| 8.01.14 | Brachytherapy for Clinically Localized Prostate Cancer Using Permanently Implanted Seeds | | |
|---|---|---|---|
| **Original Policy Date:** | January 1, 2008 | **Effective Date:** | September 1, 2023 |
| **Section:** | 8.0 Therapy | **Page:** | Page 1 of 22 |

## Policy Statement

I. Brachytherapy using permanent transperineal implantation of radioactive seeds may be considered **medically necessary** for the treatment of localized prostate cancer when used for **either** of the following criteria (see Policy Guidelines section):
   A. In conjunction with external-beam radiotherapy
   B. As monotherapy

II. Brachytherapy using permanent transperineal implantation of radioactive seeds for the treatment of localized prostate cancer is considered **investigational** for:
   A. Focal prostate brachytherapy
   B. Prostate cancer not localized to the prostate

See Policy Guidelines for allowable codes/number of units.

**NOTE**: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

## Policy Guidelines

Permanent brachytherapy with only implanted seeds is generally used in individuals whose prostate cancer is considered low risk. Active surveillance is generally recommended for very low risk prostate cancer. Permanent brachytherapy combined with external-beam radiotherapy (3-dimensional conformal radiotherapy [3D-CRT], intensity-modulated radiotherapy, or proton beam therapy) is used, sometimes with androgen deprivation therapy, to treat higher risk disease. Adequate dose escalation should be achieved with combination permanent brachytherapy and 3D-CRT. Intensity-modulated radiotherapy should be limited to cases in which 3D-CRT planning is unable to meet dose-volume constraints for normal tissue tolerance.

**Remote afterloading brachytherapy** systems automatically administer a radioisotope directly to cancerous tissue, thereby minimizing the radiation dose to surrounding tissue and eliminating the radiation exposure to hospital staff. The amount of the radiation dose varies with the brachytherapy method chosen for treatment delivery: low-dose-rate (LDR) brachytherapy uses an implanted source that delivers a dose of 40 to 60 centigrays (cGy) per hour over several days; high-dose-rate (HDR) brachytherapy uses a traveling (stepping) source that delivers a dose greater than 100 cGy per minute for 5 to 30 minutes; pulsed-dose-rate (PDR) brachytherapy uses a cable-driven source delivering a dose of up to about 300 cGy per hour for 10 to 30 minutes, repeated over several days.

Prostate cancer risk is often defined using the following criteria (Epstein):

- Low risk: PSA (prostate-specific antigen) level of 10 ng/mL or less, Gleason score of 6 or less, and clinical stage T1c (very low risk) or T1 to T2a
- Intermediate risk: PSA level greater than 10 ng/mL but 20 ng/mL or less, or Gleason score of 7, or clinical stage T2b to T2c
- High risk: PSA level greater than 20 ng/mL or Gleason score of 8 to 10, or clinical stage T3a for clinically localized disease and T3b to T4 for locally advanced disease

Permanent low-dose rate brachytherapy, as monotherapy, in the treatment of localized prostate cancer may be best used in individuals older than 60 years with small volume cancer of low-risk disease (Gleason score, less than 7; PSA level, less than 10 mg/mL; stage T1c). Individuals in their 50s

or younger may not be considered ideal candidates for brachytherapy based on concerns about the durability of treatment and quality of life outcomes. However, favorable outcomes in individuals 60 years or younger treated with brachytherapy for localized prostate cancer have been reported. Ideally, the cancer should be within a prostate with a volume of less than 60 mL. Individuals with locally advanced prostate cancer may be undertreated by permanent brachytherapy alone.

### Coding

The procedure is usually performed in 2 stages: a prostate volume study (CPT code 76873) followed at a later date by the implant itself, which is performed in the operating room with the individual under general or epidural anesthesia. Typical isotopes include iodine and palladium, and the selection of isotope is usually based on physician preference. A computed tomography scan is usually performed at some stage after the procedure to determine the quality of the seed placement.

The following codes may also be used for this application:

- **77261**: Therapeutic radiology treatment planning; simple
- **77262**: Therapeutic radiology treatment planning; intermediate
- **77263**: Therapeutic radiology treatment planning; complex
- **77295** (if used in place of 77316-77318): 3-dimensional radiotherapy plan, including dose-volume histograms
- **77370**: Special medical radiation physics consultation
- **77470**: Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)

The following CPT codes for prostate brachytherapy consists of a series of codes describing the treatment planning, dosimetry, and delivery of radiotherapy:

- **76873**: Ultrasound, transrectal; prostate volume study for brachytherapy treatment planning (separate procedure)
- **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)
- **77778**: Interstitial radiation source application, complex, includes supervision, handling, loading of radiation source, when performed
- **77790**: Supervision, handling, loading of radiation source

The following CPT code is a surgical code for placement of the brachytherapy catheter:

- **55875**: Transperineal placement of needles or catheters into prostate for interstitial radioelement application, with or without cystoscopy

### Allowable Codes and Frequencies for Brachytherapy

| Description | Code | Maximum per course of treatment | Notes |
|---|---|---|---|
| Clinical Treatment Planning | 77261, 77262 or 77263 | 1 | When used as standalone or with external beam, only one plan is allowed. |
| Simulation | 77280, 77285, 77290 | 5 | May not be billed with 77301 |
| Verification Simulation | 77280 | 5 | May not be billed with 77301 |
| Respiratory Motion Management | 77293 | 0 | Not needed for brachytherapy alone |
| 3D CRT Plan | 77295 | 1 per insertion, max 5 | May not be billed with 77301 or with 77316/77317/77318 |

| Description | Code | Maximum per course of treatment | Notes |
|---|---|---|---|
| Brachytherapy Isodose Plan | 77316, 77317 or 77318 | 1 per insertion, max 5 | cannot be billed along with 77295 |
| Special Radiation Physics Consult | 77370 | 0 | May allow x 1; documentation of medical necessity required |
| Special MD Consultation (Special Tx Procedure) | 77470 | 1 | May allow x 1; documentation of medical necessity required for more than 1 unit |
| Supervision, Handling, Loading of Radiation Source | 77790 | 1 | May not be billed with 77761, 77762, 77763, 77770, 77771, 77772 or 77778 |
| Application of Radiation Sources: LDR Brachytherapy | 77761, 77762, 77763, 77778 | 1 | May not be billed with 77770, 77771, 77772 |
| Application of Radiation Sources: HDR Brachytherapy | 77770, 77771, 77772 | 4 | Only one delivery code allowed per day per course of therapy. May not be billed with 77761, 77762, 77763, 77778, 77790. |
| High Dose Rate Electronic Brachytherapy, per fraction | 0394T-0395T | 0 | Investigational for the treatment of skin lesions. |
| Placement of Radiotherapy Afterloading Catheters | 19296, 19297, 19298 | 1 | |

## Description

Brachytherapy is a procedure in which a radioactive source (e.g., radioisotope "seeds") is permanently or temporarily implanted in or near the tumor (e.g., placed into the prostate gland to treat localized prostate cancer). The radiation from brachytherapy penetrates only short distances and is intended to deliver tumoricidal radioactivity directly to the tumor to improve local control while sparing surrounding normal tissue. Focal (subtotal) prostate brachytherapy is a form of organ-preserving therapy for small localized prostate cancers. This evidence review only assesses permanent low-dose rate (LDR) brachytherapy in prostate cancer.

## Related Policies

- Focal Treatments for Prostate Cancer
- Intensity-Modulated Radiotherapy of the Prostate
- Radiation Oncology
- Whole Gland Cryoablation of Prostate Cancer

## Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

## Regulatory Status

A large number of permanently implanted seeds for brachytherapy of prostate cancer are available. They have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process, including I-Seed® (Atherogenic), Proxcelan™ Cs-131 (IsoRay Medical), and Brachy Source® Brachytherapy Seed Implants (C.R. Bard). FDA product code: KXK.

## Rationale

### Background

#### Prostate Cancer

In 2022, it has been estimated that 14.0% of all new cancer diagnoses will involve the prostate. In addition, as of 2019 , estimates have suggested that over 3.2 million men in the U.S. are living with prostate cancer.[1,]There are also racial and ethnic disparities in prostate cancer, as shown by epidemiologic studies; in the U.S., Black men have a 1.5 times greater chance of developing prostate cancer than White men and are 2.2 times more likely to die due to prostate cancer.[2,]

#### Brachytherapy

Brachytherapy is a procedure in which a radioactive source (e.g., radioisotope "seeds") is used to provide extremely localized radiation doses. With brachytherapy, the radiation penetrates only short distances; this procedure is intended to deliver tumoricidal radioactivity directly to the tumor and improve local control while sparing surrounding normal tissue. Brachytherapy has been used for localized prostate cancer to provide local tumor control, which has been associated with lower distant metastasis rates and improved patient survival. Seeds can be permanently or temporarily implanted. Permanent (low-dose rate [LDR]) brachytherapy is generally used for low-risk disease; temporary (high-dose rate) brachytherapy is typically reserved for intermediate- or high-risk disease. This evidence review only assesses permanent LDR brachytherapy in prostate cancer.

The proposed biologic advantages of brachytherapy compared with external-beam radiotherapy (EBRT) are related to the dose delivered to the target and the dose delivery rate. The dose rate of brachytherapy sources is generally in the range of 40 to 60 centigray per hour, whereas conventional fractionated EBRT dose rates exceed 200 centigray per minute. Enhanced normal tissue repair occurs at the LDRs. Repair of tumor cells does not occur as quickly, and these cells continue to die during continued exposure. Thus, from a radiobiologic perspective, LDR radiation causes ongoing tumor destruction in the setting of normal tissue repair. Additionally, brachytherapy is performed as a single procedure in the outpatient setting, which many patients may find preferable to multiple EBRT sessions. The total doses of radiotherapy that can be delivered may also vary between EBRT and brachytherapy, especially with newer forms of EBRT such as 3-dimensional conformal radiotherapy and intensity-modulated radiotherapy.

Brachytherapy has not been considered appropriate for patients with a large prostate or those with a urethral stricture because the procedure results in short-term swelling of the prostate, which can lead to urinary obstruction. As with all forms of radiotherapy, concerns exist with the long-term risk of treatment-related secondary malignancies. Reports have also suggested that the clinician's level of experience with brachytherapy correlates with disease recurrence rates.

Studies of permanent brachytherapy have generally used iodine 125 or palladium 103. Use of cesium 131 is also being studied. Iodine 125 requires more seeds, thus reducing dosimetric dependence on any single seed. Postimplant dosimetric assessment should be performed to ensure the quality of the implant and optimal source placement (i.e., targeted tumor areas receive the predetermined radiation dosages while nearby structures and tissues are preserved).

Permanent brachytherapy may be used as monotherapy or as combination therapy with EBRT as a way to boost the dose of radiotherapy delivered to the tumor; this combined modality therapy can be performed with permanent or temporary brachytherapy. The brachytherapy boost is typically done 2 to 6 weeks after completion of EBRT, although the sequence can vary. In some cases, patients also receive androgen deprivation therapy.

Focal or subtotal prostate brachytherapy is a form of more localized, organ-preserving therapy for small localized prostate cancers. Brachytherapy seeds are placed only in the areas where the tumor has been identified rather than throughout the whole prostate gland. The aim of focal therapy is to reduce the occurrence of adverse events associated with brachytherapy, including urinary, bowel, and sexual dysfunction.

### Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

### Permanent Low-Dose Rate Brachytherapy Plus External-Beam Radiotherapy

### Clinical Context and Therapy Purpose

The purpose of permanent low-dose rate (LDR) brachytherapy plus external-beam radiotherapy (EBRT) is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as active surveillance, EBRT alone, surgery, and cryoablation, in individuals with localized prostate cancer.

The following PICO was used to select literature to inform this review.

#### *Populations*

The relevant population of interest is individuals with localized prostate cancer.

Brachytherapy has not been considered appropriate for patients with a large prostate or those with a urethral stricture because the procedure results in short-term swelling of the prostate, which can

lead to urinary obstruction. As with all forms of radiotherapy, concerns exist with the long-term risk of treatment-related secondary malignancies.

*Interventions*
The therapy being considered is permanent LDR brachytherapy plus EBRT.

Brachytherapy is a procedure in which a radioactive source (e.g., radioisotope "seeds") is permanently or temporarily implanted in or near the tumor (e.g., placed into the prostate gland to treat localized prostate cancer). The radiation from brachytherapy penetrates only short distances and is intended to deliver tumoricidal radioactivity directly to the tumor to improve local control while sparing surrounding normal tissue.

Studies of permanent brachytherapy have generally used iodine 125 or palladium 103. Use of cesium 131 is also being studied. Iodine 125 requires more seeds, thus reducing dosimetric dependence on any single seed.

*Comparators*
Comparators of interest include active surveillance, EBRT alone, surgery, and cryoablation.

*Outcomes*
The general outcomes of interest are overall survival (OS), disease-specific survival, and treatment-related morbidity (Table 1).

**Table 1. Outcomes of Interest for Individuals with Localized Prostate Cancer**

| Outcomes | Details |
|---|---|
| **Disease-specific survival** | Outcomes of interest include progression-free survival and tumor progression [Timing: ≥1 year] |
| **Treatment-related morbidity** | Outcomes of interest include treatment-related adverse events such as urinary blockage, sexual dysfunction, or gastrointestinal toxicities [Timing: ≥1 year] |

## Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

## Review of Evidence
### Systematic Reviews
Kee et al (2018) published a systematic review and meta-analysis comparing brachytherapy boost and EBRT boost after EBRT for patients with prostate cancer.[3,] Three RCTs with a total of 703 participants were included. Brachytherapy boost had a significant benefit over EBRT boost for 5-year progression-free survival (hazard ratio [HR], 0.49; 95% confidence interval [CI], 0.37 to 0.66; p<.01); there was no significant difference between the 2 treatments for OS (HR, 0.92; 95% CI, 0.64 to 1.33; p=.65). There was also no difference in rates of ≥ grade 3 late genitourinary (GU) (relative risk [RR], 2.19; 95% CI, 0.76 to 6.30; p=.15) or late gastrointestinal (GI) toxicities (RR, 1.85; 95% CI, 1.00 to 3.41; p=.05). No limitations for this analysis were reported.

### Randomized Controlled Trials

No RCTs not included in the meta-analysis above were identified that compared LDR brachytherapy plus EBRT with LDR brachytherapy or with EBRT alone in patients who have clinically localized prostate cancer. Morris et al (2017) reported on the Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy trial, which evaluated patients who received androgen deprivation therapy (ADT) and EBRT.[4,] The investigators compared EBRT boost with an LDR brachytherapy boost. The primary outcome (biochemical progression-free survival [PFS]) at a median follow-up of 6.5 years significantly favored the LDR brachytherapy group (p=.004). In a subgroup analysis limited to patients with intermediate-risk prostate cancer (i.e., clinically localized disease), biochemical PFS was significantly higher in the brachytherapy boost group (p=.003). Overall and disease-specific survival did not differ significantly between the LDR brachytherapy boost and the EBRT boost groups.

Morris et al (2018) published a reanalysis of the Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy trial comparing biochemical failure using a prostate-specific antigen (PSA) threshold of >0.2 ng/mL to the Phoenix threshold (nadir +2 ng/mL).[5,] At follow-up times >4 years, patients receiving LDR-permanent brachytherapy were less likely to experience biochemical failure (log rank p=.001). The Kaplan-Meier biochemical PFS was superior for LDR-permanent brachytherapy compared with dose-escalated EBRT when applying the nadir + 2 ng/mL threshold (5-, 7-, and 9-year results were 90%, 88%, and 85% vs. 84%, 76%, and 63%, respectively).

### Observational Studies

Pasalic et al (2021) reported on the Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study, which was a prospective, multicenter study that evaluated 695 patients who received EBRT alone (n=583) and EBRT plus LDR brachytherapy (n=112) for localized prostate cancer.[6,] Adjunctive ADT was given based on a risk-based assessment at the discretion of each clinician. Patient-reported outcomes were the primary outcomes assessed, including Expanded Prostate Cancer Index Composite domains (e.g., urinary irritative function, bowel function). After a median follow-up of 73 months, no significant differences were found between EBRT alone and EBRT plus LDR brachytherapy for 5-year OS (92.8% vs. 95.2%), 7-year OS (84% vs. 91%), 5-year prostate cancer-specific survival (99.6% vs. 99%), and 7-year prostate cancer-specific survival (96.9% vs. 97.3%). Treatment with EBRT plus LDR brachytherapy was associated with clinically meaningful worse urinary irritative function (adjusted mean difference, -5.4; 95% CI, -9.3 to -1.6; p=.006) and bowel function scores (-4.1; 95% CI, -7.6 to -0.5; p=.027) through 3 years; the differences between treatment groups were no longer considered clinically meaningful at 5 years.

Abugharib et al (2017) reported on 579 patients with localized prostate cancer treated using LDR brachytherapy plus EBRT (n=191) or EBRT alone (n=388).[7,] Patients were not randomized to a treatment group, and ADT was given at the physician's discretion to patients in both groups. After a median follow-up of 7.5 years, 13 (7%) patients in the combined treatment group and 77 (20%) patients in the EBRT alone group had a biochemical recurrence. Actutimes biochemical PFS up to 10 years was significantly higher in the combined treatment group than in the EBRT-only group (p=.014). Additionally, local PFS significantly favored the combined treatment group (p=.042), but distant metastasis-free survival did not differ significantly between groups (p=.21). There was no significant difference between groups in the rate of GI toxicity (grade ≥2), but the combined treatment group had a significantly higher incidence of grade 3 GU toxicity than the EBRT-only group.

Serrano et al (2016) evaluated long-term rectal toxicity from LDR brachytherapy patients with prostate cancer (stage T1c to T2b).[8,] A total of 245 patients were followed for at least 5 years (median follow-up, 7.5 years). Eighty-five (33.5%) patients received EBRT plus LDR brachytherapy. Sixteen (6.5%) patients developed rectal toxicity (grade ≥2) and 7 (2.9%) developed rectal toxicity (grade ≥3). Six of the 7 patients who developed grade 3 or 4 rectal toxicity had received combined treatment. The authors did not report the number of patients with grade 2, 3, or 4 rectal toxicity in either group. Moreover, survival outcomes were not reported.

Findings of the Radiation Therapy Oncology Group 0019 multicenter study, published by Lawton et al (2012), evaluated data from 131 patients followed for a median of 8.3 years.[9,] All patients received EBRT followed by permanent LDR brachytherapy. Late GU and/or GI tract toxicity greater than grade 3 was estimated to be 15%, and most commonly included urinary frequency, dysuria, and proctitis. Grade 3 impotence was reported in 42% of patients. These adverse events rates with combined modality therapy were higher than often reported for either brachytherapy or EBRT treatment alone. Estimates of biochemical failure were 18% using the Phoenix definition and 21% using the American Society for Radiation Oncology's definition, and were similar to either treatment alone.

Long-term efficacy and/or toxicity results are also available from large cohorts treated at single institutions. For example, Sylvester et al (2007) reported on results of treatment with EBRT at 45 gray followed by permanent brachytherapy.[10,] In this series, ADT was not used. This report was based on a series of 223 consecutive patients treated between 1987 and 1993; patients had stage T1 to T3 disease. Permanent brachytherapy was performed with radioactive palladium or iodine 4 weeks after EBRT. Fifteen-year biochemical PFS was 88% in the low-risk group, 80% in the intermediate-risk group, and 53% in the high-risk group. Additionally, long-term outcomes were compared with those of 2 institutions that had results for radical prostatectomy (RP). Results were similar across Gleason score categories (e.g., the relapse-free survival was 25% to 30% for those with a Gleason score of 7 for the 3 series of patients but varied for other prognostic factors such as PSA level).

In another single-center report, results were summarized for combined modality therapy using 3-dimensional conformal radiotherapy followed by permanent (palladium) brachytherapy.[11,] This 2007 study involved 282 intermediate- and high-risk patients treated from 1992 to 1996. Fourteen-year biochemical PFS in the intermediate-risk group was 87% and 72% in the high-risk group.

**Section Summary: Permanent Low-Dose Rate Brachytherapy Plus External-Beam Radiotherapy**
No RCTs comparing permanent LDR brachytherapy plus EBRT with EBRT alone in patients with clinically localized prostate cancer have been identified. One RCT compared boost LDR brachytherapy plus boost EBRT with EBRT alone. It found better biochemical PFS but not OS or disease-specific survival in patients who had combined treatment. There are also a number of observational studies, including 2 nonrandomized studies comparing LDR brachytherapy plus EBRT with EBRT alone. One found that the biochemical PFS rate was significantly higher in the combined treatment group; rates of GU but not GI toxicity were significantly higher with combined treatment. The other found differences in urinary irritative function and bowel function were significantly worse at 3 years with combination treatment, but the differences were no longer clinically meaningful at 5 years. Multicenter and single-center uncontrolled studies have found relatively high rates of biochemical PFS after LDR brachytherapy plus EBRT.

### Permanent Low-Dose Rate Brachytherapy As Monotherapy

#### Clinical Context and Therapy Purpose

The purpose of permanent LDR brachytherapy as monotherapy is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as active surveillance, EBRT alone, surgery, and cryoablation, in individuals with localized prostate cancer.

The following PICO was used to select literature to inform this review.

*Populations*
The relevant population of interest is individuals with localized prostate cancer.

*Interventions*
The therapy being considered is permanent LDR brachytherapy as monotherapy.

Brachytherapy is a procedure in which a radioactive source (e.g., radioisotope "seeds") is permanently or temporarily implanted in or near the tumor (e.g., placed into the prostate gland to treat localized prostate cancer). The radiation from brachytherapy penetrates only short distances and is intended to deliver tumoricidal radioactivity directly to the tumor to improve local control while sparing surrounding normal tissue.

Studies of permanent brachytherapy have generally used iodine 125 or palladium 103. Use of cesium 131 is also being studied. Iodine 125 requires more seeds, thus reducing dosimetric dependence on any single seed.

### *Comparators*

Comparators of interest include active surveillance, EBRT alone, surgery, and cryoablation.

### *Outcomes*

The general outcomes of interest are OS, disease-specific survival, and treatment-related morbidity (Table 2).

**Table 2. Outcomes of Interest for Individuals with Localized Prostate Cancer**

| Outcomes | Details |
|---|---|
| **Disease-specific survival** | Outcomes of interest include progression-free survival and tumor progression [Timing: ≥1 year] |
| **Treatment-related morbidity** | Outcomes of interest include treatment-related adverse events such as urinary blockage, sexual dysfunction, or gastrointestinal toxicities [Timing: ≥1 year] |

## Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

## Review of Evidence

### Systematic Reviews

A Cochrane review by Peinemann et al (2011) evaluated the literature on LDR brachytherapy for prostate cancer.[12,] Reviewers focused on the only identified RCT, Giberti et al (2009).[13,] The Giberti et al (2009) trial (detailed below) compared brachytherapy with RP and was considered to have a high risk of bias. Peinemann et al (2011) also conducted a systematic review of brachytherapy.[14,] In this review, the Giberti et al (2009) RCT and 30 nonrandomized studies were included, all of which were also found to have a high risk of bias.

### Randomized Controlled Trials

The Giberti et al (2009) RCT reported on results for 200 low-risk prostate cancer patients randomized to RP or to brachytherapy.[13,] Biochemical PFS rates at 5 years were 90% for RP and 91.7% for brachytherapy. Both treatment groups experienced decreases in quality of life at 6 months and 1 year posttreatment, although brachytherapy patients reported more urinary disorders but better erectile function than the RP group. At 5 year follow-up, functional outcomes did not differ between arms.

### Observational Studies

Several nonrandomized comparative studies have reported outcomes in patients with localized prostate cancer who received one of the several comparative treatments.

### Brachytherapy Monotherapy versus Cryoablation

Williams et al (2012) compared data from the U.S. Surveillance, Epidemiology, and End Results Program, Medicare-linked data on 10,928 patients with localized prostate cancer treated with primary cryoablation or brachytherapy.[15,] Urinary dysfunction occurred more frequently with cryoablation (41.4%) than with brachytherapy (22.2%; p<.001). Erectile dysfunction was also more common after cryoablation (34.7%) than after brachytherapy (21.0%; p<.001). Additionally, the use of ADT was significantly more common after cryoablation than after brachytherapy, suggesting a higher rate of prostate cancer recurrence after cryoablation (1.4 vs. 0.5 per 100 person-years). Bowel complications, however, occurred significantly more frequently with brachytherapy (19%) than with cryoablation (12.1%).

### Brachytherapy Monotherapy versus Radical Prostatectomy

Nepple et al (2013) analyzed data prospectively from 2 centers on 4459 men treated with RP, 972 men treated with brachytherapy, and 1261 men treated with EBRT.[16,]After treatment, the median follow-up was 7.2 years. Brachytherapy did not significantly increase prostate cancer mortality compared with RP using Cox analysis or competing risk analysis; however, EBRT did increase prostate cancer mortality under Cox analysis. Overall mortality increased with both brachytherapy (HR, 1.78; 95% CI, 1.37 to 2.31) and EBRT (HR, 1.71; 95% CI, 1.40 to 2.08) compared with RP.

Urabe et al (2023) published a retrospective, single-center, propensity score matched cohort study analyzing patients with intermediate-risk prostate cancer treated with LDR brachytherapy (n=710) or RP (n=531).[17,] Median follow-up was 108 months for RP and 99 months for LDR brachytherapy. After propensity adjustments, 642 (321 in each group) patients were analyzed. There was no significant difference in OS (p=.99), however, LDR brachytherapy was associated with improved biochemical recurrence-free survival and salvage therapy-free survival compared to RP (p<.001). Compared to LDR brachytherapy, RP was associated with improved metastasis-free survival (p<.001).

### Brachytherapy Monotherapy versus External-Beam Radiotherapy

Several observational studies have used matching to control for potential confounding due to lack of randomization. Loblaw et al (2017) evaluated data on men with clinically localized prostate cancer from the Genitourinary Radiation Oncologists of Canada prostate cancer database.[18,] They identified 458 men treated with LDR brachytherapy, 64 men treated with EBRT, and 90 men treated with stereotactic ablative body radiotherapy (SABR), a high-precision EBRT technique. The investigators created 2 sets of matched cohorts to control for confounding factors: SABR versus LDR brachytherapy and SABR versus EBRT. Cohorts were matched on age, baseline PSA level, T stage, and the number of positive cores. The SABR versus LDR cohorts included 284 patients, 71 of whom received SABR and 213 of whom received LDR brachytherapy. Analysis of SABR versus LDR brachytherapy outcomes found no significant differences between groups in biochemical PFS or OS either before matching (p=.52 and p=.71, respectively) or after matching (p=.33 and p=.56, respectively).

In a 1:1 matched-pair design, Pickles et al (2010) prospectively followed 278 low- and intermediate-risk, localized prostate cancer patients treated with brachytherapy or EBRT (139 patients in each group).[19,] The biochemical control (nadir + 2 ng/mL) at 5 years was 95% in the brachytherapy group and 85% in the EBRT group (p<.001). This rate was unchanged at 7 years in the brachytherapy group but decreased to 75% in the EBRT group. Brachytherapy patients experienced more urinary complaints, whereas EBRT patients had more rectal and bowel issues.

Delouya et al (2017) published a retrospective, single-center cohort study analyzing patients with D'Amico intermediate-risk prostate cancer treated with brachytherapy or EBRT.[20,] Of the 475 patients identified, 222 were treated with brachytherapy and 253 with EBRT. Median follow-up for

patients without biochemical failure was 56 months, and the median time to biochemical failure was 44.5 months. The brachytherapy group had significantly less biochemical failure than EBRT (5.4% vs. 14.2%, respectively; p=.036), and the 7-year biochemical recurrence-free survival rates were 91% and 83%, respectively. In multivariate analysis, only the Cancer of the Prostate Risk Assessment (CAPRA) score was a significant predictor of biochemical failure. Of patients with CAPRA scores of 0, 1, or 2, a better outcome was observed in those treated with brachytherapy (p=.042), but there was no difference in patients with CAPRA scores of 3, 4, or 5 (p=.5). The study was limited by its retrospective design and did not report toxicity data.

Sanmamed et al (2023) reported on a retrospective, single-center cohort study analyzing patients with intermediate-risk prostate cancer treated with either LDR brachytherapy (n=122) or EBRT (n=124).[21,] Median follow-up in the LDR brachytherapy group and the EBRT group was 95 months (interquartile range [IQR], 79 to 118) and 96 months (IQR, 63 to 123), respectively. Biochemical relapse was observed in 5 patients in the LDR brachytherapy group and 24 in the EBRT group. At 60 and 90 months post-initial treatment, the cumulative incidence function of biochemical relapse was 0.9% and 3.5% in the LDR brachytherapy group, respectively, versus 16.6% and 23.7% in the EBRT group, respectively (p<.001 for both comparisons). The incidence of metastases at 90 and 108 months was 0% and 1.6% versus 3.4% and 9.1% in the LDR brachytherapy and EBRT groups, respectively (p=.003). At the last follow-up (8 years), 3 patients treated with EBRT had died from their cancer (prostate cancer specific survival of 97.5%), and no patients had died in the brachytherapy group (p=.09).

### Uncontrolled Studies

Several large uncontrolled observational studies have also been published. A large multicenter study from Italy, published by Fellin et al (2016), included 2237 patients with clinically localized prostate cancer, who were treated with LDR brachytherapy as monotherapy and followed for at least 2 years.[22,] Median follow-up was 65 months. Three-, 5-, and 7-year OS rates were 96.7%, 94.0%, and 89.2%, respectively. Three-, 5-, and 7-year disease-specific survival rates were 99.7%, 99.5%, and 98.4%, respectively. A total of 207 patients experienced biochemical failure after a median of 42 months. The 3-, 5-, and 7-year biochemical PFS rates were 95.7%, 91.9%, and 88.5%, respectively.

An analysis by Pham et al (2016) evaluated outcomes of permanent brachytherapy alone in men with large prostates (>60 mL).[23,] The study included 2076 men with prostate cancer from a prospectively collected database who were treated with iodine-125 brachytherapy without ADT. Two hundred sixty-nine (13%) of the 2076 patients had prostate volumes greater than 60 mL (median volume, 72.5 mL). Men with prostate volumes greater than 60 mL were significantly older than men with prostate volumes of 60 mL or less, and a significantly larger proportion had Gleason scores of 6 and higher for initial PSA levels. Median follow-up was 55 months. The 5-year biochemical PFS rate (the primary efficacy outcome) was 96.7% (95% CI, 94.4% to 98.9%) in men with prostate volumes greater than 60 mL and 92.9% (95% CI, 91.4% to 94.3%) in men with prostate volumes of 60 mL or less (p=.02). Men with prostate volume greater than 60 mL had significantly higher rates of grade 3 and 4 GU and GI toxicity at 5 years (7.2%) than men with prostate volumes of 60 mL or less (3.2%; p<.001). In multivariate analyses, a prostate volume greater than 60 mL was a statistically significant predictor for better biochemical recurrence-free survival and for higher rates of late grade 3 and 4 GU toxicity.

### Section Summary: Permanent Low-Dose Rate Brachytherapy as Monotherapy

One RCT compared LDR brachytherapy as monotherapy with RP and found the 5 year biochemical PFS rate was as high for brachytherapy as it was for RP, and erectile function was better after brachytherapy. Comparative observational studies have found similar survival outcomes with LDR brachytherapy and other treatments; there were lower rates of some adverse events and higher rates of others.

### Focal Prostate Brachytherapy Alone or Combined With External-Beam Radiotherapy

#### Clinical Context and Therapy Purpose

The purpose of focal permanent LDR brachytherapy alone or combined with EBRT is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as active surveillance, EBRT alone, surgery, and cryoablation, in individuals with localized prostate cancer.

The following PICO was used to select literature to inform this review.

*Populations*

The relevant population of interest is individuals with localized prostate cancer.

*Interventions*

The therapy being considered is focal permanent LDR brachytherapy alone or combined with EBRT.

Brachytherapy is a procedure in which a radioactive source (e.g., radioisotope "seeds") is permanently or temporarily implanted in or near the tumor (e.g., placed into the prostate gland to treat localized prostate cancer). The radiation from brachytherapy penetrates only short distances and is intended to deliver tumoricidal radioactivity directly to the tumor to improve local control while sparing surrounding normal tissue. Focal (subtotal) prostate brachytherapy is a form of organ-preserving therapy for small localized prostate cancers.

Studies of permanent brachytherapy have generally used iodine 125 or palladium 103. Use of cesium 131 is also being studied. Iodine 125 requires more seeds, thus reducing dosimetric dependence on any single seed.

*Comparators*

Comparators of interest include active surveillance, EBRT alone, surgery, and cryoablation.

*Outcomes*

The general outcomes of interest are OS, disease-specific survival, and treatment-related morbidity (Table 3).

**Table 3. Outcomes of Interest for Individuals with Localized Prostate Cancer**

| Outcomes | Details |
|---|---|
| **Disease-specific survival** | Outcomes of interest include progression-free survival and tumor progression [Timing: ≥1 year] |
| **Treatment-related morbidity** | Outcomes of interest include treatment-related adverse events such as urinary blockage, sexual dysfunction, or gastrointestinal toxicities [Timing: ≥1 year] |

#### Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

#### Review of Evidence

#### Systematic Reviews

Evidence in the published literature on focal prostate brachytherapy is limited. Reports have primarily focused on methods to delineate and evaluate tumor areas to identify appropriate

candidates for focal prostate therapy and treatment planning approaches. Original clinical reports on patient outcomes after focal brachytherapy are limited.

In a systematic review, Valerio et al (2014) assessed studies on focal prostate cancer therapies.[24,] Only 1 series on focal brachytherapy was included. In that study by Nguyen et al (2012), 318 men received brachytherapy only to the peripheral zone.[25,] In low-risk and intermediate-risk cases, freedom from PSA failure (nadir + 2 ng/mL) was 95.1% and 73% at 5 years and 80.4% and 66.4% at 8 years, respectively. Many questions remain, including treatment effectiveness, patient selection criteria, and posttreatment monitoring approaches.

A systematic review by Baydoun et al (2017) assessing focal therapy for prostate cancer identified the Nguyen et al (2012) series (described above) and another relevant series.[26,] The other study, by Cosset et al (2013), included 21 patients who underwent permanent iodine seed implants for low-risk prostate cancer.[27,] The series reported on toxicity but not on biochemical control or survival outcomes. One patient experienced mild rectal toxicity at 2 months, and no rectal toxicity was reported at 6 or 12 months. The mean score on the International Index of Erectile Function 5 scale was 20.1 at baseline and 19.8 at 12 months (this scale ranges from 0 to 25, with a higher score indicating better function).

### Observational Studies

A nonrandomized comparative study by Kim et al (2020) has reported outcomes in patients with localized prostate cancer who received focal or partial LDR brachytherapy or whole gland LDR brachytherapy.[28,] Sixty patients were identified retrospectively that received focal/partial LDR brachytherapy (n=30) or whole gland LDR brachytherapy (n=30) without supplemental EBRT at a single institution between January 2015 and January 2017. After a median follow-up duration of 45 months, the 3-year biochemical recurrence-free survival was 91.8% and 89.6% for the focal/partial LDR brachytherapy group and whole gland LDR brachytherapy group, respectively, which was not significantly different (p=.554). However, the proportion of patients who reached the 3-year follow-up was significantly lower in the focal/partial LDR brachytherapy group (60%) versus the whole gland LDR brachytherapy group (86.7%). The incidence of GU symptoms were significantly greater with whole gland LDR brachytherapy, as measured by the change in the International Prostate Symptom Score from baseline to 6 months (whole vs. focal/partial change, 5.0 vs. 3.0; p=.018). The incidence of rectal toxicity was numerically higher, but not statistically significant, with whole gland LDR brachytherapy versus focal/partial LDR brachytherapy (33.3% vs. 16.7% ; p=.136).Matsuoka et al (2022) reported on outcomes of focal LDR brachytherapy in 51 patients with low- to intermediate-risk prostate cancer. Propensity scoring was used to select an additional 51 pair-matched patients who received RP.[29,] Patients were followed for a median of 5.7 years, and biochemical failure, additional treatment, and systemic salvage therapy in the focal LDR brachytherapy patients occurred in 24%, 20%, and 8% of patients, respectively. In the RP cohort, 6% of patients underwent systemic salvage therapy. Five-year OS in the focal LDR brachytherapy and RP cohorts were 98% and 100%, respectively (p=.947). Focal LDR brachytherapy patients also achieved greater GU function compared to the RP cohort.

Several uncontrolled observational studies have also been published that have reported longer-term survival outcomes. Saito et al (2021) examined outcomes of hemi-gland LDR brachytherapy for intermediate-risk, unilateral prostate cancer.[30,] Twenty-four patients were included and followed for a median of 61 months. Biochemical failure (PSA failure [nadir + 2 ng/mL])-free survival rates at 3 and 5 years were 86% and 71%, respectively. Treatment failure-free survival (freedom from radical or systemic therapy, metastases, and cancer-specific mortality) rates at 3 and 5 years were 95% and 90%, respectively. The 5-year rate of metastasis-free survival was 100%. Ta et al (2021) reported on outcomes of focal LDR brachytherapy for low- to intermediate-risk prostate cancer.[31,] Thirty-nine patients were included and followed for a mean of 65 months. Biochemical relapse-free survival at 5 years, disease-free survival, and OS were 96.8% ± 0.032%, 79.5% ± 0.076%, and 100%, respectively.

### Section Summary: Focal Prostate Brachytherapy Alone or Combined With External-Beam Radiotherapy

Systematic reviews of focal prostate cancer therapies have identified case series evaluating focal brachytherapy. One nonrandomized comparative study reported similar 3-year biochemical recurrence-free survival with focal/partial LDR brachytherapy versus whole gland LDR brachytherapy. Another nonrandomized comparative study reported superior GU function with focal LDR brachytherapy compared to RP, but similar 5-year OS rates. Small, single center observational studies have reported favorable medium-term oncologic outcomes. Clinical outcomes in larger studies, preferably from RCTs or nonrandomized comparative studies, and long-term follow-up are needed before conclusions can be drawn about the effect of focal brachytherapy on health outcomes in patients with localized prostate cancer.

### Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

### Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

### American Brachytherapy Society

The American Brachytherapy Society (ABS; 2021) convened a task force to provide evidence-based consensus recommendations for low-dose rate (LDR) brachytherapy for the primary treatment of prostate cancer.[32,] Relevant recommendations are:

"Brachytherapy monotherapy could be considered for patients with low-risk disease who decline active surveillance and favorable intermediate risk disease."

"Patients with unfavorable intermediate risk or high-risk disease could be considered for brachytherapy boost in combination with EBRT [external-beam radiotherapy]."

### American College of Radiology

The American College of Radiology (ACR) (2017) published appropriateness criteria for permanent brachytherapy for prostate cancer.[33,] Relevant recommendations are:

> "PPB [permanent prostate brachytherapy] monotherapy remains an appropriate and effective curative treatment for low-risk prostate cancer patients."
>
> "PPB monotherapy can be considered for select intermediate-risk patients. Multiparametric MRI [magnetic resonance imaging] may be useful in selecting such patients."
>
> "High-risk localized prostate cancer treated with PPB should be managed in conjunction with EBRT and ADT [androgen-deprivation therapy]."

In 2022, the ACR, ABS, and the American Society for Radiation Oncology (ASTRO) jointly released a practice parameter for transperineal permanent brachytherapy of prostate cancer.[34,] The practice parameter provides a framework for the appropriate use of LDR brachytherapy either as monotherapy or as a combination treatment with EBRT.

### American Society of Clinical Oncology and Cancer Care Ontario

The American Society of Clinical Oncology and Cancer Care Ontario (2017) issued joint guidelines on brachytherapy for prostate cancer that included the following statement[35,]:

"For patients with intermediate-risk prostate cancer choosing EBRT with or without ADT, brachytherapy boost ( LDR or high-dose rate [HDR]) should be offered to eligible patients. For low-intermediate risk prostate cancer (Gleason 7, prostate-specific antigen, 10 ng/mL or Gleason 6, prostate-specific antigen, 10 to 20 ng/mL), LDR brachytherapy alone may be offered as monotherapy. For patients with high-risk prostate cancer receiving EBRT and ADT, brachytherapy boost (LDR or HDR) should be offered to eligible patients."

### American Urological Association

The American Urological Association (AUA) and ASTRO jointly released a guideline on the management of clinically localized prostate cancer in 2022.[36,] The recommendations made that included guidance on LDR brachytherapy are as follows:

"In patients with low- or favorable intermediate-risk prostate cancer electing radiation therapy, clinicians should offer dose-escalated hypofractionated EBRT (moderate or ultra), permanent LDR seed implant, or temporary HDR prostate implant as equivalent forms of treatment (Strong Recommendation; Evidence Level: Grade B)."

"In patients with unfavorable intermediate- or high-risk prostate cancer electing radiation therapy, clinicians should offer dose-escalated hypofractionated EBRT or combined EBRT + brachytherapy (LDR, HDR) along with a risk-appropriate course of ADT (Strong Reommendation; Evidence Level: Grade B)."

### National Comprehensive Cancer Network

National Comprehensive Cancer Network (v.1.2023) guidelines for prostate cancer note that LDR brachytherapy as monotherapy is indicated for patients with very low-, low-, or favorable intermediate-risk prostate cancer. [37,] Additionally, "LDR or HDR brachytherapy can be added as a boost to EBRT plus ADT in patients with unfavorable intermediate-, high-, or very high-risk prostate cancer being treated with curative intent. Combining EBRT and brachytherapy allows dose escalation while minimizing acute or late toxicity in patients with high-risk localized or locally advanced cancer. This combination has demonstrated improved biochemical control over EBRT plus ADT alone in randomized trials, but with higher toxicity."

The guidelines further state that patients with very large or very small prostates (size cutoffs were not discussed), symptoms of bladder outlet obstruction, or previous transurethral resection of the prostate are more difficult to implant and may suffer an increased risk of adverse events. In cases of an enlarged prostate, neoadjuvant ADT may be used to shrink the prostate. However, increased toxicity would be expected, and prostate size may not shrink.

### National Institute for Health and Care Excellence

In 2005, NICE published guidance on LDR brachytherapy for localized prostate cancer [IPG132].[38,] They state that current evidence on the safety and short- to medium-term efficacy of LDR brachytherapy for localized prostate cancer appears adequate to support the use of the procedure. They note that effects on quality of life and long-term survival remain uncertain.

### U.S. Preventive Services Task Force Recommendations

Not applicable.

### Medicare National Coverage

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

### Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 4.

**Table 4. Summary of Key Trials**

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| *Ongoing* | | | |
| **NCT02692105** | A Phase III Randomized Pilot Study of Low Dose Rate Compared to High Dose Rate Prostate Brachytherapy for Favourable Risk and Low Tier Intermediate Risk Prostate Cancer | 60 | Apr 2026 |
| **NCT02960087** | A Randomized Phase II Trial Evaluating High Dose Rate Brachytherapy and Low Dose Rate Brachytherapy as Monotherapy in Localized Prostate Cancer | 232 | Mar 2028 |
| *Unpublished* | | | |
| **NCT02895854** | LDR Brachytherapy Versus Hypofractionated SBRT for Low and Intermediate Risk Prostate Cancer Patients | 44 | Dec 2021 (unknown) |

NCT: national clinical trial.

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## Documentation for Clinical Review

**Please provide the following documentation:**

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| Type | Code | Description |
|---|---|---|
| CPT® | 55875 | Transperineal placement of needles or catheters into prostate for interstitial radioelement application, with or without cystoscopy |
| | 76873 | Ultrasound, transrectal; prostate volume study for brachytherapy treatment planning (separate procedure) |

| Type | Code | Description |
|---|---|---|
| | 77014 | Computed tomography guidance for placement of radiation therapy fields |
| | 77261 | Therapeutic radiology treatment planning; simple |
| | 77262 | Therapeutic radiology treatment planning; intermediate |
| | 77263 | Therapeutic radiology treatment planning; complex |
| | 77280 | Therapeutic radiology simulation-aided field setting; simple |
| | 77285 | Therapeutic radiology simulation-aided field setting; intermediate |
| | 77290 | Therapeutic radiology simulation-aided field setting; complex |
| | 77293 | Respiratory motion management simulation (List separately in addition to code for primary procedure) |
| | 77295 | 3-dimensional radiotherapy plan, including dose-volume histograms |
| | 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) |
| | 77370 | Special medical radiation physics consultation |
| | 77387 | Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed |
| | 77402 | Radiation treatment delivery, => 1 MeV; simple |
| | 77407 | Radiation treatment delivery, => 1 MeV; intermediate |
| | 77412 | Radiation treatment delivery, => 1 MeV; complex |
| | 77417 | Therapeutic radiology port image(s) |
| | 77470 | Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation) |
| | 77778 | Interstitial radiation source application, complex, includes supervision, handling, loading of radiation source, when performed |
| HCPCS | C1715 | Brachytherapy needle |
| | C1728 | Catheter, brachytherapy seed administration |
| | C2634 | Brachytherapy source, nonstranded, high activity, iodine-125, greater than 1.01 mCi (NIST), per source |
| | C2635 | Brachytherapy source, nonstranded, high activity, palladium-103, greater than 2.2 mCi (NIST), per source |
| | C2636 | Brachytherapy linear source, nonstranded, palladium-103, per 1 mm |
| | C2637 | Brachytherapy source, nonstranded, ytterbium-169, per source |
| | C2638 | Brachytherapy source, stranded, iodine-125, per source |
| | C2639 | Brachytherapy source, nonstranded, iodine-125, per source |
| | C2640 | Brachytherapy source, stranded, palladium-103, per source |
| | C2641 | Brachytherapy source, nonstranded, palladium-103, per source |
| | C2642 | Brachytherapy source, stranded, cesium-131, per source |
| | C2643 | Brachytherapy source, nonstranded, cesium-131, per source |
| | C2644 | Brachytherapy source, cesium-131 chloride solution, per mCi |
| | C2645 | Brachytherapy planar source, palladium-103, per sq mm |
| | C2698 | Brachytherapy source, stranded, not otherwise specified, per source |
| | C2699 | Brachytherapy source, nonstranded, not otherwise specified, per source |
| | G6001 | Ultrasonic guidance for placement of radiation therapy fields |

| Type | Code | Description |
|---|---|---|
| | G6002 | Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy |
| | G6017 | Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface tracking), each fraction of treatment |
| | Q3001 | Radioelements for brachytherapy, any type, each |

## Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

| Effective Date | Action |
|---|---|
| 01/01/2008 | New Policy Adoption Combined the following BSC policies and addressed medical necessity for additional cancer diagnoses.<br>• Brachytherapy for Prostate Cancer<br>• Breast Brachytherapy after Breast-Conserving Surgery, as Boost with Whole Breast Irradiation, or Alone as Accelerated Partial Breast Irradiation(APBI)<br>Interstitial or Balloon Breast Brachytherapy |
| 03/01/2009 | Coding Update<br>Updated codes for 2009 CPT Updates |
| 11/04/2009 | Coding update |
| 04/01/2011 | Policy revision with position change |
| 02/22/2013 | Coding update |
| 07/03/2014 | Coding update |
| 01/30/2015 | Coding update |
| 06/30/2015 | Policy title change from Brachytherapy for Oncologic Indications<br>Policy revision with position change<br>BCBSA Medical Policy adoption |
| 09/30/2015 | Coding update |
| 01/01/2016 | Coding update |
| 09/01/2016 | Policy revision without position change |
| 09/01/2017 | Policy revision without position change |
| 02/01/2018 | Coding update |
| 09/01/2018 | Policy revision without position change |
| 09/01/2019 | Policy revision without position change |
| 06/01/2020 | Administrative update. Policy statement updated. |
| 10/01/2020 | Annual review. No change to policy statement. Coding update. |
| 11/20/2020 | Annual review. No change to policy statement. Policy guidelines and literature updated. Coding update. |
| 08/01/2021 | Annual review. Policy statement and guidelines updated. |
| 09/01/2021 | Administrative update. No change to policy statement.<br>Literature review updated. |
| 12/01/2021 | Administrative update. No change to policy statement. Policy guidelines updated. |
| 08/01/2022 | Annual review. No change to policy statement. |
| 09/01/2022 | Administrative update. No change to policy statement. Literature review updated. |
| 09/01/2023 | Annual review. No change to policy statement. Literature review updated. |

## Definitions of Decision Determinations

**Medically Necessary:** Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

## Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

*Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.*

## Appendix A

| POLICY STATEMENT (No changes) | |
|---|---|
| **BEFORE** | **AFTER** |
| **Brachytherapy for Clinically Localized Prostate Cancer Using Permanently Implanted Seeds 8.01.14**<br><br>**Policy Statement:**<br>I. Brachytherapy using permanent transperineal implantation of radioactive seeds may be considered **medically necessary** for the treatment of localized prostate cancer when used for **either** of the following criteria (see Policy Guidelines section):<br>A. In conjunction with external-beam radiotherapy<br>B. As monotherapy<br><br>II. Brachytherapy using permanent transperineal implantation of radioactive seeds for the treatment of localized prostate cancer is considered **investigational** for:<br>A. Focal prostate brachytherapy<br>B. Prostate cancer not localized to the prostate<br><br>See Policy Guidelines for allowable codes/number of units. | **Brachytherapy for Clinically Localized Prostate Cancer Using Permanently Implanted Seeds 8.01.14**<br><br>**Policy Statement:**<br>I. Brachytherapy using permanent transperineal implantation of radioactive seeds may be considered **medically necessary** for the treatment of localized prostate cancer when used for **either** of the following criteria (see Policy Guidelines section):<br>A. In conjunction with external-beam radiotherapy<br>B. As monotherapy<br><br>II. Brachytherapy using permanent transperineal implantation of radioactive seeds for the treatment of localized prostate cancer is considered **investigational** for:<br>A. Focal prostate brachytherapy<br>B. Prostate cancer not localized to the prostate<br><br>See Policy Guidelines for allowable codes/number of units. |