



American College of
RADIATION ONCOLOGY
Integrating Science and Technology into Patient Care

5272 River Road | Suite 630 | Bethesda, MD 20816 | 301.718.6515 | Fax 301.656.0989 | Email info@acro.org

In 1990 the National Institutes of Health issued a consensus statement on early stage breast cancer, supporting breast conservation surgery followed by radiotherapy as an appropriate method of primary therapy for women with stage I – II breast cancer.¹ Further support has been published with long term follow-up from the National Surgical Adjuvant Breast and Bowel Project and European Institutes of Oncology.^{2,3} This twenty year data continues to report excellent results obtained with breast conserving surgery (BCT) and post-operative radiation. The major advantages of BCT are superior cosmetic results and the potential for reduced psychological and emotional trauma compared to mastectomy. Despite the obvious cosmetic and potential emotional advantages of BCT, only 10% - 40% of patients who are candidates for BCT actually receive it. In addition, a clearly defined sub-population of patients that would not benefit from irradiation has not been identified.

Traditional whole-breast irradiation is delivered daily over 6-7 weeks after primary tumor removal. With more frequent use of adjuvant chemotherapy in patients with both node-negative and node-positive patients, substantial delays can occur prior to initiation of either breast irradiation or hormonal therapy. This protracted treatment with conventional whole breast irradiation can result in logistical barrier of time and travel. This barrier has resulted in a number of women choosing mastectomy or lumpectomy only, which results in an increased risk of in-breast failure.^{4 5 6} This trend toward breast conserving therapy only, resulting from patient choice or physician bias, has been documented through data from the National Cancer Institute Surveillance, Epidemiology, and End Results registry.⁷

Accelerated Partial Breast Irradiation (APBI) can potentially reverse this trend of breast conservation surgery only in the management of early stage breast cancer by overcoming some of the barriers to radiation therapy. APBI delivers radiation therapy only to the area of the breast at risk of failure and provides complete treatment in one week, offering women an additional treatment option. Additionally, toxicity to adjacent normal structures such as the heart, underlying chest wall, and contra-lateral breast should be significantly reduced by APBI. Also recent meta-analyses of cancer-specific mortality during the first 5 – 10 years after treatment are partially offset by late effects of radiation on adjacent tissue.

Holland, in his original pathologic evaluation of mastectomy specimens revealed multicentric microscopic disease with a relatively high frequency.⁸ This supported the concept of whole breast irradiation in the 1980s. However, with the advances in the selection of appropriate patients for BCT, it is not clear how many patients in the Holland study would be considered appropriate candidates by today's standards. Many of the patients were clinically detected and the sensitivity of mammography was not comparable to today's mammography. This study may not be applicable to patients who are candidates for BCT with modern mammographic evaluation and rigorous pathologic analysis of negative margins achieved by surgeons today. Data supports the

understanding that the majority of failures occur at the site of the resected primary lesion. Elsewhere failures, considered as any in-breast failure beyond the area of the lumpectomy cavity, occurs 1.5-3.5%. Elsewhere failure rates have been documented with equal frequency in patients treated with lumpectomy only and in patients treated with lumpectomy and whole breast irradiation.^{9 10 11} Reviewing this data suggests that whole breast irradiation benefits the reduction of failures in the breast tissue surrounding the tumor resection and equivalent local control rates can be achieved with appropriately delivered partial breast irradiation.¹² This suggests that acceptable outcomes can be achieved with APBI for the appropriately selected patient, shortening treatment time and potentially reducing health care cost.

There currently is a large body of mature Phase I & II data and maturing Phase III data supporting the replacement of whole breast irradiation with APBI. (Table I)

Partial Breast Irradiation

	IBRT	TR/MM	Elsewhere	Median F/U	DATA Set
Vicini, F et al Int J Radiat Oncol Biol Phys 2007; 68 (2) 341-346	6/199 5 yr act. = 1.6% 10 yr act. = 3.8%	3/199 based on clinical criteria 5/199 based on molecular-based assay 5 yr act. = 1.6% 10 yr act. = 3.1%	3/199 based on clinical criteria 1/199 based on molecular based clonality assay 5 yr act. = 0.8% 10yr act. = 0.8%	8.6 yrs	William Beaumont interstitial data
Chao et al Int J Radiat Oncol Biol Phys 2007; 69 (1) 32-40	2/80 = 2.5% 3 yr act. = 2.9%	1/80 according to clinical criteria 2/80 defined clonally	1/80 according to clinical criteria 0/80 based on molecular based clonality assay	22.1 m	William Beaumont <i>MammoSite</i> data
Vicini F Journal on Clin Oncol 2006; 24 (18S): 529	11/1449 = 1.2% 2 yr act. = 0.8%	6/1449 2 yr act. = 0.6%	5/1449 2 yr act. = 0.6%	14 m	<i>MammoSite</i> ASBS registry 2 year data
Polgar Int J Radiat Oncol Biol Phys 2007; 69(3) 694-702	5 yr act. = 4.7%	1.6% clinical criteria Crude rate: 3/128 = 2.3%	3.1% Clinical criteria Crude rate: 3/123 = 2.35	66m	Hungary Phase III WBRT vs. PBI 5 yr data
Benitez Am J Sur 2007; 194: 456-462	0/36	0/36	0/36	5 yr	<i>MammoSite</i> Initial Clinical Study
Chen S et al. Int J Radiat Oncol Biol Phys 2007; 69 (1): 25-31	4/70 = 5.7%	1/70	7/70	26.1 m	Rush University <i>MammoSite</i> Experience

IBRT Ipsilateral breast tumor recurrence - defined as the pathologic confirmation of cancer after disease-free interval in the treated breast

TR/MM True recurrence/marginal miss

Chen et al - termed lumpectomy bed failure; defined as within 2 cm of lumpectomy bed

Chao et al - recurrence of treated cancer within or immediately adjacent to the primary tumor site

Elsewhere failure

Chen et al - 2 cm away from original surgical bed

Chao et al - an IBRT several centimeters from the primary site, and generally felt to be clinically new primary cancer

Molecular-based clonality

Chao et al - assay used to accurately establish the type of local recurrence

Clonally distinct = new primary

Clonally related = recurrence of the index lesion

Based on available pathologic and clinical data, the target requiring treatment with adjuvant irradiation is less than the whole breast and related to the extent of surgical resection as measured by microscopic margins. When using APBI the data further suggests that a target defined as the lumpectomy cavity plus a 1-2 cm margin after resection with negative microscopic margins is appropriate. Fisher reported that 5 yr data is appropriate since that >75% of the recurrences occurred in that time frame.¹³ This demonstrates that 5 year data is sufficient to assess the efficacy of APBI

Multiple methods of partial breast irradiation have been established:

- Multiple catheters
- Brachytherapy devices (balloon)
- Single-fraction intraoperative radiation delivery
- Partial breast external beam

With all of these techniques patient selection criteria and brachytherapy quality assurance are critical components in order to assure successful treatment outcomes. The American College of Radiation Oncology supports the following selection criteria:

1. All patients who are appropriate candidates for BCT
2. \geq 45 years old
3. Unifocal, invasive cancer or ductal carcinoma in situ (DCIS)
4. \leq 3 cm tumor
5. Negative microscopic surgical margin of excision
6. Axillary node negative by level I/II axillary dissection or sentinel node evaluation

Louis L. Munoz, MD, MBA, FACRO
President
American College of Radiation Oncology

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