

Transperineal TRUS-guided prostate brachytherapy using loose seeds versus RAPIDStrand: A dosimetric analysis

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ABSTRACT **PURPOSE:** An analysis of the effect of stranded ¹²⁵I and loose (predominantly ¹⁰³Pd) sources on dosimetric outcomes of brachytherapy of the prostate. **METHODS AND MATERIALS:** Between September 1998 and December 2003, 473 patients were treated with brachytherapy for biopsy-proven carcinoma of the prostate. Of these, 337 (71%) procedures were performed using free seeds placed with a Mick applicator. Beginning in April 2002, a program of stranded ¹²⁵I sources (RAPIDStrand) was implemented; 136 (29%) patients were treated via this approach. Dosimetric variables were collected, as were events of urinary retention. **RESULTS:** Mean V100 values for the stranded ¹²⁵I approach were greater than those for free seeds ($p < 0.0005$), whether ¹²⁵I or ¹⁰³Pd ($p < 0.005$). Use of the strand was the most significant determinant of V100 of all variables examined. The stranded ¹²⁵I approach was also associated with higher mean D90 values and lower V150-urethral doses. **CONCLUSIONS:** Use of stranded ¹²⁵I was associated with superior dosimetric outcomes in this group of patients. © 2004 American Brachytherapy Society. All rights reserved.

Keywords: Prostate cancer; Brachytherapy; Dosimetry; V100; D90

Introduction

Prostate cancer is the most commonly diagnosed malignancy in American men, with an estimated 220,900 new cases in 2003 (1). Since the introduction of PSA screening, a growing number of patients will be diagnosed with organ-confined disease (2). The well-established treatment options for patients with early disease include radical prostatectomy, external beam radiation, or prostate brachytherapy (3). In the absence of a prospective randomized trial, retrospective studies have shown these therapies to provide comparable cure rates (4–11).

Transperineal prostate brachytherapy is a complex procedure that can be performed via a number of different approaches. This variety in technique arises from several

factors, including the method of seed delivery (applicator or pre-loaded needle), the nature of implanted sources (individual, stranded, linked), and the planned distribution of the radiation dose. Several seed delivery techniques and dosimetric philosophies are currently described in the literature (12–25).

Our program started in 1998, using a technique employing loose seeds delivered with the Mick applicator (Mick Nuclear, Bronx, NY). In March of 2002, we modified our technique to employ suture-embedded radioactive sources (RAPIDStrand; Oncura, Plymouth Meeting, PA) delivered by pre-loaded needles using the Utrecht University method described by Battermann *et al.* (25). The objective of this study is a comparison of the postprocedure dosimetric outcomes resulting from the two distinct approaches.

Methods and materials

Our ultrasound-guided transperineal prostate brachytherapy program began in September 1998. All cases involved replanned methodology, where a transrectal ultrasound

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(TRUS) volume study serves as the basis for a treatment plan, which is carried out in the operating room.

A total of 473 patients with localized prostate cancer were treated between September 1998 and December 2002.

Technique 1

The technique used from September 1998 through March 2002 employed loose seeds placed with a Mick applicator (26, 27). Three hundred thirty-seven patients were treated with this technique. Of 337 patients, 28 (8%) received loose ^{125}I (0.32 mCi/seed, 0.425 U) whereas 309 (92%) patients received ^{103}Pd [NIST 99, 2.15 U (28)]. The prescription dose was 145 Gy for ^{125}I patients treated with monotherapy and 120 Gy when combined with external beam radiation. Prescription doses for ^{103}Pd patients were 125 Gy (pre-NIST 99, 115 Gy) for monotherapy and 100 Gy (pre-NIST 99, 90 Gy) for the combined modality.

Technique 2

Beginning in April 2002, we changed our technique to employ ^{125}I RAPIDStrand as described by Battermann (25). RAPIDStrand consists of ^{125}I sources embedded in a dried vicryl suture material. Approximately 80–85% of the seeds placed in the prostate were stranded, while 15–20% were placed as loose seeds, primarily to cover the base and apex around the urethra. The sources consisted of 0.33/0.34 mCi, 0.425 U ^{125}I RAPIDStrand for both monotherapy and combined modality. One hundred thirty-six patients were treated by this technique. Planned doses were identical to that of the earlier, free seed ^{125}I cases.

In all cases a peripherally weighted plan was used, in which 75–80% of seeds were placed in the periphery of the prostate gland. The clinical target volume (CTV) included the prostate gland as defined by the TRUS volume study images and the planning target volume (PTV) included a 5 mm margin around the CTV with the exception of the posterior aspect of the prostate, where the margin was minimal.

Both techniques were similar with regard to the surgical implant. On the day of the implant patients were brought into the operating room and placed either under general or spinal anesthesia. Patients were positioned in the lithotomy position and the rectum was suctioned. The perineum was scrubbed with betadine and a Foley catheter was placed with 50 cc contrast instilled into the bladder. The Foley was clamped and a C-arm X-ray unit was positioned over the pelvis. The perineum was dried and a scrotal drape was attached. A TRUS probe was inserted into the rectum and attached to the stand and stepping unit along with the template. Once the images reproduced the original volume study images, that is, aligning the prostate gland with the previous prostate volume study images, insertion of sources according to the pre-plan commenced. Extra seeds were placed at the end of the procedure at the discretion of the radiation oncologist. The Foley catheter remained in place until the completion of a CT scan

either the same day or the morning following the procedure. As recommended by the American Brachytherapy Society (29), postimplant dosimetric parameters were quantified including V100, V150 prostate, V150 urethra, and D90.

Differences between the dosimetric parameters using loose seeds and RAPIDStrand were evaluated using a general linear model method (GLM; SPSS Inc., Chicago, IL), specifically a linear regression analysis solving for V100.

Results

Patient characteristics are outlined in Table 1. Given the relatively short follow-up interval, disease-free and overall survival data will not be addressed in this article.

Dosimetric outcomes as determined by 24-h CT-based postplan analysis are listed in Table 2. The observed V100 was significantly greater for the ^{125}I RAPIDStrand patients (mean, 92.5%; $n = 136$) than for the loose seed patients (mean, 88.4%; $n = 336$), $p < 0.005$ by independent samples t-test (Fig. 1).

The mean V100 for RAPIDStrand (92.5%) was significantly greater than both loose ^{125}I (78.8%) and loose ^{103}Pd (89.3%) seeds, $p < 0.005$ by F-test (Fig. 2).

Linear regression analysis solving for V100 using strand versus no strand, isotope (^{125}I versus ^{103}Pd), and type of therapy (implant combined with external beam versus implant monotherapy) revealed RAPIDStrand as the most powerful determinant of V100 in this series ($p < 0.005$, partial $h^2 = 0.12$, Table 3). Preimplant prostate volume, administration of antiandrogen therapy, and age were included in the regression and found to be insignificant.

The mean D90 for RAPIDStrand cases was significantly greater than that of ^{103}Pd free seed cases, whereas the mean V150-prostate and V150-urethra were lower (Table 2). No data on these parameters was available for the ^{125}I free seed cases.

Table 1
Patient characteristics

Presenting serum PSA	n (%)	Gleason sum	n (%)
0–9.9 ng/ml	409 (86)	2–4	3 (1)
10–19.9 ng/ml	48 (10)	5–6	322 (68)
>20 ng/ml	13 (3)	7	126 (27)
none	3 (1)	8–10	19 (4)
		none	3 (1)
Clinical stage			n%
T1a/b			1 (–)
T1c			257 (54)
T2a			176 (37)
T2b			17 (4)
T2c			10 (2)
T3a			4 (1)
none			8 (2)

Table 2
Dosimetric parameters by treatment type

	n	Mean V100 (SD)	Mean D90 ¹ (SD)	Mean V150 (SD)	Mean V150-U (SD)
Free ¹⁰³ Pd	309	89.3 (7.7)	103.4 ² (17.2)	59.8 (12.3)	9.8 (15.0)
Free ¹²⁵ I	28	78.8 (12.9)	not done	not done	not done
RAPID Strand ¹²⁵ I	136	92.5 ³ (5.9)	108.8 ³ (13.0)	46.5 ³ (12.1)	3.6 ³ (8.6)

¹ Normalized to prescription dose.

² n = 284.

³ p < 0.005 vs. other treatment(s).

The rate of retention for free ¹²⁵I was 1/27 (3.6%), for free ¹⁰³Pd 30/309 (9.7%), and for RAPIDStrand 4/136 (2.9%). These differences were significant (exact p = 0.01).

Discussion

Several authors have compared postimplant dosimetry using loose versus suture-embedded seeds. Battermann (25) reported the Utrecht University experience using loose and stranded ¹²⁵I. Based on a series of 249 patients, he noted an increase in mean coverage from 55–68% of the prostate volume with loose seeds to 90% with RAPIDStrand. In addition, the reported seed migration dropped from 10% to 1–3% following the implementation of stranded seeds.

Lee *et al.* (17) used loose sources for 3 years before changing to embedded ¹²⁵I seeds. Patients treated with suture-embedded seeds were found to have significantly improved dosimetric coverage of the prostate gland. In that series, the observed mean V100 was 94.1% versus 86.54% for the patients treated with loose seeds (p < 0.001).

Fagundes *et al.* (30) reported dosimetric results from Porto Alegre, Brazil using the Mick applicator with loose ¹²⁵I and RAPIDStrand. They noted an improvement in

the V100 from 82.8% with loose seeds to 93.6% with RAPIDStrand.

The present series revealed a statistically significant improvement in the dosimetry when RAPIDStrand was used. The observed V100 improved from 88.4% to 92.5% based on postimplant CT scan done within 24 h following implementation of RAPIDStrand. Since this series includes patients treated by free ¹²⁵I, free ¹⁰³Pd, and stranded ¹²⁵I, we are able to show a greater V100 for RAPIDStrand cases than both free ¹⁰³Pd and free ¹²⁵I cases. Likewise, upon regression analysis, while both isotope and implant dose (for boost or primary therapy) are significant factors for V100, the use of RAPIDStrand retains significance as a predictor in the final model (Table 3).

Patients implanted by the RAPIDStrand technique also experienced less acute urinary retention: 8.9% with loose seeds versus 2.9% with RAPIDStrand (p = 0.01). This decline in urinary retention correlated with a lower V150 urethra, 9.7% versus 2.8%. However, given the lack of detailed dosimetry data for the early loose ¹²⁵I cases, we are unable to attribute this difference unequivocally to RAPIDStrand, as isotope selection may play an important role. The same is true of D90, V150 prostate, and V150 urethra,

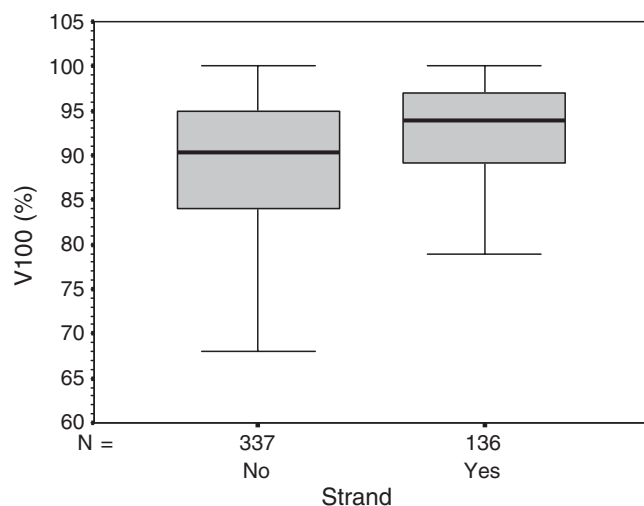


Fig. 1. Boxplot of V100 by strand vs. no strand.

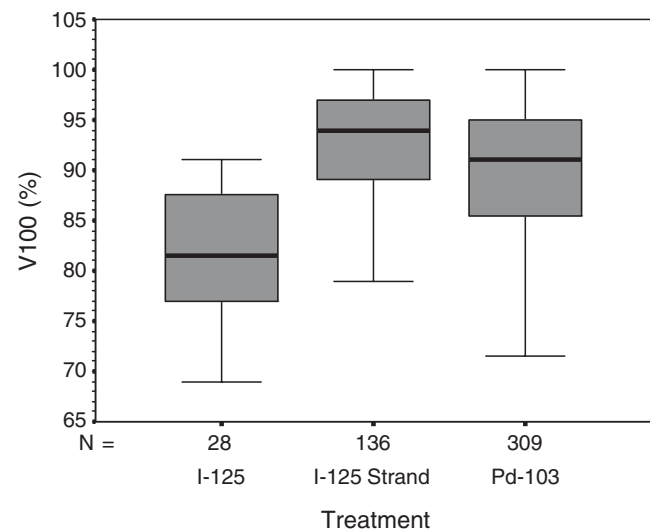


Fig. 2. Boxplot of V100 by isotope and strand.

Table 3
Best fit linear regression for V100

	P	Effect size ¹
¹⁰⁰ Pd vs. ¹²⁵ I	<0.005	0.08
Primary vs. boost	<0.005	0.03
RAPID Strand vs. loose	<0.005	0.12
Hormone treatment	0.4	n/a
Pre-implant prostate volume	0.9	n/a
Age	0.5	n/a

¹ Partial η^2 .

where significant differences were also noted (Table 2). These data support the notion of improved dose homogeneity within the prostate gland with RAPIDStrand over free seed techniques, although isotope selection cannot be ruled out as a determinant.

Other authors have compared ¹⁰³Pd versus ¹²⁵I (14, 31). Even though it has been theorized that ¹⁰³Pd might be a better choice for high-grade lesions and ¹²⁵I for lower grade ones, Wallner et al. (31) and Cha et al. (14) observed similar biochemical control rates for the two isotopes. Fuller and Koziol (32) evaluated several factors using V100 as an indicator of implant quality. They found stranded source type and ¹²⁵I to be significant predictors of a higher V100, resulting in a better implant.

An additional factor not well described in the literature is the use of extra seeds used to fill in “cold spots” at the completion of the implant. In the loose seed era, we customarily used extra seeds in about 10–15% of the cases based on cold spots on fluoroscopy due to intraprostatic seed migration as well as peripheral seeds migrating away from the prostate gland. In the RAPIDStrand era, it is unusual for us to use added seeds since we have rarely observed seed migration within or outside the prostate (less than 2%).

It is possible that a “learning curve” contributed to the differences in outcome, especially with reference to free ¹²⁵I, as improved outcomes mirrored the temporal sequence of free ¹²⁵I, free ¹⁰³Pd, and RAPIDStrand ¹²⁵I techniques.

In summary, using V100 as an indicator of implant quality for our patients, this RAPIDStrand approach demonstrates an advantage over the standard, free-seed method previously used. This technique has also been associated with a lower urinary retention rate, although isotope selection may also play an important role.

References

- [1] American Cancer Society. Cancer facts and figures. Atlanta: American Cancer Society; 2003.
- [2] Amling CL, Blute ML, Lerner SE, et al. Influence of prostate-specific antigen testing on the spectrum of patients with prostate cancer undergoing radical prostatectomy at a large referral practice. *Mayo Clin Proc* 1998;73:401–406.
- [3] Bahnon RR, Hanks GE, Huben RP, et al. NCCN Practice Guidelines for Prostate Cancer. *Oncology (Huntington)* 2000;14(11A):111–119.
- [4] Blasko JC, Grimm PD, Sylvester JE, et al. Palladium-103 brachytherapy for prostate carcinoma. *Int J Radiat Oncol Biol Phys* 2000;46:839–850.
- [5] Catalona WJ, Smith DS. Cancer recurrence and survival rates after anatomic radical retropubic prostatectomy for prostate cancer: Intermediate-term results. *J Urol* 1998;160:2428–2434.
- [6] Ragde H, Grado GL, Nadir BS. Brachytherapy for clinically localized prostate cancer: Thirteen-year disease-free survival of 769 consecutive prostate cancer patients treated with permanent implants alone. *Arch Esp Urol* 2001;54:739–747.
- [7] Grimm PD, Blasko JC, Sylvester JE, et al. Ten-year biochemical (prostate-specific antigen) control of prostate cancer with ¹²⁵I brachytherapy. *Int J Radiat Oncol Biol Phys* 2001;51:31–40.
- [8] Han M, Partin AW, Piantadosi S, et al. Era-specific biochemical recurrence-free survival following radical prostatectomy for clinically localized prostate cancer. *J Urol* 2001;166:416–419.
- [9] Sharkey J, Cantor A, Solc Z, et al. Brachytherapy versus radical prostatectomy in patients with clinically localized prostate cancer. *Curr Urol Rep* 2002;3:250–257.
- [10] Wallner K, Roy J, Harrison L. Tumor control and morbidity following transperineal ¹²⁵I implantation for stage T1/T2 prostatic carcinoma. *J Clin Oncol* 1996;14:449–453.
- [11] 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* 1998;41:491–500.
- [12] Bice WS Jr, Prestidge BR, Grimm PD, et al. Centralized multi-institutional postimplant analysis for interstitial prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 1998;41:921–927.
- [13] Butler WM, Merrick GS, Dorsey AT, et al. Comparison of dose length, area, and volume histograms as quantifiers of urethral dose in prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;48:1575–1582.
- [14] Cha CM, Potters L, Ashley R, et al. Isotope selection for patients undergoing prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 1999;45:391–395.
- [15] Horwitz EM, Mitra RK, Uzzo RG, et al. Impact of target volume coverage with Radiation Therapy Oncology Group (RTOG) 98-05 guidelines for transrectal ultrasound guided permanent ¹²⁵I prostate implants. *Radiother Oncol* 2003;66:173–179.
- [16] Lee WR, deGuzman AF, Bare RL, et al. Postimplant analysis of transperineal interstitial permanent prostate brachytherapy: Evidence for a learning curve in the first year at a single institution. *Int J Radiat Oncol Biol Phys* 2000;46:83–88.
- [17] Lee WR, deGuzman AF, Tomlinson SK, et al. Radioactive sources embedded in suture are associated with improved postimplant dosimetry in men treated with prostate brachytherapy. *Radiother Oncol* 2002;65:123–127.
- [18] Merrick GS, Butler WM, Lief JH, et al. Temporal resolution of urinary morbidity following prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;47:121–128.
- [19] Merrick GS, Butler WM, Dorsey AT, et al. Potential role of various dosimetric quality indicators in prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 1999;44:717–724.
- [20] Merrick GS, Butler WM, Dorsey AT, et al. Prostatic conformal brachytherapy: ¹²⁵I/¹⁰³Pd postoperative dosimetric analysis. *Radiat Oncol Investig* 1997;5:305–313.
- [21] Merrick GS, Butler WM, Dorsey AT, et al. Influence of timing on the dosimetric analysis of transperineal ultrasound-guided, prostatic conformal brachytherapy. *Radiat Oncol Investig* 1998;6:182–190.
- [22] Ove R, Wallner K, Badiozamani K, et al. Standardization of prostate brachytherapy treatment plans. *Int J Radiat Oncol Biol Phys* 2001;50:257–263.
- [23] Stock RG, Stone NN, Tabert A, et al. A dose–response study for ¹²⁵I prostate implants. *Int J Radiat Oncol Biol Phys* 1998;41:101–108.
- [24] Potters L, Huang D, Fearn P, et al. The effect of isotope selection on the prostate-specific antigen response in patients treated with permanent prostate brachytherapy. *Brachytherapy* 2003;2:26–31.

- [25] Battermann JJ. I-125 implantation for localized prostate cancer: The Utrecht University experience. *Radiother Oncol* 2000;57:269–272.
- [26] Grado GL, Larson TR, Balch CS, et al. Actuarial disease-free survival after prostate cancer brachytherapy using interactive techniques with biplane ultrasound and fluoroscopic guidance. *Int J Radiat Oncol Biol Phys* 1998;42:289–298.
- [27] Sharkey J, Chovnick SD, Behar RJ, et al. Evolution of techniques for ultrasound-guided ^{103}Pd brachytherapy in 950 patients with prostate cancer. *Tech Urol* 2000;6:128–134.
- [28] Williamson JF, Coursey BM. Recommendations of the American Association of Physicists in Medicine on ^{103}Pd interstitial source calibration and dosimetry: Implications for dose specification and prescription. *Med Phys* 2000;27:634–642.
- [29] Nag S, Beyer D, Friedland J, et al. American Brachytherapy Society (ABS) recommendations for transperineal permanent brachytherapy of prostate cancer. *Int J Radiat Oncol Biol Phys* 1999;44:789–799.
- [30] Fagundes MA, Leick M, Sabrito C, et al. Permanent prostate gland seed implant: A dosimetry report of the Porto Alegre, Brazil experience comparing two different brachytherapy techniques. *Radiother Oncol* 2003;66(Suppl. 95):S33.
- [31] Wallner K, Merrick G, True L, et al. I-125 versus Pd-103 for low-risk prostate cancer: Morbidity outcomes from a prospective randomized multicenter trial. *Cancer J* 2002;8:67–73.
- [32] Fuller DB, Koziol JA. Prostate brachytherapy seed migration and dosimetry: Analysis of potential predictive factors. *Brachytherapy* 2003;2:47.