



**Clinical Review Criteria  
Brachytherapy**

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**Criteria  
For Medicare Members**

| Source                                 | Policy  |
|--|---|
| CMS Coverage Manuals                   | None  |
| National Coverage Determinations (NCD) | None  |
| Local Coverage Determinations (LCD)    | 4/01/2016 Noridian retired Local Coverage Determination <a href="#">LCD Brachytherapy: Non-Intracoronary (L34065)</a> . These services still need to meet medical necessity as outlined in the LCD and will require review. LCDs are retired due to lack of evidence of current problems, or in some cases because the material is addressed by a National Coverage Decision (NCD), a coverage provision in a CMS interpretative manual or an LCD. Most LCDs are not retired because they are incorrect. The criteria should be still referenced when making an initial decision. However, if the decision is appealed, the retired LCD cannot be specifically referenced. Maximus instead looks for "medical judgment" which could be based on our commercial criteria or literature search. |
| Local Coverage Article                 | None  |

**For Non-Medicare Members**

1) Breast Cancer - Brachytherapy as an adjunct to whole breast radiation is covered when recommended by the treating practitioner. Patients eligible for brachytherapy as a sole treatment alternative to whole breast radiation therapy must meet **ALL of the following** criteria:

- A. Age ≥ 50\*
- AND**
- B. Diagnosis of unifocal invasive ductal cancer with **ALL** of the following:
  - a. Tumor size ≤ 3cm
  - b. Negative surgical margins at 2mm
  - c. Negative nodal status
- OR**
- C. Diagnosis of ductal carcinoma in situ (DCIS) with **ALL** of the following:
  - a. Detected on screening
  - b. Low to intermediate nuclear grade
  - c. Tumor size ≤ 2.5 cm
  - d. Resected with margins negative at ≥ 3 mm

\*Age 40-49 meeting requirements above on a case by case basis.

Contraindicated for any of the following:

- A. age < 40
- B. lobular disease
- C. DCIS that does not meet the indications above
- D. EIC
- E. anatomic limitations or
- F. angiolymphatic space invasion

2) High-Dose Rate Brachytherapy for Prostate Cancer

a) High-dose rate (temporary seed implantation) prostate brachytherapy may be considered medically necessary under the following conditions:

- When combined with external beam radiation as a “boost” or
- When used for early stage prostate disease as monotherapy.

**Standard brachytherapy is covered without medical necessity review for:**

Coronary Artery Brachytherapy, Intravascular Coronary Brachytherapy  
 Endobronchial Brachytherapy - Lung Cancer  
 High-Dose or Low-Dose Brachytherapy for Cervical and Endometrial Cancer  
 Prostate Cancer

| Procedure  | Criteria   |
|--|--|
| AccuBoost peripheral breast brachytherapy                            | There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies. |
| Radioactive Seeds for Treatment of Recurrent High-Grade Glioblastoma |  |

**If requesting this service, please send the following documentation to support medical necessity:**

- Last 6 months of clinical notes from requesting provider &/or specialist

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage

## Background

Brachytherapy, also called internal radiation therapy, allows a physician to use a higher total dose of radiation to treat a smaller area and in a shorter time than is possible with external radiation treatment. Brachytherapy involves placing a radioactive material directly inside or next to the tumor. It has been proven to be very effective and safe, providing a good alternative to surgical removal of the prostate, breast, and cervix, while reducing the risk of certain long-term side effects.

There are two types of brachytherapy – temporary and permanent. In temporary brachytherapy, the radioactive material is placed inside or near a tumor for a specific amount of time and then withdrawn. Temporary brachytherapy can be administered at a low-dose rate (LDR) or high-dose rate (HDR).

Permanent brachytherapy, also called seed implantation, involves placing radioactive seeds or pellets (about the size of a grain of rice) in or near the tumor and leaving them there permanently. After several weeks or months, the radioactivity level of the implants eventually diminishes to nothing. The inactive seeds then remain in the body, with no lasting effect on the patient.

## Evidence and Source Documents

[Breast Cancer](#)

[Coronary Artery Brachytherapy, Intravascular Coronary Brachytherapy](#)

[Endobronchial Brachytherapy - Lung Cancer](#)

[High-Dose vs. Low-Dose Brachytherapy for Cervical and Endometrial Cancer](#)

[High-Dose Rate Brachytherapy for Prostate Cancer](#)

[Prostate Cancer](#)

[Radioactive Seeds for Treatment of Recurrent High-Grade Glioblastoma](#)

## Medical Technology Assessment Committee (MTAC)

### Breast Cancer Brachytherapy

#### BACKGROUND

In the last two decades, the treatment of early-stage breast cancer has shifted from radical mastectomy to breast conserving therapy (BCT). This involves lumpectomy followed by whole breast external beam radiotherapy (WBRT). Several large randomized controlled trials with long-term follow-up showed that BCT has equivalent survival rates to the modified radical mastectomy among patients with early stage breast cancer. In addition, BCT has better cosmesis and less psychological and emotional trauma for women compared to mastectomy. Researchers believe that whole breast irradiation after lumpectomy reduces local breast recurrence by eliminating residual cancer at the surgical site, as well as occult areas of in-situ or infiltrating cancer in remote areas in the breast. The use of BCT is underutilized in the United States mainly due to the long course of conventional whole-breast radiation therapy, which is typically delivered daily 5 days per week for 5 to 7 weeks. This may be a problem for working women, elderly patients, or those living at a considerable distance from a treatment center. WBRT may also delay or be delayed by the initiation of systemic adjuvant chemotherapy. Investigators also found that treating the entire volume of the breast may deliver small radiation doses to the adjacent tissues leading to acute and chronic toxicity to the skin, heart, lung, and contralateral breast (Fisher 1995, 2002, Baglan 2001, Veronesi 2002, Chen 2007, Cuttino 2007). Recently, accelerated partial breast radiation therapy (APBI) has been proposed as an alternative approach to WBRT. APBI involves the treatment of the lumpectomy bed plus a 1-2 cm margin of breast tissue. This is based on the assumption that the microscopic tumor rarely extends 2 cm beyond the initial resection cavity when the margins are negative on final pathologic examination. Reducing the target allows the delivery of APBI and completing the treatment in less than one week. Several methods for delivering APBI were proposed and/or used. These approaches include multicatheter interstitial brachytherapy, balloon catheter brachytherapy, 3-D CRT (conformal radiation therapy) and intraoperative radiation therapy. These techniques are widely different in terms of radiation delivery, degree of invasiveness, length of treatment, and acceptance by radiation oncologists (Chen 2007, Chao 2007). Breast brachytherapy involves the placement of radioactive sources inside the breast to deliver a relatively high dose of radiation to the tissue immediately surrounding the lumpectomy site, and very little dose to the surrounding normal structure. The interstitial multicatheter system, the most common method used, involves the placement of a number of catheters into the breast to guide the radioactive materials to the intended area. Pellets of iridium-192 are then inserted into the catheters over the course of the treatment. The catheters are briefly connected to a dose-rate brachytherapy machine for internal radiation treatment, which takes about ten minutes each. After the course of treatment is completed the catheters are removed. The procedure requires significant technical expertise, and can be difficult and challenging (Chen 2007, Bovi 2007, Haley 2008, Kacso 2008). Balloon-based brachytherapy Several balloon-based brachytherapy devices were developed as an alternative to the interstitial multicatheter system to be more user-friendly to the clinician and more accessible and better tolerated by the patient. The MammoSite brachytherapy (MSB) system (Hologic, Marlborough, MA) was the first developed balloon-based brachytherapy device. It consists of a small balloon connected to an inflation channel and a catheter for the passage of a high dose rate brachytherapy dose (Iridium-192 [192Ir]). The device is implanted in the lumpectomy cavity during or following breast surgery. The balloon is inflated with sterile saline containing a small amount of radiographic contrast to a size that completely fills the cavity and ensures conformance of the tissue to the balloon. A computed tomography scan is obtained to assess the balloon conformance to the lumpectomy cavity and determine its symmetry, diameter, distance from skin, planning target volume, and the dose distribution. After treatment is completed in several days, the balloon is deflated, and the catheter is removed. The treatment with the MammoSite device generally delivers 34 Gy in 10 fractions (3.4 Gy /fraction twice daily with a minimum of 6 hours between the fractions on the same day). Investigators recommend the system for patients with ductal carcinoma in situ, invasive ductal carcinoma, and primary tumors with a diameter less than 3cm. It may not be suitable for patients with small breast or for tumors located in the upper inner quadrant because of the requirement for skin-to-cavity distances (Bensaleh 2009, Njeh 2010). Xoft Axxent® (Xoft, Inc., Fremont, CA) electronic brachytherapy is a modified form of balloon-based brachytherapy. Similar to MammoSite, Xoft Axxent consists of a balloon catheter that is percutaneously inserted into the lumpectomy cavity. The system uses 50 kiloVolt (kV) X-ray source (an electronic radiation source) rather than radioisotope, such as iridium-192 high dose rate (HDR) source. The x-ray source consists of a miniature x-ray tube that is inserted in the balloon catheter and delivers the radiation therapy to the patient. The system may be operated at variable currents and voltages to change the dose rate and penetration properties. The Xoft Axxent does not require a high-dose rate afterloader unit, or treatment in a shielded vault. Another potential advantage is the lower energy dose deposited in adjacent normal tissues, compared to other forms of balloon brachytherapy. It is unknown if these advantages would be outweighed by a potential harm of fat necrosis as a result of a significant dose inhomogeneity (Strauss 2009, Dickler 2009). SenoRx Contura device (SenoRx, Inc, Aliso Viejo, CA) differs from MammoSite in that it has multiple lumens for passage of 192Ir HDR source. In addition to the central lumen, the Contura balloon has 4

surrounding channels to accommodate the HDR source. The surrounding channels have 5 mm offset around the central channel. The approach provides additional flexibility and has the potential of improving normal tissue sparing. The device includes a port which can be connected to suction to remove seroma fluid or air in an effort to improve conformity (Strauss 2009, Njeh 2010). Image guided radiation therapy: AccuBoost peripheral breast brachytherapy. The AccuBoost® peripheral breast brachytherapy system (Advanced Radiation Therapy of Billerica, MA) was developed to provide a means of delivering partial breast irradiation treatment regimen noninvasively under mammographic image guidance. The AccuBoost system consists of three main components: (1) A conventional mammography unit to immobilize the breast and localize the lumpectomy site. (2) Computed Radiography (CR) system to provide radiographic images of the lumpectomy cavity (and/or implanted fiducial markers) for cavity/ margin localization at the beginning of each fraction. The CR system can also record the exit dose distribution and provide information on the therapeutic dose. (3) AccuBoost Applicators: high dose rate (HDR) Ir192 brachytherapy source remote afterloading system to deliver brachytherapy in a peripheral noninvasive manner. The applicators are made from tungsten in the form of half-cylinders. The patient's breast is compressed to a thickness of 3-8 cm between two mammography paddles and imaged with a radiopaque coordinate grid. The radiation oncologist determines the isocenter coordinates and appropriate applicator size and shape based on the image. The collimating HDR 192Ir brachytherapy applicators are then applied on either side of the breast along a common axis and the brachytherapy dose delivered. The process is repeated along an orthogonal axis to distribute the entrance dose (Rivard 2009, Yang 2009, AccuBoost website). MammoSite, multi-lumen MammoSite, Axxent Electronic brachytherapy, and SenoRx Contura device are all FDA approved to deliver intracavity radiation to the surgical margins following lumpectomy for breast cancer. AccuBoost® system for delivering guided radiation therapy is also FDA approved.

#### **06/12/2002: MTAC REVIEW**

##### **Breast Cancer Brachytherapy**

**Evidence Conclusion:** The studies reviewed aimed at determining the equivalence between brachytherapy and external beam radiation, yet none of them was designed or analyzed in a fashion to study equivalence, which is a major threat to their validity. The authors set no equivalence boundary but took the lack of statistically significant difference between the two treatments as a proof of equivalence, which could lead to an erroneous judgment. Moreover, the studies were prospective, with a historical control group. The patients were not randomly assigned to the treatment group, and it is not discussed if they were consecutive, which may be a source of selection bias. The cohorts of women treated with brachytherapy were prospectively followed for a variable period of time (median 36 months in Vicini's study, and 74 months in King's study). The follow-up period was as short as a few months among some patients, and the dropout rate in the brachytherapy group was 82% after 5 years in Vicini's study. The reason for this high dropout rate was not discussed. In the two studies, data on the control group were obtained from retrospective chart reviews. Patients in the brachytherapy group received the treatment at either a low- or high-dose rate but were analyzed as one group. There were some differences in the baseline characteristics that were not adjusted for in the analysis of the results. The overall control and cosmetic outcomes of the brachytherapy as a sole treatment after lumpectomy were similar to that achieved by the external beam radiation therapy. However, these results cannot be generalized mainly due to the design of the study as well as the selection, observation and other biases in the studies. Randomized controlled studies with large sample size, power, and longer follow-up periods are needed to determine the long-term benefits and harms of brachytherapy used as a sole treatment after breast conservative therapy.

**Articles:** The search yielded 81 articles. Many were review articles, opinion pieces, or addressed brachytherapy as a boost, not a sole treatment after lumpectomy. The literature did not include any randomized controlled trials, or meta-analyses. There was a number of small case series with no control group, and two prospective studies that compared brachytherapy with external beam irradiation. These two studies were selected for critical appraisal. Vicini FA, Baglan KL, Kestin KL, et al. Accelerated treatment of breast cancer. *J Clin Oncol* 2001; 19:1993-2001. See [Evidence Table](#). King TA, Bolton JS, Kuske RR, et al. Long-term results of wide field brachytherapy as the sole method of radiation therapy after segmental mastectomy for T<sub>is, 1, 2</sub> breast cancer. *Am J Surg* 2000; 180:299-304. See [Evidence Table](#).

The use of brachytherapy in the treatment of breast cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

#### **02/07/2005: MTAC REVIEW**

##### **Breast Cancer Brachytherapy**

**Evidence Conclusion:** Brachytherapy as an adjunct or boost to whole breast radiation therapy:

The two randomized controlled trials reviewed (Polgar 2002, and Poortmans 2004) evaluated brachytherapy for early stage breast cancer with no or limited spread to the axillary lymph nodes. Both trials compared boost to no boost therapy after breast conserving surgery and whole breast external radiation therapy. Different techniques for the boost therapy were used (brachytherapy and electrons in Polgar's trial, and electrons, photon beams, and

interstitial brachytherapy in Poortman's trial). The trials were not blinded, and the patients were randomized to boost or no boost treatment but were not randomized to the different boost techniques used. The latter was selected according to the physicians' preference. Poortman et al's trial was still ongoing, and in this publication the authors did not present a comparison between boost and no boost treatments but compared the outcomes of the different boost techniques used. Polgar et al reported a significant improvement with the boost vs. no boost treatment. The analysis provided however does not indicate that there was a statistically significant improvement as reported by the authors. The boost treatment was also found to be associated with an increased incidence of moderate to severe complications. [Brachytherapy as a sole treatment alternative to whole breast radiation therapy](#). Vicini 2003, and Polgar 2004 were prospective cohort studies with a comparison group. Patients, however, were not randomly assigned to the treatment groups but matched to historical controls from the records or databases. The criteria used to assess the effect of the treatment included the degree of local control, disease free, relapse-free, and cancer free survival, as well as cosmetic outcome, and side effects. These two studies aimed at determining the similarity between brachytherapy and external beam radiation, yet none of them was designed or analyzed in a fashion to study equivalence, which is a major threat to their validity. The authors set no equivalence boundary but took the lack of statistically significant difference between the two treatments as a proof of equivalence, which could lead to an erroneous judgment. In conclusion, interstitial brachytherapy may be a promising treatment, but the studies reviewed do not provided sufficient evidence to conclude that it may be used as an alternative to whole breast radiation therapy after breast conserving surgery. Randomized controlled studies with large sample size, power, and longer follow-up periods are underway to determine the long-term benefits and harms of brachytherapy used as a sole treatment after breast conservative therapy.

**Articles:** The search revealed more than 200 articles. Many were reviews, editorials, or dealt with the technical aspects of the technology. There were several case series, retrospective studies, and small trials. Others compared mastectomy with external beam radiation therapy, and in one trial brachytherapy was compared to WBRT without breast lumpectomy. Studies were selected for review according to the following criteria: 1. Evaluating brachytherapy as an adjunct to whole breast radiation therapy or as a sole treatment after breast-conserving surgery, 2. Prospective design, and 3. Including a comparison or control group. Two large RCTs on the use of brachytherapy as a boost to WBRT were identified and critically appraised. Several studies on the use of brachytherapy as an alternative to WBRT were published after MTAC reviewed the technology in 2002. All evaluated brachytherapy for early stage breast cancer with no or limited spread to axillary lymph nodes. Harms et al (2002), Keisch et al (2003), Perera et al (2003), Richard et al (2004), and Shah et al (2004) studies were case series with no control or comparison groups. These studies mainly evaluated the safety of the treatment rather than efficacy. Only two of the identified studies (Vicini 2003 and Polgar 2004) included a comparison group and were selected for critical appraisal. *Evidence tables were created for the following studies: For the use of brachytherapy as an adjunct to whole breast radiation therapy: Polgar C, Fodor J, Orosz Z, et al. Electron and high dose-rate brachytherapy boost in the conservative treatment of stage I-II breast cancer. First results of the Randomized Budapest Boost Trial. *Strahlenther Onkol* 2002; 178:1205-1211. See [Evidence Table](#) Poortmans P, Bartelink H, Horiot JC, et al. The influence of the boost technique on local control in breast conserving treatment in the EORTC "boost versus no boost randomized trial. *Radiother Oncol* 2004; 72:25-33. See [Evidence Table](#) For the use of brachytherapy as a sole treatment alternative to whole breast radiation therapy: Vicini F, Kestin L, Chen P, et al. Limited field radiation therapy in the management of early-stage breast cancer. *J Natl Cancer Inst* 2003; 95:1205-1211. See [Evidence Table](#) Polgar C, Major T, Fodor J, et al. High dose-rate brachytherapy alone versus whole breast radiotherapy with or without tumor bed boost after breast conserving surgery: seven-year results of a comparative study. *Int J Radiat Oncol* 2004; 60:1173-1181 See [Evidence Table](#)*

The use of brachytherapy as an adjunct or boost to whole breast radiation therapy in the treatment of breast cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

The use of brachytherapy as a sole treatment alternative to whole breast radiation therapy in the treatment of breast cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## **08/15/2011: MTAC REVIEW**

### **Breast Cancer Brachytherapy**

**Evidence Conclusion:** There is insufficient evidence to date to determine whether accelerated partial breast irradiation delivered by balloon-based brachytherapy or AccuBoost is safe and provides non-inferior or superior local tumor control and survival compared to conventional whole breast irradiation in patients with early stage breast cancer treated with breast conservative therapy. Polgar and colleagues' (2008) RCT, reviewed earlier, and Antonucci et al's study (evidence table 1) had several methodological flaws which limit generalization of their results. Large RCTs with long-term follow-up are needed to determine the equivalence or superiority of accelerated partial breast irradiation therapy to whole breast external beam radiation therapy. A phase 3 trial comparing APBI to whole breast irradiation in over 4,000 women with stage 0, I, or II breast cancer is underway. The trial is jointly conducted by the National Surgical

Adjuvant breast and Bowel Project (NSABP) and the Radiation Therapy Oncology Group (RTOG). Patients in the APBI will be treated using one of three modalities: interstitial brachytherapy, MammoSite brachytherapy, or 3-D conformal EBRT. Outcome measures include overall survival, recurrence free survival, distant disease-free survival, toxicity, cosmesis, and convenience of the care. The primary aim of the trial is determining whether APBI would provide equivalent local breast control as WBRT in early stage breast cancer. Other ongoing trials include the Canadian RAPID trial which is recruiting over 2000 patients to be randomized to either whole breast irradiation or 3-D CRT, and an international phase III large trial supported by the European Brachytherapy Breast Cancer GEC-ESTRO Working Group. This trial will randomize 1170 women between WBRT and APBI using high-dose rate or pulsed-dose rate brachytherapy. The results of these, and a number of other ongoing trials, will provide data on the efficacy and toxicity of partial breast irradiation in the treatment of early stage breast cancer as compared to WBRT. They may also provide data on appropriate candidates for APBI and on the advantages and disadvantages of each method.

**Articles:** Objectives: To determine whether accelerated partial breast irradiation leads to non-inferior or superior local tumor control and survival compared to conventional whole breast irradiation, when used as an adjuvant therapy after lumpectomy in patients with early stage breast cancer. To determine whether the use of balloon-based brachytherapy systems is safe and effective for delivering adjuvant radiation therapy after lumpectomy in patients with early stage breast cancer. To determine whether the image guided radiation therapy using AccuBoost peripheral breast brachytherapy system is safe and effective for delivering adjuvant radiation therapy after lumpectomy in patients with early stage breast cancer.

Screening of articles/selection: The search revealed around 150 articles on accelerated partial breast irradiation (APBI). The majority of the published empirical studies were phase I/II trials with no comparison group, different sizes, and follow-up durations. There were no new randomized trials, published after the last review, on APBI therapy delivered by MammoSite, Axxent, Contura, or AccuBoost systems. The search identified a recently published interim analysis on the acute toxicity in a trial that compared conventional whole breast radiation with APBI plus IMRT, a nonrandomized study that examined the dosimetric advantage of Contura catheter vs. MammoSite, and a small case series of patients treated with Contura catheter. The literature search also revealed a report on four-year outcomes of a prospective study, with no control group, on the efficacy and toxicity of 3-D-CRT to deliver APBI, and a feasibility study with 11 patients treated with intraoperative radiation using the Axxent electronic brachytherapy system. No published clinical studies on AccuBoost system were identified. A recent analysis comparing APBI with WBRT was critically appraised. See [Evidence Table](#). Antonucci JV, Wallace M, Goldstein NS, et al. Differences in patterns of failure in patients treated with accelerated partial breast irradiation versus whole-breast irradiation: a matched-pair analysis with 10-year follow-up. *Int J Radiat Oncol Biol Phys*. 2009;74:447-452. See [Evidence Table](#).

The use of brachytherapy as an adjunct or boost to whole breast radiation therapy in the treatment of breast cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

### **Coronary Artery Brachytherapy Intravascular Coronary Brachytherapy**

#### **BACKGROUND**

Percutaneous transluminal coronary angioplasty (PTCA) is a widely used therapy for obstructive coronary artery disease. It is limited however by the high rate of restenosis which occurs in 30-60% of patients after a successful PTCA. The main mechanisms of restenosis include elastic recoil of the vessel, rapid platelet deposition, vascular remodeling and neointimal hyperplasia. Endovascular stents have been shown to reduce stenosis by preventing the elastic recoil and pathological remodeling. However, stents do not prevent the restenosis caused by neointimal hyperplasia, but rather initiate an inflammatory reaction that induces more proliferation than other coronary devices. An effective treatment of restenosis within the stent will be the suppression of this neointimal hyperplasia. Radiation therapy which is known for its antiproliferative effect has been proposed as a treatment for in-stent restenosis. Over the past six years, studies on the use of various techniques to apply intracoronary radiation which is known as intracoronary brachytherapy have been showing encouraging results. Brachytherapy uses a relatively large localized dose of beta or gamma radiation. It does not provide an immediate outcome. If effective, it reduces the rate of restenosis in the vessel in the target area. This effect can be measured by angiograms performed six months after the procedure. Brachytherapy requires a multidisciplinary team to deliver it including an interventionist cardiologist, a radiation oncologist, physicist and safety officer.

#### **06/13/2001: MTAC REVIEW**

### **Coronary Artery Brachytherapy Intravascular Coronary Brachytherapy**

**Evidence Conclusion:** GAMMA-One (Leon et al), beta-WRIST (Waksman et al), SCRIPPS (Teirstein et al), and the START (In press) trials are four of the well-designed RCTs evaluating the use of brachytherapy in the management of in-stent restenosis. There are several other ongoing studies. These trials showed that patients

with in-stent restenosis treated with brachytherapy needed less revascularization than those treated with PTCA or PTCA and stents without radiation. In two of the studies, intracoronary brachytherapy tended to increase the risk of late thrombus formation, but this was statistically insignificant. Although these trials reported that major cardiac events (MACE) were lower among patients who received brachytherapy, none of them had adequate power, or follow-up to detect the difference in myocardial infarction and death rates alone. Brachytherapy may also cause acute damage in the coronary arteries including aneurysm, pseudoaneurysm, arterial dissection, or rupture of the artery. None of these acute complications was reported in any of these trials. In addition, radiation may lead to a long-term damage on the surrounding tissue and have adverse effects on the clinical personnel. These long-term complications are unknown. The longest data available is the three-year follow-up in the SCRIPP trial (Teirstein et al). The nature of radiation needs a long-term follow-up.

**Articles:** The search yielded 79 articles. Many were just reviews and literature. There were eleven articles on randomized controlled studies, more than one publication for each of the major trials, GAMMA-one, beta-WRIST and SCRIPPS. The START trial was still in press. These major randomized controlled studies were evaluated in detail. *Evidence tables were created for the following studies:* Leon MB, Teirstein PS, Moses JW, et al. Localized Intracoronary Gamma-Radiation Therapy to Inhibit the Recurrence of Restenosis After Stenting. *N Engl J Med* 2001; 344: 250-256 See [Evidence Table](#) Teirstein PS, Massulo V, Jani S, Popma JJ, et al. Three-Year Clinical and Angiographic Follow-up After Intracoronary Radiation. *Circulation* 2000; 101: 360-365. See [Evidence Table](#) Waksman R, White L, Chan RC, et al. Intracoronary Gamma -Radiation Therapy After Angioplasty Inhibits Recurrence In Patients With In-Stent Restenosis. *Circulation* 2000; 101: 2165-2171 See [Evidence Table](#) The use of Coronary Artery Brachytherapy for the treatment of restenosis of stent passes all *Kaiser Permanente Medical Technology Assessment Criteria*.

## **Endobronchial Brachytherapy - Lung Cancer**

### **BACKGROUND**

Among all types of malignancy, lung cancer is one of the most difficult to manage and is associated with the highest mortality rate. Its incidence is continuously increasing, with no improvement in mortality. 80-85% of the cases is non-small cell lung cancer (NSCLC). Squamous cell carcinoma and adenocarcinoma account for the majority of the NSCLC. Regardless of the histological type, surgery offers the best potential for cure. However, approximately 75% of the patients present with locally advanced non-resectable disease at the time of diagnosis. The treatment options for these patients are chemotherapy and / or external irradiation therapy, which have low survival rates, and high rates of local recurrence. Endobronchial brachytherapy (EBT or EBB) is an additional treatment increasingly used for centrally localized lung cancer. It can be used alone, or with the external radiation therapy (XRT) to boost the total dose of irradiation used. In earlier studies, it was used as a palliative treatment in case of endobronchial recurrence after XRT. In later studies it is used in combination with high-dose of XRT as a potential curative primary treatment in selected cases. With brachytherapy, radioactive sources usually iridium-192 are placed at the tumor site in the involved branch of the tracheobronchial tree. These will deliver a radiation dose that rapidly and progressively declines with the increasing distance from the source. Any adverse effects on normal tissue should be confined to the immediate vicinity of the bronchus, sparing the lung parenchyma and the esophagus. The procedure is done on outpatient basis. Bronchoscopy is performed under topical anesthesia to determine the field of treatment. A guidewire is then placed in the instrumentation channel of the endoscope, and the bronchoscope is removed. An after-loading catheter is passed on the guidewire, the guidewire is removed, and an applicator for placement of the radiation source is inserted in the catheter. Depending on the number of airway branches involved, 1 to 4 catheters may be placed. The position of the catheter is verified by fluoroscopy. The applicator is then connected to the iridium192 afterloading unit and the irradiation source advanced to the intended position under computer control. The application time ranges from 2 to 15 minutes depending on the dose, and length of the irradiated area. After removing the radioactive source, the catheters are removed, and the patient is observed for 30 minutes. High-dose brachytherapy may be delivered in fractionated doses by repeating the procedure at weekly or biweekly intervals, or twice a day until the entire dose is delivered. The dose varies individually and depends on the patient's clinical condition, history, and concurrent use of XRT. Endobronchial brachytherapy may be associated with acute complications. It could lead to fibrotic airway obstruction and may be linked to fatal hemoptysis depending on the dose, dose per fraction and the concurrent use of XRT.

### **08/08/2001: MTAC REVIEW**

#### **Endobronchial Brachytherapy - Lung Cancer**

**Evidence Conclusion:** The RCTs reviewed were conducted to evaluate the effect of endobronchial brachytherapy either used alone, or in addition to external radiation therapy. Langendijk's study found a statistically significant benefit of adding EBT to XRT in treating atelectasis in patients with endobronchial obstruction in the main bronchus. Huber's study did not show any statistical difference between the two treatments. On the other hand, Stout's study found that external irradiation therapy, had a statistically significant better outcome than EBT (used alone) on the patients' survival and palliation of some symptoms. EBT was not found to be associated with a higher rate of fatal hemoptysis in all three trials. The studies had some limitations

including likelihood of observation bias, incomplete data (all three RCTs), premature termination and lack of power (Langendijk). In conclusion, the efficacy and safety of endobronchial brachytherapy cannot be fully determined from the available evidence.

**Articles:** The search yielded 54 articles. Selection was based on study type. There were 3 articles on randomized control trials comparing the effect of external irradiation therapy (XRT) vs. endobronchial brachytherapy (EBT) / XRT + EBT, on patients with non-small cell lung cancer. Reviews, editorials and comments were reviewed, but no evidence tables were created. *The three RCTs selected for critical appraisal were:*

Huber RM, Fischer R, Hautmann H, et al. Does Additional Brachytherapy Improve the Effect of External Irradiation? A Prospective, Randomized Study in Central Lung Tumors. *Int.J.Radiation Oncology Biol. Phys.* 1997; 38 (3): 533-540. See [Evidence Table](#) Langendijk H, Jong JD, Tjwa M, et al. External Irradiation Plus Endobronchial Brachytherapy in Inoperable Non-small Cell Lung Cancer: a Prospective Study. *Radiotherapy and Oncology* 2001; 58: 257-268 See [Evidence Table](#) Stout R, Barber P, Burt P, et al. Clinical and Quality of Life Outcomes in the First United Kingdom Randomized Trial of Endobronchial Brachytherapy Treatment of Inoperable non-small Cell Lung Cancer. *Radiotherapy and Oncology* 2000; 56: 323-327 See [Evidence Table](#)

The use of endobronchial brachytherapy in the treatment of lung cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria 2* for effectiveness.

### **High-Dose Rate Brachytherapy for Prostate Cancer**

#### **BACKGROUND**

Prostate cancer is one of the most common cancers, and the second leading cause of cancer death in men in the United States. The standard management options for localized disease included surgery, radiotherapy, and watchful waiting. However, the optimal treatment is not well defined. Both surgery and radiation therapy are reported to have equivalent outcomes, and each approach has its advantages and disadvantages. Researchers reported that for intermediate and high-risk disease, external beam radiation therapy (EBRT) is the standard treatment, and that there is a dose response for biochemical relapse-free survival. However, dose escalation to >70 Gy is associated with an increase in genitourinary and gastrointestinal side effects. Several techniques have been developed to deliver high doses of radiation to the prostate while sparing surrounding normal tissue. Among these are the three-dimensional conformal radiotherapy (3DCRT), intensity modulated radiation therapy (IMRT), photon therapy, and brachytherapy (Vordermark 2006, Hoskin 2007, Rades 2007). Prostate brachytherapy was introduced in the late 1980s after the development of transrectal ultrasonography and sophisticated treatment planning software. It can be performed as monotherapy or in conjunction with hormone therapy or EBRT. Monotherapy is usually reserved for low-risk cancer, and the combined therapies are used for high-risk disease (Nelson 2007). Interstitial brachytherapy can be delivered using permanent low-dose-rate (LDR) seed implants or temporary high-dose-rate (HDR) implants. The latter entails the temporary placement of higher energy radioactive sources in and near the tumor. An automated machine called an afterloader sequentially moves a high-intensity radioactive source to and from a set of catheters in and around the prostate to deliver a pre-determined radiation dose to the patient's tumor. Following treatment, the radioactive source is withdrawn. Both LDR and HDR have the advantage of conforming high doses of radiation according to the precisely localized target, rapid dose fall-off, and no target movement during treatment. The dose distribution of the LDR mainly depends on the position of the implanted seed, while the HDR uses a steeping source, usually iridium-192, and is thus able to vary both the position and /or dwell time of the source. This has the potential of better target volume coverage and a greater sparing of neighboring organs at risk (Chin 2006). Unlike LDR brachytherapy, HDR brachytherapy usually requires hospitalization of the patient. HDR brachytherapy is also associated with a number of acute and chronic side effects, including urinary urgency and frequency, dysuria, nocturia, urinary retention, urethral stricture, rectal irritation, and impotence.

#### **06/06/2006: MTAC REVIEW**

##### **High-Dose Rate Brachytherapy for Prostate Cancer**

**Evidence Conclusion:** There is insufficient evidence to draw conclusions about the effectiveness and safety of HDR brachytherapy monotherapy compared to an accepted treatment for prostate cancer.

There is some evidence that HDR brachytherapy plus EBRT results in better biochemical control than EBRT alone. Data are from 2 comparative studies, one randomized and one non-randomized; both studies have threats to validity. There is insufficient evidence to determine whether HDR brachytherapy added to EBRT improves disease-specific or overall survival. In the randomized controlled trial, there was no significant increase in overall survival with HDR brachytherapy plus EBRT; data were not reported for disease-specific mortality. In the non-randomized study, there was not a significant difference in disease-specific mortality. Overall survival was significantly higher in the combined treatment group when 5-year outcomes were modeled using Kaplan-Meier analysis—actual patient data on survival were not reported.

There is insufficient evidence on adverse effects associated with HDR brachytherapy plus EBRT. In the RCT, rates of adverse effects did not differ significantly between groups—however, these comparisons were likely



underpowered. In the cohort study, adverse effects were only reported for the HDR brachytherapy plus EBRT group; 29% of patients developed impotence.

**Articles:** Note: Studies were identified using N California report but selection of articles for critical appraisal was re-done for the MTAC report. *HDR brachytherapy monotherapy:* There were no randomized controlled trials or non-randomized controlled trials that compared the safety and effectiveness of HDR brachytherapy monotherapy to a different treatment such as observation, surgery or EBRT. All of the studies were case series. Two publications from a single institution compared series of patients who received either HDR brachytherapy or LDR brachytherapy (Vargas et al., 2005 ; Grills et al., 2004 ). No studies were selected for critical appraisal since none compared HRD brachytherapy to another treatment for prostate cancer. *Combination therapy (HRD brachytherapy plus EBRT):* There was one randomized controlled trial comparing HRD brachytherapy plus EBRT to EBRT alone. There were also two nonrandomized comparison studies and nine case series. One of the non-randomized comparative studies (Jo et al., 2005 ) was a survey that only reported on quality of life, not clinical outcomes and thus this study was excluded from further review. The RCT (Sathya et al., 2005) and the other non-randomized comparison study (Kestin et al., 2000) were critically appraised. *The studies reviewed were:* Sathya JR, Davis IR, Julian JA et al. Randomized trial comparing iridium implant plus external-beam radiation therapy with external-beam radiation therapy alone in node-negative locally advanced cancer of the prostate. J Clin Oncol 2005; 23: 1192-1199. See [Evidence Table](#) Kestin LL, Martinez AA, Stromberg JS et al. Matched-pair analysis of conformal high-dose-rate brachytherapy boost versus external-beam radiation therapy alone for locally advanced prostate cancer. J Clin Oncol 2000; 18: 2869-2880. See [Evidence Table](#)

The use of High-dose rate brachytherapy in the treatment of prostate cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## 10/01/2007: MTAC REVIEW

### High-Dose Rate Brachytherapy for Prostate Cancer

**Evidence Conclusion:** High-dose rate (HDR) brachytherapy for prostate cancer was previously reviewed by MTAC on 6/5/06. The report conclusion indicated that there was insufficient evidence to determine the effectiveness and safety of HDR brachytherapy monotherapy compared to an accepted treatment for prostate cancer. For the current review, the literature search revealed one more recent RCT conducted in the UK (Hoskin 2007), that compared external-beam radiation therapy (EBRT) given as a monotherapy vs. its combination with high-dose rate brachytherapy boost for the treatment of prostate cancer. The primary outcome was biochemical relapse free survival. The secondary outcomes were the overall and relapse-free survival, acute and late toxicity, and quality of life. The study had its advantages and limitations. It was randomized, controlled, had sufficient statistical power, high completeness rate, and analysis was based on intention to treat. However, the authors did not discuss blinding of the investigators to the patient allocation, the 55 Gy dose of external beam radiotherapy is considered suboptimal, and the technique of delivering the EBRT changed along the study. Moreover, the follow-up duration was relatively short, and the primary outcome was biochemical relapse free survival which is a surrogate outcome for overall survival. It is considered acceptable by some investigators, due to the long natural history of the disease. Overall, the results of the trial indicate that that the biochemical relapse-free survival was significantly higher among patients in the HDR brachytherapy in combination with external beam radiotherapy group versus those treated with external beam radiotherapy alone. The HDR brachytherapy was also associated with an improved quality of life, without any increase in toxicity. Soumarova and colleagues (2007) compared the acute genitourinary and gastrointestinal toxicity in 97 patients treated with external beam radiotherapy (3D conformal radiotherapy [CRT]) or 3D CRT combined with interstitial conformal HDR brachytherapy for the treatment of histologically verified localized carcinoma of the prostate. The study was prospective but non-randomized: 57 patients received 3D CRT and 40 patients were irradiated with 3D CRT+ HDR brachytherapy. The patients were followed by a radiation oncologist and urologist at 1-3 months intervals, and the acute genitourinary and gastrointestinal toxicities were evaluated using the RTOG criteria. The overall results of the study showed a lower incidence of acute gastrointestinal toxicity in HDR brachytherapy combination therapy group versus those in the 3D CRT monotherapy group. In conclusion the studies published to date do not provide sufficient evidence to determine the efficacy and safety of HDR brachytherapy in the treatment of histologically proven carcinoma of the prostate.

**Articles:** *HDR brachytherapy monotherapy:* The literature search did not reveal any randomized controlled trials or non-randomized controlled trials that compared the safety and effectiveness of HDR brachytherapy monotherapy to no, or a different mode of treatment as surgery or EBRT. All published studies on monotherapeutic brachytherapy for organ confined or locally advanced prostate cancer, were case series with variable sizes and duration of follow-up. None included a comparison or control group and thus were not critically appraised. *HDR brachytherapy in combination with external beam radiotherapy (EBRT):* There was one recent randomized controlled trial (Hoskin 2007) that compared HDR brachytherapy plus EBRT to EBRT alone, and a non-randomized controlled trial (Soumarova 2007) that compared the acute toxicity of EBRT with and without

HDR brachytherapy, as well as several case series. The two studies were reviewed, Hoskin and colleagues RCT was presented in an evidence table.

Hoskin PJ, Motohashi K, Bownes P, et al. High dose rate brachytherapy in combination with external beam radiotherapy in the radical treatment of prostate cancer: initial results of a randomized phase three trial. *Radiother Oncol* 2007; May 24. See [Evidence Table](#)

The use of High-dose rate brachytherapy in the treatment of prostate cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

#### 10/18/2010: MTAC REVIEW

##### **High-Dose Rate Brachytherapy for Prostate Cancer**

**Evidence Conclusion:** HDR brachytherapy as a monotherapy A recent retrospective cohort study combined data from two centers to evaluate the safety and efficacy of HDR brachytherapy compared to LDR brachytherapy for the treatment of prostate cancer. The primary outcome measures were biochemical control and rate of acute and chronic toxicities. There was no significant difference in biochemical control rates between the HDR brachytherapy and the LDR brachytherapy groups (88% vs. 89%, P=0.62). However, compared to patients treated with LDR brachytherapy, patients treated with HDR brachytherapy experienced significantly lower rates of acute and chronic dysuria, acute urinary frequency and urgency, and acute rectal pain. Results from this study should be interpreted with caution as there was no adjustment for confounding factors, treatment techniques evolved over the study period, the two centers had different treatment procedures, and approximately 29% of patients received neoadjuvant androgen deprivation (Martinez 2009). HDR brachytherapy combined with external beam radiation therapy. A retrospective cohort study that compared the efficacy of HDR brachytherapy in combination with 3D-conformal external beam radiation (3DCRT) with 3DCRT alone for the treatment of prostate cancer found no significant difference in biochemical control, overall survival, or cause-specific mortality between the treatment groups. As side effects were only reported for the combined group, it cannot be determined if patients in the combined group experienced more side effects compared to patients in the 3DCRT alone group (Zwahlen 2010). Conclusion: There is insufficient evidence to determine whether HDR brachytherapy given alone or in combination with EBRT is safe and effective for the treatment of prostate cancer.

**Articles:** The literature search did not reveal any randomized controlled trials that addressed the safety and efficacy of HDR brachytherapy. A retrospective cohort study was identified that evaluated the safety and efficacy of HDR brachytherapy given as a monotherapy compared to LDR brachytherapy was selected for review. There were several studies that evaluated the safety and efficacy of HDR brachytherapy combined with EBRT; however, the majority of these were case series. A recent study by Zwahlen and colleagues was selected for review as it was the only study with a control group. The following studies were critically appraised:

Martinez AA, Demanes J, Vargas C, et al. High-dose-rate prostate brachytherapy: An excellent accelerated hypofractionated treatment for favorable prostate cancer. *Am J Clin Oncol* 2009 November 30. See [Evidence Table](#)

Zwahlen DR, Andrianopoulos N, Matheson B, et al. High-dose-rate brachytherapy in combination with conformal external beam radiotherapy in the treatment of prostate cancer. *Brachytherapy* 2010; 9:27-35. See [Evidence Table](#)

The use of High-dose rate brachytherapy in the treatment of prostate cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

##### **High-Dose vs. Low-Dose Brachytherapy for Cervical and Endometrial Cancer**

###### BACKGROUND

The standard treatment for cervical cancer is external beam radiation therapy (EBRT) combined with intracavity brachytherapy. There is no accepted standard treatment for early endometrial cancer. However, brachytherapy is often used, alone or in combination with EBRT. Intravaginal brachytherapy is believed to be useful for endometrial cancer in part because the vaginal apex is a common site of endometrial cancer recurrence. Brachytherapy refers to internal or local irradiation. In intracavity brachytherapy, radioactive sources are placed in body cavities that are close to the tumor. The relative balance between the two types of radiation treatment (brachytherapy and EBRT) depends on the stage and volume of disease. Generally, as the tumor volume increases, EBRT is favored to achieve a larger volume of homogenous dose (Stitt, 1999). Low-dose rate (LDR) brachytherapy has been available longer and is still used more frequently than high-dose rate (HDR) brachytherapy. There are several potential advantages of HDR brachytherapy, including the ability to treat large clinical patient volume, the lack of need for general anesthesia or bed rest, the ability to individualize treatment, complete radiation protection for staff and the application of multiple fractions on an outpatient basis. Disadvantages of HDR brachytherapy are the higher costs of staffing, equipment and the changing of iridium source every three months. In addition, optimal fractionation schemes for HDR brachytherapy are yet to be well defined and long-term complications are unclear (Stitt, 1999). In a LDR brachytherapy session, instruments need to be in place for 2-3 days. Cervical cancer treatment involves two procedures, approximately one week apart. Radium was used originally, but now cesium-

137 is used. In contrast, with HDR brachytherapy, a treatment session takes minutes. Multiple sessions are generally required; five is a common number for treating cervical cancer. For the treatment of endometrial cancer (brachytherapy alone or in combination with EBRT after a hysterectomy), two sessions of about 1 hour each are required. High-dose rate is generally accepted as being between 50-500 cGy/minute (Tewari & DiSaia, 2002; Hogberg et al., 1999).

### 06/11/2003: MTAC REVIEW

#### High-Dose vs. Low-Dose Brachytherapy for Cervical and Endometrial Cancer

**Evidence Conclusion:** Cervical cancer: With few exceptions, the studies reviewed did not find statistically significant differences in survival between patients receiving HDR and LDR brachytherapy for the treatment of cervical cancer. There were also no significant differences in adverse effects between the HDR and LDR groups. Although the studies suggest that the safety and effectiveness of the two treatments are similar, the studies were not designed as equivalence studies. The lack of a statistically significant finding could be due to a design flaw such as insufficient statistical power or bias. Neither of the RCTs discussed statistical power and both may have been underpowered to detect differences in survival and/or adverse effects between groups. This is particularly true because the results were reported separately by stage of disease which resulted in a smaller sample size for each comparison. The studies also had several threats to validity. Neither of the RCTs had adequate randomization (one allocated patients by birth month and the other alternated patient assignment to treatment group) which could introduce selection bias. In all three studies, there may have been baseline differences between groups that were not controlled for in the statistical analyses. The studies also differed in the extent of external beam radiation treatment the patients received. Endometrial cancer: There are no studies that specifically compare the safety and effectiveness of HDR and LDR brachytherapy for the treatment of endometrial cancer.

**Articles:** *Cervical cancer:* The search yielded 135 articles. Many of the studies were reviews, opinion pieces or dealt with technical aspects of the procedure. There were four studies that compared the outcomes of patients who received high-dose or low-dose brachytherapy. Two of the studies were randomized and two were non-randomized. The two randomized studies and the prospective non-randomized study were critically appraised: Hareyama M, Sakata K, Oouchi A et al. High-dose versus low-dose-rate intracavity therapy for carcinoma of the uterine cervix. *Cancer* 2002; 94: 117-124. See [Evidence Table](#)  
Teshima T, Inoue T, Ikeda H. High-dose rate and low-dose rate intracavity therapy for carcinoma of the uterine cervix. *Cancer* 1993; 72: 2409-2414. See [Evidence Table](#)  
*Endometrial cancer:* The search yielded 36 articles. No randomized controlled trials were identified. There were no empirical studies comparing low-dose rate and high-dose rate brachytherapy. No articles were critically appraised.

The use of high-dose brachytherapy in the treatment of cervical and endometrial cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

### Prostate Cancer Brachytherapy

#### BACKGROUND

At the December 14, 1994 Committee on Medically Emerging Technologies the efficacy of Transperineal Ultrasound Guided Iodine<sup>125</sup> or Palladium<sup>103</sup> Brachytherapy for Prostate Cancer was originally discussed. Dr. Blasko presented information on the 800 patients for which the procedure was performed. Only 252 of those patients had a minimum follow-up of two years. The conclusion of the committee was that there was inadequate follow-up data supporting the efficacy of Transperineal Ultrasound Guided Iodine<sup>125</sup> or Palladium<sup>103</sup> Brachytherapy for Prostate Cancer. The question of Transperineal Ultrasound Guided Iodine<sup>125</sup> or Palladium<sup>103</sup> Brachytherapy for Prostate Cancer was restated and evaluated at the January 16, 1997 Clinical Policy Committee Meeting. Committee members agreed that there was inadequate evidence to compare the benefits of the three active treatment options but that there was adequate evidence (large case series) to compare the complications of the three options. Among the three active treatment options, it was agreed that brachytherapy appeared to have the lowest rate of complications. Based on this information the Committee recommended to the Clinical Planning and Improvement Council and the Delivery System Operating Team that brachytherapy be added to the list of covered treatment options for localized prostate cancer. This recommendation was accompanied by the stipulation that educational material outlining the treatment options be developed for patient education in order that they can make an informed decision about their treatment course. Not all patients with Prostate Cancer are eligible candidates for Transperineal Ultrasound Guided Iodine<sup>125</sup> or Palladium<sup>103</sup> Brachytherapy for Prostate Cancer. Documentation of the screening criteria used to identification of the eligible candidates is the purpose of this document. In late 2001 the criteria were reviewed by Dr. Nico DeWette and updated based on the current practice and experience with Prostate Seed Implant and Combined Therapy

## 12/14/1994: MTAC REVIEW

### Prostate Cancer Brachytherapy

**Evidence Conclusion:** The conclusion of the committee was that there was inadequate follow-up data supporting the efficacy of Transperineal Ultrasound Guided Iodine<sup>125</sup> or Palladium<sup>103</sup> Brachytherapy for Prostate Cancer.

## 01/16/1997: MTAC REVIEW

### Prostate Cancer Brachytherapy

**Evidence Conclusion:** Committee members agreed that there was inadequate evidence to compare the benefits of the three active treatment options but that there was adequate evidence (large case series) to compare the complications of the three options. Among the three active treatment options, it was agreed that brachytherapy appeared to have the lowest rate of complications. Based on this information the Committee recommended to the Clinical Planning and Improvement Council and the Delivery System Operating Team that brachytherapy be added to the list of covered treatment options for localized prostate cancer. This recommendation was accompanied by the stipulation that educational material outlining the treatment options be developed for patient education in order that they can make an informed decision about their treatment course.

## 2001: MTAC REVIEW

### Prostate Cancer Brachytherapy

**Evidence Conclusion:** In late 2001 the criteria were reviewed by Dr. Nico DeWette and updated based on the current practice and experience with Prostate Seed Implant and Combined Therapy.

**Articles:** Wennberg, John E., Assessing Therapies for Benign Prostatic Hypertrophy and Localized Prostate Cancer (PORT), Agency for Health Care Policy and Research, Medical Outcomes and Guidelines Sourcebook, 273-288 Stock et al. Prostate Specific Antigen and Biopsy Results following Interactive Ultrasound Guided Transperineal Brachytherapy for Early Stage Prostate Carcinoma. Cancer. 1996, 77:2386-92

Wallner et al. Tumor Control and Morbidity Following Transperineal Iodine 125 Implantation for Stage T1/T2 Prostatic Carcinoma. Journal of Clinical Oncology. 1996, 14:449-53.

Kaye, Keith W., et al. Detailed Preliminary Analysis of <sup>125</sup>Iodine Implantation for Localized Prostate Cancer Using Percutaneous Approach. The Journal of Urology. March 1995. 153: 1020-1025.

Blasko, John C., et al., Brachytherapy and Organ Preservation in the Management of Carcinoma of the Prostate. Seminars in Radiation Oncology. 1993: 3(4), 240-249.

## **Radioactive Seeds for Treatment of Recurrent High-Grade Glioblastoma**

### BACKGROUND

Gliomas are the most common primary tumors of the adult brain. Primary brain tumors are those that arise from brain tissue itself, rather than metastasizing to the brain from another location. One of the most commonly diagnosed types of glioma is glioblastoma multiforme (GBM) which is defined as a Grade 4 (high-grade) astrocytoma. High-grade tumors are by definition, rapidly growing and typically develop at a distinct focus in the brain and become more diffuse in their spread as they progress. Several therapies for high-grade glioblastomas are currently employed. No treatment has been shown to cure these tumors, most likely because tumor cells infiltrate into surrounding tissue and this tumor cell type has been shown to be moderately resistant to chemo and radiation therapy. Treatment for glioblastoma multiforme typically involves surgery to reduce the size of the tumor and external beam radiation therapy. External beam radiotherapy can be delivered using a standard x-ray machine or focused on a small area of three dimensionally localized tissue using stereotactic radiosurgery. Systematic chemotherapy is usually a third line treatment and. One proposed treatment for glioblastoma is the use of stereotactically implanted radioactive seeds (brachytherapy) at the site of the tumor. The potential advantage of brachytherapy is that it allows high dose radiation to be applied directly to the tumor site and may avoid radionecrosis caused by high doses of externally applied radiation and toxic effects of chemotherapy. Glioblastoma is typically associated with a fatal outcome. Brachytherapy for malignant brain tumors has been practiced since the early 1980s. Brachytherapy applied as a boost to external beam radiation therapy has become part of the initial treatment of patients with malignant gliomas. Previous reports on the use of brachytherapy for patients with malignant gliomas have suggested improved survival for some patients. The largest experience to date has been with temporary high-activity brachytherapy implants. However, temporary implants have certain disadvantages compared with permanently implanted seeds, including higher costs and the need for more rigorous radiation safety precautions during the period of implantation.

## 13/13/2000: MTAC REVIEW

### Radioactive Seeds for Treatment of Recurrent High-Grade Glioblastoma

**Evidence Conclusion:** Evidence identification was conducted by searching MEDLINE from 1990-1999 using the terms: glioblastoma, brachytherapy and neoplasm recurrence. The published scientific evidence consists of 4 case series with no comparison group or comparison only to historical controls. Case series do not provide

reliable information regarding efficacy as they are subject to bias because they lack control groups that allow elimination of confounding and selection bias. Publication bias can also influence whether negative results are reported in the literature. The studies reviewed in November 2000 have a number of limitations including a small sample size, potential selection bias, lack of a proper control group, and in one of the studies, the fact that different methods variables were used to compare groups of patients. Given these limitations, there is insufficient evidence to draw conclusions about the efficacy and safety of brachytherapy for patients with glioblastoma. It was noted that glioblastoma has the worst prognosis and shortest survival times of any type of primary brain tumor. All treatments serve only to extend survival, usually by a matter of 2-3 months usually at the cost of significant treatment related morbidity. Recent improvement in imaging techniques and more complete surgical resection makes it impossible to use historical control patients as valid comparisons with respect to clinical outcomes.

**Articles:** The search yielded 20 articles. 18 articles were not directly relevant or were review articles, letters, or case reports. Two (2) empirically relevant case series were identified (evidence tables attached). *The articles selected for critical appraisal include:* Patel et al. Permanent Iodine-125 interstitial implants for the treatment of recurrent glioblastoma multiforme. *Neurosurgery* 2000; 46:1123-1130. See [Evidence Table](#)  
 J Clin Oncol 1998;16:2202-12 entitled Iodine 131-labeled antitenascin monoclonal antibody 81C6 treatment of patients with recurrent malignant Gliomas: Phase I trial results. See [Evidence Table](#)  
 Shrieve, DC et al, *Neurosurgery*, 1995, 36:275-284 See [Evidence Table](#)  
 Halligan, JB et al, *Int J. Radiation Oncology Biol. Phys.* 1996, 35:541-547 See [Evidence Table](#)  
 Sneed, PK et al, *Seminars in Surgical Oncology*, 1997;13 See [Evidence Table](#)  
 Gaspar, LE, et al. *Int J. Radiation Oncology Biol. Phys.* 1999, 43:977-82 See [Evidence Table](#)  
 Gaspar, LE, et al. *Int J. Radiation Oncology Biol. Phys.* 1999, 43:977-82 See [Evidence Table](#)  
 Koot et al. Brachytherapy: Results of two different therapy strategies for patients with primary glioblastoma. *Cancer* 2000;88:2796-802. See [Evidence Table](#)

Radioactive Seeds for Treatment of Recurrent Malignant High-Grade Glioblastoma does not meet *Kaiser Permanente Medical Technology Assessment Criteria*.

## Applicable Codes

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

| CPT® Codes | Description   |
|------------|---|
| 19296      | Placement of radiotherapy afterloading expandable catheter (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   |
| 20555      | Placement of needles or catheters into muscle and/or soft tissue for subsequent interstitial radioelement application (at the time of or subsequent to the procedure)   |
| 31643      | Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with placement of catheter(s) for intracavitary radioelement application  |
| 41019      | Placement of needles, catheters, or other device(s) into the head and/or neck region (percutaneous, transoral, or transnasal) for subsequent interstitial radioelement application  |
| 58346      | Insertion of Heyman capsules for clinical brachytherapy   |
| 61770      | Stereotactic localization, including burr hole(s), with insertion of catheter(s) or probe(s) for placement of radiation source  |
| 76965      | Ultrasonic guidance for interstitial radioelement application   |
| 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)  |
| <b>77750</b>      | Infusion or instillation of radioelement solution (includes 3-month follow-up care)   |
| <b>77761</b>      | Intracavitary radiation source application; simple  |
| <b>77762</b>      | Intracavitary radiation source application; intermediate  |
| <b>77763</b>      | Intracavitary radiation source application; complex   |
| <b>77768</b>      | Remote afterloading high dose rate radionuclide skin surface brachytherapy, includes basic dosimetry, when performed; lesion diameter over 2.0 cm and 2 or more channels, or multiple lesions |
| <b>77770</b>      | Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 1 channel  |
| <b>77771</b>      | Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 2-12 channels  |
| <b>77772</b>      | Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; over 12 channels                                       |
| <b>77778</b>      | Interstitial radiation source application, complex, includes supervision, handling, loading of radiation source, when performed   |
| <b>77789</b>      | Surface application of low dose rate radionuclide source  |
| <b>77799</b>      | Unlisted procedure, clinical brachytherapy  |
| <b>0395T</b>      | High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per fraction, includes basic dosimetry, when performed  |
| <b>HCPC Codes</b> | <b>Description</b>  |
| <b>G0458</b>      | Low dose rate (LDR) prostate brachytherapy services, composite rate   |

**\*Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

\*\*To verify authorization requirements for a specific code by plan type, please use the [Pre-authorization Code Check](#).

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| Date Created | Date Reviewed   | Date Last Revised |
|--------------|---|-------------------|
| 1998         | 06/01/2010 <sup>MDCRPC</sup> , 12/07/2010 <sup>MDCRPC</sup> , 09/06/2011 <sup>MDCRPC</sup> , 10/04/2011 <sup>MDCRPC</sup> , 08/07/2012 <sup>MDCRPC</sup> , 06/04/2013 <sup>MDCRPC</sup> , 04/01/2014 <sup>MPC</sup> , 02/03/2015 <sup>MPC</sup> , 12/01/2015 <sup>MPC</sup> , 10/04/2016 <sup>MPC</sup> , 08/01/2017 <sup>MPC</sup> , 06/05/2018 <sup>MPC</sup> , 06/04/2019 <sup>MPC</sup> , 06/02/2020 <sup>MPC</sup> , 06/01/2021 <sup>MPC</sup> , 06/07/2022 <sup>MPC</sup> , 06/06/2023 <sup>MPC</sup> , 03/12/2024 <sup>MPC</sup> | 07/07/2020        |

<sup>MDCRPC</sup> Medical Director Clinical Review and Policy Committee

<sup>MPC</sup> Medical Policy Committee

| Revision History | Description of change  |
|------------------|--|
| 06/14/2016       | Added retired LCD language   |
| 05/18/2015       | Added AccuBoost to insufficient evidence table   |
| 09/08/2015       | Revised LCD L34065   |
| 11/10/2015       | Removed Electronic Brachytherapy for non-melanoma skin cancer. See separate criteria.  |
| 04/19/2016       | Changed Medicare language as LCD 34065 was retired.  |
| 08/11/2016       | Revised retired LCD language   |
| 06/02/2020       | Removed deleted codes 77326, 77327, 77328, 77785, 77786, 77787, 0182T  |
| 06/24/2022       | Remove codes 55875, 55876, 55920, 57155, 57156   |
| 07/07/2020       | MPC approved to adopt updates to the clinical indications for Non-Medicare. Requires 60-day notice, effective date 12/01/2020. |