MP 8.01.33
High-Dose Rate Temporary Prostate Brachytherapy

DISCLAIMER
Our medical policies are designed for informational purposes only and are not an authorization, explanation of benefits or a contract. Receipt of benefits is subject to satisfaction of all terms and conditions of the coverage. Medical technology is constantly changing, and we reserve the right to review and update our policies periodically.

POLICY
High-dose rate prostate brachytherapy may be considered medically necessary as monotherapy or in conjunction with external-beam radiotherapy in the treatment of localized prostate cancer.

High-dose rate prostate brachytherapy is considered investigational in the treatment of prostate cancer when used as salvage therapy.

POLICY GUIDELINES
High-dose rate (HDR) brachytherapy as monotherapy is being used in low- and intermediate-risk patients with localized prostate cancer. HDR brachytherapy combined with external-beam radiotherapy (3-dimensional conformal radiotherapy [3D-CRT], intensity-modulated radiotherapy, or proton beam therapy) may be used for more advanced or aggressive prostate cancers. Adequate dose escalation should be achieved with combination HDR temporary brachytherapy and 3D-CRT. Intensity-modulated radiotherapy should be limited only to cases in which 3D-CRT planning is not able to meet dose-volume constraints for normal tissue tolerance. Permanent low-dose rate brachytherapy using only implanted seeds is generally used in patients 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 is used (sometimes along with androgen deprivation therapy) to treat higher risk disease.

Prostate cancer risk is often defined using the following criteria:

- Low risk: prostate-specific antigen (PSA) level of 10 ng/mL or less, Gleason score of 6 or less, and clinical stage T1c (very low risk) or T1-T2a.
- Intermediate risk: PSA level greater than 10 but 20 ng/mL or less, or Gleason score of 7, or clinical stage T2b-T2c.
- High risk: PSA level greater than 20 ng/mL or Gleason score of 8 to 10, or clinical stage T3a for
High-Dose Rate Temporary Prostate Brachytherapy

CODING
CPT coding for HDR prostate brachytherapy will consist of a series of codes describing the treatment planning, dosimetry, and delivery of radiotherapy. These codes overlap with those describing brachytherapy using permanent seed implantation. However, because the therapy is given over several days, the last 2 CPT codes listed below may be used more than once.

76873 Ultrasound, transrectal; prostate volume study for brachytherapy treatment planning
77316-77318 Brachytherapy isodose plan; simple, intermediate, or complex
77778 Interstitial radiation source application complex
77790 Supervision handling, loading of radiation source.

The surgical code for placement of the brachytherapy catheter is:

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

There are codes specific to afterloading of HDR brachytherapy:

77770 Remote afterloading high-dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 1 channel
77771 2-12 channels
77772 over 12 channels.

BENEFIT APPLICATION

BLUECARD/NATIONAL ACCOUNT ISSUES
State or federal mandates (eg, Federal Employee Program) may dictate that certain U.S. Food and Drug Administration–approved devices, drugs, or biologics may not be considered investigational, and thus these devices may be assessed only by their medical necessity.

High-dose rate brachytherapy is not a widely disseminated procedure, and thus patients seeking this therapy may request access to an out-of-network facility.

BACKGROUND

Brachytherapy for prostate cancer can be delivered in a variety of ways. Perhaps the most common technique uses radioactive seeds permanently implanted into prostate tissue. These seeds contain isotopes that slowly emit radiation of relatively low energy. In contrast, temporary prostate brachytherapy involves the use of higher energy radioisotopes such as iridium 192. The latter isotopes deliver radiation at higher dose rates than permanent seeds and may be more effective in destroying rapidly dividing cancer cells. For implantation, needle catheters are placed into the prostate gland using transrectal ultrasound guidance. Once placed, a dosimetric plan is developed, and the radioactive source is inserted into each needle using an afterloading device. The radioactive source is left in the needle for a predetermined time, called the “dwell” time. The radiation usually is delivered once or twice daily over several days. The dwell time can be altered at various positions along the needle’s length to control dose distribution to the target volume and critical surrounding structures (eg, rectum, urethra). This strategy contrasts with permanent seed implantation in which dosimetry is calculated before needle placement and which cannot be altered after seed implantation. Treatment typically consists of delivering a dose of 4000 to 5000 centigray with external-beam radiotherapy (EBRT) to the prostate and peri-prostatic tissues, while high-dose rate (HDR) brachytherapy is used as the method of dose escalation to the
prostate gland. Total boost doses vary. Additionally, studies are also being conducted using HDR brachytherapy as the sole treatment modality (monotherapy) for prostate cancer.

It is accepted that increasing doses of radiotherapy are associated with improved biochemical control (i.e., stable levels of prostate-specific antigen), and thus there has been an interest in exploring different techniques of dose escalation, simultaneously limiting both early and late toxicities in surrounding tissues. In patients with the locally advanced disease, it has been hypothesized that local failure might be related to large tumor volume and radioresistant cell clones, both of which might respond to higher radiation doses. HDR brachytherapy has been primarily investigated as an adjunct to EBRT for dose escalation. Other techniques for dose escalation include EBRT using intensity-modulated radiotherapy for treatment planning and delivery, proton beam therapy (which may also use intensity-modulated radiotherapy), or EBRT combined with brachytherapy using interstitial seeds.

**REGULATORY STATUS**

A number of devices have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process to deliver HDR brachytherapy to the prostate. The Martinez Prostate Template Set and the Photon Technologies HDR Prostate Template and Accessories are examples of radiation application devices. These devices are intended as accessories to commercially available HDR remote afterloader systems for prostate brachytherapy. Food and Drug Administration product code: JAQ.

**RATIONALE**

This evidence review was created in April 2000 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through May 7, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are 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 to 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 a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one 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.

**HIGH-DOSE RATE BRACHYTHERAPY PLUS EXTERNAL-BEAM RADIOTHERAPY**

**Clinical Context and Therapy Purpose**

The purpose of high-dose rate (HDR) temporary brachytherapy plus external-beam radiotherapy (EBRT) in patients who have localized prostate cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.
The question addressed in this evidence review is: Does use of HDR temporary brachytherapy plus EBRT improve the net health outcome in patients with localized prostate cancer?

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest is patients with localized prostate cancer.

**Interventions**
The therapy being considered is HDR temporary brachytherapy plus EBRT.

**Comparators**
The following therapies are currently being used to make decisions about localized prostate cancer: EBRT, surgery, and cryoablation.

**Outcomes**
The general outcomes of interest are locoregional recurrence, overall survival (OS), and adverse events.

**Timing**
Regular follow-up (every 6 to 12 months) are suggested for the first 5 years posttreatment.

**Setting**
Brachytherapy and EBRT are administered in an outpatient oncology setting.

**Systematic Reviews**
Zaorsky et al (2014) reviewed 38 prospective and retrospective studies (total N=8008 patients) reporting on HDR brachytherapy boost with EBRT for prostate cancer.\(^1\) Five-year freedom from biochemical failure rates were 85% to 100% for low-risk, 80% to 98% for intermediate-risk, 59% to 96% for high-risk patients, and 34% to 85% for locally advanced patients. In all risk groups, 5-year rates of cancer-specific survival, OS, local recurrence, and distant metastases were 99% to 100%, 85% to 100%, 0% to 8%, and 2% to 12%, respectively. Late Radiation Therapy Oncology Group (RTOG) grade 3 or 4 genitourinary (GU) or gastrointestinal (GI) toxicities occurred in less than 6% of patients. Comparisons of HDR brachytherapy with other radiation techniques were inconclusive. Interpretation of results of this systematic review was limited by the number of reports from single-institution studies, the lack of comparative studies, and insufficient reporting on toxicity and quality of life.

**Randomized Controlled Trials**
In a multicenter open-label RCT in Sweden, Lennernäs et al (2015) allocated patients with localized and locally advanced (T1b-T3a, N0, M0) prostate cancer to open radical prostatectomy (RP; n=45) or to combined EBRT (3-dimensional conformal radiotherapy, 25×2 Gray [Gy]) and HDR brachytherapy (2×10 Gy) between 1996 and 2001 (n=44).\(^2\) All patients received total androgen blockade that comprised a combination of leuprorelin and flutamide for 6 months. Follow-up assessments included digital rectal examinations if serum prostate-specific antigen (PSA) levels exceeded 10 ng/mL. Quality of life changes were assessed using the European Organization of Research and Treatment of Cancer Quality of Life Questionnaire C33.\(^3\) Patients completed the RTOG/European Organization of Research and Treatment of Cancer Toxicity Scale at 12, 24, and 60 months posttreatment. No statistically significant between-group differences were reported for any of the European Organization of Research and Treatment of Cancer Quality of Life Questionnaire C33 variables or treatment-associated toxicities. Sixty-eight (76%) patients were alive at 10-year follow-up; 8 patients (6 in the RP group, 2 in the 3-dimensional conformal
radiotherapy group; 9% total) died of prostate cancer, 13 (n=6 in the RP group, n=7 in the 3-dimensional conformal radiotherapy group) died of other causes.

Hoskin et al (2007) reported on a European single-center randomized trial of 220 patients conducted between 1997 and 2005. It compared EBRT at 55 Gy with EBRT at 35.75 Gy plus HDR brachytherapy in patients with prostate cancer. With a median follow-up of 30 months, an improvement was reported in actuarial biochemical recurrence-free survival (BRFS), as well as a lower incidence of acute rectal discharge. Hoskin et al (2012) later reported on longer term follow-up of 218 patients from this phase 3 trial. Seventy-six percent of patients also received androgen-deprivation therapy. BRFS was greater in the combination treatment group after 4 years (median time to relapse, 116 months) than in the EBRT-only treatment group (median time to relapse, 74 months). Estimates of BRFS rates for the combination group at 5, 7, and 10 years were 75%, 66%, and 46% compared with 61%, 48%, and 39% for the EBRT-only group, all respectively (p=0.04). However, OS did not differ significantly between treatment arms. Estimates of OS rates for the combination group at 5, 7, and 10 years were 88%, 81%, and 67% compared with 89%, 88%, and 79% for the EBRT-only group, all respectively (p=0.2). Severe urinary symptoms (26%-31%) and bowel events (6%-7%) did not differ significantly between groups at 5 years or 7 years. Erectile dysfunction rates were not reported.

**Observational Studies**

Boehm et al (2016) published a single-center retrospective analysis of 5619 patients with clinically localized prostate cancer who were treated between 1999 and 2009 with HDR brachytherapy plus EBRT (n=419) or RP (n=5200). Eligibility criteria included stage cT1 or cT2 prostate cancer, a prostate volume of 60 mL or less, no neoadjuvant androgen suppression therapy, and no urinary retention symptoms. HDR brachytherapy treatment (18 Gy in 2 fractions) preceded EBRT (50.4 Gy, 1.8 Gy per fraction with 5 fractions per week). In an unmatched analysis of the overall cohort (N=5619), 5-year OS rates were 97.1% in the RP group and 92.4% in the HDR brachytherapy plus EBRT group (p<0.01). An analysis was also conducted after matching the 2 groups on a number of variables including age, cardiovascular disease, diabetes, PSA level, Gleason score, clinical stage, and years of treatment. Five-year OS rates in the matched cohort (n=1257) did not differ significantly between groups. Rates were 95.7% after RP and 92.4% after HDR brachytherapy plus EBRT (p=0.5).

Khor et al (2013) reported on a matched pair analysis that compared 344 patients who received EBRT (46 Gy in 23 fractions) plus HDR brachytherapy (19.5 Gy in 3 fractions) with 344 patients who received only EBRT (74 Gy in 37 fractions) for intermediate- or high-risk prostate cancer. Median biochemical follow-up was 60.5 months. Freedom from biochemical failure at 5 years was 79.8% (95% confidence interval [CI], 74.3% to 85.0%) for the HDR brachytherapy plus EBRT group and 70.9% (95% CI, 65.4% to 76.0%) for the EBRT-only group. However, significantly more grade 3 urethral strictures occurred with HDR brachytherapy (11.8%) than with EBRT (0.3%; p<0.001).

Long-term outcomes of treatment with HDR brachytherapy and EBRT were reported by Yaxley et al (2017). The analysis included 507 patients with localized prostate cancer who were followed for at least 6 years; the median follow-up was 10.3 years. For 271 men with a minimum follow-up of 10 years, the actuarial 10-year OS rate was 85%, and the actual 10-year disease-specific survival rate was 90%. The overall urethral stricture rate was 28.9% (28.9% for men treated before 2005 vs 4.2% for men treated after 2005).

**Section Summary: High-Dose Rate Brachytherapy Plus External-Beam Radiotherapy**

Two RCTs comparing HDR brachytherapy plus EBRT with an alternative therapy were identified. One RCT found no statistically significant differences in outcomes between patients treated with HDR.
brachytherapy and EBRT and those given RP. Another RCT found significantly better BRFS, but not better OS, in patients treated with HDR brachytherapy plus EBRT compared with EBRT alone. Among several controlled observational studies with matched analyses, one reported 5-year OS rates for HDR brachytherapy plus EBRT similar to those of one of the RCTs. In another study, 4-year BPFS was significantly higher after HDR brachytherapy plus EBRT than after EBRT alone. Long-term (at least 10 years) outcomes after HDR brachytherapy and EBRT were reported in a case series: the actuarial 10-year OS rate was 85%, and the disease-specific survival rate was 90%.

### HDR Brachytherapy as Monotherapy

The purpose of high-dose rate (HDR) temporary brachytherapy as monotherapy in patients who have localized prostate cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of HDR temporary brachytherapy as monotherapy improve the net health outcome in patients with localized prostate cancer?

The following PICOTS were used to select literature to inform this review.

- **Patients**
  The relevant population of interest is patients with localized prostate cancer.

- **Interventions**
  The therapy being considered is HDR temporary brachytherapy as monotherapy.

- **Comparators**
  The following therapies are currently being used to make decisions about localized prostate cancer: EBRT, surgery, and cryoablation.

- **Outcomes**
  The general outcomes of interest are locoregional recurrence, OS, and adverse events.

- **Timing**
  Regular follow-up (every 6 to 12 months) are suggested for the first 5 years posttreatment.

- **Setting**
  Brachytherapy and EBRT are administered in an outpatient oncology setting.

### Systematic Reviews

Zaorsky et al (2015), in a comparative effectiveness review, assessed the relative clinical effectiveness of HDR brachytherapy as monotherapy and robotic arm stereotactic body radiotherapy (SBRT). This review was performed using Preferred Reporting Items for Systematic Reviews and Meta-Analyses conventions. Studies selected enrolled 35 or more men with localized (T1-T2, N0-Nx, M0) and locally advanced (T3-T4, N0-Nx, M0) prostate cancer who underwent either therapy and were followed for 12 or more months. To be included, studies had to report disease-related outcomes such as BPFS, PSA kinetics, and late GU or GI tract toxicities. For SBRT, BPFS rates were generally 90% or greater at up to 5 years; for HDR brachytherapy as monotherapy, rates were generally 85% or greater at up to 5 years. Median follow-up was 2.9 years, and longest reported actuarial outcomes were at 8 years. For SBRT, late GU RTOG grade 3 or 4 toxicity rates ranged from 0% to 12%; RTOG late grade 3 or 4 GI toxicity rates ranged from 0% to 5%; for HDR brachytherapy, these rates were 0% to 26% and 0% to 16%, respectively.
Demanes and Ghilezan (2014) published a systematic review analyzing evidence on HDR brachytherapy as monotherapy for prostate cancer. Thirteen studies met selection criteria; they presented clinical outcomes and toxicity data with follow-up ranging from 1.5 to 8.0 years. All risk groups (low, intermediate, high) were represented in selected articles, and a variety of dose and fractionation schedules were reported. Information on study designs, study quality, and other study and patient characteristics were very limited in this review. BPF5 rates reported among the studies ranged from 79% to 100%, and local control rates ranged from 97% to 100%. Grade 3 GU toxicity rates, mainly related to urinary urgency or frequency, ranged from 0% to 16%; grade 3 GI tract toxicity rates ranged from 0% to 2%. Erectile functional preservation rates ranged from 67% to 89%.

Observational Studies

Hegde et al (2018) reported on 437 patients with intermediate-risk prostate cancer who were treated with HDR brachytherapy (n=137) or SBRT (n=300). After a median follow-up of 4 years, the BRFS rate was 98.5% in the HDR brachytherapy group and 95.3% in the SBRT group (p=0.17). There were no statistically significant differences in subgroup analyses (eg, comparing patients with a PSA level <10 and ≥10 ng/mL or clinical stage T1 with T2). OS and disease-specific survival were not reported.

A study by Chiang and Liu (2016) reported on a nonrandomized comparison of outcomes after HDR brachytherapy (n=161), RP (n=97), cryoablation (n=114), or high-intensity focused ultrasound (HIFU; n=12). The study included patients with clinically localized prostate cancer (stage T3a or lower). Mean follow-up was approximately 3 years. In an unadjusted analysis, the length of PSA BRFS differed significantly across the 4 groups (p<0.001). The mean number of months of BRFS was 21.2 in the HDR group, 22.1 in the RP group, 26.4 in the cryotherapy group, and 27.7 in the HIFU group. There was a longer duration of BRFS in the HDR brachytherapy group than in the other 3 groups. Moreover, patients treated with HDR brachytherapy had a significantly lower metastasis-free rate (90.7%) than those who received other treatments (94.8% in the RP group, 99.1% in the cryotherapy group, 99.2% in the HIFU group; p<0.001). OS and disease-specific survival were not reported. The study was not randomized, and baseline differences across groups might have affected outcomes. For example, patients differed at baseline in a number of characteristics, including age, preoperative prostate volume, and Gleason score. The authors did not report adjusted analyses.

Strom et al (2015) published a nonrandomized comparative study assessing 413 men who had low- or intermediate-risk prostate cancer. Patients received HDR brachytherapy (n=85), low-dose rate brachytherapy (n=249), or intensity-modulated radiotherapy (n=79). Median follow-up was 32 months. Primary outcomes were patient-reported and validated health-related quality of life (HRQOL) measures obtained before treatment and at 1, 3, 5, 12, and 18 months posttreatment. Sixty-percent of patients completed pre- and posttreatment HRQOL questionnaires. HRQOL outcomes were mixed. At 1 and 3 months posttreatment, HDR brachytherapy patients reported significantly less deterioration in urinary HRQOL than low-dose rate brachytherapy patients (p=0.005). However, HDR brachytherapy patients had significantly worse sexual HRQOL than low-dose rate brachytherapy at 1, 6, 9, and 18 months after irradiation (p=0.02, p=0.003, p=0.006, p=0.02, respectively). At 18 months, the intensity-modulated radiotherapy group had significantly worse bowel HRQOL scores than either brachytherapy group (p=0.007 for both comparisons).

Long-term survival data have also been reported in uncontrolled series. For example, Demanes et al (2011) reported on 298 patients with previously untreated low- to intermediate-risk localized prostate cancer (median PSA, 6.0 ng/mL) treated with HDR brachytherapy as monotherapy between 1996 and 2005, using 2 treatment protocols. Forty-two gray units in six 7-Gy fractions were delivered using computed tomography for treatment planning in 1 protocol; the other treatment planning delivered 38
Gy units in four 9.5-Gy fractions using ultrasonography. At 8-year follow-up, outcomes included 99% local control, 97% biochemical control (using the Phoenix definition of PSA nadir plus 2 ng/mL), 99% distant metastasis-free survival, 99% cause-specific survival, and 95% OS rate. Grade 2 urinary frequency or urgency was transient in 10% of patients, whereas grade 3 urinary retention was experienced in 3% of patients. GI toxicity was reported as less than 1%.

Hauswald et al (2016) reported on 448 previously untreated men with low- to intermediate-risk localized prostate cancer patients treated with HDR brachytherapy. Median follow-up was 78 months (range, 3-216 months). The actuarial 10-year OS rate was 76.7% (95% CI, 69.9% to 82.2%) and the actuarial 10-year BPFS rate was 97.8% (95% CI, 95.5% to 98.9%) The incidence of grade 3 or 4 GU toxicity during follow-up was 4.9%. No grade 3 or 4 GI toxicity occurred.

Section Summary: HDR Brachytherapy as Monotherapy
A number of observational studies, controlled and uncontrolled, have been published. Systematic reviews have reported BRFS rates of 80% to 100%. One nonrandomized comparative study found similar rates of BRFS in patients treated with HDR brachytherapy and SBRT. However, another comparative study found significantly shorter BRFS and a lower metastases-free rate in patients who were treated with HDR brachytherapy compared with those treated with RP, cryotherapy, or HIFU. As a nonrandomized study, patients differences in baseline characteristics might have affected outcomes. Long-term survival data are available from case series; one found an 8-year OS rate of 95% and another reported an actuarial 10-year survival rate of 77%.

HDR BRACHYTHERAPY AS SALVAGE TREATMENT
The purpose of high-dose rate (HDR) temporary brachytherapy as salvage treatment with or without EBRT in patients who have treatment-resistant or recurrent prostate cancer and no disseminated disease is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of HDR temporary brachytherapy as salvage treatment with or without EBRT improve the net health outcome in patients with localized prostate cancer?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is patients with localized prostate cancer.

Interventions
The therapy being considered is HDR temporary brachytherapy as salvage treatment with or without EBRT.

Comparators
The following therapies are currently being used to make decisions about localized prostate cancer: active surveillance, surgery, and cryoablation.

Outcomes
The general outcomes of interest are locoregional recurrence, OS, and adverse events.

Timing
Regular follow-up (every 6 to 12 months) are suggested for the first 5 years posttreatment.
High-Dose Rate Temporary Prostate Brachytherapy

Setting
Brachytherapy and EBRT are administered in an outpatient oncology setting.

Case Series
Data on HDR brachytherapy as salvage treatment after failed prior radiotherapy are limited; there are no RCTs or nonrandomized comparative studies. Several retrospective case series reporting survival outcomes are described next.

Wojcieszek et al (2016) reported retrospectively on 83 men with locally recurrent prostate cancer treated with salvage HDR brachytherapy (30 Gy in three 10-Gy fractions). Median follow-up was 41 months. OS rates were 93% at 3 years and 86% at 5 years. Biochemical disease-free survival was 76% at 3 years and 67% at 5 years. The most common adverse event was GU toxicity. Acute grade 2 GU toxicity occurred in 29 (33%) men and acute grade 3 GU toxicity in 1 (1%) man. Comparable rates for late GU toxicity were 32 (39%) for grade 2 and 11 (13%) for grade 3. No grade 4 toxicities were reported.

Chen et al (2013) retrospectively analyzed 52 men with locally recurrent prostate cancer treated with salvage HDR brachytherapy (36 Gy in 6 fractions). Median follow-up was 59.6 months. At reporting, median survival had not yet been reached, but the estimated 5-year OS rate was 92% (95% CI, 80% to 97%), and the 5-year biochemical control rate using the Phoenix definition was 51% (95% CI, 34% to 66%). Acute (grade ≥2) GI tract events were not reported. Late grade 2 GI events occurred in 4% of patients. Acute grade 3 GU toxicity occurred in 2%, and late grade 3 GU toxicity occurred in 2%.

Jiang et al (2017) published a retrospective series assessing 29 patients with local failure after EBRT who received HDR brachytherapy as salvage therapy. The minimum length of follow-up was 60 months. The 5-year OS rate was 95.5%, and the 5-year biochemical control rate was 45%. There were no grade 3 or 4 late GI toxicities, but 2 patients experienced grade 2 late GI toxicity. Two patients also experienced urinary incontinence and another experienced urinary tract obstruction.

Section Summary: HDR Brachytherapy as Salvage Treatment
No controlled studies were identified; several retrospective case series with sample sizes ranging from 29 to 83 patients were. In the series, median 5-year OS rates after salvage HDR brachytherapy ranged from 83% to 95.5% and median 5-year biochemical control rates ranged from 45% to 67%. Rates of grade 3 or 4 toxicities were relatively low.

SUMMARY OF EVIDENCE
For individuals who have localized prostate cancer who receive HDR temporary brachytherapy plus EBRT, the evidence includes RCTs, observational studies, and a systematic review. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity. One of the RCTs found no statistically significant differences in outcomes between patients treated with HDR brachytherapy plus EBRT and those receiving radical prostatectomy. The other RCT found significantly better biochemical recurrence-free survival, but not better overall survival, in patients treated with HDR brachytherapy plus EBRT compared with EBRT alone. Among several controlled observational studies with matched analyses, one has reported 5-year overall survival rates for HDR brachytherapy plus EBRT similar to those of one of the RCTs. In another study, 4-year biochemical recurrence-free survival was significantly higher after HDR brachytherapy plus EBRT than after EBRT alone. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have localized prostate cancer who receive HDR temporary brachytherapy as monotherapy, the evidence includes large observational studies and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity. A number of
observational studies, controlled and uncontrolled, have been published. Systematic reviews have found biochemical recurrence-free survival rates of 80% to 100%. Long-term survival data are available from case series; one found an 8-year survival rate of 95% and another found an actuarial 10-year survival rate of 77%. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have treatment-resistant or recurrent prostate cancer and no disseminated disease who receive HDR temporary brachytherapy as salvage treatment with or without EBRT, the evidence includes case series. Relevant outcomes are overall survival, disease-specific survival, and treatment-related morbidity. Only 3 cases series have reported survival outcomes; no comparative studies have been published. In these series, median 5-year overall survival rates after salvage HDR brachytherapy ranged from 83% to 95.5% and the median 5-year biochemical control rate ranged from 45% to 67%. Rates of grade 3 or 4 toxicities were relatively low. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

**CLINICAL INPUT FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 2 physician specialty societies (4 reviews) and 2 academic medical centers while this policy was under review in 2009. There was generally strong support for the use of high-dose rate (as monotherapy and with external-beam radiotherapy) as a treatment option for prostate cancer.

**PRACTICE GUIDELINES AND POSITION STATEMENTS**

**National Comprehensive Cancer Network**

The National Comprehensive Cancer Network guidelines (v.2.2018) on the treatment of prostate cancer state that brachytherapy monotherapy is indicated for patients with very low and low-risk prostate cancer as well patients at intermediate risk with “favorable or good” prognosis. For intermediate-, high-, and very high risk cancers, combination brachytherapy, including high-dose rate (HDR) brachytherapy, with external-beam radiotherapy (EBRT; 40-50.4 gray) is indicated. Permanent low-dose radiotherapy or temporary HDR is indicated for local recurrence following EBRT or primary brachytherapy.

**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:

“For patients with intermediate-risk prostate cancer choosing EBRT with or without androgen-deprivation therapy, brachytherapy boost (LDR [low-dose rate] 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 androgen-deprivation therapy, brachytherapy boost (LDR or HDR) should be offered to eligible patients.”
These guidelines did not address HDR brachytherapy as salvage treatment.

**American College of Radiology**

American College of Radiology Appropriateness Criteria for use of HDR brachytherapy to treat prostate cancer were issued in 2014. The College indicated HDR monotherapy, HDR plus EBRT, and HDR as salvage treatment might be appropriate treatment options.

**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 1.

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NCT: national clinical trial.

**REFERENCES**


**CODES**

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>55875</td>
<td>Transperineal placement of needles or catheters into prostate for</td>
</tr>
</tbody>
</table>
### High-Dose Rate Temporary Prostate Brachytherapy

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>76873</td>
<td>Ultrasound, transrectal, prostate volume study for brachytherapy treatment planning</td>
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<tr>
<td>77316-77318</td>
<td>Brachytherapy isodose plan, code range</td>
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<tr>
<td>77778</td>
<td>Interstitial radioelement application, complex</td>
</tr>
<tr>
<td>77770-77772</td>
<td>Remote afterloading high dose rate radionuclide brachytherapy code range</td>
</tr>
<tr>
<td>77790</td>
<td>Supervision handling, loading of radioelement</td>
</tr>
</tbody>
</table>

### HCPCS
- **C1717**: Brachytherapy source, nonstranded, high dose rate iridium 192, per source
- **Q3001**: Radioelements for brachytherapy, any type, each

### ICD-10-CM
- **C61**: Malignant neoplasm of prostate

### ICD-10-PCS
- **0VH031**: Surgical, male reproductive system, insertion, prostate percutaneous, radioactive element

### Type of Service
- Therapy

### Place of Service
- Outpatient

### POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>06/12/14</td>
<td>Replace policy</td>
<td>Policy updated with literature review through May 26, 2014; references 7, 18, and 27 added; reference 25 updated. Policy statements unchanged</td>
</tr>
<tr>
<td>06/11/15</td>
<td>Replace policy</td>
<td>Policy updated with literature review through April 28, 2015; references 7-8 and 12 added; reference 29 updated. Policy statements unchanged.</td>
</tr>
<tr>
<td>08/13/15</td>
<td>Replace policy</td>
<td>Policy updated with literature review through July 2, 2015; no references added. Policy statements unchanged.</td>
</tr>
<tr>
<td>07/14/16</td>
<td>Replace policy</td>
<td>Policy updated with literature review through June 7, 2016; references 6, 10-11, and 15 added. Policy statements unchanged.</td>
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<tr>
<td>07/25/17</td>
<td>Replace policy</td>
<td>Policy updated with literature review through June 6, 2017; references 8, 11-12, 18, and 20 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>07/25/18</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted. Policy updated with literature review through May 7, 2018; no references added; reference 19 updated. Policy statements unchanged.</td>
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</table>