BRACHYTHERAPY FOLLOWING BREAST CONSERVING SURGERY FOR STAGE I OR II BREAST CANCER

ISSUE

Blue Shield has received requests for brachytherapy for treatment of breast cancer. Brachytherapy involves the placement of radioactive sources inside the breast to deliver a relatively high dose of radiation either to gross tumor or to tissue immediately surrounding the site from which the tumor was surgically removed. The Medical Policy Committee on Quality and Technology is asked to review the scientific evidence for the use of this procedure in the clinical setting.

BACKGROUND

In 2002, there will be an estimated 203,500 new cases of invasive breast cancer in the United States and an estimated 40,000 deaths from this cancer. This represents approximately 31% of all new cancer cases in women and 15% of all cancer deaths in women (ACS 2002). In addition to invasive breast cancer, 54,300 new cases of in situ breast cancer are expected to be diagnosed in women in 2002. Cancer of the breast is the most common form of cancer in women. Every American woman is estimated to have a 1 in 8 chance of developing breast cancer at some time during her life.

The staging system of the American Joint Committee on Cancer (1997) defines early stage (Stage I and Stage II) invasive breast cancer as tumors = 5 cm in largest dimension and without distant metastasis or involvement of the fixed axillary or internal mammary lymph nodes (T1-2, N0-1, M0). In the TNM (Tumor Node Metastasis) staging system for breast cancer, stage T1 refers to carcinomas 2.0 cm or less in greatest dimension; stage T2 refers to tumors more than 2.0 cm, but not more than 5.0 cm in greatest dimension; stage T3, to tumors more than 5.0 cm in greatest dimension; and stage T4, to tumors with direct extension to chest wall or skin. Stage N0 refers to tumors without regional lymph node metastasis and N1 to tumors with ipsilateral lymph nodes metastases that are not fixed or grouped. M0 refers to tumors without distant metastases.
BACKGROUND, continued

Options for surgical management of the primary tumor include breast-conserving surgery (BCS) plus radiation therapy, mastectomy plus reconstruction, and mastectomy alone. Surgical staging of the axilla is usually performed.

Survival is equivalent with any of these options as documented in randomized prospective trials and a meta-analysis of the trials (Fisher et al 1995; Blichert-Toft et al 1992; van Dongen et al 1992; Sarrazin et al 1989; Jacobson et al 1995; Veronesi et al 1990; Veronesi et al 1995; van Dongen et al 2000). Selection of a local therapeutic approach depends on the location and size of the lesion, analysis of the mammogram, breast size, and the patient’s attitude toward preserving the breast. The presence of multi-focal disease in the breast or a history of collagen vascular disease are relative contraindications to breast-conserving therapy (Abrams et al 1995).

Common Abbreviations Used Throughout the Review

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Phrase</th>
<th>Explanation</th>
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<tbody>
<tr>
<td>BT</td>
<td>Brachytherapy</td>
<td>Radiation from a source in the breast</td>
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<tr>
<td>EBR</td>
<td>External beam radiation</td>
<td>Traditional source of radiation for treatment of cancer</td>
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<td>WBRT</td>
<td>Whole breast radiation therapy</td>
<td>Irradiation of the entire breast for prevention of local recurrence</td>
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<td>LDR</td>
<td>Low dose rate</td>
<td>Continuous low dose brachytherapy</td>
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<tr>
<td>HDR</td>
<td>High dose rate</td>
<td>Intermittent high dose brachytherapy</td>
</tr>
<tr>
<td>BCS</td>
<td>Breast conserving surgery</td>
<td>Lumpectomy, tylectomy, quadrantectomy.</td>
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</table>
Breast Conserving Surgery

A patient’s age should not be a determining factor in the selection of breast-conserving treatment versus mastectomy. A study has shown that treatment with lumpectomy and radiation therapy in women 65 years of age and older produces survival and freedom-from-recurrence rates similar to those of women younger than 65 years of age (Solin et al 1995). It is uncertain whether young women with germ-line mutations or strong family histories are good candidates for breast-conserving therapy. Retrospective studies indicate no difference in local failure rates or overall survival when women with strong family histories are compared to similarly-treated women without such histories (Chabner et al 1998).

Radiation Therapy

Radiation therapy (as part of breast-conserving local therapy) consists of postoperative external-beam radiation (EBR) to the entire breast with doses of 45 Gy to 50 Gy, in 1.8 Gy to 2.0 Gy daily fractions over a 5-week period. A further radiation boost is commonly given to the tumor bed. Two randomized trials conducted in Europe have shown that using boosts from EBR of 10 Gy to 16 Gy reduces the risk of local recurrence from 4.6% to 3.6% at 3 years (p=.044) (Romestaing et al 1997), and from 7.3% to 4.3% at 5 years (p<.0001), respectively (Bartelink et al 2001). The NCI’s PDQ on Breast Cancer Treatment cites Wazer et al (1997) in concluding that if a boost is used, it can be delivered either by external-beam radiation with electrons or by using an interstitial radioactive implant (NCI 2002).

Breast-conserving surgery alone without radiation therapy has been compared with breast-conserving surgery followed by radiation therapy in 4 prospective randomized trials (Fisher et al 1995; Veronesi et al 1995; Veronesi et al 1993; Liljegren et al 1999; Clark et al 1992). All of the trials demonstrated a higher in-breast recurrence rate with breast-conserving surgery alone. No subset has been identified that did not benefit from the addition of radiation therapy. Investigation is ongoing to determine whether some women in certain favorable risk subsets can be spared breast irradiation.
Radiation Therapy, continued

Despite this evidence, in the United States less than half the patients eligible for breast preservation surgery receive such treatment. In some cases, fears about local recurrence affect the decision. In other cases, the fact that radiation therapy is required after partial mastectomy affects the decision about mastectomy versus breast preservation. Many patients maintain a deep-rooted fear of radiation. In some places radiation therapy facilities are not easily accessible. Because the conventional postoperative course of radiation requires daily attendance (Monday to Friday) for 5 to 6 weeks, it is often perceived as a major inconvenience.

Brachytherapy (BT)

Brachytherapy, or interstitial implantation of seeds, wires, or other materials that contain radioisotopes, has been used in the treatment of breast cancer since the 1920’s (Nag 1995). Brachytherapy was hypothesized to provide more localized delivery of radiation, particularly avoiding irradiation of the skin and intervening tissues when treating deep-seated tumors. This was thought to result in less damage to normal tissue at comparable doses to the tumor site when compared with orthovoltage x-rays.

Subsequently, megavoltage machines were developed that produced x-rays of sufficient energy to penetrate more deeply into tissues without energy absorption at or near the surface. Consequently, brachytherapy was used less widely for breast cancer. The use of brachytherapy for breast cancer has declined even further since linear accelerators that generate electrons for EBR became widely available. At present electron beams are used most frequently both for irradiation of the whole breast and for local boost to the tumor bed.

A variety of brachytherapy techniques have been developed, differing in the timing of implantation relative to other components of breast conserving therapy, the dose rate, the loading technique, and the radioisotopes used. Older studies of local boost brachytherapy described temporary implantation of the needles, wires, or seeds after recovery from surgery and completion of whole breast radiation therapy (WBRT). More recently, investigators have used perioperative implantation of the hollow needles and catheters that guide placement of the radioactive material.
Brachytherapy (BT), continued

This can be done during the initial lumpectomy if the decision to use brachytherapy has already been made, or at the time of a re-excision if the lumpectomy specimen has positive surgical margins. Intraoperative implantation avoids the need for a separate surgical procedure with anesthesia for brachytherapy. Depending on the technique used it may require 15-20 catheters to assure the target area of the breast is covered with an even dose of radiation. Once the catheters are placed, computer-assisted dosimetry is performed to determine where and how much radiation will be delivered. The FDA recently approved an interstitial balloon catheter device that is inserted into the lumpectomy cavity so that the surrounding tissue conforms to the balloons surface. There is little clinical experience with this device reported in the published literature.

Both low-dose-rate (LDR) and high-dose-rate (HDR) techniques have been used, with HDR techniques increasing in popularity. In the LDR technique, temporarily implanted radioactive seeds deliver radiation therapy continuously over a course of 4-5 days and then are removed. This treatment is generally given as an inpatient. The patient is confined to an isolated hospital room with limited visitation. In the HDR technique, a computer-controlled device pushes a highly radioactive isotope into a catheter that has been placed in the tumor bed. The patient is exposed to the radiation therapy for a brief period – 5 to 15 minutes – and then the radioactive source is withdrawn. HDR brachytherapy is typically administered on an outpatient basis in fractions given twice daily over 4-5 days. After the treatment session is finished, the catheters are disconnected and the patient is free to go until the next treatment session. Following the last treatment session, the catheters are easily removed in the clinic and the treatment area is cleaned and dressed.

Current interest in brachytherapy is partly based on the observation that the majority of ipsilateral breast recurrences after BCS with radiation therapy occur at or near the tumor bed, with only a small proportion of recurrences located in the remote breast. In addition, in trials of BCS without radiation therapy, the majority of recurrences occurred at or near the tumor bed, suggesting that multicentric disease is not a common cause of recurrence.
Brachytherapy (BT), continued

Together these findings suggest that the major benefit of external beam radiation therapy is related to radiation of the tumor bed. Since in the United States breast-preservation surgery is mostly tylectomy, a form of segmental mastectomy that achieves less generous margins than quadrantectomy and results in better cosmetic outcome, adjuvant radiotherapy to the tumor bed could compensate for less extensive surgery.

The advantages of primary brachytherapy include: (1) the procedure is performed over 4-5 days on an outpatient basis if the HDR technique is used and (2) the relative sparing of surrounding normal tissue, resulting in an apparent lower incidence of adverse effects. The disadvantages include: (1) the placement of catheters for 4-5 days may increase the risk of local infection; (2) the energy levels involved and the potential for placement errors can result in areas of underdosage or overdosage resulting in inadequate treatment or worse cosmetic outcomes; (3) the energy levels mean that the effect dose is confined to the tumor bed with an additional margin of about 2 cm, such that locally advanced disease extending beyond this margin is not adequately treated.

TECHNOLOGY ASSESSMENT (TA)

TA Criterion 1: The technology must have final approval from the appropriate governmental regulatory bodies.

Iodine-125 radioisotope seeds became available and were marketed prior to the 1976 enactment of the Medical Devices Amendments. Subsequent radioactive isotope seeds (such as iridium-192) have received FDA 510(k) approval as being substantially equivalent to the I-125 seeds.

The MammoSite RTS (Proxima Therapeutics, Inc., Alpharetta, GA) received FDA 510K clearance on May 24, 2002. The intended use of the MammoSite Radiation Therapy System is to provide brachytherapy when the physician chooses to deliver intracavitary radiation to the surgical margins following lumpectomy for breast cancer.
TA Criterion 1, continued

The FDA notes “Although the indication for use is not identical to the predicate devices, the intended use is the same and the difference does not introduce any new questions about safety or effectiveness”.

TA criterion 1 is met.

TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.


Comparisons of published series are handicapped by variable patient selection, varying technical methods, variability and brevity of follow-up times, and addition of hormonal or other therapies. Unfortunately, many of the reported studies of brachytherapy have not separated outcomes for patients based on tumor stage or other important prognostic factors.

The most important health outcome of breast cancer treatment is survival. Most authorities agree that the long natural history of breast cancer means that 10- to 15-year follow-up is required for meaningful survival data (Early Breast Cancer Trialists’ Collaborative Group 2000). Series reporting overall survival are most numerous; however, differences in overall survival between series may often be explained by patient selection factors.
TA Criterion 2, continued

In addition, because many women with breast cancer are older at the time of diagnosis, comorbid conditions often determine overall survival. Therefore, cause-specific survival is sometimes reported. However, morbidity from cancer progression may determine the quality of the last few years of life. Therefore, long-term disease-free survival is probably the most important outcome. Local control is an important intermediate outcome as most patients with recurrent local disease are treated with mastectomy and the primary goal of BCS with radiation is to preserve the breast. For this reason, cosmetic outcomes are also of high importance. This is usually measured on a 4 point scale (excellent, good, fair, poor) using visual comparison of the treated and untreated breast. Adverse effects include delayed wound healing, local infection and abscess formation, and fibrosis.

TA criterion 2 is met.

Level of Evidence: 2,3,4,5

TA Criterion 3: The technology must improve the net health outcomes.

(1) Primary brachytherapy after breast-conserving surgery

Table 1 summarizes data from 1 published randomized clinical trial (Polgar et al 2002) and 3 cohort comparisons (Vicini et al 2001; King et al 2000; Fentiman et al 1996) of brachytherapy as monotherapy versus WBRT alone. Table 2 reports data from 5 case series of brachytherapy monotherapy without controls (Polgar et al 2002; Wazer et al 2002; Krishnan et al 2001; Samuel et al 1999; Perera et al 1997).

The only randomized clinical trial comparing primary brachytherapy to WBRT after BCS was published in 2002 (Polgar et al 2002) Polgar and colleagues reported on 126 patients randomized to receive 50 Gy WBRT (n = 63) or brachytherapy alone (n = 63); the latter consisted of either 7 x 5.2 Gy HDR-BT using Ir-192 (n = 46) or 50-Gy wide-field electron irradiation (n = 17). They limited their participants to women with stage 1, T1, N0 cancers with clear surgical margins after BCS and excluded women with EIC. These selection criteria limit the study to women at very low risk for local recurrence. Not surprisingly, after a median follow-up of 30 months, the locoregional tumor control was 100% in both arms.
TA Criterion 3, continued

The 3-year probability of cancer-specific and relapse-free survival was 98.1% and 98.4% in the WBRT group and 100% and 94.4% in the BT group, respectively (P = NS). The overall cosmetic outcomes were not reported, however the incidence of fat necrosis was higher in the BT group (16%) than in the WBRT group (9%, p=0.22). There was no significant difference between the two treatment arms regarding the incidence of radiation side effects. They conclude that long-term results of phase III trials are required to determine the equivalence of BT alone, compared with WBRT in the management of selected patients with early breast cancer. The median follow-up in this study is too short for meaningful comparison to the literature, but the results appear promising.

In their 2001 report, Vicini and colleagues update their prior results (Baglan et al 2001; Vicini et al 1999; Vicini et al 1997) on this use of primary BT in women with Stage I or II breast cancer undergoing BCS. 174 women treated with BT were compared to 174 historical controls matched for age, tumor size and histology, surgical margins, estrogen receptor status, and use of tamoxifen. No statistically significant differences were noted in the 5-year actuarial rates of ipsilateral breast treatment failure or locoregional failure between WBRT and brachytherapy patients (1% v 0%, P =.31 and 2% v 1%, P =.63, respectively). In addition, there were no statistically significant differences noted in rates of disease-free survival (87% v 91%, P =.55), overall survival (90% v 93%, P =.66), or cause-specific survival (97% v 99%, P =.28). Cosmetic outcomes were judged good or excellent in 90% of the BT group and 83% of the WBRT group. The authors conclude that treatment of breast cancer using an interstitial implant to deliver radiation to the tumor bed alone over 4 to 5 days seems to produce 5-year results equivalent to those achieved with conventional ERT. However, they state that “extended follow-up will be required to determine the long-term efficacy of this treatment approach.”

In their 2000 non-randomized comparative trial, King and colleagues (King et al 2000) compared outcomes for 144 women with Stage Tis, T1 or T2 tumors ≤4cm with negative surgical margins and no positive lymph nodes. Important prognostic variables were not evenly distributed: the WBRT group (n=94) was 6 years younger (p=0.002), more often premenopausal (27% vs 12%, p=0.03) and had more T2 tumors (16% vs. 8%, p=0.17). No statistically significant differences were noted in the 6-year rates of locoregional failure between WBRT (2%) and BT patients (1%) or disease-free survival (92% v 88%). Cosmetic outcomes were judged good or excellent in 75% of the BT group and 84% of the WBRT group.
TA Criterion 3, continued

Finally, Fentiman and colleagues, reported on 27 women with tumors =4 cm treated with BT and compared their outcomes with 221 women who were treated with WBRT and BT boost (Fentiman et al 1996; Fentiman et al 1991). After 6 years median follow-up, the local recurrence rate was high (37%). Compared with historical controls there was significantly lower disease free survival (60% vs. 88%, p<0.003). The incidence of distant metastases and overall survival were similar in the two groups. The authors concluded that LDR BT was not an effective means of achieving local control in patients with operable breast cancer.

Table 2 summarizes the outcomes reported from 5 small case series with a total of 151 patients treated with primary brachytherapy after BCS (Polgar et al 2002; Wazer et al 2002; Krishnan et al 2001; Samuel et al 1999; Perera et al 1997). Median follow-up ranged from 1.7 to 5.6 years. The 5-year rates of local recurrence ranged from 0 to 4%. The largest of the 5 case series Polgar (2002) et al reported a 5-year disease free survival rate of 86%. No other survival data were reported by the studies. Cosmetic outcomes were good or excellent in 88-98% of the patients. Both LDR and HDR BRT were used with tissue dosages ranging from 20-55 Gy.

In general, published data suggest that brachytherapy can now be performed with acceptably low morbidity rates. However, due to lack of numbers and short follow-up, the long-term outcomes for primary brachytherapy remain to be clarified.

(2) Brachytherapy as boost in conjunction with WBRT

Table 3 summarizes outcomes from 10 non-randomized retrospective studies comparing brachytherapy to EBR as boost radiation therapy. Factors governing the selection of brachytherapy or EBR for individual patients varied among the studies. In some, patients given brachytherapy as local boost may have been at greater risk for tumor recurrence or poor cosmetic outcome than those give EBR as boost. Perez et al (1996) selected patients for brachytherapy if they had deep seated tumors (>4 cm below the skin) or if they had positive or unknown surgical margins. Vicini et al (1993) selected patients for BT if they had margins that were close to or included malignant cells, extensive intraductal disease, high grade tumors, or large breasts.
Wazer et al (1992) varied the dose used for local boost irradiation based on similar risk factors and selected patients for brachytherapy if the maximal dose for local boost (20 Gy) was prescribed. Women in this study who received BT were also 5-9 years younger than those receiving EBR, which also increases their risk for local recurrence. Equivalent outcomes for the two forms of boost irradiation in these studies suggest that brachytherapy is useful in patients selected based on similar risk factors. Mansfield et al used brachytherapy for all patients “…except where the surgeon’s preference, patient’s refusal, or tumor location negated its use.” (Mansfield et al 1995; Mansfield et al 1994). In the study by Touboul et al (1995), one hospital treated all its patients with brachytherapy, the other used only EBR. In the other studies, the reasons for receipt of BT were not clear (Deo et al 2001; Deore et al 1993; de la Rochefordiere et al 1992; Berberich et al 2001; Olivotto et al 1989).

More than 3250 patients were treated with BCS, WBRT, and BR for local boost in the 10 studies summarized in Table 3. This combination of therapies prevented local tumor recurrence, and thus the need for salvage mastectomy, in 93-97% of patients at 5 years and 85-95% of patients at 10 years in the studies with sufficient numbers and length of follow-up (Wazer et al 1997; Perez et al 1996; Mansfield et al 1994; Mansfield et al 1995; Touboul et al 1995; Deore et al 1993; Berberich et al 2001; Frazier et al 2001; Kramer et al 1999; Sarin et al 1993). Disease free survival was 82-87% at 5 years (Mansfield et al 1994; Mansfield et al 1995; Touboul et al 1995) and 54-80% at 10 years. (Perez et al 1996; Mansfield et al 1994; Mansfield et al 1995; Berberich et al 2001). Overall survival was 91-96% at 5 years (Mansfield et al 1994; Mansfield et al 1995; Touboul et al 1995; Berberich et al 2001) and 66-77% at 10 years. (Mansfield et al 1994; Mansfield et al 1995; Frazier et al 2001).

Only 61% of those given brachytherapy in the study of Touboul et al (1995) achieved acceptable cosmetic results: this was the poorest result for all of the controlled studies of brachytherapy. One other study had only a 69% rate of acceptable cosmetic results; this study was criticized for using a higher dose per fraction (2.5 Gy per dose vs. 1.2 Gy) and a higher total boost dosage (18 Gy vs. 12 Gy). The remainder of the studies reported acceptable cosmetic results in 75-94% of cases. One study reported an acute complication rate of 5% (Mansfield et al 1995) and two studies reported the frequency of chronic complications to be 6-9% (Mansfield et al 1995; Deore et al 1993).
TA Criterion 3, continued

Table 4 summarizes the outcomes reported from 14 additional uncontrolled case series (van Dongen et al 1992; Resch et al 2002; Manning et al 2000; Moreno et al 2000; Hennequin et al 1999; Formenti et al 1995; Hammer et al 1994; Baillet et al 1993; Krishnan et al 1992; Krishnan et al 1993; Lichter 1992; Pierquin et al 1991; Van Zyl 1989; McCormick et al 1988; Syed et al 1980; Syed et al 1984) with a total of 2820 women given BT for local boost after BCS and WBRT. The rates of local control ranged from 88-98% at 5 years and 79-96% at 10 years. Disease free survival was 82-94% at 5 years (Resch et al 2002; Moreno et al 2000; Hennequin et al 1999; Hammer et al 1994); one study reported a 10 year disease free survival rate of 79% (Resch et al 2002). Overall survival ranged from 64-97% at 5 years (van Dongen et al 1992; Resch et al 2002; Manning et al 2000; Moreno et al 2000; Hennequin et al 1999; Formenti et al 1995; Hammer et al 1994; Lichter 1992) and from 50-85% at 10 years (van Dongen et al 1992; Resch et al 2002; Formenti et al 1995; Hammer et al 1994; Lichter 1992). In these studies, 59-90% of the women had acceptable cosmetic outcomes (Manning et al 2000; Moreno et al 2000; Hennequin et al 1999; Formenti et al 1995; Hammer et al 1994; Baillet et al 1993; Krishnan et al 1992; Krishnan et al 1993; Pierquin et al 1991; Syed et al 1980; Syed et al 1984) with the exception of the study of Resch and colleagues (2002) who reported a rate of 38%. They report that the poor cosmetic outcomes were due to the high volume of tissue resected at surgery and not due to the BT boost. Of note, Pierquin and colleagues (1991) reported their results by tumor size; cosmetic results were acceptable in 87% of the patients with T1 tumors, 59% of those with T2 tumors, and only 33% of T3 tumors., underscoring the importance of tumor characteristics in determining outcomes. The frequency of acute complications ranged from 1-10% and the frequency of chronic complications ranged from 1-9%.

TA Criterion 3 is met
### Table 1: Comparative studies of primary brachytherapy to the tumor bed alone compared to whole breast external beam radiation therapy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>N</th>
<th>Median Follow-up (yr)</th>
<th>Study subjects</th>
<th>BT isotope</th>
<th>BT Method</th>
<th>Dose (Gy)</th>
<th>Excellent/Good Cosmetic result</th>
<th>Local recurrence rate (%)</th>
<th>Disease free survival (%)</th>
<th>Overall survival (%)</th>
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<tr>
<td>Polgar 2002&lt;sup&gt;22&lt;/sup&gt;</td>
<td>RCT</td>
<td>126</td>
<td>2.5</td>
<td>Stage I, T1 N0 BCS, clear margins, no LCIS, no DCIS, no EIC</td>
<td>– Ir-192 BT</td>
<td>46/53 received BT, the remainder EBR</td>
<td>Ir-192 HDR</td>
<td>36-36</td>
<td>0</td>
<td>94</td>
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<tr>
<td>Vicini 2001&lt;sup&gt;23&lt;/sup&gt;</td>
<td>HC</td>
<td>348</td>
<td></td>
<td>Stage III BCS with AD</td>
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<td>Vicini 1997&lt;sup&gt;26&lt;/sup&gt;</td>
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<td>144</td>
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<td>Tis T1 T2 =4 cm, negative margins, =3 positive nodes</td>
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Table 2: Uncontrolled studies of primary brachytherapy to the tumor bed alone

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>N</th>
<th>Median Follow-up (yr)</th>
<th>BT isotope</th>
<th>BT Method</th>
<th>Dose (Gy)</th>
<th>Excellent/Good Cosmetic result</th>
<th>Local recurrence rate (%)</th>
<th>Disease free survival (%)</th>
<th>Overall survival (%)</th>
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BT: Brachytherapy, BCS: Breast conserving surgery, N: Node
WBRT: Whole breast radiation therapy, LCIS: Lobular carcinoma in situ, ER: Estrogen receptor
EBT: External beam radiation therapy, DCIS: Ductal carcinoma in situ, RCT: Randomized clinical trial
LDR: Low dose rate, EID: Extensive intraductal disease, CC: Concurrent controls
HDR: High dose rate, AD: Axillary node dissection, HC: Historical controls
NR: Not reported, T: Tumor, CS: Case series
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>N</th>
<th>Median Follow-up (yr)</th>
<th>BT isotope</th>
<th>BT Method</th>
<th>Boost</th>
<th>Boost dose (Gy)</th>
<th>Excellent/Good Cosmetic result</th>
<th>Local recurrence rate (%)</th>
<th>Disease free survival (%)</th>
<th>Overall survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deo 2001&lt;sup&gt;11&lt;/sup&gt;</td>
<td>CC</td>
<td>200</td>
<td>3.5</td>
<td>Stage I/II, =4 cm</td>
<td>- Ir-192 boost</td>
<td>51</td>
<td>BCS</td>
<td>Ir-192</td>
<td>Immediate RT</td>
<td>15-20</td>
<td>80</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- No boost</td>
<td>149</td>
<td>Mastectomy</td>
<td>None</td>
<td></td>
<td></td>
<td>NR</td>
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<tr>
<td>Frazier 2001&lt;sup&gt;12&lt;/sup&gt;</td>
<td>CC</td>
<td>548</td>
<td>9.7</td>
<td>Stage I/II, BCS then 45-50 Gy WBRT then boost to total 60 Gy</td>
<td>- I-125 boost</td>
<td>122</td>
<td>I-125</td>
<td>LDR BT</td>
<td>15-20</td>
<td>94</td>
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<td></td>
<td>- Ir-192 boost</td>
<td>194</td>
<td>I-125</td>
<td>LDR BT</td>
<td>15</td>
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<td>15</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>- EBR boost</td>
<td>232</td>
<td>EBR</td>
<td>10-15</td>
<td>89</td>
<td>5</td>
<td>6</td>
<td>70</td>
</tr>
<tr>
<td>Kramer 1999&lt;sup&gt;13&lt;/sup&gt;</td>
<td>CC</td>
<td>498</td>
<td>Stage III treated with BCS and 50 Gy RT</td>
<td>- Ir-192 boost</td>
<td>127</td>
<td>6.2</td>
<td>Margin = 2 mm; age 52.5 yrs</td>
<td>Ir-192</td>
<td>LDR BT after WBRT</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- EBR boost (1)</td>
<td>87</td>
<td>3.4</td>
<td>Margin = 2 mm; age 61.4 yrs, p=0.001</td>
<td>EBR after WBRT</td>
<td>20</td>
<td>83</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- EBR boost (2)</td>
<td>295</td>
<td>5.0</td>
<td>Margin &gt; 2 mm; age 57.0 yrs, p=0.004</td>
<td>EBR after WBRT</td>
<td>0, 10, or 14</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Perco 1996&lt;sup&gt;14&lt;/sup&gt;</td>
<td>CC</td>
<td>619</td>
<td>5.6</td>
<td>T1/T2 BCS WBRT 48-50 Gy</td>
<td>- Ir-192 boost</td>
<td>129</td>
<td>Ir-192</td>
<td>BT after WBRT</td>
<td>10-20</td>
<td>75</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- EBR boost</td>
<td>490</td>
<td>EBR</td>
<td>10-20</td>
<td>81</td>
<td>6</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Touboul 1995&lt;sup&gt;15&lt;/sup&gt;</td>
<td>CC</td>
<td>329</td>
<td>6.8</td>
<td>Stage I/II =3 cm</td>
<td>- Ir-192 boost</td>
<td>169</td>
<td>51 years old, 13% T2, 45-50 Gy WBRT.</td>
<td>Ir-192</td>
<td>LDR BT after WBRT</td>
<td>15</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- EBR boost</td>
<td>160</td>
<td>54 years old p=0.03, 31% T2 p=0.001, 40-50 Gy WBRT</td>
<td>EBR</td>
<td>15</td>
<td>83</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Reference</td>
<td>Study design</td>
<td>Median Follow-up (yr)</td>
<td>Study subjects</td>
<td>BT isotope</td>
<td>BT Method</td>
<td>Boost</td>
<td>Boost dose (Gy)</td>
<td>Excellent/Good Cosmetic result</td>
<td>Local recurrence rate (%)</td>
<td>Disease free survival (%)</td>
<td>Overall survival (%)</td>
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<td>---------------------</td>
</tr>
<tr>
<td>Mallinsfield 1995&lt;sup&gt;23&lt;/sup&gt;</td>
<td>CC</td>
<td>3.3</td>
<td>Stage III BCS, AD, WBRT 45 Gy</td>
<td>Ir-192</td>
<td>LDR</td>
<td>Immediate BT</td>
<td>654</td>
<td>10 Gy</td>
<td>20</td>
<td>91</td>
<td>7</td>
</tr>
<tr>
<td>– Ir-192 boost</td>
<td>5 yr</td>
<td>10 yr</td>
<td>5 yr</td>
<td>10 yr</td>
<td>5 yr</td>
<td>10 yr</td>
<td>5 yr</td>
<td>10 yr</td>
<td></td>
<td></td>
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<tr>
<td>– EBR boost</td>
<td>416</td>
<td>Refused BT or T location poor; more Stage I, less ER+; younger, fewer N+, fewer + margins</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EBR after WBRT</td>
<td>20</td>
<td>95</td>
<td>8</td>
<td>19</td>
<td>87</td>
<td>78</td>
<td>91</td>
<td>69</td>
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<tr>
<td>Sarin 1993&lt;sup&gt;20&lt;/sup&gt;</td>
<td>CC</td>
<td>3.6</td>
<td>Stage III BCS WBRT 40-50 Gy</td>
<td>Ir-192</td>
<td>LDR</td>
<td>BT</td>
<td>219</td>
<td>81</td>
<td>7</td>
<td>15-30</td>
<td>79</td>
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<td>– EBR boost</td>
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<td>EBR</td>
<td>40</td>
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<td></td>
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<tr>
<td>De la Rochefordiere 1992&lt;sup&gt;22&lt;/sup&gt;</td>
<td>CC</td>
<td>3.6</td>
<td>Stage III BCS WBRT 46 Gy</td>
<td>Ir-192</td>
<td>LDR</td>
<td>BT</td>
<td>504</td>
<td>95% BT, 5% EBR</td>
<td>21</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>– 1970-1981</td>
<td>504</td>
<td>8.9</td>
<td>655</td>
<td>5.6</td>
<td>655</td>
<td>5.6</td>
<td>18</td>
<td>84</td>
<td></td>
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<tr>
<td>– 1982-1985</td>
<td>504</td>
<td>8.9</td>
<td>655</td>
<td>5.6</td>
<td>655</td>
<td>5.6</td>
<td>18</td>
<td>84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olivatto 1989&lt;sup&gt;21&lt;/sup&gt;</td>
<td>CC</td>
<td>3.6</td>
<td>BCS WBRT</td>
<td>Ir-192</td>
<td>LDR</td>
<td>BT</td>
<td>497</td>
<td>87</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– EBR boost</td>
<td>36</td>
<td>EBR</td>
<td>100</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Berberich 2001&lt;sup&gt;24&lt;/sup&gt;</td>
<td>HC</td>
<td>3.6</td>
<td>BCS WBRT</td>
<td>Ir-192</td>
<td>LDR</td>
<td>BT</td>
<td>100</td>
<td>60% T1, 39% T2, 43 Gy WBRT</td>
<td>18</td>
<td>67</td>
<td>5</td>
</tr>
<tr>
<td>– EBR boost</td>
<td>129</td>
<td>4.2</td>
<td>95% T1, 38% T2, 59 Gy WBRT</td>
<td>EBR</td>
<td>12</td>
<td>84, p&lt;.001</td>
<td>2</td>
<td>87</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**BT**: Brachytherapy, **BCS**: Breast conserving surgery, **N**: Node, **WBRT**: Whole breast radiation therapy, **LCIS**: Lobular carcinoma in situ, **ER**: Estrogen receptor, **DCIS**: Ductal carcinoma in situ, **RCT**: Randomized clinical trial, **EID**: Extensive intraductal disease, **CC**: Concurrent controls, **AD**: Axillary node dissection, **HC**: Historical controls. **NR**: Not reported, **T**: Tumor, **CS**: Case series.
### Table 4: Uncontrolled studies of brachytherapy boost to the tumor bed in addition to whole breast external beam radiation therapy

| Reference          | Study design | N  | Median Follow-up (yr) | Study subjects | BT isotope | BT Method | Boost | Boost dose (Gy) | Excellent/Good Cosmetic result | 5 yr Local recurrence rate (%) | 10 yr Local recurrence rate (%) | 5 yr Disease free survival (%) | 10 yr Disease free survival (%) | 5 yr Overall survival (%) | 10 yr Overall survival (%) |
|--------------------|--------------|----|-----------------------|----------------|------------|-----------|-------|----------------|---------------------------------|-------------------------------|-------------------------------|-------------------------------|---------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Resch 2002         | CS           | 49 | 8.7                   | BCS WBRT       | Ir-192     | 33% LDR, 67% HDR | Before, during, or after WBRT | 10-28 | 38             | 2                               | 4                             | 90                           | 79                           | 97                           | 85                             |
| Van Dongen 1992    | CS           | 5  | 4.2                   | Stage I/II BCS with margins < 2 mm, parenchyma, post BT boost, 33% DCIS | Ir-192     | HDR       | BT    | 15             | 67                             | 0                             |                               | 89                           |                               |                               |                               |
| Manning 2000       | CS           | 18 | 4.2                   | Stage I/II BCS WBRT 69 Gy | Ir-192     | HDR       | BT after WBRT | 17              | 90             | 5                             | 82                           |                               |                               |                               | 89                             |
| Moreno 2000        | CS           | 530| 3.3                  | Stage I/II BCS WBRT 69 Gy | Ir-192     | HDR       | BT after WBRT | 17              | 90             | 5                             | 82                           |                               |                               |                               | 89                             |
| Hennequin 1999     | CS           | 106| 3.7                  | Stage I/II tumors treated with BCS (6) WBRT 45 Gy, 13% DCIS | Ir-192     | HDR       | BT 23% periop, 77% post-WBRT | 10             | 63             | 5                             | 94                           |                               |                               |                               | 93                             |
| Formenzi 1995      | CS           | 100| 7                    | Stage I/II BCS with boost BT (6) WBRT 45-50 Gy | Ir-192     | HDR       | Immediate BT | 20             | 77             | 5                             | 7                            |                               |                               |                               | 85                             |
| Hammer 1994        | CS           | 212| 5.2                  | Stage I/II BCS WBRT 45-50 Gy | Ir-192     | HDR       | BT    | 10             | 77             | 4                             | 7                            | 81                           | 84                           |                               | 84                             |
| Baillet 1993       | CS           | 135| 8                    | T1 >5 cm, neoadjuvant chemo (5) WBRT 45 Gy | Ir-192     | LDR       | BT    | 20-30          | 66             | -                            | -                            | 64                           | 55                           |                               |                               |
| Krishnan 1993      | CS           | 243| 5.8                  | T1/T2 BCS WBRT 45-50 Gy | Ir-192     | LDR       | Immediate BT | 15-20 | 87             | 4                             | 8                            |                               |                               |                               |                               |
| Krishnan 1992      | CS           | 243| 5.8                  | T1/T2 BCS WBRT 45-50 Gy | Ir-192     | LDR       | Immediate BT | 15-20 | 87             | 4                             | 8                            |                               |                               |                               |                               |
| Van Dongen 1992    | CS           | 456|                      | Stage I/II BCS WBRT 50 Gy | Ir-192     | LDR       | BT after WBRT | 25              | 11             | 13                           |                               |                               |                               |                               | 50                             |
| Lichter 1992       | CS           | 121|                      | 81% BT, 19% EBR   |                        |           |       |                 |                               |                               |                               |                               |                               |                               | 89                           |
| Pierquin 1991      | CS           | 245|                      | T1 >5 cm, neoadjuvant chemo (5) WBRT 45 Gy, after surgery if T>5 cm. | Ir-192     | LDR       | BT after WBRT | 25             | T1: 87, 81 | T2: 59, 52 | T3: 33, 36 | T1: 63, 65 | T2: 51, 54 | T3: 26, 27 | T4: 30, 30 |                               |                               |                               |                               |                               |                               | 89                           |

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<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design</th>
<th>N</th>
<th>Median Follow-up (yr)</th>
<th>RT isotope</th>
<th>RT Method</th>
<th>Boost</th>
<th>Boost dose (Gy)</th>
<th>Excellent/Good Cosmetic result</th>
<th>Local recurrence rate (%)</th>
<th>Disease free survival (%)</th>
<th>Overall survival (%)</th>
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<tr>
<td>Van Zyl 1989**</td>
<td>CS</td>
<td>60</td>
<td>2.2</td>
<td>Ir-192</td>
<td>LDR</td>
<td>Immediate RT</td>
<td>25</td>
<td>NR</td>
<td>&lt;2</td>
<td>5 yr 10 yr</td>
<td>5 yr 10 yr</td>
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<tr>
<td>McCormick 1988**</td>
<td>CS</td>
<td>52</td>
<td>2.2</td>
<td>Ir-192</td>
<td>LDR</td>
<td>Immediate RT</td>
<td>15-22</td>
<td>NR</td>
<td>0</td>
<td>5 yr 10 yr</td>
<td>5 yr 10 yr</td>
</tr>
<tr>
<td>Syed 1984**</td>
<td>CS</td>
<td>64</td>
<td>&gt;4</td>
<td>Ir-192</td>
<td>LDR</td>
<td>BT after WBRT</td>
<td>25-30</td>
<td>&gt;75</td>
<td>6</td>
<td>5 yr 10 yr</td>
<td>5 yr 10 yr</td>
</tr>
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<td>BT: Brachytherapy,</td>
<td></td>
<td></td>
<td></td>
<td>BCS: Breast conserving surgery,</td>
<td>N: Node</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>WBRT: Whole breast radiation therapy,</td>
<td></td>
<td></td>
<td></td>
<td>LCIS: Lobular carcinoma in situ,</td>
<td>ER: Estrogen receptor</td>
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<td></td>
</tr>
<tr>
<td>EBR: External beam radiation therapy,</td>
<td></td>
<td></td>
<td></td>
<td>DCIS: Ductal carcinoma in situ,</td>
<td>RCT: Randomized clinical trial</td>
<td></td>
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</tr>
<tr>
<td>LDR: Low dose rate,</td>
<td></td>
<td></td>
<td></td>
<td>EID: Extensive intraductal disease,</td>
<td>CC: Concurrent controls</td>
<td></td>
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<tr>
<td>HDR: High dose rate,</td>
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<td></td>
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<td>AD: Axillary node dissection,</td>
<td>HC: Historical controls</td>
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<td>CS: Case series</td>
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</table>

Table 5: Summary table of brachytherapy as boost radiation therapy versus external beam radiation in comparative cohort studies

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Brachytherapy for boost</th>
<th>EBR for Boost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local control at 5 years (%)</td>
<td>93-95</td>
<td>92-98</td>
</tr>
<tr>
<td>Local control at 10 years</td>
<td>85-95</td>
<td>81-97</td>
</tr>
<tr>
<td>Disease-free survival at 5 years</td>
<td>82-87</td>
<td>85-87</td>
</tr>
<tr>
<td>Disease-free survival at 10 years</td>
<td>54-80</td>
<td>70-79</td>
</tr>
<tr>
<td>Overall survival at 5 years</td>
<td>91-96</td>
<td>87-94</td>
</tr>
<tr>
<td>Overall survival at 10 years</td>
<td>66-77</td>
<td>69-75</td>
</tr>
<tr>
<td>Acceptable cosmetic outcome (Excellent/Good)</td>
<td>61-94</td>
<td>81-95</td>
</tr>
</tbody>
</table>

TA Criterion 4: The technology must be as beneficial as any established alternatives.

(1) Primary brachytherapy after breast-conserving surgery

The results from the randomized clinical trial of Polgar and colleagues (2002) are encouraging. There have been no local recurrences in either arm and the disease free survival rates (94 and 98%) are better than those reported in comparable clinical trials of radiation therapy (Romestaing et al 1997, Bartelink et al 2001; Early Breast Cancer Trialists Collaborative Group 2000 and 1995). However, the median follow-up time is only 2.5 years and the number of participants (63 in each arm) too small to draw any meaningful conclusions.
TA Criterion 4, continued

The three cohort studies with controls (Vicini et al 2001; King et al 2000; Fentiman et al 1996) have longer follow-up (median 6 years), but only a total of 251 participants received brachytherapy. The best of these studies (Vicini et al 2001) has well matched controls and a trend towards better disease free survival at 5 years for BT (91%) compared with EBR (87%). However, Fentiman and colleagues (1991; 1996) reported significantly weak disease free survival at 5 years for BT group (60%) compared with EBR (88%, p<0.003)). Their BT group was too small (27) to have much confidence in the findings.

A study by Magee and colleagues reported on 708 women with localized breast cancer treated with BCS and then randomized to either local radiation to the tumor bed or WBRT (Magee et al 1996). After a median 8 years of follow-up the local recurrence rate was significantly higher in the group randomized to local radiation therapy (25%) compared to the group randomized to WBRT (13%, p<0.0001).

In summary, the authors of the two best studies (Polgar et al 2002, Vicini et al 2001) comparing BT to WBRT both conclude that the results are promising, but that phase 3 trials with longer follow-up are needed to assess the long term efficacy of BT compared with standard therapy. One of the four comparative studies reported significantly worse outcomes with BT (Fentiman et al 1996). Finally, the only large clinical trial comparing local radiation therapy alone (with EBR) to WBRT found significantly higher local recurrence rates with local therapy (Magee et al 1996). It is not yet clear that primary brachytherapy is equivalent to standard therapy with WBRT after BCS.

TA criterion 4 is not met for primary brachytherapy.

(2) Brachytherapy as boost in conjunction with WBRT

Of the 10 studies with control groups, only one reported a substantial difference in local control (Deore et al 1993), however only 15 participants were in the brachytherapy group. None of the studies reported important differences in disease free survival or overall survival. The cohort with the longest follow-up (9.7 years), published by Frazier and colleagues (2001), reported on a large cohort with 3 arms: I-125 boost, Ir-192 boost, and EBR boost.
TA Criterion 4, continued

The 10-year local recurrence rates were 5% for I-125, 15% for Ir-192, and 6% for EBR boost (p=NS). The 10-year disease free survival rates were 71% for I-125, 54% for Ir-192, and 70% for EBR boost (p=NS). It is unclear why there was a trend towards worse outcome in the I-125 group. Mansfield and colleagues (1994; 1995) reported on the largest cohort, although median follow-up time was only 3.3 years. The actuarial local recurrence rates and survival rates in this study were similar at 5 and 10-years follow-up.

Only 2 studies found large differences in cosmetic results. The first reported that 81% of participants receiving BT boost had acceptable cosmetic results, while only 40% of those receiving EBR boost had acceptable cosmetic results (Deore et al 1993; Sarin et al 1993). The second, reported that 67% of participants receiving BT boost had acceptable cosmetic results, while 84% of those receiving EBR boost had acceptable cosmetic results (Berberich et al 2001). Multivariable analysis found that the volume of tissue removed at surgery was significantly associated with poor cosmetic outcomes; type of boost therapy was no longer a significant predictor of cosmetic outcome.

Table 5 summarizes the outcomes from the studies with control groups. The table shows that the recurrence and survival results reported in studies of BT for boost are similar to EBR for boost. The cosmetic results may be slightly worse for brachytherapy, though the range is broad. Figure one on page 15 of the Blue Cross Blue Shield Tec assessment of the same technology combined similar data using a random effects model. They found no differences in local control or survival between the two approaches to boost therapy and a trend towards better cosmetic results with BT.

Every 5 years, the Early Breast Cancer Trialists’ Collaborative Group performs a meta-analysis (1995; 2000) using the long term follow-up from 40 randomized clinical trials of radiation therapy including 20,000 women. The 5 and 10-year local recurrence rates for women randomized to radiation therapy were 92% and 91%, compared to 77% and 73% in the no radiation group. The 5 and 10-year overall survival rates were 73% and 57% in the radiation arms compared to 72% and 55% in the no radiation arms. The BT boost studies summarized in Table 5 appear to have better overall outcomes than the summary data from these 40 randomized clinical trials of radiation therapy.
TA Criterion 4, continued

Because none of the studies reviewed are randomized comparisons, any differences observed could be due to selection bias. However, as noted under TA criterion 3, the selection criteria for many of the studies were biased towards a higher probability of local recurrence.

The available evidence supports the conclusion that BT or EBR as local boost radiotherapy provide equally beneficial health outcomes when combined with BCS and WBRT as initial treatment for stage I or II breast cancer.

TA criterion 4 is met for brachytherapy as boost therapy.

TA Criterion 5: The improvement must be attainable outside the investigational setting.

The published data represent brachytherapy used primarily in investigational settings with considerable expertise in brachytherapy. Additionally, most radiation oncologists do not have extensive experience in breast brachytherapy. However many clinical centers, particularly in Europe, are represented in the literature. With appropriate training, the outcomes reported in studies of brachytherapy for local boost irradiation in women with Stage I and II breast cancer should be reproducible outside the investigational setting. Given the limited experience of most radiation oncologists with this technique, close adherence to the American Brachytherapy Society guidelines (Nag et al 2001) is advisable.

TA criterion 5 is met

RECOMMENDATIONS OF OTHERS

Blue Cross Blue Shield Association

In July 1996, a Blue Cross Blue Shield Association Medical Advisory Panel concluded that brachytherapy when used as the sole form of radiation in patients treated with breast conserving surgery did not meet BCBSA Technology Evaluation Center (TEC) criteria for treatment of Breast Cancer. This finding was reaffirmed after an updated review in April 2002.
Blue Cross Blue Shield Association, continued

In July 1996, a Blue Cross Blue Shield Association Medical Advisory Panel concluded that brachytherapy when used as local boost irradiation in patients treated with breast conserving surgery and whole breast external beam radiotherapy met BCBSA Technology Evaluation Center (TEC) criteria for treatment of Breast Cancer. This finding was reaffirmed after an updated review in April 2002.

California Radiological Society (CRS)
American Society for Therapeutic Radiology and Oncology
American College of Radiology

The American College of Radiology and the American Society for Therapeutic Radiology and Oncology Joint Economics Committee does not have a formal position on this topic. A representative will be attending.

Association of Northern California Oncologists (ANCO)

The Association does not have a formal position on this topic and is unable to provide representation at the meeting.

Medical Oncology Association of Southern California (MOASC)

The Association has been asked to provide a position statement and representation at the meeting.

American Brachytherapy Society

The Society has been asked to provide a position statement and representation at the meeting.

American Society of Breast Surgeons

The Society is in the process of developing a formal position statement on this topic and has been asked to provide representation at the meeting.
CancerNet from the National Cancer Institute

Regarding interstitial implantation of radioisotopes for breast cancer, the NCI’s PDQ Information for Health Care Professionals (2002) says “If a boost is used, it can be delivered either by external-beam radiation, generally with electrons, or by using an interstitial radioactive implant”. The statement is silent on the use of implants as the primary source of radiation therapy.

CONCLUSION

(1) Primary brachytherapy after breast-conserving surgery

One small prospective randomized, controlled trial has been published assessing the effectiveness and morbidity of primary brachytherapy after BCS for Stage I or II breast cancer compared to WBRT after BCS. The results were promising, but the small number of participants and short follow-up do not permit any firm conclusions. Three cohort studies with controls have been reported, but are too small and short to establish equivalence with existing alternatives. One of the three reported significantly worse outcomes with BT. One large clinical trial compared local EBR to WBRT and reported significantly higher rates of local recurrence in the group randomized to local radiation therapy. It is not yet clear that local brachytherapy after BCS results in rates of local recurrence and disease-free survival that are equivalent to those obtained by the standard therapy of WBRT after BCS.

(2) Brachytherapy as boost in conjunction with WBRT

No prospective randomized, controlled trial has been done to report the effectiveness and morbidity of brachytherapy in comparison to EBR for boost therapy in addition to WBRT after BCS. However, at least 10 cohorts with controls are available (level 3 and 4 evidence) with median follow-up times as long as 9.7 years. Overall survival, disease-free survival, local recurrence, and cosmetic outcomes appear equivalent to the current standards of external beam radiation boost.
RECOMMENDATION

(1) Primary brachytherapy after breast-conserving surgery

Brachytherapy, without external beam radiation therapy, for breast cancer does not meet Blue Shield TA criteria

(2) Brachytherapy as boost in conjunction with WBRT

Brachytherapy boost with external beam whole breast radiation therapy for breast cancer meets Blue Shield TA criteria and is an acceptable alternative to the use of external beam radiation for boost therapy when performed at centers with the appropriate training and expertise.

Committee approval as recommended

October 16, 2002

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REFERENCES


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