

RESEARCH ARTICLE

Impact of nominal photon energies on normal tissue sparing in knowledge-based radiotherapy treatment planning for rectal cancer patients

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Abstract

The interactive adjustment of the optimization objectives during the treatment planning process has made it difficult to evaluate the impact of beam quality exclusively in radiotherapy. Without consensus in the published results, the arbitrary selection of photon energies increased the probability of suboptimal plans. This work aims to evaluate the dosimetric impact of various photon energies on the sparing of normal tissues by applying a preconfigured knowledge-based planning (RapidPlan) model to various clinically available photon energies for rectal cancer patients, based on model-generated optimization objectives, which provide a comparison basis with less human interference. A RapidPlan model based on 81 historical VMAT plans for pre-surgical rectal cancer patients using 10MV flattened beam (10X) was used to generate patient-specific objectives for the automated optimization of other 20 patients using 6X, 8X, 10X (reference), 6MV flattening-filter-free (6F) and 10F beams respectively on a TrueBeam accelerator. It was observed that flattened beams produced very comparable target dose coverage yet the conformity index using 6F and 10F were clinically unacceptable (>1.29). Therefore, dose to organs-at-risk (OARs) and normal tissues were only evaluated for flattened beams. RapidPlan-generated objectives for 6X and 8X beams can achieve comparable target dose coverage as that of 10X, yet the dose to normal tissues increased monotonically with decreased energies. Differences were statistically significant except femoral heads. From the radiological perspective of view, higher beam energy is still preferable for deep seated tumors, even if multiple field entries such as VMAT technique can accumulate enough dose to the target using lower energies, as reported in the literature. In conclusion, RapidPlan model configured for flattened beams cannot optimize un-flattened beams before adjusting the target objectives, yet works for flattened beams of other energies. For the investigated 10X, 8X and 6X photons, higher energies provide better normal tissue sparing.

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Introduction

The inherent photon beam characteristics of different energies, such as penetrating power and penumbra, have provided planners with more options[1], but the choices also vary subjectively among different centers. There have been a lot of dosimetric researches on the beam energies [2,3,4,5], but consensus can hardly be made providing contradictory literature reports. Coming to the era of knowledge-based planning, the impact of beam energies on the model configuration and applications remains unknown, and is worthy of more investigations.

Varian RapidPlan (Varian Medical Systems, Palo Alto, CA) uses Principal Component Analysis (PCA) regression to fit the correlation between the geometric features (including patient anatomy and beam geometry) and the historical 'achievable' dose distribution without using the actual beam energy as regression input at the training stage. When the trained model is used to predict DVHs for upcoming cases, Geometry-Based Expected Dose (GED) metric was used to estimate the achievable dose to a voxel by considering patient anatomy (such as distance from the targets surfaces), dose prescriptions, and field geometry (such as in- vs. out-of-field) [6,7] and beam energy, etc. According to the manufacturer[8], the total dose-distance value in voxel v (ged_v) is defined as:

$$ged_v = \sum_{t=1}^m \delta_t \times \sum_{f=1}^n C_{tv} \times \frac{e^{-\lambda_f \times d_{fv}}}{d_{fv}^2} \tag{1}$$

Where m is number of target levels, δ_t is incremental target level, n is number of fields, C_{TV} is a scaling factor of modulation, d_{fv} is Euclidean distance from field f to voxel v , and λ_f is a parameter depending on the nominal photon beam energy of field f . A sum of the voxels yields a predicted dose volume histogram (DVH) range that can be used to generate patient specific optimization objectives. RapidPlan generated different objectives for the same patient in an automatic and mathematical manner if various beam energies were selected as input to the model prediction.

Previous studies on the dosimetric effects of photon energies were vulnerable to potential bias of different optimization objectives[9], or limitations of planner experience [5, 10]. By introducing λ_f , RapidPlan generates various energy-dependent and patient specific objectives without subjective manual iterative adjustment and inter-planner variability, hence provides a more objective comparison basis.

This study aims to evaluate the dosimetric impact of beam qualities on the sparing of normal tissues by applying a preconfigured RapidPlan model to various clinically available photon energies for rectal cancer patients.

Methods

This retrospective, anonymous and computation-based study is approved by Medical Ethics Committee of Peking University Cancer Hospital & Institute with exemption of informed consent. All experiments were conducted on Varian RapidPlan knowledge-based treatment planning system V. 13.5 with appropriate anonymization.

The RapidPlan DVH estimation model

A published RapidPlan model for pre-surgical rectal cancer patients was used in this study [11,12,13]. As a brief review, the model was trained with 81 historical plans that were contoured and planned following Li's study [14]. Dose-volume constraints for normal tissues were in accordance with RTOG 0822 protocols [15]. Attempts were also made to reduce the organ mean dose to minimize long-term toxicity associated with low-dose region [16,17,18].

Considering the large target volumes were relatively deep-seated, all historical plans were optimized with 10 MV flattened photon beams (10X) by experts. The robustness of the model has been validated on over 100 cases [11–13].

Knowledge-based planning using various energies

On the Eclipse treatment planning system V13.5, the aforementioned RapidPlan model was applied to estimate the best achievable DVHs under five photon beam qualities from a Varian TrueBeam accelerator equipped with Millennium 120 multi-leaf collimator (MLC), including 6-MV flattened (6X), 6-MV flattening-filter-free mode (6F), 8X, 10X and 10F respectively, for 20 historical patients that were not included in the model library. Higher energies are not used at our center for the consideration of secondary neutron contamination [19], hence were not tested in this study. Without any human intervention, VMAT plans were optimized using the RapidPlan-generated patient-specific objectives [20], keeping the original beam geometries of the clinical plans unchanged. The prescription dose was 41.8Gy for PTV and 50.6Gy for PTV_{boost}. The volume dose was calculated using analytical anisotropic algorithm (AAA). All plans were normalized to cover 95% target volume with 100% prescription dose before comparison.

Dosimetric assessment and statistical analysis

Consistent with our clinical choice and characteristics of model library, RapidPlan results of 10X photon were used as references, against which the performances of other beam energies were evaluated. Target homogeneity index (HI) was calculated as $(D_{2\%} - D_{98\%})/D_{50\%}$, and conformity index (CI) was defined according to Paddick, et al [21]. $D_{x\%}$ indicates the minimum dose received by x% of the volume. In addition to conventional OARs such as urinary bladder, femoral heads and small bowel, the normal tissue integral dose (NTID) was calculated for the in-field body volume excluding PTV, and the in-field skin dose was calculated in the volume 5 mm under the body surface in accordance with previous dosimetric studies on photon energies [4,10]. Normality test was first performed to the results of each group, followed by two-way ANOVA (repeated measures on the same individual without replication in each subgroup) and multiple paired T test (with significant level adjusted to 0.016) for further comparison if AVOVA tests reported $P < 0.05$ (statistically significant, right-tailed).

Results

Patient characteristics

Table 1 summarizes the tumor characteristics of 81 training cases (53 males) and 20 validation cases (14 males). The ranges and medium age of the training set were 39~89 and 62 year, and were 34~75 and 60 year for the validation set respectively. The concurrent chemotherapy regimen was capecitabine 825mg/m² twice daily, 5d/w.

Target dose coverage using various photon energies

Fig 1 plots the target DVHs of 20 patients, as optimized automatically using various photon energies. Subfigures (a-d) present the target DVHs of 6X, 6F, 8X and 10 F (dotted lines) relative to the reference 10X results (solid lines) respectively. The figure-in-figure shows the corresponding mean target DVHs of 20 patients, as optimized using the same beam energy. The target DVHs of 10X, 8X and 6X largely overlapped with each other, providing comparable basis for OAR dose evaluation. Echoing numerically, the mean CI values for 6X, 8X and 10X were 1.05, 1.05, 1.04 for planning target volume (PTV), and 1.14, 1.12, 1.10 for PTV_{boost}.

Table 1. Tumor volumes [cm³] of 81 training cases and 20 validation cases.

	PTV _{boost}		PTV	
	Training	Validation	Training	Validation
Mean	179.54	170.70	1207.99	1151.71
Standard deviation	92.00	96.85	165.91	187.73
Minimum	53.31	60.5	844.12	802.40
Maximum	618.09	478.2	1675.05	1562.00

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respectively. The corresponding mean HI values for all flattened beams were 0.27 (PTV) and 0.05 (PTV_{boost}) respectively. However, the dosimetric features such as dose falloff and hot spots were severely worsened using 6F and 10 F beams, making those plans clinically unacceptable which were thus excluded from further OAR dose comparison. Specifically, the mean CI values for 6F and 10F were 1.10, 1.10 (PTV), and 1.29, 1.34 (PTV_{boost}) respectively. The corresponding mean HI values for 6F and 10F were 0.29, 0.30 (PTV) and 0.07, 0.08 (PTV_{boost}) respectively.

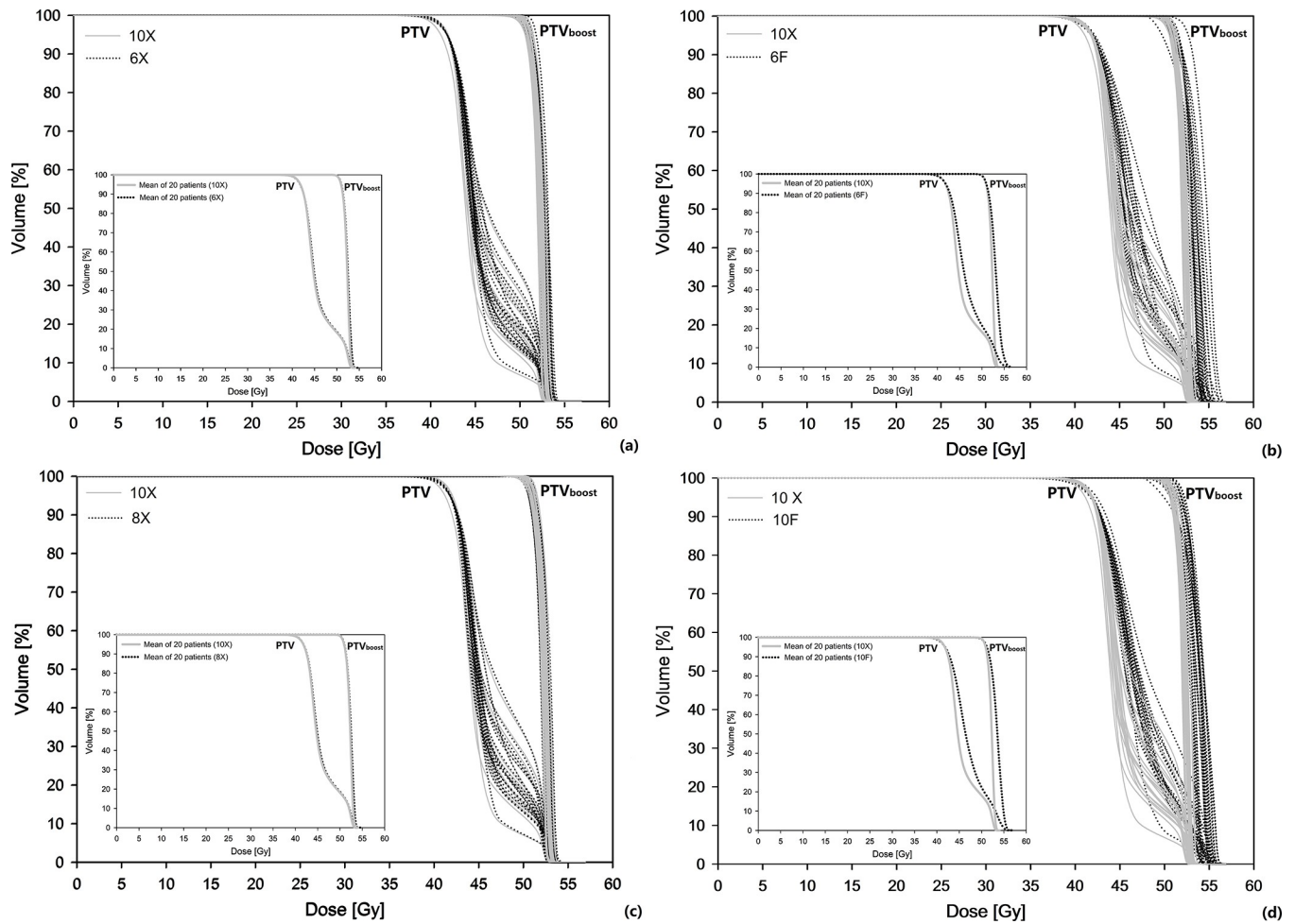


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Impact of photon energies on normal tissue sparing

The dosimetric statistics of OARs comparing the performance of 6X and 8X using 10X results as reference were listed in Table 2.

Fig 2 displays the DVH differences of the OARs as optimized using various beam energies relative to 10X photons. The differences were calculated by subtracting the DVHs of evaluated energy from the DVHs of 10X, hence curves above zero horizontal levels indicate worsened OAR sparing than those using 10X beams. The dashed lines plot the data of 20 patients, and the solid lines are their average. The left and right column shows the results of 6X-10X and 8X-10X respectively. Subfigures (a-b), (c-d), (e-f), (g-h) and (i-j) plot the results for the urinary bladder, femoral heads, NTID, skin and small bowel respectively.

Discussion

According to the manufacturer, RapidPlan does not estimate DVHs for the targets, which is determined by the fixed objectives as imbedded in the model template. It seems that these parameters can be shared by flattened beams of various energies, yielding comparable target dose coverage as suggested by the largely overlapping DVHs in Fig 1. These observations agreed with the reports that satisfactory deep-seated target coverage can be achieved by using lower photon energies if more fields were used [5]. Dramatically differed in beam characteristics, these settings did not work well for un-flattened beams of either 6F or 10F. The insufficient dose coverage induced unacceptable hot spot after renormalization (severely worsened

Table 2. Dosimetric statistics of OARs comparing the results of 6X and 8X against 10X.

		6X	10X	8X
Urinary bladder				
	V _{40Gy}	14.19	13.37	13.98
	V _{45Gy}	3.23	3.24	3.10
	D _{mean}	24.30	22.86	23.68
	P	<0.01		<0.01
Femoral heads				
	V _{40Gy}	0	0.01	0
	V _{45Gy}	0	0	0
	D _{mean}	13.58	13.00	13.40
	P	0.32	0.50	
NTID				
	D _{mean}	17.92	17.27	17.41
	P	<0.01	0.02	
Skin				
	D _{mean}	10.80	9.66	9.99
	P	<0.01	<0.01	
Small bowel				
	V _{35Gy}	7.10	5.52	6.61
	V _{40Gy}	1.09	0.67	1.01
	V _{45Gy}	0	0	0
	D _{mean}	22.78	21.42	22.28
	P	<0.01	<0.01	

P values were calculated for the mean dose. The units for the volume and dose are % and Gy respectively.

Abbreviations: V_{xGy} = volume receiving at least x Gy dose; D_{mean} = mean dose; NTID = normal tissue integral dose.

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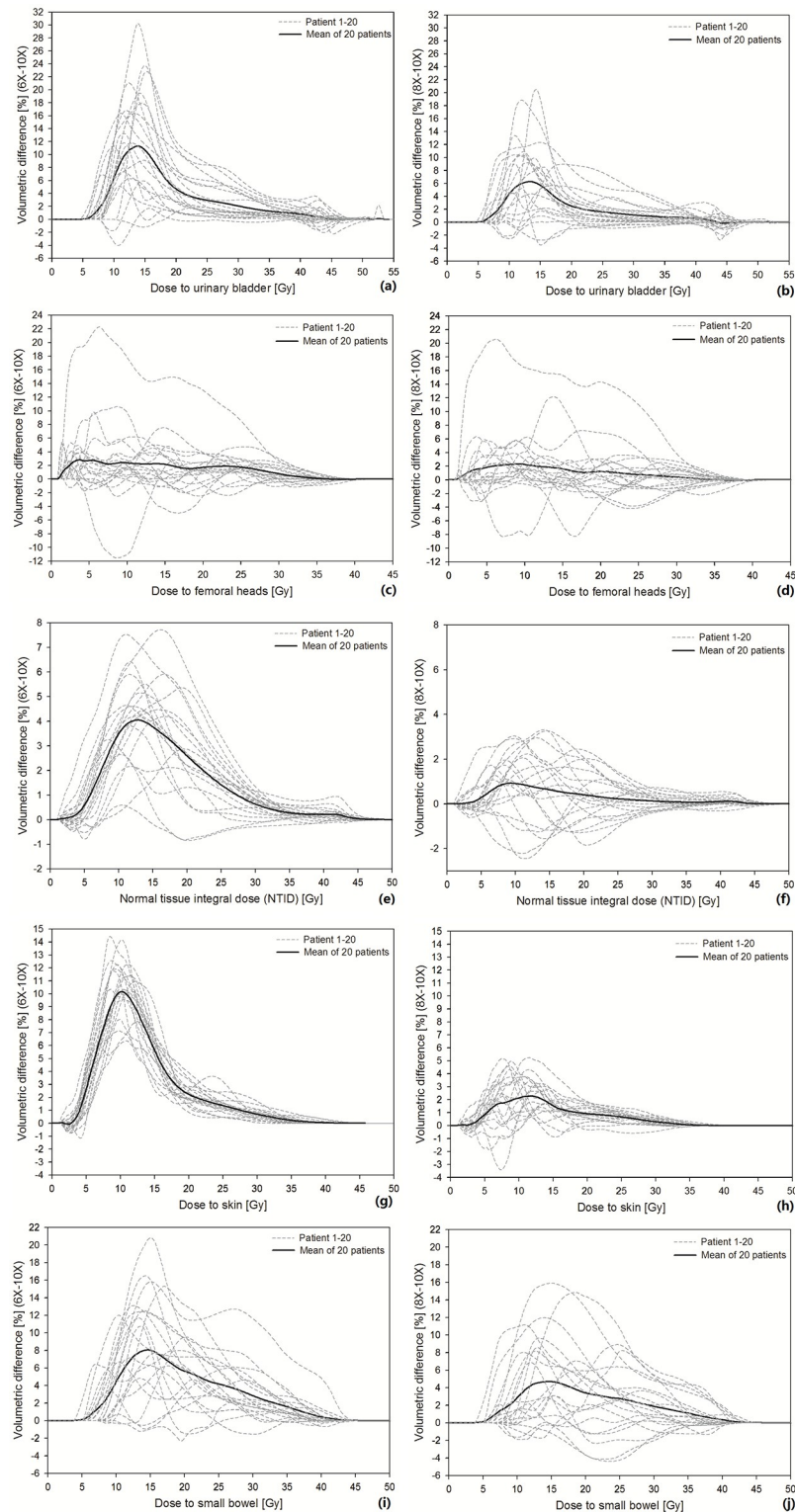


Fig 2. The DVH differences of the OARs as optimized using various beam energies relative to 10X photons. The dashed lines plot the data of 20 patients, and the solid lines are their average. The left and right column shows the results of 6X-10X and 8X-10X respectively. Subfigures (a-b), (c-d), (e-f), (g-h) and (i-j) plot the results for the urinary bladder, femoral heads, NTID, skin and small bowel respectively.

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CI for PTV_{boost}), suggesting that new optimization objectives for target dose should be configured before the RapidPlan model can be possibly used to optimize the modulation of un-flattened beams.

Although tremendous inter-patient varieties were observed for all OARs and beam energies in Fig 2, a majority of individual OAR curves and all the mean curves were overwhelmingly above zero, suggesting inferior OAR sparing using 6X and 8X than 10X. Excessive exposure was dominantly distributed in low dose regions (<20 Gy). The amplitudes of 8X curves were consistently lower than those of 6X, as echoed by the significantly higher dose to most OARs using lower beam energies in Table 2 (except for femoral heads, probably due to limited sample size), suggesting lower OAR exposures are associated with higher beam energies, at least for pelvic planning using a RapidPlan model configured with historical plans that were optimized using 10X photons. Individual lines of 8X showed more negative values and larger fluctuations than those of 6X, suggesting other factors started to play relatively more important roles in determining the OAR dose, when the energy difference reduces. These differences might be jointly contributed by multiple resources, such as beam energy (λ_p) in the modeling of ged_v , inherent photon behaviors, patient and beam geometries, etc., which can be hardly differentiated from each other. Due to relatively low values, the disparities of high dose volumes in Table 2 did not vary too much.

It should be noted that the skin and NTID are not typical OARs for rectal planning, hence were not configured in the RapidPlan model. They were analyzed in this work as indicators of superficial dose and normal tissue sparing in accordance with previous studies on beam energies [4,10]. Classical radiotherapy principle recommended higher beam energy for deep seated large tumors [1], but lower energy can reduce exit dose [22] and Pirzkall et al reported negligible difference among different energies when more than 9 IMRT fields were used [5]. In the context of knowledge-based planning, our results suggested that higher beam energies were still advantageous in normal tissue sparing for deep seated tumors of large volumes, even if many beam entries were used such as VMAT technique. Without potential bias from manual adjustments, the RapidPlan-generated optimization objectives assessed the beam quality collectively with other influential parameters such as patient anatomy and beam geometry in Eq (1), hence the dosimetric comparison between various beam energies were more objective.

Conclusion

In conclusion, a RapidPlan model configured with flattened high energy beams does not satisfy target dose coverage using un-flattened photons, and may increase normal tissue exposure if applied to optimize lower energy beams.

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Methodology: Yibao Zhang.

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Resources: Hao Wu.

Validation: Tian Li.

Visualization: Haiyang Wang.

Writing – original draft: Yibao Zhang.

Writing – review & editing: Tian Li, Yibao Zhang.

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