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Technical Note

Optimizing volumetric modulated arc therapy prostate planning using an automated Fine-Tuning process through dynamic adjustment of optimization parameters

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A R T I C L E I N F O

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A B S T R A C T

In radiotherapy treatment planning, optimization is essential for achieving the most favorable plan by adjusting optimization criteria. This study introduced an innovative approach to automatically fine-tune optimization parameters for volumetric modulated arc therapy prostate planning, ensuring all constraints were met. A knowledge-based planning model was invoked, and the fine-tuning process was applied through an in-house developed script. Among 25 prostate plans, this fine-tuning increased the number of plans meeting all constraints from 10/25 to 22/25, with a reduction in mean monitor units per gray without increasing plan's complexity. This automation improved efficiency by saving time and resources in treatment planning.

1. Introduction

Treatment planning in radiation therapy is performed by the medical physics team utilizing the treatment planning system (TPS) and computed tomography images. Recent advancements in auto-planning have significantly enhanced modern radiation therapy, aiming to improve efficiency, consistency and treatment plans quality [1,2]. Knowledge-based planning (KBP), employing machine learning, is one approach in this field [3]. It requires a dataset of high-quality plans to establish a disease model. The model then identifies correlations between dosimetric and geometric features in the training dataset for each organ at risk (OAR) and planning target volume (PTV) to estimate the dose-volume histogram (DVH). Despite its lower inter-operator variability and better efficiency, manual adjustments are often necessary once the treatment plan is generated [4,5]. An alternative auto-planning technique utilizes deep learning, typically employing a U-Net model to predict an entire dose distribution [6]. Nonetheless, manual refinement of optimization objectives may still be necessary to achieve clinical goals [7]. Another auto-planning technique is multi-criteria optimization (MCO) [8,9], where multiple plans are automatically generated, each meeting the constraints following the Pareto principle. Each plan is optimized to the extent that it cannot be improved without affecting at least one other criterion. Although an interactive navigator facilitates the selection of a clinically optimal plan, this task may prove challenging and requires intensive computing resources. Another auto-planning method adopts an a priori strategy [10,11], using a constraint-based "wish-list" per protocol to generate the solution. However, this "wish-list" may require modification for individual patient cases. Since this adaptation is not integrated into the workflow and requires generating and saving a new initial set of protocol-based constraints, it can be a time-consuming. An alternative approach allows for the automatic generation of plans using an intelligent optimization engine (IOE) [12]. Users are required to rank the clinical goals from the most to the least important. IOE then converts these clinical goals for both PTVs and OARs into the optimization objective function. While this method generates plan more efficiently than manual planning, adapting the initial

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objectives may be necessary [13,14].

In the majority of the aforementioned options for auto-planning, manual adjustments are typically necessary to meet the prespecified constraints. Therefore, the purpose of this paper was to develop a novel approach to automatically fine-tune the optimization parameters for volumetric modulated arc therapy (VMAT) plans as a proof-of-principle generated using the KBP method, specifically for patients with prostate cancer. To achieve this, a script was developed to automate the process by invoking the KBP model and applying the fine-tuning process without manual user input.

2. Materials and methods

2.1. Patient data and treatment plan

A random retrospective selection of 25 patients with prostate cancer, treated in 2022 and 2023, was chosen from the clinical database for testing the automated fine-tuning process. Varian Eclipse TPS (v 15.6) was used to perform this study. The treatment dose prescription was 60 Gy for the prostate and 44 Gy for the seminal vesicle over 20 fractions. Anisotropic margins from the clinical target volume (CTV) to PTV were applied (6 mm laterally and 8 mm in other directions). All patients underwent VMAT treatment using two opposing full arcs with a beam energy of 6 MV and collimator rotations of 30° and 330°, respectively. The dose calculation algorithm was Acuros XB (v 15.6, Varian Medical Systems). The grid sizes used in the dose calculation and the optimization were 0.25 cm. The institute constraints used to evaluate these treatment plans were presented in the supplementary material.

The study was approved by the ethical committee of the Jessa Hospital Hasselt, Belgium on 8/09/2021 (registration number 2021/086).

2.2. Knowledge-Based planning model

RapidPlan™ (RP) is a commercially available auto-planning application that uses a KBP approach developed by Varian Medical Systems. A KBP model for prostate plans using the VMAT technique was created in the RP application using high-quality plans (N=41) from cases treated between April 2020 and July 2022. The structures used to train the model included the PTV, bladder, rectum, bowel, left femoral head, and right femoral head. This KBP model can be integrated into the Varian Eclipse TPS.

2.3. Script design

An in-house C# binary plug-in script was developed using the Eclipse Scripting API™ (Varian Medical Systems, Palo Alto) for VMAT prostate plans. This script invoked the KBP model and applied the fine-tuning process with a single click. The script was divided into three parts:

First, data preparation was conducted prior to optimization. This involved generating the PTVs (PTV-high and PTV-low) and the necessary structures for optimization. Two arcs were then created and configured according to the previously described specifications. The treatment isocenter was positioned at the center of the total PTV (sum of PTV-high and PTV-low), with the jaws adjusted to be 5 mm from this total PTV. Additionally, dynamic multileaf collimators were incorporated within both arcs.

Second, the KBP model was invoked. To accomplish this, the PTVs and OARs were matched with the corresponding structures in the KBP model. Prescribed doses for each PTV were then assigned, allowing the KBP model to estimate the DVH. The optimizer function was started, and once completed, the dose distribution was calculated. A treatment plan was generated and normalized to ensure that the mean target volume (PTV-high) matched the prescribed dose.

Lastly, the fine-tuning process was performed. For this, the plan generated with KBP model was evaluated using the predefined constraints (supplementary material). If all constraints were met, the script stopped, and the plan was saved in the database. However, if one or more constraints were not met, additional objectives presented in Table 1 were incorporated into the optimizer based on the relevant structures. Subsequently, the optimization function restarted, and the dose distribution was recalculated. The treatment plan underwent re-evaluation, and if the same constraint remained unmet, the priority value of the corresponding objective was increased by 10 units. If a new constraint was unmet, additional objectives were once again integrated in the optimizer.

The fine-tuning process automatically stopped after 10 loops if one or more constraints remained unmet, as an additional loop did not provide significant benefits. In such cases, the script generated all 10 plans, allowing for selection of the least unfavorable plan.

2.4. Evaluation: Monitor unit and complexity metric

The first metric used to compare plans was the number of monitor units per gray (MU/Gy). The second parameter, introduced by Younge et al. (2012) [15], for evaluation was the complexity metric (CM). This metric is defined as:

$$CM = \frac{1}{MU}\sum_{i=1}^{n} MU_i \text{ x } \frac{y_i}{A_i}$$

where MU is the number of monitor units of the arc, n is the number of control point apertures, MU_i is the number of MUs of the i-th aperture, A_i is the area of the i-th aperture and y_i is the aperture perimeter excluding the MLC leaf ends of the i-th aperture. An increase in the CM of a plan indicates that the plan is more complex. This metric was automatically calculated using an in-house C# binary plug-in script.

3. Results

Among the 25 prostate cases tested using this script, all constraints of 10 treatment plans were met with only the KBP model. The fine-tuning process addressed the unmet constraint in another 12 cases, resulting in an increase in the number of total plans meeting all constraints from 10/25 to 22/25. Specifically, the fine-tuning process resolved the D_{max} (body) constraint in 7 cases, V_{60Gy} (rectum) constraint in 7 cases, V_{60Gy} (bladder) constraint in 2 cases, and $D_{50\%}$ (PTV-high) constraint in 1 case

Table 1
Objectives and priorities for each structure added to the optimizer via the developed script during the fine-tuning process if one of more constraints were not met.

Type	ID	Objective type	Vol (%)	Dose (Gy)	Priority
Target	PTV-high (60 Gy)	Lower	100	58.8	120
		Upper	0	61.8	120
Target	PTV-low (44 Gy)	Lower	100	43.56	120
		Upper	0	61.8	120
Body	External	Upper	0	63.9	550
Organ	Bladder	Upper	0	63	150
		Upper	4.5	54	120
		Upper	22.5	44.1	100
		Upper	45	36.9	100
		Upper	54	27.9	100
Organ	Rectum	Upper	0	54	150
		Upper	20	45	100
		Upper	33.9	36	100
		Upper	51	27	100
		Upper	61.4	23.4	100
		Upper	76.7	18	100
		Mean	/	27	100
Organ	Bowel	Upper	V58.5Gy x 0.9	52.7	80
		Upper	V41Gy x 0.9	36.9	80
		Upper	V36Gy x 0.9	32.4	80
Organ	Femoral heads	Upper	45	36.9	50

by adding the corresponding objectives presented in Table 1 into the optimizer. The convergence of a plan for which all constraints were initially unmet, through the fine-tuning process for one case is shown in Table 2. However, for 3 cases not all constraints could be met after 10 loops.

Fig. 1a and 1b respectively display the comparison between the result of the KBP (first loop) and fine-tuning (last loop) regarding the MU/Gy and the CM for the 12 cases that required the fine-tuning process to generate plans meeting all constraints. The mean MU/Gy was 381 ± 50 for KBP and 357 ± 42 for fine-tuning, while the mean CM was 0.19 ± 0.04 for KBP and 0.18 ± 0.03 for fine-tuning. Fig. 1c illustrates the estimated planning time of the script in the background for these 12 cases. This estimation assumes that the initial loop (KBP) lasted 5 min, with each loop of the fine-tuning process requiring an additional 2 min.

4. Discussion

The focus of this study was to improve prostate VMAT plans, initially generated by a KBP model through an in-house developed automatic fine-tuning process. While the KBP model is known to be more efficient than manual planning [16], manual refinement is often necessary to achieve clinical goals [17]. To improve planning efficiency and reduce manual interaction, a one-click script was developed. This script first utilized the KBP model and then applied a fine-tuning process. Consequently, both processes were fully automated within this script, allowing the generation of more plans meeting constraints without manual intervention.

Among the plans requiring the fine-tuning process to meet all constraints, the values of constraints between the first loop (KBP) and the last loop (fine-tuning) were slightly different, except for hot spots within the target volume. Despite the KBP model being configured from high-quality plans, it often had difficulties to manage high doses within the target volume [18]. Ayuthaya et al (2022) [19] improved the KBP model by increasing the number of VMAT plans used for KBP model training for prostate cancer. While this enhancement improved the treatment plans, manual refinements remained necessary. The fine-tuning process introduced in this study evaluated the treatment plans and automatically added additional optimization objectives to address unmet constraints.

A parameter used to compare both plans was the number of MU/Gy. An increase in this parameter typically results in a higher total body radiation dose due to radiation leakage and internal scatter [20], which increases the risk of radiation-induced second malignancies [21,22]. Previous studies have indicated that the KBP approach used in this research tends to increase the MU/Gy compared to manual planning [23,24]. However, in this study the plans generated with the fine-tuning process had a slightly lower mean MU/Gy than those generated by the KBP model. Furthermore, the comparison of CM showed no significant difference between both plans. The fine-tuning process did not increase the plan's complexity, thereby dose accuracy for prostate cases [25,26]. Additionally, the estimation of script's execution time in the background was considered acceptable for routine clinical use. Although the patient's treatment plan was unavailable in the TPS during this process, no time was wasted for the user.

The main strength of this work lies in the general and rapid applicability of the fine-tuning process in daily clinical practice. The script was developed to be easily applicable in the TPS where the KBP model was already in use for prostate VMAT plans. Additionally, the script ran completely in the background. However, further refinement of the script could be developed to achieve the same goal more efficiently.

Although the results are promising, their current scope is limited to patients with prostate cancer undergoing radiotherapy treatment following a prescription, as detailed in section 2.1. However, prostate cancer treatments may involve different dose prescriptions and additional dose levels for secondary boost volumes. Additionally, other type of cancer has a unique anatomical region nearby, leading to different sets of dose constraints. Therefore, an interesting direction for future research is to expand the scope of the study to generalize the method, ensuring its applicability across various type of dose prescriptions, target volumes, and disease sites (such as rectum, lung, etc.).

In conclusion, the current study aimed to develop a one-click script utilizing a KBP model and a fine-tuning process to generate more plans meeting all constraints. The results demonstrated that this script effectively addressed a significant number of plans that initially did not meet the constraints. Furthermore, the observed reduction in MU/Gy with the fine-tuning process, without affecting plan's complexity, indicated that

Table 2
The adjustment of the DVH parameter against institute constraints within the script for a particular case necessitated the fine-tuning process to meet all constraints. PTV-high: PTV volume receives 60 Gy; PTV-low: PTV volume receives 44 Gy. (*) Unmet constraint before rounding.

Structures	Constraints	KBP	Fine-Tuning							
		Loop1	Loop2	Loop3	Loop4	Loop5	Loop6	Loop7	Loop8	Loop9
PTV-high	D99 (%)	92.0	90.7	91.4	91.2	91.2	91.2	91.2	91.4	91.2
	D95 (%)	95.6	94.9	95.0*	95.1	95.1	95.1	94.9	95.2	95.1
	D50 (%)	100.2	100.3	100.3	100.3	100.4	100.4	100.3	100.3	100.4
	D5 (%)	103.5	103.9	103.8	103.7	103.5	103.6	103.7	103.6	103.4
	V107 (cm^3)	0.1	0.4	0.1	0.1	0.0	0.0*	0.0	0.0*	0.0
PTV-low	D99 (%)	96.9	95.7	97.6	98.0	97.7	97.9	98.1	98.1	97.9
	D95 (%)	98.0	98.4	98.8	99.0	99.1	99.1	99.1	99.1	98.8
Body	V107 (cm^3)	0.1	0.5	0.2	0.2	0.0*	0.1	0.0*	0.0*	0.0
Bladder	V63.6 (cm^3)	0.3	0.2	0.2	0.2	0.1	0.2	0.1	0.1	0.1
	V60 (%)	6.0	6.9	3.2	3.9	4.0	4.1	4.0	4.7	4.4
	V49 (%)	17.3	17.2	17.2	17.2	17.2	17.1	17.3	17.3	17.3
	V41 (%)	21.0	21.3	21.3	21.4	21.4	21.3	21.5	21.6	21.7
	V31 (%)	26.2	26.4	27.0	27.1	27.1	27.0	27.0	27.3	27.2
Rectum	V60 (cm^3)	0.6	0.8	1.5	0.9	1.3	0.9	1.3	1.0	0.9
	V50 (%)	17.7	17.5	17.9	17.9	17.9	17.9	17.9	17.8	18.1
	V40 (%)	23.6	23.7	23.9	24.2	24.2	24.4	24.7	24.3	24.8
	V30 (%)	30.4	30.8	31.1	31.7	31.5	31.8	32.1	31.7	32.3
	V26 (%)	33.7	34.0	34.5	35.1	35.0	35.1	35.7	35.2	35.8
	V20 (%)	40.6	39.9	40.7	41.3	41.3	41.4	42.3	42.1	42.8
	D_{mean} (Gy)	23.4	23.3	23.9	24.1	24.1	24.2	24.4	24.3	24.4
Bowel	V58.5 (cm^3)	0.7	0.5	0.7	1.0*	0.9	0.8	0.6	1.0	0.7
	V41 (cm^3)	10.3	11.2	11.7	11.6	11.7	12.1	11.8	12.5	12.6
	V36 (cm^3)	13.5	15.3	15.6	15.3	15.5	16.0	16.1	16.8	16.5
Femoral head left	V41 (%)	2.7	1.3	7.3	9.3	7.8	7.5	10.3	9.9	9.3
Femoral head right	V41 (%)	0.7	1.2	3.5	2.8	4.6	3.3	6.2	3.0	3.2

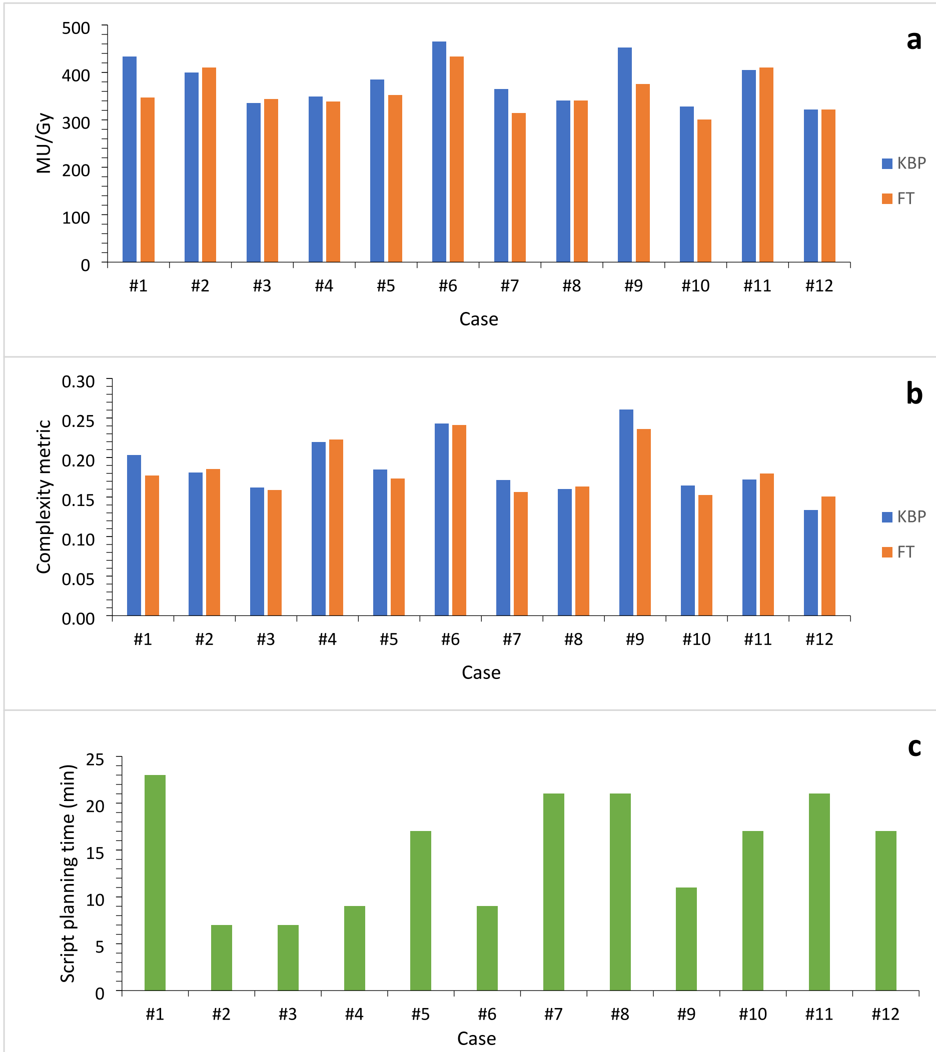

Fig. 1. MU/Gy and the complexity metric values for the 12 cases that needed the fine-tuning (FT) process are presented in (a) and (b) respectively. The blue represents the values of the first loop (KBP) and the orange the value of the last loop (FT). (c) shows script's estimated planning time in the background of these 12 cases.

it allowed for the generation of treatment plans that deliver the dose more efficiently without compromising dosimetric accuracy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2024.100619.

References

[1] Ouyang Z, Liu Shen Z, Murray E, Kolar M, LaHurd D, Yu N, et al. Evaluation of auto-planning in IMRT and VMAT for head and neck cancer. J Appl Clin Med Phys 2019;20:39–47. https://doi: 10.1002/acm2.12652.
[2] Kawamura M, Kamomae T, Yanagawa M, Kamagata K, Fujita S, Ueda D, et al. Revolutionizing radiation therapy: the role of AI in clinical practice. J Radiat Res 2024;65:1–9. https://doi: 10.1093/jrr/rrad090.
[3] Masi K, Archer P, Jackson W, Sun Y, Schipper M, Hamstra D, et al. Knowledge-based treatment planning and its potential role in the transition between treatment planning systems. Med Dosim 2018;43:251–7. https://doi: 10.1016/j.meddos.2017.10.001.
[4] Kaderka R, Hild SJ, Bry VN, Cornell M, Ray XJ, Murphy JD, et al. Wide-Scale Clinical Implementation of Knowledge-Based Planning: An Investigation of Workforce Efficiency, Need for Post-automation Refinement, and Data-Driven Model Maintenance. Int J Radiat Oncol Biol Phys 2021;111:705–15. https://doi: 10.1016/j.ijrobp.2021.06.028.
[5] Chang ATY, Hung AWM, Cheung FWK, Lee MCH, Chan OSH, Philips H, et al. Comparison of Planning Quality and Efficiency Between Conventional and Knowledge-based Algorithms in Nasopharyngeal Cancer Patients Using Intensity Modulated Radiation Therapy. Int J Radiat Oncol Biol Phys 2016;95:981–90. https://doi:10.1016/j.ijrobp.2016.02.017.
[6] Nguyen D, Lin MH, Sher D, Lu W, Jia X, Jiang S. Advances in Automated Treatment Planning. Semin Radiat Oncol 2022;32:343–50. https://doi: 10.1016/j.semradonc.2022.06.004.
[7] Borderias-Villarroel E, Huet Dastarac M, Barragán-Montero AM, Helander R, Holmstrom M, Geets X, et al. Machine learning-based automatic proton therapy planning: Impact of post-processing and dose-mimicking in plan robustness. Med Phys 2023;50:4480–90. https://doi: 10.1002/mp.16408.
[8] Craft D, Halabi T, Shih HA, Bortfeld T. An approach for practical multiobjective IMRT treatment planning. Int J Radiat Oncol Biol Phys 2007;69:1600–7. https://doi: 10.1016/j.ijrobp.2007.08.019.
[9] Craft D, Monz M. Simultaneous navigation of multiple Pareto surfaces, with an application to multicriteria IMRT planning with multiple beam angle configurations. Med Phys 2010;37:736–41. https://doi: 10.1118/1.3292636.
[10] Heijmen B, Voet P, Fransen D, Penninkhof J, Milder M, Akhiat H, et al. Fully automated, multi-criterial planning for Volumetric Modulated Arc Therapy - An international multi-center validation for prostate cancer. Radiother Oncol 2018;128:343–8. https://doi: 10.1016/j.radonc.2018.06.023.

[11] Sharfo AW, Voet PW, Breedveld S, Mens JW, Hoogeman MS, Heijmen BJ. Comparison of VMAT and IMRT strategies for cervical cancer patients using automated planning. Radiother Oncol 2015;114:395–401. https://doi: 10.1016/j.radonc.2015.02.006.

[12] Varian. Ethos Algorithms Reference Guide. Publication ID: P1035867-330-C; 2019.

[13] Pokharel S, Pacheco A, Tanner S. Assessment of efficacy in automated plan generation for Varian Ethos intelligent optimization engine. J Appl Clin Med Phys 2022;23:e13539. https://doi: 10.1002/acm2.13539.

[14] Calmels L, Sibolt P, Åström LM, Serup-Hansen E, Lindberg H, Fromm AL, et al. Evaluation of an automated template-based treatment planning system for radiotherapy of anal, rectal and prostate cancer. Tech Innov Patient Support. Radiat Oncol 2022;22:30–6. https://doi: 10.1016/j.tipsro.2022.04.001.

[15] Younge KC, Matuszak MM, Moran JM, McShan DL, Fraass BA, Roberts DA. Penalization of aperture complexity in inversely planned volumetric modulated arc therapy. Med Phys 2012;39:7160–70. https://doi: 10.1118/1.4762566.

[16] Amaloo C, Hayes L, Manning M, Liu H, Wiant D. Can automated treatment plans gain traction in the clinic? J Appl Clin Med Phys 2019;20:29–35. https://doi: 10.1002/acm2.12674.

[17] Hussein M, South CP, Barry MA, Adams EJ, Jordan TJ, Stewart AJ, et al. Clinical validation and benchmarking of knowledge-based IMRT and VMAT treatment planning in pelvic anatomy. Radiother Oncol 2016;120:473–9. https://doi: 10.1016/j.radonc.2016.06.022.

[18] Wu H, Jiang F, Yue H, Zhang H, Wang K, Zhang Y. Applying a RapidPlan model trained on a technique and orientation to another: a feasibility and dosimetric evaluation. Radiat Oncol 2016;11:108. https://doi.org/10.1186/s13014-016-0684-9.

[19] Ayuthaya IIN, Suriyapee S, Sanghangthum T. Validation of RapidPlan Knowledge-Based Model for Volumetric-Modulated Arc Therapy in Prostate Cancer. J Med Phys 2022;47:250–5. https://doi: 10.4103/jmp.jmp_138_21.

[20] Clemente S, Cozzolino M, Chiumento C, Fiorentino A, Caivano R, Fusco V. Monitor unit optimization in RapidArc plans for prostate cancer. J Appl Clin Med Phys 2013;14:4114. https://doi: 10.1120/jacmp.v14i3.4114.

[21] Hall EJ. Intensity-modulated radiation therapy, protons, and the risk of second cancers. Int J Radiat Oncol Biol Phys 2006;65:1–7. https://doi: 10.1016/j.ijrobp.2006.01.027.

[22] Cashmore J, Ramtohul M, Ford D. Lowering whole-body radiation doses in pediatric intensity-modulated radiotherapy through the use of unflattened photon beams. Int J Radiat Oncol Biol Phys 2011;80:1220–7. https://doi: 10.1016/j.ijrobp.2010.10.002.

[23] Ito T, Tamura M, Monzen H, Matsumoto K, Nakamatsu K, Harada T, et al. Impact of Aperture Shape Controller on Knowledge-based VMAT Planning of Prostate Cancer. Nihon Hoshasen Gijutsu Gakkai Zasshi 2021;77:23–31. https://doi: 10.6009/jjrt.2021_JSRT_77.1.23.

[24] Kubo K, Monzen H, Ishii K, Tamura M, Kawamorita R, Sumida I, et al. Dosimetric comparison of RapidPlan and manually optimized plans in volumetric modulated arc therapy for prostate cancer. Phys Med 2017;44:199–204. https://doi:10.1016/j.ejmp.2017.06.026.

[25] Bush K, Zavgorodni S, Gagne I, Townson R, Ansbacher W, Beckham W. Monte Carlo evaluation of RapidArc oropharynx treatment planning strategies for sparing of midline structures. Phys Med Biol 2010;55:4465–79. https://doi.org/10.1088/0031-9155/55/16/S03.

[26] Fog LS, Rasmussen JF, Aznar M, Kjær-Kristoffersen F, Vogelius IR, Engelholm SA, et al. A closer look at RapidArc® radiosurgery plans using very small fields. Phys Med Biol 2011;56:1853–63. https://doi.org/10.1088/0031-9155/56/6/020.