

# Long-Term Results of Intraoperative Dose Escalation Using I-125 Monotherapy: An Analysis of Prostate Implants with a Minimum D90 of 180 Gy

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**Background:** There has been significant interest in dose escalation using external beam radiation for prostate cancer. In contrast, the safety and efficacy of doses above the ABS recommended D90 of 145 Gy using brachytherapy has not been established.

**Purpose/Objective(s):** The purpose of this study is to characterize the oncologic results and toxicity profile of patients treated with a D90 of  $\geq 180$  Gy.

**Materials/Methods:** At Mount Sinai, the prescription D90 for I-125 monotherapy has been 160 Gy (TG-43) using real-time intraoperative planning since 1997. Consequently, some patients are noted with a D90 of  $\geq 180$  Gy at the time of post-implant dosimetry. From 6/1995 to 2/2004, 598 patients were treated with I-125 alone for T1-2 prostate cancer with a D90 of  $\geq 180$  Gy (median 197, range 180 – 267). The implants were performed using a real-time ultrasound guided seed placement method and intraoperative dosimetry to optimize target coverage and homogeneity using modified peripheral loading. A median of 92 seeds (range 31 to 220) were implanted into a prostate with a median US volume of 44.0 cc (range 14.3-125.0cc). The median activity implanted was 44.6 mCi (range 7.6-96.9 mCi) and the median V150 was 70.7% (range 21.0-94.1%). The median urethral D30 was 240.0 Gy (range 2.4-515.5 Gy) and the median rectal V100 was 1.00 cc (range 0.00-6.19 cc). We analyzed the biochemical control of 435 patients that had a minimum 2 year PSA follow-up (median f/u 6.7 years; range 2.0-11.1 years). 9.2% of the patients were intermediate or high risk based on one or more of the following factors: PSA>10, Gleason 7-10 or T2c disease. 31% received neo-adjuvant hormonal therapy. Of the 509 patients with available potency data, 375 (73.7%) were potent prior to implant. Longitudinal urinary function was assessed in 249 patients with pretreatment IPSS and a follow-up IPSS at least 3 years after implant (median 4.5 years, range 3 to 10 years). Post-brachytherapy prostate biopsy results were available for 120 (20.1%) patients.

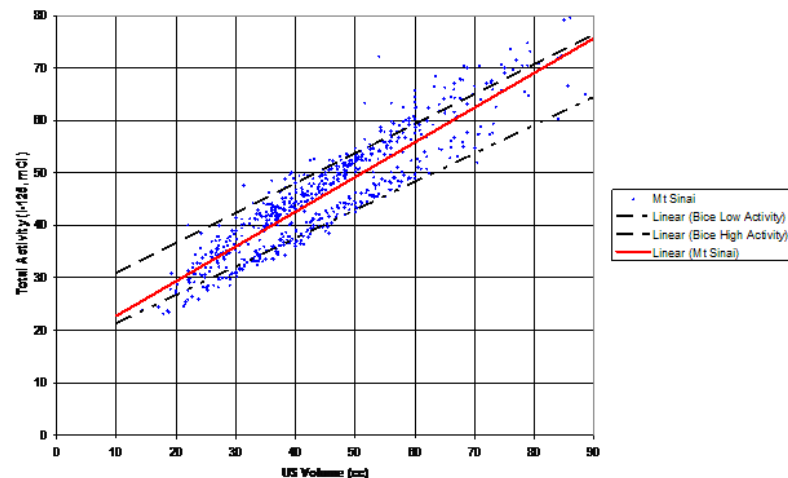
**Results:** The 5 year bDFS (ASTRO definition) for the entire cohort was 96.6%. The positive biopsy rate was 4.1%. For low risk patients, the 5 year bDFS was 97.1% while for intermediate/high risk patients, the 5 year bDFS was 92.6%. There were no PSA failures beyond 6 years. Freedom from  $\geq$  grade 2 rectal bleeding at 5 years was 88.5%. Acute urinary retention occurred in 10.7%, more commonly in patients with high pretreatment IPSS scores ( $p < 0.01$ ). The median IPSS scores increased significantly during the first six months after implant. The median IPSS was 6 (range 0-28) pre-implant compared to 6 (range 0-31) post-implant with 3-year minimum follow-up. Using a 2-tailed t-test with unequal variance, there was no significant differences between the groups ( $p = 0.14$ ). Among patients who were potent prior to treatment, 73.4% remained potent at 5 years after implant.

**Conclusions:** Patients with a minimum D90 of 180 Gy had outstanding local control based on PSA control and biopsy data. The absence of late failures with extended follow-up suggests durable tumor control. The toxicity profile, particularly long-term urinary and sexual function, was excellent and demonstrates that D90 doses  $\geq 180$  Gy are well tolerated.

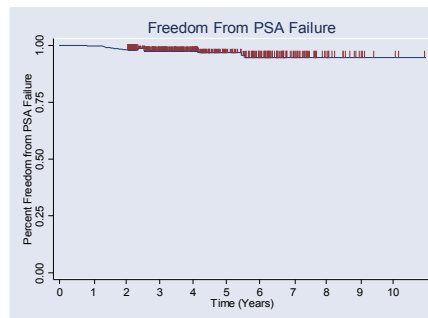
**Table 1. Patient Characteristics**

	Number (n)	Percentage (%)
<b>Clinical Stage</b>		
T1a	1	0.2
T1b	2	0.3
T1c	444	69.1
T2a	144	22.4
T2b	46	7.2
T2c	6	9.3
<b>Gleason Score</b>		
2	3	.5
3	2	.3
4	15	2.3
5	41	6.4
6	581	90.4
7	1	.2
<b>Pretreatment PSA</b>	Median 6.1	
0-4	66	10.3
4.1-10	526	81.8
10.1-20	50	7.8
$\geq 20$	2	0.3
<b>Hormonal therapy</b>		
No	444	69.0
Yes	199	31.0
<b>Prior TURP</b>		
No	624	97.0
Yes	19	3.0
<b>US Volume</b>	Median 44.0 cc	
14.3-40 cc	268	41.7
40.1-60 cc	283	44.0
60-80	76	11.8
$> 80$	16	2.5
Unknown	1	0.2

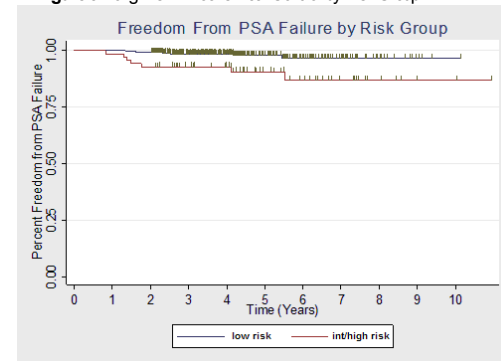
**Figure 1. Total Activity vs. Prostate Volume Compared to National Benchmarks for I-125 Brachytherapy**



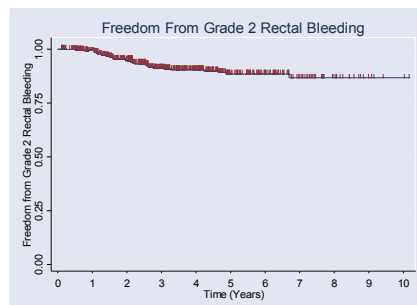
**Figure 2. Long-Term Biochemical Control**



**Figure 3. Long-Term Biochemical Control by Risk Group**



**Figure 4. Long-Term Biochemical Control**



**Figure 5. Distribution of IPSS Scores Before and After Seed Implantation Among 249 Patients with Available Pre-Treatment IPSS and Post-Treatment IPSS Scores with Minimum of 3 year Follow-up**

