Case Rep Oncol 2011;4:492–498
DOI: 10.1159/000332759

Published online:
October 3, 2011

ISSN 1662–6575
www.karger.com/cro

6 Fujii M, Tsukuda M, Satake B, Kubota AA, Kida A, Kohno N, Okami K, Inuyama Y: Phase I/II trial of weekly docetaxel and concomitant radiotherapy for squamous cell carcinoma of the head and neck. Int J Clin Oncol 2004;9:107–112.

7 Calais G, Bardet E, Sire C, Alfonsi M, Bourhis J, Rhein B, Tortochaux J, Man YT, Auvray H, Garaud P: Radiotherapy with concomitant weekly docetaxel for stages III/IV oropharynx carcinoma. Results of the 98–02 GORTEC Phase II trial, Int J Radiat Oncol Biol Phys 2004;58:161–166.

8 Maruya S, Namba A, Matsubara A, Kakehata S, Takeda I, Shirasaki T, Hatayama Y, Nagahata M, Yokoyama J, Shinkawa H: Salivary gland carcinoma treated with concomitant chemoradiation with intraarterial cisplatin and docetaxel. Int J Clin Oncol 2006;11:403–406.

9 Mitsudo K, Shigetomi T, Fujimoto Y, Nishiguchi H, Yamamoto N, Furue H, Ueda M, Itoh Y, Fuwa N, Tohnai I: Organ preservation with daily concurrent chemoradiotherapy using superselective intra-arterial infusion via a superficial temporal artery for T3 and T4 head and neck cancer. Int J Radiat Oncol Biol Phys 2011;79:1428–1435.

10 Shirasaka T, Shimamato Y, Ohshimo H, Yamaguchi M, Kato T, Yonekura K, Fukushima M: Development of a novel form of an oral 5-fluorouracil derivative (S-1) directed to the potentiation of the tumor selective cytotoxicity of 5-fluorouracil by two biochemical modulators. Anticancer Drugs 1996;7:548–557.

11 Ohnishi K, Shioyama Y, Nakamura K, Nakashima T, Ohga S, Nonoshita T, Yoshitake T, Terashima K, Komune S, Honda H: Concurrent chemoradiotherapy with S-1 as first-line treatment for patients with oropharyngeal cancer. J Radiat Res (Tokyo) 2011;52:47–53.

12 Nonoshita T, Shioyama Y, Nakamura K, Nakashima T, Ohga S, Yoshitake T, Ohnishi K, Terashima K, Asai K, Honda H: Concurrent chemoradiotherapy with S-1 for T2N0 glottic squamous cell carcinoma. J Radiat Res (Tokyo) 2010;51:481–484.

13 Inohara H, Inoue T, Akahani S, Yamamoto Y, Takenaka Y, Nakagawa T, Isohashi F, Kubo T: Concurrent chemoradiotherapy with cisplatin and docetaxel for advanced head and neck cancer. A phase I study. Anticancer Res 2004;24:4135–4140.

14 Maeda S, Sugiura T, Saikawa Y, Kubota T, Otani Y, Kumai K, Kitajima M: Docetaxel enhances the cytotoxicity of cisplatin to gastric cancer cells by modification of intracellular platinum metabolism. Cancer Sci 2004;95:679–684.

15 Kreis W, Petrylak D, Savarese D, Budman D: Colitis and docetaxel-based chemotherapy. Lancet 2000;355:2164.

Radiol Phys Technol (2011) 4:173–179
DOI 10.1007/s12194-011-0118-1

Estimation of focal and extra-focal radiation profiles based on Gaussian modeling in medical linear accelerators

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Received: 31 October 2010 / Revised: 6 March 2011 / Accepted: 8 March 2011 / Published online: 24 March 2011

Abstract The X-ray source or focal radiation is one of the factors that can degrade the conformal field edge in stereotactic body radiotherapy. For that reason, it is very important to estimate the total focal radiation profiles of linear accelerators, which consists of X-ray focal-spot radiation and extra-focal radiation profiles. Our purpose in this study was to propose an experimental method for estimating the focal-spot and extra-focal radiation profiles of linear accelerators based on triple Gaussian functions. We measured the total X-ray focal radiation profiles of the accelerators by moving a slit in conjunction with a photon field *p*-type silicon diode. The slit width was changed so that the extra-focal radiation could be optimally included in the total focal radiation. The total focal radiation profiles of an accelerator at 4-MV and 10-MV energies were approximated with a combination of triple Gaussian functions, which correspond to the focal-spot radiation, extra-focal radiation, and radiation transmitted through the slit assembly. As a result, the ratios of the Gaussian peak value of the extra-focal radiation to that of the focal spot for 4 and 10 MV were 0.077 and 0.159, respectively. The peak widths of the focal-spot and extra-focal radiation profiles were 0.57 and 25.0 mm for 4 MV, respectively, and 0.60 and 22.0 mm for 10 MV, respectively. We concluded that the proposed focal radiation profile model based on the triple Gaussian functions may be feasible for estimating the X-ray focal-spot and extra-focal radiation profiles.

Keywords Medical linear accelerator · X-ray focal spot · Extra-focal radiation · SBRT (stereotactic body radiation therapy) · Gaussian modeling

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1 Introduction

Stereotactic body radiation therapy (SBRT) is a precise irradiation method for an extracranial lesion by use of a small number of high-dose fractions [1]. The advantages of SBRT for treating lung tumors are a shortened treatment course that requires fewer trips to the clinic than does a conventional treatment, and the improvement of tumor coverage and normal tissue sparing allowed by greater precision of the setup [2]. Therefore, steep dose gradients outside a target volume must be required with higher precision, because a high dose per fraction should be delivered to a small tumor within a conformal irradiation field in SBRT.

The X-ray source or focal spot is one of the factors which can degrade the conformal field edge in the SBRT. Wang and Leszczynski [3] reported that the dose profile penumbra depends on the X-ray focal-spot size and shape. Therefore, if the focal-spot size became wider, the dose profile penumbra would be larger. As a result, the conformal edge would be blurred. On the other hand, radiation treatment planning (RTP) algorithms based on Monte Carlo simulation have been widely used in several commercial RTP systems [4–8]. In Monte Carlo simulations, the X-ray focal-spot size and shape of each linear accelerator are required for estimation of a more accurate three-dimensional dose distribution in lung cancer patients for SBRT. For that reason, it is very important to estimate the focal-spot radiation of linear accelerators.

Some researchers hypothesized that the total focal radiation consisted of focal-spot radiation and extra-focal radiation [9–11]. Because the characteristics of the focal-spot and extra-focal radiations differ from each other, many methods for determination of extra-focal radiation have been investigated based on (1) direct measurement [9–11], (2) indirect measurement [12–16], and (3) Monte Carlo simulations [7, 17, 18]. However, further studies are needed for investigation of the experimental methods for the total focal radiation and more accurate modeling for them. Therefore, our purpose in this study was to develop a method for measuring the total focal radiation including focal-spot radiation and extra-focal radiation, and then estimating the focal and extra-focal radiation profiles of linear accelerators separately based on Gaussian modeling.

2 Methods and materials

2.1 Total X-ray focal radiation profile model based on Gaussian functions

The total X-ray focal radiation profile measured by a slit assembly has been modeled by double Gaussian functions representing a direct focal-spot radiation and an extra-focal radiation [9–11]. In this study, the extra-focal radiation is considered the scatter source, which is produced mainly by Compton scattering in the field-flattening filter and primary collimator [19]. However, the radiation transmitted through the slit assembly has not been taken into account in the total focal radiation profile model. Therefore, we propose a total focal radiation profile model approximated with triple Gaussian functions, which is given by

$$F(x) = G_f(x) + G_e(x) + G_t(x) + b \tag{1}$$

and

$$G_i(x) = a_i \exp\left(-\frac{1}{2}\frac{x^2}{\sigma_i^2}\right) (i = f, e, t) \tag{2}$$

where f, e, and t correspond to the focal-spot radiation, extra-focal radiation, and radiation transmitted [20] through and around the edge of the slit assembly (slit corner), respectively, a_i as well as σ_i are the peak height and width parameters of each Gaussian function, respectively, and b is the background signal. Because the peak width parameter σ_i is related to the spread of each radiation profile rather than the statistical standard deviation (SD), the parameter σ_i of a Gaussian function is called a "peak width" of the Gaussian function in this study. It is common knowledge that the full width at half maximum is $2\sqrt{2\ln 2}\,\sigma$. All parameters in Eq. 1 were determined by following two steps so that the approximate model of Eq. 1 can fit the experimental data of the total focal radiation profile obtained by a method described in the next section. In the first step, the peak width σ_f of the focal-spot radiation profile was determined by fitting of Eq. 1 with the narrow total focal radiation profile obtained by use of a 0.1-mm slit. In the second step, all other parameters in Eq 1 except the peak width σ_f of the focal-spot radiation profile, i.e., the peak heights (a_f, a_e, and a_t) and peak widths (σ_e, σ_t), were determined by fitting of Eq. 1 with the broad total focal radiation profile obtained by use of a 0.4-mm slit.

2.2 Measurement of total X-ray focal radiation profiles

The total X-ray focal radiation profiles of a linear accelerator were measured by moving a collimator-slit assembly in conjunction with a photon field p-type silicon diode. Figure 1 shows an illustration of the experimental setup for measurement of a total focal radiation profile of the linear accelerator. A megavoltage linear accelerator (Clinac 21 EX; Varian, Palo Alto, USA) producing 4-MV and 10-MV photon beams was used as the radiation source in our experiments. The irradiation field was set to 5.0 × 5.0 cm^2 at an isocenter of 100 cm. The collimator-slit assembly consisted of one to five sheets of paper (each thickness: 0.1 mm) sandwiched by two solid iron blocks [6 cm

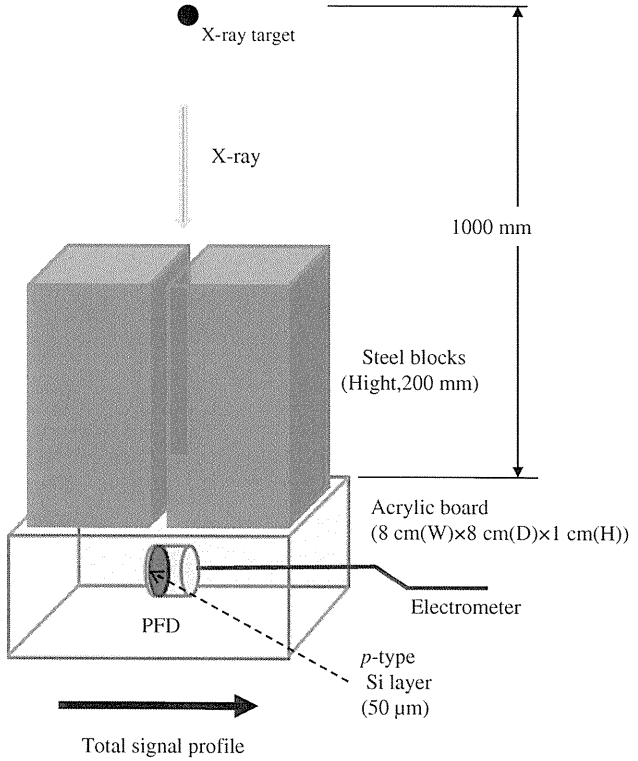

Fig. 1 Illustration of the experimental setup for measurement of total focal radiation profiles of a linear accelerator

(W) × 6 cm (D) × 20 cm (H), PLAT-SSB-A200-B60-T60, MISUMI, Japan], whose flatness was 200 ± 0.2 mm. The collimator-slit assembly in conjunction with a photon field detector (PFD; Scanditronix Medical AB, Uppsala, Sweden) was moved in a horizontal direction by use of a stepping motor (Suruga Seiki stepping motor controller Model D70) across the focal spot. The PFD was mounted below the center of the collimator-slit assembly. The other end of the PFD was connected to an electrometer (RAMTEC 1000 plus TOYO MEDIC, Japan). The PFD has an effective diameter of 2.0 ± 0.1 mm and a 50-μm thick *p*-type Si layer, and can be used for 1–50 MV.

For investigation of the dependence of slit width on the total focal-spot radiation profiles, the total focal radiation profiles were scanned by a slit assembly with slit widths of 0.1, 0.2, 0.3, 0.4, or 0.5 mm within ±10 mm from a beam axis with a scanning pitch of 0.2 mm for 10-MV X-rays. For determination of the Guassian parameters in Eq. 2, two types of total focal radiation profiles, i.e., narrow and broad total focal radiation profiles, were measured by use of two slit widths of 0.1 and 0.4 mm, respectively. The narrow total focal radiation profile was scanned within ±5 mm from a beam axis with a slit width of 0.1 mm and a scanning pitch of 0.1 mm, but a 1-mm pitch outside ±5 mm. The broad total focal radiation profile was measured within ±15 mm from a beam axis with a slit width of 0.4 mm and a scanning pitch of 0.2 mm.

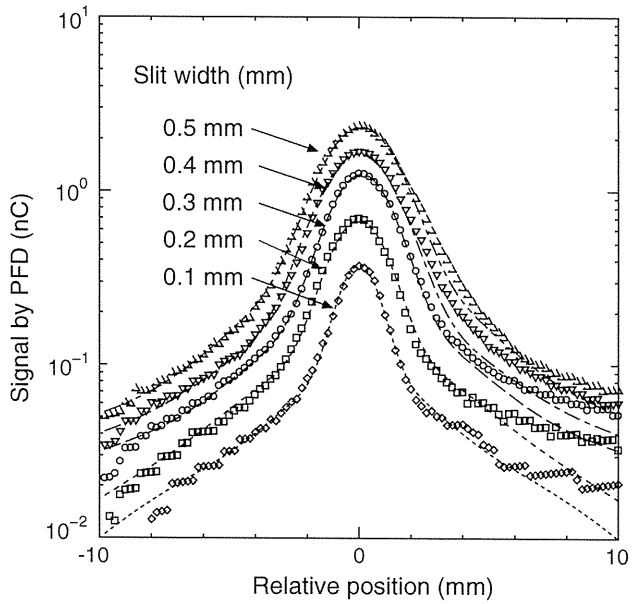

Fig. 2 Total focal radiation profiles measured for 10-MV X-rays by a slit assembly with slit widths of 0.1, 0.2, 0.3, 0.4, or 0.5 mm. The *open symbols* correspond to the signal measured by a PFD, and the *dotted lines* indicate the approximated models

Because both profiles contained the background signal, the background signal was subtracted from the measured profiles for determination of the net profiles, which were used in this study. We considered the background signal as diode dark signal and very weak radiation transmitted through the iron block used for the slit assembly, which would not include the radiation transmitted through and around the edge of the slit assembly. The background signal was measured by moving an iron block without a slit under the same conditions as those of the profile measurement at a scanning pitch of 1 mm.

3 Results

Figure 2 shows the total focal radiation profiles measured by a slit assembly with slit widths of 0.1, 0.2, 0.3, 0.4, or 0.5 mm for 10-MV X-rays. The approximate models indicated by dotted lines were fitted with the measured signal. However, the tail data in the radiation profile obtained by the 0.1-mm slit fluctuated greatly. Figure 3 shows the relationship between the slit width and the average fluctuation of the measured data around the tail. The average fluctuation of the measured data was defined by the average difference between the measured data and the approximate model around the tail (−9.8 to −7.2 mm, 7.2 to 9.8 mm). The data measured by the 0.1-mm slit were the most unstable because of the very small number of photons. Therefore, this result suggested that the

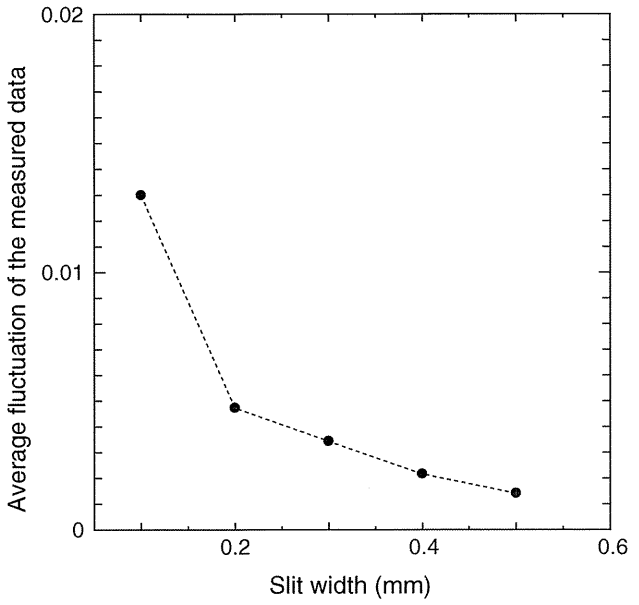

Fig. 3 Relationship between the slit width and the average fluctuation of the measured data around tail outside ±2 standard deviations

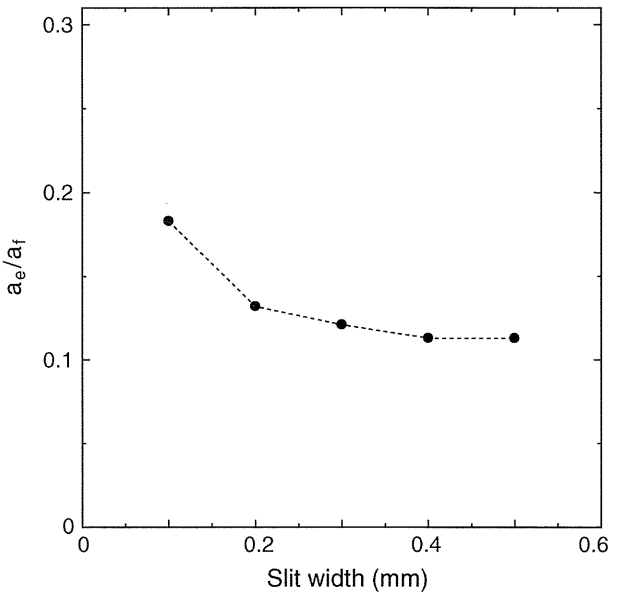

Fig. 4 Relationship between the slit width and the ratio (a_e/a_f) of the Gaussian height of the extra-focal radiation (a_e) to that of the focal-spot radiation (a_f) in the approximated model expressed by Eq. 2

parameters of the extra-focal radiation profile and the transmitted radiation would be considered to be inaccurate when the parameters were determined for such inaccurate tail data. Consequently, we decided to use the 0.1-mm slit only for determination of the peak width σ_f of the focal-spot radiation.

Figure 4 shows the relationship between the slit width and the ratio (a_e/a_f) of the Gaussian height of the extra-focal radiation (a_e) to that of the focal-spot radiation (a_f) in the approximate model expressed by Eq. 2. Figure 5 shows the relationship between the slit width and the peak widths of the focal-spot (σ_f), extra-focal (σ_e), and transmitted radiation (σ_t) profiles expressed by the Gaussian function in Eq. 2. According to Fig. 4, slits with a width larger than 0.4 mm would be better, because the ratio (a_e/a_f) did not change from the 0.4-mm width to the 0.5-mm width. In addition, because the extra-focal radiation and transmitted radiation contribute to the tail region of the total radiation profile, we need stable experimental data in the tail region, which was fitted by the approximate model. The data fluctuation around the tail region of the total focal radiation profile shown in Fig. 3 seems to be small for slit widths larger than 0.4 mm. Furthermore, as shown in Fig. 5, the peak width of the extra-focal radiation profile seems to become constant for slit widths larger than 0.4 mm. Therefore, we considered that the 0.4-mm slit width would be proper for determination of the peak heights and peak widths for the extra-focal radiation and transmitted radiation profiles.

Figure 6 shows the measured signal (solid circle) and the approximate model (solid line) of the narrow total

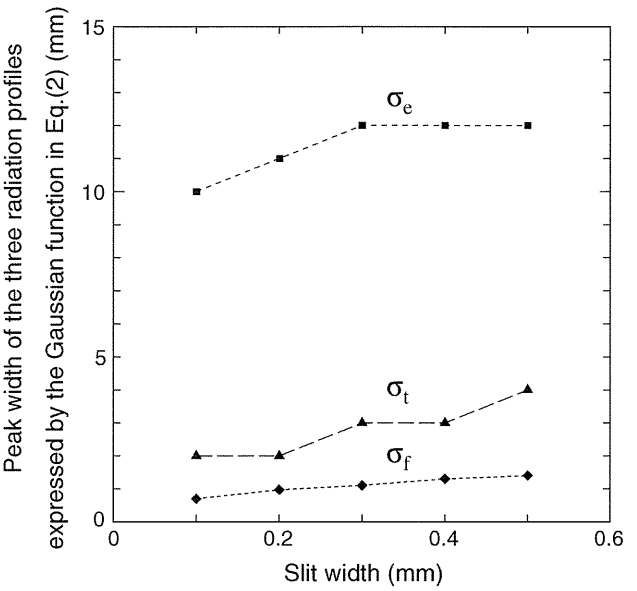

Fig. 5 Relationship between the slit width and the peak widths of focal-spot (σ_f), extra-focal (σ_e), and transmitted radiation (σ_t) profiles expressed by the Gaussian function in Eq. 2

X-ray focal radiation profile with use of a 0.1-mm slit obtained for 4-MV and 10-MV X-ray beams. The measured data fluctuate on the tail of the total X-ray focal radiation profile outside ±5 mm, because the number of photons decreases on the tail of the radiation profile obtained with a 0.1-mm narrow slit.

Figure 7 shows the relative error in the total focal radiation profile within ±5 mm between the measured

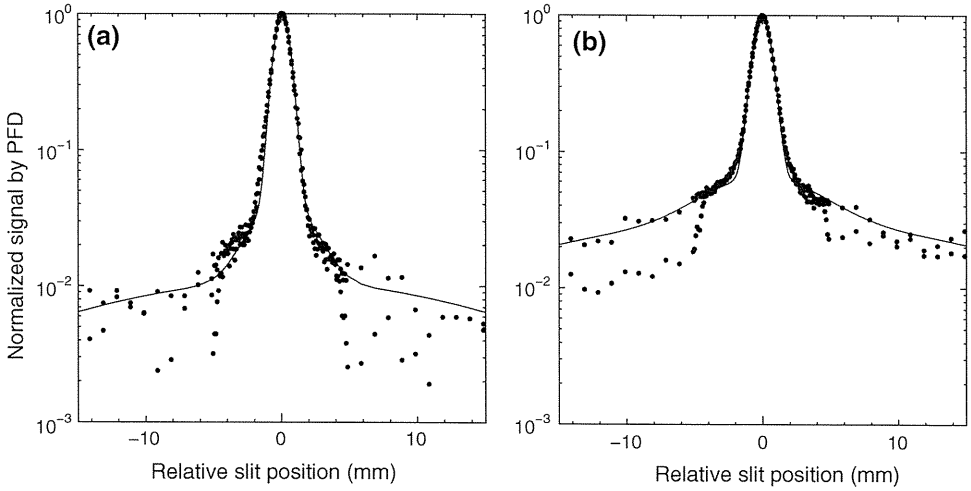

Fig. 6 Measured signal (*solid circle*) and the approximated model (*solid line*) of the narrow total X-ray focal radiation profile with a 0.1-mm slit obtained for (**a**) 4-MV and (**b**) 10-MV X-ray beams

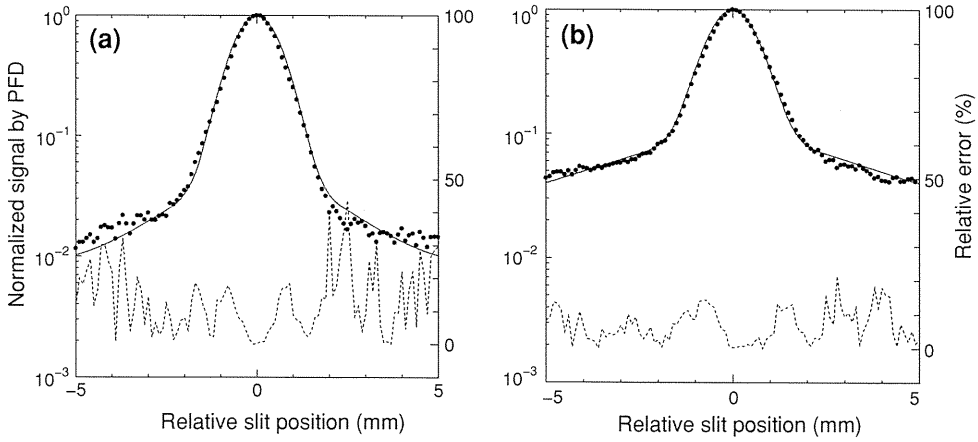

Fig. 7 Relative error (*dotted line*) in the total focal radiation profile within ±5 mm between the measured signal and approximated model for a 0.1-mm slit obtained for (**a**) 4-MV and (**b**) 10-MV X-ray beams. The *solid circles* and *solid lines* indicate the measured signal and the approximated model, respectively, which are the same data as shown in Fig. 6

signal and the approximate model for a 0.1-mm slit, obtained for 4-MV and 10-MV X-ray beams. The solid circles and solid lines indicate the measured signal and the approximated model, respectively, which are the same data as shown in Fig. 6. The relative error (%) was defined by the measured value minus the approximated value divided by the measured value. The relative error was smaller than 50% for 4 MV, but was 20% for 10 MV.

Figure 8 shows the measured signal (solid circle) and the approximate model (solid line) of the broad total focal radiation profile measured and approximated by the proposed method with a slit width of 0.4 mm for 4-MV and 10-MV X-rays. Figure 8 also shows the relative error in the total focal radiation profile between the measured signal and the approximated model. The relative errors for 4 and 10 MV were smaller than 20 and 10%, respectively.

Table 1 shows the parameters in Gaussian models, which were obtained by the proposed method, approximated for total focal radiation profiles for 4 and 10 MV. As a result, the ratios of the Gaussian peak value of the extra-focal radiation to that of the focal spot for 4 and 10 MV were 0.077 and 0.159, respectively. The peak widths of the focal-spot and extra-focal radiations were 0.57 and 25.0 mm for 4 MV, respectively, and 0.60 and 22.0 mm for 10 MV, respectively.

4 Discussion

We have developed an experimental method for measuring the total focal radiation distribution including focal-spot radiation and extra-focal radiation, and then estimating the focal and extra-focal radiation profiles of linear accelerators separately based on a triple Gaussian model. Sham et al. [11] published a study similar to ours, and they proposed an experimental method for measurement of the total focal radiation profile using a slit width of 0.3 mm, where the profiles were approximated by two Gaussian functions. On the other hand, we used an approximate model of triple Gaussian functions, taking into account radiation transmitted through and around the edge of the slit assembly. Furthermore, we proposed a two-step method

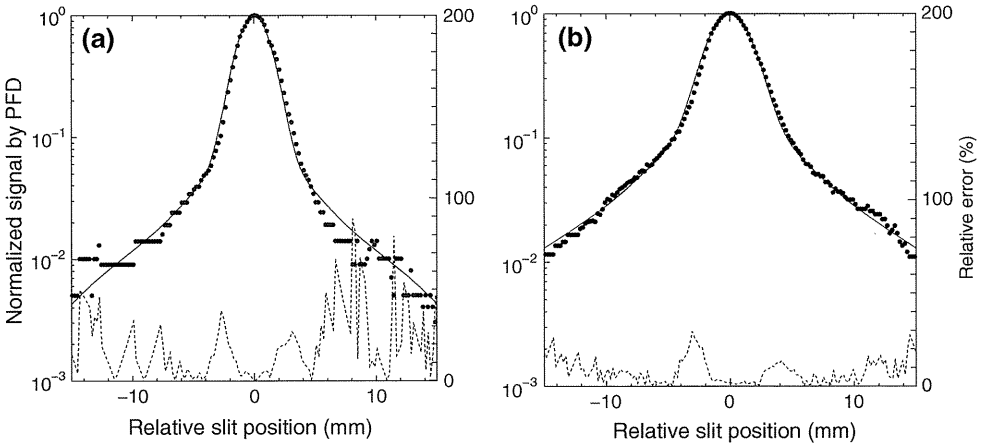

Fig. 8 Measured signal (*solid circle*) and the approximated model (*solid line*) of the total broad X-ray focal radiation profile with a 0.4-mm slit obtained for (**a**) 4-MV and (**b**) 10-MV X-ray beams. This figure also shows the relative error (*dotted line*) in the total focal radiation profile within ±15 mm between the measured signal and the approximated model for a 0.4-mm slit obtained for (**a**) 4-MV and (**b**) 10-MV X-ray beams

Table 1 Parameters in a Gaussian model approximating total focal radiation profiles obtained by the proposed method

X-ray energy (MV)	Triple-Gaussian model parameters						
	a_f	σ_f (mm)	a_e	σ_e (mm)	a_t	σ_t (mm)	a_e/a_f
4	3.00	0.57	0.23	25.0	0.65	4.20	0.077
10	3.47	0.60	0.55	22.0	1.23	6.10	0.159

Table 2 Peak width: comparisons of the focal-spot radiation profile and extra-focal radiation profile between our study and other studies

	X-ray energy (MV)	σ_f (mm)	σ_e (mm)	a_e/a_f
Jaffray et al. [9]	6	0.30–1.45	0.93	0.020
Sharpe et al. [10]	6	0.43–0.85	–	0.120
Sham et al. [11]	6	0.65	9.93	0.162
Our study	4, 10	0.57, 0.60	25.0, 22.0	0.077, 0.159

for determination of Gaussian parameters of the focal-spot radiation profile and the extra-focal radiation profile using narrow and broad total focal radiation profiles measured by slits with two widths.

Gaussian models of the focal-spot radiation profile and the extra-focal radiation profile based on experimental data are useful and necessary for Monte Carlo simulations for estimating accurate dose distributions at penumbral area [3]. If the focal radiation profiles were incorrect, the dose profiles at the penumbral area obtained by the Monte Carlo simulation could not be consistent with measured data. In particular, the discrepancy could become large in the SBRT, where steep dose gradients outside a tumor should be required in a small irradiation field.

Table 2 shows a comparison of the peak widths of the focal-spot radiation profile and the extra-focal radiation profile between our study and other studies based on experimental methods. Jaffray et al. [9] obtained nine focal-spot radiation profiles of linear accelerators using a computed tomography reconstruction technique. The peak width of the focal-spot radiation profile ranged from 0.30 to 1.45 mm, the peak width of the extra-focal radiation profile was 0.93 mm, and the a_e/a_f ratio was 0.02. Sharpe et al. [10] measured the extra-focal radiation for a 6-MV X-ray beam, where the peak widths of the focal-spot radiation profiles were from 0.43 to 0.85 mm, and the a_e/a_f ratio was approximately 12%. Sham et al. [11] evaluated the total focal radiation profiles using a simplified moving slit technique in conjunction with a diode detector for a megavoltage 6-MV linac. They reported that the peak widths of the focal-spot and extra-focal radiation profiles were 0.65 and 9.93 mm, respectively, and the a_e/a_f ratio was 0.162. On the other hand, the a_e/a_f ratios obtained based on Monte Carlo simulation ranged from 0.065 to 0.088 according to Mohan et al. [18], and from 0.03 to 0.09 according to Chaney et al. [17]. As a result, our data on the focal-spot radiation profile and the a_e/a_f ratio were close to the data of Sharpe et al. except for the peak width of the extra-focal radiation profiles. Because few data on the peak width of the extra-focal radiation profiles were reported in past studies, we should continue to investigate the methods for measurement of the extra-focal radiation profiles.

5 Conclusions

We have proposed an experimental method for estimating focal-spot and extra-focal radiation profiles of linear accelerators based on triple Gaussian functions. As a result, the ratios of the Gaussian peak height of the extra-focal radiation to that of the direct focal spot, which were measured by this proposed method, were close to previous results. Therefore, we conclude that the proposed focal-profile model based on the triple Gaussian functions may

be feasible for estimating the X-ray focal-spot and extra-focal radiation profiles.

Acknowledgments The authors thank Mr. Kazuharu Nishitani and Mr. Tokuhiro Hayashi for assistance in measurements of the total focal radiation profile.

References

1. Martin A, Gaya A. Stereotactic body radiotherapy: a review. Clin Oncol. 2010;22(3):157–72.
2. Nagata Y, Matsuo Y, Takayama K, Norihisa Y, Mizowaki T, Mitsumori M, et al. Current status of stereotactic body radiotherapy for lung cancer. Int J Clin Oncol. 2007;12(1):3–7.
3. Wang LLW, Leszczynski K. Estimation of the focal size and shape for a medical linear accelerator by Monte Carlo simulation. Med Phys. 2007;34(2):485–8.
4. Mackie TR, Scrimger JW, Battista JJ. A convolution method of calculating dose for 15-MV X rays. Med Phys. 1985;12(2): 188–96.
5. Boyer AL, Mok EC. Calculation of photon dose distributions in an inhomogeneous medium using convolutions. Med Phys. 1986;13:503–9.
6. Ahnesjö A. Collapsed cone convolution of radiant energy for photon dose calculation in heterogeneous media. Med Phys. 1989; 16(4):577–92.
7. Liu HH, Mackie TR, McCullough EC. Correcting kernel tilting and hardening in convolution/superposition dose calculations for clinical divergent and polychromatic photon beams. Med Phys. 1997;24(11):1729–41.
8. Battista JJ, Sharpe MB. True three-dimensional dose computations for megavoltage X-ray therapy: a role for the superposition principle. Australas Phys Eng Sci Med. 1992;15(4):159–78.
9. Jaffray DA, Battista JJ, Fenster A, Munro P. X-ray source of medical liner accelerators: focal and extra-focal radiation. Med Phys. 1993;20(5):1417–27.
10. Sharpe MB, Jaffray DA, Battista JJ, Munro P. Extrafocal radiation: a unified approach to the prediction of beam penumbra and output factors for megavoltage X-ray beams. Med Phys. 1995; 22(12):2065–74.
11. Sham E, Seuntjens J, Devic S, Podgorsak EB. Influence of focal spot on characteristics of very small diameter radiosurgical beams. Med Phys. 2008;35(7):3317–30.
12. Ahnesjö A, Knöös T. Application of the convolution method for calculation of output factors for therapy photon beams. Med Phys. 1992;19(2):295–301.
13. Ahnesjö A. Analytic modeling of photon scatter from flattening filters in photon therapy beams. Med Phys. 1994;21(8):1227–35.
14. Zhu TC, Bjarngard BE. The head-scatter factor for small field sizes. Med Phys. 1994;21(1):65–8.
15. Das IJ, Ding GX, Ahnesjö A. Small fields : nonequilibrium radiation dosimetry. Med Phys. 2008;35(1):206–15.
16. Scott AJD, Nahum AE, Fenwick JD. Monte Carlo modeling of small photon fields: quantifying the impact of focal spot size on source occlusion and output factors, and exploring mini phantom design for small-field measurements. Med Phys. 2009;36(7): 3132–44.
17. Chaney EL, Cullip TJ, Gabriel TA. A Monte Carlo study of accelerator head scatter. Med Phys. 1994;21(9):1383–90.
18. Mohan R, Chui C, Lidofsky L. Energy and angular distributions of photons from medical linear accelerators. Med Phys. 1985; 12(1):592–7.
19. DeLuca P, Jones D, Gahbauer R. Prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT). ICRU report 83. 2010;10(1):60–6
20. Sawant A, Antonuk L, El-Mohri Y. Slit design for efficient and accurate MTF measurement at megavoltage X-ray energies. Med Phys. 2007;34(5):1535–45.

II. 臨　　床

前立腺癌の治療
放射線療法　外照射

外照射療法の現状と展望

Trends and future of external radiotherapy for prostate cancer

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Key words：外照射，強度変調放射線治療，画像誘導放射線治療，寡分割照射，hypofractionation

はじめに

外照射を含めた放射線治療は，近年急速に進歩している．我が国においても，三次元原体放射線治療(three-dimensional conformal radiotherapy: 3DCRT)，強度変調放射線治療(intensity-modulated radiotherapy: IMRT)，画像誘導放射線治療(image-guided radiotherapy: IGRT)などの最新の技術が実際に臨床の現場に導入されてきている．また，線量増加の有用性などに関する臨床試験の結果が次々と明らかとなり，臨床現場へフィードバックされることにより，前立腺癌に対する放射線治療の照射法，線量などは急速に変化しつつある．

本稿では，外照射の現状とその将来展望について解説する．

1. 外照射の現状

外照射の技術的な進歩は，悪性腫瘍に対する放射線治療の成績の向上に大きく貢献してきた．特に，前立腺癌に対しては，直腸線量を低減することで，更に多くの線量を照射できるため，積極的に最新技術が導入されている．このような状況で，前立腺癌の放射線治療が我が国においてどのように行われており，どのように変化しているかを恒常的にモニタすることは非常に重要である．これらを明らかにする研究の一つが，医療実態調査研究(Patterns of Care Study: PCS)である．

PCSは，米国で開発された臨床的精度管理QAの手法の一つで，structure，process，outcomeの分析を行うものである[1]．我が国には1996年より本格的に導入され，厚生労働省がん研究助成金の援助を受け，研究者がランダムに選択された全国の放射線治療施設を訪問し，ランダムに抽出された各疾患の治療のプロセス，成績などを調査してきた[2]．前立腺癌に対しては，1996-98年，1999-2001年，2003-05年に放射線治療が行われた遠隔転移または重複癌を伴わない前立腺癌症例が調査され[3,4]，計177施設より，根治的外照射例852例，術後照射例278例，内分泌療法抵抗・再燃例189例，その他104例(組織内照射施行例84例含む)，合計1,423例が集積されている．

根治的外照射852例についてみると[5]，T因子は，T1: 16.6%，T2: 38.7%，T3: 38.2%，T4: 6.5%であった．また，リンパ節転移例は6.5%であった．Gleasonスコアは，2-6: 35.5%，7: 31.8%，8-10: 32.7%であった．全治療前のPSA(prostate specific antigen)値は，<10 ng/mL:

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0047-1852/11/¥60/頁/JCOPY

29.8％，10-19.9ng/mL: 24.4％，≧20ng/mL: 45.9％であった．経年的変化としては，T1-2の割合は1996-98年34.6％から，2003-05年64.6％と上昇しており，PSA値の中央値は，1996-98年22ng/mLから2003-05年14.9ng/mLと低下していた．すなわち，放射線治療にて治療される早期前立腺癌症例が増加していることがわかる．内分泌療法施行割合は84.9％と，多くの症例に内分泌療法が併用されていた．放射線治療に関しては，58.0％に3DCRTが施行されていたが，その割合は，1996-98年49.1％から2003-05年66.4％と上昇している．照射線量の中央値は，1996-98年65 Gyから2003-05年70 Gyと上昇しており，経年的に，より高精度な照射方法にて高い線量が投与される傾向にあることを示している．

このように，PCSは，放射線治療の構造面，診療過程を全国規模で調査し，解析することによって，診療上の変化に加えて，照射野設定，線量分割などを含めた診療の質を同時にモニタでき，日本の放射線治療の質の向上に寄与してきた．米国では，このような研究はThe Quality Research in Radiation Oncology(QRRO)として継続されており，米国での放射線治療の質の維持・向上に重要な役割を果たしている．今後，我が国での前立腺癌の放射線治療では，IMRTやIGRTなどの新しい技術が更に普及してくるものと思われる．また，粒子線治療により治療される前立腺癌症例も増加するであろう．このように，今後とも急激に変化していく放射線治療の実態を調査し，その診療の質を評価する研究の重要性は更に増すものと考えられる．

2. 画像誘導放射線治療

放射線治療のターゲットとなる前立腺の位置は，毎回の治療ごとに変動することが知られている．これは，セットアップエラーに加えて，直腸，膀胱容量などによっても前立腺の位置が影響されることによる．もし，この治療ごとの位置変動を小さくすることができれば，より小さい照射野で照射でき，有害事象を低減化できる可能性がある．

前立腺の位置の不確定要素を低減する方法としては，金属マーカーを前立腺周囲に挿入し，治療直前にX線透視などでマーカーの位置を確認する方法，治療装置に連携した超音波装置やCTなどにより位置確認を行う方法などがある．このような方法は，画像誘導放射線治療(image-guided radiotherapy: IGRT)と呼ばれ，近年急速に普及しつつある．

我が国において，IGRTが前立腺癌の外照射においてどのように使用されているか，不明であった．そこで，厚生労働省科学研究費による'放射線治療期間の短縮による治療法の有効性と安全性に関する研究'では，IGRT，IMRTの実施状況に対してアンケートを行った．平成22年に全国大学病院/がんセンター，都道府県がん診療連携拠点病院を含む主要139施設にアンケートを送付し，117施設(84.2％)より回答を得た．IMRT実施施設は67施設(57.3％)，IGRT実施施設は71施設(60.7％)であった．しかし，IMRT未導入施設のうち75％，IGRT未導入施設のうち65％が3年以内に導入予定としている．すなわち，数年以内に多くの施設でIMRT，IGRTが行われるようになると考えられる．照射については，93.0％の施設が週5回法，86.6％の施設が1回2 Gyにて治療を行っていた．投与線量は，図1に示すように，3DCRTでは中央値70 Gy，IMRTでは中央値76 Gyであり，明らかにIMRTにて高線量が投与されていた．IGRTについては，kVCT，MVCT，透視装置，超音波装置，金属マーカーなど，様々な手法で行われており，IMRTなどの高精度治療が実施される場合にはほぼ全例に，ほぼ毎日IGRTでの位置確認が行われていた．位置確認については，47.1％が骨情報，40.0％が前立腺などの軟部組織，12.9％が金属マーカーでの位置合わせであった．

このアンケートからもわかるように，少なくとも大規模施設においては，数年以内にIMRT，IGRTが広く普及すると予想され，今後の前立腺癌の外照射の成績向上が期待される．

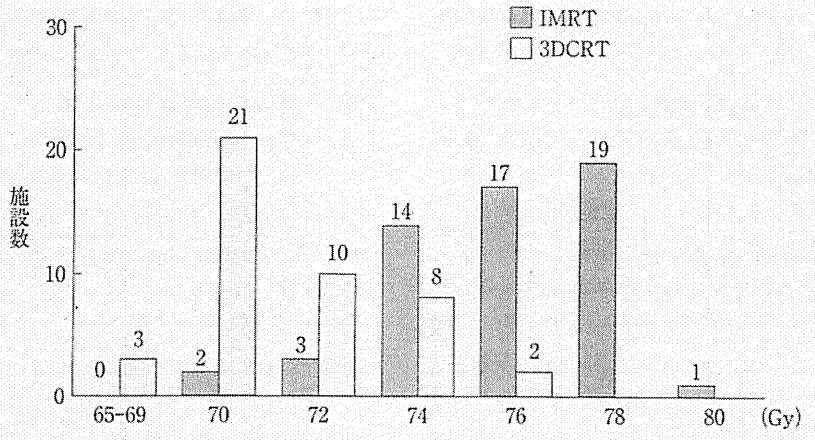

図1 治療法別の前立腺に対する総線量の分布
1回線量1.8-2.0 Gyにて治療している全国100施設を対象とした.
IMRT: 強度変調放射線治療, 3DCRT: 三次元原体放射線治療.

3. 寡分割照射

上述のように, IGRTが普及することのメリットの一つは, 毎回の治療ごとのセットアップエラーなどによる位置変動を小さくすることにより, 治療成績向上に貢献することである. 実は, もう一つの利点として, 1回線量を増加させ, 治療回数を減らす(寡分割照射, hypofractionation)ことが可能となる点があげられる.

放射線に対する感受性の指標としてα/β比が知られており, 通常の悪性腫瘍は10程度, 直腸などの正常組織では3程度とされており, 1回線量を大きくすると, α/β比の小さい正常組織では有害事象の可能性が高くなり, 腫瘍のコントロール率向上のメリットよりもマイナス面の方が大きいとされている. しかし, 増殖速度の遅い前立腺癌のα/β比は非常に小さく, 周囲の正常組織である直腸や尿道などのα/β比よりも小さいと推測されている[6]. もしこの予想が正しければ, 1回線量の増加により, 有害事象の発生率は変えずに治療成績を向上させることができるかもしれない.

通常分割(1回線量1.8-2 Gy)での前立腺癌に対する照射回数は37-40回程度であり, セットアップエラーや直腸容積などによる前立腺位置の変動があっても, 多数回の照射により平均化されるため, それほど治療成績に影響しない. しかし, 照射野のマージンが小さい場合, 1回線量をより大きくし, 分割回数を小さくすればするほど, 前立腺の位置の不確定要素が治療成績に大きく関係してくるようになる[7]. すなわち, 毎回の前立腺の位置の不確定要素を低減させるIGRTを用いることで, 初めて寡分割照射を安全にかつ効果的に実現できると考えられている.

寡分割照射については, 既に多くの報告がある. レトロスペクティブな報告で, 大規模なものとして, Cleveland Clinicからの1回2.5 Gy, total 70 Gyの治療成績の報告がある[8]. 超音波装置を使って前立腺の位置を同定してIMRTにて治療された770例の5年PSA無再発率は82%と良好であり, Grade 2以上の直腸障害, 尿路系障害はそれぞれ4.5%, 5.2%と通常分割法と同程度であったとしている.

現在, 寡分割照射の有効性を確認するために, IGRTを使って, 通常分割照射(1回1.8-2 Gy)と寡分割照射(1回2.5-3 Gy程度)との大規模なランダム化比較試験が幾つか実施されており[9], これらの結果によっては, 寡分割照射がスタンダードの一つとなる可能性を秘めている.

前立腺癌に定位的に放射線治療を行い, 更に少ない回数で, 1回大線量を投与する試みもある. Bolzicco ら[10]は, 低~中リスク前立腺癌45例に対して, Cyberknifeにより定位的に35

Gy/7分割(1回7Gy)を照射し，20カ月の経過観察期間にて，Grade 2以上の晩期有害事象は4.4％と良好であったと報告している．しかし，このような大線量，少数分割の長期成績は不明であり，いまだ研究的な治療法であることに注意しなければならない．

おわりに

いままで述べてきたように，IMRT，IGRTが前立腺癌の外照射に急速に応用されるようになっており，より有害事象の発生を抑えた治療が可能となっている．更に，それらの技術的な進歩を背景として，寡分割照射の有用性が世界中で検討されている．外照射の欠点は，7-8週間程度と治療期間が長期にわたる点であったが，もし寡分割照射の大規模比較試験の結果が明らかとなれば，より短期間で外照射が実施可能となるかもしれない．今後の研究成果が期待される．

文献

1) Hanks GE, et al: Patterns of Care Studies—Past, Present, and Future—. Semin Radiat Oncol 7: 97-100, 1997.
2) 手島昭樹：放射線腫瘍学における医療実態調査研究—わが国における臨床施行の成果と意義，将来目標—．日放線腫瘍会誌 12: 1-12, 2000.
3) Nakamura K, et al: Trends in the practice of radiotherapy for localized prostate cancer in Japan: a preliminary patterns of care study report. Jpn J Clin Oncol 33: 527-532, 2003.
4) Ogawa K, et al: Radical External Beam Radiotherapy for Clinically Localized Prostate Cancer in Japan: Changing Trends in the Patterns of Care Process Survey. Int J Radiat Oncol Biol Phys, 2010. Oct 13. [Epub ahead of print]
5) 中村和正：外照射—3DCRT，IMRT，陽子・重粒子線．限局性(T1，T2)前立腺癌の治療．第36回尿路悪性腫瘍研究会記録，p54-58, 2010.
6) Williams SG, et al: Use of individual fraction size data from 3756 patients to directly determine the alpha/beta ratio of prostate cancer. Int J Radiat Oncol Biol Phys 68: 24-33, 2007.
7) Song WY, et al: Evaluation of image-guided radiation therapy(IGRT) technologies and their impact on the outcomes of hypofractionated prostate cancer treatments: a radiobiologic analysis. Int J Radiat Oncol Biol Phys 64: 289-300, 2006.
8) Kupelian PA, et al: Hypofractionated intensity-modulated radiotherapy(70Gy at 2.5Gy per fraction) for localized prostate cancer: Cleveland Clinic experience. Int J Radiat Oncol Biol Phys 68: 1424-1430, 2007.
9) Miles EF, Lee WR: Hypofractionation for prostate cancer: a critical review. Semin Radiat Oncol 18: 41-47, 2008.
10) Bolzicco G, et al: Image-guided stereotactic body radiation therapy for clinically localized prostate cancer: preliminary clinical results. Technol Cancer Res Treat 9: 473-477, 2010.

Q28 前立腺がん

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point

- 前立腺がんの放射線治療は大きな進歩をとげ，3次元原体照射，強度変調放射線治療，小線源療法など，前立腺に線量を集中し，その周囲への被曝を低減する種々の技術が開発された．
- 早期前立腺がんに対する放射線治療の治療成績は手術とほぼ同等である．
- 放射線治療の主な有害事象は直腸障害であるが，男性機能，尿路系機能などを含めた生活の質を高く保つことができる．
- 放射線治療は，前立腺全摘除術後のアジュバント療法または救済療法として行われることがある．
- 骨転移の痛み，脊髄圧迫，下部尿路閉塞などの症状緩和にも放射線治療が用いられる．

Q 前立腺がんに対する放射線治療の役割は何ですか？

A 前立腺がんの放射線治療は，治す目的で行う根治的放射線治療，手術後に行う術後照射，がんの進行に伴う症状を緩和するために行う緩和的放射線治療に分かれます．根治的放射線治療は，後述するように近年急速に進歩し，治療成績は手術とほぼ同等のレベルに向上し，根治的な治療を検討する場合の重要な選択肢の一つとなっています．また，前立腺全摘除術が行われた後に，再発を予防するためや再発した場合の治療として，術後に放射線治療が行われることがあります．骨転移による痛みやホルモン療法抵抗性で腫大した前立腺による排尿障害などの症状を緩和するためにも，放射線治療が用いられます．

Q 前立腺がんの根治的な治療を考えるにあたり，注意すべき点は何ですか？

A 前立腺がんの特徴は，他の悪性腫瘍と比較して予後が良好であることです．早期の前立腺がんであれば，適切な治療を行うことにより前立腺がんで命を落とす可能性はかなり低いと考えられます．また，前立腺がんは，前立腺特異抗原（prostate specific

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antigen：PSA）というきわめて鋭敏な腫瘍マーカーをもつことも特徴です．PSAは早期診断や治療効果の優れた指標として用いられ，再発の早期発見にも威力を発揮します．しかし，たとえPSA再発が起こっても，それがすぐに前立腺がん死と結びつくわけではないことが多いため，前立腺がんの治療方針を決定する場合，治療後の患者の生活の質（quality of life：QOL）をいかに高く保つかが重要になります．年齢，合併症などで患者の期待生存期間が短い場合や，進行のリスクが非常に小さいと判断される場合には，無治療も一つの選択肢となる場合があります．

前立腺がんは，通常の悪性腫瘍のように病期分類としてTNM分類が用いられ，遠隔転移やリンパ節転移があれば，それだけ予後が不良となります．さらに，治療前PSA値，Gleason scoreなども重要な予後予測因子となります[1]．つまり，前立腺がんの放射線治療は，単にTNM分類のみならず，これらのリスク因子を考慮に入れた治療戦略を立てる必要があります．リスク分類にはいろいろなものがありますが，米国のNCCN Clinical Practice Guidelines in Oncology[2]では，T1～2aかつGleason score 2～6かつPSA＜10 ng/mLを低リスク群，T3a以上またはGleason score 8～10またはPSA＞20 ng/mLを高リスク群，それ以外を中リスク群と分類し，治療方針の決定を行っています．

メモ

●Gleason score

前立腺がんの病理組織学的分類として用いられます．がんの悪性度を5段階に評価し，前立腺がんの組織像の多様性を考慮して，量的に最も優位なパターンと次に優性なパターンの数の合計をグリーソンスコア（＝Gleason score, Gleason sum）として表現します．グリーソンスコアでは，6以下が低リスク，7は中リスク，8～10は高リスクとされ，治療法選択の重要な情報の一つです．

Q 前立腺がんの根治的放射線治療には，どのようなものがありますか？

A 前立腺がんの放射線治療は，大きく外部照射と小線源療法に分かれます．外部照射は体外からX線などの放射線を照射する方法で，3次元放射線治療（3 dimentional conformal radiation therapy：3DCRT），強度変調放射線治療（intensity-modulated radiation therapy：IMRT）などの照射方法があります．また，これらの治療を行う直前に治療計画との位置のずれを補正して照射する，画像誘導放射線治療（image-guided radiation therapy：IGRT）が近年普及しています．さらに，陽子イオンや炭素イオンを使った粒子線治療も近年普及しつつあります（3DCRT，IMRT，IGRTについての詳細は総論の項を参照ください）．前立腺がんは，このような高精度放射線治療の利点を最も生かすことができる疾患の一つです．なぜなら，前立腺がんの放射線治療では直腸出血の頻度をいかに低減させるかが重要なポイントとなり，これらの高精度放射線治療は直腸の被曝線量を効率的

に低減できるからです.

小線源療法では，小さい金属容器に密封された放射性同位元素（これを小線源といいます）から放出されるγ線などを治療に用います．前立腺がんに対する小線源療法は，経直腸的超音波のガイドを用いることにより，線源またはアプリケータ針を正確に挿入できるようになり，成績が飛躍的に向上しました．小線源療法は，直接前立腺またはその周囲に線源を挿入するため，組織内照射ともよばれます.

前立腺がんに対する小線源療法には低線量率，高線量率の２種類の方法があります．低線量率による小線源療法は，ヨード125という放射線を放出する物質を直径0.5 mm，長さ約５mmの筒型容器に封入した小さい線源を，会陰部より前立腺組織に永久的に挿入します．数日程度の短期入院での治療が可能です.

小線源療法には，高線量率組織内照射という方法もあり，前立腺にアプリケータ針とよばれる細いチューブを数日間挿入したままにし，そのチューブ内に小さいイリジウム192などの線源を繰返し一時的に挿入して治療する方法です．線量率が高いため，まずチューブのみを挿入し，遠隔から操作して線源をチューブ内に挿入するため，術者の被曝がありません．この方法は，remote after-loading system（RALS）ともよばれます.

小線源療法は麻酔が必要なため，外部照射より侵襲的ですが，外部照射よりさらに多くの線量を前立腺に照射でき，短期の入院のみで治療が終了するなどの利点があります.

Q 根治目的での放射線治療は，どのように実施されますか？ またその治療成績はどのくらいですか？

A 外部照射では，通常，一回1.8～2 GyのX線にて70～78 Gy程度の総線量が選択されます．3DCRTでは70～72 Gyが，IMRTでは74～78 Gyが投与されることが多いようです．外部照射は，外来での治療で十分ですが，治療期間として７～８週間程度必要となります.

前立腺がんの根治的外部照射では，リスク分類に従って，治療方針が変わります．たとえば，NCCNガイドラインでは，低リスク群では外部照射単独が推奨されています[2]．一方で，リスクが高くなるにしたがって前立腺外への浸潤やリンパ節転移の可能性が高くなり，ホルモン療法と併用することによって再発率を低下させることができます．中リスク群には，４～６ヵ月の短期間のホルモン療法との併用，高リスク群では２～３年以上の長期のホルモン療法との併用が推奨されています[2].

低線量率での小線源療法は，低リスク群に関しては小線源療法単独にて，中リスク群には外部照射との併用にて治療が行われることが一般的です[3]．高リスクでは再発する可能性も高いため，あまり推奨されていません．高線量率での小線源療法は，外部照射と併用したブースト照射として使用されることが多く，本邦では比較的高リスクの症例に行われます.

局所療法，すなわち手術や放射線治療での10年PSA非再発率は，低リスク群で約80%，中等度リスク群で約50%，高リスク群で約30%とされています[4]．しかし，中～高リスク群では高線量投与により治療成績が向上する可能性があり，また，内分泌療法を併

用することによっても成績の向上が見込めます．これはあくまでPSAの非再発率であり，全生存率は通常の悪性腫瘍と比べて，一般的に非常に良好です．

Q 放射線治療に伴う副作用（有害事象）について教えてください

A 急性の有害事象として，下痢・軟便，頻尿，排尿痛などがありますが，可逆的です．晩期有害事象として最も問題となるものは直腸出血です．手術を要するような出血などをきたす頻度は1％以下ですが，輸血を含めた内科的な処置の必要な出血の起こる頻度は，数パーセントから20％程度にみられます[5]．これは直腸の線量に依存しますので，強度変調放射線治療などの高精度放射線治療を行うことにより，有害事象の頻度を低減することができます．尿路系の有害事象として，血尿，尿道狭窄などがあります．性機能障害が起こる可能性もありますが，手術に比べ頻度は低いとされています．

Q 前立腺がんの手術後に放射線治療を行うことがあるのですか？

A 前立腺全摘除術を行い，断端陽性などで再発のリスクが高いと判断した場合，アジュバント療法として外部照射を行うことがあります．一方，たとえ再発のリスクが高くても，PSAの上昇を確認してから救済放射線治療を行う場合もあり，一定のコンセンサスは得られていません[6]．近年，pT3，断端陽性など，再発のリスクの高い症例に，アジュバント放射線治療を加える群と加えない群の比較試験の結果がいくつか報告され，外部照射を加えたほうが，PSA再発率が低いことが証明されました[6]．ただし，全生存率に影響するかどうかについては，はっきりしていません．

術後にPSAが上昇し，明らかな遠隔転移がない場合には，救済療法として外部照射を考慮する必要があります．治療開始の目安となるPSA値は0.4～1.0 ng/mL程度とされ，早い時期での治療開始がよいとされています．膀胱尿道吻合部を十分含めた前立腺床を照射野とし，64 Gy以上の線量が推奨されています[7]．有害事象として，尿道狭窄などの合併症が1～3％に認められます．

Q 前立腺がんの緩和的な放射線治療について教えてください

A 緩和的な放射線治療としては，骨転移の痛みの緩和，脊髄圧迫の解除，下部尿路閉塞などの症状緩和などを目的として行われます[8]．

骨転移の痛みに対する治療効果は，一般的な疼痛改善率は約70～85％で，完全除痛率は30～50％程度といわれています．30 Gy/10分割，20 Gy/5分割などの線量分割が一般的に用いられ，1～2週間の短期間で治療を終了しますが，さらに短期照射として，8 Gy程

度の１回照射が行われることがあります．この利点としては，１回来院するだけで治療が完了することや，費用も安価であることなどがあり，外来通院が困難な患者さんなどで行われます．前立腺がんの骨転移は多発する場合も多いのですが，すべての骨転移部位への照射は容易ではなく，近年はストロンチウム89という放射性同位元素を注射して，骨転移部位に集積させ，痛みを改善する治療も導入されています．

骨転移に伴う脊髄圧迫は，患者のQOLを大きく低下させるため，その予防・治療は，進行前立腺がんのマネジメントにとってきわめて重要です．手術が第一選択ですが，手術は侵襲性も大きく，状態の安定した患者が主に適応となりますので，実際には放射線治療が行われることも多くみられます．

ホルモン療法に抵抗・再燃となった場合で，前立腺の腫大に伴う下部尿路閉塞などの症状緩和に対しても放射線治療は有効で，通常の前立腺がん根治照射と異なり，比較的少ない線量で，短い期間で治療を終了します．

前立腺がんに対する緩和的医療として治療を行う場合には，患者のQOLを考えながら，なるべく短い期間で，患者の身体的負担がなるべく少なくなるように治療する必要があります．

[文　献]

1) Makarov DV, Trock BJ, Humphreys EB et al：Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. Urology 69：1095-1101, 2007
2) NCCN Clinical Practice Guidelines in Oncology, Prostate Cancer v3.2010 http://www.nccn.org/professionals/physician_gls/f_guidelines.asp
3) 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 44：789-799, 1999
4) D'Amico AV, Whittington R, Malkowicz SB et al：Predicting prostate specific antigen outcome preoperatively in the prostate specific antigen era. J Urol 166：2185-2188, 2001
5) Cahlon O, Hunt M, Zelefsky MJ：Intensity-modulated radiation therapy：supportive data for prostate cancer. Semin Radiat Oncol 18：48-57, 2008
6) 中村和正：術後照射・再発前立腺癌．"がん・放射線療法2010" 大西　洋 他編．篠原出版新社，pp968-975，2010
7) Cox JD, Gallagher MJ, Hammond EH et al：Consensus statements on radiation therapy of prostate cancer：guidelines for prostate re-biopsy after radiation and for radiation therapy with rising prostate-specific antigen levels after radical prostatectomy. American Society for Therapeutic Radiology and Oncology Consensus Panel. J Clin Oncol 17：1155, 1999
8) 中村和正，桑原康雄，吉満研吾：緩和療法としての放射線療法．Urology View 7：77-81，2009

Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 5, pp. 1310–1318, 2011

0360-3016/$ - see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2010.08.014

CLINICAL INVESTIGATION **Prostate**

RADICAL EXTERNAL BEAM RADIOTHERAPY FOR CLINICALLY LOCALIZED PROSTATE CANCER IN JAPAN: CHANGING TRENDS IN THE PATTERNS OF CARE PROCESS SURVEY

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Purpose: To delineate changing trends in radical external beam radiotherapy (EBRT) for prostate cancer in Japan.
Methods and Materials: Data from 841 patients with clinically localized prostate cancer treated with EBRT in the Japanese Patterns of Care Study (PCS) from 1996 to 2005 were analyzed.
Results: Significant increases in the proportions of patients with stage T1 to T2 disease and decrease in prostate-specific antigen values were observed. Also, there were significant increases in the percentages of patients treated with radiotherapy by their own choice. Median radiation doses were 65.0 Gy and 68.4 Gy from 1996 to 1998 and from 1999 to 2001, respectively, increasing to 70 Gy from 2003 to 2005. Moreover, conformal therapy was more frequently used from 2003 to 2005 (84.9%) than from 1996 to 1998 (49.1%) and from 1999 to 2001 (50.2%). On the other hand, the percentage of patients receiving hormone therapy from 2003 to 2005 (81.1%) was almost the same as that from 1996 to 1998 (86.3%) and from 1999 to 2001 (89.7%). Compared with the PCS in the United States, patient characteristics and patterns of treatments from 2003 to 2005 have become more similar to those in the United States than those from 1996 to 1998 and those from 1999 to 2001.
Conclusions: This study indicates a trend toward increasing numbers of patients with early-stage disease and increasing proportions of patients treated with higher radiation doses with advanced equipment among Japanese prostate cancer patients treated with EBRT during 1996 to 2005 survey periods. Patterns of care for prostate cancer in Japan are becoming more similar to those in the United States. © 2011 Elsevier Inc.

Patterns of care study, Prostate cancer, Radical external beam radiotherapy, Changing trend.

INTRODUCTION

The Patterns of Care Study (PCS) national survey is a retrospective study designed to establish the national practice process of therapies for selected malignancies over a specific time period (1–3). In addition to documenting the practice process, data from PCS surveys are important for developing and disseminating national guidelines for cancer treatment that help promote a more uniform care process in the country. The PCS is also designed to complement the role of clinical trials in enhancing the standard of care for cancer patients (1, 4).

To improve the quality of radiation oncology, PCS methodology has been imported to Japan from the United States. The Japanese PCS Working Group of Prostate Cancer started a nationwide process survey of patients treated with radiotherapy between 1996 and 1998 (5, 6). Subsequently, the Working Group conducted a second PCS of patients treated with radiotherapy between 1999 and 2001 and previously reported the results of this second PCS for prostate cancer patients in Japan treated with radiotherapy (7–18). At present, we have conducted a third PCS of patients treated with radiotherapy from 2003 to 2005 (19).

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This work was supported by Grants-in-Aid for Cancer Research (Grant no. 10-17, 14-6, 18-4 and H22-3rd Term Cancer Control-General-043) from the Ministry of Health, Labor and Welfare of Japan.

Conflict of interest: none.

Acknowledgment—We thank the radiation oncologists who participated in this study. We are grateful for the continuous thoughtful support from the US Patterns of Care Survey committee for more than 10 years.

Received April 12, 2010, and in revised form July 2, 2010. Accepted for publication Aug 1, 2010.

Over the past 10 years, remarkable changes have occurred in prostate cancer treatment policy in Japan. The number of deaths due to prostate cancer has been on a steep increase, especially in elderly patients. The proportion of prostate cancer deaths to total cancer deaths also showed an increase from 0.9% in 1960 to 4.2% in 2000 (20). Since the introduction of prostate-specific antigen (PSA) screening, prostate cancer cases are being detected at earlier stages of disease, which allows early-stage patients a better chance of successful treatment and reduction of death from prostate cancer (21, 22). Moreover, recently, the use of radical external beam radiotherapy (EBRT) for prostate cancer has increased rapidly, as significant new radiation treatment planning technologies and methodologies have become available. Therefore, to optimally treat Japanese prostate cancer patients, it is important to accurately delineate the intrinsic changes taking place in the national practice process of radiotherapy for prostate cancer in Japan. In this report, we present the results of our analysis of the time-dependent transition of the process of care for prostate cancer patients treated with radical EBRT in the time periods from 1996 to 1998, 1999 to 2001, and 2003 to 2005.

METHODS AND MATERIALS

PCS surveys from 1996 to 1998, 1999 to 2001, and 2003 to 2005 in Japan contain detailed information about a total of 1,286 patients with prostate cancer treated with radiotherapy during the respective survey periods (307 patients were treated in 1996-1998; 387 patients in 1999-2001 PCS; and 592 patients in 2003-2005). PCS methodology has been described previously (1–4). Briefly, the PCS surveys were extramural audits that utilized a stratified two-stage cluster sampling design. The Japanese PCS used an original data format developed in collaboration with the American College of Radiology (Philadelphia, PA). The PCS surveyors consisted of 20 radiation oncologists from academic institutions. For each institution, one radiation oncologist collected data by reviewing patients' charts. To validate the quality of the collected data, the PCS used an Internet mailing list including all of the surveyors. On-site real-time checks and adjustments of the data input were available to each surveyor and to the PCS committee.

Of the 1,286 patients comprising the PCS 1996 to 1998, 1999 to 2001, and 2003 to 2005 surveys, patients with a diagnosis of adenocarcinoma of the prostate were eligible for inclusion in the present study unless they had one or more of the following conditions: (*1*) hormone-refractory cancer; (*2*) evidence of distant metastasis; (*3*) concurrent or prior diagnosis of any other malignancy; (*4*) prior radiotherapy; (*5*) or prior prostatectomy. In the current study, we considered the exclusion of patients with concurrent or prior diagnosis of nonmelanoma skin cancer would not affect the results of our PCS survey because the incidence of nonmelanoma skin cancers in Japan has been low compared to those in Western countries. A total of 841 patients with clinically localized prostate cancer treated with EBRT met these eligibility criteria and were selected for analysis (1996-1998 PCS included 161 patients from 51 institutions; 1999-2001 PCS included 283 patients from 66 institutions; and 2003-2005 PCS included 397 patients from 61 institutions). Criteria for institutional categories in the 1996 to 1998, 1999 to 2001, and 2003 to 2005 surveys have been detailed elsewhere (10, 11). Briefly, the PCS divided Japanese institutions into academic institutions (university hospital or cancer center) and nonacademic institutions (other hospitals).

In the current study, we used the risk groups utilized by D'Amico *et al.* (23), based on serum PSA level, biopsy, Gleason combined score, and 1992 American Joint Commission on Cancer (AJCC) clinical tumor category. Low-risk patients had a PSA of 10 μg/l or less, a Gleason score of 6 or less, and a 1992 tumor category of stage T1c or T2a. Intermediate-risk patients had PSA levels of 10.1 to 20 μg/l or a Gleason combined score of 7 or a 1992 AJCC tumor category of stage T2b. High-risk patients had a PSA level of more than 20 μg/l or a Gleason combined score of 8 or a 1992 AJCC tumor category of stage T2c.

Statistical analyses were performed using the Statistical Analysis System at the PCS data center at Osaka University (24). Statistical significance was tested using the chi-square test, Student's *t* test, and the Mann-Whitney U test. A probability level of 0.05 was chosen for statistical significance.

RESULTS

Patient characteristics

Patient characteristics for the PCS surveys from 1996 to 1998, 1999 to 2001, and 2003 to 2005 are shown in Table 1. There were significant increases over time in the proportion of patients with stage T1 to T2 disease (34.6% of patients in the 1996-1998 PCS; 48.2% of patients in the1999-2001 PCS; and 61.4% of patients in the 2003-2005 PCS) and decreases in median PSA values at diagnosis (: 22.0 ng/ml in the 1996-1998 PCS; 20.0 ng/ml in the 1999-2001 PCS; and 14.9 ng/ml in the 2003-2005 PCS). Data for the Gleason combined score were missing for 73.9% (119/161) of the patients in the 1996 to 1998 PCS and for 39.6% (112/283) of the patients in the 1999 to 2001 PCS, while only 5.5% (22/397) of patients were missing in the 2003 to 2005 PCS. The number of patients in the low-risk group increased gradually over time, while the number of patients in the high-risk group decreased gradually (Fig. 1). Table 1 and Fig. 2 indicate the reasons for selecting radiotherapy during these different time periods. There were significant increases over time in the number of patients treated with radiotherapy by their own choice (5.9% of patients in the 1996-1998 PCS; 26.5% of patients in the 1999-2001 PCS; and 41.4% of patients in the 2003-2005). This change in the rate of "patient choice" was significantly different ($p < 0.0001$).

Treatment characteristics

Treatment characteristics are shown in Table 2. The frequencies of radiation energies >10 MV, the use of portal or electronic portal images, and all field treatment each day increased gradually from 1996 to 1998 to 2003 to 2005. Also, the frequency of computed tomography (CT)-based treatment planning was 90.9% in 2003 to 2005, but 80.7% in 1996 to 1998, and 85.5% in 1999 to 2001. Moreover, the frequency of conformal therapy increased more rapidly from 2003 to 2005 (84.9%) than from 1996 to 1998 (49.1%) and 1999 to 2001 (50.2%).

Median radiation doses were 65.0 Gy and 68.4 Gy from 1996 to 1998 and from 1999 to 2001, respectively, increasing up to 70 Gy from 2003 to 2005. Stratifying patients by

Table 1. Patient and disease characteristics

Patient characteristic	PCS survey 1996-1998 (n = 161 patients)	PCS survey 1999-2001 (n = 283 patients)	PCS survey 2003-2005 (n = 397 patients)	Significance (p value)
Institution	51	66	61	
Median age, years (range)	70.4 (46.5–89.8)	71.8 (49.7–92.2)	72.1 (50.7–87.7)	0.4556
Mean age ± SD	70.8 ± 8.1	71.8 ± 6.6	71.5 ± 6.1	0.3446
Median KPS % (range)	90 (40–100)	90 (50–100)	90 (60–100)	<0.0001
Mean ± SD	87.0 ± 8.9	89.1 ± 7.1	90.9 ± 8.5	<0.0001
Missing data	7	8	0	
Pretreatment PSA level (%)				
Median PSA level (range)	21.95 (0.3–900.0)	19.99 (0.6–856.9)	14.94 (0.7–3,058.0)	0.0176
Mean PSA level ± SD	51.5 ± 93.5	54.1 ± 99.5	48.2 ± 179.2	0.8719
<10	41/146 (28.1%)	77/268 (28.7%)	121/391 (30.9%)	0.0066
10-19.9	25/146 (17.1%)	57/268 (21.3%)	113/391 (28.9%)	
≥20	80/146 (54.8%)	134/268 (50.0%)	157/391 (40.2%)	
Missing data	15	15	6	
Lower pretreatment PSA level (%)				
<4	17/146 (11.6%)	8/268 (3.0%)	9/391 (2.3%)	<0.0001
≥4	129/146 (88.4%)	260/268 (97.0%)	382/391 (97.7%)	
Missing data	15	15	6	
Differentiation (no. patients/total) (%)				
Well	24/159 (15.1%)	62/264 (23.5%)	67/376 (17.8%)	0.0148
Moderate	79/159 (49.7%)	93/264 (35.2%)	152/376 (40.4%)	
Poor	46/159 (28.9%)	93/264 (35.2%)	99/376 (26.3%)	
Other	0/159 (0.0%)	2/264 (0.8%)	7/376 (1.9%)	
Unknown	10/159 (6.3%)	14/264 (5.3%)	51/376 (13.6%)	
Missing data	2	19	21	
Gleason combined score (%)				
2-6	11/42 (26.2%)	77/171 (45.0%)	118/375 (31.5%)	0.0014
7	18/42 (42.9%)	35/171 (20.5%)	134/375 (35.7%)	
8-10	13/42 (31.0%)	59/171 (34.5%)	123/375 (32.8%)	
Missing data	119	112	22	
T stage (no. patients/total) (%)				
TX-T0	1/159 (0.6%)	10/272 (3.7%)	1/394 (0.3%)	<0.0001
T1	8/159 (5.0%)	22/272 (8.1%)	88/394 (22.3%)	
T2	47/159 (29.6%)	109/272 (40.1%)	154/394 (39.1%)	
T3-T4	102/159 (64.2%)	124/272 (45.6%)	134/394 (34.0%)	
Unknown	1/159 (0.6%)	7/272 (2.6%)	17/394 (4.3%)	
Missing data	2	11	3	
N stage (no. patients/total) (%)				
NX-N0	136/157 (86.6%)	249/270 (92.2%)	372/394 (94.4%)	0.0038
N1	18/157 (11.5%)	15/270 (5.6%)	12/394 (3.0%)	
Unknown	3/157 (1.9%)	6/270 (2.2%)	10/394 (2.5%)	
Missing data	4	13	3	
Risk group (no. patients/total) (%)				
Low risk	1/127 (0.8%)	16/242 (6.6%)	40/381 (10.5%)	< 0.0001
Intermediate risk	7/127 (5.5%)	26/242 (10.7%)	107/381 (28.1%)	
High risk	119/127 (93.7%)	200/242 (82.6%)	234/381 (61.4%)	
Missing patient data	34	41	16	
Reason for selection of RT (no. patients/total) (%)				
Patient choice	8/136 (5.9%)	71/268 (26.5%)	159/384 (41.4%)	
Advanced or high-risk disease	43/136 (31.6%)	83/268 (31.0%)	121/384 (31.5%)	
Intercurrent disease	0/136 (0.0%)	0/268 (0.0%)	62/384 (16.1%)	
Medical contraindication	7/136 (5.1%)	36/268 (13.4%)	0/384 (0.0%)	
Old age	37/136 (27.2%)	44/268 (16.4%)	94/384 (24.5%)	
Other	9/136 (6.6%)	8/268 (3.0%)	6/384 (1.6%)	
NA or unknown	32/136 (23.5%)	26/268 (9.7%)	27/384 (7.0%)	
Missing data	25	15	13	

Abbreviations: KPS = karnofsky performance status; PSA = prostate-specific antigen; RT = radiotherapy; NA = data not available; SD = standard deviation.