Research Consent Form
Dana-Farber/ Harvard Cancer Center
BIDMC/BWH/DFCI/MGH/Partners Network Affiliates

OPRS: 11-02

DFCI IRB PROTOCOL NUMBER: 03-179

PROTOCOL TITLE: Partial Breast Irradiation (PBI) for Selected Patients with Early Invasive or Non Invasive Breast Cancer: A Phase I/II Study with Dose Escalation

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INTRODUCTION

We are inviting you to participate in a research study. A clinical research trial is a study of a treatment, procedure or medication done in a medical setting. The title of the study is shown above. This study is being funded by internal funds through the Massachusetts General Hospital (MGH). This form was created to help explain to you the nature of this study and if you choose to participate, it will be used to document your agreement to be part of this study. This study is being performed in several hospitals. We plan to enroll 400 people through DFHCC.

Included in this form is a description of why this study is being done, what will be asked of you if you choose to participate, any possible risks, inconveniences or discomforts you may experience and any other important information that you may need to help you make a decision about whether or not to enroll in this study. This form can be used as a guide for discussion between you and the investigator and may also be helpful as a reference if you choose to participate, as a reminder of what your role in the study is, and whom to contact if you have questions at any time during your participation.

You are urged to discuss any questions you have about this study with members of the research team.

WHY IS THIS STUDY BEING DONE?

You are being asked to participate in this study because your doctor believes that you should receive radiation therapy for your recently diagnosed breast cancer. Radiation therapy (also known as "radiotherapy") is usually given as a series of daily treatments (Monday through Friday) that last for about 6-7 weeks. The entire breast is treated for most of this period.

However, several studies have been performed in which only a portion of the breast near the cancer (called the "tumor bed") is treated. This approach is called "partial breast irradiation". Because only a small portion of the breast is treated, the entire course of radiation treatments on this study can be given in a 1-week period.

These previous studies were done by placing catheters (tubes) in the breast in the operating room, then placing radioactive materials in the catheters. This procedure is called an "interstitial implant". So far, these studies have had results very similar to conventional radiation treatments, with a low risk of the cancer reappearing in the breast and low complication rates. It is also hoped that this approach will also reduce the chance of complications arising in the lungs and heart that may happen years after treatment.

In this study, radiotherapy is given only to a portion of the breast around the tumor bed using external radiation treatments instead of an interstitial implant. This study treatment will be completed in 4-7 days. No further surgery will be needed.

WHAT OTHER OPTIONS ARE THERE?

Taking part in this study is voluntary. Instead of being in this study, you have these options:

- Conventional radiation treatment.
- Mastectomy (as an alternative to breast-preserving surgery and radiotherapy).
- Other investigational treatments
- No anti-cancer therapy at this time, with supportive care.

Please discuss these and other options with your study doctor.

WHAT IS INVOLVED IN THE STUDY?

You will undergo a thorough evaluation before entering this study. This is to determine if you are eligible for this study. Many of the following evaluations are commonly done to determine diagnosis and/or stage of disease. You may have already had some or all of these evaluations.

Evaluations may include: physical examination, medical history, blood tests, a pregnancy test if you are a woman of child-bearing age, and a mammogram. At the discretion of your treating physician, abdominal (stomach), chest and pelvic CT and/or MRI scan and other tests as appropriate for your illness could be ordered. MRIs use powerful magnets to make images. CT scans are X-ray examinations.

You will undergo a planning session for the radiation treatments. This planning will be done by CT scan days or weeks before you start study treatment. This planning process is the same as that commonly used to plan conventional radiation therapy treatments. You may be given an intravenous dye ("contrast") to help see the tumor bed; your study doctor will discuss this with you at the time of planning if it is felt to be needed. After this planning session, your radiation oncologist may decide that he or she cannot identify the area of the tumor bed well enough to do partial breast irradiation adequately. In this case, you will not be treated in this study, and conventional radiation treatments will be given.

You will also be asked about any drugs you are taking, your ability to carry out normal activities, and how you are currently feeling. If you are pregnant, you will not be able to participate in this study.

If these tests indicate you are eligible for this study, you will receive study treatment as an outpatient.

Your radiation therapy will begin 4-12 weeks after the last surgery of the breast in individuals not receiving chemotherapy first. For individuals receiving chemotherapy before radiation therapy, radiation therapy will start 2-6 weeks after ending chemotherapy. (Chemotherapy and radiation therapy will not be given at the same time.)

Radiation Treatments

Radiation therapy doses are measured in Grays (Gy). We will be studying three levels of doses of radiation therapy to see which is best. The first 100 women who participate in the study will receive the first level; the second 100, the second level; and patients 201-400 will receive the third level. Depending on the level you are enrolled to, you will be given radiation treatment twice each day for 4 or 5 treatment days, within an overall treatment time of one week. You will receive 8-10 treatments in total. There will be an interval of at least 6 hours between each treatment. (For example, you may receive the first treatment each day at 8 AM, and the second at 2 PM). The chart below summarized the doses and number of treatments for each group.

Group 1	→	Group 2	→	Group 3
Study Patients 1-100 32 Gy – 8 treatments 4 treatment days		Study Patients 101-200 36 Gy – 9 treatments 4½ treatment days		Study Patients 201-400 40 Gy – 10 treatments 5 treatment days

After your radiation, you will have follow-up office visits, initially one to two visits within 3-9 weeks after treatment and then every 6 months (+/- 2 months) for five years, then once a year (+/- 3 months) for five years thereafter. These visits will include physical examination and

history, X-rays and other tests as appropriate. Photographs of your breasts will be taken before radiation treatment and at subsequent follow-up visits. These photographs will be confidential, and are for the purpose of evaluating the cosmetic outcome of your treatment. You will be asked to fill out a 1-page cosmetic and satisfaction questionnaire at every radiation follow-up visit.

No further radiation treatment for your breast cancer will be necessary unless the disease reappears. You may be treated with chemotherapy or hormonal therapy in addition.

We may also ask you to participate in another part of this study that will use video images to look at variations in patient positioning during radiation treatments. Normally during radiation treatments, you are monitored from outside the treatment room by closed circuit television (to ensure you do not move during treatment), but images are not normally recorded. This part of the research involves recording digital images during your treatment planning simulation and treatment sessions. These images are captured by two video cameras, one in the ceiling and one on the wall, or both might be in the ceiling, and may be taken during a single session and/or multiple treatment sessions. These images are then studied to quantify how much variation in patient setup occurs from day to day or during a treatment session. You will not be identifiable in these images. The images will be securely stored and your identity will be protected. If you choose not to participate in this part of the study, you will still be monitored by closed circuit TV by the radiation therapist, to ensure you do not move during treatment. However, the images will not be recorded.

HOW LONG WILL I BE IN THE STUDY?

You will receive radiation treatments on this study for only 1 week. After your radiation, follow-up office visits will be initially one to two visits at 3-9 weeks, every 6 months (+/- 2 months) for five years, then once a year (+/- 3 months) for the next five years.

The study doctor may decide to take you off this study without your consent for any of the following reasons:

- Discontinuation of this study treatment is felt to be in your best medical interest
- You are unable to follow the study plan
- Your disease worsens
- You experience unacceptable and/or harmful side effects
- If you are a woman and become pregnant

You may choose not to take part in this study. If you decide to enroll on this study, you can stop participating at any time. Choosing to not participate or leaving the study will not result in any

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penalty or loss of benefits, for example medical care, to which you are entitled. If you do decide to stop participating in the study, we encourage you to discuss your decision with your doctor. New findings developed during the course of this research, which may relate to your willingness to continue participation, will be provided to you by your study doctor.

WHAT ARE THE RISKS OF THE STUDY?

While on this study, you are at risk for the side effects described below. Since this radiation procedure is investigational, there may also be other side effects that we cannot predict. Your study doctor can prescribe drugs to make some of these side effects less serious and make you more comfortable.

A significant risk to taking part in this study is the small likelihood of receiving a dose of a radiation that is not fully effective in helping to treat your disease. This means that you may spend time and experience side effects undergoing radiation that does not provide you with the equivalent health-related benefits of standard radiation treatments.

Other less common or unexpected side effects may also develop and may be irreversible. This intervention has not yet been proven safe and therefore, may potentially result in death (unlikely). During your therapy you will be monitored closely for potential side effects. You are expected to report to the study doctor(s) any adverse sign(s) or symptom(s) which may develop while you are on this study.

For your safety, please disclose to the study doctor all of your present and past diseases and known allergies. It is important that you share with the study doctor any prescription and/or over-the-counter drugs, herbal preparations and nutritional supplements you are taking.

During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

Radiation Therapy

Very likely*:* These symptoms usually recover in the first few weeks following completion of radiation therapy

- Irritation, redness and discoloration of the skin in the radiation area similar to a sunburn
- Fatigue (tiredness) which can occur even 2-4 weeks after treatment
- Tenderness likely around the scar area

Less Likely

- Peeling of the skin, like that from a sunburn
- Permanent discoloration of the skin
- Hardness of the treated area which may include retraction of the breast (similar to a dent)
- Damage to fat cells in the breast that cause a red, swollen, or tender area in the breast (These damaged cells can look/feel like a lump and a biopsy may be needed which may be immediate or delayed.) (fat necrosis)
- Infection, which may be immediate or delayed and may develop as breast redness and/or pain (cellulitis)
- Small visible blood vessels on the skin surface over the treated area (telangiectasia)
- Poor cosmetic outcome due to fat and/or skin necrosis which may require surgery

Rarely

- Nausea
- Decreased appetite
- Inflammation in the lung under the treated breast, usually months after the radiotherapy course. Although this is usually mild, sometimes medication or hospitalization may be needed to treat this reaction. This reaction does not seem to cause any lasting damage to lung functioning, although rarely it is possible that it might do so.
- Fractures of the ribs. These usually heal slowly.
- Damage to the heart muscles or coronary arteries years after treatment which might very rarely cause a heart attack or other major problems.
- Severe infection that may develop as redness, pain, or a collection of infected cells (abscess)
- Severe scar tissue caused by infection or damage to the fat cells and surrounding tissue (fat necrosis and severe fibrosis)
- Breast pain in the treated breast that may come early or late and last for an extended period of time or permanently
- Delayed healing following a biopsy or fine needle aspiration (FNA) in a previously treated breast with PBI, which might cause blackened skin (skin necrosis)
- Cause new cancers to appear in the treated breast years later
- Cause new cancers to appear in the radiation field years later. This includes the breast, soft tissue, and lungs.

When the left breast is treated (but not when the right breast is treated), subjects may very rarely develop inflammation of the membranes around the heart or the heart itself months after radiation therapy. This causes discomfort.

If you have these symptoms you should report them to your study doctor who will determine if they are related to the radiation treatments given in the study or to infection. If radiation is the cause, the symptoms are usually temporary and relieved with medication. With medication for pain, you should be able to continue on the protocol.

It is not anticipated that these side effects will prevent you from finishing radiotherapy in 4 days. If it becomes necessary to stop your radiation treatments due to other problems (such as a medical illness), you may be taken off this study. At this time, your study doctor will discuss with you other treatment options.

MRIs use powerful magnets to make images. Therefore, persons with metal implants, such as surgical clips or pacemakers should not have an MRI. However, there are no known health risks associated with this exposure. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. The MRI makes loud banging noises as it takes images. Earplugs can be used to reduce the noises. The MRI can be stopped at any time at your request.

Radiology Tests (Mammograms/CT Scans): The radiation associated with these diagnostic radioactive drug and diagnostic x-ray studies will not adversely affect the treatment of your disease.

Reproductive risks: Because radiation can affect an unborn baby, you should not become pregnant while on this study. If you have any questions about the reproductive issues or about preventing pregnancy, please discuss them with your study doctor.

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

If you enroll on this study and experience any of the side effects listed above or others that you are concerned about, you can contact the investigator or another study physician any time of day or night by paging (617) 726-1818.

WHAT ARE THE BENEFITS OF THE STUDY?

If you agree to take part in this study, there may be no direct medical benefit to you.

Radiation treatment in general is destruction of any tumor cells remaining in the breast following surgery while attempting to preserve a cosmetically satisfactory appearance of the breast and causing very few complications.

The way radiation therapy is given in this study will allow you to complete study treatment much

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more quickly than if you had conventional treatment. We hope that this approach will be as effective as conventional treatments in preventing the cancer from reappearing in the breast. We also hope there may be fewer side effects from treating only part of the breast and that the cosmetic results will be as good as, or better than, conventional radiation therapy.

We hope the information learned from this study will benefit other people with breast cancer in the future.

WHAT ARE THE COSTS?

Taking part in this study may lead to added costs to you or your insurance company.

You or your insurance company will be charged for any other portion of your care that is considered standard care. This includes any blood work, office visits, radiation treatments and all other tests associated with this study. You may be responsible for any co-payments and deductibles that are standard for your insurance coverage.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services:

- Dana-Farber Cancer Institute: (617) 632-3455
- Massachusetts General Hospital: (617) 726-2191
- Brigham and Women's Hospital: (617) 732-5524 or (617) 732-7485
- Beth Israel Deaconess Medical Center: (617) 667-7082

There is no cost to you associated with the video recording portion of the study.

You will receive no payment for taking part in this study.

WHAT HAPPENS IF I AM INJURED OR SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

Providing your care does not mean that DF/HCC or the research doctors are at fault, or that there was wrongdoing. There are no plans for DF/HCC to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

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If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this study may become part of your hospital medical record. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database called CORIS.

Information contained in your records is used by study staff. There may be times when we are required by law to share your information. In those cases, we do not need your permission.

The results of this study may be published. You will not be identified in any publication without your permission.

PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana Farber/Harvard Cancer Center (DF/HCC) and its affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health an conditions ("protected health information"). If you enroll in the research described in this consent form, your "protected health information" will be used and shared with others as explained below.

1. **What protected health information about me will be used or shared with others during this research?**

    - Existing medical records
    - New health information created from study-related tests, procedures, visits, and/or questionnaires

2. **Why will protected information about me be used or shared with others?**

    The main reasons include:

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- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements; and
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm)
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for Use and Sharing of Protected Health Information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated researchers and entities participating in the research will use and share your protected health information. In addition, the DF/HCC review board that oversees the research at DF/HCC and its affiliated staff who have a need to access this information to carry out their responsibilities (for example, oversight, quality improvement, and billing) will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

All reasonable efforts will be made to protect the confidentiality of your protected health information, which may be shared with the following others for the reasons noted above:

- Outside individuals or entities that have a need to access this information to perform functions on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor(s) of the study, its subcontractors, and its agents: 2003 Avon Pilot Grant Awardee
- Other researchers and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. **For how long will protected health information about me be used or shared with others?**

   - There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process. Research information may be analyzed and re-analyzed in light of scientific and medical advances, or reviewed for quality assurance, oversight or other purposes.

6. **Statement of privacy rights:**

   - You have the right to withdraw you permission for the researchers and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. If you withdraw your permission, you must do so in writing by contacting the researcher listed as the Study Contact.
   - You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study. However, refusing to sign will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.
   - You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed under Study Contacts on the consent form.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

You are encouraged to ask questions about the study or your role as a participant at any time.

For questions about the study or a research-related injury, contact:

Alphonse Taghian, M.D.	MGH	(617) 726-8650
Abram Recht, M.D.	BIDMC	(617) 667-2345
Jay Harris, M.D.	DFCI	(617) 632-2291

For questions about your rights as a research participant, please contact a representative of the Office for the Protection of Research Subjects at DFCI (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research-related injury, or if you feel/felt under any pressure to enroll in this study or to continue to participate in this study.

You will receive a signed copy of this consent form.

Documentation of Consent

My signature below indicates that I have read this consent form in its entirety, my willingness to participate in this study and my understanding that I can withdraw at any time.

_____ _____

Signature of Subject or Legally Authorized Representative — Date

To be completed by person obtaining consent:

The consent discussion was initiated on _____ (date) at _____ (time.)

☐ A copy of this signed consent form was given to the subject or legally authorized representative, or, where the subject is a minor, the subject's parent or legal guardian.

For Adult Subjects

☐ The subject is an adult and provided consent to participate.

☐ The subject is an adult who lacks capacity to provide consent and his/her legally authorized representative:

- ☐ gave permission for the adult subject to participate
- ☐ did not give permission for the adult subject to participate

Signature of Individual obtaining consent: _____

Printed name of above: _____

Date: _____

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Agreement to Video Recording Procedures

Your consent to participate should be voluntary and informed.

___ I do ___ I do not consent to video images being recorded during my treatment.

Patient Initials: _____ Date: _____

For MGH Office Use Only: Date Consent Drafted or Revised: 10/20/09