

High Dose Rate Brachytherapy as Monotherapy for Clinically Localized Prostate Cancer

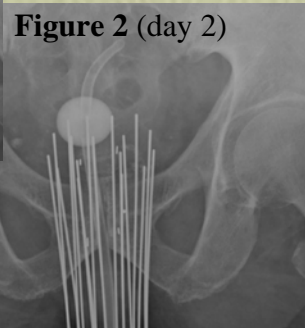
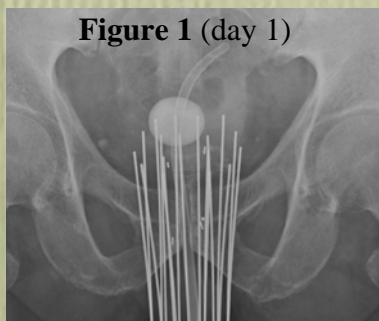
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Purpose: To review our initial single institution prospective experience with high dose rate brachytherapy as monotherapy (HDR-MT) for patients with clinically localized prostate cancer, emphasizing tolerance, toxicity, and freedom from biochemical failure.

Methods and Materials: Since May 2002 we have treated 401 low and intermediate risk prostate cancer patients with HDR-MT. Limiting analysis to patients with ≥ 6 months follow-up establishes a cohort of 326 patients. Median age was 69.1 years (range 47.9-85.7), and median pretreatment PSA 6.3 (range 0.8-19.7). Patients were stratified into 2 risk groups incorporating AJCC clinical stage, Gleason's score (GS), and pretreatment PSA: low risk (stage $\leq T2a$, GS ≤ 6 , PSA ≤ 10), and intermediate risk (stage T2b or c, GS 7, PSA 10-20), rendering 209 (63.7%) low risk and 117 (36.3%) intermediate risk patients. Median follow-up for the entire cohort was 13.4 months (range 6.0-39). By risk group, median follow-up was 13.3 months for low risk (range 6.1-39), and 13.6 months (range 6.0-37) for intermediate risk patients.

Treatment consisted of 2 brachytherapy procedures, each with 3 fractions of 6.5 Gy over a one-night hospitalization. Thus from both procedures, the total dose was 39 Gy in 6 fractions delivered over a median of 16 days (range 6-35). For each procedure, catheters were placed in the operating suite with transrectal ultrasound and fluoroscopic guidance. Treatment planning was CT based. One brachytherapy fraction was given in the afternoon of day 1, a second fraction the morning of day 2, and the third fraction the afternoon of day 2. The mean interfraction interval on day 2 was 5.5 hours. As demonstrated with the plain film images below (Figures 1 and 2), catheter positions were evaluated on day 2 relative to 4 gold fiducials placed intraoperatively (2 at the prostatic base and 2 at the apex). If needed, needle depth adjustments were made, keeping implant geometry consistent.



Methods and Materials (cont'd): Dose distributions were carefully planned such that the prescription isodose (100%) covered the entire prostate, and such that the 120% isodose encompassed the transitional zone. As depicted in Figure 3 and exhibited numerically in Table 1, the 110% isodose was not permitted to touch the urethral catheter surface anywhere in the treated volume, and the urethral central point doses were limited to 105%. The rectal mucosa (defined by contrast within the rectal lumen) was limited to $\leq 60\%$, and no portion of rectum was permitted to receive $> 100\%$. Bladder doses were also limited to 100%.

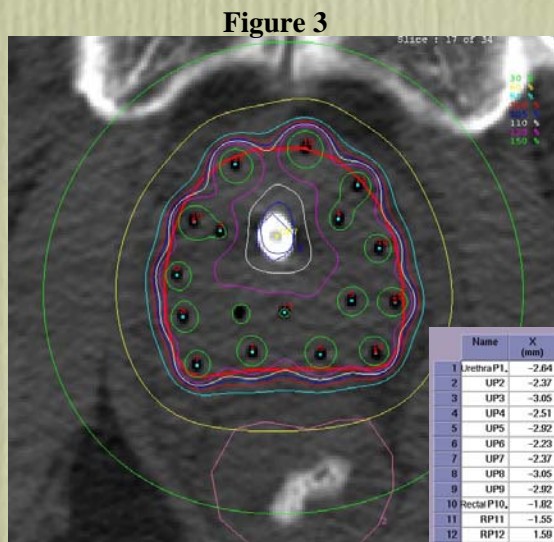


Table 1

Name	X (mm)	Y (mm)	Z (mm)	Norm dose	Act dose (%)	Act dose (cGy)
1 UretraP1	-2.64	-4.77	-22.70	100.00	93.87	610.18
2 UP2	-2.37	-3.82	-17.79	100.00	101.40	659.07
3 UP3	-3.05	-2.87	-12.88	100.00	103.78	674.59
4 UP4	-2.51	-3.13	-7.70	100.00	103.98	675.89
5 UP5	-2.92	-3.51	-2.50	100.00	103.98	675.75
6 UP6	-2.23	-4.97	2.95	100.00	103.75	674.35
7 UP7	-2.37	-6.42	8.39	100.00	103.14	670.40
8 UP8	-3.05	-8.14	13.89	100.00	99.63	647.82
9 UP9	-2.92	-8.93	18.19	100.00	95.39	587.54
10 RectalP10	-1.82	32.74	-31.02	100.00	30.29	196.87
11 RP11	-1.55	32.89	-23.37	100.00	36.69	238.51
12 RP12	1.59	30.38	-12.57	100.00	40.28	260.32
13 RP13	1.59	31.61	-2.60	100.00	49.97	324.70
14 RP14	4.74	34.98	6.90	100.00	43.32	281.55
15 RP15	7.34	41.15	15.77	100.00	32.51	211.29
16 RP16	7.61	45.71	25.00	100.00	25.87	168.17
17 RP17	4.88	49.75	34.35	100.00	20.65	134.19
18 Bladder18	2.96	-13.59	22.79	100.00	82.55	536.56
19 BP19	-3.33	-0.49	27.56	100.00	87.95	571.70
20 BP20	-1.82	1.00	34.91	100.00	69.68	452.91
21 BP21	-1.00	1.55	42.47	100.00	51.18	332.74

Follow-up was scheduled at 3 months after HDR-MT, then every 6 months. Two definitions for PSA failure were analyzed: ASTRO, and nadir + 2. Each patient recorded his International Prostate Symptom Score (IPSS), and International Index of Erectile Function (IIEF-5) score at baseline and at follow-up. Rectal side effects were evaluated using RTOG criteria.

Results: In our cohort of 326 patients, median follow-up was 13.4 months (range 6-39). Using the Kaplan-Meier method, 3-year overall survival was 99.1%, and cause-specific survival 100%. 3-year rates of biochemical disease-free survival (bDFS) are listed in Table 2.

Table 2
3-year Actuarial bDFS Rates by Risk Group

Patient Risk Group	ASTRO	Nadir + 2
Low (n = 209)	99.4%	99.4%
Intermediate (n = 117)	97.8%	97.8%
All Patients (n = 326)	98.8%	98.8%

Results (cont'd): Urinary symptoms were the most frequently encountered side effects. However, only 3 (0.9%) patients required intermittent self-catheterization or a temporary indwelling catheter. No patient required these beyond 3 months. Urinary IPSS scores tended to improve modestly following HDR-MT. Respectively at baseline, 6 months and 12 months, IPSS scores were 8.9 ± 6.6 , 10.2 ± 6.2 , and 10.2 ± 7.2 . Prior to treatment, the IIEF-5 erectile function scores were 12.5 ± 9.5 . At 6 and 12 months, the respective IIEF-5 scores were 13.5 ± 6.2 , and 14.7 ± 7.0 with the use of PDE-5 inhibitors, and 8.2 ± 5.1 , and 8.3 ± 5.5 without such erectile aid. Defining potency as an IIEF-5 score > 10 , 165 patients were potent before HDR-MT, 75% of whom were potent at 1 year. We recorded rectal toxicity data on our patients at each follow-up visit. Rectal toxicity was mild, and in no case required intervention or chronic medication. The highest rectal toxicity at any post-treatment interval was RTOG grade 1.

As referenced below,¹ we separately undertook an analysis of PSA kinetics in 3 of our patient cohorts with the longest-term follow-up. Group 1 (low risk) received permanent I-125 seed brachytherapy, Group 2 (intermediate risk) external beam radiation therapy (EBRT) with an HDR brachytherapy boost, and Group 3 (high risk) short course (median 4 months) neoadjuvant and adjuvant androgen blockade, EBRT to the prostate and pelvis, and an HDR brachytherapy boost. Group 2 patients were the most likely to experience a PSA bounce (41%), had the highest bounce magnitude (mean 0.86) and the shortest mean time to bounce (mean 13.8 months). The median bounce duration in these patients was 6.6 months (range 0.9 to 46 months).

With this prior data in mind, and with a further 6 months follow-up since the present abstract was originally submitted, we re-analyzed the HDR-MT cohort. Of our 326 patients, 15 were previously scored as PSA failures (8 low risk, 7 intermediate risk). Twelve of these 15 patients have now been documented as PSA bounces rather than failures (7 of 8 low risk, 5 of 7 intermediate risk). Thus only 1 low risk patient, and 2 intermediate risk patients have had PSA failures, in each case meeting both the ASTRO and nadir + 2 definitions.

Conclusion: High-dose-rate brachytherapy as monotherapy results in excellent intermediate-term outcomes for patients with low and intermediate-risk prostate cancer. It is well tolerated, and toxicities are limited in severity and scope. We have been offering HDR-MT to low and intermediate risk prostate cancer patients for over 3 years, and will continue to study their outcome, side effects and PSA kinetics carefully. HDR-MT is very promising, well deserving of further analysis, and of careful investigation in single institution and cooperative group settings.

Bibliography: ¹ Hayes, JK, Hansen, RS, Rogers CL, *et al*. Post-treatment PSA Kinetics of Three Prostate Cancer Treatment Regimens Involving Brachytherapy. Brachytherapy 2006;5:113 (Abst P-106)