ACR Appropriateness Criteria® Postradical Prostatectomy Irradiation in Prostate Cancer

By Gary S. Gustafson, MD [6], Paul L. Nguyen, MD [7], Dean G. Assimos, MD [8], Anthony V. D’Amico, MD, PhD [9], Alexander R. Gottschalk, MD, PhD [10], I-Chow Joe Hsu, MD [11], Shane Lloyd, MD [12], Patrick W. Mclaughlin, MD [13], Gregory S. Merrick, MD [14], Timothy N. Showalter, MD [15], Al V. Taira, MD [16], Neha Vapiwala, MD [17], Yoshiya Yamada, MD [18], and Brian J. Davis, MD, PhD [19]

The purpose of this article is to present an updated set of American College of Radiology consensus guidelines formed from an expert panel on the appropriate use of radiation therapy in postprostatectomy prostate cancer.

Source:

Summary of Literature Review

Introduction/Background

Radical prostatectomy (RP) and radiation therapy (RT), including brachytherapy, are the primary treatment options for organ-confined prostate cancer (T1-2, stages I or II). Eventually, 50% to 70% of postprostatectomy patients with high-risk pathologic features, such as a positive margin, extracapsular extension (ECE), and/or seminal vesicle involvement (SVI), will develop biochemical failure (BF).[1] Thus, RT may play a role either immediately following prostatectomy, based on various known high-risk pathologic features, or at the time of BF.[2-5]

There are three main clinical scenarios in which RT is given after RP: (1) adjuvant radiotherapy (ART) for men with undetectable or barely detectable levels of prostate-specific antigen (PSA; < 0.2 ng/mL) who have high-risk pathologic features; (2) salvage radiotherapy (SRT) for men with undetectable or barely detectable PSA levels (< 0.2 ng/mL) immediately postoperatively but whose PSA rises at some later date—a delayed rise in PSA (DR-PSA); and (3) SRT for men whose PSA remains at 0.2 ng/mL or above postoperatively—a persistently detectable PSA (PD-PSA).

The purpose of distinguishing between ART and SRT is rooted in the observation that there are significant differences between the two groups in terms of prognosis after RT, dose of RT administered, and prognostic factors. The further subdivision of salvage patients into two groups, those with a DR-PSA vs those with a PD-PSA, is useful because their outcomes after RT appear to be different,[6-10] with a worse prognosis for those with a PD-PSA. In general, the earlier the rise in PSA after RP, the worse the outcome because of a higher risk of metastatic disease.

Adjuvant Radiotherapy

The rationale for administering ART after RP is predicated on the assumption that microscopic local disease remains. Local therapy reduces the rate of recurrence in the prostate bed and may reduce the risk that the residual nidus of prostate cancer will disseminate distantly. The decision to administer ART is based on the presence of high-risk pathologic findings in the prostatectomy specimen. The primary high-risk features are ECE, positive margins (prostate cancer at the margin of resection), and SVI.[11] The rate of adverse pathologic findings may vary considerably due to patient selection and prognostic factors, as well as surgical technique and pathologic evaluation, but adverse findings occur at approximate rates of 40% for ECE, 25% for margin positivity, 10% for SVI, and 5% for lymph node involvement (LNI).[12-22]

The prevalence of persistent local disease following RP is significant. Residual disease has been documented in approximately 50% of prostatectomy cases at autopsy,[23] and in biopsy specimens of the prostatic fossa and urethrovessical anastomosis.[11,24-26] Long-term follow-up has revealed that the risk of BF following prostatectomy is substantial. Various surgical series have reported that this risk continues to be present between 5 and 10 years after prostatectomy, with an average relative risk of 2%–3% per year, without reaching a plateau.[22,27-29] Late BFs are not insignificant.
and may eventually lead to the development of painful bony metastases in 50% of patients within 7–8 years.[30-32] ART has the potential to reduce failure and ultimately improve quality of life, leading to fewer local and systemic failures.[33] Failure may lead to the need for additional therapy using androgen deprivation, and the associated treatment side effects. Patients with a life expectancy of > 10 years should benefit from ART.

A powerful predictor of biochemical and local failure after prostatectomy is margin positivity. It is estimated that approximately 40% of men with a positive surgical margin will experience a rise in PSA to detectable levels within 5–10 years.[13,34-40] Other pathologic features that predict for BF include ECE, also referred to as extraprostatic extension, Gleason score ≥ 7, and SVI.[4,13,36,37,39-43] The extent of margin positivity is another factor shown to influence BF[37,44,45] that has only been examined in retrospective series. ART may have less of an effect in the case of a small focal positive margin in the absence of other unfavorable pathologic features.[46] In this setting, other factors, such as the degree of extraprostatic extension[47] and/or Gleason score ≥ 7, appear to contribute to a greater risk of BF and provide a stronger rationale for ART. Similarly, a focal area of ECE alone is associated with a lower risk of biochemical progression, as compared with more extensive ECE, but the risk will be higher when the ECE is accompanied by Gleason score ≥ 7 disease.

In the setting of negative margins and a rising PSA, a complete biochemical response to SRT is still achieved in the majority of cases, suggesting that local disease persists in the prostatic fossa only. A rising PSA after a negative margin has been associated with a worse prognosis in some prostatectomy series[48,49]; however, it should be kept in mind that not every micron of tissue in the prostatectomy specimen is pathologically assessed. The RT response data suggest that tumor cells were left behind (a focal positive margin) but were not identified on pathologic evaluation. The risk of local disease persistence when there is obvious ECE in addition to a Gleason score ≥ 7,[47] even with negative margins, is significant enough that ART should be considered.

Adjuvant radiotherapy outcomes

Many retrospective studies have examined the role of ART.[50-55] Three prospective randomized trials comparing prostatectomy alone with prostatectomy plus ART have been reported.[22,55,56] All three trials have demonstrated an improvement in biochemical control of approximately 20% when ART is employed, with one trial demonstrating an improvement in both metastasis-free and overall survival. The European Organisation for Research and Treatment of Cancer (EORTC) 22911 study included 972 patients with pT2-3 prostate cancer with at least one high-risk feature (ECE, positive margins, or SVI). Freedom from biochemical failure (FFBF) at 5 years was 53% in the RP-alone group vs 74% in the RP plus RT (60 Gy) group (P < .0001)[56,57] and at 10 years was 41% vs 61%, respectively.

A similar study was conducted by the Southwest Oncology Group (SWOG).[33] A total of 473 patients with pathologically determined ECE, positive margins, and/or SVI were randomized to RT (at 60–64 Gy) vs observation. FFBF was significantly improved by the addition of radiation, from 38% to 61% at 5 years and from 23% to 47% at 10 years. This benefit was shared by each of the three pathologic risk groups. ART also obviated the need for androgen deprivation therapy (ADT) in some patients and delayed its use significantly (by 2.5 years) in others. The most recent update of this study demonstrates an improvement in its primary endpoint of metastasis-free survival, as well as in overall survival. With a median follow-up of 12.7 years, out of 425 evaluable patients, metastasis developed in 114 of 211 patients in the observation arm vs 93 of 214 patients who received early adjuvant therapy (P = .016). In addition, there have been 110 deaths in the observation arm vs 88 deaths among the irradiated patients (P = .023). Although ART initially resulted in some adverse impacts on quality of life, this difference disappeared by 2 years after treatment, and the irradiated patients actually fared better beyond 3 years after RT in terms of overall quality of life.[33] A third study (the German Cancer Society trial ARO 96-02) randomized 388 men with pT3 disease after prostatectomy and an undetectable postoperative PSA to either RT (60 Gy) or observation.[58] The 5-year FFBF rate was 54% in the RP-alone group vs 72% in the RP plus RT group (P = .0015). ART was very well tolerated, with a 0.3% rate of grade 3/4 late adverse events (see Variant 1 and Variant 2).

Salvage Radiotherapy

RT is given for salvage after RP in three settings: (1) for a DR-PSA after the PSA has dropped to an undetectable level immediately postprostatectomy, (2) for a PD-PSA after surgery, and (3) for
treatment of a documented recurrence within the prostatic fossa. This distinction in categorizing patients suitable for SRT is relevant because the initial considerations in evaluation may be different. Furthermore, there are reported differences in outcome. However, many retrospective series were based on small patient numbers and did not separate these patients, making conclusions difficult.

Time to development of a rising PSA after prostatectomy, the prostatectomy Gleason score, and the PSA doubling time (PSADT) are independent predictors of distant metastasis and mortality.[30,31,59] When the time to BF is < 3 years (the PD-PSA patients would be included in this group), Gleason score is ≥ 8, and PSADT is < 9 months, the risk of death due to prostate cancer at 5 years is ≥ 19%. This risk increases to ≥ 74% at 10 years.[31] In another study, PSADT of < 6 months was associated with an increase in BF, distant metastasis, and prostate cancer–specific mortality.[59] PSADT has taken on much more importance over the last 5 years.[49,60,61] If the above parameters included a postoperative PSADT of < 3 months, nearly 50% would die within 5 years. PSA kinetics prior to prostatectomy may also be an independent determinant of mortality.[62-64] A rapidly rising PSA prior to RP or RT connotes a poor prognosis and is suggestive of occult metastatic disease even if the metastatic workup is negative. Nonetheless, salvage RT has the potential to improve prostate cancer–specific survival rates with short PSADT, as reported by Trock et al.[65] Thus, patients with short PSADT, although their prognosis is poorer than it would be otherwise, should be considered for SRT. Although the ability to predict progression after SRT has improved, definitive statements regarding optimal treatment regimens are difficult due to the absence of contemporary prospective clinical trials. There is a need to optimize treatment selection, with the goal of prolonging survival without unnecessary toxicity, particularly in the setting of rapid PSA kinetics and negative metastatic workup.

Factors indicating that postprostatectomy RT for a PD-PSA might be beneficial include extensive extraprostatic extension (particularly in patients with high-grade disease) or positive margins. Other indicators that there may be disease in the prostatic fossa are SVI, a cut-through of the prostate (a partial prostatectomy when there is evidence of prostate remaining, from palpation, biopsy, or imaging), or incomplete removal of the seminal vesicles in the setting of T3 disease (especially with ECE at the base or with SVI). In the absence of these features, and with a PSA that rises quickly (doubling time < 6 months), the probability of distant metastasis is high,[30,60,66-68] and SRT may be less beneficial.

The results of SRT have been relatively poor, with 5-year FFBF rates in most series ranging from 10% to 66%.[7-10,48,67,69-74] The following factors have been correlated with worse FFBF rates: Gleason score > 7, SVI, high pre-RT PSA level (> 1 ng/mL to > 2.5 ng/mL), short PSADT, negative prostatectomy margins, treatment for a PD-PSA (vs a DR-PSA), a palpable prostatic fossa mass, and RT dose < 65 Gy.

Salvage radiotherapy outcomes

In general, when the PSA remains detectable after RP, the risk of distant metastasis is greater than when the PSA becomes undetectable following prostatectomy and then rises later. Thus, outcomes of SRT in most series have been worse for patients with a PD-PSA compared with a DR-PSA.[7,8,10,71] However, some series have not found a significant difference in FFBF rates between the two groups.[9,49,73,75] Although distinguishing between the groups seems to be the most objective way of evaluating the utility of SRT, most of the studies reporting SRT outcomes do not separately analyze the DR-PSA and the PD-PSA patients. In addition, all of these studies are retrospective, and most include small numbers of patients.

As described above, the PSADT is an important predictor of SRT outcome. The shorter its duration, the greater the risk of death due to prostate cancer. A doubling time of ≤ 10 months in the setting of a DR-PSA or a PD-PSA indicates a higher likelihood of occult metastatic disease.[30,49,59,60,66-68] thus rendering postoperative RT much less effective. Another study showed that a PSADT of ≥ 5 months predicted a response to SRT (a response was defined as a PSA nadir of ≤ 0.1 ng/mL).[76] One caveat concerning the PSADT as a reliable predictor of distant metastasis is that when the PSA is below 1 ng/mL, the estimates may be inaccurate.[68,77,78] In reports of postoperative RT, few have identified PSADT as a predictor of FFBF. In a preliminary recursive partitioning analysis of 1,168 men in a pooled multi-institutional database, PSADT was not independently related to outcome, although pre-RT PSA, Gleason score, and margin status were related.[79] Standardization is needed both for when the PSADT calculation begins (from the PSA just prior to when an accelerated rise occurs or from the time of the first detectable PSA) and for the minimum number of PSA values required to accurately calculate a PSADT.

The pre-RT PSA has been found to be the most consistent predictor of FFBF in both univariate and
multivariate analyses of SRT.[80-83] Although a clear pre-RT PSA cutpoint has not yet been defined, evidence suggests that lower pre-RT PSAs are associated with higher FFBF rates. The best results have been seen when the pre-RT PSA is ≤ 1 ng/mL. A significant decline in FFBF is seen when the pre-RT PSA increases from ≤1 ng/mL to 2 ng/mL, and then to > 2 ng/mL. Data suggest that initiating SRT at a lower PSA level leads to an improved outcome, with each incremental 0.1 ng/mL PSA increase resulting in an average 2.6% loss in the percentage of patients with relapse-free survival.[84]

Other important prognostic factors include the Gleason score, margin status, and seminal vesicle invasion. Gleason scores of ≤ 7 predict for a better prognosis compared with scores of 8-10. A positive margin often indicates residual disease in the prostate bed, for which SRT is effective, and FFBF rates are higher when this is the case. Seminal vesicle invasion has also been found to be a determinant of outcome in multivariate analysis in many series, with worse FFBF rates when the seminal vesicles were involved, due to these patients being at a higher risk for the development of subsequent metastatic failure[7,48,49] (see Variant 3).

External Beam Therapy

Intensity-modulated radiation therapy (IMRT) and image-guided RT

External beam therapy is the standard mode of delivery. Multiple studies, as described above, demonstrate its effectiveness. As with definitive external beam therapy for prostate cancer, multiple techniques may be used in the postoperative setting. IMRT or three-dimensional–conformal radiation therapy (3D-CRT) and image guidance are the preferred techniques. Dosimetric studies have been done comparing 3D-CRT vs IMRT in the postoperative setting. IMRT may be the preferred technique, as it may allow for dose escalation with limited toxicity.[85-94] Koontz et al[91] compared 3D-CRT and IMRT for postprostatectomy RT. In their comparison, IMRT reduced the volume of bladder and rectum receiving high radiation doses during treatment. Ost et al[93] evaluated 104 patients using IMRT to a median dose of 74 Gy in the postprostatectomy setting. The toxicity profile was acceptable. Using European Organisation for Research and Treatment of Cancer consensus guidelines for target volumes, Harrison et al[90] compared IMRT (at 72 Gy) vs 3D-CRT (to 68.4 Gy) in 28 patients. The dosimetric parameters were improved with IMRT with respect to dose to the rectum and bladder.

In the SRT setting, in a comparison study of 3D-CRT and IMRT, Goenka et al[88] demonstrated a similar risk of grade > 2 genitourinary (GU) toxicity and a reduction in the risk of grade > 2 gastrointestinal (GI) toxicity. In the salvage setting, with or without androgen deprivation, Ost et al[94] were able to deliver 76 Gy with a toxicity profile similar to that of 3D-CRT delivered at a dose of 68 Gy. In addition, Ost et al[92] did a matched-control analysis of ART and SRT using IMRT. First, for ART the dose was 74 Gy and for SRT the dose was 76 Gy. Secondly, the authors demonstrated a benefit for ART over SRT. Lastly, for ART, the GI and GU toxicity rates were zero and 4%, respectively. In the SRT group, GI and GU toxicity rates were 3% and 3%, respectively. In a large group comparison study, Crandley et al[87] analyzed complications related to IMRT vs 3D-CRT. There has been an increased use of IMRT as the technique of choice. The study showed a decrease in GI complications but a higher rate of GU incontinence with IMRT, compared with 3D-CRT. Nonetheless, a comparison review of IMRT and 3D-CRT by Goldin et al[89] showed no significant difference in rates of long-term GI complications, nonurinary incontinence morbidity, GU incontinence, or erectile dysfunction. Using these comparisons, the bulk of the data favor IMRT over 3D-CRT.

Furthermore, based on the experience gleaned from multiple studies in the setting of treatment for primary intact prostate cancer, IMRT may be considered the technique of choice. Zelefsky et al[95] showed a decrease in rectal toxicity with IMRT compared with 3D-CRT, with a reduction of grade 2/3 rectal bleeding, from 15% with 3D-CRT to 3% with IMRT. In a 2002 report by Zelefsky et al[96] involving 772 patients, the 3-year actuarial rectal grade 2 toxicity was 4%, and the urinary grade 2 toxicity was 15%, comparing favorably with the results of 3D-CRT. In this study, 90% of patients were treated to a dose of 81 Gy, and 10% were treated to 86.4 Gy. The 3-year actuarial PSA biochemical control rates were 92% for favorable disease, 86% for intermediate disease, and 81% for unfavorable disease.

Spratt et al[97] recently updated the Memorial Sloan Kettering experience with prostate cancer patients treated to 86.4 Gy. In this study of 1,002 patients, the 7-year prostate cancer–specific mortality rates were 0%, 3.3%, and 8.1% in the low-risk, intermediate-risk, and high-risk groups, respectively. Rates of Common Terminology Criteria for Adverse Events (CTCAE) v4.0 grade 3 GI and GU toxicity were only 0.7% (mainly rectal bleeding) and 2.2% (mainly urethral strictures and
hemorrhagic cystitis), respectively. Michalski et al.[98] recently published in abstract form a re-analysis of the RTOG 9406 dose-escalation studies in which patients were treated to 79.2 Gy using either 3D-CRT or IMRT (in a nonrandomized fashion). The authors found an association between use of IMRT and reduced CTCAE grade 2 or higher acute GU and GI toxicity, although no significant difference in late toxicity was seen.

A study reported by Chung et al.[99] also addressed the additional technical improvement of implanting fiducial markers to facilitate image-guided radiation therapy (IGRT). In this study, prostate margins were reduced from 1 cm to 2-3 mm with placement of fiducials, resulting in a decrease in grade 2 rectal toxicity (80% vs 13%, respectively) and bladder toxicity (60% vs 13%, respectively). Zelefsky et al.[100] also recently reported on a retrospective series in which men treated to the same dose with IGRT vs IMRT had significantly lower 3-year grade 2+ late urinary toxicity (10.4% vs 20.0%, respectively, \(P = .03\)), although no difference in rectal toxicity was seen (\(P = .81\)).

Therefore, based on these dosimetric studies and clinical experience, IMRT and image guidance are considered preferable, if not essential, in the delivery of postprostatectomy RT. The appropriate radiation dose to the prostatic fossa in the adjuvant or salvage setting ranges from 64.8 Gy to 70.2 Gy.[11,29-31,101] Higher doses have been delivered with acceptable toxicity[90,93] and may be appropriate under certain conditions.

Summary

- A high percentage of radical prostatectomy (RP) patients with high-risk pathologic features (positive surgical margins, extraprostatic extension of cancer, seminal vesicle involvement) will experience a subsequent biochemical failure, often due to progression of residual disease within the surgical bed.
- The addition of adjuvant RT <br/>directed at the prostatic fossa in these patients has been shown in three prospective randomized trials to improve the biochemical freedom-from-failure rate in the irradiated patients and, in one trial, provided improvement in metastasis-free and overall survival.
- Salvage RT, in which patients with biochemically detectable disease receive RT to the prostate bed, has been associated with improvements in cancer-specific and overall survival in retrospective series but has not been tested in a randomized fashion.
- The appropriate radiation dose to the prostatic fossa in the adjuvant or salvage setting ranges from 64.8 Gy to 70.2 Gy. Higher doses may be appropriate if there is evidence of gross recurrence within the prostate bed.
- Addition of pelvic RT to prostatic fossa radiation is generally discouraged, but it may be appropriate in certain clinical situations (eg, absence of lymph node dissection, evidence of nodal involvement at prostatectomy or on imaging studies).
- The benefit of neoadjuvant/adjuvant androgen deprivation therapy with adjuvant or salvage radiation is the subject of ongoing clinical trials.

Androgen Deprivation Therapy

Use of concurrent ADT with ART or SRT may have an impact on the course of the disease by three principal mechanisms: (1) better disease eradication locally (recurrence in a hypoxic scar may be radioresistant), (2) improved disease control distantly (cells in microscopic metastatic deposits might retain sensitivity to ADT), and (3) possible alteration of PSA kinetics by the combination of ADT and RT in patients who eventually relapse.[102,103] The mechanism of the effect on the kinetics of BF and the delayed appearance of distant metastasis is unknown. In some reports,[8,10,22,48,104-111] ADT had positive results in patients at high risk for a rising PSA after SRT (eg, those with a pre-RT PSA > 1 ng/mL).

Randomized trials are needed to further evaluate this finding, and are in progress.[112-114] The RTOG 9601 randomized trial has thus far been reported in abstract form (Shipley et al, ASTRO 2010 and ASCO GU 2011), and found that among 771 men with pT3 or margin-positive disease in whom PSA recurrence developed, those randomized to SRT plus 2 years of bicalutamide as opposed to SRT alone had a significantly improved freedom from PSA progression (57% vs 40% at 7 years, \(P < .0001\)) and significantly reduced risk of metastases (7.4% vs 12.6%, \(P = .04\)). The impact on overall survival awaits further follow-up and more events (see Variant 4).
Adjuvant vs Salvage Radiotherapy

The optimal timing of ART vs SRT for patients with high-risk pathologic features remains controversial.[21,23,24,84,115-117] Presently, there are no published randomized trials comparing ART to planned SRT at established predefined thresholds of BF.[118] Thus, some have supported watchful waiting before administering SRT.[119] The rationale for this approach is based on three points: First, half of all men will be treated unnecessarily. Second, salvage rates are fairly good when the pre-RT PSA is low (≤ 1.0 ng/mL).[69,104,120-122] Third, the progression to distant metastasis after BF may be long.[30,31,59] An important observation is that the addition of SRT in patients who were originally in the observation arm of the SWOG randomized trial still resulted in a higher rate of metastatic failure and reduced overall survival in these patients compared with early adjuvant therapy.[33] Consequently, a recent joint American Urologic Association and American Society of Radiation Oncology guideline supports offering ART to patients with adverse pathologic features.[2,5,15] Similarly, the European Association of Urology developed guidelines on the treatment of advanced, relapsing, and castration-resistant prostate cancer.[3] Without a randomized trial to eliminate selection bias, it is impossible to ascribe an advantage to one strategy over the other based on FFBF outcomes. ART has a proven benefit in randomized prospective studies, supporting first principles that RT treatment should be used if the risk of local failure is > 20% and the side-effect profile is acceptable. Local persistence may lead to the development of distant metastasis in many malignancies. There is evidence that this is the case for prostate cancer.[123-126] In younger men with a long life expectancy and adverse pathologic features, ART should be strongly considered.

Irradiation in Patients With Positive Lymph Nodes

Lymph node involvement (LNI) portends a poor prognosis with a high rate of distant failure. Although there are data indicating that RP or RT should be used along with ADT when LNI is identified,[127] there is no well-established benefit from this approach as yet. ART might be of some value when there is evidence of an appreciable local-regional tumor burden, such as extensive positive margins. There are insufficient data on the subject of pelvic nodal irradiation to make any recommendations, even when LNI has been documented[127-130] (see Variant 5). The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document.

Financial Disclosure: The authors have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article. Copyright © 2014 American College of Radiology. Reprinted with permission of the American College of Radiology. For additional information on ACR Appropriateness Criteria®, refer to www.acr.org/ac.
Variant 1: Postradical prostatectomy irradiation in a 65-year-old man ...

Variant 2: Postradical prostatectomy irradiation in a 58-year-old man ...

Variant 3: Postradical prostatectomy irradiation in a 58-year-old man ...

Variant 4: Postradical prostatectomy irradiation in a 67-year-old man ...
Variant 5: Postradical prostatectomy irradiation in a 64-year-old man...

References:


28. Catalona WJ, Smith DS. Cancer recurrence and survival rates after anatomic radical retropubic...


82. Rogers R, Grossfeld GD, Roach M 3rd, et al. Radiation therapy for the management of 


84. King CR. The timing of salvage radiotherapy after radical prostatectomy: a systematic review. Int 

85. Alongi F, Fiorino C, Cozzarini C, et al. IMRT significantly reduces acute toxicity of whole-pelvis 
irradiation in patients treated with post-operative adjuvant or salvage radiotherapy after radical 

86. Bastasch MD, Teh BS, Mai WY, et al. Post-nerve-sparing prostatectomy, dose-escalated 

after radical prostatectomy: comparative effectiveness of intensity-modulated versus conformal 

88. Goenka A, Magsanoc JM, Pei X, et al. Improved toxicity profile following high-dose 
2011;60:1142-8.

radiotherapy and conventional conformal radiotherapy in the treatment of prostate cancer after 

setting with intensity-modulated radiotherapy: a dosimetric study using EORTC consensus 

versus intensity modulated planning techniques for prostate bed radiotherapy. Medl Dosim. 
2009;34:256-60.

high-dose postoperative intensity-modulated radiotherapy for prostate cancer. Int J Radiat Oncol Biol 


without androgen deprivation after radical prostatectomy for rising or persisting prostate-specific 

1998;41:491-500.


high-dose intensity modulated radiation therapy for localized prostate cancer. Int J Radiat Oncol Biol


