Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. The NCCN Clinical Practice Guidelines in Oncology™ Prostate Cancer V.1.2015 © 2015 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf.	Review/Other-Tx	N/A	To provide guidelines in prostate cancer.	No abstract available.	4
2. Morris WJ, Keyes M, Spadinger I, et al. Population-based 10-year oncologic outcomes after low-dose-rate brachytherapy for low-risk and intermediate-risk prostate cancer. *Cancer.* 2013;119(8):1537-1546.	Observational-Tx	1,006 patients	To report the rates of DFS, CSS, and OS after LDR prostate brachytherapy.	The median follow-up was 7.5 years. By using Fine and Gray competing risks analysis, the 5-year and 10-year actuarial DFS rates were 96.7% (95% CI, 95.2%–97.7%) and 94.1% (95% CI, 92%–95.6%), respectively. When applied to the whole cohort, none of the usual prognostic variables, including dose metrics, were correlated with DFS. However, in both univariate and multivariate models, increasing dose was the only covariate that correlated with improved DFS for the subset of men (n = 348) who did not receive ADT (*P*=.043). The actuarial 10-year CSS rate was 99.1% (95% CI, 97.3%–99.7%). The OS rate was 93.8% at 5 years (95% CI, 92%–95.1%) and 83.5% at 10 years (95% CI, 79.8%–86.6%). Only age at implantation (*P*=.0001) was correlated with OS in multivariate analysis.	2
3. Sylvester JE, Grimm PD, Wong J, Galbreath RW, Merrick G, Blasko JC. Fifteen-year biochemical relapse-free survival, cause-specific survival, and overall survival following I(125) prostate brachytherapy in clinically localized prostate cancer: Seattle experience. *Int J Radiat Oncol Biol Phys.* 2011;81(2):376-381.	Observational-Tx	215 patients	To report 15-year bRFS, CSS, and OS outcomes of patients treated with I-125brachytherapy monotherapy for clinically localized prostate cancer early in the Seattle experience.	15-year bRFS for the entire cohort was 80.4%. bRFS by D'Amico risk group classification cohort analysis was 85.9%, 79.9%, and 62.2% for low, intermediate, and high-risk patients, respectively. Follow-up ranged from 3.6 to 18.4 years; median follow-up was 15.4 years for biochemically free of disease patients. Overall median follow-up was 11.7 years. The median time to biochemical failure in those who failed was 5.1 years. CSS was 84%. OS was 37.1%. Average age at time of treatment was 70 years. There was no significant difference in bRFS between low and intermediate risk groups.	1

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4. Taira AV, Merrick GS, Butler WM, et al. Long-term outcome for clinically localized prostate cancer treated with permanent interstitial brachytherapy. *Int J Radiat Oncol Biol Phys*. 2011;79(5):1336-1342.	Observational-Tx	1,656 patients	To present the largest series of prostate cancer brachytherapy patients treated with modern brachytherapy techniques and postimplant day 0 dosimetric evaluation.	At 12 years, bPFS, CSS, and OS for the entire cohort was 95.6%, 98.2%, and 72.6%, respectively. For low-, intermediate-, and high-risk patients, bPFS was 98.6%, 96.5%, and 90.5%; CSS was 99.8%, 99.3%, and 95.2%; and OS was 77.5%, 71.1%, and 69.2%, respectively. For biochemically controlled patients, the median post-treatment PSA concentration was 0.02 ng/mL. bPFS was most closely related to percent positive biopsy specimens and risk group, while GS was the strongest predictor of CSS. OS was best predicted by patient age, hypertension, diabetes, and tobacco use. At 12 years, biochemical failure and cause-specific mortality were 1.8% and 0.2%, 5.1% and 2.1%, and 10.4% and 7.1% for GSs 5 to 6 and 7 and ≥8, respectively.	2
5. Zelefsky MJ, Yamada Y, Pei X, et al. Comparison of tumor control and toxicity outcomes of high-dose intensity-modulated radiotherapy and brachytherapy for patients with favorable risk prostate cancer. *Urology*. 2011;77(4):986-990.	Observational-Tx	729 patients	To compare the long-term, PSA relapse-free survival outcome and incidence of toxicity for patients with low-risk prostate cancer who underwent brachytherapy or IMRT.	The 7-year PSA relapse-free survival rate for the brachytherapy and IMRT groups was 95% and 89% for low-risk patients, respectively (P=.004). Cox regression analysis demonstrated that brachytherapy was associated with improved PSA relapse-free survival, even after adjustment for other variables. The incidence of metastatic disease between treatment sessions was low for both treatment groups. Late grade 2 GI toxicity was observed in 5.1% and 1.4% of the brachytherapy and IMRT groups, respectively (P=.02). No significant differences were seen between treatment groups for late grade 3 or greater rectal complications (brachytherapy 1.1% and IMRT 0%; P=.19). Late grade 2 urinary toxicity occurred more often in the brachytherapy group than in the IMRT group (15.6% and 4.3%, respectively; P<.0001). No significant differences were seen between the 2 treatment groups for late grade 3 urinary toxicity (brachytherapy 2.2% and IMRT 1.4%; P=.62).	2

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6. Alemozaffar M, Regan MM, Cooperberg MR, et al. Prediction of erectile function following treatment for prostate cancer. *Jama.* 2011;306(11):1205-1214.	Observational-Tx	1027 patients; prostatectomy (n=524), EBRT (n=241), or brachytherapy (n=262).	To predict long-term erectile function following prostate cancer treatment based on individual patient and treatment characteristics.	2-years after prostate cancer treatment, 368 (37% [95% CI, 34%–40%]) of all patients and 335 (48% [95% CI, 45%–52%]) of those with functional erections prior to treatment reported functional erections; 531 (53% [95% CI, 50%–56%]) of patients without penile prostheses reported use of medications or other devices for erectile dysfunction. Pretreatment sexual health-related quality of life score, age, serum PSA level, race/ethnicity, body mass index, and intended treatment details were associated with functional erections 2 years after treatment. Multivariable logistic regression models predicting erectile function estimated 2-year function probabilities from as low as 10% or less to as high as 70% or greater depending on the individual's pretreatment patient characteristics and treatment details. The models performed well in predicting erections in external validation among Cancer of the Prostate Strategic Urologic Research Endeavor [CaPSURE] cohort patients (areas under the receiver operating characteristic curve, 0.77 [95% CI, 0.74–0.80] for prostatectomy; 0.87 [95% CI, 0.80–0.94] for EBRT; and 0.90 [95% CI, 0.85–0.95] for brachytherapy).	1
7. Pardo Y, Guedea F, Aguilo F, et al. Quality-of-life impact of primary treatments for localized prostate cancer in patients without hormonal treatment. *J Clin Oncol.* 2010;28(31):4687-4696.	Observational-Tx	435 patients	To compare the quality-of-life impact of the 3 most common primary treatments on patients who were not receiving adjuvant hormonal treatment.	Compared with the brachytherapy group, the prostatectomy group showed greater deterioration on urinary incontinence and sexual scores but better urinary irritative-obstructive results (-18.22, -13.19, and +6.38, respectively, at 3 years; $P<.001$). In patients with urinary irritative-obstructive symptoms at baseline, improvement was observed in 64% of those treated with nerve-sparing RP. Higher bowel worsening (-2.87, $P=.04$) was observed in the EBRT group, with 20% of patients reporting bowel symptoms.	1

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8. Sanda MG, Dunn RL, Michalski J, et al. Quality of life and satisfaction with outcome among prostate-cancer survivors. *N Engl J Med.* 2008;358(12):1250-1261.	Observational-Tx	1,201 patients and 625 spouses or partners	To identify determinants of health-related quality of life after primary treatment of prostate cancer and to measure the effects of such determinants on satisfaction with the outcome of treatment in patients and their spouses or partners.	Adjuvant hormone therapy was associated with worse outcomes across multiple quality-of-life domains among patients receiving brachytherapy or RT. Patients in the brachytherapy group reported having long-lasting urinary irritation, bowel and sexual symptoms, and transient problems with vitality or hormonal function. Adverse effects of prostatectomy on sexual function were mitigated by nerve-sparing procedures. After prostatectomy, urinary incontinence was observed, but urinary irritation and obstruction improved, particularly in patients with large prostates. No treatment-related deaths occurred; serious adverse events were rare. Treatment-related symptoms were exacerbated by obesity, a large prostate size, a high PSA score, and older age. Black patients reported lower satisfaction with the degree of overall treatment outcomes. Changes in quality of life were significantly associated with the degree of outcome satisfaction among patients and their spouses or partners.	1
9. Grimm P, Billiet I, Bostwick D, et al. Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group. *BJU Int.* 2012;109 Suppl 1:22-29.	Review/Other-Tx	N/A	A comprehensive review of the literature comparing risk stratified patients by treatment option and with long-term follow-up.	A statistical analysis (standard deviational ellipse) of the study outcomes suggested that, in terms of biochemical-free progression, brachytherapy provides superior outcome in patients with low-risk disease. For intermediate-risk disease, the combination of EBRT and brachytherapy appears equivalent to brachytherapy alone. For high-risk patients, combination therapies involving EBRT and brachytherapy plus or minus ADT appear superior to more localized treatments such as seed implant alone, surgery alone or EBRT.	4

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10. Morris WJ, Tyldesley S, Pai H, et al. Low-Dose-Rate Brachytherapy Is Superior to Dose-Escalated EBRT for Unfavourable Risk Prostate Cancer: The Results of the ASCENDE-RT* Randomized Control Trial. *Brachytherapy.* 2015;14, Supplement 1:S12.	Experimental-Tx	276 high-risk and 122 intermediate-risk patients	To compare the rates of biochemically-defined DFS following either: 1) a LDR prostate brachytherapy boost or 2) a dose-escalated EBRT boost for men with National Comprehensive Cancer Network (NCCN) intermediate- and high-risk prostate cancer.	The median follow up is 6.5 years. There were 12 major protocol violations in each arm. Using the nadir+2 ng/mL threshold, men assigned to LDR prostate brachytherapy boost were less than half as likely to have a biochemical relapse compared to those assigned to dose-escalated EBRT boost (HR 5 0.473; 95% CI 0.292–0.765; *P* 5 0.0022). Using surgical thresholds of O0.4 ng/mL or O0.2 ng/mL to define biochemical relapse greatly magnified the difference between the 2 treatment arms. Using the lowest threshold for biochemical failure (O0.2 ng/mL), the 7-year Kaplan-Meier DFS estimate was 82% for men randomized to LDR prostate brachytherapy boost compared to only 39% for men assigned to dose-escalated EBRT boost.	1

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11. Shilkrut M, Merrick GS, McLaughlin PW, et al. The addition of low-dose-rate brachytherapy and androgen-deprivation therapy decreases biochemical failure and prostate cancer death compared with dose-escalated external-beam radiation therapy for high-risk prostate cancer. *Cancer.* 2013;119(3):681-690.	Observational-Tx	958 patients	To determine whether the addition of LDR brachytherapy or ADT improves clinical outcome in patients with high-risk prostate cancer who received dose-escalated RT.	The median follow-up was 63.2 months (interquartile range, 35.4–99.0 months), and 250 patients were followed for >8 years. Compared with combined-modality RT, patients who received EBRT had higher PSA levels, higher tumor classification, lower Gleason sum, and more frequent receipt of ADT for a longer duration. The 8-year incidence biochemical failure and prostate cancer-specific mortality among patients who received EBRT was 40% (standard error, 38%–44%) and 13% (standard error, 11%–15%) compared with 14% (standard error, 12%–16%; $P<.0001$) and 7% (standard error 6%–9%; $P=.003$) among patients who received combined-modality RT. On multivariate analysis, the HRs for biochemical failure and prostate cancer-specific mortality were 0.35 (95% CI, 0.23–0.52; $P<.0001$) and 0.41 (95% CI, 0.23–0.75; $P<.003$), favoring combined-modality RT. Increasing duration of ADT predicted decreased biochemical failure ($P=.04$) and prostate cancer-specific mortality ($P=.001$), which was greatest with long-term ADT (biochemical failure: HR, 0.33; $P<.0001$; 95% CI, 0.21–0.52; prostate cancer-specific mortality: HR, 0.30; $P=.001$; 95% CI, 0.15–0.6) even in the subgroup that received combined-modality RT.	2
12. Frank SJ, Arterbery VE, Hsu IC, et al. American College of Radiology Appropriateness Criteria permanent source brachytherapy for prostate cancer. *Brachytherapy.* 2011;10(5):357-362.	Review/Other-Tx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for a specific clinical condition.	N/A	4

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13. Nath R, Bice WS, Butler WM, et al. AAPM recommendations on dose prescription and reporting methods for permanent interstitial brachytherapy for prostate cancer: report of Task Group 137. *Med Phys.* 2009;36(11):5310-5322.	Review/Other-Tx	N/A	AAPM recommendations on dose prescription and reporting methods for permanent interstitial brachytherapy for prostate cancer.	The AAPM recommends guidelines for dose prescription from a physics perspective for routine patient treatment, clinical trials, and for treatment planning software developers. The authors continue to follow the current recommendations on using D90 and V100 as the primary quantitles, with more specific guidelines on the use of the imaging modalities and the timing of the imaging. The AAPM recommends that the postimplant evaluation should be performed at the optimum time for specific radionuclides. In addition, they encourage the use of a radiobiological model with a specific set of parameters to facilitate relative comparisons of treatment plans reported by different institutions using different loading patterns or radionuclides.	4
14. Davis BJ, Horwitz EM, Lee WR, et al. American Brachytherapy Society consensus guidelines for transrectal ultrasound-guided permanent prostate brachytherapy. *Brachytherapy.* 2012;11(1):6-19.	Review/Other-Tx	N/A	To provide updated American Brachytherapy Society (ABS) guidelines for TRUS-guided transperineal interstitial PPB.	Patients with high probability of organ-confined disease or limited EPE are considered appropriate candidates for PPB monotherapy. Low-risk patients may be treated with PPB alone without the need for supplemental EBRT. High-risk patients should receive supplemental EBRT if PPB is used. Intermediate-risk patients should be considered on an individual case basis. Intermediate-risk patients with favorable features may appropriately be treated with PPB monotherapy but results from confirmatory clinical trials are pending. CT-based postimplant dosimetry performed within 60 days of the implant is considered essential for maintenance of a satisfactory quality assurance program. Postimplant CT-MRI fusion is viewed as useful, but not mandatory.	4

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15. Nag S, Beyer D, Friedland J, Grimm P, Nath R. American Brachytherapy Society (ABS) recommendations for transperineal permanent brachytherapy of prostate cancer. *Int J Radiat Oncol Biol Phys.* 1999;44(4):789-799.	Review/Other-Tx	N/A	To develop and disseminate the ABS recommendations for the clinical quality assurance and guidelines of permanent transperineal prostate brachytherapy with I-125 or Pd-103.	Patients with high probability of organ-confined disease are appropriately treated with brachytherapy alone. Brachytherapy candidates with a significant risk of EPE should be treated with supplemental EBRT. Patient selection guidelines were developed. Dosimetric planning of the implant should be carried out for all patients before seed insertion. A modified peripheral loading is preferred. The AAPM TG-43 recommendations requiring a change in prescription dose for I-125 sources should be universally implemented. The recommended prescription doses for monotherapy are 145 Gy for I-125 and 115–120 Gy for Pd-103. The corresponding boost doses (after 40–50 Gy EBRT) are 100–110 Gy and 80–90 Gy, respectively. Clinical evidence to guide selection of radionuclide (Pd-103 or I-125) is lacking. Post implant dosimetry and evaluation must be performed on all patients. It is suggested that the dose that covers 90% (D90) and 100% (D100) of the PV and the percentage of the PV receiving the prescribed dose (V100) be obtained from a dose-volume histogram and reported.	4

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16. Nag S, Ciezki JP, Cormack R, et al. Intraoperative planning and evaluation of permanent prostate brachytherapy: report of the American Brachytherapy Society. *Int J Radiat Oncol Biol Phys.* 2001;51(5):1422-1430.	Review/Other-Tx	N/A	To assess the current intraoperative planning process and explore the potential for improvement in intraoperative treatment planning.	The ABS proposes the following terminology in regard to prostate planning process: Preplanning-Creation of a plan a few days or weeks before the implant procedure. Intraoperative planning-Treatment planning in the operating room: the patient and TRUS probe are not moved between the volume study and the seed insertion procedure. Intraoperative preplanning-Creation of a plan in the operating room just before the implant procedure, with immediate execution of the plan. Interactive planning-Stepwise refinement of the treatment plan using computerized dose calculations derived from image-based needle position feedback. Dynamic dose calculation-Constant updating of dose distribution calculations using continuous deposited seed position feedback. Both intraoperative preplanning and interactive planning are currently feasible and commercially available and may help to overcome many of the limitations of the preplanning technique. Dosimetric feedback based on imaged needle positions can be used to modify the intraoperative treatment planning. However, the dynamic changes in prostate size and shape and in seed position that occur during the implant are not yet quantifiable with current technology, and intraoperative treatment planning does not obviate the need for postimplant dosimetric analysis. The major current limitation of intraoperative treatment planning is the inability to localize the seeds in relation to the prostate. Dynamic dose calculation can become a reality once these issues are solved. Future advances can be expected in methods of enhancing seed identification, in imaging techniques, and in the development of better source delivery systems. Additionally, intraoperative treatment planning should be correlated with outcome studies, using dosimetric, toxicity, and efficacy endpoints.	4

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17. Rosenthal SA, Bittner NH, Beyer DC, et al. American Society for Radiation Oncology (ASTRO) and American College of Radiology (ACR) practice guideline for the transperineal permanent brachytherapy of prostate cancer. *Int J Radiat Oncol Biol Phys.* 2011;79(2):335-341.	Review/Other-Tx	N/A	To define the qualifications and responsibilities of all the involved personnel, including the radiation oncologist, physicist and dosimetrist.	Factors with respect to patient selection and appropriate use of supplemental treatment modalities such as EBRT and androgen suppression therapy are discussed. Logistics with respect to the brachytherapy implant procedure, the importance of dosimetric parameters, and attention to radiation safety procedures and documentation are presented. Adherence to these practice guidelines can be part of ensuring quality and safety in a successful prostate brachytherapy program.	4
18. Ash D, Flynn A, Battermann J, de Reijke T, Lavagnini P, Blank L. ESTRO/EAU/EORTC recommendations on permanent seed implantation for localized prostate cancer. *Radiother Oncol.* 2000;57(3):315-321.	Review/Other-Tx	N/A	To indicate to those embarking on brachytherapy the factors which may be related to successful outcomes.	There is general consensus about which groups of patients can be expected to do well with brachytherapy alone and which do poorly. There is an intermediate group where it remains unclear whether there is an advantage from adjuvant therapy or whether they may do better with alternative treatment. On the whole, however, patients with poor prognostic factors do poorly however treated. These questions can only be resolved by clinical trials but it seems unlikely that these will either be done or at least available within the next 8±10 years. In the meantime patients should be carefully selected and counselled on the basis of experience from nonrandomized studies.	4
19. Salembier C, Lavagnini P, Nickers P, et al. Tumour and target volumes in permanent prostate brachytherapy: a supplement to the ESTRO/EAU/EORTC recommendations on prostate brachytherapy. *Radiother Oncol.* 2007;83(1):3-10.	Review/Other-Tx	N/A	To supplement the GEC/ESTRO/EAU recommendations for permanent seed implantations in prostate cancer to develop consistency in target and volume definition for permanent seed prostate brachytherapy.	Recommendations on target and organ at risk definitions and dosimetry parameters to be reported on post implant planning are given.	4
20. Bellon J, Wallner K, Ellis W, Russell K, Cavanagh W, Blasko J. Use of pelvic CT scanning to evaluate pubic arch interference of transperineal prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 1999;43(3):579-581.	Observational-Dx	97 patients	To determine the necessity of preoperative evaluation of pubic arch interference in patients with small PVs.	There was considerable variability in pubic arch interference between patients. The mm of pubic arch overlap with the prostatic margin varied from -11 mm to 20 mm. Patients with larger PVs generally had more pubic arch interference, but the degree of interference was only loosely related to the PV (r = 0.46).	3

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21. Ryu B, Bax J, Edirisinge C, et al. Prostate brachytherapy with oblique needles to treat large glands and overcome pubic arch interference. *Int J Radiat Oncol Biol Phys.* 2012;83(5):1463-1472.	Observational-Tx	5 subjects; 2 types of planning studies per subject; 3 plans for each study type	To show that LDR prostate brachytherapy plans using oblique needle trajectories are more successful than parallel trajectories for large prostates with pubic arch interference; and, to test the accuracy of delivering an oblique plan by using a 3D TRUS-guided mechatronic system.	In the increasing-PV study, oblique needle no-template plans were successful for prostates of ≤80 cc, and parallel needle template plans were successful for prostates of <65 cc. In paired, one-sided t tests for the 60-cc volume study, oblique needle no-template plans showed dosimetric improvements for all organs compared to both of the parallel type plans (P<0.05); parallel needle no-template plans showed a benefit only in planning target volumes receiving more than 100 Gy compared to parallel needle template plans. A CT scan of the phantom showed submillimeter seed placement accuracy in all directions.	2
22. Wallner K, Ellis W, Russell K, Cavanagh W, Blasko J. Use of TRUS to predict pubic arch interference of prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 1999;43(3):583-585.	Observational-Dx	22 patients	To demonstrate the potential for TRUS to predict pubic arch interference of transperineal needle placement for prostate brachytherapy.	The pubic arch was readily visualized by TRUS in 21 of the 22 patients. There was good correlation between TRUS and CT for evaluating the amount of pubic arch interference (r = 0.90).	3
23. Stone NN, Stock RG. Prostate brachytherapy in men with gland volume of 100cc or greater: Technique, cancer control, and morbidity. *Brachytherapy.* 2013;12(3):217-221.	Observational-Tx	2,051 patients	To determine the outcomes of prostate seed implantation in men with PV of 100 cc or greater (PV100).	The biochemical freedom from failure at 10 years was no different between PV100 and smaller glands (82.4% vs 84.5%, P=0.71). At last follow-up, mean IPSS for PV100 increased from 8.5 to 9.1 against 7.4 to 9.2 for smaller glands (P=0.935). Urinary retention rates were higher for PV100 (6/34, 17.6% vs 148/2017, 7.3%; odds ratio, 2.71; 95% CI, 1.1–6.6; P=0.038). Postimplant TURP was performed in none of the 34 patients with PV100 against 66/2017 patients (3.3%, P<0.001). Long-term radiation proctitis for PV100 were 1 of 34 (2.9%) against 82/2017 (4.1%, P=0.741). Rectourethral fistula occurred in 4 patients (0.19%), that is, 1 of 34 (2.9%) in PV100 group and 3 of 2017 (0.1%, P<0.001).	2

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24. Merrick GS, Wallner KE, Butler WM. Patient selection for prostate brachytherapy: more myth than fact. *Oncology (Williston Park).* 2004;18(4):445-452; discussion 452, 455-447.	Review/Other-Tx	N/A	To summarize evidence-based vs unsubstantiated patient selection factors that affect outcome.	Most brachytherapy studies have demonstrated favorable and durable biochemical outcomes with acceptable morbidity. While there is no shortage of opinions regarding symptoms or circumstances that render the use of brachytherapy inadvisable, most are baseless: Reports to date have failed to establish any firm contraindication. Even in situations where patients present with alleged contraindications, brachytherapy may still be the best choice compared to the alternatives. Continued efforts to refine patient selection, brachytherapy quality, and postimplant management should further decrease brachytherapy- related morbidity.	4
25. Wallner K, Smathers S, Sutlief S, Corman J, Ellis W. Prostate brachytherapy in patients with median lobe hyperplasia. *Int J Cancer.* 2000;90(3):152-156.	Review/Other-Tx	8 patients with median lobe hyperplasia	To document the technical and clinical course of prostate brachytherapy patients with radiographic evidence of median lobe hyperplasia.	There was no apparent association between the degree of median lobe hyperplasia and preimplant PV or AUA score. Intraoperatively, we were able to visualize median lobe hyperplasia by TRUS and did not notice any particular difficulty placing sources in the median lobe hyperplasia tissue or migration of sources out of the tissue. The prescription isodose covered from 81% to 99% of the postimplant CT-defined target volume, achieving adequate dose to the median lobe tissue in all patients. 2 of the 8 patients developed acute, postimplant urinary retention. The first patient required intermittent self-catheterization for 3 months and then resumed spontaneous urination. Median lobe hyperplasia does not appear to be a strong contraindication to prostate brachytherapy, and prophylactic resection of hypertrophic tissue in such patients is probably not warranted.	4

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26. Keyes M, Miller S, Moravan V, et al. Predictive factors for acute and late urinary toxicity after permanent prostate brachytherapy: long-term outcome in 712 consecutive patients. *Int J Radiat Oncol Biol Phys.* 2009;73(4):1023-1032.	Observational-Tx	712 patients	To describe the frequency of acute and late Radiation Therapy Oncology Group (RTOG) urinary toxicity, associated predictive factors, and resolution of IPSS in 712 consecutive prostate brachytherapy patients.	The IPSS returned to baseline at a median of 12.6 months. On multivariate analysis, patients with a high baseline IPSS had a quicker resolution of their IPSS. Higher prostate D90 (dose covering 90% of the prostate), maximal postimplant IPSS, and urinary retention slowed the IPSS resolution time. The rate of the actuarial 5-year late urinary (>12 months) RTOG Grade 0, 1, 2, 3, and 4 was 32%, 36%, 24%, 6.2%, and 0.1%, respectively. At 7 years, the prevalence of RTOG Grade 0-1 was 92.5%. Patients with a larger PV, greater number of needles, greater baseline IPSS, and use of hormonal therapy had more acute toxicity. On multivariate analysis, the significant predictors for late greater than or equal to RTOG toxicity 2 were a greater baseline IPSS, maximal postimplant IPSS, presence of acute toxicity, and higher prostate V150 (volume of the prostate covered by 150% of the dose). More recently implanted patients had less acute urinary toxicity and patients given hormonal therapy had less late urinary toxicity (all $P<0.02$).	2

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27. Terk MD, Stock RG, Stone NN. Identification of patients at increased risk for prolonged urinary retention following radioactive seed implantation of the prostate. *J Urol.* 1998;160(4):1379-1382.	Observational-Tx	251 patients	To determine the incidence of prolonged urinary retention and to analyze the effect of pretreatment and treatment related factors to identify high risk patients.	Urinary retention developed in 14 patients requiring catheterization for more than 48 hours. Median time to onset was 1 day after implant. Of these patients 6 ultimately required transurethral prostatic resection to relieve urinary obstruction. No patient had urinary incontinence following implantation or transurethral prostatic resection. Multivariate analysis revealed that pretreatment IPSS, and combined treatment with hormonal therapy and Pd-103 predicted for the development of retention. Patients with IPSS 20 or greater had a 29% risk, IPSS 10 to 19, 11% risk and IPSS <10, 2% risk of retention. Neither patient age, clinical stage, prostate specific antigen, GS, use of I-125 nor PV was significant. A subgroup analysis of patients receiving hormonal therapy and Pd-103 revealed that those with persistent urinary symptoms (IPSS 10 or greater) following 3 months of hormonal therapy had the greatest risk of prolonged retention (37%).	2
28. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Lief JH. Long-term urinary quality of life after permanent prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2003;56(2):454-461.	Observational-Tx	195 patients and 51 controls	To evaluate late urinary function following PPB using a validated patient-administered quality of life instrument Expanded Prostate Cancer Index.	When the survey scores for the implant patients were compared with the control group, no significant differences in either the IPSS or function, bother, incontinence, or irritation/obstruction subscales of the urinary EPIC were discernible. In addition, no significant difference was observed between the implant and control groups when the EPIC and IPSS surveys were evaluated by each individual question. Of all the evaluated parameters, the use of tobacco was the best predictive variable for diminished quality of life.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
29. Merrick GS, Butler WM, Wallner KE, Lief JH, Galbreath RW. Prophylactic versus therapeutic alpha-blockers after permanent prostate brachytherapy. *Urology.* 2002;60(4):650-655.	Experimental-Tx	234 patients	To evaluate the influence of prophylactic vs therapeutic alpha-blockers on urinary morbidity after PPB.	In both the prophylactic and the therapeutic cohorts, the IPSS peaked 1 month after implantation. Patients receiving a prophylactic alpha-blocker returned to baseline at a mean of 4 months and a median of 3 months postoperatively. For those patients not receiving prophylactic alpha-blockers, the IPSS returned to the antecedent value at a mean and median of 10 months and 6 months, respectively. Of the 125 patients receiving prophylactic alpha-blockers, 102 (81.2%) remained medication dependent at the conclusion of the study, and 140 (78.2%) of 179 patients receiving alpha-blockers other than for hypertensive purposes did so. The incidence of prolonged urinary catheter dependency (greater than 3 days) and the need for postimplant transurethral incision of the prostate/TURP were not affected by alpha-blocker use. Cox regression analysis revealed that only the prophylactic use of alpha-blockers and the difference between the preimplant IPSS and the 1-month IPSS were predictive of the time to return to the referent zone.	1
30. Stone NN, Ratnow ER, Stock RG. Prior transurethral resection does not increase morbidity following real-time ultrasound-guided prostate seed implantation. *Tech Urol.* 2000;6(2):123-127.	Observational-Tx	419 patients	To examine the morbidity following brachytherapy using the real-time method to determine if patients with a history of TURP are at increased risk for developing complications.	Median follow-up for group 1 was 12 months and for group 2 was 18 months. No patients suffered from radiation-related proctitis or cystitis in either group of patients. 2 patients in group 2 implanted with I-125 and who had a history of 2 prior TURPs developed mild superficial urethral necrosis. The actuarial freedom from developing superficial urethral necrosis at 4 years was 84% in patients with a history of prior TURP. There were no episodes of superficial urethral necrosis in group 1 and no cases of incontinence reported in either group of patients. The actuarial rate of potency was 78% at 2 years.	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Wallner K, Lee H, Wasserman S, Dattoli M. Low risk of urinary incontinence following prostate brachytherapy in patients with a prior transurethral prostate resection. *Int J Radiat Oncol Biol Phys.* 1997;37(3):565-569.	Observational-Tx	19 patients	To review post implant morbidity in patients with prior TURP.	Only one patient developed mild urinary stress incontinence, 6 months following his I-125 implant. The actuarial freedom from permanent urinary incontinence at 3 years after implantation was 94%. No patient required urethral dilatation for urethral stricture. 11 patients were sexually potent prior to implantation. At 3 years after treatment, all patients had maintained potency.	3
32. Merrick GS, Butler WM, Wallner KE, Galbreath RW. Effect of transurethral resection on urinary quality of life after permanent prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2004;58(1):81-88.	Observational-Tx	27 brachytherapy patients	To determine the effect of transurethral resection on urinary function after PPB using a validated, patient-administered, quality-of-life instrument.	For all evaluated parameters, superior urinary scores were noted in the preimplant TURP group, with intermediate scores in the postimplant TURP patients and poor urinary quality-of-life scores in the pre- and postimplant TURP patients. With time, the EPIC scores improved in the pre- and postimplant TURP cohorts. In multivariate linear regression analysis of the EPIC urinary summary score, the number of TURPs and supplemental EBRT were the strongest predictors for diminished quality-of-life.	1
33. Mayadev J, Merrick GS, Reed JR, et al. Permanent prostate brachytherapy in prostate glands <20 cm(3). *Int J Radiat Oncol Biol Phys.* 2010;76(5):1450-1455.	Observational-Tx	104 patients	To investigate the dosimetry, treatment-related morbidity, and biochemical outcomes for brachytherapy in patients with prostate glands <20 cm(3).	The median patient age, follow up, and pre-treatment US volume was 64 years, 5.0 years and 17.6cm(3), respectively. Median day 0 dosimetry was significant for the following: V100 98.5%, D90 126.1% and R100 <0.5% of prescription dose. The mean urethral and maximum urethral doses were 119.6% and 133.8% of prescription. The median time to IPSS resolution was 4 months. There were no RTOG grade III or IV rectal complications. The CSS, bPFS, and OS rates were 100%, 92.5%, and 77.8% at 9 years. For biochemically disease-free patients, the median most recent postbrachytherapy PSA value was 0.02 ng/mL.	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Merrick GS, Butler WM, Galbreath RW, et al. Prostate cancer death is unlikely in high-risk patients following quality permanent interstitial brachytherapy. *BJU Int.* 2011;107(2):226-232.	Observational-Tx	284 patients	To evaluate CSS, bPFS and OS in high-risk prostate cancer brachytherapy patients.	12-year CSS, bPFS and OS were 94.2%, 89.0% and 69.7%. On multivariate analysis, bPFS was best predicted by percent positive biopsies and ADT. The analysis failed to identify any predictors for CSS, while OS was highly correlated with patient age, percent positive biopsies and diabetes. 14% of patients died from diseases of the heart, while 8%, 8% and 6% of patients died from nonprostate cancer, other causes and prostate cancer, respectively. When OS was stratified by patients with 0–3 vs ≥4 comorbidities, the 12-year OS was 73.0% and 52.7% (*P*=0.036).	2
35. Quan AL, Ciezki JP, Reddy CA, et al. Improved biochemical relapse-free survival for patients with large/wide glands treated with prostate seed implantation for localized adenocarcinoma of prostate. *Urology.* 2006;68(6):1237-1241.	Observational-Tx	390 patients	To analyze whether prostate size affects bRFS.	Most patients had low-risk disease, and the median follow-up was 45 months (range 24 to 102). Using the ASTRO definition of biochemical failure, the overall 5-year bRFS rate was 89.3%. On separate multivariate analyses, only the pretreatment prostate width and volume significantly influenced bRFS favorably (*P*=0.0069 and *P*=0.0255, respectively). No association was found between gland size/width and postimplant dosimetry.	2
36. Stone NN, Stock RG. Prostate brachytherapy in patients with prostate volumes >/= 50 cm(3): dosimetic analysis of implant quality. *Int J Radiat Oncol Biol Phys.* 2000;46(5):1199-1204.	Observational-Tx	66 patients	To describe dosimetry outcomes in a group of patients who were implanted using the real-time US-guided technique who had PVs ≥50 cm(3).	PVs in the 66 patients ranged from 50 to 93 cm(3) (median 57, mean 61 cm(3)). Total activity implanted was 27.8–89.1 mCi (median 57 mCi), with a range in activity per seed of 0.36–0.56 mCi (median 0.4 mCi). The prostate D90s and D95s ranged from 13,245 to 22,637 cGy (median 18,750) and 11,856 to 20,853 cGy (median 16,725), respectively. Only 1 patient (1.5%) had a D90 <140 Gy. The DURE30 values ranged from 15,014 to 27,800 cGy (median 20,410) and the DRECT30 values were 3137–9910 cGy (median 5515).	3

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Grann A, Wallner K. Prostate brachytherapy in patients with inflammatory bowel disease. *Int J Radiat Oncol Biol Phys.* 1998;40(1):135-138.	Review/Other-Tx	6 patients	To report on the post-treatment course for 6 patients with a history of inflammatory bowel disease who were treated with I-125 prostate brachytherapy for early stage prostate cancer.	None of the 6 patients experienced unusual or significant GI side effects following implantation. All 6 patients remain free of GI complications. The rectal surface area that received >100 Gy was kept below 10 mm2 in all patients, in accordance with previously published guidelines.	4
38. Peters CA, Cesaretti JA, Stone NN, Stock RG. Low-dose rate prostate brachytherapy is well tolerated in patients with a history of inflammatory bowel disease. *Int J Radiat Oncol Biol Phys.* 2006;66(2):424-429.	Observational-Tx	24 patients	To report on the follow-up of 24 patients with a prior history of inflammatory bowel disease treated with brachytherapy for early-stage prostate cancer.	None of the patients experienced Grade 3 or 4 rectal toxicity. 4 patients experienced Grade 2 late rectal toxicity. The 5-year actuarial freedom from developing late Grade 2 rectal toxicity was 81%. At a median follow-up of 48.5 months, 23 patients were alive and had no evidence of disease with a median PSA for the sample of 0.1 ng/mL (range, <0.05–0.88 ng/mL). 1 patient died of other causes unrelated to his prostate cancer.	2
39. Crook JM, Gomez-Iturriaga A, Wallace K, et al. Comparison of health-related quality of life 5 years after SPIRIT: Surgical Prostatectomy Versus Interstitial Radiation Intervention Trial. *J Clin Oncol.* 2011;29(4):362-368.	Observational-Tx	168 survey responders	To report health-related quality of life at a mean of 5.3 years for 168 trial-eligible men who either chose or were randomly assigned to RP or brachytherapy following a multidisciplinary educational session.	Of 168 survey responders, 60.7% had brachytherapy (9.5% randomly assigned) and 39.3% had RP (9.5% randomly assigned). Median age was 61.4 years for brachytherapy and 59.4 for RP (P=.05). Median follow-up was 5.2 years (range, 3.2 to 6.5 years). For brachytherapy vs RP, there was no difference in bowel or hormonal domains, but men treated with brachytherapy scored better in urinary (91.8 vs 88.1; P=.02) and sexual (52.5 vs 39.2; P=.001) domains, and in patient satisfaction (93.6 vs 76.9; P<.001).	1

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Benoit RM, Smith RP, Beriwal S. Five year prostate-specific antigen outcomes after caesium prostate brachytherapy. *Clin Oncol (R Coll Radiol)*. 2014;26(12):776-780.	Observational-Tx	367 patients	To report 5 year PSA outcomes in men undergoing prostate brachytherapy with Cs-131 at a single institution.	485 patients underwent prostate brachytherapy with Cs-131 at our institution and 367 patients had at least 24 months of follow-up and were included in this analysis. Using the Phoenix criteria, 5 year actuarial biochemical freedom from disease was 96.0% for patients in the low-risk category, 92.7% for patients in the intermediate-risk category and 82.9% for patients in the high-risk category. By treatment category, 95.7% of men treated with monotherapy had biochemical freedom from disease, 84.9% of men treated with combination therapy had biochemical freedom from disease and 92.0% of men treated with trimodal therapy had biochemical freedom from disease.	2
41. Bradley RP, William SB. Clinical outcomes of a Phase II, multi-institutional Cesium-131 permanent prostate brachytherapy trial. *Brachytherapy*. 2007;6(2):78.	Experimental-Tx	80 patients	To report the preliminary clinical results of the first clinical trial using Cs-131 for permanent brachytherapy to treat early stage prostate cancer.	80 patients are currently enrolled in the study. All patients received Cs-131 PPB as monotherapy for early stage prostate cancer (GSS <6 or 7, Stage <T2b, PSA <10 or 10e20). The average pretreatment PSA was 6.75. PVs measured by US ranged from 15.5 to 77.0 cm3 with a mean of 37.5 cm3. 63% of the patients experienced some level of urinary morbidity, by the end of the first year post implant this number decreased to 30%. Patients most often complained of frequency, urgency or dysuria. Rectal morbidity occurred in 38% of the patients, dropping to less than 6% by the end of the first year. Only one, grade 3 rectal complication was noted in this study; the remainder, Grades 1 and 2. The objective measures of morbidity, IPSS, urinary Quality of Life, and IIEF-5, all showed an early peak in symptoms in the 2-week to 1-month time frame, with a resolution to about 1/3 of the maximum levels by 4 months. Both urinary and rectal morbidity correlated with total implanted source strength. There was also a demonstrated correlation between urinary morbidity and prostate V100.	3

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Eshleman JS, Davis BJ, Pisansky TM, et al. Radioactive seed migration to the chest after transperineal interstitial prostate brachytherapy: extraprostatic seed placement correlates with migration. *Int J Radiat Oncol Biol Phys*. 2004;59(2):419-425.	Observational-Tx	100 patients	To examine the incidence of seed migration detected on chest X-ray and to identify the predictors associated with its occurrence.	One or more seeds were identified on the chest X-rays of 55 (55%) of 100 patients. The mean number of intrathoracic seeds in patients with migration was 2.2 (range, 1–10), and the proportion of seeds that migrated to the thorax was 0.98%. The rate of extraprostatic seeds planned was 43.9%, and postimplant CT identified 37.9% in such a location. The number of seeds planned for extraprostatic placement and below the apex were statistically significant (alpha = 0.05) predictors in univariate logistic analysis. Multivariate analysis revealed the planned number of extraprostatic seeds as the only statistically significant predictor (*P*=0.04).	3
43. Stone NN, Stock RG. Reduction of pulmonary migration of permanent interstitial sources in patients undergoing prostate brachytherapy. *Urology*. 2005;66(1):119-123.	Observational-Tx	238 patients	To investigate a method to decrease the problem of seed migration after PPB.	A total of 21,654 seeds were implanted (median 89, range 27 to 220). Postimplant chest x-rays were obtained at a median of 912 days (range 147 to 3023), and 4 patients (1.7%) experienced at least 1 seed embolus to the lung. Of the 21,654 seeds, 10 (0.005%) were found in the lungs. All 4 patients had received an I-125 implant, resulting in a pulmonary embolus rate for I-125 of 2.7% (4 of 146) and for Pd-103 of 0% (0 of 92). No patients experienced subsequent seed migration if it was not seen on the initial film. The median dose delivered to 90% of the PV for all patients undergoing I-125 implantation was 172 Gy and for the 4 patients with seed migration it was 174 Gy.	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Reed DR, Wallner KE, Merrick GS, et al. A prospective randomized comparison of stranded vs. loose 125I seeds for prostate brachytherapy. *Brachytherapy.* 2007;6(2):129-134.	Experimental-Tx	62 patients	To compare seed loss and dosimetric parameters between stranded and loose I-125 seeds for prostate brachytherapy.	Overall, 21/62 patients (30%) experienced seed loss. Seed loss occurred in 15/32 of loose I-125 seeds patients (47%) vs 6/30 RAPID Strand I-125 seeds patients (23%; p=0.053). Mean seed loss was 1.09 in the loose I-125 seeds patient vs. 0.43 in RAPID Strand I-125 seeds patients (*P*=0.062). 8 loose I-125 seeds patients (25%) lost multiple seeds, compared to 3 stranded patients (10%). Despite the lesser degree of seed loss in patients who received stranded seeds, they had a paradoxical trend toward lower V100 and D90 values.	1

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Merrell K, Davis B, Goulet C, et al. PO-1039: Comparison of seed migration to the chest after permanent prostate brachytherapy with loose, stranded or mixed seeds. *Radiotherapy and Oncology.* 2015;115:S560-S561.	Observational-Tx	990 patients	To review our institutional experience of seed migration after PPB comparing loose seeds, mixed loose and stranded seeds, and stranded seeds in an absorbable vicryl suture.	The mean PV and number of seeds implanted in each group was 39.9 cc (range, 8–98) and 116 seeds (range, 49–214), 37.8 cc (range, 17.5–75) and 93.2 seeds (range, 62–145), and 36.8 cc (range, 13.5–77) and 77.9 seeds (range, 44–116) for loose seeds, mixed loose and stranded seeds, and stranded seeds in an absorbable vicryl suture, respectively. The overall rate of seed migration was 0.38% (351/93,230). The rate of seed migration per group was 0.73% (339/46,346) for loose seeds, 0.16% (7/4,288) for mixed loose and stranded seeds, and 0.012% (5/42,596) for stranded seeds in an absorbable vicryl suture. The percent of patients with seed migration and the mean number of migrated seeds per patient was 45% and 1.9 seeds (range, 1–10) 13% and 1.2 seeds (range, 1–2), and 0.9% and 1 seed (range, 1), for loose seeds, mixed loose and stranded seeds, and stranded seeds in an absorbable vicryl suture, respectively. The right and left lower lobe were the most frequent sites of pulmonary seed migration. Pairwise comparison showed a significantly higher rate of seed migration in the loose seeds group compared to the mixed loose and stranded seeds ($P<0.001$) and stranded seeds in an absorbable vicryl suture group ($P<0.001$). Patients treated with any number of loose seeds had a significantly higher rate of seed migration than patients with completely stranded seed implants ($P<0.001$).	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Chen WC, Katcher J, Nunez C, Tirgan AM, Ellis RJ. Radioactive seed migration after transperineal interstitial prostate brachytherapy and associated development of small-cell lung cancer. *Brachytherapy.* 2012;11(5):354-358.	Review/Other-Tx	1 patient	To report a case of lung carcinoma developing in the location of a migrated prostate brachytherapy seed.	The treatment was unremarkable for any complications, and immediate postimplant evaluation did not reveal any loose seeds. The patient remained clinically without evidence of disease and was asymptomatic until an isolated episode of hematuria in December 2009. Radiographic evaluation noted an incidental right lower lobe lung mass with a 4 mm hyperdensity slightly off-center. Biopsy confirmed stage IB limited-stage small-cell lung cancer, and he underwent thoracic radiation with concurrent systemic chemotherapy. The mass remained mildly avid on a positron emission tomographic scan after treatment, and he underwent surgical evaluation with final pathology demonstrating no residual tumor but a metal rod-like implant consistent with a migrated radioactive brachytherapy seed.	4
47. Zhu AX, Wallner KE, Frivold GP, Ferry D, Jutzy KR, Foster GP. Prostate brachytherapy seed migration to the right coronary artery associated with an acute myocardial infarction. *Brachytherapy.* 2006;5(4):262-265.	Review/Other-Tx	1 patient	To report a case of prostate brachytherapy seed migration to the right coronary artery associated with an acute myocardial infarction.	Postimplant pelvic radiography at Day 30 showed 5 seeds missing. No chest radiography was done until hospital admission on October 10, 2005 for acute myocardial infarction. Cine radiography from cardiac catheterization revealed 86 metallic seeds remaining in the pelvic region, 4 that had migrated to the lungs (2 left and 2 right) and 2 to the heart. 2 seeds were unaccounted for. Of the 2 cardiac seeds, 1 was lodged in the right ventricle endocardium and the other in the midsegment of the right coronary artery at the site of a severely stenotic lesion that resulted in an acute myocardial infarction.	4
48. McLaughlin P, Narayana V, Pan C, et al. Comparison of day 0 and day 14 dosimetry for permanent prostate implants using stranded seeds. *Int J Radiat Oncol Biol Phys.* 2006;64(1):144-150.	Observational-Tx	28 patients	To determine, using MRI-based dosimetry (Day 0 and Day 14), whether clinically significant changes in the dose to the prostate and critical adjacent structures occur between Day 0 and 14, and to determine to what degree any changes in dosimetry are due to swelling or its resolution.	The D90 changed in 27/28 patients between Days 0 and 14. No relationship was found between a change in PV and the change in D90 (R2 = 0.01). A paradoxic dosimetric result was noted in 11/28 patients. The rectal dose increased in 23/28 patients, with a >30 Gy change in 6. The external sphincter D90 increased in 19/28, with a >50 Gy increase in 6.	2

Permanent Source Brachytherapy for Prostate Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Pinkawa M, Asadpour B, Gagel B, et al. Evaluation of source displacement and dose--volume changes after permanent prostate brachytherapy with stranded seeds. *Radiother Oncol.* 2007;84(2):190-196.	Observational-Tx	51 patients	To analyze source displacements and dose-volume changes in the first month after a permanent implant.	Seed positions have moved significantly between day 1 and 30 in the posterior (mean 1.0 mm; $P<0.001$) and inferior (mean 3.8 mm; $P<0.001$) directions. Treatment margins increased particularly at the posterior (mean 2.2 mm; $P<0.001$) and apical (median 3.0 mm; $P<0.001$) prostate contour with decreasing oedema. With a stable apex position and a mean inward posterior surface displacement of 1.1 mm ($P<0.001$) relative to pelvic bones, seed displacements could be well correlated with prescription isodose displacements (Pearson correlation coefficients ≥0.81; $P<0.001$).	3
50. Saibishkumar EP, Borg J, Yeung I, Cummins-Holder C, Landon A, Crook J. Sequential comparison of seed loss and prostate dosimetry of stranded seeds with loose seeds in 125I permanent implant for low-risk prostate cancer. *Int J Radiat Oncol Biol Phys.* 2009;73(1):61-68.	Observational-Tx	40 patients	To compare stranded seeds with loose seeds in terms of prostate edema, dosimetry, and seed loss after I-125 brachytherapy.	Prostate edema was less in the stranded seeds cohort at all points (P=NS). On Day 0, all the prostate dosimetric factors were greater in the loose seeds group than in the stranded seeds group (P=0.003). However, by Days 7 and 30, the dosimetry was similar between the 2 cohorts. No seeds migrated to the lung in the stranded seeds cohort compared with a total of 5 seeds in 4 patients in the loose seeds cohort. However, the overall seed loss was greater in the stranded seeds cohort (24 seeds in 6 patients; 1.1% of total vs 0.6% for loose seeds), with most seeds lost through urine (22 seeds in 5 patients).	2
51. Heysek RV, Gwede CK, Torres-Roca J, et al. A dosimetric analysis of unstranded seeds versus customized stranded seeds in transperineal interstitial permanent prostate seed brachytherapy. *Brachytherapy.* 2006;5(4):244-250.	Observational-Tx	272 patients	To retrospectively analyze the dosimetric and toxicity results from 272 patients with localized prostate cancer treated consecutively using loose or stranded radioactive seeds by TRUS-guided transperineal permanent prostate seed brachytherapy.	There was a slight improvement in the dosimetric parameter D90 between the customized stranded seeds (101.9%) and unstranded or loose seeds (99.3%) groups (P=0.041). However, overall implant quality based on RTOG guidelines was similar between both groups.	2
52. Lin K, Lee SP, Cho JS, Reiter RE, DeMarco JJ, Solberg TD. Improvements in prostate brachytherapy dosimetry due to seed stranding. *Brachytherapy.* 2007;6(1):44-48.	Observational-Tx	80 patients	To contribute to the understanding of whether seed stranding improves dosimetry.	Dosimetry of patients treated with stranded seeds showed significant improvement. Specifically, the V100 (volume of the prostate receiving 100% of the prescribed dose) improved from 88% to 92% ($P<0.05$), and the D90 (maximum dose received by 90% of the prostate) improved from 143 to 155 Gy ($P<0.05$).	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Fagundes HM, Keys RJ, Wojcik MF, Radden MA, Bertelsman CG, Cavanagh WA. Transperineal TRUS-guided prostate brachytherapy using loose seeds versus RAPIDStrand: a dosimetric analysis. *Brachytherapy.* 2004;3(3):136-140.	Observational-Tx	473 patients	To analyze the effect of stranded I-125 and loose (predominantly Pd-103 sources on dosimetric outcomes of brachytherapy of the prostate.	Mean V100 values for the stranded I-125 approach were greater than those for free seeds (P<0.0005), whether I-125 or Pd-103 (P<0.005). Use of the strand was the most significant determinant of V100 of all variables examined. The stranded I-125 approach was also associated with higher mean D90 values and lower V150-urethral doses.	2
54. Bice WS, Prestidge BR, Kurtzman SM, et al. Recommendations for permanent prostate brachytherapy with (131)Cs: a consensus report from the Cesium Advisory Group. *Brachytherapy.* 2008;7(4):290-296.	Review/Other-Tx	N/A	To provide consensus recommendations for Cs-131 prostate brachytherapy based on experience to date.	We recommend using 1.059cGyh(-1)U(-1) as the dose rate constant for the IsoRay source. The prescription for monotherapy implants is 115 Gy and when combined with 45–50 Gy EBRT it is 85 Gy. Suggested individual source strength ranges from 1.6 to 2.2U. The release criterion for Cs-131 implants is 6mRh(-1) at 1m. Cs-131 brachytherapy should be performed differently from I-125 and Pd-103 brachytherapy: source placement is further from the urethra and rectum; the prostate V(150) should be ≤45%; sufficient margins may be obtained while limiting source placement to the capsule or close to the capsule. The increased dose rate may cause degradation of postimplant quantifiers due to edema. However, large variability in the magnitude and rate of resolution of edema make determination of the most representative postoperative imaging time impossible. The Cesium Advisory Group recommends postimplant imaging on the day of the implant. Recommended postimplant evaluation goals include prostate D(90) greater than the prescription dose; maintaining D(u)(,30)<140% of the prescription dose and keeping V(r)(,100)<0.5cm(3).	4

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Cohen GN, Amols HI, Zelefsky MJ, Zaider M. The Anderson nomograms for permanent interstitial prostate implants: a briefing for practitioners. *Int J Radiat Oncol Biol Phys.* 2002;53(2):504-511.	Observational-Tx	20 patients to assess plan optimization; 61 patients to assess implant quality	To re-evaluate the role of the Anderson nomograms in treatment planning for permanent prostate implants.	Nomogram predictions of the total activity required are in good agreement (within 10%) with the genetic algorithm-planned activity. However, computer-optimized plans consistently yield superior plans, as reflected in both pre- and postimplant analyses. We find also that user (specifically, treatment planner) implementation of the nomograms may be a major source of variability in nomogram planning-a difficulty to which robust computer optimization is less prone.	3
56. Davis BJ, Pisansky TM, Wilson TM, et al. The radial distance of extraprostatic extension of prostate carcinoma: implications for prostate brachytherapy. *Cancer.* 1999;85(12):2630-2637.	Review/Other-Tx	376 specimens	To define and evaluate a novel measure of EPE in a large series of RP specimens.	EPE was identified in 105/376 specimens (28%) at 248 sites. The radial EPE distance in these specimens had a mean of 0.8 mm (range, 0.04–4.4 mm) and a median of 0.5 mm. Of these 105 patients, the median and mean preoperative PSA concentrations were 11.8 ng/mL and 17.9 ng/mL, respectively. The mean and range of the GS and PV for all specimens were 6.3 (range, 3–9) and 39 cc (range, 8–294 cc), respectively. In 107 patients who met the selection criteria for prostate brachytherapy eligibility of a PSA level <10 ng/mL, GS <7, and gland volume <60 cc, the maximum and mean radial EPE distances were 0.6 mm and 0.03 mm, respectively.	4
57. Waterman FM, Yue N, Corn BW, Dicker AP. Edema associated with I-125 or Pd-103 prostate brachytherapy and its impact on post-implant dosimetry: an analysis based on serial CT acquisition. *Int J Radiat Oncol Biol Phys.* 1998;41(5):1069-1077.	Review/Other-Tx	10 patients	To characterize the magnitude and duration of post-implant edema following the implantation of I-125 or Pd-103 seeds into the prostate and to investigate its effect on the CT-based calculation of the total dose delivered by the implant.	The magnitude of the edema, expressed as the ratio of the post- to pre-implant volume on the day of the procedure, ranged from 1.33 to 1.96 (mean 1.52). The edema decreased exponentially with time; however, the edema half-life (time for the edema to decrease by 1/2) varied from 4 to 25 days (mean 9.3 days). As the edema resolved, the percentage of the prostate that received a dose equal to or greater than the prescribed dose increased by at least 7% in 7 of the 10 patients and increased by more than 15% in 2. In those patients in whom dose coverage was unaffected by the resolution of edema, more than 90% of the prostate was covered by the prescribed dose in the initial CT scan.	4

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
58. Buyyounouski MK, Davis BJ, Prestidge BR, et al. A survey of current clinical practice in permanent and temporary prostate brachytherapy: 2010 update. *Brachytherapy.* 2012;11(4):299-305.	Review/Other-Tx	65 practitioner survey responders	To help establish patterns of care and standards of care of interstitial permanent LDR and temporary high-dose-rate brachytherapy for prostate cancer and to compare the results with a similar 1998 ABS survey.	65 brachytherapy practitioners responded to the survey. 89% of respondents performed LDR and 49% perform high-dose-rate brachytherapy. The median number of years of experience for LDR brachytherapists increased from 5 to 10 years over the course of the 12 years since the preceding survey. Compared with the first ABS, a smaller proportion of respondents received formal brachytherapy residency training (43% vs 56%) or formal "hands-on" brachytherapy training (15% vs 63%). There has been a marked decline in the utilization of the Mick applicator (Mick Radio-Nuclear Instruments, Inc., Mount Vernon, NY, USA) (60% vs 28%) and an increase in the use of stranded seeds (40% vs 11%). Compliance with postimplant dosimetry was higher in the 2010 survey.	4
59. Crook J, Patil N, Ma C, McLean M, Borg J. Magnetic resonance imaging-defined treatment margins in iodine-125 prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2010;77(4):1079-1084.	Observational-Tx	131 patients	To calculate implant quality parameters, D90 and V100, for the MRI-defined prostate plus 2, 3, and 5 mm.	Mean prostate V100 (SD) and D90 (SD) were 95.6% (4.1) and 117.2% (12.7). For prostate plus a 2-mm margin the D90 was 107.9% (14.3) and for a 3-mm margin 96.0 % (14.0). For prostate plus a 5-mm margin, the D90 was only 78.4% (11.0). The 8 patients experiencing local failure, despite adequate implants, had a lower mean V100 of 91.2% (SD, 2.8; P=0.0008) and D90 of 103.7% (SD, 8.3; P=0.002) and significantly inferior margin coverage.	2

Permanent Source Brachytherapy for Prostate Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
60. Stock RG, Stone NN, Tabert A, Iannuzzi C, DeWyngaert JK. A dose-response study for I-125 prostate implants. *Int J Radiat Oncol Biol Phys*. 1998;41(1):101-108.	Observational-Tx	134 patients	To explore the relationship between dose, biochemical failure and biopsy results.	Improvements in freedom from biochemical failure rates were seen with increasing D90 levels. The 4-year freedom from biochemical failure rates for patients with D90 values <100 Gy, 100–119.9 Gy, 120–13.9 Gy, 140–159.9 Gy, and ≥160 Gy were 53%, 82%, 80%, 95%, and 89%, respectively (P=0.02). Patients receiving a D90 <140 Gy (65 patients) were similar with respect to presenting disease prognostic factors to those receiving a D90 ≥140 Gy (69 patients). Patients receiving a D90 <140 Gy had a 4-year freedom from biochemical failure rate of 68% compared to a rate of 92% for those receiving a D90 ≥140 Gy (P=0.02). 2-year post-treatment biopsies were negative in 70% (33/47) of patients with a D90 <140 Gy compared to a rate of 83% (24/29) in patients with a D90 ≥140 Gy (P=0.2). A multivariate analysis using dose, PSA, score, and stage revealed that dose was the most significant predictor of biochemical failure (P=0.001). This dose response was more pronounced in patients presenting with PSA levels >10 ng/ml. In these patients, the 4-year freedom from biochemical failure rates were 51% and 100% for the low and high dose groups, respectively (P=0.009) and the negative biopsy rates were 64% (14/22) and 100% (8 of 8), respectively (P=0.05). In patients with presenting PSA <10 ng/ml, the 4-year freedom from biochemical failure rates were 82% and 88% for the low and high dose groups, respectively (P=0.29).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Keyes M, Spadinger I, Liu M, et al. Rectal toxicity and rectal dosimetry in low-dose-rate (125)I permanent prostate implants: a long-term study in 1006 patients. *Brachytherapy.* 2012;11(3):199-208.	Observational-Tx	1,006 patients	To describe the acute and late rectal toxicity in 1006 prostate brachytherapy patients implanted 1998-2003. To determine whether rectal dose-volume histogram as well as patient and treatment factors were associated with rectal toxicity.	Rectal dosimetry in 93.5% and rectal toxicity in 96.2% have been recorded. Median VR(100)=1.05cc. Late RTOG Grades 0, 1, 2, 3, and 4 were recorded in 68%, 23%, 7.3%, 0.9%, and 0.2% patients, respectively. On multivariate analysis, acute RTOG ≥2 rectal toxicity was associated with urinary retention (P=0.036) and learning curve (P=0.015); late RTOG ≥2 was associated with the presence of acute toxicity (P=0.0074), higher VR(100) (P=0.030) and learning curve (P=0.027).	2
62. Edge SB, American Joint Committee on Cancer. *AJCC cancer staging manual.* 7th ed. New York: Springer; 2010.	Review/Other-Dx	N/A	N/A	N/A	4
63. Gomez-Iturriaga Pina A, Crook J, Borg J, Lockwood G, Fleshner N. Median 5 year follow-up of 125iodine brachytherapy as monotherapy in men aged<or=55 years with favorable prostate cancer. *Urology.* 2010;75(6):1412-1416.	Observational-Tx	96 patients	To report the GU and GI toxicity rates, erectile function preservation, and bPFS rate in men aged ≤55 years treated with I-125 brachytherapy.	Only 1 patient experienced a biochemical failure; the actuarial 7-year bPFS rate is 98.9%. Median nadir is 0.05 ng/mL, reached at 48 months of follow-up. Median 5- and 7-year PSA was 0.09 and 0.06 ng/mL, respectively. Grade 2 acute and late GU toxicity rates (urinary frequency, urgency, and/or dysuria) were 9.8% and 10.6%, respectively. Grade 3 GU toxicity (urethral stricture) was observed in 3 men and was corrected with urethral dilatation or transurethral resection. 2 (2.2%) patients developed grade 2 GI toxicity (proctitis). Erectile function was preserved in 85/91 men with prior good function (93.4%); 41 (45%) used phosphodiesterase-5 inhibitors.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Potters L, Morgenstern C, Calugaru E, et al. 12-year outcomes following permanent prostate brachytherapy in patients with clinically localized prostate cancer. *J Urol.* 2005;173(5):1562-1566.	Observational-Tx	1,449 patients	To review the outcomes in men treated with PPB.	Median follow-up was 82 months with 39 patients at risk at for 144 months. OS and disease specific survival at 12 years was 81% and 93%, respectively. The 12-year biochemical freedom from recurrence was 81%, 78%, 74% and 77% according to the ASTRO, ASTRO-Kattan, ASTRO-Last Call and Houston definitions, respectively. The 12-year ASTRO-Kattan biochemical freedom from recurrence using risk stratification was 89%, 78% and 63% in patients at low, intermediate and high risk, respectively (P=0.0001). Multivariate analysis identified the dose that 90% of the target volume received (P<0.0001), pretreatment PSA (P=0.001), GS (P=0.002), the percent positive core biopsies (P=0.037), clinical stage (P=0.689), the addition of hormones (P=0.655) and the addition of EBRT (P=0.724) for predicting biochemical freedom from recurrence-ASTRO. 5-year disease specific survival was 44% in patients with a PSA doubling time of <12 months vs 88% in those with a PSA doubling time of 12 months or greater (P=0.0001).	2
65. Sohayda C, Kupelian PA, Levin HS, Klein EA. Extent of extracapsular extension in localized prostate cancer. *Urology.* 2000;55(3):382-386.	Observational-Dx	265 RP specimens	To measure the radial extent of extracapsular penetration by tumor cells, thereby providing estimates of the margins needed around target volumes.	The site of extracapsular extension was posterolateral in 53% of cases, lateral in 24%, posterior in 13%, and at the base in 10%. The median amount of extracapsular extension at all sites was 1.1 mm (mean 1.7). However, the range was wide; the minimum measurable extent was 0.1 mm and the maximum 10.0 mm. The extent was within 3.8 mm for 90% of all cases. By stratifying cases with favorable and unfavorable tumors, the 90th percentiles of extracapsular extension were as follows: 3.3 mm for favorable tumors (clinical stage T1-2, initial PSA 10 ng/mL or less, and biopsy GS 6 or less) and 3.9 mm for unfavorable tumors (clinical stage T3, initial PSA greater than 10 ng/mL, or biopsy GS 7 or greater).	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Pugh TJ, Frank SJ, Achim M, et al. Endorectal magnetic resonance imaging for predicting pathologic T3 disease in Gleason score 7 prostate cancer: implications for prostate brachytherapy. *Brachytherapy.* 2013;12(3):204-209.	Observational-Dx	171 patients	To determine the ability of endorectal MRI and other pretreatment factors to predict the presence and extent of EPE in men with GS 7 prostate cancer.	171 men were eligible for inclusion. Pretreatment characteristics were: median age=60 years (42–76); median PSA 4.9ng/mL (0.4–9.9); GS 3+4=61%; T1c=51%; T2a=25%; T2b=21%; T2c=3%; ≥50% positive cores=46%; EPE+ endorectal MRI =28%. 33% had pathologic EPE. Increasing T-stage (P<0.0001) and EPE+ endorectal MRI (P<0.0001) were significant predictors of pathologic EPE, whereas GS (4+3 vs 3+4) (P=0.14), percentage of positive core biopsies (P=0.15), and pretreatment PSA (P=0.41) were not. Median EPE distance was 1.75 mm (range, <1–15mm). The rates of EPE >5 mm and EPE >3 mm were 11% and 15%, respectively. The odds ratios for endorectal MRI detection of any EPE and of EPE >5 mm were 3.06 and 3.75, respectively.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
67. Brachman DG, Thomas T, Hilbe J, Beyer DC. Failure-free survival following brachytherapy alone or external beam irradiation alone for T1-2 prostate tumors in 2222 patients: results from a single practice. *Int J Radiat Oncol Biol Phys.* 2000;48(1):111-117.	Observational-Tx	2,222 total patients; 1,527 EBRT; 695 brachytherapy	To evaluate failure-free survival for brachytherapy alone compared to EBRT alone for stage T1-2 Nx-NoMo patients over the same time period by a single community-based practice in the PSA era.	Failure-free survival at 5 years for EBRT and brachytherapy are 69% and 71%, respectively (P=0.91). For T stage, no significant difference in failure-free survival at 5 years is observed between EBRT and brachytherapy for either T1 (78% vs 83%, P=0.47) or T2 (67% vs 67%, P=0.89) tumors. Analysis by GS shows superior outcomes for Gleason 8–10 lesions treated with EBRT vs brachytherapy (5-year failure-free survival 52% vs 28%, P=0.04); outcomes for lower grade lesions (Gleason 4-6) when analyzed by GS alone do not significantly differ according to treatment received. Patients with initial PSA values of 10–20 ng/dL have an improved failure-free survival with EBRT vs brachytherapy at 5 years (70% vs 53%, P=0.001); outcomes for patients with initial PSA ranges of 0–4 ng/dL, of > 4–10 ng/dL, and >20 ng/dL did not differ significantly by treatment received. Failure-free survival was also determined for presenting GS/PSA combinations; all Gleason combinations in the initial PSA range >10–20 ng/dL had superior outcomes with EBRT compared to brachytherapy, and this reached statistical significance for GSs of 2–4 (72% vs 58%, P=0.026), Gleason 7 (67% vs 28%, P=0.002), and Gleason 8–10 (63% vs 23%, P=0.05).	2
68. 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

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. Kwok Y, DiBiase SJ, Amin PP, Naslund M, Sklar G, Jacobs SC. Risk group stratification in patients undergoing permanent (125)I prostate brachytherapy as monotherapy. *Int J Radiat Oncol Biol Phys.* 2002;53(3):588-594.	Observational-Tx	102 patients with clinically localized prostate cancer	To report the outcome of patients undergoing prostate brachytherapy as monotherapy who were stratified into low-, intermediate-, and high-risk groups with extended follow-up.	40 patients experienced a biochemical relapse at a median of 1.9 years (range 0.4–4.2). The 5-year actuarial PSA relapse-free survival rate for patients with favorable, intermediate, and unfavorable risk was 85%, 63%, and 24%, respectively (P<0.0001). All but 1 patient had the relapse within the first 5 years of treatment. When stratifying patients on the basis of their pretreatment PSA level, the 5-year PSA relapse-free survival rate for men with a PSA ≤10 ng/mL vs >10 ng/mL was 78% vs 35%, respectively (P=0.0005). Furthermore, the 5-year PSA relapse-free survival rate for men with a GS of ≤6 vs ≥7 was 74% vs 33%, respectively (P=0.0001). No difference was found between stage T1-T2a and stage T2b or higher (64% vs 54%, respectively; P=0.353).	2
70. Blasko JC, Grimm PD, Sylsvester JE, Cavanagh W. The role of external beam radiotherapy with I-125/Pd-103 brachytherapy for prostate carcinoma. *Radiother Oncol.* 2000;57(3):273-278.	Observational-Tx	634 total; 403 patients treated with brachytherapy; 231 brachytherapy combined with 45 Gy of EBRT	To compare the biochemical outcomes of patients treated with Pd-103/I-125 brachytherapy alone vs brachytherapy combined with EBRT for early stage prostate carcinoma.	The actuarial bPFS rate for the entire 634 patients was 85% at 10 years. The bPFS rate outcomes by risk group for monotherapy vs combined therapy respectively were: low risk, 94% vs 87%; intermediate risk, 84% vs 85%; high risk, 54% vs 62%. These differences did not reach statistical significance for any risk group. Rectal morbidity was slightly greater in the combined treatment patients.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Grimm PD, Blasko JC, Sylvester JE, Meier RM, Cavanagh W. 10-year biochemical (prostate-specific antigen) control of prostate cancer with (125)I brachytherapy. *Int J Radiat Oncol Biol Phys.* 2001;51(1):31-40.	Observational-Tx	125 patients with T1-T2	To report 10-year biochemical PSA outcomes for patients treated with I-125 brachytherapy as monotherapy for early-stage prostate cancer with comparisons made to an earlier-treated cohort.	The overall PSA PFS rate achieved at 10 years was 87% for low-risk patients (PSA <10, Gleason Sum 2–6, T1–T2b). Of 59 patients (47%) followed beyond 7 years, 51 (86%) had serum PSAs <0.5 ng/mL; 48 (81%) had serum PSAs <0.2 ng/mL. Failures were local, 3.0%; distant, 3.0%. No patients have died of prostate carcinoma. The proportion of patients with a PSA ≤0.2 ng/mL continued to increase until at least 7–8 years post-therapy. A plot of PSA PFS against the proportion of patients achieving serum PSA of <0.2 ng/mL suggests a convergence of these 2 endpoints at 10 years. Patients treated in the era of this study (1988-1990) experienced a statistically improved PFS compared with an earlier era (1986-1987). This difference appears independent of patient selection, suggesting that the maturation of the technique resulted in improved biochemical control.	2
72. Taira AV, Merrick GS, Galbreath RW, Wallner KE, Butler WM. Natural history of clinically staged low- and intermediate-risk prostate cancer treated with monotherapeutic permanent interstitial brachytherapy. *Int J Radiat Oncol Biol Phys.* 2010;76(2):349-354.	Observational-Tx	463 patients	To evaluate the natural history of clinically staged low- and intermediate-risk prostate cancer treated with permanent interstitial seed implants as monotherapy.	The 12-year bPFS, CSS, and OS rates for the entire cohort were 97.1%, 99.7%, and 75.4%, respectively. Only pretreatment PSA level, percent positive biopsy cores, and minimum dose that covered 90% of the target volume were significant predictors of biochemical recurrence. The bPFS, CSS, and OS rates were 97.4%, 99.6%, and 76.2%, respectively, for low-risk patients and 96.4%, 100%, and 74.0%, respectively, for intermediate-risk patients. The bPFS rate was 98.8% for low-risk patients with high-quality implants vs 92.1% for those with less adequate implants (P<0.01), and it was 98.3% for intermediate-risk patients with high-quality implants vs 86.4% for those with less adequate implants (P<0.01).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. Munro NP, Al-Qaisieh B, Bownes P, et al. Outcomes from Gleason 7, intermediate risk, localized prostate cancer treated with Iodine-125 monotherapy over 10 years. *Radiother Oncol.* 2010;96(1):34-37.	Observational-Tx	187 patients	To review the 10 year experience of permanent brachytherapy monotherapy at a single UK center for GS 7, intermediate risk (MSK model), PSA 6 10 ng/mL, localized prostate cancer.	Median follow-up was 5.0 years (range 2.0–10.1 years). 1 patient has died of prostate cancer. At 10 years, PSA-RFS was 82.4%/78% (ASTRO consensus and nadir +2 definitions). For GS 3+4, 5 year PSA-RFS was 86.7%/87.9% and for GS 4+3: 85.2%/96.6% respectively, with no significant difference between groups. 5-year PSA-RFS (ASTRO) of 92.6% was seen for D(90) ≥140 Gy (50% total), compared with 77.0% below 140 Gy (P=0.08).	2
74. Blasko JC, Grimm PD, Sylvester JE, Badiozamani KR, Hoak D, Cavanagh W. Palladium-103 brachytherapy for prostate carcinoma. *Int J Radiat Oncol Biol Phys.* 2000;46(4):839-850.	Observational-Tx	230 patients with T1-T2	To evaluate biochemical outcome following monotherapeutic Pd-103.	The overall biochemical control rate achieved at 9 years was 83.5%. Failures were local 3.0%; distant 6.1%; PSA progression only 4.3%. Significant risk factors contributing to failure were serum PSA >10 ng/mL and Gleason sum of 7 or greater. 5-year biochemical control for those exhibiting neither risk factor was 94%; 1 risk factor, 82%; both risk factors, 65%. When all 1354 PSA determinations obtained for this cohort were considered, the patients with a proportion of PSAs ≤0.5 ng/ml continued to increase until at least 48 months post-therapy. These data conformed to a median PSA half-life of 96.2 days.	2
75. Merrick GS, Butler WM, Wallner KE, et al. Impact of supplemental external beam radiotherapy and/or androgen deprivation therapy on biochemical outcome after permanent prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2005;61(1):32-43.	Observational-Tx	668 clinical stage T1b-T3aNxM0	To evaluate the impact of supplemental EBRT and/or ADT on 8-year biochemical outcome after PPB.	For the entire group, the actuarial 8-year bPFS rate was 98.2%, 98.4%, and 88.2% for low-, intermediate-, and high-risk patients, respectively, with a median PSA level of <0.1 ng/mL for all risk groups and ADT and EBRT subgroups. At last follow-up, only 5 patients (0.8%) had died of metastatic prostate cancer. In multivariate analysis, GS, percentage of positive biopsies, and ADT predicted for biochemical outcome in high-risk patients. In low- and intermediate-risk patients, none of the evaluated variables predicted for biochemical outcome. For the entire population, pretreatment PSA level, GS, ADT, and clinical stage predicted for 8-year bPFS, with the percentage of positive biopsies approaching statistical significance.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. D'Amico AV, Moran BJ, Braccioforte MH, et al. Risk of death from prostate cancer after brachytherapy alone or with radiation, androgen suppression therapy, or both in men with high-risk disease. *J Clin Oncol.* 2009;27(24):3923-3928.	Observational-Tx	1,342 men	To estimate the risk of prostate cancer-specific mortality after brachytherapy alone or in conjunction with androgen suppression therapy, EBRT, or both in men with high-risk prostate cancer.	Despite higher baseline probabilities of prostate cancer-specific mortality after a median follow-up of 5.1 years, there was a significant reduction in the risk of prostate cancer-specific mortality (adjusted HR, 0.32; 95% CI, 0.14 to 0.73; *P*=.006) in men treated with brachytherapy and both androgen suppression therapy and EBRT as compared with neither. When compared with brachytherapy alone, a significant decrease in the risk of prostate cancer-specific mortality was not observed in men treated with either supplemental androgen suppression therapy (adjusted HR, 0.63; 95% CI, 0.27 to 1.47; *P*=.28) or EBRT (adjusted HR, 0.57; 95% CI, 0.21 to 1.52; *P*=.26). There was a near-significant reduction (adjusted HR, 0.53; 95% CI, 0.27 to 1.07; *P*=.079) in the risk of prostate cancer-specific mortality in men treated with tri- as compared with bimodality therapy.	2

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77. Zelefsky MJ, Kuban DA, Levy LB, et al. Multi-institutional analysis of long-term outcome for stages T1-T2 prostate cancer treated with permanent seed implantation. *Int J Radiat Oncol Biol Phys.* 2007;67(2):327-333.	Observational-Tx	2,693 patients treated with permanent interstitial BT monotherapy for T1-T2 prostate cancer	To assess long-term PSA (PSA) outcome after PPB and identify predictors of improved DFS.	Among patients where the I-125 dose to 90% of the prostate (D90) was ≥130 Gy, the 8-year PSA relapse-free survival was 93% compared with 76% for those with lower D90 dose levels (P<0.001). A multivariable analysis identified tumor stage (P=0.002), GS (P<0.001), pretreatment PSA level (P<0.001), treatment year (P=0.001), and the isotope used (P=0.004) as pretreatment and treatment variables associated with PSA relapse-free survival. When restricted to patients with available postimplantation dosimetric information, D90 emerged as a significant predictor of biochemical outcome (P=0.01), and isotope was not significant. The 8-year PSA relapse-free survival was 92%, 86%, 79%, and 67%, respectively, for patients with PSA nadir values of 0–0.49, 0.5–0.99, 1.0–1.99, and >2.0 ng/mL (P<0.001). Among patients free of biochemical relapse at 8 years, the median nadir level was 0.1 ng/mL, and 90% of these patients achieved a nadir PSA level <0.6 ng/mL.	2

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78. Sabolch A, Feng FY, Daignault-Newton S, et al. Gleason pattern 5 is the greatest risk factor for clinical failure and death from prostate cancer after dose-escalated radiation therapy and hormonal ablation. *Int J Radiat Oncol Biol Phys.* 2011;81(4):e351-360.	Observational-Tx	718 men	To analyze the clinical outcomes in patients treated with dose-escalated RT based on the presence or absence of Gleason pattern 5.	At biopsy, 89% of patients had no Gleason pattern 5, and 11% (76/718) had Gleason pattern 5. There were no differences in age, comorbid illness, T stage, PSA, or the use or duration of ADT between GS 8 without Gleason pattern 5 and GS 8-10 with Gleason pattern 5. The presence of Gleason pattern 5 predicted lower freedom from metastasis (P<0.002; HR 3.4 [1.7–7.1]); CSS (P<0.0001; HR 12.9 [5.4–31]); and OS (P<0.0001; HR 3.6 [2.0–6.5]) in comparison with GS 8 (without Gleason pattern 5). The 8-year freedom from metastasis, CSS, and OS were 89%, 98%, and 57%, respectively, for those with Gleason 8 prostate cancer without Gleason pattern 5 in comparison with 61%, 55%, and 31%, respectively, for those with Gleason pattern 5. In addition, both freedom from metastasis and CSS were strongly influenced by ADT given concurrently with RT. On multivariate analysis, Gleason pattern 5 was the strongest prognostic factor for all clinical endpoints, including OS.	2
79. Taira AV, Merrick GS, Galbreath RW, et al. Long-term outcomes of prostate cancer patients with Gleason pattern 5 treated with combined brachytherapy and external beam radiotherapy. *Brachytherapy.* 2013;12(5):408-414.	Observational-Tx	329 patients	To report outcomes of men with Gleason grade 5 treated with brachytherapy to help determine the efficacy of brachytherapy in this patient population.	At 10 years, bPFS, CSS, and OS for the group of high-risk patients as a whole was 91.1%, 95.5%, and 72.5%, respectively. There was no difference in bPFS between men with and without Gleason pattern 5 (89.7% vs 91.8%; P=0.56). However, men with Gleason pattern 5 had lower prostate cancer CSS (90.3% vs 98.1%; P=0.011). There was no difference in OS comparing men with and without Gleason pattern 5 disease (67.7% vs 75.4%; P=0.14).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
80. Frank SJ, Pisters LL, Davis J, Lee AK, Bassett R, Kuban DA. An assessment of quality of life following radical prostatectomy, high dose external beam radiation therapy and brachytherapy iodine implantation as monotherapies for localized prostate cancer. *J Urol.* 2007;177(6):2151-2156; discussion 2156.	Observational-Tx	234 with RP; 135 with EBRT; 74 with a I-125 implant	To assess the health related quality of life associated with monotherapy with RP, high dose EBRT, and a I-125 implant.	A total of 234 patients with RP, 135 with EBRT and 74 with a I-125 implant were treated with a monotherapy approach. Median age was 61 years in the RP group, 68 years in the high dose EBRT group and 64 years in the I-125 implant group ($P<0.001$). Of the patients 97% [corrected] had cT1-2 disease and GS 7 or less [corrected] Median time from treatment was 4.0 years for RP, 4.7 years for high dose EBRT and 3.5 years for I-125 implantation. Radiation caused significantly worse bowel bother and bowel function than RP ($P\leq0.018$). Patients with high dose EBRT had significantly better urinary function than patients with RP ($P<0.001$). While patients with RP had significantly worse urinary incontinence than those with a I-125 implant or high dose EBRT ($P<0.0001$), patients with a I-125 implant had more urinary irritation than those with high dose EBRT and RP ($P<0.01$ and <0.0001, respectively). Patients with a I-125 implant had significantly better sexual function than those with high dose EBRT and RP ($P=0.01$ and 0.0003, respectively).	2

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81. Merrick GS. The role of hormonal therapy in prostate brachytherapy. Counterpoint. *Brachytherapy.* 2003;2(1):2-4.	Review/Other-Tx	N/A	A counterpoint stating that improvements in DFS and OS in patients with locally advanced prostate cancer may be a result of the inability of conventional doses of EBRT as a monotherapeutic approach to sterilize large, bulky prostate cancers and as such may not be applicable to brachytherapy.	The vast majority of hormone-naïve intermediate- and high-risk patients remain free of biochemical failure after prostate brachytherapy, and the delivered radiation dose is paramount in securing freedom from biochemical failure. Although it is possible that subgroups of higher-risk patients may benefit from hormonal therapy, that patient population has not been definitively identified. In addition, in series reporting a biochemical advantage for high-risk patients, the follow-up of the hormone-naïve patients has been statistically longer than that of the hormonally manipulated patients, and, as such, additional follow-up will be mandatory to confirm the durability of those findings. With multiple institutions reporting favorable biochemical outcomes for hormone- naïve brachytherapy patients, the potential population that may benefit from hormonal therapy continues to shrink.	4
82. Radiation Thearpy Oncology Group. 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. Available at: https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0924.	Review/Other-Tx	Ongoing	To demonstrate that prophylactic neoadjuvant ADT and whole-pelvic RT will result in improvement in OS in patients with "unfavorable" intermediate risk or "favorable" high risk prostate cancer compared to NADT and high dose prostate and seminal vesicle 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

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83. Burri RJ, Stone NN, Unger P, Stock RG. Long-term outcome and toxicity of salvage brachytherapy for local failure after initial radiotherapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2010;77(5):1338-1344.	Observational-Tx	37 men: local failure after initial prostate RT (32 EBRT and 5 brachytherapy)	To describe long-term outcomes and toxicity after salvage brachytherapy for local failure after initial RT for prostate cancer.	Median follow-up was 86 months (range, 2–156). The median dose to 90% of the PV was 122 Gy (range, 67–166). The 10-year freedom from biochemical failure and cancer-specific survival were 54% and 96%, respectively. On univariate analysis, PSA >10 ng/mL at initial diagnosis was significantly associated with freedom from biochemical failure (P=0.01), and there were trends for both age <70 years (P=0.08) and PSA <6 ng/mL (P=0.08) at the time of salvage brachytherapy. On multivariate analysis, only presalvage PSA <6 ng/mL (P=0.046) was significantly associated with improved freedom from biochemical failure. There were three Grade 3 toxicities and one Grade 4 toxicity. Pelvic lymph node dissection before salvage brachytherapy was the only variable significantly associated with Grade ≥2 toxicity (P=0.03).	2
84. Lee HK, Adams MT, Motta J. Salvage prostate brachytherapy for localized prostate cancer failure after external beam radiation therapy. *Brachytherapy.* 2008;7(1):17-21.	Observational-Tx	21 patients	To determine the toxicity and clinical outcome of salvage prostate brachytherapy for localized prostate cancer failure after EBRT.	With a median follow-up of 36 months, the actuarial 3-year and 5-year OS rates were 81% and 81%, and the biochemical failure-free survival rates were 94% and 38%, respectively. There was no significant difference in biochemical failure-free survival (P=0.98) and OS (P=0.13) for patients who had androgen ablation. 4 patients developed biochemical failure and 1 patient developed distant metastasis at 59 months from treatment. 4 patients had Grade 2 GU adverse events, 2 patients had Grade 1 GU adverse events, and 1 patient had a Grade 2 GI adverse event. There were no Grade 3 or higher adverse events. All 3 deaths were secondary to other medical comorbidities.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
85. Nguyen PL, Chen MH, D'Amico AV, et al. Magnetic resonance image-guided salvage brachytherapy after radiation in select men who initially presented with favorable-risk prostate cancer: a prospective phase 2 study. *Cancer.* 2007;110(7):1485-1492.	Experimental-Tx	25 patients	To evaluate the late GI and GU toxicity and PSA control of MRI-guided brachytherapy used as salvage for RT failure.	The median follow-up was 47 months. The 4-year estimate of grade 3 or 4 GI or GU toxicity was 30%, and 13% of patients required a colostomy and/or urostomy to repair a fistula. An interval <4.5 years between RT courses was associated with both outcomes with a HR of 12 (95% CI, 1.4–100; *P*=.02) for grade 3 or 4 toxicity and 25 (95% CI, 1.1–529; *P*=.04) for colostomy and/or urostomy. PSA control (nadir +2 definition) was 70% at 4 years.	2
86. Caloglu M, Ciezki J. Prostate-specific antigen bounce after prostate brachytherapy: review of a confusing phenomenon. *Urology.* 2009;74(6):1183-1190.	Review/Other-Tx	N/A	A review of 19 articles summarized to delineate the facts of PSA level fluctuation and increase.	Although several patient and treatment related factors were assessed by studies, only age remained as the most consistent predictor.	4
87. Satoh T, Ishiyama H, Matsumoto K, et al. Prostate-specific antigen 'bounce' after permanent 125I-implant brachytherapy in Japanese men: a multi-institutional pooled analysis. *BJU Int.* 2009;103(8):1064-1068.	Observational-Tx	388 patients	To examine the incidence, timing, and magnitude of the PSA level 'bounce' after PPB and correlate the PSA bounce with clinical and dosimetric factors in Japanese patients with prostate cancer.	The actuarial likelihood of having PSA bounce at 24 months was 50.8% for definition A, 23.5% for definition B, and 19.4% for definition C. The median time to develop PSA bounce was 12 months for definition A, 18 months for definition B, and 18 months for definition C. There was a PSA bounce magnitude of 2 ng/mL in 5.3% of patients, and 95.3% of PSA bounce occurred within 24 months after I-125-brachytherapy. Among the before and after I-125-brachytherapy factors, clinical stage, initial PSA level, and GS did not predict for PSA bounce using any definition; only being younger predicted for PSA bounce on multivariate analysis (*P*<0.001).	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
88. Thompson A, Keyes M, Pickles T, et al. Evaluating the Phoenix definition of biochemical failure after (125)I prostate brachytherapy: Can PSA kinetics distinguish PSA failures from PSA bounces? *Int J Radiat Oncol Biol Phys.* 2010;78(2):415-421.	Observational-Tx	1,006 patients	To evaluate the PSA kinetics of PSA failure and PSA bounce after permanent I-125 PPB.	Median follow-up was 54 months. Of the 1,006 men, 57 patients triggered the Phoenix definition of PSA failure, 32 (56%) were true PSA failure, and 25 PSA bounce (44%). The median time to trigger nadir + 2 was 20.6 months (range, 6–36) vs 49 months (range, 12–83) for PSA bounce vs PSA failure groups (P<0.001). The PSA bounce patients were significantly younger (P<0.0001), had shorter time to reach the nadir (median 6 vs 11.5 months, P=0.001) and had a shorter PSA doubling time (P=0.05). Men younger than age 70 who trigger nadir +2 PSA failure within 38 months of implant have an 80% likelihood of having PSA bounce and 20% chance of PSA failure.	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
89. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Anderson RL. Prostate-specific antigen spikes after permanent prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2002;54(2):450-456.	Observational-Tx	218 hormone-naïve patients free of biochemical or clinical failure	To evaluate whether any clinical, treatment, or dosimetric parameters correlated with the development of a PSA spike after PPB.	52 patients (23.9%) developed a PSA spike at a mean and median of 19.5 +/- 9.4 months and 16.3 months (range 6.5–59.9), respectively. The median serum PSA before the PSA spike was 0.50 ng/mL, and the median PSA at the time of the spike was 0.90 ng/mL (range 0.3–3.0). On average, patients experiencing a PSA spike were 3.4 years younger (63.9 vs 67.3 years, P=0.002) than patients not experiencing a spike and were more likely to have been implanted with I-125 than with Pd-103 (32.7% vs 16.7%, P=0.006). In addition, the mean first postimplant PSA level was significantly higher in the spike than in the nonspike patients (1.2 vs 0.7 ng/mL, P<0.001). By 66 months, the mean and median serum PSA levels for the spike and nonspike patients were all ≤0.1 ng/mL. Stratified into 3 nadir PSA groups, patients with a nadir PSA ≤0.2 ng/mL were significantly less likely to develop a PSA spike than those patients with a PSA nadir >0.2 to ≤0.5 ng/mL or >0.5 to 1.0 ng/mL (20%, 50%, and 80%, respectively, P<0.001). In Cox multivariate regression analysis, patient age, clinical stage, first postimplant PSA level, and V(150) were predictive for the development of a PSA spike. A postimplant dosimetric threshold of either <115% of the minimal peripheral dose for D(90) or <55% of the PV for V(150) was strongly predictive of a spike. When the variables only determinable after the occurrence of the PSA spike were included in the multivariate analysis, V(150), preimplant PSA level, and nadir PSA were the significant predictors.	2

Permanent Source Brachytherapy for Prostate Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
90. Reed D, Wallner K, Merrick G, Buskirk S, True L. Clinical correlates to PSA spikes and positive repeat biopsies after prostate brachytherapy. *Urology.* 2003;62(4):683-688.	Review/Other-Tx	8	To make some preliminary observations regarding the biochemical characteristics of the doubly confusing picture of PSA spikes and histologically positive biopsies after prostate brachytherapy.	Patients' prespike nadir ranged from 0.9 to 1.7 ng/mL (median 1.2). The time from the implant to the start of the spike ranged from 9 to 24 months (median 13). The time from implant to the spike peak ranged from 12 to 30 months (median 22). The peak spike height ranged from 2.6 to 8.4 ng/mL (median 3.1). Patients' last PSA value ranged from 0.1 to 0.5 ng/mL (median 0.2).	4
91. Crook J, Gillan C, Yeung I, Austen L, McLean M, Lockwood G. PSA kinetics and PSA bounce following permanent seed prostate brachytherapy. *Int J Radiat Oncol Biol Phys.* 2007;69(2):426-433.	Observational-Tx	292 men	To report the incidence, timing, and magnitude of the benign PSA bounce after I-125 prostate brachytherapy and correlate the bounce with clinical and/or dosimetric factors.	Resolved PSA bounces were seen in 40% of men with follow-up >30 months. Median onset was 15 months, and median magnitude was 0.76 ng/ml. Magnitude >2 ng/ml was seen in 15%. The only clinical or dosimetric factor predictive of bounce in multivariate analysis was younger age. Median time to increasing PSA level indicative of failure was 30 months.	2

Evidence Table Key

Study Quality Category Definitions

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

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

ADT = Androgen deprivation therapy

bPFS = Biochemical progression-free survival

bRFS = Biochemical relapse-free survival

CI = Confidence interval

CSS = Cause-specific survival

CT = Computed tomography

DFS = Disease-free survival

EBRT = External-beam radiation therapy

EPE = Extraprostatic extension

GI = Gastrointestinal

GS = Gleason score

GU = Genitourinary

HR = Hazard ratio

IMRT = Intensity-modulated radiotherapy

IPSS = International Prostate Symptom Score

LDR = Low-dose-rate

MRI = Magnetic resonance imaging

OS = Overall survival

PFS = Progression-free survival

PPB = Permanent prostate brachytherapy

PSA = Prostate-specific antigen

PV = Prostate volume

RP = Radical prostatectomy

RT = Radiotherapy

TURP =Transurethral resection of the prostate

TRUS = Transrectal ultrasound

US = Ultrasound