External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin.* 2015;65(1):5-29.	Review/Other-Tx	N/A	To provide the expected numbers of new cancer cases and deaths in 2015 nationally and for each state, as well as a comprehensive overview of cancer incidence, mortality, and survival rates and trends using the most current population-based data. The article also estimates the total number of deaths averted nationally during the past 2 decades and by state in 2011 as a result of the continual decline in cancer death rates and present actual number of deaths reported in 2011 by age for the 10 leading causes of death and for the 5 leading causes of cancer death.	Cancer death rates have been continuously declining for the past 2 decades. Overall, the risk of dying from cancer decreased by 22% between 1991 and 2011. Regionally, progress has been most rapid for residents of the Northeast, among whom death rates have declined by 25% to 30%, and slowest in the South, where rates declined by about 15%. Further reductions in cancer death rates can be accelerated by applying existing cancer control knowledge across all segments of the population, with an emphasis on those in the lowest socioeconomic bracket and other disadvantaged populations.	4
2. Cooperberg MR, Broering JM, Carroll PR. Time trends and local variation in primary treatment of localized prostate cancer. *J Clin Oncol.* 2010;28(7):1117-1123.	Review/Other-Tx	11,892 men at 36 sites	To determine trends over time in treatment of cancers at varying levels of progression risk, and to characterize and quantify variation in primary treatment at the level of the clinical practice site.	Among 11,892 men analyzed, 6.8% elected surveillance, 49.9% prostatectomy, 11.6% EBRT, 13.3% brachytherapy, 4.0% cryoablation, and 14.4% androgen deprivation monotherapy. Prostate cancer risk drives treatment selection, but the data suggest both overtreatment of low-risk disease and undertreatment of high-risk disease. The former trend appears to be improving over time, while the latter is worsening. Treatment varies with age, comorbidity, and socioeconomic status. However, treatment patterns vary markedly across clinical sites, and this variation is not explained by case-mix variability or known patient factors. Practice site explains a proportion of this variation ranging from 13% for androgen deprivation monotherapy to 74% for cryoablation.	4

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3. Aizer AA, Yu JB, Colberg JW, McKeon AM, Decker RH, Peschel RE. Radical prostatectomy vs. intensity-modulated radiation therapy in the management of localized prostate adenocarcinoma. *Radiother Oncol.* 2009;93(2):185-191.	Observational-Tx	556 patients RP (n=204) or IMRT (n=352)	To determine whether RP or IMRT to ≥72 Gy, plus hormonal therapy if indicated, results in improved BDFS in localized prostate adenocarcinoma.	IMRT patients had more advanced disease at baseline (P<.001). There was no difference in 5-year BDFS rates between RP and IMRT in the favorable (92.8% vs 85.3%, P=.20) or intermediate prognosis (86.7% vs 82.2%, P=.46) subsets. A difference favoring IMRT plus hormonal therapy was seen in the poor prognosis (38.4% vs 62.2%, P<.001) subset. Within the entire cohort, after adjustment for confounding variables, GS (P<.001) and clinical stage (P<.001) predicted BDFS, but treatment modality (P=.06) did not. Within the poor prognosis subset, treatment modality (P=.006) predicted BDFS.	2
4. Klein EA, Ciezki J, Kupelian PA, Mahadevan A. Outcomes for intermediate risk prostate cancer: are there advantages for surgery, external radiation, or brachytherapy? *Urol Oncol.* 2009;27(1):67-71.	Review/Other-Tx	N/A	To review recent results from an institutional database and prospective quality of life study comparing cancer-related and quality of life outcomes among different treatment modalities for intermediate risk prostate cancer.	The results suggest similar short-term survival but domain-specific effects on quality of life after treatment with RP, brachytherapy, or EBRT.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
5. Kupelian PA, Potters L, Khuntia D, et al. Radical prostatectomy, external beam radiotherapy <72 Gy, external beam radiotherapy > or =72 Gy, permanent seed implantation, or combined seeds/external beam radiotherapy for stage T1-T2 prostate cancer. *Int J Radiat Oncol Biol Phys.* 2004;58(1):25-33.	Observational-Tx	2,991 patients	To review the bRFS rates after treatment with permanent seed implantation, EBRT <72 Gy, EBRT ≥72 Gy, combined seeds and EBRT, or RP for clinical Stage T1-T2 localized prostate cancer treated between 1990 and 1998.	The 5-year bRFS rate for RP, EBRT <72 Gy, EBRT ≥72 Gy, permanent seed implantation, and combined seeds and EBRT was 81%, 51%, 81%, 83%, and 77%, respectively (P<0.001). The 7-year bRFS rate for RP, EBRT <72 Gy, EBRT ≥72 Gy, permanent seed implantation, and combined seeds and EBRT was 76%, 48%, 81%, 75%, and 77%, respectively. Multivariate analysis, including all cases, showed iPSA (P<0.001), biopsy GS (P<0.001), year of therapy (P<0.001), and treatment modality (P<0.001) to be independent predictors of relapse. Because EBRT <72 Gy cases had distinctly worse outcomes, the analysis was repeated after excluding these cases to discern any differences among the other modalities. The multivariate analysis excluding the EBRT <72 Gy cases revealed iPSA (P<0.001), biopsy GS (P<0.001), and year of therapy (P=0.001) to be the only independent predictors of relapse. Treatment modality (P=0.95), clinical T stage (P=0.09), and androgen deprivation (P=0.56) were not independent predictors for failure.	2
6. Mohler JL, Kantoff PW, Armstrong AJ, et al. Prostate cancer, version 2.2014. *Journal of the National Comprehensive Cancer Network.* 2014;12(5):686-718.	Review/Other-Tx	N/A	To provide multidisciplinary recommendations on the clinical management of patients with prostate cancer based on clinical evidence and expert consensus.	No results stated in abstract.	4
7. Gustafson GS, Nguyen PL, Assimos DG, et al. ACR Appropriateness Criteria(R) Postradical Prostatectomy Irradiation in Prostate Cancer. *Oncology (Williston Park).* 2014;28(12).	Review/Other-Tx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate treatment decisions for postradical prostatectomy irradiation in prostate cancer.	N/A	4
8. Nguyen PL, Aizer A, Assimos DG, et al. ACR Appropriateness Criteria(R) Definitive External-Beam Irradiation in Stage T1 and T2 Prostate Cancer. *Am J Clin Oncol.* 2014;37(3):278-288.	Review/Other-Tx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate treatment decisions for definitive EBRT in Stage T1 and T2 prostate cancer.	N/A	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. D'Amico AV, Whittington R, Malkowicz SB, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA*. 1998;280(11):969-974.	Observational-Tx	1,872 patients/ 888 treated with RP/ 218 treated with implant with or without neoadjuvant ADT/ 766 treated with RT	To estimate control of PSA after RP, EBRT, or implant with or without neoadjuvant ADT in patients with clinically localized prostate cancer.	The relative risk of PSA failure in low-risk patients (stage T1c, T2a and PSA level ≤10 ng/mL and GS ≤6) treated using RT, implant plus ADT, or implant therapy was 1.1 compared with those patients treated with RP. The addition of ADT to implant therapy did not improve PSA outcome in high-risk patients but resulted in a PSA outcome that was not statistically different compared with the results obtained using RP or RT in intermediate-risk patients. Intermediate- and high-risk patients treated with EBRT or RP fared better than brachytherapy.	2
10. Zaorsky NG, Ohri N, Showalter TN, Dicker AP, Den RB. Systematic review of hypofractionated radiation therapy for prostate cancer. *Cancer Treat Rev.* 2013;39(7):728-736.	Review/Other-Tx	N/A	To review the impetus behind moderate hypofractionation and the current clinical evidence supporting moderate hypofractionated RT for prostate cancer.	EBRT is an established treatment modality for almost all prostate cancer patients. Determining the optimal fractionation scheme has been one of the goals of radiation oncologists. Hypofractionated RT is hypothesized to improve tumor control, patient quality of life, and cost. Randomized controlled trials comparing hypofractionated RT and CRT have been inconsistent in their results: the methods of earlier studies are not comparable to modern techniques, and the modern studies have rejected their hypotheses of superiority of hypofractionated RT. While it is difficult to infer the findings of 1 study to any other, as they use different doses, treatment techniques, target margins, and outcome measures, noninferiority studies with more robust databases of patient outcomes will help to determine which patients would benefit from hypofractionated RT.	4

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11. Zaorsky NG, Studenski MT, Dicker AP, Gomella L, Den RB. Stereotactic body radiation therapy for prostate cancer: is the technology ready to be the standard of care? *Cancer Treat Rev.* 2013;39(3):212-218.	Review/Other-Tx	N/A	To review the impetus behind SBRT and the current clinical evidence supporting its use for prostate cancer, thus providing oncologists and primary care physicians with an understanding of the continually evolving field of prostate RT.	EBRT is an established treatment modality for almost all prostate cancer patients. Determining the optimal fractionation scheme has been one of the goals of radiation oncologists. SBRT is hypothesized to improve tumor control, decrease toxicity, patient quality of life, and reduce resource consumption. Phase I/II studies of SBRT have had some encouraging results in terms of biochemical control and treatment toxicity. However, a number of limitations are still present among all of the trials that preclude recommending SBRT monotherapy for prostate cancer outside the setting of a clinical trial. SBRT should be considered experimental at present.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Perez CA, Michalski JM, Mansur D, Lockett MA. Three-dimensional conformal therapy versus standard radiation therapy in localized carcinoma of prostate: an update. *Clin Prostate Cancer*. 2002;1(2):97-104.	Observational-Tx	312 patients treated with 3D-CRT and 135 with standard RT alone	To update technical principles and results of 3D-CRT in localized carcinoma of the prostate.	Dose-volume histograms showed a two-thirds reduction with 3D-CRT in normal bladder or rectum receiving ≥70 Gy with 3D-CRT. Higher 5-year chemical DFS was observed with 3D-CRT (75%; for T1b-c and 79%; for T2 tumors) compared with SRT (61% and 65%, P=0.01 and P=0.12, respectively). There was no statistically significant difference in chemical DFS in patients with GS of ≤4 (P=0.85), but, with GS of 5-7, the 5-year survival rates were 83% with 3D-CRT and 59% with standard RT (P≤0.01). In 245 patients with pretreatment PSA of ≤10 ng/mL treated with 3D-CRT, the chemical disease-free rate was 80% vs 72% in 98 patients treated with standard RT (P=0.21). In patients with PSA of 10.1–20 ng/mL, the chemical DFS rate for 50 patients treated with 3D-CRT was 71% compared with 43% for 20 patients treated with standard RT (P=0.02). The corresponding values were 59% and 16%, respectively, for patients with PSA levels >20 ng/mL (P=0.09). On multivariate analysis, the most important prognostic factors for chemical failure were pretreatment PSA (P=0.004), nadir PSA (P=0.001), and 3D-CRT technique (P=0.012). Moderate dysuria was reported by 2%–5% of patients treated with 3D-CRT in contrast to 6%–9% of patients treated with standard RT. The incidence of moderate loose stools or diarrhea, usually after the fourth week of treatment, was 3%-5% in the 3D-CRT patients and 8%-19% in the standard RT group. Late intestinal grade 2 morbidity (proctitis or rectal bleeding) was 1% in the 3D-CRT group in contrast to 7% in standard RT patients.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
13. Kuban DA, Levy LB, Cheung MR, et al. Long-term failure patterns and survival in a randomized dose-escalation trial for prostate cancer. Who dies of disease? *Int J Radiat Oncol Biol Phys.* 2011;79(5):1310-1317.	Experimental-Tx	301 patients	To report long-term failure patterns and survival in a randomized RT dose escalation trial for prostate cancer.	Patients with pretreatment PSA >10 ng/mL or high-risk disease had higher biochemical and clinical failures rates when treated to 70 Gy. These patients also had a significantly higher risk of dying of prostate cancer. Patients <70 years old at treatment died of prostate cancer nearly 3 times more frequently than of other causes when they were radiated to 70 Gy, whereas those treated to 78 Gy died of other causes more frequently. Patients age 70 or older treated to 70 Gy died of prostate cancer as often as other causes, and those receiving 78 Gy never died of prostate cancer within 10 years of follow-up. In regression analysis, factors predicting for death from prostate cancer were pretreatment PSA >10.5 ng/mL, GS 9 and 10, recurrence within 2.6 years of radiation, and doubling time of <3.6 months at the time of recurrence.	1
14. Kuban DA, Tucker SL, Dong L, et al. Long-term results of the M. D. Anderson randomized dose-escalation trial for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2008;70(1):67-74.	Experimental-Tx	301 patients	To report the long-term results of a randomized RT dose escalation trial for prostate cancer.	For all patients, FFBF or clinical failure was superior for the 78 Gy arm, 78%, as compared with 59% for the 70 Gy arm (P=0.004, and an even greater benefit was seen in patients with initial PSA >10 ng/ml (78% vs 39%, P=0.001). Clinical failure rate was significantly reduced in the 78 Gy arm as well (7% vs 15%, P=0.014).	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Michalski J, Winter K, Roach M, et al. Clinical outcome of patients treated with 3D conformal radiation therapy (3D-CRT) for prostate cancer on RTOG 9406. *Int J Radiat Oncol Biol Phys.* 2012;83(3):e363-370.	Experimental-Tx	1,051 patients	To report the 5- and 10-year biochemical control and clinical outcomes in patients treated in this trial at all 5 dose levels.	34 institutions enrolled 1,084 patients and 1,051 patients are analyzable. Median follow-up for levels I, II, III, IV, and V was 11.7, 10.4, 11.8, 10.4, and 9.2 years, respectively. 36% of patients received nonhormonal therapy. The 5-year OS was 90%, 87%, 88%, 89%, and 88% for dose levels I-V, respectively. The 5-year clinical DFS (excluding protocol PSA definition) for levels I-V is 84%, 78%, 81%, 82%, and 82%, respectively. By ASTRO definition, the 5-year DFSs were 57%, 59%, 52%, 64% and 75% (low risk); 46%, 52%, 54%, 56%, and 63% (intermediate risk); and 50%, 34%, 46%, 34%, and 61% (high risk) for levels I-V, respectively. By the Phoenix definition, the 5-year DFSs were 68%, 73%, 67%, 84%, and 80% (low risk); 70%, 62%, 70%, 74%, and 69% (intermediate risk); and 42%, 62%, 68%, 54%, and 67% (high risk) for levels I-V, respectively.	1
16. Michalski JM, Bae K, Roach M, et al. Long-term toxicity following 3D conformal radiation therapy for prostate cancer from the RTOG 9406 phase I/II dose escalation study. *Int J Radiat Oncol Biol Phys.* 2010;76(1):14-22.	Experimental-Tx	1,084 total patients	To update the incidence of late toxicity of RTOG 9406, a 3D-CRT dose escalation trial for prostate cancer.	The incidence rates of RTOG grade 3 or less GI or GU toxicity were 3%, 4%, 6%, 7%, and 9% in group 1 and 6%, 2%, 6%, 9%, and 12% in group 2 at dose levels of I, II, III, IV, and V, respectively. In group 1, level V patients had a higher probability of grade 2 late or greater GI or GU toxicity than those in levels I, II, and III (HR = 1.93, P=0.0101; HR = 2.29, P=0.0007; HR = 2.52, P=0.0002, respectively). In group 2, dose level V patients had a higher probability of grade 2 or greater late GI or GU toxicity than those in dose levels II, III, and IV (HR = 2.61, P=0.0002; HR = 2.22, P=0.0051; HR = 1.60, P=0.0276, respectively). Tolerance to high-dose 3D-CRT remains excellent. There is significantly more grade 2 or greater toxicity with a dose of 78 Gy at 2 Gy/fraction than with 68.4 Gy to 79.2 Gy at 1.8 Gy/fraction and with 74 Gy at 2 Gy/fraction.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
17. Zelefsky MJ, Fuks Z, Happersett L, et al. Clinical experience with intensity modulated radiation therapy (IMRT) in prostate cancer. *Radiother Oncol.* 2000;55(3):241-249.	Experimental-Tx	232 patients	To compare acute and late toxicities of high-dose radiation for prostate cancer delivered by either conventional 3D-CRT or IMRT.	Compared with conventional 3D-CRT, IMRT improved the coverage of the CTV by the prescription dose and reduced the volumes of the rectal and bladder walls carried to high dose levels ($P<0.01$), indicating improved conformality with IMRT. Acute and late urinary toxicities were not significantly different for the two methods. However, the combined rates of acute grade 1 and 2 rectal toxicities and the risk of late grade 2 rectal bleeding were significantly lower in the IMRT patients. The 2-year actuarial risk of grade 2 bleeding was 2% for IMRT and 10% for conventional 3D-CRT ($P<0.001$).	2
18. Pollack A, Walker G, Horwitz EM, et al. Randomized trial of hypofractionated external-beam radiotherapy for prostate cancer. *J Clin Oncol.* 2013;31(31):3860-3868.	Experimental-Tx	303 patients	To determine if escalated radiation dose using hypofractionation significantly reduces biochemical and/or clinical disease failure in men treated primarily for prostate cancer.	There were 303 assessable patients with a median follow-up of 68.4 months. No significant differences were seen between the treatment arms in terms of the distribution of patients by clinicopathologic or treatment-related (ADT use and length) factors. The 5-year rates of biochemical and/or clinical disease failure were 21.4% (95% CI, 14.8% to 28.7%) for conventional fractionation IMRT and 23.3% (95% CI, 16.4% to 31.0%) for hypofractionated IMRT ($P=.745$). There were no statistically significant differences in late toxicity between the arms; however, in subgroup analysis, patients with compromised urinary function before enrollment had significantly worse urinary function after hypofractionated IMRT.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
19. Sheets NC, Goldin GH, Meyer AM, et al. Intensity-modulated radiation therapy, proton therapy, or conformal radiation therapy and morbidity and disease control in localized prostate cancer. *JAMA*. 2012;307(15):1611-1620.	Observational-Tx	12,976 patients	To determine the comparative morbidity and disease control of IMRT, proton therapy, and CRT for primary prostate cancer treatment.	Use of IMRT vs CRT increased from 0.15% in 2000 to 95.9% in 2008. In propensity score-adjusted analyses (N = 12,976), men who received IMRT vs CRT were less likely to receive a diagnosis of GI morbidities (absolute risk, 13.4 vs 14.7 per 100 person-years; relative risk, 0.91; 95% CI, 0.86–0.96) and hip fractures (absolute risk, 0.8 vs 1.0 per 100 person-years; RR, 0.78; 95% CI, 0.65–0.93) but more likely to receive a diagnosis of erectile dysfunction (absolute risk, 5.9 vs 5.3 per 100 person-years; RR, 1.12; 95% CI, 1.03–1.20). IMRT patients were less likely to receive additional cancer therapy (absolute risk, 2.5 vs 3.1 per 100 person-years; RR, 0.81; 95% CI, 0.73–0.89). In a propensity score-matched comparison between IMRT and proton therapy (n = 1368), IMRT patients had a lower rate of GI morbidity (absolute risk, 12.2 vs 17.8 per 100 person-years; RR, 0.66; 95% CI, 0.55-0.79). There were no significant differences in rates of other morbidities or additional therapies between IMRT and proton therapy.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. 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 relapse-free survival 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
21. Katz AJ, Santoro M, Ashley R, Diblasio F, Witten M. Stereotactic body radiotherapy as boost for organ-confined prostate cancer. *Technol Cancer Res Treat.* 2010;9(6):575-582.	Observational-Tx	73 patients	To present preliminary biochemical control and urinary, rectal and sexual toxicities for 73 patients treated with SBRT as a boost to EBRT.	The median follow-up was 33 months (range, 22–43 months). Less than 7% Grade II and no higher grade acute toxicities occurred. To date, 1 Grade III and no Grade IV late toxicities occurred. For the 97% of patients with 24 months minimum follow-up, 71.8% achieved a PSA nadir threshold of 0.5 ng/mL. 3 intermediate-risk and 7 high-risk biochemical failures occurred; one high-risk patient died of his cancer. 3-year actuarial biochemical control rates were 89.5% and 77.7% for intermediate- and high-risk patients, respectively.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
22. Katz AJ, Santoro M, DiBlasio F, Ashley R. Stereotactic Body Radiation Therapy for Low, Intermediate, and High-risk Prostate Cancer: Disease Control and Quality of Life. *Int J Radiat Oncol Biol Phys.* 2011;81(2):S100-S100.	Experimental-Tx	304 patients	To expand upon prior studies to further evaluate SBRT efficacy and quality of life for a large patient population that includes low-, intermediate-, and high-risk prostate cancer patients.	At a median follow-up of 40 months (range, 9–58 months), 10 patients died of other causes and 9 were lost to follow-up. The median PSAs at 36 and 48 months were 0.20 ng/mL and 0.11ng/mL. Biochemical failures occurred for 4 low-risk patients (2 had negative biopsies and 2 failed distantly), 5 intermediate-risk patients (none locally), and 3 high-risk patients (1 proven local failure). The 4-year actuarial FFBF is 98.5%, 93.0%, and 75%, for the low-, intermediate- and high-risk groups (P<0.001). Late RTOG toxicity was mild with 4.2% Grade 2 rectal, 7.8% Grade 2 urinary, and 1.4% Grade 3 urinary. Mean EPIC urinary and bowel quality of life declined at 1 month post-treatment and returned to baseline by 2 years where it remains. Mean EPIC sexual quality of life declined by 23% at 1 month where it remains. 80% of the patients potent at baseline remain potent.	1
23. Katz AJ, Kang J. Quality of Life and Toxicity after SBRT for Organ-Confined Prostate Cancer, a 7-Year Study. *Front Oncol.* 2014;4:301.	Observational-Tx	515 patients	To present a 7-year update on treatment toxicity and quality of life from 515 patients treated with prostate SBRT.	Median follow-up was 72 months. The actuarial 7-year FFBF was 95.8%, 89.3%, and 68.5% for low-, intermediate-, and high-risk groups, respectively (P<0.001). No patients experienced acute Grade 3 or 4 acute complications. Fewer than 5% of patients had any acute Grade 2 urinary or rectal toxicity. Late toxicity was low, with Grade 2 rectal and urinary toxicity of 4 and 9.1%, respectively, and Grade 3 urinary toxicity of 1.7%. Mean EPIC urinary and bowel quality of life declined at 1 month post-treatment, returned to baseline by 2 years and remained stable thereafter. EPIC sexual quality of life declined by 23% at 6-12 months and remained stable afterwards. Of patients potent at baseline evaluation, 67% remained potent at last follow-up.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
24. Zietman AL, Bae K, Slater JD, et al. Randomized trial comparing conventional-dose with high-dose conformal radiation therapy in early-stage adenocarcinoma of the prostate: long-term results from proton radiation oncology group/american college of radiology 95-09. *J Clin Oncol.* 2010;28(7):1106-1111.	Experimental-Tx	393 men	Randomized study to determine whether increasing radiation dose delivered to men with early-stage prostate cancer improves clinical outcomes.	Median follow-up was 8.9 years. Men receiving high-dose RT were significantly less likely to have local failure, with a HR of 0.57. The 10-year ASTRO biochemical free rates were 32.4% for conventional-dose and 16.7% for high-dose RT ($P<.0001$). Trial shows superior long-term cancer control for men with localized prostate cancer receiving high-dose vs conventional-dose radiation. This was achieved without an increase in grade ≥3 late urinary or rectal morbidity.	1
25. Beckendorf V, Guerif S, Le Prise E, et al. 70 Gy versus 80 Gy in localized prostate cancer: 5-year results of GETUG 06 randomized trial. *Int J Radiat Oncol Biol Phys.* 2011;80(4):1056-1063.	Experimental-Tx	306 patients	To perform a randomized trial comparing 70 and 80 Gy RT for prostate cancer.	The median follow-up was 61 months. According to the 1997-ASTRO definition, the 5-year biochemical relapse rate was 39% and 28% in the 70- and 80-Gy arms, respectively ($P=.036$). Using the Phoenix definition, the 5-year biochemical relapse rate was 32% and 23.5%, respectively ($P=.09$). The subgroup analysis showed a better biochemical outcome for the higher dose group with an initial PSA level >15 ng/mL. At the last follow-up date, 26 patients had died, 10 of their disease and none of toxicity, with no differences between the 2 arms. According to the RTOG scale, the Grade 2 or greater rectal toxicity rate was 14% and 19.5% for the 70- and 80-Gy arms ($P=.22$), respectively. The Grade 2 or greater urinary toxicity was 10% at 70 Gy and 17.5% at 80 Gy ($P=.046$). Similar results were observed using the LENT-SOMA scale. Bladder toxicity was more frequent at 80 Gy than at 70 Gy ($P=.039$). The quality-of-life questionnaire results before and 5 years after treatment were available for 103 patients with no differences found between the 70- and 80-Gy arms.	1

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26. Al-Mamgani A, van Putten WL, Heemsbergen WD, et al. Update of Dutch multicenter dose-escalation trial of radiotherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys.* 2008;72(4):980-988.	Experimental-Tx	669 patients	To update the analysis of the Dutch dose-escalation trial of RT for prostate cancer.	After a median follow-up of 70 months, the freedom from failure using the ASTRO definition was significantly better in the 78-Gy arm than in the 68-Gy arm (7-year freedom from failure rate, 54% vs 47%, respectively; *P*=0.04). The freedom from failure using the Phoenix definition was also significantly better in the 78-Gy arm than in the 68-Gy arm (7-year freedom from failure rate, 56% vs 45%, respectively; *P*=0.03). However, no differences in freedom from clinical failure or OS were observed. The incidence of late Grade 2 or greater GU toxicity was similar in both arms (40% and 41% at 7 years; *P*=0.6). However, the cumulative incidence of late Grade 2 or greater GI toxicity was increased in the 78-Gy arm compared with the 68-Gy arm (35% vs 25% at 7 years; *P*=0.04).	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
27. Dearnaley DP, Sydes MR, Graham JD, et al. Escalated-dose versus standard-dose conformal radiotherapy in prostate cancer: first results from the MRC RT01 randomised controlled trial. *Lancet Oncol.* 2007;8(6):475-487.	Experimental-Tx	843 men randomized to escalated-dose CRT (n=422) or standard-dose CRT (n=421)	Present first results from the MRC RTO1 randomized controlled trial. Escalated-dose was compared to standard-dose CRT in prostate cancer.	Between January, 1998, and December, 2002, 843 men were randomly assigned to escalated-dose CRT (n=422) or standard-dose CRT (n=421). In the escalated group, the HR for bPFS was 0.67 (95% CI 0.53–0.85, *P*=0.0007). We noted 71% bPFS (108 cumulative events) and 60% bPFS (149 cumulative events) by 5 years in the escalated and standard groups, respectively. HR for clinical PFS was 0.69 (0.47–1.02; *P*=0.064); local control was 0.65 (0.36–1.18; *P*=0.16); freedom from salvage androgen suppression was 0.78 (0.57–1.07; *P*=0.12); and metastases-free survival was 0.74 (0.47–1.18; *P*=0.21). HR for late bowel toxicity in the escalated group was 1.47 (1.12–1.92) according to the RTOG (grade ≥2) scale; 1.44 (1.16–1.80) according to the LENT/SOM (grade ≥2) scales; and 1.28 (1.03–1.60) according to the UCLA PCI (score ≥30) scale. 33% of the escalated and 24% of the standard group reported late bowel toxicity within 5 years of starting treatment. HR for late bladder toxicity according to the RTOG (grade ≥2) scale was 1.36 (0.90–2.06), but this finding was not supported by the LENT/SOM (grade ≥2) scales (HR 1.07 [0.90–1.29]), nor the UCLA PCI (score ≥30) scale (HR 1.05 [0.81–1.36]).	1
28. Seddon B, Bidmead M, Wilson J, Khoo V, Dearnaley D. Target volume definition in conformal radiotherapy for prostate cancer: quality assurance in the MRC RT-01 trial. *Radiother Oncol.* 2000;56(1):73-83.	Review/Other-Tx	15 clinicians	To assess the reproducibility of outlining the GTV, bladder and rectum by oncologists in the UK Medical Research Council Radiotherapy Working Party RT-01 multicenter trial of CRT in prostate cancer.	GTV central slice and length were defined with reasonable consistency. The radial line measurement variation analysis showed that the main part of the prostate gland, bladder and inferior rectum were outlined with good consistency among clinicians. However, the outlining of the prostatic apex, superior aspect of the prostate projecting into the bladder, SVs, the base of SVs and superior rectum were more variable.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
29. Michalski J. RTOG 0126: A Phase III Randomized Study of High Dose 3DCRT/IMRT versus Standard Dose 3DCRT/IMRT in Patients Treated for Localized Prostate Cancer. 2014; Available at: http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0126.	Review/Other-Tx	N/A	To determine whether 3D-CRT/IMRT to 79.2 Gy in 44 fractions will lead to improved OS in patients treated for prostate cancer compared to a group of patients treated with 3D-CRT/ IMRT to 70.2 Gy in 39 fractions.	No abstract available.	4
30. Roach M. RTOG 0924: Androgen Deprivation Therapy and High Dose Radiotherapy With or Without Whole-Pelvic Radiotherapy in Unfavorable Intermediate or Favorable High Risk Prostate Cancer: A Phase III Randomized Trial. 2011; http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0924.	Review/Other-Tx	Ongoing	To demonstrate that prophylactic neoadjuvant ADT and WPRT will result in improvement in OS in patients with "unfavorable" intermediate risk or "favorable" high risk prostate cancer compared to neoadjuvant ADT and high dose prostate and SV RT using IMRT or EBRT with a high dose rate or a permanent prostate (radioactive seed) implant boost.	This trial is still recruiting study subjects and results are not available yet.	4
31. Gregoire V, Mackie TR. State of the art on dose prescription, reporting and recording in Intensity-Modulated Radiation Therapy (ICRU report No. 83). *Cancer Radiother.* 2011;15(6-7):555-559.	Review/Other-Tx	N/A	The International Commission on Radiation Units and Measurements (ICRU) report No. 83 provides the information necessary to standardize techniques and procedures and to harmonize the prescribing, recording, and reporting of IMRT.	IMRT is characterized by nonuniform intensity distributions that have been optimized to collectively deliver an adequately homogenous dose to the target volume and spare normal tissues as much as possible. Usually these intensity patterns are iteratively optimized by specifying dose and dose-volume constraints to the target volume and normal tissues. The optimization leads to an approved treatment planned, which is specified by the prescription (which also includes specifications for organs at risk as well as the target volume) and the technical data needed to deliver the plan. Treatment plans can be altered during the course of RT to take into account patient anatomy changes due to tumor shrinkage or weight loss. This so called adaptive therapy can result in new target volume and organ at risk delineations.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
32. Boehmer D, Maingon P, Poortmans P, et al. Guidelines for primary radiotherapy of patients with prostate cancer. *Radiother Oncol.* 2006;79(3):259-269.	Review/Other-Tx	N/A	To standardize target delineation as well as clinical quality assurance procedures for patients undergoing RT for prostate cancer.	Target volume definitions for different risk groups of prostate cancer patients based on pathological and imaging studies are provided. Available imaging modalities, patient positioning and treatment preparation studies as well as verification procedures are collected from literature studies. These studies are summarized and recommendations are given where appropriate.	4
33. Cox J. RTOG 9406: A Phase I/II Dose Escalation Study Using Three Dimensional Conformal Radiation Therapy for Adenocarcinoma of the Prostate. 2008; Available at: http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=9406. Accessed April 22, 2015.	Review/Other-Tx	N/A	To establish the maximum tolerated dose of radiation that can be delivered to the prostate gland and immediate surrounding tissues in patients with carcinoma of the prostate using 3D-CRT.	No abstract available.	4
34. Litzenberg DW, Balter JM, Hadley SW, et al. Influence of intrafraction motion on margins for prostate radiotherapy. *Int J Radiat Oncol Biol Phys.* 2006;65(2):548-553.	Review/Other-Tx	11 patients	To assess the impact of intrafraction intervention on margins for prostate RT.	For skin-based setup without and with inclusion of intrafraction motion, prostate treatments would have required average margins of 8.0, 7.3, and 10.0 mm and 8.2, 10.2, and 12.5 mm, about the left-right, AP, and cranial-caudal directions, respectively. Positioning by prostate markers at the start of the treatment fraction reduced these values to 1.8, 5.8, and 7.1 mm, respectively. Interbeam adjustment further reduced margins to an average of 1.4, 2.3, and 1.8 mm. Intrabeam adjustment yielded margins of 1.3, 1.5, and 1.5 mm, respectively. Significant reductions in margins might be achieved by repositioning the patient before each beam, either radiographically or electromagnetically. However, 2 of the 11 patients would have benefited from continuous target tracking and threshold-based intervention.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Gay HA, Barthold HJ, O'Meara E, et al. Pelvic normal tissue contouring guidelines for radiation therapy: a Radiation Therapy Oncology Group consensus panel atlas. *Int J Radiat Oncol Biol Phys.* 2012;83(3):e353-362.	Review/Other-Tx	N/A	To define a male and female pelvic normal tissue contouring atlas for Radiation Therapy Oncology Group (RTOG) trials.	The panel achieved consensus definitions for pelvic normal tissue contouring in RTOG trials with these standardized names: Rectum, AnoRectum, SmallBowel, Colon, BowelBag, Bladder, UteroCervix, Adnexa_R, Adnexa_L, Prostate, SeminalVesc, PenileBulb, Femur_R, and Femur_L. Two additional normal structures whose purpose is to serve as targets in anal and rectal cancer were defined: AnoRectumSig and Mesorectum. Detailed target volume contouring guidelines and images are discussed.	4
36. McLaughlin PW, Evans C, Feng M, Narayana V. Radiographic and anatomic basis for prostate contouring errors and methods to improve prostate contouring accuracy. *Int J Radiat Oncol Biol Phys.* 2010;76(2):369-378.	Review/Other-Dx	300 patients	A retrospective study to analyze the radiographic and anatomic basis of common errors in CT contouring and suggest methods to correct them.	Contouring errors were identified at the prostatic apex, mid gland, and base on CT. At the apex, the GU diaphragm, rectum, and anterior fascia contribute to overestimation. At the mid prostate, the anterior and lateral fasciae contribute to overestimation. At the base, the bladder and anterior fascia contribute to anterior overestimation. Transition zone hypertrophy and bladder neck variability contribute to errors of overestimation and underestimation at the superior base, whereas variable prostate-to-SV relationships with prostate hypertrophy contribute to contouring errors at the posterior base. Most CT contouring errors can be detected by (1) inspection of a lateral view of prostate contours to detect projection from the expected globular form and (2) recognition of anatomic structures (GU diaphragm) on the CT scans that are clearly visible on MRI. This study shows that many CT prostate contouring errors can be improved without direct incorporation of MRI data.	4

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Cazzaniga LF, Marinoni MA, Bossi A, et al. Interphysician variability in defining the planning target volume in the irradiation of prostate and seminal vesicles. *Radiother Oncol.* 1998;47(3):293-296.	Observational-Dx	6 physicians, 3 test cases	To assess the variability between 6 radiotherapists in defining the PTV on CT slices for 3 prostate tumor cases.	Percentage differences between measured volumes and mean values calculated for each case ranged from -53.64 to +60.48% (SD 36.00%). There is a considerable variation in delineating the PTV, both in the cranio-caudal direction and in the in-slice extension of the areas drawn on each slice (SDs ranged from 0.35 to 2.64 cm2). We also checked the uncertainty in the shape and position of the contours on each CT image. The analysis was performed on 3 slices of 1 test case. As we expected, the uncertainty seems largest for SV slices and smallest for prostatic apex slices.	3
38. Rasch C, Steenbakkers R, van Herk M. Target definition in prostate, head, and neck. *Semin Radiat Oncol.* 2005;15(3):136-145.	Review/Other-Tx	N/A	To review target definition as a major source of errors in both prostate and head and neck EBRT.	No results stated in the abstract.	4
39. Debois M, Oyen R, Maes F, et al. The contribution of magnetic resonance imaging to the three-dimensional treatment planning of localized prostate cancer. *Int J Radiat Oncol Biol Phys.* 1999;45(4):857-865.	Experimental-Dx	10 patients	To investigate whether the use of transaxial and coronal MRI improves the ability to localize the apex of the prostate and the anterior part of the rectum compared to the use of transaxial CT alone, and whether the incorporation of MRI could improve the coverage of the prostate by the RT field and change the volume of rectum irradiated.	The interobserver variation of the prostatic apex location was largest on CT ranging from 0.54 to 1.07 cm, and smallest on coronal MRI ranging from 0.17 to 0.25 cm. The interobserver variation of the delineation of the anterior rectum on MRI was small and constant along the whole length of the prostate (0.09+/-0.02 cm), while for CT it was comparable to that for the MRI delineation at the base of the prostate, but it increased gradually towards the apex, where the variation reached 0.39 cm. The volume of MRI rectum receiving more than 80% of the prescribed dose was on average reduced by 23.8+/-11.2% from the CT to the MRI treatment plan.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Usmani N, Sloboda R, Kamal W, et al. Can images obtained with high field strength magnetic resonance imaging reduce contouring variability of the prostate? *Int J Radiat Oncol Biol Phys.* 2011;80(3):728-734.	Experimental-Dx	40 patients; 5 radiation oncologists	To determine whether there is less contouring variability of the prostate using higher-strength MRI compared with standard MRI and CT.	Although there was less interobserver contouring variability in the overall prostate volumes in 1.5-T MRI compared with 3.0-T MRI ($P<0.01$), there was no significant differences in contouring variability in the different regions of the prostate between 1.5-T MRI and 3.0-T MRI. MRI demonstrated significantly less interobserver contouring variability in both 1.5-T and 3.0-T compared with CT in overall prostate volumes ($P<0.01$, $P=0.01$), with the greatest benefits being appreciated in the base of the prostate. Overall, there was less intraobserver contouring variability than interobserver contouring variability for all of the measurements analyzed.	1
41. Rasch C, Barillot I, Remeijer P, Touw A, van Herk M, Lebesque JV. Definition of the prostate in CT and MRI: a multi-observer study. *Int J Radiat Oncol Biol Phys.* 1999;43(1):57-66.	Experimental-Dx	18 patients; 3 radiation oncologists	To determine, in three-dimensions, the difference between prostate delineation in MR and CT images for RT treatment planning.	Interscan variation: CT volumes were larger than the axial MR volumes in 52/54 delineations. The average ratio between the CT and MR volumes was 1.4 (standard error of mean, SE: 0.04) which was significantly different from 1 ($P<0.005$). Only small differences were observed between the volumes outlined in the various MR scans, although the coronal MR volumes were smallest. The CT derived prostate was 8 mm (SD: 6 mm) larger at the base of the SVs and 6 mm (SD 4 mm) larger at the apex of the prostate than the axial MRI. Similar figures were obtained for the CT and the other MRI scans. Interobserver variation: The average ratio between the volume derived by one observer for a particular scan and patient and the average volume was 0.95, 0.97, and 1.08 (SE 0.01) for the 3 observers, respectively. The 3D pattern of the overall observer variation (1 SD) for CT and axial MRI was similar and equal to 3.5 to 2.8 mm at the base of the SVs and 3 mm at the apex.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Kalkner KM, Kubicek G, Nilsson J, Lundell M, Levitt S, Nilsson S. Prostate volume determination: differential volume measurements comparing CT and TRUS. *Radiother Oncol.* 2006;81(2):179-183.	Observational-Dx	31 patients	To compare the differences in prostate volume assessed by CT, TRUS-step and TRUS with ellipsoid-formula volume calculation.	The prostate volume was on average 34 cc (range 18–60 cc) according to CT, 28 cc (range 12–57 cc) and 24 cc (range 13–44 cc) according to TRUS-step and TRUS-ellipsoid, respectively. The differences between the lengths measured were most pronounced with a mean length of 4.5 cm (range 3.0–6.0 cm) defined by CT as compared to 3.6 cm (range 3.0–5.0 cm) and 3.6 cm (range 2.8–5.0 cm) when defined by TRUS-step and TRUS-ellipsoid, respectively.	3
43. Smith WL, Lewis C, Bauman G, et al. Prostate volume contouring: a 3D analysis of segmentation using 3DTRUS, CT, and MR. *Int J Radiat Oncol Biol Phys.* 2007;67(4):1238-1247.	Experimental-Dx	10 patients; 7 observers	To evaluate the reproducibility and modality differences of prostate contouring after brachytherapy implant using 3DTRUS, T2-weighted MR, and CT imaging.	Average volume ratios were 1.16 for CT/MR, 0.90 for 3DTRUS/MR, and 1.30 for CT/3DTRUS. Overall contouring variability was largest for CT and similar for MR and 3DTRUS. The greatest variability of CT contours occurred at the posterior and anterior portions of the midgland. On MR, overall variability was smaller, with a maximum in the anterior region. On 3DTRUS, high variability occurred in anterior regions of the apex and base, whereas the prostate-rectum interface had the smallest variability. The shape of the prostate on MR was rounder, with the base and apex of similar size, whereas CT contours had broad, flat bases narrowing toward the apex. The average percent of surface area that was significantly different (95% confidence interval) for CT/MR was 4.1%; 3DTRUS/MR, 10.7%; and CT/3DTRUS, 6.3%. The larger variability of CT measurements made significant differences more difficult to detect.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. McLaughlin PW, Troyer S, Berri S, et al. Functional anatomy of the prostate: implications for treatment planning. *Int J Radiat Oncol Biol Phys.* 2005;63(2):479-491.	Review/Other-Dx	N/A	To summarize the functional anatomy relevant to prostate cancer treatment planning.	The 3 major prostate zones (inner, outer, and anterior fibromuscular) are visible by T2 MRI. The bladder, bladder neck, and internal (preprostatic) sphincter are a continuous muscular structure and clear definition of the preprostatic sphincter is difficult by MRI. Transition zone hypertrophy may efface the bladder neck and internal sphincter. The external "lower" sphincter is clearly visible by T2 MRI with wide variations in length. The critical erectile structures are the internal pudendal artery (defined by MRI angiogram or T2 MRI), corpus cavernosum, and neurovascular bundle. The neurovascular bundle is visible along the posterior lateral surface of the prostate on CT and MRI, but its terminal branches (cavernosal nerves) are not visible and must be defined by their relationship to the urethra within the GU diaphragm. Visualization of the ejaculatory ducts within the prostate is possible on sagittal MRI. The anatomy of the prostate-rectum interface is clarified by MRI, as is the potentially important distinction of rectal muscle and rectal mucosa. Improved understanding of functional anatomy and imaging of the prostate and critical adjacent structures will improve prostate RT by improvement of dose and toxicity correlation, limitation of dose to critical structures, and potential improvement in post therapy quality of life.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. McLaughlin PW, Narayana V, Meirovitz A, et al. Vessel-sparing prostate radiotherapy: dose limitation to critical erectile vascular structures (internal pudendal artery and corpus cavernosum) defined by MRI. *Int J Radiat Oncol Biol Phys*. 2005;61(1):20-31.	Review/Other-Dx	25 patients: 10 EBRT; 15 brachytherapy	To determine feasibility to decrease radiation dose to the corpora cavernos and the internal pudendal artery.	The combination of coronal, sagittal, and axial MRI data sets allowed superior definition of the prostate apex and its relationship to critical vascular structures. The apex to penile bulb distance averaged 1.45 cm (0.36 SD) with a range of 0.7 cm to 2.1 cm. Peak dose (D5) to the proximal corpus cavernosum in the MRI-planned 80 Gy course was 26 (9) Gy (0.36 of CT-planned dose), and peak dose to the internal pudendal artery was 39 (13) Gy (0.61 of CT-planned dose). The distance between the prostate apex and critical vascular structures is highly variable. Current empiric rules for CT contouring (apex 1.5 cm above penile bulb) overestimate or underestimate the distance between the prostate apex and critical vascular structures. When defined by MRI T2 and MRI angiogram with CT registration, limitation of dose to critical erectile structures is possible, with a more significant gain than has been previously reported using dose limitation by commonly applied IMRT studies based on CT imaging. These techniques make "vessel-sparing" prostate RT feasible.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Steenbakkers RJ, Deurloo KE, Nowak PJ, Lebesque JV, van Herk M, Rasch CR. Reduction of dose delivered to the rectum and bulb of the penis using MRI delineation for radiotherapy of the prostate. *Int J Radiat Oncol Biol Phys.* 2003;57(5):1269-1279.	Experimental-Dx	18 patients	To determine the influence of MRI- vs CT-based prostate delineation using multiple observers on the dose to the target and organs at risk.	The equivalent uniform dose of the CT rectal wall in plans based on the CT-delineated prostate was, on average, 5.1 Gy (SEM 0.5) greater than in the plans based on the MRI-delineated prostate. For the MRI rectal wall, this difference was 3.6 Gy (SEM 0.4). Allowing for the same equivalent uniform dose to the CT rectal wall, the prescribed dose to the PTV could be raised from 78 to 85 Gy when using the MRI-delineated prostate for treatment planning. The mean dose to the bulb of the penis was 11.6 Gy (SEM 1.8) lower for plans based on the MRI-delineated prostate. The mean coverage (volume of the PTV receiving ≥95% of the prescribed dose) was 99.9% for both modalities. The interobserver coverage (coverage of the PTV by a treatment plan designed for the PTV delineated by another observer in the same modality) was 97% for both modalities. The MRI rectum was significantly more ventrally localized than the CT rectum, probably because of the rounded tabletop and no knee support on the MRI scanner. The dose delivered to the rectal wall and bulb of the penis is significantly reduced with treatment plans based on the MRI-delineated prostate compared with the CT-delineated prostate.	2
47. Villeirs GM, Van Vaerenbergh K, Vakaet L, et al. Interobserver delineation variation using CT versus combined CT + MRI in intensity-modulated radiotherapy for prostate cancer. *Strahlenther Onkol.* 2005;181(7):424-430.	Observational-Dx	13 patients	To quantify interobserver variation of prostate and SV delineations using CT only vs CT + MRI in consensus reading with a radiologist.	Using CT + MRI as compared to CT alone, the mean CTV, prostate and SV volumes significantly decreased by 6.54%, 5.21% and 10.47%, respectively. More importantly, their SDs significantly decreased by 63.06%, 62.65% and 44.83%, respectively. The highest level of variation was found at the prostatic apex, followed by the prostatic base and SVs.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Parker CC, Damyanovich A, Haycocks T, Haider M, Bayley A, Catton CN. Magnetic resonance imaging in the radiation treatment planning of localized prostate cancer using intra-prostatic fiducial markers for computed tomography co-registration. *Radiother Oncol.* 2003;66(2):217-224.	Experimental-Dx	6 patients	To assess the feasibility of intra-prostatic fiducial markers, rather than bony landmarks, for the co-registration of CT and MRI in the radiation treatment planning.	Phantom measurements demonstrated trivial image distortion within the required field of view, and an 18K Au/Cu alloy to be the marker composition most suitable for CT-MRI image fusion purposes. Inter-observer variation in prostate contouring was significantly less for MR compared to CT. The mean SEV/SCV ratio was 1.58 (CI: 1.47–1.69) for CT scans and 1.37 (CI: 1.33–1.41) for MR scans (paired t-test; P=0.036). The overall magnitude of contoured gross tumor volume was similar for MR and CT; however, there were spatial discrepancies in contouring between the 2 modalities. The greatest systematic discrepancy was at the posterior apical prostate border, which was defined 3.6 mm (SD 3.5 mm) more posterior on MR- than CT-defined contouring. Prostate contouring on MR is associated with less inter-observer variation than on CT. In addition, we have demonstrated the feasibility of using intra-prostatic fiducial markers, rather than bony landmarks, for the co-registration of CT and MR images in the radiation treatment planning of localized prostate cancer. This technique, together with on-line correction of treatment set-up according to the fiducial marker position on electronic portal imaging, may enable a reduction in the PTV margin needed to account for inter-observer error in target delineation, and for prostate motion.	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Chen L, Price RA, Jr., Wang L, et al. MRI-based treatment planning for radiotherapy: dosimetric verification for prostate IMRT. *Int J Radiat Oncol Biol Phys*. 2004;60(2):636-647.	Review/Other-Dx	15 patients	To investigate the dosimetric accuracy of MRI-based treatment planning for prostate IMRT.	Dose distributions between CT-based and MRI-based plans were equally acceptable based on our clinical criteria. The absolute dose agreement for the PTV was within 2% between CT-based and MR-based plans and 3% between measured dose and dose predicted by the planning system in the physical phantom. MRI is a useful tool for RT simulation. Compared with CT-based treatment planning, MR imaging-based treatment planning meets the accuracy for dose calculation and provides consistent treatment plans for prostate IMRT. Because MRI-based digitally reconstructed radiographs do not provide adequate bony structure information, a technique is suggested for producing a wire-frame image that is intended to replace the traditional digitally reconstructed radiographs that are made from CT information.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Petersch B, Bogner J, Fransson A, Lorang T, Potter R. Effects of geometric distortion in 0.2T MRI on radiotherapy treatment planning of prostate cancer. *Radiother Oncol.* 2004;71(1):55-64.	Observational-Dx	5 patients	To evaluate the impact of 2 different methods of geometric distortion correction of MRI.	Maximum distortions of 28 mm (mean 2.2 mm) were found within the FOV in frequency encode direction. Maximum distortions could be reduced by a factor of 2 (mean factor 4) by our phantom measurement based technique. Distortion patterns were found to be stable and reproducible over several weeks with this MR unit. For 4/5 patients, relative doses at the normalization point as calculated on the distortion corrected MRI only (all tissues taken water equivalent) were all within 1% of the corresponding value from the standard CT-based plan (actual Hounsfield units). The largest differences in isocentric dose found in 1 case were 3.1% MR uncorrected vs CT and 2.6% MR corrected vs CT. Typical sites of internal anatomical landmarks chosen for image registration show distortions up to 3 mm. Object induced distortions are negligible at such low field strengths compared to system related distortions. Treatment plans for prostate cancer do not seem to differ significantly from "standard" plans calculated on CT images when calculated on distortion corrected MRI, even if all tissues are assigned the electron density of water. Distortion correction of MRI can theoretically improve the starting point for image registration of MRI and CT images.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Lee YK, Bollet M, Charles-Edwards G, et al. Radiotherapy treatment planning of prostate cancer using magnetic resonance imaging alone. *Radiother Oncol.* 2003;66(2):203-216.	Experimental-Dx	5 patients	To study the possibility and practicality of using MR only for RT treatment planning.	The differences between dose-plans on bulk-density assigned images when compared to CT were <2% when water and bone values were assigned. Dose differences >2% were observed when images of homogeneous-density assignment were compared to the CT. Phantom measurements showed that the distortions in the FLASH 3D T1-weighted MR averaged 2 mm in the volume of interest for prostate RT planning. For the CT and MR prostate planning study, doses delivered to the PTV in CT and MR were always inside a 93%–107% dose range normalized to the isocenter. Also, the doses to the organs-at-risk in the MRIs were similar to the doses delivered to the volumes in the registered CT image when the organ volumes between the 2 images were similar.	2
52. Sciarra A, Barentsz J, Bjartell A, et al. Advances in magnetic resonance imaging: how they are changing the management of prostate cancer. *Eur Urol.* 2011;59(6):962-977.	Review/Other-Dx	N/A	To review the current roles of these MR techniques in different aspects of prostate cancer management: initial diagnosis, biopsy strategies, planning of RP and external RT, and implementation of alternative focal therapies.	Initial diagnosis: The data suggest that the combination of T2W MRI and diffusion-weighted imaging or MRSI with DCE-MRI has the potential to guide biopsy to the most aggressive cancer foci in patients with previously negative biopsies, increasing the accuracy of the procedure. Transrectal MR-guided prostate biopsy can improve prostate cancer detection, but its availability is still limited and the examination time is rather long. Planning of RP: It appears that adding MRSI, diffusion-weighted imaging, and/or DCE-MRI to T2W MRI can facilitate better preoperative characterization of cancer with regard to location, size, and relationship to prostatic and extraprostatic structures, and it may also facilitate early detection of local recurrence. Thus, use of these MR techniques may improve surgical, oncologic, and functional management. Planning of external RT and focal therapies: MR techniques have similar potential in these areas, but the published data remain very limited.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Sciarra A, Panebianco V, Salciccia S, et al. Role of dynamic contrast-enhanced magnetic resonance (MR) imaging and proton MR spectroscopic imaging in the detection of local recurrence after radical prostatectomy for prostate cancer. *Eur Urol.* 2008;54(3):589-600.	Experimental-Dx	70 total patients	To assess the accuracy of 1H-MRSI and DCE-MRI in the depiction of local prostate cancer recurrence in patients with biochemical progression after RP.	In group A, 1H-MRSI analysis alone showed a sensitivity of 84% and a specificity of 88%; the DCE-MRI analysis alone, a sensitivity of 71% and a specificity of 94%; combined 1H-MRSI-DCE-MRI, a sensitivity of 87% and specificity of 94%. AUC for 1H-MRSI, DCE-MRI, and combined 1HMRSI/DCE-MRI were 0.942, 0.93,1 and 0.964, respectively. In group B, 1H-MRSI alone showed a sensitivity of 71% and a specificity of 83%; DCE-MRI, a sensitivity of 79% and a specificity of 100%; combined 1H-MRSI and DCE-MRI, a sensitivity of 86% and a specificity of 100%. AUC for each of these groups were 0.81, 0.923, and 0.94, respectively.	2
54. Turkbey B, Choyke PL. Multiparametric MRI and prostate cancer diagnosis and risk stratification. *Curr Opin Urol.* 2012;22(4):310-315.	Review/Other-Dx	N/A	To review multiparametric MRI in the detection and risk stratification of prostate cancer.	Multiparametric-MRI has been shown to be the most accurate noninvasive technique to localize prostate cancer. Recent studies reported that using MRI for guidance during prostate biopsies increases the yield of prostate biopsies. Moreover, multiparametric and particular MRI sequences such as apparent diffusion coefficient values of diffusion-weighted MRI have been found to correlate negatively with tumor GSs.	4
55. Seitz M, Shukla-Dave A, Bjartell A, et al. Functional magnetic resonance imaging in prostate cancer. *Eur Urol.* 2009;55(4):801-814.	Review/Other-Dx	N/A	To emphasize different functional MRI techniques in the diagnosis of prostate cancer and includes information about their clinical value and usefulness.	The combination of conventional MRI with functional MRI techniques is more reliable for differentiating benign and malignant prostate tissues than any other diagnostic procedure. At present, no guideline is available that outlines which technique is best in a specific clinical situation. It also remains uncertain whether improved spatial resolution and signal-to-noise ratio of 3-T MRI will improve diagnostic performance.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Chao KK, Goldstein NS, Yan D, et al. Clinicopathologic analysis of extracapsular extension in prostate cancer: should the clinical target volume be expanded posterolaterally to account for microscopic extension? *Int J Radiat Oncol Biol Phys.* 2006;65(4):999-1007.	Observational-Dx	371 prostatectomy specimens	To perform a complete pathologic analysis examining ECE and microscopic spread of malignant cells beyond the prostate capsule to determine whether and when CTV expansion should be performed.	A total of 121 patients (33%) were found to have ECE (68 unilateral, 53 bilateral). Median ECE distance =2.4 mm [range: 0.05–7.0 mm]. The 90th-percentile distance = 5.0 mm. Of the 121 cases with ECE, 55% had ECE distance ≥2 mm, 19% ≥4 mm, and 6% ≥6 mm. ECE occurred primarily posterolaterally along the neurovascular bundle in all cases. Pretreatment PSA, biopsy Gleason, pathologic Gleason, clinical stage, bilateral involvement, positive margins, percentage of gland involved, and maximal tumor dimension were associated with presence of ECE. Both PSA and GS were associated with ECE distance. In all 371 patients, for those with either pretreatment PSA ≥10 or biopsy GS ≥7, 21% had ECE ≥2 mm and 5% ≥4 mm beyond the capsule. For patients with both of these risk factors, 49% had ECE ≥2 mm and 21% ≥4 mm.	3
57. Zlotta AR, Roumeguere T, Ravery V, et al. Is seminal vesicle ablation mandatory for all patients undergoing radical prostatectomy? A multivariate analysis on 1283 patients. *Eur Urol.* 2004;46(1):42-49.	Observational-Tx	1,283 patients	To determine which patients could be safely spared SV excision during RP.	Out of 1,283 patients, 137 (10.6%) had SV involvement, 41/777 (5.2%) with PSA <10.0 ng/ml, 16.1% in the 10-20 ng/mL range and 26.2% when PSA was >20 ng/ mL. Percentage of biopsies affected by prostate cancer and biopsy GS were significant predictors of SVI in multivariate analysis, both in the entire population and in the subset of patients with PSA <10.0 ng/ mL (P<0.0001). Probability graphs created for patients with PSA <10 ng/ mL indicate a risk of seminal invasion <5% when GS on biopsy is <7 or when the percentage of biopsies affected by cancer is <50%.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
58. Schwartz DJ, Sengupta S, Hillman DW, et al. Prediction of radial distance of extraprostatic extension from pretherapy factors. *Int J Radiat Oncol Biol Phys.* 2007;69(2):411-418.	Observational-Dx	404 patients	To evaluate clinical determinants of radial distance extraprostatic extension from a RP series with whole-mount specimen pathologic examination to develop a multivariate model that would be useful in planning EBRT and permanent prostate brachytherapy target volumes.	The range of the radial distance extraprostatic extension distance was 0.0–5.7 mm. A three-category model was used that included 283 patients (70%) with no extraprostatic extension, 59 (15%) with "near extraprostatic extension" (range, 0.01–0.59 mm), and 62 (15%) with "far extraprostatic extension" (≥0.6 mm). Univariate analysis revealed that patient age and prostate volume did not correlate with radial distance extraprostatic extension, in contrast to all other factors evaluated. Multivariate analysis identified the preoperative serum PSA, the percentage of cancer in the biopsy cores, and clinical tumor stage as significant. However, the GS was not associated with the radial distance extraprostatic extension. Greater discrimination was possible in estimating the probability of extension in the "near" category than in the "far" category.	3
59. Eifler JB, Feng Z, Lin BM, et al. An updated prostate cancer staging nomogram (Partin tables) based on cases from 2006 to 2011. *BJU Int.* 2013;111(1):22-29.	Review/Other-Dx	5,629 consecutive men	To update the 2007 Partin tables in a contemporary patient population.	The median PSA was 4.9 ng/mL, 63% had Gleason 6 disease, and 78% of men had T1c disease. 73% of patients had organ-confined disease, 23% had extraprostatic extension, 3% had SV+ but not LN+, and 1% had LN+ disease. Compared to the previous Partin nomogram, there was no change in the distribution of pathologic state. The risk of LN+ disease was significantly higher for tumors with biopsy Gleason 9–10 than Gleason 8 (organ-confined disease 3.2, 95% CI 1.3–7.6). The c-indexes for extraprostatic extension vs organ-confined disease, SV+ vs organ-confined disease, and LN+ vs organ-confined disease were 0.702, 0.853, and 0.917, respectively. Men with biopsy Gleason 4+3 and Gleason 8 had similar predicted probabilities for all pathologic stages. Most men presenting with Gleason 6 disease or Gleason 3+4 disease have <2% risk of harboring LN+ disease and may have lymphadenectomy omitted at RP.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
60. Kestin L, Goldstein N, Vicini F, Yan D, Korman H, Martinez A. Treatment of prostate cancer with radiotherapy: should the entire seminal vesicles be included in the clinical target volume? *Int J Radiat Oncol Biol Phys.* 2002;54(3):686-697.	Observational-Dx	344 specimens	To determine the appropriate length of SV to include within the CTV when SV treatment is indicated.	51 patients (15%) demonstrated SV involvement in 81 SVs (21 unilateral, 30 bilateral SV involvement). The median SV length was 3.5 cm (range: 0.7–8.5 cm). Factors associated with SV involvement included the pretreatment PSA level, biopsy GS, and clinical T classification. The commonly used risk group stratification was very effective at predicting SV positivity. Only 1% of low-risk patients (PSA <10 ng/mL, Gleason ≤6, and clinical stage ≤T2a) demonstrated SV involvement vs 27% of high-risk patients. Patients with only 1 high-risk feature still demonstrated a 15% risk of SV involvement, whereas 58% of patients with all 3 high-risk features had positive SVs The median length of SV involvement was 1.0 cm (90th percentile: 2.0 cm, range: 0.2-3.8 cm). A median of 25% of each SV was involved with adenocarcinoma (90th percentile: 54%, range: 4%–75%). For the 81 positive SVs, no factor was associated with a greater length or percentage of SV involvement. In the entire population, 7% had SV involvement beyond 1.0 cm. There was an approximate 1% risk of SV involvement beyond 2.0 cm or 60% of the SV. In addition, this risk was <4% for all subgroups, including high-risk patients. A portion of the SV should be included in the CTV only for higher-risk patients (PSA >10 ng/ml, biopsy Gleason >7, or clinical T stage >T2b).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Lawton CA, Michalski J, El-Naqa I, et al. Variation in the definition of clinical target volumes for pelvic nodal conformal radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2009;74(2):377-382.	Observational-Dx	Scans from 2 patients; 14 radiation oncologists	To look at the congruence or levels of discrepancies of CTV definition of pelvic LNs in the treatment of prostate cancer by multiple GU radiation oncologists.	Significant variation in the definition of the iliac and presacral CTVs was seen among the physicians. The minimum, maximum, mean (SD) iliac volumes (mL) were 81.8, 876.6, 337.6 +/- 203 for case 1 and 60.3, 627.7, 251.8 +/- 159.3 for case 2. The volume of 100% agreement was 30.6 and 17.4 for case 1 and 2 and the volume of the union of all contours was 1,012.0 and 807.4 for case 1 and 2, respectively. The overall agreement was judged to be moderate in both cases (kappa = 0.53 (P<0.0001) and kappa = 0.48 (P<0.0001). There was no volume of 100% agreement for either of the 2 presacral volumes. These variations were confirmed in the responses to the associated questionnaire.	3
62. Lawton CA, Michalski J, El-Naqa I, et al. RTOG GU Radiation oncology specialists reach consensus on pelvic lymph node volumes for high-risk prostate cancer. *Int J Radiat Oncol Biol Phys.* 2009;74(2):383-387.	Review/Other-Dx	N/A	To establish a consensus of the appropriate nodal volumes for these patients so that the relative safety and merit of such treatment can be established.	Consensus was obtained resulting in CT image-based pelvic LN CTVs. Based on this consensus, the pelvic LN volumes to be irradiated include: distal common iliac, presacral LNs (S(1)-S(3)), external iliac LNs, internal iliac LNs, and obturator LNs. LN CTVs include the vessels (artery and vein) and a 7-mm radial margin being careful to "carve out" bowel, bladder, bone, and muscle. Volumes begin at the L5/S1 interspace and end at the superior aspect of the pubic bone. Consensus on dose-volume histogram constraints for organs-at-risk was also attained.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
63. Sidhom MA, Kneebone AB, Lehman M, et al. Post-prostatectomy radiation therapy: consensus guidelines of the Australian and New Zealand Radiation Oncology Genito-Urinary Group. *Radiother Oncol.* 2008;88(1):10-19.	Review/Other-Tx	N/A	To develop consensus guidelines on to whom, when and how to deliver post-prostatectomy RT.	Central to the recommendations is that patients with positive surgical margins, SVI and/or ECE have a high risk of residual local disease and should be informed of the options of either immediate adjuvant RT or active surveillance with early salvage in the event of biochemical recurrence. Salvage RT should be instituted at the earliest confirmation of biochemical recurrence. Detailed contouring guidelines have been developed, defining the regions at risk of residual microscopic disease which should be included in the CTV. The recommended doses are 60-64Gy for adjuvant, and 60-66Gy for salvage RT. The role of hormone therapy in conjunction with post-prostatectomy RT is yet to be defined.	4
64. Poortmans P, Bossi A, Vandeputte K, et al. Guidelines for target volume definition in post-operative radiotherapy for prostate cancer, on behalf of the EORTC Radiation Oncology Group. *Radiother Oncol.* 2007;84(2):121-127.	Review/Other-Tx	N/A	To provide standardization of the target volume definition and delineation as well as standardization of the clinical quality assurance procedures for patients undergoing postoperative 3D-CRT, IMRT or IGRT for prostate cancer.	No results stated in the abstract.	4
65. Wiltshire KL, Brock KK, Haider MA, et al. Anatomic boundaries of the clinical target volume (prostate bed) after radical prostatectomy. *Int J Radiat Oncol Biol Phys.* 2007;69(4):1090-1099.	Experimental-Dx	30 patients	To derive and validate an interdisciplinary consensus definition for the anatomic boundaries of the postoperative CTV, prostate bed.	Anatomic boundaries of the consensus CTV (prostate bed) are described. Surgical clips (n = 339) were well distributed throughout the CTV. The vesicourethral anastomosis was accurately localized using central sagittal CT reconstruction, with a mean +/- SD uncertainty of 1.8 +/- 2.5 mm. Delineation uncertainties were small for both MRI and CT (mean reproducibility, 0-3.8 mm; SD, 1.0-2.3); they were most pronounced in the a AP and SI dimensions and at the superior/posterior-most aspect of the CTV. Retrospectively, the mean +/- SD CTV (prostate bed) percentage of volume receiving 100% of prescribed dose was only 77% +/- 26%.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Michalski JM, Lawton C, El Naqa I, et al. Development of RTOG consensus guidelines for the definition of the clinical target volume for postoperative conformal radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2010;76(2):361-368.	Review/Other-Dx	N/A	To define a prostate fossa-CTV for RTOG trials using postoperative RT for prostate cancer.	Starting from the model-derived CTV, consensus was reached for a CT image-based prostate fossa-CTV. The prostate fossa-CTV should extend superiorly from the level of the caudal vas deferens remnant to >8–12 mm inferior to vesicourethral anastomosis. Below the superior border of the pubic symphysis, the anterior border extends to the posterior aspect of the pubis and posteriorly to the rectum, where it may be concave at the level of the vesicourethral anastomosis. At this level, the lateral border extends to the levator ani. Above the pubic symphysis, the anterior border should encompass the posterior 1–2 cm of the bladder wall; posteriorly, it is bounded by the mesorectal fascia. At this level, the lateral border is the sacrorectogenitopubic fascia. SV remnants, if present, should be included in the CTV if there is pathologic evidence of their involvement.	4
67. Wang J, Kudchadker R, Choi S, et al. Local recurrence map to guide target volume delineation after radical prostatectomy. *Pract Radiat Oncol.* 2014;4(6):e239-246.	Review/Other-Dx	10 patients	To describe the various anatomic locations of recurrent disease, in a cohort of men with radiographically visualized, biopsy-proven recurrent prostate cancer after RP, in order to help guide contouring of the prostatic fossa-CTV when no gross recurrence is visible or when MRI is not used.	The median age at the time of RP was 61 years (range, 50–73). In the SI direction, recurrences ranged from the superior retrovesical region, to the inferior retrovesical region, to the posterior anastomosis, and as inferiorly as the posterior urogenital diaphragm. In the anteroposterior direction, the areas of recurrence ranged from involving the posterior bladder wall anteriorly to invading the rectum posteriorly. Recurrences were found at the center, right, and left of the prostate and SV fossa. When target volumes were delineated using RTOG-defined consensus prostatic fossa-CTV contours, coverage was marginal on recurrences in the posterolateral aspects of the CTV near the rectum and mesorectal fascia and lacking on recurrences occurring inferiorly at the posterior urogenital diaphragm.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Kim BS, Lashkari A, Vongtama R, Lee SP, Parker RG. Effect of pelvic lymph node irradiation in salvage therapy for patients with prostate cancer with a biochemical relapse following radical prostatectomy. *Clin Prostate Cancer.* 2004;3(2):93-97.	Observational-Tx	46 patients	To compare the results of postoperative RT delivered to extended fields (EFs), prostatic fossa, and pelvic LNs encompassing at least the obturator LNs with treatment of limited fields (LFs), prostatic fossa only, as salvage treatment for patients with a biochemical relapse.	The 10-year actuarial BDFS rates for the extended field and limited field groups were 52% and 47%, respectively (P=0.523). The distant metastasis-free survival rates were 77% and 78% (P=0.925), and OS rates were 88% and 68% (P=0.615) for the extended field and limited field group, respectively. A subset analysis of patients with adverse pathologic features (including tumor-involved surgical margins, LN involvement, SV involvement, ECE, and/or perineural invasion) showed BDFS rates of 57% and 44% (P=0.217) for the extended field and limited field groups, respectively. The distant metastasis-free survival rates were 84% and 72% (P=0.423), and OS rates 92% and 61% (P=0.366) for the extended field and limited field groups, respectively. For patients with increasing PSA levels after a RP, salvage irradiation is a viable option for biochemical control.	2
69. Spiotto MT, Hancock SL, King CR. Radiotherapy after prostatectomy: improved biochemical relapse-free survival with whole pelvic compared with prostate bed only for high-risk patients. *Int J Radiat Oncol Biol Phys.* 2007;69(1):54-61.	Observational-Tx	160 patients	To compare the bRFS among patients receiving WPRT vs PBRT after RP.	WPRT resulted in superior bRFS compared with PBRT (P=0.03). The advantage of WPRT was limited to high-risk patients, with a 5-year bRFS rate of 47% (95% confidence interval, 35-59%) after WPRT vs 21% (95% confidence interval, 8-35%) after PBRT (P=0.008). For low-risk patients, no difference (P=0.9) was found. On multivariate analysis, only WPRT (P=0.02) and a preoperative PSA level <1.0 ng/mL (P=0.002) were significantly associated with bRFS. The benefit from total androgen suppression with postoperative RT was only observed when given concurrently with WPRT (P=0.04) and not with PBRT (P=0.4).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
70. Deville C, Vapiwala N, Hwang WT, et al. Comparative toxicity and dosimetric profile of whole-pelvis versus prostate bed-only intensity-modulated radiation therapy after prostatectomy. *Int J Radiat Oncol Biol Phys.* 2012;82(4):1389-1396.	Observational-Tx	67 patients	To assess whether whole-pelvis IMRT for prostate cancer after prostatectomy is associated with increased toxicity compared to prostate-bed only IMRT.	Pretreatment demographics including age and comorbidities were similar between groups. Whole-pelvis patients had higher GSs, T stages, and preoperative PSA levels, and more whole-pelvis patients underwent ADT. Whole-pelvis minimum (Dmin) and mean bladder doses, bladder volumes receiving >5 Gy (V5) and V20, rectal Dmin, and prostate-bed bladder and rectal V65 were significantly increased. Maximum acute GI toxicity was Grade 2 and was increased for whole-pelvis (61%) vs prostate-bed (29%) patients (P=0.001); there was no significant difference in acute Grade ≥2 GU toxicity (22% whole-pelvis vs 10% prostate-bed; P=0.193), late Grade ≥2 GI toxicity (3% whole-pelvis vs 0% prostate-bed; P=0.678), or late Grade ≥2 GU toxicity (28% whole-pelvis vs 19% prostate-bed; P=0.274) with 25-month median follow-up (range, 12–44 months). On multivariate analysis, long-term ADT use was associated with Grade ≥2 late GU toxicity (P=0.02).	2
71. Pollack A. RTOG 0534: A Phase III Trial of Short Term Androgen Deprivation With Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients With a Rising PSA After Radical Prostatectomy. 2014; https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0534.	Review/Other-Tx	Ongoing	To determine whether the addition of NC-STAD to PBRT improves freedom from progression [maintenance of a PSA less than the nadir+2 ng/mL, absence of clinical failure and absence of death from any cause] for 5 years, over that of PBRT alone in men treated with salvage RT after RP; To determine whether NC-STAD+PLNRT+PBRT improves freedom from progression over that of NC-STAD+PBRT and PBRT alone in men treated with salvage RT after RP.	This trial is still recruiting study subjects and results are not available yet.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
72. Malone S, Croke J, Roustan-Delatour N, et al. Postoperative radiotherapy for prostate cancer: a comparison of four consensus guidelines and dosimetric evaluation of 3D-CRT versus tomotherapy IMRT. *Int J Radiat Oncol Biol Phys.* 2012;84(3):725-732.	Observational-Dx	20 patients	To compare the CTVs and the volume of normal tissue irradiated using the current consensus recommendations with the aim of achieving a better understanding of how the choice of treatment guideline affects the parameters that can affect the treatment outcomes and toxicity. To determine the ability of the different consensus CTV guidelines to meet the rectal and bladder dose-volume histogram constraints proposed in QUANTEC and the ongoing RADICALS trial. To compare the 3D-CRT plans and the tomotherapy IMRT plans using the CTV RTOG guideline to evaluate the potential benefits of IMRT.	The CTV differed significantly between guidelines (P<0.001). The European Organization for Research and Treatment of Cancer-CTVs were significantly smaller than the other CTVs (P<0.001). Differences in prostate bed coverage superiorly accounted for the major volumetric differences between the guidelines. Using 3D-CRT, the dose-volume histograms rarely met the QUANTEC or RADICALS rectal constraints, independent of the guideline used. The RADICALS bladder constraints were met most often by the European Organization for Research and Treatment of Cancer consensus guideline (14/20). The tomotherapy IMRT plans resulted in significant organs-at-risk sparing compared with the 3D-CRT plans; however, the RADICALS and QUANTEC criteria were still missed in a large percentage of cases.	3
73. Ost P, De Meerleer G, Vercauteren T, et al. Delineation of the postprostatectomy prostate bed using computed tomography: interobserver variability following the EORTC delineation guidelines. *Int J Radiat Oncol Biol Phys.* 2011;81(3):e143-149.	Observational-Dx	10 patients; 6 observers	To assess the interobserver agreement of prostate bed delineation after RP using CT alone as proposed by the European Organization for Research and Treatment of Cancer guidelines.	The mean volume of 100% agreement (+/-1 SD) was only 5.0 (+/-3.3) mL for the prostate bed and 0.9 (+/-1.5) mL for the SV, whereas the mean union of all contours (+/-1 SD) was 41.1 (+/-11.8) mL and 25.3 (+/-13.4) mL, respectively. The mean overall agreement corrected for chance was moderate for both the prostate bed (mean kappa, 0.49; range, 0.35–0.62) and SV (mean kappa, 0.42; range, 0.22–0.59). The overall SD of the outer margins of the PB ranged from 4.6 to 7.0 mm.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
74. Sefrova J, Odrazka K, Paluska P, et al. Magnetic resonance imaging in postprostatectomy radiotherapy planning. *Int J Radiat Oncol Biol Phys.* 2012;82(2):911-918.	Observational-Dx	21 patients	To investigate whether the use of MRI in prostate bed treatment planning could influence definition of the CTV and organs at risk.	The CTV was significantly reduced on the T1- and T2-weighted MRI scans (13% and 9%, respectively) compared with the CT scans. The urinary bladder was drawn smaller on the CT scans and the rectum was smaller on the MRI scans. On T1 MRI, the rectum and urinary bladder were delineated larger than on T2 MRI. Minimal agreement was observed between the CT and T2 images. The main spatial differences were measured in the superior and superolateral directions in which the CTV on the MRI scans was 1.8–2.9 mm smaller. In the posterior and inferior border, no difference was seen between the CT and T1 MRI scans. On the T2 MRI scans, the CTV was larger in these directions (by 1.3 and 1.7 mm, respectively).	3
75. Croke J, Malone S, Roustan Delatour N, et al. Postoperative radiotherapy in prostate cancer: the case of the missing target. *Int J Radiat Oncol Biol Phys.* 2012;83(4):1160-1168.	Observational-Dx	20 patients	To evaluate the utility of preoperative MRI in defining prostate bed CTV.	Gross tumor was visible in 18 cases. In all 20 cases, the consensus CTVs did not fully cover the MRI-defined prostate. On average, 35% of the prostate volume and 32% of the gross tumor volume were missed using six-field 3D treatment plans. The entire MRI-defined gross tumor volume was completely covered in only 2 cases (six-field plans). The expanded PTVs did not cover the entire prostate bed in 50% of cases. Prostate base and mid-zones were the predominant site of inadequate coverage.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Kitamura K, Shirato H, Seppenwoolde Y, et al. Three-dimensional intrafractional movement of prostate measured during real-time tumor-tracking radiotherapy in supine and prone treatment positions. *Int J Radiat Oncol Biol Phys.* 2002;53(5):1117-1123.	Experimental-Tx	50 sets for 10 patients	To quantify 3D movement of the prostate gland with the patient in the supine and prone positions and to analyze the movement frequency for each treatment position.	No apparent difference in movement was found among individuals. The amplitude of 3D movement was 0.1–2.7 mm in the supine and 0.4–24 mm in the prone positions. The amplitude in the supine position was statistically smaller in all directions than that in the prone position ($P<0.0001$). The amplitude in the craniocaudal and AP directions was larger than in the left-right direction in the prone position ($P<0.0001$). No characteristic movement frequency was detected in the supine position. The respiratory frequency was detected for all patients regarding movement in the craniocaudal and AP directions in the prone position. The results of the frequency analysis suggest that prostate movement is affected by the respiratory cycle and is influenced by bowel movement in the prone position.	2
77. McLaughlin PW, Wygoda A, Sahijdak W, et al. The effect of patient position and treatment technique in conformal treatment of prostate cancer. *Int J Radiat Oncol Biol Phys.* 1999;45(2):407-413.	Experimental-Tx	10 patients	To show that the prone treatment position would lead to better stabilization than supine positioning as the prostate would rest against the bony symphysis rather than the less rigid, less stable rectum and pelvic soft tissues.	For prostate or prostate/SV treatments, prone flat was advantageous or equivalent to other positions with regard to rectal sparing. The mechanism of rectal sparing in the prone position may be related to a paradoxical retraction of the rectum against the sacrum, away from the prostate/SV. Although there was no clear overall preference for beam arrangement, substantial improvements in rectal sparing could be realized for individual patients. In this limited number of patients, there was no convincing evidence prostate position was stabilized by prone relative to supine position.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
78. Vargas C, Saito AI, Hsi WC, et al. Cine-magnetic resonance imaging assessment of intrafraction motion for prostate cancer patients supine or prone with and without a rectal balloon. *Am J Clin Oncol.* 2010;33(1):11-16.	Experimental-Dx	68 studies: 17 different series on 7 patients	To determine prostate intrafraction motion with Cine-MRI and deformable registration.	The variation/SD of the prostate position during 240 seconds was: supine with rectal balloon: 0.55 mm, without rectal balloon: 1.2 mm, and prone with rectal balloon: 1.48 mm, without rectal balloon: 2.15 mm (P<0.001). A strong relationship was observed between time and prostate motion. For the initial 120 s the SD was smaller than for the second 120 s supine with rectal balloon 0.54 mm vs 1.37 mm; supine without rectal balloon 0.61 mm vs 1.70 mm; prone with rectal balloon 0.85 mm vs 1.85 mm; and prone without rectal balloon 1.60 mm vs 2.56 mm. The probabilities for prostate staying within +/-2 mm to its initial position are: 94.8% supine with rectal balloon; 91.5% supine without rectal balloon; 92.3% prone with rectal balloon; 79.2% prone without rectal balloon. Intrafraction prostate motion was found dependent on time, patient position, and the use of a rectal balloon. Relatively stable positions can be obtained for 4 minutes or less especially in the supine position with a rectal balloon.	2
79. Wilder RB, Chittenden L, Mesa AV, et al. A prospective study of intrafraction prostate motion in the prone vs. supine position. *Int J Radiat Oncol Biol Phys.* 2010;77(1):165-170.	Experimental-Tx	15 patients	To prospectively analyze prostate intrafraction motion in the prone vs supine position and to assess patient satisfaction with these 2 positions.	Mean +/- SD intrafraction prostate motion was 2.1 +/- 1.2 mm and 1.7 +/- 1.4 mm (AP, P=0.47) 2.2 +/- 2.0 mm and 1.6 +/- 1.8 mm (SI, P=0.16), and 1.0 +/- 1.2 mm and 0.6 +/- 0.9 mm (left-right, P=0.03) in the prone and supine positions, respectively. 80% of patients stated that they were more comfortable in the supine position (P=0.02). Prone and supine positions resulted in a similar magnitude of AP and SI intrafraction prostate motion (2 mm). Because there was no significant difference in the magnitude of AP and SI prostate motion prone vs supine and patients were more comfortable in the supine position, patients now undergo IMRT to the prostate and SVs at our center in the supine position.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
80. Liu B, Lerma FA, Patel S, et al. Dosimetric effects of the prone and supine positions on image guided localized prostate cancer radiotherapy. *Radiother Oncol.* 2008;88(1):67-76.	Experimental-Tx	20 patients	To compare target coverage and doses to rectum and bladder in IMRT of localized prostate cancer in the supine vs prone position, with the inclusion of image guidance.	As expected, alignment based on skin marks yielded unacceptable dose coverage for both groups of patients. Under bony alignment, the target coverage index, V95, was 97.3% and 93.6% for prone and supine patients (P<0.0001), respectively. The mean PTV overlap indices were 90.7% and 84.7% for prone and supine patients (P<0.0002), respectively. In the supine position 36% of cases showed a V95<95% after bony alignment, while only 12.5% of prone patients with V95<95% following bony alignment. Under soft-tissue alignment matching the center of mass of the prostate, the mean V95 was 99.3% and 98.6% (P<0.03) and the PTV overlap index was 97.7% and 94.8% (P<0.0002) for prone and supine groups, respectively.	1
81. Dawson LA, Litzenberg DW, Brock KK, et al. A comparison of ventilatory prostate movement in four treatment positions. *Int J Radiat Oncol Biol Phys.* 2000;48(2):319-323.	Experimental-Tx	4 patients	To report the influence of patient orientation and immobilization on prostate movement due to breathing.	During normal breathing, maximal movement of the prostate markers was seen in the prone position (cranial-caudal range: 0.9–5.1 mm; AP range: up to 3.5 mm). In the supine position, prostate movement during normal breathing was <1 mm in all directions. Deep breathing resulted in cranial-caudal movements of 3.8–10.5 mm in the prone position (with and without an aquaplast mold). This range was reduced to 2.0–7.3 mm in the supine position and 0.5–2.1 mm with the use of the false table top. Deep breathing resulted in AP skeletal movements of 2.7–13.1 mm in the prone position, whereas AP skeletal movements in the supine position were negligible. Ventilatory movement of the prostate is substantial in the prone position and is reduced in the supine position. The potential for breathing to influence prostate movement, and thus the dose delivered to the prostate and normal tissues, should be considered when positioning and planning patients for CRT.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
82. Malone S, Crook JM, Kendal WS, Szanto J. Respiratory-induced prostate motion: quantification and characterization. *Int J Radiat Oncol Biol Phys.* 2000;48(1):105-109.	Experimental-Tx	40 total patients: 20 consecutive patients evaluated prone; 20 patients evaluated prone and supine	To identify and characterize a potential cause of inaccurate prostatic localization-respiratory-induced movement.	When the patients were immobilized prone in thermoplastic shells, the prostate moved synchronously with respiration. In the study the prostate was displaced a mean distance of 3.3 +/- 1.8 (SD) mm (range, 1–10.2 mm), with 23% (9/40) of the displacements being ≥4 mm. The respiratory-associated prostate movement decreased significantly when the thermoplastic shells were removed. Significant prostate movement can be induced by respiration when patients are immobilized in thermoplastic shells. This movement presumably is related to transmitted intra-abdominal pressure within the confined space of the shells. Careful attention to the details of immobilization and to the possibility of respiratory-induced prostate movements is important when employing small field margins in prostatic RT.	2
83. Kneebone A, Gebski V, Hogendoorn N, Turner S. A randomized trial evaluating rigid immobilization for pelvic irradiation. *Int J Radiat Oncol Biol Phys.* 2003;56(4):1105-1111.	Experimental-Tx	100 total patients	To assess whether the use of rigid immobilization devices improve the accuracy and reproducibility of prostate irradiation to a clinically useful degree.	The average simulation-to-treatment deviation of the isocenter position was 8.5 mm in the control group and 6.2 mm in the immobilization group ($P<0.001$). In the control arm, 30.9% of port films had isocenter deviations >10 mm compared with 10.6% in the immobilized arm ($P=0.001$). For the control group, average deviations in the AP, right-left, and SI directions were 5.2 mm, 3.2 mm, and 4.3 mm, respectively, compared with 2.9 mm, 2.1 mm, and 3.9 mm for the immobilized group ($P\leq0.001$, $P<0.001$, $P=0.55$). Treatment times were very similar between the 2 groups: the average treatment time was 15.5 min in the control group vs 16.1 min in the immobilized group ($P=0.82$). The use of rigid immobilization improves the accuracy of treatment delivery for the prone position, especially in the AP direction. Of clinical importance, the number of major deviations >10 mm (that is, that would result in a geographic miss) was reduced from 31% to 11%.	1

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
84. Rosewall T, Chung P, Bayley A, et al. A randomized comparison of interfraction and intrafraction prostate motion with and without abdominal compression. *Radiother Oncol.* 2008;88(1):88-94.	Experimental-Tx	32 patients	To quantify inter- and intrafraction prostate motion in a standard VacLok immobilization device or in the BodyFix system incorporating a compression element which may reduce abdominal movement.	There were no significant differences in interfraction (P=0.002) or intrafraction (P=0.16) prostate motion with or without abdominal compression. Median intrafraction motion was slightly smaller than interfraction motion in the AP (7.0 mm vs 7.6 mm) and SI direction (3.2 mm vs 4.7 mm). The final image captured the maximal intrafraction displacement in only 40% of fractions. Our PTV incorporated >95% of total prostate motion. Intrafraction motion became the major source of error during RT after online correction of interfraction prostate motion. The addition of 120 mbar abdominal compression to custom pelvic immobilization influenced neither interfraction nor intrafraction prostate motion.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
85. Bayley AJ, Catton CN, Haycocks T, et al. A randomized trial of supine vs. prone positioning in patients undergoing escalated dose conformal radiotherapy for prostate cancer. *Radiother Oncol.* 2004;70(1):37-44.	Experimental-Tx	28 patients	Randomized trial to evaluate the effects of supine and prone positioning on organ motion, positioning errors, and dose to critical organs and satisfaction with setup technique.	Prostate motion in AP direction was statistically significantly less in the supine position ($P<0.05$). More pretreatment corrections were required for patients in the prone position. The dose volume histogram analysis demonstrated larger volumes of the bladder wall, rectal wall and small bowel within the D95, D80 and D50% when comparing the PTV actually treated for prone positioning. When the prone PTV was expanded to account for the greater prostate motion encountered in that position, a statistically significant difference ($P<0.007$) was observed in favor of the supine position at all dose levels. In the prone position, 4 patients had small bowel within the 60 Gy isodose and in the supine position. Supine position was significantly more comfortable for the patients and setup was significantly easier for the radiation therapists. There were statistically significant improvements at all dose levels for small bowel, rectal wall and bladder wall doses in the supine position once corrections were made for differences in organ motion. Supine positioning has been adopted as the standard for conformal prostatic irradiation at our center.	1
86. Shah AP, Kupelian PA, Willoughby TR, Langen KM, Meeks SL. An evaluation of intrafraction motion of the prostate in the prone and supine positions using electromagnetic tracking. *Radiother Oncol.* 2011;99(1):37-43.	Experimental-Tx	20 patients	To evaluate differences in target motion during prostate irradiation in the prone vs supine position using electromagnetic tracking to measure prostate mobility.	Clear patterns of respiratory motion were seen in the prone tracks due to the influence of increased abdominal motion. Averaged over all patients, the prostate was displaced >3 and 5 mm for 37.8% and 10.1% of the total tracking time in the prone position, respectively. In the supine position, the prostate was displaced >3 and 5 mm for 12.6% and 2.9%, respectively. With both patient setups, inferior and posterior drifts of the prostate position were observed. Averaged over all prone tracking sessions, the prostate was displaced >3 mm in the posterior and inferior directions for 11.7% and 9.5% of the total time, respectively.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
87. de Crevoisier R, Melancon AD, Kuban DA, et al. Changes in the pelvic anatomy after an IMRT treatment fraction of prostate cancer. *Int J Radiat Oncol Biol Phys.* 2007;68(5):1529-1536.	Experimental-Tx	46 patients	To quantify the 3D variations of pelvic anatomy after a single treatment fraction.	During 1 treatment fraction (21 +/- 4 min), both the prostate and SVs showed statistically significant systematic trends in the superior and anterior directions of the patient's anatomy. The net increase in bladder volume was huge (127 +/- 79 cm(3)), yet this change did not translate into large target displacements. Although the population mean displacements in either direction were 1.3 +/- 2.9 mm for the prostate and 1.2 +/- 4.1 mm for the SVs in the anterior direction, a few patients had displacements as large as 8.4 mm and 15.6 mm, respectively. These large displacements correlated strongly ($P<0.001$) with large rectal volume increases caused by gaseous build-up in the rectum.	2
88. Guckenberger M, Pohl F, Baier K, Meyer J, Vordermark D, Flentje M. Adverse effect of a distended rectum in intensity-modulated radiotherapy (IMRT) treatment planning of prostate cancer. *Radiother Oncol.* 2006;79(1):59-64.	Observational-Tx	10 patients	To evaluate whether proximal rectum and supra-anal rectum/anal canal should be delineated as separated organs-at-risk to achieve optimal dose distributions to the anorectal region in IMRT of prostate cancer.	Results from both TPS showed significantly increased doses to the distal rectum/anal canal for plans Rec-tot compared with Rec-sep in case of a distended rectum in the planning CT study: doses were increased by up to mean 31% ($P=0.02$) and 18% ($P=0.03$), respectively, in both TPS. For the patient with the largest rectum, the maximum dose increase was 61%. No significant differences in doses to target, bladder, femoral head and proximal rectum were seen.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
89. de Crevoisier R, Tucker SL, Dong L, et al. Increased risk of biochemical and local failure in patients with distended rectum on the planning CT for prostate cancer radiotherapy. *Int J Radiat Oncol Biol Phys*. 2005;62(4):965-973.	Observational-Tx	127 patients	To retrospectively test the hypothesis that rectal distension on the planning CT scan is associated with an increased risk of biochemical and local failure among patients irradiated for prostate carcinoma when a daily repositioning technique based on direct prostate-organ localization is not used.	The incidence of biochemical failure was significantly higher among patients with distended rectums (cross-sectional rectal area >11.2 cm(2)) on the planning CT scan (P=0.0009, log-rank test). Multivariate analysis indicates that rectal distension and high-risk disease are independent risk factors for biochemical failure, with HR of 3.89 (95% CI, 1.58 to 9.56, P=0.003) and 2.45 (95% CI, 1.18 to 5.08, P=0.016), respectively. The probability of residual tumor without evidence of radiation treatment (as scored by the pathologist) increased significantly with rectal distension (P=0.010, logistic analysis), and a lower incidence of Grade 2 or greater late rectal bleeding within 2 years was simultaneously observed with higher cross-sectional rectal area values (P=0.031, logistic analysis). We found strong evidence that rectal distension on the treatment-planning CT scan decreased the probability of biochemical control, local control, and rectal toxicity in patients who were treated without daily image-guided prostate localization, presumably because of geographic misses. Therefore, an empty rectum is warranted at the time of simulation. These results also emphasize the need for IGRT to improve local control in irradiating prostate cancer.	2
90. Hynds S, McGarry CK, Mitchell DM, et al. Assessing the daily consistency of bladder filling using an ultrasonic Bladderscan device in men receiving radical conformal radiotherapy for prostate cancer. *Br J Radiol.* 2011;84(1005):813-818.	Experimental-Tx	30 men	To evaluate the effectiveness of bladder-filling instructions in achieving a consistent and reproducible bladder volume at the time of planning CT and daily during the course of radical RT for prostate cancer and to assess the rate of bladder filling before and at the end of RT.	The mean bladder volume at the time of planning was 282 mL (range 89–608 ml, SD = 144.5 ml). This fell during treatment, with a mean value for all treatments of 189 mL (range 11–781 mL, SD = 134 ml). During RT, 76% (828/1090), 53% (579/1090) and 36% (393/1090) of bladder volumes had >50 mL, >100 mL and >150 mL difference, respectively when compared with their volume at the time of planning. Inflow reduced from 4.6 mL min(-1), SD = 2.9 min(-1) at planning to 2.5 min(-1), SD = 1.8 min(-1) after RT.	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
91. Tsai CL, Wu JK, Wang CW, Hsu FM, Lai MK, Cheng JC. Using cone-beam computed tomography to evaluate the impact of bladder filling status on target position in prostate radiotherapy. *Strahlenther Onkol.* 2009;185(9):588-595.	Experimental-Dx	23 patients	To assess bladder filling status and its impact on target position during daily IMRT using CBCT in prostate cancer patients.	A total of 867 CBCT images were evaluated. The average left-right, AP, and SI bladder dimensions were 7.8 +/- 1.5 cm, 6.7 +/- 1.4 cm, and 5.6 +/- 1.7 cm, respectively. The average left-right, AP, and SI bladder dimension change ratios were 0.88 +/- 0.17, 0.90 +/- 0.15, and 0.86 +/- 0.32, respectively. The SD was significantly greater in SI dimension than in left-right (P<0.001) and AP (P<0.001) dimensions. The interfraction changes in the 3 bladder dimensions were significantly larger than those of target position, and did not correlate with target position changes.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
92. Moiseenko V, Liu M, Kristensen S, Gelowitz G, Berthelet E. Effect of bladder filling on doses to prostate and organs at risk: a treatment planning study. *J Appl Clin Med Phys.* 2007;8(1):55-68.	Experimental-Dx	21 patients	To evaluate effects of bladder filling on dose-volume distributions for bladder, rectum, PTV, and prostate in RT of prostate cancer.	Mean bladder volume was 354.3 cm3 when full and 118.2 cm3 when empty. Median prostate equivalent uniform dose was 70 Gy for plans based on full- and empty-bladder scans alike. The median rectal Deff was 55.6 Gy for full-bladder anatomy and 56.8 Gy for empty-bladder anatomy, and the corresponding bladder Deff was 29.0 Gy and 49.3 Gy respectively. In 1 patient, part of the small bowel (7.5 cm3) received more than 50 Gy with full-bladder anatomy, and in 6 patients, part (2.5 cm3–30 cm3) received more than 50 Gy with empty-bladder anatomy. Bladder filling had no significant impact on prostate equivalent uniform dose or rectal Deff. A minimal volume of the small bowel received more than 50 Gy in both groups, which is below dose tolerance. The bladder Deff was higher with empty-bladder anatomy; however, the predicted complication rates were clinically insignificant. When the multileaf collimator pattern was applied in reverse, substantial underdosing of the PTV was observed, particularly for patients with prostate shifts in excess of 0.5 cm in any 1 direction. However, the prostate shifts showed no correlation with bladder filling, and therefore the PTV underdosing also cannot be related to bladder filling. For some patients, bladder dose-volume constraints were not fulfilled in the worst-case scenario-that is, when a patient planned with full bladder consistently arrived for treatment with an empty bladder.	2
93. Heemsbergen WD, Hoogeman MS, Witte MG, Peeters ST, Incrocci L, Lebesque JV. Increased risk of biochemical and clinical failure for prostate patients with a large rectum at radiotherapy planning: results from the Dutch trial of 68 GY versus 78 Gy. *Int J Radiat Oncol Biol Phys.* 2007;67(5):1418-1424.	Experimental-Tx	549 patients	To investigate whether a large rectum filling visible on the planning CT scan was associated with a decrease in freedom from any failure and freedom from clinical failure for prostate cancer patients.	Significant results were observed only for patients with a risk of SV involvement >25% (dose of 68–78 Gy to the SVs, n = 349). We found a decrease in freedom from any failure (P=0.001) and freedom from clinical failure (P=0.01) for the 87 patients with RF1 (for RF2, P=0.02 and P=0.01, respectively). The estimated decrease in the freedom from clinical failure rate at 5 years was 15%.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
94. Smitsmans MH, Pos FJ, de Bois J, et al. The influence of a dietary protocol on cone beam CT-guided radiotherapy for prostate cancer patients. *Int J Radiat Oncol Biol Phys.* 2008;71(4):1279-1286.	Experimental-Tx	49 total patients	To evaluate the influence of a dietary protocol on CBCT image quality, which is an indirect indicator for short-term (intrafraction) prostate motion, and on interfraction motion.	Feces, gas, and moving gas significantly decreased from 55%, 61%, and 43% of scans in the nondiet group to 31%, 47%, and 28% in the diet group (all $P<0.001$). Since there is a known relation between gas and short-term prostate motion, intrafraction prostate motion probably also decreased. The success rate of 3D-gray-value registration improved from 83% to 94% ($P<0.001$). A decrease in random interfraction prostate motion also was found, which was not significant after Bonferroni's correction. Significant deviations from planning CT position for rotations around the left-right axis were found in both groups.	2
95. Nichol AM, Warde PR, Lockwood GA, et al. A cinematic magnetic resonance imaging study of milk of magnesia laxative and an antiflatulent diet to reduce intrafraction prostate motion. *Int J Radiat Oncol Biol Phys.* 2010;77(4):1072-1078.	Experimental-Tx	42 patients	To determine the reduction of prostate motion during a typical RT fraction from a bowel regimen comprising an antiflatulent diet and daily milk of magnesia.	The mean rectal area was: 13.5 cm(2) at MRI-baseline, 12.7 cm(2) at MRI-CT, and 12.3 cm(2) at MRI-RT (MRI-baseline vs MRI-CT, $P=0.11$; MRI-baseline vs MRI-CT, $P=0.07$). Moving rectal gas alone (56%) and moving gas and stool (18%) caused 74% of intrafraction prostate motion. The PTPM3 was 11.3% at MRI-baseline, 4.8% at MRI-CT, and 12.0% at MRI-RT (MRI-baseline vs MRI-CT, $P=0.12$; MRI-baseline vs MRI-RT, $P=0.89$). For subjects voiding their rectum before imaging, an antiflatulent diet and milk of magnesia laxative did not significantly reduce initial rectal area or intrafraction prostate motion.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
96. Button MR, Staffurth JN. Clinical application of image-guided radiotherapy in bladder and prostate cancer. *Clin Oncol (R Coll Radiol)*. 2010;22(8):698-706.	Review/Other-Tx	N/A	To review issues associated with internal organ motion for bladder and prostate cancer.	Bladder cancer and prostate cancer are 2 malignancies where significant target motion occurs, necessitating the use of margins to account for this. The causes and solutions are different: for bladder cancer, changes in the shape of the target volume require changes to the volume treated; for prostate cancer, a 3D vector displacement requires accurate alignment of the isocenter. Historically these margins have been population derived yet this is now known to be suboptimal individualized margins are desirable and are possible, optimizing the accuracy of RT delivery for each patient. The optimal method for this is yet to be defined.	4
97. Yahya S, Zarkar A, Southgate E, Nightingale P, Webster G. Which bowel preparation is best? Comparison of a high-fibre diet leaflet, daily microenema and no preparation in prostate cancer patients treated with radical radiotherapy to assess the effect on planned target volume shifts due to rectal distension. *Br J Radiol.* 2013;86(1031):20130457.	Observational-Tx	3 cohorts of 10 patients	To evaluate and compare a high-fiber diet leaflet, daily microenema and no preparation to establish how best to achieve consistent bowel preparation in prostate cancer patients being treated with radical RT.	Mean rectal cross-sectional area in the post-enema group was reduced compared with both pre-leaflet (P=0.010) and post-leaflet values (P=0.031). The magnitude of observed mean prostate shifts was significantly reduced in the post-enema group compared with the pre-leaflet group (P=0.014). The proportion of scans showing geometric miss (i.e. shift >5 mm) in the post-enema group (31%) was significantly lower than in the pre-leaflet (62%, P<0.001) or post-leaflet groups (56%, P<0.001).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
98. Court LE, D'Amico AV, Kadam D, Cormack R. Motion and shape change when using an endorectal balloon during prostate radiation therapy. *Radiother Oncol.* 2006;81(2):184-189.	Review/Other-Tx	9 patients	To investigate motion and shape change when using an endorectal balloon in patients receiving RT for prostate cancer.	86% of all inter-imaging shifts of the anterior wall of the endorectal balloon were in the posterior direction (mean: 1.8 mm, 1 SD: 1.8 mm, maximum posterior shift: 2.8–7.2 mm). The inter-fraction shape change (1 SD) of the anterior wall was equivalent to a change in the angle of the balloon of 2.5–5.7 degrees, with a range of 8–20 degrees, depending on the patient. Inter-imaging shape changes were similar in size. The inter-imaging motion and shape changes may be explained by the patient relaxing sometime after insertion of the endorectal balloon, indicating that it could be reduced by a waiting period after insertion before irradiation. Development of image-guided localization strategies should consider intra-fraction motion and also inter- and intra-fraction shape change.	4
99. Smeenk RJ, Teh BS, Butler EB, van Lin EN, Kaanders JH. Is there a role for endorectal balloons in prostate radiotherapy? A systematic review. *Radiother Oncol.* 2010;95(3):277-282.	Review/Other-Tx	N/A	To give an overview of published data concerning endorectal balloon application in prostate RT.	Overall, endorectal balloons are tolerated well, although patients with pre-existing anorectal disease have an increased risk of developing endorectal balloon-related toxicity. Planning studies show reduced rectal wall and anal wall doses with endorectal balloon application. Clinical data, however, are scarce, as only 1 study shows reduced late rectal damage. There is no consensus about the immobilizing properties of endorectal balloons and it is recommended to use additional set-up and correction protocols, especially because there are potential pitfalls.	4
100. Smeenk RJ, van Lin EN, van Kollenburg P, Kunze-Busch M, Kaanders JH. Anal wall sparing effect of an endorectal balloon in 3D conformal and intensity-modulated prostate radiotherapy. *Radiother Oncol.* 2009;93(1):131-136.	Experimental-Tx	24 patients	To investigate the anal wall sparing effect of an endorectal balloon in 3D-CRT and IMRT for prostate cancer.	In the 3D-CRT plans, an endorectal balloon significantly reduced D(mean), D(max), and V(30)-V(70). For IMRT all investigated dose parameters were significantly reduced by the endorectal balloon. The absolute reduction of D(mean) was 12 Gy in 3D-CRT and was 7.5 Gy in IMRT for both methods of anal wall delineation. Application of an endorectal balloon showed a significant anal wall sparing effect in both 3D-CRT and IMRT. This may lead to reduced late anal toxicity in prostate RT.	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
101. van Lin EN, Kristinsson J, Philippens ME, et al. Reduced late rectal mucosal changes after prostate three-dimensional conformal radiotherapy with endorectal balloon as observed in repeated endoscopy. *Int J Radiat Oncol Biol Phys.* 2007;67(3):799-811.	Experimental-Tx	48 patients, 146 endoscopies, 2,336 mucosal areas	To investigate prospectively the rectal wall spatial dose distribution, toxicity, and mucosal changes after prostate cancer RT with or without an endorectal balloon.	The endorectal balloon significantly reduced the rectal wall volume exposed to doses >40 Gy. Late rectal toxicity (grade ≥1, including excess of bowel movements and slight rectal discharge) was reduced significantly in the endorectal balloon group. A total of 146 endoscopies and 2,336 mucosal areas were analyzed. Telangiectases were most frequently seen and appeared after 6 months. At 1 and 2 years, significantly less high-grade telangiectasia (T 2-3) was observed in the endorectal balloon group at the lateral and posterior part of the rectal wall. In mucosal areas exposed to doses >40 Gy, less high-grade telangiectases (T 2-3) were seen in the endorectal balloon group compared with the No-endorectal balloon group. An endorectal balloon reduced the rectal wall volume exposed to doses >40 Gy, resulting in reduction of late rectal mucosal changes and reduced late rectal toxicity. Although further analysis is needed, these data suggest an endorectal balloon-induced increased tolerance for late rectal wall damage.	1

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
102. Zaorsky NG, Harrison AS, Trabulsi EJ, et al. Evolution of advanced technologies in prostate cancer radiotherapy. *Nat Rev Urol.* 2013;10(10):565-579.	Review/Other-Tx	N/A	To review advanced technologies in prostate cancer RT.	Advances in IGRT since the 1980s, the development of IMRT during the 1990s and evidence from radiobiological models–which support the use of high doses per fraction–have developed alongside novel advanced RT modalities that include high-dose-rate brachytherapy, SBRT and proton beam therapy. The relationship between the outcomes of and toxicities experienced by patients with prostate cancer treated with high-dose-rate brachytherapy, SBRT and particle-beam therapy should provide urologists and oncologists an understanding of the continually evolving technology in prostate RT. On the basis of published evidence, conventionally fractionated EBRT with IMRT is considered the standard of care over conventional 3D-CRT, whereas high-dose-rate brachytherapy boost is an acceptable treatment option for selected patients with intermediate-risk and high-risk prostate cancer. SBRT and proton therapy should not be used for patients (regardless of disease risk group) outside the setting of a clinical trial.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
103. Bastasch MD, Teh BS, Mai WY, McGary JE, Grant WH, 3rd, Butler EB. Tolerance of endorectal balloon in 396 patients treated with intensity-modulated radiation therapy (IMRT) for prostate cancer. *Am J Clin Oncol.* 2006;29(1):8-11.	Observational-Tx	396 patients	To report patient tolerance and acute anorectal toxicity of an endorectal balloon used for prostate immobilization during 35 daily fractions.	RTOG grades 1 and 2 rectal toxicity occurred in 55/396 (13.9%) and 73/396 (18.4%), respectively. Topical anal medications were prescribed for 46/396 (11.6%) patients and antidiarrhea medication for 27/396 (6.8%) patients. Of patients with pretreatment anorectal disease, 50% developed rectal toxicities over the 7 weeks. Rectal toxicity occurred most frequently in the third, fourth, fifth, or sixth week; 19.5%, 20.8%, 18.2%, and 16.9%, respectively. The duration of the toxicity measured lasted 1 week, 35.2%; 2 weeks, 31.0%; 3 weeks, 15.5%; 4 weeks, 11.3%; 5 weeks, 4.2%; and 6 weeks, 2.8%. Most of the patients, 393/396 (99.2%), tolerated a 100 mL endorectal immobilization balloon for IMRT. The rate of acute anorectal toxicity was acceptable with no grade 3 or 4 toxicities. Duration of the toxicities typically was 1 to 2 weeks. Patients with pre-existing anorectal disease are at higher risk of developing acute anorectal toxicity with the use of an endorectal balloon.	2
104. Wachter S, Gerstner N, Dorner D, et al. The influence of a rectal balloon tube as internal immobilization device on variations of volumes and dose-volume histograms during treatment course of conformal radiotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2002;52(1):91-100.	Experimental-Tx	10 consecutive patients	To describe the effects of an air-inflated rectal balloon tube that has been used for prostate immobilization.	By use of the balloon, rectum filling variations (P=0.04) and maximum AP displacements of the prostate (P=0.008) were reduced significantly, leading to a reduction in dose-volume histograms variations during treatment. Maximum displacements of posterior prostate border (>5 mm) were found in 8/10 patients without a rectum balloon and in only 2/10 patients with the balloon. The balloon led to a significant reduction in partial posterior rectal wall volumes included in the high-dose regions, without significant changes at the anterior rectum wall in cases of irradiation of the prostate only. However, when entirely irradiating the whole SV, this advantage was lost. A rectal balloon catheter can immobilize the prostate and determine the position of the anterior rectal wall at daily treatment. This allows a reduction of margins.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
105. Patel RR, Orton N, Tome WA, Chappell R, Ritter MA. Rectal dose sparing with a balloon catheter and ultrasound localization in conformal radiation therapy for prostate cancer. *Radiother Oncol.* 2003;67(3):285-294.	Experimental-Tx	5 patients	To compare the rectal wall and bladder volume in the high dose region with or without the use of a balloon catheter.	Daily balloon placement was well-tolerated with good patient positional reproducibility. Inflation of the rectal balloon in all cases resulted in a significant decrease in the absolute volume of rectal wall receiving >60, 65, or 70Gy. The rectal sparing ratio, consisting of a structure's high dose volume with the catheter inflated, divided by the volume with the catheter deflated, was calculated for each patient with and without SV inclusion for 3D-CRT and IMRT. For 3D-CRT, rectal sparing ratio with SV included were 0.59, 0.59, and 0.56 and with SV excluded were 0.60, 0.58, and 0.54 at doses of greater than 60, 65, and 70 Gy, respectively. Similarly, for IMRT, the mean rectal sparing ratio was 0.59, 0.59, and 0.63 including SV and 0.71, 0.66, and 0.67 excluding SV at these same dose levels, respectively. Averaged over all conditions, inflation of the rectal balloon resulted in a significant reduction in rectal volume receiving ≥65Gy to a mean ratio of 0.61 (P=0.01) or, in other words, a mean fractional high dose rectal sparing of 39%. There was a slight overall increase to 1.13 in the relative volume of bladder receiving at least 65 Gy; however, this was not significant (P=0.6). Use of an endorectal balloon with a non-image-guided 3D-CRT plan produced about as much rectal dose sparing as a highly conformal, image-guided IMRT approach without a balloon. However, inclusion of a balloon with IMRT produced further rectal sparing still. The use of a rectal balloon with a 3D-CRT plan will produce significant rectal sparing.	1

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
106. Kim DW, Straka C, Cho LC, Timmerman RD. Stereotactic Body Radiation Therapy for Prostate Cancer: Review of Experience of a Multicenter Phase I/II Dose-Escalation Study. *Front Oncol.* 2014;4:319.	Experimental-Tx	91 patients	To review our experiences of dose-escalated SBRT for localized prostate cancer.	91 patients were enrolled from 5 institutions. Median follow-up for PSA evaluation was 42 months. PSA control remains at 99%. While the maximum tolerated dose was not reached in the phase I study, excess high grade rectal toxicity (10.6%) was noted in the phase II study. The 13 patients treated to 50 Gy in the phase I study that did not have high grade rectal toxicity, in retrospect met these parameters and have not had further events on longer follow-up.	2
107. Boike TP, Lotan Y, Cho LC, et al. Phase I dose-escalation study of stereotactic body radiation therapy for low- and intermediate-risk prostate cancer. *J Clin Oncol.* 2011;29(15):2020-2026.	Experimental-Tx	45 patients	To evaluate the tolerability of escalating doses of SBRT in the treatment of localized prostate cancer.	Groups of 15 patients received 45 Gy, 47.5 Gy, and 50 Gy in 5 fractions (45 total patients). The median follow-up is 30 months (range, 3 to 36 months), 18 months (range, 0 to 30 months), and 12 months (range, 3 to 18 months) for the 45 Gy, 47.5 Gy, and 50 Gy groups, respectively. For all patients, GI grade ≥2 and grade ≥3 toxicity occurred in 18% and 2%, respectively, and GU grade ≥2 and grade ≥3 toxicity occurred in 31% and 4%, respectively. Mean AUA scores increased significantly from baseline in the 47.5-Gy dose level (P=.002) as compared with the other dose levels, where mean values returned to baseline. Rectal quality-of-life scores (Expanded Prostate Cancer Index Composite) fell from baseline up to 12 months but trended back at 18 months. In all patients, PSA control is 100% by the nadir + 2 ng/mL failure definition.	1

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
108. Susil RC, McNutt TR, DeWeese TL, Song D. Effects of prostate-rectum separation on rectal dose from external beam radiotherapy. *Int J Radiat Oncol Biol Phys.* 2010;76(4):1251-1258.	Experimental-Tx	2 cadavers; 10 IMRT plans	To describe and characterize the dosimetric effects of creating prostate-rectum separation.	In the cadaveric studies, an average of 12.5 mm of prostate-rectum separation was generated with the 20-mL hydrogel injections (the SVs were also separated from the rectum). The average rectal volume receiving 70 Gy decreased from 19.9% to 4.5% ($P<.05$). In the simulation studies, a prostate-rectum separation of 10 mm was sufficient to reduce the mean rectal volume receiving 70 Gy by 83.1% ($P<.05$). No additional reduction in the average rectal volume receiving 70 Gy was noted after 15 mm of separation. In addition, spacer placement allowed for increased PTV margins without exceeding the rectal dose tolerance.	2
109. Chapet O, Udrescu C, Devonec M, et al. Prostate hypofractionated radiation therapy: injection of hyaluronic acid to better preserve the rectal wall. *Int J Radiat Oncol Biol Phys.* 2013;86(1):72-76.	Experimental-Tx	16 patients	To evaluate the contribution of an injection of hyaluronic acid between the rectum and the prostate for reducing the dose to the rectal wall in a hypofractionated irradiation for prostate cancer.	The mean V90, V80, V70, V60, and V50 values were reduced by 73.8% ($P<.0001$), 55.7% ($P=.0003$), 43.0% ($P=.007$), 34% ($P=.002$), and 25% ($P=.036$), respectively. The average values of D2.5, D5, D10, D15, and D20 were reduced by 8.5 Gy ($P<.0001$), 12.3 Gy ($P<.0001$), 8.4 Gy ($P=.005$), 3.7 Gy ($P=.026$), and 1.2 Gy ($P=.25$), respectively.	2
110. Eckert F, Alloussi S, Paulsen F, et al. Prospective evaluation of a hydrogel spacer for rectal separation in dose-escalated intensity-modulated radiotherapy for clinically localized prostate cancer. *BMC Cancer.* 2013;13:27.	Experimental-Tx	10 patients	To assess an innovative approach of hydrogel injection between prostate and rectum to reduce the radiation dose to the rectum and thus side effects in dose-escalated prostate RT.	From 11 patients scheduled for spacer injection the procedure could be performed in 10. In 1 patient hydrodissection of the Denonvillier space was not possible. Radiation treatment planning showed low rectal doses despite dose-escalation to the target. In accordance with this, acute rectal toxicity was mild without grade 2 events and there was complete resolution within four to twelve weeks.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
111. Pinkawa M, Corral NE, Caffaro M, et al. Application of a spacer gel to optimize three-dimensional conformal and intensity modulated radiotherapy for prostate cancer. *Radiother Oncol.* 2011;100(3):436-441.	Experimental-Tx	18 patients	To evaluate the impact of a spacer gel on the dose distribution, applying 3D-CRT and IMRT planning techniques.	In contrast to the PTV and bladder, significant advantages ($P<0.01$) resulted in respect of all analyzed rectal dose values comparing pre spacer with post spacer plans for both techniques. Rectal normal tissue complication probability reached the lowest percentage after spacer injection irrespective of the technique, with a mean reduction of >50% for both IMRT and 3D-CRT. Significantly ($P<0.01$) higher D(mean), and V(78) for the PTV were reached with IMRT vs 3D-CRT plans, with a smaller rectum V(76) but larger rectum V(50).	2
112. Song DY, Herfarth KK, Uhl M, et al. A multi-institutional clinical trial of rectal dose reduction via injected polyethylene-glycol hydrogel during intensity modulated radiation therapy for prostate cancer: analysis of dosimetric outcomes. *Int J Radiat Oncol Biol Phys.* 2013;87(1):81-87.	Experimental-Tx	48 patients	To characterize the effect of a prostate-rectum spacer on dose to rectum during EBRT for prostate cancer and to assess for factors correlated with rectal dose reduction.	Hydrogel resulted in ≥7.5-mm prostate-rectal separation in 95.8% of patients; 95.7% had decreased rectal V70 of ≥25%, with a mean reduction of 8.0 Gy. There were no significant differences in preinjection and postinjection prostate, PTV, rectal, and bladder volumes. Plan conformities were significantly different before vs after injection ($P=.02$); plans with worse conformity indexes after injection compared with before injection (n=13) still had improvements in rectal V70. In multiple regression analysis, greater postinjection reduction in V70 was associated with decreased relative postinjection plan conformity ($P=.01$). Reductions in V70 did not significantly vary by institution, despite significant interinstitutional variations in plan conformity. There were no significant relationships between reduction in V70 and the other characteristics analyzed.	2
113. Noyes WR, Hosford CC, Schultz SE. Human collagen injections to reduce rectal dose during radiotherapy. *Int J Radiat Oncol Biol Phys.* 2012;82(5):1918-1922.	Experimental-Tx	11 patients	To report an investigational trial using human collagen to increase the distance between the prostate and anterior rectal wall, thereby decreasing the radiation dose to the rectum.	11 patients were enrolled into the study. The injection of human collagen in the outpatient setting was well tolerated. The mean separation between the prostate and anterior rectum was 12.7 mm. The mean reduction in dose to the anterior rectal wall was 50%. All men denied any rectal symptoms during the study.	1

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
114. Melchert C, Gez E, Bohlen G, et al. Interstitial biodegradable balloon for reduced rectal dose during prostate radiotherapy: results of a virtual planning investigation based on the pre- and post-implant imaging data of an international multicenter study. *Radiother Oncol.* 2013;106(2):210-214.	Experimental-Tx	22 patients	To evaluate dose reduction caused by the implantation of an interstitial inflatable and biodegradable balloon device aiming to achieve lower rectal doses with virtual 3D-CRT.	The dorsal prostate-ventral rectal wall separation resulted in an average reduction of the rectal V70% by 55.3% (+/- 16.8%), V80% by 64.0% (+/- 17.7%), V90% by 72.0% (+/- 17.1%), and V100% by 82.3% (+/- 24.1%). In parallel, rectal D2 ml and D0.1 ml were reduced by 15.8% (+/- 11.4%) and 3.9% (+/- 6.4%), respectively.	1
115. Gez E, Cytron S, Ben Yosef R, et al. Application of an interstitial and biodegradable balloon system for prostate-rectum separation during prostate cancer radiotherapy: a prospective multi-center study. *Radiat Oncol.* 2013;8:96.	Experimental-Tx	23 patients	To evaluate the safety and efficacy of an implantable and biodegradable balloon specifically designed to protect rectal tissue during RT by increasing the prostate-rectum interspace.	4 of 27 patients were excluded from the evaluation. One was excluded due to a technical failure during implant, and 3 patients were excluded because the balloon prematurely deflated. The balloon status was evaluated for the duration of the RT period in 23 patients. With the balloon implant, the distance between the prostate and rectum increased 10-fold, from a mean 0.22 +/- 0.2 cm to 2.47 +/- 0.47 cm. During the RT period the balloon length changed from 4.25 +/- 0.49 cm to 3.81 +/- 0.84 cm and the balloon height from 1.86 +/- 0.24 cm to 1.67 +/- 0.22 cm. But the prostate-rectum interspace distance remained constant from beginning to end of RT: 2.47 +/- 0.47 cm and 2.41 +/- 0.43 cm, respectively. A significant mean reduction in calculated rectal radiation exposure was achieved. The implant procedure was well tolerated. The adverse events included mild pain at the perineal skin and in the anus. 3 patients experienced acute urinary retention which resolved in a few hours following conservative treatment. No infections or thromboembolic events occurred during the implant procedure or during the RT period.	1

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
116. Weber DC, Zilli T, Vallee JP, Rouzaud M, Miralbell R, Cozzi L. Intensity modulated proton and photon therapy for early prostate cancer with or without transperineal injection of a polyethylen glycol spacer: a treatment planning comparison study. *Int J Radiat Oncol Biol Phys.* 2012;84(3):e311-318.	Experimental-Tx	8 patients	To assess the dosimetric impact of the polyethylen glycol spacer with advanced delivery RT techniques, including IMRT, VMAT, and intensity modulated proton beam RT.	Regardless of the radiation technique, spacer injection decreased significantly the rectal dose in the 60- to 70-Gy range. Mean V(70 Gy) and V(60 Gy) with IMRT, VMAT, and intensity modulated proton beam RT planning were 5.3 +/- 3.3%/13.9 +/- 10.0%, 3.9 +/- 3.2%/9.7 +/- 5.7%, and 5.0 +/- 3.5%/9.5 +/- 4.7% after spacer injection. Before spacer administration, the corresponding values were 9.8 +/- 5.4% (*P*=.012)/24.8 +/- 7.8% (*P*=.012), 10.1 +/- 3.0% (*P*=.002)/17.9 +/- 3.9% (*P*=.003), and 9.7 +/- 2.6% (*P*=.003)/14.7% +/- 2.7% (*P*=.003). Importantly, spacer injection usually improved the PTV coverage for IMRT. With this technique, mean V(70.2 Gy) (*P*=.07) and V(74.1 Gy) (*P*=0.03) were 100 +/- 0% to 99.8 +/- 0.2% and 99.1 +/- 1.2% to 95.8 +/- 4.6% with and without Spacer, respectively. As a result of spacer injection, bladder doses were usually higher but not significantly so. Only intensity modulated proton beam RT managed to decrease the rectal dose after spacer injection for all dose levels, generally with no observed increase to the bladder dose.	2
117. Chapet O, Udrescu C, Tanguy R, et al. Dosimetric implications of an injection of hyaluronic acid for preserving the rectal wall in prostate stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys.* 2014;88(2):425-432.	Experimental-Tx	10 patients	To assess the contribution of a hyaluronic acid injection between the rectum and the prostate to reducing the dose to the rectal wall in SBRT.	For both plans, the average volume of the rectal wall receiving the 90% isodose line (V90%) was reduced up to 90% after injection. There was no significant difference (*P*=.32) between doses received by the rectal wall on CT1 and CT2 at the base of the prostate. This variation became significant from the median plane to the apex of the prostate (*P*=.002). No significant differences were found between Plan A without hyaluronic acid and Plan B with hyaluronic acid for each level of the prostate (*P*=.77, at the isocenter of the prostate).	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
118. Reddy NM, Nori D, Chang H, Lange CS, Ravi A. Prostate and seminal vesicle volume based consideration of prostate cancer patients for treatment with 3D-conformal or intensity-modulated radiation therapy. *Med Phys.* 2010;37(7):3791-3801.	Observational-Tx	48 patients	To determine the suitability of the prostate and SV volumes as factors to consider patients for treatment with image-guided 3D-CRT or IMRT, using common dosimetry parameters as comparison tools.	When the data for all patients were combined, mean dose to prostate and CDPTV was higher with 3D than IMRT plans ($P<0.01$). Mean D95 to CDPTV was the same for 3D and IMRT plans ($P > 0.2$). On average, among all cases, the minimum point dose was less for 3D-CRT plans and the maximum point dose was greater for 3D-CRT than for IMRT ($P<0.01$). Mean dose to 30%, rectum with 3D and IMRT plans was comparable ($P > 0.1$). V30 was less ($P<0.01$), V50 was the same ($P > 0.2$), and V70 was more ($P<0.01$) for rectum with 3D than IMRT plans. Mean dose to bladder was less with 3D than IMRT plans ($P<0.01$). V30 for bladder with 3D plans was less than that of IMRT plans ($P<0.01$). V50 and V70 for 3D plans were the same for 3D and IMRT plans ($P>0.2$). Mean dose to femurs was more with 3D than IMRT plans ($P<0.01$). For a given patient, mean dose and dose to 30% rectum and bladder were less with 3D than IMRT plans for prostate or prostate + SV volumes <65 (38/48) and 85 cm3 (39/48), respectively ($P<0.01$). The larger the dose to rectum or bladder with 3D plans, the larger also was the dose to these structures with IMRT ($P<0.001$). For both 3D and IMRT plans, dose to rectum and bladder increased with the increase in the volumes of prostate and SVs ($P<0.02$ to 0.001).	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
119. Gibbons EP, Jacobs BL, Smith RP, Beriwal S, Krishna K, Benoit RM. Dosimetric outcomes in prostate brachytherapy: is downsizing the prostate with androgen deprivation necessary? *Brachytherapy.* 2009;8(3):304-308.	Observational-Tx	145 patients	To compare postimplant dosimetry in patients with prostate volumes >50 cc with those with prostate volumes ≤50 cc.	145 out of a total of 148 patients had available dosimetry. In the 113 patients with prostate volumes ≤50 cc (mean, 35.4 cc, range, 14.2–49.7 cc); the mean D(90) (dose which covers 90% of the prostate), V(100) (volume of prostate receiving 100% of the prescribed dose), V(150) (volume of prostate receiving 150% of the prescribed dose), and V(200) (volume of prostate receiving 200% of the prescribed dose) was 128.9%, 95.6%, 73.9%, and 51.2%, respectively. In the 32 patients with prostate volumes >50 cc (mean 58.1 cc, range 50.2–86.0 cc); the mean D(90), V(100), V(150), and V(200) was 125.1%, 95.2%, 68.2%, and 41.7%, respectively. The rectal V(100) was 1.0 cc for both cohorts. There was no statistically significant difference between the cohorts with respect to postimplant dosimetry for D(90), V(100), and V(150). The V(200) for prostate volumes >50 cc was significantly lower ($P<0.05$).	2
120. Kucway R, Vicini F, Huang R, Stromberg J, Gonzalez J, Martinez A. Prostate volume reduction with androgen deprivation therapy before interstitial brachytherapy. *J Urol.* 2002;167(6):2443-2447.	Observational-Tx	107 patients	To assess the degree of prostate downsizing using ADT, and determine its relation to clinical and pathological variables.	Mean percent volume reduction of the prostate was 33% after a 3.7-month average duration of androgen deprivation. Larger prostate volume before ADT and longer deprivation duration statistically correlated with mean percent volume reduction. Simple linear and multiple regression analyses revealed that these 2 variables remained significant predictors of percent volume reduction. Subgroup analysis indicated that a significant difference was seen in patients who received ADT with luteinizing hormone releasing hormone agonists alone vs those who received treatment with total androgen blockade (luteinizing hormone releasing hormone agonists plus antiandrogens 30% vs 35%, $P=0.04$), and when prostate volume before androgen deprivation was less than 50 cc vs larger volumes (30% vs 35%, $P=0.01$). Of patients with an initial prostate volume of >50 cc 82% achieved a volume of <50 cc after ADT.	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
121. Zelefsky MJ, Harrison A. Neoadjuvant androgen ablation prior to radiotherapy for prostate cancer: reducing the potential morbidity of therapy. *Urology.* 1997;49(3A Suppl):38-45.	Experimental-Tx	45 patients	To determine the impact of neoadjuvant hormonal therapy prior to CRT on the reduction of volume of normal tissue structures exposed to high doses of RT and to evaluate the overall late toxicity and response to treatment among patients treated with this approach.	In the 45 patients evaluated, the median reduction of the rectal and bladder volumes receiving 95% of the prescription dose (D95) were 18% and 46%, respectively, while 91% showed a reduction of small bowel volume in a range of 27% to 100% of the prehormonal values. Among the entire group of 214 patients treated with neoadjuvant hormonal therapy and 3D-CRT, no grade 3 or 4 toxicity was observed with a median follow-up of 15 months after 3D-CRT. The 3-year actuarial grade 2 late GI and GU toxicity rates were 6% and 18%, respectively.	2
122. McGee L, Mendenhall NP, Henderson RH, et al. Outcomes in men with large prostates (>/= 60 cm(3)) treated with definitive proton therapy for prostate cancer. *Acta Oncol.* 2013;52(3):470-476.	Observational-Tx	186 patients	To investigate GU and GI toxicity in men with large prostates (>60 cm(3)) undergoing definitive proton therapy for prostate cancer.	Median follow-up was 2 years. Grade 3 GU toxicities occurred in 14 men, including temporary catheterization (n = 7), TURP (n = 6), and balloon dilation for urethral stricture (n = 1). Multivariate analysis demonstrated pretreatment medical management (P=0.0065) and pretreatment TURP (P=0.0002) were significantly associated with grade 3 GU toxicity. One man experienced grade 3 GI toxicity and 15 men had grade 2 GI toxicities. On multivariate analysis, dose >78 CGE was associated with increased grade 2 + GI toxicity (P=0.0142).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
123. Melancon AD, Lee AK, Kudchadker R, et al. Anatomic variation and dosimetric consequences of neoadjuvant hormone therapy before radiation therapy for prostate cancer. *Pract Radiat Oncol.* 2013;3(4):329-336.	Observational-Tx	44 patients	To characterize anatomic variation during neoadjuvant androgen deprivation and determine a treatment planning strategy to maintain acceptable normal tissue dose while treating potential microscopic disease in the original (pre-neoadjuvant androgen deprivation) tumor bed.	The prostate decreased in volume by an average of about 14 cm(3) (24.3%) and was correlated with neoadjuvant androgen deprivation duration (P=.002). The prostate center of volume systematically shifted in the inferior direction (mean = 1.4 mm, P=.005) and inferior shift was correlated with absolute volume reduction of the prostate (P=.044) in a multivariate model containing rectal and bladder volume change and initial prostate volume. Pre-neoadjuvant androgen deprivation treatment planning resulted in a significant increase in the bladder volume (P<.01) but little increase in the rectal volume treated to all dose levels. Post-neoadjuvant androgen deprivation treatment planning resulted in decreased treatment of the prostate and SVs (on the pre-neoadjuvant androgen deprivation anatomy) at the prescribed and 95% isodose levels (prostate: P=.033 and 0.025; SVs: P<.001).	2
124. Martin DA, Hruby G, Whitaker MK, Foo KY. Constrained-beam inverse planning for intensity-modulated radiation therapy of prostate cancer patients with bilateral hip prostheses. *J Med Imaging Radiat Oncol.* 2012;56(6):703-707.	Review/Other-Tx	1 patient	To report a novel inverse planning technique for IMRT of patients with prostate cancer and bilateral hip prostheses, by constraining beam characteristics rather than dose in the inverse planning process.	No results stated in the abstract.	4

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
125. Han SC, Chung YE, Lee YH, Park KK, Kim MJ, Kim KW. Metal artifact reduction software used with abdominopelvic dual-energy CT of patients with metal hip prostheses: assessment of image quality and clinical feasibility. *AJR Am J Roentgenol.* 2014;203(4):788-795.	Observational-Dx	33 patients with hip replacements ; 20 patients with no metal prostheses	To determine the feasibility of using Metal Artifact Reduction software for abdominopelvic dual-energy CT in patients with metal hip prostheses.	Image quality was significantly better with Metal Artifact Reduction reconstruction than without at all sites except the rectal shelf, where the image quality either had not changed or had worsened after Metal Artifact Reduction reconstruction. The mean attenuation value was changed after Metal Artifact Reduction reconstruction to its original expected value at the pelvic sidewall ($P<0.001$) and inside the bladder ($P<0.001$). The SD attenuation value was significantly decreased after Metal Artifact Reduction reconstruction at the pelvic sidewall ($P=0.019$) but did not show significant differences at the bladder ($P=0.173$) or rectal shelf ($P=0.478$). In the phantom study, all lesions obscured by metal artifacts on the standard reconstruction images were visualized after Metal Artifact Reduction reconstruction; however, new artifacts had developed in other parts of the Metal Artifact Reduction reconstruction images.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
126. Li H, Noel C, Chen H, et al. Clinical evaluation of a commercial orthopedic metal artifact reduction tool for CT simulations in radiation therapy. *Med Phys.* 2012;39(12):7507-7517.	Experimental-Dx	10 patients; 5 sets from phantom	To evaluate the performance of the first commercial orthopedic metal artifact reduction function for RT, and investigate its clinical applications in treatment planning.	Results of the phantom study indicated that CT Hounsfield number accuracy and noise were improved on the orthopedic metal artifact reduction corrected images, especially for images with bilateral metal implants. The gamma pass rates of the simulated dose distributions computed on the uncorrected and orthopedic metal artifact reduction corrected images referenced to those of the true densities were higher than 99.9% (even when using 1% and 3 mm distance-to-agreement criterion), suggesting that dose distributions were clinically identical. In all patient cases, radiation oncologists rated orthopedic metal artifact reduction corrected images as higher quality. Formerly obscured critical structures were able to be visualized. The overall image quality and the conspicuity in critical organs were significantly improved compared with the uncorrected images: overall quality score (1.35 vs 3.25, P=0.0022); bladder (2.15 vs 3.7, P=0.0023); prostate and SVsvagina (1.3 vs 3.275, P=0.0020); rectum (2.8 vs 3.9, P=0.0021). The noise levels of the selected ROIs were reduced from 93.7 to 38.2 HU. On most cases (810), the average CT Hounsfield numbers of the prostatevagina on the orthopedic metal artifact reduction corrected images were closer to the referenced value (41.2 HU, an average measured from patients without metal implants) than those on the uncorrected images. High gamma pass rates of the 5 IMRT dose distribution pairs indicated that the dose distributions were not significantly affected by the CT image improvements.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
127. Su A, Reft C, Rash C, Price J, Jani AB. A case study of radiotherapy planning for a bilateral metal hip prosthesis prostate cancer patient. *Med Dosim.* 2005;30(3):169-175.	Review/Other-Tx	1 patient	To communicate the observed advantage of IMRT in a patient with bilateral metallic hip prostheses.	The results of the analysis demonstrated that IMRT provided superior target coverage with reduced dose to normal tissues for both individual phases of the treatment plan as well as for the composite treatment plan. The dose to the rectum was significantly reduced with the IMRT technique, with a composite V80 of 35% for the IMRT plan vs 70% for 3D-CRT plan. Similarly, the dose to the bladder was significantly reduced with a V80 of 9% vs 20%. Overall, various dosimetric parameters revealed the corresponding 3D-CRT plan would not have been acceptable.	4
128. van der Est H, Prins P, Heijmen BJ, Dirkx ML. Intensity modulated radiation therapy planning for patients with a metal hip prosthesis based on class solutions. *Pract Radiat Oncol.* 2012;2(1):35-40.	Review/Other-Tx	2 patients	To present a new approach for IMRT planning allowing the use of a default beam setup.	For both IMRT techniques a similar PTV coverage was achieved, but with the IMRT-prosthesis avoidance volumes technique the mean doses to the bladder and the rectum were reduced by up to 25%. While the IMRT-prosthesis avoidance volumes technique required more time for delineation, the time for treatment planning reduced because the default beam setup could be applied. The number of segments needed for dose delivery was comparable for both techniques.	4
129. Voet PW, Dirkx ML, Breedveld S, Heijmen BJ. Automated generation of IMRT treatment plans for prostate cancer patients with metal hip prostheses: comparison of different planning strategies. *Med Phys.* 2013;40(7):071704.	Observational-Tx	18 patients	To compare IMRT planning strategies for prostate cancer patients with metal hip prostheses.	Especially for patients with bilateral hip prostheses, IMRT cut significantly improved rectum and bladder sparing compared to IMRT remove. For 9-beam coplanar plans, rectum V60 Gy reduced by 17.5% +/- 15.0% (maximum 37.4%, P=0.036) and rectum D mean by 9.4% +/- 7.8% (maximum 19.8%, P=0.036). Further improvements in organs-at-risk sparing were achievable by using noncoplanar beam setups, reducing rectum V 60Gy by another 4.6% +/- 4.9% (P=0.012) for noncoplanar 9-beam IMRT cut plans. Large reductions in rectum dose delivery were also observed when increasing the number of beam directions in the plans. For bilateral implants, the rectum V 60 Gy was 37.3% +/- 12.1% for coplanar 7-beam plans and reduced on average by 13.5% (maximum 30.1%, P=0.012) for 15 directions.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
130. Chapman D, Smith S, Barnett R, Bauman G, Yartsev S. Optimization of tomotherapy treatment planning for patients with bilateral hip prostheses. *Radiat Oncol.* 2014;9:43.	Experimental-Dx	3 patients, 1 phantom	To determine the effect of different imaging options and the most efficient imaging strategy for treatment planning of patients with hip prostheses.	On average for 3 patients, the D35% for the bladder was 8% higher in plans based on MVCT images and 7% higher in plans based on hybrid images, compared to the plans based on kVCT images alone. Likewise, the D35% for the rectum was 3% higher than the kVCT based plan for both hybrid and MVCT plans. The average difference in planned D99% in the PTV compared to kVCT plans was 0.9% and 0.1% for MVCT and hybrid plans, respectively. For the water tank with hip prostheses phantom, the kVCT plan with orthopedic metal artifact reduction correction applied showed better agreement between the measured and calculated dose than the original image set, with a difference of -1.9% compared to 3.3%. The measured doses for the MVCT plans were lower than the calculated dose due to image size limitations. The best agreement was for the kVCT/MVCT hybrid plans with the difference between calculated and measured dose around 1%.	3
131. Alongi F, Fodor A, Maggio A, et al. Megavoltage CT images of helical tomotherapy unit for radiation treatment simulation: impact on feasibility of treatment planning in a prostate cancer patient with bilateral femoral prostheses. *Tumori.* 2011;97(2):221-224.	Review/Other-Dx	1 patient	To review the use of MVCT images to overcome the problem of hip prosthesis artefacts.	MVCT images of the patient in the treatment position obtained using a helical tomotherapy unit can provide sufficient morphological information to define the pelvic anatomic structures for radical prostate treatment planning.	4
132. Charnley N, Morgan A, Thomas E, et al. The use of CT-MR image registration to define target volumes in pelvic radiotherapy in the presence of bilateral hip replacements. *Br J Radiol.* 2005;78(931):634-636.	Review/Other-Dx	N/A	To describe a small series of patients with bilateral hip replacements on whom CT-MRI registration has been used to successfully define adequate target volumes.	No results stated in the abstract.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
133. Rosewall T, Kong V, Vesprini D, et al. Prostate delineation using CT and MRI for radiotherapy patients with bilateral hip prostheses. *Radiother Oncol.* 2009;90(3):325-330.	Observational-Dx	7 patients	To determine the effect of b-HP on prostate delineation using CT and MR.	Prostate volumes on CT were consistently larger than MR volumes in all patients when averaged over the 4 observers (+10% to +46%, $P<0.001$). The mean inter-modality volume overlap was 1.59, which varied significantly between patients (1.35 to 1.82, $P=0.04$). There was a trend toward smaller inter-observer variability in the MR volumes (1.95 vs 1.71, $P=0.08$). No differences could be identified between the IPM vectors on CT and MR.	2
134. Boda-Heggemann J, Haneder S, Ehmann M, et al. Stereotactic ultrasound for target volume definition in a patient with prostate cancer and bilateral total hip replacement. *Pract Radiat Oncol.* 2015;5(3):197-202.	Review/Other-Tx	1 patient	To present a method to define prostate target volumes based on US images acquired during CT simulation and online-matched to the CT data set directly at the planning CT.	Because of variations in bladder and rectal filling and metal-induced image distortion in MRI, soft-tissue-based matching of the MRI to CT was not sufficient for unequivocal prostate target definition. US-based images could be matched, and prostate, SVs, and target volumes were reliably defined. Daily IGRT could be successfully completed with transabdominal US with good accordance between CBCT and US.	4
135. Bittner N, Butler WM, Kurko BS, Merrick GS. Effect of metal hip prosthesis on the accuracy of electromagnetic localization tracking. *Pract Radiat Oncol.* 2015;5(1):43-48.	Experimental-Tx	2 phantoms	To quantify the effect of metal hip prosthesis on the ability to track and localize electromagnetic transponders.	Regardless of hip prosthesis composition, the average vector displacement in the presence of a unilateral prosthesis was <0.5 mm. The greatest contribution to overall vector displacement occurred in the lateral dimension. With bilateral hip prosthesis, the average vector displacement was 0.3 mm. The displacement in the lateral dimension was markedly reduced compared with a unilateral hip, suggesting that there was a countervailing effect with bilateral hip prosthesis. The greatest average vector displacement was 0.6 mm and occurred when bilateral hip prostheses were placed within 4 cm of the detector array.	2
136. Reft C, Alecu R, Das IJ, et al. Dosimetric considerations for patients with HIP prostheses undergoing pelvic irradiation. Report of the AAPM Radiation Therapy Committee Task Group 63. *Med Phys.* 2003;30(6):1162-1182.	Review/Other-Tx	N/A	To make the radiation oncology community aware of the problems arising from the presence of these devices in the radiation beam, to quantify the dose perturbations they cause, and, finally, to provide recommendations for treatment planning and delivery.	No results stated in the abstract.	4

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
137. Rana SB, Pokharel S. A dosimetric study of volumetric modulated arc therapy planning techniques for treatment of low-risk prostate cancer in patients with bilateral hip prostheses. *South Asian J Cancer.* 2014;3(1):18-21.	Review/Other-Tx	1 patient; 3 treatment plans	To compare the dosimetric quality of VMAT techniques in the form of Rapid Arc for treating low-risk prostate cancer patient with bilateral prostheses.	The mean and maximum doses to the PTV as well as the homogeneity index among all 3 Rapid Arc plans were comparable. The plan conformity index was highest in the 2-Arc plan (1.19) and lowest in the 4-Arc plan (1.10). In comparison to the 2-Rapid Arc technique, the 4-Rapid Arc technique reduced the doses to rectum by up to 18.8% and to bladder by up to 7.8%. In comparison to the 3-Rapid Arc technique, the 4-Rapid Arc technique reduced the doses to rectum by up to 14.6% and to bladder by up to 3.5%.	4
138. Sterzing F, Kalz J, Sroka-Perez G, et al. Megavoltage CT in helical tomotherapy - clinical advantages and limitations of special physical characteristics. *Technol Cancer Res Treat.* 2009;8(5):343-352.	Observational-Tx	456 patients	To describe the clinical experience with MVCT and provide a review of the current literature of the possibilities and limitations of MVCT.	Mean shifts were lateral 0.9 mm (SD 5.0 mm), mean longitudinal shift 1.0 mm (SD 5.1 mm) and mean vertical shift 3.2 mm (SD 5.2 mm). The MVCT enables imaging of anatomical structures in the presence of dental metal or orthopedic implants. Especially in these cases, dose recomputations can increase the precision of dose calculations. Due to a mean 3D correction vector of >7 mm and a variation of corrections of >5 mm daily image-guidance is recommended to achieve a precise dose application. The MVCT shows evident advantages in cases with metal implants but has limitations due to a reduced soft tissue contrast. Compared with MVCT the tomotherapy fan beam CT adds less extra dose for the patient and has a better soft tissue contrast.	3

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
139. Cuaron JJ, Harris AA, Chon B, et al. Anterior-oriented proton beams for prostate cancer: A multi-institutional experience. *Acta Oncol.* 2015;54(6):868-874.	Observational-Tx	20 patients	To report a multi-institutional experience for patients treated with at least one non-lateral proton beam for prostate cancer.	The median follow-up was 6.4 months. No patients have developed PSA failure or distant metastases. The median PTV D95 was 79.2 Gy (RBE) (range 69.7–79.9). The median rectal V70 was 9.2% (2.5–15.4). The median bladder V50, V80, and mean dose were 12.4% (3.7–27.1), 3.5 cm3 (0–7.1), and 14.9 Gy (RBE) (4.6–37.8), respectively. The median contralateral femur head V45 and max dose were 0.01 cm3 (0–16.6) and 43.7 Gy (RBE) (15.6–52.5), respectively. The incidence of acute Grade 2 urinary toxicity was 40%. There were no Grade ≥3 urinary toxicities. There was 1 patient who developed late Grade 2 rectal proctitis, with no other cases of acute or late ≥Grade 2 GI toxicity. Grade 2 erectile dysfunction occurred in 2 patients (11.1%). Mild hip pain was experienced by 5 patients (25%). There were no cases of hip fracture.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
140. Rana S, Cheng C, Zheng Y, et al. Dosimetric study of uniform scanning proton therapy planning for prostate cancer patients with a metal hip prosthesis, and comparison with volumetric-modulated arc therapy. *J Appl Clin Med Phys.* 2014;15(3):4611.	Observational-Tx	4 patients	To investigate the dosimetric quality of uniform scanning proton therapy planning for prostate cancer patients with a metal hip prosthesis, and to compare the dosimetric results of uniform scanning proton therapy with that of VMAT.	In comparison to the proton plans, on average, the maximum and mean doses to the PTV were higher in the VMAT plans by 1.4% and 0.5%, respectively, whereas the minimum PTV dose was lower in the VMAT plans by 3.4%. The proton plans had lower (or better) average homogeneity index of 0.03 compared to the 1 for VMAT (homogeneity index = 0.04). The relative rectal volume exposed to radiation was lower in the proton plan, with an average absolute difference ranging from 0.1% to 32.6%. In contrast, using proton planning, the relative bladder volume exposed to radiation was higher at high-dose region with an average absolute difference ranging from 0.4% to 0.8%, and lower at low- and medium-dose regions with an average absolute difference ranging from 2.7% to 10.1%. The average mean dose to the rectum and bladder was lower in the proton plans by 45.1% and 22.0%, respectively, whereas the mean dose to femoral head was lower in VMAT plans by an average difference of 79.6%. In comparison to the VMAT, the proton planning produced lower equivalent uniform dose for the rectum (43.7 CGE vs 51.4 Gy) and higher equivalent uniform dose for the femoral head (16.7 CGE vs 9.5 Gy), whereas both the VMAT and proton planning produced comparable equivalent uniform doses for the prostate tumor (76.2 CGE vs 76.8 Gy) and bladder (50.3 CGE vs 51.1 Gy).	3
141. Newhauser WD, Giebeler A, Langen KM, Mirkovic D, Mohan R. Can megavoltage computed tomography reduce proton range uncertainties in treatment plans for patients with large metal implants? *Phys Med Biol.* 2008;53(9):2327-2344.	Review/Other-Tx	1 patient, 1 phantom	To quantify streak-related range errors and to determine if they could be avoided by using artifact-free MVCT images in treatment planning.	Streak-induced range errors of 5–12 mm were present in the uncorrected kVCT-based patient plan. Correcting the streaks by manually assigning estimated true Hounsfield units improved the range accuracy. In a rigid heterogeneous phantom, the implant-related range uncertainty was estimated at <3 mm for both the corrected kVCT-based plan and the uncorrected MVCT-based plan.	4

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
142. Millender LE, Aubin M, Pouliot J, Shinohara K, Roach M, 3rd. Daily electronic portal imaging for morbidly obese men undergoing radiotherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys.* 2004;59(1):6-10.	Experimental-Tx	3 patients	To summarize our experience with a series of morbidly obese men treated using daily online portal imaging and implanted gold markers to guide EBRT.	The absolute magnitude of positioning error was greatest in the left-right direction with a mean of 11.4 mm/fraction (median, 8 mm; range, 0–42 mm). Mean error in the SI direction was also substantial at 7.2 mm/fraction (median, 5 mm; range, 0–47 mm). Anteroposterior error was the least problematic with a mean value of 2.6 mm/fraction (median, 2.5 mm; range, 0–8 mm).	2
143. Wong JR, Gao Z, Uematsu M, et al. Interfractional prostate shifts: review of 1870 computed tomography (CT) scans obtained during image-guided radiotherapy using CT-on-rails for the treatment of prostate cancer. *Int J Radiat Oncol Biol Phys.* 2008;72(5):1396-1401.	Observational-Tx	329 patients; 1,870 CT scans	To review 1,870 CT scans of interfractional prostate shift obtained during IGRT.	Of the 1,870 scans reviewed, 44% required no setup adjustments in the AP direction, 14% had shifts of 3–5 mm, 29% had shifts of 6–10 mm, and 13% had shifts of >10 mm. In the SI direction, 81% had no adjustments, 2% had shifts of 3–5 mm, 15% had shifts of 6–10 mm, and 2% had shifts of >10 mm. In the left-right direction, 65% had no adjustment, 13% had shifts of 3–5 mm, 17% had shifts of 6–10 mm, and 5% had shifts of >10 mm. Further analysis of the first 66 consecutive patients divided into 3 groups according to body mass index indicates that the shift in the AP direction for the overweight subgroup was statistically larger than those for the control and obese subgroups ($P<0.05$). The interfractional shift in the lateral direction for the obese group (1 SD, 5.5 mm) was significantly larger than those for the overweight and control groups (4.1 and 2.9 mm, respectively) ($P<0.001$).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
144. Den RB, Nowak K, Buzurovic I, et al. Implanted dosimeters identify radiation overdoses during IMRT for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2012;83(3):e371-376.	Experimental-Tx	20 patients	To report our initial clinical experience using implantable dosimeters to quantify and adjust the dose received during IMRT.	Using implanted in vivo dosimeters, dose measurements consistently >6% greater than the predicted values were observed during treatment for 3 of 20 prostate cancer patients who received IMRT with daily image guidance. A review of the daily CBCT images revealed acceptable alignment of the prostate target volumes and implanted dosimeters but identified significant anatomic changes within the treated region. Repeat CT simulation and RT planning was performed, with resolution of the dose discrepancies in all 3 cases with the adoption of a new IMRT plan.	2
145. Strom SS, Kamat AM, Gruschkus SK, et al. Influence of obesity on biochemical and clinical failure after external-beam radiotherapy for localized prostate cancer. *Cancer.* 2006;107(3):631-639.	Observational-Tx	873 patients	To determine whether obesity was an independent predictor of biochemical failure and clinical recurrence among patients treated with EBRT.	Of the 873 patients, 18% were mildly obese and 5% were moderately to severely obese. Obesity was related to younger age at diagnosis (P<.001), more recent year of diagnosis (P=.03), and race (P=.03), with African-American men having the highest obesity rates. During a mean follow-up of 96 months, 295 patients experienced biochemical failure and 127 had clinical recurrence. On multivariate analysis, controlling for clinical and treatment characteristics, increased body mass index significantly predicted biochemical failure (HR = 1.04; 95% confidence interval [95% CI, 1.02–1.07) with a positive trend by body mass index category (P=.001). Similar results were found when the outcome was clinical recurrence; body mass index remained an independent predictor of progression (HR = 1.05; 95% CI, 1.01–1.09), with a statistically significant trend by increased body mass index category (P=.03).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
146. Wang LS, Murphy CT, Ruth K, et al. Impact of obesity on outcomes after definitive dose-escalated intensity-modulated radiotherapy for localized prostate cancer. *Cancer.* 2015;121(17):3010-3017.	Observational-Tx	1,442 patients	To determine whether increasing BMI was associated with outcomes in men with localized prostate cancer who were treated with dose-escalated RT.	Of the 1442 patients identified, approximately 20% had a BMI <25 kg/m(2) , 48% had a BMI of 25 to 29.9 kg/m(2) , 23% had a BMI of 30 to 34.9 kg/m(2) , 6% had a BMI of 35 to 39.9 kg/m(2) , and 4% had a BMI of ≥40 kg/m(2). The median follow-up was 47.6 months (range, 1–145 months), with a median age of 68 years (range, 36–89 years). The median dose was 78 Gy (range, 76-80 Gy) and 30% of patients received androgen deprivation therapy. Increasing BMI was found to be inversely associated with age (*P*<.001) and pretreatment prostate-specific antigen level (*P*=.018). On multivariable analysis, increasing BMI was associated with an increased risk of BF (HR, 1.03; 95% CI, 1.00–1.07 [*P*=.042]), DM (HR, 1.07; 95% CI, 1.02–1.11 [*P*=.004]), CSM (HR, 1.15; 95% CI, 1.07–1.23 [*P*<.001]), and overall mortality (HR, 1.05; 95% CI, 1.02–1.08 [*P*=.004]).	2
147. Moseley DJ, White EA, Wiltshire KL, et al. Comparison of localization performance with implanted fiducial markers and cone-beam computed tomography for on-line image-guided radiotherapy of the prostate. *Int J Radiat Oncol Biol Phys.* 2007;67(3):942-953.	Experimental-Tx	15 patients; 256 volumetric images	To assess the accuracy of kV CBCT setup corrections as compared with orthogonal MV portal image-based corrections for patients undergoing EBRT of the prostate.	The Pearson coefficient of correlation for the patient position shifts using fiducial markers in MV vs kV was (R2 = 0.95, 0.84, 0.81) in the left-right, AP, and SI directions, respectively. The correlation using soft-tissue matching was as follows: R2 = 0.90, 0.49, and 0.51 in the left-right, AP, and SI directions. A Bland-Altman analysis showed no significant trends in the data. The percentage of shifts within a +/-3-mm tolerance (the clinical action level) was 99.7%, 95.5%, 91.3% for fiducial marker matching and 99.5%, 70.3%, 78.4% for soft-tissue matching. CBCT is an accurate and precise tool for image guidance. It provides an equivalent means of patient setup correction for prostate patients with implanted gold fiducial markers. Use of the additional information provided by the visualization of soft-tissue structures is an active area of research.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
148. Martin JM, Frantzis J, Eade T, Chung P. Clinician's guide to prostate IMRT plan assessment and optimisation. *J Med Imaging Radiat Oncol.* 2010;54(6):569-575.	Review/Other-Tx	N/A	To present aspects of IMRT planning relevant to clinicians to aid in plan critiquing.	No results stated in the abstract.	4
149. Lee W. RTOG 0415: A Phase III Randomized Study of Hypofractionated 3DCRT/IMRT versus Conventionally Fractionated 3DCRT/IMRT in Patients Treated for Favorable-Risk Prostate Cancer. 2009; Available at: http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0415.	Review/Other-Tx	N/A	To determine if hypofractionated 3D-CRT/IMRT (70 Gy in 28 fractions over 5.6 weeks) will result in DFS that is no worse than DFS following conventionally fractionated 3D-CRT/IMRT (73.8 Gy in 41 fractions over 8.2 weeks) in patients treated for favorable-risk prostate cancer.	No abstract available.	4
150. Lukka H. RTOG 0938: A Randomized Phase II Trial Of Hypofractionated Radiotherapy For Favorable Risk Prostate Cancer. 2011; http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0938.	Review/Other-Tx	N/A	To demonstrate that 1-year health-related quality of life for at least one hypofractionated arm is not significantly lower than baseline as measured by the Bowel and Urinary domains of the Expanded Prostate Cancer Index Composite (EPIC) instrument.	No abstract available.	4
151. Bauman G, Haider M, Van der Heide UA, Menard C. Boosting imaging defined dominant prostatic tumors: a systematic review. *Radiother Oncol.* 2013;107(3):274-281.	Review/Other-Tx	13 papers; 833 patients	To address the question: "what is the clinical evidence to support differential boosting to an imaging defined GTV volume within the prostate when delivered by external beam or brachytherapy".	13 papers describing 11 unique patient series and 833 patients in total were identified. Methods and details of GTV definition and treatment varied substantially between series. GTV boosts were on average 8 Gy (range 3–35 Gy) for external beam, or 150% for brachytherapy (range 130%–155%) and GTV volumes were small (<10 ml). Reported toxicity rates were low and may reflect the modest boost doses, small volumes and conservative dose-volume histogram constraints employed in most studies. Variability in patient populations, study methodologies and outcomes reporting precluded conclusions regarding efficacy.	4
152. Emami B, Lyman J, Brown A, et al. Tolerance of normal tissue to therapeutic irradiation. *Int J Radiat Oncol Biol Phys.* 1991;21(1):109-122.	Review/Other-Tx	N/A	To present the updated information on tolerance of normal tissues of concern, based on available data, with a special emphasis on partial volume effects.	No results stated in the abstract.	4
153. Marks LB, Ten Haken RK, Martel MK. Guest editor's introduction to QUANTEC: a users guide. *Int J Radiat Oncol Biol Phys.* 2010;76(3 Suppl):S1-2.	Review/Other-Tx	N/A	No abstract available.	No abstract available.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
154. Michalski JM, Gay H, Jackson A, Tucker SL, Deasy JO. Radiation dose-volume effects in radiation-induced rectal injury. *Int J Radiat Oncol Biol Phys.* 2010;76(3 Suppl):S123-129.	Review/Other-Tx	4 clinical series	To review the available dose/volume/outcome data for rectal injury.	No results stated in the abstract.	4
155. Chennupati SK, Pelizzari CA, Kunnavakkam R, Liauw SL. Late toxicity and quality of life after definitive treatment of prostate cancer: redefining optimal rectal sparing constraints for intensity-modulated radiation therapy. *Cancer Med.* 2014;3(4):954-961.	Observational-Tx	372 patients	To assess late toxicity and quality of life for patients receiving definitive IMRT and IGRT with regard to normal tissue sparing objectives.	The median age and prescription dose was 69 years and 76 Gy, respectively. Median follow-up was 47 months. At 4 years, freedom from Grade 2 GI toxicity was 92% and freedom from Grade 2 GU toxicity was 76%. On univariate analysis, current smoking, larger bladder volume, and higher RT dose were associated with decreased freedom from Grade 2 GU toxicity, while use of anticoagulation, increasing age, and not meeting ideal rectal constraints were associated with decreased freedom from Grade 2 GI toxicity (all $P \leq 0.05$). Bowel quality of life remained stable over the 2-year follow-up period and was higher for patients who met ideal rectal constraints ($P=0.05$).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
156. Michalski JM, Yan Y, Watkins-Bruner D, et al. Preliminary toxicity analysis of 3-dimensional conformal radiation therapy versus intensity modulated radiation therapy on the high-dose arm of the Radiation Therapy Oncology Group 0126 prostate cancer trial. *Int J Radiat Oncol Biol Phys.* 2013;87(5):932-938.	Experimental-Tx	748 patients	To give a preliminary report of clinical and treatment factors associated with toxicity in men receiving high-dose RT on a phase 3 dose-escalation trial.	Of 763 patients randomized to the 79.2-Gy arm of RTOG 0126 protocol, 748 were eligible and evaluable: 491 and 257 were treated with 3D-CRT and IMRT, respectively. For both bladder and rectum, the volumes receiving 65, 70, and 75 Gy were significantly lower with IMRT (all $P<.0001$). For grade 2+ acute GI/GU toxicity, both univariate and multivariate analyses showed a statistically significant decrease in grade 2+ acute collective GI/GU toxicity for IMRT. There were no significant differences with 3D-CRT or IMRT for acute or late grade 2+ or 3+ GU toxicities. Univariate analysis showed a statistically significant decrease in late grade2+ GI toxicity for IMRT ($P=.039$). On multivariate analysis, IMRT showed a 26% reduction in grade2+ late GI toxicity ($P=.099$). Acute grade2+ toxicity was associated with late grade3+ toxicity ($P=.005$). With dose-volume histogram data in the multivariate analysis, RT modality was not significant, whereas white race ($P=.001$) and rectal V70 ≥15% were associated with grade2+ rectal toxicity ($P=.034$).	1
157. Viswanathan AN, Yorke ED, Marks LB, Eifel PJ, Shipley WU. Radiation dose-volume effects of the urinary bladder. *Int J Radiat Oncol Biol Phys.* 2010;76(3 Suppl):S116-122.	Review/Other-Tx	N/A	To present an in-depth overview of the normal-tissue radiation tolerance of the urinary bladder.	No results stated in the abstract.	4
158. Roach M, 3rd, Nam J, Gagliardi G, El Naqa I, Deasy JO, Marks LB. Radiation dose-volume effects and the penile bulb. *Int J Radiat Oncol Biol Phys.* 2010;76(3 Suppl):S130-134.	Review/Other-Tx	N/A	To review the dose, volume, and clinical outcome data for penile bulb for patients treated with EBRT.	According to the data available, it is prudent to keep the mean dose to 95% of the penile bulb volume to <50 Gy. It may also be prudent to limit the D70 and D90 to 70 Gy and 50 Gy, respectively, but coverage of the PTV should not be compromised.	4

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
159. Kupelian PA, Willoughby TR, Reddy CA, Klein EA, Mahadevan A. Hypofractionated intensity-modulated radiotherapy (70 Gy at 2.5 Gy per fraction) for localized prostate cancer: Cleveland Clinic experience. *Int J Radiat Oncol Biol Phys.* 2007;68(5):1424-1430.	Observational-Tx	770 patients	To study the outcomes in patients treated for localized prostate cancer with 70 Gy delivered at 2.5 Gy/fraction within 5 weeks.	The overall 5-year ASTRO bRFS rate was 82% (95% CI, 79%–85%), and the 5-year nadir + 2 ng/mL rate was 83% (95% CI, 79%–86%). For patients with low-risk, intermediate-risk, and high-risk disease, the 5-year ASTRO rate was 95%, 85%, and 68%, respectively. The 5-year nadir + 2 ng/mL rate for patients with low-, intermediate-, and high-risk disease was 94%, 83%, and 72%, respectively. The RTOG acute rectal toxicity scores were 0 in 51%, 1 in 40%, and 2 in 9% of patients. The acute urinary toxicity scores were 0 in 33%, 1 in 48%, 2 in 18%, and 3 in 1% of patients. The late rectal toxicity scores were 0 in 89.6%, 1 in 5.9%, 2 in 3.1%, 3 in 1.3%, and 4 in 0.1% (1 patient). The late urinary toxicity scores were 0 in 90.5%, 1 in 4.3%, 2 in 5.1%, and 3 in 0.1% (1 patient).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
160. Hamstra DA, Stenmark MH, Ritter T, et al. Age and comorbid illness are associated with late rectal toxicity following dose-escalated radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys*. 2013;85(5):1246-1253.	Observational-Tx	718 patients	To assess the impacts of patient age and comorbid illness on rectal toxicity following EBRT for prostate cancer and to assess the QUANTEC normal tissue complication probability model in this context.	The cumulative incidence of rectal toxicity grade ≥2 was 9.5% and 11.6% at 3 and 5 years and 3.3% and 3.9% at 3 and 5 years for grade ≥3 toxicity, respectively. Each year of age predicted an increasing relative risk of grade ≥2 (P<.03; HR, 1.04 [95% CI, 1.01–1.06]) and ≥3 rectal toxicity (P<.0001; HR, 1.14 [95% CI, 1.07–1.22]). Increasing CCMI predicted rectal toxicity where a history of either myocardial infarction (P<.0001; HR, 5.1 [95% CI, 1.9–13.7]) or congestive heart failure (P<.0006; HR, 5.4 [95% CI, 0.6–47.5]) predicted grade ≥3 rectal toxicity, with lesser correlation with grade ≥2 toxicity (P<.02 for myocardial infarction, and P<.09 for congestive heart failure). An age comorbidity model to predict rectal toxicity was developed and confirmed in a validation cohort. The use of anticoagulants increased toxicity independent of age and comorbidity. Normal tissue complication probability was prognostic for grade ≥3 (P=.015) but not grade ≥2 (P=.49) toxicity. On multivariate analysis, age, myocardial infarction, congestive heart failure, and normal tissue complication probability >20% all correlated with late rectal toxicity.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
161. Murphy CT, Heller S, Ruth K, et al. Evaluating toxicity from definitive radiation therapy for prostate cancer in men with inflammatory bowel disease: Patient selection and dosimetric parameters with modern treatment techniques. *Pract Radiat Oncol.* 2015;5(3):e215-222.	Observational-Tx	84 patients	To examine our experience in men with IBD who were treated with definitive RT for prostate cancer.	Between 1990 and 2010, 84 men were included. 63 men served as matched controls and 21 with IBD: 13 ulcerative colitis, 7 Crohn disease, and 1 IBD not otherwise specified. For men with IBD, median age was 69 years, and median follow-up was 49 months. Median flare-free interval before RT was 10 years. 7 were taking IBD medications during RT. There was no difference in acute or late GI toxicity in the IBD group vs controls. Among IBD patients, IBD medication use was the only predictor of acute ≥G2 GI toxicity: 57.1% with medication vs7% without (49.4% absolute difference, 95% CI, 10.0%–88.9%, *P*=.03). The 5-year risk of late GI toxicity in men with IBD vs controls was not statistically significant (HR = 1.19, 95% CI, 0.28–5.01, *P*=.83). The crude incidence of late ≥G2 GI toxicity was 10%.	2
162. White EC, Murphy JD, Chang DT, Koong AC. Low Toxicity in Inflammatory Bowel Disease Patients Treated With Abdominal and Pelvic Radiation Therapy. *Am J Clin Oncol.* 2015;38(6):564-569.	Observational-Tx	19 patients	To determine the short-term and long-term toxicity of abdominal and pelvic RT in a cohort of patients with IBD.	Acute grade ≥3 toxicity occurred in 2 patients (11%). Late grade ≥3 toxicity occurred in 1 patient (6%). Acute grade ≥2 toxicity occurred in 28% of patients treated with IMRT vs 100% of patients treated with 3D-CRT (*P*=0.01). Acute grade ≥2 GI toxicity was lower in patients treated with IMRT vs 3D-CRT (14% vs 100%, respectively, *P*=0.002). Late grade ≥2 toxicity occurred in 21% of patients. Higher total dose (Gy) and biologically effective dose (Gy) were associated with increased rates of late grade ≥2 toxicity (*P*=0.02 and 0.03, respectively).	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
163. Beltran C, Herman MG, Davis BJ. Planning target margin calculations for prostate radiotherapy based on intrafraction and interfraction motion using four localization methods. *Int J Radiat Oncol Biol Phys.* 2008;70(1):289-295.	Observational-Dx	40 patients	To determine PTV margins for prostate RT based on the internal margin (intrafractional motion) and the setup margin (interfractional motion) for 4 daily localization methods: skin marks (tattoo), pelvic bony anatomy (bone), intraprostatic gold seeds using a 5-mm action threshold, and using no threshold.	A total of 1,532 fractions were analyzed. Tattoo localization requires a setup margin of 6.8 mm left-right, 7.2 mm inferior-superior, and 9.8 mm AP. Bone localization requires 3.1, 8.9, and 10.7 mm, respectively. The 5-mm threshold localization requires 4.0, 3.9, and 3.7 mm. No threshold localization requires 3.4, 3.2, and 3.2 mm. The intrafractional prostate motion requires an internal margin of 2.4 mm left-right, 3.4 mm inferior-superior and AP. The PTV margin using the 5-mm threshold, including interobserver uncertainty, internal margin, and setup margin, is 4.8 mm left-right, 5.4 mm inferior-superior, and 5.2 mm AP.	3
164. Graf R, Boehmer D, Budach V, Wust P. Interfraction rotation of the prostate as evaluated by kilovoltage X-ray fiducial marker imaging in intensity-modulated radiotherapy of localized prostate cancer. *Med Dosim.* 2012;37(4):396-400.	Experimental-Tx	38 patients	To quantify the daily rotation of the prostate during a RT course using stereoscopic kV X-ray imaging and intraprostatic fiducials for localization and positioning correction.	The interfraction rotation errors of the prostate as assessed from the radiodense surrogate markers around the 3 axes Y, Z, and X were on average 0.09, -0.52, and -0.01 degrees with SDs of 2.01, 2.30, and 3.95 degrees , respectively. The systematic uncertainty per patient for prostate rotation was estimated with 2.30, 1.56, and 4.13 degrees and the mean random components with 1.81, 2.02, and 3.09 degrees. The largest rotational errors occurred around the X-axis (pitch), but without preferring a certain orientation. Although the error around Z (roll) can be compensated on average by a transformation with 4 coordinates, a significant error around X remains and advocates the full correction with 6 coordinates.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
165. Badakhshi H, Wust P, Budach V, Graf R. Image-guided radiotherapy with implanted markers and kilovoltage imaging and 6-dimensional position corrections for intrafractional motion of the prostate. *Anticancer Res.* 2013;33(9):4117-4121.	Experimental-Tx	13 patients, 427 treatment fractions	To assess intrafractional prostate and patient movement using intra-prostatic fiducials and stereoscopic kV X-ray imaging in a 6D position correction protocol. To evaluate potential gains of intra-treatment repositioning with respect to treatment margins.	The mean treatment duration was 14.2+/-2.6 min. SDs of the effective intrafractional target displacement in SI and AP axes were 2.4 mm and 2.1 mm, respectively. Systematic errors for patient were 1.8 and 1.7 mm, and for prostate movement were 2.1 and 2.0 mm in SI and AP, respectively. The SDs of intrafractional rotation errors of the prostate around SI and left right were on average 2.2 and 3.6 degrees, respectively. Margins covering intrafractional motion were 4.5 and 4.3 mm in SI and AP without intrafractional correction and were estimated to 2.9 mm and 2.8 mm in SI and AP, respectively for simulated intra-treatment intervention.	2
166. Cramer AK, Haile AG, Ognjenovic S, et al. Real-time prostate motion assessment: image-guidance and the temporal dependence of intra-fraction motion. *BMC Med Phys.* 2013;13(1):4.	Observational-Tx	143 patients	To qualify and quantify the contribution of image-guidance to the temporal dependence of intrafraction motion during prostate IMRT.	Mean/median session times were 4.15/3.99 min intensity-modulated arc therapy (transponder only localization), 12.74/12.19 min intensity-modulated arc therapy (transponder + CBCT localization), 5.99/5.77 min IMRT (transponder only localization), and 12.98/12.39 min IMRT (transponder + CBCT localization), with significant pair-wise difference ($P<0.0001$) between all category combinations except for IMRT (transponder + CBCT localization) vs intensity-modulated arc therapy (transponder + CBCT localization) ($P>0.05$). Median intrafraction motion difference between CBCT and non-CBCT categories strongly correlated with time for root-mean-square (t-value=17.29; $P<0.0001$), SI (t-value=-4.25; $P<0.0001$), and AP (t-value=2.76; $P<0.0066$), with a weak correlation for RL (t-value=1.67; $P=0.0971$). Treatment time reduction with non-CBCT treatment categories showed reductions in the observed intrafraction motion: systematic error (Sigma)<0.6 mm and random error (sigma)<1.2 mm compared with ≤0.8 mm and <1.6 mm, respectively, for CBCT-involved treatment categories.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
167. Shelton J, Rossi PJ, Chen H, Liu Y, Master VA, Jani AB. Observations on prostate intrafraction motion and the effect of reduced treatment time using volumetric modulated arc therapy. *Pract Radiat Oncol.* 2011;1(4):243-250.	Observational-Tx	37 patients, 1,332 treatment sessions	To provide a detailed analysis of observed intrafraction prostate motion and to evaluate the impact of various factors on this motion; in particular, treatment time.	37 patients were included, accounting for 1,332 treatment sessions. Mean session time was 7.4 minutes (range, 0.5–37.2; interquartile range, 4.8–9.2). R (0.06, 0.08, 0.11, 0.18) and R95 (0.14, 0.18, 0.23, 0.36) values (RL, SI, AP, 3D, respectively) were evaluated for the entire cohort. Regression analysis showed treatment time to be the strongest predictor of observed displacements (P<.001 AP, SI, 3D; P<0.05 RL). 95 displacements increased continuously from 0.05 cm, 0.09 cm, 0.12 cm, and 0.16 cm after 1 minute to 0.21 cm, 0.20 cm, 0.29 cm, and 0.47 after 10 minutes (RL, SI, AP, and 3D). Mean session time for VMAT was 4.6 minutes compared to 8.4 minutes for IMRT (difference = 3.8 min, P<.0001); VMAT was associated with reduced motion for both (difference = 0.02, 0.03, 0.05, 0.07 cm) and (0.03, 0.04, 0.11, 0.12 cm) displacements.	2
168. Gill S, Dang K, Fox C, et al. Seminal vesicle intrafraction motion analysed with cinematic magnetic resonance imaging. *Radiat Oncol.* 2014;9:174.	Experimental-Dx	11 patients	To analyze SV displacement relative to the prostate and in relation to treatment time.	The 2.5% trimmed range for 3, 5, 10 and 15 minutes for the SV centroids in the SI direction measured 4.7 mm; 5.8 mm; 6.5 mm and 7.2 mm respectively. In the AP direction, it was 4.0 mm, 4.5 mm, 6.5 mm, and 7.0 mm. In the left-right direction for 3, 5 and 10 minutes; for the left SV, it was 2.7 mm, 2.8 mm, 3.4 mm and for the right SV, it was 3.4 mm, 3.3 mm, and 3.4 mm. The correlation between the real-time prostate and SV displacement varied substantially between patients indicating that the relationship between prostate displacement and SVs displacement is patient specific with the majority of the patients not having a strong relationship.	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
169. Frank SJ, Dong L, Kudchadker RJ, et al. Quantification of prostate and seminal vesicle interfraction variation during IMRT. *Int J Radiat Oncol Biol Phys.* 2008;71(3):813-820.	Experimental-Tx	15 patients	To quantify the interfraction variability in prostate and SV positions during a course of IMRT using an integrated CT-linear accelerator system and to assess the impact of rectal and bladder volume changes.	For all 15 patients, the mean systematic internal prostate and SV variation was 0.1 +/- 4.1 mm and 1.2 +/- 7.3 mm in the anteroposterior axis, -0.5 +/- 2.9 mm and -0.7 +/- 4.5 mm in the SI axis, and 0.2 +/- 0.9 mm and -0.9 +/- 1.9 mm in the lateral axis, respectively. The mean magnitude of the 3D displacement vector was 4.6 +/- 3.5 mm for the prostate and 7.6 +/- 4.7 mm for the SVs. The rectal and bladder volume changes during treatment correlated with the anterior and superior displacement of the prostate and SVs.	2
170. Liang J, Wu Q, Yan D. The role of seminal vesicle motion in target margin assessment for online image-guided radiotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2009;73(3):935-943.	Observational-Dx	24 patients	To investigate interfraction motion characteristics of the SVs and determine proper margins for online CT image guidance.	The prostate and SVs move significantly more in the AP and SI than right-left directions. The AP motion of the prostate and SVs correlated (R(2) = 0.7). The SVs move significantly more than the prostate. The minimum margins found were 2.5 mm for 3D-CRT and 4.5, 4.5, and 3.0 mm for Margins A, B, and C for IMRT, respectively. Margins for IMRT were larger, but the irradiated volume and doses to critical structures were smaller. Minimum margins of 4.5 mm to the SVs and 3 mm to the prostate are recommended for IMRT with prostate-only guidance.	3
171. Adamczyk M, Piotrowski T, Adamiak E, Malicki J. Dosimetric consequences of prostate-based couch shifts on the precision of dose delivery during simultaneous IMRT irradiation of the prostate, seminal vesicles and pelvic lymph nodes. *Phys Med.* 2014;30(2):228-233.	Observational-Dx	28 patients, 253 studies	To evaluate the impact interfraction prostate (CTV1) motion corrections on doses delivered to SVs (CTV2) and LNs (CTV3), and to determine ideal PTV margins for these targets with prostate-based position verification.	The tracked shifts influenced the minimum, maximum and mean CTV2 and CTV3 doses, with a range differential of 0.17%–2.63% (prostate shifts) and 0.13%–1.92% (bony shifts) compared to the corresponding original parameters. Friedman's test revealed significant differences in the minimum doses to the CTV3 and maximum doses to both the CTV2 and CTV3. The calculated set-up margins of 1.22 cm (vertical), 0.19 cm (longitudinal) and 0.39 cm (lateral) should be added to CTV3 while performing prostate-based positioning.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
172. Huang K, Palma DA, Scott D, et al. Inter- and intrafraction uncertainty in prostate bed image-guided radiotherapy. *Int J Radiat Oncol Biol Phys.* 2012;84(2):402-407.	Experimental-Dx	14 patients	To measure inter- and intrafraction setup error and prostate bed motion in patients undergoing post-prostatectomy IGRT and to propose appropriate population-based 3D CTV-PTV margins in both non-IGRT and IGRT scenarios.	The magnitude of interfraction prostate bed motion was 2.1 mm, and intrafraction prostate bed motion was 0.4 mm. The maximum inter- and intrafraction prostate bed motion was primarily in the AP direction. Margins of at least 3–5 mm with IGRT and 4–7 mm without IGRT (aligning to skin marks) will ensure 95% of the prescribed dose to the CTV in 90% of patients.	2
173. Klayton T, Price R, Buyyounouski MK, et al. Prostate bed motion during intensity-modulated radiotherapy treatment. *Int J Radiat Oncol Biol Phys.* 2012;84(1):130-136.	Observational-Dx	18 patients	To report prostate bed localization and motion characteristics, using data collected from implanted radiofrequency transponders.	At localization, prostate bed displacement relative to bony anatomy exceeded 5 mm in 9% of fractions in the AP direction and 21% of fractions in the SI direction. The 3D vector length from skin marks to Calypso alignment exceeded 1 cm in 24% of all 652 fractions with available setup data. During treatment, the target exceeded the 5-mm tracking limit for at least 30 sec in 11% of all fractions, generally in the AP or SI direction. In the AP direction, target motion was twice as likely to move posteriorly, toward the rectum, than anteriorly. 15% of all treatments were interrupted for repositioning, and 70% of patients were repositioned at least once during their treatment course.	3
174. Stephans KL, Xia P, Tendulkar RD, Ciezki JP. The current status of image-guided external beam radiotherapy for prostate cancer. *Curr Opin Urol.* 2010;20(3):223-228.	Review/Other-Tx	N/A	To assess the current status and technological advances in image-guided EBRT for prostate cancer.	Modern imaging has improved the ability to define RT target volumes. Specifically, treatment margins have been reduced through the use of treatment planning and image-guidance technology. Increasing dose has led to increased disease control. Concurrent technological advances may improve treatment-related toxicity. Data continues to emerge on patient selection, treatment schedule, and use of additional systemic therapy in conjunction with radiation.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
175. Das S, Liu T, Jani AB, et al. Comparison of image-guided radiotherapy technologies for prostate cancer. *Am J Clin Oncol.* 2014;37(6):616-623.	Review/Other-Tx	N/A	To summarize the advantages, disadvantages, and the limitations of IGRT technologies.	Radiation oncology has seen a rapid increase in the use of IGRT technology for prostate cancer patients over the past decade. The increase in the use of IGRT is largely driven by the fact that these technologies have been approved by the Food and Drug Administration and are now readily reimbursed by many insurance companies. Prostate cancer patients undergoing IMRT now have access to a wide variety of IGRTs that can cost anywhere from $500,000 or more in upfront costs, and can add anywhere from 10 to 15 thousand dollars to a course of IMRT. Some of the IGRT options include daily CBCT, US, orthogonal X-ray units using implanted fiducial markers, implanted radiofrequency markers with the ability to localize and track prostate motion during RT (Calypso 4D), and cine MRI. Although these technologies add to the cost of IMRT, there is little direct comparative effectiveness data to help patients, physicians, and policy makers decide if 1 technology is better than another.	4
176. Park SS, Yan D, McGrath S, et al. Adaptive image-guided radiotherapy (IGRT) eliminates the risk of biochemical failure caused by the bias of rectal distension in prostate cancer treatment planning: clinical evidence. *Int J Radiat Oncol Biol Phys.* 2012;83(3):947-952.	Observational-Tx	962 patients	To study the effect of rectal volume/distension on biochemical control and GI/GU toxicity in patients treated with the adaptive RT technique.	Median follow-up was 5.5 years. Median minimum dose covering confidence-limited-PTV was 75.6 Gy. Median values for rectal volume, cross-sectional area, and SV to the inferior prostate were 82.8 cm(3), 5.6 cm(2), and 53.3 cm(3), respectively. The 5-year BC was 89% for the entire group: 96% for low risk and 83% for intermediate/high risk ($P<0.001$). No statistically significant differences in biochemical control were seen with stratification by rectal volume, cross-sectional area, and SV to the inferior prostate in quartiles. Maximum chronic Grades ≥2 and 3 GI toxicities were 21.2% and 2.9%, respectively. Respective values for GU toxicities were 15.5% and 4.3%. No differences in GI or GU toxicities were noted when patients were stratified by rectal volume.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
177. Kupelian PA, Langen KM, Willoughby TR, Zeidan OA, Meeks SL. Image-guided radiotherapy for localized prostate cancer: treating a moving target. *Semin Radiat Oncol.* 2008;18(1):58-66.	Review/Other-Tx	N/A	To present our current understanding of prostate motion and deformation, to clarify how different current targeting methods attempt to address prostate motion and deformation, and review the limited available clinical outcome data (tumor control and toxicity) resulting from the use of such targeting techniques.	No results stated in the abstract.	4
178. Poli ME, Parker W, Patrocinio H, et al. An assessment of PTV margin definitions for patients undergoing conformal 3D external beam radiation therapy for prostate cancer based on an analysis of 10,327 pretreatment daily ultrasound localizations. *Int J Radiat Oncol Biol Phys.* 2007;67(5):1430-1437.	Observational-Tx	387 patients	To assess the PTV margins required for adequate treatment of the prostate in the absence of daily localization imaging based on the statistical analysis of a large data set obtained from 5 years of use of a 2D US pretreatment localization device.	The mean displacements required to shift the target to the required position were 6.1 mm posterior (4.4 mm SD), 2.1 mm superior (4.5 mm SD), and 0.5 mm right (3.6 mm SD). The 6.1 mm shift posterior is indicative of a systematic uncertainty. Differences in planning conditions between the CT simulation and the treatment room may account for this discrepancy. The study reveals systematic intertreatment uncertainties that would have required a nonuniform PTV margin ranging in dimensions between 2.7 mm anterior, 14.9 mm posterior, 7.7 mm right, 6.7 mm left, 11 mm superior, and 7 mm inferior to encompass the prostate for 95% of our sample if the US localization system were not used. In the absence of systematic uncertainties, a uniform PTV margin of 9 mm would suffice.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
179. Boda-Heggemann J, Kohler FM, Kupper B, et al. Accuracy of ultrasound-based (BAT) prostate-repositioning: a three-dimensional on-line fiducial-based assessment with cone-beam computed tomography. *Int J Radiat Oncol Biol Phys.* 2008;70(4):1247-1255.	Experimental-Tx	8 patients	To assess the accuracy of US-based repositioning before prostate radiation with fiducial-based 3D matching with CBCT.	Overall mean value (MV+/-SD) residual error after US-based repositioning based on fiducial registration by CBCT was 0.7+/-1.7 mm in x (group systematic error [M]=0.5 mm; SD of systematic error [sigma]=0.8 mm; SD of random error [sigma]=1.4 mm), 0.9+/-3.3 mm in y (M=0.5 mm, sigma=2.2 mm, sigma=2.8 mm), and -1.7+/-3.4 mm in z (M=-1.7 mm, sigma=2.3 mm, sigma=3.0 mm) directions, whereas residual error relative to positioning based on skin marks was 2.1+/-4.6 mm in x (M=2.6 mm, Sigma=3.3 mm, sigma=3.9 mm), -4.8+/-8.5 mm in y (M=-4.4 mm, sigma=3.7 mm, sigma=6.7 mm), and -5.2+/-3.6 mm in z (M=-4.8 mm, sigma=1.7 mm, sigma=3.5 mm) directions and relative to positioning based on bony anatomy was 0+/-1.8 mm in x (M=0.2 mm, Sigma=0.9 mm, sigma=1.1 mm), -3.5+/-6.8 mm in y (M=-3.0 mm, sigma=1.8 mm, sigma=3.7 mm), and -1.9+/-5.2 mm in z (M=-2.0 mm, sigma=1.3 mm, sigma=4.0 mm) directions. BAT improved the daily repositioning accuracy over skin marks or even bony anatomy. The results obtained with b-mode US are within the precision of extracranial stereotactic procedures and represent values that can be achieved with several users with different education levels. If sonographic visibility is insufficient, CBCT or kV/MV portal imaging with implanted fiducials are recommended.	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
180. Greer PB, Dahl K, Ebert MA, Wratten C, White M, Denham JW. Comparison of prostate set-up accuracy and margins with off-line bony anatomy corrections and online implanted fiducial-based corrections. *J Med Imaging Radiat Oncol.* 2008;52(5):511-516.	Experimental-Tx	11 patients	To determine prostate set-up accuracy and set-up margins with off-line bony anatomy-based imaging protocols compared with online implanted fiducial marker-based imaging with daily corrections.	The prostate systematic set-up errors in the medial-lateral, SI and AP directions for skin marker set-up were 2.2, 3.6, and 4.5 mm (1 SD). For our bony anatomy-based off-line protocol the prostate systematic set-up errors were 1.6, 2.5, and 4.4 mm. For the online fiducial based set-up the results were 0.5, 1.4, and 1.4 mm. A prostate systematic error of 10.2 mm was uncorrected by the off-line bone protocol in 1 patient. Set-up margins calculated to encompass 98% of prostate set-up shifts were 11–14 mm with bone off-line set-up and 4–7 mm with online fiducial markers. Margins from the van Herk margin recipe were generally 1–2 mm smaller. Bony anatomy-based set-up protocols improve the group prostate set-up error compared with skin marks; however, large prostate systematic errors can remain undetected or systematic errors increased for individual patients. The margin required for set-up errors was found to be 10–15 mm unless implanted fiducial markers are available for treatment guidance.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
181. Chung PW, Haycocks T, Brown T, et al. On-line aSi portal imaging of implanted fiducial markers for the reduction of interfraction error during conformal radiotherapy of prostate carcinoma. *Int J Radiat Oncol Biol Phys.* 2004;60(1):329-334.	Experimental-Tx	17 patients; 239 portal images	To report the results and accuracy of patient setup a fiducial marker system with daily portal images were reported.	After identification and correction, prostate center of mass displacements were <3 mm in all directions. The therapists found it simple to match markers 88% of the time using this system. Treatment delivery times were in the order of 9 min for patients requiring isocenter adjustment and 6 min for those who did not. Fiducial markers with daily imaging is technically possible to implement and use as part of an on-line correction protocol and does not require a longer than standard daily appointment time at our center with the current action limit of 3 mm. The system is commercially available and is more efficient and user-friendly than portal film analysis. It provides the opportunity to identify and accommodate interfraction organ motion and may also permit the use of smaller margins during conformal prostate RT. Further integration of the system such as remote table control would improve efficiency.	3
182. Beaulieu L, Girouard LM, Aubin S, et al. Performing daily prostate targeting with a standard V-EPID and an automated radio-opaque marker detection algorithm. *Radiother Oncol.* 2004;73(1):61-64.	Experimental-Tx	14 patients	To show the feasibility of implementing an automated online 3D target verification and position correction procedure on a daily basis, using a widely available standard video-based electronic portal imaging device as an online guiding tool.	The average systematic (random) errors have been reduced from 2.1 mm (2.7 mm) to 0.5 mm (1.5 mm) in AP direction, 1.1 mm (1.7 mm) to 0.7 mm (1.2 mm) SI and 1.2 mm (1.7 mm) to 0.6 mm (1.3 mm) left-right. Even though the image quality of such a system is generally considered poor, target position correction using fiducial markers is feasible and yields results comparable to that of a standard video-based electronic portal imaging device. The present approach is easily exportable to the community with almost no addition of equipment and has a limited impact on the overall treatment times. Based on the results, margin reduction, if appropriate, is possible with an online correction procedure. The residual errors from prostate inter-fraction motion were found to be smaller than the systematic contouring uncertainties. Therefore, margin reduction would be limited by the ability to define precisely the target volume.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
183. Graf R, Wust P, Budach V, Boehmer D. Potentials of on-line repositioning based on implanted fiducial markers and electronic portal imaging in prostate cancer radiotherapy. *Radiat Oncol.* 2009;4:13.	Experimental-Tx	23 patients	To compare the use of bony anatomy vs implanted markers for calculation of setup-error plus/minus prostate movement. To estimate the error reduction (and the corresponding margin reduction) by reducing the total error to 3 mm once a week, 3 times per week or every treatment day.	The systematic error (1 SD) in left-right, SI and AP direction contributes for the setup 1.6 mm, 2.1 mm and 2.4 mm and for prostate motion 1.1 mm, 1.9 mm and 2.3 mm. The random error (1 SD) in left-right, SI and AP direction amounts for the setup 2.3 mm, 2.7 mm and 2.7 mm and for motion 1.4 mm, 2.3 mm and 2.7 mm. The resulting total error suggests margins of 7.0 mm left-right, 9.5 mm SI and 9.5 mm AP between CTV and PTV. After correction once a week the margins were lowered to 6.7, 8.2 and 8.7 mm and furthermore down to 4.9, 5.1 and 4.8 mm after correcting every treatment day. Prostate movement relative to adjacent bony anatomy is significant and contributes substantially to the target position variability. Performing on-line setup correction using implanted radiopaque markers and megavoltage radiography results in reduced treatment margins depending on the online imaging protocol (once a week or more frequently).	1
184. Rossi PJ, Schreibmann E, Jani AB, Master VA, Johnstone PA. Boost first, eliminate systematic error, and individualize CTV to PTV margin when treating lymph nodes in high-risk prostate cancer. *Radiother Oncol.* 2009;90(3):353-358.	Observational-Tx	10 consecutive patients	To evaluate the movement of the PTV in relation to the pelvic LNs during treatment of high-risk prostate cancer.	Pelvic LNs CTV was identified in each man using CT-based treatment planning. At treatment planning, median minimum planned dose to the pelvic LNs was 95%, maximum 101%, and mean 97%. Daily couch shifting to prostate markers degraded the dose slightly; median minimum dose to the pelvic LNs was 92%, maximum, 101%, and mean delivered, 96%. Demonstrated degradation of the delivered dose to pelvic LNs PTV, which may occur if daily alignment only to the prostate is considered.	3

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
185. Shi W, Li JG, Zlotecki RA, et al. Evaluation of kV cone-beam ct performance for prostate IGRT: a comparison of automatic grey-value alignment to implanted fiducial-marker alignment. *Am J Clin Oncol.* 2011;34(1):16-21.	Observational-Tx	12 patients	To assess the accuracy of soft-tissue-based automatic alignment as compared with manual alignment using intraprostatic fiducials.	The distribution of the 3D vectors between gray-value and fiducial registrations demonstrated notable differences. The mean summed vector was 0.75 cm, with a SD of 0.52 cm and range from 0.04 to 2.06 cm. There was minimal difference along the lateral direction, with a mean +/- SD of -0.02 cm +/- 0.13 cm. However, there were large discrepancies along the SI and AP direction alignments, with mean +/- SD values of -0.55 +/- 0.48 cm and -0.31 +/- 0.43 cm, respectively.	2
186. Ng M, Brown E, Williams A, Chao M, Lawrentschuk N, Chee R. Fiducial markers and spacers in prostate radiotherapy: current applications. *BJU Int.* 2014;113 Suppl 2:13-20.	Review/Other-Tx	N/A	To review the use of fiducial markers and spacers in prostate RT.	Prostate motion is a significant problem both during and between RT treatments. Intraprostatic fiducials allow accurate prostate localization ensuring RT treatment accuracy. Insertion of gold fiducials is a cost-effective marker that can be easily and quickly implanted and at least three fiducials are recommended. Severe complications from fiducial implantation are uncommon and marker migration is very rarely clinically significant. Spacers are a novel method to distance the rectum from the prostate during RT, reducing acute rectal toxicity, and have no detrimental impact on health-related quality of life.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
187. Schallenkamp JM, Herman MG, Kruse JJ, Pisansky TM. Prostate position relative to pelvic bony anatomy based on intraprostatic gold markers and electronic portal imaging. *Int J Radiat Oncol Biol Phys.* 2005;63(3):800-811.	Observational-Tx	20 patients	To describe the relative positions and motions of the prostate, pelvic bony anatomy, and intraprostatic gold fiducial markers during daily electronic portal localization of the prostate.	A total of 22,266 data points were obtained from daily pre-therapy and through-treatment electronic portal imaging. The pre-therapy 3D average displacement of the fiducial markers, as a surrogate for the prostate, was 5.6 mm, which improved to 2.8 mm after use of the localization protocol. The bony anatomy 3D average displacement was 4.4 mm both before and after localization to the prostate (P=0.46). Along the SI, AP, and right-left axes, the average prostate displacement improved from 2.5, 3.7, and 1.9 mm, respectively, before localization to 1.4, 1.6, and 1.1 mm after (all P<0.001). The pre-therapy to through-treatment position of the bony landmarks worsened from 1.7 to 2.5 mm (P<0.001) in the SI axis, remained statistically unchanged at 2.8 mm (P=0.39) in the AP axis, and improved from 2.0 to 1.2 mm in the right-left axis (P<0.001). There was no significant intrafractional displacement of prostate position or bony anatomic landmarks. An intermarker distance was identified for all fiducial markers, and 96 were followed daily. 79% had a SD of <1 mm, and 96% were <1.5 mm. Margins were 5.1, 7.3, and 5.0 mm in the SI, AP, and RL axes, respectively, before localization and 2.7, 2.9, and 2.8 mm after localization.	2
188. Kumar KA, Wu T, Tonlaar N, Stepaniak C, Yenice KM, Liauw SL. Image-guided radiation therapy for prostate cancer: A computed tomography-based assessment of fiducial marker migration between placement and 7 days. *Pract Radiat Oncol.* 2015;5(4):241-247.	Observational-Tx	100 patients	To determine whether clinically significant fiducial marker migration occurs immediately after prostatic implantation.	The average d (mean distance) for all patients was 0.78 +/- 0.45 mm; only 1 patient had d >2 mm. Placement technique, hormonal therapy, prostate size, and marker distance from the capsule were not associated with d (P>.05). The mean percentages of day 7 prostate volumes covered by the day 0 prostate plus 1, 3, and 5 mm were 98.3%, 99.8%, and 100%, respectively. With an expansion of 3 mm, 98% of men had >95% of day 0 volume covered; with an expansion of 5 mm, 100% of men had 100% of the day 0 volume covered.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
189. Nichol AM, Brock KK, Lockwood GA, et al. A magnetic resonance imaging study of prostate deformation relative to implanted gold fiducial markers. *Int J Radiat Oncol Biol Phys*. 2007;67(1):48-56.	Experimental-Tx	25 patients	To describe prostate deformation during RT and determine the margins required to account for prostate deformation after setup to intraprostatic fiducial markers.	During RT, the prostate volume decreased by 0.5%/fraction (P=0.03) and the fiducial markers in-migrated by 0.05 mm/fraction (P<0.05). Prostate deformation was unrelated to differential bladder and bowel filling, but was related to a TURP (P=0.003). The SD for systematic uncertainty of prostate surface contouring was 0.8 mm and for fiducial markers centroid localization was 0.4 mm. The SD of random interfraction prostate deformation was 1.5 mm and for fiducial markers centroid variability was 1.1 mm. These uncertainties from prostate deformation can be incorporated into a margin recipe to determine the total margins required for RT. During RT, the prostate exhibited: volume decrease, deformation, and in-migration of fiducial markers. Patients with TURP were prone to prostate deformation.	2
190. Chua B, Min M, Wood M, et al. Implementation of an image guided intensity-modulated protocol for post-prostatectomy radiotherapy: planning data and acute toxicity outcomes. *J Med Imaging Radiat Oncol.* 2013;57(4):482-489.	Review/Other-Tx	75 patients	To describe our implementation of IG-IMRT, to examine how often published organ-at-risk constraints were met, and to evaluate the incidence of acute GU and GI toxicities when patients were treated according to our protocol.	75 eligible patients received either 64 Gy (19%) or 66 Gy (81%) in a single phase to the prostate bed. Suggested rectal dose-constraints of V40Gy <60% and V60Gy <40% were met in 64 (85%) and 75 (100%) patients, respectively. IMRT-specific rectal dose-constraints of V40Gy <35% and V65Gy <17% were achieved in 5 (7%) and 57 (76%) of patients. Bladder dose-constraint (V50Gy <50%) was met in 58 (77%) patients. 2 patients (3%) experienced new grade 3 GU toxicity and 1 patient (1%) experienced new grade 3 GI toxicity. All grade 3 toxicities had improved by 3-month review. Overall deterioration in urinary and GI symptoms occurred in 33 (44%) and 35 (47%) of patients respectively.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
191. Eldredge HB, Studenski M, Keith SW, et al. Post-prostatectomy image-guided radiation therapy: evaluation of toxicity and inter-fraction variation using online cone-beam CT. *J Med Imaging Radiat Oncol.* 2011;55(5):507-515.	Observational-Tx	68 patients with CBCT; 150 patients with port film	To assess the acute and late GU and GI toxicities of CBCT guided conformal adjuvant and salvage post-prostatectomy RT compared with RT with port films.	Grades 2 and 3 acute GU toxicity were experienced by 13% (n=9) and 2% (n=1) of patients in group 1, respectively, while 13% (n=19) had grade 2 acute GU toxicity in the control group (group 2). Grade 2 acute GI toxicity was experienced by 13% (n=9) and 15% (n=23) in groups 1 and 2, respectively. Acute GU (P=0.67) and GI (P=0.84) toxicities were not significantly different between the 2 groups. There were no associations detected between CBCT and acute GI toxicity (OR 0.76, P=0.57) or acute GU (OR 1.16, P=0.75). Increased odds of acute GU toxicity were observed for doses >68.4 Gy (OR 12.81, P=0.04), which were only delivered in the CBCT group. CBCT mean variations (SD) for 1,053 fractions were 2.8mm (2.8), 2.0mm (2.4) and 3.1mm (2.9) in the left-to-right, AP and SI axes, respectively. Corrective shifts for variance ≥5 mm were required for 15%, 6% and 19% of fractions in the left-to-right, AP and SI axes, respectively.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
192. Court LE, Dong L, Lee AK, et al. An automatic CT-guided adaptive radiation therapy technique by online modification of multileaf collimator leaf positions for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2005;62(1):154-163.	Review/Other-Tx	2 patients; 46 CT image sets (23 each)	To propose and evaluate online adaptive RT using in-room CT imaging that detects changes in the target position and shape of the prostate and SV and then automatically modifies the multileaf collimator leaf pairs in a slice-by-slice fashion.	The shifts and shape change of the prostate and SV could be separated into 3D global shifts in the right-left, AP, and SI directions, plus local shifts in the AP direction, which were different for each CT slice. The multileaf collimator leaf positions were successfully modified to compensate for these global shifts and local shape variations. The adaptive RT method improved geometric coverage of the prostate and SV compared with the couch-shift method, particularly for the superior part of the prostate and all the SV, for which the interfraction shape change was the largest. The dosimetric comparison showed that the adaptive RT method covered the target better and reduced the rectal dose more than a simple couch-translation method. Adaptive RT corrected for interfraction changes in the position and shape of the prostate and SV and gave dose distributions that were considerably closer to the planned dose distributions than could be achieved with simple alignment strategies that neglect shape change. The adaptive RT proposed in this investigation requires neither contouring of the daily CT images nor extensive calculations; therefore, it may prove to be an effective and clinically practical solution to the problem of interfraction shape changes.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
193. Stutzel J, Oelfke U, Nill S. A quantitative image quality comparison of four different image guided radiotherapy devices. *Radiother Oncol.* 2008;86(1):20-24.	Review/Other-Dx	3 different head-sized phantoms	To quantitatively compare the image quality of 4 different IGRT devices based on phantom measurements with respect to the additional dose delivered to the patient.	Based on the current findings for head-sized phantoms all devices show an electron density-to-CT-number conversion almost independent of the imaging parameters and hence can be suited for treatment planning purposes. The evaluation of the image quality, however, points out clear differences due to the different energies and geometries. The Primatom standard CT scanner shows throughout the best performance, especially for soft tissue contrast and spatial resolution with low imaging doses. Considering the entire investigations, especially in terms of contrast and spatial resolution, a rough tendency for decreasing image quality can be given: Primatom, Artíste prototype kV CB, Tomotherapy, Artíste prototype MVCB.	4
194. Hammoud R, Patel SH, Pradhan D, et al. Examining margin reduction and its impact on dose distribution for prostate cancer patients undergoing daily cone-beam computed tomography. *Int J Radiat Oncol Biol Phys.* 2008;71(1):265-273.	Observational-Tx	5 patients; 140 CBCT	To examine the dosimetric impact of margin reduction and quantify residual error after 3D image registration using daily CBCT for prostate cancer patients.	Prostate coverage was within 2% between the 10/6 and 5/3 plans. SV coverage was reduced with the 5/3 plan compared with the 10/6 plan, with coverage difference within 7%. The 5/3 plan allowed 30%–50% sparing of bladder and rectal high-dose regions. For residual error quantification, center of mass data show that 99%, 93%, and 96% of observations fall within 3 mm in the left-right, AP, and SI directions, respectively. Maximal border displacement observations range from 79% to 99%, within 5 mm for all directions. CBCT dosimetrically validated a 10/6 margin when soft-tissue localization is not used. Intensity-based 3D image registration has the potential to improve target localization and to provide guidelines for margin definition.	3

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
195. Pawlowski JM, Yang ES, Malcolm AW, Coffey CW, Ding GX. Reduction of dose delivered to organs at risk in prostate cancer patients via image-guided radiation therapy. *Int J Radiat Oncol Biol Phys.* 2010;76(3):924-934.	Observational-Tx	8 patients	To determine whether image guidance can improve the dose delivered to target organs and organs at risk for prostate cancer patients treated with IMRT.	For the 8 treatment plans on the 56 CBCT scans, the average doses to 98% of the prostate (D98) were 102% (range, 99%–104%) and 99% (range, 45%–104%) with and without image guidance, respectively. Using margin reduction, the average D98s were 100% (range, 84%–104%) and 92% (range, 40%–104%) with and without image guidance, respectively. Currently, margins used in IMRT plans are adequate to deliver a dose to the prostate with conventional patient positioning using skin tattoos or bony anatomy. The use of image guidance may facilitate significant reduction of planning margins. Future studies to assess the efficacy of decreasing margins and improvement of treatment-related toxicities are warranted.	3
196. Ramsey CR, Scaperoth D, Seibert R, Chase D, Byrne T, Mahan S. Image-guided helical tomotherapy for localized prostate cancer: technique and initial clinical observations. *J Appl Clin Med Phys.* 2007;8(3):2320.	Observational-Tx	33 patients	To implement a technique for daily CT-based IGRT and to report observations on treatment planning, imaging, and delivery based on the first 2 years of clinical experience.	The prostate, rectum, bladder, femoral heads, and pubis symphysis were visible in 1 or more slices for all 1,266 MVCT image sets. The typical range of measured prostate displacement relative to a 3-point external laser setup in this study was 2–10 mm [3.4 mm SD] in the AP direction, 2–8 mm (3.7 mm SD) in the lateral direction, and 1–6 mm (2.4 mm SD) in the SI direction. The obese patients in this study had a substantially larger lateral variation (8.2 mm SD) attributable to mobility of skin marks. The prostate, SV, rectum, and bladder anatomy were used to position the patient relative to the desired treatment position without the use of implanted markers. Acute toxicities were within the expected range given the number of patients treated and the dose level.	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
197. Schubert LK, Westerly DC, Tome WA, et al. A comprehensive assessment by tumor site of patient setup using daily MVCT imaging from more than 3,800 helical tomotherapy treatments. *Int J Radiat Oncol Biol Phys.* 2009;73(4):1260-1269.	Observational-Tx	3,867 total fractions: 1,179 brain and head and neck; 1,414 lung; 1,274 prostate	To assess patient setup corrections based on daily MVCT imaging for 4 anatomic treatment sites treated on tomotherapy.	Brain and head and neck had lower magnitude positioning corrections and smaller variations in translational setup errors but were comparable in roll rotations. 3Dl vector translational shifts of larger magnitudes occurred more frequently for lung and prostate than for brain and head and neck treatments, yet this was not observed for roll rotations. The global systematic error for prostate was 4.7 mm in the vertical direction, most likely due to couch sag caused by large couch extension distances. Variations in systematic errors and magnitudes of random translational errors ranged from 1.6 to 2.6 mm for brain and head and neck and 3.2 to 7.2 mm for lung and prostate, whereas roll rotational errors ranged from 0.8 degrees to 1.2 degrees for brain and head and neck and 0.5 degrees to 1.0 degrees for lung and prostate. Differences in setup were observed between brain, head and neck, lung, and prostate treatments. Patient setup can be improved if daily imaging is performed. This analysis can assess the utilization of daily image guidance and allows for further investigation into improved anatomic site-specific and patient-specific treatments.	1
198. Murphy MJ, Balter J, Balter S, et al. The management of imaging dose during image-guided radiotherapy: report of the AAPM Task Group 75. *Med Phys.* 2007;34(10):4041-4063.	Review/Other-Dx	N/A	To review the management of imaging dose during IGRT.	The management of imaging dose during RT is a different problem than its management during routine diagnostic or image-guided surgical procedures. The imaging dose received as part of a RT treatment has long been regarded as negligible and thus has been quantified in a fairly loose manner. On the other hand, radiation oncologists examine the therapy dose distribution in minute detail. The introduction of more intensive imaging procedures for IGRT now obligates the clinician to evaluate therapeutic and imaging doses in a more balanced manner.	4

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
199. Fu W, Yang Y, Yue NJ, Heron DE, Huq MS. A cone beam CT-guided online plan modification technique to correct interfractional anatomic changes for prostate cancer IMRT treatment. *Phys Med Biol.* 2009;54(6):1691-1703.	Review/Other-Tx	3 typical cases evaluated	To develop an online plan modification technique to compensate for the interfractional anatomic changes for prostate cancer IMRT treatment based on daily CBCT images.	The study revealed that the proposed modification technique is superior to the bony-structure-based and prostate-based correction techniques, especially when interfractional target deformation exists. Its dosimetric performance is closer to that of the re-planned strategy, but with much higher efficiency, indicating that the introduced online CBCT-guided plan modification technique may be an efficient and practical method to compensate for the interfractional target position and shape changes for prostate IMRT.	4
200. Cheung J, Aubry JF, Yom SS, Gottschalk AR, Celi JC, Pouliot J. Dose recalculation and the Dose-Guided Radiation Therapy (DGRT) process using megavoltage cone-beam CT. *Int J Radiat Oncol Biol Phys.* 2009;74(2):583-592.	Review/Other-Tx	8 patient datasets (6 head and neck, 2 prostate)	To present the process of performing dose recalculation on MVCT images and discusses possible strategies for dose-guided RT.	Analysis of the head-and-neck datasets shows that interfraction treatment doses vary compared with the planning dose for the organs at risk, with the mean parotid dose and spinal cord D(1) increasing by as much as 52% and 10%, respectively. Variation of the coverage to the target volumes was small, with an average D(5) dose difference of 1%. The prostate patient datasets revealed accurate dose coverage to the targeted prostate and varying interfraction dose distributions to the organs at risk. An effective workflow for the clinical implementation of dose-guided RT has been established. With these techniques in place, future clinical developments in adaptive RT through daily or weekly dosimetric measurements of treatment day images are possible.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
201. Varadhan R, Hui SK, Way S, Nisi K. Assessing prostate, bladder and rectal doses during image guided radiation therapy--need for plan adaptation? *J Appl Clin Med Phys.* 2009;10(3):2883.	Observational-Tx	10 patients	To evaluate the dosimetric uncertainties caused by inter-fraction organ variation during IGRT using kV CBCT on the Elekta Synergy system and MVCT on the Tomotherapy Hi-ART system.	Due to the large deviation in CT number (300 HU) between the kV CBCT images and the kV CT, a direct dose recomputation on the kV CBCT images from the Elekta Synergy system was found to be inaccurate. The maximum deviation to the prostate was only 2.7% in our kV CBCT study when compared to the daily prescribed dose. However, there was a large daily variation in rectum and bladder doses based on the anatomy of the day. The maximum variation in rectum and bladder volumes receiving the percentage of prescribed dose was 12% and 40% respectively. The researchers have shown that by using Planned Adaptive software on the Tomotherapy Hi-ART system, plans can be adapted based on the image feedback from daily MVCT scans to allow the actual delivered doses to closely track the original planned doses.	3
202. Balter JM, Wright JN, Newell LJ, et al. Accuracy of a wireless localization system for radiotherapy. *Int J Radiat Oncol Biol Phys.* 2005;61(3):933-937.	Review/Other-Tx	N/A	To demonstrate the accuracy of the system before clinical trials.	Submillimeter accuracy was maintained throughout all experiments. Precision was greater proximal to the source plane (sigmax = 0.006 mm, sigmay = 0.01 mm, sigmaz = 0.006 mm), but continued to be submillimeter at the end of the designed tracking range at 270 mm from the array (sigmax = 0.27 mm, sigmay = 0.36 mm, sigmaz = 0.48 mm). The introduction of saline and the use of multiple beacons did not affect accuracy. Submillimeter accuracy was maintained using the dynamic phantom at speeds of up to 3 cm/s. This system has demonstrated the accuracy needed for localization and monitoring of position during treatment.	4

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
203. Langen KM, Willoughby TR, Meeks SL, et al. Observations on real-time prostate gland motion using electromagnetic tracking. *Int J Radiat Oncol Biol Phys.* 2008;71(4):1084-1090.	Experimental-Tx	17 patients	To quantify and describe the real-time movement of the prostate gland in a large data set of patients treated with RT.	Averaged over all patients, the prostate was displaced >3 and >5 mm for 13.6% and 3.3% of the total treatment time, respectively. For individual patients, the corresponding maximal values were 36.2% and 10.9%. For individual fractions, the corresponding maximal values were 98.7% and 98.6%. Displacements >3 mm were observed at 5 min after initial alignment in about one-eighth of the observations, and increased to one-quarter by 10 min. For individual patients, the maximal value of the displacements >3 mm at 5 and 10 min after initial positioning was 43% and 75%, respectively. On average, the prostate was displaced by >3 mm and >5 mm approximately 14% and 3% of the time, respectively. For individual patients, these values were up to 3 times greater. After the initial positioning, the likelihood of displacement of the prostate gland increased with elapsed time. This highlights the importance of initiating treatment shortly after initially positioning the patient.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
204. Zhu X, Bourland JD, Yuan Y, et al. Tradeoffs of integrating real-time tracking into IGRT for prostate cancer treatment. *Phys Med Biol.* 2009;54(17):N393-401.	Review/Other-Tx	N/A (phantoms)	To investigate the integration of the Calypso real-time tracking system based on implanted ferromagnetic transponders and a detector array, into the current process for IGRT of prostate cancer at our institution.	The measurements show that the Calypso system is safe with all the imaging systems. Transponder position displacements due to the MR field are minimal (<1.0 mm) for both 1.5 T and 3 T MRI scanners, and the temperature variation due to MRI RF heating is <0.2 degrees C. The visibility of transponders and bony anatomy was not affected on the OBI kV and CT images. Image quality degradation caused by the detector antenna array is observed in the CBCT image. Image artifacts are most significant with the gradient echo sequence in the MRI, producing null signals surrounding the transponders with radii approximately 1.5 cm and length approximately 4 cm. Thus, Calypso transponders can preclude the use of MRI/MRS in post-treatment assessment. Modifications of the clinical flow are required to accommodate and minimize the substantial MRI artifacts induced by the Calypso transponders.	4
205. van Herk M. Errors and margins in radiotherapy. *Semin Radiat Oncol.* 2004;14(1):52-64.	Review/Other-Tx	N/A	To give an overview of errors in RT and margin recipes, based on physical and biological considerations.	No results stated in the abstract.	4
206. Perez-Romasanta LA, Lozano-Martin E, Velasco-Jimenez J, et al. CTV to PTV margins for prostate irradiation. Three-dimensional quantitative assessment of interfraction uncertainties using portal imaging and serial CT scans. *Clin Transl Oncol.* 2009;11(9):615-621.	Experimental-Tx	20 patients	To determine the magnitude of setup and organ motion errors from a subset of prostate cancer patients treated with conventional CRT, and to estimate the CTV-PTV margin according to published margin recipes.	Tattoo localization requires a margin of 9–10.5 mm (left-right), 15.2–17.8 mm (AP) and 10.6–12.4 mm (SI). Systematic displacements due to prostatic motion, with SDs of 2.4 mm (left-right), 4.2 mm (AP) and 3.1 mm (SI) were found to be larger than setup errors (1.8, 3.0 and 1.7 mm respectively).	2

External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
207. Wu Q, Ivaldi G, Liang J, Lockman D, Yan D, Martinez A. Geometric and dosimetric evaluations of an online image-guidance strategy for 3D-CRT of prostate cancer. *Int J Radiat Oncol Biol Phys.* 2006;64(5):1596-1609.	Observational-Tx	28 patients	To evaluate an online image-guidance strategy for conformal treatment of prostate cancer and to estimate margin-reduction benefits.	Average isocenter shift and rotation were (dX,dY,dZ,theta) = (0.0 +/- 0.7,-1.1 +/- 4.0,-0.1 +/- 2.5,0.7 degrees +/- 2.0 degrees) mm. Prostate motion in AP direction was significantly higher than SI and left-right directions. This observation was confirmed by isocenter shift in perspectives AP (1.8 +/- 1.8 mm) and RL (3.7 +/- 3.0 mm). Organ motion degrades target coverage and reduces doses to rectum. If 2% dose reduction on prostate D(99) is allowed for 90% patients, then minimum 3 mm margins are necessary with ideal image registration.	2
208. Letourneau D, Martinez AA, Lockman D, et al. Assessment of residual error for online cone-beam CT-guided treatment of prostate cancer patients. *Int J Radiat Oncol Biol Phys.* 2005;62(4):1239-1246.	Experimental-Tx	8 patients, 1 phantom	To assess the magnitude and stability of the residual setup error associated with CBCT online-guided prostate cancer patient setup.	For ideal rigid phantoms, CBCT image-guided treatment can usually achieve setup accuracy of 1 mm or better. For the patients, after CBCT correction, the target setup error was reduced in almost all cases and was generally within +/-1.5 mm. The image guidance process took 23-35 min, dictated by the computer speed and network configuration. The contribution of the intrafraction motion to the residual setup error was small, with a SD of +/-0.9 mm. The average difference between the setup corrections obtained with coil and soft-tissue registration was greatest in the superoinferior direction and was equal to -1.1 +/- 2.9 mm.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
209. Ghilezan M, Yan D, Liang J, Jaffray D, Wong J, Martinez A. Online image-guided intensity-modulated radiotherapy for prostate cancer: How much improvement can we expect? A theoretical assessment of clinical benefits and potential dose escalation by improving precision and accuracy of radiation delivery. *Int J Radiat Oncol Biol Phys.* 2004;60(5):1602-1610.	Observational-Tx	22 patients	To quantify the theoretical benefit, in terms of improvement in precision and accuracy of treatment delivery and in dose increase, of using online IG-IMRT performed with onboard CBCT, in an ideal setting of no intrafraction motion/deformation, in the treatment of prostate cancer.	With respect to radiosensitive tumor, the average equivalent uniform dose for the target (prostate plus SVs) was 96.8% for conventional IMRT and 98.9% for online IG-IMRT, with SDs of 5.6% and 0.7%, respectively ($P<0.0001$). The average equivalent uniform doses of bladder wall and rectal wall for conventional IMRT vs online IG-IMRT were 70.1% vs 47.3%, and 79.4% vs 72.2%, respectively. On average, a target dose increase of 13% (SD = 9.7%) can be achieved with online IG-IMRT based on rectal wall equivalent uniform doses and 53.3% (SD = 15.3%) based on bladder wall equivalent uniform doses. However, the variation (SD = 9.7%) is fairly large among patients; 27% of patients had only minimal benefit (<5% of dose increment) from online IG-IMRT, and 32% had significant benefit (>15%-41% of dose increment).	2
210. Yan D, Lockman D, Brabbins D, Tyburski L, Martinez A. An off-line strategy for constructing a patient-specific planning target volume in adaptive treatment process for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2000;48(1):289-302.	Experimental-Tx	30 patients	To propose a patient-specific confidence-limited PTV in an adaptive treatment process for prostate cancer.	The bounding volume constructed using daily CT measurements in the first week of treatment are adequate for the conventional beam delivery to achieve maximum dose reduction in the CTV of 2% or less of the prescription dose, for at least 80% of patients ($P=0.08$), and 4.5% or less for 95% of patients ($P=0.1$). However, for IMRT delivery, 2 weeks of daily CT measurements are required to achieve a similar level of the dosimetric criterion; otherwise the maximum dose reduction of 7%, on average, in the CTV is expected. Furthermore, the patient-specific setup margin required for the IMRT treatment is at least twice larger than that for the conventional treatment, to maintain the same dosimetric criterion. As compared to the conventional PTV, the volume of confidence-limited PTV is significantly reduced, while maintaining the same dosimetric criterion.	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
211. Schulze D, Liang J, Yan D, Zhang T. Comparison of various online IGRT strategies: The benefits of online treatment plan re-optimization. *Radiother Oncol.* 2009;90(3):367-376.	Observational-Tx	9 patients	To compare the dosimetric differences of various online IGRT strategies and to predict potential benefits of online re-optimization techniques in prostate cancer radiation treatments.	With the same margin, rectum and bladder doses in IMRT plans were about 10% and 5% less than those in CRT plans, respectively. Rectum and bladder doses were reduced as much as 20% if motion margin is reduced by 1cm. IMRT is more sensitive to organ motion. Large discrepancies of bladder and rectum doses were observed compared to the actual delivered dose with treatment plan predication. The therapeutic ratio can be improved by 14% and 25% for rectum and bladder, respectively, if IMRT online re-planning is employed compared to the IMRT bone alignment approach. The improvement of target alignment approach is similar with 11% and 21% dose reduction to rectum and bladder, respectively. However, underdosing in SVs was observed on certain patients.	3
212. Engels B, Soete G, Gevaert T, Storme G, Michielsen D, De Ridder M. Impact of planning target volume margins and rectal distention on biochemical failure in image-guided radiotherapy of prostate cancer. *Radiother Oncol.* 2014;111(1):106-109.	Observational-Tx	50 patients	To investigate the impact of appropriate PTV margins and rectal distention on FFBF.	The overall 5-year FFBF was 83%. A 6 mm PTV margin was related to increased 5-year FFBF on univariate analysis (96% vs 74% with the tighter PTV margins, P=0.04). The 5-year FFBF of patients with a rectal distention on the planning CT was worse compared to those with limited rectal filling (75% for cross-sectional area(2) vs 89% for cross-sectional area<9cm(2), P=0.02), which remained significant on multivariate analysis (P=0.04).	2

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
213. Hummel S, Simpson EL, Hemingway P, Stevenson MD, Rees A. Intensity-modulated radiotherapy for the treatment of prostate cancer: a systematic review and economic evaluation. *Health Technol Assess.* 2010;14(47):1-108, iii-iv.	Review/Other-Tx	N/A	To evaluate the clinical effectiveness and cost-effectiveness of IMRT for the radical treatment of prostate cancer.	No randomized controlled trials of IMRT vs 3D-CRT in prostate cancer were available, but 13 nonrandomized studies comparing IMRT with 3D-CRT were found, of which 5 were available only as abstracts. One abstract reported OS. bRFS was not affected by treatment group, except where there was a dose difference between groups, in which case higher dose IMRT was favored over lower dose 3D-CRT. Most studies reported an advantage for IMRT in GI toxicity, attributed to increased conformality of treatment compared with 3D-CRT, particularly with regard to volume of rectum treated. There was some indication that GU toxicity was worse for patients treated with dose escalated IMRT, although most studies did not find a significant treatment effect. health-related quality of life improved for both treatment groups following RT, with any group difference resolved by 6 months after treatment. No comparative studies of IMRT vs prostatectomy were identified. No comparative studies of IMRT in prostate cancer patients with bone metastasis were identified.	4
214. Martinez AA. RTOG 0815: A Phase III Prospective Randomized Trial of Dose-Escalated Radiotherapy with or without Short-Term Androgen Deprivation Therapy for Patients with Intermediate-Risk Prostate Cancer. 2012; http://www.rtog.org/clinicaltrials/protocoltable/studydetails.aspx?study=0815.	Review/Other-Tx	Ongoing	To demonstrate an OS advantage for the addition of short-term (6 months) ADT to dose-escalated RT for patients with intermediate-risk prostate cancer. The events for OS will be defined as death due to any cause.	This trial is still recruiting study subjects and results are not available yet.	4
215. American College of Radiology. ACR–ASTRO Practice Parameter for Intensity Modulated Radiation Therapy (IMRT). Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/IMRT.pdf. Accessed April 24, 2015.	Review/Other-Tx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
216. American College of Radiology. ACR Technical Standard for the Performance of Radiation Oncology Physics for External Beam Therapy. Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/standards/ROPhysicsExtBeamTherapy.pdf. Accessed April 24, 2015.	Review/Other-Tx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4
217. Ezzell GA, Galvin JM, Low D, et al. Guidance document on delivery, treatment planning, and clinical implementation of IMRT: report of the IMRT Subcommittee of the AAPM Radiation Therapy Committee. *Med Phys.* 2003;30(8):2089-2115.	Review/Other-Tx	N/A	To guide and assist the clinical medical physicist in developing and implementing a viable and safe IMRT program.	This report, while not prescribing specific procedures, provides the framework and guidance to allow clinical radiation oncology physicists to make judicious decisions in implementing a safe and efficient IMRT program in their clinics.	4
218. Wolff D, Stieler F, Welzel G, et al. Volumetric modulated arc therapy (VMAT) vs. serial tomotherapy, step-and-shoot IMRT and 3D-conformal RT for treatment of prostate cancer. *Radiother Oncol.* 2009;93(2):226-233.	Observational-Tx	9 patient datasets	To compare VMAT against established IMRT and 3D-CRT delivery techniques.	For MIMiC/IMRT(MLC)/VMAT2x/VMAT1x/3D-CRT, mean CI was 1.5/1.23/1.45/1.51/1.46 and HI was 1.19/1.1/1.09/1.11/1.04. For a prescribed dose of 76 Gy, mean doses to organs-at-risk were 50.69 Gy/53.99 Gy/60.29 Gy/61.59 Gy/66.33 Gy for the anterior half of the rectum and 31.85 Gy/34.89 Gy/38.75 Gy/38.57 Gy/55.43 Gy for the posterior rectum. Volumes of nontarget normal tissue receiving ≥70% of prescribed dose (53 Gy) were 337 ml/284 ml/482 ml/505 ml/414 ml, for ≥50% (38 Gy) 869 ml/933 ml/1155 ml/1231 ml/1993 ml and for ≥30% (23 Gy) 2819 ml/3414 ml/3340 ml/3438 ml /3061 ml. D(95%) was 69.79 Gy/70.51 Gy/71,7 Gy/71.59 Gy/73.42 Gy. Mean treatment time was 12 min/6 min/3.7 min/1.8 min/2.5 min.	3
219. American College of Radiology. ACR–ASTRO Practice Parameter for the Performance of Stereotactic Body Radiation Therapy. Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Stereo_body_radiation.pdf. Accessed April 24, 2015.	Review/Other-Tx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
220. American College of Radiology. ACR–ASTRO Practice Parameter for the Performance of Proton Beam Radiation Therapy. Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/Rad_Onc_Proton_Therapy.pdf. Accessed April 24, 2015.	Review/Other-Tx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4
221. Benedict SH, Yenice KM, Followill D, et al. Stereotactic body radiation therapy: the report of AAPM Task Group 101. *Med Phys*. 2010;37(8):4078-4101.	Review/Other-Tx	N/A	A review of the literature to identify reported clinical findings and expected outcomes for SBRT.	No results stated in the abstract.	4
222. Kim DW, Cho LC, Straka C, et al. Predictors of rectal tolerance observed in a dose-escalated phase 1-2 trial of stereotactic body radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys*. 2014;89(3):509-517.	Experimental-Tx	91 patients	To convey the occurrence of isolated cases of severe rectal toxicity at the highest dose level tested in 5-fraction SBRT for localized prostate cancer; and to rationally test potential causal mechanisms to guide future studies and experiments to aid in mitigating or altogether avoiding such severe bowel injury.	At the highest dose level, 6.6% of patients treated (6/91) developed high-grade rectal toxicity, 5 of whom required colostomy. Grade 3+ delayed rectal toxicity was strongly correlated with volume of rectal wall receiving 50 Gy >3 cm(3) (P<.0001), and treatment of >35% circumference of rectal wall to 39 Gy (P=.003). Grade 2+ acute rectal toxicity was significantly correlated with treatment of >50% circumference of rectal wall to 24 Gy (P=.010).	1
223. American College of Radiology. ACR–ASTRO Practice Parameter for Image-Guided Radiation Therapy (IGRT). Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/IGRT.pdf. Accessed April 24, 2015.	Review/Other-Tx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4
224. Bissonnette JP, Balter PA, Dong L, et al. Quality assurance for image-guided radiation therapy utilizing CT-based technologies: a report of the AAPM TG-179. *Med Phys*. 2012;39(4):1946-1963.	Review/Other-Tx	N/A	To provide consensus recommendations for quality assurance protocols that ensure patient safety and patient treatment fidelity for such systems.	This report proposes a generic quality assurance program for CT-based IGRT systems in an effort to provide a vendor-independent program for clinical users. Published data from long-term, repeated quality control tests form the basis of the proposed test frequencies and tolerances.	4
225. Molloy JA, Chan G, Markovic A, et al. Quality assurance of U.S.-guided external beam radiotherapy for prostate cancer: report of AAPM Task Group 154. *Med Phys*. 2011;38(2):857-871.	Review/Other-Tx	N/A	To produce a guidance document for clinical medical physicists describing recommended quality assurance procedures for US-guided EBRT localization.	No results stated in the abstract.	4

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.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

3D-CRT = 3D-confromal radiation therapy
ADT = Androgen deprivation therapy
AP = Anterior-posterior
AUC = Areas under the receiver operating characteristic curve
BAT = B-mode acquisition and targeting
BDFS = Biochemical disease-free survival
BMI = Body mass index
bNED = Biochemical no evidence of disease
bPFS = Biochemical progression-free survival
bRFS = Biochemical relapse-free survival
CBCT = Cone-beam computed tomography
CRT = Conformal radiation therapy
CT = Computed tomography
CTV = Clinical target volume
DCE-MRI = Dynamic contrast-enhanced magnetic resonance imaging
DFS = Disease-free survival
DIL = Dominant intraprostatic lesion
EBRT = External-beam radiation therapy
ECE = Extracapsular extension
FFBF = Freedom from biochemical failure
GI = Gastrointestinal
GS = Gleason score
GU = Genitourinary
HR = Hazard ratio
IBD = Inflammatory bowel disease
IGRT = Image-guided radiotherapy
IMRT = Intensity-modulated radiotherapy
iPSA = Initial pretreatment prostate-specific antigen
kV = Kilovoltage
LN = Lymph node
MRI = Magnetic resonance imaging
MRSI = Magnetic resonance spectroscopic imaging
MVCT = Megavoltage computed tomography
NPV = Negative predictive value
OS = Overall survival
PBRT = Prostate bed radiotherapy
PET = Positron emission tomography
PFS = Progression-free survival
PPV = Positive predictive value
PSA = Prostate-specific antigen
PTV = Planning target volume
RP = Radical prostatectomy
RT = Radiation therapy
SBRT = Stereotactic body radiation therapy
SD = Standard deviation
SI = Superior-inferior
SV = Seminal vesicle
SVI = Seminal vesicle invasion
TRUS = Transrectal ultrasound
TURP = Transurethral resection of the prostate
US = Ultrasound
VMAT = Volumetric modulated arc therapy
WPRT = Whole-pelvic radiotherapy