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ORIGINAL ARTICLE

Interfraction variation in prostate cancer - analysis of 11726 cone-beam CT

Martin Dolezel[1,2,3], Peter Slezak[4], Karel Odrazka[1,2,5], Jaroslav Vanasek[1], Ales Hlavka[1], Vit Ulrych[1], Jan Stuk[1], Iveta Waczulikova[4], Igor Hartmann[6]

[1]Oncology Centre, Multiscan & Pardubice Regional Hospital, Pardubice, Czech Republic; [2]First Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; [3]Faculty of Medicine, University Hospital Olomouc, Czech Republic;; [4]Faculty of Mathematics, Physics and Informatics, Comenius University in Bratislava, Slovakia; [5]Third Faculty of Medicine, Charles University in Prague, Prague, Czech Republic; [6]Department of Urology, University Hospital Olomouc, Czech Republic

Summary

Purpose: *To investigate the setup margins in prostate cancer treatment without using daily online repositioning methods.*

Methods: *We analysed the data from patients treated with curative-intend radiotherapy. Each patient underwent a series of pretreatment online localizations during daily setup using cone-beam CT. The skin-prostate shifts and bone-prostate shifts were recorded in anteroposterior (AP), craniocaudal (CC), and laterolateral (LL) direction. The safety margins based on van Herk equation (2.5Σ+0.7σ) were calculated and the correlations between margins and various patient characteristics and prostate locations were investigated.*

Results: *A total of 307 patients were included, representing 11,726 localizations resulting in 70,356 shifts. The mean skin-prostate setup inaccuracy was 0.8 ± 5.4mm in AP, 1.3 ± 4.8mm for CC, and 0.1 ± 5.6mm in LL direction. The mean bone-prostate setup inaccuracy was 0.4 ± 3.3mm in AP, 0.1 ± 2.5mm for CC, and 0.1 ± 1.4mm in LL direction. According to van Herk equation, clinical target volume (CTV)-planning target volume (PTV) margins of 11.4, 10.6, and 11.8 mm (AP, CC, and LL, respectively) would be required for setup using skin markers and margins of 7.0, 4.7, and 2.1mm would be necessary for setup using bone structures. The average rectal area < 11cm^2 and volume of bladder > 300 cm^3 were associated with smaller CTV-PTV margins for setup using bone structures. The largest margins (15.8 mm in LL direction) were needed in patients with body mass index (BMI) > 35 using skin markers.*

Conclusions: *Our results confirm that the commonly used CTV-PTV margins are inadequate.*

Key words: *cone-beam CT, image-guided radiotherapy, prostate cancer*

Introduction

The knowledge of interfraction variation plays an important role in the assessment of set-up margins in prostate cancer treatment without using daily online repositioning methods. Both randomized trials and retrospective studies have confirmed benefit of dose escalation [1-6]. The increasing use of dose escalation with 3D-CRT techniques leads to higher morbidity, especially long-term rectal toxicity [7]. Implementation of intensity-modulated radiation therapy (IMRT) in clinical practice makes it possible to minimize the volume of irradiated normal tissue by producing steeper dose gradients. However, high conformity of treatment and the reduction of margin around the target volume can increase the risk of geographic miss. Accurate treatment dose delivery can lead to further decrease of toxicity and better biochemical tumor control [8]. In the past years,

Correspondence to: Martin Dolezel, MD, PhD. Oncology Centre, Multiscan a Pardubice Regional Hospital, Kyjevska 44, Pardubice 532 03, Czech Republic. Tel: +420 467 436 410, Fax: +420 467 436 413, E-mail: dolezelm@email.cz
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image-guided radiotherapy (IGRT) became available in clinical practice with target position verified with electronic portal imaging device (EPID), orthogonal kV imaging, cone-beam CT (CBCT) and ultrasound localization [9-13]. The frequency of imaging throughout a course of radiotherapy and the appropriate methods of evaluation of the setup data are still being debated.

The primary endpoint of this study was to investigate the setup margins in the treatment of prostate cancer without using daily online repositioning methods. The secondary endpoint was to evaluate the correlations between CTV-PTV margins and various patient characteristics and prostate locations.

Methods

We analysed data from 307 patients with localized prostate cancer treated with curative-intend radiation therapy between 2009 and 2012. Each patient underwent a series of pretreatment online localizations during daily setup (with a minimum of 35).

The radiation treatment technique used was described earlier [14-17]. Briefly, patients were planned and treated in a supine position. A vacuum cushion or knee and feet support (VacLok/Dual Leg Positioner Cushion, MED-TEC) have been used for immobilization. The patients had been instructed prior to treatment to adhere (a week before planning CT and during radiotherapy) to a specific dietary protocol designed to minimize flatulence, achieve pre-radiation rectum evacuation, and ensure a constant urinary bladder volume. CT simulation was performed without contrast, at a slice thickness of 3 mm.

Two IMRT techniques were used. The IMRT with a dose 78 Gy in 39 fractions to prostate and seminal vesicles (IMRT 78) and simultaneous integrated boost to 84.84, 80 and 76 Gy in 40 fractions to the intraprostatic lesion, high risk volume and prostate with seminal vesicles. In patients with the conventional IMRT – IMRT 78, CTV consisted of the entire prostate and the base of seminal vesicles; in patients with seminal vesicles invasion, the prostate and the whole seminal vesicles were included. The PTV was generated by a 6 mm expansion of the CTV. In patients with simultaneous integrated boost (IMRT/SIB 84.84), the dominant intraprostatic lesion was contoured based on multiparametric MR, the high risk volume was defined as adjacent area (in case of peripheral lesion, we contoured the whole peripheral lobe), and the low risk volume was the rest of the prostate and seminal vesicles. The PTV was generated by a 3 mm expansion for intraprostatic lesion and the high risk volume and by a 6 mm expansion for prostate and seminal vesicles.The intensity-modulated treatment was delivered with a dynamic MLC, using the RapidArc technique (Clinac 2100, Varian Medical Systems, Palo Alto, CA, USA).

Patients were positioned for radiotherapy using skin marks. Verification of patient position and its corrections were performed online prior to each radiation fraction by means of CBCT (OBI 1.3, Varian Medical Systems, Palo Alto, CA, USA). CBCT images were obtained after one 180- or 360-degree gantry rotation and compared with the reference planning CT images. First, the pelvic skeleton was registered and the setup errors in all axes (AP, CC, and LL) were recorded. Second, the target volume (prostate) was registered, setup errors were recorded again and the treatment table was shifted accordingly before treatment.

Systematic errors (Σ) were calculated as standard deviation of the average setup deviations per patient. The random error (σ) was defined as the root mean square of the standard deviations of all patients. The CTV-PTV margin was calculated using van Herk equation to ensure a minimum of 95% prescription dose to cover the clinical target volume for 90% of the population (2.5 Σ+0.7 σ).

Statistics

Variance F test was used to analyze differences in the Σ and σ values between two groups. All presented p values are two-sided and are not adjusted for multiple comparisons. p values < 0.05 were considered significant.

Results

A total of 307 patients were included in this study, which represented 11,726 localizations resulting in 35,178 skin-prostate shifts (AP, CC, and LL) and 35,178 bone-prostate shift (AP, CC, and LL). Tables 1 and 2 contain the results from the shifts with respect to direction and setup inaccuracy. The mean skin-prostate setup inaccuracy was 0.8±5.4 mm in AP direction, 1.3±4.8 mm for CC, and 0.1±5.6 mm in LL direction. The mean bone-prostate setup inaccuracy was 0.4±3.3 mm in AP direction, 0.1±2.5 mm for CC, and 0.1±1.4 mm in LL direction. Histograms for each group of directions are presented in Figures 1 and 2.

According to van Herk equation, the CTV-PTV margins of 11.4, 10.6, and 11.8 mm (AP, CC, and LL, respectively) would be required for setup using skin markers and margins of 7.0, 4.7, and 2.1 mm would be necessary for setup using bone structures.

We also investigated the minimum number of fractions for a representative calculation of safety margins. The growing number of fractions leads to more accurate margins in comparison with all fractions. The margins using the first two setup shifts were 13.7, 12.0 and 13.5 mm (AP, CC, LL)

Table 1. Results of prostate displacement – mean, median, range

	Skin - Prostate				*Bone- Prostate*			
Axis	*Mean shift and direction (mm)*	*Median shift and direction (mm)*	*SD (mm)*	*Range (mm)*	*Mean shift and direction (mm)*	*Median shift and direction (mm)*	*SD (mm)*	*Range (mm)*
AP	0.8 posterior	1.0 posterior	5.4	20.0 posterior – 31.0 anterior	0.4 posterior	0	3.3	15.0 posterior – 15.0 anterior
CC	1.3 caudal	1.0 caudal	4.8	20.0 cranial - 26.0 caudal	0.1 caudal	0	2.5	14.0 cranial - 18.0 caudal
LL	0.1 left	0	5.6	31.0 right - 32.0 left	0.1 left	0	1.4	13.0 right - 15.0 left

AP: anteroposterior, CC: craniocaudal, LL: laterolateral, SD: standard deviation

Table 2. Results of prostate displacement according to setup error range

Setup error	*Skin - Prostate*			*Bone - Prostate*		
	AP (%)	*CC (%)*	*LL (%)*	*AP (%)*	*CC (%)*	*LL (%)*
≤ 4 mm	7 624 (65.02)	8 184 (69.79)	7 287 (62.14)	9 929 (84.68)	10 706 (91.30)	11 586 (98.80)
> 4 mm; ≤ 6 mm	1 980 (16.88)	1 739 (14.83)	1 935 (16.50)	1 177 (10.04)	663 (5.65)	71 (0.60)
> 6 mm; ≤ 8 mm	1 152 (9.82)	918 (7.83)	1161 (9.90)	405 (3.45)	238 (2.03)	23 (0.20)
> 8 mm; ≤ 10 mm	558 (4.76)	545 (4.65)	669 (5.71)	152 (1.30)	71 (0.61)	21 (0.18)
> 10 mm; ≤ 12 mm	254 (2.17)	195 (1.66)	326 (2.78)	45 (0.38)	36 (0.31)	16 (0.14)
> 12 mm; ≤ 15 mm	105 (0.90)	97 (0.83)	238 (2.03)	18 (0.15)	11 (0.09)	9 (0.08)
> 15 mm	53 (0.45)	48 (0.41)	110 (0.94)	0	1 (0.01)	0

AP: anteroposterior, CC: craniocaudal, LL: laterolateral

for skin marks and 8.2, 6.3, 3.4 mm for bone structures. Setup margins using the first 5 fractions were 12.4, 10.9, 12.1 mm and 7.3, 5.1, and 2.8 mm, respectively. The CTV-PTV margins using the first 10 fractions were 11.8, 10.5, 11.9 mm and 7.1, 4.7, and 2.4 mm, respectively. Further increase of the number of fractions has led to only limited changes (Figures 3 and 4).

The correlations between CTV-PTV margins and various patient characteristics (average rectal area, volume of bladder, volume of CTV, age, BMI, hormonal therapy) and prostate locations were further investigated. Table 3 summarizes the Σ, σ, and calculated margins in the AP, CC, and LL directions and the p values for statistical differences between the groups. The average rectal area <11cm^2 and volume of bladder >300 cm^3 were associated with smaller CTV-PTV margins for setup using bones structures. Unfortunately, this difference did not translate into the setup margins using skin marks. Conversely, margins for patiens with voluminous bladder were larger. Largest margins (15.8 mm in LL direction) were needed in patients with BMI > 35 using skin markers. This difference disappeared in setup using bone structures. Age and extent of CTV had no significant influence on setup margins.

Discussion

Interfractional variation implies the differences in patient anatomic position and shape, appearing at treatment delivery with respect to those at treatment simulation. Major causes of interfractional patient variation are patient positioning and organ filling [18]. These differences can produce relevant uncertainties in organ dose-volume determination and target underdosage [19]. Herein we presented the largest study concerning interfraction motion in prostate cancer radiotherapy

Table 3. Statistical results of prostate displacement for different patient characteristics

	Skin-Prostate									*Bone-Prostate*								
	Σ			Σ			*Set-up margin*			Σ			Σ			*Set-up margin*		
	AP	*CC*	*LL*	*AP*	*CC*	*LL*	*AP*	*CC*	*LL*	*AP*	*CC*	*LL*	*AP*	*CC*	*LL*	*AP*	*CC*	*LL*
Entire cohort	*3.4*	*3.2*	*3.5*	*4.3*	*3.6*	*4.5*	*11.4*	*10.6*	*11.8*	*2.1*	*1.3*	*0.5*	*2.6*	*2.1*	*1.4*	7.0	4.7	2.1
ARA (cm^2)																		
<11	3.4	3.2	3.5	4.2	3.6	4.5	11.4	10.6	11.9	2.0	1.3	0.4	2.5	2.1	1.4	6.8	4.6	2.1
≥11	3.3	3.6	2.8	4.4	4.2	4.2	11.3	12.0	9.9	2.7	1.9	0.7	3.1	2.6	1.3	9.0	6.6	2.6
p value	*0.99*	*0.49*	*0.37*	*0.84*	*0.35*	*0.85*				*0.09*	*0.02*	*0.01*	*0.23*	*0.20*	*0.88*			
Bladder (cm^3)																		
<300	3.3	3.2	3.4	4.3	3.6	4.5	11.2	10.6	11.6	2.1	1.3	0.4	2.6	2.2	1.4	7.0	4.8	2.1
≥300	4.8	3.6	4.3	3.9	3.3	4.5	14.8	11.2	14.0	1.4	1.0	0.4	2.5	1.8	1.2	5.1	3.8	2.0
p value	*0.01*	*0.51*	*0.13*	*0.71*	*0.72*	*0.87*				*0.045*	*0.27*	*0.99*	*0.92*	*0.38*	*0.57*			
CTV (cm^3)																		
<35	3.6	3.3	3.8	4.3	3.6	3.9	12.1	10.8	12.3	2.3	1.3	0.5	2.5	2.1	1.3	7.4	4.8	2.1
≥35	3.3	3.2	3.4	4.3	3.6	4.5	11.4	10.6	11.7	2.0	1.3	0.4	2.6	2.1	1.4	6.9	4.7	2.1
p value	*0.46*	*0.79*	*0.33*	*0.91*	*0.99*	*0.27*				*0.37*	*0.68*	*0.47*	*0.82*	*0.99*	*0.73*			
Age (years)																		
<75	3.5	3.1	3.6	4.4	3.7	4.5	11.7	10.4	12.1	2.0	1.3	0.4	2.5	2.1	1.4	6.8	4.8	2.0
≥75	3.2	3.5	3.2	4.2	3.4	4.4	10.9	11.1	11.2	2.2	1.2	0.5	2.6	2.1	1.3	7.3	4.5	2.2
p value	*0.35*	*0.22*	*0.31*	*0.66*	*0.44*	*0.89*				*0.32*	*0.38*	*0.07*	*0.75*	*0.87*	*0.64*			
BMI (kg/m^2)																		
<35	3.4	3.3	3.4	4.3	3.6	4.2	11.6	10.8	11.4	2.1	1.3	0.4	2.6	2.1	1.4	7.1	4.8	2.1
≥35	2.7	2.5	4.5	4.5	3.3	6.6	9.9	8.6	15.8	1.3	0.9	0.5	2.4	2.1	1.4	5.1	3.8	2.3
p value	*0.18*	*0.11*	*0.03*	*0.73*	*0.67*	*0.001*				*0.32*	*0.38*	*0.07*	*0.75*	*0.87*	*0.64*			
Hormonotherapy																		
Yes	3.3	3.5	3.6	4.3	3.5	4.5	11.3	11.1	12.0	2.0	1.2	0.4	2.5	2.1	1.4	6.8	4.6	2.1
No	3.5	2.6	3.2	4.4	3.8	4.5	11.9	9.1	11.2	2.2	1.4	0.5	2.7	2.2	1.3	7.4	5.1	2.1
p value	*0.52*	*0.002*	*0.29*	*0.75*	*0.33*	*0.82*				*0.29*	*0.10*	*0.51*	*0.38*	*0.75*	*0.66*			

AP: anteroposterior, CC: craniocaudal, LL: laterolateral, Σ: systematic errors, σ: random errors, ARA: average rectal area, CTV: clinical target volume, BMI: body mass index

and prostate variability with regard to bone structures using cone-beam CT. We analyzed 11,726 fractions and 70,356 shifts in 307 patients. Poli and colleagues published an analysis of 10,327 pretreatment daily localizations using ultrasound [20]. However ultrasound is associated with significant systematic error, especially in AP and CC directions. Other authors presented results with only a limited number of patients (less than one thousand localisations) [21-23].

Our results confirm that commonly used CTV-PTV margins (especially for AP direction) are inadequate. The margin of 9 mm for AP direction ensures only 80% minimum dose for 80% of the patients without using IGRT. The margin of 7 mm for identical direction is adequate only for daily online setup using bone structures. While the setup using bone structures was associated with reduced safely margins in left-right and CC directions, it had only limited impact on CTV-PTV margin in AP direction despite using dietary protocol. The hypothesis that accurate dose delivery to the target can improve tumor control was recently confirmed by Zelefsky et al. [8].

A number of adaptive offline protocols have been introduced to reduce systematic errors. Adaptive radiotherapy uses information from the first few treatment fractions to reoptimize the treatment plan. Unfortunately, the question remains about what number of fractions is sufficient to calculate the representative safety margins. Based on our data, information from the first 5-10 fractions is adequate. Further increase in fractions leads to only limited changes. However, setup using bone structures is not an ideal way for online protocol. Our results are in agreement with the data published by Schallenkamp et al. based on 20 patients [22].

To analyze various correlations, we divided the group of patients into subgroups by average rectal area (ARA), volume of bladder, CTV, age, BMI and administration of neoadjuvant hormonal

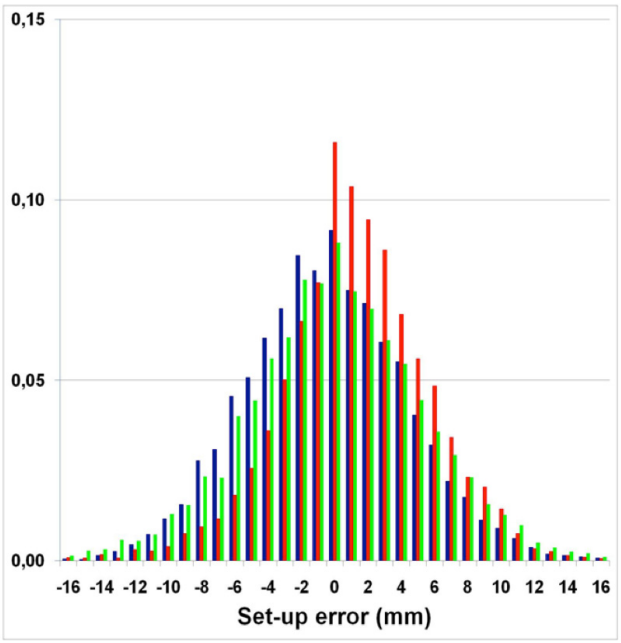

Figure 1. Frequency histogram of prostate displacement - setup using skin marks. Anteroposterior direction – blue, Laterolateral direction – green, Craniocaudal direction – red.

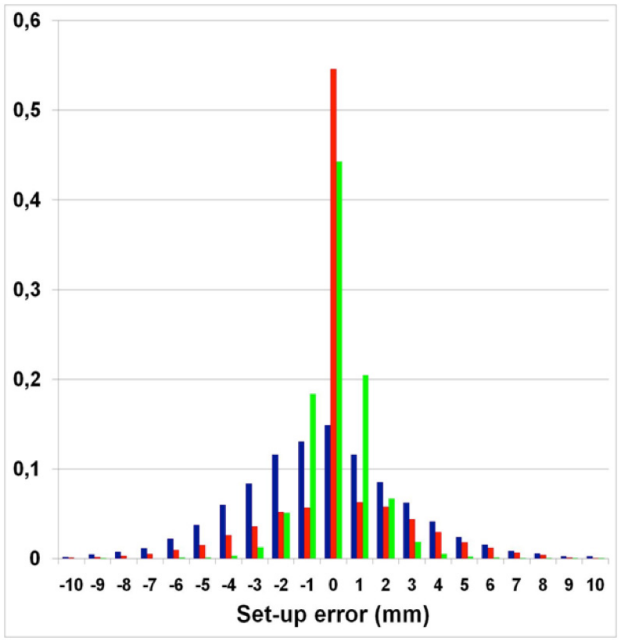

Figure 2. Frequency histogram of prostate displacement - setup using bone structures. Anteroposterior direction: blue, Laterolateral direction: green, Craniocaudal direction: red.

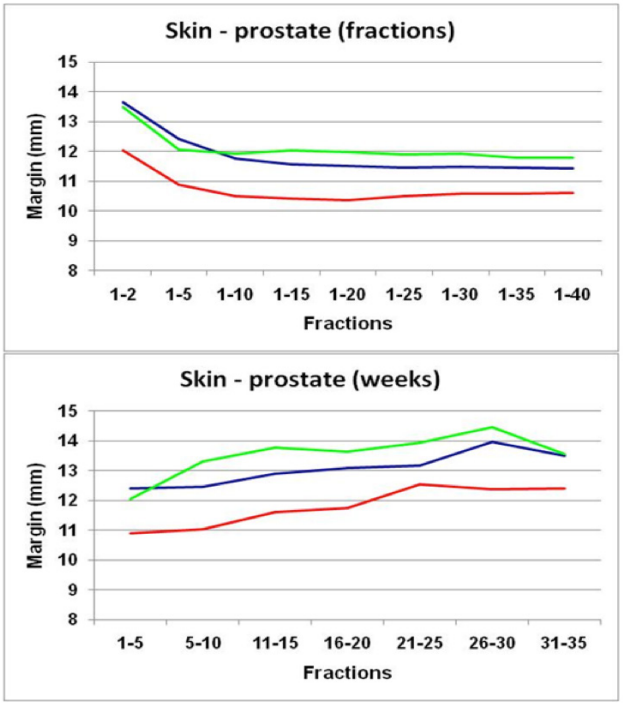

Figure 3. Calculated margins for setup using skin marks according to the number of fractions or particular weeks. Anteroposterior direction: blue, Laterolateral direction: green, Craniocaudal direction: red.

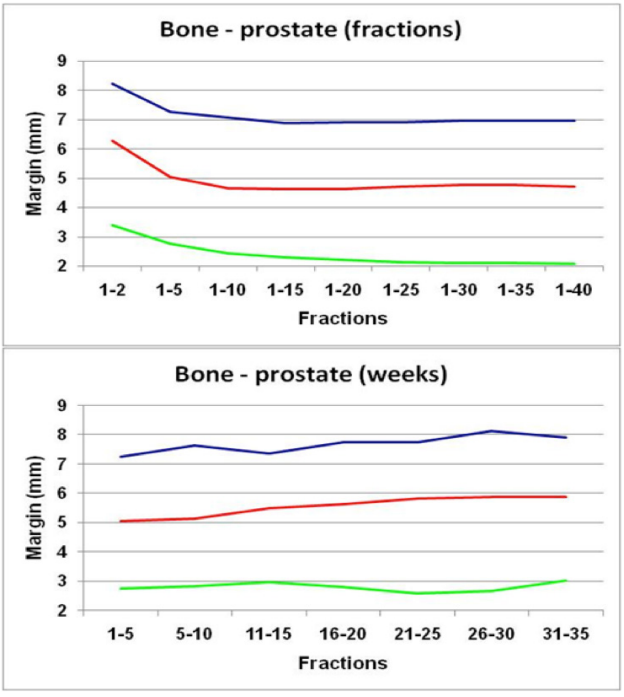

Figure 4. Calculated margins for setup using bone structures according to the number of fractions or particular weeks. Anteroposterior direction: blue, Laterolateral direction: green, Craniocaudal direction: red.

therapy. Although de Crevoisier et al. proved that the incidence of biochemical failure was significantly higher among patients with cross-sectional rectal area >11.2 cm^2, we found significantly greater CTV-PTV margins only for setup using bone structures [24].This greater interfractional variability did not modify the safety margins for setup using skin marks. We are convinced that only limited interfraction variability was caused by the application of a dietary protocol [25]. Blad-

der filling is the dominant factor which predicted acute genitourinary toxicity [26,27]. We investigated its impact on CTV-PTV margins. Full bladder (> 300 cm^3) was associated with smaller margins using bones structures. On the other hand, margins for setup using skin markers for patiens with voluminous bladder were larger. Presumably patients with full bladder are difficult to setup accurately. The limited impact of bladder filling status on target position is consistent with data from Tsai and colleagues [21]. The largest margins (15.8 mm in LL direction) were calculated for patients with BMI > 35 using skin markers. This finding is consistent with published data confirming increased risk of recurrence in patients with higher body mass index [28].

Conclusion

Our results confirm that the commonly used CTV-PTV margins are inadequate. We are convinced that image-guided radiotherapy is an integral part of modern radiotherapy. In our opinion, online corrections using cone-beam CT or fiducial markers should be the preferred approach for patients with prostate cancer undergoing radical radiotherapy because setup using bone stuctures resulted in significant interfraction variation in the AP direction.

References

1. Hanks GE, Hanlon AL, Epstein B, Horwitz EM. Dose response in prostate cancer with 8-12 years' follow-up. Int J Radiat Oncol Biol Phys 2008;54:427-435.
2. Zelefsky MJ, Pei X, Chou JF et al. Dose escalation for prostate cancer radiotherapy: predictors of long-term biochemical tumor control and distant metastases-free survival outcomes. Eur Urol 2011;60:1133-1139.
3. Al-Mamgani A, van Putten WLJ, Heemsbergen WD et al. Update of the Dutch multicenter dose escalation trial of radiotherapy for prostate cancer. Int J Radiat Oncol Biol Phys 2008;72:980-988.
4. Dearnaley DP, Hall E, Lawrence D et al. Phase III pilot study of dose escalation using conformal radiotherapy in prostate cancer: PSA control and side effects. B J Cancer 2005;92:488-498.
5. Pollack A, Zagars GK, Starkschall G et al. Prostate cancer radiation dose response:Result of the M.D.Anderson phase III randomized trial. Int J Radiat Oncol Biol Phys 2002;53:1097-1105.
6. Zietman AL, DeSilvio ML, Slater JD et al. Comparison of conventional-dose vs high dose conformal radiation therapy in clinically localized adenocarcinoma of the prostate: A randomized controlled trial. JAMA 2005;294:1233-1239.
7. Odrazka K, Dolezel M, Vanasek J et al. Time course of late rectal toxicity after radiation therapy for prostate cancer. Prostate Cancer Prostatic Dis 2010;13:138-143.
8. Zelefsky MJ, Kollmeier M, Cox B et al. Improved clinical outcomes with high-dose image guided radiotherapy compared with non-IGRT for the treatment of clinically localized prostate cancer. Int J Radiat Oncol Biol Phys 2012;84:125-129.
9. Stephans KL, Xia P, Tendulkar RD, Ciezki JP. The current status of image-guided external beam radiotherapy for prostate cancer. Curr Opin Urol 2010;20:223-228.
10. Eminowicz G, Dean C, Shoffren O, Macdougall N, Wells P, Muirhead R. Intensity-modulated radiotherapy (IMRT) to prostate and pelvic nodes-is pelvic lymph node coverage adequate with fiducial-based image-guided radiotherapy? Br J Radiol 2014;87(1037):20130696.
11. Kasaova L, Sirak I, Jansa J, Paluska P, Petera J. Quantitative evaluation of the benefit of fiducial image-guidance for prostate cancer intensity modulated radiation therapy using daily dose volume histogram analysis. Technol Cancer Res Treat 2014;13:47-55.
12. Nath SK, Sandhu AP, Sethi RA et al. Target localization and toxicity in dose-escalated prostate radiotherapy with image-guided approach using daily planar kilovoltage imaging. Technol Cancer Res Treat 2011;10:31-37.
13. Piotrowski T, Kaczmarek K, Bajon T, Ryczkowski A, Jodda A, Kazmierska J. Evaluation of Image-guidance Strategies for Prostate Cancer. Technol Cancer Res Treat 2014;13:583-591.
14. Odrazka K, Zouhar M, Petera J et al. Comparison of rectal dose-volume constraints for IMRT prostate treatment planning. Phys Med 2005;21:129-135.
15. Dolezel M, Odrazka K, Vaculikova M et al. Dose escalation in prostate radiotherapy up to 82 Gy using simultaneous integrated boost: direct comparison of acute and late toxicity with 3D-CRT 74 Gy and IMRT 78 Gy. Strahlenther Onkol 2010;186:197-202.
16. Dolezel M, Odrazka K, Vanasek J, Milan Mrklovsky, Petr Hoffmann, Karel Lucky. Dose escalation to the intraprostatic lesion – the results of acute and early late toxicity. Czech Urol 2013;17:175-182.

17. Dolezel M, Odrazka K, Vanasek J et al. Neoadjuvant hormonal therapy in prostate cancer - impact of PSA level before radiotherapy. J BUON 2013;18:949-953.
18. Yan D, Lockman D, Martinez A et al. Computed tomography guided management of interfractional patient variation. Semin Radiat Oncol 2005;15:168-179.
19. Yan D, Lockman D. Organ/patient geometric variation in external beam radiotherapy and its effects. Med Phys 2001;28:593-602.
20. Poli ME, Parker W, Patrocinio H et al. An assessment of PTV margin definitions for patients undergoing conformal 3D external beam radiation therapy for prostate cancer based on an analysis of 10,327 pretreatment daily ultrasound localizations. Int J Radiat Oncol Biol Phys 2007;67:1430-1437.
21. Tsai CL, Wu JK, Wang CW, Hsu FM, Lai MK, Cheng JC. Using cone-beam computed tomography to evaluate the impact of bladder filling status on target position in prostate radiotherapy. Strahlenther Onkol 2009;185:588-595.
22. Schallenkamp JM, Herman MG, Kruse JJ, Pisansky TM. Prostate position relative to pelvic bony anatomy based on intraprostatic gold markers and electronic portal imaging. Int J Radiat Oncol Biol Phys 2005;63:800-811.
23. Trofimov A, Nguyen PL, Efstathiou JA et al. Interfractional variations in the setup of pelvic bony anatomy and soft tissue, and their implications on the delivery of proton therapy for localized prostate cancer. Int J Radiat Oncol Biol Phys 2011;80:928-937.
24. de Crevoisier R, Tucker SL, Dong L et al. Increased risk of biochemical and local failure in patients with distended rectum on the planning CT for prostate cancer radiotherapy. Int J Radiat Oncol Biol Phys 2005;62:965-973.
25. Smitsmans MH, Pos FJ, de Bois J et al. The influence of a dietary protocol on cone beam CT-guided radiotherapy for prostate cancer patients. Int J Radiat Oncol Biol Phys 2008;71:1279-1286.
26. Pinkawa M, Fischedick K, Asadpour B et al. Low-grade toxicity after conformal radiation therapy for prostate cancer – impact of bladder volume. Int J Radiat Oncol Biol Phys 2006;64:835-841.
27. Nakamura N, Shikama N, Takahashi O et al. The relationship between the bladder volume and optimal treatment planning in definitive radiotherapy for localized prostate cancer. Acta Oncol 2012;51:730-734.
28. Stroup SP, Cullen J, Auge BK, L'Esperance JO, Kang SK. Effect of obesity on prostate-specific antigen recurrence after radiation therapy for localized prostate cancer as measured by the 2006 Radiation Therapy Oncology Group-American Society for Therapeutic Radiation and Oncology (RTOG-ASTRO) Phoenix consensus definition.Cancer 2007;110:1003-1009.