Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Bottke D, de Reijke TM, Bartkowiak D, Wiegel T. Salvage radiotherapy in patients with persisting/rising PSA after radical prostatectomy for prostate cancer. *Eur J Cancer.* 2009;45 Suppl 1:148-157.	Review/Other-Tx	N/A	Review role of SRT in patients with persisting PSA after RP for prostate cancer.	SRT should be offered to patients with persisting PSA after RP provided distant metastases have been adequately ruled out. Of these patients, 30%–70% will experience a decrease in their PSA to an undetectable range, and in about 40%–50% of these patients, the PSA will remain stable after 5 years.	4
2. Valicenti RK, Thompson I, Jr., Albertsen P, et al. Adjuvant and salvage radiation therapy after prostatectomy: American Society for Radiation Oncology/American Urological Association guidelines. *Int J Radiat Oncol Biol Phys.* 2013;86(5):822-828.	Review/Other-Tx	N/A	To provide a clinical framework for the use of RT after RP as adjuvant or salvage therapy.	Guideline statements are provided for patient counseling, use of RT in the adjuvant and salvage contexts, defining biochemical recurrence, and conducting a restaging evaluation.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
3. Mottet N, Bellmunt J, Bolla M, et al. EAU guidelines on prostate cancer. Part II: Treatment of advanced, relapsing, and castration-resistant prostate cancer. *Eur Urol.* 2011;59(4):572-583.	Review/Other-Tx	N/A	To present a summary of the 2010 version of the European Association of Urology guidelines on the treatment of advanced, relapsing, and castration-resistant prostate cancer.	Luteinising hormone-releasing hormone agonists are the standard of care in metastatic prostate cancer. Although luteinising hormone-releasing hormone antagonists decrease testosterone without any testosterone surge, their clinical benefit remains to be determined. Complete androgen blockade has a small survival benefit of about 5%. Intermittent androgen deprivation results in equivalent oncologic efficacy when compared with continuous ADT in well-selected populations. In locally advanced and metastatic prostate cancer, early ADT does not result in a significant survival advantage when compared with delayed ADT. Relapse after local therapy is defined by PSA values >0.2 ng/mL following RP and >2 ng/mL above the nadir after RT. Therapy for PSA relapse after RP includes SRT at PSA levels <0.5 ng/mL and salvage RP or cryosurgical ablation of the prostate in radiation failures. Endorectal magnetic resonance imaging and (11)C-choline positron emission tomography/CT are of limited importance if the PSA is <2.5 ng/mL; bone scans and CT can be omitted unless PSA is >20 ng/mL. Follow-up after ADT should include screening for the metabolic syndrome and an analysis of PSA and testosterone levels. Treatment of castration-resistant prostate cancer includes second-line hormonal therapy, novel agents, and chemotherapy with docetaxel at 75 mg/m(2) every 3 weeks. Cabazitaxel as a second-line therapy for relapse after docetaxel might become a future option. Zoledronic acid and denusomab can be used in men with castration-resistant prostate cancer and osseous metastases to prevent skeletal-related complications.	4

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4. Swindle P, Eastham JA, Ohori M, et al. Do margins matter? The prognostic significance of positive surgical margins in radical prostatectomy specimens. *J Urol.* 2005;174(3):903-907.	Observational-Tx	1,389 consecutive patients	To evaluate the prognostic significance of positive surgical margins using multiple methods of analysis accounting for patients who received adjuvant therapy.	Overall 179 patients (12.9%) had a positive surgical margin, including 6.8% of 847 patients with pT2 and 23% of 522 patients with pT3 disease. A positive surgical margin was a significant predictor of cancer recurrence when analyzed using methods 1, 3, 4 and 5 (P=0.005, P=0.014, P=0.0005, P=0.002, respectively). However, it was not a predictor of recurrence using method 2 in which adjuvant therapy was ignored (P=0.283). Using method 5 multivariate analysis demonstrated that a positive surgical margin (P=0.002) was an independent predictor of 10-year progression-free probability along with Gleason score (P=0.0005), extracapsular extension (P=0.0005), SVI (P<0.0005), positive lymph nodes (P<0.0005) and preoperative serum prostate specific antigen (P<0.0001). Using method 5 the 10-year progression-free probability was 58% +/- 12% and 81% +/- 3% for patients with and without a positive surgical margin, respectively (P<0.00005). The RR of recurrence in men with a positive surgical margin using method 5 was 1.52 (95% CI, 1.06–2.16).	2
5. Thompson IM, Valicenti RK, Albertsen P, et al. Adjuvant and salvage radiotherapy after prostatectomy: AUA/ASTRO Guideline. *J Urol.* 2013;190(2):441-449.	Review/Other-Tx	N/A	Guideline to provide a clinical framework for the use of RT after RP as adjuvant or salvage therapy.	Guideline statements are provided for patient counseling, the use of RT in the adjuvant and salvage contexts, defining biochemical recurrence, and conducting a re-staging evaluation.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
6. Choo R, Hruby G, Hong J, et al. (IN)-efficacy of salvage radiotherapy for rising PSA or clinically isolated local recurrence after radical prostatectomy. *Int J Radiat Oncol Biol Phys.* 2002;53(2):269-276.	Observational-Tx	98 patients	Retrospective analysis to determine the efficacy of EBRT as salvage treatment for PSA failure or local recurrence after RP.	Initial PSA response rate was at a range of 86%–94%.Complete PSA response rate (PSA ≤0.2 ng/mL) ranged from 53%–62%. Actuarial relapse-free rate, including freedom from PSA failure, at 4 years was 26%, 39%, and 14% for Groups A, B, and C, respectively. The actuarial survival rate at 4 years was 89%, 95%, and 94% for Groups A, B, and C, respectively. Efficacy of SRT for PSA failure or local recurrence after RT was limited, reflected by very low relapse-free rates. SRT appeared more efficacious for patients with a delayed PSA rise than for those with either persistently detectable postoperative PSA levels or clinically palpable local recurrence.	2
7. Chawla AK, Thakral HK, Zietman AL, Shipley WU. Salvage radiotherapy after radical prostatectomy for prostate adenocarcinoma: analysis of efficacy and prognostic factors. *Urology.* 2002;59(5):726-731.	Observational-Tx	54 patients	Review patients' records to determine the probability of biochemical control for patients treated with SRT and identify prognostic factors associated with successful salvage.	SRT yields a 76% complete response rate, with 35% of treated patients free of a detectable PSA at 5 years. Those with favorable biochemical and pathologic tumor features are most likely to remain disease free.	2
8. Taylor N, Kelly JF, Kuban DA, Babaian RJ, Pisters LL, Pollack A. Adjuvant and salvage radiotherapy after radical prostatectomy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2003;56(3):755-763.	Observational-Tx	71 patients	Retrospective review of a large post-RP RT experience to determine optimal timing of RT and determinants of outcome. The results of ART and SRT were compared.	ART group - 8 patients subsequently developed a rising PSA level. The 5-year bNED rate was 88%. SVI was the strongest predictor of outcome, with a 5-year bNED rate of 94% for those without SVI and 65% for those with SVI (P=0.0002). SRT group - 20 patients developed a rising PSA level after RT. The 5-year bNED rate was 66% for all SRT patients, and 43% and 78% in those with a persistently detectable PSA and those with a delayed rise in PSA, respectively.	2
9. Garg MK, Tekyi-Mensah S, Bolton S, et al. Impact of postprostatectomy prostate-specific antigen nadir on outcomes following salvage radiotherapy. *Urology.* 1998;51(6):998-1002.	Observational-Tx	78 patients	To evaluate the relationship between the postprostatectomy PSA nadir and the outcome of patients treated with SRT.	Overall DFS rate at 3 years was 78% in patients with a PSA level ≤2 ng/mL at the time of RT compared to 31% with a PSA >2 ng/mL (P<0.0001). Many patients who never achieve an undetectable postprostatectomy PSA level may still be salvaged with therapeutic RT. The best predictor of a favorable outcome is a low (≤2 ng/mL) PSA level at the time of radiation.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
10. Song DY, Thompson TL, Ramakrishnan V, et al. Salvage radiotherapy for rising or persistent PSA after radical prostatectomy. *Urology.* 2002;60(2):281-287.	Observational-Tx	61 patients	To assess the effectiveness of SRT for a persistent or rising PSA level after RP, and to identify the pretreatment factors that may predict for patients likely to benefit from this treatment.	The actuarial PSA-free survival rate at 4 years was 39%. Univariate analysis showed a pre-RT PSA level of <1.0 ng/mL (P=0.001), Gleason score <8 (P=0.003), and achievement of an undetectable PSA level after prostatectomy (P=0.018) were significant predictors of improved DFS. On multivariate analysis, both a pre-RT PSA level of <1.0 ng/mL and a Gleason score <8 maintained statistical significance.	2
11. Swanson GP, Hussey MA, Tangen CM, et al. Predominant treatment failure in postprostatectomy patients is local: analysis of patterns of treatment failure in SWOG 8794. *J Clin Oncol.* 2007;25(16):2225-2229.	Observational-Tx	374 patients	To evaluate the data from SWOG 8794 to try to gain additional insight into failure patterns as related to PSA and effect on long-term control.	374 eligible patients had immediate postprostatectomy and follow-up PSA data. Median follow-up was 10.2 years. For patients with a postsurgical PSA of 0.2 ng/mL, radiation was associated with reductions in the 10-year risk of biochemical treatment failure (72% to 42%), local failures (20% to 7%), and distant failures (12% to 4%). For patients with a postsurgical PSA between higher than 0.2 and ≤1.0 ng/mL, reductions in the 10-year risk of biochemical failure (80% to 73%), local failures (25% to 9%), and distant failures (16% to 12%) were realized. In patients with postsurgical PSA higher than 1.0, the respective findings were 94% vs 100%, 28% vs 9%, and 44% vs 18%.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Kupelian P, Katcher J, Levin H, Zippe C, Klein E. Correlation of clinical and pathologic factors with rising prostate-specific antigen profiles after radical prostatectomy alone for clinically localized prostate cancer. *Urology.* 1996;48(2):249-260.	Observational-Tx	337 patients	Review charts of patients treated with RP alone to better identify factors affecting PSA level elevation after RP alone in men with clinical stage T1-2 prostate cancer.	3- and 5-year RFS rates were 74% and 61%, respectively. 5-year RFS was 89% in patients with preoperative PSA levels of ≤4 ng/mL; 62% for PSA level of 4 to 10 ng/mL; 56% for PSA level to 10 to 20 ng/mL; and 26% for a PSA level >20 ng/mL. 5-year RFS rates for margin-positive vs margin-negative patients were 37% vs 80%, respectively (P<0.001). With pretreatment PSA levels of ≤10 ng/mL, lymph node involvement was seen in 3%, and margin involvement in 36%; the 5-year RFS rate was 71%. With pretreatment PSA levels of >10 ng/mL, lymph node involvement was seen in 16%, and margin involvement in 57%; the 5-year RFS rate was 42%. However, patients with an initial PSA level >10 ng/mL and positive margins had a 5-year RFS rate of 22% vs 73% in patients with a PSA level of ≤10 ng/mL or negative margins (P<0.001).	2
13. Epstein JI, Partin AW, Sauvageot J, Walsh PC. Prediction of progression following radical prostatectomy. A multivariate analysis of 721 men with long-term follow-up. *Am J Surg Pathol.* 1996;20(3):286-292.	Observational-Tx	721 men	To examine men with clinically confined disease who had RP. Study was focused on men without lymph node metastases or SVI.	Tumors with a Gleason score of 2 through 4 had a 10-year progression-free risk of 96%. The 10-year actuarial progression-free risk for men with a Gleason score of 8 through 9 was 35%. Men with Gleason score 2 through 4 or 8 through 9 tumors could not be stratified into different risks of progression based on the presence or extent of capsular penetration or margin status. Men with Gleason score 5 through 7 tumors (88.2% of cases), predicting their risk of progression was enhanced by knowledge of their tumor's capsular penetration and margin status. Tumors with a Gleason score of 5 through 6 and 7 were each stratified into 3 groups with different risks of progression.	2
14. Ramos CG, Carvalhal GF, Smith DS, Mager DE, Catalona WJ. Clinical and pathological characteristics, and recurrence rates of stage T1c versus T2a or T2b prostate cancer. *J Urol.* 1999;161(5):1525-1529.	Observational-Tx	1,620 patients	To compare clinicopathological features, and cancer recurrence and survival rates in men with stage T1c vs T2a or T2b prostate cancer. Univariate statistics were used to compare clinical and pathological features by clinical stage, and multivariate Cox models were used to compare 5-year recurrence-free probabilities.	5-year recurrence-free survival rate was 85% for T1c, 83% for T2a and 72% for T2b cases. 5-year disease specific survival rate was 100% for the T1c and T2a groups, and 97% for the T2b group. Clinical and pathological features were similar for stages T1c and T2a, and different from stage T2b cancers.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Gilliland FD, Hoffman RM, Hamilton A, et al. Predicting extracapsular extension of prostate cancer in men treated with radical prostatectomy: results from the population based prostate cancer outcomes study. *J Urol.* 1999;162(4):1341-1345.	Observational-Tx	3,826 patients	To determine whether clinical information routinely available in community practice could predict extracapsular extension of clinically localized prostate cancer in men undergoing RP.	Strongest predictors were elevated PSA >20 vs <4 ng/mL Gleason score >8 vs <6 and age >70 vs <50 years. In a population based analysis of prostate cancer practice patterns PSA, Gleason score and age are clinically useful predictors of extracapsular extension.	3
16. Cheng L, Slezak J, Bergstralh EJ, Myers RP, Zincke H, Bostwick DG. Preoperative prediction of surgical margin status in patients with prostate cancer treated by radical prostatectomy. *J Clin Oncol.* 2000;18(15):2862-2868.	Observational-Tx	339 patients	To predict the margin status based on various preoperative clinical features in patients undergoing RP for prostate cancer.	Overall margin positivity rate was 24%. In multivariate analysis, preoperative serum PSA level (P<.001) and percentage of cancer in the biopsy specimens (P<.001) were predictive of margin status in RP.	2
17. Shah O, Robbins DA, Melamed J, Lepor H. The New York University nerve sparing algorithm decreases the rate of positive surgical margins following radical retropubic prostatectomy. *J Urol.* 2003;169(6):2147-2152.	Observational-Dx	272 patients	Developed an algorithm that prospectively defines when to excise the neurovascular bundles during RRP to maximize the performance of nerve sparing procedures while minimizing positive surgical margins.	The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of algorithm were 18%, 93%, 28%, 89% and 84%, respectively. In sides of the prostate with extraprostatic extension ipsilateral wide excision of the neurovascular bundle was associated with positive margins in 33% of cases compared with 22% when the neurovascular bundle was preserved (P=0.42).	3
18. Cagiannos I, Karakiewicz P, Eastham JA, et al. A preoperative nomogram identifying decreased risk of positive pelvic lymph nodes in patients with prostate cancer. *J Urol.* 2003;170(5):1798-1803.	Observational-Dx	5,510 patients	Retrospective, nonrandomized analysis of 7,014 patients treated with RP at 6 institutions. Developed a preoperative nomogram for prediction of lymph node metastases in patients with clinically localized prostate cancer.	Pretreatment PSA, biopsy Gleason score, clinical stage and institution represented predictors of lymph node status (P<0.001). Bootstrap corrected predictive accuracy of the 3-variable nomogram (clinical stage, Gleason sum, and PSA) was 0.76. Negative predictive value of the nomograms was 0.99 when they predicted 3% or less chance of positive lymph nodes.	4
19. Han M, Partin AW, Zahurak M, Piantadosi S, Epstein JI, Walsh PC. Biochemical (prostate specific antigen) recurrence probability following radical prostatectomy for clinically localized prostate cancer. *J Urol.* 2003;169(2):517-523.	Observational-Tx	2,091 patients	Retrospective review to identify clinical and/or pathological predictors of biochemical recurrence and to use them to develop multivariate models to determine probability of recurrence following RRP.	5-, 10- and 15-year biochemical recurrence-free survival rates were 84%, 72% and 61%, respectively. Variables identified for the preoperative model were biopsy Gleason score, clinical TNM stage and PSA. Variables identified for the postoperative model were prostatectomy Gleason score, PSA and pathological organ confinement status.	2

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20. Roehl KA, Han M, Ramos CG, Antenor JA, Catalona WJ. Cancer progression and survival rates following anatomical radical retropubic prostatectomy in 3,478 consecutive patients: long-term results. *J Urol.* 2004;172(3):910-914.	Observational-Tx	3,478 patients	To update the long-term cancer control outcome in a large anatomical RRP series and to evaluate the perioperative parameters that predicts cancer specific outcomes following surgery.	10-year biochemical progression-free, cancer specific and OS probabilities were 68%, 97% and 83%, respectively. On multivariate analysis bPFS probability was significantly associated with preoperative PSA, clinical tumor stage, Gleason sum, pathological stage and treatment era. Cancer specific survival and OS rates were also significantly associated with clinicopathological parameters.	3
21. Hull GW, Rabbani F, Abbas F, Wheeler TM, Kattan MW, Scardino PT. Cancer control with radical prostatectomy alone in 1,000 consecutive patients. *J Urol.* 2002;167(2 Pt 1):528-534.	Observational-Tx	1,000 patients	To analyze the long-term progression-free probability after RRP in a consecutive series of patients with localized prostate cancer.	10 years - the mean probability +/- 2 standard errors that patients remained free of progression was 75.0% +/- 3.7% and of metastasis 84.2% +/- 4.4%. Mean actuarial cancer specific survival rate +/- 2 standard errors was 97.6% +/- 1.7%. Radical RRP provided long-term cancer control in 75% of patients with clinically localized prostate cancer and was effective in the majority of those with high risk cancer, including T2c or biopsy Gleason sum 8 to 10, or PSA >20 ng/mL.	2
22. Han M, Partin AW, Pound CR, Epstein JI, Walsh PC. Long-term biochemical disease-free and cancer-specific survival following anatomic radical retropubic prostatectomy. The 15-year Johns Hopkins experience. *Urol Clin North Am.* 2001;28(3):555-565.	Observational-Tx	2,404 men	To provide long-term outcome of patients with clinically localized cancer who underwent RRP between 1982 and 1999.	The overall actuarial 5-, 10-, and 15-year recurrence-free survival rates for these men were 84%, 74%, and 66%, respectively. As demonstrated in the authors' previous reports, the actuarial likelihood of a postoperative recurrence increased with advancing clinical stage, Gleason-score, preoperative PSA level, and pathologic stage. Subdivision of men with Gleason 7 tumors resulted in better stratification. There was a similar actuarial likelihood of postoperative recurrence for men with Gleason 4 + 3 and Gleason score 8 to 10 disease. The actuarial rate of recurrence of tumor for men with Gleason 3 + 4 disease was statistically different from the rate for men with Gleason score 6 or Gleason 4 + 3 disease.	2

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23. Oesterling JE, Epstein JI, Walsh PC. Long-term autopsy findings following radical prostatectomy. *Urology.* 1987;29(6):584-588.	Review/Other-Tx	10 men	Review hospital records of over 1,000 radical prostatectomies performed since 1904.	10 men have had a subsequent autopsy. All were managed by radical perineal prostatectomy without adjunctive therapy; 4 had pathologic stage B disease, and 6 had pathologic stage C cancer. Data suggest: RP alone provides excellent local control of the primary tumor, irrespective of the pathologic stage.	4
24. Saleem MD, Sanders H, Abu El Naser M, El-Galley R. Factors predicting cancer detection in biopsy of the prostatic fossa after radical prostatectomy. *Urology.* 1998;51(2):283-286.	Observational-Dx	91consecutive patients; 131 exams	To determine whether the results of anastomotic biopsy for PSA recurrence after RP could be predicted by either PSA, PSAV, DRE, TRUS, or the interval from prostatectomy to biopsy.	Of 131 exams, there were 50 positive biopsy specimens for a detection rate of 38%. Although patients with a negative DRE can have a positive biopsy and patients with a PSA of ≤1.0 ng/mL can have a positive biopsy, no patient with a negative DRE and a PSA of ≤0.5ng/mL has a positive biopsy.	3
25. Foster LS, Jajodia P, Fournier G, Jr., Shinohara K, Carroll P, Narayan P. The value of prostate specific antigen and transrectal ultrasound guided biopsy in detecting prostatic fossa recurrences following radical prostatectomy. *J Urol.* 1993;149(5):1024-1028.	Observational-Dx	43 patients	To determine the value of PSA and TRUS guided biopsy in detecting prostatic fossa recurrences following RP. DRE and TRUS were compared.	Of 22 patients (51%) with biopsy proved cancer, 21 (95%) had positive TRUS, while DRE was able to detect cancer in only 10 (45%). Among TRUS detected recurrences, 15 (68%) were detected at the initial biopsy and 7 (32%) at repeat biopsies. Study shows that the combination of PSA and TRUS provides a more effective method than DRE and PSA to detect biopsy proved cancer following RP.	3
26. Naya Y, Okihara K, Evans RB, Babaian RJ. Efficacy of prostatic fossa biopsy in detecting local recurrence after radical prostatectomy. *Urology.* 2005;66(2):350-355.	Observational-Dx	100 patients	To retrospectively evaluate the efficacy of prostatic fossa biopsy in detecting local recurrence of prostate cancer in men with bNED after RP. TRUS findings, DRE findings, serum total PSA level at TRUS, PSAV, and pathologic stage and Gleason score of the RP specimen were correlated with biopsy results.	29 (29%) of 100 men had documented local recurrence. The sensitivity and specificity of DRE to detect biopsy-proven local recurrence was 72.4% and 64.8%, respectively. The corresponding values for TRUS were 86.2% and 53.5%. None of the men with a serum PSA concentration <0.5 ng/mL at biopsy who had normal results for both TRUS and DRE had a biopsy-proven local recurrence. The best predictive model for a positive fossa biopsy result was a combination of TRUS and serum PSA concentration.	3
27. Trapasso JG, deKernion JB, Smith RB, Dorey F. The incidence and significance of detectable levels of serum prostate specific antigen after radical prostatectomy. *J Urol.* 1994;152(5 Pt 2):1821-1825.	Observational-Tx	601 patients	Patients who underwent RRP for localized prostate cancer were followed with serial PSA determinations.	5- and 10-year DFS rates were 86% +/- 2% and 78% +/- 3%, respectively. The rate of detectable PSA (>0.4 ng/mL), revealed 5- and 10-year DFS of 69% +/- 2% and 47% +/- 3%, respectively. RRP has showed excellent DFS rates.	2

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28. Catalona WJ, Smith DS. Cancer recurrence and survival rates after anatomic radical retropubic prostatectomy for prostate cancer: intermediate-term results. *J Urol.* 1998;160(6 Pt 2):2428-2434.	Observational-Tx	1,778 patients	To evaluate cancer recurrence and survival rates after anatomic RRP.	7-year recurrence-free survival was significantly associated with lower preoperative PSA (estimated probability of nonprogression 76% to 93% for PSA <10), nonpalpable, localized clinical stage (79%), lower tumor grade (84% and 68% for well and moderately differentiated, respectively) and localized pathological stage (81% for pT1 or pT2) (all log rank test P<0.0001) but not age at surgery. Estimated 7-year prostate cancer specific survival rate was 97% and the all cause survival rate was 90%. Cancer specific and all cause survival were significantly associated with lower grade and localized pathological stage.	2
29. Amling CL, Blute ML, Bergstralh EJ, Seay TM, Slezak J, Zincke H. Long-term hazard of progression after radical prostatectomy for clinically localized prostate cancer: continued risk of biochemical failure after 5 years. *J Urol.* 2000;164(1):101-105.	Observational-Tx	2,782 patients	To analyze clinical and biochemical progression rates after RRP for men with clinically localized prostate cancer with particular attention to recurrence beyond 5 years. Annual hazard rates of progression were calculated to determine the probability of recurrence at specific intervals following surgery.	bPFS at 5- and 10-years was 76% and 59%, respectively, for the entire study population while those with pathologically organ confined (pT2, N0) cancers had progression-free survival rates of 82% and 68% at 5- and 10-years, respectively. Annual hazard rates were highest during the first 2 years after RP for the entire population. Patients with adverse prognostic features (pT3b, PSA >10, Gleason score 8-10 and nondiploid cancers) had high initial hazard rates that decreased with time to lower levels. Those with pathologically organ confined cancer had low but constant hazard rates throughout follow-up.	2

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30. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. *JAMA.* 1999;281(17):1591-1597.	Observational-Tx	1,997 patients	Retrospective review of a large surgical series to characterize the time course of disease progression in men with biochemical recurrence after RP.	MFS for all the men was 82% at 15 years after surgery. Of the 1,997 men, 315 (15%) developed biochemical PSA level elevation. The median actuarial time to metastases was 8 years from the time of PSA level elevation. In survival analysis, time to biochemical progression (P<.001), Gleason score (P<.001), and PSADT (P<.001) were predictive of the probability and time to the development of metastatic disease. Once men developed metastatic disease, the median actuarial time to death was 5 years. The time interval from surgery to the appearance of metastatic disease was predictive of time until death (P<.02).	2
31. Freedland SJ, Humphreys EB, Mangold LA, et al. Risk of prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. *JAMA.* 2005;294(4):433-439.	Observational-Tx	379 men	To define risk factors for prostate cancer death following RP and to develop tables to risk stratify for prostate cancer-specific survival.	Median survival had not been reached after 16 years of follow-up after biochemical recurrence. PSADT (<3.0 vs 3.0-8.9 vs 9.0-14.9 vs ≥15.0 months), pathological Gleason score (≤7 vs 8-10), and time from surgery to biochemical recurrence (≤3 vs >3 years) were all significant risk factors for time to prostate-specific mortality. Using these 3 variables, tables were constructed to estimate the risk of prostate cancer-specific survival at year 15 after biochemical recurrence.	2
32. Antonarakis ES, Feng Z, Trock BJ, et al. The natural history of metastatic progression in men with prostate-specific antigen recurrence after radical prostatectomy: long-term follow-up. *BJU Int.* 2012;109(1):32-39.	Observational-Tx	450 men	To describe MFS in men with PSA recurrence following RP, and to define clinical prognostic factors modifying metastatic risk.	Median follow-up after prostatectomy was 8.0 years, and after biochemical recurrence was 4.0 years. At last follow-up, 134/450 patients (29.8%) had developed metastases, while median MFS was 10.0 years. Using multivariable regressions, 2 variables emerged as independently predictive of MFS: PSADT (<3.0 vs 3.0–8.9 vs 9.0–14.9 vs ≥15.0 months) and Gleason score (≤6 vs 7 vs 8–10). Using these stratifications of Gleason score and PSADT, tables were constructed to predict median, 5- and 10-year MFS after PSA recurrence. In different patient subsets, median MFS ranged from 1 to 15 years.	2

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33. Thompson IM, Tangen CM, Paradelo J, et al. Adjuvant radiotherapy for pathological T3N0M0 prostate cancer significantly reduces risk of metastases and improves survival: long-term followup of a randomized clinical trial. *J Urol.* 2009;181(3):956-962.	Experimental-Tx	425 patients	Long-term follow-up of a randomized clinical trial of RT to reduce the risk of subsequent metastatic disease and death. 211 men were randomized to observation and 214 to ART.	MFS was significantly greater with RT (93/214 events on the RT arm vs 114/211 events on observation). Survival improved significantly with ART (88 deaths of 214 on the RT arm vs 110 deaths of 211 on observation). ART after RP for a man with pT3N0M0 prostate cancer significantly reduces the risk of metastasis and increases survival.	1
34. Paulson DF. Impact of radical prostatectomy in the management of clinically localized disease. *J Urol.* 1994;152(5 Pt 2):1826-1830.	Review/Other-Tx	N/A	To review the impact of RP in the management of clinically localized disease.	Disease detected by PSA seems to be of smaller volume and to have a higher probability of negative margins. Disease recurrence or persistence by PSA detection seems to precede clinical detection of disease by 3 to 5 years. Disease recurrence by PSA detection does not predict survival outcome, probably does not differentiate between local and distant microscopic recurrence, and is not predictive of biological aggressiveness.	4
35. Zietman AL, Edelstein RA, Coen JJ, Babayan RK, Krane RJ. Radical prostatectomy for adenocarcinoma of the prostate: the influence of preoperative and pathologic findings on biochemical disease-free outcome. *Urology.* 1994;43(6):828-833.	Observational-Tx	62 patients	Retrospective study to evaluate the outcome for a cohort of men undergoing RRP alone as primary treatment for clinical T1-2 prostate adenocarcinoma.	Strongest preoperative predictors of pT3 disease were the biopsy Gleason grade and the initial serum PSA value. Actuarial analysis showed the overall likelihood of remaining free from detectable PSA at 4 years to be 43% (75% for those with organ-confined disease and 27% for those who were pT3).	2
36. Epstein JI. Incidence and significance of positive margins in radical prostatectomy specimens. *Urol Clin North Am.* 1996;23(4):651-663.	Review/Other-Tx	N/A	Review on how the incidence of positive margins may be affected by patient selection, technical differences in performing RP, and processing and analysis of RP specimens.	No results stated.	4
37. Watson RB, Civantos F, Soloway MS. Positive surgical margins with radical prostatectomy: detailed pathological analysis and prognosis. *Urology.* 1996;48(1):80-90.	Observational-Tx	215 consecutive RP specimens	To examine the extent and location of positive surgical margins and their influence on progression. RP specimens, using 2-3 mm step-sections, were reviewed.	Multivariate analysis of margin-positive patients identified tumor volume and grade as the most significant predictors, with the location and extent of the positive margin not significant. Although more frequent at the prostatic apex, tumor at the inked margin at any location is a risk factor for postoperative biochemical progression.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Kupelian PA, Katcher J, Levin HS, Klein EA. Stage T1-2 prostate cancer: a multivariate analysis of factors affecting biochemical and clinical failures after radical prostatectomy. *Int J Radiat Oncol Biol Phys.* 1997;37(5):1043-1052.	Observational-Tx	423 patients	Review stage T1-2 prostate cancer treated with RP to understand the impact of PSA on pathologic findings, outcome, and salvage treatment.	5-year clinical RFS rate was 84%. At 5 years, the local control and distant failure rates were 92% and 91%, respectively. Pretreatment PSA is the most potent clinical factor independently predicting biochemical relapse.	2
39. Kausik SJ, Blute ML, Sebo TJ, et al. Prognostic significance of positive surgical margins in patients with extraprostatic carcinoma after radical prostatectomy. *Cancer.* 2002;95(6):1215-1219.	Observational-Tx	842 patients	To evaluate the impact of positive surgical margins as an independent predictive factor for PSA progression in patients with pT3a/b N0M0 carcinoma.	5-year survival free of clinical recurrence and/or bNED (postoperative PSA level >0.2 ng/mL) for patients with no positive surgical margins was 76% and was 65% for patients with 1 positive surgical margin (P=0.0001). There was no significant difference in biochemical disease progression between patients with 1 vs those with ≥2 surgical margins (65% vs 62%). Analysis showed that the positive surgical margins were a significant predictor (P=0.0017) of clinical disease recurrence and bNED after controlling for preoperative PSA, Gleason score, and DNA ploidy.	2
40. Karakiewicz PI, Eastham JA, Graefen M, et al. Prognostic impact of positive surgical margins in surgically treated prostate cancer: multi-institutional assessment of 5831 patients. *Urology.* 2005;66(6):1245-1250.	Observational-Tx	5,831 patients	To assess the prognostic significance of a positive surgical margin in the RP specimen, and to test for the presence of statistically significant interactions between surgical margin status and select pathologic stage variables. Study combined prospectively collected data from 7,816 consecutive patients treated with RP at 8 institutions.	Pretreatment PSA, pathologic Gleason score, surgical margin status (positive vs negative), presence of extracapsular extension, SVI, and pelvic lymph node status were examined as predictors of biochemical progression. In multivariate Cox regression models a positive surgical margin was associated with a 3.7-fold greater risk of progression (P=0.001).A statistically significant interaction was found between surgical margin status and Gleason score 7 to 10 (P=0.008) as well as lymph node invasion (P<0.001).	2
41. Jones EC. Resection margin status in radical retropubic prostatectomy specimens: relationship to type of operation, tumor size, tumor grade and local tumor extension. *J Urol.* 1990;144(1):89-93.	Review/Other-Tx	199 patients (1980-1987) 52 patients (1987)	Review charts of radical RP patients from 1980 to 1987 and slides from patients in 1987 to identify factors that determine resection margin status.	92 (46%) of 199 patients had positive resection margins; there was no difference in the frequency between the nerve-sparing and standard procedures. The 1987 slide review showed a positive resection margin frequency of 58%. Determination of these risk factors identifies patients at greatest risk for positive resection margins.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Epstein JI, Pizov G, Walsh PC. Correlation of pathologic findings with progression after radical retropubic prostatectomy. *Cancer.* 1993;71(11):3582-3593.	Observational-Tx	507 patients	To evaluate the effect of positive margins, Gleason grade, and capsular penetration on progression after RP. Authors followed men with totally embedded RRP specimens performed for clinical Stages A and B prostate cancer.	Positive margins and Gleason sum strongly correlated with progression in a multivariate analysis. Approximately 50% of patients with positive margins experienced disease progression during 5 years of follow-up. The most common single sites of positive margins were distal (22%), posterior (17%), and posterolateral (14%); 22% of positive margins were extensive. RP provided excellent local control, with only 8% of patients exhibiting local recurrence. 61% of men with progression had an elevated serum PSA level as their only manifestation of progression.	2
43. Epstein JI, Pound CR, Partin AW, Walsh PC. Disease progression following radical prostatectomy in men with Gleason score 7 tumor. *J Urol.* 1998;160(1):97-100; discussion 101.	Observational-Tx	488 patients	To determine the long-term prognosis of men with Gleason score 7 adenocarcinoma of the prostate.	Margins status greatly influences the risk of progression in men with Gleason score 7 tumors. Among men with Gleason score 7 tumors, except for those with established extraprostatic extension and positive margins, more than 50% appear to be cured at long-term follow-up. Because of the high risk of progression in patients with positive margins, clinical studies of ART in this population appear warranted.	2
44. Obek C, Sadek S, Lai S, Civantos F, Rubinowicz D, Soloway MS. Positive surgical margins with radical retropubic prostatectomy: anatomic site-specific pathologic analysis and impact on prognosis. *Urology.* 1999;54(4):682-688.	Observational-Tx	495 patients	To correlate the extent and location of positive surgical margins after RP with disease progression. Data on patients who underwent RP by 1 surgeon were analyzed.	Overall recurrence rate was 13.3%. Patients with positive surgical margins had a higher incidence of recurrence compared with those with negative margins (27.8% vs 6.9%, P=0.001). Multivariate analyses indicated that age older than 70 (P=0.005), a prostatectomy Gleason score of 7 (P=0.015) or 8 to 10 (P=0.003), and positive margin(s) at the bladder neck (P=0.003) were independently associated with a shorter time to recurrence among patients with a positive margin.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Emerson RE, Koch MO, Jones TD, Daggy JK, Juliar BE, Cheng L. The influence of extent of surgical margin positivity on prostate specific antigen recurrence. *J Clin Pathol.* 2005;58(10):1028-1032.	Observational-Tx	86 consecutive margin positive prostate-ectomy specimens	To evaluate the linear extent of margin positivity and the number and location of positive sites as prognostic indicators in a series of prostatectomy specimens. All pathology data were collected prospectively.	The linear extent of margin positivity was associated with PSA recurrence in univariate logistic regression (P=0.031).The extent of margin positivity correlated with preoperative PSA (P=0.017) and tumor volume (P=0.013), but not with age, prostate weight, Gleason score, pathological stage, or perineural invasion. The total number of positive sites was significantly higher in patients with PSA recurrence (P=0.037).The location of the positive margin site was not associated with PSA recurrence. The extent of margin positivity correlated with PSA recurrence in univariate analysis, although it had only marginal predictive value when adjusted for Gleason score (P=0.076).	2
46. Freedland SJ, Aronson W, Presti JC, Jr., et al. Should a positive surgical margin following radical prostatectomy be pathological stage T2 or T3? Results from the SEARCH database. *J Urol.* 2003;169(6):2142-2146.	Observational-Tx	1,621 patients	To examine the significance of various pathological features of positive surgical margin and extracapsular extension for predicting bNED following RP.	SVI predicted for the highest PSA recurrence rates. Negative surgical margin and no extracapsular extension had the lowest PSA recurrence rates. There were no differences in PSA failure rates between a positive surgical margin and no extracapsular extension vs a negative surgical margin and extracapsular extension vs extracapsular extension and a positive surgical margin. In the subset of patients with a positive surgical margin and/or extracapsular extension but no SVI only serum PSA was a significant independent predictor of biochemical recurrence.	2
47. Wheeler TM, Dillioglugil O, Kattan MW, et al. Clinical and pathological significance of the level and extent of capsular invasion in clinical stage T1-2 prostate cancer. *Hum Pathol.* 1998;29(8):856-862.	Observational-Tx	688 patients	Retrospective analysis to assess the relationship between the level and extent of prostatic capsular invasion by cancer and the clinical and pathological features and prognosis of early-stage prostate cancer.	The level of prostatic capsular invasion was an independent prognostic factor (P<.001) in a multivariate analysis. Strong association between the level of invasion of cancer into or through the prostatic capsule and the volume, grade, pathological stage, and rate of recurrence after RP. Subclassifications of patients according to the levels of prostatic capsular invasion provide valuable prognostic information.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Katz MS, Zelefsky MJ, Venkatraman ES, Fuks Z, Hummer A, Leibel SA. Predictors of biochemical outcome with salvage conformal radiotherapy after radical prostatectomy for prostate cancer. *J Clin Oncol.* 2003;21(3):483-489.	Observational-Tx	115 patients	To identify predictors of biochemical outcome following RT in patients with a rising PSA after RP for prostate cancer. Patients with a rising PSA after RP received salvage 3D-CRT alone or with neoadjuvant androgen deprivation.	4-year actuarial PSA RFS, distant MFS, and OS rates were 46%, 83%, and 95%, respectively. Multivariate analysis showed that negative/close margins (P=.03), absence of extracapsular extension (P<.01), and presence of SVI (P<.01) were independent predictors of PSA relapse after RT. Neoadjuvant androgen deprivation did not improve the 4-year PSA RFS in patients with positive margins, extracapsular extension, and no SVI (P=.24). However, neoadjuvant androgen deprivation did improve PSA RFS when 1 or more of these variables were absent (P=.03).	2
49. Stephenson AJ, Shariat SF, Zelefsky MJ, et al. Salvage radiotherapy for recurrent prostate cancer after radical prostatectomy. *JAMA.* 2004;291(11):1325-1332.	Observational-Tx	501 patients	Retrospective review of patients at 5 centers to define patients who may benefit from SRT for prostate cancer recurrence by identifying variables associated with a durable response.	4-year progression-free probability was 45%. By multivariable analysis, predictors of progression were Gleason score of 8 to 10, pre-RT PSA level >2.0 ng/mL, negative surgical margins, PSADT of 10 months or less, and SVI. Selected patients with high-grade disease and/or a rapid PSADT who were previously thought to be destined to develop progressive metastatic disease may achieve a durable response to SRT.	2
50. Valicenti RK, Gomella LG, Perez CA. Radiation therapy after radical prostatectomy: a review of the issues and options. *Semin Radiat Oncol.* 2003;13(2):130-140.	Review/Other-Tx	N/A	To summarize the published retrospective and prospective data to guide decision making in selecting appropriate candidates for post prostatectomy RT.	Postoperative radiation is a safe option in the patient at high risk for local recurrence based on adverse pathology or clinical features. Administration of an adequate dose of prostate bed radiation (ie, >64 Gy) in men with these adverse prognostic features appears to effectively reduce PSA recurrence rates.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Leibovich BC, Engen DE, Patterson DE, et al. Benefit of adjuvant radiation therapy for localized prostate cancer with a positive surgical margin. *J Urol.* 2000;163(4):1178-1182.	Observational-Tx	152 patients	Retrospective study to determine the benefit of postoperative EBRT in patients with margin positive prostate cancer with respect to biochemical progression or cancer recurrence. Study was limited to men with organ confined cancer and a single positive margin.	Significant estimated improvement plus or minus standard error in 5-year clinical and bPFS in 88% +/- 5% vs 59% +/- 11% of patients treated with ART vs no RT (P=0.005). No patient who received RT had local or distant recurrence, while 16% of controls had recurrence (P=0.015). When stratified by site of margin positivity, the 5-year estimated clinical and biochemical progression-free rate in 18 cases and controls with a positive base margin was 95%+/-15% and 65%+/-13%, respectively (P=0.02). The rate in 35 cases and cases with a positive apex margin was 95% +/- 5% and 64% +/- 15%, respectively (P=0.07).	2
52. Do LV, Do TM, Smith R, Parker RG. Postoperative radiotherapy for carcinoma of the prostate: impact on both local control and distant disease-free survival. *Am J Clin Oncol.* 2002;25(1):1-8.	Observational-Tx	179 patients	To evaluate the impact of postoperative RT on patients diagnosed with prostate cancer with respect to biochemical and clinical disease free survival.	10-year biochemical RFS from date of surgery were 88%, 45%, and 25% for patients treated with postoperative ART, SRT, and with surgery alone, respectively (P=0.046). 10-year distant RFS from date of surgery were 82%, 74%, and 44% for adjuvantly treated patients, those with SRT, and those with surgery alone, respectively (P=0.0180). 10-year overall disease RFS from date of surgery was 89%, 76%, and 30% for adjuvantly treated patients, those with SRT, and those with surgery alone, respectively (P=0.0237). Multivariate analyses revealed that a preoperative PSA >20 ng/mL and pathologic Gleason Score of 8 to 10 were adverse predictors for biochemical relapse, whereas pathologic Gleason Score of 8 to 10, SVI, and extracapsular extension were adverse predictors of distant metastases.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Petrovich Z, Lieskovsky G, Stein JP, Huberman M, Skinner DG. Comparison of surgery alone with surgery and adjuvant radiotherapy for pT3N0 prostate cancer. *BJU Int.* 2002;89(6):604-611.	Observational-Tx	622 patients	To compare the outcome between patients with pT3N0 adenocarcinoma of the prostate treated with RP and those receiving RP followed by a planned course of postoperative RT.	5- and 10-year actuarial survival was 92% and 73%, respectively, for RP+RT patients, and nearly identical for those in the RP alone group (P=0.73). 5- and 10-year DFS; PSA <0.05 ng/mL) was 69% and 51%, respectively, for RP + RT patients, and 71% and 60%, respectively, for the RP alone group. A preoperative PSA level of <10 vs 10-25 vs >25 ng/mL did not influence OS but a PSA of >25 ng/mL was predictive of DFS (P+0.02). In a multivariate analysis the Gleason score was the most important predictor for OS and DFS (P<0.001). Postoperative RT helped reduce the incidence of local recurrence and improved DFS to equal that of a lower-risk group of patients treated with RP alone.	3
54. Vargas C, Kestin LL, Weed DW, Krauss D, Vicini FA, Martinez AA. Improved biochemical outcome with adjuvant radiotherapy after radical prostatectomy for prostate cancer with poor pathologic features. *Int J Radiat Oncol Biol Phys.* 2005;61(3):714-724.	Observational-Tx	617 patients	Retrospective comparison of RP vs RP followed by adjuvant EBRT in the treatment of prostate cancer.	5-year biochemical control rate (PSA <0.1 ng/mL) was 57% for RP+RT and 47% for RP (P=0.28). For patients with extracapsular extension, the 5-year biochemical rate was 52% for RP+RT vs 30% for RP (P<0.01). The 5-year biochemical control rate for patients with SVI was 60% for RP+RT vs 18% for RP (P<0.01). For those with positive margins, the 5-year biochemical rate was 64% for RP+RT vs 27% for RP (P<0.01). ART demonstrated improved efficacy against prostate cancer. For patients with poor pathologic features (extracapsular extension, SVI, positive margins), ART improved the biochemical outcome independent of other prognostic factors.	2
55. Lee HM, Solan MJ, Lupinacci P, Gomella LG, Valicenti RK. Long-term outcome of patients with prostate cancer and pathologic seminal vesicle invasion (pT3b): effect of adjuvant radiotherapy. *Urology.* 2004;64(1):84-89.	Observational-Tx	43 patients	To evaluate the long-term outcome of patients with prostate cancer who have pathologic SVI without lymph node metastasis (pT3bN0M0) and compare management strategies.	5-year survival estimates for distant metastasis were 0% for the ART vs 17% for the observed patient group. Patients with a preoperative PSA level of <20 ng/mL showed significantly greater 5-year bNED survival than those with a preoperative PSA level of 20 ng/mL or greater (56% vs 32%, P<0.05). The survival curves for risk of distant metastasis and death from prostate cancer for those 2 patient groups were not significantly different statistically.	2

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56. Bolla M, van Poppel H, Collette L, et al. Postoperative radiotherapy after radical prostatectomy: a randomised controlled trial (EORTC trial 22911). *Lancet.* 2005;366(9485):572-578.	Experimental-Tx	972 patients	Randomized controlled trial to compare RP followed by immediate external RT with prostatectomy alone for patients with positive surgical margin or pT3 prostate cancer.	After a median follow-up of 5 years, bPFS was significantly improved in the irradiated group (74.0%, 98% CI 68.7-79.3 vs 52.6%, 46.6-58.5; P<0.0001). Immediate external RT after RP improves bPFS and local control in patients with positive surgical margins or pT3 prostate cancer who are at high risk of progression.	1
57. Bolla M, van Poppel H, Tombal B, et al. Postoperative radiotherapy after radical prostatectomy for high-risk prostate cancer: long-term results of a randomised controlled trial (EORTC trial 22911). *Lancet.* 2012;380(9858):2018-2027.	Experimental-Tx	1,005 patients	To report the long-term results of a trial of immediate postoperative irradiation vs a wait-and-see policy in patients with prostate cancer extending beyond the prostate, to confirm whether previously reported progression-free survival was sustained.	1,005 patients were randomly assigned to a wait-and-see policy (n=503) or postoperative RT (n=502) and were followed up for a median of 10.6 years (range 2 months to 16.6 years). Postoperative RT significantly improved bPFS compared with the wait-and-see policy (198 [39.4%] of 502 patients in postoperative irradiation group vs 311 [61.8%] of 503 patients in wait-and-see group had biochemical or clinical progression or died; HR 0.49 [95% CI; 0.41–0.59]; P<0.0001). Late adverse effects (any type of any grade) were more frequent in the postoperative irradiation group than in the wait-and-see group (10 year cumulative incidence 70.8% [66.6–75.0] vs 59.7% [55.3–64.1]; P=0.001).	1
58. Wiegel T, Bottke D, Steiner U, et al. Phase III postoperative adjuvant radiotherapy after radical prostatectomy compared with radical prostatectomy alone in pT3 prostate cancer with postoperative undetectable prostate-specific antigen: ARO 96-02/AUO AP 09/95. *J Clin Oncol.* 2009;27(18):2924-2930.	Experimental-Tx	388 patients (114 had RT and 154 "wait and see")	Randomized phase III results of ART vs "wait and see" in patients with pT3 prostate cancer following RP.	Biochemical control at 5 years increased to 72% for RT arm compared with 54% for wait and see (P=.0015, HR 0.53). The rate of late grade 3-4 side effects was 0.3%. ART for pT3 prostate cancer significantly reduces the risk of biochemical progression after RP. The rate of side effects is very low.	1

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59. Jackson WC, Johnson SB, Li D, et al. A prostate-specific antigen doubling time of <6 months is prognostic for metastasis and prostate cancer-specific death for patients receiving salvage radiation therapy post radical prostatectomy. *Radiat Oncol.* 2013;8:170.	Observational-Tx	277 patients	To assess what PSADT threshold is most clinically prognostic in this setting.	Sufficient data to calculate PSADTs were available for 277 patients. PSADT was prognostic for biochemical failure, distant metastasis, prostate cancer-specific mortality, and overall mortality on univariate analysis regardless of threshold. HR assessment identified 6 months as a strong threshold. No statistically significant difference was observed in biochemical failure, distant metastasis, prostate cancer-specific mortality, or overall mortality between patients with PSADT <3 (n=40) and 3-6 months (n=61) or between 6-10 (n=62) and >10 months (n=114). However significant differences were seen in biochemical failure (HR: 2.2, [95% CI: 1.4-3.5], P<0.01) and distant metastasis (HR: 2.2, [95% CI: 1.2-4.3], P=0.02) between a PSADT of 3-6 and 6-10 months. On multivariate analysis a PSADT <6 months predicted biochemical failure (HR: 2.0, [95% CI: 1.4-2.9], P=0.0001), distant metastasis (HR: 2.0, [95% CI: 1.2-3.4], P=0.01), and prostate cancer-specific mortality (HR: 2.6, [95% CI: 1.1-5.9], P=0.02).	2
60. D'Amico AV, Moul JW, Carroll PR, Sun L, Lubeck D, Chen MH. Surrogate end point for prostate cancer-specific mortality after radical prostatectomy or radiation therapy. *J Natl Cancer Inst.* 2003;95(18):1376-1383.	Observational-Tx	8,669 patients	To evaluate the hypothesis that a short post-treatment PSADT after RT is a surrogate end point for prostate cancer-specific mortality by analyzing 2 multi-institutional databases of patients with localized or locally advanced, non-metastatic prostate cancer.	Post-treatment PSADT was statistically significantly associated with time to prostate cancer-specific mortality and with time to all-cause mortality (P<.001). Treatment received was not statistically significantly associated with time to prostate cancer-specific mortality after PSA-defined disease recurrence for patients with a PSADT <3 months (P=0.90) and for patients with a PSADT of >3 months (P=.28) when controlling for the specific value of the PSADT. After a PSA-defined recurrence, a PSADT <3 months was statistically significantly associated with time to prostate cancer-specific mortality.	2

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61. Ward JF, Blute ML, Slezak J, Bergstralh EJ, Zincke H. The long-term clinical impact of biochemical recurrence of prostate cancer 5 or more years after radical prostatectomy. *J Urol.* 2003;170(5):1872-1876.	Observational-Tx	3,903 patients	To differentiate the innocuous recurrence of serum PSA from that which heralds an eventual clinical failure, and to determine if there is a period following RP when a patient is cured of clinical disease.	Overall bNED rate >5 disease-free years was 27%. Progression from bNED to clinical failure was not significantly altered by the disease-free interval (P=0.544). A PSADT <12 months significantly increased the risk of chronic failure regardless of the interval from surgery. Risk factors for bNED were significant throughout the duration of follow-up.	2
62. Sengupta S, Myers RP, Slezak JM, Bergstralh EJ, Zincke H, Blute ML. Preoperative prostate specific antigen doubling time and velocity are strong and independent predictors of outcomes following radical prostatectomy. *J Urol.* 2005;174(6):2191-2196.	Observational-Tx	2,290 patients	To assess preoperative PSADT and PSAV as predictors of outcome following RRP.	The HR for death from prostate cancer was 6.22 in men with PSADT <18 month's vs ≥18 and 6.54 in men with PSAV >3.4 ng/mL yearly vs 3.4 or less. On multivariate analysis adjusting for preoperative or postoperative variables PSADT and PSAV remained significant predictors of each outcome. When assessed jointly, PSAV was significant as a predictor of biochemical progression, while PSADT was a significant predictor of clinical progression and cancer death.	2
63. Patel DA, Presti JC, Jr., McNeal JE, Gill H, Brooks JD, King CR. Preoperative PSA velocity is an independent prognostic factor for relapse after radical prostatectomy. *J Clin Oncol.* 2005;23(25):6157-6162.	Observational-Tx	202 patients	Retrospective review to evaluate the relative merit of established preoperative factors, including biopsy indices and preoperative PSAV, for their impact on relapse after RP.	Kaplan-Meier RFS at 5 years was 89%, compared with 73% for PSAV ≤2 vs >2 ng/mL/year (P=.003). On multivariate analysis, only the biopsy Gleason sum (P<.008; RR, >4.8) and the preoperative PSAV (P<.04; RR, 3.0 to 4.7) remained significant. Preoperative PSAV is a significant independent clinical factor predicting for relapse after RP and also predicts for larger, more aggressive, and more locally advanced tumors.	2

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64. D'Amico AV, Chen MH, Roehl KA, Catalona WJ. Preoperative PSA velocity and the risk of death from prostate cancer after radical prostatectomy. *N Engl J Med.* 2004;351(2):125-135.	Observational-Tx	1,095 men	To determine whether men at risk for death from prostate cancer after RP can be identified using information available at diagnosis.	As compared with an annual PSAV of 2.0 ng/mL or less, an annual PSAV of more than 2.0 ng/mL was associated with a significantly shorter time to death from prostate cancer (P<0.001) and death from any cause (P=0.01). An increasing PSA level at diagnosis (P=0.01), a Gleason score of 8, 9, or 10 (P=0.02), and a clinical tumor stage of T2 (P<0.001) also predicted the time to death from prostate cancer. For men with an annual PSAV of more than 2.0 ng/mL, estimates of the risk of death from prostate cancer and death from any cause 7 years after RP were also influenced by the PSA level, tumor stage, and Gleason score at diagnosis.	2
65. Trock BJ, Han M, Freedland SJ, et al. Prostate cancer-specific survival following salvage radiotherapy vs observation in men with biochemical recurrence after radical prostatectomy. *JAMA.* 2008;299(23):2760-2769.	Observational-Tx	635 men	To quantify the relative improvement in prostate cancer-specific survival of SRT vs no therapy after biochemical recurrence following prostatectomy, and to identify subgroups for whom salvage treatment is most beneficial.	With a median follow-up of 6 years after recurrence and 9 years after prostatectomy, 116 men (18%) died from prostate cancer, including 89 (22%) who received no salvage treatment, 18 (11%) who received SRT alone, and 9 (12%) who received SRT and hormonal therapy. SRT alone was associated with a significant 3-fold increase in prostate cancer-specific survival relative to those who received no salvage treatment (HR, 0.32 [95% CI, 0.19–0.54]; P<.001). Addition of hormonal therapy to SRT was not associated with any additional increase in prostate cancer-specific survival (HR, 0.34 [95% CI, 0.17-0.69]; P=.003). The increase in prostate cancer-specific survival associated with SRT was limited to men with a PSADT of <6 months and remained after adjustment for pathological stage and other established prognostic factors. SRT initiated more than 2 years after recurrence provided no significant increase in prostate cancer-specific survival. Men whose PSA level never became undetectable after SRT did not experience a significant increase in prostate cancer-specific survival. SRT also was associated with a significant increase in OS.	2

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66. Patel A, Dorey F, Franklin J, deKernion JB. Recurrence patterns after radical retropubic prostatectomy: clinical usefulness of prostate specific antigen doubling times and log slope prostate specific antigen. *J Urol.* 1997;158(4):1441-1445.	Observational-Tx	77 patients	To examine the correlation between PSADT or equivalently, log slope PSA and clinical recurrence in patients with detectable PSA after RRP.	80% with PSADT of 6 months or greater remained clinically disease-free compared to 64% with PSADT <6 months. After PSA became detectable PSADT or, equivalently, log slope PSA, was a better indicator of the risk and time to clinical recurrence after RRP than preoperative PSA, specimen Gleason sum or pathological stage.	2
67. Leventis AK, Shariat SF, Kattan MW, Butler EB, Wheeler TM, Slawin KM. Prediction of response to salvage radiation therapy in patients with prostate cancer recurrence after radical prostatectomy. *J Clin Oncol.* 2001;19(4):1030-1039.	Observational-Tx	49 patients	To study a group of patients who were treated with SRT for control of presumed or biopsy-proven local recurrence and to identify factors predictive of local recurrence as defined by a complete response to SRT.	Multivariate analysis showed prebiopsy PSA level, postrecurrence PSADT, and positive DRE of the prostatic fossa were all statistically significant predictors of a positive biopsy. For the 49 patients subsequently treated with SRT, the overall actuarial 3- and 5-year PSA relapse-free probabilities were 43% and 24%, respectively. In multivariate analysis, preradiation PSA and postrecurrence PSADT measured before radiation were the only statistically significant predictors of outcome. DRE of the prostatic fossa, prebiopsy PSA, and postrecurrence PSADT predict which patients will have biopsy-proven local recurrence.	2

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68. Roberts SG, Blute ML, Bergstralh EJ, Slezak JM, Zincke H. PSA doubling time as a predictor of clinical progression after biochemical failure following radical prostatectomy for prostate cancer. *Mayo Clin Proc.* 2001;76(6):576-581.	Observational-Tx	2,809 patients	To characterize the clinical progression of disease in men who have undergone prostatectomy for clinically localized prostate cancer and have postoperative bNED and to identify predictors of clinical disease progression, including the possible effect of PSADT.	31% of patients experienced bNED with mean follow-up from time of bNED of 4.7 years. Mean time to bNED was 2.9 years (median, 2.4 years).Overall mean systemic progression (SP)-free survival from time of bNED was 94% and 91% at 5 and 10 years, respectively. Mean local recurrence/systemic progression-free survival was 64% and 53% at 5- and 10-years, respectively. Univariate analysis on the 587 patients with PSADT data, significant risk factors for systemic progression were PSADT (P<.001) and pathologic Gleason score (P=.005); for local recurrence/systemic progression, significant risk factors included PSADT (P<.001) and pathologic Gleason score (P<.001). For multivariate analysis, only PSADT remained a significant risk factor for systemic progression and local recurrence/systemic progression (P<.001). Mean 5-year systemic progression-free survival was 99%, 95%, 93%, and 64% for patients with PSADT of >10 years, 1.0-9.9 years, 0.5-0.9 years, and <0.5 years, respectively; the respective mean local recurrence/systemic progression-free survivals were 87%, 62%, 46%, and 38%, respectively. The percentage of patients with PSADT of <0.5 years was considerably higher if the type of first clinical event was systemic progression (48%) compared with local recurrence (18%) (P<.001).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. Brooks JP, Albert PS, Wilder RB, Gant DA, McLeod DG, Poggi MM. Long-term salvage radiotherapy outcome after radical prostatectomy and relapse predictors. *J Urol.* 2005;174(6):2204-2208, discussion 2208.	Observational-Tx	114 patients	Retrospective review to assess the efficacy of SRT and analyze predictors of bPFS and distant MFS in patients with clinically localized disease recurrence after RP.	At a median follow-up of 6.3 years for SRT, 4 and 6-year bPFS was 50% and 33%, respectively. The 6-year actuarial probability of distant metastases after SRT was 14%. Multivariate analysis demonstrated an independent association of increasing Gleason score, lymphovascular invasion and lack of a complete response to SRT. These factors were associated with significantly less 5-year distant MFS. Pre-RT PSA >2.0 ng/mL was associated with significantly decreased 5-year bDFS and distant MFS, although it was not maintained on multivariate analysis.	2
70. Nudell DM, Grossfeld GD, Weinberg VK, Roach M, 3rd, Carroll PR. Radiotherapy after radical prostatectomy: treatment outcomes and failure patterns. *Urology.* 1999;54(6):1049-1057.	Observational-Tx	105 patients	Review records of patients to define the optimal role for RT after RP and to characterize specific patterns of PSA failure in this setting.	Actuarial 3- and 5-year progression-free survival estimates for all patients were 55% and 43%, respectively. Significant favorable predictors of response to RT by multivariate analysis were preoperative PSA <20 ng/mL and the use of ART. However, patients who received therapeutic RT with a pre-RT PSA <1.0 ng/mL demonstrated progression-free outcome equivalent to those who received ART. Patients whose PSA failed to reach a nadir <0.2 ng/mL after RT had progression with a high PSAV (1.5 ng/mL/year). Patients whose PSA reached a nadir <0.2 ng/mL but who subsequently had treatment failure progressed later with a lower PSAV (0.36 ng/mL/year). RT is effective in select patients after RP.	2
71. Anscher MS, Clough R, Dodge R. Radiotherapy for a rising prostate-specific antigen after radical prostatectomy: the first 10 years. *Int J Radiat Oncol Biol Phys.* 2000;48(2):369-375.	Observational-Tx	89 patients	To determine the results of RT to the prostate bed for a presumed local recurrence heralded by a rising PSA after RP for adenocarcinoma of the prostate.	Estimated 4-year DFS for all patients is 50%. The DFS at 4 years was 61% for the 3D-RT patients vs 41% for those treated without 3D-RT (P=0.006). Late complications (grade 1/2 only), however, were significantly more common in the 3D-RT group. On multivariate analysis, only dose >65 Gy predicted for better DFS. Pelvic RT may achieve sustained remission of prostate cancer for about half of patients with a rising PSA after RP, at least in the intermediate term. Doses >65 Gy are recommended.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
72. Mosbacher MR, Schiff PB, Otoole KM, et al. Postprostatectomy salvage radiation therapy for prostate cancer: impact of pathological and biochemical variables and prostate fossa biopsy. *Cancer J.* 2002;8(3):242-246.	Observational-Tx	62 patients	To examine the impact of pathological and biochemical variables and pre-RT biopsy of the prostate fossa on biochemical DFS and initial PSA response.	Complete biochemical response was observed in 50% of patients, and a partial biochemical response was observed in an additional 34%, yielding an overall biochemical response rate of 84%. Gleason's score and SVI predicted bNED DFS after post-RRP RT. Overall biochemical response rates were high in all subgroups. Pre-RT biopsy was predictive of neither bNED nor overall biochemical response.	2
73. Macdonald OK, Schild SE, Vora SA, et al. Radiotherapy for men with isolated increase in serum prostate specific antigen after radical prostatectomy. *J Urol.* 2003;170(5):1833-1837.	Observational-Tx	60 patients	Retrospective study to determine the results of salvage EBRT to the prostate bed for isolated increase of serum PSA after RP.	5-year actuarial bDFS was 45%. PSA before RT (P=0.016), RT dose (P=0.026), surgical margin involvement (P=0.017) and Gleason score (P=0.018) were identified as prognostic factors for bDFS. A significant association with bDFS was present at 5 years of 65%, 34% and 0% for PSA before RT <0.6, 0.6 to 1.2, and >1.2 ng/mL, respectively (P=0.036). Patients with PSA before RT <0.6 ng/mL and total RT dose >64.8 Gy had improved bDFS at 5 years compared to all others (77% vs 32%, P=0.04). Of 60 patients 3 (5%) experienced chronic grade 3 toxicity.	2
74. MacDonald OK, Schild SE, Vora S, et al. Salvage radiotherapy for men with isolated rising PSA or locally palpable recurrence after radical prostatectomy: do outcomes differ? *Urology.* 2004;64(4):760-764.	Observational-Tx	102 patients	To compare, in a retrospective analysis, the outcome of EBRT for isolated PSA elevation or palpable local recurrence after RP.	5-year rate of biochemical DFS, local control, freedom from distant metastasis, and OS for all patients was 38%, 94%, 87%, and 88%, respectively. The greatest 5-year rate of biochemical control (69%) was obtained in patients with a pre-EBRT PSA level of ≤0.5 ng/mL. The 5-year OS rate was significantly better for those who underwent salvage EBRT for a rising PSA level than for those with palpable recurrence (96% vs 78%, P=0.02). Salvage EBRT provides excellent local control of recurrent disease after RP.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
75. Peyromaure M, Allouch M, Eschwege F, Verpillat P, Debre B, Zerbib M. Salvage radiotherapy for biochemical recurrence after radical prostatectomy: a study of 62 patients. *Urology.* 2003;62(3):503-507.	Observational-Tx	62 patients	To determine the predictive factors of PSA recurrence after SRT for biochemical recurrence following RP to identify patients who may benefit from this treatment.	With a mean follow-up of 44 months (range 3 to 110), 23 patients (37.1%) experienced PSA recurrence after RT. Using univariate analysis, 6 factors were found to be predictive of PSA recurrence after RT: the length of follow-up after RT (P<0.0001), PSA nadir after RP (P=0.0004),time to PSA recurrence after RP (P=0.003),pre-RP PSA level (P=0.008),Gleason score (P=0.011), pre-RT PSA level (P=0.028). Using multivariate analysis, only the Gleason score (P=0.015) and length of follow-up after RT (P=0.02) were found to be predictive of PSA recurrence after RT. A Gleason score >7 was a significant predictor of PSA recurrence after SRT (P=0.04).	2
76. Numata K, Azuma K, Hashine K, Sumiyoshi Y. Predictor of response to salvage radiotherapy in patients with PSA recurrence after radical prostatectomy: the usefulness of PSA doubling time. *Jpn J Clin Oncol.* 2005;35(5):256-259.	Observational-Tx	21 patients	Retrospective review to assess predictors of response to SRT in patients with PSA recurrence after RP.	Only predictive factor was PSADT. The median PSADT in responders was 6.2 months vs 1.9 months in nonresponders (P=0.019). PSADT appears to be a good predictor of response to SRT. SRT was especially effective when PSADT was ≥5 months.	2
77. Ng MK, Van As N, Thomas K, et al. Prostate-specific antigen (PSA) kinetics in untreated, localized prostate cancer: PSA velocity vs PSA doubling time. *BJU Int.* 2009;103(7):872-876.	Observational-Dx	199 patients	To compare the accuracy of PSAV vs PSADT for predicting the repeat biopsy results in men with localized prostate cancer on active surveillance.	The median PSAV and PSADT were 0.71 ng/mL/year and 5.29 years, respectively. 53 patients (27%) had adverse histology on repeat biopsy. On univariate analyses, PSAV (P<0.001) and PSADT (P=0.019) were associated with adverse histology. PSAV is more accurate than PSADT for predicting adverse histology on repeat biopsies.	3
78. Swindle PW, Kattan MW, Scardino PT. Markers and meaning of primary treatment failure. *Urol Clin North Am.* 2003;30(2):377-401.	Review/Other-Tx	N/A	Review markers and meaning of primary treatment failure. Focus on management of biochemical recurrence.	Time to biochemical progression, Gleason score, and PSADT are predictive of the probability and time to development of metastatic disease, and allow for stratification of patients into different risk groups. TRUS, CT, positron emission tomography, and DRE all have limited utility in the identification of local recurrence.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
79. Pollack A, Hanlon AL, Pisansky TM, et al. A multi-institutional analysis of adjuvant and salvage radiotherapy after radical prostatectomy. *International Journal of Radiation Oncology*Biology*Physics.* 2004;60(1, Supplement):S186-S187.	Review/Other-Tx	N/A	Review of the data for prostate cancer patients with pathologically documented regional lymph node + disease treated with EBRT + androgen deprivation or RP + androgen deprivation shows promising results.	For patients with subclinical lymph node involvement:10 year FFBF à 20%10 year OS à 70%Patients with a 10 year life expectancy should be treated aggressively with long-term androgen deprivation combined with either EBRT or RP.	4
80. Forman JD, Meetze K, Pontes E, et al. Therapeutic irradiation for patients with an elevated post-prostatectomy prostate specific antigen level. *J Urol.* 1997;158(4):1436-1439; discussion 1439-1440.	Observational-Tx	47 patients	To determine the efficacy of post-prostatectomy therapeutic radiation for patients with elevated PSA. Univariate and multivariate survival analyses were performed to identify prognostic variables.	Therapeutic RT for patients with elevated PSA postoperatively is highly effective. At a median follow-up of 36 months, 64% of the patients remain disease-free.	2
81. Morris MM, Dallow KC, Zietman AL, et al. Adjuvant and salvage irradiation following radical prostatectomy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 1997;38(4):731-736.	Observational-Tx	88 patients	Retrospective analysis to assess the durability of benefit derived from RT after prostatectomy for pT3N0 disease, and the possibility of cure.	88% of adjuvant patients were bNED at 3 years from prostatectomy. 68% of those receiving SRT were bNED 3 years after surgery. On univariate analysis, treatment group, preoperative PSA, and the status of seminal vesicles were significant prognostic factors. On multivariate analysis, the only significant predictor of outcome was treatment group, with ART having better outcome than salvage. For patients with stage pT3N0 prostate cancer following RP, data support the use of either routine postoperative ART or close PSA follow-up with early salvage treatment.	2
82. Rogers R, Grossfeld GD, Roach M, 3rd, Shinohara K, Presti JC, Jr., Carroll PR. Radiation therapy for the management of biopsy proved local recurrence after radical prostatectomy. *J Urol.* 1998;160(5):1748-1753.	Observational-Tx	34 patients	Review clinical records to determine which clinical characteristics correlate with a successful outcome following EBRT for the management of biopsy proved, locally recurrent prostate cancer after RP.	Likelihood of successful treatment at 3 years after RT for all patients was 48%. Preoperative PSA, PSA at first elevation, postoperative PSAV and pathological stage were not significant predictors of a successful outcome following radiation treatment. Patients with a serum PSA of ≤4 ng/mL before receiving RT and those with a prostatectomy specimen Gleason score of ≤7 were significantly more likely to be successfully treated by RT. RT is a viable treatment option for select patients with biopsy proved local disease recurrence following RP.	2

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
83. Valicenti RK, Gomella LG, Ismail M, Mulholland SG, Petersen RO, Corn BW. Effect of higher radiation dose on biochemical control after radical prostatectomy for PT3N0 prostate cancer. *Int J Radiat Oncol Biol Phys.* 1998;42(3):501-506.	Observational-Tx	86 consecutive patients	To examine the effect of higher radiation dose on biochemical control after RP for PT3N0 prostate cancer.	Univariate and multivariate analyses of variables showed that the pre-RT PSA level was the most significant predictor of improved bNED survival (P<0.001). Actuarial analyses of radiation dose grouped with pre-RT PSA levels found higher RT dose to be significant (P<0.05). For the 52 patients with an undetectable pre-RT PSA level, the 3-year bNED rate was 91% for patients irradiated to 61.5 Gy or more and 57% for those irradiated to lower doses (P=0.01). For the 21 patients with pre-RT PSA level >0.2 and ≤2.0 ng/mL, the 3-year bNED rate was 79% for patients irradiated to 64.8 Gy or more and 33% for those irradiated to a lower dose (P=0.02).	2
84. King CR. The timing of salvage radiotherapy after radical prostatectomy: a systematic review. *Int J Radiat Oncol Biol Phys.* 2012;84(1):104-111.	Review/Other-Tx	41 studies	A systematic review of all published SRT studies was performed to identify the pathologic, clinical, and treatment factors associated with RFS after SRT.	PSA level before SRT (P<.0001) and RT dose (P=.0052) had a significant and independent association with RFS. There was an average 2.6% loss of RFS for each incremental 0.1 ng/mL PSA at the time of SRT (95% CI, approximately 2.2-3.1). With a PSA level of 0.2 ng/mL or less before SRT, the RFS approached 64%. The dose for SRT in the range of 60-70 Gy seemed to be on the steep part of the sigmoidal dose-response curve, with a dose of 70 Gy achieving 54% RFS compared with only 34% for 60 Gy. There was a 2% improvement in RFS for each additional Gy (95% CI, approximately 0.9-3.2). The observed dose-response was less robust on sensitivity analysis.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
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 prostatectomy. *Radiother Oncol.* 2009;93(2):207-212.	Observational-Tx	172 consecutive patients	To investigate the role of IMRT in reducing the risk of acute GU, upper GI and lower GI toxicity following whole-pelvis RT after RP.	Patients treated with IMRT experienced a decreased risk of acute toxicity. The crude incidence of grade ≥2 toxicity was GU 12.3% vs 6.6% (P=0.19); lower GI 8.6% vs 3.2% (P=0.14); upper GI 22.2% vs 6.6% (P=0.004), for 3D-CRT and IMRT, respectively. With respect to upper GI and lower GI, the acute toxicity profile of the helical tomotherapy patients was even better when compared to that of 3D-CRT patients (crude incidence: 1.8% and 0.0%, respectively). Treatment interruptions due to upper GI toxicity were 11/81 in the 3D-CRT group vs 2/91 in the IMRT group (P=0.006).	2
86. Bastasch MD, Teh BS, Mai WY, et al. Post-nerve-sparing prostatectomy, dose-escalated intensity-modulated radiotherapy: effect on erectile function. *Int J Radiat Oncol Biol Phys.* 2002;54(1):101-106.	Observational-Tx	51 patients	To investigate the effect of postprostatectomy, high-dose IMRT on patients' erectile function.	Of the 51 patients, 18 (35.3%) maintained their potency and 33 (64.7%) became impotent after nerve-sparing prostatectomy. Patients who underwent bilateral nerve-sparing prostatectomy had higher rates of postoperative potency than did those who underwent unilateral nerve-sparing surgery (72.2% vs 27.8%; P=0.025). The follow-up for the entire group was 19.5 months. All 18 patients (100%) who were potent postoperatively remained potent after RT. The median follow-up for the 18 potent patients was 27.2 months, significantly longer than that of the impotent group, 13.0 months (P<0.001).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
87. Crandley EF, Hegarty SE, Hyslop T, Wilson DD, Dicker AP, Showalter TN. Treatment-related complications of radiation therapy after radical prostatectomy: comparative effectiveness of intensity-modulated versus conformal radiation therapy. *Cancer Med.* 2014;3(2):397-405.	Observational-Tx	1,686 patients	To analyze a large group of patients treated with RT after RP to compare complications after IMRT and CRT.	First complication events, based upon administrative procedure or diagnosis codes occurring >1 year after start of RT, were compared for IMRT vs CRT groups. Propensity score adjustment was performed to adjust for potential confounders. Multivariable Cox proportional hazards models of time to first complication were performed. A total of 1,686 patients were identified who received RT after RP (IMRT = 634, CRT = 1,052). Patients treated with IMRT were more likely to be diagnosed after 2004 (P<0.001), have minimally invasive prostatectomy (P<0.001) and have positive margins (P=0.019). IMRT use increased over time. After propensity score adjustment, IMRT was associated with lower rate of GI complications, and higher rate of GU-incontinence complications, compared to CRT.	2
88. Goenka A, Magsanoc JM, Pei X, et al. Improved toxicity profile following high-dose postprostatectomy salvage radiation therapy with intensity-modulated radiation therapy. *Eur Urol.* 2011;60(6):1142-1148.	Observational-Tx	285 patients	To compare acute and late toxicities in patients treated with IMRT and 3D-CRT in the postprostatectomy salvage setting.	The 5-year actuarial rates of late grade ≥2 GI and GU toxicity were 5.2% and 17.0%, respectively. IMRT was independently associated with a reduction in grade ≥2 GI toxicity compared with 3D-CRT (5-year IMRT, 1.9%; 5-year 3D-CRT, 10.2%; P=0.02). IMRT was not associated with a reduction in risk of grade ≥2 GU toxicity (5-year IMRT, 16.8%; 5-year 3D-CRT, 15.8%; P=0.86), urinary incontinence (5-year IMRT, 13.6%; 5-year 3D-CRT, 7.9%; P=0.25), or grade 3 erectile dysfunction (5-year IMRT, 26%; 5-year 3D-CRT, 30%; P=0.82). Of patients who developed late grade ≥2 GI or GU toxicity, 38% and 44%, respectively, experienced resolution of their symptoms prior to the last follow-up.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
89. Goldin GH, Sheets NC, Meyer AM, et al. Comparative effectiveness of intensity-modulated radiotherapy and conventional conformal radiotherapy in the treatment of prostate cancer after radical prostatectomy. *JAMA Intern Med.* 2013;173(12):1136-1143.	Observational-Tx	457 IMRT and 557 CRT patients	To examine the patterns of use of IMRT, a newer, more expensive technology that may reduce radiation dose to adjacent organs compared with the older CRT in the postprostatectomy setting, and to compare disease control and morbidity outcomes of these treatments.	Use of IMRT increased from zero in 2000 to 82.1% in 2009. Men who received IMRT vs CRT showed no significant difference in rates of long-term GI morbidity (RR, 0.95; 95% CI, 0.66–1.37), urinary nonincontinent morbidity (0.93; 0.66–1.33), urinary incontinence (0.98; 0.71–1.35), or erectile dysfunction (0.85; 0.61–1.19). There was no significant difference in subsequent treatment for recurrent disease (RR, 1.31; 95% CI, 0.90–1.92).	2
90. Harrison A, Studenski M, Harvey A, et al. Potential for dose escalation in the postprostatectomy setting with intensity-modulated radiation therapy: a dosimetric study using EORTC consensus guidelines for target volume contours. *Practical Radiation Oncology.* 2011;1(2):105-114.	Observational-Tx	20 patients	To compare IMRT vs 3D-CRT planning.	The 9-field IMRT plans (vs 3D-CRT) improved bladder mean dose and volume receiving 65 Gy or more (V65), as well as rectum mean dose (31.6 Gy vs 36.1 Gy; P<.001), volume receiving 75% or more of the prescription dose (24.4% vs 31.0%; P<.001), and V65 (10.5% vs 20.0%; P<.001). Advantages of IMRT were at the cost of small increases in maximum point doses delivered to the bladder and rectum. Cone beam CT images (n = 132) were analyzed for 8 patients; rectum mean dose and V65 were also improved by IMRT on these scans. IMRT allowed increasing dose to 72.0 Gy with similar bladder and rectum mean doses, V65, and V40 compared to 3D-CRT to a total dose of 68.4 Gy.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
91. Koontz BF, Das S, Temple K, et al. Dosimetric and radiobiologic comparison of 3D conformal versus intensity modulated planning techniques for prostate bed radiotherapy. *Med Dosim.* 2009;34(3):256-260.	Observational-Tx	15 patients	To compare normal tissue and target dosimetry and radiobiological modeling of IMRT vs 3D-CRT planning in the postoperative setting.	3D-CRT plans were designed for 15 patients who had been treated with IMRT planning for salvage post-prostatectomy RT. The same CT and target/normal structure contours, as well as prescription dose, was used for both IMRT and 3D plans. Normal tissue complication probabilities were calculated based on the dose given to the bladder and rectum by both plans. Dose-volume histogram and normal tissue complication probabilities data were compared by paired t-test. Bladder and rectal sparing were improved with IMRT planning compared to 3D conformal planning. The volume of the bladder receiving at least 75% (V75) and 50% (V50) of the dose was significantly reduced by 28% and 17%, respectively (P=0.002 and 0.037). Rectal dose was similarly reduced, V75 by 33% and V50 by 17% (P=0.001 and 0.004). While there was no difference in the volume of rectum receiving at least 65 Gy (V65), IMRT planning significant reduced the volume receiving 40 Gy or more (V40, P=0.009).	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
92. Ost P, De Troyer B, Fonteyne V, Oosterlinck W, De Meerleer G. A matched control analysis of adjuvant and salvage high-dose postoperative intensity-modulated radiotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2011;80(5):1316-1322.	Observational-Tx	178 patients	To perform a matched case analysis comparing high-dose adjuvant IMRT with salvage IMRT.	A total of 178 patients were matched (89:89). From the end of RT, the median follow-up was 36 months for both groups. The 3-year bRFS rate for the adjuvant IMRT group was 90% compared to 65% for the salvage IMRT group (P<0.05). On multivariate analysis, salvage IMRT, Gleason grades of ≥4+3, perineural invasion, preoperative PSA level of ≥10 ng/mL, and omission of ADT were independent predictors for a reduced bRFS (P<0.05). From the date of surgery, the median follow-up was 43 and 60 months for adjuvant IMRT and salvage IMRT, respectively. The 3-year bRFS rate for adjuvant IMRT was 91% compared to 79% for salvage IMRT (P<0.05). On multivariate analysis, Gleason grades of ≥4+3, perineural invasion, and omission of ADT were independent predictors for a reduced bRFS (P<0.05). Salvage IMRT was no longer an independent prognostic factor (P=0.08).	2
93. Ost P, Fonteyne V, Villeirs G, Lumen N, Oosterlinck W, De Meerleer G. Adjuvant high-dose intensity-modulated radiotherapy after radical prostatectomy for prostate cancer: clinical results in 104 patients. *Eur Urol.* 2009;56(4):669-675.	Observational-Tx	104 patients	To report on the safety and biochemical outcome of adjuvant IMRT with doses >70 Gy.	With respect to acute toxicity, no patients developed grade 3 GI toxicity, and 8 patients developed grade 3 GU toxicity (8%). With respect to late toxicity, no patients developed grade 3 GI toxicity, and 4 patients (4%) developed grade 3 GU toxicity. A urethral stricture was observed in 6 patients (6%). The 3- and 5-year actuarial bRFS was 93%. On univariate analysis, bRFS rates were worse when SVI (P<0.02), Gleason score ≥4+3 (P<0.02), or negative surgical margins (P<0.02) were present. ADT did not influence bRFS. 6 patients had a clinical relapse.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
94. Ost P, Lumen N, Goessaert AS, et al. High-dose salvage intensity-modulated radiotherapy with or without androgen deprivation after radical prostatectomy for rising or persisting prostate-specific antigen: 5-year results. *Eur Urol.* 2011;60(4):842-849.	Observational-Tx	136 patients	To report on the late toxicity profile and outcome of patients treated with high-dose salvage IMRT with or without ADT.	The 5-year actuarial bRFS and clinical RFS were 56% and 86%, respectively. On multivariate analysis, the presence of perineural invasion at RP (HR: 6.19, P=0.001) and an increasing pre-SRT PSA (PSA 0.5 ng/mL: HR: 1; PSA 1–1.5 ng/mL: HR: 1.60, P=0.30; and PSA >1 ng/mL: HR: 2.70, P=0.02) were independent factors for a decreased bRFS. The addition of AD improved bRFS (HR: 0.33, P=0.005). On multivariate analysis, none of the variables was a predictor of clinical RFS. The 5-year risk of grade 2-3 toxicity was 22% and 8% for GU and GI symptoms, respectively.	2
95. Zelefsky MJ, Leibel SA, Gaudin PB, et al. Dose escalation with three-dimensional conformal radiation therapy affects the outcome in prostate cancer. *Int J Radiat Oncol Biol Phys.* 1998;41(3):491-500.	Observational-Tx	743 patients	To determine whether dose escalation with 3D-CRT improves outcomes.	The median follow-up was 3 years (range: 1-7.6 years). Induction of an initial clinical response was dose-dependent, with 90% of patients receiving 75.6 or 81.0 Gy achieving a PSA nadir ≤1.0 ng compared with 76% and 56% for those treated with 70.2 Gy and 64.8 Gy, respectively (P<0.001). The 5-year actuarial PSA RFS for patients with favorable prognostic indicators (stage T1-2, pretreatment PSA ≤10.0 ng/mL and Gleason score ≤6) was 85%, compared to 65% for those with intermediate prognosis (1 of the prognostic indicators with a higher value) and 35% for the group with unfavorable prognosis (2 or more indicators with higher values) (P<0.001). PSA RFS was significantly improved in patients with intermediate and unfavorable prognosis receiving ≥75.6 Gy (P<0.05). A positive biopsy at ≥2.5 years after 3D-CRT was observed in only 1/15 (7%) of patients receiving 81.0 Gy, compared with 12/25 (48%) after 75.6 Gy, 19/42 (45%) after 70.2 Gy, and 13/23 (57%) after 64.8 Gy (P<0.05).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
96. Zelefsky MJ, Fuks Z, Hunt M, et al. High-dose intensity modulated radiation therapy for prostate cancer: early toxicity and biochemical outcome in 772 patients. *Int J Radiat Oncol Biol Phys*. 2002;53(5):1111-1116.	Observational-Tx	772 patients	Report on the toxicity and biochemical outcomes for patients treated with IMRT.	4.5% had Grade 2 rectal toxicity (no Grade 3), 28% had Grade 2 urinary symptoms (1 with Grade 3). The 3 year relapse free survival was 92%, 86%, and 81%, respectively by risk group. This shows that IMRT can achieve good outcomes while reducing morbidity.	2
97. Spratt DE, Pei X, Yamada J, Kollmeier MA, Cox B, Zelefsky MJ. Long-term survival and toxicity in patients treated with high-dose intensity modulated radiation therapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys*. 2013;85(3):686-692.	Observational-Tx	1,002 patients; 587 patients treated with neoadjuvant and concurrent ADT	To report long-term survival and toxicity outcomes with the use of high-dose IMRT to 86.4 Gy for patients with localized prostate cancer.	For low-, intermediate-, and high-risk groups, 7-year biochemical RFS outcomes were 98.8%, 85.6%, and 67.9%, respectively (P<.001), and distant MFS rates were 99.4%, 94.1%, and 82.0% (P<.001), respectively. On multivariate analysis, T stage (P<.001), Gleason score (P<.001), and >50% of initial biopsy positive core (P=.001) were predictive for distant metastases. No prostate cancer-related deaths were observed in the low-risk group. The 7-year prostate cancer-specific mortality rates, using competing risk analysis for intermediate- and high-risk groups, were 3.3% and 8.1%, respectively (P=.008). On multivariate analysis, Gleason score (P=.004), percentage of biopsy core positivity (P=.003), and T-stage (P=.033) were predictive for prostate cancer-specific mortality. Actuarial 7-year grade 2 or higher late GI and GU toxicities were 4.4% and 21.1%, respectively. Late grade 3 GI and GU toxicity was experienced by 7 patients (0.7%) and 22 patients (2.2%), respectively. Of the 427 men with full potency at baseline, 317 men (74%) retained sexual function at time of last follow-up.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
98. Michalski JM, Yan Y, Watkins-Bruner D, et al. Preliminary Analysis of 3D-CRT vs. IMRT on the High Dose Arm of the RTOG 0126 Prostate Cancer Trial: Toxicity Report. *International journal of radiation oncology, biology, physics.* 2011;81(2):S1-S2.	Observational-Tx	748 patients	Preliminary analysis of clinical and treatment characteristics associated with acute and late toxicity in men receiving high dose RT on a Phase III RTOG dose escalation trial.	Median follow-up was 4.6 years and 3.5 years for 3D-CRT and IMRT patients. Median D98 delivered to the PTV7920 was 80 Gy for 3D-CRT and 79.2 Gy for IMRT. The median percentage of the bladder receiving at least x Gy (pVx) for pV65, pV70, and pV75 were 25.3%, 22.2%, and 17.7%, respectively, for 3D-CRT, and 19.7%, 16.6%, and 13.1%, respectively, for IMRT. The median rectum pV65, pV70, and pV75 were 27.4%, 21.7%, and 15.8% for 3D-CRT and 23.0%, 18.2%, and 13.0% for IMRT. For both bladder and rectum, the pVx was significantly lower with IMRT for 65, 70, and 75 Gy (all P=0.0001). Acute toxicity; there are 16.9% Grade (G2), 2.5% G3, and no G4 or 5 in the 3D-CRT group; there are 13.9% G2, 2.4% G3, 0.4% G4, and no G5 in the IMRT group. Late toxicity; there are 23.6% G2, 8.9% G3, 0.4% G4, and 0.2% G5 (1 death) with 3D-CRT group; there are 19.9% G2, 4.7% G3, 0.4% G4, and no G5 with IMRT. For G2+ acute GI/GU toxicity, both univariate and multivariate analyses show a statistically significant decrease in G2+ acute collective GI/GU toxicity for IMRT.	1
99. Chung HT, Xia P, Chan LW, Park-Somers E, Roach M, 3rd. Does image-guided radiotherapy improve toxicity profile in whole pelvic-treated high-risk prostate cancer? Comparison between IG-IMRT and IMRT. *Int J Radiat Oncol Biol Phys.* 2009;73(1):53-60.	Observational-Tx	25 consecutively treated patients	To evaluate the impact of adding image-guided technique to IMRT on dosimetric avoidance of organs at risk and acute toxicities.	The planning target volume dose coverage was not significantly different between IMRT and image-guided-IMRT for the prostate, seminal vesicles, and lymph nodes. The volume of rectum and bladder receiving ≥40, ≥60, and ≥70 Gy were all significantly less using image-guided-IMRT (P<.001). Image-guided-IMRT yielded lower acute RTOG Grade 2 rectal (80% vs 13%, P= 0.004) and bladder (60% vs 13%, P= 0.014) toxicities.	2

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
100. Zelefsky MJ, Kollmeier M, Cox B, et al. Improved clinical outcomes with high-dose image guided radiotherapy compared with non-IGRT for the treatment of clinically localized prostate cancer. *Int J Radiat Oncol Biol Phys*. 2012;84(1):125-129.	Observational-Tx	186 patients	To compare toxicity profiles and biochemical tumor control outcomes between patients treated with high-dose IGRT and high-dose IMRT for clinically localized prostate cancer.	A significant reduction in late urinary toxicity was observed for IGRT patients compared with the non-IGRT patients. The 3-year likelihood of grade 2 and higher urinary toxicity for the IGRT and non-IGRT cohorts were 10.4% and 20.0%, respectively (P=0.02). Multivariate analysis identifying predictors for grade 2 or higher late urinary toxicity demonstrated that, in addition to the baseline International Prostate Symptom Score, IGRT was associated with significantly less late urinary toxicity compared with non-IGRT. The incidence of grade 2 and higher rectal toxicity was low for both treatment groups (1.0% and 1.6%, respectively; P=0.81). No differences in PSA RFS outcomes were observed for low- and intermediate-risk patients when treated with IGRT and non-IGRT. For high-risk patients, a significant improvement was observed at 3 years for patients treated with IGRT compared with non-IGRT.	2
101. King CR, Kapp DS. Radiotherapy after prostatectomy: is the evidence for dose escalation out there? *Int J Radiat Oncol Biol Phys*. 2008;71(2):346-350.	Review/Other-Tx	N/A	To study the effective doses of RT after prostatectomy in search for evidence of a dose-response.	The tumor control rates after SRT were consistent with the tumor control probability dose-response curve of radical RT, suggesting the presence of macroscopic-equivalent disease among salvage patients. For radical RT, the dose to achieve 50% biochemical tumor control was 65.9 Gy (95% CI, 64.8–66.8) and the Slope(50) was 2.6%/Gy (95% CI, 2.3–3.0). For SRT, the corresponding values were 66.8 Gy (95% CI, 65.1–68.4) and 3.8%/Gy (95% CI, 2.5–7.6). For a comparable tumor control probability, the dose for ART was approximately 6 Gy lower, consistent with one-tenth the burden of local disease. The present doses for adjuvant or SRT in the range of 60–70 Gy appear to be still on the steep part of the tumor control probability dose-response curve.	4

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
102. Hanlon AL, Horwitz EM, Hanks GE, Pollack A. Short-term androgen deprivation and PSA doubling time: their association and relationship to disease progression after radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2004;58(1):43-52.	Observational-Tx	284 patients	To examine the relationship between PSADT and initial management of prostate cancer with short-term androgen deprivation and the impact of these factors on disease progression after RT.	19% of patients developed distant metastasis, 20 (7%) died of prostate cancer, and 53 (19%) died of any cause. Median PSADT was 12 months. Predictors of a longer PSADT were time to bNED >12 months, Gleason score 2-6, and short-term androgen deprivation. Significant predictors of higher freedom from distant metastasis rates were longer PSADT, short-term androgen deprivation, lower PSA nadir, higher RT dose, and Gleason score 2-6. Predictors of higher cause-specific survival rates were lower nadir, longer PSADT, T1/T2ab tumors, the composite covariate, and short-term androgen deprivation. The most significant predictor of a higher OS rate was short-term androgen deprivation, followed by longer PSADT, younger age at diagnosis, the composite covariate, lower nadir, and T1/T2ab tumors.	1
103. Kaminski JM, Hanlon AL, Joon DL, Meistrich M, Hachem P, Pollack A. Effect of sequencing of androgen deprivation and radiotherapy on prostate cancer growth. *Int J Radiat Oncol Biol Phys.* 2003;57(1):24-28.	Observational-Tx	35 rats	To examine the effect of the sequencing of androgen deprivation and RT on prostate cancer growth.	Analysis of the differences in the tumor volume doubling time as measured from the end of treatment suggests that Groups 1 and 7 were statistically different from the other groups (P=0.02). The sham control group had the shortest doubling time at 5.4 days and Group 7 (14 days of androgen deprivation administered before RT) had the longest doubling time at 32.6 days. Neoadjuvant androgen deprivation resulted in prolonged suppression of tumor growth, even after testosterone replacement.	1
104. Cheung R, Kamat AM, de Crevoisier R, et al. Outcome of salvage radiotherapy for biochemical failure after radical prostatectomy with or without hormonal therapy. *Int J Radiat Oncol Biol Phys.* 2005;63(1):134-140.	Observational-Tx	101 patients	To analyze the outcome of SRT for bNED after RP. Potential benefits of hormonal therapy were assessed by comparing the outcomes for patients who received RT alone and for those who received combined RT and hormonal therapy.	Pre-RT PSA was the only significant prognostic factor for the combined-therapy group. 5-year PSA control probabilities for the favorable vs the unfavorable group were 83.7% vs 61.7% with RT alone (P=0.03). Androgen ablation seemed to be most beneficial in the unfavorable group.	2

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
105. Corn BW, Winter K, Pilepich MV. Does androgen suppression enhance the efficacy of postoperative irradiation? A secondary analysis of RTOG 85-31. Radiation Therapy Oncology Group. *Urology.* 1999;54(3):495-502.	Experimental-Tx	139 patients	To evaluate the outcome of a subset of patients from the RTOG trial 85-31 who were treated with postoperative RT (with immediate or delayed hormonal manipulation) after primary surgery. The RTOG 85-31, a randomized trial, comparing standard EBRT plus immediate androgen suppression vs EBRT alone with delayed hormonal treatment at relapse was initiated for patients with locally advanced adenocarcinoma of the prostate.	Follow-up of 5 years estimated progression-free survival rate was 65% for the men who received combination therapy and 42% for those treated by RT alone with hormones reserved for relapse. Differences in the rates of bNED relapse were observed when failure was defined as PSA of 1.0 to 3.9 ng/mL (71% vs 46%; P=0.008) and PSA >4.0 ng/mL (76% vs 55%; P=0.05), respectively.	1
106. de la Taille A, Flam TA, Thiounn N, et al. Predictive factors of radiation therapy for patients with prostate specific antigen recurrence after radical prostatectomy. *BJU Int.* 2002;90(9):887-892.	Observational-Tx	52 patients	To assess the efficacy of salvage/ART for patients with PSA recurrence after RP.	3-year bPFS was 51%. Using univariate analysis, an age <65 years, a Gleason score on the RP specimen of ≥8, stage pT3 , a detectable nadir PSA after RT and the absence of hormonal therapy were associated with a lower bPFS. However, only the Gleason score and nadir serum PSA after RT remained independent predictive factors on multivariate analysis.	2
107. Jani AB, Sokoloff M, Shalhav A, Stadler W. Androgen ablation adjuvant to postprostatectomy radiotherapy: complication-adjusted number needed to treat analysis. *Urology.* 2004;64(5):976-981.	Review/Other-Tx	N/A	To quantify the benefits and harm of androgen ablation adjuvant to RT in the postprostatectomy setting. Literature review was performed to estimate the absolute biochemical control advantage for the use of androgen ablation concomitant with postprostatectomy EBRT.	The unadjusted number needed to treat analysis showed very low values (<20), suggesting a strong benefit for the use of androgen ablation, in both ART and SRT settings. Even after adjustment for hormone-induced functional loss, a significant advantage of androgen ablation was demonstrated.	4

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
108. King CR, Presti JC, Jr., Gill H, Brooks J, Hancock SL. Radiotherapy after radical prostatectomy: does transient androgen suppression improve outcomes? *Int J Radiat Oncol Biol Phys.* 2004;59(2):341-347.	Observational-Tx	122 patients	Retrospective study. Long-term biochemical RFS and OS were compared for patients receiving either RT alone or RT combined with a short-course of total androgen suppression for failure after RP.	At 5 years, the actuarial bNED rates were 57% for the combined therapy group compared with 31% for the RT alone group. OS rates at 5 years were 100% for the combined therapy group compared with 87% for the RT alone group (P=0.0008). For pathologic Gleason sum ≤7, the 5-year bNED rates were 58% for combined therapy and 38% for RT alone (P=0.0155). For pathologic Gleason sum ≥8 the 5-year bNED rates were 65% for combined therapy and 17% for RT alone (P=0.075). The 5-year OS rates for pathologic Gleason sum ≤7 were 100% for combined therapy and 98% for RT alone group (P=0.106), and the 5-year OS for pathologic Gleason sum ≥8 was 100% for combined therapy and 54% for RT alone (P=0.04). RT combined with short-course total androgen suppression after RP appears to confer a PSA RFS advantage and possibly an OS advantage when compared with RT alone.	2
109. Tiguert R, Rigaud J, Lacombe L, Laverdiere J, Fradet Y. Neoadjuvant hormone therapy before salvage radiotherapy for an increasing post-radical prostatectomy serum prostate specific antigen level. *J Urol.* 2003;170(2 Pt 1):447-450.	Observational-Tx	81 patients	Retrospectively evaluate the benefit of neoadjuvant ADT administered before salvage EBRT in patients with bNED following RRP.	Free bNED rates at 3- and 5-years were 75% and 50%, respectively. EBRT with neoadjuvant ADT is a viable option for patients with an increasing post-prostatectomy serum PSA. The most powerful predictor of bNED was pre-RT serum PSA.	2
110. Jang JW, Hwang WT, Guzzo TJ, et al. Upfront androgen deprivation therapy with salvage radiation may improve biochemical outcomes in prostate cancer patients with post-prostatectomy rising PSA. *Int J Radiat Oncol Biol Phys.* 2012;83(5):1493-1499.	Observational-Tx	191 patients	To compare biochemical outcomes in post-prostatectomy patients who received SRT with or without concurrent ADT.	129 patients received SRT alone, and 62 patients received combined ADT and SRT. Median follow-up was 5.4 years. Patients who received combined ADT and SRT were younger, had higher pathologic Gleason scores, and higher rates of SVI, lymph node involvement, and pelvic nodal irradiation compared with patients who received SRT alone. Patients who received combined therapy had improved bPFS compared with patients who received RT alone (P=0.048). For patients with pathologic Gleason scores ≤7, combined RT and ADT resulted in significantly improved bPFS compared to RT alone (P=0.013).	2

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
111. Soto DE, Passarelli MN, Daignault S, Sandler HM. Concurrent androgen deprivation therapy during salvage prostate radiotherapy improves treatment outcomes in high-risk patients. *Int J Radiat Oncol Biol Phys.* 2012;82(3):1227-1232.	Observational-Tx	441 patients	To determine whether concurrent ADT during SRT improves prostate cancer treatment outcomes.	Low-, intermediate-, and high-risk patients made up 10%, 24%, and 66% of patients, respectively. The mean RT dose was 68 Gy. 24% of patients received concurrent ADT. Regional pelvic nodes were treated in 16% of patients. With a median follow-up of 3 years, the 3-year PFS was 4.0 years for concurrent ADT vs 3.4 years for concurrent ADT patients (P=0.22). Multivariate analysis showed that concurrent ADT (P=0.05), Gleason score (P<0.001), and pre-RT PSA (P=0.03) were independent predictors of PFS. When patients were stratified by risk group, the benefits of concurrent ADT (HR, 0.65; P=0.046) were significant only for high-risk patients.	2
112. Dorff TB, Flaig TW, Tangen CM, et al. Adjuvant androgen deprivation for high-risk prostate cancer after radical prostatectomy: SWOG S9921 study. *J Clin Oncol.* 2011;29(15):2040-2045.	Experimental-Tx	481 patients	To investigate whether the addition of mitoxantrone chemotherapy to ADT using zoladex plus bicalutamide would improve survival after prostatectomy, compared with ADT alone.	Although the final primary treatment comparison results are not ready for publication, this article reports results in the ADT-alone control arm with a median follow-up of 4.4 years. For these 481 men, the estimated 5-year biochemical failure-free survival is 92.5% (95% CI, 90 to 95), and 5-year OS is 95.9% (95% CI, 93.9 to 97.9).	1
113. Parker C, Sydes MR, Catton C, et al. Radiotherapy and androgen deprivation in combination after local surgery (RADICALS): a new Medical Research Council/National Cancer Institute of Canada phase III trial of adjuvant treatment after radical prostatectomy. *BJU Int.* 2007;99(6):1376-1379.	Review/Other-Tx	N/A	To describe the background to, and the design of an international, phase III randomized controlled trial, funded by Cancer Research-UK and sponsored by the UK Medical Research Council (MRC), of RT and ADT combined after local surgery (RADICALS).	No results stated.	4

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
114. Trans-Tasman Radiation Oncology Group (TROG). Radiotherapy - Adjuvant Versus Early Salvage. A Phase III Multi-centre Randomised Trial Comparing Adjuvant Radiotherapy (RT) With Early Salvage RT in Patients With Positive Margins or Extraprostatic Disease Following Radical Prostatectomy. In: ClinicalTrials.gov. Bethesda (MD): National Library of Medicine (US). March 13, 2014. Available from: http://clinicaltrials.gov/ct2/show/record/NCT00860652?term=nct00860652&rank=1. NLM Identifier: NCT00860652.	Review/Other-Tx	Ongoing	RP is the most common curative approach offered to men with newly diagnosed prostate cancer. Unfortunately, up to half of these patients will have factors placing them at high risk of their cancer recurring. Having RT after RP is known to improve cure rates, but what is not known is whether it should be given straight after the operation or only when there is a rising PSA after surgery indicating active cancer. Immediate RT may not benefit all men, and can cause serious side effects such as bladder and bowel problems and impotence. International lack of consensus on the optimal timing of RT has resulted in varied clinical practice. This phase 3 trial will compare the 2 approaches.	This trial is still recruiting study subjects and results are not available yet.	4
115. D'Amico AV, Chen MH, Sun L, et al. Adjuvant versus salvage radiation therapy for prostate cancer and the risk of death. *BJU Int.* 2010;106(11):1618-1622.	Observational-Tx	1,638 men	To investigate whether SRT for PSA failure can provide the same result as ART, which decreases the risk of all-cause mortality for men with positive margins (R1), or extra-capsular or seminal vesicle extension (pT3).	Despite fewer men with 2 or more adverse features (61 vs 82%; P=0.016), salvage for a rapid PSADT vs ART increased the risk of all-cause mortality [adjusted HR=3.42; 95% CI=1.27–9.20; P=0.015]. There was no difference (adjusted HR=1.39; 95% CI=0.50–3.90; P=0.53) in the risk of all-cause mortality among men who received salvage for a slow PSADT or ART. Nearly all (90%) men with a slow PSA DT had Gleason score ≤7 and the majority (59%) had at most pT3 or R1 disease.	1
116. King CR. Adjuvant versus salvage radiotherapy after prostatectomy: the apple versus the orange. *Int J Radiat Oncol Biol Phys.* 2012;82(3):1045-1046.	Review/Other-Tx	N/A	A critical review to compare adjuvant vs SRT after prostatectomy.	No results stated.	4
117. King CR. Adjuvant versus salvage radiotherapy for high-risk prostate cancer patients. *Semin Radiat Oncol.* 2013;23(3):215-221.	Review/Other-Tx	N/A	To summarize the evidence of (a) whether ART is superior to early SRT, (b) what the optimal timing for SRT is, (c) whether there is benefit of ADT with postop RT, and (d) what the optimal treatment specifics are (dose and fields).	No results stated.	4

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
118. Bottke D, Bartkowiak D, Schrader M, Wiegel T. Radiotherapy after radical prostatectomy: immediate or early delayed? *Strahlenther Onkol.* 2012;188(12):1096-1101.	Review/Other-Tx	N/A	To review published data on ART and SRT to allow a comparison of the 2 treatment approaches.	3 randomized phase III trials demonstrated an almost 20% absolute benefit for bPFS after ART (60-64 Gy) compared to a "wait and see" policy. The greatest benefit was achieved in patients with positive margins and pT3 tumors. SRT can be offered to patients with elevated PSA after RP. In 30%–70% of SRT patients, PSA will decrease to an undetectable level, thus giving a second curative chance. The rate of side effects for both treatments is comparably low. The role of irradiation of pelvic lymph nodes and the additional use of hormone therapy and radiation dose are discussed.	4
119. Forman JD, Velasco J. Therapeutic radiation in patients with a rising post-prostatectomy PSA level. *Oncology (Williston Park).* 1998;12(1):33-39; discussion 39, 43-34, 47.	Review/Other-Tx	N/A	Review management of patients with an elevated post-prostatectomy PSA level.	A suitable therapeutic option for high-risk patients following prostatectomy would be to wait for an elevated PSA and then proceed with a course of potentially curative RT.	4
120. Terai A, Matsui Y, Yoshimura K, Arai Y, Dodo Y. Salvage radiotherapy for biochemical recurrence after radical prostatectomy. *BJU Int.* 2005;96(7):1009-1013.	Observational-Tx	37 patients	To evaluate the clinical outcome of SRT for biochemical recurrence after RP.	11 patients (30%) had disease progression after RT and the 3- and 5-year progression-free probability was 74% and 54%, respectively. SRT for bNED after RP at a low PSA level, using ultrasensitive immunoassays for monitoring, is a reasonably effective treatment. A relatively low radiation dose (60 Gy) seems to be effective.	2
121. Pazona JF, Han M, Hawkins SA, Roehl KA, Catalona WJ. Salvage radiation therapy for prostate specific antigen progression following radical prostatectomy: 10-year outcome estimates. *J Urol.* 2005;174(4 Pt 1):1282-1286.	Observational-Tx	3478 patients	Retrospective study to evaluate men treated with SRT for increasing serum PSA following RRP.	5- and 10-year progression-free (PSA <0.3 ng/mL) survival probabilities following SRT were 40%, respectively. Actuarial 5- and 10-year bPFS estimates following SRT in responders only were 55% and 35%, respectively. An undetectable PSA level following SRT is more frequently achieved in men with lower pre-radiation serum PSA and those without seminal vesicle or lymph node involvement.	2

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
122. Choo R, Morton G, Danjoux C, Hong E, Szumacher E, DeBoer G. Limited efficacy of salvage radiotherapy for biopsy confirmed or clinically palpable local recurrence of prostate carcinoma after surgery. *Radiother Oncol.* 2005;74(2):163-167.	Observational-Tx	44 patients	Retrospective analysis to assess the efficacy of SRT for biopsy confirmed or clinically palpable local recurrence of prostate adenocarcinoma after RP.	Median follow-ups from RP and SRT were 8.7 and 5.5 years, respectively. PSA relapse-free and survival rate at 5 years were 11% and 87%, respectively. On Cox regression analysis, significant predictors for relapse were PSA level prior to SRT, and Gleason score. The efficacy of SRT alone for local recurrence was limited.	2
123. Coen JJ, Zietman AL, Thakral H, Shipley WU. Radical radiation for localized prostate cancer: local persistence of disease results in a late wave of metastases. *J Clin Oncol.* 2002;20(15):3199-3205.	Observational-Tx	1,469 patients	Retrospective review to assess whether failure to maintain local failure of prostate cancer after RT results in a higher incidence of distant metastasis.	10-year local control rate was 79%. Gleason score ≥7, PSA >15, and T3 to T4 tumors predicted a higher incidence of local failure (palpable recurrence or positive re-biopsy). 10-year distant MFS was 74%. Gleason score ≥7, PSA >15, and T3 to T4 tumors predicted a higher incidence of distant failure. Local failure was the strongest predictor for distant metastasis in a multivariate model.10-year distant MFS for local failure and local failure patients was 77% and 61%, respectively. Median time to distant failure was prolonged in patients with local failure compared with patients with locally controlled disease (54 vs 34 months). Hazard rate analysis of the time to distant metastasis revealed that patients who maintain local failure have a lower rate of distant metastasis, which remains constant over time. Patients who ultimately develop local failure have a higher initial rate of distant metastasis, which increases with time.	2
124. Zagars GK, von Eschenbach AC, Ayala AG, Schultheiss TE, Sherman NE. The influence of local control on metastatic dissemination of prostate cancer treated by external beam megavoltage radiation therapy. *Cancer.* 1991;68(11):2370-2377.	Observational-Tx	601 patients	To examine the influence of local control on metastatic dissemination in patients with clinically staged A2 to C prostate cancer treated by high-energy EBRT who did not undergo hormonal manipulation before disease progression.	93 patients had locally recurrent disease. The actuarial incidence of metastases in these patients (70% at 13 years) was significantly higher than in the 508 patients without local failure (40% at 13 years, P<0.001).Local control of prostate cancer does decrease the likelihood of metastatic disease.	2

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
125. Kuban DA, el-Mahdi AM, Schellhammer PF. Effect of local tumor control on distant metastasis and survival in prostatic adenocarcinoma. *Urology.* 1987;30(5):420-426.	Observational-Tx	286 patients	To examine the effect of local tumor control on distant metastasis and survival in prostatic adenocarcinoma.	While tumor histology appeared to predict prognosis, the poorly differentiated tumors showing the highest incidence of distant metastasis and the lowest survival, local tumor control was an important factor within the poorly differentiated group. Of those with local recurrence, distant metastases developed in 68% compared with 37% of those with no local disease (P=0.025). Survival was similarly affected with 86% of those with locally controlled tumor who were alive at 5 years vs a 56% actuarial survival in those with locally recurrent disease (P<0.05).	2
126. Fuks Z, Leibel SA, Wallner KE, et al. The effect of local control on metastatic dissemination in carcinoma of the prostate: long-term results in patients treated with 125I implantation. *Int J Radiat Oncol Biol Phys.* 1991;21(3):537-547.	Observational-Tx	679 patients	To evaluate the effect of the locally recurring tumor on the incidence of metastatic disease in early stage carcinoma of the prostate.	Distant MFS for patients at risk at 15 years after initial therapy was 37%. 15-year distant MFS in 351 patients with local control was 77% compared to 24% in 328 patients who developed local relapses (P<0.00001). Median local RFS in the 268 patients with local recurrences who did not receive hormonal therapy before distant metastases were detected was 51 months, compared to a median of 71 months for distant MFS in the same patients (P<0.001), Data suggest that the existence and re-growth of local residual disease in localized prostatic carcinoma promotes an enhanced spread of metastatic disease, and that early and complete eradication of the primary tumor is required if a long term cure is to be achieved.	2
127. Pollack A, Horwitz EM, Movsas B. Treatment of prostate cancer with regional lymph node (N1) metastasis. *Semin Radiat Oncol.* 2003;13(2):121-129.	Review/Other-Tx	N/A	To determine the role of EBRT or RP +/- androgen deprivation in patients with lymph node metastasis at the time of presentation of prostate cancer.	Patients with a 10-year life expectancy should be treated aggressively with long-term androgen deprivation combined with either EBRT or RP.	4

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
128. Cheng CW, Bergstralh EJ, Zincke H. Stage D1 prostate cancer. A nonrandomized comparison of conservative treatment options versus radical prostatectomy. *Cancer.* 1993;71(3 Suppl):996-1004.	Observational-Tx	631 patients	To evaluate the impact of combination therapy, local (surgery or radiation) and systemic (hormonal), compared with that of monotherapy on disease outcome.	Cause-specific survival rates for prostatectomy-orchiectomy-treated patients at 5 and 10 years were 91% and 78%, respectively; they were 84% and 54% for irradiation-orchiectomy-treated patients and 66% and 39% for orchiectomy alone-treated patients, respectively. Controlling for the number of nodes, the difference between prostatectomy-orchiectomy-treated and irradiation-orchiectomy-treated patients was not significant; the former group had a significantly longer survival than the orchiectomy alone-treated patients (P=0.037). The 5-year and 10-year cause-specific survival rates for prostatectomy alone-treated patients were 91% and 75%, respectively, and 84% and 45% for RT alone-treated patients. Thus, cause-specific survival rates in prostatectomy alone-treated patients were significantly better (P=0.0085).	2
129. Galalae RM, Kovacs G, Schultze J, et al. Long-term outcome after elective irradiation of the pelvic lymphatics and local dose escalation using high-dose-rate brachytherapy for locally advanced prostate cancer. *Int J Radiat Oncol Biol Phys.* 2002;52(1):81-90.	Observational-Tx	144 patients	To report the 8-year outcome of local dose escalation using high-dose-rate conformal brachytherapy combined with elective RT of the pelvic lymphatics for localized prostate cancer. 144 consecutively treated men (1986-1992) were recorded prospectively.	OS rate was 71.5%; DFS rate was 82.6%. The bNED survival rate was 72.9%. Freedom from local recurrence for T3 stage was 91.3%, whereas for G3 lesions it was 88.23%. Freedom from distant recurrence for T3 stage was 82.6% and for G3 lesions 70.59%. The 8-year results confirm the feasibility and effectiveness of combined elective RT of the pelvic lymphatics and local dose escalation using high-dose-rate brachytherapy for cure of localized and especially high-risk prostate cancer.	1

Postradical Prostatectomy Irradiation in Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
130. Rusthoven CG, Carlson JA, Waxweiler TV, et al. The impact of definitive local therapy for lymph node-positive prostate cancer: a population-based study. *Int J Radiat Oncol Biol Phys*. 2014;88(5):1064-1073.	Observational-Tx	796 cN+ and 2,991 pN+ patients	To evaluate the survival outcomes for patients with lymph node-positive, nonmetastatic prostate cancer undergoing definitive local therapy (RP, EBRT, or both) vs no local therapy in the U.S. population in the modern PSA era.	A total of 796 cN+ and 2,991 pN+ patients were evaluable. Among cN+ patients, 43% underwent EBRT and 57% had no local therapy. Outcomes for cN+ patients favored EBRT, with 10-year OS rates of 45% vs 29% (P<.001) and prostate cancer-specific survival rates of 67% vs 53% (P<.001). Among pN+ patients, 78% underwent local therapy (RP 57%, EBRT 10%, or both 11%) and 22% had no local therapy. Outcomes for pN+ also favored local therapy, with 10-year OS rates of 65% vs 42% (P<.001) and prostate cancer-specific survival rates of 78% vs 56% (P<.001). On multivariate analysis, local therapy in both the cN+ and pN+ cohorts remained independently associated with improved OS and prostate cancer-specific survival (all P<.001). Local therapy was associated with favorable HRs across subgroups, including patients aged ≥70 years and those with multiple positive lymph nodes. Among pN+ patients, no significant differences in survival were observed between RP vs EBRT and RP with or without adjuvant EBRT.	2

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

3D-CRT = 3D-confromal radiation therapy
ADT = Androgen-deprivation therapy
ART = Adjuvant radiation therapy
bDFS = biochemical disease-free survival
bNED = Freedom from biochemical failure
bPFS = biochemical progression-free survival
bRFS = biochemical relapse-free survival
CI = Confidence interval
CT = Computed tomography
DFS = Disease-free survival
DRE = Digital rectal examination
EBRT = External-beam radiation therapy
GI = Gastrointestinal
GU = Genitourinary
HR = Hazard ratio
IGRT = Image-guided radiotherapy
IMRT = Intensity-modulated radiotherapy
MFS = Metastasis-free survival
OS = Overall survival
PSA = Prostate-specific antigen
PSADT = Prostate-specific antigen doubling time
PSAV = Prostate-specific antigen velocity
RFS = Relapse-free survival
RR = Relative risk
RRP = Radical retropubic prostatectomy
RP = Radical prostatectomy
RT = Radiation therapy
SRT = Salvage radiotherapy
SVI = Seminal vesicle invasion
TRUS = Transrectal ultrasound