Intensity Modulated Radiotherapy (IMRT) of the Prostate

Effective: October 1, 2018

Next Review: August 2019
Last Review: September 2018

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

IMRT is a form of radiation therapy that conforms closely to the targeted tumor shape and allows higher doses of radiation to be delivered while minimizing toxicity to surrounding healthy tissues.

MEDICAL POLICY CRITERIA

I. Intensity-modulated radiotherapy (IMRT) may be considered medically necessary for the treatment of prostate cancer when any of the following criteria are met:

   A. Primary treatment of local (clinical or pathological T1, T2, N0, M0) or locally advanced (clinical or pathological T3, T4, N0, N1, M0) prostate cancer; or

   B. There is documented prior radiation treatment within the planned target volume (quality assurance of IMRT plan is not required for a preauthorization request); or

   C. For tumors in close proximity to organs at risk, when comparative 3D versus IMRT dose/volume histograms are submitted AND the summary analysis (table preferred; with preauthorization request) is completed demonstrating that only through IMRT can published dose/volume constraints be met for organs at risk (quality assurance procedures are not required for preauthorization).
II. IMRT may be considered **medically necessary** post radical prostatectomy as either adjuvant or salvage treatment when any of the following are met:

A. Documentation includes evidence of adverse pathologic findings post-prostatectomy, defined as capsular penetration, seminal vesicle involvement, or positive surgical margins; or

B. There is clinical documentation of persistence of detectable PSA post-surgery; or

C. Increase in PSA after non-detectability, post-surgery.

III. IMRT is considered **investigational** for the treatment of prostate cancer when the above criteria are not met.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

**POLICY GUIDELINES**

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome. Quality assurance for 3D and IMRT submitted plans are not required with a preauthorization request.

- Clinical history, physical examination, PSA measurements, and/or imaging documenting patient's current clinical and/or pathologic stage.
- Documentation clarifying if the treatment is considered definitive, adjuvant, or salvage (see below).
  - If adjuvant, documentation must include pathologic evidence of the presence of adverse pathologic factors.
  - If salvage, documentation must include either clinical evidence of local recurrence, and/or PSA measurements showing either persistent detectable PSA post-surgery or subsequent rise in PSA after non-detectability, post-surgery.
- For tumors close to organ(s) at risk, the provider must submit comparative 3D versus IMRT dose/volume histograms and the completed analysis as described in Criterion I.C. above. The submitted information must demonstrate the need for IMRT to meet dose constraints not achievable through 3D planning. The best way to ensure criteria are met is to submit the provided summary analysis table. If using the table, please ensure all components are completed prior to submission. If any of these items are not provided it could impact our review and decision outcome.

**ORGANS AT RISK**

Example table *(Click here for a template to use)*:

<table>
<thead>
<tr>
<th>Organ(s) At Risk</th>
<th>Quantec Constraint</th>
<th>3D</th>
<th>IMRT</th>
<th>Can constraint only be met with IMRT?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example: Rectum</td>
<td>V70 &lt; 15%</td>
<td>28%</td>
<td>14%</td>
<td>Yes</td>
</tr>
<tr>
<td>Example: Rectum</td>
<td>V70 &lt; 15%</td>
<td>28%</td>
<td>20%</td>
<td>No</td>
</tr>
<tr>
<td>Example: Rectum</td>
<td>V70 &lt; 15%</td>
<td>14%</td>
<td>10%</td>
<td>No</td>
</tr>
</tbody>
</table>
Organs at risk are defined as normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed radiation dose. These organs at risk may be particularly vulnerable to clinically important complications from radiation toxicity.

**CROSS REFERENCES**

1. [Charged-Particle (Proton) Radiotherapy](#), Medicine, Policy No. 49
2. [Intensity Modulated Radiotherapy (IMRT) of the Thorax](#), Medicine, Policy No. 136
3. [Intensity Modulated Radiotherapy (IMRT) of the Head and Neck](#), Medicine, Policy No. 138
4. [Intensity-Modulated Radiotherapy (IMRT) of the Abdomen and Pelvis](#), Medicine, Policy No. 139
5. [Intensity-Modulated Radiotherapy (IMRT) for Central Nervous System (CNS) Tumors](#), Medicine, Policy No. 147
6. [Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy](#), Surgery, Policy No. 16

**BACKGROUND**

For localized prostate cancer, radiotherapy (RT) is one accepted option for primary (definitive) treatment. Other options include surgery (radical prostatectomy [RP]) or active surveillance. Adjuvant hormonal treatment may be considered along with the other definitive methods of treatment.

In the postoperative setting, RT to the prostate, seminal vesicle, nodal drainage bed is an accepted procedure for patients with an increased risk of local recurrence, based on three randomized controlled trials, which showed a significant increase in biochemical recurrence-free survival, and one study, which reported long-term increase in overall survival.[1-3] Major society guidelines recommend adjuvant radiotherapy to patients with adverse pathologic findings at the time of prostatectomy and salvage RT to patients with prostate-specific antigen (PSA) or clinical evidence of local recurrence after prostatectomy in the absence of metastatic disease.[4]

**RADIOThERAPY TECHNIQUES**

**Conventional (2-Dimensional) External Beam Radiotherapy**

Over the past several decades, methods to plan and deliver RT have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used two-dimensional treatment planning based on flat images and radiation beams with cross-sections of uniform intensity that were sequentially aimed at the tumor along two or three intersecting axes. Collectively, these methods are termed conventional external beam radiotherapy (2-D, EBRT) and is largely of historical application.

**Three-Dimensional Conformal Radiation**

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

**Intensity-Modulated Radiotherapy**
IMRT, which uses computer software and CT and magnetic resonance imaging images, offers better conformality than 3D-CRT, as it is able to modulate the intensity of the overlapping radiation beams projected on the target and to use multiple-shaped treatment fields. It uses a device (a multileaf collimator) which, coupled to a computer algorithm, allows for “inverse” treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target’s prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, and adjacent normal tissue volumes to minimize dose/volume distribution to neighboring organs at risk. Based on these parameters and a digitally reconstructed radiographic image of the tumor and surrounding tissues and organs at risk, computer software optimizes the location, shape, and intensities of the beam’s 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 minimize dose/volume distribution to neighboring organs at risk. IMRT based radiotherapy planning has largely replaced 3-D treatment planning in university and clinical settings across the United States.

REGULATORY STATUS

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

A number of intensity modulators have received marketing clearance through the FDA 510(k) process.Intensity modulators include the Innocure Intensity Modulating Radiation Therapy Compensators (Innocure) and decimal tissue compensator (Southeastern Radiation Products) FDA product code: IXI. Intensity modulators may be added to standard linear accelerators to deliver IMRT when used with proper treatment planning systems.

Radiotherapy treatment planning systems have also received FDA 510(k) marketing clearance. These include the Prowess Panther (Prowess), TiGRT (LinaTech), Ray Dose (Ray Search Laboratories), 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 to receive FDA 510(k) clearance is the Varian IMRT system (Varian Medical Systems). FDA product code: IYE.

EVIDENCE SUMMARY

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

Comparative studies of radiation-induced adverse effects from IMRT versus alternative radiation delivery are probably the most important type of evidence in establishing the benefit of IMRT. Such studies would answer the question of whether the theoretic benefit of IMRT in sparing normal tissue translates into real health outcomes. Single-arm series of IMRT can give some insights into the potential for benefit, particularly if an adverse effect 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 that IMRT is at least as good as other types of delivery, but in the absence of such comparative trials, it is likely that benefit from IMRT is at least as good as with other types of delivery.

This evidence review includes systematic reviews that evaluate outcomes of intensity-modulated radiotherapy (IMRT) treatment in patients with prostate cancer, summarizes the data on adverse effects from these systematic reviews and includes representative primary studies. A reduction in adverse effects is likely to be the greatest potential benefit of IMRT, and, in this regard, the most relevant studies are comparative trials of IMRT versus 3D-CRT that report on rates of adverse events following treatment.

**PRIMARY (DEFINITIVE) THERAPY FOR LOCALIZED PROSTATE CANCER**

**Systematic Reviews**

A 2016 meta-analysis by Yu included 23 studies (total N=9556 patients) that compared IMRT with 3D-CRT for gastrointestinal (GI), genitourinary (GU), and rectal toxicity, biochemical control, and overall survival (OS). The meta-analysis included 16 retrospective comparisons and five prospective cohort studies published before July 2015. The relative risk for the pooled analysis was considered significant if the 95% confidence interval did not overlap 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 two 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 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>
<tr>
<td>Late GU toxicity</td>
<td>14</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 two to four toxicity; GU: genitourinary, grade two to four toxicity; IMRT: intensity modulated radiotherapy; No.: number; RR: relative risk; 3D-CRT: three-dimensional conformal radiotherapy.

In 2012, Bauman published a systematic review that examined the evidence for IMRT in the treatment of prostate cancer to quantify its potential benefits and to make recommendations for
radiation treatment programs considering adopting this technique within the province of Ontario, Canada.\textsuperscript{6} Based on a review of 11 published reports through March 2009 (nine retrospective cohort studies and two randomized clinical trials [RCTs]) including 4559 patients, the authors put forth the recommendation for IMRT over 3D-CRT for aggressive treatment of localized prostate cancer where an escalated radiation (>70 gray [Gy]) dose is required. There were insufficient data to recommend IMRT over 3D-CRT in the postoperative setting.\textsuperscript{6}

Nine of 11 studies reviewed by Bauman reported on adverse effects. Six of nine studies reported on acute gastrointestinal (GI) effects.\textsuperscript{6} Four studies (three retrospective cohort studies, one RCT) reported differences in adverse effects between IMRT and 3D-CRT. The RCT included a total of 78 patients and reported that acute GI toxicity was significantly less frequent in the IMRT group compared with 3D-CRT. This was true for grade two or higher toxicities (20\% vs 61\%, \textit{p}=0.001), grade three or higher toxicity (0 vs 13\%, \textit{p}=0.001) and for acute proctitis (15\% vs 38\%, \textit{p}=0.03). In contrast, the second RCT included in this systematic review reported that there were no differences in toxicity between IMRT and 3D-CRT.\textsuperscript{6}

Six of nine studies reported on acute genitourinary (GU) effects. One study, which was a retrospective cohort study including 1571 patients, reported a difference in overall acute GU effects in favor of 3D-CRT (37\% IMRT vs 22\% 3D-CRT, \textit{p}=0.001). For late GI toxicity, four of nine studies, all retrospective cohort studies with a total of 3333 patients, reported differences between IMRT and 3D-CRT. One RCT reported on late GI toxicity and did not find any differences between IMRT and 3D-CRT. Five of nine studies reported on late GU effects, and only one reported a difference in late GU effects in favor of 3D-CRT (20\% vs 12\%, \textit{p}=0.01). Two retrospective cohort studies reported mixed findings on quality-of-life outcomes.\textsuperscript{6} A subsequent economic analysis (based on this systematic review data) demonstrated that for radical radiation treatment (>70 Gy) of prostate cancer, IMRT seems to be cost-effective when compared with an equivalent dose of 3D-CRT from the perspective of the Canadian health care system for 2009.\textsuperscript{7}

In 2008, the Agency for Healthcare Research and Quality (AHRQ) published a systematic review comparing the relative effectiveness and safety of various treatment options for clinically localized prostate cancer.\textsuperscript{8} Studies on IMRT were included in the assessment under the category of external beam radiotherapy (EBRT). Based on review of RCTs and nonrandomized studies published from 2000 to September 2007, there was no direct evidence (i.e., from RCTs) that IMRT resulted in better survival or disease-free survival (DFS) than other therapies for localized prostate cancer. Based on case-series data, the absolute risks of clinical and biochemical outcomes (including tumor recurrence), toxicity, and quality of life after IMRT were comparable with conformal radiation. For IMRT, the percent of patients with grade one and two acute GI toxicity was 22\% and 4\%, respectively; the percent of patients with rectal bleeding was 1.6\% to 10\%; and the percent of patients with grade two GU toxicity was 28\% to 31\%. This review concluded that there was low-level evidence that IMRT provides at least as good a radiation dose to the prostate with less radiation to the surrounding tissues compared with CRT.\textsuperscript{8}

In 2010, an update of the 2008 AHRQ systematic review was undertaken by the AHRQ Technology Assessment Program.\textsuperscript{9} As with the 2008 review, this review concluded that the available data were insufficient to compare the effectiveness of the various forms of radiation treatments. Studies on IMRT were included in the assessment under the category of EBRT and thus reported data were not specific to IMRT. While higher EBRT dosages may result in longer-term biochemical control than lower EBRT dosages, overall and disease-specific
survival data were inconclusive. Additionally, GU and GI toxicities experienced with EBRT did not seem to differ when standard fractionation was compared with moderate hypofractionization. The authors noted the need for further studies to evaluate outcomes of IMRT for the treatment of prostate cancer.\[9\] In addition, a subsequent report was undertaken by the AHRQ Comparative Effectiveness Review Surveillance Program using the search strategy employed for the 2008 systematic review in 2014.\[10\]

Similar findings were observed in a systematic review by Hummell of the clinical effectiveness of IMRT for the radical treatment of prostate cancer undertaken by the U.K. Health Technology Assessment Programme in 2010.\[11\] The literature search was through May 2009, from which eight full-length, non-randomized studies of IMRT versus 3D-CRT were identified. Clinical outcomes were overall survival, biochemical (PSA) relapse-free survival, toxicity, and health-related quality of life. The biochemical relapse-free survival was not affected by treatment received, except when there was a dose difference between groups; in these cases a higher dose with IMRT was favored over lower doses with 3D-CRT. There was some indication that genitourinary toxicity was worse for patients treated with dose escalated IMRT, however, any group difference resolved by six months after treatment. Comparative data of IMRT versus 3D-CRT seem to support the theory that higher doses, up to 81 Gy, can improve biochemical survival for patients with localized prostate cancer, concurring with data on 3D-CRT. Most studies reported an advantage for IMRT in GI toxicity, particularly with regard to the volume of the rectum treated, as toxicity can be reduced by increasing conformality of treatment, which can be more easily achieved with IMRT than 3D-CRT.

A 2007 review by the Institute for Clinical and Economic Review reached the following conclusions:\[12\]

The literature on comparative rates of toxicity has serious methodological weaknesses. There are no prospective randomized trials or cohort trials, and the case series that exist are hampered by the lack of contemporaneous cohorts and/or by a failure to describe the selection process by which patients were assigned to IMRT vs. 3D-CRT. Published case series demonstrate consistent findings of a reduced rate of GI toxicity for IMRT at radiation doses from approximately 75–80 Gy [grays]. Data on GU toxicity have not shown superiority of IMRT over 3D-CRT, nor do the existing data suggest that IMRT provided a lower risk of erectile dysfunction.

and

The literature suggests that the risk of Grade two GI toxicity is approximately 14% with 3D-CRT and 4% with IMRT. Thus, the number of patients needed to treat to prevent one case of moderate-severe proctitis is 10, and for every 100 patients treated with IMRT instead of 3D-CRT, 10 cases of GI toxicity would be expected to be prevented.

**Randomized Controlled Trials**

Additional studies not included in the 2016 meta-analysis by Yu are described next.

In 2016, Viani reported a pseudorandomized trial (sequential allocation) that compared toxicity between IMRT and 3D-CRT in 215 men who had localized prostate cancer.\[13\] Treatment consisted of hypofractionated radiotherapy (RT) at a total dose of 70 Gy at 2.8 Gy per fraction using either IMRT or 3D-CRT. The primary endpoint of the trial was toxicity, defined as any symptom up to six months after treatment (acute) or that started six months after treatment.
Quality of life was assessed with a prostate-specific module. The study 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 acute and late GI and GU toxicity, with similar rates of biochemical control (PSA nadir + 2 ng/mL). The combined incidence of acute GI/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 after treatment.

### 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 GI toxicity</td>
<td>24</td>
<td>7</td>
<td>0.001</td>
</tr>
<tr>
<td>Acute GU toxicity</td>
<td>27</td>
<td>9</td>
<td>0.001</td>
</tr>
<tr>
<td>Late GI toxicity</td>
<td>21.7</td>
<td>6.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Late GU toxicity</td>
<td>12.3</td>
<td>3.7</td>
<td>0.02</td>
</tr>
<tr>
<td>Biochemical control</td>
<td>94.3</td>
<td>96.4</td>
<td>NS</td>
</tr>
</tbody>
</table>

GI: gastrointestinal, grade two or greater toxicity; GU: genitourinary, grade two or greater toxicity; IMRT: intensity modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy.

### Nonrandomized Studies

Sujenthiran (2017) published a retrospective cohort study evaluating 23222 men who were treated for localized prostate cancer with IMRT (n=6933) 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.[14] 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=5962 [68.5%] of 8701 diagnoses). Of 4061 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.

In 2015, Dolezel published a nonrandomized retrospective study with a total of 553 patients with prostate cancer who were treated with 3D-CRT at a dose of 70 or 74 Gy (3D-CRT 70, 3D-CRT 74, respectively) or IMRT at a dose of 78 Gy or a total dose of 82 Gy that included IMRT and a simultaneous integrated boost (SIB) (IMRT 78, IMRT/SIB 82, respectively).[15] Late toxicity was scored according to the Fox Chase Modification of the Radiation Therapy Oncology Group and late Effects Normal Tissue Task Force (FC-RTOG/LENT) late toxicity criteria. Biochemical failure was defined using the Phoenix and American Society for Therapeutic Radiation Oncology (ASTRO) definitions. The five-year risk of grade two to four genitourinary toxicity was 26% in the 3D-CRT 70 group, 27% in the 3D-CRT 74 group, 17% in the IMRT 78 group, and 25% in the IMRT/SIB 82 group, with no intergroup statistical...
differences. The five-year risk of grade two to four gastrointestinal toxicity was 19% (3D-CRT 70), 42% (3D-CRT 74), 20% (IMRT 78), and 27% (IMRT/SIB 82); the differences between the 3D-CRT 74 and 3D-CRT 70 and between 3D-CRT 74 and IMRT 78 groups were statistically significant (log rank, p=0.03). The five-year Phoenix PSA relapse-free survival (PSA-RFS) in low-risk, intermediate-risk, and high-risk patients treated using 3D-CRT were 89%, 66%, and 58%, respectively. Among patients treated with IMRT, the five-year PSA-RFS was 91%, 89%, and 84% among low-, intermediate-, and high-risk patients, respectively. Among patients treated using 3D-CRT versus IMRT for the aforementioned risk groups, clinical relapse-free survival rates (C-RFS) were 95% versus 100%, 87% versus 99%, and, 84% versus 94%, respectively. DFS rates for low-, intermediate- and high-risk patients treated using 3D-CRT were 83%, 71%, and 72%, respectively. For those categories, the IMRT group had DFS rates of 96%, 89%, and 88%, respectively. The differences in PSA-RFS rates for intermediate- and high-risk patients were statistically significant compared with low- risk patients, while C-RFS and DFS rate differences did not differ statistically.

A 2014 nonrandomized study by Morimoto compared acute and subacute urinary and rectal toxicity in patients with localized prostate cancer who received treatment with one of the following four RT techniques: IMRT, 3D-CRT, low-dose-rate permanent implant brachytherapy using I-125 seeds (LDRB), and high-dose-rate brachytherapy (HDRB). Among 156 patients with localized prostate cancer, 57 underwent IMRT; 35 underwent 3D-CRT; 37 underwent I-125 LDRB implant, and 27 underwent HDRB. The prescribed doses were 70 to 74 Gy/35-37 fractions, 70 Gy/35 fractions, 145 Gy, and 45.5 Gy/7 fraction/4 days for IMRT, 3D-CRT, LDRB, and HDRB, respectively. Toxicities (≤6 months) were retrospectively evaluated using the Common Terminology Criteria for Adverse Events, version 4.03. The frequency of grade one or two urinary toxicities using 3D-CRT (33/35 [94%]) was significantly higher than that with HDRB (18/27 [67%]) or IMRT (37/57 [65%]) (p<0.05). The frequency of grade one or two urinary toxicities using LDRB was 31 of 37 (84%). The frequency of grade one or two gastrointestinal toxicities using 3D-CRT (17/35 [49%]) was significantly higher than that using LDRB (4/37 [11%]) or HDRB (0/27 [0%]) (p<0.05). With IMRT, the frequency of grade one or two gastrointestinal toxicities was 32% (18/57), which was significantly higher than that using HDRB (0/27 [0%]) (p<0.05). Grade three or greater adverse events were not observed.

A 2013 study by Michalski reported comparative data of IMRT compared with 3D-CRT in a publication from the high-dose arm of the Radiation Therapy Oncology Group 0126 prostate cancer trial. In this trial, the initial protocol was for 3D-CRT, but during the trial, the protocol was amended to provide 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 were treated to the prostate and seminal vesicles to 79.2 Gy. Radiation exposure for the bladder and rectum were significantly reduced with IMRT. There was a significant decrease in grade two or greater late GI toxicity for IMRT on univariate analysis (p=0.039). On multivariate analysis, there was a 26% reduction in grade two or higher GI toxicity for the IMRT group, but this difference did not meet statistical significance (p=0.099). There were no differences in early or late GU toxicity between groups.

In 2013, Vora reported on nine-year tumor control and chronic toxicities observed in 302 patients treated with IMRT for clinically localized prostate cancer at one institution. The 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 nine years, biochemical control rates were close to 77% for low-risk, 70% for intermediate-risk,
and 53% for high-risk patients (log rank, p=0.05). At last follow-up, only 0%/0.7% had persistent grade ≥3 GI/GU toxicity. The high-risk group was associated with a higher distant metastasis rate (p=0.02) and death from prostate cancer (p=0.001). \[18\]

In 2011, Alicikus reported on 10-year outcomes in 170 patients treated after high-dose IMRT (81 Gy).\[19\] The 10-year actuarial PSA relapse-free survival rates were 81% for the low-risk group, 78% for the intermediate-risk group, and 62% for the high-risk group. The 10-year distant metastases-free rates were 100%, 94%, and 90%, respectively, and cause-specific mortality rates were 0%, 3%, and 14%, respectively. The 10-year likelihood of developing grade two and three late GU toxicity was 11% and 5%, respectively, and the likelihood of developing grade two and three late GI toxicity was 2% and 1%, respectively. No grade four toxicities were observed.

In 2009, Wong reported on a retrospective study of radiation dose escalation in 853 patients with localized (T1c-T3N0M0) prostate cancer.\[20\] 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 EBRT plus brachytherapy boost (n=44). All patients were followed for a median of 58 months (range, 3-121 months). The five-year overall survival for the entire group was 97%. The five-year [biochemical control] bNED 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 BRT alone; and 94%, 100%, and 97%, respectively, for EBRT plus BRT. The bNED rates for 3D-CRT were significantly less than those of the other higher dose modalities (p<.0001).

In 2008, Zelefsky reported on the incidence and predictors of treatment-related toxicity at 10 years after 3D-CRT and IMRT for localized prostate cancer.\[21\] Between 1988 and 2000, 1571 patients with stages T1-T3 prostate cancer were treated with 3D-CRT or IMRT, with doses ranging from 66 to 81 Gy. Twenty-two percent were considered to be at low risk, as based on National Comprehensive Cancer Network (NCCN) guidelines. The median follow-up was 10 years. The actuarial likelihood at 10 years for the development of grade two or higher GI toxicities was 9%. The use of IMRT significantly reduced the risk of GI toxicities compared with conventional 3D-CRT (13% to 5%, p<0.001). Among patients who experienced acute symptoms, the 10-year incidence of late toxicity was 42%, compared with 9% for those who did not experience acute symptoms. The 10-year incidence of late grade two or higher GU toxicity was 15%. Patients treated with 81 Gy (IMRT) had a 20% incidence of GU symptoms at 10 years, compared with 12% for patients treated with lower doses (p=0.01). Among patients who had developed acute symptoms during treatment, the incidence of late toxicity at 10 years was 35%, compared with 12%. The incidence of grade three GI and GU toxicities was 1% and 3%, respectively.

In 2008, Cahlon reported on preliminary biochemical outcomes and toxicity with high-dose IMRT to a dose of 86.4 Gy for localized prostate cancer.\[22\] For this study, 478 patients were treated between August 1997 and March 2004 with 86.4 Gy using a five- to seven-field IMRT technique. The median follow-up was 53 months. Thirty-seven patients (8%) experienced acute grade two GI toxicity; none had acute grade three or four GI toxicity; 105 patients (22%) experienced acute grade two GU toxicity; and three patients (0.6%) had grade three GU toxicity. Sixteen patients (3%) developed late grade two GI toxicity; two patients (<1%) developed late grade three GI toxicity; 60 patients (13%) had late grade two GU toxicity; and 12 (<3%) experienced late grade three GU toxicity. The five-year actuarial PSA relapse-free survival, according to the nadir plus 2 ng/mL definition, was 98%, 85%, and 70% for the low-,
intermediate-, and high-risk NCCN prognostic groups.

**NCCN Recommendations for RT Dose for Low-Risk vs Intermediate to High-Risk Prostate Cancer**

NCCN has made recommendations for the use of RT for patients with prostate cancer, based on risk stratification by clinical and pathologic findings. These recommendations are based on some studies that did include the use of IMRT as the mode of radiation therapy and others that did not.

In 1993, the University of Texas M.D. Anderson Cancer Center activated an RCT to compare toxicity and patient outcomes after 78 Gy using 3D-CRT versus 70 Gy using conventional (2D) in patients with localized prostate cancer. The long term results of this study were reported by Kuban and colleagues in 2008.[23] 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 groups in the 70 and 78 Gy groups were low risk (n=31 and n=30), intermediate risk (n=71 and n=68), and high risk (n=48 and n=53), respectively. When analyzed by risk group, patients with low risk disease treated to 78 Gy versus 70 Gy, had a freedom from biochemical or clinical failure (FFF) of 88% and 63%, respectively (p=0.042). The intermediate-risk patients showed no statistically significant difference in FFF based on dose level (p=0.36). Patients with high-risk disease showed a significant difference in FFF based on dose (63% vs 26%, p=0.004), although when these high-risk patients were divided by PSA level, only those patients with a PSA level greater than 10 ng/mL showed a difference in FFF based on dose level.

NCCN guidelines cite the 2008 Kuban study as evidence for a dose of 75.6 to 79.2 Gy (with or without 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 cites the following studies.

In 2011, Xu reported a toxicity analysis of dose escalation from 75.6 to 81.0 Gy in 189 patients receiving definitive radiation therapy for prostate cancer.[24] Patients were a mixture of high, intermediate, and low risk according the NCCN definitions, and received dose according to physician discretion. A total of 119 patients received 75.6 Gy and 70 received 81.0 Gy. Patients were followed up at intervals of three to six months for five years and yearly thereafter (median follow-up, 3.0 years). The method of RT was at the discretion of the treating physician, and included IMRT in 60% and conventional RT in 40%. The 81.0 Gy group had higher rates of grade two 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 when compared with the 75.6 Gy group.

In 2008, Zelefsky reported on the incidence and predictors of treatment-related toxicity at 10 years after 3D-CRT and IMRT for localized prostate cancer.[21] This study is described previously in this review.

In 2007, Eade reported the results of 1530 consecutive patients treated for localized prostate cancer with 3D-CRT between 1989 and 2002.[25] The patients were divided into four dose groups: <70 Gy (n=43), 70-74.9 Gy (n=552), 75-79.9 Gy (n=568), and ≥80 Gy (n=367). Median follow-up ranged from 46 to 86 months. The group that received ≥80 Gy had a median follow-up of 45.6 months. The group of patients that received ≥80 Gy was mixed, with 64 (17%) with
low-risk cancer, 247 (67%) intermediate-risk, and 56 (16%) high-risk. Intermediate- and high-risk patients made up 44%, 46%, and 48% of the <70 Gy, 70-74.9 Gy, and 75-79.9 Gy groups, respectively. Adjusted five-year estimates of freedom from biochemical failure (FFBF) for the four groups were 60%, 68%, 76%, and 84% using ASTRO criteria and 70%, 81%, 83%, and 89% using Phoenix criteria. Adjusted five-year and 10-year estimates of freedom from distant metastases for the four groups were 96% and 93%, 97% and 93%, 99% and 95%, and 98% and 96%. The authors concluded that a pronounced RT dose-response by FFBF was seen after adjusting for pretreatment PSA, GS and tumor stage and that the vast majority of patients should receive 80 Gy or more although a subgroup of favorable patients may be adequately treated with less than 80 Gy.

Section Summary: Primary (Definitive) RT for Localized Prostate Cancer

The evidence on IMRT for definitive treatment of localized prostate cancer includes a few prospective comparative studies, retrospective comparative studies, and systematic reviews of these studies. Results generally show that IMRT provides tumor control and survival outcomes similar to 3D-CRT, with a reduction in GI and GU toxicity. A reduction in clinically significant complications of RT is likely to improve quality of life for treated patients.

THERAPY FOR PROSTATE CANCER AFTER PROSTATECTOMY

The 2012 Bauman systematic review found insufficient data to recommend IMRT over 3D-CRT in the postprostatectomy setting.[6]

In 2014, initial results of the PLATIN three trial (Prostate and Lymph Node Irradiation with Integrated-Boost- IMRT after Neoadjuvant Antihormonal Treatment) were published.[26] This phase two trial evaluated the safety and feasibility of irradiation of the pelvic lymph nodes simultaneously with a boost to the prostate bed. From 2009 to 2011, 40 patients with high-risk features or inadequate lymphadenectomy after RP were enrolled; 39 patients finished the treatment. Treatment consisted of two 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 acute grade three or four toxicity occurred. 22.5% of patients experienced acute grade two GI and GU toxicity and 10% late grade two GI and 5% late grade two GU toxicity. One patient developed late grade three proctitis and enteritis. After a median of 24 months, 89% of patients were free of a PSA recurrence.

In 2014, acute toxicity results from the PRIAMOS1 (Hypofractionated Radiotherapy of the Prostate Bed With or Without the Pelvic Lymph Nodes) trial were reported.[27] This prospective phase two trial assessed 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 completion of therapy, there were no adverse events grade three or greater. Acute GI toxicity rates were 56.4% and 17.9% for grade one and two, respectively, and acute GU toxicity was recorded in 35.9% of patients at a maximum grade of one.

In 2013, Corbin reported adverse effects in high-risk men two years after IMRT post-prostatectomy.[28] Between 2007 and 2010, 78 consecutive men received either adjuvant RT
(n=17 [22%]) or salvage RT (n=61 [78%]). 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 two-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 lower at two months but improved or unaffected over follow-up.

### 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 GI toxicity</td>
<td>7 (8.6)</td>
<td>3 (3.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Acute upper GI toxicity</td>
<td>18 (22.2)</td>
<td>6 (6.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Acute GU toxicity</td>
<td>10 (12.3)</td>
<td>6 (6.6)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

GI: gastrointestinal, grade two or greater toxicity; GU: genitourinary, grade two or greater toxicity; IMRT: intensity modulated radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy.

In 2013, Massaccesi reported preliminary results of acute toxicities during a phase two trial of hypofractionated IMRT with simultaneous integrated boost (SIB) to the pelvic nodes and prostate bed after prostatectomy.[29] Between November 2008 and February 2012, 49 patients considered to be at high risk of relapse after RP or who had biochemical relapse received 45 GY in 1.8 Gy fractions to the whole pelvis and 62.5 Gy, 2.5 Gy fractions (equivalent dose, 68.75) to the prostate bed. The toxicity findings were compared to those of 52 consecutive patients who underwent adjuvant or salvage 3D-CRT with standard 2 Gy fractionation to the prostatic bed and regional pelvic nodes who were selected from an electronic database. Grade one or greater 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 two 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 three acute GU toxicity. Thirty (29.7%) patients developed grade two acute GI toxicity; the difference between groups was not significant. No cases of grade three acute GI toxicity were reported. The authors concluded that the acute toxicity profile for hypofractionated high-dose SIB-IMRT in the post prostatectomy setting compares favorably with that of conventionally fractionated high-dose 3D-CRT.

A 2013 AUA/ASTRO guideline on the use of adjuvant and salvage RT after prostatectomy was based on a systematic review of the literature from 1990 to 2012, which yielded 294 articles.[4] The panel’s comments on RT technique state that they attempted to determine which technique and doses produced optimal outcomes, but that it was not possible to answer these questions from available data, as the majority of the data come from observational studies and approximately one-third treated patients with conventional (2D) external beam modalities. Of the literature included in the review, less than 5% reported using IMRT. The panel stated that 64 to 65 Gy is the minimum dose that should be delivered after prostatectomy, but that this should be individualized to the patient.

Alongi 2009 reported the results of acute toxicity of whole-pelvis irradiation in 172 consecutive patients with clinically localized prostate cancer who were treated with either IMRT or 3D-CRT as adjuvant (n=100) or salvage (n=72) RT after radical prostatectomy and pelvic lymph node dissection.[30] 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 >7 and/or preoperative PSA >10 ng/mL). Eighty-one patients underwent 3D-CRT and 91 underwent IMRT. No grade three or higher acute GU or lower GI side effects were observed. Acute grade two GU occurred in 10 (12.3%) of 81 of the 3D-CRT group and in 6 (6.6%) of 91 of the IMRT group (p=0.19). For acute lower GI grade two events, the incidence was 7 (8.6%) of 81 in the 3D-CRT group versus 3 of 91 (3.3%) in IMRT (p=0.14) group. Acute upper GI grade two or higher toxicities were 18 of 81 (22.2%) of 81 and 6 of 91 (6.6%) of 91 in 3D-CRT and IMRT group, respectively (p=0.004). The authors concluded that acute toxicity following postoperative whole pelvis irradiation was reduced with the use of IMRT as compared to 3D-CRT; this effect was most significant for upper GI symptoms, owing mainly to better bowel sparing with IMRT.

Section Summary: RT for Prostate Cancer After Prostatectomy

The evidence on IMRT for prostate cancer after prostatectomy includes nonrandomized comparative studies, single-arm phase two 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 improvement 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

The evidence for IMRT in individuals who have localized prostate cancer and are undergoing definitive radiotherapy includes a few prospective comparative studies, retrospective cohort studies and case series, and systematic reviews of these studies; well-designed randomized controlled studies comparing IMRT with 3D-CRT are lacking. Relevant outcomes are overall survival, disease-free survival, quality of life, and treatment-related morbidity. Although the available evidence is of lower quality, limited evidence suggests that IMRT provides tumor control and survival outcomes comparable with 3D-CRT with a reduction in GI and GU toxicity. These findings are supported by treatment planning studies which predict that IMRT improves target volume coverage and sparing of adjacent organs at risk compared with 3D-CRT. In the treatment of localized prostate cancer, although results are not uniform, some studies have shown reductions in gastrointestinal and genitourinary toxicity with the use of IMRT. A reduction in clinically significant complications of RT is likely to lead to an improved quality of life for treated patients. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for IMRT in individuals who have prostate cancer and are undergoing radiotherapy after prostatectomy includes early results from phase two trials, case series, and evidence-based society guidelines. Relevant outcomes are overall survival, disease-free survival, quality of life, and treatment-related morbidity. Although the available evidence is of lower quality, limited evidence suggests that IMRT provides tumor control and survival outcomes comparable with 3D-CRT. Treatment planning studies have shown that the use of IMRT provides better target volume coverage and better sparing of adjacent organs at risk than with 3D-CRT. In the treatment of prostate cancer after prostatectomy, a small series
found a significant improvement in acute gastrointestinal toxicity with the use of IMRT compared to 3D-CRT, mainly due to the ability of IMRT to provide better bowel sparing. A reduction in clinically significant complications of radiotherapy is likely to lead to an improved quality of life for treated patients. The evidence is sufficient to determine qualitatively 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 two trials, and systematic reviews of these studies. Relevant outcomes are OS, disease-free survival, quality of life, and treatment related morbidity. Although the comparative studies are primarily retrospective, the evidence generally shows that IMRT provides tumor control and survival outcomes similar to 3D-CRT. Notably, one retrospective comparative study found a significant improvement 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.

**PRACTICE GUIDELINE SUMMARY**

**NATIONAL COMPREHENSIVE CANCER NETWORK**

The most recent National Comprehensive Cancer Network (NCCN) guidelines (v.4.2018) for prostate cancer indicate, in the principles of radiotherapy (RT) for primary external beam radiation therapy, highly conformal radiotherapy (CRT) should be used in conventional fraction doses of 75.6 to 79.2 Gy for low-risk prostate cancer and up to 81 Gy for intermediate- and high-risk prostate cancer.[31] A reference in the discussion section indicates IMRT is preferred over 3D-CRT because it seems to decrease salvage therapy rates while the risk of adverse effects such as gastrointestinal toxicities are reduced with IMRT.

NCCN states that evidence supports offering adjuvant/salvage RT in most men with adverse pathologic features or detectable PSA and no evidence of disseminated disease. Indications for adjuvant RT include pT3 disease, positive margins, or seminal vesicle involvement. Indications for salvage RT include an undetectable PSA that becomes detectable and then increases on two subsequent measurements. The recommended prescribed doses for adjuvant/salvage post-prostatectomy RT are 64-72 Gy in standard fractionation. NCCN guidelines also indicate 3D-CRT or IMRT may be considered as initial treatment options in all prostate cancer patients except for patients with a very low risk of recurrence and less than 20 years’ expected survival.

**AMERICAN UROLOGICAL ASSOCIATION AND AMERICAN SOCIETY FOR RADIATION ONCOLOGY**

American Urological Association (AUA) and American Society for Radiation Oncology (ASTRO) guidelines (2013) address the use of adjuvant and salvage radiotherapy after radical prostatectomy.[4] The guidelines state that adjuvant RT should be given to patients with adverse pathologic findings at prostatectomy and salvage RT to patients with PSA or local recurrence after prostatectomy if there is no evidence of distant metastases, but that the available data do not answer the question of which RT technique and dose produces optimal outcomes in this setting.
The UAU, ASTRO, and the Society of Urologic Oncology (SUO) published guidelines for clinically localized prostate cancer in 2017.[32] The guidelines state that external beam radiotherapy is an option for low-, intermediate-, and high-risk localized prostate cancer and one of the options for treatment is IMRT.

The American College of Radiology Appropriateness Criteria indicates IMRT is the standard for definitive external beam RT of the prostate.[33]

**SUMMARY**

There is enough research to show improved health outcomes with use of radiotherapy in the treatment of prostate cancer. The use of intensity-modulated radiotherapy (IMRT) can minimize the radiation dose to surrounding normal tissues and structures. In addition, practice guidelines recommend IMRT for the treatment of prostate cancer. Therefore, IMRT may be considered medically necessary for the treatment of prostate cancer when policy criteria are met. IMRT is considered not medically necessary when policy criteria are not met due to the tumor not being in close proximity to organs at risk and when a clinical analysis fails to show that only through IMRT planning can published dose/volume constraints be met for organ(s) at risk.

**REFERENCES**


34. BlueCross BlueShield Association Medical Policy Reference Manual "Intensity-Modulated Radiotherapy of the Prostate." Policy No. 8.01.47
**NOTE:** The correct code to use for image fusion performed to provide enhanced delineation of target and normal critical structures is CPT code 77399 (Unlisted procedure, medical radiation physics, dosimetry and treatment devices, and special services); however, it is considered part of the treatment planning.

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<td></td>
<td>77385</td>
<td>Intensity modulated radiation treatment deliver (IMRT), includes guidance and tracking, when performed; simple</td>
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<tr>
<td></td>
<td>77386</td>
<td>;complex</td>
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<td>G6015</td>
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<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>
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**Date of Origin:** April 2011