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Dosimetric and Radiobiological Evaluation of Dose Volume Optimizer (DVO) and Progressive Resolution Optimizer (PRO) Algorithm against Photon Optimizer on IMRT and VMAT Plan for Prostate Cancer

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This study aimed to compare the performance of previous optimization algorithms against new a photon optimizer (PO) algorithm for intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) plans for prostate cancer. Eighteen patients with prostate cancer were retrospectively selected and planned to receive 78 Gy in 39 fractions of the planning target volume (PTV). All plans for each patient optimized with the dose volume optimizer (DVO) and progressive resolution optimizer (PRO) algorithms for IMRT and VMAT were compared against plans optimized with the PO within Eclipse version 13.7. No interactive action was performed during optimization. Dosimetric and radiobiological indices for the PTV and organs at risk were analyzed. The monitor units (MU) per plan were recorded. Based on the plan quality for the target coverage, prostate IMRT and VMAT plans using the PO showed an improvement over DVO and PRO. In addition, the PO generally showed improvement in the tumor control probability for the PTV and normal tissue control probability for the rectum. From a technical perspective, the PO generated IMRT treatment plans with fewer MUs than DVO, whereas it produced slightly more MUs in the VMAT plan, compared with PRO. The PO showed over potentiality of DVO and PRO whenever available, although it led to more MUs in VMAT than PRO. Therefore, the PO has become the preferred choice for planning prostate IMRT and VMAT at our institution.

Keywords: Optimization algorithm, Photon optimizer, IMRT, VMAT

Introduction

The planning process for intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) is based on an optimization algorithm to attain the desired dose distribution. These optimization algorithms are used to determine the combination of field shapes and segment weights which achieve the desired planning. Many optimization algorithms, such as, dose volume optimizer (DVO) and progressive resolution optimizer (PRO) have been developed for IMRT and VMAT planning optimization.[1-4]

Recently, the new photon optimizer (PO) algorithm has been introduced to add the usage of possibly advanced personalized optimization objectives as generated by the dose-volume histogram (DVH) estimation models. It is

a new dose calculation optimizer currently supported in VMAT optimization as well as static field IMRT optimization for the Eclipse treatment planning system (V 13.5 or later, Varian Medical Systems, Palo Alto, CA, USA).[5]

In the previous version, the Eclipse treatment planning system used separate optimizers, with DVO for IMRT and PRO for VMAT optimization. As it is known, DVO optimizes the field shape and intensity using a simple gradient optimization to approach the desired dose-volume objectives.[6] The fluences are back-projected from the derivatives of the costs at each cloud point representing the patient volume. PRO, described by Cozzi et al., is based on the assumption that a complex problem like optimization of continuous variables, such as, multileaf collimator (MLC) shape, leaf positions and segment weights based on control point segmentations of the entire arc angle and could be solved in discrete steps of progressively increasing resolution without compromising on the quality of results.[7] As the optimization progresses, the accuracy of angle resolution and dose calculation segments increase. PRO was feasible as a VMAT optimization engine, which was clinically usable and converged to a desired dose distribution. Two generations of the PRO algorithm were investigated: the first generation PRO2 and the second generation PRO3. In PRO2 reported by Otto, an arc is modeled by a sequence of control points (CPs), defined on an aperture basis, equally spaced every roughly 2 at the end of the optimization cycle.[8] In PRO3, the full collection of 178 CPs is optimized in all phases of the algorithm, while the dose calculation is still progressive and calculated in sectors, from a coarse (about 18°) to a fine resolution (about 2°) in terms of the angles between adjacent calculations according to the four phases.[9] One of the major differences is that PRO2 was fully based on direct aperture optimization (DAO), whereas PRO3 calculates an intermediate fluence. Additionally, PRO3 offers the option of a so-called intermediate dose calculation, which takes the results of the dose calculation of a previous run into account.[10] The new PO provides a new volume representation replacing the old point cloud model of PRO and DVO. It also provides an approximation of the dose distribution shown in the 2D view during optimization.

In order to evaluate the different optimization engines based on the same optimization objectives that can produce clinically acceptable dose plans without interactive human interference, the capability of the PO was compared with those of IMRT and VMAT planning using DVO and PRO, respectively. In a previous study, Vanetti et al. assessed the performance of two versions of PRO (PRO2 and PRO3) for VMAT planning.[9] They reported that PRO3 is either clinically beneficial or neutral in terms of dosimetric quality while it showed significant advantage for acquiring a desired dose distribution in a sufficiently short time. Shende et al. also performed a study to compare PO relative to prior optimizers for both IMRT and VMAT using a virtual phantom.[6] They stated that PO generates plans with better quality compared to DVO and PRO. So far, no study has been conducted to confirm whether PO was attributable to better planning quality in clinical case. Therefore, the aim of the present study is to compare a new PO algorithm (Version 13.7.16), which has been released for clinical usage, with previously used DVO and PRO (Version 13.7.16) for IMRT and VMAT optimization of prostate cancer.

Materials and Methods

1. IMRT and VMAT prostate planning using DVO, PRO, and PO algorithms

For this retrospective study, we chose 18 patients diagnosed with prostate cancer that had previously been treated in our department from March 2017 to July 2018. All prostate cancer patients were enrolled in IMRT and VMAT planning study, which was approved by the institutional review board of Seoul National University Bundang Hospital (IRB No. B-1810/501-108). Prior to the planning computed tomography (CT) simulation, all patients were asked to drink 300 ml of water before 1 hour of simulation to ensure that the bladder was completely filled. An endorectal balloon (ERB) was inserted into the rectum and inflated with approximately 70 cm3 with air. After 1 minute, the ERB was pulled toward the patient's anal sphincter to the pre-marketed position on the ERB catheter.[11] CT scan was obtained with a Philips Big Bore CT scanner (Philips Medical Systems, Amsterdam, Netherlands). The gross target volume (GTV) on the planning CT was delineated as

the prostate volume determined using magnetic resonance image. The clinical target volume (CTV) also included gross tumor and subclinical microscopic disease. The planning target volume (PTV) was created by expanding 5 mm posteriorly and 7 mm elsewhere to the CTV. The rectum, bladder, left and right femoral heads were delineated as the organs at risk (OARs). Varian couch is modeled in our treatment planning system (TPS) and was inserted in each treatment plan (used for dose calculation). The prostate treatment plans were generated using the Eclipse TPS (version 13.7. 16, Varian Medical System, Palo Alto, CA, USA) to compare PO versus DVO and PO versus PRO for IMRT and VMAT technique, respectively. A total of 72 plans were generated for this study. A target dose of 78 Gy was prescribed to 95% of PTV in 39 fractions. VMAT plans using PO and PRO were created with gantry angle of two full arcs and 30° and 330° of collimation rotations. IMRT plans using PO and DVO were generated with five sliding-window fields of 0°, 72°, 144°, 216°, and 288° gantry angles. All clinical plans were optimized initially with PRO for VMAT and DVO for IMRT. All plans were reoptimized with the new PO algorithm which is based on initial dose-volume constraints. The dose volume constrains used in the study are summarized in Table 1. All VMAT and IMRT plans were delivered with 10-MV photon beams modulated by high definition (HD) 120 MLC from a Varian TrueBeam (Varian Medical Systems, Palo Alto, USA) linear accelerator.

Table 1. Dose volume constraints used in this study for both volumetric modulated arc therapy and intensity modulated radiation therapy.

Structure	Function type	Physical dose (Gy)
Rectum	$V_{30\%}$	<70
	$V_{50\%}$	<54.3
Bladder	$V_{30\%}$	<70
	$V_{50\%}$	<54.3
Femoral heads	$V_{5\%}$	<54.3
GTV	$V_{99\%}$	>78
PTV	$V_{0\%}$	<81.9
	$V_{2\%}$	<81
	$V_{97\%}$	>76.5
	$V_{99\%}$	>74.1
Ring	D_{max}	<60

D_{max}, the maximum dose; $V_{xx\%}$, the volume receiving dose of xx Gy (x% of the prescription dose).

In order to obtain a conformal dose distribution, a ring structure around the PTV was created. The ring is a pseudo planning structure used in dose volume optimization to conformal dose to the target and reduce dose to OARs. All plans were used by Acuros XB algorithm with 2.5 mm dose calculation grid size to perform finial dose calculation. All other parameters, such as energy, dose prescription as well as upper and lower dose objective, were kept as original conditions without interactive manual adjustment during the optimization. Therefore, the observable discrepancies were mostly ascribed to the disparities of different optimizer algorithms.

2. Evaluation of dosimetric and radiobiological indices

For dosimetric and radiobiological comparison of plans using various optimization algorithms, the cumulative DVH was used. PO versus DVO plans and PO versus PRO plans for both IMRT and VMAT technique were evaluated mutually by using dosimetric and radiobiological indices. As dosimetric indices for target coverage, D_{mean} (mean dose), $D_{2\%}$, and $D_{98\%}$ (dose to 2% and 98% volume), and $V_{95\%}$ (percent volume irradiated by 95% of the prescription dose) of PTV were calculated and compared. In order to evaluate the plan quality parameters, homogeneity index (HI), conformity index (CI), and conformation number (CN) of PTV were calculated. The HI (as defined by the International Commission on Radiation Units and Measurements, report 83) is mathematically defined as,[12]

$$HI=\frac{D_{2\%}-D_{95\%}}{D_{50\%}} \quad (1)$$

where $D_{2\%}$, $D_{95\%}$, and $D_{50\%}$ represent the dose to 2%, 95%, and 50% volume for the PTV, respectively. A lower HI value indicates that the plan is more conformal to the prescription dose for target.

According to the Radiation Therapy Oncology Group, the conformity index (CI) is mathematically defined as,

$$CI=\frac{V_{RI}}{TV} \quad (2)$$

where V_{RI} is the treatment volume covered by reference isodose (95% isodose of the prescribed dose), and TV is the PTV volume as the target volume. CI is a measure of conformity of isodose encompassing the target volume. A CI equal to 1 corresponds to an ideal conformation, whereas a CI>1 indicates irradiation of healthy tissues.[13]

CN is mathematically defined as,

$$CN=\frac{TV_{RI}}{TV}\times\frac{TV_{RI}}{V_{RI}} \quad (3)$$

where TV_{RI} represents the target volume covered with reference isodose.

For OARs, D_{mean}, $V_{40\%}$, and $V_{70\%}$ (the volumes receiving 40% and 70% of the prescribed dose) of bladder, D_{mean}, $V_{10\%}$, $V_{40\%}$, $V_{60\%}$, and $V_{70\%}$ of rectum, and D_{mean} and D_{max} (Maximum dose) of left and right femoral heads were evaluated.

In order to evaluation the percentage difference of calculated dosimetric parameters among optimization algorithms, the following equation was used.

$$\text{Percentage difference}=\frac{(\text{Dosimetric parameter}_{DVO,PRO}-\text{Dosimetric paramter}_{PO})}{\text{Dosimetric parameter}_{DVO,PRO}} \quad (4)$$

where, Dosimetic $\text{parameter}_{DVO,PRO}$ represents the calculated dosimetric parameter using DVO and RPO algorithms, and Dosimetic parameter_{PO} refers to the calculated dosimetric parameter using PO algorithm.

To investigate the radiobiological impact for the target volume and various OARs, the tumor control probability (TCP) and normal tissue complication probability (NTCP) were calculated from the DVH of plan using different optimization algorithms for IMRT and VMAT technique. Equivalent uniform dose (EUD) is defined as the dose with uniform distribution over a structure, which would produce the same effect as the dose specified by the DVH. The EUD calculated by Niemierko's phenomenological model is expressed as,

$$EUD=(\sum_{i=1}(v_i D_i^a))^{\frac{1}{a}} \quad (5)$$

This model can be used for both tumor and normal tissues by applying different input parameters. a is a unitless model parameter that is derived specifically from normal tissues or tumor of interest. v_i represents the i^{th} partial volume that received a dose of D_i in Gy. Therefore, the sum of all v_i is equal to 1 in the above EUD formula.[14] D_i^a is the biologically equivalent physical dose of 2 Gy. Differential DVHs were obtained from a given IMRT and VMAT plan to obtain the D_i and v_i for each structure. NTCP and TCP are expressed as,

$$NTCP=\frac{1}{1+\left(\frac{TD_{50}}{EUD}\right)^{\gamma_{50}}} \quad (6)$$

$$TCP=\frac{1}{1+\left(\frac{TCD_{50}}{EUD}\right)^{\gamma_{50}}} \quad (7)$$

TD_{50} is the tolerance dose for a 50% complication probability at a specific time interval. TCD_{50} is the tumor dose to control 50% of the tumor when irradiated homogeneously, and γ_{50} is a unitless parameter derived from the slope of the dose-response curve that is specific to the normal organ or tumor of interest. Table 2 lists the input parameters used to calculate TCP and NTCP. These parameters were referenced from other studies.[14,15]

3. Technical and statistical evaluation

To assess the impact of the optimization algorithms on the technical aspect, total monitor unit (MU) is determined in this study. The analysis is aimed to investigate the planning efficiency of two optimizers.

Based on the SPSS Statistics 19 software (IBM SPSS, Chicago, IL), the statistical significance between DVO and PO,

Table 2. Parameters used to calculate Niemierko's EUD-based TCP and NTCP.

Tissue	Volume Type	a	γ_{50}	TCD50/TD50	α/β
Prostate	Tumor	–13	2.2	67.5	1.5
Rectum	Normal	8.33	2.66	80	5.4
Bladder		2	3.63	80	7.5
Right FH		13	2.7	65	3
Left FH		13	2.7	65	3

FH, femoral head; α/β, Alpha-beta ratio.

as well as PRO and PO were investigated using the Wilcoxon signed rank test in this study. The result was considered statistically significant when $P<0.05$.

Results

1. Dosimetric indices

The dosimetric impact of different optimization algorithms on the dose distribution of IMRT and VMAT plans for patient 1 is shown in Fig. 1a, 1b, which illustrates the comparison of DVH of PTV and OARs for PO versus DVO and PO versus PRO.

Table 3 indicates the comparative dosimetric indices in IMRT plans optimized with DVO and PO, and VMAT plans optimized with PRO and PO. For the PTV, the average percentage difference of D_{mean}, $D_{2\%}$, $D_{95\%}$, and $V_{95\%}$ between DVO and PO optimized plan was –0.49%, 0.39%, –2.62%, and –2.78%, respectively. The average percentage difference of the same parameters between PRO and PO optimized plan was –0.38%, 0.43%, –1.22%, and –1.40%, respectively. For the evaluated indices to assess plan quality, the average percentage difference of HI, CI, and CN was –60%, 22.56%, and –23.29%, respectively, in IMRT plan optimized with the DVO versus PO. In VMAT plan optimized with the PRO versus PO, the corresponding difference was 22.22%, –2.91%, and –1.10%, respectively.

For dosimetric indices of QARs, the average percentage difference of D_{mean}, $V_{40\%}$, and $V_{70\%}$ on bladder for IMRT plans optimized with PO in comparison with DVO was –0.02%, –4.74%, and 10.89%, respectively. The corresponding difference for VMAT plans optimized with PO in comparison with PRO was –5.11%, –4.56%, and –4.32%, respectively. The average percentage difference of D_{mean}, $V_{10\%}$, $V_{40\%}$, $V_{60\%}$, and $V_{70\%}$ on rectum was 9.98%, –1.12%, 4.72%, 33.11%, and 32.40%, respectively, for IMRT plans optimized with PO in comparison with DVO and 5.39%, 1.76%, 8.38%, 8.81% and 11.38%, respectively, for VMAT plans optimized with PO in comparison with PRO. In the left and right femoral heads, the average percentage difference of D_{mean} and D_{max} in plans optimized with PO in comparison with DVO was 6.69% and 1.72% for the left femoral head and 11.00% and –0.32% for the right femoral head, respectively. The average percentage difference in plan optimized with the PRO versus PO was 6.20 % and 3.77% for the left femoral head and 2.57% and 3.23% for the right femoral head, respectively.

2. Radiobiological indices

For radiobiological comparison of plans using the different optimization algorithms for PTV and OARs, the average and standard deviation (SD) of TCP and NTCP calculated on the basis of the planned DVHs are listed in Table 4.

The average TCP value of plans optimized with DVO and PO for IMRT was 84.49% and 86.00%, respectively. The average percentage difference for both optimization algorithms was 1.51%. In addition, the average TCP values of plans optimized with PRO and PO for VMAT were 84.31%

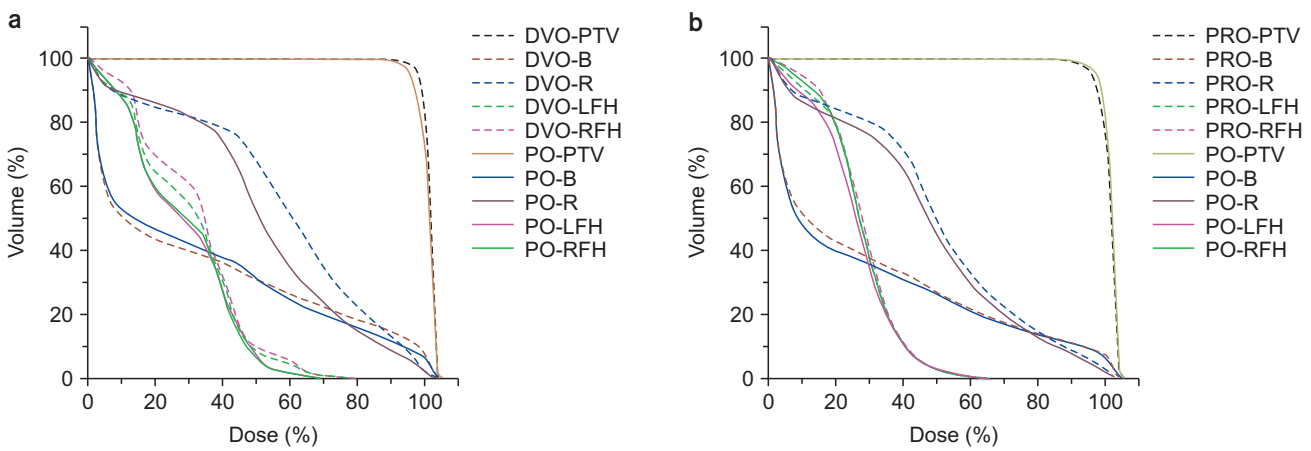

Fig. 1. Comparison of DVH of (a) PO versus DVO for IMRT plan and (b) PO versus PRO for VMAT plan. Solid lines correspond to PO while the dashed lines correspond to DVO and PRO used in the optimization.

Table 3. Comparison of dosimetric index for PTV and OARs in IMRT plans optimized with DVO and PO, and VMAT plans optimized with PRO and PO.

Organ	Dosimetric Index	IMRT		VMAT	
		DVO	PO	PRO	PO
PTV	D_{mean} (%)	100.90	101.39	101.30	101.69
	$D_{2\%}$ (%)	103.91	103.50	104.93	104.48
	$D_{95\%}$ (%)	95.79	98.30	96.16	97.33
	$V_{95\%}$ (%)	95.89	98.56	96.60	97.95
	HI	0.05	0.08	0.09	0.07
	CI	1.33	1.03	1.03	1.06
	CN	0.73	0.90	0.91	0.90
Bladder	D_{mean} (%)	33.18	33.10	28.95	30.43
	$V_{40\%}$ (%)	36.28	38.00	31.13	32.55
	$V_{70\%}$ (%)	22.32	19.89	16.89	17.62
Rectum	D_{mean} (%)	57.50	51.76	50.27	47.56
	$V_{10\%}$ (%)	88.41	89.40	88.15	86.60
	$V_{40\%}$ (%)	78.21	74.52	71.09	65.13
	$V_{60\%}$ (%)	51.82	34.66	32.79	29.90
	$V_{70\%}$ (%)	34.53	23.34	22.40	19.85
Right FH	D_{mean} (%)	31.83	28.33	27.97	27.25
	D_{max} (%)	56.90	57.08	48.68	47.11
Left FH	D_{mean} (%)	30.20	28.18	27.44	25.74
	D_{max} (%)	57.66	56.67	48.26	46.44

D_{mean}, the mean dose; D_{max}, the maximum dose; D_{min}, the minimum dose; $D_{95\%}$, the dose received at least 95% volume; $V_{XX\%}$, the volume received xx% of prescription dose; HI, homogeneity index; CI, conformity index; CN, conformal number.

Table 4. Average and standard deviation of TCP and NTCP from DVHs of 20 patient plans using different optimization algorithms for IMRT and VMAT technique.

Radiobiological Index	Organ	IMRT		VMAT	
		DVO Average (SD)	PO Average (SD)	PRO Average (SD)	PO Average (SD)
TCP (%)	PTV	84.49 (3.53)	86.00 (4.94)	84.31 (2.43)	86.27 (2.11)
NTCP (%)	Bladder	0.064 (0.150)	0.060 (0.184)	0.051 (0.181)	0.053 (0.176)
	Rectum	6.693 (3.297)	4.384 (2.325)	4.586 (2.219)	3.659 (2.199)
	Left FH	0.548 (1.418)	0.126 (0.337)	0.041 (0.119)	0.035 (0.103)
	Right FH	0.618 (1.835)	0.168 (0.514)	0.030 (0.080)	0.031 (0.088)

SD, standard deviation; FH, femoral head.

and 86.27%, respectively. The average TCP values of plans optimized with PO for IMRT and VMAT were comparable with the average difference of 0.27%. TCP values for both delivery techniques are higher for the plan optimized with PO than with DVO and PRO.

The average NTCP values of bladder for both delivery techniques were very small for plans optimized with different optimization algorithms. Only the average NTCP values of rectum were observed to have a remarkably large difference than those of the other OARs. The average NTCP values of left and right femoral head for plans optimized with different optimization algorithms were negligible, ranging between 10^{-4}% and less than a percent.

3. Technical parameters and statistical analysis

Table 5 summaries the total MU for technical aspect. The data were reported for different delivery techniques and optimization algorithms and also as average and standard deviation for 18 plans. These MUs correspond to IMRT and

Table 5. Average and standard deviation of total MUs and optimization time for different delivery techniques and optimization algorithms.

Technical parameter	IMRT		VMAT	
	DVO Average (SD)	PO Average (SD)	PRO Average (SD)	PO Average (SD)
MUs	604 (32)	555 (25)	439 (19)	452 (22)

SD, standard deviation; MUs, monitor units.

Table 6. *P*-value of estimated parameters by statistical analysis on plans with DVO and PRO against PO for IMRT and VMAT.

Organ	Index	DVO vs PO	PRO vs PO
PTV	D_{mean} (%)	<.01	<.01
	$D_{2\%}$ (%)	<.01	<.01
	$D_{95\%}$ (%)	<.01	<.01
	$V_{95\%}$ (%)	<.01	<.01
	HI	<.01	<.01
	CI	<.01	<.01
	CN	<.01	0.03
	TCP	<.01	<.01
Bladder	D_{mean} (%)	0.64	<.01
	$V_{40\%}$ (%)	<.01	<.01
	$V_{70\%}$ (%)	<.01	<.01
	NTCP	0.03	<.01
Rectum	D_{mean} (%)	<.01	<.01
	$V_{10\%}$ (%)	<.01	<.01
	$V_{40\%}$ (%)	<.01	<.01
	$V_{60\%}$ (%)	<.01	<.01
	$V_{70\%}$ (%)	<.01	<.01
	NTCP	<.01	<.01
Right Femoral Head	D_{mean} (%)	<.01	0.11
	D_{max} (%)	0.78	0.02
	NTCP	0.91	0.53
Left Femoral Head	D_{mean} (%)	<.01	<.01
	D_{max} (%)	0.81	<.01
	NTCP	0.25	0.03
	MU	<.01	<.01

VMAT plans optimized without any interactive adjustment.

PO for IMRT technique showed reduction in total MUs compared to DVO. On the other hand, total MUs for VMAT were slightly higher with PO than that with PRO. The average percentage difference of MUs between PO and DVO for IMRT was 8.8%, and that between PO and PRO for VMAT was –2.9%.

Table 6 shows *P*-value of estimated parameters for statistical analysis on IMRT and VMAT plans with DVO and PRO against PO. A *P*-value <0.05 is observed when plans optimized with DVO and PRO were compared with plans optimized with PO for various parameters. Except the D_{mean} of bladder and the D_{max} and NTCP of both femoral heads, all the evaluated indices show significant differences between DVO and PO. In statistical analysis between PRO and PO, only the *P*-values of the D_{mean} and NTCP of right femoral head was higher than 0.05 among all the evaluated indices.

Discussion

The treatment planning process for radiation therapy is based on various optimization algorithms. These optimization algorithms are used to determine the combination of field shape and segment weight with dose rate and gantry speed variations, which best approximates the desired dose distribution in the inverse planning for IMRT and VMAT.[9,16] In a previous study performed with a virtual phantom, difference of dosimetric performance was observed between newly incorporated PO versus the conventional DVO and PRO for both delivery techniques. We compared the performance between PO and the conventional optimization algorithms in IMRT and VMAT plans for application in clinical prostate cancer treatment using ERB. In this study, radiobiological and technical parameters as well as dosimetric parameters were evaluated quantitatively and qualitatively to plans optimized using different optimization algorithms without any interactive adjustment of planning parameters, such as, all dose-volume constraints and priorities.

With the dosimetric indices to HI, CI, and CN, plans optimized with DVO and PRO have lower quality than those optimized with PO. Variation of these indices was lower in VMAT plan optimized with PRO and PO than IMRT plan optimized with DVO and PO. For both delivery techniques, the PO was higher the mean target dose than DVO and PRO. $D_{2\%}$ indicating reduced hot spots in the target was lower in PO than in DVO and PRO. For HI, there is a contrary trend for both delivery techniques. For OARs sparing, the PO presented more remarkable improvement than

DVO and PRO, excepted in bladder dose of IMRT as shown in Fig. 1. This is consistent with earlier studies.[9,17,18] The improvement of OARs sparing may not be clinically significant, but it complies with the as low as reasonably achievable (ALARA) principle. Overall, variations of dosimetric indices between optimization algorithms were more in OARs than in PTV.

In order to study the impact of the different algorithms on radiobiological parameters, we used Niemierko's EUD-based model to calculate TCP and NTCP.[14] For radiobiological indices, the TCP of the target volume was higher for both delivery techniques with PO than with DVO and PRO. This suggests that the PO results in dose distribution with superior target coverage. However, the difference between TCPs obtained from plans optimized with PO for IMRT and VMAT are also small and insignificant. The magnitudes of the difference for NTCP of OARs were relatively small, except for the rectum. Hence, it may be clinically negligible, as shown in Table 4. No difference between PO and the other optimization algorithms occurred to bias any results of the comparison of radiobiological indices for OARs. The difference of NTCP on rectum was, however, the largest among all OARs, and this might depend on the ERB including an air cavity.

For the technical aspect, total MUs and optimization times were investigated to evaluate the efficiency of PO against DVO and PRO algorithm for IMRT and VMAT techniques. Planned total MUs showed opposing consequence trends for the two delivery techniques. The MUs were found to be less in IMRT plan optimized with PO than with DVO and higher in VMAT plan optimized with PO than with PRO. Higher MU corresponded to higher modulation in several IMRT plans. The considerably increased MUs might be associated with smaller MLC apertures.

Although some of the evaluated parameters showed a statistically significant difference according to the optimizer, the differences of those parameters were not large in the PTV. Only the differences of $D_{95\%}$ and $V_{95\%}$ between optimizers were relatively larger compared to the others, and the difference in VMAT was greater than that in IMRT. In the rectum, all parameters were significantly different with the optimizers and the difference in D_{mean} was 5.74% of the prescribed dose for IMRT, which was larger than 2.71% for VMAT. In addition, $V_{60\%}$ and $V_{70\%}$ of rectum showed significant difference, which were 17.16% and 11.19% of rectal volume, respectively. This means that clinically significant dose differences can occur with a high probability depending on the optimizer.

The limitation of the current study is that it was performed only on patients with prostate cancer, whose target shape is relatively simple. Thus, further assessment of the clinical impact of the optimizer may need to be performed by application to treatment sites with relatively complex targets, such as, brain and head and neck cancer.

Conclusion

This study compared the impact of dosimetric and radiobiological parameters on the prostate VMAT and IMRT plans using different optimization algorithms. The plan quality was generally improved with PO and, although not for all parameters, some of the estimated dosimetric indices showed also an improvement with PO than with DVO and PRO. For radiobiological parameters, the PO showed clear improvement in TCP of the PTV and NTCP of the rectum. Furthermore, the PO generated IMRT treatment plans with less number of MUs than DVO, although there is an increase in the number of MUs produced by VMAT treatment plans optimized using PO compared with those using PRO. Overall, PO had more potential than DVO and PRO whenever it was used for optimization. Thus, PO was the primary choice for planning prostate IMRT and VMAT in our institution. Finally, we suggest employing PO algorithm for optimizing prostate IMRT and VMAT plan.

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Conflicts of Interest

The authors have nothing to disclose.

Availability of Data and Materials

All relevant data are within the paper and its Supporting Information files.

Ethics Approval and Consent to Participate

The study was approved by the institutional review board (IRB approval number; B-1810/501-108).

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