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CLINICAL INVESTIGATION **Prostate**

A COMPREHENSIVE REVIEW OF CT-BASED DOSIMETRY PARAMETERS AND BIOCHEMICAL CONTROL IN PATIENTS TREATED WITH PERMANENT PROSTATE BRACHYTHERAPY

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Purpose: The American Brachytherapy Society recommends that postprostate implant dosimetry be performed on all patients undergoing transperineal interstitial permanent prostate brachytherapy (TIPPB) utilizing CT scan clinical target volume reconstructions. This study was undertaken to assess the recommended dosimetry parameters from a large cohort of patients undergoing TIPPB that would predict for PSA relapse-free survival (PSA-RFS).

Methods and Materials: Seven hundred nineteen consecutive patients with clinical stage T1/T2 adenocarcinoma of the prostate underwent TIPPB using either I-125 or Pd-103. Postimplant dosimetry was performed at 2 to 3 weeks with CT scan 3-dimensional reconstructions obtained on all patients. The D90 and D100 doses (defined as the minimum dose covering 90% and 100% of the prostate volume, respectively) and the V100 (defined as the percent of the prostate receiving 100% of the prescribed dose) were obtained for each patient. Regression analysis was performed on the D90 dose, D100 dose, and V100 to test for cutoff points that would predict for PSA-RFS, defined by a modification of the American Society for Therapeutic Radiology and Oncology consensus panel statement. A cutoff value was found and was subjected to subset analysis to assess for its robustness. Treatment-related factors were tested for their ability to achieve dosimetry at or above the cutoff dose.

Results: The median follow-up from this cohort is 30 months (7–71 months) with a 48-month PSA-RFS of 89.5%. A D90 dose-response cutoff value ≥90% of the prescribed dose was identified. Prostate implants with a D90 dose <90% of the prescribed dose had an 80.4% 4-year PSA-RFS, while those with a D90 dose ≥90% of the prescribed dose had a 92.4% 4-year PSA-RFS ($p = 0.001$). No cutoff value was found for the V100 and D100 dose that predicted for PSA-RFS. Using the cutoff value, the D90 dose at 90% of the prescribed dose, a difference in 4-year PSA-RFS survival was identified for patients treated with I-125 ($p = 0.04$), Pd-103 ($p = 0.01$), TIPPB as monotherapy ($p = 0.001$), the addition of hormone therapy ($p = 0.005$), and TIPPB without hormone therapy ($p = 0.001$). The D90 dose was not significant for the group of patients treated with external beam radiotherapy and TIPPB ($p = 0.15$). The only significant finding from Cox regression analysis to predict for a poor D90 dose (<90% of the prescribed dose) was a CT/TRUS volume ratio >1.5 ($p = 0.02$).

Conclusions: The American Brachytherapy Society recommends that postimplant CT-based dosimetry be performed for all patients treated with TIPPB. This prospective study identified that the D90 dose ≥90% of the prescribed dose can be used as a factor for predicting PSA-RFS in patients treated with brachytherapy. A dose-response using the D90 dose was observed for several typical clinical treatment variations used in the practice of TIPPB. Using the D90 dose appears to be a satisfactory parameter for predicting outcome in patients treated with TIPPB. **© 2001 Elsevier Science Inc.**

Prostate cancer, Brachytherapy, Dosimetry, Iodine, Palladium.

INTRODUCTION

Transperineal interstitial permanent prostate brachytherapy (TIPPB) is an effective modality for the treatment of early-stage prostate cancer (1–6). Clinical factors such as the Gleason score, pretreatment PSA value, and clinical stage have been identified in most series to be important prognostic factors in predicting the biochemical freedom from disease (1, 2, 6). Data from the suprapubic era of iodine (I-125) prostate brachytherapy have identified that implant "adequacy" can have a profound effect on clinical recurrence rates (7). In patients treated with TIPPB, Stock *et al.* have shown that the use of CT scan–based implant dosimetry can likewise identify a dose-response cutoff value that

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Table 1. Patient characteristics

	MSKCC at Mercy Medical Center (n = 719 [%])
Implant dates	06/10/95–10/30/99
Biopsy Gleason sum (n)	
2	3 (0.4%)
3	6 (0.8%)
4	8 (1.1%)
5	25 (3.5%)
6	402 (55.9%)
7	226 (31.5%)
8	38 (5.3%)
9	10 (1.4%)
10	0
Clinical stage (n)	
T1ab	3 (0.4%)
T1c	438 (60.9%)
T2a	224 (33.9%)
T2b	34 (4.8%)
External beam (n)	
No	520 (71.6%)
Yes	199 (28.4%)
Hormones	
No	469 (65.2%)
Yes	250 (34.8%)
Pretreatment PSA (ng/ml)	
Minimum	1.1
First quartile	5.8
Median	8.0
Mean	9.7
Third quartile	10.7
Maximum	112.0

predicts for prostatic specific antigen relapse-free survival (PSA-RFS) (8).

Currently, the American Brachytherapy Society (ABS) recommends that postimplant CT-based dosimetry be performed for all patients undergoing TIPPB (9). Nonetheless, there are few data on what defines an "adequate" implant, and the ABS is currently unable to recommend specific parameters that define implant quality.

This prospective study examines various CT-based implant parameters from a large cohort of patients treated with TIPPB to define a dose-response cutoff that can predict for PSA-RFS.

METHODS AND MATERIALS

Seven hundred nineteen consecutive patients with clinically localized prostate cancer were treated with TIPPB between April 1995 and October 1999. The clinical characteristics of these patients are presented in Table 1. Six hundred one patients were treated using palladium (Pd-103), while 118 received I-125. Five hundred twenty patients received TIPPB as monotherapy, and 199 patients were treated with a combination of external beam irradiation (EBT) and TIPPB. The treatment approach used in our clinic has been previously published (10). All patients underwent a preimplant transrectal ultrasound (TRUS) study to determine the prostate volume, defined as the clinical target volume (CTV), three to six weeks before surgery. The total activity and total number of seeds used in each case were based on the dimensions of the CTV using a modified version of the Anderson nomogram (11). The prescribed dose to the CTV for patients treated with Pd-103 was 120 Gy (pre-NIST 99 [12]) and with I-125 was 144 Gy (AAPM TG-43 modification [13]). The delivered doses were kept constant within this study cohort, which means that the written prescription doses have changed to account for changes in the air to water kerma strength for I-125 and a change in the calibration standard for Pd-103 that was identified in 1997. The seed activity range for I-125 (NIST 85) was 0.31–0.62 mCi (median of 0.509 mCi) and 1.02–1.70 mCi for Pd-103 (median of 1.45 mCi). Patients treated with EBT received a dose of either 41.4 Gy (n = 119) or 45.0 Gy (n = 80) at 1.8 Gy fractions to a standard pelvic 4-field box (typical anterior:posterior field size was 11 × 11 cm) 4 weeks before undergoing TIPPB. When EBT was used, the prescribed implant dose for Pd-103 and I-125 was 90 Gy and 104 Gy, respectively. Our TIPPB technique involves using a Mick interstitial gun (Mick Nuclear, Bronx, NY) to place the seeds with peripheral alignment using real-time TRUS guidance with the patient in high lithotomy position.

All patients included in this study had a postimplant CT scan obtained at a median of 3.1 weeks (1.6–6.5 weeks). A commercial treatment planning system (Prowess, Chico, CA) was used to generate the 3-dimensional dose distribution to the target as drawn on the CT images by the treating physician (L.P. and T.T.). Doses to the target were calculated for the D90 and D100 (the minimum dose that covers 90% and 100% of the target volume, respectively). The percents of the target volume treated to the 100% isodose line (V100) and to the 150% isodose line (V150) were calculated for each patient.

Patients were followed post-TIPPB at 3–4-month intervals for 2 years, then at 6–8-month intervals thereafter. A clinical digital examination was performed, and a PSA value was obtained at each follow-up visit. The PSA-RFS was determined using the Kattan modification to the American Society for Therapeutic Radiology and Oncology con-

Table 2. Evidence of failure information from the entire cohort

First evidence of failure	n = 719
Biochemical relapse	45
Clinical relapse	1
Hormonal therapy	5
Salvage prostatectomy	2
Death from disease	0
Median (maximum) months of follow-up for censored patients	30 (71)
Total number of PSA values obtained at follow-up (mean per patient)	5312 (7.3)
Percent of censored patients who did not have their PSA measured within 1 year of analysis	18

Table 3a. Parameters for volumetric and seed strength subgroups for target volume

Target volume	Small (≤20 cc)	Medium (>20, ≤40 cc)	Large (>40 cc)
I-125	$n = 26$	$n = 77$	$n = 15$
Pd-103	$n = 156$	$n = 393$	$n = 52$

Table 3b. Parameters for volumetric and seed strength subgroups for seed activity

Seed activity	Low	Medium	High
I-125	≤0.4 mCi $n = 8$	>0.4, ≤0.55 mCi $n = 81$	>0.55 mCi $n = 29$
Pd-103	≤1.35 mCi $n = 63$	>1.35, ≤1.55 mCi $n = 345$	>1.55 mCi $n = 193$

sensus panel definition that is applied to external beam radiotherapy (14, 15). This definition marks failure at the midpoint in time between the post-treatment nadir and the first of three consecutive PSA rises with two important conservative modifications. First, the requirement that the three rises have to be consecutive was relaxed. If three rises occurred with intervening stable PSA values, but the PSA never decreased, the patient was considered a failure at the midpoint in time between his first rise and the PSA immediately before the first rise. Second, for patients whose most recent PSA values were rising at the time of their last follow-up, but in whom failure had not occurred, follow-up time was truncated at the PSA immediately before the first rise. This technique reduces the "backdating" problem whereby patients are currently judged to be disease-free but later declared failures at a prior date. With this early censoring adjustment, patients with equivocal PSA values are not considered disease-free beyond the time of the nadir PSA value. Clinical relapse, death from disease, and secondary treatments were also considered treatment failures if they occurred before a PSA failure. The specific types of failure experienced by these patients appear in Table 2. All patients were entered into a data management tool to assist in record keeping (ProstaBase).

Statistical analysis was performed using software by SPSS (Chicago, IL). Regression analysis was performed on the D90 and D100 dose and on the V100 to identify a cutoff value that could predict for PSA-RFS. Kaplan-Meier curves were compared for each of these cutoff values to determine their significance (16). Once a cutoff value was determined, analysis was performed to validate the cutoff value for several typical clinical treatment approaches: isotope selection, TIPPB as monotherapy, TIPPB combined with EBT, and TIPPB performed with and without neoadjuvant hormones. In addition, the chi-square test and Cox regression analysis were used to test isotope activity, prostate size, CT/TRUS ratio, case order, and the addition of EBT to identify which factors may improve the implant quality (17). Prostate target volumes were divided into small, in-

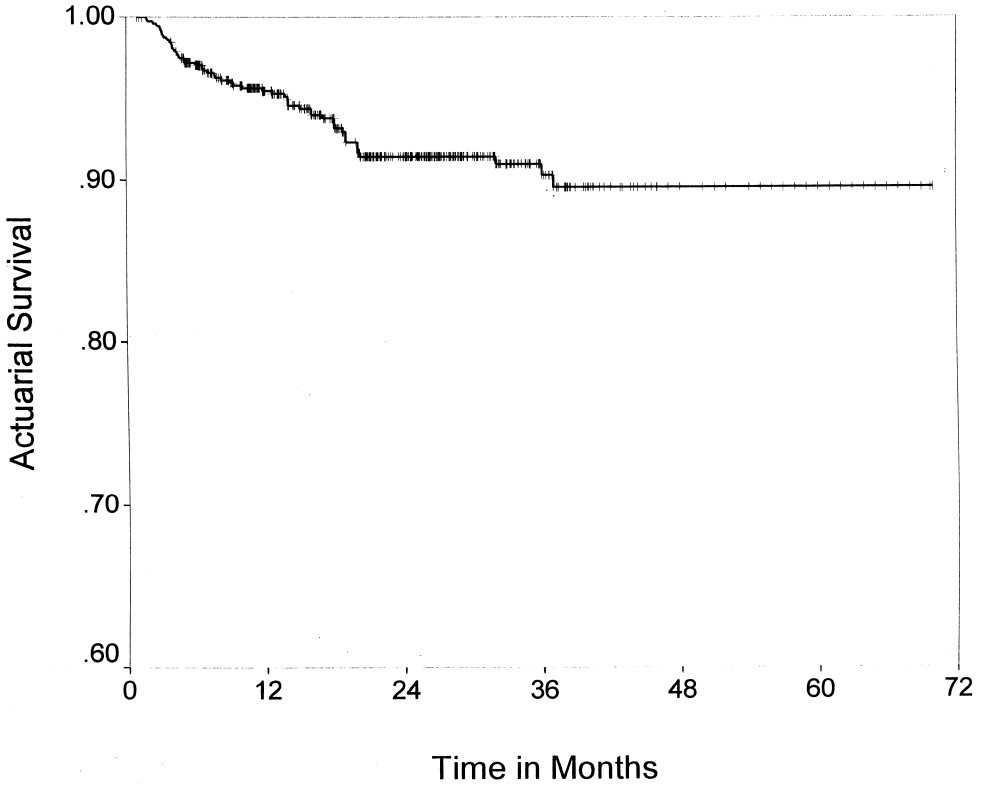

Fig. 1. Actuarial PSA relapse-free survival for all 719 patients.

Table 4. PSA relapse-free survival broken down by cutoff points based on CT scan–based postimplant dosimetry

Factor	% dose	4-yr. PSA-RFS	*n*	*p* value
V100				0.150
	<90%	89.4	353	
	≥90%	89.6	363	
D90				0.001
	<90%	80.4	216	
	≥90%	92.4	503	
D90				0.193
	<100%	87.1	305	
	≥100%	92.1	414	

% dose: Calculated dose relative to the prescribed dose.
D90: Minimum dose to 90% of the target volume.
V100: Percent of prescribed dose covering the target volume.

termediate, and large sizes, and individual seed activity was divided into low, medium, and high activity as outlined in Table 3a and 3b. The CT/TRUS volume ratio is defined as the postimplant CT scan volume relative to the ratio of the pre-implant TRUS volume.

RESULTS

The median follow-up for all 715 patients is 30 months (7–71 months), with a 4-year PSA-RFS of 89.5% (Fig. 1).

Table 5. Cox regression analysis to predict PSA relapse-free survival from all 717 patients

Factor	*p* value
Gleason score	0.0001
Pretreatment PSA value	0.0003
D90 dose	0.003
Stage	0.01
Addition of EBT	0.16
Isotope	0.24
Age	0.21

Table 2 presents the evidence of failure information from this study cohort.

Several cutoff values that were tested are presented in Table 4. The only dosimetric value with a significant difference in 4-year PSA-RFS was the D90 dose ≥90% of the prescribed dose (*p* value of 0.001, Fig. 2). Cox regression analysis identified that the 90% cutoff of the D90 dose, in addition to the Gleason score and pretreatment PSA value, was found significant for predicting PSA-RFS (Table 5).

The 90% cutoff of the D90 dose cutoff value was stratified by isotope, the addition of neoadjuvant hormone therapy, and the addition of EBT to assess PSA-RFS. A significant difference was identified for patients treated with I-125 ($p = 0.04$), Pd-103 ($p = 0.01$), TIPPB as monotherapy ($p = 0.001$), the addition of neoadjuvant hormones

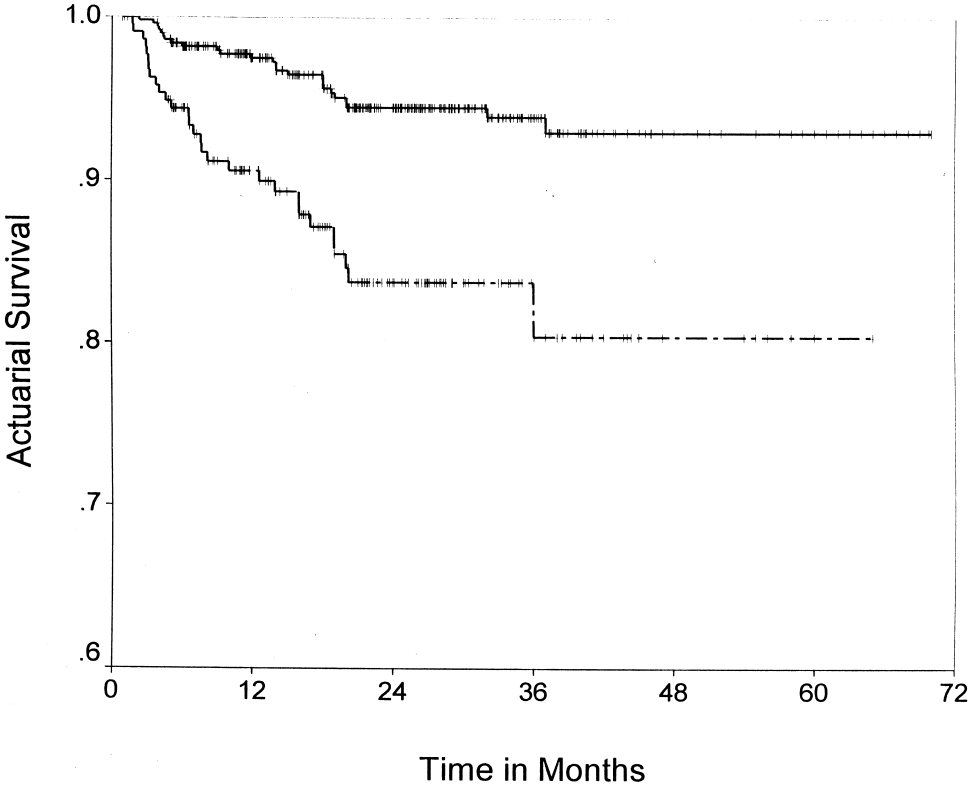

Fig. 2. Actuarial PSA relapse-free survival for patients divided by the dose cutoff value of the D90 dose <90%, ≥90% of the prescribed dose ($p = 0.0001$) (Solid line, D90 ≥90% of the prescribed dose; dashed line, D90 <90% of the prescribed dose).

Table 6. Actuarial 48-month PSA-RFS comparing the D90 dose <90% or ≥90% of the prescribed dose for Pd-103, I-125, TIPPB as monotherapy, and TIPPB combined with EBT

Factor	D90 dose	4-yr. PSA-RFS	*n*	*p* value
Palladium				.01
	<90	83.4	178	
	≥90	93.3	423	
Iodine				.04
	<90	63.8	38	
	≥90	93.0	80	
No hormones				.001
	<90	81.0	134	
	≥90	93.4	335	
Hormones				.001
	<90	79.3	82	
	≤90	92.5	168	
EBT + TIPPB				.13
	<90	87.9	77	
	≥90	88.23	122	
TIPPB alone				.001
	<90	74.3	136	
	≥90	94.6	384	

($p = 0.005$), and treated without hormones ($p = 0.001$) (Table 6, Figs. 3, 4, 5, 6). For patients treated with combination external beam radiation and TIPPB, there was no significant difference in outcome based on the D90 cutoff value ($p = 0.13$) (Fig. 7).

The mean CT/TRUS ratio was 1.43 (0.75–2.34). A significant correlation was identified by the Wilcoxon test associating a lower CT/TRUS ratio and patients treated with neoadjuvant hormone therapy ($p = 0.0001$) (18). Cox regression analysis was performed to assess which factors (isotope, case order, prostate volume, seed activity, the CT/TRUS ratio [for patients treated without hormones], and seed activity) may predict for a D90 dose ≥90% of the prescribed dose. Only a high CT/TRUS ratio (>1.5) was predictive for the D90 dose <90% of the prescribed dose (Table 7).

DISCUSSION

This study examined prospective data from patients treated with TIPPB that had postimplant CT-based dosimetric evaluations and found a significant dose-response relationship for the D90 dose that predicted for 4-year PSA-RFS. The identified cutoff dose was 90% of the D90 dose, 108 Gy for Pd-103 and 130 Gy for I-125 when TIPPB was performed without EBT.

The robustness of the D90 dose ≥90% of the prescribed dose was tested for typical clinical conditions common in the practice of TIPPB. Using the D90 cutoff value ≥90% of the prescribed dose, a significant difference in 4-year PSA-RFS was seen for patients treated with I-125, with Pd-103, with and without the addition neoadjuvant hormones, and

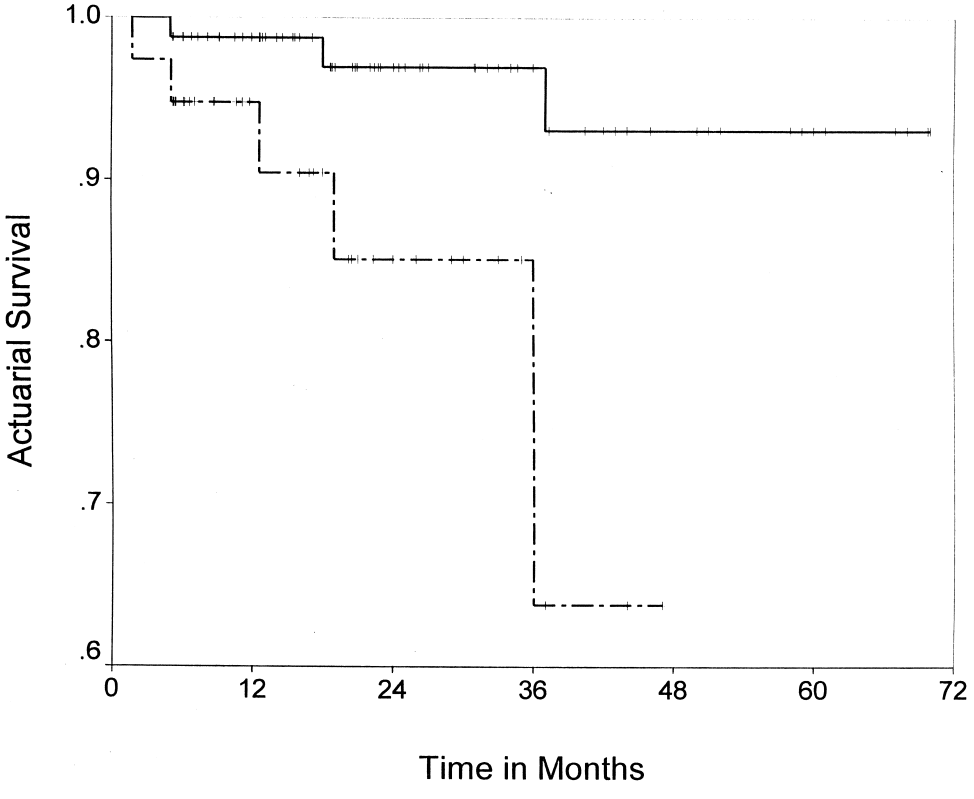

Fig. 3. Actuarial PSA relapse-free survival for patients treated with iodine divided by the dose cutoff value of the D90 dose <90%, ≥90% of the prescribed dose ($p = 0.04$) (Solid line, D90 ≥90% of the prescribed dose; dashed line, D90 <90% of the prescribed dose).

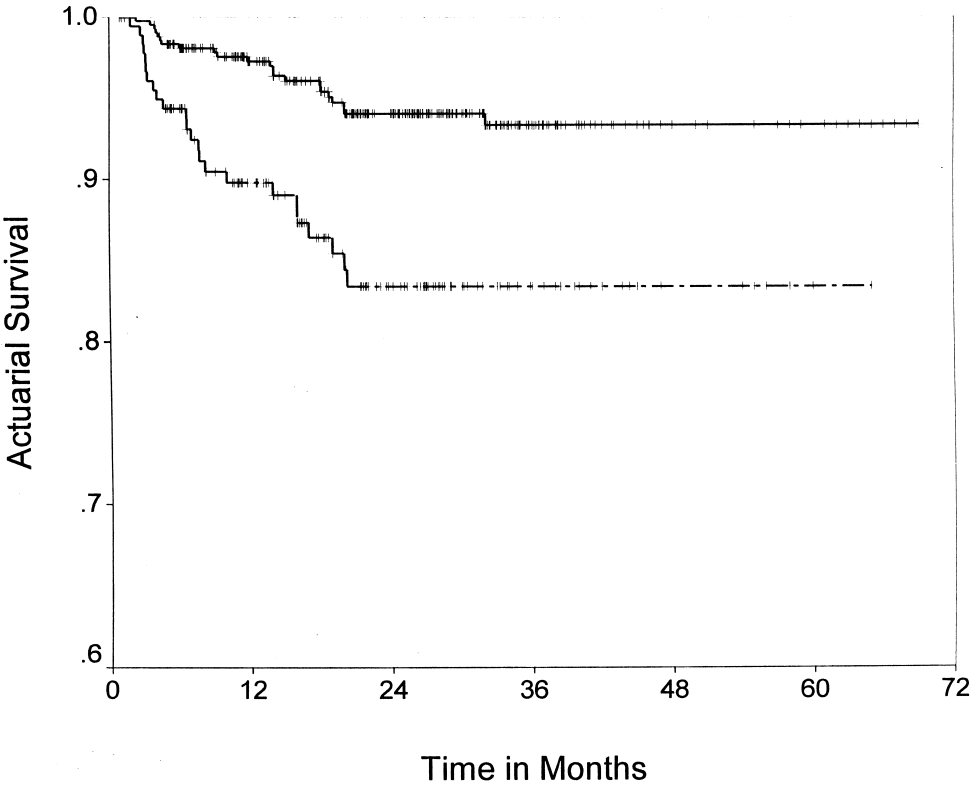

Fig. 4. Actuarial PSA relapse-free survival for patients treated with palladium divided by the dose cutoff value of the D90 dose <90%, ≥90% of the prescribed dose ($p = 0.01$) (Solid line, D90 ≥90% of the prescribed dose; dashed line, D90 <90% of the prescribed dose).

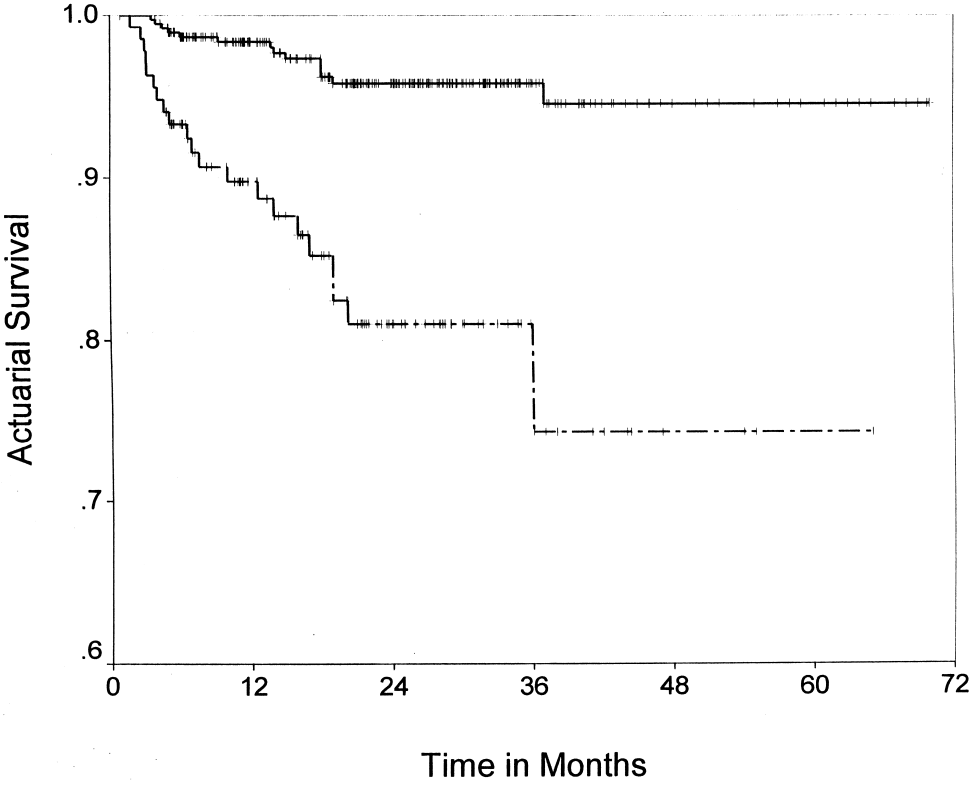

Fig. 5. Actuarial PSA relapse-free survival for patients treated with TIPPB as monotherapy divided by the dose cutoff value of the D90 dose <90%, ≥90% of the prescribed dose ($p = 0.001$) (Solid line, D90 ≥90% of the prescribed dose; dashed line, D90 <90% of the prescribed dose).

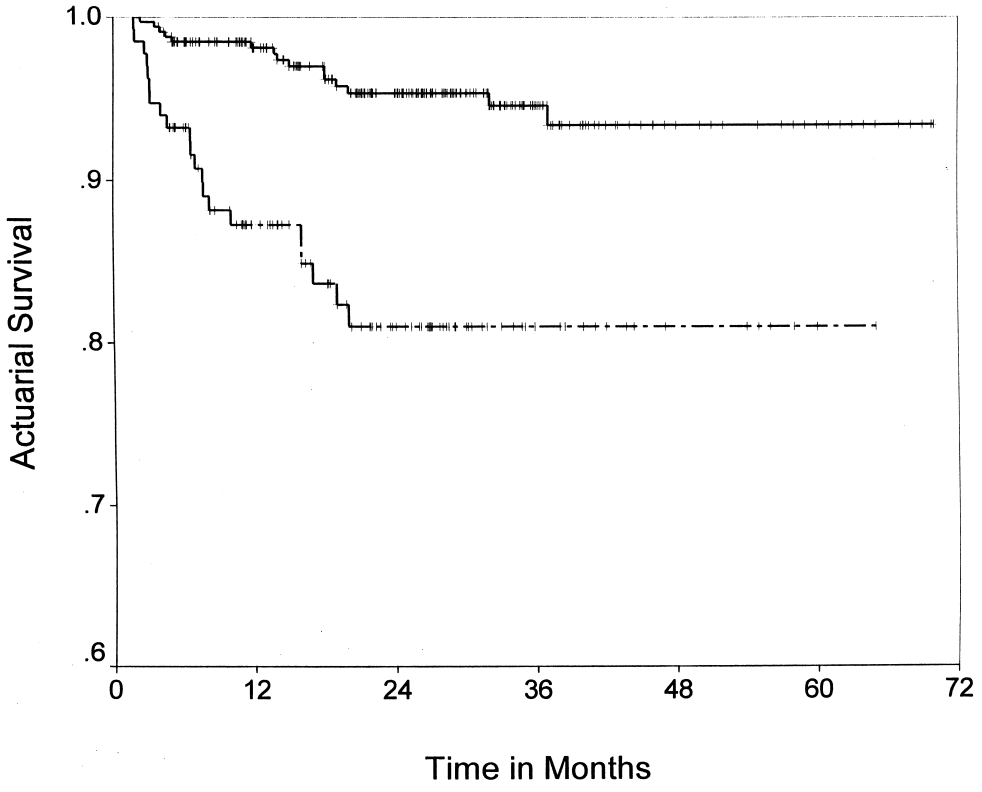

Fig. 6. Actuarial PSA relapse-free survival for patients treated without hormonal therapy divided by the dose cutoff value of the D90 dose <90%, ≥90% of the prescribed dose ($p = 0.001$) (Solid line, D90 ≥90% of the prescribed dose; dashed line, D90 <90% of the prescribed dose).

with TIPPB as monotherapy. There was no difference for patients treated with EBT and TIPPB.

The ABS recommends that CT scan–based postimplant dosimetry be mandatory for all patients undergoing TIPPB (9). The recommended parameters that should be considered for all patients include the following: the D80, D90, and D100 doses and the fractional volume that receives 200%, 150%, 100%, 90%, and 80% of the prescribed dose, respectively. Nonetheless, the ABS is currently unable to provide recommendations as to which parameters are important to define an adequate implant. In the current study, CT scan–based dosimetry was instituted at our facility in 1995 with only the D90, V100, and V150 doses calculated and, as such, only these parameters were analyzed in this study.

The prescribed implant dose for patients treated with TIPPB evolved from the suprapubic experience that used the original Anderson nomogram to 160 Gy for I-125 as measured by the matched peripheral dose (19). Manual measurements of the target, as well as other problems with the open surgical technique, limited the ability to deliver accurate doses to the prostate and precluded its continued use (7). Developments such as real-time intraoperative TRUS have improved our ability to more effectively deliver the prescribed dose to the prostate and, coupled with the closed surgical transperineal approach, is responsible for the resurgence of prostate brachytherapy as definitive therapy for localized prostate cancer. The original I-125 dose of 160 Gy was maintained until the AAPM in 1997 changed the calibration of the seeds from an air to water constant, effectively decreasing the prescribed dose to 144 Gy. Similarly, the original dose for Pd-103 of 115–120 Gy was calibrated based on its relative biologic equivalence to I-125 (20). In 1997, there was a change in the dosing of Pd-103 due to a change in the calibration standard, and again in early 2000 with the establishment of the NIST standard. While the ABS has recommended prescription doses for both I-125 and Pd-103, reported retrospective data collected during these changes need to identify specifically the prescribed doses used. In the current study, the delivered doses for I-125 and Pd-103 have been kept constant.

Data from the retropubic era identified that a dose of 140 Gy measured by the matched peripheral dose was a significant cutoff dose to predict for local recurrence-free survival (21). In a recent retrospective review from the retropubic implants using modern CT-based dosimetry, Nath *et al.* were able to establish other significant cutoff values that predict for clinical relapse-free survival (7). These include the total activity implanted, the activity per unit dimension, the V50, V100, and V150.

In patients undergoing TIPPB, Stock *et al.* identified a cutoff D90 dose response for I-125 similar to the current study (8). Their study reported a significant 4-year freedom from biochemical failure of 92% for implants with a D90 dose >140 Gy and 68% for a D90 dose <140 Gy ($p = 0.02$). Other studies have tried to correlate implant dosim-

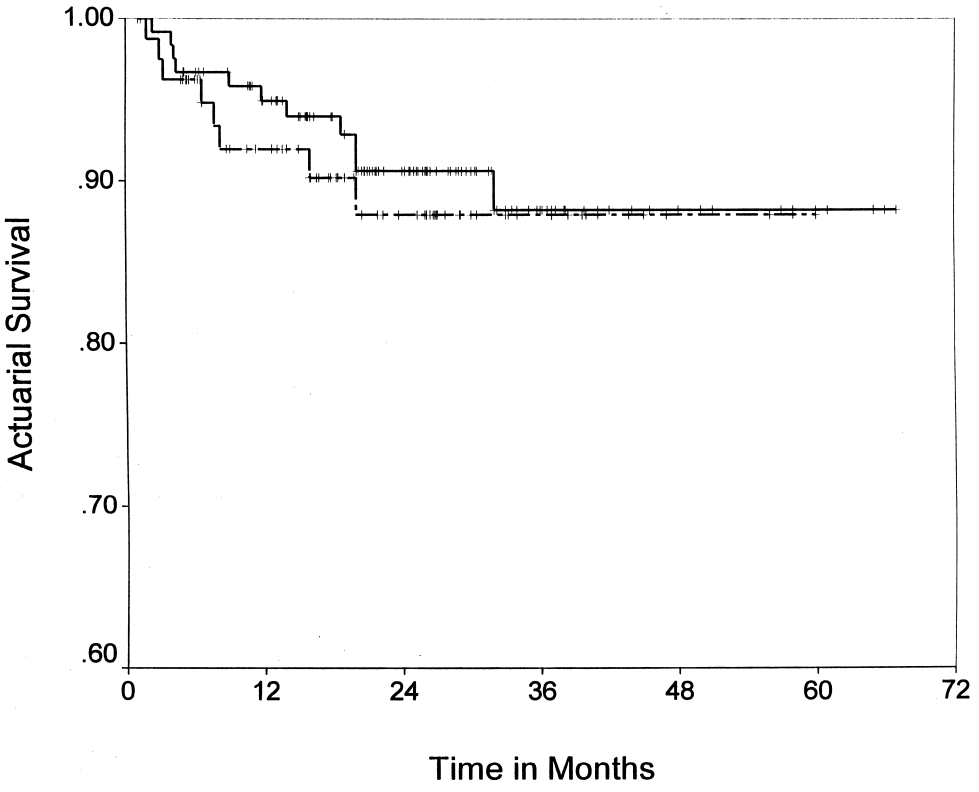

Fig. 7. Actuarial PSA relapse-free survival for patients treated with external beam irradiation and TIPPB divided by the dose cutoff value of the D90 dose <90%, ≥90% of the prescribed dose ($p = 0.13$) (Solid line, D90 ≥90% of the prescribed dose; dashed line, D90 <90% of the prescribed dose).

etry and toxicity, but not biochemical freedom from disease (22, 23).

It is estimated that up to 40,000 TIPPB procedures were performed in the United States in 2000. Vicini *et al.*, in a review of published TIPPB series, were unable to determine how postimplant dosimetry was performed in a majority of the peer-reviewed papers (24). Only 14% of the papers reviewed in that study performed CT-based dosimetry, although it is possible that other centers obtained postimplant CT scans but did not report on them. As it appears that postimplant dosimetry can have a profound effect on the reported outcome after TIPPB, all future studies reporting data on TIPPB should report dosimetry data along with clinical and biochemical outcome data (9).

Table 7. Cox regression analysis of implant-related factors that predict for a D90 dose <90% of the prescribed dose

Factor	*p* value
CT/TRUS volume ratio <1.5*	0.02
Addition of EBT	n.s.
Seed activity I-125	n.s.
Case order	n.s.
Isotope selection	n.s.
Prostate size	n.s.
Seed activity Pd-103	n.s.

* Postimplant CT scan target volume in cc/Preimplant ultrasound volume in cc.

Analyzing the postimplant CT scans of the prostate is difficult, and accurate delineation of the prostate tissue around the apex, the periprostatic muscle, vessels, or nerve bundles takes considerable time and practice. Technology to improve the mapping of the prostate may become available via fusion of magnetic resonant imaging studies, TRUS studies, and CT scan data. Until such time, the process of evaluating CT scan images of the prostate can be difficult and is subject to bias. Whereas the data presented in this study are subject to this same bias, our results are internally consistent and reflect a dose response in our patients that is consistent with others (7, 8). Further, the exercise of drawing prostate CTVs for calculating the dosimetry can provide important feedback to the physician on his or her technique. A study from Lee *et al.* demonstrated sequential improvement in TIPPB dosimetry with experience (25). Likewise, Prestidge *et al.* showed that case sequence was significant for predicting improved dosimetry (26). Centers that perform CT scan analysis may, by virtue of the exercise, potentially shorten the learning curve required to obtain good dosimetry with TIPPB. Having quality assurance programs that evaluate the CTV delineation on the CT scan remains an important part of the process. In the current study, CT-based dosimetry was initiated several years and several hundred patients into the development of the TIPPB program, which likely explains why case sequence was not predictive of the D90 dose.

As was pointed out by Stock et al. (8) and confirmed in the study by Nath *et al.* (7), an increase in the isotope activity per unit volume of the target improved the implant dosimetry and was found to be a significant cutoff point measuring clinical control of disease (7, 8). Therefore, the practice of putting "extra" seeds into the prostate will likely work to improve the D90 dose. Nonetheless, if perfect seed geometry could be achieved, the activity per unit volume should be lower without having a negative impact on the implant dosimetry. This would at the same time decrease the integral dose and hot areas within the prostate, potentially decreasing toxicity. We are currently examining the integral dose to the CTV expressed as the homogeneity index, which measures the V150 dose relative to the V100 dose to see if there is a relationship to the D90 dose and clinical outcome. Further study of the dose homogeneity within the CTV may in fact become an important dosimetric tool, not only to help predict adequate implants, but to help reduce toxicity.

There was no dose response found in those patients treated with EBT and TIPPB in this study. This is likely explained by the delivery of a uniform dose to the CTV by the EBT, in addition to the implant dose. In an earlier publication, we examined the difference in D90 dose between patients treated with EBT and TIPPB and TIPPB alone and found that there was no significant difference in PSA-RFS (27). There was also no difference in 5-year PSA-RFS in a matched pair analysis between TIPPB as monotherapy or TIPPB and EBT, even for patients with high-risk localized prostate cancer. Therefore, implant dosimetry appears to play a more important role for patients treated with TIPPB as monotherapy. If TIPPB techniques can assure acceptable dosimetry, there may in fact not be a need for combined EBT and TIPPB, as our data do not identify a significant difference for biochemical control when treatments are combined (27). We are currently updating our results examining the role of EBT and TIPPB in conjunction with the implant dosimetry. Nonetheless, prospective data will be needed to ultimately address the role of adding EBT to TIPPB for localized prostate cancer.

The CT/TRUS ratio reflects the difference between the preimplant CTV and the postimplant volume. Differences between these volumes are most likely attributable to prostate edema but may also include the inaccuracies of estimating the target volume from two different imaging modalities. In our study, the CT/TRUS ratio was significantly lower for patients treated with neoadjuvant hormones. This is likely due to additional shrinkage of the prostate gland between the preplanning time and the date of the postimplant CT scan. Patients treated with neoadjuvant hormones were excluded from the Cox regression analysis that identified that a high CT/TRUS ratio (>1.5) predicts for a poor D90 dose $<90\%$ of the prescribed dose ($p = 0.02$, Table 7). A high CT/TRUS ratio likely represents prostate edema after TIPPB and prostate edema appears to be universal to some degree for all patients treated with TIPPB (28). The "best" time for performing the postimplant CT scan to decrease the effects of edema is estimated at one month but may be variable (29). In the current study, the CT scans were obtained at a mean of 3.1 weeks, which may be too early for all of the prostate edema to resolve. As prostate edema may account for the high CT/TRUS ratio, which in turn accounts for a lower D90 dose, methods to deliver a prostate dose that compensate for edema will likely improve implant dosimetry. This could be performed by increasing the activity for I-125 by 5% or Pd-103 by 12% as proposed by Yue *et al.* (30). Using this approach of a single edema factor for each isotope implies that prostate edema is identical for all patients, which is unlikely. Increasing the total activity without knowing how much edema is present may compensate too much or too little for prostate volume changes. Other methods to account for edema include using intraoperative treatment planning or an edema nomogram after all needles are placed into the prostate, as it appears that edema develops acutely during the procedure (31). Further study is necessary to establish the appropriate time to obtain the postimplant CT scan and to evaluate different methods to account for edema.

If implant dosimetry can predict PSA-RFS, then it could possibly be used as a marker to determine the need for adjuvant therapy. Nonetheless, the role of adjuvant therapy after TIPPB has not been prospectively studied and remains controversial. Should patients who fail to meet the D90 dose cutoff be reimplanted or treated with adjuvant EBT? Currently we do not add adjuvant therapy to patients with implants that have a D90 dose $<90\%$. As a result of this study, we intend on studying the role of adjuvant therapy prospectively when dosimetry is poor.

In conclusion, this study demonstrated a significant dose response for the D90 dose $\geq 90\%$ of the prescribed TIPPB dose. This study, along with the Stock series (8), affirms the utility of postimplant dosimetry and, in particular, the predictive value of the D90 dose.

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