UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: TARGIT: Targeted Intraoperative Radiotherapy after conservative breast surgery for women with early stage breast cancer

This is a clinical trial, a type of research study. Your study doctors, Catherine Park, M.D., Michael Alvarado, M.D., and associates in the Departments of Surgery and Radiation Oncology at the University of California San Francisco (UCSF), will explain the clinical trial to you.

Clinical trials include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study doctor.

You are being asked to take part in this study because you have early stage invasive breast cancer that is suitable for breast conserving surgery.

Why is this study being done?

At the present time, many women who have a lumpectomy for breast cancer also receive radiation therapy after surgery, which requires 3-6 weeks of five treatments per week. The purpose of this study is to evaluate the use of targeted intraoperative radiation therapy (IORT), where radiation is given one time during surgery. We are looking to see if there are any differences between women who receive standard radiation after surgery versus those who have IORT.

IORT is given during surgery after the tumor has been removed. The IORT device, called Intrabeam Device®, is FDA approved to be used in all parts of the body to deliver radiation. It can deliver radiation therapy accurately targeted to the area of the breast where the tumor has been removed while you are in the operating room.

A similar trial has already been completed with over 3400 patients internationally. The results showed that both radiation treatment options were similarly effective after 5 years of follow-up. This new trial is to look at the long term outcome after IORT for women in the United States with early stage breast cancer.

Carl Zeiss Meditec Inc., the maker of the Intrabeam Device®, is providing funding for this study.

How many people will take part in this study?

About 1200 patients will be participating in this study nationally, and about 100 patients will participate in this study at UCSF.

What will happen if I take part in this research study?

If you agree to participate in the study, your medical chart will be reviewed. If the review shows that you are eligible to participate, the following will happen:

Before you begin the main part of the study...

1) Consultation: You will meet with a radiation oncologist to see whether you are eligible for the study. The risks of study participation will be emphasized during this visit.

2) During the main part of the study:

- If the consultation shows that you can be in the main part of the study, and you choose to take part, you will be assigned to undergo intraoperative radiation as the sole radiation treatment following lumpectomy.
    - You will receive targeted IORT at the time of your initial lumpectomy, while you are still under general anesthesia in the operating room. The IORT procedure will take approximately 15-40 minutes. Radiation is delivered only to the part of the breast from which the cancer was removed. Therefore, there is minimal exposure to the heart and ribs and to the unaffected parts of the breast. However, if the final pathology report shows that you need further treatment, you may either need additional surgery, five-six weeks of standard radiation therapy given to the whole breast after surgery, or both. For the IORT, the doctor will place a round applicator directly in to the breast where the tumor has been removed to deliver the radiation dose. The doctor may use sutures (stitches) to hold the tissue around the applicator so that the radiation can be delivered more effectively. After the radiation is delivered, the doctor will suture (stitch) the incision as part of the normal surgery.
    - If you are not given IORT during surgery for any reason or your physician decides that you are no longer eligible for IORT after signing consent you will be considered “Off Study” and no longer followed by study staff.

3) Additional Operative Time

The IORT will add approximately 15-40 minutes of additional operative time to the surgery procedure. You will be under general anesthesia during the procedure.

The need for further treatment may arise if:

- The cancer is of a special type called “invasive lobular cancer”
- The cancer is associated with a large amount of pre-invasive cancer (DCIS or Ductal Carcinoma In Situ)
- The cancer has not been completely removed (close or positive margins), that is, some cancer cells are still present after the tumor was removed
- The cancer is larger than originally suspected
- There are cancer cells in your lymph nodes

Your doctor will discuss these possibilities with you, if the need arises.

Patients with high-risk pathological features (changes in your tissue or cells associated with cancer that may mean your cancer has a high risk of coming back in the breast) will be discussed in a gathering of UCSF breast physicians and alternative recommendations may be advised.

4) Photographs: Photographs of your breasts may be taken if you agree to allow it. These photographs may be shared with international researchers, but your name and/or other identifiable information will not be used. You can choose to be in the study and refuse to allow any pictures to be taken.

Please put your initials in the "YES" or "NO" box to indicate your answer.

Photographs of my breasts may be taken for the study:

YES	*NO*

When you are finished receiving IORT...

After completion of surgery and radiation, you will come to the breast care center for a follow-up visit within 6 weeks. If you undergo postoperative radiation therapy, this will require 3-6 weeks of outpatient treatment. All patients will then be followed at the breast care center with a physical examination and monitoring of side effects every 6 months for the first 3 years, then annually thereafter for 2 years. Your doctor may recommend that you have a mammogram at your 6 month follow-up visit.

Many patients with breast cancer are advised to take additional therapy such as chemotherapy or hormone therapy to try and stop the cancer from coming back. These treatments are not part of this trial and will be given in the usual way, and will not affect your participation in this trial.

Study location: All study procedures will be done at University of California San Francisco Mt. Zion Hospital or San Francisco General Hospital. If you undergo postoperative radiation therapy, you may have the option of seeing your local doctor for these visits.

How long will I be in the study?

After you are finished with your radiation treatment, the study doctor will ask you to visit the office for follow-up exams every 6 months for 3 years, then annually thereafter for 2 years. During these follow-up visits, we will perform a physical exam and ask if you have experienced any adverse events since the last visit. These visits will take approximately 15-30 minutes.

In addition, we would like to keep track of your medical condition for 10 years after your treatment. We would like to do this by looking at your medical records during the follow-up period to get updated information on your health status. If you are no longer being seen at the breast care center, we may call you on the telephone to see how you are doing. Keeping in touch with you and checking on your condition helps us look at the long-term effects of the study.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from your treatment can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen.

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

The amount of radiation you will receive during this procedure is similar to that received in many standard x-ray procedures and less than standard post-operative radiation therapy. However, the amount of radiation received is more than you would receive from natural daily exposure, and carries at least a theoretical risk. If you are especially concerned with radiation exposure, you should discuss this with the researchers.

Risks and side effects related to IORT are the same as that for standard postoperative radiotherapy. The targeted intraoperative radiation therapy device has been tested on over 4000 patients worldwide. In the International trial comparing IORT to standard postoperative radiation therapy, the number of patients with any complication was similar in both groups. Specifically, bleeding complication, skin breakdown and delayed healing were the same for IORT and standard radiation. In general the same side effects seen in radiation therapy may also occur in IORT, but are less likely. Patients who must undergo a surgical re-excision (additional surgery to remove any remaining cancer cells) following IORT may experience some complications, such as delayed wound healing.

Standard postoperative radiation therapy and IORT side effects may include:

- Redness and soreness of the skin (<1% of patients)
- Breast pain (<1% of patients)
- Infection requiring IV antibiotics (2% of patients)
- Delayed wound healing (3% of patients)

Increased Risk of Recurrence:

It is possible that the risk of local recurrence of your breast cancer could be somewhat higher in women who do not have whole breast radiation. However, the 5-year results of the International trial suggest that the difference between IORT and standard postoperative radiation therapy is likely to be small.

In addition, it is possible that subjects assigned to receive IORT may also have to undergo postoperative radiation treatment, which will result in greater radiation exposure.

Patients who need postoperative radiation therapy after IORT and also need chemotherapy may have a slightly higher risk of distant metastases (spread of your cancer to other parts of the body) due to the delay in starting chemotherapy**.**

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

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope IORT will be as effective against cancer compared to the usual treatment, its safety and effectiveness will be further tested in this study. We do know that the information from this study will help doctors learn more about IORT as a treatment for cancer. This information could help future cancer patients.

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

Your other choices may include:

- You may choose to undergo intraoperative radiation therapy (IORT) without participating in this study.
- You may choose to undergo postoperative radiation therapy without participating in this study.
- You may choose to decline radiotherapy altogether
- You may choose some other investigative treatment
- You may choose to obtain a second opinion

Please talk to your doctor about your choices before deciding if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Principal Investigators and the study team
- University of California
- Carl Zeiss Meditec Inc., the maker of the Intrabeam Device®, and the company that is providing funding for this study.
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in keeping research safe for people.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other doctors may become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

What are the costs of taking part in this study?

You or your insurance companies will be billed for all tests and procedures performed as part of this study. If you meet criteria to be part of this study, you or your insurance carrier will be responsible for costs resulting from the additional time in the operating room. In addition, if you decide to receive your IORT after your initial lumpectomy, you or your insurance company will incur additional costs from having the IORT as a separate second procedure. Insurance companies and other third party payers for health care have sometimes refused to pay for the costs of treatment for patients on research studies, in which case patients will be responsible for all costs. Financial counselors are available through the hospital accounting department to discuss this with patients. We do make every effort to obtain pre-authorization from insurance carriers before treatment on the study begins. If your insurance company does not authorize the procedures, you may not be able to take part in the 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.

Will I be paid for taking part in this study?

There is no financial reimbursement to patients for participating in the study.

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

It is important that you tell your study doctor, Dr. Catherine Park or Dr. Michael Alvarado, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at 415-353-7111.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, treatment will be available. The costs of the treatment may be covered by the University of California, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

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

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this 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 regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

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

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions, concerns, or complaints you have about this study. Contact your study doctors Dr. Catherine Park or Dr. Michael Alvarado at 415-353-7111.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814.

ClinicalTrials.gov is a website that provides information about clinical trials. 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.

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent
Date	Translator's Signature (if applicable)