**MP 8.01.47**
Intensity-Modulated Radiotherapy of the Prostate

**BCBSA Ref. Policy:** 8.01.47  
**Last Review:** 07/25/2018  
**Effective Date:** 07/25/2018  
**Section:** Therapy

**Related Policies**
- 6.01.10 Stereotactic Radiosurgery and Stereotactic Body Radiotherapy  
- 8.01.10 Charged-Particle (Proton or Helium Ion) Radiotherapy  
- 8.01.14 Brachytherapy for Clinically Localized Prostate Cancer Using Permanently Implanted Seeds  
- 8.01.33 High-Dose Rate Temporary Prostate Brachytherapy

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**POLICY**
Intensity-modulated radiotherapy may be considered **medically necessary** in the treatment of localized prostate cancer (see Policy Guidelines).

Intensity-modulated radiotherapy may be considered **medically necessary** after radical prostatectomy as:

- Adjuvant therapy when there are adverse pathologic findings at prostatectomy or with a persistently detectable prostate-specific antigen level after prostatectomy (see Policy Guidelines), or
- Salvage therapy when there is evidence of biochemical or local recurrence when there is no evidence of distant metastatic disease (see Policy Guidelines).

Intensity-modulated radiotherapy is considered **investigational** for the treatment of prostate cancer when the above criteria are not met.

**POLICY GUIDELINES**

**LOCALIZED PROSTATE CANCER: RADIOTHERAPY AS DEFINITIVE TREATMENT**
Localized prostate cancer can be defined as cancer confined to the prostate gland T1-T2N0-NXM0 or as locally advanced cancer. Locally advanced cancer is confined to adjacent structures and includes T3a-T3bN0-NXM0. The presence of tumor invasion beyond extracapsular extension or other than seminal vesicles, or with evidence of regional lymph node involvement, in the absence of distant metastases T4N0-N1M0, does not necessarily preclude definitive therapy.

The National Comprehensive Cancer Network (NCCN) has recommended a dose of 75.6 to 79.2 gray (Gy) in conventional fractions (with or without seminal vesicles) for patients with low-risk cancers (based on findings from Kuban et al [2008]). Low-risk features in localized prostate cancer are defined as stage T1...
to T2a, a Gleason score of 6 or less, and a prostate-specific antigen (PSA) level less than 10 ng/mL.

NCCN has recommended doses up to 81.0 Gy for patients with intermediate- and high-risk cancers, defined as: intermediate risk: stage T2b to T2c or Gleason score of 7 or PSA levels between 10 ng/mL and 20 ng/mL; and high risk: stage T3a or Gleason score of 8 to 10 or PSA level greater than 20 ng/mL (based on Eade et al [2007]; and Xu et al [2011]).

**POST PROSTATECTOMY: RADIOTHERAPY AS ADJUVANT OR SALVAGE THERAPY**

Radiotherapy (RT) after prostatectomy is used as adjuvant therapy in patients at a higher risk of recurrence. In the adjuvant setting, adverse pathologic findings at prostatectomy include positive surgical margins, seminal vesicle invasion, extraprostatic extension, and Gleason scores of 8 to 10.

Use of RT as salvage therapy included treating the prostate bed and possibly surrounding tissues, including lymph nodes, in a patient with locoregional recurrence after surgery. In the salvage setting, biochemical recurrence is defined as a detectable or rising PSA level of 0.2 ng/mL or more after surgery, with a confirmatory test level of 0.2 ng/mL or higher.

American Urological Association and American Society for Radiation Oncology (Thompson et al [2013]) guidelines recommend a minimum dose of 64 to 65 Gy in the post prostatectomy setting.

**FRACTIONATION**

In the treatment of prostate cancer, conventional RT applies total doses in excess of 74 Gy over up to 9 weeks, whereas hypofractionated RT involves daily doses greater than 2 Gy and has an overall shorter treatment time. Published randomized controlled trials have failed to demonstrate the superiority of hypofractionation in definitive RT for prostate cancer, either for efficacy or late toxicity. Ongoing phase 3 noninferiority trials might provide insight.

NCCN guidelines state that because, in the treatment of prostate cancer, moderately hypofractionated intensity-modulated radiotherapy (IMRT) regimens (2.4-4 Gy per fraction over 4-6 weeks) have been tested in randomized controlled trials, and efficacy and toxicity have been found similar to conventionally fractionated IMRT, hypofractionation may be considered as an alternative to conventionally fractionated regimens when clinically indicated.

**RADIATION TOLERANCE OF NORMAL TISSUE**

Organs at risk are defined as normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed radiation dose. Organs at risk may be particularly vulnerable to clinically important complications from radiation toxicity.

IMRT should be considered when a tumor is near organs at risk, and 3-dimensional conformal radiotherapy planning does not meet dose-volume constraints for normal tissue tolerance.

Tables PG1 and 2 outline radiation doses generally considered tolerance thresholds for these normal structures in the pelvis.

**Table PG1. Radiation Tolerance Doses for Normal Tissues of the Pelvis**

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5, Gray&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TD 50/5, Gray&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Complication End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Portion of Organ Involved</td>
<td>Portion of Organ Involved</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1/3</td>
<td>2/3</td>
<td>3/3</td>
</tr>
<tr>
<td></td>
<td>1/3</td>
<td>2/3</td>
<td>3/3</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>50</td>
<td>50</td>
<td>47</td>
</tr>
<tr>
<td>Small</td>
<td>50</td>
<td>NP</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>NP</td>
<td>55</td>
</tr>
</tbody>
</table>

<sup>a</sup> TD 5/5: Dose to a specified portion of the organ to cause 5% late normal tissue complication.

<sup>b</sup> TD 50/5: Dose to a specified portion of the organ to cause 50% late normal tissue complication.
intestine

<table>
<thead>
<tr>
<th>Site</th>
<th>Radiation Dose Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>55</td>
</tr>
<tr>
<td>Rectum</td>
<td>NP</td>
</tr>
<tr>
<td>Bladder</td>
<td>NP</td>
</tr>
<tr>
<td>Femoral head</td>
<td>NP</td>
</tr>
</tbody>
</table>


NP: not provided; TD: tolerance dose.

\(^a\) TD 5/5 is the average dose that results in a 5% complication risk within 5 years.

\(^b\) TD 50/5 is the average dose that results in a 50% complication risk within 5 years.

**Table PG2. Radiation Dose Volume (1.8-2.0 Gray per Fraction) for Normal Tissues of the Pelvis**

<table>
<thead>
<tr>
<th>Site</th>
<th>Radiation Dose Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectum</td>
<td>V75 &lt;15%, V70 &lt;20%, V65 &lt;25%, V60 &lt;35%, V50 &lt;50%</td>
</tr>
<tr>
<td>Bladder</td>
<td>V80 &lt;15%, V75 &lt;25%, V70 &lt;35%, V65 &lt;50%</td>
</tr>
<tr>
<td>Femoral head</td>
<td>V50 &lt;5%</td>
</tr>
</tbody>
</table>


**CODING**

The following CPT codes for simple and complex IMRT delivery are available:

77385 Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple
77386 complex.

The Centers for Medicare & Medicaid Services decided not to implement these CPT codes and instead created HCPCS G codes using the language of the previous CPT codes. So the following codes may be used for IMRT:

G6015 Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
G6016 Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session.

Code 77301 remains valid:

77301 Intensity-modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications.

The following CPT code may also be used:
77338 Multi-leaf collimator (MLC) device(s) for intensity-modulated radiation therapy (IMRT), design and construction per IMRT plan.

Code 77338 is to be reported only once per IMRT plan and should not be reported with 0073T.

**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

**BACKGROUND**

**PROSTATE CANCER TREATMENT**
For localized prostate cancer, radiotherapy (RT) is an accepted option for primary (definitive) treatment. Other options include surgery (radical prostatectomy), hormonal treatment, or active surveillance.

In the postoperative setting, RT to the prostate bed is an accepted procedure for patients with an increased risk of local recurrence, based on 3 randomized controlled trials that showed a significant increase in biochemical recurrence-free survival. Professional society guidelines have recommended adjuvant RT to patients with adverse pathologic findings at the time of prostatectomy and salvage RT for patients with prostate-specific antigen recurrence or local recurrence after prostatectomy in the absence of metastatic disease.

**RT Techniques**

*Conventional External-Beam Radiotherapy*
Methods to plan and deliver RT have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used 2-dimensional treatment planning, based on flat images and radiation beams with cross-sections of uniform intensity that were sequentially aimed at the tumor along 2 or 3 intersecting axes. Collectively, these methods are termed *conventional external-beam radiotherapy*.

*Three-Dimensional Conformal Radiotherapy*
Treatment planning evolved by using 3-dimensional images, usually from computed tomography scans, to delineate the boundaries of the tumor and to discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Computer algorithms were developed to estimate cumulative radiation doses delivered to each volume of interest by summing the contribution from each shaped beam. Methods were also developed to position the patient and the radiation portal reproducibly for each fraction and to immobilize the patient, thus maintaining consistent beam axes across treatment sessions. Collectively, these methods are termed *3-dimensional conformal radiotherapy* (3D-CRT).

*Intensity-Modulated Radiotherapy*
Intensity-modulated radiotherapy (IMRT), which uses computer software along with computed tomography and magnetic resonance images, offers better conformality than 3D-CRT because it modulates the intensity of the overlapping radiation beams projected on the target and uses multiple shaped treatment fields. Treatment planning and delivery are more complex, time-consuming, and labor intensive for IMRT than for 3D-CRT. The technique uses a multileaf collimator (MLC), which, when coupled with a computer algorithm, allows for “inverse” treatment planning. The radiation oncologist
delineates the target on each slice of a computed tomography scan and specifies the target’s prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose limits within the normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan’s goals.

Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and thus may improve local tumor control, with decreased exposure to surrounding, normal tissues, potentially reducing acute and late radiation toxicities. Better dose homogeneity within the target may also improve local tumor control by avoiding underdosing within the tumor and may decrease toxicity by avoiding overdosing.

Technologic development has advanced techniques that may further improve RT treatment by improving dose distribution. These techniques are considered variations of IMRT. Volumetric modulated arc therapy delivers radiation from a continuous rotation of the radiation source. The principal advantage of volumetric modulated arc therapy is greater efficiency in treatment delivery time, reducing radiation exposure and improving target radiation delivery due to less patient motion. Image-guided RT involves the incorporation of imaging before and/or during treatment to more precisely deliver RT to the target volume.

IMRT methods to plan and deliver RT are not uniform. IMRT may use beams that remain on as MLCs move around the patient (dynamic MLC) or that are off during movement and turn on once the MLC reaches prespecified positions (“step and shoot” technique). A third alternative uses a very narrow single beam that moves spirally around the patient (tomotherapy). Each method uses different computer algorithms to plan treatment and yields somewhat different dose distributions in and outside the target. Patient position can alter target shape and thus affect treatment plans. Treatment plans are usually based on a single imaging scan, a static 3D-CT image. Current methods seek to reduce positional uncertainty for tumors and adjacent normal tissues by various techniques. Patient immobilization cradles and skin or bony markers are used to minimize day-to-day variability in patient positioning. In addition, many tumors have irregular edges that preclude drawing tight margins on computed tomography scan slices when radiation oncologists contour the tumor volume. It is unknown whether omitting some tumor cells or including some normal cells in the resulting target affects the outcomes of IMRT.

REGULATORY STATUS
In general, IMRT systems include intensity modulators, which control, block, or filter the intensity of radiation; and RT planning systems, which plan the radiation dose to be delivered.

A number of intensity modulators have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Intensity modulators include the Innocure Intensity Modulating Radiation Therapy Compensators (Innocure), cleared in 2006, and the decimal tissue compensator (Southeastern Radiation Products), cleared in 2004. FDA product code: IXI. Intensity modulators may be added to standard linear accelerators to deliver IMRT when used with proper treatment planning systems.

RT planning systems have also been cleared for marketing by FDA through the 510(k) process. They include the Prowess Panther™ (Prowess) in 2003, TiGRT (LinaTech) in 2009, the RayDose (RaySearch Laboratories) in 2008, and the eIMRT Calculator (Standard Imaging). FDA product code: MUJ.
Fully integrated IMRT systems also are available. These devices are customizable and support all stages of IMRT delivery, including planning, treatment delivery, and health record management. One such device cleared for marketing by FDA through the 510(k) process is the Varian IMRT system (Varian Medical Systems). FDA product code: IYE.

RATIONALE

This evidence review was created in February 2008 and has been updated regularly with searches of the MEDLINE database. The most recent literature review was performed through May 24, 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.

Multiple-dose planning studies have generated 3-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT) treatment plans from the same scans, and then compared predicted dose distributions within the target and adjacent organs at risk. Results of such studies have shown that IMRT improves on 3D-CRT on conformality to, and dose homogeneity within, the target. Dosimetry using stationary targets generally confirms these predictions. Thus, radiation oncologists have hypothesized that IMRT may provide better treatment outcomes than 3D-CRT. However, these types of studies offer indirect evidence for IMRT treatment benefit, and it is difficult to relate dosing study results to actual effects on health outcomes.

Comparative studies of radiation-induced adverse events from IMRT vs alternative radiation delivery would constitute definitive evidence of establishing the benefit of IMRT. Single-arm series of IMRT can give insights into the potential for benefit, particularly if an adverse event that is expected to occur at high rates is shown to decrease by a large amount. Studies of treatment benefit are also important to establish whether IMRT is at least as good as other types of delivery, but, absent such comparative trials, it is likely that benefit from IMRT is at least as good as with other types of delivery.

In general, when the indication for IMRT is to avoid radiation to sensitive areas, dosimetry studies have been considered sufficient evidence to demonstrate that harm would be avoided using IMRT. For other indications, such as using IMRT to provide better tumor control, comparative studies of health outcomes are needed to demonstrate such a benefit.
IMRT FOR PRIMARY (DEFINITIVE) THERAPY FOR LOCALIZED PROSTATE CANCER

Clinical Context and Test Purpose
The purpose of IMRT in patients who have localized prostate cancer and undergoing definitive RT 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 IMRT improve the net health outcome for individuals who have localized prostate cancer and are undergoing definitive therapy?

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

Patients
The relevant population of interest is individuals who have localized prostate cancer and are undergoing definitive therapy.

Interventions
The test being considered is IMRT.

Comparators
The following test is currently being used to make decisions about the treatment of localized prostate cancer: 3D-CRT.

Outcomes
The general outcomes of interest are overall survival (OS), locoregional recurrent, quality of life, and treatment-related morbidity.

Timing
Follow-up times of interest may vary from weeks to months after treatment

Setting
Patients with prostate cancer are actively managed by radiation oncologists.

Systematic Reviews
A meta-analysis by Yu et al (2016) included 23 studies (total N=9556 patients) that compared IMRT with 3D-CRT for gastrointestinal (GI), genitourinary (GU), and rectal toxicity, biochemical control, and OS. Reviewers included 16 retrospective comparisons and 5 prospective cohort studies published before July 2015. The relative risk for the pooled analysis was considered significant if the 95% confidence intervals (CIs) did not overlap at 1 at the p<0.05 level. IMRT resulted in less acute and late GI toxicity, less rectal bleeding, and improved biochemical control (see Table 1). There was a modest increase in acute GU toxicity, and no significant differences between the treatments in acute rectal toxicity, late GU toxicity, and OS.

Table 1. Outcomes for IMRT Compared With 3D-CRT

<table>
<thead>
<tr>
<th>Comparison</th>
<th>No. of Studies</th>
<th>No. of Patients</th>
<th>RR for IMRT vs 3D-CRT</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute GI toxicity</td>
<td>12</td>
<td>4142</td>
<td>0.59</td>
<td>0.44 to 0.78</td>
</tr>
<tr>
<td>Late GI toxicity</td>
<td>13</td>
<td>6519</td>
<td>0.54</td>
<td>0.38 to 0.78</td>
</tr>
<tr>
<td>Acute rectal toxicity</td>
<td>4</td>
<td>2188</td>
<td>1.03</td>
<td>0.45 to 2.36</td>
</tr>
<tr>
<td>Late rectal bleeding</td>
<td>5</td>
<td>1972</td>
<td>0.48</td>
<td>0.27 to 0.85</td>
</tr>
<tr>
<td>Acute GU toxicity</td>
<td>14</td>
<td>4603</td>
<td>1.08</td>
<td>1.00 to 1.17</td>
</tr>
</tbody>
</table>
### Comparison Table

<table>
<thead>
<tr>
<th>Comparison</th>
<th>No. of Studies</th>
<th>No. of Patients</th>
<th>RR for IMRT vs 3D-CRT</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late GU toxicity</td>
<td>12</td>
<td>5608</td>
<td>1.03</td>
<td>0.82 to 1.30</td>
</tr>
<tr>
<td>Biochemical control</td>
<td>6</td>
<td>2416</td>
<td>1.17</td>
<td>1.08 to 1.27</td>
</tr>
<tr>
<td>Overall survival</td>
<td>3</td>
<td>924</td>
<td>1.07</td>
<td>0.96 to 1.19</td>
</tr>
</tbody>
</table>

CI: confidence interval; GI: gastrointestinal, grade 2-4 toxicity; GU: genitourinary, grade 2-4 toxicity; IMRT: intensity-modulated radiotherapy; RR: relative risk; 3D-CRT: 3-dimensional conformal radiotherapy.

Bauman et al (2012) published a systematic review assessed IMRT in the treatment of prostate cancer to quantify its potential benefits and to make recommendations for radiotherapy programs considering adopting this technique within Ontario, Canada. Based on a review of 11 published reports through March 2009 (9 retrospective cohort studies, 2 RCTs) including 4559 patients, reviewers recommended IMRT over 3D-CRT for aggressive treatment of localized prostate cancer where an escalated radiation (>70 gray [Gy]) dose would be required. Four studies (3 retrospective cohort studies, 1 RCT) reported differences in adverse events between IMRT and 3D-CRT. The RCT (N=78 patients) reported significantly less frequent acute GI toxicity in the IMRT group than in the 3D-CRT group. This was true for grade 2, 3, or 4 toxicity (20% vs 61%, p=0.001), grade 3 or 4 toxicity (0% vs 13%, p=0.001), and for acute proctitis (15% vs 38%, p=0.03). A second RCT included in this systematic review reported no differences in toxicity between IMRT and 3D-CRT.

For late GI toxicity, 4 of 9 studies, all retrospective cohort studies (total N=3333 patients), reported differences between IMRT and 3D-CRT. One RCT, reporting on late GI toxicity, did not find any differences between IMRT and 3D-CRT. Five of 9 studies reported on late GU effects: only one reported a difference in late GU effects in favor of 3D-CRT. Two retrospective cohort studies reported mixed findings on quality of life outcomes.

A systematic review by Hummel et al (2010) conducted for the Health Technology Assessment Programme evaluated the clinical effectiveness of IMRT for the radical treatment of prostate cancer. The literature search through May 2009 identified 8 nonrandomized studies comparing IMRT with 3D-CRT. Clinical outcomes were OS, biochemical (prostate-specific antigen [PSA]) relapse-free survival, toxicity, and health-related quality of life. The biochemical relapse-free survival was not affected by treatment received, except when doses differed between groups; in those cases, a higher dose with IMRT was favored over lower doses with 3D-CRT. There was some indication that GU toxicity was worse for patients treated with dose-escalated IMRT. However, any group difference resolved by 6 months after treatment. Data comparing IMRT with 3D-CRT supported the theory that higher doses (up to 81 Gy) can improve biochemical survival for patients with localized prostate cancer. Most studies reported an advantage for IMRT in GI toxicity, particularly for the volume of the rectum treated, because toxicity can be reduced by increasing conformality of treatment.

### Randomized Controlled Trials

Studies not included in the Yu et al (2016) meta-analysis are described next.

Viani et al (2016) reported on a pseudorandomized trial (sequential allocation) that compared toxicity levels between IMRT and 3D-CRT in 215 men who had localized prostate cancer. Treatment consisted of hypofractionated radiotherapy (RT) at a total dose of 70 Gy in 2.8 Gy per fraction for either IMRT or 3D-CRT. The primary end point was toxicity, defined as any symptoms up to 6 months after treatment (acute) or that started 6 months after treatment (late). Quality of life was assessed with a prostate-specific module. The trial was adequately powered, and the groups were comparable at baseline.
However, blinding of patients and outcome assessors was not reported. As shown in Table 2, the 3D-CRT group reported significantly more incidence of acute and late GI and GU toxicity, with similar rates of biochemical control (PSA nadir + 2 ng/mL). The combined incidence of acute GI and GU toxicity was 28% for the 3D-CRT group compared with 11% for the IMRT group. Prostate-specific quality of life was reported to be worse in the 3D-CRT group at 6, 12, and 24 months, but not at 36 months posttreatment.

### Table 2. Acute and Late Toxicity Rates With 3D-CRT and IMRT

<table>
<thead>
<tr>
<th>Comparison</th>
<th>3D-CRT (n=109), %</th>
<th>IMRT (n=106), %</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute gastrointestinal toxicity, grade ≥2</td>
<td>24</td>
<td>7</td>
<td>0.001</td>
</tr>
<tr>
<td>Acute genitourinary toxicity, grade ≥2</td>
<td>27</td>
<td>9</td>
<td>0.001</td>
</tr>
<tr>
<td>Late gastrointestinal toxicity, grade ≥2</td>
<td>21.7</td>
<td>6.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Late genitourinary toxicity, grade ≥2</td>
<td>12.3</td>
<td>3.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Biochemical control</td>
<td>94.3</td>
<td>95.4</td>
<td>0.678</td>
</tr>
</tbody>
</table>

IMRT: intensity-modulated radiotherapy; 3D-CRT: 3-dimensional conformal radiotherapy.

### Nonrandomized Studies

Sujenthiran et al (2017) published a retrospective cohort study evaluating 23,222 men who were treated for localized prostate cancer with IMRT (n=6,933) or 3D-CRT (n=16,289) between January 2010 and December 2013 and whose data were available in various databases within the English National Health Service. Dosage was similar between treatment types: patients in both groups received a median of 2 Gy per fraction for a median total dose of 74 Gy. GI and GU toxicities were categorized as grade 3 or above using National Cancer Institute Common Terminology Criteria. On average, patients in the IMRT group experienced fewer GI toxic events per 100 person-years (4.9) than patients in the 3D-CRT group, who saw an average 6.5 GI events per 100 person-years (adjusted hazard ratio, 0.66; 95% CI, 0.61 to 0.72; p<0.01). The rate of GU toxicity events was similar between treatment groups (IMRT, 2.3 GU events per 100 person-years vs 3D-CRT, 2.4 GU events per 100 person-years; hazard ratio, 0.94; 95% CI, 0.84 to 1.06; p=0.31). The most commonly diagnosed GI toxicity events were radiation proctitis (n=5,962 [68.5%] of 8,701 diagnoses). Of 4,061 GU toxicity diagnoses, the most common was hematuria (1265 [31.1%]). Study limitations included therapeutic differences and baseline GI and GU symptoms unaccounted for in the analysis, as well as limited follow-up on GI and GU toxicity. Reviewers concluded that IMRT showed a significant reduction in GI toxicity severity over 3D-CRT and similar levels of GU toxicity severity.

Michalski et al (2013) reported on comparative data for IMRT and 3D-CRT from the high-dose arm of the Radiation Therapy Oncology Group 0126 prostate cancer trial. In this trial, the initial protocol only included 3D-CRT, but during the trial, the protocol was amended to include IMRT. As a result, 491 patients were treated with 3D-CRT and 257 were treated with IMRT. Patients treated with 3D-CRT received 55.8 Gy to the prostate and seminal vesicles and then 23.4 Gy to the prostate only. All IMRT patients received 79.2 Gy to the prostate and seminal vesicles. Radiation exposure for the bladder and rectum were significantly reduced with IMRT. There was a significant decrease in the incidence of grades 2, 3, and 4 late GI toxicity for IMRT on univariate analysis (p=0.039). On multivariate analysis, there was a 26% reduction in grade 2, 3, and 4 GI toxicity for the IMRT group, but this difference was not statistically significant (p=0.099). There were no differences in early or late GU toxicity between groups.

Vora et al (2013) reported on 9-year tumor control and chronic toxicities observed in 302 patients treated with IMRT for clinically localized prostate cancer at a single institution. Median dose delivered was 76 Gy (range, 70–77 Gy), and 35% of patients received androgen deprivation therapy. Local and
distant-recurrence rates were 5% and 8.6%, respectively. At 9 years, biochemical control rates were 77% for low-risk, 70% for intermediate-risk, and 53% for high-risk patients (p=0.05). At last follow-up, none had persistent GI and only 0.7% had persistent GU toxicities of grade 3 or 4. The high-risk group was associated with a higher distant metastasis rate (p=0.02) and death from prostate cancer (p=0.001).

Wong et al (2009) reported on a retrospective study of radiation dose escalation in 853 patients with localized (T1c-T3N0M0) prostate cancer. RTs used included conventional dose (71 Gy) 3D-CRT (n=270), high-dose (75.6 Gy) IMRT (n=314), permanent transperineal brachytherapy (n=225), and external-beam radiotherapy plus brachytherapy boost (n=44). All patients were followed for a median of 58 months (range, 3-121 months). The 5-year OS rate for the entire group was 97%. The 5-year biochemical no evidence of disease rates, local control rates, and distant control rates were 74%, 93%, and 96%, respectively, for 3D-CRT; 87%, 99%, and 97%, respectively, for IMRT; 94%, 100%, and 99%, respectively, for brachytherapy alone; and 94%, 100%, and 97%, respectively, for external-beam radiotherapy plus brachytherapy.

Dosing for Low-Risk vs Intermediate- to High-Risk Prostate Cancer
The National Comprehensive Cancer Network (NCCN) has made recommended use of RT for patients with prostate cancer based on risk stratification by clinical and pathologic findings. These recommendations are based on studies that did and did not include IMRT as the mode of RT.

In 1993, a U.S. cancer research center initiated an RCT comparing toxicity levels with outcomes after 3D-CRT (at 78 Gy) and 2-dimensional RT (at 70 Gy) in patients with localized prostate cancer. The long-term results were reported by Kuban et al (2008). The trial included 301 patients with stage T1b to T3 disease who received 70 Gy (n=150) or 78 Gy (n=151). Median follow-up was 8.7 years. Patient risk levels in the 70- and 78-Gy groups were low (n=31 and n=30), intermediate (n=71 and n=68), and high (n=48 and n=53), respectively. When analyzed by risk group, patients with low-risk disease treated to 78 Gy vs 70 Gy, had a freedom from biochemical or clinical failure of 88% and 63%, respectively (p=0.042). The intermediate-risk patients showed no statistically significant difference in freedom from biochemical or clinical failure based on dose level (p=0.36). Patients with high-risk disease showed a significant difference in freedom from biochemical or clinical failure based on dose (63% vs 26%, p=0.004), although when these high-risk patients were stratified by PSA level, only those patients with a PSA level greater than 10 ng/mL showed a difference in freedom from biochemical or clinical failure.

NCCN guidelines also cite the 2008 Kuban study as evidence for a dose of 75.6 to 79.2 Gy (with or without the inclusion of the seminal vesicles) as appropriate for patients with low-risk cancers and that the conventional dose of 70 Gy is no longer considered adequate.

For patients with intermediate- and high-risk prostate cancer, NCCN has cited the following studies. For example, Xu et al (2011) reported on a toxicity analysis of dose escalation from 75.6 to 81.0 Gy in 189 patients receiving definitive RT for prostate cancer. Patients were at high, intermediate, and low risk according to NCCN definitions, and were dosed at physician discretion. A total of 119 patients received 75.6 Gy and 70 received 81.0 Gy. Patients were followed at intervals of 3 to 6 months for 5 years and yearly after that (median follow-up, 3 years). The 81.0-Gy group had higher rates of grade 2 acute GU toxicity (p=0.001), late GU toxicity (p=0.001), and late GI toxicity (p=0.082), but a lower rate of acute GI toxicity (p=0.002). There were no notable differences in final GU (p=0.551) or final GI (p=0.194) toxicity levels compared with the 75.6-Gy group.

Eade et al (2007) reported on the results of 1530 consecutive patients treated for localized prostate cancer with 3D-CRT between 1989 and 2002. Patients were grouped by dose level: less than 70 Gy (n=43), 70 to 74.9 Gy (n=552), 75 to 79.9 Gy (n=568), and 80 Gy or more (n=367). Median follow-up
ranged from 46 to 86 months, with the group receiving 80 Gy or more having a median follow-up of 45.6 months. Adjusted 5-year estimates of freedom from biochemical failure for the 4 groups were 60%, 68%, 76%, and 84% using the American Society for Radiation Oncology criteria and 70%, 81%, 83%, and 89% using Phoenix criteria, respectively. Adjusted 5- and 10-year estimates of freedom from distant metastases for the 4 groups were 96% and 93%, 97% and 93%, 99% and 95%, and 98% and 96%, respectively. The authors concluded that a pronounced RT dose-response by freedom from biochemical failure was seen after adjusting for pretreatment PSA level, Gleason score, and tumor stage and that the vast majority of patients should receive 80 Gy or more, although a subgroup of patients might be adequately treated with radiation lower dose.

Section Summary: IMRT for Primary (Definitive) RT for Localized Prostate Cancer
The evidence on IMRT for definitive treatment of localized prostate cancer includes several prospective comparative studies, retrospective comparative studies, and systematic reviews of these studies. Results generally showed that IMRT provides tumor control and survival outcomes similar to 3D-CRT, with reductions in GI and GU toxicity. A reduction in clinically significant complications of RT is likely to improve the quality of life for treated patients.

IMRT FOR PROSTATE CANCER AFTER PROSTATECTOMY

Clinical Context and Test Purpose
The purpose of IMRT in patients who have prostate cancer and are undergoing RT after prostatectomy 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 IMRT improve the net health outcome in patients who have prostate cancer and are undergoing RT after prostatectomy?

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

Patients
The relevant population of interest is individuals who have prostate cancer and are undergoing RT after prostatectomy.

Interventions
The test being considered is IMRT.

Comparators
The following tool is currently being used to make decisions about the treatment of localized prostate cancer after prostatectomy: 3D-CRT.

Outcomes
The general outcomes of interest are OS, locoregional recurrence, quality of life, and treatment-related morbidity.

Timing
Follow-up times of interest vary from weeks to months after treatment.

Setting
Patients with prostate cancer are actively managed by radiation oncologists.
Systematic Reviews
The Bauman et al (2012) systematic review (discussed earlier) found insufficient data to recommend IMRT over 3D-CRT as adjuvant therapy after prostatectomy. The 2013 joint American Urological Association and the American Society for Radiation Oncology guidelines on the use of adjuvant and salvage RT after prostatectomy was based on a systematic review conducted by Thompson et al (2013) who searched the literature from 1990 to 2012 and selected 294 articles. Reviewers attempted to determine which RT technique and doses produced optimal outcomes, but found it impossible to answer these questions because most available data came from observational studies and approximately one-third treated patients with conventional 2-dimensional external-beam modalities. Of the literature assessed in the review, less than 5% of studies reported using IMRT. Reviewers stated that 64 to 65 Gy is the minimum dose that should be delivered after prostatectomy, but that dosage should be individualized to the patient.

Nonrandomized Comparative Studies
Alongi et al (2009) reported on acute toxicity results of whole pelvis irradiation for 172 consecutive patients with clinically localized prostate cancer treated with IMRT or 3D-CRT as adjuvant (n=100) or salvage (n=72) therapy after radical prostatectomy and pelvic lymph node dissection. Whole pelvis radiation was considered in patients with a limited lymphadenectomy and/or in the presence of a high risk of nodal involvement, in patients with positive lymph nodes and/or in the presence of adverse prognostic factors (Gleason score >7 and/or preoperative PSA level >10 ng/mL). Eighty-one patients underwent 3D-CRT, and 91 underwent IMRT. No grade 3 or 4 acute GU or lower GI side effects were observed. Acute grade 2 GU and acute lower GI grade 2 events did not differ significantly between treatment groups (see Table 3). There was a higher incidence of acute upper GI grade 2, 3, and 4 toxicity, in the 3D-CRT group. The authors concluded that acute toxicity following postoperative whole pelvis irradiation was reduced with IMRT compared with 3D-CRT; this effect was most significant for upper GI symptoms, owing mainly to better bowel sparing with IMRT.

Table 3. Acute and Late Toxicity Rates With 3D-CRT and IMRT

<table>
<thead>
<tr>
<th>Comparison</th>
<th>3D-CRT, n (%)</th>
<th>IMRT, n (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lower gastrointestinal toxicity, grade ≥2</td>
<td>7 (8.6)</td>
<td>3 (3.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Acute upper gastrointestinal toxicity, grade ≥2</td>
<td>18 (22.2)</td>
<td>6 (6.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Acute genitourinary toxicity</td>
<td>10 (12.3)</td>
<td>6 (6.6)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

IMRT: intensity-modulated radiotherapy; 3D-CRT: 3-dimensional conformal radiotherapy.

Massaccesi et al (2013) reported preliminary acute toxicity results from a phase 2 trial of hypofractionated IMRT with a simultaneous integrated boost to the pelvic nodes and prostate bed after prostatectomy. Between 2008 and 2012, 49 patients considered to be at high risk of relapse after radical prostatectomy or who had biochemical relapse received 45 Gy in 1.8-Gy fractions to the whole pelvis and 62.5 Gy in 2.5-Gy fractions (equivalent dose, 68.75 Gy) to the prostate bed. The toxicity findings were compared with those of 52 consecutive patients selected from an electronic database who underwent adjuvant or salvage 3D-CRT with standard 2-Gy fractionation to the prostatic bed and regional pelvic nodes. Grade 1, 2, 3, and 4 acute GU toxicity occurred in 71.2% of all patients without a significant difference between the groups (hypofractionated IMRT vs conventionally fractionated 3D-CRT; p=0.51). Grade 2 acute GU toxicity, reported in 19.8% of all patients, was less frequent in patients in the IMRT group (9.6% vs 28.8%, p=0.02). There were no cases of grade 3 acute GU toxicity. Thirty (29.7%) patients developed grade 2 acute GI toxicity; the difference between groups was not statistically significant. No cases of grade 3 acute GI toxicity were reported. The study concluded that the acute
toxicity profile for hypofractionated high-dose simultaneous integrated boost IMRT after prostatectomy compared favorably with that of conventionally fractionated high-dose 3D-CRT.

**Single-Arm Studies**
Several prospective single-arm phase 2 studies have evaluated the safety and efficacy of different methods of delivering IMRT (eg, integrated boost, hypofractionation).

**PLATIN 3 Trial**
Initial results of the phase 2 Prostate and Lymph Node Irradiation With Integrated Boost-IMRT After Neoadjuvant Antihormonal Treatment (PLATIN 3) trial were published by Katayama et al (2014).\(^{18}\) This trial evaluated the safety and feasibility of irradiating the pelvic lymph nodes simultaneously with a boost to the prostate bed in 40 patients with high-risk features or inadequate lymphadenectomy after radical prostatectomy. Treatment consisted of 2 months of antihormonal treatment before IMRT of the pelvic lymph nodes (51.0 Gy) with a simultaneous integrated boost to the prostate bed (68.0 Gy). No incidence of acute grade 3 or 4 toxicity occurred. Nearly 23% of patients experienced acute grade 2 GI and GU toxicity, 10% late grade 2 GI toxicity, and 5% late grade 2 GU toxicity. One patient developed late grade 3 proctitis and enteritis. At a median of 24 months, 89% of patients were free of a PSA recurrence.

**PRIAMOS1 Trial**
Acute toxicity results from the Hypofractionated RT of the Prostate Bed With or Without the Pelvic Lymph Nodes (PRIAMOS1) trial were reported by Katayama et al (2014).\(^{19}\) This prospective phase 2 trial assessed the safety and toxicity of hypofractionated RT of the prostate bed with IMRT as a basis for further prospective trials. Forty patients with indications for adjuvant or salvage therapy (pathologic stage T3 and/or R1/2 or with a PSA recurrence after prostatectomy) were enrolled from February to September 2012; 39 were evaluated. All patients received a total dose of 54.0 Gy to the prostate bed, 28 for salvage and 11 in the adjuvant setting. Based on preoperative staging, patients were risk-stratified as low (n=2), intermediate (n=27), or high (n=10). Ten weeks after completing therapy, there were no adverse events exceeding grade 3. Acute GI toxicity rates were 56.4% and 17.9% for grade 1 and 2, respectively, and acute grade 1 GU toxicity was recorded in 35.9% of patients.

Corbin et al (2013) reported on the adverse events in men at high risk of recurrence 2 years after prostatectomy and IMRT.\(^{20}\) Between 2007 and 2010, 78 consecutive men received adjuvant RT (n=17 [22%]) or salvage RT (n=61 [78%]). The median IMRT dose was 66.6 Gy (range, 60-72 Gy). Quality of life data were collected prospectively at 2, 6, 12, 18, and 24 months, and included urinary incontinence, irritation or obstruction, bowel or rectal function, and sexual function. No significant changes were observed from baseline through 2-year follow-up, with global urinary irritation or obstruction scores unchanged or improved over time from baseline, global urinary incontinence improved from baseline to 24 months in the subset of patients receiving adjuvant therapy, and global bowel and sexual domain scores improved or were unaffected over follow-up (though initially lower at 2 months).

**Section Summary: IMRT for Prostate Cancer After Prostatectomy**
The evidence on the use of IMRT for prostate cancer after prostatectomy includes nonrandomized comparative studies, single-arm phase 2 trials, retrospective series, and systematic reviews of these studies. Although the comparative studies are primarily retrospective, the evidence has generally shown that IMRT provides tumor control and survival outcomes similar to 3D-CRT. Notably, a retrospective comparative study found a significant reduction in acute GI toxicity with IMRT compared with 3D-CRT, mainly due to better bowel sparing with IMRT. Another retrospective comparative study found a
reduction in GU toxicity. A reduction in clinically significant complications of RT is likely to improve the quality of life for treated patients.

**SUMMARY OF EVIDENCE**
For individuals who have localized prostate cancer and are undergoing definitive RT who receive IMRT, the evidence includes several prospective comparative studies, retrospective studies, and systematic reviews of these studies. Relevant outcomes are overall survival, disease-free survival, quality of life, and treatment-related morbidity. Although there are few prospective comparative trials, the evidence has generally shown that IMRT provides tumor control and survival outcomes similar to 3D-CRT while reducing gastrointestinal and genitourinary toxicity. These findings are supported by treatment planning studies, which have predicted that IMRT improves target volume coverage and sparing of adjacent organs compared with 3D-CRT. A reduction in clinically significant complications of RT is likely to improve the quality of life for treated patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have prostate cancer and are undergoing RT after prostatectomy who receive IMRT, the evidence includes retrospective comparative studies, single-arm phase 2 trials, and systematic reviews of these studies. Relevant outcomes are overall survival, disease-free survival, quality of life, and treatment-related morbidity. Although the comparative studies are primarily retrospective, the evidence has generally shown that IMRT provides tumor control and survival outcomes similar to 3D-CRT. Notably, a retrospective comparative study found a significant reduction in acute upper GI toxicity with IMRT compared with 3D-CRT, mainly due to better bowel sparing with IMRT. Another retrospective comparative study found a reduction in GU toxicity. A reduction in clinically significant complications of RT is likely to improve the quality of life for treated patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

**SUPPLEMENTAL INFORMATION**

**PRACTICE GUIDELINES AND POSITION STATEMENTS**

**National Comprehensive Cancer Network**
National Comprehensive Cancer Network guidelines (v.3.2018) on prostate cancer indicate that highly conformal radiotherapy should be used in conventional fraction doses of 75.6 to 79.2 gray for low-risk prostate cancer and up to 81 gray for intermediate- and high-risk prostate cancer.²¹ For adjuvant and salvage external-beam radiotherapy, the recommended dose ranged from 64 to 72 gray in standard fractionation. The Network guidelines also indicate that intensity-modulated radiotherapy is used increasingly in clinical practice because of reduced risk of gastrointestinal toxicities and rates of salvage therapy in some studies.

**American Urological Association and American Society for Radiation Oncology**
The 2013 American Urological Association and American Society for Radiation Oncology guidelines addressed the use of adjuvant and salvage radiotherapy after radical prostatectomy.⁴ The guidelines stated that adjuvant radiotherapy should be given to patients with adverse pathologic findings after prostatectomy and salvage radiotherapy to patients with prostate-specific antigen recurrence or local recurrence after prostatectomy if there is no evidence of distant metastases. However, the available data did not identify which radiotherapy technique and dose produce optimal outcomes in this setting.
American Society of Clinical Oncology
American Society of Clinical Oncology endorsed the American Urological Association and the American Society for Radiation Oncology (2013) clinical practice guidelines for adjuvant and salvage radiotherapy after prostatectomy.22

American College of Radiology
The American College of Radiology Appropriateness Criteria (2014) have indicated intensity-modulated radiotherapy is the standard for definitive external-beam radiotherapy of the prostate.23

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 affect this review are listed in Table 4.

Table 4. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tbody>
<tr>
<td>Ongoing</td>
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<tr>
<td>NCT00331773</td>
<td>A Phase III Randomized Study of Hypofractionated 3D-CRT/MRT vs Conventionally Fractionated 3D-CRT/MRT With Favorable-Risk Prostate Cancer</td>
<td>1115</td>
<td>Jul 2015 (ongoing)</td>
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<tr>
<td>NCT00033631</td>
<td>A Phase III Randomized Study Of High Dose 3D-CRT/IMRT Versus Standard Dose 3D-CRT/IMRT In Patients Treated For Localized Prostate Cancer</td>
<td>1532</td>
<td>Apr 2014 (ongoing)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

REFERENCES


**CODES**

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>CPT</td>
<td>77301</td>
<td>Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specification</td>
</tr>
<tr>
<td></td>
<td>77338</td>
<td>Multileaf collimator (MLC) device(s) for intensity-modulated radiation therapy (IMRT), design and construction, per IMRT plan</td>
</tr>
<tr>
<td></td>
<td>77385</td>
<td>Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple</td>
</tr>
<tr>
<td></td>
<td>77386</td>
<td>complex</td>
</tr>
<tr>
<td>HCPCS</td>
<td>G6015</td>
<td>Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session</td>
</tr>
<tr>
<td></td>
<td>G6016</td>
<td>Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session</td>
</tr>
<tr>
<td>ICD-10-CM</td>
<td>C61</td>
<td>Malignant neoplasm of prostate</td>
</tr>
<tr>
<td>ICD-10-PCS</td>
<td></td>
<td>ICD-10-PCS codes are only used for inpatient services. There is no specific ICD-10-PCS code for this imaging.</td>
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**POLICY HISTORY**

<table>
<thead>
<tr>
<th>Date</th>
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<th>Description</th>
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<tbody>
<tr>
<td>04/10/14</td>
<td>Replace policy</td>
<td>Policy updated with literature review through March 18, 2014. Reference 14 added; reference 16 updated. Policy statement added indicating all other indications not meeting medically necessary criteria are investigational.</td>
</tr>
<tr>
<td>11/13/14</td>
<td>Replace policy – coding update only</td>
<td>New CPT and HCPCS codes added</td>
</tr>
<tr>
<td>04/23/15</td>
<td>Replace policy</td>
<td>Policy updated with literature review through March 3, 2015. References 9-10 and 19 added. Title changed from “radiation therapy” to “radiotherapy” to be consistent with other MPRM policies. Policy statements unchanged.</td>
</tr>
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</table>
| 09/10/15   | Replace policy              | Policy statement revised to remove RT dose constraint: “Intensity-
modulated radiotherapy (IMRT) may be considered medically necessary in the treatment of localized prostate cancer.”

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Details</th>
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<tr>
<td>03/10/16</td>
<td>Replace policy</td>
<td>Policy updated with literature review through January 12, 2016; references 1-4, 20-27, and 30 added. Policy statements changed to remove radiation dose constraints for definitive therapy of localized prostate cancer, with policy guidelines providing additional details on dose for low-risk vs intermediate- to high-risk prostate cancer. A policy statement was added to address the use of IMRT post prostatectomy.</td>
</tr>
<tr>
<td>04/25/17</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho annual review; no change to policy.</td>
</tr>
<tr>
<td>07/25/17</td>
<td>Replace policy</td>
<td>Policy updated with literature review through June 2, 2017; references 5 and 9 added; reference 22 updated; some references removed. 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 24, 2018; reference 9 added; reference 23 updated. Policy statements unchanged.</td>
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