Journal of Radiotherapy in Practice

cambridge.org/jrp

Dosimetric variations for high-risk prostate cancer by VMAT plans due to patient's weight changes

David Miguel, Victor de la Llana, Daniel Martinez, Angel del Castillo, Delfín Alonso, Jesús-María de Frutos, Carlos Andrés, Manuel Agulla, Ricardo Torres and Francisco López-Lara

Hospital Clinico Universitario de Valladolid, Valladolid, Valladolid, Spain

Original Article

Cite this article: Miguel D, de la Llana V, Martinez D, del Castillo A, Alonso D, de Frutos J-M, Andrés C, Agulla M, Torres R, and López-Lara F. (2019) Dosimetric variations for high-risk prostate cancer by VMAT plans due to patient's weight changes. *Journal of Radiotherapy in Practice* **18**: 336–342. doi: 10.1017/S1460396919000177

Received: 11 February 2019
Revised: 5 March 2019
Accepted: 6 March 2019
First published online: 21 May 2019

Key words:
dosevolume points; patient's weight changes; prostate; treatment planning evaluation; VMAT

Author for correspondence:
David Miguel, Hospital Clinico Universitario de Valladolid, Valladolid 47014, Spain.
Email: david.miguel@outlook.com

Abstract

Purpose: The aim of this study is to investigate the impact of anatomical changes in prostate cancer patients on the target coverage when using 6 MV beams-VMAT therapy and to propose strategies that allow us to evaluate the dose or correct it by normalization without having to perform a new simulation.

Methods and materials: Ten patients of high-risk prostate cancer were chosen for the study. All test plans were delivered using the same isocenter and monitor units as the original plan and compared against the original unedited plan. The expansion and contraction of body contours due to size changes was mimicked by increasing and decreasing the body contour with depths of −2, −1·5, . . . , 1·5, 2 cm, in the anterior, and both lateral directions of the patient. A total of 90 plans were evaluated, 9 for each patient. Dose-volume histogram statistics were extracted from each plan and normalized to prescription dose.

Results: Weight changes resulted in considerable dose modifications to the target and critical structures. Plans were found to be varied with 2·9% ± 0·3% per cm SSD change for VMAT treatment with a correlation index close to one. Therefore, doses variations were linear to the changes of depth. Gamma index evaluation was performed for the 10 renormalized plans. All of them passed criteria of 3%/3 mm in at least 98.2% of points. Eight of them passed criteria in 99% points. Gamma index 4%/4 mm passed 100% points in all patients for the chosen region of interest.

Conclusions: The dosimetry estimation presented in this study shows important data for the radiation oncology staff to justify whether a CT rescan is necessary or not when a patient experiences weight changes during treatment. Based on the results of our study, discrepancies between real dose and planned dose were >5% for 1·7 cm of difference in external contour in the anterior and both lateral directions of the patient.

Introduction

Prostate cancer is the second highest cause of cancer death in males in developed countries, and the incidence and death rates have been steadily increased in developing countries.[1,2] External beam radiation therapy (EBRT) is one of the primary treatments options, nevertheless, radiotherapy of prostate tumors can be toxic due to the high dose to the surrounding organs-at-risk (OARs) such as rectum and bladder.

Volumetric modulated arc therapy (VMAT) is a radiation technique, which can reach highly conformal dose distributions with enhanced target volume coverage, sparing of normal tissues compared to conventional radiotherapy techniques.[3] Therefore, it has become the gold standard for EBRT[2] in prostate cancer. In combination with image-guided radiotherapy (IGRT), it can limit the rectum and bladder to low doses allowing high doses to the target volumes including pelvic lymph node treatment, with low side effects.[4]

Simulation is a critical preparation step before radiation treatment. The simulated setup will be exactly reproduced by comparing the 3D on-board images to the simulation CT scan.[4] In current practice, for prostate cancer radiotherapy, many centers carry out the original treatment plan to completion without accounting for anatomical changes that can occur due to weight variations and normal tissue volume alterations. This fact can lead variations in patient's body shape[5,6] and the body region does not match exactly with the original CT.

Furthermore, these volumetric changes can have an impact on delivered doses to the normal tissues and target structures as planned from the original pretreatment plan. These changes can greatly influence the penetration depth of charged particles and modify target coverage.[4,7] Fractionated photon irradiation of prostate tumors is not robust against changes in body contour with dose coverage being highly affected. It can greatly modify target dose coverage when

© Cambridge University Press 2019.

CAMBRIDGE UNIVERSITY PRESS

Table 1. Volumes features of the PTV1, PV2, PTV3, rectum, bladder, and left and right femoral heads for 10 patients

Variable	Minimum	Maximum	Mean	Std. deviation
Volume [cm^3] Bladder	152·90	759·10	379·99	172·25
Volume [cm^3] rectum	51·90	105·90	72 ·82	17 ·10
Volume [cm^3] RFH	47·10	87·40	70·45	10·82
Volume [cm^3] LFH	54·60	96·50	72·27	11·76
Volume [cm^3] PTV1	53·90	226·70	134·18	53·57
Volume [cm^3] PTV2	16·70	115·20	47·68	27·90
Volume [cm^3] PTV3	377·40	808·70	553·08	162·00

using bony anatomy-based position verification.[8–10] The result of dosimetric change is a discrepancy of delivered dose to the planned target volumes (PTVs) and organs at risk (OARs).

There is little information on the effect of weight change (gain or loss) to the dosimetric impact due to the change of body contour for prostate cancer. The aim of this study is to investigate the impact of anatomical changes in prostate cancer patients on the target coverage when using 6 MV beams-VMAT therapy. Therefore, accumulated dose distributions were calculated for different anatomical changes and compared to the planned dose distributions. Another purpose of the study is to propose strategies that allow us to evaluate the dose or correct it by normalization without having to perform a new simulation. Normalization is a

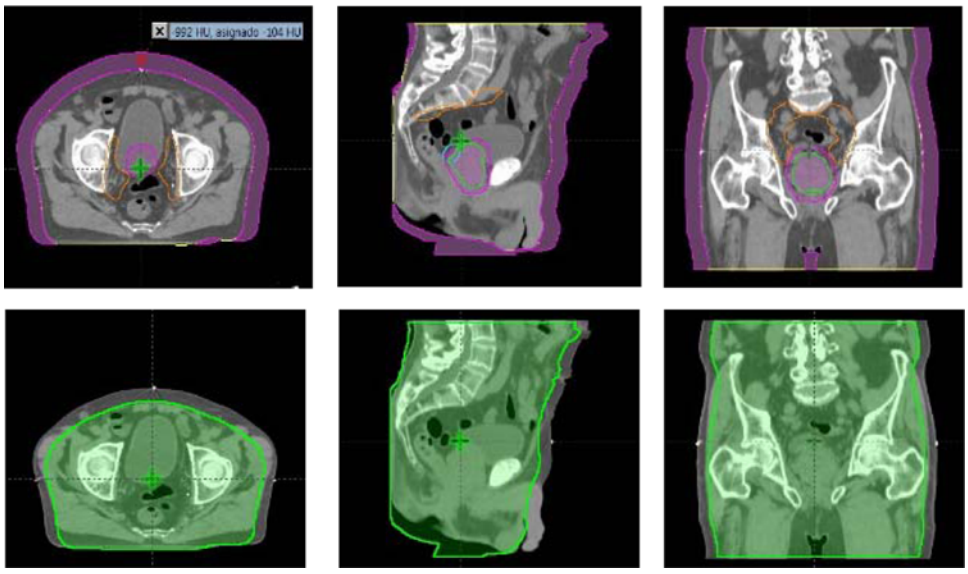


Figure 1. CT images of the axial, sagittal and coronal views for a patient with magnified (purple) and reduced (green) depths (anterior, left and right direction) of 2 cm.

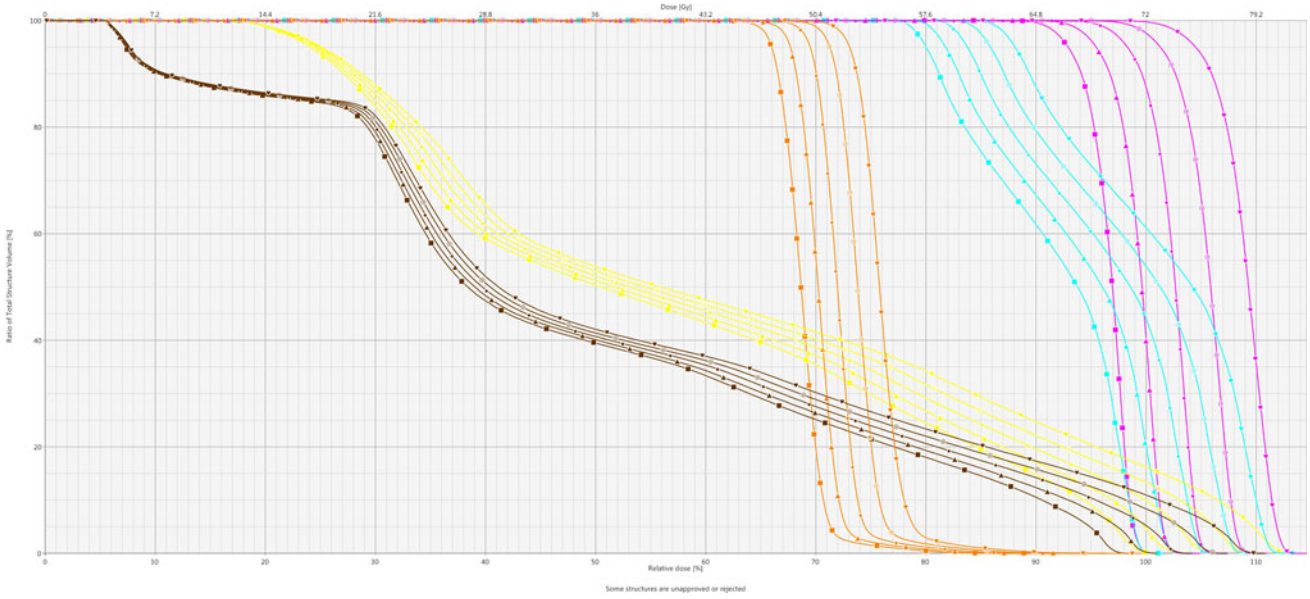


Figure 2. Comparison of the initial VMAT plan (square) with the final plans after mimicking weight gain or loss. Triangle (−2 cm), solid dot (−1 cm), not solid dot (+1 cm), heart (+2 cm) were DVH for the recalculated plans.

https://doi.org/10.1017/S1460396919000177 Published online by Cambridge University Press

Table 2. Minimum, maximum and median doses for PTV1, PTV2, PTV3. Data fitting y = a + bx and correlation index R^2

	R^2	a	b
Min Dose [Gy] PTV1	0·972	1·001	−0·032
Max Dose [Gy] PTV1	0·982	1·003	−0·033
Median Dose [Gy] PTV1	0·988	1·001	−0·032
Min Dose [Gy] PTV2	0·972	1·001	−0·026
Max Dose [Gy] PTV2	0·977	1·002	−0·028
Median Dose [Gy] PTV2	0·979	1·000	−0·025
Min Dose [Gy] PTV3	0·947	0·996	−0·026
Max Dose [Gy] PTV3	0·950	1·002	−0·029
Median Dose [Gy] PTV3	0·985	1·000	−0·025

Table 3. Data fitting for maximum and median doses for OARs for 10 patients. Y = a + bx

	Maximum			Median		
	R2	a	b	R2	a	b
Bladder	0·976	1·001	−0·031	0·974	1·000	−0·023
Rectum	0·967	1·000	−0·032	0·946	0·999	−0·020
RFH	0·967	1·000	−0·030	0·986	1·000	−0·030
LFH	0·963	1·000	−0·029	0·981	1·000	−0·029

method that is sometimes used in radiation therapy planning as a means of satisfying or obtaining acceptable dose coverage to the PTVs. The results may be transferred to other types of cancers in the pelvic area such as endometrium, rectum or anal cancer.

Material and Method

Patients

Ten patients of high-risk prostate cancer were chosen for the study. All of them were simulated with an empty rectum and a comfortably full bladder in the supine position with ankle stocks. An enema per rectum was given before simulation to empty the rectum as much as possible.

Planning CT images were acquired using a CT simulator (Aquilion™ LB, Canon Medical Systems). The structures outlined included the prostate (PTV1), seminal vesicles (PTV2), pelvic lymph nodes (PTV3), rectum (entire contents) from the ischial tuberosities to the sigmoid flexure, bladder (entire contents), right and left femoral heads and the external contour.

Each treatment was planned with a 6 MV photon beam for a Varian Clinac 21 DHX (Varian Medical System, Palo Alto, CA), and a 120-leaf Millennium MLC system was used. Treatment plans were created using inverse plan optimized by the Eclipse RapidArc algorithm v15·1·51 (Varian Medical Systems, Palo Alto, CA). Dose grid resolution was set to 0·25 cm and calculation was performed using Acuros algorithm (v15·6·03).

Mimicking weight gain or loss

The expansion and contraction of body contours due to size changes were mimicked by increasing and decreasing the body contour with depths of −2, −1·5, −1, −0·5, 0, 0·5, 1, 1·5 and 2 cm, in the anterior, and both lateral directions of the patient based on our clinical experience and in a similar way (only for reduced depths) as in Chow and Jiang.[11] For expansion, we used in the new contour, the mean value of Hounsfield units that were measured for the abdominal fat in each patient. For contraction, the external volume was evaluated by cutting. The missing tissue was assigned a density of air equivalent.

Dose-volume histogram statistics

All test plans were delivered using the same isocenter and monitor units as the original plan and compared against the original unedited plan. A total of 90 plans were evaluated, 9 for each patient. Dose-volume histogram statistics were extracted from each plan and normalized to prescription dose.

Normalize

The evolution of all items mentioned (PTVs and OARs) was studied by least squares data fitting. For the target volumes (PTVs), we focused on the maximum, minimum and medium doses. For OAR's (rectum, bladder and femoral heads), we focused on the maximum and median dosages. Then, we evaluated the mean slope of the evolution forms of data fitting that was computed as the value of normalization.

To evaluate the value of normalization computed previously as an alternative to re-simulation, dosimetric effects of the modified plan were compared to the original plan. The dose differences between the plans were determined by comparing dose-volume histograms and analyzing the 3D-gamma index between them. To do this, dose matrices were exported from the treatment planning system.

The use of the gamma index evaluation has become a standard technique to contrast measured distributions against the ones predicted by commercial treatment planning systems.[12] The comparison between plans and dose distributions was performed with the software Verisoft 5·1 (PTW). Measured dose was compared with the 3D dose distribution from the treatment planification system using a 3D global gamma analysis.[13] For the VMAT plans, the gamma pass rates were calculated using gamma parameters 3 mm and 3%,[13,14] a dose threshold of 10% of the measured maximum dose and a pass criterion of 95% or higher was used. To avoid close skin tissue, what obviously will not match, we performed the analysis in a cube of 18 cm × 20 cm × 20 cm (height × length × width) centered in the isocenter of the treatment.

Results

Size expansions or reductions used to modify patient's body contour were performed while the bone anatomy remained unchanged. Figure 1 shows a typical patient anatomy in the axial, coronal and sagittal view after the body contour was expanded (purple) or contracted (green) for a thickness of 2 cm.

Table 1 shows volumes features of the PTV1, PV2, PTV3, rectum, bladder, and left and right femoral heads for 10 patients of the study. Weight changes resulted in considerable dose modifications to the target and critical structures. Plans with simulated weight gain had significantly reduced doses. Figure 2 is an example of dose-volume histogram (DVH) plots for the patient with a prostate volume of 61 cm^3 and a PTV1 volume of 141 cm^3, which is close to the median volume value of PTV1 in our patient group. For PTVs, rectum and bladder (femoral heads have been omitted for the sake

https://doi.org/10.1017/S1460396919000177 Published online by Cambridge University Press

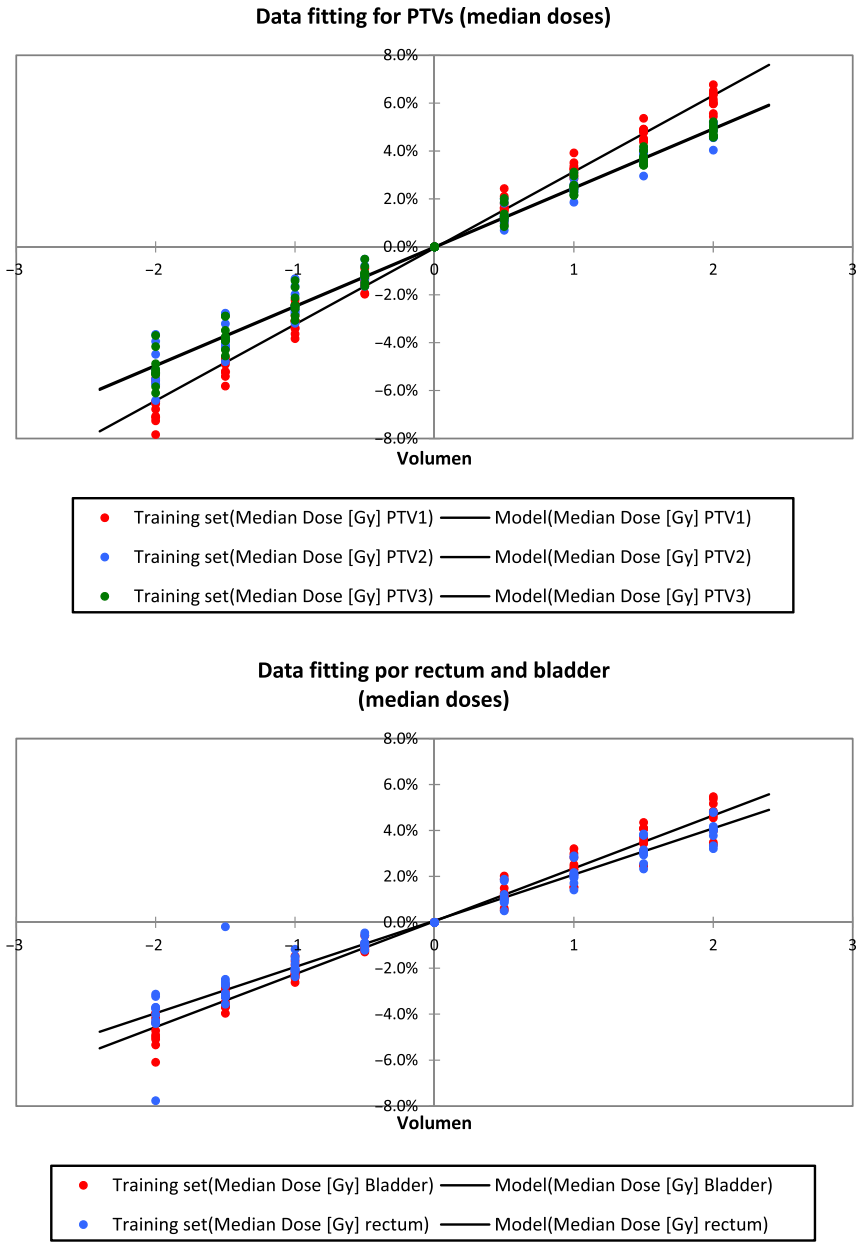


Figure 3. Data fitting for PTVs, rectum and bladder (median doses).

of simplicity) DVH curves vary with the patient's fat layer thickness from −2 to +2 cm with a 1 cm step. This pattern is maintained for all patients analyzed.

The data fitting of the points of interest from DVH curves can be found in Tables 2 and 3 and Figure 3. Slopes of curves are found to be varied with 2·9% ± 0·3% per cm with a correlation index close to one. Therefore, doses variations were linear to the changes of depth.

To evaluate the effect of application of normalization for VMAT planning, the normalization value was applied to treatment plans. The DVH curves of the patient after normalization are shown in Figure 4.

Figures 5–7 show the evaluation of gamma index for 10 patient plans. All of them passed criteria of 3%/3 mm in at least 98.2% of points. Eight of them passed criteria in 99% points. Gamma index 4%/4 mm passed 100% points in all patients for the chosen region of interest.

Discussion

Although this is a relatively small study, the cohort of 10 patients allows the study of individual data, thus enabling recognition of important outcomes. A total of 90 plans have been evaluated. Anatomical changes were associated with significant dosimetric differences.

Anatomical alterations should have a critical impact in VMAT plans due to the sharp dose gradient between the edges of target volumes and critical OARs.[15] These changes could potentially lead to overdosing of normal tissues and under dosing or marginal geographical misses of target volumes during a course of treatment based on a single planning data set.

Evaluation of treatment plans in radiation oncology is heavily dependent on DVHs. However, such evaluations typically are limited to a small set of points from the DVH.[15] In this study, we

https://doi.org/10.1017/S1460396919000177 Published online by Cambridge University Press

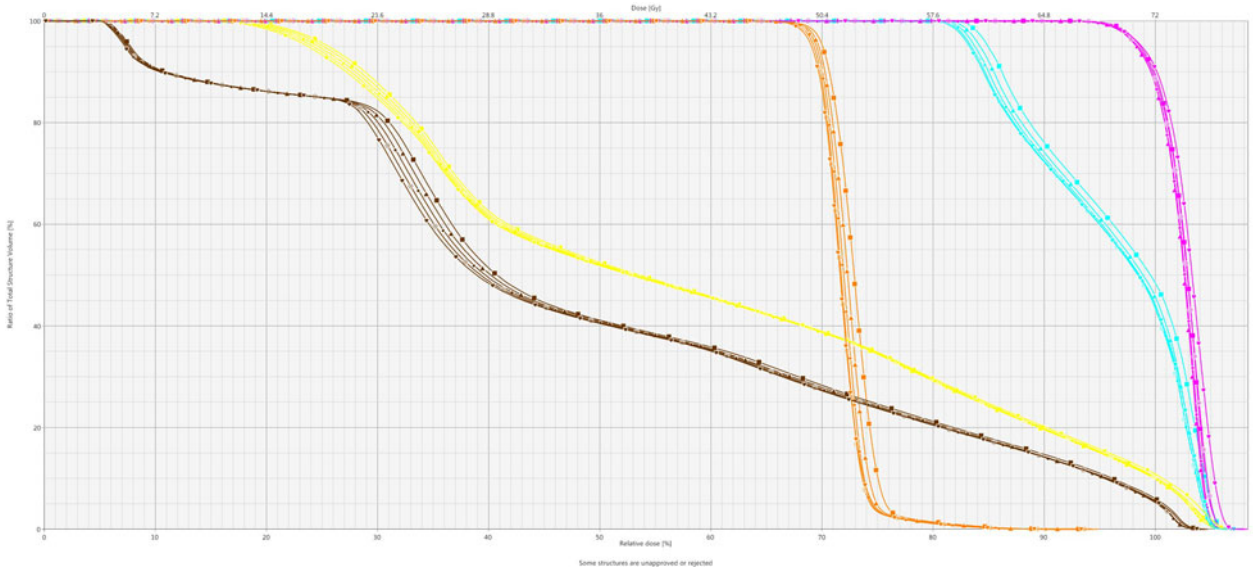


Figure 4. DVHs of the PTV1, PTV2, PTV3, rectum and bladder for a patient varying with reduced depths of −2 cm to +2 cm after normalization a value of 2·9% per centimeter.

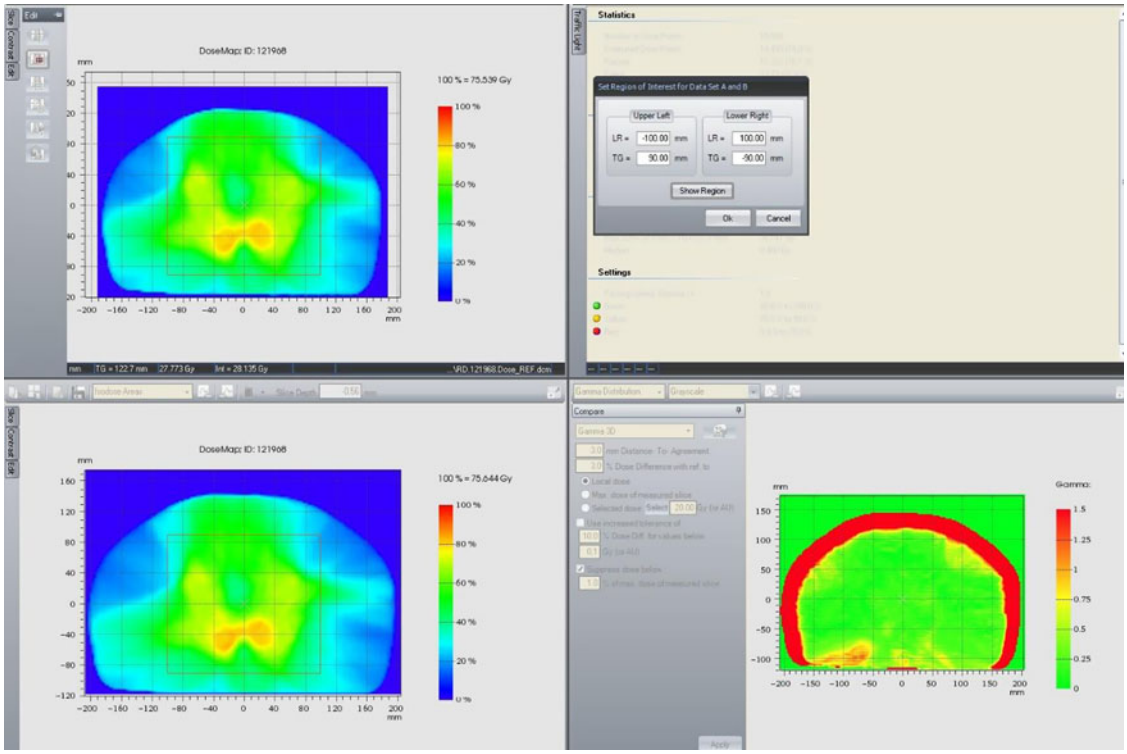


Figure 5. Region of interest in transversal plan to perform the 3D-gamma index evaluation.

conclude that it is possible to use the plots to illustrate the trend and agreement of different DVHs against the independent predicted SSD changes.

Normalization for VMAT plans should be used with caution to avoid potential pitfalls that may occur. Normalizations help meet the volume coverage goals may result in avoidable delivery of additional doses to the normal tissues. Although this is a widely utilized technique to aid in achieving volume coverage, recommendations would favor re-optimization over normalization in most planning situations.[16]

Finally, renormalized plans passed gamma index criteria of 3%/3 mm by almost all cases. Furthermore, all plans passed 4%/4 mm criteria. Therefore, there was statistically a good agreement between the predicted gamma between original plans and the renormalized ones. One final important fact, normalization does not allow us to predict the dose close to skin. From our measurements, it is considered to be approximately 20% of prescription dose in the first 1·5 cm (15 Gy) for a 6 MV beam.

Resimulation, replanning and performing quality assurance are usually unnecessary when the SSD changes by a small amount.

https://doi.org/10.1017/S1460396919000177 Published online by Cambridge University Press

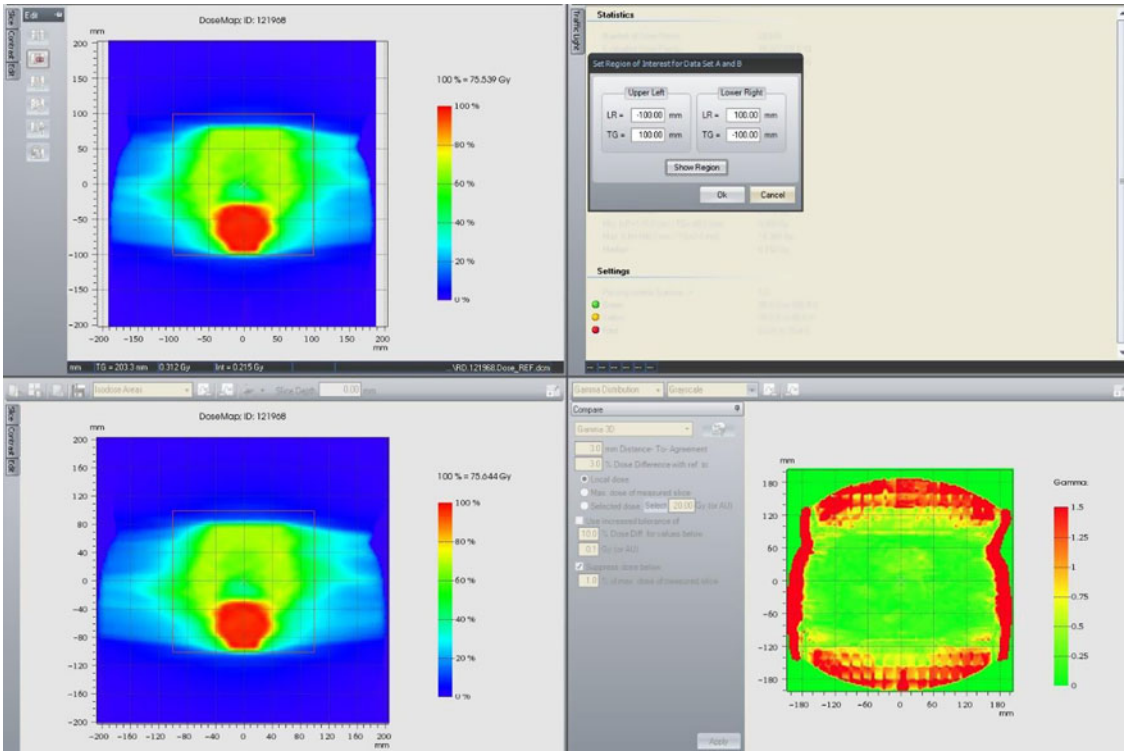


Figure 6. Region of interest in sagital plan to perform the 3D-gamma index evaluation.

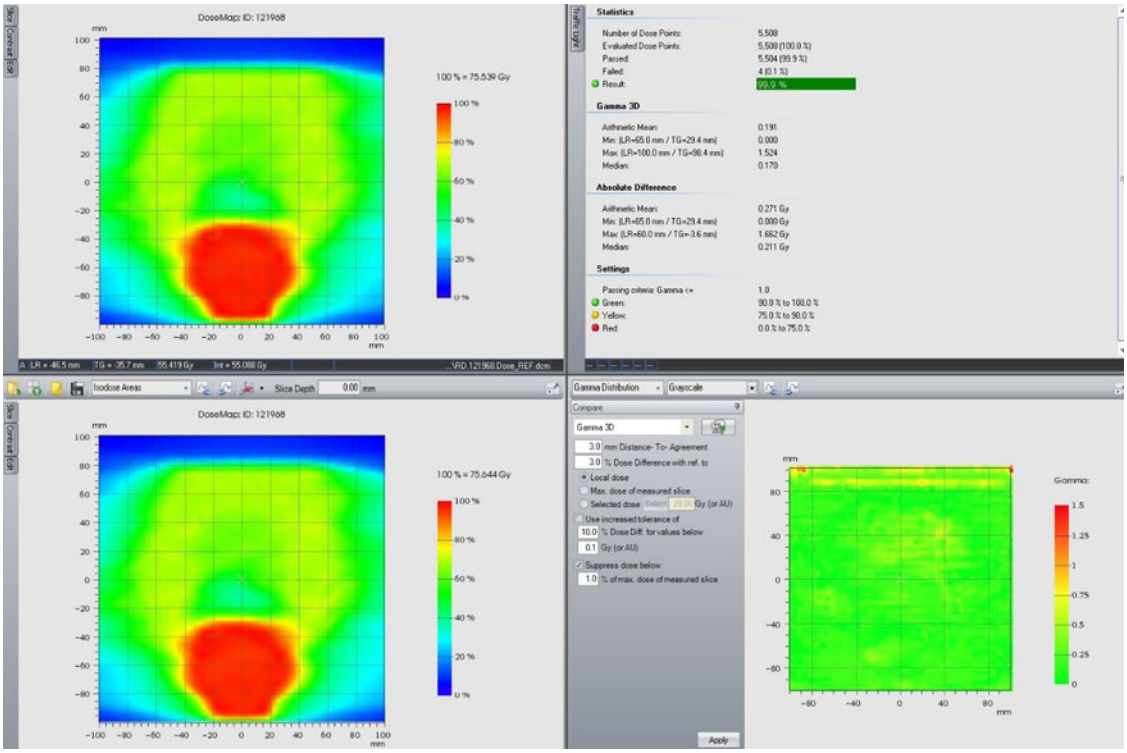


Figure 7. An example of 3 mm/3% 3D-gamma analysis for a patient of the study.

https://doi.org/10.1017/S1460396919000177 Published online by Cambridge University Press

Replanning is clearly resource and time intensive. When discrepancies between real dose and planned dose were >5%, which is the limit of the treatment delivery tolerance,[17] doctors and medical physicists should rescan the patient. Based on the results of our study, 2·9% ± 0·3% per cm, 1·7 cm of difference in external contour in the anterior and both lateral directions of the patient, must be the maximum discrepancy value. For lesser difference, it can be considered normalization in order to preserve planned DVH.

These results match with those of Chow and Jiang.[11] (only for patient's weight loss and low-risk prostate cancer), where D99% for the PTV was found to have increased 2·86% ± 0·34% per centimeter of reduced depth. Otherwise, Pair et al.[9] (for low-risk prostate cancer) found a value of 3·6% ± 0·2% per centimeter. On the other hand, Klein et al.[18] recommend using both optical distance indicator values and vertical couch settings to avoid treatment distance setup errors because dose difference is about 2% change per centimeter.

Therefore, the tendency found by the previous authors is maintained for the case of high-risk prostate cancer patients, such as those analyzed in this study. The values found, not only for the volumes of interest, but for all the points, are corroborated with the gamma index evaluation carried out.

The study presents two main limitations. First, the model used to simulate the fattening or thinning of patients is an approximation, changes in volume may be slightly different from those assumed here. Second, to carry out the treatment plans by means of inverse calculation, no irradiation angle has been restricted; it is probable that plans with prohibited sectors of irradiation will produce different results.

Conclusions

Patient setup should be verified using SSD measurements before and during the radiotherapy course to ensure that patient dimensions remain stable because it should have an important dosimetry impact.

The dosimetry estimation presented in this study shows important data for the radiation oncology staff to justify whether a CT rescan is necessary or not when a patient experiences weight changes during treatment.

Author ORCiD. David Miguel 0000-0001-7573-2642

Acknowledgment. The authors would like to thank the referees for the valuable comments on our manuscript.

Conflict of interest. The authors declare that they have no conflict of interest.

References

1. Torre L A, Bray F, Siegel R L, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65 (2): 87–108.
2. Mottet N, Bellmunt J, Bolla M et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol 2017; 71 (4): 618–629.
3. Pollack A, Hanlon A L, Horwitz E M et al. Dosimetry and preliminary acute toxicity in the first 100 men treated for prostate cancer on a randomized hypofractionation dose escalation trial. Int J Radiat Oncol 2006; 64 (2): 518–526.
4. Nguyen N P, Davis R, Bose S R et al. International Geriatric Radiotherapy Group the IGR. Potential applications of image-guided radiotherapy for radiation dose escalation in patients with early stage high-risk prostate cancer. Front Oncol 2015; 5 (18): 1–7.
5. Rodriguez C, Freedland S J, Deka A et al. Body mass index, weight change, and risk of prostate cancer in the cancer prevention study II nutrition cohort. Cancer Epidemiol Biomarkers Prev 2007; 16 (1): 63–69.
6. Bolze M S, Fosmire G J, Stryker J A, Chung C K, Flipse B G. Taste acuity, plasma zinc levels, and weight loss during radiotherapy: a study of relationships. Radiology 1982; 144 (1): 163–169.
7. Houweling A C, Fukata K, Kubota Y et al. The impact of interfractional anatomical changes on the accumulated dose in carbon ion therapy of pancreatic cancer patients. Radiother Oncol 2016; 119 (2): 319–325.
8. Choi H S, Jo G S, Chae J P et al. Defining the optimal time of adaptive replanning in prostate cancer patients with weight change during volumetric arc radiotherapy: a dosimetric and mathematical analysis using the gamma index. Comput Math Methods Med 2017; 2017: 4149591.
9. Pair M L, Du W, Rojas H D et al. Dosimetric effects of weight loss or gain during volumetric modulated arc therapy and intensity-modulated radiation therapy for prostate cancer. Med Dosim 2013; 38 (3): 251–254.
10. Chow J C L, Jiang R. Dosimetry estimation on variations of patient size in prostate volumetric-modulated arc therapy. Med Dosim 2013; 38 (1): 42–47.
11. Chow J C L, Jiang R. Comparison of dosimetric variation between prostate IMRT and VMAT due to patient's weight loss: patient and phantom study. Reports Pract Oncol Radiother 2013; 18 (5): 272–278.
12. Low D A, Harms W B, Mutic S, Purdy J A. A technique for the quantitative evaluation of dose distributions. Med Phys 1998; 25 (5): 656–661.
13. Low D A, Harms W B, Mutic S, Purdy J A. A technique for the quantitative evaluation of dose distributions. Med Phys 1998; 25 (5): 656–661.
14. Mans A, Schuring D, Arends M P et al. The NCS code of practice for the quality assurance and control for volumetric modulated arc therapy. Phys Med Biol 2016; 61 (19): 7221–7235.
15. Cutright D, Gopalakrishnan M, Roy A, Panchal A, Mittal B B. DVH Analytics: a DVH database for clinicians and researchers. J Appl Clin Med Phys 2018; 19 (5): 413–427.
16. Williams G, Tobler M, Leavitt D. Pitfalls in normalization for intensity-modulated radiation therapy planning. Med Dosim 2005; 30 (4): 194–200.
17. Kouloulias V E. Quality assurance in radiotherapy. Eur J Cancer 2003; 39 (4): 415–422.
18. Klein E E, Drzymala R E, Purdy J A, Michalski J. Errors in radiation oncology: a study in pathways and dosimetric impact. J Appl Clin Med Phys 2005; 6 (3): 81–94.

https://doi.org/10.1017/S1460396919000177 Published online by Cambridge University Press