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POSTRADICAL PROSTATECTOMY IRRADIATION IN PROSTATE CANCER

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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%–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 3 main clinical scenarios in which RT is given after RP: 1) adjuvant radiotherapy (ART) for men with an undetectable or barely detectable prostate specific antigen (PSA) (<0.2 ng/mL) who have high-risk pathologic features; 2) salvage radiotherapy (SRT) for men who had an undetectable or barely detectable PSA (<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 2 groups in terms of prognosis after RT, dose of RT administered, and prognostic factors. The further subdivision of salvage patients into 2 groups, those with a DR-PSA and those with a PD-PSA, is useful because their outcomes after RT appear to be different [6-10], with a worse prognosis for those having 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 disseminates 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 based on patient selection and prognostic factors as well as surgical technique and pathologic evaluation, but they 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 urethrovesical anastamosis [11,24-26]. Long-term follow-up has revealed that the risk of BF following

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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]. This failure may lead to the need for additional therapy using androgen deprivation and its associated 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 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 to 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 considered 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 such that ART should be considered.

Adjuvant Radiotherapy Outcome

Many retrospective studies have examined the role of ART [50-55]. Three prospective randomized trials comparing prostatectomy alone to prostatectomy plus ART have been reported [22,55,56]. All 3 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 versus 74% in the RP plus RT (60 Gy) group (P<.0001) [56,57] and at 10 years was 41% versus 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 (60–64 Gy) versus 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 3 pathologic risk groups. ART also prevented 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 on the observation arm versus 93 of 214 patients who received early adjuvant therapy (P=.016). In addition, there have been 110 deaths on the observation arm versus 88 deaths in the irradiated patients (P=.023). Although ART initially resulted in some adverse impact 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 overall quality of life [33].

A third study (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 versus 72% in the RP plus RT group (P=.0015). ART was very well tolerated; with the rate of grade 3–4 late adverse events being 0.3% (see Variant 1 and Variant 2).

Salvage Radiotherapy

RT is given for salvage after RP in 3 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% [31]. This risk increases to ≥74% at 10 years. 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% will 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 prior to RT connotes a poor prognosis, 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 having a poorer prognosis than they would otherwise have, 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 those 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 palpable, biopsy, or imaging evidence of prostate remaining), 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 (>1 to >2.5 ng/mL), short PSADT, negative prostatectomy margins, treatment for a PD-PSA (versus a DR-PSA), a palpable prostatic fossa mass, and RT dose <65 Gy.

Salvage Radiotherapy Outcome

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 2 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 it is, 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 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 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 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 of 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 been found to be a determinant of outcome in multivariate analysis in many series as well, with worse FFBF rates when the seminal vesicles were involved, due to these patients being at a higher risk of developing subsequent metastatic failure [7,48,49] (see Variant 3).

External Beam Therapy

Intensity-Modulated Radiation Therapy and Image-Guided Radiation Therapy

External beam therapy is the standard mode for 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. Intensity-modulated radation therapy (IMRT) or 3-D-conformal radiation therapy (3-D-CRT) and image guidance are the preferred techniques. Dosimetric studies have been done in this setting comparing 3-D-CRT and IMRT in the postoperative setting. In comparison, IMRT may be the preferred technique as it may allow for dose escalation with limited toxicity [85-94]. Koontz et al [91]compared 3-D-CRT and IMRT for postprostatectomy RT. In their comparison IMRT reduced the volume of bladder and rectum receiving high doses during treatment. Ost et al [93] evaluated 104 patients using IMRT in the postprostatectomy setting to a median dose of 74 Gy. The toxicity profile was acceptable. Using EORTC consensus guidelines for target volumes, Harrison et al [90] compared IMRT and 3-D-CRT in 28 patients. They compared 72 Gy with IMRT to 68.4 Gy with 3-D-CRT. The dosimetric parameters were improved with IMRT with respect to dose to the rectum and bladder. In the SRT setting a comparison study of 3-D-CRT and IMRT, Goenka et al [88] demonstrated a similar risk of grade >2 genitourinary (GU) toxicity and a reduction in risk of grade >2 gastrointestinal (GI) toxicity. Ost et al [94] in the salvage setting, with or without androgen deprivation, were able to deliver 76 Gy with a toxicity profile similar to 3-D-CRT 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, they demonstrated a benefit to ART over SRT. Lastly, for ART the GI and GU toxicity was zero and 4%, respectively. In the SRT group, GI and GU toxicity was 3% and 3%, respectively. In a large group comparison study, Crandley et al [87] analyzed complications between IMRT and 3-D-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 over 3-D-CRT. Nonetheless, a comparison review of IMRT and 3-D-CRT by Goldin et al [89] showed no significant difference in rates of long-term GI, nonurinary incontinence morbidity, GU incontinence, or erectile dysfunction. Using these comparisons, the bulk of the data favors IMRT compared to 3-D-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 compared to 3-D-CRT with a reduction of grade 2–3 rectal bleeding from 15% 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 to the results of 3-D-CRT. Ninety percent of those patients were treated to 81 Gy, and 10% 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 on prostate cancer patients treated with 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 reanalysis of the RTOG 9406 dose escalation studies in which patients were treated to 79.2 Gy using either 3-D-CRT or IMRT (in a nonrandomized fashion) and found an association between the 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 implanted fiducial markers to facilitate image-guided radiation therapy (IGRT). In this study prostate margins were reduced from 1 cm to 2–3 mm with the placement of fiducials, resulting in a decrease in grade 2 rectal toxicity (80% to 13%) and bladder toxicity (60% versus 13%). Zelefsky et al [100] also recently reported on a retrospective series in which men treated to the same dose with IGRT versus IMRT had significantly lower 3-year grade 2+ late urinary toxicity (10.4% versus 20.0%, 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 prostate fossa in the adjuvant or salvage setting is 64.8–70.2 Gy [11,29-31,101]. Higher doses have been delivered with acceptable toxicity [90,93] and may be appropriate under certain conditions.

Androgen Deprivation Therapy

The use of concurrent ADT with ART or SRT may impact the course of the disease by 3 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) the combination of ADT and RT may alter the PSA kinetics 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 of experiencing a rising PSA after SRT (eg, a pre-RT PSA >1 ng/mL). Randomized trials are needed and are in progress [112-114]. The RTOG 9601 randomized trial has thus far been reported in abstract form (Shipley ASTRO 2010 and ASCO GU 2011), and found that among 771 men with pT3 or margin positive disease who developed PSA recurrence, those randomized to SRT plus 2 years of bicalutamide as opposed to SRT alone had a significantly improved freedom from PSA progression (57% versus 40% at 7 years, P<.0001) and significantly reduced risk of metastases (7.4% versus 12.6%, P=.04). The impact on overall survival awaits further follow-up and more events (see Variant 4).

Adjuvant Versus Salvage Radiotherapy

The optimal timing of ART versus 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]. As such, some have supported watchful waiting before administering SRT [119]. This rationale is based on 3 points. First, half of 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 to 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 to 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).

Summary

- A high percentage of RP patients with high-risk pathologic features (positive surgical margins, extraprostatic extension of cancer, SVI) will experience a subsequent BF, with failure often due to progression of residual disease within the surgical bed.

- The addition of adjuvant RT directed at the prostate fossa to these patients has been shown in 3 prospective randomized trials to improve the biochemical freedom-from-failure rate among the irradiated patients and, in one trial, to provide an improvement in metastasis-free and overall survival.
- Salvage RT, in which patients with biochemically detectable disease undergo 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 prostate fossa in the adjuvant or salvage setting is 64.8–70.2 Gy. Higher doses may be appropriate if there is evidence of gross recurrence within the prostate bed.
- The addition of pelvic RT to prostate fossa radiation is generally discouraged, although 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 ADT with adjuvant or salvage radiation is the subject of ongoing clinical trials.

Supporting Documents

- ACR Appropriateness Criteria® Overview
- Evidence Table

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Clinical Condition: **Postradical Prostatectomy Irradiation in Prostate Cancer**

Variant 1: **65-year-old man, stage T2A, Gleason score 6, adenocarcinoma. PSA 14.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy. Right seminal vesicle involved by tumor, but surgical margins of prostatectomy specimen negative (pT3bN0M0R0). Negative lymph nodes. Postprostatectomy PSA nondetectable.**

Treatment	Rating	Comments
Radiation therapy alone	9	
RT plus neoadjuvant and concurrent hormone therapy (HT)	5	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	3	
Observation	3	
HT alone	3	
Radiation Therapy		
Pelvis and prostate bed	4	
Prostate bed	9	
Pelvic Irradiation, if given		
40 Gy/20 fractions	2	
45 Gy/25 fractions	7	
50.4 Gy/28 fractions	6	
54 Gy/30 fractions	2	
Dose to Prostate Bed (may include dose to pelvis)		
45 Gy/25 fractions	2	
50.4 Gy/28 fractions	2	
54 Gy/30 fractions	3	
59.4 Gy/33 fractions	4	
66.6 Gy/37 fractions	8	
70.2 Gy/39 fractions	6	
72 Gy/40 fractions	3	
Treatment Plan		
IMRT	8	
3-D-CT based plan	8	
2-D-CT based plan	3	
Non-CT based plan	2	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Postradical Prostatectomy Irradiation in Prostate Cancer**

Variant 2: **58-year-old man, stage T1C, Gleason score 7, adenocarcinoma. PSA 10.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy (pT2cN0M0R1). Positive margins at prostate apex. Negative lymph nodes. Postprostatectomy PSA nondetectable.**

Treatment	Rating	Comments
Radiation therapy alone	8	
Observation	3	
RT plus neoadjuvant and concurrent HT	2	
HT alone	2	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	2	
Radiation Therapy		
Pelvis and prostate bed	3	
Prostate bed	8	
Pelvic Irradiation, if given		
40 Gy/20 fractions	2	
45 Gy/25 fractions	7	
50.4 Gy/28 fractions	6	
54 Gy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
45 Gy/25 fractions	2	
50.4 Gy/28 fractions	2	
54 Gy/30 fractions	2	
59.4 Gy/33 fractions	4	
66.6 Gy/37 fractions	8	
70.2 Gy/39 fractions	7	
72 Gy/40 fractions	4	
Treatment Plan		
IMRT	8	
3-D-CT based plan	8	
2-D-CT based plan	3	
Non-CT based plan	2	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Postradical Prostatectomy Irradiation in Prostate Cancer**

Variant 3: **58-year-old man, stage T1C, Gleason score 7, adenocarcinoma. PSA 10.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy (pT2cN0M0R1). Positive margins at prostate apex. Negative lymph nodes. Postprostatectomy PSA detectable at 0.3 ng/mL.**

Treatment	Rating	Comments
Radiation therapy alone	8	
RT plus neoadjuvant and concurrent HT	6	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	3	
HT alone	2	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	4	
Prostate bed	8	
Pelvic Irradiation, if given		
40 Gy/20 fractions	2	
45 Gy/25 fractions	7	
50.4 Gy/28 fractions	5	
54 Gy/30 fractions	3	
Dose to Prostate Bed (may include dose to pelvis)		
45 Gy/25 fractions	2	
50.4 Gy/28 fractions	2	
54 Gy/30 fractions	2	
59.4 Gy/33 fractions	4	
66.6 Gy/37 fractions	8	
70.2 Gy/39 fractions	7	
72 Gy/40 fractions	5	
Treatment Plan		
IMRT	8	
3-D-CT based plan	8	
2-D-CT based plan	3	
Non-CT based plan	2	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**

Clinical Condition: **Postradical Prostatectomy Irradiation in Prostate Cancer**

Variant 4: **67-year-old man, stage T1C, Gleason score 8, adenocarcinoma. PSA 8.0 ng/mL. Negative metastatic workup. Nerve-sparing radical prostatectomy performed (pT2cN0M0R0). No ECE. Margins negative. No seminal vesicle extension. Negative lymph nodes. Postoperative PSA nonmeasurable. Six months later PSA rose to 9.0 ng/mL. Metastatic workup, including pelvic MRI, negative.**

Treatment	Rating	Comments
HT alone	8	
Radiation therapy alone	3	
RT plus neoadjuvant and concurrent HT	3	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	3	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	2	
Prostate bed	2	
Pelvic Irradiation, if given		
40 Gy/20 fractions	2	
45 Gy/25 fractions	2	
50.4 Gy/28 fractions	2	
54 Gy/30 fractions	2	
Dose to Prostate Bed (may include dose to pelvis)		
45 Gy/25 fractions	2	
50.4 Gy/28 fractions	2	
54 Gy/30 fractions	2	
59.4 Gy/33 fractions	2	
66.6 Gy/37 fractions	2	
70.2 Gy/39 fractions	2	
72 Gy/40 fractions	2	
Treatment Plan		
IMRT	2	
3-D-CT based plan	2	
2-D-CT based plan	2	
Non-CT based plan	2	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate		

Clinical Condition: **Postradical Prostatectomy Irradiation in Prostate Cancer**

Variant 5: **64-year-old man, stage T2A, Gleason score 7, adenocarcinoma. PSA 10.5 ng/mL. Negative metastatic workup. Treated with nerve-sparing radical prostatectomy (pT2cN1M0R0). Prostatectomy margins negative. No seminal vesicle extension. One positive obturator lymph node. Postprostatectomy PSA nondetectable.**

Treatment	Rating	Comments
HT alone	7	
RT plus neoadjuvant, concurrent, and long-term adjuvant HT	7	
RT plus neoadjuvant and concurrent HT	4	
Radiation therapy alone	3	
Observation	2	
Radiation Therapy		
Pelvis and prostate bed	8	
Prostate bed	2	
Pelvic Irradiation, if given		
40 Gy/20 fractions	2	
45 Gy/25 fractions	7	
50.4 Gy/28 fractions	8	
54 Gy/30 fractions	4	
Dose to Prostate Bed (may include dose to pelvis)		
45 Gy/25 fractions	2	
50.4 Gy/28 fractions	3	
54 Gy/30 fractions	3	
59.4 Gy/33 fractions	5	
66.6 Gy/37 fractions	8	
70.2 Gy/39 fractions	7	
72 Gy/40 fractions	4	
Treatment Plan		
IMRT	8	
3-D-CT based plan	7	
2-D-CT based plan	3	
Non-CT based plan	2	

Rating Scale: **1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate**