Informed Consent Form: A Phase II Study of MRI-Based Pre-Operative Accelerated Partial Breast Irradiation

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EFFECTIVE
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MCW/FH IRB

Medical College of Wisconsin and Froedtert Hospital
CONSENT TO PARTICIPATE IN RESEARCH

Name of Study Subject: _____

A PHASE II STUDY OF MRI-BASED PRE-OPERATIVE ACCELERATED PARTIAL BREAST IRRADIATION

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You are invited to take part in this research study. This form tells you why this research study is being done, what will happen in the research study, possible risks and benefits to you, your choices, and other important information. If there is anything that you do not understand, please ask questions. Then you can decide if you want to join this study or not.

A1. INTRODUCTION – WHY ARE WE ASKING YOU ABOUT THIS STUDY?

You are being invited to participate in this research study because you have an early stage breast cancer. Because of your condition, you may be eligible for a research study that uses a new radiation technique called pre-operative accelerated partial breast irradiation in conjunction with breast conserving surgery (otherwise known as a lumpectomy). Accelerated partial breast irradiation with external radiation has been used in patients before, but traditionally it has been given after surgery. While this treatment has been effective at treating breast cancer, it can cause some side effects to

the surrounding breast tissue. The purpose of this study is to see if giving accelerated partial breast irradiation prior to surgery might reduce the side effects of the partial breast irradiation while keeping the risks of surgical complications at a low level.

Typically, radiation therapy for early stage breast cancer is delivered after surgery over a period of 3-6 weeks. If you are treated on this study, your radiation will be given before surgery as 5 treatments given over 2 weeks. The radiation oncologist who is treating you will design a radiation plan that will radiate the tumor in your breast and a small portion of the surrounding breast tissue. The radiation oncologist will use an MRI scan to help him/her more accurately target the tumor and the breast tissue at highest risk for recurrence. The radiation treatment will be given in five treatment sessions that will occur on non-consecutive days. Between 5-8 weeks after your radiation is complete, you will then undergo a lumpectomy, similar to the surgery you would have if you choose to not enroll on the study.

Patients who are eligible for this study include women over the age of 50 with a stage 1 or stage 2 breast cancer that doesn't appear to involve the lymph nodes of the underarm.

A total of about 40 people are expected to participate in this study the Medical College of Wisconsin/Froedtert Hospital as well as Community Memorial Hospital in Menomonee Falls and St. Joseph's Hospital in West Bend.

The Director of the study is Adam Currey, MD in the Department of Radiation Oncology. A study team works with Dr. Currey You can ask who these people are.

The study is being funded by the Dr. Nancy Laning Sobczak Award for Breast Cancer.

A2. DO I HAVE TO BE IN THIS STUDY?

You can decide whether to take part in this study or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this study, you do not have to stay in it. You may stop at any time.

A research study is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the study procedures, tests and visits follow a set plan that must be kept.

A3. WHY IS THIS RESEARCH STUDY BEING DONE?

In this study we want to find out more about pre-operative accelerated partial breast irradiation in people with early stage breast cancer. Delivering radiation prior to surgery might have the potential to reduce some of the long term effects of radiation. It may also increase in surgical complications. The main purpose of this study is find out whether

the new radiation technique is safe and doesn't cause an excessive number of surgical complications. We also want to see if using MRI to help guide radiation and delivering the radiation in the pre-operative setting reduces the long term side effects of accelerated partial breast irradiation. Because most patients receive radiation after their tumor is removed from their breast, it is difficulty to study the effects of the radiation on the tumor. In this study, we also plan to investigate how the appearance of your tumor on an MRI scan changes after radiation treatments and how the genetic make-up of that tumor changes after radiation treatment.

Everyone in this study will receive pre-operative accelerated partial breast irradiation, which is still experimental and is not a standard treatment at this time. We are testing this novel radiation approach to see what effect it has on people with breast cancer. We don't know if this study will help you. Your condition may get better but it could stay the same or even get worse. We hope the information from this study will help us develop a better treatment for breast cancer in the future.

B1. WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

Screening procedures:

If you decide to join the study, some screening tests that are standard of care will be done first to see if you are eligible. Many of these tests you may have already had or are part of the standard evaluation for someone with breast cancer. These include:

- History and physical, height, weight and performance status
- Breast exam
- Bilateral mammogram
- Axilla ultrasound and biopsy of enlarged/abnormal lymph nodes
- Lab work (CBC with diff and ANC) and chemistry panel
- Breast biopsy tissue and blood for research
- Hormone receptor and her2 status
- Medical Oncologist consultation
- OncotypeDX testing if recommended

If you are interested in participating in the study, you will also need to meet with a medical oncologist prior to enrollment. A medical oncologist is a physician who specializes in drug-based treatments for cancer (for example chemotherapy and hormone therapy). Patients treated for early stage breast cancer usually see a medical oncologist after surgery, so this is a physician you would see regardless of whether you participate in the study.

The reason you need to meet with a medical oncologist is to determine whether you need to have a special genetic test on your tumor. Typically this test is called OncotypeDX and is used to help determine whether or not you would benefit from

chemotherapy. If the medical oncologist does not recommend an OncotypeDX be performed in your case, or you decide to not receive chemotherapy regardless of the results of the OncotypeDX testing, you may then be able to enroll on the study.

If an OncotypeDX test is recommended and you are willing to receive chemotherapy, then the doctors treating you will perform that test prior to surgery. The test will be performed on the tissue obtained at the time of the biopsy that diagnosed your cancer. The reason this needs to be done is that the radiation you get on the study prior to surgery could affect the results of the OncotypeDX test, and may cause a loss of information that would guide your treatment in the future. If there is insufficient tissue from the biopsy to perform the OncotypeDX test, you may be ineligible for the study. In that case, you may choose to undergo an additional biopsy to obtain additional tissue to perform the OncotypeDX test and thus become eligible for the study. However, if you choose that option, you or your insurance company will be charged for that additional biopsy.

If the screening evaluations show that you meet the requirements for the study, then you will be able to start the study. If the screening information shows that you cannot be in the research study, the study doctors will discuss other options with you and/or refer you back to your regular doctor.

Summary of Study Procedures :

You will receive 5 radiation treatments given every other day, Monday-Friday.
The following procedures will be done:

Prior to radiation treatment

- CT scan and MRI to plan the radiation therapy (creating a device to keep you in the same position for each of your radiation treatments, and then obtaining a CT and MRI scan in the treatment position). The only exception is that for the CT and MRI scan, a few additional imaging sequences will be performed. This will mean that you are on the MRI table an additional 5-10 minutes longer than you normally would be, but would otherwise have no adverse effects on your health.
- History and physical, weight and performance status
- Breast examination
- Blood collection and tissue storage
- Physician Cosmetic and Quality of life questionnaire
- Breast photos

During radiation therapy

- History and physical, weight and performance status
- Breast examination

- Adverse event evaluation

Last day of radiation therapy

- Breast examination
- Adverse event evaluation
- Breast photos
- Physician Cosmetic and Quality of life questionnaire

Surgery

About 5-8 weeks after your radiation has finished, you will undergo a lumpectomy and possibly a sentinel lymph node biopsy. The surgery will be no different than the surgery you would have if you had not participated on the study. After your surgery, you may receive treatment with chemotherapy and/or anti-hormone therapy at the discretion of you and your medical oncologist.

Sometime after your surgery, tests will be performed on your tumor tissue and on the tissue from your biopsy to see if the genes expressed in each sample have changed. These research tests will also be paid for by the funds of the study.

Follow up assessments

1 month after completion of radiation therapy and prior surgery

- History and physical, weight and performance status
- Breast examination
- Adverse event evaluation
- Blood collection and storage
- Blood draw for research
- Quality of life questionnaire
- MRI that will be used to compare how your tumor changed in response to radiation. This MRI is one that you would not normally undergo, and the cost of that test will be covered by the funds for the study.

1 month after last surgery

- History and physical, weight and performance status
- Breast examination
- Adverse event evaluation
- Quality of life questionnaire
- Breast photos

6 months after last surgery

- History and physical, weight and performance status
- Breast examination
- Adverse event evaluation

- Quality of life questionnaire
- Breast photos
- Mammogram of Ipsilateral Breast

12 months after surgery or chemotherapy then annually until year 5

- History and physical, weight and performance status
- Breast examination
- Adverse event evaluation
- Quality of life questionnaire
- Breast photos (to year **3**)
- Mammogram of bilateral breasts (based on surgical date)

B2. HOW LONG WILL I BE IN THE STUDY?

You will be in this research study for 5 years. You may have additional follow-up with your physicians beyond that time.

After your treatment is finished, we want to keep in touch with you to follow your health over time. After some initial visits a few weeks after your surgery, we will ask you to come in to the clinic at least once a year for the next five years. These visits would happen even if you received treatment outside the study. At these visits, we will ask you about any side effects that you might have, other updates to your health, and will perform a physical exam.

B3. CAN I STOP BEING IN THE STUDY?

You are free to withdraw from the study at any time. If you leave, your regular medical care will not change. If you are thinking about leaving, please tell the study doctor.

The doctor can tell you about the effects of stopping, and the doctor can talk about what follow-up care would help you the most. You might be asked to come back for one more visit to check your health.

The study doctor may take you out of this study at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the study rules.
- The whole study is stopped.

If this happens, the study doctor will tell you.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE STUDY?

There are risks to taking part in any research study. There is a risk that you may get a treatment that does not help your condition or may make it worse. There also may be

problems (side effects) we do not know about yet, from the radiation itself, or how it combines with other treatment you receive. If we learn about new important side effects, we will tell you.

C2. RISKS OF RADIATION THERAPY

The research radiation therapy itself may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away.

Side effects of radiation therapy are often divided into side effects that happen during treatment or shortly after treatment is over, and side effects that can occur months to years after treatment is over.

Side effects that can happen during radiation or shortly thereafter can include:

- Fatigue
- Redness of the skin that can itch or be uncomfortable
- Peeling of the skin that can be painful

Side effects that can happen months to years after radiation is completed can include

- Permanent changes to the appearance of the treated breast such as a permanent darkening of the skin, or scaring to the breast tissue that may affect the breast's shape
- Swelling of the breast tissue
- Scaring of the breast tissue that can be firm and at times tender or painful.
- Radiation injury to the lung that can cause cough or shortness of breath
- If your cancer is on the left side, radiation injury to the heart that may lead to a slightly increased risk for heart disease later in life
- Cancer that is caused by radiation (this is extremely unlikely).

Please note that these side effects are general side effects of radiation therapy that may occur regardless of whether you enroll on the study or not. One potential benefit of pre-operative partial breast irradiation is to reduce the risk of some of these complications.

In addition to the common side effects of radiation described above, the following are possible side effects of pre-operative treatment that would be unique to this study:

- Delayed wound healing after your lumpectomy surgery
- A fluid collection in the breast that may become uncomfortable (this is called a seroma). This may require a procedure or even another surgery to correct.
- Infection
- A collection of blood in the breast that may become uncomfortable (this is called a hematoma). This may require a procedure or even another surgery to correct.

It is also possible that the doctors and tests done up to this point have underestimated the extent of your disease. After this short course of radiation and your surgery, it is possible your doctors could discover disease in the lymph nodes of your underarm. If that occurs, you may need to have additional radiation treatments after your surgery. While inconvenient, the total number of radiation treatments both before and after surgery will be roughly the same as the number of treatments you would have if surgery was done first and all your radiation done after surgery.

C5. ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

We don't know if this study will help you. Your condition may get better but it could stay the same or even get worse. We hope the information from this study will help us develop better treatments for breast cancer.

One potential benefit of pre-operative partial breast irradiation is that patients may be less likely to need a second surgery to ensure all cancer is removed from the breast. This is known as a positive margin, and for other cancers where pre-operative radiation therapy is used routinely, lower risks of positive margins is one benefit. It is also possible that the pre-operative radiation treatment may cause less scaring and improve the cosmetic appearance of the breast after treatment is complete when compared to patients treated in the post-operative setting.

D1. ARE THERE ANY COSTS TO BEING IN THE STUDY?

Some of / Most of the medical care that you will receive in this study is considered routine care for your condition and would be recommended whether you join the study or not. Costs for routine care will be billed to you or your insurance carrier. Activities / costs that are part of the study will not be billed to you or your insurance company. These are MRI at 4 weeks after radiation therapy has been completed, blood draw and tissue analysis for research. Some insurers will not pay for drugs, tests or hospitalization that are part of research studies, so check with your insurer before you join this study. If you have questions regarding study costs, please contact Dr. Currey.

D2. WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

There is no payment for being in this study.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this study. You are free to say yes or no. If you do not join this study, your doctor can discuss other healthcare choices with you.

Your other choices may include:

- Standard radiation therapy delivered after surgery
- Joining a different research study

- Surgery without radiation, but this may place you at a higher risk of breast cancer recurrence
- No treatment

The study doctor can explain both the possible benefits and the risks of other options that are available to you.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE STUDY?

If we learn any important new information about the radiation therapy that might change your mind about being in the study, we will tell you about it right away. You can then decide if you want to stay in the study.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE STUDY?

If you have been following directions, the injury is directly related to the research, and not the result of an underlying condition, then MCW will compensate you for the injury.

If you think you have been injured because of this study, let the study doctors know right away by calling414-805-4400.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

- If you have more questions about this study at any time, you can call Dr. Currey at 414-805-4400 or Dr. Bovi at 262-257-5110or Dr. Candice Johnstone at 262 836-7200.
- If you have questions about your rights as a study participant, want to report any problems or complaints, obtain information about the study, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this study?

To be in this research study, the study team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the study.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); BloodCenter of Wisconsin (BCW); any Froedtert Health Affiliate- Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc.

(FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information to be collected and used for this study is:
Past medical records and records dating from when you join this study until the end of the study.

E2. Who will see the health information collected for this study?
The only MCW/Froedtert Hospital/ Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; employees allowed to handle your health information are those on the study team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different study without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed, the information might be used or released for other purposes without asking you. Results of the study may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?
One risk of taking part in a research study is that more people will handle your personal health information collected for this study. The study team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the study doctor about whether this could apply to you.

E4. How long will you keep the health information for this study?
If you sign this form, we plan to keep your information without any end-date in case we need to check it again for this study.

E5. Can I cancel my permission to share this health information?
If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Adam Currey, MD at 9200 W. Wisconsin Ave. Milwaukee, WI 53226*,* Community Memorial Hospital (CMH) N8085 Town Hall Road, Menomonee Falls, WI 53051 Co-Investigator Joseph Bovi, MD or St. Joseph's Community Hospital (SJH) West Bend, Inc. 3200 Pleasant Valley Road, West Bend, WI

53095 Co-Investigator Candice Johnstone, MD. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the study. We may still use the information we have already collected.

F1. FOR MORE INFORMATION ABOUT THE STUDY

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 look up this study by referring to the ClinicalTrials.gov number (NCT02728076) or by asking the study team for a printed copy.

CONSENT TO PARTICIPATE IN THE STUDY

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The study's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the study team use and share the health information and other information gathered for this study.
- I voluntarily agree to participate in this research study. I agree to follow the study procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date**
Name of Witness (if applicable**)** *please print* (for short form consent process, or consent of blind or illiterate subject)	**Signature of Witness**	**Date**

*** Name of person discussing/ obtaining consent** *please print*	**Signature of person discussing/obtaining consent**	**Date**

** A member of the study team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. In all research study protocols the Principal Investigator is responsible and accountable for the study.*