In 65 men with normal potency at 5 years, 35 men (54%) used PDE-5 inhibitors at least once.

Discussion

We performed 2200 cases of prostate BT in a decade since September 2003. We adopted the preplanning technique and shifted to the intraoperative planning with dose escalation, step by step. With careful analysis of postplan results in the study period, average D_{90} of 183 Gy (range, 126-233 Gy) was achieved at Day 30 in monotherapy. In this dose range, BT was definitely an ablative treatment. The median PSA nadir was 0.05 ng/mL, and many patients are still showing a decreasing trend even after 7 years. The biochemical control rates we report here were excellent for all risk groups and consistent with other published results (1-11).

In patient selection, we followed American Brachytherapy Society recommendation and consensus guidelines (18, 19). Certain intermediate-risk patients with low-risk features of low-volume disease (a biopsy positive core rate of <34%) (20), predominant Pattern 3 and low PSA were treated with BT alone without supplemental EBRT. Patients with other high-risk features were treated with BT and supplemental EBRT. We excluded patients with PSA >50 ng/mL (21) or having massive invasion to the seminal vesicles on MRI.

In this series, 40% of the patients were treated with NADT. There were some special issues in Japan. ADT alone was used as a common treatment option for any patients with any stages throughout the country. Many patients treated with ADT in other institutions all over Japan came to us seeking for BT during the early study period. The median duration of 8 months of NADT was not intentional. Moreover, the Japanese Guidelines for Safety Control of Brachytherapy with Permanently Implanted Sealed Radiation Sources for Prostate Cancer recommend the regulation of two types of release criteria, not exceeding the measured radiation dose rate of 1.8 µSv/h at a distance of 1 m from the patient and also not exceeding the administered radionuclide activity of 1300 MBq (22). This special situation arises from a general anxiety about radiation risk among the population. Therefore, we usually had to reduce the prostate volume to around 30 cc with NADT for radiation safety (12). Now we can manage to treat a patient with a prostate of 40-60 cc without NADT, following the regulation (22).

Based on the univariate analysis, the risk groups, biopsy Gleason score, positive biopsy rates, initial PSA level, T-stage, and EBRT were all confirmed to be significant predictors of biochemical tumor control after prostate BT (1-4). In addition, we found that the dose and NADT significantly impacted on biochemical outcomes in the multivariate analysis. The dose—response relationship is still controversial in permanent prostate BT (23, 24). In the low-risk and low-tier intermediate-risk groups treated

using BT alone, postimplant D_{90} at Day 30 was significantly associated with improved biochemical control when the dose delivered to the prostate was >150 Gy in our previous report (25). Zelefsky et al. (3) reported that at Day 0, D_{90} of >140 Gy was associated with improved biochemical tumor control compared with lower doses. In a series by Morris et al. (6), D_{90} values of <130 Gy at Day 0 or Day 30 were predictive of an increased risk of recurrence in the non-NADT subset. Because D_{90} values change greatly from 0 to 30 days postimplant (16), this factor may have accounted for a variable threshold of the dose-response relationship (3, 6-8). Our planning technique showed that the average D_{90} was 156 Gy at Day 1 and 183 Gy at Day 30; the difference was as large as 17%. In this study, patients with intermediate-risk disease had an improved outcome with BED of ≥180 Gy₂ compared with a lower BED. Stone et al. (7) reported BED-response relationship for the intermediate-risk group in a multiinstitutional analysis. Our results are comparable with reports of favorable oncologic results of the prostate D_{90} of ≥180 Gy (26). In our patient selection, patients with bulky disease or Gleason score 4 + 3 are treated with BT and supplemental EBRT. Advantage of supplemental EBRT is intraprostatic dose escalation as well as good coverage of extracapsular extension and seminal vesicle invasion (27). In contrast, we did not find a dose—response relationship for the high-risk patients with very high BED setting in our previous study (28).

The addition of ADT to combined BT with EBRT is still controversial. A clinical randomized trial has been conducted to investigate the efficacy of short-term vs. long-term adjuvant ADT after the combination of BT and EBRT for high-risk patients in Japan (29). At the Tokyo Medical Center, low- to intermediate-risk patients are now less likely to have NADT, and high-risk patients are now prescribed with short-term ADT. Implant planning technique was not a prognostic factor as we previously reported (13).

Most patients had no long-term treatment-related severe toxicity. The 7-year actuarial developing Grade 3+ GU and GI toxicity was 2% and 0.3%, respectively. These severe toxicity rates are comparable with those in other reports (1, 4, 5, 10, 11, 30). Acute urinary retention is a major toxicity in prostate BT (30). In the present series, 5.2% of patients experienced urinary retentions, but most of them resolved spontaneously within several weeks. Our previous data suggest that the number of needles and hormonal manipulation increased the risk of catheterization (31). Grade 2+ GI toxicity developed in 12.6% of patients treated with the supplemental EBRT. We previously reported rectal dose constraint for minimizing Grade 2+ rectal bleeding (32). Since 2011, intensity-modulated radiotherapy has been available using EBRT, and GI toxicity has been reduced in our department (10, 11). The rectal volumes receiving doses higher than 30, 35, and 40 Gy by supplemental EBRT should be kept under 15%, 25%, and 35%, respectively (32). In this setting, the Grade 2+ rectal

toxicity has decreased to 5%. We showed a satisfactory return to baseline urinary function in 70% of patients 12 months later; however, recovery was not complete even at 60 months. Managing long-term GU toxicity is still challenging for prostate BT (30). Maintenance of erectile function is modest (33), and we report 44% of men who were potent at baseline reported normal erections at 5 years, with an additional 18% having suboptimal erections. We propose that PDE-5 inhibitor use should be encouraged after BT (34).

Conclusions

Our results demonstrated excellent results with permanent prostate BT in a high-volume center in Japan. ¹²⁵I prostate BT is a highly effective treatment option for low, intermediate-, and selected high-risk prostate cancers. Urinary, rectal, and sexual side effects were tolerable. Adequate dose may need to be delivered to achieve successful biochemical control. Outcomes with technical shifts or dose escalation should be analyzed with rigorous and longer followup periods including investigations into patterns of failure.

Acknowledgments

This work was presented at the International Symposium on 10th Anniversary of Permanent Prostate Brachytherapy in Japan. We are grateful to the Japan Permanent Prostate Brachytherapy Study Group for valuable suggestions and clerical supports. We also thank Enago (www.enago.jp) for the English language review.

References

- [1] Sylvester JE, Grimm PD, Wong J, et al. 15-Year biochemical relapsefree survival, cause-specific survival, and overall survival following I(125) prostate brachytherapy in clinically localized prostate cancer: Seattle experience. Int J Radiat Oncol Biol Phys 2011;81:376—381.
- [2] Stock RG, Stone NN, Cesaretti JA, et al. Biologically effective dose values for prostate brachytherapy: Effects on PSA failure and posttreatment biopsy results. Int J Radiat Oncol Biol Phys 2006;64: 527-533.
- [3] Zelefsky MJ, Chou JF, Pei X, et al. Predicting biochemical tumor control after brachytherapy for clinically localized prostate cancer: The Memorial Sloan-Kettering Cancer Center experience. Brachytherapy 2012;11:245—249.
- [4] Taira A, Merrick GS, Butler WM, et al. Long-term outcome for clinically localized prostate cancer treated with permanent interstitial brachytherapy. Int J Radiat Oncol Biol Phys 2011;79:1336—1342.
- [5] Crook J, Borg J, Evans A, et al. 10-Year experience with I-125 prostate brachytherapy at the Princess Margaret Hospital: Results for 1100 patients. Int J Radiat Oncol Biol Phys 2011;81:96—101.
- [6] Morris WJ. Spadinger I, Keyes M, et al. Whole prostate D90 and V100: A dose-response analysis of 2000 consecutive I-125 monotherapy patients. Brachytherapy 2014;13:32—41.
- [7] Stone NN, Potters L. Davis BJ, et al. Customized dose prescription for permanent prostate brachytherapy: Insights from a multicenter analysis of dosimetry outcomes. Int J Radiat Oncol Biol Phys 2007;69:1472-1477.

- [8] Zelefsky MJ, Kuban DA, Levy LB, et al. Multi-institutional analysis of long-term outcome for stages T1-T2 prostate cancer treated with permanent seed implantation. Int J Radiat Oncol Biol Phys 2007: 67:327-333.
- [9] Grimm P, Billiet I, Bostwick D, et al. Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group, BJU Int 2012;109 Suppl.:22—29.
- [10] Zelefsky MJ, Nedelka MA, Arican ZL, et al. Combined brachytherapy with external beam radiotherapy for localized prostate cancer: Reduced morbidity with an intraoperative brachytherapy planning technique and supplemental intensity-modulated radiation therapy. Brachytherapy 2008;7:1—6.
- [11] Forsythe K, Blacksburg S, Stock RG. Intensity-modulated radiotherapy causes fewer side effects than three-dimensional conformal radiotherapy when used in combination with brachytherapy for the treatment of prostate cancer. Int J Radiat Oncol Biol Phys 2012;1:630—635.
- [12] Saito S, Ito K, Yorozu A, et al. Nationwide Japanese Prostate Cancer Outcome Study of permanent iodine-125 seed implantation (J-POPS). Int J Clin Oncol 2014; Epub ahead of print.
- [13] Yoshida K. Yorozu A, Ohashi T, et al. Comparison of preplanning and intraoperative planning for 1-125 prostate brachytherapy. Jpn J Clin Oncol 2013;43:383—389.
- [14] National Comprehensive Cancer Network guidelines. Available at: www.nccn.org. 2014.
- [15] Ohashi T, Yorozu A, Toya K, et al. Acute urinary mortality following I-125 prostate brachytherapy. Int J Clin Oncol 2005;10:262–268.
- [16] Ohashi T, Yorozu A, Toya K, et al. Comparison of intraoperative ultrasound with postimplant computed tomography—Dosimetric values at Day 1 and Day 30 after prostate brachytherapy. Brachytherapy 2007;6:246—253.
- [17] Crook JM, Potters L. Stock RG, ct al. Critical organ dosimetry in permanent seed prostate brachytherapy: Defining the organ at risk. Brachytherapy 2005:4:186—194.
- [18] Davis BJ, Horwitz EM, Lee WR, et al. American Brachytherapy Society consensus guidelines for transrectal ultrasound-guided permanent prostate brachytherapy. Brachytherapy 2012;11:6—19.
- [19] 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.
- [20] Merrick GS, Zelefsky MJ, Sylvester J, et al. American Brachytherapy Society Prostate Low-Dose Rate Task Group. Available at: www. americanbrachytherapy.org.
- [21] Kestin LL, Goldstein NS. Vicini FA, et al. Percentage of positive biopsy cores as predictor of clinical outcome in prostate cancer treated with radiotherapy. J Urol 2002;168:1994—1999.
- [22] Hanada T, Yorozu A, Kikumura R, et al. Assessing protection against radiation exposure after prostate I-125 brachytherapy. Brachytherapy 2014;13:311—318.
- [23] Stone NN. Stock RG. Does dose matter? Editorial comments to Morris et al. Whole prostate D90 and V100: A dose-response analysis of 2000 consecutive 125-I monotherapy cases. *Brachytherapy* 2014;13:42—43.
- [24] Spadinger I, Morris WJ. Rebuttal to Drs Stone and Stock. Brachytherapy 2014:13:44–45.
- [25] Ohashi T, Yorozu A, Saito S, et al. Outcomes following iodine-125 prostate brachytherapy with or without neoadjuvant androgen deprivation. Radiother Oncol 2013;109:241—245.
- [26] Kao J, Stone NN, Lavaf A, et al. (125)I monotherapy using D90 implant doses of 180Gy or greater. Int J Radiat Oncol Biol Phys 2008;70:96—101.
- [27] Spratt DE, Zelefsky MJ. There is a need for supplemental XRT with brachytherapy in the treatment of intermediate-risk prostate cancer patients. *Brachytherapy* 2013;12:389—392.
- [28] Ohashi T, Yorozu A, Saito S, et al. Combined brachytherapy and external beam radiotherapy without adjuvant androgen deprivation therapy for high-risk prostate cancer. Radiat Oncol 2014;9:13.

A. Yorozu et al. / Brachytherapy ■ (2014) ■

- [29] Konaka H, Egawa S, Saito S, et al. Tri-modality therapy with I-125 brachytherapy, external beam radiation therapy, and short or long-term hormone therapy for high-risk localized prostate cancer (TRIP): Study protocol for a phase III, multicenter, randomized, controlled trial. BMC Cancer 2012;12:110.
- [30] Chan EK, Keyes M, Pickles T, et al. Decline in acute urinary toxicity: A long-term study in 2011 patients with prostate brachytherapy within a provincial institution. *Brachytherapy* 2014;13:46–52.
- [31] Ohashi T, Yorozu A, Toya K, et al. Predictive factors of acute urinary retention requiring catheterization following I-125 prostate brachytherapy. Jpn J Clin Oncol 2006;36:285—289.
- [32] Shiraishi Y, Yorozu A, Ohashi T, et al. Dose constraint for minimizing grade 2 rectal bleeding following brachytherapy combined with external beam radiotherapy for localized prostate cancer: Rectal dose-volume histogram analysis of 457 patients. *Int J Radiat Oncol Biol Phys* 2011;81:e127—e133.
- [33] Nishimura S, Yorozu A, Ohashi T, et al. Five-year potency preservation after iodine-125 brachytherapy. Int J Clin Oncol 2013: Epub ahead of print.
- [34] Zelefsky MJ, Shasha D, Branco RD, et al. Prophylactic sildenafil citrate improves selected aspects of sexual function in men treated by radiotherapy for prostate cancer. J Urol 2014; Epub ahead of print.

7







Brachytherapy 13 (2014) 311-318

Assessing protection against radiation exposure after prostate ¹²⁵I brachytherapy

Takashi Hanada^{1,2,*}, Atsunori Yorozu², Riki Kikumura³, Toshio Ohashi^{1,3}, Naoyuki Shigematsu¹

¹Department of Radiology, Keio University, School of Medicine, Tokyo, Japan ²Department of Radiology, Tokyo Medical Center, National Hospital Organization, Tokyo, Japan ³Department of Radiology, Saitama Hospital, National Hospital Organization, Saitama, Japan

ABSTRACT

PURPOSE: To expand the radiation dose rate measurement data set by measuring radiation under various prostate ¹²⁵I brachytherapy situations.

METHODS AND MATERIALS: Measurements were obtained from 63 consecutive unselected patients at Tokyo Medical Center, Japan. Differences in factors during measurements, such as body postures, distances from the skin surface, and measurement directions were considered. Furthermore, shielding effects of lead-lined underwear, consisting mainly of 0.1-mm thickness of lead, were also assessed.

RESULTS: Radiation exposure varies according to the patient's body posture, with results differing as much as approximately 40.0% in measured radiation dose rates at 30 cm from the anterior skin surface. Weight, body mass index, and tissue thickness showed good correlations with measured radiation dose rates. The magnitude of radiation exposure attenuation by shielding was approximately 95.8%, similar to the attenuation ratio based on tissue measurements made in the lateral direction. The respective mean times required to reach 1 mSv were 1.2, 7.6, and 65.4 days in the standing position and 0.6, 4.6, and 40.4 days in the supine position at the site of contact, and at 30 and 100 cm from the anterior skin surface.

CONCLUSIONS: This study obtained supplemental information pertaining to radiological protection and confirmed that shielding can be an effective tool for reducing exposures. © 2014 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords:

Brachytherapy; Iodine-125; Radiation exposure; Prostate cancer; Radiation safety

Introduction

Permanent seed implant treatment using ¹²⁵I is currently a common procedure for localized prostate cancer (1—3), as this method is now viewed worldwide as being on par with external beam radiation therapy and prostatectomy (4, 5). In Japan as well, about 27,000 patients have undergone ultrasound-guided transperineal permanent implantation brachytherapy for early-stage prostate cancer. To avoid unnecessarily high radiation exposure to the general public,

the International Commission on Radiological Protection (ICRP) recommends that a medical facility may authorize release from its control of any individual who has been administered a byproduct material if the effective dose to any other persons from exposure to this individual is not likely to exceed 5 mSv, and the effective dose to a member of the general public is not likely to exceed 1 mSv (6). Furthermore, according to Nuclear Regulatory Commission (NRC) regulations, prostate brachytherapy patients are given instructions regarding precautions against unnecessarily exposing others, with the recommendations that radiation exposures to others be kept as low as reasonably achievable (ALARA) (7, 8).

The NRC does not require a specific set of patient instructions. Instead, instructions are left to the discretion of the facility. Radiation safety precaution instructions given to patients, therefore, have relied on a community consensus developed from the literature and actual practice

Received 20 August 2013; received in revised form 7 November 2013; accepted 5 December 2013.

Conflict of interest statement: The authors have no conflicts of interest to declare.

^{*} Corresponding author. Department of Radiology, Keio University, School of Medicine, Shinanomachi 35, Shinjuku-ku, Tokyo 160-8582, Japan. Tel.: +81-3-5363-3835; fax: +81-3-3359-7425.

E-mail address: thanada@rad.med.keio.ac.jp (T. Hanada).

(9-11). The Japanese Guidelines for Safety Control of Brachytherapy with Permanently Implanted Sealed Radiation Sources for Prostate Cancer recommend a much more sophisticated approach, taking into account attenuation by a possible protective device, such as lead-lined underwear, the duration of wearing such an undergarment, and the contact time of the involved person per day at given distances (12). This approach results in introducing the regulation of two types of release criteria, not exceeding the measured radiation dose rate of 1.8 μSv/h at a distance of 1 m from the patient, and also not exceeding the administered radionuclide activity of 1300 MBq. This special situation arises from a general anxiety about radiation risks among the population, although some peer-reviewed publications with data showing that the radiation exposure to family members, support providers, care givers, and members of the general population coming into contact with patients harboring prostate permanent implants with radioactive seeds is very low (9, 10, 13-15).

The authors are frequently asked for more detailed information regarding the true exposure rates and associated risk that patients pose to the public. However, there are no data for specific measurements situations, such as the patient's body postures, or considering lifestyle habits. In addition, published data have been limited to Europeans and North Americans who are physically different from Asian populations. These data thus do not provide peace of mind for Asian patients. Magnitudes of radiation exposures are directly linked to not only by the activity of the administered radionuclides but also to the tissue attenuation associated with the patient's physical build. The purpose of this study was to provide appropriate assessment expanding the radiation dose rate measurement data, by taking into consideration lifestyle habits, and to provide reassurance regarding the safety of radiation exposure after prostate ¹²⁵I brachytherapy.

Methods and materials

A total of 63 consecutive patients with stage T1–T3a localized prostate cancer who underwent transperineal ¹²⁵I implantation at Tokyo Medical Center, National Hospital Organization, during the period from May 2012 through February 2013 were studied. The characteristics of these patients are listed in Table 1, which describes their states at the time of radiation dose rate measurements. Seed implantations were performed by the standard technique, using an intraoperative three-dimensional conformal treatment planning system (16, 17). In the case of a permanent implant being the sole treatment, prescription doses at the external surface of the prostate were 160 Gy for 46 patients;and in the 17 patients who had received prior 45-Gy external beam radiotherapy, the prescription dose was 110 Gy (18).

Various radiation dose rate measurements were performed the day after implantation, focusing particularly

Table 1 Characteristics of 63 patients in this study

		Standard		
Characteristics	Mean	deviation	Minimum	Maximum
Age (y)	69	6	57	83
Number of implanted seeds	82	15	46	115
Total implant activity (mCi)	29.2	7.7	12.6	46.3
Weight (kg)	66.0	7.9	48.0	82.9
BMI (kg/m ²)	23.9	2.7	17.3	29.7
Prostate volume (mL)	33.4	8.7	11.3	58.7

BMI = body mass index.

on different body postures of patients and lifestyle habits. Radiation dose rate measurements were performed in two different positions, standing and supine, on the anterior skin surface at the point of the symphysis pubis, and at distances 30 and 100 cm perpendicular to the surface of the anterior skin. Measurements at the skin surfaces of the right or left lateral torso at the locations of the femoral heads, at 30 cm from the surface of the lateral skin, were also performed. Furthermore, we assessed the magnitude of attenuation of the measured radiation dose rate by having each subject wear personal lead-lined underwear, consisting mainly of 0.1-mm thickness of lead, known as Radiation Guard, a product handled by Atlantic Nuclear. Radiation dose rate measurements were obtained using a Fluke model 451B ion chamber survey meter calibrated with energy at 30 keV. Calibration-corrected readings for ¹²⁵I energy were used in this study. The total activity (mCi) of the implant; measured radiation dose rate (µSv/h); and the preoperative weight (kg), height (cm), number of sources implanted, and prostate volume (mL) were recorded and then subsequently evaluated retrospectively. The lifetime exposures of individuals near the patient under various conditions were calculated using the following equation (11)

$$D(\infty) = 34.6 \cdot T_{1/2} \cdot \dot{D}(0) \cdot E$$

where D (∞) is the committed dose in μ Sv, 34.6 is the conversion factor of 24 h/d times the total integration of decay (1.44), $T_{1/2}$ is the half-life in days (59.4 days), $\dot{D}(0)$ is the measured radiation dose rate (μ Sv/h), and E is the occupancy factor based on the fraction of time a person could be in the vicinity of the implanted patient. The time required to reach a given total dose D (t) (μ Sv) is given by following equation (11)

$$t = \frac{-T_{1/2} \cdot \ln\left(1 - \frac{D(t)}{34.6 \cdot T_{1/2} \cdot \dot{D}(0) \cdot E}\right)}{0.693}$$

Two sets of calculations were made using the mean radiation dose rate measurements. In the first set of calculations, the occupancy factor was assumed to be 1.00 (100%), representing the dose to a caregiver who is present 100% of the time under the conditions of which the radiation dose rate was measured. In the second set of calculations, the

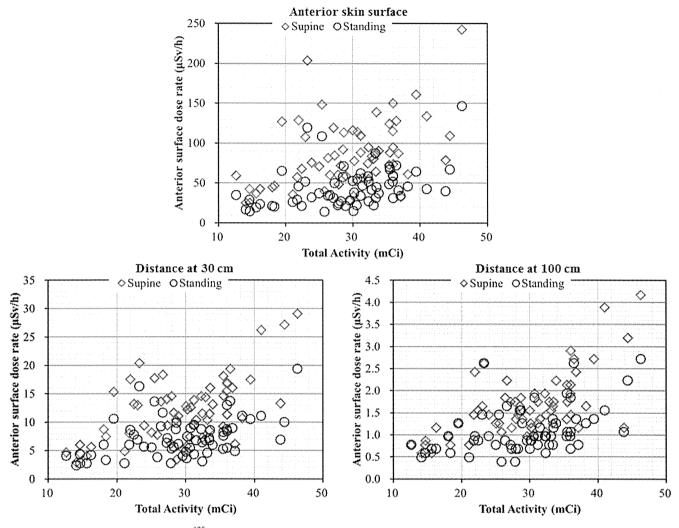


Fig. 1. Radiation dose rate correlates with ¹²⁵I activity with the patient in the supine and standing positions. Measurements were made at the anterior skin surface, and at 30 and 100 cm from the skin.

occupancy factor was assumed to be 0.33, representing the dose to a caregiver who is present 1 of the 3 of any day at the given distances. This second set of calculations was intended to represent the typical sleeping arrangement of a caregiver near the patient for 8 of 24 h or as a conservative estimate for other members of the public in proximity to the patient with an implant.

Results

The mean measured radiation dose rate at the anterior skin surface after ^{125}I implantation was 85.4 $\mu Sv/h$ (range, 25.2–242.5) with the patient in the supine position. The measured radiation dose rates at 30 and 100 cm from the skin surface decreased to mean values of 12.0 $\mu Sv/h$ (range, 2.9–29.1) and 1.6 $\mu Sv/h$ (range, 0.6–4.2), respectively. When the patient's body posture was changed to the standing position, the mean measured radiation dose rates at the anterior skin surface and at 30 and 100 cm from the skin were lower than those measured in the supine

position, resulting in mean values of 44.3 μ Sv/h (range, 13.8—146.5), 7.2 μ Sv/h (range, 2.3—19.4), and 1.1 μ Sv/h (range, 0.4—2.7), respectively.

The correlations between total activity of the implant and the measured radiation dose rates for both patient body postures were calculated. Figure 1 shows variation in the radiation dose rates values measured in treated patients. The wide range of measured values is probably because of the variability in the total activities of the implants (from 12.6 to 46.3 mCi) and to the different depths of the prostate.

Figure 2 shows that measured radiation dose rates rise as the patient's physical characteristics normalize with activity. Physical characteristics include weight (kg), body mass index (kg/m²), and the thickness of the tissues between radiation sources and the skin (millimeter). Therefore, the horizontal axes for each of these parameters are expressed in units of mCi/kg, mCi·m²/kg, and mCi/mL, respectively. Measurements of the distance between the radiation sources nearer to the anterior body surface and the anterior skin

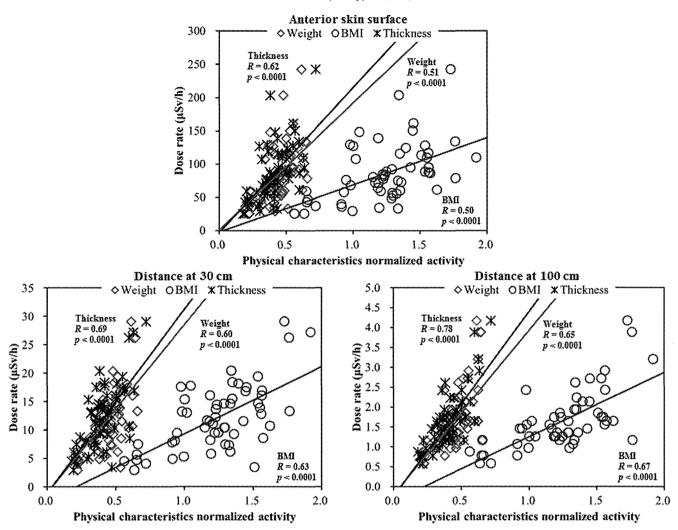


Fig. 2. Radiation dose rate correlates with patient's physical characteristics, as normalized by activity. Measurements were made at the anterior skin surface, and at 30 and 100 cm from the skin. Units of the horizontal axis are expressed as mCi/kg for weight, mCi·m²/kg for BMI, and mCi/mm for tissue thickness. BMI = body mass index.

surface were taken from the computed tomography scans, which were carried out for each patient within 1 day after implantation. With higher weights, body mass index, and/ or tissue thickness, lower measured radiation dose rate measurements are expected.

The mean measured radiation dose rate 30 cm from the patient's lateral skin while in the supine position was 0.5 $\mu Sv/h$ (range, 0.1–1.2). This result was similar to that obtained with a measurement point at 30 cm from the anterior skin surface while the patient was in the supine position wearing personal lead-lined underwear, resulting in a mean value of 0.5 $\mu Sv/h$ (range, 0.1–1.5), resulting in attenuation of approximately 95.8% of the exposure dose rate, as compared with radiation dose rates obtained 30 cm from the anterior skin with patient in the supine position. Specific radiation dose rate attenuations are shown in Fig. 3.

Table 2 summarizes the mean theoretical durations in days to reach the 1 and 5 mSv limits established by the

ICRP and NRC (7, 8, 11). Assuming that the fraction of time a person could be in the vicinity of the implanted patient to be 1.00, the time required for a family member to reach the 5-mSv limit, in the standing position, was 6.4 days (range, 1.4-16.6) at the site of contact and 53.0 days (range, 11.5-193.2) at 30 cm from the anterior skin surface. The mean durations required to reach the 1-mSv general population limit were 1.2 days (range, 0.3-3.1), 7.6 days (range, 2.2–20.1), and 65.4 days (range, 16.9-154.6) at the site of contact, and at 30 and 100 cm from the anterior skin surface, respectively. Obviously, these times decrease toward the mean values of 0.6 days (range, 0.2–1.7), 4.6 days (range, 1.4–15.7), and 40.4 days (range, 10.6–154.6) when the patient is in the supine position. The values presented above significantly overestimate the doses received both by family members and the general population because the occupancy factor was assumed to be 1.00. The results of the mean theoretical time using an occupancy factor of 0.33, and percentage values (%) reaching

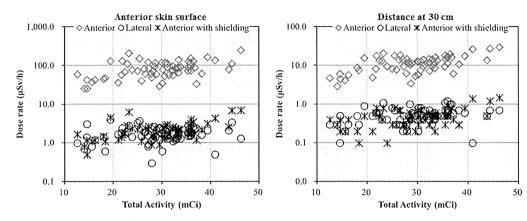


Fig. 3. Radiation dose rate correlates with ¹²⁵I activity measured from the anterior direction, the anterior direction with shielding and the lateral direction. Measurements were made at the anterior skin surface and at 30 cm from the skin.

the dose limit in their lifetime by performing the calculations using each occupancy factor within the patient group undergoing measurement (i.e., values of 100.0% represent measurements from all 63 patients who could possibly reach the dose limit at the distance at which the radiation dose rates were measured) are also shown in Table 2.

Discussion

The study is based on the direct radiation dose rate measurements taken the day after ¹²⁵I permanent interstitial

brachytherapy. Such a data set facilitates meaningful evaluation of the variability in patient radiation dose rates (Figs. 1–3) and providing a foundation for making general assumptions using mean values, representing typical patients. Although differing in methodology and numbers of data points, these results are in agreement with those of other studies, supporting the findings of our research (9, 10, 13). Smathers *et al.* (15) measured radiation dose rates from 38 ¹²⁵I or ¹⁰³Pd prostate brachytherapy patients and suggested that these patients need not be concerned about being a radiation risk to the general public after their procedures.

Table 2 Mean times required to reach 1 and 5 mSv

Posture		Shielding	Occupancy factor	Distance (cm)	Time to reach the dose limit in days (ratio)		
	Direction				1 mSv	5 mSv	
Supine	Anterior	_	0.33	Skin surface	1.9 (100.0)	10.1 (100.0)	
				30	15.1 (100.0)	93.2 (79.4)	
				100	127.3 (49.2)	N/A (0.0)	
			1.00	Skin surface	0.6 (100.0)	3.2 (100.0)	
				30	4.6 (100.0)	28.4 (100.0)	
				100	40.4 (100.0)	149.8 (11.1)	
		+	0.33	Skin surface	96.9 (31.8)	N/A (0.0)	
				30	N/A (0.0)	N/A (0.0)	
			1.00	Skin surface	28.6 (98.4)	148.5 (28.6)	
				30	98.8 (30.2)	N/A (0.0)	
	Lateral	_	0.33	Skin surface	128.3 (55.6)	N/A (0.0)	
				30	N/A (0.0)	N/A (0.0)	
			1.00	Skin surface	38.0 (96.8)	168.4 (14.3)	
				30	107.7 (42.9)	N/A (0.0)	
Standing	Anterior	_	0.33	Skin surface	3.8 (100.0)	21.5 (100.0)	
C				30	26.2 (100.0)	135.9 (41.3)	
				100	144.7 (17.5)	N/A (0.0)	
			1.00	Skin surface	1.2 (100.0)	6.4 (100.0)	
				30	7.6 (100.0)	53.0 (98.4)	
				100	65.4 (93.7)	214.9 (4.8)	
	Lateral	_	0.33	Skin surface	113.7 (71.4)	N/A (0.0)	
				30	169.8 (3.2)	N/A (0.0)	
			1.00	Skin surface	30.9 (100.0)	144.6 (20.6)	
				30	93.3 (60.3)	N/A (0.0)	

N/A = not available.

Ratio (%) describes the percentage reaching the dose limit in their lifetime. The number (N/A) of days has not been calculated because committed doses have not reached the dose limit.

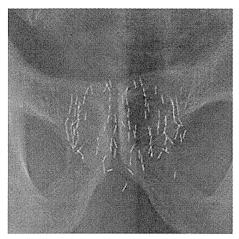




Fig. 4. Two plain radiographs of the pelvis with a seed-implanted in prostate in the standing (left) and supine (right) position body postures.

Michalski *et al.* (14) measured patient exposures and those to members of their families for 44 patients receiving a permanent prostate brachytherapy implant using optically stimulated dosimeters to measure the doses. They concluded that the exposures of family members from patients were well below the ICRP and NRC limits (6-8).

There is marked variability in measured radiation dose rates among patients (Fig. 1). The wide range of reported dose measurements is in large part because of the variability in the total activities of the implants and variability in the depth of the prostate. It was shown previously that activity-normalized anterior surface effective dose rates (µSv/h/GBq) generally decrease as patient weight increases, likely because the prostate is located at greater depth in large patients (9, 10, 15). In addition, Cattani et al. have clearly shown the activity-normalized anterior surface radiation dose rates to be inversely correlated with distance between the implanted seeds and the skin surface (13). Our results indicate that the radiation dose rate

generally increases as the patient's physical characteristics are normalized by activity, results similar to those obtained by other researchers (9, 10, 13, 15). In addition, good clear correlations between the measured radiation dose rate and these parameters were demonstrated (Fig. 2).

Associated with these findings, radiation exposure varies with the patient's body posture, even when measured under the same conditions (Fig. 1). This is the first report describing differences in body posture, showing important results, for instance, a difference in the rate of decrease of approximately 40.0% in measured radiation dose rates between two situations at 30 cm from the anterior skin surface. We consider two factors to account for this dose reduction in the standing position. First, the location of the prostate differs between the supine and standing positions. With a seed implant in the prostate, there is a tendency to move down to the same level as the pubic bone, causing significant crossover between the two. Figure 4 shows two plain radiographs of the pelvis containing a seed

Table 3
Characteristic data of Japanese patients in our study and other published data

Characteristics	Occupancy factor	Distance	This study		Dauer et al. (10)	Cattani <i>et al.</i> (13) Posterior
			Anterior and supine	Anterior and standing	Anterior	
Total implanted activity (GBq)			1.08 (0.47-1.71)		1.50 (0.48-2.67)	1.14 (0.60-1.76)
Number of implants seeds			82 (46-115)			82 (42-124)
Weight (kg)			66.0 (48.0-82.9)		86.4 (65.9-115)	
Prostate volume (mL)			33.4 (11.3-58.7)			33 (10-58)
Mean dose rate (μSv)		Skin surface	85.4 (25.2-242.5)	44.3 (13.8-146.5)	37.3 (0.9-221)	41.3 (6.2-99.4)
		30 cm	12.0 (2.9-29.1)	7.2 (2.3-19.4)	6.0 (0.9-33)	
Time to reach 1 mSv (d)	0.33	Skin surface	1.9	3.8	3.5	1.4
		30 cm	15.1	26.2	24.1	
	1.00	Skin surface	0.6	1.2	1.1	
		30 cm	4.6	7.6	7.3	
Time to reach 5 mSv (d)	0.33	Skin surface	10.1	21.5	18.8	
		30 cm	93.2ª	135.9 ^a	N/A	
	1.00	Skin surface	3.2	6.4	5.8	
		30 cm	28.4	53.0°	44.4	

N/A = not available.

^a Some of the patients have not reached the dose limit.

implanted in prostate, and illustrates how the prostate shifts behind the pubic bone with postural change. This observation is enough to corroborate our assumption that the pubic bone serves as a shield against radiation exposure. Second, we consider that the thickness of the tissues between radiation sources and the skin differs between the two positions. Fat in the abdomen seems to spread and thereby flatten in the supine position, as a consequence of reducing the thickness of tissues between sources and the skin. In the standing position, fat hangs loosely and is weighted down because of gravity, and there is an increase in tissue thickness. Thus, with more overlying tissue providing shielding, lower radiation dose rates can be expected, and are generally observed.

In practical terms, our data and those from other researchers (9, 10, 13, 15) suggest that patients need not be concerned about being a radiation risk to the general public after ¹²⁵I brachytherapy. However, it is prudent to practice the ALARA principle in radiological protection. Furthermore, it is true that there are national differences in the degree of fear associated with radiation exposure. For example, patients and their families, as well as the general public in Japan, have stronger feelings because of their national circumstances, leading to the introduction of strict regulations (12, 19, 20). For individuals who are still concerned about the possibility of radiation exposure, a lead apron, fabricated from lead-lined sheeting or purchased from a radiology supply company, is feasible and would shield the individual from virtually all radiation. The results of our present study clarify the degree of radiation exposure risk by calculating the mean time required to reach 1 and 5 mSv assuming occupancy factors 1.00 and 0.33 (Table 2). Moreover, our data were obtained from various radiation dose rate measurements (different patient body postures, distances from the skin surface, and measurement directions, and whether or not shielding was applied), taking the patient's lifestyle habits into consideration. Table 3 shows characteristic data of Japanese patients in our study and other published data. Although total implanted activity and patient weight differs among studies, calculated mean times required to reach 1 mSv measured in standing position were similar to results reported by Dauer et al. (9, 10), which represents North American data. It is difficult to compare the data from Cattani et al. (13), which represents Italian data because no direct comparable values are reported. However, physical characteristics were similar to those seen in our study. These data suggest that precautions for radiation safety in Asian patients could be less restrictive, considering that other countries declare radiation exposure from patients who receive ¹²⁵I implants is very low. This detailed information is quite helpful for evaluating the magnitude of radiation exposure to the general public and provides a basis for the validation of current radiation safety recommendations. It also provides clinicians with more concrete information regarding allowable exposure times for caregivers and members of the public.

The use of brachytherapy to treat selected localized prostate cancers continues to increase rapidly worldwide, especially because of the low degree of toxicity; improved quality of life; and a general, long-term, positive prognosis. Also because brachytherapy is likely to expand in Asian countries because this treatment is more convenient and cost-effective than external beam radiation therapy, it is necessary to prove the safety of radiation exposure from the viewpoint of environmental protection. The ongoing growth in the application of low-dose-rate seed brachytherapy worldwide underscores the need for consistent and sound radiologic protection practices and precautions, meeting the ALARA recommendations. Because the target patients' builds in our study were somewhat smaller than those in previous studies (9, 10, 13, 14), our results may fill a previous information gap.

A limitation of this retrospective study is that only ¹²⁵I was examined. We have no data for ¹⁰³Pd because this form of seed implantation is now not allowed in Japan. However, it is well known that radiation exposures from ¹⁰³Pd patients are lower than that from ¹²⁵I patients and are therefore not a cause for concern (9, 10). Allowable exposure times for ¹⁰³Pd are generally much longer than those for ¹²⁵I owing to the lower energies and typically lower initial dose rates from ¹⁰³Pd. Therefore, we consider our study data to be broadly applicable to implantation brachytherapy in general.

Conclusions

This study provided appropriate assessment, expanding measurement data by taking into consideration lifestyle habits, and can be used to reassure patients, family members, and caregivers about radiation exposure based on the safety of radiation after prostate ¹²⁵I brachytherapy. It is important to make patients worldwide feel comfortable and allow them to maintain a good quality of life. The present study is an essential aspect of obtaining continuous supplemental data and improving protection from radiation by providing useful information and suggesting areas for additional regional, national, and international research.

Acknowledgments

The authors thank staff members from the Department of Radiology, The National Hospital Organization, Tokyo Medical Center, for their help in carrying out the radiation dose rate measurements. The authors appreciate the support and assistance with data management provided by Mrs. Kazuko Ogawa at Keio University School of Medicine.

References

[1] Holm HH. The history of interstitial brachytherapy of prostatic cancer. Semin Surg Oncol 1997;13:431-437.

- [2] Nag S, Ciezki JP, Cormack R, et al. Intraoperative planning and evaluation of permanent prostate brachytherapy: Report of the American Brachytherapy Society. Int J Rudiat Oncol Biol Phys 2001;51: 1422–1430.
- [3] Stock RG, Stone NN, Wesson MF, et al. A modified technique allowing interactive ultrasound-guided three-dimensional transperineal prostate implantation. Int J Radiat Oncol Biol Phys 1995;32: 219–225.
- [4] Ciezki JP. Klein EA, Angermeier K, et al. A retrospective comparison of androgen deprivation (AD) vs. no AD among low-risk and intermediate-risk prostate cancer patients treated with brachytherapy, external beam radiotherapy, or radical prostatectomy. Int J Radiat Oncol Biol Phys 2004;60:1347–1350.
- [5] Stokes SH. Real JD, Adams PW, et al. Transperineal ultrasound-guided radioactive seed implantation for organ-confined carcinoma of the prostate. Im J Radiat Oncol Biol Phys 1997;37:337—341.
- [6] ICRP. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP publication 103. Ann ICRP 2007; 37:1–332.
- [7] Commission UNR. Consolidated guidance about materials licensees: Program-specific guidance about medical use licenses. NUREG-1556. Washington, DC: US Nuclear Regulatory Commission; 2002. p. 9.
- [8] Commission UNR. Regulatory Guide 8.39: Release of patients administered radioactive materials. Washington, DC: US Nuclear Regulatory Commission; 1997.
- [9] Dauer LT, Kollmeier MA, Williamson MJ, et al. Less-restrictive, patient-specific radiation safety precautions can be safely prescribed after permanent seed implantation. Brachytherapy 2010;9: 101-111
- [10] Dauer LT, Zelefsky MJ, Horan C, et al. Assessment of radiation safety instructions to patients based on measured dose rates following prostate brachytherapy. Brachytherapy 2004;3:1–6.

- [11] ICRP. Radiation safety aspects of brachytherapy for prostate cancer using permanently implanted sources. A report of ICRP Publication 98. Ann ICRP 2005;35:iii-ivi. 3-50.
- [12] Guideline for safety control of permanent implantation brachytherapy of prostate cancer. Editorial supervision by the Japanese Society for Therapeutic Radiology and Oncology/Japanese Urological Association/Japan Radiological Society; 2003.
- [13] Cattani F, Vavassori A, Polo A, et al. Radiation exposure after permanent prostate brachytherapy. Radiother Oncol 2006;79:65-69.
- [14] Michalski J, Mutic S, Eichling J, et al. Radiation exposure to family and household members after prostate brachytherapy. Int J Radiat Oncol Biol Phys 2003;56:764—768.
- [15] Smathers S, Wallner K. Korssjoen T. et al. Radiation safety parameters following prostate brachytherapy. Int J Radiat Oncol Biol Phys 1999;45:397—399.
- [16] Matzkin H, Kaver I. Bramante-Schreiber L, et al. Comparison between two iodine-125 brachytherapy implant techniques: Pre-planning and intra-operative by various dosimetry quality indicators. Radiother Oncol 2003;68:289—294.
- [17] Zelefsky MJ, Yamada Y, Marion C, et al. Improved conformality and decreased toxicity with intraoperative computer-optimized transperineal ultrasound-guided prostate brachytherapy. Int J Radiat Oncol Biol Phys 2003:55:956–963.
- [18] Nickers P, Thissen B, Jansen N, et al. 192 Ir or 125 I prostate brachytherapy as a boost to external beam radiotherapy in locally advanced prostatic cancer: A dosimetric point of view. Radiother Oncol 2006;78:47—52.
- [19] Dauer LT. Globalization, implantation, cremation...Oh, my!. Bruchytherapy 2012;11:197—198.
- [20] Satoh T, Yamanaka H, Yamashita T, et al. Deaths within 12 months after ¹²⁵I implantation for brachytherapy of prostate cancer: An investigation of radiation safety issues in Japan (2003-2010). Brachytherapy 2012;11:192—196.

