Comparison of the 5-Year Outcome and Morbidity of Three-Dimensional Conformal Radiotherapy Versus Transperineal Permanent Iodine-125 Implantation for Early-Stage Prostatic Cancer

By Michael J. Zelefsky, Kent E. Wallner, C. Clifton Ling, Adam Raben, Timothy Hollister, Theresa Wolfe, Alison Grann, Paul Gaudin, Zvi Fuks, and Steven A. Leibel

Purpose: **To compare the prostate-specific antigen (PSA) relapse-free survival outcome and incidence of late toxicity for patients with early-stage prostate cancer treated at a single institution with either three-dimensional conformal radiotherapy (3D-CRT) or transperineal permanent implantation (TPI) with iodine-125 seeds.**

Materials and Methods: **Patients with favorable-risk prostate cancer, defined as a pretreatment PSA of less than or equal to 10.0 ng/mL, Gleason score of 6 or lower, and stage less than or equal to T2b, were selected for this analysis. Between 1989 and 1996, 137 such patients were treated with 3D-CRT and 145 with TPI. The median ages of the 3D-CRT and TPI groups were 68 years and 64 years, respectively. The median dose of 3D-CRT was 70.2 Gy, and the median implant dose was 150 Gy. Prostate-specific antigen relapse was defined according to the American Society of Therapeutic Radiation Oncology Consensus Statement, and toxicity was graded according to the Radiation Therapy Oncology Group morbidity scoring scale. The median follow-up times for the 3D-CRT and TPI groups were 36 and 24 months, respectively.**

Results: **Eleven patients (8%) in the 3D-CRT group and 12 patients (8%) in the TPI group developed a biochemical relapse. The 5-year PSA relapse-free survival rates for the 3D-CRT and the TPI groups were 88% and 82%, respectively ($P = .09$). Protracted grade 2 urinary symptoms were more prevalent among patients treated with TPI compared with 3D-CRT. Grade 2 urinary toxicity, which was manifest after the implant and persisted for more than 1 year after this procedure, was observed in 45 patients (31%) in the TPI group. In these 45 patients, the median duration of grade 2 urinary symptoms was 23 months (range, 12 to 70 months). On the other hand, acute grade 2 urinary symptoms resolved within 4 to 6 weeks after completion of 3D-CRT, and the 5-year actuarial likelihood of late grade 2 urinary toxicity for the 3D-CRT group was only 8%. The 5-year actuarial likelihood of developing a urethral stricture (grade 3 urinary toxicity) for the 3D-CRT and TPI groups was 2% and 12%, respectively ($P < .0002$). Of 45 patients who developed grade 2 or higher urinary toxicity after TPI, the likelihood of resolution or significant improvement of these symptoms at 36 months from onset was 59%. The 5-year likelihood of grade 2 late rectal toxicity for the 3D-CRT and TPI patients was similar (6% and 11%, respectively; $P = .97$). No patient in either group developed grade 3 or higher late rectal toxicity. The 5-year likelihood of posttreatment erectile dysfunction among patients who were initially potent before therapy was 43% for the 3D-CRT group and 53% for the TPI group ($P = .52$).**

Conclusion: **Both 3D-CRT and TPI are associated with an excellent PSA outcome for patients with early-stage prostate cancer. Urinary toxicities are more prevalent for the TPI group and subsequently resolve or improve in most patients. In addition to evaluating long-term follow-up, future comparisons will require detailed quality-of-life assessments to further determine the impact of these toxicities on the overall well-being and quality of life of the individual patient.**

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RADICAL PROSTATECTOMY, external-beam radiotherapy, and brachytherapy are commonly used treatment approaches for patients with early-stage prostate cancer. Recent reports have demonstrated excellent biochemical outcomes for patients with similar stage and favorable prognostic variables treated with any of these therapeutic interventions. Kupelian et al[1] reported similar biochemical relapse-free survival rates for patients with favorable prognostic features who underwent radical prostatectomy or external-beam radiotherapy at the same institution. Similar findings have been reported by D'Amico et al.[2,3] Prostate-specific antigen (PSA) relapse-free survival rates for early-stage patients treated by transperineal permanent implantation (TPI) have also been excellent and are comparable to those obtained in patients who underwent surgery or external-beam irradiation.[4-7]

The patient with cancer of the prostate confronts the difficult task of selecting the optimal treatment modality. Weighing the pros and cons of such treatment approaches must not only incorporate the likelihood of achieving an

From the Departments of Radiation Oncology and Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY.

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Address reprint requests to Michael J. Zelefsky, MD, Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, 1275 York Ave, New York, NY 10021.

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excellent disease-free survival outcome but also include an assessment of the incidence of potential treatment-related morbidities and its resultant impact on the quality of life for the individual patient. Although the available data suggest comparable biochemical outcomes for early-stage patients with these treatment approaches,[3] there is limited information comparing the associated toxicities or complication-free survival rates of each modality.

At the Memorial Sloan-Kettering Cancer Center, 282 patients with favorable-risk prostate cancer were treated with three-dimensional conformal radiotherapy (3D-CRT) or computed tomography (CT)-planned transperineal permanent iodine-125 implantation of the prostate. In general, as all patients with such favorable prognostic features were routinely offered each of these treatment modalities, the final decision for a particular mode of therapy was made by the patient. The data presented in this article indicate comparable biochemical outcomes for the two groups, with a higher incidence of moderate, but transient, urinary toxicity in the TPI cohort.

MATERIALS AND METHODS

3D-CRT Group

Between 1988 and 1995, 743 patients with clinically localized adenocarcinoma of the prostate were treated using 3D-CRT with photon beams.[8] Of these, 137 (18%) were characterized as having favorable prognostic features and constitute the 3D-CRT group in this analysis. For the purposes of this study, the criteria necessary for inclusion in this group were less than or equal to stage T2b disease, pretreatment PSA less than or equal to 10.0 ng/mL, and a Gleason score of 6 or lower. These patients represent a cohort with a high likelihood of organ-confined disease who are also optimal candidates for implant therapy. Clinical stage was defined according to the American Joint Committee on Cancer 1992 Staging System.[9] The details of the pretreatment diagnostic evaluation have previously been published.[10,11] The details of 3D-CRT treatment planning and treatment delivery have also been described in previous publications.[8,10,11]

The patient characteristics of the 3D-CRT group are shown in Table 1. Briefly, these patients were treated with six individually shaped coplanar fields, delivered with 15- or 25-MV x-rays in daily fractions of 1.8 Gy, prescribed to the maximum isodose surface distribution that completely encompassed the planning target volume. A prescription dose of 64.8 Gy was given to 21 patients (15%), 70.2 Gy to 54 patients (39%), 75.6 Gy to 59 patients (43%), and 81.0 Gy to three patients (2%). For patients treated with 81 Gy, the last five fractions (9 Gy) were delivered with a separate boost plan in which the anterior rectal wall was shielded in each of the fields.[10,11] Twenty-three patients (17%) with large-volume prostate glands were treated with neoadjuvant androgen deprivation (NAAD) for 3 months to reduce the volume of rectum or bladder exposed to the high doses of therapy.[12] This treatment was continued during 3D-CRT and stopped when radiotherapy was completed.

Table 1. Characteristics of 3D-CRT and TPI Cohorts

	3D-CRT (n = 137)		TPI (n = 145)		
	No.	%	No.	%	*P*
Median age, years	68		64		
T stage					
T1c	58	43	98	68	< .01
T2a	32	23	29	20	NS*
T2b	47	34	18	12	NS
Median pretreatment PSA, ng/mL	6.6		6.1		
Potent pretreatment	105	77	128	88	< .01
NAAD	23	17	16	11	NS
Prior TURP	21	15	9	6	NS

*NS, not significant ($P > .5$).

Transperineal ^{125}I Implant Group

Between 1988 and 1997, 245 patients were treated with CT-planned TPI of the prostate. Of these patients, 145 (58%) were characterized as having favorable prognostic features,[8] ie, PSA less than or equal to 10 ng/mL, Gleason score lower than 7, and clinical stage less than or equal to T2b, and constitute the TPI group in this analysis. The patient characteristics of this group are also shown in Table 1.

The TPI procedure has also been described in detail.[4] Briefly, a preimplantation CT scan and a computer-aided optimization method were used to determine the needle placement, the number of sources, and their respective locations.[13] Fluoroscopy was used to monitor needle placement during the implantation procedure, as previously described.[14] In general, ultrasound guidance was not routinely used with this approach. The prescribed, minimum radiation dose to the prostate was 140 to 160 Gy. The median value of implanted activity was 45 mCi of ^{125}I (range, 32 to 77 mCi), and the median seed strength was 0.70 mCi (range, 0.5 to 0.92 mCi). The median matched peripheral dose (MPD) was 150 Gy (range, 110 to 257 Gy), and the median implanted volume was 59 ml (range, 29 to 135 ml). Neoadjuvant androgen deprivation was given to 16 patients (11%) in this group for a median duration of 2 months before TPI.

In general, follow-up evaluations were performed at 1 and 4 months after treatment and at 6-month intervals thereafter. The median follow-up time in the 3D-CRT group was 36 months (range, 12 to 109 months), with 25 patients (15%) followed for 5 years or more. The median follow-up time in the TPI group was 24 months (range, 6 to 103 months), and 17 patients (12%) were followed for 5 years or more. Disease status and late complications were determined as of the time of analysis in April 1998. PSA relapse was defined as three successive PSA elevations observed from the posttreatment nadir PSA value, and the date of the PSA relapse was calculated from the midpoint between the postirradiation nadir PSA and the first rising value.[15] Late treatment complications, graded according to the morbidity grading system of the Radiation Therapy Oncology Group,[16] were defined as those developing more than 90 days after the completion of irradiation or those that started during treatment and persisted for longer than 90 days after its completion. In a similar fashion, late complications after TPI were defined as those developing or persisting 90 days after the effective treatment time of the implant. For the purposes of this study, this time point was taken at 1 year from the date of the implant procedure.

Time-adjusted rates of the appearance of late complications and PSA relapse-free survival were calculated using the product-limit (Kaplan-Meier) method.[17] Differences between time-adjusted incidence rates were evaluated using the Mantel log-rank test for censored data.[18] Covariates that affect the time-adjusted incidence of chemical relapse and treatment-related toxicity were examined using the stepwise Cox proportional hazards regression model.[19]

RESULTS

PSA Relapse-Free Survival

Eleven patients (8%) in the 3D-CRT group and 12 patients (8%) in the TPI group developed a PSA relapse. The median times to biochemical failure in the 3D-CRT and the TPI groups were 25 months and 20 months, respectively, with corresponding 5-year actuarial PSA relapse-free survival rates of 88% and 82%, respectively ($P = .09$) (Fig 1). In a multivariate analysis, neither mode of therapy (3D-CRT *v* TPI), NAAD, clinical stage (T1c *v* T2), age (> 60 years *v* ≤ 60 years), nor higher doses had an impact upon the biochemical outcome in these patients.

Urinary Toxicity

In the 3D-CRT group, 80 patients (58%) had no or only mild (grade 1) acute gastrourinary (GU) toxicity that required no therapeutic intervention, whereas 57 patients (42%) required medications for relief of urinary symptoms (grade 2). Acute urinary retention (grade 3) was observed in five patients (3%) in the TPI group and necessitated catheterization, but this form of toxicity was not observed in the 3D-CRT group ($P = .08$). No grade 4 acute GU toxicities were observed in either group.

In the 3D-CRT group, minimal to no late GU toxicity was observed in 124 patients (91%), and 11 patients (8%) experienced late grade 2 urinary symptoms requiring medications such as terazosin hydrochloride. In the TPI group, minimal to no late GU toxicity was observed in 90 patients (62%). In general, grade 2 symptoms in the TPI group were manifest immediately after the procedure but were classified as ''late'' toxicity as these symptoms persisted beyond 90 days from the effective treatment time or activity of the implant. Protracted grade 2 urinary symptoms were more prevalent among patients treated with TPI compared with 3D-CRT. Grade 2 urinary toxicity that persisted for more than 1 year after this procedure was observed in 45 patients (31%) in the TPI group. In these 45 patients, the median duration of grade 2 urinary symptoms was 23 months (range, 12 to 70 months). On the other hand, acute grade 2 urinary symptoms resolved within 4 to 6 weeks after completion of 3D-CRT, and the 5-year actuarial likelihood of late grade 2 urinary toxicity for the 3D-CRT group was 8%. The higher incidence of late grade 2 urinary symptoms in the TPI group was similar for patients with implanted volumes of less than or equal to 60 ml and with larger volumes (data not shown). In most cases, these symptoms gradually resolved with time. In the 3D-CRT group, the median duration of grade 2 symptoms was 19 months, and the likelihood of symptom resolution or improvement at 36 months from their onset was 68%. In the TPI group, the median duration of persistent grade 2 symptoms from the time of implantation was 23 months, and the likelihood of resolution or improvement at 36 months from their onset was 59%.

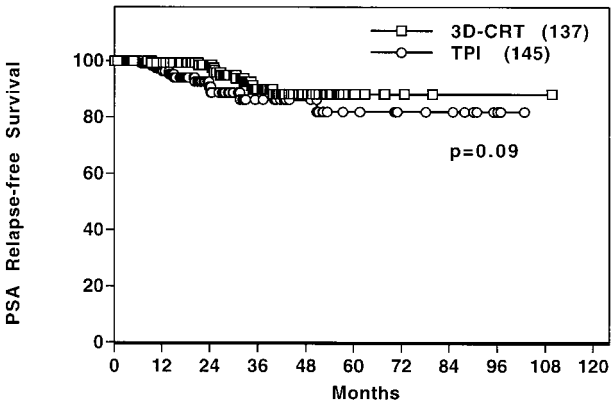

Fig 1. Actuarial PSA relapse-free survival for favorable-risk patients treated with 3D-CRT and TPI.

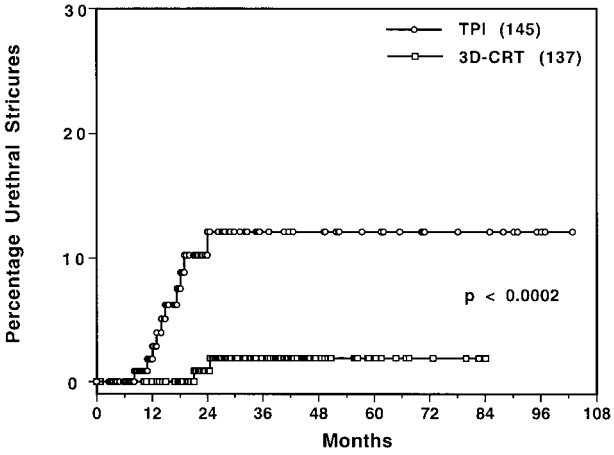

Fig 2. Actuarial likelihood of grade 3 GU toxicity-urethral stricture development, according to treatment received.

Late grade 3 urinary toxicity (urethral stricture) developed in two patients (1%) in the 3D-CRT group and in 10 (7%) patients in the TPI group ($P = .05$). Both patients who developed urethral stricures in the 3D-CRT group had a prior transurethral resection of prostate (TURP) compared with one of 10 who developed a stricture in the TPI group. The 5-year actuarial likelihood of late grade 3 urinary toxicity for the 3D-CRT and TPI groups was 2% and 12%, respectively ($P < .0002$) (Fig 2). No late grade 4 urinary toxicities were observed in either group. As shown in Table 2, the only predictor for late grade 2 or higher urinary toxicity was the mode of therapy (TPI $>$ 3D-CRT; $P < .0001$). Because the mode of therapy was an overwhelming predictor of late urinary toxicity in these patients, this variable was excluded from the Cox regression analysis to identify additional variables that may impact upon the likelihood of GU

Table 2. Cox Regression Analysis of Variables Affecting Late Grade 2 or Higher GU Toxicity

Variable	*P*	Regression Coefficient ± SE	Regression Coefficient Exponent
TPI *v* 3D-CRT	< .001	1.97 ± 0.34	7.19
Age ≥ 60 years	NS*		
NAAD	NS		
Prior TURP	NS		
Higher radiation doses	NS		

*NS, not significant ($P > .5$).

toxicity. In this analysis, higher radiation dose (3D-CRT dose > 75.6 Gy; TPI MPD ≥ 160 Gy) was the only other variable that predicted for late urinary toxicity ($P = .01$; regression coefficient, 2.0), whereas the clinical stage, prior TURP, and age younger than 60 years had no impact on this end point.

Rectal Toxicity

In the 3D-CRT group, 118 patients (86%) had no or only mild (grade 1) acute gastrointestinal (GI) toxicity not requiring therapeutic intervention, and 19 (14%) required medications for relief of GI symptoms (grade 2). No acute rectal symptoms were observed in the TPI group.

Minimal to no late rectal toxicity (grade 0-1) was observed in 157 patients (94%) and 139 patients (96%) in the 3D-CRT and TPI groups, respectively. Ten patients (6%) in the 3D-CRT group and six patients (4%) in the TPI group experienced late grade 2 GI toxicity (rectal bleeding), which was treated with conservative measures such as cortisone enemas. The 5-year actuarial likelihood of developing late grade 2 GI toxicity for the 3D-CRT and the TPI groups was 6% and 11%, respectively ($P = .71$). In the 3D-CRT group, the median duration of late grade 2 toxicity was 12 months (range, 8 to 39 months), and the likelihood of symptomatic resolution or improvement at 36 months from its onset was 75%. In the TPI group, the median duration of late grade 2 GI toxicity was 8 months (range, 5 to 47 months), and the likelihood of resolution or improvement of these symptoms at 36 months from onset was 86%. No grade 3 or higher late GI toxicities were observed in either treatment group.

Potency Preservation

Among patients who were potent before treatment, 32 (32%) of 101 patients in the 3D-CRT group and 28 (21%) of 132 patients in the TPI group became impotent after therapy. The median time for development of posttreatment impotence after 3D-CRT and TPI was 22 months and 17 months, respectively. The 2- and 5-year likelihoods of posttreatment erectile dysfunction among patients who were initially potent before therapy were 28% and 43% for the 3D-CRT group, respectively, and 21% and 53% for the TPI group, respectively ($P = .64$). A Cox regression analysis was performed to identify variables predicting for posttreatment erectile dysfunction. Higher radiation dose (3D-CRT dose > 75.6 Gy; TPI MPD ≥ 160 Gy) was the only predictor for impotence ($P = .008$; regression coefficient, 2.0), whereas age younger 60 years, prior TURP, the use of NAAD, and the mode of radiotherapy (3D-CRT *v* TPI) were not significant predictors of this end point.

DISCUSSION

The absence of a randomized trial comparing external-beam radiotherapy and permanent interstitial implantation for early-stage prostate cancer has created confusion for patients faced with the challenge of choosing a treatment for their disease. Both of these radiotherapeutic interventions have undergone significant technologic improvements that have enhanced their respective capabilities to target high-radiation doses to the prostate more precisely than in the past. Transperineal ultrasound-based or CT-planned permanent seed implantation has supplanted the open retropubic technique, and this modification in technique has likely contributed to the excellent biochemical outcome seen in patients with favorable-risk disease treated with this modality. Similarly, technologic enhancements in the delivery of external radiotherapy, such as three-dimensional conformal radiotherapy, have led to improved precision of therapy compared with conventional treatment techniques and a further reduction of dose to normal tissue structures, resulting in a decrease in the incidence of treatment-related toxicities.

Comparison of the outcome of these two treatment approaches has been fraught with difficulties. In particular, the varying definitions of PSA relapse used in many reports as well as the paucity of available outcome data reported for prognostic risk groups have confounded any attempt to appropriately compare the results of TPI and external-beam radiotherapy for patients with localized prostate cancer. The data presented in this article are unique in that the recently established American Society of Therapeutic Radiation Oncology consensus definition for PSA relapse[15] was used to compare TPI and 3D-CRT for patients with similar prognostic features treated at a single institution. The 5-year outcome was excellent for both groups (88% and 82% for the 3D-CRT and TPI groups, respectively) and is consistent with reports from other institutions.[1,2,5-7]

Comparison of the morbidity of these procedures has also been hampered because of the absence of consistent toxicity scoring criteria as well as the lack of the use of actuarial methods to report late toxicity for patients treated with TPI.

Previous studies have documented a low incidence of grade 3 or higher urinary or rectal toxicities after TPI,[5-7] but the extent of less severe, but nonetheless important, symptoms has not been routinely reported. Prior reports from our institution, however, have, in particular, highlighted the incidence of moderate grade 2 urinary symptoms that may persist for at least 6 to 12 months after TPI.[20,21] The current report confirms these findings in larger numbers of patients. The incidence of late grade 2 urinary morbidity was observed in a higher percentage patients treated with TPI compared with 3D-CRT, although most patients experienced significant improvement or resolution of such symptoms over time.

Wallner et al[22] have previously demonstrated a correlation of late urethral toxicity with the urethral dose from TPI. In that study, the average maximal urethral dose among patients with late grade 2 and 3 urinary toxicities was 592 Gy compared with 447 Gy for those who had minimal (grade 1) or no late urinary toxicity ($P = .03$). In the current analysis, the higher incidence of grade 2 GU symptoms with TPI compared with 3D-CRT is likely related to the higher urethral doses with TPI, which on average are 150% of the prescription dose. These findings are consistent with our observations in this article of a higher incidence of grade 2 GU symptoms for patients treated with higher radiation doses. Although the median dose of 3D-CRT in this study was 70.2 Gy, a higher incidence of late grade 2 toxicity was nevertheless observed among the cohort of patients in this study treated with higher doses consistent with our previous reports.[8,11] In addition, it is also possible that the higher incidence of late grade 2 urinary symptoms in this study may relate to technical factors, such as the use of higher activity seeds or a nonperipheral-based seed placement approach compared with other techniques that use peripheral loading patterns. Nevertheless, as a computerized optimization program was used for the treatment planning of our patients which constrained the dose to urethra and minimized seed placement in close proximity to this structure, the impact of the loading pattern and seed activity on the incidence of late toxicity remains uncertain.

A surprising finding in this study was the identification of a higher than expected incidence of erectile dysfunction among patients treated with TPI. Although the incidence of impotence at 2 years after TPI was only 21% after implantation, the actuarial incidence increased to 53% by 5 years. Prior reports have noted a relatively low incidence of impotence after TPI,[23,24] although, in general, this end point was only evaluated at 2 years after implantation. Whereas age of the patient at the time of therapy had no significant impact on the likelihood of developing posttherapy impotence, the use of higher radiation doses was found in this analysis to be a significant predictor of impotence. Clearly, careful prospective assessments of long-term sexual function among similar patients will be necessary to confirm these findings.

To reduce the incidence of treatment-related toxicities, continued technologic advances are needed to deliver high radiation doses to the tumor concomitant with reduction of dose to the normal tissues. In external-beam radiotherapy, an important and recent innovation is intensity-modulated radiation therapy using the inverse planning method and treatment delivery with dynamic multileaf collimators.[25] We have already successfully treated over 300 patients with this approach for 3D-CRT, and the application of inverse treatment planning for TPI is currently being investigated. These potential improvements may further enhance our ability to optimize the dose distribution and reduce treatment-related morbidity. In addition, improved preimplant planning and postimplant evaluation, using concepts such as dose volume histogram analyses, tumor control probability, and normal tissue complication probability, may also enhance our ability to design the most optimal dose distribution. In fact, these capabilities may be even more critical for brachytherapy plans, where the dose fall-off is more rapid and less forgiving than that associated with external-beam radiotherapy.

In conclusion, our data demonstrate that excellent outcome can be obtained with either 3D-CRT or TPI for patients with early-stage favorable-risk prostate cancer. Although the short-term urinary morbidity is higher with implantation using the CT-based technique, these symptoms, nevertheless, abate in the majority of patients. Careful selection of patients for a particular therapy needs to account for multiple factors that may influence the suitability of that therapeutic intervention for the individual patient. The patient with a prior history of TURP or severe urinary obstructive symptoms may not be an ideal candidate for TPI because of an increased risk for GU toxicity. On the other hand, the patient with a history of inflammatory bowel disease or bowel in close proximity to the planning target volume may be better suited for TPI because of a potential lower risk for GI-related complications. In addition, prospective assessments of quality of life need to be performed in this patient population to provide information based on which patients can more easily choose the appropriate therapy more suitable for their lifestyle. Lastly, whereas available data indicate excellent and equivalent biochemical outcome for 3D-CRT and TPI for patients with favorable prognostic features, the ongoing technologic advances will likely reduce doses to normal tissue and thus decrease morbidity associated with each of these treatment modalities.

REFERENCES

1. Kupelian P, Katcher J, Levin H, et al: External beam radiotherapy versus radical prostatectomy for clinical stage T1-T2 prostate cancer: Therapeutic implications of stratification by pretreatment PSA levels and biopsy gleason scores. Cancer J Sci Am 3:78-87, 1997
2. D'Amico AV, Whittington R, Kaplan I, et al: Equivalent biochemical failure-free survival after external beam radiation therapy or radical prostatectomy in patients with a pretreatment prostate specific antigen of 4 > 20 ng/ml. Int J Radiat Oncol Biol Phys 37:1053-1058, 1997
3. 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 280:969-974, 1998
4. Wallner K, Roy J, Harrison L: Tumor control and morbidity following transperineal iodine 125 implantation for stage T1/T2 prostatic carcinoma. J Clin Oncol 14:449-453, 1996
5. Blasko JC, Wallner K, Grimm PD, et al: Prostate specific antigen based disease control following ultrasound guided 125-iodine implantation for stage T1/T2 prostatic carcinoma. J Urol 154:1096-1099, 1995
6. Stock RG, Stone NN: The effect of prognostic factors on therapeutic outcome following transperineal prostate brachytherapy. Semin Surg Oncol 13:454-460, 1997
7. Beyer DC, Priestley JB: Biochemical disease-free survival following I-125 prostate implantation. Int J Radiat Oncol Biol Phys 37:559-563, 1997
8. Zelefsky MJ, Leibel SA, Gaudin PB, et al: Dose escalation with three dimensional conformal radiation therapy affects the outcome in prostate cancer. Int J Radiat Oncol Biol Phys 41:491-500, 1998
9. American Joint Committee on Cancer: Prostate, in Beahrs OH, Henson DE, Hutter RVP, et al (eds): Manual for Staging of Cancer (ed 4). Philadelphia, PA, Lippincott, 1992, pp 181-183
11. Zelefsky MJ, Leibel SA, Kutcher GJ, et al: Three-dimensional conformal radiotherapy and dose escalation: Where do we stand? Semin Radiat Oncol 8:107-114, 1998
12. Zelefsky MJ, Leibel SA, Burman CA, et al: Neoadjuvant hormonal therapy improves the therapeutic ratio in patients with bulky prostatic cancer treated with three-dimensional conformal radiation therapy. Int J Radiat Oncol Biol Phys 29:755-761, 1994
13. Roy JN, Wallner KE, Chiu-Tsao S, et al: CT-based optimizedplanning for transperineal prostate implant with customized template. Int J Radiat Oncol Biol Phys 29:755-761, 1991
14. Wallner K, Roy J, Zelefsky MJ, et al: Fluoroscopic visualization of the prostatic urethra to guide transperineal prostate implantation. Int J Radiat Oncol Biol Phys 29:863-868, 1994
15. American Society for Therapeutic Radiology and Oncology Consensus Panel: Consensus statement: Guidelines for PSA following radiation therapy. Int J Radiat Oncol Biol Phys 37:1035-1041, 1997
16. Lawton CA, Won M, Pilepich MV, et al: Long-term treatment sequelae following external beam irradiation for adenocarcinoma of the prostate: Analysis of RTOG studies 7506 and 7706. Int J Radiat Oncol Biol Phys 21:935-936, 1991
17. Kaplan EL, Meier P: Nonparametic estimation from incomplete observations. J Am Stat Assoc 53:447-457, 1958
18. Mantel N: Evaluation of survival data and two rank order statistics arising in its consideration. Cancer Chemo Rep 50:163-168, 1966
19. Cox DR: Regression models and life tables. J R Stat Soc Series B 34:187-220, 1972
20. Kleinberg L, Wallner K, Roy J, et al: Treatment-related symptoms during the first year following transperineal I-125 prostate implantation. Int J Radiat Oncol Biol Phys 28:985-990, 1994
21. Arterberry VE, Wallner K, Roy J, et al: Short-term morbidity from CT-planned transperinral I-125 prostate implants. Int J Radiat Oncol Biol Phys 25:661-667, 1993
22. Wallner KE, Roy J, Harrison L, et al: Dosimetry guidelines to minimize urethral and rectal morbidity following transperineal I-125 prostate brachytherapy. Int J Radiat Oncol Biol Phys 32:465-471, 1995
23. Stock RG, Stone NN, Iannuzzi C: Sexual potency following interactive ultrasound guided brachytherapy for prostate cancer. Int J Radiat Oncol Biol Phys 35:267-272, 1996
24. Ragde H, Blasko JC, Grimm PD, et al: Brachytherapy for clinically localized prostate cancer: Results at 7- and 8-year follow-up. Semin Surg Oncol 13:438-443, 1997
25. Ling CC, Burman C, Chui CS, et al: Conformal radiation treatment of prostate cancer using inversely-planned intensity-modulated photon beams produced with multileaf collimation. Int J Radiat Oncol Biol Phys 35:721-730, 1996