Brachytherapy Treatment of Breast Cancer

Radiation therapy is the standard care for patients with breast cancer undergoing breast-conserving surgery (BCS), as it reduces recurrences and lengthens survival. The conventional radiation therapy regimen consists of approximately 25 treatments of 2 Gray (Gy; a measure of absorbed radiation dose) delivered over 5 to 6 weeks. Nonetheless, not all patients undergo radiation therapy following breast-conserving surgery; 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 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. This approach has been commonly used in Canada and Europe.
- Accelerated partial-breast irradiation (APBI) irradiates 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. Several approaches can be used to deliver APBI, including interstitial brachytherapy, balloon brachytherapy, external beam radiotherapy, or intraoperative radiotherapy (which occurs on only 1 day).

The critical question is whether these three approaches are equivalent in outcomes and adverse events to the conventional radiation therapy regimen.

Background

Breast Conservation Therapy

Survival after breast-conservation therapy (BCT) is equivalent to survival after mastectomy for patients diagnosed with tumors categorized as stage I or II. BCT is a multimodality treatment that initially consisted of breast conservation therapy (BCS) to excise the tumor with adequate margins, followed by whole-breast external-beam radiation therapy 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 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 individual-level meta-analysis, the Early Breast Cancer Trialists’ Collaborative Group (EBCTCG) reported that radiotherapy halved the annual recurrence rate after 10 years for women with node-negative disease (n=7,287), from 31.0% for those not receiving radiotherapy to 15.6% for those receiving it. (1) 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=1,050), 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%.
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Consequently, radiation therapy is generally recommended following BCS. A potential exception is for older women at low risk of recurrence. For example, the National Comprehensive Cancer Network (NCCN) guidelines state that women aged 70 or older may omit radiotherapy if they have estrogen receptor positive, T1 tumors, clinically negative lymph nodes, and plans to take adjuvant endocrine therapy.

Controversy continues on the length of follow-up needed to determine whether APBI is equivalent to whole breast irradiation (for more information, see the most recent update to the TEC Assessment on Accelerated Radiotherapy after Breast-Conserving Surgery for Early Stage Breast Cancer) (3); some 10- year data are already available on accelerated whole breast irradiation. However, the issue may be resolved by statistical issues rather than biological ones. Because recurrences are relatively rare among low-risk early breast cancer patients, it may take considerable time for there to be enough recurrences to achieve sufficient power to compare rates for each radiotherapy approach. Additionally, radiation-induced adverse cardiovascular effects and radiation-induced non-breast cancers tend to occur 10 or more years after treatment. For example, in the large NSABP-39/RTOG 0413 trial comparing whole breast irradiation versus APBI, enrollment has reached the revised target of 4,216. The length of the trial (presumably barring early termination) is determined by the occurrence of a pre-specified number (175) of in-breast recurrences. The researchers expect that reaching that number of recurrences will take about 10 years.

Most patients diagnosed with stage I or II breast cancer now are offered a choice of BCT or modified radical mastectomy, but BCT is selected less often than expected. Studies have shown that those living furthest from treatment facilities are least likely to select BCT instead of mastectomy and most likely to forgo radiation therapy after breast-conserving surgery. A study using data from the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) tumor registries from 1992 to 2002 examined how many women with early stage (I or II) breast cancer received radiotherapy within 4 months following breast-conserving surgery. After adjusting for age, they found that in 2002, 30.8% of Caucasian women and 44.7% of African-American women had not received radiotherapy. Furthermore, these rates had increased from 24.7% for Caucasians and 34.0% for African Americans in 1992.

Given that duration and logistics appear to be barriers to completion of treatment, there has been interest in developing shorter radiotherapy regimens. Two approaches have been explored.

The first method 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 to target the tumor more effectively might induce more severe adverse events from radiation exposure, thus, tipping the balance between benefits and harms. More recent research, some of which is highlighted below, has allayed most of these concerns. Accelerated whole breast irradiation (AWBI) has been used especially in Canada and Europe.

The second approach to reducing radiotherapy treatment time is accelerated partial-breast irradiation (APBI). It differs from conventional whole-breast irradiation in several ways. First, the radiation targets only 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 4 to 5 days (or 1 day with intraoperative radiotherapy) rather than 5 to 6 weeks, because the radiation is delivered in fewer fractions at larger doses per fraction to the tumor bed. 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).

To appreciate the differences among radiotherapy techniques, it is useful to understand attributes of radiation delivery. The goals of cancer radiotherapy are usually to provide the tumor or tumor bed with a high dose of homogeneous radiation (e.g., all parts of the tumor cavity receive close to the targeted dose). Areas adjacent to the tumor may be treated with a lower dose of radiation (e.g., with whole-
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breast irradiation, to treat any unobserved cancerous lesions). Radiation outside the treatment area should be minimal or non-existent. The goal is to target the tumor or adjacent areas at risk of harboring unseen cancer with an optimum dose, while avoiding healthy tissues.

**Brachytherapy Boost with Whole Breast Irradiation**

Brachytherapy can also be used as an alternative to external beam radiation therapy to deliver boost radiation therapy combined with whole-breast external-beam radiation therapy. Most of the studies of local boost brachytherapy use temporarily implanted needles, wires, or seeds after patients recovered from surgery and completed whole-breast radiation therapy.

**Regulatory Status**

The various radiotherapy modalities presented in this report have been approved or cleared for marketing by the U.S. Food and Drug Administration (FDA) (TEC 2013). All brachytherapy devices have been approved for marketing through the 510(k) process and are either balloon brachytherapy or hybrid balloon-Interstitial brachytherapy devices. One device can provide either intraoperative or intracavitary treatments. The FDA has required a black box warning on each stating that “The safety and effectiveness of the … [brachytherapy device] as a replacement for whole breast irradiation in the treatment of breast cancer has not been established.” The breast brachytherapy applicator used for noninvasive brachtherapy (a precursor of Accuboost ®) was approved for marketing through the 510(k) process in June 2006. It does not have the black box warning.

Axxent® electronic brachytherapy (by iCAD; formerly by Xoft, Inc) refers to both a type of balloon brachytherapy and an alternative to the high-dose rate afterloader unit often used to deliver the radiotherapy. FDA has approved this device for marketing through the 510(k) process for use with balloon and interstitial brachytherapy, intraoperative brachytherapy, vaginal brachytherapy, and delivery of radiation to the skin. A balloon brachytherapy device is also approved for marketing. Intrabeam® Photon Radiosurgery Device (Carl Zeiss Surgical) is another electronic brachytherapy device that is used for intraoperative radiotherapy. It was used for the TARGIT trial and may be used in other organs.

**Related Policies:**
Accelerated Partial Breast Radiotherapy (Breast Brachytherapy)

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

**Policy**

BCBSNC will provide coverage for Brachytherapy Treatment of Breast Cancer when it is determined to be medically necessary because the medical criteria and guidelines shown below are met. Some members may be eligible for specific coverage of accelerated partial breast radiotherapy through their benefit plan. Please see separate BCBSNC Corporate Medical Policy Accelerated Partial Breast Radiotherapy. (Breast Brachytherapy)

**Benefits Application**

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.
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When Brachytherapy Treatment of Breast Cancer is covered

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 patients who are also treated with breast-conserving surgery and whole breast external beam radiotherapy.

Accelerated whole breast irradiation may be considered medically necessary for patients who meet the following conditions:

- invasive carcinoma of the breast. Exclude invasive disease or ductal carcinoma in situ involving the margins of excision; tumors >5 cm in diameter; breast width >25 cm at posterior border of medical and lateral tangential beams.
- negative lymph nodes
- technically clear surgical margins

When Brachytherapy Treatment of Breast Cancer is not covered

1. Brachytherapy is considered investigational when used in patients with Stage I or II diseases as the sole form of radiotherapy after surgical excision.

2. Brachytherapy is considered investigational for local boost irradiation when combined with whole breast radiotherapy but without surgical excision.

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

Accelerated whole breast irradiation is considered investigational when medical necessity criteria under “When Brachytherapy Treatment of Breast Cancer is covered” are not met.

Policy Guidelines

Refer to the member’s benefit booklet for prior plan review/precertification requirements.

The overall body of evidence on accelerated whole-breast irradiation (AWBI) compared to conventional whole-breast irradiation suggests local recurrence rates with accelerated whole breast radiotherapy were not worse than conventional whole breast irradiation in patients meeting the criteria of the Canadian trial, when applying a non-inferiority margin of 5%. Patient selection is important, and at this point, only patients similar to those in the Canadian trial should be considered for this therapy.

Thus, accelerated whole-breast irradiation may be considered medically necessary for these patients with clinical characteristics noted in the medically necessary policy statement. Outcomes could vary in women with other disease characteristics.

For patients treated with whole breast external beam radiation and breast-conserving surgery, local boost irradiation via interstitial or balloon brachytherapy is likely to result in equivalent outcomes compared to local boost given by external beam. This is based on results on nonrandomized, comparative studies, a TEC Assessment, and specialty society guidelines. As a result, interstitial or balloon brachytherapy may be considered medically necessary for these patients when used as local boost irradiation.
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The evidence on noninvasive breast brachytherapy using Accuboost to provide the boost radiation to the tumor bed is very weak, therefore this technique is considered investigational.

Given the available evidence, interstitial or balloon brachytherapy may be considered medically necessary for these patients when used as local boost irradiation.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 0395T, 19296, 19297, 19298, 77316, 77770, 77771, 77772, 77778

Diagnoses that are subject to medical necessity review: C50.0 - C50.929, C79.81, D05.0 – D05.92, D48.60 - D48.62, D49.3  (Effective 3/11/2016)

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

TEC Assessment - 5/96
National Association issued policy 7/96
Medical Policy Advisory Group 12/2/1999
BCBSA Medical Policy Reference Manual, 8.01.13; 12/16/02


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BCBSA Medical Policy Reference Manual [Electronic version]. 8.01.13, 10/10/06


TEC assessment 7/2010


Specialty Matched Consultant Advisory Panel 8/2012


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Specialty Matched Consultant Advisory Panel 5/2017

Policy Implementation/Update Information

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<tr>
<td>7/96</td>
<td>Original policy issued.</td>
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<tr>
<td>6/99</td>
<td>Reformatted, Description of Procedure or Service revised, Medical Term Definitions added.</td>
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<td>12/99</td>
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<tr>
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<td>Specialty Matched Consultant Advisory Panel - Revised section under when it is covered. Format changes.</td>
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<tr>
<td>8/02</td>
<td>Reaffirmed. Source added to Scientific Reference Sources section.</td>
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| 10/8/05 | Specialty Matched Advisory Panel review 9/19/2005. Updated "Description of Procedure or Services" section. Added the statement; "BCBSNC will cover partial breast radiotherapy when performed in a National Cancer Institute-approved Phase III Clinical Trial (for members who have clinical trial benefits). An example of such a trial is "Phase III Randomized Study of Adjuvant Whole Breast Versus Partial Breast Irradiation in Women

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with Ductal Carcinoma In Situ or Stage I or II Breast Cancer" (Protocol IDs NSABP-B-39, NCT00103181, RTOG-0413, SWOG-NSABP-B-39). Information regarding this trial can be found at http://cancernet.nci.nih.gov. ***Please note that prior approval for phase III clinical trials is required for BCBSNC members." to the "Policy" section. Added "Partial breast radiotherapy when performed in a National Cancer Institute-approved Phase III Clinical Trial for members who have clinical trial benefits." under the "When covered" section. Rationale updated in the "Policy Guidelines" section. Key words added. "3-D conformal external beam radiation" and "lumpectomy" added to "Medical Term Definitions". References added.

4/1/07 Added statement in "Policy" section, "Some patients may be eligible for specific coverage of accelerated partial breast radiotherapy through their benefit plan. Please see Accelerated Partial Breast Radiotherapy (Breast Brachytherapy), policy number ADM9100." Removed the following from the "Policy" section; "BCBSNC will cover partial breast radiotherapy when performed in a National Cancer Institute-approved Phase III Clinical Trial (for members who have clinical trial benefits). An example of such a trial is "Phase III Randomized Study of Adjuvant Whole Breast Versus Partial Breast Irradiation in Women with Ductal Carcinoma In Situ or Stage I or II Breast Cancer" (Protocol IDs NSABP-B-39, NCT00103181, RTOG-0413, SWOG-NSABP-B-39). Information regarding this trial can be found at http://cancernet.nci.nih.gov." Removed coverage indication under the "When Covered" section indicating "Partial breast radiotherapy when performed in a National Cancer Institute-approved Phase III Clinical Trial for members who have clinical trial benefits." Updated "Policy Guidelines" section and added statement, "Refer to the individual certificate for prior approval/precertification requirements." References added.

7/16/07 Added new CPT code 0182T to "Billing/Coding" section.


1/5/09 Added new CPT codes 77785, 77786, and 77787 to the "Billing/Coding" section. Removed deleted CPT codes 77781 and 77782. (btw)


9/30/11 Description section extensively revised. Under “When Covered” section added: Interstitial or balloon brachytherapy may be considered medically necessary. Also added accelerated whole breast irradiation may be considered medically necessary for patients who meet the following conditions: invasive carcinoma of the breast. Exclude invasive disease or ductal carcinoma in situ involving the margins of excision; tumors >5 cm in diameter; breast width >25 cm at posterior border of medical and lateral tangential beams; negative lymph nodes and negative surgical margins. Under “When Not Covered” section added: Accelerated whole breast irradiation is considered investigational when medical necessity criteria not met. Specialty Matched Consultant Advisory Panel review 8/31/2011. (lpr)

9/4/12 Specialty Matched Consultant Advisory Panel review 8/15/2012. No changes to policy statement. Reference added. (lpr)

7/1/13 Updated Description section. Under When Covered section 3rd bullet: added technically clear and removed the word “negative” from the statement ending in surgical margins.
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Specialty Matched Consultant Advisory panel meeting 5/15/2013. Reference added. No change to policy statement. (lpr)

4/15/14 Updated Description, Regulatory status, and Policy Guidelines sections. Under “When Not Covered” section added Accuboost as investigational: “Noninvasive brachytherapy using Accuboost® for patients undergoing initial treatment for stage I or II breast cancer when used as local boost irradiation in patients who are also treated with BCS and whole breast external beam radiotherapy”. References added. Medical director review 3/2014. Policy noticed 4/15/14 for effective date 7/1/14. (lpr)

7/29/14 Specialty matched consultant advisory panel review meeting 6/24/14. No change to policy statement. (lpr)

12/30/14 Added CPT code 77316 and deleted CPT code 77326 in Billing/Coding section for effective date 1/1/2015. (lpr)

2/10/15 Updated Description and Policy Guidelines sections. No change to policy statement. Reference added. (lpr)

7/1/15 Specialty Matched Consultant Advisory Panel review 5/27/2015. No change to policy statement. (lpr)

12/30/15 Added the following CPT codes: 0395T, 77770, 77771, 77772 and deleted the following CPT codes: 0182T, 77776, 77777, 77785, 77786, 77787 in Billing/Coding section for effective date 1/1/2016. (lpr)

2/29/16 Added the following ICD-10 Diagnoses codes to the Billing/Coding section: Diagnoses that are subject to medical necessity review: C50.0 - C50.929, C79.81, D05.0 – D05.92, D48.60 - D48.62, D49.3 (Effective 3/11/2016). No change to policy statement. (lpr)

7/26/16 Specialty Matched Consultant Advisory Panel review 5/25/2016. No change to policy statement. (lpr)

8/30/16 Corrected format in “When Covered” section. No change to policy statement. (lpr)

6/30/17 Specialty Matched Consultant Advisory Panel review 5/31/2017. No change to policy statement. (lpr)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.