SEMINARS IN BREAST DISEASE

# Partial Breast Irradiation: Is This a Viable Option?

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**In the treatment of early invasive and in situ breast carcinomas, lumpectomy followed by whole breast radiation are generally accepted as standard of care in breast conservation. Long-term data from early breast conservation trials has shown that most local failures occur in close proximity to the tumor bed. This has been observed in both radiated and unradiated breasts treated with breast conservation techniques, suggesting that occult multifocal disease is less ominous than once believed. Improvements in breast imaging and radiation treatment planning and delivery allow the experienced radiation oncologist to deliver high doses of radiation to the region of the tumor bed alone in less than 2 weeks. Preliminary data suggests that this abbreviated course of radiation offers cosmetic and disease control outcomes equal to that of traditional whole breast radiation in selected populations. This article reviews current techniques, outcomes of clinical trials, and novel techniques in partial breast radiation for early and locally recurrent breast carcinomas.**


**KEYWORDS** breast cancer, partial breast radiation, recurrent breast cancer, intraoperative radiation, brachytherapy, breast conservation

Breast cancer remains the most commonly diagnosed cancer among women in the United States with 212,920 estimated new cases in 2006.[1] Fortunately, most are early stage malignancies, due to increased screening and public awareness. The treatment of early stage breast cancer has undergone massive changes since the advent of breast conservation (BC) in the late 1960s and 1970s. Original attempts at local excision (lumpectomy) without adjuvant radiation proved inferior to mastectomy. Multiple phase II and phase III trials have proven lumpectomy with adjuvant whole breast radiation to be a safe and effective option.[2-4] Simulated mastectomies performed by Rosen and coworkers showed a multicentric pattern of breast cancer.[5] Interestingly, follow-up data from these early trials suggest that these occult, multicentric foci may not be clinically relevant. Veronesi and coworkers examined the benefits of whole breast irradiation (WBI) following quadrantectomy and axillary dissection.[6] Long-term follow-up data showed 56 in-breast recurrences in the surgery alone arm and 13 in the adjuvant WBI arm at 10 years. In both arms, 85% of the local failures were within the area of the quadrantectomy, suggesting that occult, multifocal disease may have little clinical significance. This predilection for local failure at the previous tumor bed has long been known. It was hypothesized and tested by Bartelink and coworkers that an additional dose, or boost, of radiation to the tumor bed may improve local control. This proved to be true and, an additional 16 to 20 Gy of radiation to the excisional cavity and scar are considered standard by most radiation oncologists today.[7]

Furthermore, the treatment of early stage breast cancer has improved with the advent of selective estrogen receptor modulators, such as tamoxifen.[8] More recently, aromatase inhibitors have shown a decrease in local failure rates more than tamoxifen in postmenopausal women.[9]

Despite these incremental improvements in breast-conserving therapy for early stage cancers, only 40% of patients undergo breast conservation therapy (BCT).[10] Factors contributing to this discrepancy include patient choice, distance to treatment facility,[11] time away from work/life, expense of WBI, prior history of radiation therapy, and patient age.

Given the high likelihood of local failure occurring within 2 cm of the tumor bed and antihormonal oncologics, WBI may be treating an unnecessarily large volume of normal breast tissue. Herein lies the hypothesis of partial breast irradiation. By virtue of the smaller volumes of normal tissue involved, partial breast irradiation therapy may take advantage of several key principles of radiobiology allowing for an accelerated course of treatment. First, smaller volumes of tissue treated, in general, show fewer side effects of radiation. In the case of breast tissue, this includes less erythema and fibrosis and therefore an improved cosmetic result. Second,

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**Table 1** Patient Selection Criteria for APBI

| | ABS[14] | ASBS[15] |
|---|---|---|
| Age | ≥45 years | ≥50 years |
| Histology | Unifocal, invasive ductal, or DCIS | Invasive ductal or DCIS |
| Mammogram findings | ≤3 cm | ≤2 cm |
| Surgical margins | Negative (≥2 mm) | ≥2 mm |
| Clinical target volume | 2 cm around excision cavity, remaining ≥0.5 cm from skin and ribs | |
| Nodal status | Negative with axillary dissection | Axillary/sentinel LN negative |

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compared with conventional breast radiation, larger doses of radiation per treatment, or fraction, may be delivered to lower total dose with equivalent biological effect. This principle is based on the Linear-Quadratic Model, on which most current theories of radiobiology are based.[12]

Accelerated partial breast irradiation (APBI) describes the delivery of full course, curative radiation to the tumor bed usually over 1 to 5 days. APBI has been developed over the past 20 years, with the first cases being described in the United Kingdom in the early 1980s.[13] In its infancy, APBI was performed solely through interstitial brachytherapy catheters using low-dose rate sources. APBI has gained wider acceptance with the development of high-dose rate remote afterloaders/associated applicators, improved three-dimensional treatment planning, and delivery.

The goal of this article is to provide an overview of the various modalities employed in the delivery of APBI, appropriate patient selection, and results of current clinical trials and research in the field of radiation oncology regarding APBI.

## Patient Selection and Techniques

When using APBI therapy for the treatment of breast cancer, patient selection plays a critical role in achieving successful outcomes. Patient selection criteria have been developed in consensus panels and described in previous publications by the American Brachytherapy Society (ABS) and the American Society of Breast Surgeons (ASBS). A summary of these recommendations is provided in Table 1.

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## Multicatheter-Based Interstitial Brachytherapy

The APBI treatment protocols first began with the use of multicatheter-based interstitial brachytherapy (IB).[14] At that time, IB was used to deliver a boost of radiation directly to the lumpectomy cavity before or after whole breast radiation. This has evolved into the investigational use of IB as the sole modality to deliver postexcision treatment with both low dose rate (LDR) and high dose rate (HDR) radioactive sources.

IB consists of placement of multiple after-loading catheters around the lumpectomy cavity, as this is the region most likely to harbor residual microscopic malignant foci. The catheters are placed every 1 to 1.5 cm and arranged in planes through the breast tissue. The number of catheters required depends on the size and the geometry of the excision cavity, but typically requires >10 catheters. The catheters are then used to house radioactive sources inserted after surgery to provide direct irradiation to the excision cavity margins and the adjacent tissues. The catheters remain in place for the duration of the treatment, and are generally well tolerated. Interstitial brachytherapy is applicable to patients with a wide variety of excision cavity dimensions, due to the flexibility in configuring the catheters. The treatment volume which receives the prescribed dose usually includes a margin of 1 to 2 cm of tissue surrounding the excision cavity.

One of the challenges of IB is not only the steep learning curve that exists in the placement of the catheters, but also the consistency of catheter placement between physicians. During the initial use of IB, the catheters were placed by palpation of the postoperative induration and seroma, but this has been reported to lead to misplacement relative to the tumor bed of up to 2.5 cm in up to 50% of the cases.[15] The use of image-based treatment planning, along with the development of rigid templates, has increased the reproducibility between centers.

At the time of implantation, one can use the seroma fluid to base placement of the catheters under ultrasound guidance. Kuske[16] described the introduction of contrast medium into the excision cavity, allowing one to better delineate the boundaries of the lumpectomy cavity. In addition, one can use a rigid template system in conjunction with CT imaging to accurately plan the catheter placement. The template is applied to the breast, stabilizing the area to be implanted between the two template grids. During the treatment planning process, a series of grid coordinates are selected that correspond with possible catheter positions. The treatment plan is then developed to deliver a radiation dose that conforms to the size and shape of the lumpectomy cavity and surrounding tissue margins. This plan can then be implemented, allowing the accurate placement of the IB catheters in a parallel orientation and minimizing deviation. Fluoroscopic imaging or stereotactic mammography tables can also be used to assist with proper catheter placement.

The multicatheter-based brachytherapy system can be used for HDR or LDR treatments. HDR brachytherapy deliv-