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High-dose-rate brachytherapy for prostate cancer is well tolerated with acceptable morbidity and without treatment mortality.

High-Dose-Rate Brachytherapy in the Treatment of Carcinoma of the Prostate

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Background: *Although radical prostatectomy for localized disease is considered as a standard of care, external-beam radiotherapy and brachytherapy are equally effective. We report on the technique and preliminary results of high-dose-rate (HDR) brachytherapy using a temporary iridium-192 implant technique.*

Methods: *The authors reviewed the literature on the techniques, treatment protocols, and results of HDR brachytherapy in the treatment of carcinoma of the prostate, and they report their own protocols, technique, and results.*

Results: *The combination of HDR brachytherapy and external irradiation has been well tolerated by all 200 patients in our series, with less than 3% grade 3 late complications and with 95% PSA relapse-free survival with a median follow-up of 24 months.*

Conclusions: *HDR brachytherapy may be the most conformal type of irradiation in the treatment of carcinoma of the prostate regardless of tumor size, anatomical distortion, and organ mobility.*

Introduction

Carcinoma of the prostate is a common cancer in men in the United States. Treatment options include radical prostatectomy and radiation therapy (external-beam and brachytherapy), among others. Most reported series of treatment with radical prostatectomy with or without nerve-sparing treatment include patients who are younger than 70 years of age in good medical condition and exclude those with metastatic pelvic lymph nodes or gross extracapsular tumor extension.[1-6]

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In contrast, patients treated with irradiation are older, they are in less than ideal medical condition, and they frequently have more extensive local tumors.

The effect of surgical staging on outcome of irradiation was documented by Asbell et al[7] in patients with clinical stages A2 and B carcinoma of the prostate. The 5-year disease-free survival rate was 76% in patients with surgically evaluated negative pelvic lymph nodes vs 63% for those with radiographically evaluated negative lymph nodes. The disease-free, metastasis-free, and overall survival rates were similar in patients with positive or negative radiographically assessed lymph nodes, indicating the limitations of this procedure in correctly evaluating lymph node status in these patients. The authors concluded that radiographic determination of lymph node status had no prognostic value and should not be used for stratification of patients in clinical trials. Thus, for a true comparison of results of radical prostatectomy or radiation therapy, all patients treated with either modality should be surgically staged or all patients should be randomized before treatment and receive therapy based on the findings of various staging procedures.

External irradiation is used as a definitive therapy in a large number of patients with clinical stage A, B, and C or locally extensive tumors. Tumor doses have ranged from 60-64 Gy for stage A1 (T1a) tumors, 65-70 Gy for stage A2 (T1b) and B (T2) tumors, and 70-72 Gy for stage C (T3) tumors.[8-10] Several retrospective studies indicate that dose affects local tumor control. Hanks and colleagues[11] reported the following actuarial 5-year local recurrence rates: 37% for patients treated with doses less than 60 Gy, 36% for 60-64.9 Gy, 29% for 65-69.9 Gy, and 19% for 70 Gy or more.

In most instances, the failure of radiotherapy to control organ-confined prostate cancer results from the persistence of prostatic tumor clonogens with inherent resistance to the radiation doses used. To avoid underdosage relative to the prescribed schedule or even a complete miss of part of the tumor-containing prostate, conventional radiotherapy techniques should uniformly encompass significant portions of the bladder and rectum. Consequently, attempts to increase the tumor dose are frequently restricted by the high sensitivity of the rectum and bladder to the effects of radiation. The recently introduced high-precision radiation techniques, ie, three-dimensional (3D) conformal photon therapy, intensity-modulated radiation therapy, and proton-beam radiation therapy, provide a way to overcome these limitations on dose escalation, and preliminary reports are encouraging.[12-16] Neoadjuvant hormonal deprivation with external-beam radiotherapy (EBRT) in patients with locally advanced carcinoma of the prostate, metastatic pelvic lymph nodes, or Gleason score of 8-10 has significantly improved local control and survival in prospective, randomized trials by the European Organization for Research and Treatment of Cancer (EORTC)[17] and the Radiation Therapy Oncology Group (RTOG).[18]

The incidence of fatal complications in localized carcinoma of the prostate treated with conventional external irradiation is approximately 0.2%. The overall incidence of severe urinary and rectosigmoid sequelae is approximately 3%; moderate complications occur in 7%-10% of patients. The incidence of impotence from different series ranges from 31%-60%.[19-21]

Brachytherapy in the treatment of carcinoma of the prostate was reported as early as 1972 by Whitmore et al[22] using a retropubic approach with bilateral pelvic lymphadenopathy. In general, brachytherapy alone is used for tumors clinically staged as T1 and T2a, whereas stage T2b and T2c lesions with high risk of extracapsular extension and pelvic node metastases are usually treated by a combination of external irradiation and brachytherapy. Zelefsky et al[23] reported 56% and 34% local control rates in patients with T2a lesions at 10 and 15 years, respectively, following permanent iodine-125 implantation using a retropubic approach. Several authors have reported 5-year prostate-specific antigen (PSA) relapse-free survival rates of 85%-94% in low-risk patients, 33%-82% in intermediate-risk patients, and 5%-65% in high-risk patients using the transrectal ultrasound (TRUS)-guided implant technique.[24-27] A majority of patients develop early grade 1 and 2 urinary symptoms (frequency, dysuria, and urgency of micturition) following brachytherapy. Late grade 3 and 4 genitourinary complications such as urethral stricture and incontinence occur in 3%-11% of patients, which increases to 18% in patients who had prior transurethral resection of the prostate. Grade 3-4 rectal complications were reported in 1%-2% of patients.[28,29]

Although the TRUS-guided technique significantly improved source distribution compared with the retropubic approach, several disadvantages of the permanent implant technique remain unresolved, such as the inability to implant seminal vesicles, extracapsular extension, apical lesions, and patients who had transurethral resection of the prostate. The most significant disadvantages are the inability to alter position of the seeds once implanted and migration of seeds in 5%-10% of patients.

We previously reported our technique and the results of a low-dose-rate (LDR) temporary iridium-192 implant technique using transperineal approach under ultrasound guidance, which resulted in positive biop-

Table 1. — Prostate Cancer HDR Brachytherapy and External Irradiation Protocol: Stage and Gleason Score

Stage	No. of Patients	Gleason Score:		
		0-4	5-7	8-10
T1c (A2)	28	8	19	1
T2a (B1)	65	14	49	2
T2b (B2)	64	4	53	7
T3a-b (C)	43	2	30	11
Total	200	28	151	21

sies following irradiation in 15% and an 85% actuarial survival rate.[30-34] Mate et al[35] and others[36-40] employed a similar technique but used high-dose-rate (HDR) rather than LDR with excellent PSA relapse-free survival and minimal complications. Encouraged by the long-term results of our LDR brachytherapy using a temporary iridium-192 implant technique and preliminary data of HDR brachytherapy, we developed an HDR brachytherapy protocol and began treating patients 6 years ago.[41,42]

Materials and Methods

From June 1996 to July 1999, we treated 200 patients with clinically localized carcinoma of the prostate with a combination of HDR iridium-192 brachytherapy and external irradiation. The average patient age was 64 years (range = 45-84 years). All patients had biopsy-proven carcinoma of the prostate with Gleason score and were staged according to the TNM classification (Table 1). All patients underwent clinical examination including digital rectal examination (DRE), chest radiograph, complete blood count, PSA testing, and bone scan. Most of the high-risk patients with locally advanced tumors, Gleason score >7, and PSA level >10 ng/mL had either computed tomography (CT) scan and/or magnetic resonance imaging (MRI) with endorectal coil to evaluate capsular or seminal vesicle invasion and the status of the pelvic lymph nodes. The pretreatment PSA ranged from 1.2-96 ng/mL, with an average of 10 ng/mL. Patients with PSA >20 ng/mL, Gleason score 8-10, or capsular and seminal vesicle invasion received monthly leuprolide injections for 2-3 months (3.5 mg intramuscularly [IM] per month) or one injection of goserelin (10.5 mg IM) plus oral bicaludamide daily (5 mg) for 2 weeks following the leuprolide injection and prior to irradiation. Approximately 70% of the patients had HDR brachytherapy before external irradiation to the prostate and 30% following EBRT. A majority of the patients started external irradiation 2-3 weeks following brachytherapy. The HDR brachytherapy dose ranged from 22-26 Gy in four equal HDR fractions and 39.6 to 45 Gy to the prostate by EBRT, depending on the stage of the tumor (Table 2).

Technique

The patients were given an enema the night prior to the procedure. Most patients had an epidural block for pain management and general anesthesia for the procedure. The procedure was performed with the patient in an extended lithotomy position. General clinical examination and DRE were performed to evaluate the size of the prostate and tumor nodules. Proctosigmoidoscopic examination was routinely done to clean the rectum of feces and to rule out any abnormalities of the rectum and rectosigmoid colon such as polyps, cancer, and inflammation.[30-32]

The scrotum and perineum were prepared with a betadine solution, and a transparent plastic "O'Connor" sterile drape was applied against the perineum to minimize rectal contamination. A three-way 18F Foley

Table 2. — HDR Prostate Cancer Treatment Protocol: Interstitial and External Irradiation

Stage	Interstitial Irradiation Gy (min TD)	No. of Fractions	External Irradiation Gy	Total Gy
T1c (A2)	1st = 21 + 2nd = 21 or 22	4 4 4	0 39.6	42 61.6
T2a (B1)	22	4	39.6	61.6
T2b (B2)	24	4	45	69
T3a-c (C)	26 ± hyperthermia	4	45	71

TD = tumor dose

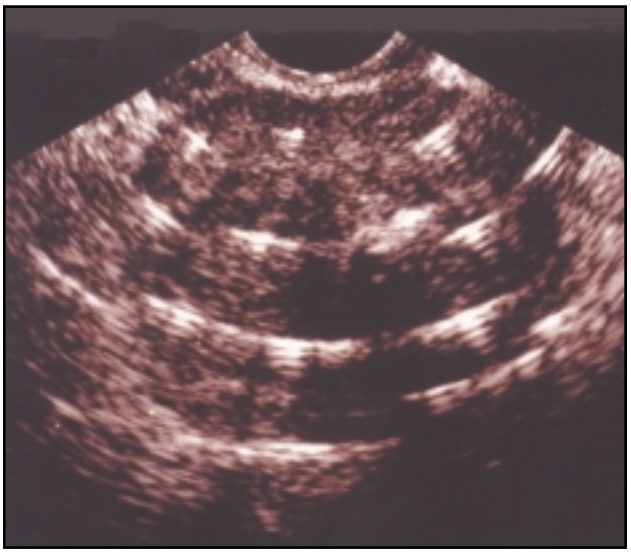


Fig 1. — Needle insertion under ultrasound guidance, coronal view.

catheter was inserted into the bladder and a Foley balloon was filled with 7 mL of diatrizoate sodium. An ultrasound transducer was introduced into the rectum through the O'Connor drape to evaluate the prostate, seminal vesicles, and bladder. The hypoechoic nodule size, position of the urethra throughout the prostate (from base to apex), and capsular and seminal invasions were determined. The size of the prostate and the tumor nodules were measured and the volume was calculated. Two marker seeds were implanted into each lobe of the prostate, one at the base and one at the apex. The technique of implant has been previously published.[30,31]

The Syed-Neblett prostate template was used to maintain the position of the needles. The template was never fixed to the ultrasound transducer (unlike permanent implant techniques) in order to have the flexibility of moving the template to circumvent the bony obstruction by ischial tuberosity and pubic rami. We implanted 12 to 22 HDR needles (an average of 14 needles), 17-gauge with blunt and closed proximal ends and 20 cm in length, transperineally in and around the prostate and seminal vesicles. Each needle was viewed during its insertion from the base to the apex of the prostate to keep the needles at least 8-10 mm from the urethra, 5-6 mm from the rectum, and 1 cm from other needles (Fig 1). The needles were inserted till their tips were 1-2 cm above the base of the prostate into the bladder neck and seminal vesicles. Plastic, steel, or MRI-compatible titanium needles were implanted using alcohol as a lubricant through the prostate template. The template was secured in position with 00 silk sutures through the perineal skin and anterior two corner holes on the template. The space between the template and perineum was filled with antibiotic-soaked roller gauze (Fig 2). The patient's legs were then brought down to the supine position. Initially, patients had anterior-posterior (AP) and lateral localization films with diluted contrast in the bladder in the operating room to confirm that the needles still encompassed the prostate despite a 1- to 2-cm downward movement of the needles in a few patients.

The patients had AP and lateral orthogonal radiographic localization films with inactive "dummy sources" and CT scans of the implant for 3D computerized dose distribution planning and volume analysis (Fig 3). In 5%-10% of patients, the needles needed to be pushed up in the simulator or CT room to adequately encompass the base of the prostate and the lower half of the seminal vesicles (due to a downward movement of the needles). This was accomplished without difficulty since the majority of patients had an epidural for pain control and others received an injection of morphine sulfate. However, since December 2000, CT-based dosimetry has been done with a treatment planning system (BrachyVision, Varian Medical Systems, Palo Alto, Calif). From the CT data, 3D reconstruction of the implant was performed from the CT data, and the planning target volume was independently obtained by delineating prostate and seminal vesicles on the transverse CT slices.[43] Similarly, the organs at risk such as the rectum, bladder, and urethra were reconstructed from the CT data (Fig 4). Dwell positions were defined in the needles according to their intersection with planning target volume. Dwell times were obtained after geometrical optimization defining the dose distribution in the volume of interest. The brachytherapy dose to the prostate was 15 Gy given in three equal fractions in the initial 20 patients and was escalated to 22-26 Gy in four HDR fractions in the remaining patients. In most patients, two fractions were delivered during the first day of the implant and another two fractions during the second day. On completion of the treatment, the implant and Foley catheters were

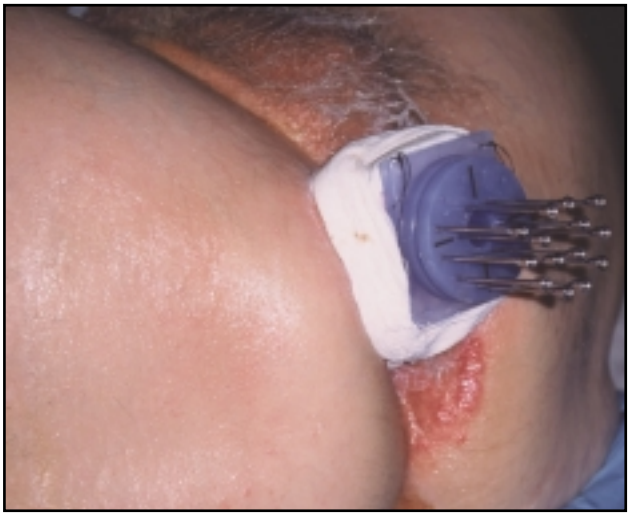
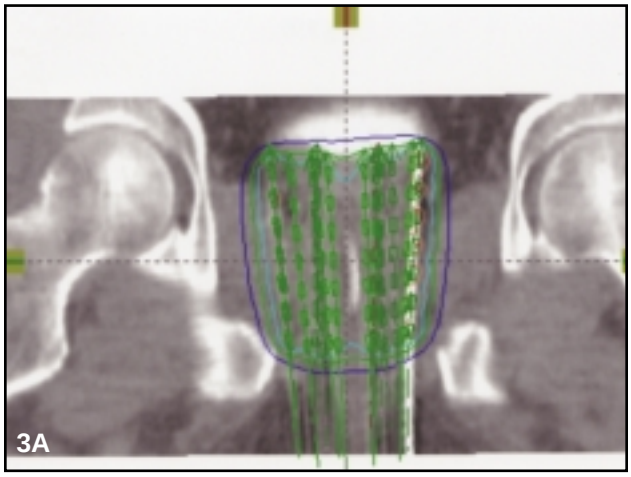
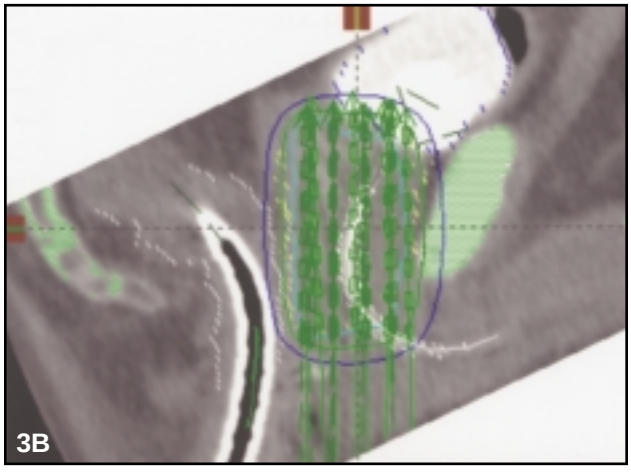


Fig 2. — Implant procedure completed.

removed and the patients were discharged with a prescription for an antibiotic, tamsulosin, phenazopyridine and acetaminophen/codeine for 10 days.

Due to a downward movement of the needles ranging from 0.5 to 2 cm in 25% of the patients, lateral x-ray localization of the implant was performed before each fraction to adjust the position of the needles as needed.[44] The prescribed minimum tumor dose was defined as the isodose line encompassing the prostate and sem-





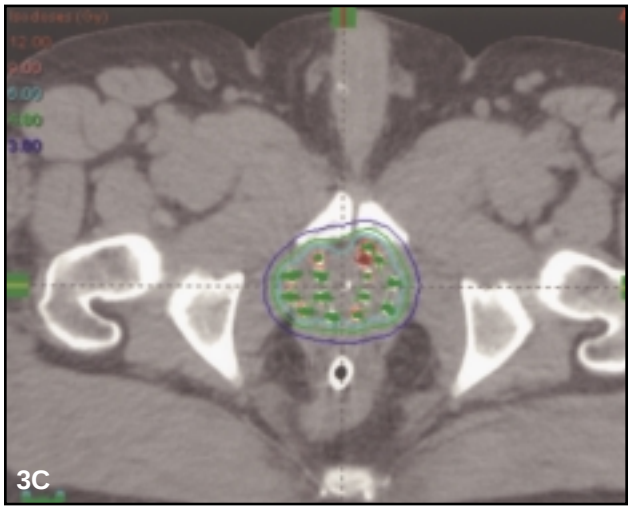
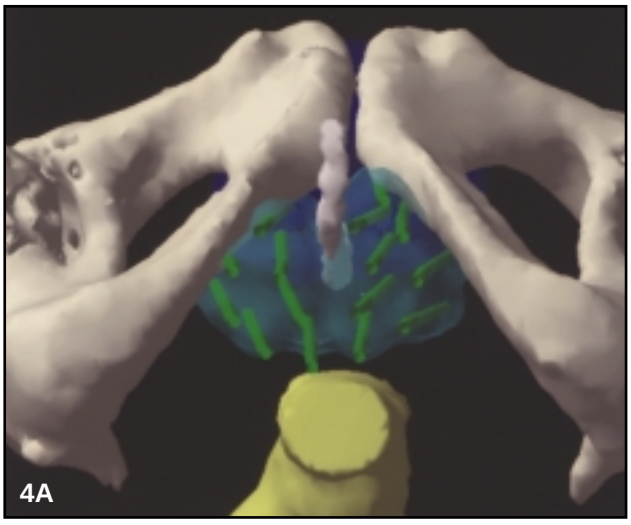
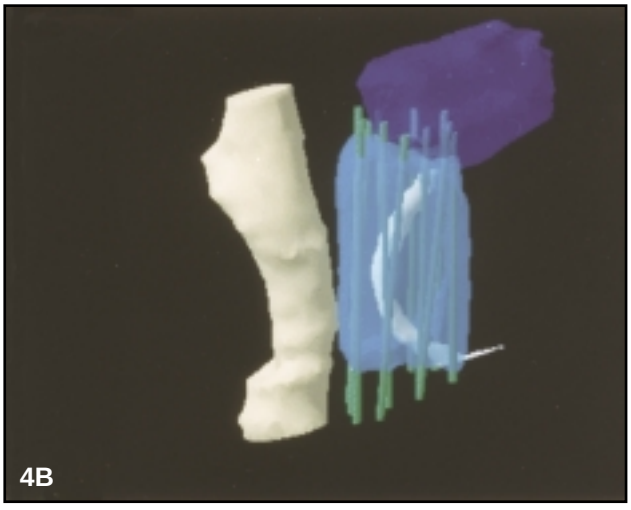


Fig 3. — (A) AP view with isodose plots, (B) lateral view with isodose plots, and (C) CT cross section with isodose plots.





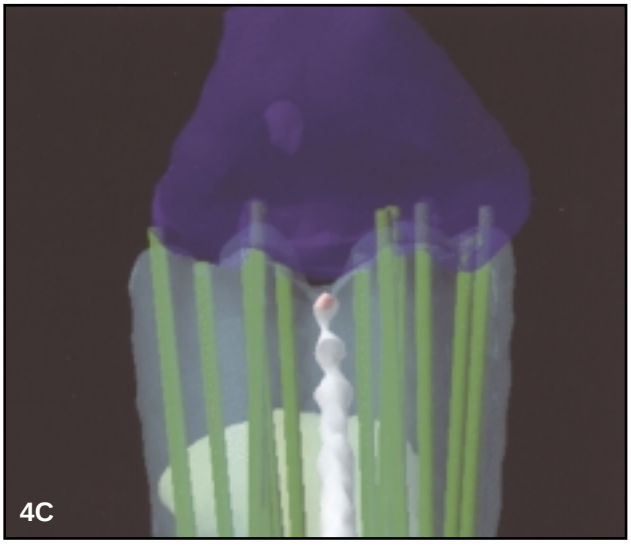


Fig 4. — (A) 3D reconstruction of the implant with dose distribution, (B) 3D reconstruction, lateral view with dose distribution, and (C) 3D reconstruction, AP view with dose distribution.

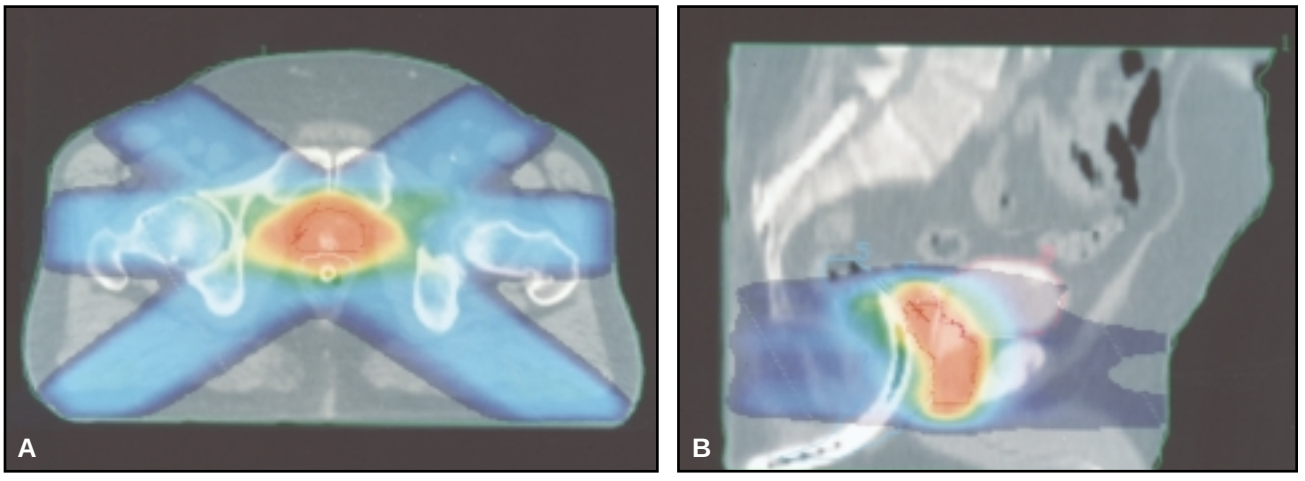


Fig 5. — (A) Transverse view of conformal six-field plan, (B) reconstructed lateral view of the six-field plan.

inal vesicles with 0.5-1.0 cm margins all around, with the rectal dose not exceeding 60% of the prescribed tumor dose and the urethral dose at 100%-110% of the prescribed tumor dose.

External Irradiation

All patients received a dose of 39.6 to 45.0 Gy to the prostate and seminal vesicles with wide margins (1.5-2.0 cm). The posterior half circumference of the rectum was blocked from irradiation. We used either a four-field box technique with anterior and posterior beams and bilateral opposed fields or a six-field conformal technique, utilizing 6 or 18 MV photon beams with 1.80 Gy per fraction and five fractions per week (Fig 5A-B). All patients were clinically evaluated for tumor regression and complications. DRE and PSA levels were obtained at 3-month intervals during the first 2 years, then every 6 months for up to 5 years, and then yearly. Clinical local control was defined as complete resolution of palpable nodules or induration following completion of irradiation. Biochemical relapse or treatment failure was defined according to American Society of Therapeutic Radiology and Oncology (ASTRO) criteria with three consecutive rising PSA levels.

Results

The 200 patients in our series were treated with a combination of HDR brachytherapy and external irradiation from June 1996 to July 1999. The staging and Gleason scores are presented in Table 1. The average follow-up was 30 months, with a minimum of 25 months and a maximum of 61 months. Clinical local control was achieved in 194 patients (97%). An overall

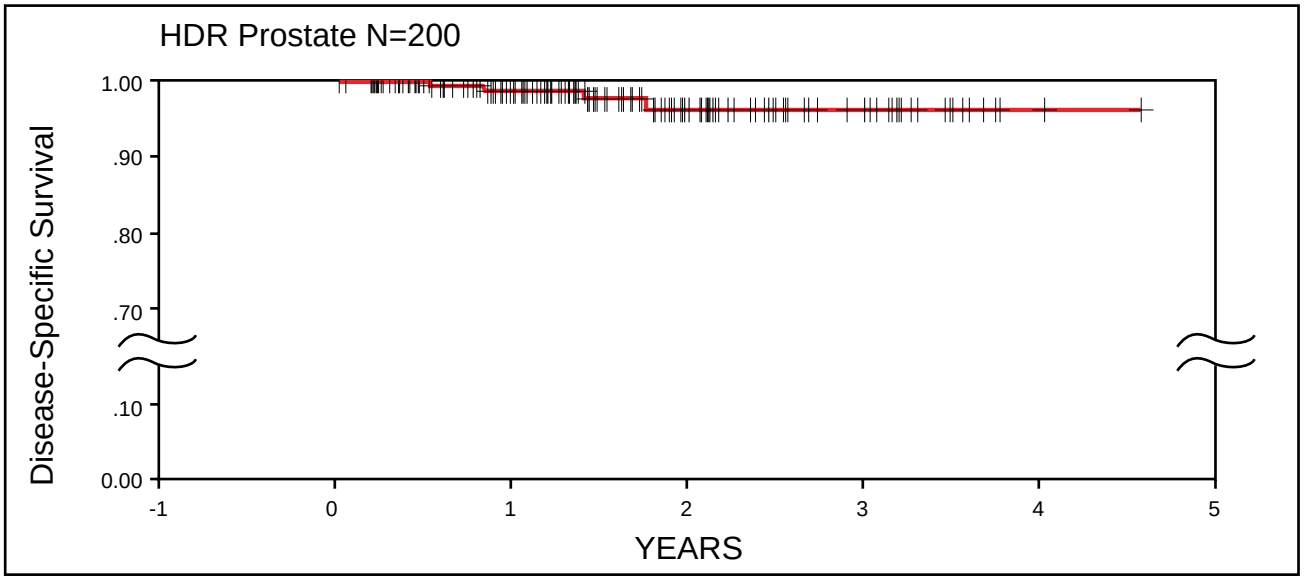


Fig 6. — Disease-specific survival (clinical and PSA relapse-free) of all 200 patients.

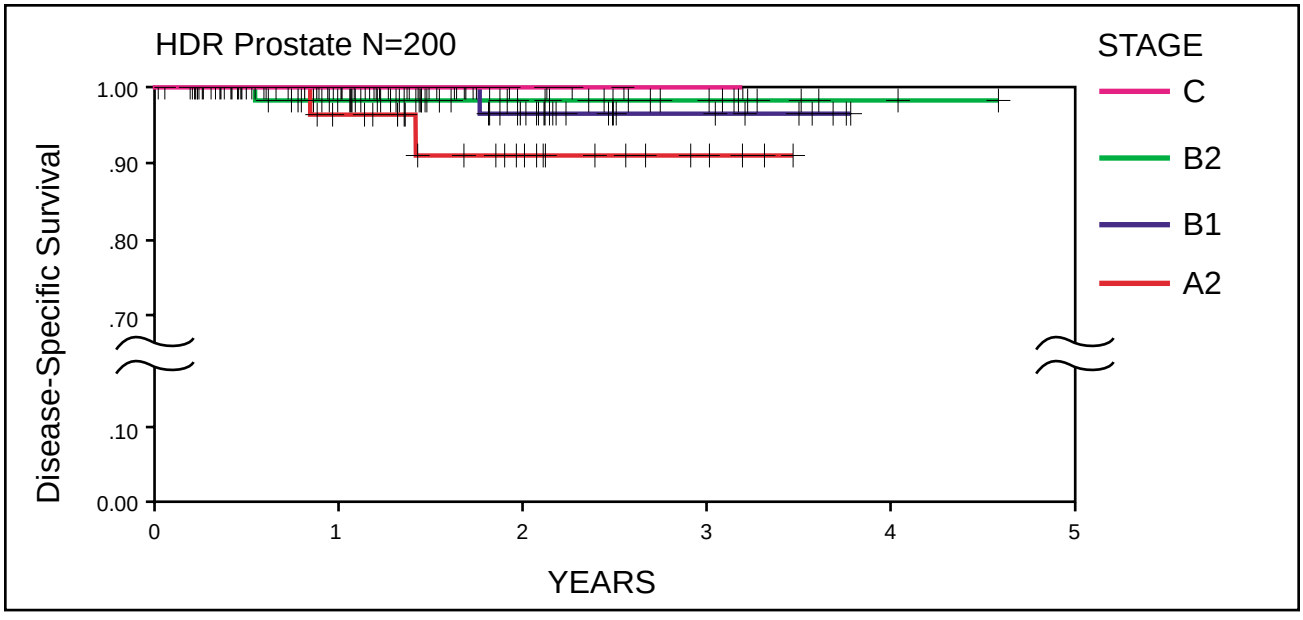


Fig 7. — Disease-specific survival (clinical and PSA relapse-free) according to staging.

disease-specific survival rate (clinical and PSA relapse-free, according to ASTRO criteria) of 97% was achieved for a minimum follow-up of 25 months (Figs 6-7). Of the remaining six patients, four died of unrelated causes (eg, coronary artery disease, chronic obstructive pulmonary disease), one died with locally persistent tumor, and one died of pulmonary metastasis. Seventy-two high-risk patients (PSA >20, Gleason score 8-10, and stage C lesions) received androgen blockade before irradiation. The average pretreatment PSA level of 10 ng/mL in these 200 patients declined to 1.1 ng/mL; 170 patients (85%) achieved a nadir of <1 ng/mL and 22 patients (11%) between 1-2 ng/mL (Table 3). The PSA level was 1 ng/mL or less in 101 (78%) of 128 patients who had no androgen blockade. The PSA is still declining in many patients and has not yet reached the nadir. In 69 (95%) of 72 patients who received androgen blockade before irradiation, the PSA level reached a nadir of <1 ng/mL within 1 year of treatment (Table 4).

In the majority of these patients, the PSA achieved a nadir within 1 year of completion of the treatment. In six patients, the PSA level fluctuated for up to 2 years as a result of prostatitis or urinary infection, which responded to antibiotic treatment. The overall clinical and PSA relapse-free survival rate was 93% (Figs 6-7).

Table 3. — PSA Post-Treatment Levels

No. of Patients	PSA (ng/mL)	
5	>4	2.5%
3	>2-4	1.5%
22	1-2	11%
170	<1 (0-1)	85%
90	<0.5	45%

No grade IV gastrointestinal (GI) or genitourinary (GU) postirradiation complications occurred. Acute GI and GU toxicity (grade 3-4) occurred in 20% and 10% of patients, respectively, according to the RTOG criteria (Table 5). Late GI toxicity (grade 3) occurred in three patients, and they responded to conservative management. Blood in ejaculum was observed in 10% of the patients up to 3 months following treatments. Late GU complications occurred in four patients — urethral strictures in three patients and incontinence in one patient. The three patients with strictures had posteri-

Table 4. — Pretreatment and Postoperative PSA Levels in Patients With vs Without Androgen Blockade

With No Androgen Blockage (n=128):			
Pretreatment PSA (ng/mL)	1.2 minimum 76.3 maximum 8.1 average		
Postoperative PSA (ng/mL)	0-0.5	42 pts	(33%)
	0-1.0	101 pts	(78%)
	1.1-1.5	14 pts	(10.9%)
	1.6-2.0	7 pts	(5.4%)
	2.1-4	2 pts	(1.6%)
	> 4	4 pts	(3%)
	Average: 1.25		
With Androgen Blockade (n=72):			
Pretreatment PSA (ng/mL)	0.6 minimum 96 maximum 10.5 average		
Postoperative PSA (ng/mL)	0-0.5	34 pts	(47%)
	0-1	69 pts	(95.1%)
	1.1-1.5	0 pts	(0%)
	1.6 -2.0	1 pt	(1.3%)
	2.1-4	1 pt	(1.3%)
	>4	1 pt	(1.3%)
	Average: 0.9		

Table 5. — Late Complications (Grade 3)*

Stage	No. of Patients	Genitourinary	Gastrointestinal
T1c (A2)	28	0	0
T2a (B1)	65	0	1
T2a (B2)	64	2	1
T3a,b (C)	43	2	1
Total	200	4 (2%)	3 (1.5%)

*Radiation Therapy Oncology Group, grade 1-4

or laser urethrotomy, which resulted in two of them requiring pads for partial incontinence.

In patients who were potent before treatment, impotency occurred in 30% who did not receive androgen blockade and in 50% of those who did receive androgen blockade. Most of these patients achieved erections with sildenafil (Viagra), urethral suppositories, and vacuum pumps. Numbness of the penis occurred in 10 patients and resolved over a period of 3 months to 2 years after completion of the treatment.

Discussion

Radical prostatectomy considered as a standard treatment for carcinoma of the prostate is based on selection of patients who have prostate-confined tumors, are surgically staged with negative pelvic nodes, are less than 70 years of age, and are in good medical condition.[1-6] Most of the reported series using EBRT alone, brachytherapy alone, or a combination of both included elderly patients (>70 years of age) who lacked surgical staging of the pelvic lymph nodes and had high-grade tumors and high PSA levels. However, it is clear from the surgical and radiation series that local eradication of the tumor is an important factor in determining the prognosis. Freiha et al[45] and others[46-48] have reported that patients with persistent or recurrent tumors following irradiation had four times more distal metastases than patients with negative biopsies.

Hanks et al[11] and others[12-15] reported improvement in PSA relapse-free survival and less morbidity in both randomized and nonrandomized studies with escalating doses of external irradiation up to 78 Gy using 3D conformal radiotherapy and, more recently, intensity-modulated radiation therapy (IMRT). The use of 3D conformal radiotherapy and IMRT improves the therapeutic ratio by delivering the dose more precisely. Local failures may occur due to prostate movement during radiation or possibly to tumor clonogens that have possibly tumor clonogens that have inherent resistance to the radiation doses. A retropubic interstitial iodine-125 implant technique reported by Whitmore et al[22] and others[23] had several disadvantages, and long-term follow-up showed local failures in 40%-60% of patients. There have been significant improvements in the distribution of seeds in the prostate since Holm and associates[49] introduced the TRUS-guided transperineal permanent interstitial implant technique in 1980. However, several inherent technical and radiobiological problems remain unresolved, including migration of seeds, inability to implant seminal vesicles following transurethral resection of the prostate, and inability to fill in cold spots or remove seeds from areas of clus-

Table 6. — Selected Treatment Protocols

Institution	Stage	No. of Implants	Dose (Gy) and No. of HDR Fractions/Implants	Brachytherapy Dose (Gy)	External Irradiation (Gy)	Total Physical Dose (Gy)
LBMMC	T1c, T2a	1	5.5 × 4	22	45	57
	T2b,c	1	6.0 × 4	24	45	69
	T3a,b	1	6.5 × 4	26	45	71
SPI	All	1	4.0 × 4 (study #1)	16	50.4	66.4
	All	1	5.5 × 3 (study #2)	16.5	45	61.5
WBH	All	2	9.5 × 1	19	46	65
CET	All	2	6.0 × 2	24	36	60
SC	All	1	5.5 × 3	16.5	50.4	66.9
MMC	All	1	5.5 × 4	22	45	67

LBMMC = Long Beach Memorial Medical Center, Long Beach, California
SPI = Seattle Prostate Institute, Seattle, Washington
WBH = William Beaumont Hospital, Royal Oak, Michigan
CET = California Endocurietherapy Cancer Center, Oakland, California
SC = Scripps Clinic, La Jolla, California
MMC = Memorial Medical Center, New Orleans, Louisiana

Table 7. — HDR Prostate Cancer Results

Authors	No. of Patients	PSA Relapse-Free Survival (%)	Grade 3 Complications: GU (%)	GI (%)
Mate et al[35]	104	84% (5 yrs)	6.7	0
Vicini et al[53]	161	86% (2 yrs) 67% (5 yrs)	4.5	0
Kovacs et al[54]	174	83% (5 yrs)	7	3
Rodriguez et al[39]	110	85% (3 yrs)	4	1
Borghede et al[55]	50	84%	8	3.5
Syed et al	200	89% (No ADT, avg 2.5 yrs) 95% (ADT)	2	1.5

ADT = androgen deprivation treatment

tered seeds near the rectum or urethra. The resultant matched peripheral dose isodose coverage frequently does not match the idealized preplan, thus yielding poor dosimetry following implant.

We have already reported on the technique and long-term results with an LDR temporary interstitial iridium-192 implant using a transperineal template technique under ultrasound guidance with an 85% actuarial disease-free survival rate and 15% positive post-irradiation biopsies.[50] Khan et al[51] and others[52] have reported similar results. However, this technique involves manual loading of radioactive iridium-192 sources and radiation exposure (although within tolerance to personnel) during 40-48 hours of continuous irradiation.

In 1997, Mate and colleagues[35] reported on the technique and results of HDR brachytherapy in the treatment of carcinoma of the prostate. This implant technique is similar to our technique using an LDR iridium-192 implant. However, four fractions of 4 Gy each were delivered using a remote afterloader with a high-intensity iridium-192 source followed by 50.4 Gy EBRT. Of the 104 patients whose pretreatment PSA levels were less than 20 ng/mL, 84% were free of progression at 5 years by actuarial analysis, with 6.7% of patients having developed urethral strictures.

Martinez and associates[37] published recent preliminary data of monotherapy in patients with favorable prognostic factors (Gleason score <7, PSA <10 ng/mL, and stage T1-T2a). A total dose of 38 Gy in four fractions was delivered over 2 days, two fractions per day. The dose to the rectum and urethra was limited to ≤75% and ≤125%, respectively, of the prescription dose. All 41 patients treated with HDR monotherapy tolerated the treatment well with modest acute toxicity. Late toxicity and tumor control have not been reported.

Vicini et al[53] reported the results of combined HDR brachytherapy and EBRT. All 161 patients received pelvic EBRT to 46 Gy. HDR brachytherapy boosts were performed in the first, second, and third week of EBRT. Seventy-two patients received three implants of 5.5-6.5 Gy each and 89 patients received 10.5 Gy each. The 2- and 5-year actuarial biochemical control rates were 86% and 67%, respectively, with 4% grade 3 late toxicity consisting of strictures (five patients), incontinence (one patient), and impotency (27%). Table 6 and Table 7 show the protocols used by major investigators with preliminary results in the United States.

We previously published the technique, protocol, preliminary results, and complications of HDR brachytherapy.[41,42]

Our series of 200 patients treated from June 1996 to July 1999 by a combination of HDR brachytherapy and EBRT to the prostate was well tolerated with relatively few acute and late complications and compares favorably with other reports, published protocols, and data (Figs 6-7). PSA relapse-free survival, with 30 months of median follow-up according to the ASTRO criteria, was achieved in 91% of the patients. The low- and intermediate-risk patients did not receive androgen blockade. The average pretreatment PSA level of 8.1 ng/mL in 128 patients with low- and intermediate-risk factors reached a nadir of <1 ng/mL in 78% of the patients and <1.5 ng/mL in 89%. PSA relapse-free survival with a minimum follow-up of 2 years in 72 patients with high-risk factors treated by androgen blockade in addition to irradiation was 95%. PSA level reached a nadir of <1 ng/mL in 95% of the patients.

Acute GI and GU toxicity (RTOG grade 3-4) occurred in 20% and 10% of patients, respectively, which resolved with conservative management. Late GI and GU toxicity (RTOG grade 3) occurred in 1.5% and 2%, respectively. Four patients required urethrotomy,

two of whom became partially incontinent. Of the patients who were potent before irradiation, impotency occurred in 50% of those receiving androgen blockade and in 30% of those not receiving androgen blockade. Most patients achieved erection following treatment with sildenafil (Viagra), urethral suppositories, etc.

Conclusions

HDR brachytherapy is well tolerated with no treatment mortality and with acceptable morbidity. Combined HDR brachytherapy and EBRT provides superior conformal irradiation in low-, intermediate-, and high-risk patients, yielding a PSA relapse-free survival rate of 97%. This compares favorably to surgical, conformal external-beam, proton-beam treatments, and permanent implant techniques with minimal morbidity.

Androgen blockade for 2-3 months prior to irradiation and up to 2-3 years following irradiation may improve survival and reduce local failure in patients with high-risk factors (T3 lesions, PSA >20 ng/mL, and Gleason score 8-10). HDR brachytherapy offers total control of source and dose distribution so that the maximum dose can be delivered to the prostate and less to the rectum, bladder, and urethra. HDR procedures can be performed even after transurethral resection of the prostate because a "donut" type of dose distribution reduces the dose to the urethra and thus decreases the risk of complications. No radiation precautions are required as there is no exposure to the personnel. The learning curve for the radiation oncologist and urologist for HDR procedures is shorter than that needed for permanent implant techniques and does not compromise the outcome as irradiation is not delivered if the dose distribution is unsatisfactory. HDR procedures deliver the maximum dose to the prostate with less integral dose compared to conformal or IMRT.

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