiation and does not pose additional risks or side effects.

Likely
These side effects occur in **10% or more** of patients:

- Reddening of the skin during treatment and for several weeks following treatment
- Tanning of the skin in the radiated region lasting months and may be permanent
- Slightly smaller breast size or change in the way the breast looks
- Mild thickening or firming of the breast on touch
- Tiredness and weakness during treatment and for several weeks following treatment
- Swelling of breast
- Peeling of the skin in the area treated with radiation
- Mild pain at the site of radiation treatment requiring over the counter pain relievers

Less likely
These side effects occur in **3–9%** patients:

- Soreness or tightness in muscles of the chest wall under the treated breast
- Severe pain at the site of radiation treatment requiring prescription pain relievers
- Prominent thickening or firming of the breast on touch

- Wound complications following surgery

Rare but serious
These side effects are **rare but serious**, occurring in **less than 1 %** of patients:

- Cough
- Difficulty breathing
- Inflammation of the heart muscle. Damage to the cells in the wall of the heart may not result in any symptoms at all or could cause you to have a fever, achy feeling in your chest, and severe fatigue. Some people have irregular heartbeat or trouble breathing. Usually, a mild case of myocarditis (heart muscle inflammation) will go away on its own without any lasting damage. Severe cases can sometimes resolve but may result in symptoms of heart failure and irreversible damage.
- Increased risk for heart disease for patients with cancer in the left breast. Because the heart is near the left breast, it is often exposed to some of the radiation. However, the overall increase in risk is still very small, less than 1-2% increase in overall risk of major heart events occurring.
- Rib fracture
- Risk of developing another cancer

Risks related to Magnetic Resonance Imaging (MRI):

There are no known harmful side-effects associated with temporary exposure to the strong magnetic field used by MRI scanners. Patients with claustrophobia may have difficulty tolerating the MRI scanner. If you feel too confined in the MRI scanner you can inform the technologist and the MRI scan will be stopped. We will ask you about metal within your body as the magnet could attract certain kinds of metal that may cause injury to you. Patients with metal objects in their bodies may be excluded from MRI scanning. The MRI machine makes loud knocking sounds when it is scanning. Because of this, you will be given earplugs and/or headphones to wear while getting your MRI examinations. This helps minimize discomfort from noise and keep the MRI noise within the safety range. If a contrast agent is used, there is a slight risk of an allergic reaction. MRI contrast agents can cause problems in patients with significant kidney disease.

Risks related to Computed Tomography (CT) Scans:

For the purposes of this research, you will undergo 2 CT scans of your chest. This radiation exposure is not necessary for your medical care and is for research purposes only. The total amount of radiation that you will receive during these CT scans is about 26mSv or 2600 mrem, and is approximately equivalent to a whole body exposure of 3163 days (8.666 years) of exposure to natural background radiation. This use involves minimal risk and is necessary to obtain the research information desired.

Risks related to blood sample collection:

When blood samples are taken from a vein, there may be pain, bleeding, bruising and, rarely, infection at the place where the blood was drawn. Rarely, a person may become dizzy or faint when blood is drawn. The risk of bleeding and bruising can be reduced by putting pressure on the place where the blood was taken. The chance of infection is lowered by using standard skin cleaning and sterile needles.

For more information about risks and side effects, ask your study doctor.

7. What benefits can I expect from being in the study?

Taking part in this study may or may not make your health better. Doctors hope that administering accelerated partial breast irradiation before lumpectomy will help target the tumor cells and prevent cancer from coming back, reduce the side effects of radiation therapy, and to improve cosmetic appearance of the breast after radiation, there is no proof of this yet. The information from this study will help doctors learn more about methods to best deliver radiation therapy to early stage breast cancer patients. This information could help future breast cancer patients.

8. What other choices do I have if I do not take part in the study?

Your other choices may include:

- Getting treatment or care for your cancer without being in this study
- Taking part in another study
- Getting no treatment

Talk to your study doctor about your options before you decide to participate in this study.

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;

- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search the website at any time.

You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

10. What are the costs of taking part in this study?

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

Costs that are considered standard of care (procedures or tests that you would receive whether or not you were participating in a research study) will be billed to you or your insurance company.

Those costs that are performed solely for the purpose of research will be paid by the sponsor of this study. For example, the breast MRI at screening and prior to your operation will not be billed to you/your insurance. You will be responsible for meeting co-pay and deductible requirements by your insurance plan while on study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site. Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

11. Will I be paid for taking part in this study?

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

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

If you are injured as a result of your participation in this study, you may obtain immediate care at The Ohio State University Medical Center. The cost of this treatment will be charged to you or your insurance company. Your health insurance company may or may not pay for treatment of injuries as a result of your participation in this study. The Ohio State University has no funding set aside for the payment of health care expenses for this study.
By signing this consent form, you will not be waiving any of the legal rights which you otherwise would have as a subject in a research study.

13. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact ***Dr. Sasha Beyer at (614) 293-3255***.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact ***Dr. Sasha Beyer at (614) 293-3255***.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form**.**

Printed name of subject	**Signature of subject**
	AM/PM
	Date and time
Printed name of person authorized to consent for subject (when applicable)	**Signature of person authorized to consent for subject (when applicable)**
Relationship to the subject	**AM/PM**
	Date and time

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time