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FIVE-YEAR RETROSPECTIVE, MULTI-INSTITUTIONAL POOLED ANALYSIS OF CANCER-RELATED OUTCOMES AFTER CRYOSURGICAL ABLATION OF THE PROSTATE

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ABSTRACT

Objectives. To define the potential role of cryosurgical ablation of the prostate (CSAP) as a treatment option for patients with localized prostate carcinoma (PCA), we performed a retrospective outcomes analysis of a large database of patients undergoing CSAP constructed from five institutions and compared this with matching outcomes from contemporary reports of patient outcomes after radiotherapy.

Methods. A total of 975 patients who underwent CSAP as primary therapy from January 1993 to January 1998 with sufficient outcomes data available were identified. Patients were stratified into three groups on the basis of their clinical features. Biochemical-free survival (BFS), post-CSAP biopsy results, and post-CSAP morbidities were calculated and recorded.

Results. The median follow-up for all patients was 24 months. The percentages of patients in the low, medium, and high-risk groups were 25%, 34%, and 41%, respectively. For prostate-specific antigen thresholds of less than 0.5 and less than 1.0 ng/mL, the 5-year actuarial BFS ranged from 36% to 61% and 45% to 76%, respectively, depending on the risk category. Overall, the positive biopsy rate was 18%. Morbidities included impotence in 93%, incontinence in 7.5%, rectourethral fistula in 0.5%, and transurethral resection of the prostate in 13% of patients (10% approved warming catheters versus 40% nonapproved).

Conclusions. For each risk group, the 5-year BFS and positive biopsy rate after CSAP was comparable to matching outcomes reported after radiotherapy. Morbidities also seemed comparable, with impotence rates higher and rectal injury rates lower after CSAP than after radiotherapy. These data indicate that CSAP can be performed with low morbidity and can produce cancer-related results comparable to those reported for patients undergoing radiotherapy.

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Prostate adenocarcinoma (PCA) continues to be the most common malignancy and second most common cause of cancer-related death in American men. Despite the voluminous reports investigating this disease, defining a standard of treatment for individual patients who present with a new diagnosis of PCA remains problematic. Historically, the dominant treatment options for localized disease have included radical prostatectomy and external beam radiotherapy. More recently, particularly during the past 5 years, novel or modified treatments for localized PCA have been introduced, including ultrasound-guided interstitial brachytherapy, three-dimensional conformal radiotherapy, high-dose combination radiotherapy, HDR-iridium 192 brachytherapy, proton beam radiotherapy, high-intensity focused ultrasound thermotherapy, and cryoablation. In the absence of randomized prospective comparisons between any two of these approaches, recommendations for treatment must be made on the basis of the available information. Some of the principal problems with deriving treatment recommendations on the basis of published data are that patient selection

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may vary considerably among reports that provide post-treatment outcomes and that the definitions of success, particularly if surrogate outcomes were relied on, may vary as well.

During the past 5 years, a number of reports have been published documenting the results after the use of transrectal ultrasound-guided cryoablation of the prostate for patients with PCA,[1–3] and these reports are not immune from the problems mentioned above. A number of investigators have suggested very promising preliminary results with regard to cancer-related outcomes such as biochemical disease-free survival or negative biopsy rates, and others have raised concerns regarding the potential morbidities of this procedure and the feasibility of safely accomplishing whole-gland ablations.

In an effort to derive a more valid overview of the outcomes that might be anticipated for patients currently undergoing cryoablation, we conducted a retrospective pooled analysis from five institutions performing cryoablation during the past 5 years with stratified patient selection criteria and uniform definitions of cancer-related outcomes. Furthermore, the outcomes chosen were derived from similar or matching outcomes reported for radiotherapy studies to examine comparatively the relative role that cryoablation may currently have as a potential tool for treating patients with PCA.

MATERIAL AND METHODS

Patient Selection

The primary patient databases for all patients undergoing cryoablation at five institutions (New England Medical Center, University of California at San Francisco, Urologic Institute of New Orleans, Crittenton Hospital, and Alhambra Hospital) between 1993 and 1998 were submitted for pooled analysis. Excluded from the analysis were all patients with metastatic disease at the time of treatment and patients in whom previous radiation therapy had failed. Patients receiving any androgen deprivation therapy before cryoablation were identified and categorized separately. Therefore, the selection criteria consisted of all patients with clinical Stages T1 to T4, any PSA level, and any Gleason grade from each program.

Risk Groups

Patients were separated into three risk groups. The low-risk group was defined as patients with Stage T2a or lower, PSA 10.0 ng/mL or less, and Gleason grade 6 or less. The moderate risk group was defined as patients with any one of the following factors: Stage T2b or greater, PSA greater than 10.0 ng/mL, or Gleason grade 7 or greater. Finally, patients in the high-risk group were those having two or three of the above factors at the time of their procedure. These risk definitions are identical to those used in a recent report[4] and similar to others[5–7] documenting outcomes for patients undergoing various forms of contemporary radiotherapy.

Procedure

For all patients, an attempt to ablate the entire prostate gland was made. In all cases, real-time transrectal ultrasound monitoring was used. However we did not stratify the procedures by the use of specific elements of cryotechnique. Aspects such as the number of cryoprobes (five to eight), number of freeze-thaw cycles/case (one to three), length of apical pullback, use of thermocouples for real-time temperature monitoring during freezing, and use of LN_2 or argon-based cooling systems varied among different institutions to a measurable degree. Consequently, for all patients examined in this study, a genuinely uniform treatment protocol was not used. All procedures typically took 2 to 3 hours, and patients were discharged with either suprapubic or urethral catheter drainage. These catheters were removed within 1 to 3 weeks or when spontaneous voiding (in the case of suprapubic tubes) resumed. After the CSAP procedure, PSA monitoring was maintained at regular but varying intervals among all institutions. After CSAP, 6 to 12 core biopsies were performed either at fixed intervals or in response to rising PSA levels. Post-treatment morbidities were identified by chart review and recorded.

Statistical Analysis

Actuarial analyses were performed by coding data on a case-by-case basis. Two criteria for success were used: maintenance of PSA at less than 0.5 ng/mL and maintenance of PSA at less than 1.0 ng/mL. Cases failing a given criterion of success were failed at the midpoint between the date of failure diagnosis and the date of the most recent preceding follow-up visit. Cases maintaining success criteria were censored at the date of the most recent follow-up visit. A separate actuarial curve was calculated for each biochemical success criterion. Nonparametric actuarial curves were generated from the resulting coded data using StatView (Statistical Analysis System Institute, Cary, NC). Additionally, two sets of stratified outcomes were created on the basis of preprocedural patient criteria. The first set was based on the three-point risk group variable. The second set stratified patients by whether they had undergone preoperative androgen ablation therapy. Curves were compared for statistical differences using the log-rank test. Analyses comparing population characteristic proportions were compared using the chi-square test.

RESULTS

Patient characteristics are listed in Table I. The median follow-up ± SD for all patients was 24 ± 16.5 months. Androgen deprivation was used for 3 to 8 months before the procedure in 30% of patients. Typically, it consisted of at least one luteinizing hormone-releasing hormone depot injection, with concomitant antiandrogen oral therapy administered on a random basis.

The 5-year actuarial biochemical-free survival (BFS) rates and positive biopsy rates for each risk group are listed in Table II and depicted in Figure 1. Not surprisingly, BFS was dependent on the risk category. When patients were divided into those receiving neoadjuvant hormonal therapy and those not, surprisingly, improved BFS rates for both the 0.5 and 1.0 thresholds were seen in the nontreatment arm, 55% versus 40% and 69% versus 47%, respectively. However, a larger number of high-risk patients were segregated into the androgen-deprivation group versus the non-androgen-deprivation group (49% versus 37%, $P < 0.0001$). The

TABLE I. ***Overall patient characteristics***

	n (%)
Stage	
T1	101 (10.7)
T2	604 (64)
T3	222 (24)
T4	15 (1.6)
ND	33 (3.3)
Total	975
Gleason grade	
2–5	138 (14.4)
6	303 (32)
7	401 (42)
8–10	115 (12)
ND	18 (1.8)
Total	975
Preoperative PSA (ng/mL)	
<4.0	131 (13)
4.0–10.0	521 (54)
10.0–20.0	203 (21)
>20.0	115 (12)
ND	5 (<1)
Total	975
Risk group	
Low	238 (25)
Medium	321 (34)
High	385 (41)
ND	31 (3)
Total	975
NAHT	
No	613 (67)
Yes	307 (33)
ND	55 (6)
Total	975

KEY: ND = not determined; PSA = prostate-specific antigen; NAHT = neoadjuvant hormonal therapy.

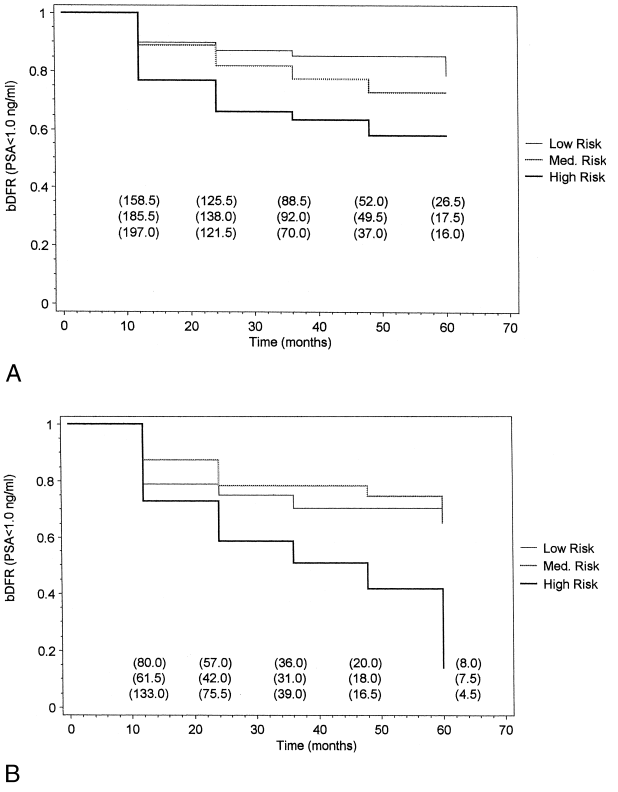

FIGURE 1. *Actuarial projections of overall biochemical-free survival stratified by risk categories for a PSA threshold of less than 1.0 for (A) patients without neoadjuvant hormonal therapy and (B) patients with neoadjuvant hormonal therapy. Numbers of patients in each group available for evaluation at 12-month intervals noted in parentheses.*

crude positive biopsy rate was 18% among patients biopsied and 14% among all treated patients. The use of neoadjuvant hormonal therapy did not appear to alter the likelihood of avoiding positive biopsies. Table III lists the rates of four morbidities measured after CSAP. The use of nonapproved urethral warming catheters was associated with a significantly higher rate of urethral sloughing and slightly higher rates of incontinence and rectal fistulas.

COMMENT

The actuarial 5-year BFS rates for patients with PCA who undergo radiotherapy vary widely in published reports. This variance is a consequence of nonuniform patient selection, the use of varying dosing and techniques, and, especially, a lack of consensus on how best to define biochemical failure. Despite this lack of consensus, an overview of the radiotherapy data can be instructive.

After conventional (ie, nonconformal) external beam radiotherapy (6600 to 7000 cGy) for patients with Stage T1-T3 PCA, most reports note 5-year BFS rates ranging from 29% to 64%,[8,9] depending on the criteria used, with rates of finding positive biopsies after radiotherapy ranging from 12% to 100%.[10] The overall 5-year BFS rates of 52% (PSA less than 0.5 ng/mL) and 63% (PSA less than 1.0 ng/mL) and overall positive biopsy rate of 18% noted in this series compares very favorably with these data.

Results after more contemporary radiotherapy techniques are typically segregated by risk group. As shown in Table II, for patients with a low risk of progression undergoing brachytherapy and conformal radiotherapy (some with three-dimensional enhancement) the reported 5-year BFS rates were very similar, ranging from 75% to 87%,[6,11–13] (brachytherapy) to 67% to 81%[4,6,7] (conformal radiotherapy), depending on the criteria used. For similar patients, we found a 5-year BFS rate of 76% using a PSA threshold of less than 1.0 ng/mL, which compares favorably with the above data.

For patients with higher risks of progression, 5-year BFS rates range from 0% to 60%[6,12,13] (brachytherapy) to 35% to 60%[4–7] (conformal ra-

TABLE II. *Comparisons between radiotherapy and cryoablation for biochemical-free survival and positive biopsy rates*

Conformal Radiotherapy Biochemical-Free Rates				Brachytherapy Biochemical-Free Rates				Cryoablation (current series) Biochemical-Free Rates		
Ref.	Tumor Characteristics	BFS Criteria	5-yr Rates (%)	Ref.	Tumor Characteristics	BFS Criteria	5-yr Rates (%)	Tumor Characteristics	BFS Criteria	5-yr Rates (%)
Low Risk										
4	T1-2, PSA <10, GG <7	PSA <1.0 ng/mL	85	11	T1-2, PSA <20, GG <7	PSA <1.0 ng/mL	87	T1-2a, PSA <10, GG <7	PSA <1.0 ng/mL	76
7	T1-2, PSA <10, GG <7	PSA <2.0 ng/mL	75	13	T1-2, PSA any, GG <7	PSA <4.0 ng/mL	65		PSA <0.5 ng/mL	60
5	T1-2, PSA <20, GG <7	PSA <1.0 ng/mL	75	12	T1-2, PSA any, GG <7	Two PSAs >1.0 ng/mL	81			
6	T1-2a, PSA <10, GG <7	ASTRO*	87	6	<T2b, PSA <10, GG <7	ASTRO*	85			
Medium-High Risk										
4	>T2, PSA >10, GG >6	PSA <1.0 ng/mL		6	T2b or PSA >10 or GG 7	ASTRO*	32	>T2a, PSA >10, GG >6	PSA <1.0 ng/mL	
	1/3 findings		65	6	>T2b or PSA >20 or GG >7	ASTRO*	0	1/3 findings		71
	2–3/3 findings		35	12	T1-2, PSA >20, GG <7	Two PSAs >1.0 ng/mL	58	2–3/3 findings		45
7	>T2, PSA >10, GG >6	PSA <2.0 ng/mL	37	13	T1-2, PSA >20, GG <8	PSA <4.0 ng/mL	35	>T2a, PSA>10, GG >6	PSA <0.5 ng/mL	
6	T2b or PSA >10 or GG 7	ASTRO*	60					1/3 findings		61
6	>T2b or PSA >20 or GG >7	ASTRO*	15					2–3/3 findings		36

Positive Biopsy Rates			Positive Biopsy Rates			Positive Biopsy Rates	
Ref.	Patients	Rates (%)	Ref.	Patients	Rates (%)	Patients	Rates (%)
4	T1-4, PSA any, GG any	43	11	T1-2, PSA <20, GG <8	22	T any, PSA any, GG any	18
14	T1-4, PSA any, GG any	62	12	T1-2, PSA any, GG <7	26	T1-2a, PSA <10, GG <7	12
15	T1-4, PSA any, GG any	43				>T2a, PSA >10, GG >6	
						1/3 findings	12
						2–3/3 findings	24

Key: Ref. = reference; BFS = biochemical-free survival; PSA = prostate-specific antigen; GG = Gleason grade; ASTRO = American Society of Therapeutic Radiation Oncology.
** Three successive rises in PSA (current ASTRO guidelines).*

TABLE III. *Comparison of reported morbidities after radiotherapy and cryoablation*

References	Morbidities	Rates (%)
Beam radiotherapy		
16, 17, 20, 21, 22	Incontinence	0–13
16, 17–19	Impotence	37–70
18, 22, 23	TURP/major GU	0–3
18–20, 22, 23	Fistula/major GI	1–9
Brachytherapy		
24, 25, 28	Incontinence	0–5
21, 24	Impotence	10–40
24, 25, 28	TURP/major GU	0–4
27, 28	Fistula/major GI	0–7

		Rates (%)		
	Morbidities	Approved	Alternate	Overall
Current series	Incontinence	7.5	10	7.5
	Impotence	93	90	93
	TURP/major GU	10	44*	13
	Fistula/major GI	0.4	1.4	0.5

KEY: TURP = transurethral resection of the prostate; GU = genitourinary; GI = gastrointestinal.
** P <0.05, chi-square test.*

diotherapy), again depending on the criteria used. In our series, we found that for patients with a medium risk of progression, the 5-year BFS rates were 67%, and for high-risk patients, 41%. Again, these results are very comparable to those noted after conformal radiotherapy techniques and appear to be superior to those reported for brachytherapy.

The recent radiotherapy reports contain fewer data on post-treatment biopsy results, but several studies noted overall rates of positive biopsies ranging from 43% to 65%,[4,14,15] with a trend toward decreasing rates with dose escalation, especially for doses greater than 75 Gy. Very few data on positive biopsy results after brachytherapy are available, but two reports noted that among those low-risk patients who underwent biopsy, positive biopsies were seen in 22% to 26%.[11,12] Our rates of 12% (low-risk) and 18% (overall) compare favorably with these findings.

The morbidities after radiotherapy vary among studies.[16–28] Table III lists a comparison between the rates of four morbidities measured in the present study with those in published reports after radiotherapy. Broadly, significant differences appeared in the rates of erectile dysfunction and rectal injury between the two groups, with lower rates of rectal problems after CSAP but higher rates of potency after radiotherapy. The incidence of voiding dysfunction after CSAP was slightly higher as well, although a meaningful comparison was difficult without a uniform outcomes assessment vehicle for all groups.

Given that others have demonstrated the beneficial effects of androgen deprivation before cryotherapy in humans,[1] the observation of poorer PSA outcomes in the patients treated with androgen deprivation was unexpected. The best explanation for this finding is most likely that there was a statistically significant preponderance of higher risk patients in the treatment arm compared with the nontreatment arm. Prospective investigations, especially with stratified treatment protocols, should consider addressing this further.

Retrospective studies such as this one usually have a number of limitations inherent in the design. Perhaps most prominent in the present study is that genuinely direct comparisons with radiotherapy are impossible without the benefit of prospective randomization. However, the risk and outcome definitions in this report, although not matching precisely all the cited comparison radiotherapy studies, were fairly close. Also, using retrospective, physician-assessed rates of treatment-related morbidities may underestimate the rates that would be found using patient-derived outcomes assessment tools. However, we chose a relatively simple panel of treatment-related side effects to facilitate comparisons with similar data in the radiotherapy reports.

The cumulative experience during the past 5 years with CSAP supports several "critical elements" that seem necessary to maximize outcome. These include two freeze cycles, approved urethral warming, thermocouple monitoring, achieving temperatures of −40°C or less, and using six to eight cryoprobes per procedure.[1,3,29,30] Although we were not able to stratify all patients in this study by actual technique, it was clear that only a small number were treated with all these features, making the pooled results reflective of a minimal treat-

ment effect. One recent report noted that when all the above features were used, only a 2% positive biopsy rate was found.[30]

The results from the present study indicate that even despite the variations in treatment technique, CSAP can achieve cancer-related outcomes that seem very comparable to similar or matching outcomes reported after radiotherapy. It is perhaps remarkable that the results seem to be reasonably similar despite a substantial disparity in resources and experience between the two therapies. It is conceivable that with only a modest increase in research/interest in CSAP that a uniformly effective technique might be developed, resulting in an even lower incidence of post-CSAP voiding dysfunction and even more reliable total prostatic ablation than was found in this report.

CONCLUSIONS

The data presented in this report suggest that CSAP can be a safe and effective treatment alternative for a significant number of patients with PCA. Future efforts designed to improve the current technique and to define clearly the mechanisms of effective in situ ablation of human prostatic tissue should be encouraged and broadly supported.

REFERENCES

1. Shinohara K, Connolly JA, Presti JC Jr, *et al:* Cryosurgical treatment of localized prostate cancer (stages T1 to T4): preliminary results. J Urol **156:** 115–121, 1996.
2. Long JP, Fallick ML, LaRock DR, *et al:* Preliminary outcomes following cryosurgical ablation of the prostate in patients with clinically localized prostate carcinoma. J Urol **159:** 477–484, 1998.
3. Wong WS, Chinn DO, Chinn M, *et al:* Cryosurgery as a treatment for prostate carcinoma. Cancer **79:** 963–974, 1997.
4. 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.
5. Seung SK, Kroll S, Wilder RB, *et al:* Candidates for prostate radioactive seed implantation treated by external beam radiotherapy. Cancer J Sci Am **4:** 168–174, 1998.
6. 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.
7. Fukunaga-Johnson N, Sanadler HM, McLaughlin PW, *et al:* Results of 3D conformal radiotherapy in the treatment of localized prostate cancer. Int J Radiat Oncol Biol Phys **38:** 311–317, 1997.
8. Zagars GK, Pollack A, Kavadi VS, *et al:* Prostate-specific antigen and radiation therapy for clinically localized prostate cancer. Int J Radiat Oncol Biol Phys **32:** 293–306, 1995.
9. Lee WR, Hanks GE, Schultheiss TE, *et al:* Localized prostate cancer treated by external-beam radiotherapy alone: serum prostate-specific antigen-driven outcome analysis. J Clin Oncol **13:** 464–469, 1995.
10. Zietman AL, Shipley WU, and Willett CG: Residual disease after radical surgery or radiation therapy for prostate cancer. Cancer **71**(3 suppl): 959–969, 1993.
11. Ragde H, Elgamal AA, Snow PB, *et al:* Ten-year disease-free survival after transperineal sonography-guided iodine-125 brachytherapy with or without 45-gray external beam irradiation in the treatment of patients with clinically localized, low to high Gleason grade prostate carcinoma. Cancer **83:** 989–1001, 1998.
12. Stock RG, Stone NN, Tabert A, *et al:* A dose-response study for I-125 prostate implants. Int J Radiat Oncol Biol Phys **41:** 101–108, 1998.
13. Beyer DC, and Priestly JB Jr: Biochemical disease-free survival following I125 prostate implantation. Int J Radiat Oncol Biol Phys **37:** 559–563, 1997.
14. Laverdiere J, Gomez JL, Cusan L, *et al:* Beneficial effect of combination hormonal therapy administered prior and following external beam radiation therapy in localized prostate cancer. Int J Radiat Oncol Biol Phys **37:** 247–252, 1997.
15. Crook JM, Bahadur YA, Perry GA, *et al:* Radiotherapy for prostate cancer: results of systematic biopsies for 479 patients (abstract). J Urol **159:** 64, 1998.
16. Lim AJ, Brandon AH, Fiedler J, *et al:* Quality of life: radical prostatectomy versus radiation therapy for prostate cancer. J Urol **154:** 1420–1425, 1995.
17. Jonler M, Ritter MA, Brinkmann R, *et al:* Sequelae of definitive radiation therapy for prostate cancer localized to the pelvis. Urology **44:** 876–882, 1994.
18. Shipley WU, Zietman AL, Hanks GE, *et al:* Treatment related sequelae following external beam radiation for prostate cancer: a review with an update in patients with Stages T1 and T2 tumor. J Urol **152:** 1799–1805, 1994.
19. Goldstein I, Feldman MI, Dickens PJ, *et al:* Radiation-associated impotence: a clinical study of its mechanism. JAMA **251:** 903–910, 1984.
20. Holzman M, Carlton CE Jr, and Scardino PT: The frequency and morbidity of local tumor recurrence after definitive radiotherapy for Stage C prostate cancer. J Urol **146:** 1578–1582, 1991.
21. Chaikin DC, Broderick GA, Malloy TA, *et al:* Erectile dysfunction following minimally invasive treatments for prostate cancer. Urology **48:** 100–104, 1996.
22. Beard CJ, Lamb C, Buswell L, *et al:* Radiation-associated morbidity in patients undergoing small-field external beam irradiation for prostate cancer. Int J Radiat Oncol Biol Phys **41:** 257–262, 1998.
23. Nguyen LN, Pollack A, and Zagars GK: Late effects after radiotherapy for prostate cancer in a randomized dose-response study: results of a self-assessment questionnaire. Urology **51:** 991–997, 1998.
24. Wallner K, Roy J, and Harrison L: Tumor control and morbidity following transperineal iodine 125 implantation for stage T1/T2 prostatic carcinoma. J Clin Oncol **14:** 449–453, 1996.
25. Desai J, Stock RG, Stone NN, *et al:* Acute urinary morbidity following I-125 interstitial implantation of the prostate gland. Radiat Oncol Invest **6:** 135–141, 1998.
26. Boersma LJ, van den Brink M, Bruce AM, *et al:* Estimation of the incidence of late bladder and rectum complications after high-dose (70-78 Gy) conformal radiotherapy for prostate cancer, using dose-volume histograms. Int J Radiat Oncol Biol Phys **41:** 83–92, 1998.
27. Hu K, and Wallner K: Clinical course of rectal bleeding following I-125 prostate brachytherapy. Int J Radiat Oncol Biol Phys **41:** 263–265, 1998.
28. Sharkey J, Chovnick SD, Behar RJ, *et al:* Outpatient ultrasound-guided palladium 103 brachytherapy for localized adenocarcinoma of the prostate: a preliminary report of 434 patients. Urology **51:** 796–803, 1998.
29. Larson TR, Robertson DW, Corica A, *et al:* In vivo interstitial temperature mapping of the human prostate during cryosurgery with correlation to histopathologic outcomes. Urology **55:** 547–552, 2000.
30. Lee F, Bahn DK, Badalament RA, *et al:* Cryosurgery for prostate cancer: improved glandular ablation by use of 6 to 8 cryoprobes. Urology **54:** 135–140, 1999.