FEP 8.01.13 Accelerated Breast Irradiation and Brachytherapy Boost After Breast-Conserving Surgery for Early-Stage Breast Cancer

Description
Radiotherapy is the standard care for patients with breast cancer undergoing breast-conserving surgery (BCS), because it reduces recurrences and lengthens survival. The 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 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.

FDA REGULATORY STATUS

In 2002, the MammoSite® Radiation Therapy System (Proxima Therapeutics; Alpharetta, GA), the first device specifically designed for breast brachytherapy,11 was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Its intended use is “to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.”12

Since 2002, several other devices for breast brachytherapy have been cleared for marketing by FDA through the 510(k) process. FDA determined that several devices (eg, Axxent® Electronic Brachytherapy System [Xoft; San Jose, CA], Strut-Adjusted Volume Implant [SAVI™] Applicator Kit [Biolucent (now Cianna Medical); Aliso Viejo, CA], Contura® Multi-Lumen Balloon Source Applicator for Brachytherapy [SenoRx; Aliso Viejo, CA], ClearPath™ Adjustable Multi-Catheter Source Applicator [North American Scientific; Chatsworth, CA], Intrabeam® System [Carl Zeiss Surgical; Oberkochen, Germany]) were substantially equivalent to predicate devices. Each includes an FDA-required warning that the safety and effectiveness of the device “as a replacement for whole-breast irradiation in the treatment of breast cancer has not been established.”

Although the Intrabeam® System (discussed in the Intraoperative Brachytherapy subsection) is subject to FDA regulation, it does not fall under the regulatory purview of the U.S. Nuclear Regulatory Commission. In some states, participation of radiation oncologists in delivering radiation is not required.
POLICY STATEMENT

When using radiotherapy 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 greater than 5 cm in diameter
- Negative lymph nodes
- Technically clear surgical margins, i.e., no ink on tumor on invasive carcinoma or ductal carcinoma in situ
- Age at least 50 years old.

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.

POLICY GUIDELINES

Electronic brachytherapy is considered a type of balloon brachytherapy that can be used to deliver accelerated partial-breast irradiation (APBI).

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 of 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).

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).
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Rationale

Summary of Evidence

Accelerated Whole-Breast Irradiation

For individuals who have node-negative, early-stage breast cancer with clear surgical margins who receive accelerated whole-breast irradiation (AWBI) after breast-conserving surgery (BCS), the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are overall survival, 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 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 more than 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.

Accelerated Partial-Breast Irradiation

For individuals who have early-stage breast cancer who receive interstitial brachytherapy, the evidence includes 1 completed RCT. Relevant outcomes are overall survival, 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 overall survival, disease-specific survival, change in disease status, and treatment-related morbidity. Several RCTs have been published, but they have not demonstrated that outcomes after intraoperative brachytherapy are noninferior to WBI. Results of 2 RCTs (TARGIT-A, ELIOT) comparing intraoperative brachytherapy to 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 accelerated partial-breast irradiation (APBI), the evidence includes RCTs. Relevant outcomes are overall survival, disease-specific survival, change in disease status, and treatment-related morbidity. The RCTs only reported outcomes after 3 to 5 years, and 10-year data are required to draw conclusions about the impact of the technology on health outcomes. Moreover, 1 of the 2 trials 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.

Brachytherapy

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 overall survival, 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 1 or 2 breast cancer, nonrandomized comparative studies have shown similar outcomes with brachytherapy.
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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.

For individuals who have early-stage breast cancer who receive noninvasive breast brachytherapy, the evidence includes 1 retrospective comparative study. Relevant outcomes are overall survival, 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.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

Current National Comprehensive Cancer Network (NCCN) guidelines (v.2. 2016) on breast cancer state: “Preliminary studies of APBI [accelerated partial-breast irradiation] suggest that rates of local control in selected patients with early-stage breast cancer may be comparable to those treated with standard whole breast RT [radiotherapy]. However, compared to standard whole breast radiation, several recent studies documented an inferior cosmetic outcome with APBI. Follow-up is limited and studies are ongoing. Patients are encouraged to participate in clinical trials.

For whole-breast radiotherapy, NCCN recommends a conventional whole-breast irradiation regimen or a total dose of 42.5 gray (Gy) with 2.66 Gy per fraction (16 fractions). Although NCCN guidelines do not specify the duration of treatment, the latter is presumably an accelerated whole-breast irradiation (AWBI) regimen. A boost to the tumor bed is recommended for higher risk patients receiving whole-breast radiotherapy (ie, those who are <50 years old with high-grade disease).

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

FEP 8.01.13 Accelerated Breast Irradiation and Brachytherapy Boost After Breast-Conserving Surgery for Early-Stage Breast Cancer


The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.
47. American Society of Breast Surgeons. Consensus statements: accelerated partial breast irradiation, revised

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POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>December 2011</td>
<td>New Policy</td>
<td>Update rationale. No change in policy statement.</td>
</tr>
<tr>
<td>December 2012</td>
<td>Update Policy</td>
<td>Policy updated with literature review. References added, removed and renumbered. 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.</td>
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<tr>
<td>June 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review. Two references updated (2-3). Nine references added (15, 34, 41-44, 46, 48, 49). Policy statement clarified. Changed “Following breast-conserving surgery for early stage breast cancer” to “When using radiation therapy after breast-conserving surgery for early stage breast cancer.” Also added text at the end of the following statement: Accelerated whole-breast irradiation is not medically necessary in all other situations involving treatment of early stage breast cancer after breast-conserving surgery. Added noninvasive brachytherapy AccuBoost to policy statements as not medically necessary.</td>
</tr>
<tr>
<td>March 2015</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references 3, 5-7, 12-13, 22-28, 50-52, 57-59, 61, 69, 73, and 77 added; references 2 and 76 updated. Rationale reorganized and references renumbered. No change to policy statements.</td>
</tr>
<tr>
<td>March 2017</td>
<td>Update Policy</td>
<td>Policy updated with literature review through June 6, 2016; references 19-20, 22-23, and 27-28 added. Breast width criterion removed from first policy statement. Title shortened to “Accelerated Breast Irradiation and Brachytherapy Boost After Breast-Conserving Surgery for Early-Stage Breast Cancer.” Clinical input added. Based on clinical input, the following changes were made: A bullet point on age at least 50 years was added to the policy statement on AWBI; The meaning of ‘technically clear surgical margins’ was clarified in the policy statement on AWBI and the Policy Guidelines; and Exclude disease involving the margins of excision” was removed from the policy statement on AWBI.</td>
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