

## RADIOACTIVE SEED MIGRATION TO THE CHEST AFTER TRANSPERINEAL INTERSTITIAL PROSTATE BRACHYTHERAPY: EXTRAPROSTATIC SEED PLACEMENT CORRELATES WITH MIGRATION

JEFFREY S. ESHLEMAN, M.D.,\* BRIAN J. DAVIS, M.D., PH.D.,\* THOMAS M. PISANSKY, M.D.,\*  
TORRENCE M. WILSON, M.D.,† MICHAEL G. HADDOCK, M.D.,\* BERNARD F. KING, M.D.,‡  
CHARLES H. DARBY, M.S.,§ WAYNE N. LAJOIE, B.S.,\* AND ANN L. OBERG, PH.D.§

\*Division of Radiation Oncology, Departments of †Urology and ‡Diagnostic Radiology, and §Division of Biostatistics, Mayo Clinic, Rochester, MN

**Purpose:** To examine the incidence of seed migration detected on chest X-ray and to identify the predictors associated with its occurrence.

**Methods and Materials:** Between May 1998 and April 2000, 102 patients underwent permanent prostate brachytherapy at our institution and 100 were eligible for the study. Chest X-rays obtained at follow-up were examined for the number and location of seeds. The patient and treatment variables potentially associated with the occurrence and number of seed migrations were analyzed.

**Results:** One or more seeds were identified on the chest X-rays of 55 (55%) of 100 patients. The mean number of intrathoracic seeds in patients with migration was 2.2 (range, 1–10), and the proportion of seeds that migrated to the thorax was 0.98%. The rate of extraprostatic seeds planned was 43.9%, and postimplant CT identified 37.9% in such a location. The number of seeds planned for extraprostatic placement and below the apex were statistically significant ( $\alpha = 0.05$ ) predictors in univariate logistic analysis. Multivariate analysis revealed the planned number of extraprostatic seeds as the only statistically significant predictor ( $p = 0.04$ ).

**Conclusion:** Extraprostatic placement of loose seeds is associated with an increased likelihood for, and frequency of, seed migration to the thorax. Nonetheless, the small proportion of implanted seeds that migrated ( $\leq 1\%$ ) is highly unlikely to have significant dosimetric consequences. © 2004 Elsevier Inc.

Brachytherapy,  $^{125}\text{I}$ , Migration, Prostatic neoplasms, Radiotherapy.

### INTRODUCTION

In 2003, an estimated 220,900 men in the United States were diagnosed with adenocarcinoma of the prostate and 28,900 men died of this cancer (1). With the advent of prostate-specific antigen screening, most prostate cancer diagnoses are made in the early stages. An increasingly used option in the management of early-stage prostate cancer is transperineal interstitial permanent prostate brachytherapy (TIPPB) (2).

A unique property of TIPPB is the possibility of radioactive seed migration. In 1988, Hempel *et al.* (3) reported on a patient who underwent  $^{125}\text{I}$  interstitial therapy for carcinoma of the anus and was later found to have metallic seeds on chest X-ray (3). Subsequently, Steinfeld *et al.* (4) reported chest migration of a radioactive seed after TIPPB. Gupta *et al.* (5) later reported seed migration to the chest from various anatomic sites after interstitial brachytherapy.

In recent years, the increased use of TIPPB has led to multiple reports of radioactive seed migration to the chest (4, 6–13). Published rates, as summarized in Table 1, range from 0.6% to 29% of patients with one or more seeds found on a postimplant chest X-ray (CXR). Published patient and treatment parameters influencing the incidence and rate of seed migration include the use of Vicryl sutures, number of seeds implanted, planning volume, and number of loose seeds placed (7, 10).

The basis of radioactive seed migration seems clear; the prostatic capsule has a rich venous plexus with vessels large enough to accommodate seeds. Seeds placed extraprostatically have access to this plexus and often migrate away from their intended position via access to the venous circulation. Through the venous pathway, seeds migrate through the inferior vena cava, right chambers of the heart and into the pulmonary circulation. Because of their size and rigid-

Reprint requests to: Brian J. Davis, M.D., Ph.D., Division of Radiation Oncology, Mayo Clinic, 200 First St. SW, Rochester, MN 55905. Tel: (507) 284-3191; Fax: (507) 284-0079; E-mail: davis.brian@mayo.edu

Originally presented at the 43rd Annual Meeting of the American Society for Therapeutic Radiology and Oncology, November 2001.

Received Jun 26, 2003. Accepted for publication Oct 15, 2003.

Table 1. Chest migration in reported TIPPB series

Study	Isotope	Patients with seed migration to chest (%)	Rate of seed migration to chest (%)	Maximum seeds to migrate in 1 patient (n)
Present study	$^{125}\text{I}$ and $^{103}\text{Pd}$	55.0% (55/100)	0.98% (119/12,135)	10
Grimm <i>et al.</i> (12)	$^{125}\text{I}$ and $^{103}\text{Pd}$	17.6% (39/221)	Not reported	3
Merrick <i>et al.</i> (7)	$^{125}\text{I}$ (Rapid STRAND in periphery)	21.4% (18/84)	0.18% (24/13,467)	Not reported
	$^{103}\text{Pd}$	22.2% (16/72)	0.28% (29/10,338)	Not reported
	Overall	21.8% (34/156)	0.22% (53/23,805)	Not reported
Nag (8)	$^{103}\text{Pd}$	17.8% (19/107)	0.30% (32/10,612)	2
Older (13)	$^{103}\text{Pd}$	29.0% (32/110)	Not reported	4
Steinfeld <i>et al.</i> (4)	$^{125}\text{I}$	20.0% (1/5)	0.80% (5/600)	5
Tapen <i>et al.</i> (10)	$^{125}\text{I}$ (Rapid STRAND in periphery)	0.7% (1/143)	Not reported	2
	$^{125}\text{I}$ loose	10.0% (1/10)	Not reported	Not reported
	$^{103}\text{Pd}$	11.0% (15/126)	Not reported	Not reported
	Overall	5.9% (17/289)	Not reported	Not reported

Abbreviation: TIPPB = transperineal interstitial permanent prostate brachytherapy.

ity, seeds lodge in the end arterioles of the pulmonary system where, owing to their metallic content, they can be easily visualized by CXR.

To date, no untoward clinical consequences have been reported when pulmonary embolization has occurred (4, 6–13). However, it is conceivable that seeds could migrate or become entrapped in other organ systems. In this regard, autopsy-documented evidence has recently been published of seeds lodged in the right ventricle of the heart (14) and in a coronary artery as visualized by angiography (15).

Other potential consequences of seed migration include dosimetric consequences (16). Seeds lost to migration detract from the overall dose meant to cover the planning target volume. Merrick *et al.* (7) reported that pulmonary seed embolization accounted for only 10% of the seeds absent after orthogonal films were taken of the pelvis after implantation. Thus, CXR detection alone may significantly under represent the total seed loss from the target volume.

Migration rates have been linked to technical differences in TIPPB, which have been previously reviewed (17). Many institutions perform a modified peripheral loading technique in which loose seeds are placed. Most seeds are placed in the periphery of the gland to administer a homogenous dose and limit severe overdosing to the urethra. A typical margin of 3–5 mm is planned around the prostate (18) to account for extraprostatic tumor extension (19, 20), the accuracy of delivering the radiation dose to the target volume (21, 22), and the accuracy of the imaging technology used in the procedure. Other factors influencing migration rates may include both patient and tumor characteristics. The purpose of this study was to examine both clinical and treatment-related factors associated with migration of seeds to the thorax.

## METHODS AND MATERIALS

### Patient characteristics

The patient characteristics are given in Table 2. Between May 1998 and April 2000, 102 patients with Stage T1-T2 prostate cancer underwent TIPPB at our institution of whom 100 were included in this study. All patients underwent transrectal ultrasound (TRUS)-based planning using a modified peripheral loading technique and loose seed placement. Post-TIPPB dosimetry was evaluated by CT within 30 days after the date of the procedure. PA and lateral CXRs obtained at follow-up were examined for the number and location of seeds. Patient and treatment variables potentially associated with the occurrence and number of seed migrations were analyzed.

### Preimplant planning

All patients underwent TRUS-based preplanning using the Theraplan Plus 3.0 system (Theratronics, MDS Inc., Toronto, Ontario, Canada). The planning target volume was created by placing a 3–5-mm margin around the prostate, except in the posterior and superior directions. Posteriorly, in proximity to the rectum, and superior to the bladder base, a smaller margin was used.

### TIPPB procedure and postimplant CT scanning

The TIPPB procedure has been previously described (23); it includes the use of a Mick applicator and a modified peripheral loading technique. Ninety-seven patients underwent  $^{125}\text{I}$  implantation and three underwent  $^{103}\text{Pd}$  implantation. Ninety-nine patients were treated with TIPPB as monotherapy, and one received combination external beam radiotherapy and TIPPB. All patients were admitted postoperatively to the hospital overnight, and a Foley catheter was placed in each. Urine and Foley catheter bags were inspected and surveyed for displaced seeds. Patients rou-

Table 2. Patient and treatment characteristics

Characteristic	Patients (n)	Mean (range)
Age (y)		68.8 55–70
Tumor stage (1997 AJCC)		
T1c	63 (63)	
T2a	35 (35)	
T2b	2 (2)	
Pretreatment PSA (ng/mL)		6.3 0.7–16.3
PSA (ng/mL)		
0.0–4.0	24 (24)	
4.1–10.0	64 (64)	
>10.0	12 (12)	
Gleason score		6 (4–7)
4–5	15 (15)	
6–7	85 (85)	
Pretreatment ultrasound volume (cm <sup>3</sup> )		43.3 (16–98)
Postimplant CT volume (cm <sup>3</sup> )		56.7 (20–124)
Time to postimplant CT (days)		5.7 (0–57)
Radioisotope (Gy)		
<sup>125</sup> I	97 (97)	
<sup>103</sup> Pd	3 (3)	
Seeds planned (n)		113.1 (58–192)
Seeds placed (n)		123.8 (60–214)
Needles implanted (n)		30.3 (18–50)
mCi per source ( <sup>125</sup> I only)		0.4 (0.3–0.5)
Total mCi implanted ( <sup>125</sup> I only)		48.1 (22.2–82.2)

Abbreviations: AJCC = American Joint Committee on Cancer; PSA = prostate-specific antigen.

Data in parentheses are percentages, unless otherwise noted.

tinely underwent postimplant CT scanning within 2 days after their procedure. The prostate was contoured on the CT image by the treating radiation oncologist. Postimplant dosimetric analysis was performed according to the American Brachytherapy Society recommendations (24).

#### Statistical analysis

The preplans were reviewed and the following information was recorded: preimplant prostate size in cubic centimeters as determined by TRUS planimetry and prolate spheroid calculation, number of needles planned, total number of seeds planned and placed, and postimplant prostate size in cubic centimeters by CT contouring. Preplanning ultrasonography and postimplant CT were then carefully reviewed for peripheral and extraprostatic seed placement. Extraprostatic seed placement was defined as any digitally reconstructed seed falling completely outside the CT-contoured prostatic capsule or planimetric margin. Peripheral seed placement was defined as any extraprostatic seed or any digitally reconstructed seed falling on the CT-contoured prostatic capsule or margin. Seeds planned and placed above the base and below the apex were analyzed separately as well as included in the extraprostatic group. An example of a preplan TRUS image identifying

extraprostatic and peripherally labeled digitally reconstructed seeds is shown in Fig. 1.

All patients whose records were used in this analysis had previously provided consent for use of their records in retrospective medical research. Univariate analyses were prepared and examined to ascertain any transformations that would be necessary before subsequent model building ensued. Predictors were transformed using the natural logarithm function to reduce skewness of distribution if appropriate. Univariate and multivariate logistic models of occurrence of seed migrations were performed.

## RESULTS

Of the 102 patients whose medical records were considered for use in this study, 1 did not have a postoperative CXR and 1 refused research authorization. Thus, 100 patients with one or more postimplant CXR were evaluated. One or more seeds were identified on the CXRs of 55 (55%) of 100 patients. A total of 119 (0.98%) of 12,135 seeds implanted were identified on CXR. The mean number of intrathoracic seeds in patients with migration was 2.2 (median, 2; range, 1–10). The distribution of seeds on CXR (Table 3) was 11 right upper lobe, 3 right middle lobe, 74 right lower lobe, 3 left upper lobe, and 26 left lower lobe and 2 autopsy proven seeds in the right cardiac ventricle. The proportion of extraprostatic seeds planned was 43.9%, and 37.9% were actually placed in an extraprostatic location as ascertained by postoperative CT imaging (Table 4). The number of seeds planned for extraprostatic placement and inferior to the apex was a statistically significant predictor of seed migration in univariate logistic analyses at the  $\alpha = 0.05$  level (Table 5).

Three additional predictors were suggestive of significance at or below  $\alpha = 0.14$ . These included the number of seeds planned for implantation above the prostate base, number of peripheral seeds for implantation, and natural log of time from the procedure to the first CXR. All five predictors were tested in multiple logistic models via a stepwise model building process. *A priori*, a four-predictor model was also considered on the basis of our knowledge. The predictors considered were the number of seeds planned for implantation at the prostate periphery and below the apex, the total number of seeds planned for placement, and the interval (expressed as natural logarithm [LnT]) from TIPPB until the first CXR. Subsequent evaluation indicated that the multiple predictor models were unstable and provided no usable information. Consequently, multivariate analysis revealed the planned number of extraprostatic seeds as the only statistically significant predictor ( $p = 0.04$ ). LnT was suggestive of an effect ( $p = 0.053$ ).

No toxicity was reported from chest migration of the radioactive seeds. Although the patient with two <sup>125</sup>I seeds found within the right ventricle died of a cardiac event, he had had a long history of heart disease, and the cause of death was not attributed to the embedded seeds (14).

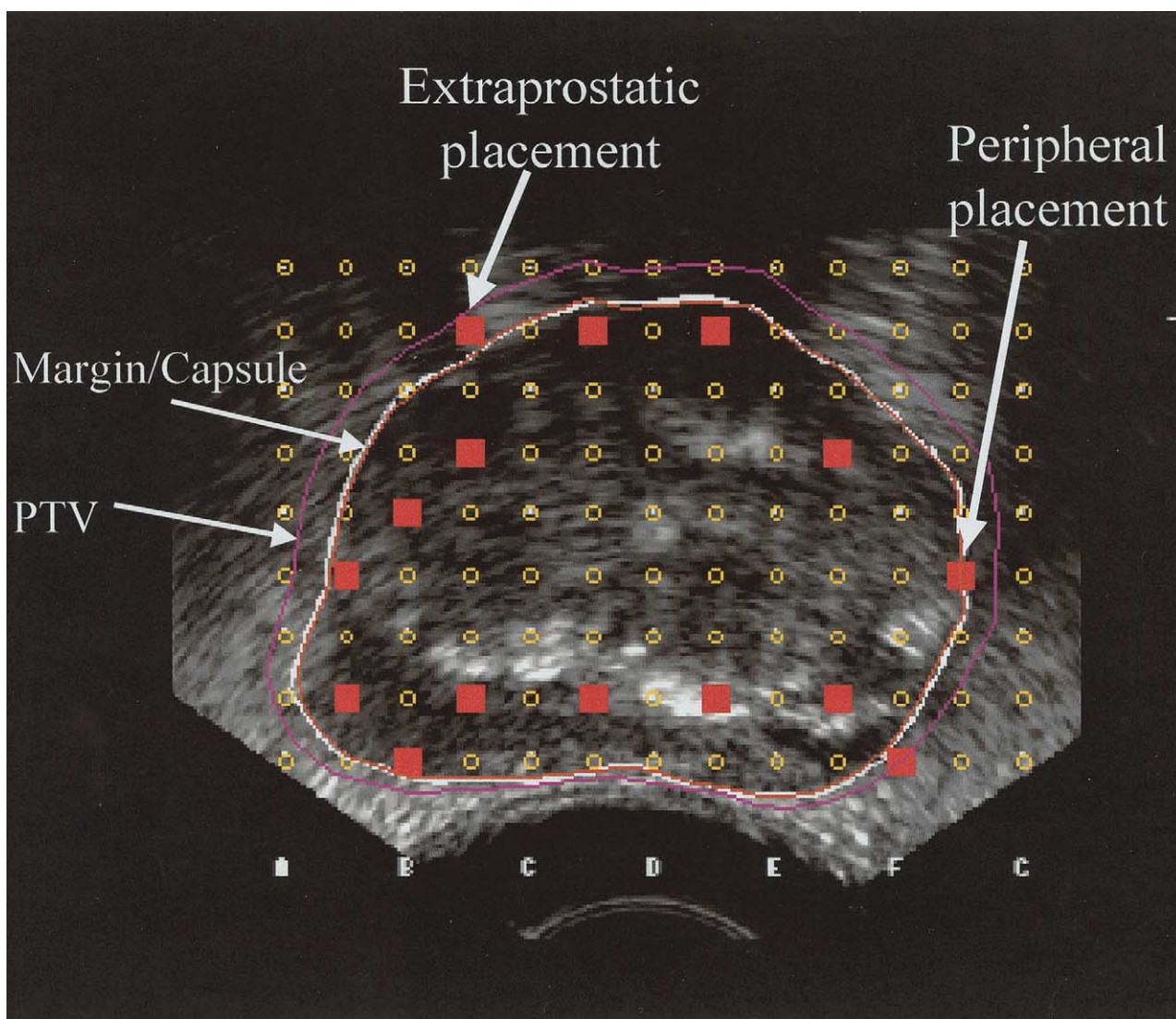


Fig. 1. Preimplant planning ultrasound scan. Extraprostatic seed placement defined as any digitally reconstructed seed falling completely outside contoured prostatic capsule or margin on ultrasound imaging. Peripheral seed placement defined as any extraprostatic seed plus any digitally reconstructed seed falling on contoured prostatic capsule or margin on ultrasound imaging. Similar method also applied to evaluation of postimplant CT scans.

## DISCUSSION

We report the postimplant seed migration rate to the chest in 100 of the first 102 consecutive patients undergoing TIPPB at our institution. Fifty-five percent of the 100 patients had seed migration to the chest after TIPPB. As summarized in Table 1, this rate was greater than in any previous study on seed migration. However, the total number of seeds found on CXR accounted for <1% of seeds implanted into the prostate and periprostatic tissue. This latter finding is consistent with that of other studies pertaining to the use of loose seeds. The results of the present study differ from many others in that the percentage of seeds planned for extraprostatic placement exhibited a high correlation with seed migration. It also differs in that a thorough review of both PA and lateral CXRs before and after TIPPB was performed.

Table 3. Seed migration to chest

Lobe of lung	Patients (n)	Total seeds migrating to chest (%)	Range
RUL	7	11/119 (9)	1.0–3.0
RML	2	3/119 (3)	1.0–2.0
RLL	41	74/119 (63)	1.0–8.0
LUL	3	3/119 (3)	1.0–2.0
LLL	19	26/119 (22)	1.0–2.0
Heart*	1	2/119 (2)	—

Abbreviations: RUL = right upper lobe; RML = right medial lobe; RLL = right lower lobe; LUL = left upper lobe; LLL = left lower lobe.

\* Autopsy proven.

Table 4. Peripheral and extraprostatic seed placement by pre- and postimplant imaging

Seed placement	Planned preimplant TRUS	Actual postimplant CT
Average proportion of extraprostatically placed seeds	39% (43.9/113.1)	31% (37.9/123.8)
Average proportion of peripherally placed seeds	60% (68.3/113.1)	47% (58.6/123.8)
Average proportion of seeds placed inferior to the apex	7% (8/113.1)	4% (4.7/123.8)
Average proportion of seeds placed superior to the base	6% (7/113.1)	3% (3.6/123.8)

Abbreviation: TRUS = transrectal ultrasonography.

The high rate of seed migration found in this report may be attributed to several factors. First, CXRs were available for review in >98% of the 100 study patients. This patient evaluation rate contrasts with several other studies such as that of Older (13) in which only 110 (60%) of 183 patients had postimplant CXRs available for review. Whether the 60% of patients was representative of the group as a whole was not indicated, so the overall seed migration rate in their patients may have been different. In the present study, preoperative CXRs were available for comparison allowing selective identification of migrated seeds even in the presence of multiple surgical clips in the chest from prior coronary artery bypass grafts or other surgical interventions. The identification of seeds from CXRs showing multiple surgical clips in patients with prior chest surgery without pre-TIPPB CXRs for comparison may add a source of uncertainty. From a review of plain film imaging, it is clear that diagnostic-quality PA and lateral CXRs more thoroughly and readily identify seeds than would a limited PA view on a fluoroscopic simulator. Some patients had seeds near the diaphragm, which were only identifiable as such on a lateral CXR. Finally, the results of our study suggest that

the timing of the CXR may be relevant to the occurrence of seed migration. The greater the duration between TIPPB and subsequent CXR, the more likely that seed migration might be detected. In our series, CXRs were usually obtained 2–3 months after TIPPB; CXRs were obtained much sooner after the procedure in some other reports. This observation is consistent with that of Merrick *et al.* (7) who observed an increasing rate of seed migration depending on the timing of post-TIPPB CXR.

In the present study, regression analysis revealed that extraprostatic seed placement in the TRUS preplan correlated with migration. This finding is consistent with observations made during TIPPB in which seed migration was witnessed by fluoroscopy, particularly as seeds were placed anterior to the prostate where abundant venous drainage exists (25). The anterior and lateral periprostatic locations appear more prone to seed migration than other periprostatic locations. Nonetheless, seed migration has also been observed with intraprostatic seed placement, albeit much less frequently than with extraprostatic placement. No other study, to our knowledge, has confirmed the clinical observation that extraprostatic seed placement as per TRUS preplanning correlates with migration. Treatment of extraprostatic extension of prostate cancer is accomplished using a 3–5-mm dosimetric margin (19, 20, 26). TIPPB may treat extraprostatic extension with placement of a portion of the seeds in extraprostatic locations (27). In a survey report on experienced brachytherapists by Prete *et al.* (28), 53% of respondents reported using a 5-mm treatment margin. On the basis of this response and radiation dosimetric considerations, it is likely that the placement of some seeds in extraprostatic locations remains a common and arguably rational approach to TIPPB (27). In a related study by Butzbach *et al.* (29), examination of treatment margins and seed placement was conducted. Seeds were implanted in extraprostatic locations only at the prostatic base and apex, and the treatment margins were judged adequate to treat extraprostatic extension by postimplant CT-based dosimetric analysis. Nonetheless, and in principle, it appears possible that a dosimetric margin may be achieved if intraprostatic peripheral seed location is within 1–2 mm of the prostatic capsule or edge. Intraprostatic seed placement, without extraprostatic placement, would then likely result in lower rates of seed migration. Technical factors, including prostate mobility, seed tracking at implantation, degradation of the TRUS image, and operator error limit such precise

Table 5. Univariate analysis of patient and treatment parameters with seed migration to chest

Parameter	<i>p</i>
Total seeds planned for extraprostatic placement (TRUS)	0.03
Total seeds planned for placement inferior to the apex (TRUS)	0.03
Total seeds planned for peripheral placement (TRUS)	0.06
Time from implant to CXR	0.14
Total seeds planned for placement superior to base (TRUS)	0.21
Total number of seeds planned	0.35
Total number of seeds placed	0.36
Radiation oncologist	0.38
Seeds placed peripherally (postimplant CT)	0.45
Seeds placed extraprostatically (postimplant CT)	0.55
Seeds placed inferior to apex (postimplant CT)	0.60
Postimplant CT volume	0.63
Pretreatment TRUS volume	0.86
Actual seeds placed superior to base (by postimplant CT)	0.92

Abbreviations: TRUS = transrectal ultrasonography; CXR = chest X-ray.

TRUS used for preplanning; CT used for postimplant imaging and dosimetry analysis.

placement of all seeds. In a study by Yu *et al.* (30), it was noted that seed placement may occasionally vary by up to 1 cm from the intended position. In a related study (21), supplemental implantation in a prostate phantom on a “mock” cold implant was examined. Seed placement accuracy under idealized conditions with an experienced practitioner using a Mick applicator was determined. Seed placement accuracy as determined by all 41 supplemental seeds implanted ranged from 0 to 7.5 mm (mean  $\pm$  standard deviation  $2.3 \pm 2.3$  mm). Roberson *et al.* (22) found similar source placement error, with an average displacement of 4.6 mm. Such findings suggest that exclusive intraprostatic seed placement may not approach the accuracy desired to ensure complete treatment of a 3–5-mm periprostatic margin and planning target volume.

Evaluation of the preimplant TRUS-based plans revealed a rate of planned extraprostatic seed placement of 39% and an observed rate of placement of 31% by postimplant CT. Another seed placement definition, termed “peripherally placed,” incorporates those seeds that are on the “line” of the contoured prostate, in addition to the seeds placed in extraprostatic locations. This latter definition is meant to account for seeds that are at the prostatic margin and may be more prone to migration than just those that are placed in extraprostatic locations. Furthermore, this definition accounts for the uncertainty in prostate segmentation whereby seeds judged to be at the prostate margin are actually in extraprostatic locations. To our knowledge, no other study, other than that of Merrick *et al.* (7), has reported either of these values, but comparisons between studies might be difficult because of the known rates of interobserver and intraobserver variability in post-TIPPB prostate contouring (31). Nevertheless, Merrick *et al.* (7) reported a rate of 41.3% extraprostatic seed placement, comparable to the rate of 39% reported in our study. Their study did not, however, find a correlation with extraprostatic seed placement and embolization; otherwise, their findings are consistent with many of those described in the present study.

It is remarkable that the planned extraprostatic placement of seeds as determined by preimplant TRUS correlated with seed migration and extraprostatic seed placement as determined by postimplant CT scanning did not. This finding may be attributable to differences in reproducibility and variability of preimplant TRUS and post-TIPPB CT imaging in segmentation of the prostate such that the preplan more accurately reflects extraprostatic seed placement. Although no recent studies directly comparing the reproducibility of preimplant TRUS with postimplant CT have been published, several studies have demonstrated that observer variability in postimplant CT segmentation is significant. In a study by Dubois *et al.* (31), interobserver and intraobserver variabilities of postimplant CT and MRI were measured and revealed that a difference of 5 mm routinely occurs in establishing prostate dimensions. Lee *et al.* (32) and Al-Qaisieh *et al.* (33) have reported that interobserver variability in postimplant prostate segmentation on CT images resulted in differences that were statistically significant

with respect to predicted dosimetry. In detailed studies by Narayana *et al.* (34, 35), difficulties and differences in registering TRUS and CT for treatment planning related to TIPPB were evident. In contrast, Sech *et al.* (36) have demonstrated relatively good interexaminer reliability of TRUS prostate volume estimation using a prolate ellipsoid calculation. Furthermore, Tong *et al.* (37) have shown that step-section TRUS planimetry similar to that used in TIPPB planning has less variability in prostate volume determination than the ellipsoid method.

Patients at our institution are counseled before TIPPB that seed migration to the chest and other locations may occur. Although no untoward effects from seed migration have been observed, reducing the rate of migration after TIPPB nonetheless seems an intrinsically worthwhile endeavor. One method of reducing seed embolization is to use seeds that are packaged in absorbable suture material (10). Tapen *et al.* studied 289 consecutive patients who underwent TIPPB with the use of sutured seeds ( $n = 143$ ) placed at the periphery or with loose seeds only ( $n = 146$ ). The rate of seed migration in those patients with sutured seeds was 0.7% and for those with loose seeds was 11%. In their study, the postimplant CXRs were performed on the day after the procedure, so that the rate of longer term seed migration from sutured seeds may have been greater, as has been noted by Merrick *et al.* (7). Nonetheless, Tapen *et al.* (10) demonstrated a clear advantage in reducing seed migration with use of seeds in absorbable suture material. A delay in the timing of seed migration, if it is to occur, may have favorable dosimetric consequences compared with immediate seed migration. Similarly, Merrick *et al.* (7) found that the proportion of Vicryl suture-encapsulated seeds implanted influenced the rate of seed migration. Histopathologic examination of salvage prostatectomies after TIPPB failure has demonstrated that a fibrous capsule may form around the seeds after a period (14). Such observations are consistent with those described in reports on radiation pathology (38) and provide an explanation for the relative “fixity” of seeds embedded in Vicryl suture material after the suture material has been absorbed. The use of seeds in Vicryl suture material may, therefore, be considered if significant extraprostatic seed placement is contemplated in the planning process, because its use may reduce seed migration.

## CONCLUSION

The number of loose seeds placed in extraprostatic locations as per the TRUS preplan correlated with an increased likelihood of seed migration to the thorax. This finding is consistent with observations made with fluoroscopy during TIPPB. Although a substantial proportion of patients had seed migration to the thorax, the small proportion of implanted seeds that migrated ( $\leq 1\%$ ) is not likely to have adverse dosimetric or patient health consequences. Until the dosimetric affects of peripheral seed loss are quantified, attention to the proportion of seeds planned for extraprostatic placement appears warranted when using a free seed approach.

## REFERENCES

- Jemal A, Murray T, Samuels A, *et al.* Cancer statistics, 2003. *CA Cancer J Clin* 2003;53:5–26.
- Prestidge BR. Radioisotopic implantation for carcinoma of the prostate: Does it work better than it used to? *Semin Radiat Oncol* 1998;8:124–131.
- Hempel M, Bruggmoser G, Wannenmacher M. [A rare complication of interstitial therapy with iodine-125 seeds: Embolization of a seed into the lung]. *Strahlenther Onkol* 1988;164:531–532.
- Steinfeld AD, Donahue BR, Plaine L. Pulmonary embolization of iodine-125 seeds following prostate implantation. *Urology* 1991;37:149–150.
- Gupta S, Nag S, Gupta J. Pulmonary embolization of permanently implanted radioactive iodine-125 seeds. *Endocurie Hypertherm Oncol* 1993;9:27–31.
- Huttner S, Lengsfeld M, Scholz H. [A rare route for the loss of a 125-iodine seed after the interstitial therapy of prostatic carcinoma]. *Urol A* 1992;31:96–97.
- Merrick GS, Butler WM, Dorsey AT, *et al.* Seed fixity in the prostate/periprostatic region following brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;46:215–220.
- Nag S. Principles and practice of brachytherapy. Armonk, NY: Futura Publishing; 1997.
- Nag S, Scaperth DD, Badalament R, *et al.* Transperineal palladium 103 prostate brachytherapy: Analysis of morbidity and seed migration. *Urology* 1995;45:87–92.
- Tapen EM, Blasko JC, Grimm PD, *et al.* Reduction of radioactive seed embolization to the lung following prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 1998;42:1063–1067.
- Sommerkamp H, Rupperecht M, Wannenmacher M. Seed loss in interstitial radiotherapy of prostatic carcinoma with I-125. *Int J Radiat Oncol Biol Phys* 1988;14:389–392.
- Grimm PD, Blasko JC, Ragde H. Migration of iodine-125 and palladium-103 seeds to the lung after transperineal brachytherapy for prostate cancer. *Endocurie Hypertherm Oncol* 2000;9:50.
- Older R, Snyder B, Krupski TL, Glembocki DJ, Gillenwater JY. Radioactive implant migration in patients treated for localized prostate cancer with interstitial brachytherapy. *J Urol* 2001;165:1590–1592.
- Davis BJ, Pfeifer EA, Wilson TM, *et al.* Prostate brachytherapy seed migration to the right ventricle found at autopsy following acute cardiac dysrhythmia. *J Urol* 2000;164:1661.
- Davis BJ, Bresnahan JF, Stafford SL, *et al.* Prostate brachytherapy seed migration to a coronary artery found during angiography. *J Urol* 2002;168:1103.
- Stock RG, Stone NN, Tabert A, *et al.* A dose-response study for I-125 prostate implants. *Int J Radiat Oncol Biol Phys* 1998;41:101–108.
- Narayana V, Roberson PL, Winfield RJ, *et al.* Optimal placement of radioisotopes for permanent prostate implants. *Radiology* 1996;199:457–460.
- Nag S, Beyer DC, Friedland J, *et al.* American Brachytherapy Society (ABS) recommendations for transperineal permanent brachytherapy for prostate cancer. *Int J Radiat Oncol Biol Phys* 1999;46:789–799.
- Davis BJ, Pisansky TM, Wilson TM, *et al.* The radial distance of extraprostatic extension of prostate cancer: Implications for prostate brachytherapy. *Cancer* 1999;85:2630–2637.
- Sohayda C, Kupelian PA, Levin HS, *et al.* Extent of extracapsular extension in localized prostate cancer. *Urology* 2000;55:382–386.
- Davis BJ, Herman MG, LaJoie WN, *et al.* Supplemental implantation for suboptimal permanent prostate brachytherapy: A prostate phantom study. *Radiother Oncol* 2000;55S:91–92.
- Roberson PL, Narayana V, McShan DL, *et al.* Source placement error for permanent implant of the prostate. *Med Phys* 1997;24:251–257.
- 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.
- Nag S, Bice W, DeWyngaert K, *et al.* The American Brachytherapy Society recommendations for permanent prostate brachytherapy postimplant dosimetric analysis. *Int J Radiat Oncol Biol Phys* 2000;46:221–230.
- Reiner WG, Walsh PC. An anatomical approach to the surgical management of the dorsal vein and Santorini's plexus during radical retropubic surgery. *J Urol* 1979;121:198–200.
- Ragde H, Balasko JC, Grimm PD, *et al.* Interstitial iodine-125 radiation without adjuvant therapy in the treatment of clinically localized prostate carcinoma. *Cancer* 1997;80:442–453.
- Davis BJ, Haddock MG, Wilson TM, *et al.* Treatment of extraprostatic cancer in clinically organ-confined prostate cancer by permanent interstitial brachytherapy: Is extraprostatic seed placement necessary? *Tech Urol* 2000;6:70–77.
- Prete JJ, Prestidge BR, Bice WS, *et al.* A survey of physics and dosimetry practice of permanent prostate brachytherapy in the United States. *Int J Radiat Oncol Biol Phys* 1998;40:1001–1005.
- Butzbach D, Waterman FM, Dicker AP. Can extraprostatic extension be treated by prostate brachytherapy? An analysis based on postimplant dosimetry. *Int J Radiat Oncol Biol Phys* 2001;51:1196–1199.
- Yu Y, Waterman FM, Suntharalingam N, *et al.* Limitations of the minimum peripheral dose as a parameter for dose specification in permanent <sup>125</sup>I prostate implants. *Int J Radiat Oncol Biol Phys* 1996;34:717–725.
- Dubois DF, Prestidge BR, Hotchkiss LA, *et al.* Intraobserver and interobserver variability of MR imaging- and CT-derived prostate volumes after transperineal interstitial permanent prostate brachytherapy. *Radiology* 1998;207:785–789.
- Lee WR, Roach M III, Michalski J, *et al.* Interobserver variability leads to significant differences in quantifiers of prostate implant adequacy. *Int J Radiat Oncol Biol Phys* 2002;54:457–461.
- Al-Qaisieh B, Ash D, Bottomley DM, *et al.* Impact of prostate volume evaluation by different observers on CT-based postimplant dosimetry. *Radiother Oncol* 2002;62:267–273.
- Narayana V, Roberson PL, Winfield RJ, *et al.* Impact of ultrasound and computed tomography prostate volume registration on evaluation of permanent prostate implants. *Int J Radiat Oncol Biol Phys* 1997;39:341–346.
- Narayana V, Roberson PL, Pu AT, *et al.* Impact of differences in ultrasound and computed tomography volumes on treatment planning of permanent prostate implants. *Int J Radiat Oncol Biol Phys* 1997;37:1181–1185.
- Sech S, Montoya J, Girman CJ, *et al.* Interexaminer reliability of transrectal ultrasound for estimating prostate volume. *J Urol* 2001;166:125–129.
- Tong S, Cardinal HN, McLoughlin RF, *et al.* Intra- and inter-observer variability and reliability of prostate volume measurement via two-dimensional and three-dimensional ultrasound imaging. *Ultrasound Med Biol* 1998;24:673–681.
- Fajardo LF. Basic mechanisms and general morphology of radiation injury. *Semin Roentgenol* 1993;28:297–302.