Application of the RapidPlan knowledge-based treatment planning system for radiation therapy of prostate cancer patients

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ABSTRACT

Background: RapidPlan (RP) knowledge-based treatment planning was developed and adopted in volumetric arc modulated radiotherapy (VMAT) planning to improve plan quality and planning efficiency. RP used plan database to train a model for predicting organ-at-risk (OAR) dose-volume-histograms (DVHs) of the new treatment plan.

Objectives: The purpose of this study was to develop and evaluate the performance of the RP knowledge-based treatment planning to generate VMAT for definitive radiotherapy of prostate cancer.

Materials and methods: Three RP models based on a number of 20, 40, and 60 previously VMAT plans were trained and validated on 10 new prostate cancer patients. Dosimetric parameters of the target volume and organs at risks (OARs) between models and manually optimized method (MO) from experienced planner were compared. The D2%, D95%, D98%, homogeneity index (HI), and conformation

number (CN) for planning target volume (PTV), V65Gy, V70Gy, V75Gy for bladder and V50Gy, V60Gy, V65Gy, V70Gy, V75Gy for rectum were collected and analyzed (one-way repeated measures ANOVA, $p<0.05$).

Results: VMAT plans between models and MO showed similar results of D95%, D98% for PTV but a significant higher of D2%, CN, and HI from RP (105.4%-105.7% for D2%, 0.06-0.07 for HI, and 0.9 for CN) when compared with MO (104% for D2%, 0.05 for HI, and 0.8 for CN). For bladder and rectum, all dose-volume parameters of RP were significantly lower than MO ($p<0.05$), only in RPmodel20 which bladder V75Gy, was similar to MO. Dosimetric analysis for model training based on a different number of VMAT plans showed no statistical difference in plan quality.

Conclusion: RP knowledge-based treatment planning in this investigation presented acceptable VMAT plan quality for definitive radiotherapy prostate in only single optimization. Twenty historic plans were found to be an acceptable minimum number of plans for the model training.

Keyword: Knowledge-based planning, Prostate planning, RapidPlan, VMAT

บทคัดย่อ

หลักการและเหตุผล: RapidPlan(RP)ถูกพัฒนาและประยุกต์ใช้เพื่อเพิ่มคุณภาพและประสิทธิภาพของแผนการรักษา โดย RP จะใช้ข้อมูลแผนการรักษาที่ถูกใช้กับผู้ป่วยในทางคลินิกมาแล้ว เพื่อสร้างเป็นแบบจำลองการรักษาและประเมิน DVHs แก่อวัยวะสำคัญในแผนการรักษาใหม่

วัตถุประสงค์: เพื่อประเมินประสิทธิภาพของระบบวางแผนการรักษาแบบจัดฐานความรู้ด้วย RP สำหรับการรักษาแบบปรับความเข้มหมุนรอบตัว(VMAT)ในผู้ป่วยมะเร็งต่อมลูกหมาก

วัสดุและวิธีการ: สร้างแบบจำลอง RP 3 แบบจากแผนการรักษาVMATที่ถูกใช้กับผู้ป่วยในทางคลินิกมาแล้วจำนวน 20, 40, และ 60 แผนตามลำดับ จากนั้นนำแบบจำลองดังกล่าวมาทดสอบกับผู้ป่วยรายใหม่จำนวน 10 ราย และเปรียบเทียบแผนการรักษาที่ได้จาก RPและวิธีด้วยมือจากผู้มีประสบการณ์ (MO) ข้อมูลปริมาณรังสีสำหรับก้อนมะเร็ง (PTV) ที่นำมาวิเคราะห์ได้แก่ค่า D2%, D95%, D98%, conformation number(CN) และhomogeneity index(HI) ส่วน

กระเพาะปัสสาวะได้แก่ค่า V65Gy, V70Gy, V75Gy และไส้ตรงที่ V50Gy, V60Gy, V65Gy, V70Gy, V75Gy จากนั้นทำการวิเคราะห์ทางสถิติโดยใช้ one-way repeated measures ANOVA, $p<0.05$ ผลการศึกษา: แผนการรักษาRPและMO แสดงผลของ D95%, D98% สำหรับ PTV ที่เหมือนกัน แต่มีค่า D2%, CN, และ HI จากแผนRP (105%-106% สำหรับ D2%, 0.06-0.07 สำหรับ HI และ 0.9 สำหรับ CN) ที่มากกว่าMO (104% สำหรับ D2%, 0.05 สำหรับ HI, และ 0.8 สำหรับ CN) อย่างมีนัยสำคัญทางสถิติ สำหรับปริมาณรังสีที่กระเพาะปัสสาวะและไส้ตรงได้รับจาก RP มีค่าต่ำกว่า MO อย่างมีนัยสำคัญด้วยเช่นกัน ยกเว้นปริมาณรังสีที่ V75Gy ของกระเพาะปัสสาวะที่ RP 20 แผน มีผลเหมือนกับการวางแผนแบบ MO ในการเปรียบเทียบแผนการรักษาที่สร้างจาก RP 3 รูปแบบใน ผู้ป่วยรายเดียวกันไม่พบความแตกต่างทางสถิติของปริมาณรังสี

ข้อสรุป: ระบบวางแผนการรักษาแบบจัดฐานความรู้ด้วย RPสามารถสร้างแผนการรักษา VMAT ในผู้ป่วยมะเร็งต่อมลูกหมากได้อย่างมีคุณภาพและแผนการรักษาจำนวนขั้นต่ำ 20 แผนเพียงพอ สำหรับการสร้างแบบจำลอง RP ได้อย่างเหมาะสมและมีประสิทธิภาพ

คำสำคัญ: ระบบการวางแผนการรักษาแบบจัดฐานความรู้, การวางแผนการรักษามะเร็งต่อมลูกหมาก, RapidPlan, การฉายรังสีแบบปรับความเข้มหมุนรอบตัว

INTRODUCTION

Intensity-modulated radiation therapy (IMRT) and volumetric modulated arc radiotherapy (VMAT) utilized the inverse planning process that is needed to solve this complexity through the optimization process. To get the satisfied results, an appropriate set of optimization parameters for organs at risk (OARs) and the target volume has to be specified by planners through a repeated trial-and-error process. Therefore, the planning outcome was strongly based on the experience and skills of the planners[1, 2]. The treatment planning could take several hours in trial-and-error optimization to achieve the planning goals. Currently, various tools were developed for IMRT and VMAT radiation therapy treatment planning. Knowledge-based (KB) approaches were introduced and adopted in treatment planning to improve planning consistency in IMRT and VMAT. KB treatment planning (KBTP) method was used to predict the dosimetric features of the new treatment plan by utilizing a database of prior plans

determined via the spatial relationship between anatomical, geometric and dosimetric features of targets and OARs [3, 4].

This method was useful to reduce variations in plan quality. Previous studies[5-7] have demonstrated that KBTP resulted in superior treatment plans in terms of planning time and dose distributions as compared to conventional IMRT and VMAT plans. Furthermore, this approach is able to decrease optimization time. RapidPlan version 13.6 (Varian Medical System, Palo Alto, CA, USA; RP) is a commercially KB planning application software which is an optional application from the Eclipse treatment planning system (TPS). Therefore, the purpose of this paper was to study and demonstrate the potential of the RP knowledge-based TPS for VMAT plans in prostate cancer in terms of plan quality and efficiency at the Division of Radiation Oncology, Department of Radiology, Faculty of Medicine, Siriraj Hospital.

MATERIALS AND METHODS

Previously clinical VMAT plans of prostate cancer selection

Sixty VMAT planning of prostate cancer patients who treated only prostate gland, not involved lymph node during January 2016 to March 2018 were collected and analyzed. All treatment plans were created with two or three arcs, using 10 MV photon beams, and total prescribed dose to PTV was 78 Gy in 39 fractions. Dose-volume constraints for the planning target volume (PTV-prostate gland), the OARs such as bladder, rectum, and the PTV overlap OARs were assigned as the planning goal for the optimization process. All treatment plans were approved by the radiation oncologist according to Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) guideline[8] as shown in **Table 1**. Volume data of the PTV and all OARs were also collected for the analysis.

Table 1. Dose-volume constraints assigned for VMAT prostate cancer optimization

Organ	Dose constraints
PTV	D2%≤ 107%, D95%≥ 95%, and D98%≥ 93%
Bladder	V65Gy≤50%, V70Gy≤35%, and V75Gy≤25%
Rectum	V50Gy≤ 50%, V60Gy≤35%, V65Gy≤25%, V70Gy≤20%, and V75Gy≤15%

Model configuration

RP system consists of two main components: model configuration and model validation. To configure a model, the geometric and dosimetric parameters of the historic treatment plans are extracted and trained by using a combination of Principal Component Analysis and regression tecniques in the RP algorithm[9]. For model validation, estimated dose volume histogram (DVH) and optimization objectives for the optimization process of new patients were generated. In this study, sixty previously VMAT prostate plans were used to generate three RP models. Model20 is the minimum number of 20 random previous plans that used for building the model as suggested by the vendor. To examine whether a number of plans result in model quality and consistency or not, Model40 and Model60 were generated from using 40 and 60 previous plans for training.

Model Validation

CT dataset of 10 new prostate cancer patients were used to validate the model. For each patient, three VMAT treatment planning were created from a total of 3 RP models. The VMAT planning parameters including the field geometry (2 arcs), 10 MV photon energy, and dose prescription 78 Gy to PTV were set. In the optimization process, the RP system was used to perform an estimation for the DVHs in any new patient. The workflow of the DVHs estimation started with a selection of the RP model. Then, the outlined structures of new patient auto-matched to the model structures using a structure code. The system automatically generated optimization priorities, setting of the upper and lower objectives to the PTV, DVH estimated boundary to the OARs, and line objectives, which placed along the inferior DVH estimated boundary[9]. The examples of the resulting RP predictive DVH estimated and priorities are shown in **Figure 1**. Generating estimated DVHs and priorities based on patient geometry of new patient and previous knowledge contained in a model database and were used in the optimization process. A single optimization without any planner intervention was performed to assess the quality of the models.

Performance of the RP plan compared to the manually optimized plans

Two expert planners with their experience in VMAT planning of more

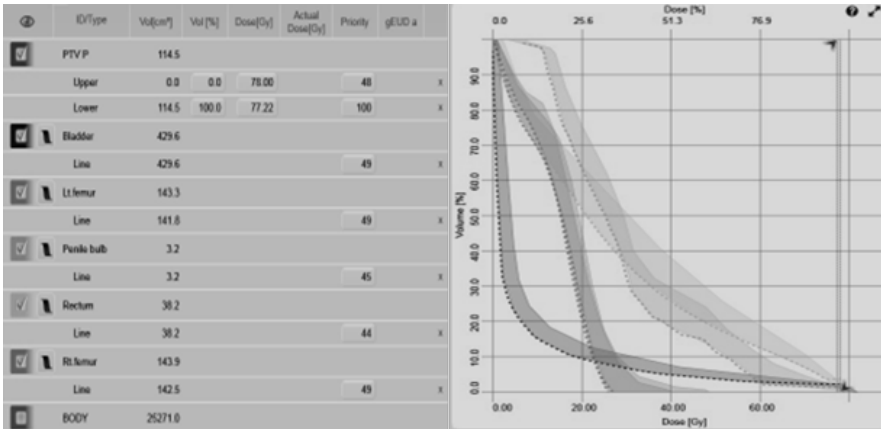

Figure 1. (a) priorities and objectives (b) the estimated range and line objectives of RP prediction

than 60 prostate cancer plans were participated in this study. Manually optimized (MO) VMAT plans were created by the planners using the same technique as the RP plans. Dosimetric parameter results of MO plans from two planners were comparable. Then, the MO plans results were averaged and compared with plans from 3 RP models. Dosimetric parameters in term of (1) dose to 2% of the PTV volume (D2%); (2) dose to 95% of the PTV volume (D95%); (3) dose to 98% of the PTV volume (D98%); (4) homogeneity index (HI)[10] of the PTV defined as HI =[D2%-D98]/D50%, the HI value is 0, representing dose homogeneous in target ; (5) conformation number (CN)[11] of the PTV defined as CN = [TVRI/TV] × [TVRI/VRI] where TVRI = target volume covered by the prescription isodose, TV = target volume, and VRI = volume of the prescription isodose, the CN value is 1, representing conformity of target; (6) dose-volume parameters to the bladder as V65Gy, V70Gy, and V75Gy; and (7) dose-volume parameters to the rectum as V50Gy, V60Gy, V65Gy, V70Gy, and V75Gy were used for the analysis.

The one-way repeated measures ANOVA ($p < 0.05$) was used to test the significance of the plan comparison results.

RESULTS

Collecting the structure's volume from the historic plans, the results in **Table 2** shows mean + SD of PTV, OARs, and OARs overlapping with PTV volumes for each RP model, compared with 10 new patients. The mean of the PTV registered in each model and test group

Table 2. Data of the structure volumes in each RP model and a test group

Volumes (cm^3) Mean ± S.D.	$Model_{20}$	$Model_{40}$	$Model_{60}$	New Patients
PTV	112.2 ± 33.9	112.6 ± 30.8	116.1 ± 35.1	110.0 ± 35.3
Bladder	264.5 ± 161.6	251.3 ± 135.4	251.1 ± 117.1	266.2 ± 141.8
Rectum	56.6 ± 24.0	57.6 ± 23.9	56.3 ± 21.6	52.6 ± 14.1
Bladder Overlap PTV	11.4 ± 4.2	14.9 ± 9.0	14.7 ± 7.8	11.31 ± 4.0
Rectum Overlap PTV	2.8 ± 1.3	3.0 ± 1.5	3.0 ± 1.7	2.7 ± 1.9

were 112.2 ± 33.9 cm^3, 112.6 ± 30.8 cm^3, 116.1 ± 35.1 cm^3 and 110.0 ± 35.3 cm^3 for $Model_{20}$, $Model_{40}$, $Model_{60}$, and test group respectively. The mean ± SD of the bladder were 264.5 ± 161.6 cm^3, 251.3 ± 135.4 cm^3, 251.1 ± 117.1 cm^3, and 266.2 ± 141.8 cm^3 for $Model_{20}$, $Model_{40}$, $Model_{60}$, and test group, respectively. In the rectum volume, the mean ± SD were 56.6 ± 24.0 cm^3, 57.6 ± 23.9 cm^3, 56.3 ± 21.6 cm^3, and 52.6 ± 14.1 cm^3 for $Model_{20}$, $Model_{40}$, $Model_{60}$, and test group, respectively. It can be seen that the volumes of the target and organs at risks among 3 models and in a test group were quite similar.

The isodose distribution for VMAT planning from both RP & MO optimization methods are shown in **Figure 2**. All plans were evaluated and passed the clinical planning goal as prescribed from QUANTEC guideline. All dosimetric results were summarized as shown in **Table 3**. The comparison of RP plans to MO plans, RP improved $D_{95\%}$ and $D_{98\%}$ of PTV, but no significant difference was seen. A significant higher of $D_{2\%}$, CN, and HI from all 3 RP models ($D_{2\%}$: 105.7 %, 105.4 %, and 105.4%, HI: 0.07, 0.07, and 0.06, CN: 0.9, 0.9, and 0.9 for $Model_{20}$, $Model_{40}$, and $Model_{60}$, respectively) was shown when compared with MO ($D2_{\%}$: 104%, HI: 0.05, and CN: 0.8), ($p<0.05$). The higher $D_{2\%}$ and HI showed more dose variation. However, the higher CN represented more conformity of target. For bladder, almost all

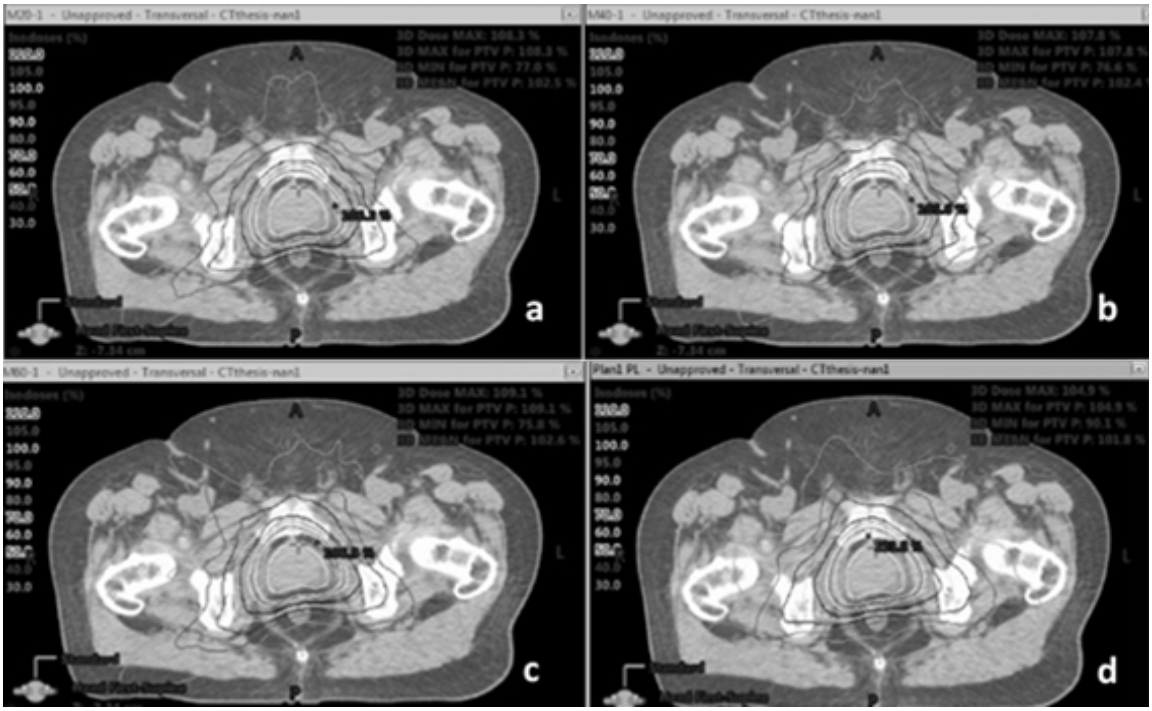

Figure 2. Isodose distributions for VMAT prostate cancer of (a) $Model_{20}$, (b) $Model_{40}$, (c) $Model_{60}$, and (d) MO

Table 3. Summary of the dosimetric results from RP and MO plans in 10 new prostate patients

		Mean ± SD	*P-value* (Model vs. MO)	P-value (Model vs. Model)
PTV; $D_{2\%}$ (%)	$Model_{20}$	105.7 ± 0.8	M_{20} vs. MO: <0.001	M_{20} vs. M40: 0.187
	$Model_{40}$	105.4 ± 0.8	M_{40} vs. MO: 0.010	M_{20} vs. M60: 0.162
	$Model_{60}$	105.4 ± 0.7	M_{60} vs. MO: <0.001	M_{40} vs. M60: 0.880
	MO	104.0 ± 0.3		
PTV; $D_{95\%}$ (%)	$Model_{20}$	100.1 ± 0.5	M_{20} vs. MO: 0.125	M_{20} vs. M40: 0.307
	$Model_{40}$	100.0 ± 0.6	M_{40} vs. MO: 0.209	M_{20} vs. M60: 0.770
	$Model_{60}$	100.0 ± 0.5	M_{60} vs. MO: 0.120	M_{40} vs. M60: 0.125
	MO	99.7 ± 0.9		

		Mean ± SD	*P-value* (Model vs. MO)	P-value (Model vs. Model)
PTV; $D_{98\%}$ (%)	$Model_{20}$	98.8 ± 0.6	M_{20} vs. MO: 0.341	M_{20} vs. M40: 0.373
	$Model_{40}$	98.7 ± 0.7	M_{40} vs. MO: 0.526	M_{20} vs. M60: 0.878
	$Model_{60}$	98.8 ± 0.6	M_{60} vs. MO: 0.328	M_{40} vs. M60: 0.052
	MO	98.5 ± 0.9		
PTV; HI	$Model_{20}$	0.07 ± 0.1	M_{20} vs. MO: 0.012	M_{20} vs. M40: 0.343
	$Model_{40}$	0.07 ± 0.1	M_{40} vs. MO: 0.037	M_{20} vs. M60: 0.177
	$Model_{60}$	0.06 ± 0.0	M_{60} vs. MO: 0.023	M_{20} vs. M60: 0.443
	MO	0.05 ± 0.1		
PTV; CN	$Model_{20}$	0.9 ± 0.0	M_{20} vs. MO: 0.001	M_{20} vs. M40: 0.343
	$Model_{40}$	0.9 ± 0.0	M_{40} vs. MO: <0.001	M_{20} vs. M60: 1.000
	$Model_{60}$	0.9 ± 0.0	M_{60} vs. MO: 0.001	M_{40} vs. M60: 0.343
	MO	0.8 ± 0.1		
Bladder; V_{65Gy} (%)	$Model_{20}$	8.6 ± 5.9	M_{20} vs. MO: 0.020	M_{20} vs. M40: 0.144
	$Model_{40}$	8.2 ± 5.1	M_{40} vs. MO: 0.001	M_{20} vs. M60: 0.534
	$Model_{60}$	8.4 ± 5.1	M_{60} vs. MO: <0.00	M_{40} vs. M60: 0.059
	MO	10.1 ± 5.3		
Bladder; V_{70Gy} (%)	$Model_{20}$	7.5 ± 5.0	M_{20} vs. MO: 0.036	M_{20} vs. M40: 0.193
	$Model_{40}$	7.1 ± 4.4	M_{40} vs. MO: 0.002	M_{20} vs. M60: 0.535
	$Model_{60}$	7.3 ± 4.4	M_{60} vs. MO: 0.001	M_{40} vs. M60: 0.120
	MO	8.6 ± 4.5		
Bladder; V_{75Gy} (%)	$Model_{20}$	6.2 ± 4.1	M_{20} vs. MO: 0.160	M_{20} vs. M40: 0.135
	$Model_{40}$	6.0 ± 3.8	M_{40} vs. MO: 0.020	M_{20} vs. M60: 0.622
	$Model_{60}$	6.1 ± 3.8	M_{60} vs. MO: 0.026	M_{40} vs. M60: 0.051
	MO	6.8 ± 3.5		
Rectum; V_{50Gy} (%)	$Model_{20}$	16.1 ± 4.6	M_{20} vs. MO: <0.001	M_{20} vs. M40: 0.109
	$Model_{40}$	17.5 ± 6.0	M_{40} vs. MO: 0.006	M_{20} vs. M60: 0.158
	$Model_{60}$	17.4 ± 6.0	M_{60} vs. MO: 0.006	M_{40} vs. M60: 0.752
	MO	20.3 ± 5.8		
Rectum; V_{60Gy} (%)	$Model_{20}$	12.0 ± 3.8	M_{20} vs. MO: 0.001	M_{20} vs. M40: 0.156
	$Model_{40}$	12.7 ± 4.6	M_{40} vs. MO: 0.001	M_{20} vs. M60: 0.242
	$Model_{60}$	12.7 ± 4.6	M_{60} vs. MO: 0.002	M_{40} vs. M60: 0.957
	MO	14.9 ± 4.7		

		Mean ± SD	*P-value* (Model vs. MO)	P-value (Model vs. Model)
Rectum; V_{65Gy} (%)	$Model_{20}$	10.2 ± 3.4	M_{20} vs. MO: 0.001	M_{20} vs. M40: 0.216
	$Model_{40}$	10.7 ± 4.0	M_{40} vs. MO: 0.001	M_{20} vs. M60: 0.305
	$Model_{60}$	10.7 ± 4.1	M_{60} vs. MO: 0.001	M_{40} vs. M60: 0.957
	MO	12.6 ± 4.2		
Rectum; V_{70Gy} (%)	$Model_{20}$	8.4 ± 3.1	M_{20} vs. MO: 0.002	M_{20} vs. M40: 0.237
	$Model_{40}$	8.7 ± 3.5	M_{40} vs. MO: 0.002	M_{20} vs. M60: 0.335
	$Model_{60}$	8.7 ± 3.6	M_{60} vs. MO: 0.003	M_{40} vs. M60: 0.826
	MO	10.1 ± 3.7		
Rectum; V_{75Gy} (%)	$Model_{20}$	6.4 ± 2.8	M_{20} vs. MO: 0.030	M_{20} vs. M40: 0.478
	$Model_{40}$	6.5 ± 3.0	M_{40} vs. MO: 0.028	M_{20} vs. M60: 0.375
	$Model_{60}$	6.6 ± 3.0	M_{60} vs. MO: 0.048	M_{40} vs. M60: 0.405
	MO	7.1 ± 3.1		

[a]M_{20} is 20 plans model training, M_{40} is 40 plans model training, and M_{60} is 60 plans model training
[b]The p-value < 0.05 is the statistical significance of this study

dose-volume parameters of RP were significantly lower than MO ($p<0.05$), only RPmodel20, V75Gy of the bladder was similar to MO (V75Gy: 6.2% and 6.8% for RPmodel20 and MO). All dose-volume parameters to the rectum in RP plans were significantly lower than MO plans ($p<0.05$). In addition, PTV parameters in terms of D2%, D95%, D98%, HI, and CN illustrated result among the models insignificantly. For bladder and rectum, all 3 RP models provided comparable the dose-volume parameters.

DISCUSSION

The complicated VMAT treatment planning needed the efficient optimization process in the inverse planning system. However, to reach the planning goals, the optimization was currently a trial-and-error approach, and quality of planning was mostly based on the experience of planners. To reduce the planner dependent variability in plan quality, the RP knowledge-based (KB) solutions for the inverse planning have been developed. Best practice models were able to apply for the clinic to increase planning efficiency. The performance of RP had been compared with manually optimized clinical plans for different treatment sites and techniques. Previous

studies[5-7, 12-14] of RP for VMAT optimization in head and neck, hepatocellular, lung, rectum, pelvic, and esophagus cancer were reported and RP optimized plan is able to improve plan quality and increase planning efficiency. For prostate cancer, better plan quality than the original clinically acceptable plans were presented, from the study of Fogliata et al.[5], Hussein et al.[14] , and Kubo et al.[15] In addition, reduction of planning time, and independently of planner's skill when they used RP was also exhibited.

In this study, after the 3 RP models for VMAT prostate cancer validation, all plans from 3 models were clearly shown the acceptable and better plan quality. For PTV dose coverage, similar results of $D_{95\%}$, $D_{98\%}$, and higher CN, from the models were exhibited when compared with MO. However, in MO plans showed lower $D_{2\%}$ and HI number due to the better control of a hotspot area in PTV from the planner. Kubo et al.[15] also showed that the dose coverage, $D_{2\%}$, $D_{98\%}$, CN, and HI to the PTV was slightly inferior in KBP plans when compared with the manually optimized planning. They suggested to manually adjust in the RP optimization process for improving PTV coverage. For OARs, almost all of the rectum and bladder doses in RP models showed significantly better results than MO, except the V75Gy to the bladder in Model20 that was comparable to the MO plans. For the head and neck studied from Tol et al.[16], they reported that the high dose-volume of OARs might be increased due to the overlap region between PTV and OARs. Therefore, Hussein et al.[14] and Kubo et al.[15] suggested that the planners should add the upper objective of OARs in the optimization process to reduce the high dose of RP plans.

The number of the plan for model training and the removing of outliers was also investigated in this study. Three different RP models, based on 20, 40, and 60 prostate cancer plans, showed similar results of PTV coverage, bladder, and rectum dose. When the organ volume used in building the model was analyzed, it can be seen that all 3 models presented a very similar volume of the PTV, bladder, and rectum. A study of Tol et al.[17], also created head and neck model using 30 and 60 plans and plan quality obtained from both models were the same and concluded that 30 plans were sufficient for building model. In addition, their study showed OAR outlier did not influence to OAR dose.

Hussein et al.[14] as well found that removing statistical outliers from the training set was insignificant effect to modal quality. In our study, removing the outliers from the model was also tested, and showed the same result of no effect on our model quality. Besides, the application of RP for VMAT optimization was found to reduce the optimization time from 30 min in MO plans to 6-7 min. However, the result of this study was limited from a number of sample size in the model validation and further study with more number of data or applied in other clinical cases should be conducted.

CONCLUSION

RP knowledge-based treatment planning system is able to increase planning efficiency and plan quality. Satisfactorily and acceptable prostate VMAT plans from 3 RP trained models in this investigation can be obtained in only single optimization. The 20 historic plans were also found to be an acceptable minimum number of plans for the model training.

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