THE AMERICAN SOCIETY OF Breast Surgeons

Resource Guide

Accelerated Partial Breast Irradiation

Purpose

To outline the use of accelerated partial breast irradiation (APBI) for the treatment of breast cancer.

Introduction/Purpose

Partial breast irradiation (PBI) is a type of treatment where radiation is delivered locally to the area where the tumor was surgically removed (lumpectomy cavity) and can encompass balloon-based, external-beam radiation or interstitial brachytherapy treatment. The duration of treatment with PBI has also been condensed from the traditional 5-6 weeks for conventionally fractionated radiation to a week or less, a technique called accelerated PBI (APBI) This document serves to aid breast surgeons in interpreting multiple guidelines on APBI and applying its use in clinical practice.

Methods

A prior ASBrS resource guide on APBI in 2018 performed a comprehensive, but not systematic, review of the modern literature on this subject. Since then, long-term results comparing PBI alone with whole breast irradiation (WBI) in over 10,000 patients with breast cancer in several randomized clinical trials have been published. In this resource guide, we updated the findings from the main trials on APBI. We have also focused our update on the two main clinical guidelines available for PBI from the American Society for Radiation Oncology (ASTRO) and the American Brachytherapy Society (ABS). The ASBrS Critical Writing, Editing and Review Committee (CWERC) updated and reviewed this resource guide, which the ASBrS Board of Directors then reviewed and approved.

Summary of Data Reviewed

Background

The surgical and adjuvant radiation treatment of breast cancer has evolved dramatically over the past 50 years. In 1976, the National Surgical Adjuvant Breast and Bowel Project (NSABP) initiated the B-06 trial, which randomized patients with invasive breast cancers to receive modified radical mastectomy, lumpectomy, or lumpectomy plus whole breast irradiation (WBI), each with axillary dissection. After 20 years of follow-up, published data from this study and other randomized trials have established that both mastectomy and breast-conserving surgery (BCS) with WBI are appropriate treatment options for Stage I and II breast cancer, with equivalent survival.[1-7] In 1990, the National Institutes of Health issued a consensus statement that supported the use of BCS and WBI as the preferred management for patients with invasive breast cancer.[8] This report was followed by widespread adoption of BCS with WBI. BCS without WBI is associated with a higher rate of recurrence.[1,9-11]

Despite the advantages of BCS, which involves less extensive surgical intervention than mastectomy, many eligible women opt to undergo mastectomy instead of BCS[12] because of the long- and short-term side effects of WBI and the burden of treatment, which involves traveling to a radiation treatment facility for daily treatments for 3-6 weeks.[13] In addition, 10-30% of women who are

treated with BCS never receive radiation as part of their treatment.[14-16] Multiple factors contribute to underutilization of BCS and adjuvant radiation, including: specific tumor characteristics, cost, patient social and demographic factors, physician/patient bias, racial and ethnic disparities[16], distance from the radiation facility, and lack of social support.[13-18] Furthermore, WBI has other potential downsides, such as deleterious effects upon adjacent tissues including the heart, lung, contralateral breast, adjacent normal breast, and skin.[19-21] Data on the use of WBI administered from 1958 to 2001 have demonstrated that its use is associated with a dose-dependent increase in long-term incidence of ischemic heart disease.[22] A safer and more convenient approach to adjuvant radiation therapy could allow more patients to choose BCS, decrease the number of patients treated with BCS who never received adjuvant radiation, and reduce the complications associated with radiation therapy after BCS.[23]

Accelerated Partial Breast Irradiation (APBI)

APBI has been studied as an alternative to whole breast radiation to potentially increase the number of individuals eligible for breast conservation. APBI can be delivered via multi-catheter interstitial brachytherapy, balloon-based applicators, external beam radiotherapy, or intraoperative radiation therapy (IORT). All of the APBI modes involve treating a limited and targeted volume of breast tissue in a much shorter course than traditional whole breast radiation.

Clinical Trials examining APBI

Numerous studies have shown that a majority of ipsilateral breast tumor recurrences (IBTR), after treatment with BCS and WBI, occur within the index quadrant.[24-26] The concept that irradiation of the immediate vicinity of the primary tumor is adequate to achieve local control of early-stage breast cancer was used to initiate numerous clinical trials involving APBI to show equivalence and non-inferiority of APBI.[27-29] Several of these trials, including the National Surgical Adjuvant Breast and Bowel Project (NSABP) B39/Radiotherapy Oncology Group (RTOG)0413, APBI-IMRT-Florence, and Canadian RAPID trials are summarized here. Overall, these trials demonstrate long-term comparable rates of IBTR between PBI and WBI.

The NSABP-B39/RTOG 0413 study[30] enrolled 4216 patients who were randomized to WBI versus ABPI. ABPI techniques included external 3-D conformal radiation, interstitial multicatheter brachytherapy, or intracavitary brachytherapy. At 10-year median follow up, IBTR was 3.9% with WBI versus 4.6% with APBI. This trial employed a 90% confidence interval of a hazard ratio exceeding 1.5%. While the trial did not meet statistical equivalence (HR 1.22, 90% CI 0.94 – 1.58), there was no clinically meaningful difference in IBTR, with an absolute difference of 0.7% at 10 years. No difference was seen in disease-free survival, distant disease-free interval, overall survival, and late toxicity was equivalent. Patient-rated and blinded physician review of cosmetic outcomes noted no difference between WBI and APBI.

The APBI-IMRT Florence Trial was a single-center phase III trial comparing WBI to ABPI using intensity-modulated radiation therapy (IMRT) in early-stage breast cancer, with a primary endpoint of determining 5-year difference[31] in IBTR between 30 Gy in 5 once-daily fractions (APBI arm) and 50 Gy in 25 fractions with a tumor bed boost (WBI arm) after breast-conserving surgery. 520 patients were randomized between 2005 and 2013. At 10 years, IBTR was 2.5% with WBI versus 3.7% with APBI.[32] No difference was seen in 10-year breast cancer specific survival between groups. Less acute and long-term toxicity was seen in the APBI group as compared to the WBI group. Improved cosmetic outcome was noted in the APBI group as evaluated by both physician and patient. This trial supports

a preferred schedule of 30 Gy in 5-fractions.

The Canadian RAPID trial[33] involved 2135 patients randomized to WBI or APBI using an external-beam 3D conformal technique (87%) or IMRT (10%) at a dose of 38.5 Gy in 10 fractions administered twice per day separated by 6-8 hours over 5-8 days. At 8-year follow up, IBTR met noninferiority criteria (2.8% with WBI versus 3% with APBI). No difference was seen in disease-free and overall survival, and acute toxicity was lower with APBI as compared to WBI.

The Groupe Européen de Curiethérapie (GEC) and European Society for Radiotherapy and Oncology (ESTRO) multicatheter interstitial brachytherapy (MIB) randomized clinical trial studied 1184 patients randomized to WBI and APBI using MIB (delivered twice a day for 4 days) between 2004 and 2009. At 10 years, there was no difference in local recurrence (3.51% MIB vs. 1.58% WBI, p=0.07).[34] The UK IMPORT LOW trial performed a multicenter, phase 3, randomized controlled trial of non-accelerated external beam PBI (delivered once a day over 3 weeks) in 2018 women between 2007 and 2010 and found that IBTR rates were not inferior to PBI compared with WBI at 5 years (0.5% vs. 1.1%).[35] The Danish Breast Cancer Group randomized 865 patients to WBI versus non-accelerated PBI (all received 40 Gy in 15 fractions). While the primary end-point was 3-year grade 2-3 breast induration, after a median follow-up of 7.6 years, there was no difference in locoregional recurrence (1.4% WBI vs 2.3% PBI, P=0.28).[36]

Clinical Benefits of APBI

Reduce treatment time and costs: APBI was developed to improve access to breast-conserving therapy by reducing radiation treatment to several days (shorter treatment time). From the patient perspective, the tangible benefits of APBI may be found primarily in improved access to radiation treatment, less travel[37], reduced out-of- pocket costs[38], increased patient satisfaction, decreased radiation therapy exposure to normal tissues, and potentially improved cosmetic outcomes.[39-41]

Reduced Toxicity: In the RTOG study[30], toxicities were similar between groups: APBI (40% grade 1, 44% grade 2, 10% grade 3) vs. WBI (31% grade 1, 59% grade 2, 7% grade 3). There was <1% grade 4-5 toxicities in both groups and no difference in second primary cancers (10% WBI versus 9% APBI). The RAPID trial[33] did note increased late toxicity (32% vs 13%) and lower rates of good to excellent cosmesis with APBI. This was thought to be related to twice-daily fractionation used in the ABPI arm. This was not seen in the RTOG[30] or ESTRO[34] trials. In the Florence trial[31,32], the APBI group had better acute and late toxicities, and cosmetic outcomes at 5 years.[40] In the MIB trial at 5 years[42], there was no difference in grade 2-3 late side effects to the skin, grade 2-3 subcutaneous tissue late side effects or severe fibrosis. At 10 years[34], the APBI group had less grade 3 late side effects than WBI (1% vs 4%, p=0.02), the most common being fibrosis. The investigators surmised that this may have been due to the fact that when active sources are placed into the breast, a smaller volume of breast is treated, which may explain the lesser toxicity. In the UK IMPORT LOW trial[35], the PBI group had better breast appearance, and less breast firmness compared with WBI as judged by patients. In the Danish trial[36], the 3-year rate of grade 2-3 breast induration was better for non-accelerated PBI compared with WBI (5.1% vs. 9.7%, P=0.014), with larger breast size having worse induration.

While the different PBI techniques have not been compared head-to-head in randomized trials, a systematic review found that interstitial brachytherapy may have the lowest risk of fat necrosis, infection and breast pain. 3-D conforming radiotherapy may offer the best cosmetic outcome and be

least associated with telangiectasia.[43]

Limitations of APBI

While the randomized controlled trials assessed different kinds of APBI, no study has compared outcomes between the different modalities of APBI. The RTOG study[30] was not powered to assess different kinds of APBI delivered: 73% 3-D conformal radiotherapy (3DCRT), 21% single-entry brachytherapy and 6% multi-catheter brachytherapy. Most of the RAPID trial[33] patients also received 3DCRT (87%, IMRT in 10%), as did the Danish study[36], while the Florence[31,32] and UK IMPORT LOW[35] trials assessed IMRT. The GEC-ESTRO trial assessed MIB.[34]

Most studies included patients with invasive, node-negative breast cancer, median age over 60 years, and a large majority of tumors were grade 1-2 and hormone receptor positive (UK IMPORT LOW, ESTRO, RAPID, Florence); the RTOG study had the widest inclusion criteria with adult women over age 18, tumor size up to 3 cm and nodal positivity (up to 3 positive axillary nodes). The RAPID trial had more narrow selection criteria: node-negative breast cancer less than 3 cm in size receiving lumpectomy. Lobular and multicentric breast cancer and women young than age 40 were excluded. The Florence trial enrolled women over age 40 with maximum tumor size of 2.5 cm and excluded extensive intraductal component, multifocal cancer, and margins < 5 mm. The UK trial enrolled women over age 50 with grade 1-3, tumor size up to 3 cm and up to 3 positive nodes, and 2 mm margins.

Intraoperative Radiotherapy (IORT):

Two trials (ELIOT[44], TARGIT-A[45]) have investigated IORT use. Both studies reported high rates of local recurrence compared with WBI, which suggests that IORT may be too targeted or conformal, potentially missing areas that are at increased risk for recurrence. Despite higher rates of local recurrence, the TARGIT-A long-term results showed no difference on survival.[46] In 2020, the ESTRO IORT Task Force published a review of the existing data on IORT use suggesting that it may be considered as an alternative to WBI in carefully selected patients with low risk disease features.[47]

Per 2024 ASTRO guidelines, electron IORT is not recommended outside of a clinical trial or multi-institutional registry. Similarly, kilovoltage (kV) IORT alone (without WBI) is not recommended outside of a clinical trial or multi-institutional registry. Per 2022 ABS guidelines, recommendation for IORT is weak and considered appropriate for use on clinical trial only. This recommendation was initially published in the 2019 ABS guidelines and the 2022 update did not find sufficient evidence to justify changing this recommendation.

Decisions regarding the use of IORT outside of a clinical trial or registry should be made in a shared decision making fashion with the patient and a multidisciplinary tumor board where available.

APBI in the setting of sentinel lymph node biopsy omission

In 2016, the Society of Surgical Oncology Choosing Wisely guidelines recommended against the routine use of sentinel lymph node biopsy in women aged 70 and over with early-stage clinically node-negative hormone receptor-positive, HER2-negative invasive breast cancer[47], supported by data from the CALGB 9343 trial[48]. The recent publication of the SOUND[49] and INSEMA[50] randomized clinical trials further support the omission of sentinel lymph node biopsy in patients over the age of 50 with small invasive breast cancers and a negative pre-operative axillary ultrasound planned to receive breast-conserving therapy (lumpectomy followed by WBI). The recent ASCO guidelines now

discourage routine SLNB in post-menopausal patients 50 years of age and older with negative pre-operative axillary ultrasound for small (2 cm or less) grade 1 or 2 hormone receptor-positive, HER2-negative breast cancer planned to receiving breast conserving therapy.[51] The clinical trials examining APBI required pathologically negative sentinel lymph nodes for patients to be eligible, which risks the potential escalation of adjuvant radiotherapy in patients where SLNB is omitted. In the SOUND trial[49], 90% of participants received WBI and 10% received PBI while in the INSEMA trial, all patients received WBI as PBI was not allowed.[50] Most patients enrolled in the SOUND and INSEMA trials would have likely also been candidates for APBI because of the low likelihood of positive sentinel lymph nodes. The ASCO guidelines recommend shared decision making and multidisciplinary discussion when considering the use of APBI after omission of SLNB.[51]

APBI and Re-irradiation

There is emerging data that in the setting of a local recurrence, repeat breast-conserving therapy with lumpectomy and partial breast irradiation is safe and effective, which is reflected in the updated ABS guidelines.[52] The NRG/RTOG 1104 trial was a phase 2, single-arm, prospective clinical trial of 3DCRT as partial breast re-irradiation (1.5 Gy twice daily for 15 days) after a second lumpectomy for an ipsilateral breast cancer recurrence after prior WBI. The eligibility criteria were a unifocal IBTR on MRI, size of 3 cm or less, no evidence of skin involvement, and occurring 1 year or more after initial BCT. Among 58 evaluable patients enrolled between 2010 and 2013, the 5-year cumulative incidence of ipsilateral breast recurrence was 5%, with late grade 3 treatment-related adverse events reported in only 7% (no grade 4 or higher adverse effects were reported).[53] The GEC-ESTRO breast cancer working group found no difference in 5-year overall survival (88% vs 87%, P = .6) and cumulative incidence of a third breast event (2.3% vs 2.8%, P = .4) in a propensity matched analysis comparing 377 patients having mastectomy and 377 patients having lumpectomy and MIB for a second ipsilateral breast cancer between 1995 and 2017.[54] In a population-based study using SEER data between 1999 and 2015, there was no difference in overall survival and breast cancer-specific survival between repeat BCS with radiation versus mastectomy. Patients with an IBTR who had repeat BCS without repeat radiation had worse survival (HR 1.4), highlighting the importance of repeat radiation.[55] In the lack of Level 1 evidence comparing repeat BCT versus mastectomy after an IBTR, the ABS guidelines recommend consideration of repeat BCT in appropriately selected patients after multidisciplinary discussion and patient consent.[52] Additional factors to consider for re-irradiation are to select patients with a longer time interval between ipsilateral breast events and no prior toxicity from prior RT. The ideal patient selection criteria for repeat BCT is evolving, amid on-going prospective studies such as the international, multicentre phase 2 PRESERVE trial.[56]

CONSENSUS RECOMMENDATIONS

The American Society for Radiation Oncology (ASTRO) and the American Brachytherapy Society (ABS) have published consensus statements regarding “suitable” and “cautionary” and “unsuitable” patients for treatment with APBI.[27,48] ASTRO[58] and ABS[52] have recently updated their guidelines resulting in more open patient selection criteria. The National Comprehensive Cancer Networks (NCCN)[59] endorses the use of APBI for any patient without a germline BRCA1/2 mutation who meets criteria outlined in the updated ASTRO guidelines. The table below lists ABS and ASTRO guidelines and updates.

Criterion	ABS Updates	ASTRO update
Age	≥45 years <45 years if luminal A features and/or low-risk genomic recurrence score results	≥40 years
Histology	All invasive subtypes and DCIS	Non-lobular invasive subtypes and DCIS
Grade		1-2 3*
Tumor Size	≤3cm	≤2cm >2 - ≤3 cm*
T Stage	Tis, T1, T2 (≤ 3cm)	Tis, T1, T2 (≤ 3cm)
Margins	No tumor on ink for invasive ≥2mm for DCIS	Positive margins are a contraindication
Nodal status	Negative†	Negative†
ER status	ER+ or ER-	ER+ ER-*
HER2 status	Her2- or Her2+ if patient receives Her2 directed therapy per NCCN guidelines	Her2- or Her2+ if patient receives Her2 directed therapy per NCCN guidelines
Other factors	No extensive LVI	
Abbreviations: ABS = American Brachytherapy Society; ASTRO = American Society for Radiation Oncology; NCCN = National Comprehensive Cancer Networks *Conditional ASTRO recommendations †Omission of SLN may influence candidacy for APBI		

ASTRO **conditionally recommends** PBI if any of these factors are present: (1) grade 3 disease, (2) ER- histology, (3) tumor size >2cm - ≤3 cm. PBI may not be appropriate when multiple conditional factors are present, given possible higher risk of recurrence.

ASTRO **conditionally does not recommend** PBI if any of these factors are present: (1) HER2-positive tumors not receiving anti-HER2 therapy, (2) LVI or (3) lobular histology, due to low number of patients accrued to RCTs (and thus possibly higher risk of recurrence with PBI).

ASTRO **does not recommend** PBI for DCIS or invasive breast cancer if any of these factors are present: (1) positive lymph nodes (if invasive), (2) positive surgical margins, (3) known germline BRCA1 or BRCA2 mutation or (4) age < 40 years.

Recommendations

Patients should be carefully selected for APBI and properly informed of the current benefits and risks when considering APBI, WBI, and no radiation. Several APBI options exist and should be discussed in a multidisciplinary fashion to ensure optimal patient outcomes. There are risks and benefits to each of these approaches concerning effectiveness, side effect profile, patient access, and patient preference. These relevant techniques include:

1. External beam radiation therapy (EBRT) with 3-D conformal radiation, intensity modulated radiation therapy (IMRT) or protons

2. Brachytherapy with intercavitary or interstitial techniques
3. Per 2024 ASTRO guidelines, electron IORT is not recommended outside of a clinical trial or multi-institutional registry. Similarly, kilovoltage (kV) IORT alone (without WBI) is not recommended outside of a clinical trial or multi-institutional registry. Per 2022 ABS guidelines, recommendation for IORT is weak and considered appropriate for use on clinical trial only. This recommendation was initially published in the 2019 ABS guidelines and the 2022 update did not find sufficient evidence to justify changing this recommendation.

In consideration of the updated ASTRO and ABS guidelines, The American Society of Breast Surgeons recommends the following selection criteria when considering patients for treatment with APBI:

1. **Age:** Minimum of 40 years

2. **Histology**:
   - All invasive subtypes, recognizing that ASTRO guidelines conditionally do not recommend APBI in lobular histology due to poor representation in clinical trials (and thus possible higher recurrence rates). ABS guidelines recommend APBI in all invasive subtypes.
   - Ductal carcinoma in situ (DCIS)

3. **Total tumor size (invasive and DCIS):** less than or equal to 3 cm in size

4. **T Size:** Tis, T1, T2 (≤ 3 cm)

5. **Margins:**
   - No tumor on ink for invasive tumors and invasive tumors with associated DCIS
   - ≥ 2mm for DCIS

   Note: ASTRO guidelines state that positive margins for both DCIS and invasive disease are a contraindication for APBI, however, do not specify the definition of a negative margin for invasive or in situ disease. ABS guidelines clearly specify no tumor on ink for invasive disease and ≥ 2mm for DCIS. Per ABS guidelines, PBI may be considered for selected patients with DCIS who have negative margins <2mm in the context of appropriate multidisciplinary and shared decision-making discussions.

6. **Nodal Status:** Negative

   Note: Omission of sentinel lymph node biopsy may affect candidacy for APBI as surgical staging is a key factor in formulating these recommendations. Shared decision-making and multidisciplinary discussion are recommended for the consideration of APBI following the omission of SLNB. We discourage the routine use of WBI following SLNB omission, as most patients who are candidates for SLNB omission likely would have had pathologically negative sentinel nodes and qualified for APBI as well.

7. **Other Factors:**
   - Multifocal disease is allowed as long as the combined area of tumor is ≤3cm.
   - Tumor may be estrogen receptor positive or estrogen receptor negative.

- ABS guidelines allow for APBI for patients with tumors without extensive LVI, while recognizing the lack of a standardized definition for reporting LVI extent. ASTRO guidelines conditionally do not recommend ABPI in the setting of lymphovascular invasion due to underrepresentation in clinical trials, making it challenging to understand the implications of LVI on ipsilateral breast recurrence (IBR). Given the concerns for potential increased local recurrence rates, APBI should be considered with caution for patients with tumors exhibiting LVI.
- Patients should not be treated with APBI if they have a BRCA genetic mutation or other genetic mutation that confers an increased risk of breast cancer.
- There is no evidence to support use of APBI in male patients due to underrepresentation in clinical trials. ABS guidelines recommend offering APBI to men who have undergone breast conserving surgery and clinical and pathologic features otherwise appropriate for treatment with APBI.
- There is no contraindication to APBI in patients with history of contralateral breast cancer.
- In the absence of Level 1 data, repeat BCS with APBI may be considered for unifocal IBTRs less than 3 cm in size who have had no toxicity from prior radiation treatment. The time interval from prior radiation is a consideration.

8. Patient selection and counseling should be performed in a multidisciplinary fashion with collaboration between the treating surgeon and the treating radiation oncologist. These recommendations are intended as a guide to treat patients. Individual treatment decisions could allow treatment outside of the parameters listed above with appropriate multidisciplinary review and implementation of shared decision-making discussions with the patient.

This statement was developed and revised by the Society's Critical Writing, Editing and Review Committee and on July 12, 2025 was approved by the Board of Directors.

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