

Corporate Medical Policy

Brachytherapy Treatment of Breast Cancer

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Description of Procedure or Service

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.

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 consists of 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 5-year risk of local recurrence of 7.3% among breast-conserving-surgery patients allocated to radiotherapy versus 25.9% among those not (2p<0.00001; n=51,958 woman-years). (1) Whole-breast irradiation reduced the 15-year breast cancer mortality risk from 35.9% to 30.5% (breast cancer death rate ratio: 0.83; standard error [SE]=0.05; 95% confidence interval [CI]: 0.75, 0.91; 2p=0.0002; n=7,311 women); there was a similar reduction in mortality from all causes (5.3%, SE=1.8, 2p=0.005). Radiotherapy provided benefits for both node-negative and node-positive women.

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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.

Eight to 10 years of follow-up is needed to assess the outcomes from different treatments for early stage breast cancer. The EBCTCG individual-level meta-analysis provides data on the pattern of recurrences among BCS patients with and without radiotherapy for more than 10 years. In web figure 6a (Available online at: <http://www.ctsu.ox.ac.uk/~ebctcg/local2000/annex.pdf>), data on the percentage of patients per year with isolated local recurrence is 2.7% and 9.0% for those with and without whole-breast irradiation, respectively, in year 0; 1.5% and 4.8% in years 1–2; 1.1% and 3.7% in years 3–4; 0.8% and 1.9% in years 5–9; and 0.2% for both groups in years 10 and higher (trend $\chi^2_1=4.3$, $2p=0.04$). While the recurrence rate falls over time, it persists for more than 10 years. In another study, local recurrence was highest between years 3 to 5 of follow-up, and 67% of events took place in the first 5 years. However, that means 33% of events took place after 5 years. (3) For additional information on the length of follow-up needed, see the two TEC Assessments on APBI. (4,5)

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 some 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-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

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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 2010). All brachytherapy devices have been approved through the 510(k) process and are either balloon brachytherapy or hybrid balloon-interstitial brachytherapy devices. 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.”

*****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.

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 medial and lateral tangential beams.
- negative lymph nodes
- negative surgical margins

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When Brachytherapy Treatment of Breast Cancer is not covered

1. When the above medical criteria are not met
2. Brachytherapy is considered investigational when used in patients with Stage I or II diseases as the **sole** form of radiotherapy after surgical excision.
3. Brachytherapy is considered investigational for local boost irradiation when combined with whole breast radiotherapy **but without** surgical excision.
4. 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.

In review of the MammoSite® website in April 2009 the following statement was included in their information "About MammoSite®" that states; "The safety and effectiveness of the MammoSite® as a replacement for whole breast irradiation in the treatment of breast cancer has not been established."

The FDA 510k clearance for the MammoSite® device issued May 2002 and Axxent issued in 2005 requires of the manufacturer of the devices: "in accordance with Section 513(i)(1)(E) of the Act, the following limitation must appear in the Warnings section of the device’s labeling:"

"The safety and effectiveness of the MammoSite RTS® as a replacement for whole breast irradiation in the treatment of breast cancer has not been established."

"The safety and effectiveness of the Axxent Electronic Brachytherapy System as a replacement for whole breast irradiation in the treatment of breast cancer has not been established."

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: 0182T, 19296, 19297, 19298, 77326, 77776, 77777, 77778, 77785, 77786, 77787.

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.

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Scientific Background and Reference Sources

TEC Assessment - 5/96

National Association issued policy 7/96

Medical Policy Advisory Group Review 3/99

Specialty Matched Consultant Advisory Panel 11/1999

Medical Policy Advisory Group 12/2/1999

Specialty Matched Consultant Advisory Panel 11/2001

BCBSA Medical Policy Reference Manual, 8.01.13; 5/15/2002

BCBSA Medical Policy Reference Manual, 8.01.13; 12/16/02

Specialty Matched Consultant Advisory Panel - 10/2003

The American Society of Breast Surgeons. (2003, April). Consensus statement for accelerated partial breast irradiation. Retrieved 8/4/2004 from <http://www.breastsurgeons.org/officialstmts/officialstmt3.shtml>.

ECRI Target Report # 829. (2003, November). Intracavitary balloon brachytherapy for early-stage breast cancer. Retrieved on 1/24/04 from http://65.213.73.177/summary/detail.aspx?doc_id=4921.

NCCN Practice Guidelines in Oncology. (2004, April). Breast cancer. Retrieved 10/7/04 from http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf.

ICSI. (2004, September). Breast cancer treatment health care guideline. Retrieved 10/7/04 from <http://www.icsi.org/knowledge/detail.asp?catID=29&itemID=54>.

Proxima Therapeutics, Inc. (2004). About mammosite. Retrieved 10/8/04 from http://www.proxima.org/mammo_abomamrts.asp.

Medical Policy Advisory Group - 12/2/2004

"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). Retrieved 9/20/05 from <http://cancernet.nci.nih.gov/search/View-ClinicalTrials.aspx?cdrId=409590&version=HealthProfessional&protocolsearchid=1840297>.

BCBSA Medical Policy Reference Manual [Electronic version]. 8.01.13, 11/9/04

Specialty Matched Consultant Advisory Panel - 9/2005

The American Society of Breast Surgeons. (2005, December). Consensus statement for accelerated partial breast irradiation. Retrieved 1/29/07 from <http://www.breastsurgeons.org/apbi.shtml>.

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

National Comprehensive Cancer Network. Breast Cancer. Clinical practice guidelines in oncology, V.1.2007. Retrieved 1/29/07 from http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf

CYTYC Corporation. (2007). MammoSite targeted radiation therapy. About MammoSite RTS. Retrieved 3/27/07 from <http://www.mammosite.com/mammosite-about.htm>

Xoft Incorporated. (2007). Axxent electronic brachytherapy system. Breast cancer and brachytherapy. Retrieved 6/18/07 from <http://www.xoftmicrotube.com/axxentproductoverview.html>.

BCBSA Medical Policy Reference Manual [Electronic version]. 8.01.13, 4/17/2007

BCBSA Technology Evaluation Center. (2007). Accelerated partial breast irradiation as sole radiotherapy after breast-conserving surgery for early stage breast cancer. Retrieved 6/1/2007 from <http://>

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www.bcbsa.com/betterknowledge/tec/press/accelerated-partial-breast.html.

Specialty Matched Consultant Advisory Panel - 8/2007

CYTYC Corporation. (2009). MammoSite targeted radiation therapy. About MammoSite RTS. Retrieved 4/24/09 from <http://www.mammosite.com/physicians/radiation-therapy/about-mammosite.cfm>

BCBSA Medical Policy Reference Manual [Electronic version]. 8.01.13, 4/17/2007

Specialty Matched Consultant Advisory Panel - 8/2009

BCBSA Medical Policy Reference Manual [Electronic version]. 8.01.13, 5/2008

Specialty Matched Consultant Advisory Panel 5/2010

TEC assessment 7/2010

BCBSA Medical Policy Reference Manual [Electronic version]. 8.01.13, 4/14/11

Specialty Matched Consultant Advisory Panel 8/2011

Policy Implementation/Update Information

- 7/96 Original policy issued.
- 11/96 Reaffirm: National policy issued 7/96. No changes.
- 3/99 Reviewed by MPAG. Reaffirmed.
- 6/99 Reformatted, Description of Procedure or Service revised, Medical Term Definitions added.
- 12/99 Reaffirmed, Medical Policy Advisory Group
- 10/00 System coding changes.
- 11/01 Coding format change.
- 11/01 Specialty Matched Consultant Advisory Panel - Revised section under when it is covered. Format changes.
- 8/02 Reaffirmed. Source added to Scientific Reference Sources section.
- 11/03 Specialty Matched Consultant Advisory Panel review. No change in criteria. Updated Billing/Coding and Benefit Application sections. Scientific sources added.
- 11/25/04 No change in criteria for coverage. Added rationale to Policy Guidelines section. Added CPT code 77326 and 77781 to Billing/Coding section. References added. Notice given 11/25/2004. Effective date 2/3/2005.
- 2/3/05 Policy reviewed at the Medical Policy Advisory Group meeting 12/2/2004. No changes to criteria. Corrected wording from incision to excision under the second bullet in the When Brachytherapy Treatment of Breast Cancer is not covered section. Added new 2005 CPT codes 19296, 19297, and 19298 to Billing/Coding section.
- 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 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

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- "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 Guideline" 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.
- 9/24/07 Specialty Matched Consultant Advisory Panel review 8/23/2007. No changes to policy statement. "Policy Guidelines" updated to add information regarding the "Axxent" device. References added.
- 1/5/09 Added new CPT codes 77785, 77786, and 77787 to the "Billing/Coding" section. Removed deleted CPT codes 77781 and 77782. (btw)
- 10/12/09 Specialty Matched Consultant Advisory Panel review 8/28/09. "Description" section revised. Added an additional indication under the "When Not Covered" section to state; "Accelerated partial breast irradiation using an electronic radiotherapy device is considered investigational." Updated the rationale in the "Policy Guidelines" section. Removed "3-D conformal external beam radiation" from the "Definitions" section. References added. Notice given 10/12/09. Policy effective 1/19/2010. (btw)
- 6/22/10 Specialty Matched Consultant Advisory Panel review 5/24/10. Removed Medical Policy number. No policy statement changes. References updated. (lr)
- 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 medial 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)

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.