Journal of Radiotherapy in Practice

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RapidPlan models for prostate radiotherapy treatment planning with 10-MV photon beams

Francesco Pupillo† , Maria Antonietta Piliero† , Margherita Casiraghi, Luca Bellesi and Stefano Presilla

Medical Physics Division, Imaging Institute of Southern Switzerland, Ente Ospedaliero Cantonale, 6500 Bellinzona, Switzerland

Original Article

Cite this article: Pupillo F, Piliero MA, Casiraghi M, Bellesi L, and Presilla S. (2023) RapidPlan models for prostate radiotherapy treatment planning with 10-MV photon beams. *Journal of Radiotherapy in Practice*. **22**(e56), 1–7. doi: 10.1017/S1460396922000267

Received: 26 January 2022
Revised: 3 June 2022
Accepted: 26 August 2022

Key words:
Knowledge-based planning; Prostate radiotherapy; Rapid Plan; VMAT

Author for correspondence:
Dr Francesco Pupillo, Medical Physics Division, Imaging Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Via A. Gallino 12, 6500 Bellinzona, Switzerland.
E-mail: francesco.pupillo@eoc.ch

†Equally contributed to this work and should be considered as co-first authors.

Abstract

Introduction: The RapidPlan is a radiotherapy planning tool that uses a dataset of approved plans to predict the dose distribution and automatically generates the dose–volume constraints for optimisation of the new plan. This study compares three strategies of model building for the treatment of prostate cancer with the 10-MV photon beam.
Methods: Three models for prostate treatment were compared: *Model 6X*, *Model10X* and *Model6Xrefined*. *Model6X* is already used in our department and was trained on treatment plans based on the 6-MV photon beam. *Model10X* was trained on treatment plans based on the 10-MV photon beam and manually optimised by an experienced medical physicist. Finally, *Model6Xrefined* was trained on plans automatically created by the *Model6X*, but using the 10-MV photon beam. The three models were used to generate 25 new plans with the 10-MV photon beam.
Results: *Model10X* generated plans with 2 Gy lower mean dose to bladder-PTV and rectum-PTV volumes and 8% lower V_{15Gy} at bladder and rectum volumes, although the number of monitor units increased by 170 on average.
Conclusions: The model trained on manually optimised plans generated plans with higher normal tissue sparing. However, model building is a time-consuming process, so a cost–benefit balance should be performed.

Introduction

In 2014, Varian released RapidPlan (Varian Medical Systems, Palo Alto, USA), a knowledge-based planning module for the Eclipse treatment planning system (TPS).

RapidPlan is a statistical engine that identifies the correlation between some geometric and dosimetric features. It uses the library of already calculated and clinically accepted plans (training plans) to estimate the possible dose–volume histograms (DVHs) and define the plan optimisation objectives for new patients. The choice of the training plans is crucial, since the efficacy of the knowledge-based process relies on the quality of the training plans and the consistency between the new case and the training population.[1]

A RapidPlan model based on the 6-MV photon beam and volumetric-modulated arc therapy (VMAT) technique is already configured and routinely used in our department for prostate cancer radiotherapy treatment planning. However, lower dose to the organs at risk (OARs) can be achieved with 10-MV photon beams, especially in the case of large patients.[2–5] A new RapidPlan model based on the 10-MV photon beam was configured using a new training set of high-quality treatment plans based on the 10-MV photon beam. However, model configuration is a time-consuming procedure because it is an iterative process of model training and validation until the RapidPlan-generated plans reach the desired quality.[6–9]

Studies showed that no specific training plans are necessary to obtain clinically acceptable results.[10–12] Therefore, in this work, we used the RapidPlan model trained on the 6-MV photon beam plans to create treatment plans with the 10-MV photon beam. We then evaluated the dosimetric differences with the plans generated by the new model trained on the 10-MV photon beam plans. Moreover, an iterative process of model configuration was investigated: the 6-MV RapidPlan model was used to automatically calculate a new set of training plans with the 10-MV photon beam. A new RapidPlan model was then configured based on those automatically calculated training plans. This could be a fast approach for building a new RapidPlan model that can be considered as a refinement of an already existing model.

Methods and Materials

Patient population

Seventy-five patients who received radiotherapy treatment for the prostate and lymph nodes were retrospectively selected for this study. Each patient underwent a computed tomographic

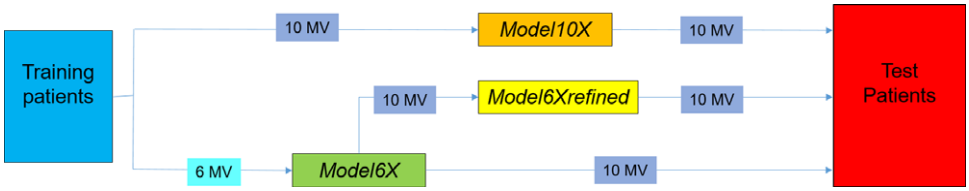

Figure 1. Outline of the generation of the three RapidPlan models.

(CT) scan in the supine position with a 3-mm slice thickness. The clinical target volume (CTV) was defined as prostate gland plus pelvic lymph nodes. The planning target volume (PTV) was obtained by adding a 7-mm isotropic margin to the CTV.[13] The dose prescription to the PTV was 50 Gy in 25 fractions.[14] The rectum, bladder and femoral heads were included in the structure set as OARs. The CTV, PTV and OARs were contoured by certified radiation oncologists. All the patients received a sequential boost dose of 28 Gy in 14 fractions to the prostate gland. However, this work focused on the dosimetric properties of the 50-Gy treatment plan only, since we believed it was worth studying the potential of a RapidPlan model for a complex-shaped target volume, which is the prostate plus lymph nodes volume, rather than a simpler shape, such as the prostate gland.

Model configuration

The RapidPlan model configuration is based on a library of clinically accepted treatment plans.

The first phase of the model configuration is data extraction. This is a calculation of the geometric features for each OAR, based on the patient characteristics and beam geometry. Those features include the total volume, the overlap volume with the target, the out-of-field volume, the target volume and the geometry-based expected dose (GED) histogram. The GED is a metric used to calculate the expected dose to a structure. It is based on the distance between the structure and the target volume.

The second phase of model configuration is the training, which is a combination of principal component and regression analysis. The principal component analysis is applied to the GED histograms and the DVH to find two or three principal scores. The regression model is used to correlate the principal scores of the GED histogram and the geometric features to the principal scores of the plan DVH.[15,16]

At the end of the training phase, the system produces a statistical summary of the model goodness and the regression plots. These parameters helps to highlight plans that differ from average dosimetrically or geometrically, the so-called outliers. Detailed descriptions of these parameters and outliers identification are provided in the literature.[15]

The final model is a set of coefficients which will be used to estimate DVHs and optimisation parameters for the new patient.

Three RapidPlan models were configured in this work. Model training was carried out on 50 of the 75 randomly selected patient plans. All the plans were created for the Varian TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA) using the Eclipse TPS (version 15.6) with the photon optimiser (PO) engine and the AcurosXB dose calculation algorithm. The plans included two full arcs with collimator angles at 30 and 330 degrees, and they were optimised with the VMAT technique.

The first RapidPlan model, called *Model6X*, was trained on plans optimised with the 6-MV photon beam quality. This model is currently used in our department. The second RapidPlan model, called *Model10X*, was trained on plans optimised with the 10-MV photon beam quality. Both models were trained on treatment plans manually optimised by an experienced medical physicist. The third RapidPlan model, named *Model6Xrefined*, was trained on plans automatically optimised using the *Model6X* with the 10-MV photon beam quality. The optimisation cycle included all the PO optimisation multiple resolution (MR) levels from MR1 to MR4, an intermediate dose calculation and a final optimisation cycle from the MR2 to the MR4 level. Figure 1 shows a schematic view of the generation of the three models.

The RapidPlan models included the following OARs: bladder, small bowel, anal canal, penile bulb, femoral heads and rectum. Four additional structures were included in the model to help with plan optimisation:

- Bladder-PTV and rectum-PTV: bladder or rectum structure without the area overlapping the PTV;
- Control5mm: a 5-mm expansion of the PTV. This structure was used to avoid dose hotspots around the PTV;
- Ring_EXT: a ring around the PTV, at 5 mm distance. The thickness was 50 mm in the anterior–posterior direction, 40 mm in the cranio-caudal direction and 30 mm in the lateral direction. This structure was used together with the manual NTO (Normal Tissue Objective) tool to control the dose fall-off.

At the end of the training phase, the model goodness was evaluated using both the statistical summary generated by the RapidPlan engine and the Varian Model Analytics tool, the cloud service solution provided by Varian to analyse the RapidPlan models. The dose distribution and the anatomic features of the plans reported as outliers were visually inspected: geometrical outliers (OAR structures that showed a marked difference in the shape compared to the average of the population) were excluded from the training set; dosimetric outliers were re-planned. The outliers identification takes place only in the training phase of model building.

An open-loop and closed-loop approach was used to fine-tune the optimisation objectives and priorities.[16] It consisted in a trial-and-error process where the RapidPlan models were used to generate automatic plans using different values of optimisation objectives and priorities, until the generated plans of both the training set and the validation set reached the following criteria:

- PTV coverage V95% > 95%;
- 90% to 70% isodose lines conformed to the PTV;
- Rectum-PTV mean dose around 20 Gy;
- Bladder-PTV mean dose below 25 Gy.

The optimisation objectives used in each model are summarised in Table 1. *Model6X* and *Model6Xrefined* share the same priorities and objectives. An additional upper objective was needed in the *Model10X* for the rectum, bladder and femoral heads structures to increase conformity of the medium–low dose isolines.

Comparison of the model performance

The comparison of the model performance was carried out on the remaining 25 patients not included in the training set. The

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Table 1. Optimisation objectives and priorities of the three models. RP gen means that the objective and/or the priority is automatically generated by RapidPlan. gEUD a is the parameter for the generalised equivalent uniform dose function.

		Model6X/Model6Xrefined				Model10X			
		Vol [%]	Dose	Priority	gEUD a	Vol [%]	Dose	Priority	gEUD a
PTV									
	Upper	0	100%	160 (180)*		0	100%	160	
	Lower	100	100%	160 (180)*		100%	100%	160	
	Lower	100	98%	160 (180)*		100%	98%	160	
	target gEUD		100%	RP gen	−1		100%	RP gen	−1
Anal canal									
	Line	RP gen	RP gen	RP gen		RP gen	RP gen	RP gen	
Bladder									
	Upper	–	–	–		20	40%	80	
	Upper	2	RP gen	80		1	RP gen	80	
	Line	RP gen	RP gen	RP gen		RP gen	RP gen	RP gen	
Bladder-PTV									
	mean		RP gen	80			17 Gy	80	
	Upper gEUD		21 Gy	RP gen	3		21 Gy	RP gen	3
	Line	RP gen	RP gen	RP gen		RP gen	RP gen	RP gen	
Bowel									
	Line	RP gen	RP gen	RP gen		RP gen	RP gen	RP gen	
Femoral heads									
	Upper	–	–	–		12	30%	80	
	Upper	0	30 Gy	RP gen		0	30 Gy	RP gen	
	Line	RP gen	RP gen	RP gen		RP gen	RP gen	RP gen	
Ring_EXT									
	Upper	0	95%	RP gen		0	95%	RP gen	
	Upper	RP gen	25 Gy	90		RP gen	25 Gy	90	
	Mean		RP gen	RP gen			RP gen	RP gen	
	Upper gEUD		60%	RP gen	8		60%	RP gen	8
	Upper gEUD		75%	110	30		75%	110	30
	Line	RP gen	RP gen	RP gen		RP gen	RP gen	RP gen	
Control5mm									
	Upper	0	102.50%	110		0	102.50%	110	
	Upper gEUD		98%	RP gen	30		97%	110	30
Penile bulb									
	Line	RP gen	RP gen	15		RP gen	RP gen	15	
Rectum									
	Upper	–	–	–		20	40%	80	
	Upper	2	RP gen	80		1	RP gen	80	
	Line	RP gen	RP gen	80		RP gen	RP gen	80	
Rectum-PTV									
	Mean		19 Gy	80			17 Gy	80	
	Upper gEUD		20 Gy	RP gen	3		20 Gy	RP gen	3
	Line	RP gen	RP gen	RP gen		RP gen	RP gen	RP gen	

(*Continued*)

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Table 1. (*Continued*)

		Model6X/Model6Xrefined	Model10X
NTO		Manual	Manual
	Priority	110	110
	Distance Target Border	0.5 cm	0.5 cm
	Start Dose	100%	100%
	End Dose	50%	50%
	Fall-off	0.5	0.5

*For the *Model6Xrefined* only.

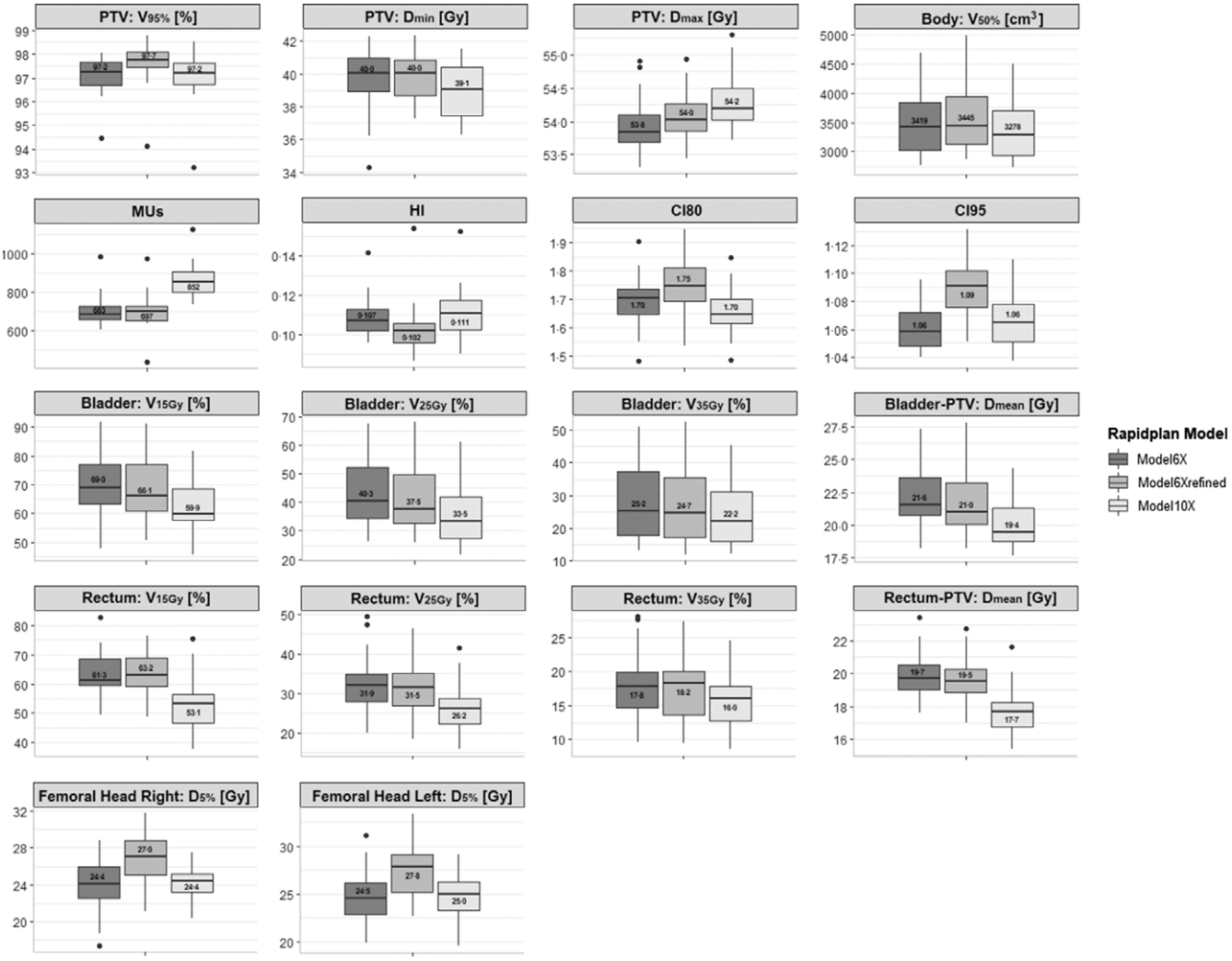

Figure 2. Boxplots of the DVH metrics of the test plans calculated with the three models. Median values are reported in the graphs.

treatment plans were automatically generated by the three models using the 10-MV photon beam and without any interaction during optimisation.

The following DVH metrics were compared:

- PTV coverage ($V_{95\%}$);
- Maximum dose to the PTV calculated as dose at 0.03 cc (D_{max});
- Minimum dose to the PTV (D_{min});
- Bladder and rectum V_{15Gy}, V_{25Gy} and V_{35Gy};
- Mean dose to rectum-PTV and bladder-PTV (D_{mean});
- Dose to 5% of the volume of femoral head right and femoral head left ($D_{5\%}$);
- Body $V_{50\%}$;
- Conformity index calculated at 80% and 95% isodose (CIx), as the ratio between the body volume receiving x% of the prescription dose ($V_{x\%}$) and the PTV volume (V_{PTV}):

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Table 2. Median values of the dose differences between the plans obtained with the Model6Xrefined or Model10X and the plans obtained with the Model6X

		Model6Xrefined – Model6X Median (1st quartile and 3rd quartile)	Model10X – Model6X Median (1st quartile and 3rd quartile)
MUs		15 (−14, 34)	166 (129, 204)**
Bladder			
	V_{15Gy} [%]	−1.3 (−3.5, 1.1)	−8.0 (−9.2, −6.1)**
	V_{25Gy} [%]	−1.5 (−2.0, −0.2)	−6.3 (−7.8, −5.1)**
	V_{35Gy} [%]	−0.5 (−1.1, −0.2)*	−2.8 (−5.0, −2.0)**
Rectum			
	V_{15Gy} [%]	−0.4 (−2.9, 1.3)	−10.4 (−13.1, −7.7)**
	V_{25Gy} [%]	−1.3 (−1.7, 0)	−5.8 (−7.2, −4.8)**
	V_{35Gy} [%]	−0.2 (−0.7, 0)	−2.2 (−2.5, −1.8)**
Bladder-PTV			
	D_{mean} [Gy]	−0.2 (−0.6, 0)	−2.2 (−2.6, −1.8)**
Rectum-PTV			
	D_{mean} [Gy]	−0.3 (−0.5, 0)	−2.1 (−2.5, −1.9)**
Femoral head right			
	$D_{5\%}$ [Gy]	3 (1.9, 3.9)**	0 (−1.0, 1.5)
Femoral head left			
	$D_{5\%}$ [Gy]	2.9 (2.3, 4.0)**	0.6 (−0.5, 1.0)
Body			
	$V_{50\%}$ [cc]	115 (49, 192)**	−103 (−171, −41)**
PTV			
	$V_{95\%}$ [%]	0.6 (0.3, 0.9)**	−0.1 (−0.4, 0.2)
	D_{min} [Gy]	−0.1 (−0.4, 0.3)	−1.0 (−1.8, −0.2)**
	D_{max}[Gy]	0.1 (0, 0.3)	0.3 (0.1, 0.5)**
CI80		0.05 (0.04, 0.06)**	−0.03 (−0.04, −0.02)**
CI95		0.03 (0.02, 0.03)**	0.003 (−0.002, 0.008)
HI		−0.007 (−0.010, −0.003)*	0.002 (−0.001, 0.008)

In brackets, the interquartile range is reported. The * symbol indicates the p-value of the Nemenyi post hoc test: *p-value < 0.05; **p-value < 0.01.

$$CI = \frac{V_{x\%}}{V_{PTV}}$$

- Total number of monitor units (MUs);
- Homogeneity index (HI) calculated using the following formula:

$$HI = \frac{D_{1\%} - D_{99\%}}{D_{50\%}}$$

where $D_{x\%}$ is the dose at x% of the PTV volume.

All the DVH metrics were compared with the Friedman test. The Nemenyi post hoc test was carried out to compare the difference between pairs of models. The level of significance was set to 0.05. The analyses were carried out using the R *stats* package.

Results

All the plans created by each model were clinically acceptable. The clinical acceptability was based on dose constraints guidelines that we internally developed together with the radiation oncologists following the literature data. More than 95% of the PTV volume received at least 95% of the prescription dose, as per protocol requirement. The 90%, 80% and 70% isodose lines were conformed to the PTV.

Figure 2 shows the boxplots of the DVH metrics of the test plans calculated with the three models. Median values are reported in the graphs.

Table 2 shows the median values (with the interquartile ranges) of the paired differences between the DVH metric values obtained with the *Model6Xrefined* or *Model10X* and the DVH metric values obtained with the *Model6X*. *Model6X was* chosen as reference because it is the model currently used in our department.

The *p*-value of the Friedman test was below 0.01 for all the dosimetric features. The Nemenyi post hoc test showed that the plans generated by *Model10X* were statistically different from the plans generated by *Model6X* and *Model6Xrefined*: *Model10X* generated plans with less dose to OARs and body without compromising the PTV coverage. The bladder V15Gy and the rectum V15Gy were 8% and 10% lower, respectively. The mean dose of bladder-PTV and

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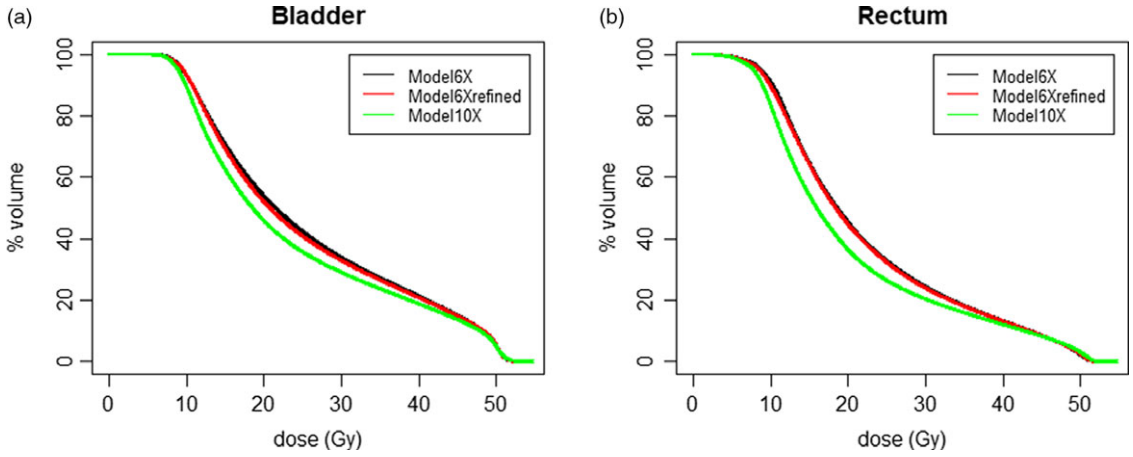

Figure 3. Average DVH plots of the bladder and rectum structures.

rectum-PTV was 2 Gy lower. However, the number of MUs was 20% higher on average. The *Model6Xrefined* also showed a lower HI, but, at the same time, this resulted in obtaining a larger CI.

The plans generated by the *Model6Xrefined* were not different from the plans obtained by the *Model6X* in terms of dose distribution. Although some DVH metrics resulted statistically significant different, the differences were not considered clinically relevant. Figure 3 shows the average DVH plots of the bladder and rectum structures.

Discussion

This study evaluates the performance of three RapidPlan models for prostate radiotherapy treatment planning with 10-MV photon beams.

A RapidPlan model for prostate radiotherapy treatment planning with the 6-MV photon beam was previously trained and validated, and it is already clinically used in our department. Using this RapidPlan model (*Model6X*) with a 10-MV photon beam created clinically acceptable plans, confirming the results of previous studies that showed how RapidPlan models trained on plans with a specific beam configuration and treatment technique can be applied to different treatment arrangements.[2,17,18]

Using the *Model6X* to automatically generate treatment plans with the 10-MV photon beam for training a new model (*Model6Xrefined*) did not improve the performance.

This finding could be explained as follows: the training plans for the *Model6Xrefined* were calculated using the *Model6X* with the 10-MV photon beam; this also is how the 25 test plans relative to *Model6X* were calculated for the comparison. Assuming that the patient population is well represented by the 50 patients used for model training, the dosimetric properties of the 25 test plans calculated by the *Model6X* are not different from the dosimetric properties of the 50 training plans for the *Model6Xrefined*. Since the outcome of a knowledge-based model reflects the properties of the training inputs, as demonstrated by Fogliata et al.[1] for the RapidPlan system, the equivalence in the performance of *Model6X* and *Model6Xrefined* could be justified.

Our results show that OAR sparing was better achieved by the RapidPlan model trained on manually optimised plans with 10-MV photon beams (*Model10X*). Manually optimised plans highlighted the need for the additional optimisation objective $V_{40\%} < 20\%$ on both the bladder and rectum structures for optimal dose distribution. Lower values of bladder and rectum V15 and lower mean dose to the bladder-PTV and rectum-PTV structures could be due to this additional optimisation objective. This finding emphasises the benefit of using manually created training plans in order to fully exploit the ability of normal tissue sparing of the 10-MV photon beam. However, the higher normal tissue sparing comes at the cost of a higher number of MUs, which means longer treatment times. Furthermore, photon beam energies higher than 8 MV produce neutrons which lead to an increase of the equivalent dose[19,20] that is not taken into account by the TPS. A recent study showed that the dose due to neutron contamination when using 15-MV photon beams is comparable to that due to the imaging during image-guided radiotherapy.[21] In our work, we used the 10-MV photon beam. The cross section for neutron production in high atomic number materials is lower for 10-MV photons compared to 15-MV photons;[22] therefore, the dose contribution due to neutron contamination is lower than the dose measured by the authors Hälg et al.[21]

Conclusion

This work shows that all the RapidPlan models generate clinically acceptable plans for prostate cancer treatments with the 10-MV photon beam. We found that higher normal tissue sparing is obtained when the RapidPlan model is trained with manually optimised plans (*Model10X*) compared to outcomes generated by the RapidPlan model (*Model6Xrefined)* trained on 10-MV photon beam plans that in turn were generated by a RapidPlan model based on the 6-MV photon beam (*Model6X)*. However, this procedure of model building is more time-consuming, and it produces plans with a higher number of MU. Therefore, a cost–benefit balance should be performed within each institute.

Acknowledgements. None.

Financial Support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflict of Interest. The authors declare none.

Ethics Standards. The Canton Ticino Ethics Committee waived the need for ethics approval and the need to obtain consent for publication of the results of this work.

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