Medical Policy

Accelerated Breast Irradiation and Brachytherapy Boost after Breast-Conserving Surgery for Early Stage Breast Cancer

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Policy Number: 326
BCBSA Reference Number: 8.01.13
NCD/LCD: N/A

Related Policies
None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

When using radiation therapy after breast-conserving surgery (BCS) for early stage breast cancer:

Accelerated whole breast irradiation (AWBI) may be considered MEDICALLY NECESSARY for patients who meet the following conditions:

• Invasive carcinoma of the breast
• Tumors ≤5 cm in diameter
• Negative lymph nodes
• Technically clear surgical margins, ie, no ink on tumor or invasive carcinoma or ductal carcinoma in situ
• Age at least 50 years old.

As recommended by the Society of Surgical Oncology and the American Society for Radiation Oncology (ASTRO), technically clear surgical margins can be defined as no ink on tumor or invasive carcinoma or ductal carcinoma in situ (http://www.redjournal.org/article/S0360-3016(13)03315-4/pdf).

As part of the clinical input process, ASTRO recommended additional criteria that should be satisfied for patients undergoing AWBI:
1. Pathologic stage is T1–2 N0 and the patient has been treated with breast-conserving surgery.
2. Patient has not been treated with systemic chemotherapy.
3. Within the breast along the central axis, the minimum dose is no less than 93% and maximum dose is no greater than 107% of the prescription dose (±7%) (as calculated with 2-dimensional treatment planning without heterogeneity corrections).
AWBI is considered **INVESTIGATIONAL** in all other situations involving treatment of early-stage breast cancer after BCS.

Interstitial or balloon brachytherapy may be considered **MEDICALLY NECESSARY** for patients undergoing initial treatment for stage I or II breast cancer when used as local boost irradiation in those who are also treated with BCS and whole-breast external-beam radiotherapy.

Accelerated partial breast-irradiation (APBI), including interstitial APBI, balloon APBI, external beam APBI, noninvasive brachytherapy using Accuboost®, and intra-operative APBI, is considered **INVESTIGATIONAL**.

Noninvasive brachytherapy using Accuboost® for patients undergoing initial treatment for stage I or II breast cancer when used as local boost irradiation in those who are also treated with BCS and whole-breast external-beam radiotherapy is considered **INVESTIGATIONAL**.

### Prior Authorization Information

**Inpatient**
- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

**Outpatient**
- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

<table>
<thead>
<tr>
<th>Product</th>
<th>Prior Authorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>Prior authorization <strong>is not required</strong>.</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
<td>Prior authorization <strong>is not required</strong>.</td>
</tr>
<tr>
<td>Medicare HMO BlueSM</td>
<td>Prior authorization <strong>is not required</strong>.</td>
</tr>
<tr>
<td>Medicare PPO BlueSM</td>
<td>Prior authorization <strong>is not required</strong>.</td>
</tr>
</tbody>
</table>

### CPT Codes / HCPCS Codes / ICD Codes

*Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.*

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

*The following codes are included below for informational purposes only; this is not an all-inclusive list.*

The above **medical necessity criteria MUST be met** for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue

### CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>19296</td>
<td>Placement of radiotherapy afterloading expandable catheter (single or multichannel) into the breast for interstitial radioelement application following partial mastectomy, includes imaging guidance; on date separate from partial mastectomy</td>
</tr>
<tr>
<td>19297</td>
<td>Placement of radiotherapy afterloading expandable catheter (single or multichannel) into the breast for interstitial radioelement application following partial mastectomy, includes imaging guidance; concurrent with partial mastectomy (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>19298</td>
<td>Placement of radiotherapy afterloading brachytherapy catheters (multiple tube and button type) into the breast for interstitial radioelement application following (at the time of or subsequent to) partial mastectomy, includes imaging guidance</td>
</tr>
</tbody>
</table>
Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 1 channel

Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 2-12 channels

Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; over 12 channels

Interstitial radiation source application, complex, includes supervision, handling, loading of radiation source, when performed

Therapeutic radiology treatment planning; simple

Therapeutic radiology treatment planning; intermediate

Therapeutic radiology treatment planning; complex

Therapeutic radiology simulation-aided field setting; simple

Therapeutic radiology simulation-aided field setting; complex

Therapeutic radiology simulation-aided field setting; complex

3-dimensional radiotherapy plan, including close volume histograms

Brachytherapy isodose plan; simple (calculation[s] made from 1 to 4 sources, or remote afterloading brachytherapy, 1 channel), includes basic dosimetry calculation(s)

Brachytherapy isodose plan; intermediate (calculation[s] made from 5 to 10 sources, or remote afterloading brachytherapy, 2-12 channels), includes basic dosimetry calculation(s)

Brachytherapy isodose plan; complex (calculation[s] made from over 10 sources, or remote afterloading brachytherapy, over 12 channels), includes basic dosimetry calculation(s)

Brachytherapy source, nonstranded, high dose rate iridium-192, per source

Placement and removal (if performed) of applicator into breast for radiation therapy

Radioelements for brachytherapy, any type, each

High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per fraction, includes basic dosimetry, when performed

Breast Cancer

Current estimates suggest that over 266000 new cases of breast cancer of any stage will occur in the U.S. in 2018. Based on adjusted data from 2011 to 2015, among women, the number of new cases is 126 per 100000 and the number of deaths 21 per 100000.1

Breast Conservation Therapy

For patients diagnosed with stage I or II breast tumors, survival after breast conservation therapy (BCT) is equivalent to survival after mastectomy. BCT is a multimodality treatment that initially comprised breast-conserving surgery (BCS) to excise the tumor with adequate margins, followed by whole-breast external-beam radiotherapy (EBRT) administered as five daily fractions per week over five to six weeks. Local boost irradiation to the tumor bed often is added to whole-breast irradiation (WBI) to provide a higher dose of radiation at the site where recurrence most frequently occurs. For some patients, BCT also includes axillary lymph node dissection, sentinel lymph node biopsy, or irradiation of the axilla. A number
of randomized controlled trials have demonstrated that the addition of radiotherapy after BCS reduces recurrences and mortality. In an expanded update of an individual patient data meta-analysis, the Early Breast Cancer Trialists’ Collaborative Group (2011) reported that radiotherapy halved the annual recurrence rate after 10 years for women with a node-negative disease (n=7287), from 31.0% for those not receiving radiotherapy to 15.6% for those receiving it. It also reduced the 15-year risk of breast cancer death from 20.5% to 17.2% (p=0.005). For women with node-positive disease (n=1050), radiotherapy reduced the 1-year recurrence risk from 26.0% to 5.1%. Radiotherapy also reduced the 15-year risk of breast cancer death from 51.3% to 42.8% (p=0.01).

Consequently, radiotherapy is generally recommended following BCS. A potential exception is for older women at low-risk of recurrence. For example, current National Comprehensive Cancer Network guidelines state that women ages 70 or older may omit radiotherapy if they are estrogen receptor-positive, have T1 tumors, have clinically negative lymph nodes, and plan to take adjuvant endocrine therapy. However, the agreement is not universal.

Controversy continues on the length of follow-up needed to determine whether accelerated partial-breast irradiation (APBI) is equivalent to WBI (see the TEC Assessment [2013] on accelerated radiotherapy after BCS for early-stage breast cancer for details). Because recurrences are relatively rare among low-risk early breast cancer patients, it may take a considerable time for enough recurrences to occur to provide sufficient power for comparing recurrence rates across radiotherapy approaches. Additionally, radiation-induced adverse cardiovascular effects and radiation-induced non-breast cancers tend to occur ten or more years after treatment. For accelerated WBI, some ten-year data are available. However, for newer approaches, the issue may be resolved by statistical issues rather than biologic ones. For example, in the large NSABP-39/RTOG 0413 trial comparing WBI with APBI (NCT00103181), enrollment has reached the revised target of 4216. Trial duration (barring early termination) is determined by the occurrence of a prespecified number (175) of in-breast recurrences. Researchers expect that reaching that number of recurrences will take approximately ten years.

Currently, most patients diagnosed with stage I or II breast cancer are offered a choice between BCT and mastectomy but BCT is selected less often than expected. Studies have shown that those living farthest from treatment facilities are least likely to select BCT instead of mastectomy and most likely to forgo radiotherapy after BCS.

**Approaches to Radiotherapy Following Breast-Conservation Treatment**

The goals of cancer radiotherapy are to deliver a high dose of homogeneous radiation (ie, all parts of the tumor cavity receive close to the targeted dose) to the tumor or tumor bed. Areas adjacent to the tumor may be given a lower dose of radiation (eg, with WBI) to treat any unobserved cancerous lesions. Radiation outside the treatment area should be minimal or nonexistent. The goal is to target the tumor or adjacent areas at risk of harboring unseen cancer with an optimum dose while avoiding healthy tissues. Table 1 outlines the major types of radiotherapy used after BCS.

<table>
<thead>
<tr>
<th>Radiation Type</th>
<th>Accelerated?</th>
<th>Whole or Partial Breast</th>
<th>EBRT or Brachytherapy</th>
<th>Treatment Duration</th>
<th>Published RCTs</th>
<th>Length of Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional WBI</td>
<td>No</td>
<td>Whole</td>
<td>EBRT</td>
<td>5-6 wk</td>
<td>Multiple</td>
<td>&gt;15 y</td>
</tr>
<tr>
<td>Accelerated WBI</td>
<td>Yes</td>
<td>Whole</td>
<td>EBRT</td>
<td>3 wk</td>
<td>4</td>
<td>10 y</td>
</tr>
<tr>
<td>Interstitial APBI</td>
<td>Yes</td>
<td>Partial</td>
<td>Brachytherapy</td>
<td>1 wk</td>
<td>2</td>
<td>5.4 y</td>
</tr>
<tr>
<td>Balloon APBI</td>
<td>Yes</td>
<td>Partial</td>
<td>Brachytherapy</td>
<td>1 wk</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>EBRT APBI</td>
<td>Yes</td>
<td>Partial</td>
<td>EBRT</td>
<td>1 wk</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
Intraoperative APBI | Yes | Partial | Not applicable | 1d | 1 | 5 y

APBI: accelerated partial-breast irradiation; EBRT: external-beam radiotherapy; RCT: randomized controlled trial; WBI: whole-breast irradiation.
Noninvasive breast brachytherapy using AccuBoost has been described by the manufacturer as capable of delivering APBI but no studies for this indication were found. Interstitial brachytherapy entails placement of multiple hollow needles and catheters to guide placement of the radioactive material by a remote afterloading device. It is more difficult to perform than other types of brachytherapy and has a steep learning curve. Balloon brachytherapy (e.g., MammoSite) entails inserting a balloon into the tumor bed, inflating the balloon, confirming its position radiographically, and then using a remote afterloader to irradiate the targeted area. Some brachytherapy systems combine aspects of interstitial and balloon brachytherapy. External-beam APBI is delivered in the same way as conventional or accelerated whole-breast radiotherapy but to a smaller area. All three external-beam regimens can use 3-dimensional conformal radiotherapy or intensity-modulated radiotherapy. Intraoperative APBI is performed during breast-conserving surgery with a single dose of radiation delivered to the exposed tumor bed.

Accelerated Whole Breast Irradiation
One approach to reducing radiotherapy treatment time is to provide the same dose to the whole breast in a shorter time by increasing the dose provided per treatment (hypofractionation). This approach was initially avoided out of concern that increasing doses might induce more severe adverse events from radiation exposure, thus tipping the balance between benefits and harms. More recent research, some of which are highlighted below, has allayed most of these concerns. Accelerated whole-breast irradiation has been adopted widely in Canada and Europe.

Accelerated Partial Breast Radiation
The second approach to reducing radiotherapy treatment time is APBI. It differs from conventional WBI in several ways. First, the radiation only targets the segment of the breast surrounding the area where the tumor was removed, rather than the entire breast. This approach was based in part on the finding that recurrences are more likely to occur close to the tumor site rather than elsewhere in the breast. Second, the duration of treatment is four to five days (or one day with intraoperative radiotherapy) rather than five to six weeks, because radiation is delivered to the tumor bed in fewer fractions at larger doses per fraction. Third, the radiation dose is intrinsically less uniform within the target volume when APBI uses brachytherapy (i.e., the implantation of radioactive material directly in the breast tissue).

Several methods to deliver APBI are available, including Interstitial brachytherapy, intraoperative brachytherapy, and external-beam APBI irradiation.

Brachytherapy Boost With WBI
Brachytherapy also can be used as an alternative to EBRT to deliver boost radiotherapy combined with whole-breast EBRT. Most studies of local boost brachytherapy use temporarily implanted needles, wires, or seeds after patients have recovered from surgery and completed whole-breast radiotherapy.

Noninvasive Breast Brachytherapy
Noninvasive breast brachytherapy (AccuBoost), has been used for local boost around the tumor bed. The AccuBoost system provides image-guided radiotherapy before each treatment to ensure that radiation is directed at the treatment target. The breast is placed between mammography paddles, where images are taken, and radiation is delivered using a distinct applicator. The paddles prevent motion during treatment. Radiation is delivered from one side of the breast to the other or from the top of the breast to the bottom. This is proposed to reduce radiation exposure to adjacent tissues, including the heart and lung. No long-term studies are available to confirm this.

Summary
Radiotherapy is the standard of care for patients with breast cancer undergoing breast-conserving surgery (BCS) because it reduces recurrences and lengthens survival. The conventional radiotherapy
A regimen consists of approximately 25 treatments of 2 gray (a measure of absorbed radiation dose) delivered over 5 to 6 weeks. Nonetheless, not all patients undergo radiotherapy following BCS; the duration and logistics of treatment may be barriers for some women. Accelerated radiotherapy approaches have been proposed to make the regimen less burdensome for patients with early-stage breast cancer at a low-risk of recurrence. Accelerated (also called hypofractionated) whole-breast irradiation (AWBI) reduces the number of fractions and the duration of treatment to about three weeks. Accelerated partial-breast irradiation (APBI) targets a limited part of the breast in and close to the tumor cavity. By reducing the area irradiated, fewer treatments are needed, and the total treatment takes about one week.

**Accelerated Whole-Breast Irradiation**

For individuals who have node-negative, early-stage breast cancer with clear surgical margins who receive AWBI after BCS, the evidence includes randomized controlled trials (RCTs) and systematic reviews. The relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, and treatment-related morbidity. Two randomized noninferiority trials both reported ten-year follow-up data on local recurrence. Both trials found that local recurrence rates with AWBI were no worse than conventional whole-breast irradiation (WBI) when applying a noninferiority margin of 5%. Conclusions apply to patients meeting eligibility criteria of the RCTs trials, including having early-stage invasive breast cancer, clear surgical margins, and negative lymph nodes. In addition, consistent with national guidelines, these conclusions apply to tumors less than or equal to 5 cm in diameter and women at least 50 years old. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Input obtained in 2017 and in 2011 supported the use of AWBI.

**Accelerated Partial-Breast Irradiation**

For individuals who have early-stage breast cancer who receive interstitial brachytherapy, the evidence includes an RCT. The relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The RCT reported five-year follow-up data and found that interstitial brachytherapy was noninferior to WBI for rates of local breast cancer recurrence when applying a noninferiority margin of 3%. Ten-year follow-up data are needed on local recurrence as well as at least one additional trial confirming these findings. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have early-stage breast cancer who receive intraoperative brachytherapy, the evidence includes RCTs. The relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. Several RCTs have been published but collectively they have not demonstrated that outcomes after intraoperative brachytherapy are noninferior to WBI. Results of two RCTs (TARGET-A, ELIOT) comparing intraoperative brachytherapy with WBI found higher rates of local recurrence with intraoperative brachytherapy than with WBI. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have early-stage breast cancer who receive external-beam APBI, the evidence includes RCTs. The relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The RCTs have reported outcomes out to three to five years, and ten-year data are required to draw conclusions about the impact of the technology on health outcomes. One trial reported higher rates of adverse cosmesis and grade 3 toxicities in the external-beam APBI group compared with the WBI group. The evidence is insufficient to determine the effects of the technology on health outcomes.

Input obtained in 2011 was mixed in its support of APBI.

**Local Boost Brachytherapy with Whole-Breast Irradiation**

For individuals who have early-stage breast cancer who receive local boost brachytherapy with WBI, the evidence includes nonrandomized studies and a systematic review. The relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. A TEC Assessment
concluded that, for women undergoing BCS plus WBI as initial treatment for stage I or II breast cancer, nonrandomized comparative studies have shown similar outcomes with brachytherapy local boost and with external-beam radiotherapy local boost. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**Noninvasive Breast Brachytherapy**

For individuals who have early-stage breast cancer who receive noninvasive breast brachytherapy, the evidence includes a retrospective comparative study. The relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The retrospective study was a matched comparison of noninvasive breast brachytherapy or electron beam radiotherapy to provide boost radiation to the tumor bed. The study was subject to selection bias, relatively short follow-up, and use of a retrospective design. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/2018</td>
<td>BCBSA National medical policy review. Policy criteria clarified to state: tumors ≤5 cm in diameter. 6/14/2018</td>
</tr>
<tr>
<td>1/2016</td>
<td>Clarified coding information.</td>
</tr>
<tr>
<td>2/2015</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>1/2015</td>
<td>Clarified coding information.</td>
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</table>

**Information Pertaining to All Blue Cross Blue Shield Medical Policies**

Click on any of the following terms to access the relevant information:

- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

**References**


accelerated partial breast irradiation for ductal carcinoma in situ: long-term follow-up from a phase 3 randomized trial. Tumori, 2018 Nov 27;105(3). PMID 30474504


