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PTV Margins for Prostate Treatments with an Endorectal Balloon

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Purpose: To determine the appropriate prostate planning target volume (PTV) margins for 3-dimensitional (3D) conformal radiotherapy (CRT) and intensity-modulated radiation therapy (IMRT) patients treated with an endorectal balloon (ERB) under our institutional treatment condition.

Materials and Methods: Patients were treated in the supine position. An ERB was inserted into the rectum with 70 cc air prior to planning a CT scan and then each treatment fraction. Electronic portal images (EPIs) and digital reconstructed radiographs (DRR) of planning CT images were used to evaluate inter-fractional patient's setup and ERB errors. To register both image sets, we developed an in-house program written in visual C^{++}. A new method to determine prostate PTV margins with an ERB was developed by using the common method.

Results: The mean value of patient setup errors was within 1 mm in all directions. The ERB inter-fractional errors in the superior-inferior (SI) and anterior-posterior (AP) directions were larger than in the left-right (LR) direction. The calculated 1D symmetric PTV margins were 3.0 mm, 8.2 mm, and 8.5 mm for 3D CRT and 4.1 mm, 7.9 mm, and 10.3 mm for IMRT in LR, SI, and AP, respectively according to the new method including ERB random errors.

Conclusion: The ERB random error contributes to the deformation of the prostate, which affects the original treatment planning. Thus, a new PTV margin method includes dose blurring effects of ERB. The correction of ERB systematic error is a prerequisite since the new method only accounts for ERB random error.

Key Words: Prostate, Endorectal balloon, PTV margin, Setup error

Introduction

The radiation treatment for prostate cancer patients has some difficulties to escalate prescription dose.[1~3] The rectum is adjacent to the prostate and thus happens to be located in the region of high dose as much as the prescribed dose in a treatment plan. Thus, dose escalation to the prostate might lead to a high risk of rectal toxicity. To increase the prescribed dose above 70 Gy, the dose volume effect of rectum becomes an important factor. Many studies showed a strong correlation between the dose-volume histograms and the toxicity of rectum.[4~7] Both prostate and rectum suffer from the internal motion during the treatment, which can often reduce target dose coverage and raise rectal dose.[8] It has been known that the inter-fractional motion of prostate is often smaller in left-right direction than in other directions.[9] The shape and the volume of rectum vary day-by-day due to the amounts of air, gas, and stools. To solve these problems, an endorectal balloon (ERB) has been introduced into the radiation treatment for prostate cancer patients to consistently maintain the shape and the volume of rectum and to minimize the error due to the prostate motion.

Many studies have described an advantage of ERB.[10~15] It decreases the prostate motion by giving a constant rectal filling toward the pubic bone and gives the dosimetric advantage of an air-tissue interface. This advantage of ERB may result in a better sparing of rectal wall and thus reduce the

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rectal toxicity.[16,17] However this advantage strongly depends on the consistence of ERB location. Human errors (when inserting an ERB into the rectum), patient setup errors, and internal motions significantly contribute to the daily variation of prostate location.[1,18] Therefore, the institutional analysis of treatment reproducibility with an ERB should be accompanied with an effort to determine an appropriate planning target volume (PTV) margin for clinical setting. For this purpose, we analyzed patient setup errors in 3D conformal radiotherapy (CRT) and intensity modulated radiation therapy (IMRT) and addressed the setup reproducibility in our institution. We used electronic portal images of treatment machines and digital reconstructed radiographs (DRR) of planning computed tomography (CT) images to evaluate the day-to-day variation of patient's treatment setup position.

In order to evaluate the inter- and intra-fractional variations of prostate motion, gold seeds are often inserted into the prostate. In this study, such an internal marker system was not available. With an assumption that the prostate motion itself was not much dependent upon individual institutions, we adopted the relevant values from the literature.[16] The common method of PTV margin calculation from van Herk et al.[19] was reviewed and became a basis of our approach. A new method accounting for the ERB effect was developed to evaluate our institutional PTV margins. We present the results of patient's setup analysis and calculated PTV margins with/without an ERB. The limitation of this study and the future work are also discussed.

Materials and Methods

1. Patient treatment setup

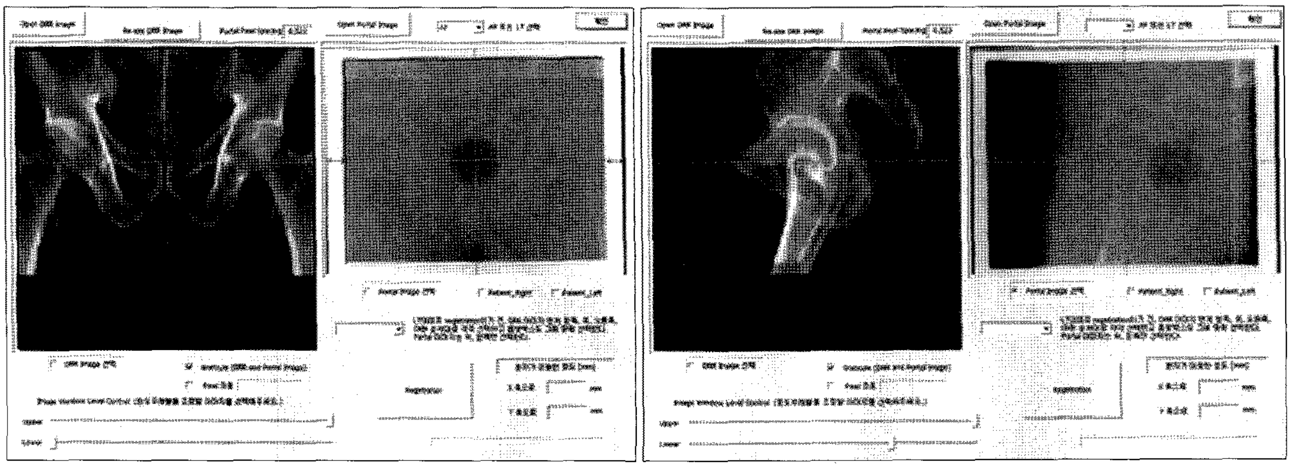
The prostate cancer patients have been treated with either 3D CRT or IMRT in supine position with an aid of immobilizers. Since October 2007, an ERB has been used for all prostate cancer patients for both 3D CRT and IMRT. Prior to planning CT scan and each treatment fraction, an ERB was inserted into the rectum and filled with 70 mL of air. The expanded ERB was pulled toward the patient's anal sphincter and ensured the pre-marked position on the ERB catheter.

2. Image collection for patient's setup analysis

The number of electronic portal images (EPIs) used for the analysis was 66 from 9 patients of 3D CRT with an ERB, and 450 from 16 patients of IMRT with an ERB. We generated DRR images of anterior-posterior (AP) and lateral views using each patient's CT images in radiation treatment planning systems. The EPIs of AP and lateral views were acquired at least twice a week during patient's treatment.

3. Image and data analysis

We used Varian Portal Vision (Varian Medical Systems, Inc., Palo Alto, CA, USA) and an in-house program written in C^{++} to register both DRR images and EPIs (Fig. 1).



AP view of EPIs and DRR image

Lateral view of EPIs and DRR image

Fig. 1. Image registration using an in-house program written in C^{++}. AP: anterior-posterior, EPI: electronic portal images, DRR: digital reconstructed radiographs.

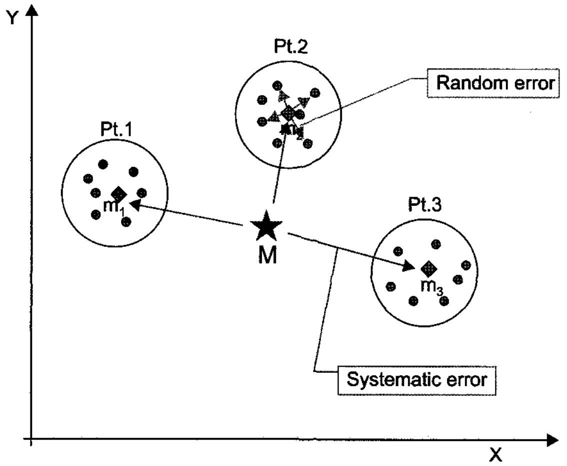


Fig. 2. A schematic overview of mean, systematic, and random errors in the distribution of patient's setup errors.

Setup errors were divided into 3 categories; variations of bony landmark with respect to isocenter, variations of balloon with respect to isocenter, and variations of balloon with respect to bony landmark. The mean, systematic and random errors were calculated in all three directions (AP, left-right [LR], and superior-inferior [SI]). Utilizing the computational environment for radiotherapy research software platform written in the Matlab language, the center of mass of ERB was determined and served as a reference point.[20] For 2D EPIs, the center of balloon was chosen a reference point.

As shown in Fig. 2, the mean, systematic and random errors are defined as follow.

$$\mathrm{m_p}=\sum_{f=1}^{F_p}\frac{x_{pf}}{F_p} \tag{1}$$

$$\mathrm{N}=\sum_{p=1}^{p}F_p \tag{2}$$

$$\mathrm{M}=\frac{1}{N}\sum_{p=1}^{p}\sum_{f=1}^{F_p}x_{pf} \tag{3}$$

$$\sigma=\sqrt{\frac{1}{N-P}\sum_{p=1}^{p}\sum_{f=1}^{Fp}(x_{pf}-m_p)^2} \tag{4}$$

$$\Sigma=\sqrt{\frac{1}{N(P-1)}\sum_{p=1}^{p}F_p(m_p-M)^2} \tag{5}$$

Where F_p is the measured fractions for each patient 'p', f is the number of fractions in a patient, x_{pf} is the measurement of a setup error for each measured fraction, m_p is the average patient error, N is the total number of measured fractions, σ is the standard deviation of the random errors, and Σ is the standard deviation of the systematic errors.[21]

4. The common method to determine PTV margin

The PTV margin recipe derived by van Herk et al.[19] was commonly used. It was assumed that the minimum dose delivered to the target for 90% of the patients under the normal distribution (Gaussian distribution) of errors is more than 95% of the nominal dose. The following equation was derived by van Herk et al.[19] for 3D symmetric margin:

$$\text{PTV margin}=2.5\Sigma+0.7\sigma \tag{6}$$

Errors were divided into systematic and random errors. The SD of systematic errors (Σ) includes those from the delineation, prostate motion, and setup errors. The standard deviation (SD) of random errors (σ) attributes to not only the prostate motion and setup errors, but also the penumbra width between 95% and 50% isodose surfaces. The systematic error shifts clinical target volume (CTV) into a certain direction, while the random error blurs dose distributions.[19] As shown in the International Commission on Radiation Units and Measurements (ICRU) report 62,[22] a simple linear addition of the margins for both setup error and organ motion results in an excessively large PTV. As an alternative, the root-sum-of-squares of setup error (external) and organ motion (internal) was suggested as follow:

$$\Sigma=\sqrt{\Sigma^2_{delineation}+\Sigma^2_{organ\ motion}+\Sigma^2_{setup}} \tag{7}$$

$$\sigma=\sqrt{\sigma^2_{organ\ motion}+\sigma^2_{setup}} \tag{8}$$

Where $\Sigma_{\mathrm{delineation}}$ is the SD of the target volume delineation errors, $\Sigma_{\mathrm{organ\ motion}}$ is the SD of the inter- fractional errors of the organ motion, and Σ_{setup} is the SD of the systematic setup errors with respect to the bony anatomy. Further, $\sigma_{\mathrm{organ\ motion}}$ is the SD of the random errors of the organ motion, σ_{setup} is the SD of the random errors of patient setup.[23]

5. A new method to determine a PTV margin including ERB effect

The PTV margins without an ERB were computed by the previous method of van Herk et al.[19] However, treatments with an ERB introduce additional errors that resulted from inconsistency of ERB insertion and biased displacements in SI direction. Although an ERB cannot decrease the prostate inter-fraction motion statistically, the movement of prostate in AP direction increased over the course of treatment in patients without an ERB.[16,24] The technical components of setup error and delineation uncertainty vary from institution to institution, but the organ motion is less likely.[21] The technical components have different magnitudes depending on institutions and/or physicians, while the SD of the organ motion doesn't.

The method derived by van Herk et al.[19] has been used as a common method to determine the PTV margin for prostate. The assumption of his method was that the rectum has no inter-fractional motion during the course of treatments and the prostate only has a motion in its position, without the change of shape. However, in real treatments, the rectum also has a motion and the inter-fractional position of rectum can be changed. This displacement of rectum can give an effect on the prostate position.[8,14,18] To reduce this inter-fractional displacement of prostate, an ERB has been used for prostate cancer treatments. As showed in Fig. 3, an ERB expands the volume of rectum and it pushes the prostate toward the pubic bone.[1,14,18] This expansion makes possible to control or restrict the extent of prostate and rectum movement during the treat-

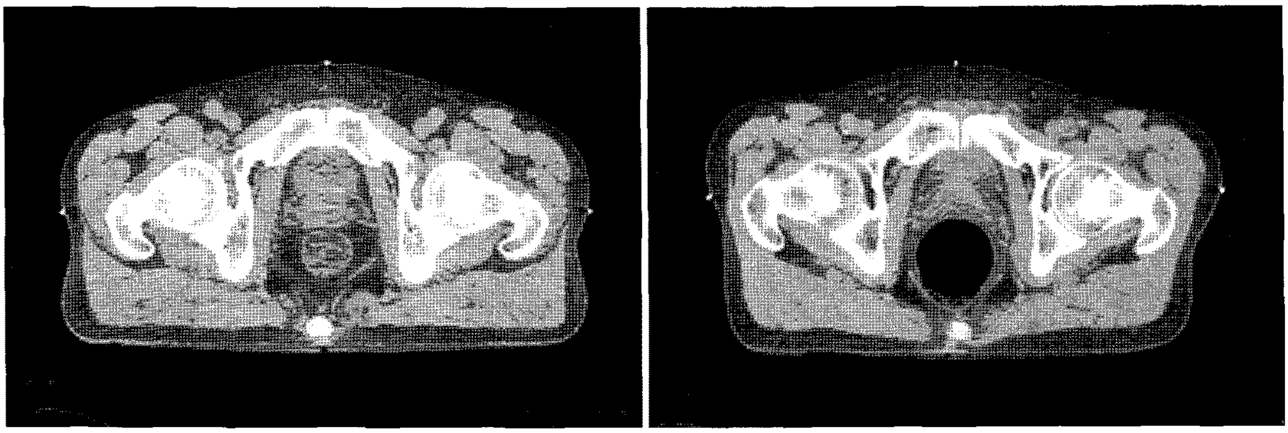


Fig. 3. Position and shape of prostate and rectum without and with an endorectal balloon.

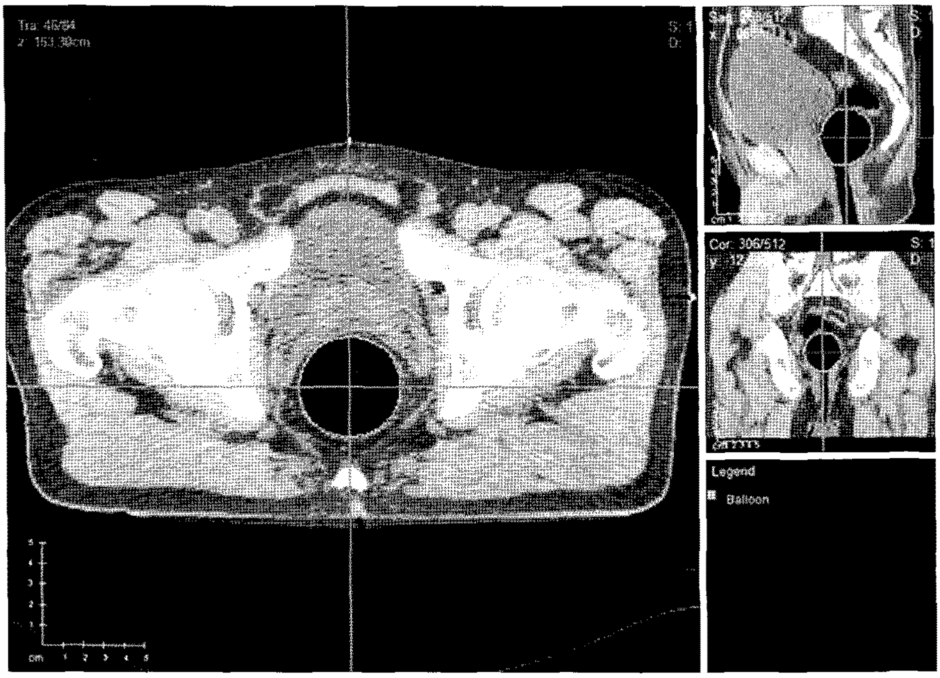


Fig. 4. Shape and location of prostate and endorectal balloon (ERB) at a daily patient's setup (including axial and sagittal views).

ment. However, the inflation and variation of ERB can lead to the displacement and deformation of the prostate anatomy, which potentially introduce the errors in the delivered dose. It was known that the shape of the prostate is changed and can be more distorted due to the rectal distention or the use of an endorectal coil or ERB.[18,25~27] Fig. 4 shows that the prostate becomes close to the rectum due to the expansion of ERB. As shown in the sagittal view of Fig. 4, the ERB movement can cause an arbitrary change in the position and shape of the prostate and the seminal vesicle.[18] This is illustrated in Fig. 5. Such day-to-day displacement of ERB can result in dose blurring of the edge of target volume due to the deformation of the prostate.

To date, there has been no proper method to determine a PTV margin including this ERB effect. In treatments with an ERB, the random error of ERB has to be incorporated into the PTV margin recipe since this ERB random variation makes dose blurring. Therefore, we propose a new method to account for the ERB effect when the PTV margin needs to be determined at individual clinical settings. To avoid any geometrical missing of target coverage, all errors resulted from treatment process should be taken into account.[21]

Due to the asymmetric behavior of patient's setup errors, we selected a 1D margin for all three directions instead of a symmetric 3D margin. The developed equation of PTV margin follows the assumption that 90% of patients must have a minimal dose to the CTV of 95%.[19] The off-line/on-line correction for the systematic error of ERB is required prior to the usage of the following equation for the PTV margin. This equation assumes that the systematic effect of prostate from the inter-fractional motion of ERB is corrected. The designed equation is

$$\mathrm{PTVmargin} = 1.64\sqrt{\Sigma_d^2+\Sigma_m^2+\Sigma_s^2}+ 1.64\sqrt{\sigma_m^2+\sigma_s^2+\sigma_p^2+\sigma_{ERB}^2}-1.64\sigma_p \qquad (9)$$

Where Σ_d is the SD of the delineation errors, Σ_m is the SD of the systematic errors of the prostate motion during treatment preparation, and Σ_s is the SD of the setup errors during treatment preparation. Further, σ_m is the SD of the random errors of the prostate motion, σ_s is the SD of the random errors of the setup motion, σ_p is the SD describing the width of the penumbra, and σ_{ERB} is the SD of the random errors of ERB.

Table 1. Setup Errors of Bone Relative to Isocenter in Three Directions

	Mean (mm)	Σ (mm)	σ (mm)
LR*	0.8	1.1	1.4
SI†	−0.2	1.1	1.3
AP†	−0.2	2.4	2.5

*left-right , †superior-inferior, †anterior-posterior.

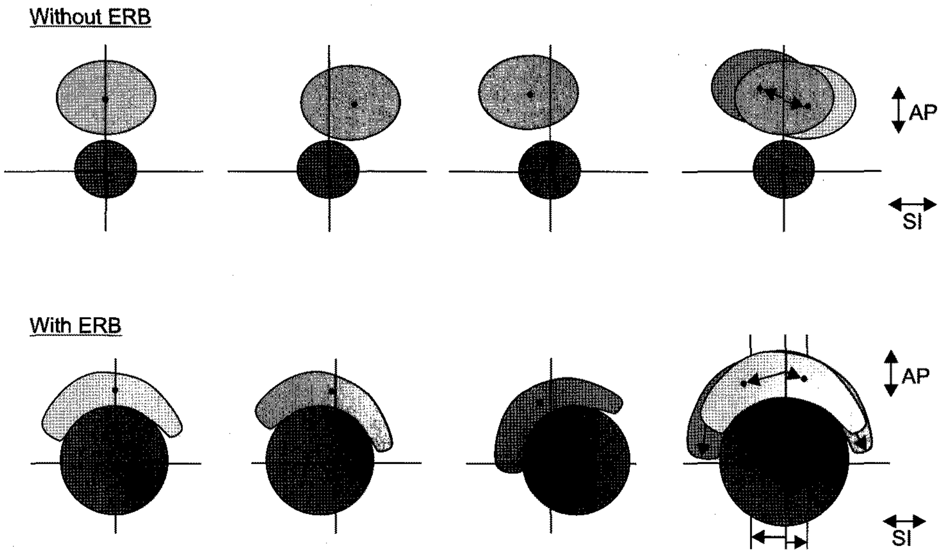


Fig. 5. An endorectal balloon (ERB) effect on the position and shape of prostate in sagittal view. For example, the ERB displacement in the superiorinferior (SI) direction can cause the prostate and the seminal vesicle position to be changed in anterior-posterior (AP) as much as in SI.

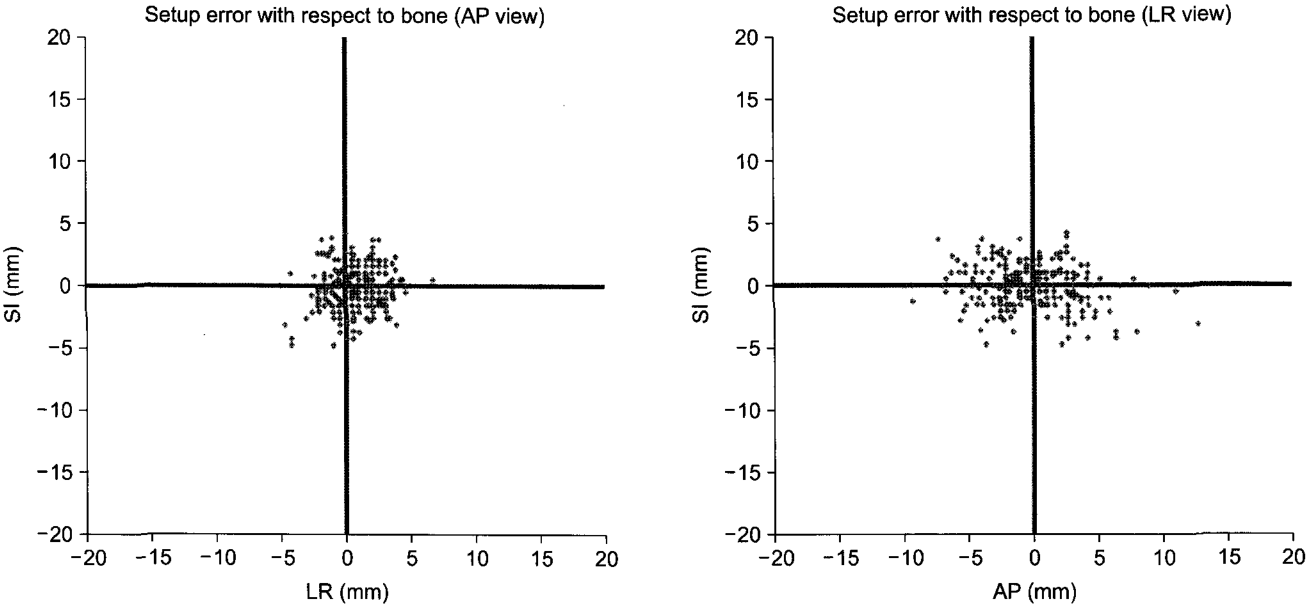


Fig. 6. Setup error distribution in three directions. SI: superior-inferior, AP: anterior-posterior. LR: left-right.

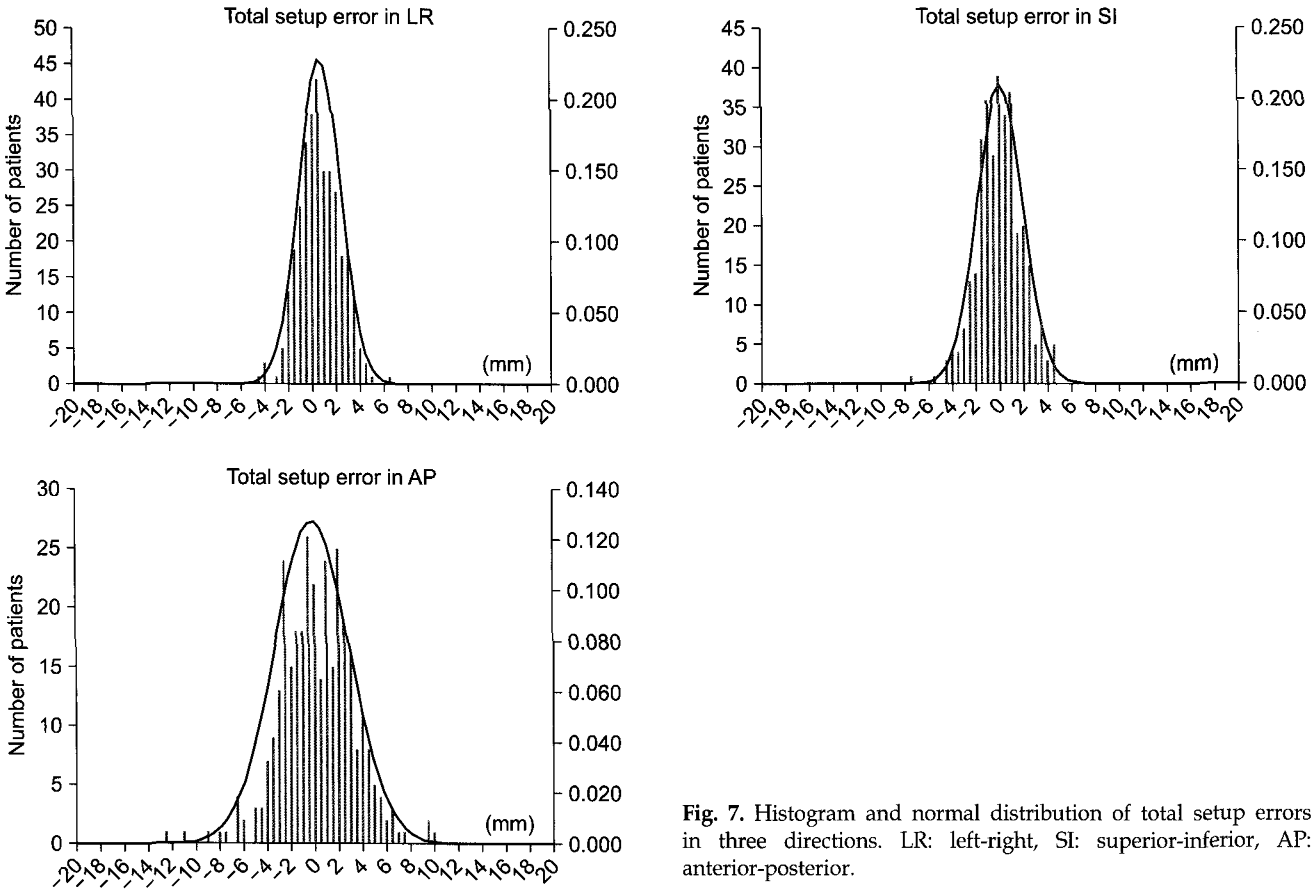


Fig. 7. Histogram and normal distribution of total setup errors in three directions. LR: left-right, SI: superior-inferior, AP: anterior-posterior.

Results

1. Setup errors

The patient's setup during treatments may change day-by-day due to many factors such as immobilizer setting, laser alignment, and human errors. We evaluated the variation of EPIs with respect to the reference images (DRR images). This variation was defined as patient's setup errors.

1) Patient setup error (bone vs. isocenter)

Setup errors of bone relative to the isocenter in three directions are listed in Table 1. The average errors are mostly less than 1 mm in all directions and both treatment modalities (*i.e.*, 3D CRT and IMRT). We found that there were no systematic errors (*e.g.*, a misaligned laser that would be applied to all patients' treatment equally). The spread of total setup errors with a directional sign (*i.e.*, ±direction) are showed in Fig. 6 and the histogram of the errors are conformable to the normal distribution (solid line) in Fig. 7. The numbers in this table are in units of mm. Σ is a SD of systematic errors and σ is a SD of random errors. The systematic and random errors of bone relative to the isocenter are almost less than 3 mm. For IMRT, we had at least 6 portal images per a patient. Fig. 8 shows the history of setup errors during the total fractions of treatment.

2) ERB setup error (ERB vs. isocenter and ERB vs. bone)

The reproducibility of ERB in the treatments was estimated with a directional sign (Table 2, 3). The mean displacements of balloon relative to isocenter and bone are large in SI direction of both 3D CRT and IMRT. The systematic and random errors are also larger in SI than in other directions. The distributions of the ERB variation with respect to isocenter in AP and LR views are shown in Fig. 9. The distributions of the ERB variations with respect to bony landmark in AP and LR views are shown in Fig. 10.

2. Calculation of PTV margins

From the analysis of isodose distributions in patient's plans, σ_p in LR, SI, and AP were 2.6, 2.0, and 3.2 mm for IMRT with an ERB, 7.9, 1.7, and 6.9 mm for 3D CRT with an ERB. However, we neglected the delineation error of target volume from the single observer (*i.e.*, one radiation oncologist involved in this study).

Using equation 9, we calculated the 1 D symmetric PTV margins for 3D CRT with an ERB and for IMRT with an ERB. In this calculation, we used real values (*i.e.*, with a directional sign [±]) of the setup errors for the 1 D symmetric margins and the prostate motion data of the literature (van Herk et al.[19]). The calculated PTV margins of 3D CRT with an ERB were 3.0 mm, 8.2 mm, and 8.5 mm in LR, SI, and AP, respectively. The calculated PTV margins of IMRT with an ERB were 4.1 mm, 7.9 mm, and 10.3 mm for LR, SI, and AP.

In equation 9, the large SD of penumbra can reduce the dose blurring effect that results from random errors. In IMRT, the penumbra was smaller than one in 3D CRT, and then the calculated PTV margins of IMRT were larger than those of 3D CRT.

Discussion and Conclusion

In order to evaluate our institutional PTV margins for prostate cancer treatment with an ERB, we first analyzed patient setup errors and daily ERB variations based on EPI and DRR images. All of cases for IMRT and 3D CRT with an ERB had a setup consistency within 3 mm. The results of ERB setup variations demonstrated a lower reproducibility in SI direction than those in the other directions. These findings agreed with the results from the literature.[1,16,19]

Table 2. ERB Errors Relative to Isocenter in Three Directions

	Mean (mm)	Σ (mm)	σ (mm)
LR*	−1.0	2.2	2.1
SI†	−2.4	6.1	3.8
AP‡	0.1	4.3	3.3

*left-right , †superior-inferior, ‡anterior-posterior.

Table 3. ERB Errors Relative to Bone in Three Directions

	Mean (mm)	Σ (mm)	σ (mm)
LR*	−1.7	2.5	2.4
SI†	−2.2	6.1	3.9
AP‡	0.2	5.4	3.7

*left-right , †superior-inferior, ‡anterior-posterior.

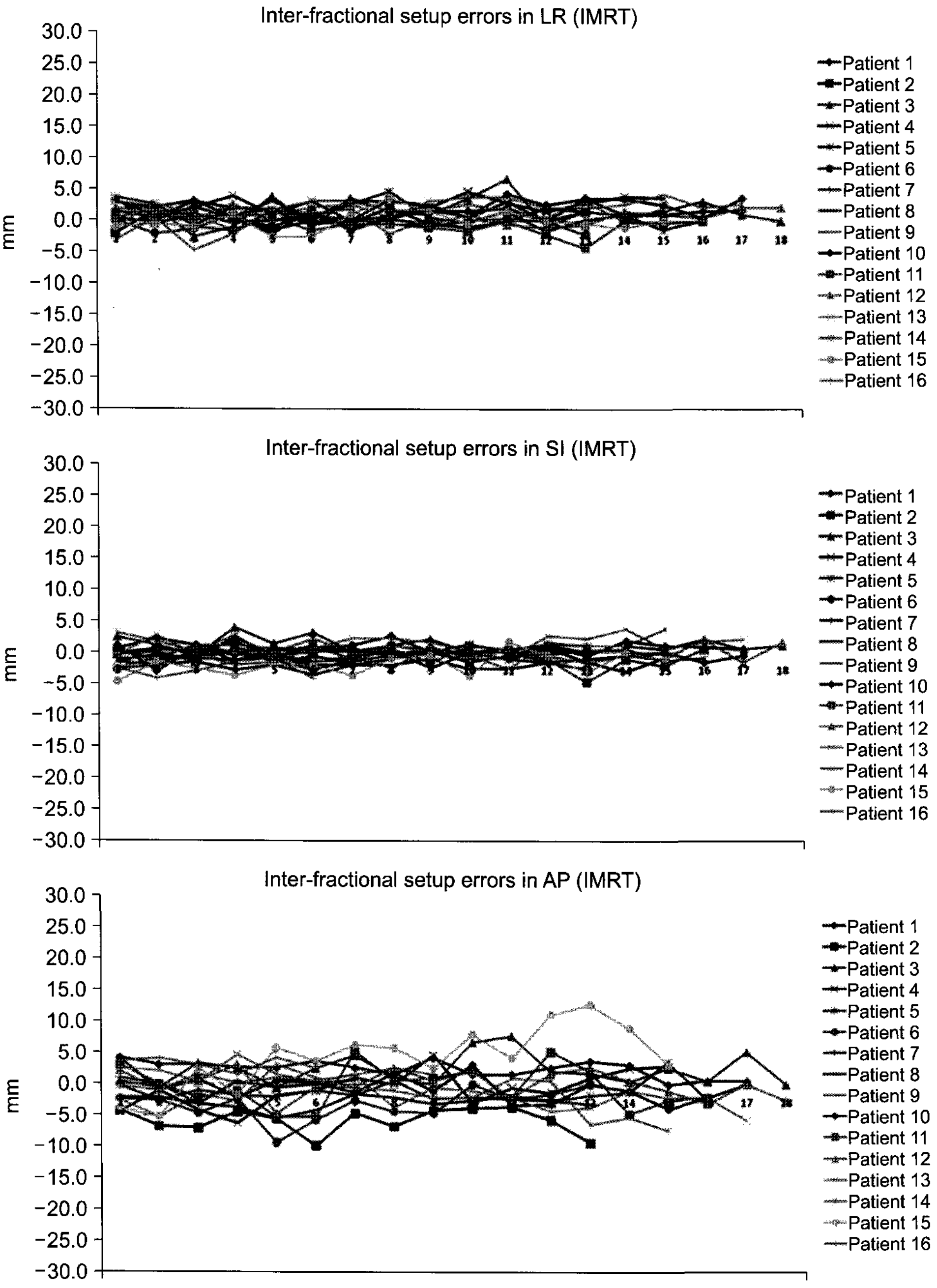


Fig. 8. History of setup errors of intensity modulated radiation therapy (IMRT) patients in three directions. LR: left-right, SI: superior-inferior, AP: anterior- posterior.

The common method (derived by van Herk et al.[19]) to determine PTV margins was not directly applicable for the prostate cancer treatments with an ERB. A new method (equation 9) can include the dose blurring effect due to the prostate displacement and shape change that resulted from the inter-fractional setup variations of ERB. It was an 1 D symmetric formula. An internal marker system to detect the inter-fractional prostate motion was not available in this study. The study of van Lin et al.[16] showed that the inter-fractional error of prostate motion with an ERB was not significantly different from the error without an ERB. We adopted the reported prostate motion data in equation 9 since the prostate motion itself doesn't much vary from institution to institution. The calculated PTV margins (*i.e.*, result from this retrospective study) were at least 2 mm smaller than our current margins, except for the posterior margin in IMRT.

Depending on user's need in treatment planning, the PRV (planning organ at risk volume by ICRU report 62[22]) margin

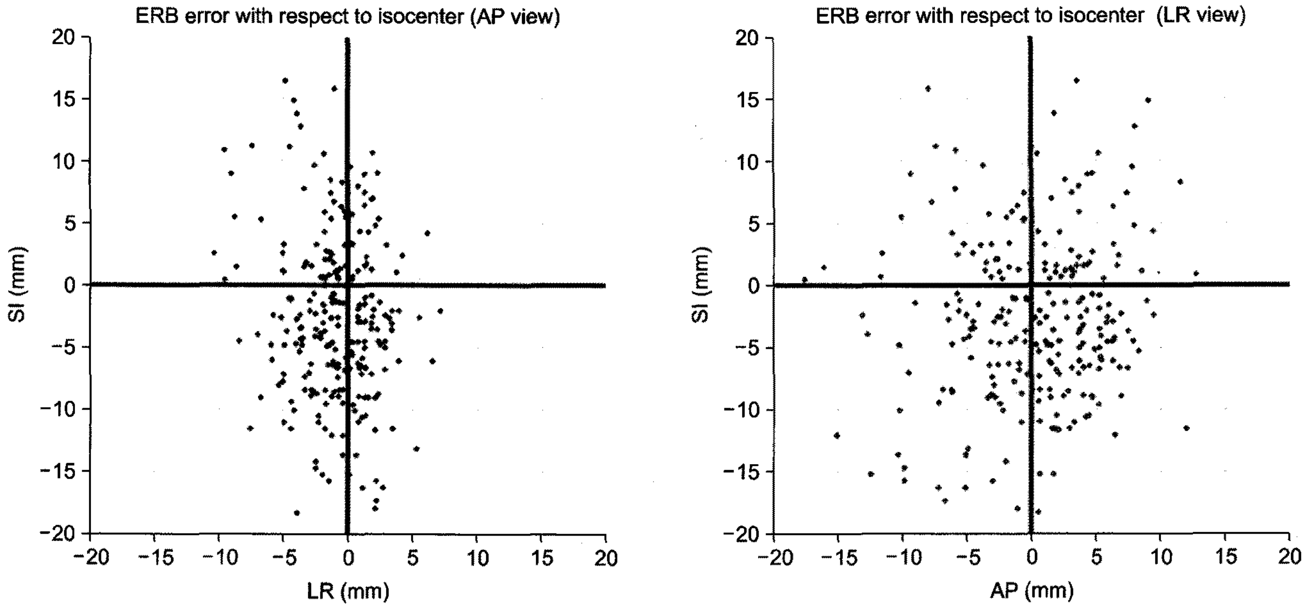


Fig. 9. Distribution of endorectal balloon (ERB) errors with respect to isocenter. LR: left-right, SI: superior-inferior, AP: anterior-posterior.

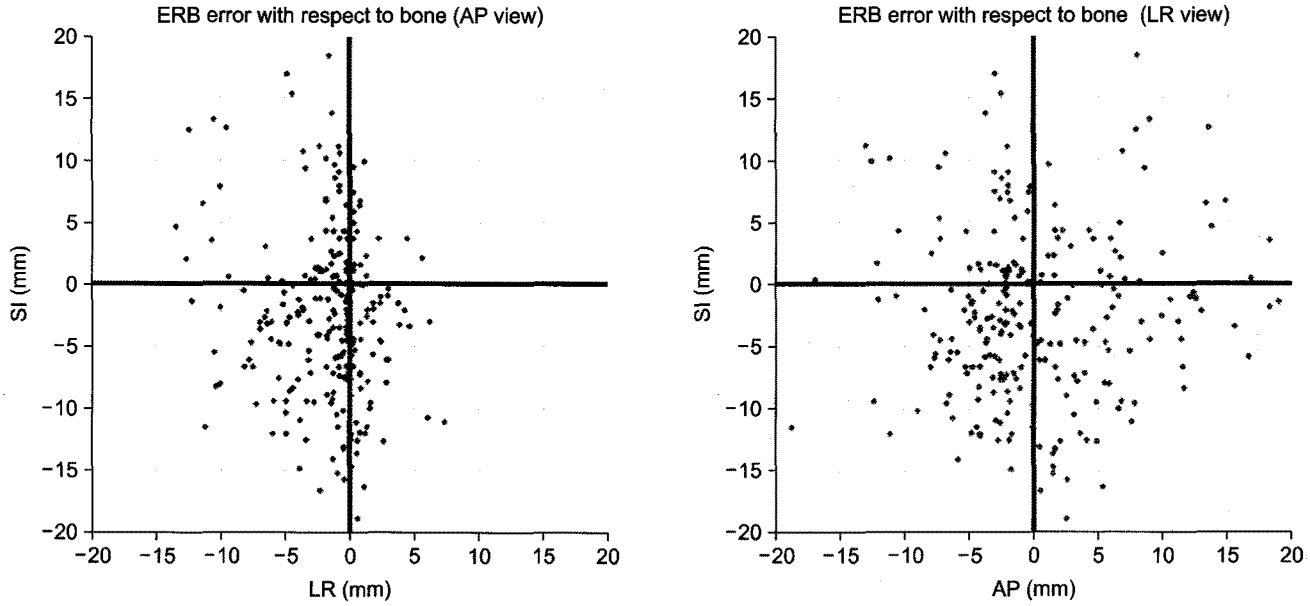


Fig. 10. Distribution of endorectal balloon (ERB) errors with respect to bone. LR: left-right, SI: superior-inferior, AP: anterior-posterior.

of rectum can be derived similarly. This margin can save the rectum from receiving high dose and to account for the uncertainty in rectal position between the treatment fractions.[28]

In conclusion, appropriate PTV margins should be carefully determined by reflecting a specific treatment condition of each instituion. The new PTV margin method for prostate patients with an ERB was developed in this study. With a correction for the systematic error of ERB it can be one of promissing methods to account for the target coverage uncertainty due to the random error of ERB insertion.

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국문초록

전립선 암의 방사선치료 시 직장 내 풍선삽입에 따른 계획표적부피마진

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목 적: 직장 내 풍선삽입을 하는 전립선 암 환자의 3차원 입체조형방사선치료(3D CRT)와 세기조절치료에 대한 적절한 계획표적부피 마진을 구하기 위하여 본 연구를 수행하였다.

대상 및 방법: 환자는 반듯이 누운 자세에서 치료계획용 CT 촬영과 매 치료 전에 환자의 직장에 풍선이 삽입되었고 70 mL의 공기로 풍선을 팽창시켰다. Anterior-posterior (AP)와 측면에서의 전자식 조사문영상 이미지와 디지털 화재구성사진을 이용하여 치료간 환자 치료위치 및 풍선의 위치 변화를 분석하였다. 두 이미지를 정합하기 위하여 Visual C^{++} 기반의 프로그램을 개발하여 사용하였다. 기존의 방법을 기반으로 풍선에 의한 선량 흐려짐 효과를 고려한 계획표적부피 마진을 구하는 방법 고안하였다.

결 과: 환자치료위치의 치료간 변화는 모든 방향에서 평균 1 mm 이내로 나타났다. 풍선의 치료간 변화는 left-right (LR) 방향에 비해 superior-inferior (SI)와 AP 방향으로 크게 나타났다. 풍선의 무작위오차를 포함시켜 새로 고안된 1차원 계획표적부피 마진 구하는 방법을 사용하여 마진을 구한 결과, 3D CRT의 경우에는 LR 방향으로 3.0 mm, SI 방향으로 8.2 mm, AP 방향으로 8.5 mm로 계산되었다. Intensity modulated radiation therapy의 경우, LR 방향으로 4.1 mm, SI 방향으로 7.9 mm, AP 방향으로 10.3 mm로 마진이 계산되었다.

결 론: 풍선의 무작위오차는 전립선 모양의 변형을 일으켜서 선량분포에 영향을 준다. 따라서, 새로 고안된 계획표적부피 마진을 구하는 방법에는 풍선에 의한 선량 흐려짐 효과가 고려되었다. 이 방법은 풍선의 무작위오차만 계산에 포함하기 때문에 풍선의 계통오차에 대한 보정을 전제로 한다.

핵심용어: 전립선, 직장 내 풍선삽입, 계획표적부피마진, 준비오차