Partial Breast Irradiation for Primary Breast Cancer

The delivery of larger doses of radiation therapy (RT) to the lumpectomy cavity and a margin of surrounding tissue after breast-conserving surgery, via brachytherapy or external beam radiation techniques, may provide several advantages to appropriately selected patients. Partial breast irradiation (PBI) may improve the documented underutilization of breast-conserving surgery by allowing RT to be completed in four or five days, instead of six to seven weeks, eliminate the acute and chronic toxicities associated with whole breast irradiation (WBI), improve cosmesis and confer societal economic benefits. Before PBI can be routinely incorporated into clinical practice, several issues must be addressed, including appropriate patient selection, optimal fractionation schedules and PBI techniques. Importantly, it must be established that long-term rates of locoregional control are similar to those achieved with WBI. A matched-pair analysis has demonstrated comparable outcomes for women treated with limited-field radiation or WBI. Several Phase III clinical trials evaluating these issues are ongoing worldwide.

PUBLISHED PBI RESULTS: BRACHYTHERAPY

Institution	N	Follow-up (months)	Local recurrence (%)
WBH – LDR patients	120	82	0.9
WBH – all patients	199	65	1.2
WBH – HDR patients	59	52	2.1
Ochsner Clinic	51	75	2.0
NIO – Hungary	45	60	4.4
University of Kansas	24	37	0
Tufts – New England Medical Center	32	33	3
NIO – Hungary Phase III	181	30	1.1
Florence, Italy	90	27	4.4
MGH	48	23	0

WBH = William Beaumont Hospital; LDR = low dose-rate brachytherapy; NIO = National Institute of Oncology; HDR = high dose-rate brachytherapy; MGH = Massachusetts General Hospital

SOURCE: Vicini F. **Partial breast irradiation: Current status.** Presentation. San Antonio Breast Cancer Symposium, 2003.

RANDOMIZED PHASE III STUDY OF CONVENTIONAL WHOLE BREAST RADIATION THERAPY VERSUS PBI FOR WOMEN WITH STAGE 0, I OR II BREAST CANCER

Protocol ID: Pending NSABP Protocol B-39
Projected Accrual: 3,000

Eligibility	**Stages 0-II breast cancer, ≤3-cm tumor size, <4 positive axillary lymph nodes and clear surgical margins**
ARM 1	**Whole breast radiation therapy**
ARM 2	**PBI* prior to adjuvant chemotherapy**

* Interstitial brachytherapy or MammoSite® balloon catheter or 3D conformal external beam irradiation. The PBI technique utilized will be at the physician's discretion and will be based on technical considerations, radiation oncology facility technique credentialing and patient preference.

SOURCE: NSABP Protocol Summaries, November 2004.

ACTIVE PARTIAL BREAST IRRADIATION TRIALS

Trial	Schema	Projected accrual
MammoSite® Registry Trial[1]	MammoSite® primary treatment MammoSite® boost treatment	1,300
National Institute of Oncology (Budapest, Hungary)[2]	External beam whole breast radiation therapy PBI (brachytherapy or external beam radiation therapy)	570
European Institute of Oncology (Milan, Italy)[2]	External beam whole breast radiation therapy PBI (intraoperative)	824
University College of London (London, England)[2]	External beam whole breast radiation therapy PBI (intraoperative)	1,666

SOURCES: [1] American Society of Breast Surgeons Patient Registry Protocol, December 2003.
[2] Vicini F. **Partial breast irradiation: Current status.** Presentation. San Antonio Breast Cancer Symposium, 2003.

FIVE-YEAR ACTUARIAL TREATMENT OUTCOMES FROM MATCHED-PAIR ANALYSIS OF PATIENTS TREATED WITH WHOLE BREAST VERSUS LIMITED-FIELD RADIATION THERAPY

Outcome	Whole breast % (95% CI)	Limited-field % (95% CI)	*p*-value
Ipsilateral recurrence	1 (0-2.4)	1 (0-2.8)	0.65
Regional failure*	1 (0-1.5)	1 (0.1-2.1)	0.54
Distant metastasis	5 (2.2-8.4)	3 (0.5-5.9)	0.17
Disease-free survival	91 (86.5-94.7)	87 (81.5-92.1)	0.30
Overall survival	93 (89.7-96.7)	87 (82.1-92.7)	0.23
Cause-specific survival	97 (95.0-99.8)	97 (93.8-99.9)	0.34
Contralateral breast failure	4 (1.0-6.4)	1 (0-2.4)	0.03

* Regional failure is defined as the recurrence of cancer in a regional nodal site before or simultaneously with the diagnosis of local recurrence or distant metastasis.

SOURCE: Vicini FA et al. **Limited-field radiation therapy in the management of early-stage breast cancer.** *J Natl Cancer Inst* 2003;95(16):1205-11.

SELECT PUBLICATIONS

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Dirbas FM et al. **Intraoperative radiation therapy following lumpectomy for breast cancer.** *Breast Cancer Res Treat* 2003;Abstract 455.

Keisch M et al. **Initial clinical experience with the MammoSite breast brachytherapy applicator in women with early-stage breast cancer treated with breast-conserving therapy.** *Int J Radiat Oncol Biol Phys* 2003;55(2):289-93.

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Van Limbergen E. **Indications and technical aspects of brachytherapy in breast conserving treatment of breast cancer.** *Cancer Radiother* 2003;7(2):107-20.

Vicini FA et al. **Limited-field radiation therapy in the management of early-stage breast cancer.** *J Natl Cancer Inst* 2003;95(16):1205-10.

Vicini F. **Partial breast irradiation: Current status.** *Breast Cancer Res Treat* 2003;Abstract MS2-1.

PARTIAL BREAST IRRADIATION

One of the advantages of PBI is that it can be completed quickly before systemic therapy is initiated. William Beaumont is one of the few institutions that offers interstitial brachytherapy, MammoSite® and conformal external beam radiation therapy.

Each technique has its advantages and none of them is applicable to all clinical scenarios. Treatment must be individualized based on factors such as the patient's access to a radiation facility and the location of the lesion within the breast.

At our institution, of the patients who receive PBI, approximately 60 percent are treated with the MammoSite®, 30 percent with conformal external beam radiation therapy and a small percentage with interstitial brachytherapy. Reducing the amount of time required and the amount of toxicity associated with radiation therapy may increase the rate of breast conservation. I believe an additional 10 to 20 percent of women making this decision would select breast-conserving therapy if PBI were an option.

— Frank A Vicini, MD

Intraoperative radiation therapy is an idea whose time has arrived. The procedure is gaining acceptance, and many competing technologies exist. I believe three-dimensional conformal, multicollimator, high-tech radiation therapy is absurd. No matter how carefully you plan your fields, you are not hitting the target.

A number of studies using MRI have demonstrated how off target this approach is. Even if the surgeon puts clips around the cavity during surgery, the cavity collapses and the clips migrate; therefore, no matter how expensive and high tech, I don't think this approach will work.

I'm interested in conforming the tissue to the source rather than the other way around. The approach I developed with Carl Zeiss is called Intrabeam. It is an elegant, simple device that a surgeon can utilize after wide local excision. In approximately 25 minutes, you can give a boost to the tumor bed and a centimeter beyond in all directions.

— Michael Baum, MD, ChM

NSABP PBI TRIAL

We are developing a trial to compare partial breast radiation therapy versus whole breast radiation therapy. The eligibility criteria will be broad and will include totally resected DCIS and invasive breast tumors up to three centimeters in size. We want to conduct this study now because there may only be a small window of opportunity before partial breast radiation therapy is widely adopted.

In this study, PBI can be administered by brachytherapy catheters, the MammoSite® device or conformal external beam radiation therapy. The physician and the hospital will determine which method to utilize, and it needs to be declared before randomization, although it can be changed if a patient is not eligible for a certain procedure.

All three options are done in 10 fractions over five days, as opposed to the five or six weeks it takes to administer whole breast radiation therapy, with or without a boost.

PBI may offer subtle advantages. Data suggest if we delay radiation therapy we may increase local recurrence; however, when we delay systemic therapy we increase systemic recurrence, so we choose to use systemic therapy first. PBI takes only five days and is then followed by adjuvant chemotherapy. By moving radiation therapy earlier into the treatment schedule, we may decrease local recurrences.

— Eleftherios P Mamounas, MD, MPH