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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 <u>MEDICALLY NECESSARY</u> 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 (<u>http://www.redjournal.org/article/S0360-3016(13)03315-4/pdf</u>).

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 <u>MEDICALLY NECESSARY</u> 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 <u>IS REQUIRED</u> for all products if the procedure is performed <u>inpatient</u>.

Outpatient

 For services described in this policy, see below for products where prior authorization <u>might be</u> <u>required</u> if the procedure is performed <u>outpatient</u>.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is not required .
Commercial PPO and Indemnity	Prior authorization is not required .
Medicare HMO Blue sm	Prior authorization is not required .
Medicare PPO Blue SM	Prior authorization is not required .

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 <u>medical necessity criteria MUST</u> 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

CPT codes:	Code Description
	Placement of radiotherapy afterloading expandable catheter (single or multichannel)
	into the breast for interstitial radioelement application following partial mastectomy,
19296	includes imaging guidance; on date separate from partial mastectomy
	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
19297	addition to code for primary procedure)
	placement of radiotherapy afterloading brachytherapy catheters (multiple tube and
	button type) into the breast for interstitial radioelement application following (at the
19298	time of or subsequent to) partial mastectomy, includes imaging guidance

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; simple
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)

HCPCS Codes

HCPCS	
codes:	Code Description
C1717	Brachytherapy source, nonstranded, high dose rate iridium-192, per source
C9726	Placement and removal (if performed) of applicator into breast for radiation therapy
Q3001	Radioelements for brachytherapy, any type, each

The following CPT codes are considered investigational for <u>Commercial Members: Managed Care</u> (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
	High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per
0395T	fraction, includes basic dosimetry, when performed

Description

Breast Cancer

Current estimates suggest that 276,480 new cases of breast cancer of any stage will occur in the U.S. in 2020. Based on adjusted data from 2013 to 2017, among women, the number of new cases is 128.5 per 100,000 and the number of deaths 20.3 per 100,000.^{2,}

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 comprises breast-conserving surgery (BCS) to excise the tumor with adequate margins, followed by whole-breast externalbeam radiotherapy (EBRT) administered as 5 daily fractions per week over 5 to 6 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 (RCTs) 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 radiotherapy.³, 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 (NCCN) 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.^{4,} However, the agreement is not universal.^{5,}

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.⁶, Because recurrences are relatively rare among low-risk early breast cancer patients, it may take 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 10 or more years after treatment.^{7,8,9}, For accelerated WBI, some 10-year data are available. However, for newer approaches, the issue may be resolved by statistical issues rather than biologic ones.

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.^{10,11,12,}

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. They differ by technique, instrumentation, dose delivery, and possible outcomes.

Radiation Type	Accelerated?	Whole or Partial Breast	EBRT or Brachytherapy	Treatment Duration	Published RCTs	Length of Follow-Up
Conventional WBI	No	Whole	EBRT	5-6 wk	Multiple	>15 y
Accelerated WBI	Yes	Whole	EBRT	3 wk	4	10 y
Interstitial APBI ^b	Yes	Partial	Brachytherapy	1 wk	2	5.4 y
Balloon APBI ^c	Yes	Partial	Brachytherapy	1 wk	0	0
EBRT APBId	Yes	Partial	EBRT	1 wk	3	0

Table 1. Major Types of Radiotherapy Following Breast-Conserving Surgery^a

Intraoperative	Yes	Partial	Not applicable	1 d	1	5 y
APBI ^e						

APBI: accelerated partial-breast irradiation; EBRT: external-beam radiotherapy; RCT: randomized controlled trial; WBI: whole-breast irradiation.

^a Noninvasive breast brachytherapy using AccuBoost has been described by the manufacturer as capable of delivering APBI but no studies for this indication were found.

^b 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.

^c Balloon brachytherapy (eg, 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. ^d 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.

^e Intraoperative APBI is performed during breast-conserving surgery with a single dose of radiation delivered to the exposed tumor bed.

Summary

Radiotherapy is the standard of care for patients with breast cancer undergoing breast-conserving surgery (BCS) because it reduces recurrences and lengthens survival. A conventional radiotherapy 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 3 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 1 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. Relevant outcomes are overall survival (OS), disease-specific survival, change in disease status, and treatment-related morbidity. Two randomized noninferiority trials both reported 10-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 , 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. Relevant outcome are OS, disease-specific survival, change in disease status, and treatment-related morbidity. The RCT reported 5-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 1 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. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. Several RCTs have been published but collectively results have not demonstrated that outcomes after intraoperative brachytherapy are noninferior to WBI. Results of 2 RCTs (TARGIT-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. Relevant outcomes are OS, disease-specific survival, change in disease status, and treatment-related morbidity. RCTs have reported outcomes from 5 to 10 years. Results from the trial with the largest number of patients and longest duration of follow-up reveal that external-beam APBI did not meet the criteria for equivalence to WBI with regard to controlling tumor recurrence; however, the the absolute difference in the 10-year cumulative incidence of ipsilateral recurrence was low and survival was not different between groups. Other RCTs found no significant differences between external beam ABPI and WBI regarding local recurrence or survival. Moreover, 1 of the trials reported higher rates of adverse cosmetic outcomes and grade 3 toxicities in the external-beam APBI group than in 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. 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. 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.

Date	Action
10/2020	BCBSA National medical policy review. Description, summary, and references
	updated. Policy statement(s) unchanged.
10/2019	BCBSA National medical policy review. No changes to policy statements. New
	references added. Background and summary clarified.
9/2018	BCBSA National medical policy review. No changes to policy statements. New
	references added. Background and summary clarified.
6/2018	BCBSA National medical policy review. Policy criteria clarified to state: tumors ≤5
	cm in diameter. 6/14/2018
6/2017	BCBSA National medical policy review. New medically necessary indications
	described. Effective 6/1/2017.
1/2016	Clarified coding information.
2/2015	New references added from BCBSA National medical policy.
1/2015	Clarified coding information.

Policy History

5/2014	BCBSA National medical policy review. New investigational indications described. Effective 5/1/2014.
6/2013	BCBSA National medical policy review. Policy statement on criteria for accelerated whole breast radiation changed from "negative surgical margins" to "technically clear surgical margins"; no change to intent of policy statement. Effective 6/1/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/1/2011	New policy, effective 12/1/2011, describing covered and non-covered indication.

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

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