

MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	Brachytherapy After Breast-Conserving Surgery, as Boost with Whole Breast Irradiation or Alone as Accelerated Partial Breast Irradiation
Policy Number	6.01.30
Category	Technology Assessment
Original Effective Date	05/21/03
Committee Approval Date	04/15/04, 03/17/05, 01/19/06, 11/16/06, 09/20/07, 07/17/08, 07/16/09, 07/15/10, 08/18/11, 08/16/12, 08/15/13, 06/19/14, 08/21/14, 07/16/15, 08/18/16, 08/17/17, 11/15/18, 11/21/19, 01/21/21, 11/18/21, 11/17/22, 01/18/24, 11/21/24
Current Effective Date	11/21/24
Archived Date	N/A
Archived Review Date	N/A
Product Disclaimer	<ul style="list-style-type: none"> • Services are contract dependent; if a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply. • If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit. • If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit. • If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit. • If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY STATEMENT

- I. Based upon our criteria and assessment of the peer-reviewed literature, accelerated partial breast irradiation (APBI) using either interstitial or balloon brachytherapy of the breast (e.g., the MammoSite Radiation Therapy System) has been medically proven to be effective and, therefore, is considered a **medically appropriate** treatment option for individuals when **EITHER A. or B.** are met:
- A. **ALL** of the following criteria are met:
1. BRCA negative;
 2. aged 50 years or greater;
 3. diagnosis of invasive ductal carcinoma measuring less than or equal to 2 cm (pT1 disease);
 4. negative margin widths are greater than or equal to 2 mm;
 5. no lymphovascular space invasion; **and**
 6. estrogen receptor (ER) positive;
- OR**
- B. **ALL** of the following criteria are met:
1. low or intermediate nuclear grade,
 2. screening-detected ductal carcinoma in situ (DCIS);
 3. measuring size is 2.5 cm or less; **and**
 4. negative margin widths are greater than or equal to 3 mm.
- II. Based upon our criteria and assessment of the peer-reviewed literature, APBI using either interstitial or balloon brachytherapy of the breast (e.g., the MammoSite Radiation Therapy System) as a boost treatment in individuals who are treated with breast-conserving surgery and whole-breast external beam radiation therapy is considered **not medically necessary**.

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III. Based upon our criteria and assessment of the peer-reviewed literature, intra-operative breast radiotherapy has not been medically proven to be effective and, therefore, is considered **investigational**.

IV. Based upon our criteria and assessment of the peer-reviewed literature, electronic brachytherapy has not been medically proven to be effective and, therefore, is considered **investigational**.

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

POLICY GUIDELINES

- I. This policy addresses the use of either interstitial or balloon brachytherapy as an alternative to external beam radiation therapy in three settings:
 - A. alone, for accelerated partial breast radiation therapy after breast-conserving surgery;
 - B. in the intra-operative setting; or
 - C. to replace external beam for boost radiation therapy, when combined with whole-breast external-beam radiation therapy and breast-conserving surgery.
- II. Methods other than brachytherapy are also used for partial breast irradiation (PBI), including several types of external beam therapy. They are not addressed in this policy.
- III. At the time of surgery, a cavity evaluation device may be inserted as a placeholder, to simplify insertion of the MammoSite balloon catheter at a later date, when final pathology and staging is known, and a decision regarding the role of brachytherapy in the patient's treatment plan is established.

DESCRIPTION

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 multi-modality treatment that consists of breast-conserving surgery to excise the tumor with adequate margins, followed by whole-breast external-beam radiation therapy (WB-EBRT), administered as five daily fractions per week over five to six weeks. For those at higher risk of recurrence, local "boost" irradiation, narrowly directed to the tumor bed is often 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 or irradiation of the axilla.

Brachytherapy for breast cancer uses radiate sources placed inside the breast. When used after breast-conserving surgery, brachytherapy is one of several methods of accelerated partial breast irradiation (APBI). APBI differs from WB-EBRT in two ways. First, APBI radiation targets only a segment surrounding the tumor, rather than the entire breast. Second, because the duration of APBI treatment is four to five days, rather than five to six weeks, radiation is delivered in fewer fractions, at larger doses per fraction. APBI brachytherapy is delivered via multi-catheter interstitial brachytherapy, balloon-based applicators, external beam radiotherapy, or intraoperative radiation therapy.

Interstitial Breast Brachytherapy

Various interstitial brachytherapy techniques have been investigated. They differ in the timing of implantation relative to other components of breast-conserving therapy, the radiation dose rate, the loading technique, the number and volumetric distribution of radioactive sources, and the radioisotopes used. Older forms of local boost irradiation brachytherapy implanted the needles, wires, or seeds for brachytherapy after recovery from surgical tumor excision and WB-EBRT. More recently, the hollow needles and catheters that guide placement of the radioactive material are peri-operatively implanted. This can be done during the initial lumpectomy, if the decision to use brachytherapy has already been made, or at the time of re-excision, if pathologic evaluation of margins shows that additional surgery is necessary. Intraoperative implantation avoids the need for a separate surgical procedure with anesthesia for brachytherapy. Both low-dose rate and high-dose rate techniques have been used. In the low-dose rate technique, radioactive seeds are temporarily implanted in hospitalized patients, to deliver radiation continuously over four days, and are then removed. In the high-dose rate technique, a computer-controlled device loads highly radioactive isotope sources into catheters that have been placed into the tumor bed. The patient is exposed to the radiation therapy for a brief period (15 minutes), then the radioactive sources

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are withdrawn. This type of brachytherapy is typically administered on an outpatient basis as eight fractions, given twice daily over four days. Most brachytherapy for Stage I or II breast cancer uses high dose-rate iridium-192 in the form of wires or needles. Sometimes seeds containing iodine-125 are used in place of iridium-192.

Balloon APBI

Balloon brachytherapy uses a single radioactive source that delivers radiation to a spherical or elliptical target volume with no radiation remaining inside the breast between treatments. The MammoSite Radiation Therapy System (RTS) (Cytac Surgical Products, formerly Proxima Therapeutics) was cleared by the U.S Food and Drug Administration (FDA) for marketing via Section 510(k) in May 2002 as substantially equivalent to other commercially available brachytherapy applicators used with sealed radiation sources. The system consists of a hollow catheter to which an inflatable balloon is attached that is implanted into the lumpectomy cavity during or shortly after breast-conserving surgery. The balloon is inflated with a sterile solution of contrast media in saline, and its position is confirmed radiographically using computed tomography. A high-dose rate source of iridium-192 is then centrally positioned within the applicator by a remote afterloader. The MammoSite balloon catheter is usually removed on the last day of treatment. The manufacturer has indicated that it may be used to deliver local boost or accelerated partial-breast radiation therapy. The FDA Office of Device Evaluation judged it reasonably likely that the Mammosite RTS would be used in ways outside those specified in the proposed labeling, and that such use could cause harm. Therefore, the FDA required inclusion of the following statement 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.” In August 2004, the FDA approved a new version of the MammoSite RTS, which offers a thinner catheter shaft and a smaller balloon profile to further minimize intrusion into the lumpectomy cavity during brachytherapy. Many other balloon brachytherapy devices have since been cleared by the FDA through the 510 (k) process as being substantially equivalent to predicate devices (e.g., ClearPath HDR Breast Brachytherapy System (NAS Medical, Chatsworth, CA), the Contura Multi-Lumen Balloon (SenoRx, Inc., Irvine, CA), or the Strut-Adjusted Volume Implant (SAVI) (Cianna Medical, Inc., Aliso Viejo, CA).

Electronic Brachytherapy

Electronic brachytherapy is x-ray radiotherapy that does not utilize a radioactive isotope or require a high-dose rate (HDR) afterloader. It can be applied directly to the excised tumor bed, or to deliver intracavitary or interstitial radiation to surgical margins following lumpectomy for breast cancer. The FDA approved the Axxent Electronic Radiotherapy device (Xoft) in December of 2005 via Section 510(k) as substantially equivalent to the MammoSite and other brachytherapy systems. It is comprised of three components: the controller (a mobile platform responsible for overall operation of the device), a balloon applicator and an x-ray source. A breast surgeon implants the balloon applicator into the lumpectomy cavity, then balloon is inflated with sterile saline. Radiation is delivered by a disposable micro-miniature x-ray source located at the end of a flexible cable, which is comparable in dosage strength to iridium-192. Given that the Axxent device utilizes low energy x-ray, it does not require the heavily shielded treatment rooms necessary for the delivery of isotope-based HDR brachytherapy. Treatments are given in 10 fractions, twice per day for five days.

Intraoperative Radiation Therapy (IORT)

IORT is delivered directly to exposed tissues during lumpectomy, allowing a patient to receive all required radiation in a single fraction. It may allow higher radiation doses by excluding nearby radiation dose-sensitive tissues and may replace post-operative WB-EBRT for early breast cancer. IORT is marketed to help patients avoid three to six weeks of daily hospital visits, be more efficient for those that do not live close to a radiation facility who may elect total mastectomy vs. breast conservation, and also substantially reduce the heavy workload of radiotherapy departments. IORT techniques include electron beam IORT (EIORT), high-dose rate brachytherapy based IORT, and low-energy x-ray IORT.

RATIONALE

Implanting the guides used to insert radioisotopes for brachytherapy is a surgical procedure and, therefore, is not subject to government regulation. As iodine-125 seeds were marketed prior to enactment of the 1976 Medical Device Regulation Act, also known as the Medical Device Amendments, they were cleared by the FDA for marketing on a “grandfathered”

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basis. Subsequent radioactive isotope implants, including iridium-192, received Section 510(k) approval from the FDA as substantially equivalent to the radioactive iodine seeds.

Interstitial, Multi-Catheter APBI

Several single-institution, non-randomized studies using the multicatheter technique have shown low local recurrence rates that are comparable to standard external beam radiation therapy.

Balloon APBI

Initial published results of the MammoSite Patient Registry addressed the cosmetic results and early toxicity rates of 1,403 women with early-stage breast cancer. Cosmetic results at 12 months were comparable to those reported with whole-breast radiation therapy. A good/excellent result was identified at the last follow-up visit in 95% of patients (1,030 of 1,084 patients) who had a cosmetic assessment. Early toxicity rates (infections, radiation recall) appeared to be acceptable. An infection in the treated breast developed in 8.1% (92 of 1,140 patients). A radiation recall reaction was reported in 3.4% (15 of 442 patients) who had this information recorded. At the time of publication, one local recurrence (0.1%) was reported, which was a new primary cancer. Of 158 ductal carcinoma in situ (DCIS) patients, two to 24 months follow-up of 104 patients showed 94% had an excellent or good cosmetic result and 5% had fair or poor results (Jeruss, 2006). Lowest toxicity was obtained in patients with the greatest device-to-skin distance. Long-term follow-up data regarding patient satisfaction, cosmesis and efficacy are needed. Data continue to accrue from uncontrolled studies on the use of Mammosite balloon brachytherapy. The longest follow-up identified was five years in a study of 36 patients, with no local recurrences reported. Based on development of recurrences beyond five years, longer follow-up is needed, as well as controlled trials.

Electronic APBI

Current literature regarding the use of electronic brachytherapy for the treatment of breast cancer is limited. The FDA required a black box warning stating, "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."

The American Brachytherapy Society published a consensus statement for electronic brachytherapy in 2018 stating that, "In light of a randomized trial in breast showing higher rates of recurrence and the lack of prospective data with mature follow up with other sites, as well as concerns regarding dosimetry, it is not recommended that [electronic brachytherapy] be utilized for accelerated partial breast irradiation, nonmelanomatous skin cancers, or vaginal cuff brachytherapy outside prospective clinical trials at this time.

The American Society for Radiation Oncology (ASTRO), in conjunction with the Agency for Healthcare Research and Quality (AHRQ) developed a clinical practice guideline for partial breast irradiation for patients with early-stage invasive breast cancer or ductal carcinoma in situ (Shaitelman et al., 2024). The clinical practice guideline aimed to support a replacement of the prior ASTRO 2009 APBI consensus statement and 2016 focused update which included the use of IORT. A systematic review was conducted from the time of database inception through June 30, 2022, only including RCTs for the comparison of partial breast irradiation (PBI) as an alternative to whole breast irradiation (WBI). Out of 52 original articles, 23 studies were included for data abstraction. Studies included adult patients with early-stage invasive breast cancer +/- DCIS who received one of six modalities (multi-catheter interstitial brachytherapy [MIB], single-entry catheter brachytherapy, 3-dimensional conformal radiation therapy [3-D CRT], Intensity Modulated Radiation Therapy [IMRT], proton radiation therapy, or IORT [electron or photon] as sole radiation therapy treatment. ASTRO recommended PBI for patients with early-stage invasive breast cancer with the following factors: Grade 1-2 disease, ER-positive histology, Age ≥ 40 years, and tumor size ≤ 2 cm. The strength of the recommendation was strong with a high quality of evidence related to grade, histology and age ≥ 50 years. The quality of evidence for size and age 40-49 years was only moderate. PBI is not recommended for individuals with positive lymph nodes, positive surgical margins, known germline BRCA 1 /2 mutations or age < 40 years (Strong recommendation based upon expert opinion). Regarding individuals with DCIS, ASTRO recommends PBI for the following factors: low to intermediate grade, age ≥ 40 years, size ≤ 2 cm as a strong recommendation based upon expert opinion. For individuals with early-stage invasive breast cancer receiving PBI, electron IORT is not recommended, unless part of a clinical trial or multi-institutional registry (Strong

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Recommendation, moderate quality of evidence) and kV IORT alone without WBI, is not recommended unless part of a clinical trial or multi-institutional registry (Strong recommendation, low quality of evidence).

The National Comprehensive Cancer Network (NCCN) Breast Cancer guidelines (V.4.2024) reports their acceptance of the updated ASTRO APBI consensus statement from 2016 and encourages participation in clinical trials for patients who do not meet the selected criteria presented by ASTRO (age >50 years, ER-positive invasive ductal carcinoma measuring \leq 2cm (pT1 disease) with negative margin widths of \geq 2mm, and no lymphovascular invasion. It also allows for PBI in patients >50 years of age with screen-detected low-or intermediate-grade DCIS measuring \leq 2.5cm, resected with \geq 3mm margins).

The American Society of Breast Surgeons, in its Consensus Statement of Accelerated Partial Breast Irradiation (revised June 2018), reached the following conclusions:

1. Outside of multi-institutional studies and institutional protocols, patients should be carefully selected for APBI and properly informed of the benefits and risks of this type of radiation treatment. The American Society of Breast Surgeons recommends the following selection criteria when considering patients for treatment with APBI, as a sole form of radiation therapy, in lieu of whole breast irradiation:
 - a. Patient is age 45 years or older;
 - b. Tumor is invasive ductal carcinoma or ductal carcinoma in situ;
 - c. Total tumor size (invasive and DCIS) less than or equal to three cm in size;
 - d. There is no tumor on ink for invasive tumors and invasive tumors with associated DCIS; tumor is greater than two mm for DCIS
 - e. Sentinel lymph node is negative;
 - f. If multifocal disease is present, the combined area of tumor is less than or equal to three cm;
 - g. Estrogen receptor positive or estrogen receptor negative tumor;
 - h. If lymphovascular invasion is present, it must be focal;
 - i. Patient has not been treated with APBI, if there is a BRCA genetic mutation or other genetic mutation that confers an increased risk of breast cancer;
 - j. There is no evidence to support use of APBI in male patients;
 - k. Patients with a history of ipsilateral breast cancer treated with radiation should only be treated with APBI as part of specific clinical trial;
 - l. There should be no contraindication to APBI in patients with history of contralateral breast cancer.
2. Patient selection and counseling should be performed in a multidisciplinary fashion with collaboration between the treating surgeon and the treating radiation oncologist.
3. It is preferred that all patients treated are part of a clinical trial or registry.
4. All patients should be monitored regularly to identify adverse events as well as local recurrences.
5. The published dataset for APBI supports the recommendations summarized above. Continuous, long-term, outcomes-based monitoring of APBI is desirable. The American Society of Breast Surgeons maintains an ongoing Mammosite Registry (registration completed in 2004) collecting data on 1440 patients treated via the Mammosite balloon catheter technique. As is the case with all cancer treatments, participation in multi-institutional clinical studies, including NSABP/RTOG B39, or in single-site protocols, or as part of data-gathering registries, is desirable, if available.
6. These recommendations are intended as a guide for patient treatment, but individual treatment decisions could allow for treatment outside of the parameters listed above with appropriate discussion with the patient.

Strnad et al. (2023) published the 10-year results of a GEC-ESTRO randomized study comparing APBI using sole interstitial multicatheter brachytherapy targeted to the original tumor bed with whole-breast irradiation (WBI) with boost for early breast cancer. Patients aged 40 years or older with invasive breast cancer (\leq 3 cm diameter, pN0-pNmi and M0 breast cancer (stage 0, I, and IIA), have undergone local excision of the breast tumor with microscopically clear resection margins of at least 2mm in all directions (in cases of invasive lobular carcinoma or DCIS at least 5 mm), and no lymph or blood vessel invasion (L0 and V0) were randomized (APBI, n=633, WBI, n=551). The difference in 10-year cumulative incidence between groups was 1.93% (95% CI -0.018-3.87, p=0.074), supporting the results of a previous analysis that the

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rate of local recurrence in APBI is similar to WBI. Additionally, there was a lower incidence of treatment-related late side effects in patients treated with APBI than in those treated with WBI. Authors conclude that APBI should be considered an attractive standard treatment option for patients with low-risk early breast cancer opting for breast-conserving surgery and postoperative radiotherapy.

Intraoperative Radiation Therapy (IORT)

RCTs have compared IORT with WB-EBRT. Vaidya et al. (2010,2014) summarized The Risk-adapted Targeted Intraoperative Radiotherapy (TARGIT-A) trial that evaluated IORT compared with WB-EBRT in a non-inferiority study with a predefined noninferiority margin of 2.5% between groups for pathologically confirmed ipsilateral local recurrence. 5-year ipsilateral local recurrence (median follow up of 29 months, 18% met 5 year follow up mark) were 3.3% (95% CI, 2.1% to 5.1%) in the TARGIT group and 1.3% (95% CI, 0.7% to 2.5%; $p=.042$) in the WB-EBRT group. Mortality was similar between the 2 groups (2.6% with TARGIT vs 1.9% with WB-EBRT; $p=.56$) and there were fewer non-breast cancer deaths in the TARGIT group (1.4%; 95% CI, 0.8% to 2.5%) than in the WB-EBRT group (3.5%; 95% CI, 2.3% to 5.2%; $p<.001$). Due to post-operative discovery of predefined factors (e.g., lobular carcinoma), the addition of external beam WB-EBRT was provided to 14% of patients. In the group that received IORT plus WB-EBRT, the mortality rate was higher at 8% (95% CI, 3.7% to 17.5%), but the percentage of women with local recurrences (0.9%; 95% CI, 0.1% to 6.1%) was similar for those who only received IORT. There was no significant difference between the IORT and WB-EBRT groups in predefined 6-month wound-related complications. However, grade 3 or 4 radiotherapy-related skin complications were more common in the WB-EBRT group (13/1730 vs 4/1731; $p=.029$). In 2016, the full final report of the TARGIT-A trial was published concluding that "for patients with breast cancer (women who are aged ≥ 45 years with hormone-sensitive invasive ductal carcinoma that is up to 3.5 cm in size), targeted IORT concurrent with lumpectomy within a risk-adapted approach is as effective as, safer than, and less expensive than postoperative EBRT. Responses to this trial have been controversial with several authors ([Cuzick 2014], Haviland et al. [2014], Silverstein et al. [2014]) questioning the statistical analysis.

Valente et al. (2021), in the TARGIT-R multi-institutional retrospective registry, recently reported notably different outcomes on 5 year results of patients who underwent lumpectomy and IORT between 2007 and 2013 to measure ipsilateral breast tumor recurrence in those who received primary IORT (at the time of lumpectomy, 72%), delayed IORT (after lumpectomy, 3%), intended boost (8%), and unintended boost (primary IORT followed by WB-EBRT, 17%). Tumor recurrence occurred in 8% for the primary IORT group, 1.7% for the unintended boost group. No recurrences were identified in the delayed IORT or intended-boost groups. Authors conclude that given the local recurrence rate difference between this and the TARGIT-A trial, more information is needed to optimize patient selection and outcomes in the future.

The electron intraoperative radiotherapy (ELIOT) trial reported by Veronesi et al. (2013) compared individuals treated with ELIOT vs. individuals treated with WB-EBRT. They evaluated 1305 patients with a median follow up of 5.8 years. 35 (4.4%) individuals in the ELIOT group and 4 (0.4%) individuals in the WB-EBRT group developed ipsilateral breast tumor recurrences (hazard ratio, 9.3; 95%CI, 3.3 to 26.3; $p<.001$) There was no statistically significant difference in 5-year overall survival. Adverse skin events were fewer in individuals who had received IORT. The ELIOT trial has also been criticized by several authors. Silverstein, et al. (2014) noted that of the individuals with 4 or more positive lymph nodes, those in the WB-EBRT group ($n=38$) received concurrent axillary radiation, while those in the IORT group were delayed by 6-12 weeks.

The 15-year results of the ELIOT trial were published by Orrechia et al. (2021) and noted that at a median of 12.4 years of follow up, 11% ($n=70$) of the IORT group experienced ipsilateral breast tumor recurrence versus 2% ($n=16$) 16 in the WB-EBRT group. Fifteen-year overall survival was 83.4% and 82.4%, respectively. The authors concluded that even though there was a higher rate of recurrence in the IORT group, long term results did not lead to an increase in overall survival.

The existing literature has not demonstrated that intraoperative radiotherapy is superior to whole breast irradiation after breast conserving surgery.

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CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
19294 (E/I)	Preparation of tumor cavity, with placement of a radiation therapy applicator for intraoperative radiation therapy (IORT) concurrent with partial mastectomy (list separately in addition to code for primary procedure)
19296	Placement of radiotherapy afterloading expandable (single or multichannel) into the breast for interstitial radioelement application following partial mastectomy, includes imaging guidance; on date separate from partial mastectomy
19297	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)
19298	Placement of radiotherapy after loading 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
77316	Brachytherapy isodose plan; simple (calculation[s] made from 1 to 4 sources, or remote afterloading brachytherapy, 1 channel), includes basic dosimetry calculation(s)
77317	Brachytherapy isodose plan; intermediate (calculation[s] made from 5 to 10 sources, or remote afterloading brachytherapy, 2-12 channels), includes basic dosimetry calculation(s)
77318	Brachytherapy isodose plan; complex (calculation[s] made from over 10 sources, or remote afterloading brachytherapy, over 12 channels), includes basic dosimetry calculation(s)
77424 (E/I)	Intraoperative radiation treatment delivery, x-ray, single treatment session
77425 (E/I)	Intraoperative radiation treatment delivery, electrons, single treatment session
0394T (E/I)	High dose rate electronic brachytherapy, skin surface application, per fraction, includes basic dosimetry, when performed
0395T (E/I)	High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per fraction, includes basic dosimetry, when performed

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HCPCS Codes

Code	Description
C9726 (E/I)	Placement and removal (if performed) of applicator into breast for intraoperative radiation therapy, add-on to primary breast procedure
Q3001	Radioelements for brachytherapy, any type, each

ICD10 Codes

Code	Description
C50.011- C50.922	Malignant neoplasm of the breast (code range)
C79.81	Secondary malignant neoplasm of breast
D05.00-D05.92	Carcinoma in situ of the breast (code range)
Z85.3	Personal history of malignant neoplasm of breast

REFERENCES

*American Society of Breast Surgeons. Consensus statement for accelerated partial breast irradiation. Revised 2018 Jun 5 [<https://breastsurgeons.org/docs/statements/Consensus-Statement-for-Accelerated-Partial-Breast-Irradiation.pdf>] accessed 10/10/24.

*Aristei C, et al. Partial breast irradiation with interstitial multi-catheter high-dose-rate brachytherapy. Long term results of a phase II prospective study. *Radiother Oncol* 2017 Aug;124(2):208-213.

*Bietsch P, et al. Five-year outcome of patients classified in the “unsuitable” category using the American Society of Therapeutic Radiology and Oncology (ASTRO) Consensus Panel Guidelines for the application of accelerated partial breast irradiation: an analysis of patients treated on the American Society of Breast Surgeons MammoSite® Registry Trial. *Ann Surg Oncol* 2010;17:S219–25.

*Beitsch PD, et al. Accelerated partial breast irradiation. *J Surg Oncol* 2011 Mar15;103(4):362-8.

*Budrukkar A, et al. A comparison of long-term clinical outcomes of accelerated partial breast irradiation using interstitial brachytherapy as per GEC-ESTRO, ASTRO, updated ASTRO, and ABS guidelines. *Brachytherapy* May-Jun 2020;19(3):337-347.

*Correa C, et al. Accelerated partial breast irradiation: executive summary for the update of an ASTRO Evidence-based Consensus Statement. *Pract Radiat Oncol* 2017 May-Jun;7(3):73-79.

*Cuzick J. Radiotherapy for breast cancer, the TARGIT-A trial. *Lancet* 2014;383:1716.

*Ferraro DJ, et al. Comparison of accelerated partial breast irradiation via multicatheter interstitial brachytherapy versus whole breast radiation. *Radiat Oncol* 2012 Mar 29;7(1):53.

*Fisher B, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *NEJM* 2002 Oct 17;347(16):1233-41.

*Gittleman M, et al. Clinical evaluation of the mammosite breast brachytherapy catheter: an analysis of technical reproducibility, acute toxicity, and patient demographics. *Int J Radiat Oncol Biol Phys* 2003 Oct 1;57(2 Suppl):S365-6.

*Haviland J et al. Radiotherapy for breast cancer, the TARGIT-A trial. *Lancet* 2014;383:1716-1717.

Hickey BE, et al. Partial breast irradiation versus whole breast radiotherapy for early breast cancer. *Cochrane Database Syst Rev* 2021 Aug 30;8:CD007077. accessed 10/10/24.

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- *Kahn AJ, et al. Six-year analysis of treatment-related toxicities in patients treated with accelerated partial breast irradiation on the American Society of Breast Surgeons Mammosite Breast Brachytherapy registry trial. Ann Surg Oncol 2012 May;19(5):1477-83.
- *Keisch M, et al. Initial clinical experience with the MammoSite breast brachytherapy applicator in women with early-stage breast cancer treated with breast-conserving therapy. Int J Radiat Oncol Biol Phys 2003 Feb 1;55(2):289-93.
- *Keisch M, et al. Two-year outcome with the mammosite breast brachytherapy applicator: factors associated with optimal cosmetic results when performing partial breast irradiation. Int J Radiat Oncol Biol Phys 2003 Oct 1;57(2 Suppl):S315.
- *Lv Y, et al. A systematic review of clinical outcomes and radiotherapy-associated toxicity in multicatheter accelerated partial breast irradiation. Medicine (Baltimore) 2019 Feb;98(6):e14407.
- *National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology, breast cancer. V4.2024 [http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf] accessed 10/10/24.
- *Orrechia et al. Intraoperative irradiation for early breast cancer (ELIOT): long-term recurrence and survival outcomes from a single-centre, randomised, phase 3 equivalence trial. Lancet Oncology 2021;22:597-608.
- *Park CC, et al. American Society for Therapeutic Radiology and Oncology (ASTRO) Emerging Technology Committee report on electronic brachytherapy. Int J Radiat Oncol Biol Phys 2010 Mar 15;76(4):963-72.
- *Poggi MM, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute randomized trial. Cancer 2003 Aug 15;98(4):697-702.
- *Polgár C, et al. Breast-conserving therapy with partial or whole breast irradiation: ten-year results of the Budapest randomized trial. Radiother Oncol 2013 Aug;108(2):197-202.
- *Polgár C, et al. Sole brachytherapy of the tumor bed after conservative surgery for T1 breast cancer: five-year results of a phase I-II study and initial findings of a randomized phase III trial. J Surg Oncol 2002 Jul;80(3):121-8.
- Schwieger MD, et al. Intraoperative radiation therapy for early-stage breast cancer. J Surg Oncol 2024 Aug 5; 1-9.
- *Shah C, et al. Modern approaches for breast brachytherapy. Semin Radiat Oncol 2020 Jan;30(1):61-67.
- *Smith GL et al. Association between treatment with brachytherapy vs whole-breast irradiation and subsequent mastectomy, complications, and survival among older women with invasive breast cancer. JAMA 2012 May 2;30(7):1827-37.
- *Shah C, et al. The American Brachytherapy Society consensus statement for accelerated partial-breast irradiation. Brachytherapy 2018 Jan-Feb;17(1):154-170.
- *Shaitelman, MD et al. Partial breast irradiation for patients with early stage invasive breast cancer or ductal carcinoma in situ: An ASTRO clinical practice guideline. Practical Rad Onc 2024 Mar-Apr;14(2):112-132.
- *Silverstein MJ, et al. Intraoperative Radiation Therapy: A Critical Analysis of the ELIOT and TARGIT Trials Part I. Ann Surg Oncol 2014 Aug 27;21:3787-3792.
- *Silverstein MJ, et al. Intraoperative Radiation Therapy: A Critical Analysis of the ELIOT and TARGIT Trials Part II. Ann Surg Oncol 2014 Aug 20;21:3793-3799.
- *Strnad V, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomized, phase 3, non-inferiority trial. Lancet 2016 Jan;387(10015):229-38.
- *Strnad V, et al. Accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy compared with whole-breast irradiation with boost for early breast cancer: 10-year results of a GEC-ESTRO randomized, phase 3, non-inferiority trial. Lancet Oncol 2023 Feb 1;24:262-272.

Medical Policy: BRACHYTHERAPY AFTER BREAST-CONSERVING SURGERY, AS BOOST WITH WHOLE BREAST IRRADIATION OR ALONE AS ACCELERATED PARTIAL BREAST IRRADIATION

Policy Number: 6.01.30

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- *Vaidya JS, et al. Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial. Lancet 2010 Jun 5;376:91-102.
- *Vaidya JS, et al. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. Lancet 2014 Feb; 383:603-613.
- *Vaidya JS, et al. Long term survival and local control outcomes from single dose targeted intraoperative radiotherapy during lumpectomy (TARGIT-IORT) for early breast cancer: TARGIT-A randomised clinical trial. BMJ 2020 Aug; 370(m2836).
- *Valente S, et al. TARGIT-R (retrospective): 5-year follow-up on intraoperative radiation therapy (IORT) for breast cancer performed in North America. Ann Surg Oncol 2021 May; 28(5):2512-2521.
- *Veronesi U, et al. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. Lancet Oncology 2013 Dec; 14:1269-1277.
- *Vicini F, et al. Five-year analysis of the treatment efficacy and cosmesis by the American Society of Breast Surgeons Mammosite Breast Brachytherapy registry trial in patients treated with accelerated partial breast irradiation. Int J Radiat Oncol Biol Phys 2011 Mar 1;79(3):808-17.
- *Vicini F, et al. Limitations of the American Society of Therapeutic Radiology and Oncology Consensus Panel guidelines on the use of accelerated partial breast irradiation. Int J Radiat Oncol Biol Phys 2011 Mar 15;79(4):977-84.
- *Vicini FA, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomized, phase 3, equivalence trial. Lancet 2019 Dec 14;394(10215):2155-2164.
- *Wazer DE, et al. Preliminary results of a phase I/II study of HDR brachytherapy alone for T1/T2 breast cancer. Int J Radiat Oncol Biol Phys 2002 Jul 15;53(4):889-97.
- *Whelan TJ, et al. External beam accelerated partial breast irradiation versus whole breast irradiation after breast conserving surgery in women with ductal carcinoma in situ and node-negative breast cancer (RAPID): a randomized controlled trial. Lancet 2019 Dec 14;394(10215):2165-2172.
- *Zannis VJ, et al. Postoperative ultrasound-guided percutaneous placement of a new breast brachytherapy balloon catheter. Am J Surg 2003 Oct;186(4):383-5.
- *Zauls AJ, et al. Outcomes in women treated with MammoSite brachytherapy or whole breast irradiation stratified by ASTRO accelerated partial breast irradiation consensus statement groups. Int J Radiat Oncol Biol Phys 2012 Jan 1;82(1):21-9

*Key Article

KEY WORDS

Accelerated partial breast irradiation; APBI, Axxent, Electronic brachytherapy, Interstitial brachytherapy, MammoSite, intraoperative radiation therapy, Xoft, Intrabeam

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

Based on our review, brachytherapy after breast conserving surgery is not addressed in National or Regional Medicare coverage determinations or policies.