

Assessment of Knowledge-Based Planning Model in Combination with Multi-Criteria Optimization in Head-and-Neck Cancers

Pichandi Anchineyan, Jerrin Amalraj, Bijina Themantavida Krishnan, Muthuselvi Chockalingampillai Ananthalakshmi, Punitha Jayaraman, Ramkumar Krishnasamy

Department of Radiation Oncology, Healthcare Global Enterprises, Bengaluru, Karnataka, India

Abstract

Aim: The aim of this study was to build knowledge-based planning model (KBPM) for head-and-neck (HN) cancers using volumetric-modulated arc therapy (VMAT), optimized with multi-criteria optimization (MCO), and to evaluate KBPM plan quality with clinical plan (CP) using in-house developed Python script. **Materials and Methods:** Two hundred previously treated simultaneously integrated boost (SIB) HN VMAT plans (RapidArc®) were selected for creating KBPM. These plans were further optimized using MCO to strike right trade-off between target and organs at risk (OARs). The script was written using Python V3.7.1 to automatically extract and analyze treatment plan dosimetric parameters through Eclipse Scripting Application Programming Interface (ESAPI). Analyzed plans that met deliverable quality were modeled using regression-based KBPM framework. The trained model is validated with 35 cohorts of HN SIB patients. **Results:** MCO plans were able to improve the OAR sparing without compromising target coverage compared to user-optimized CPs except for increased heterogeneity. With MCO, spinal cord dose D0.03cc is reduced by $3.2 \text{ Gy} \pm 1.8 \text{ Gy}$, parotid mean dose by $2 \text{ Gy} \pm 1.7 \text{ Gy}$ compared to CPs, respectively. MCO-based KBPM plans were comparable to CP with improved sparing for left and right parotids by 11.5% and 7.8%, respectively. **Conclusion:** MCO-based KBPM plans were superior to user plans in terms of OAR sparing and user need to spend more time to meet the model-based plan outcomes. Created KBPM planning is simple and efficient to generate estimate for OAR sparing to guide entry and intermittent planners to improve their clinical planning skills with lesser planning time. Python ESAPI is a powerful tool to extract plan parameters and quickly evaluate either individual or a cohort of plans.

Keywords: Knowledge-based planning model, multi-criteria optimization, Python, RapidPlan

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INTRODUCTION

Radiation therapy is a noninvasive, normal tissue preserving treatment where ionizing radiation is used to treat malignant disease. The aim of the radiotherapy is to deliver conformal dose to target, simultaneously minimizing the dose in surrounding tissues to avoid damage to healthy organs. Radiotherapy is one of the treatments of choice for head-and-neck (HN) cancers. This treatment can affect the quality of life of treated patients, also affecting their physical, mental, and social health.^[1] Radiotherapy treatment plan is generated by expert planners which involves step-by-step processes where the clinical prescription objectives given by clinical radiation oncologist are realized into deliverable dose distributions to defined region of interest. Optimizing the treatment plan is one of the major

steps in the treatment planning process. Treatment planning is a trial and error process in which the planner has to trade off the plan between target coverage and organ at risk (OAR) sparing. Literature reports on knowledge-based planning (KBP) help to standardize the treatment plans.^[2-4]

Multi-criteria optimization (MCO) is an effectual treatment planning method, in terms of planning time and dosimetric

Address for correspondence: Dr. Pichandi Anchineyan,

Department of Radiation Oncology, Healthcare Global Enterprises, Tower2,
4th Floor, Central Physics, P. Kalingarao Road, Sampangiramnagar,
Bengaluru - 560 027, Karnataka, India.
E-mail: apichu@gmail.com

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plan quality.^[5,6] MCO method relies on the plan database which lies on or near the pareto-optimal surface. The treatment plans on the pareto-optimal surface cannot be improved without degrading the other plan.^[7]

The Eclipse treatment planning system was capable to integrate scripting application programming interface (API). Eclipse Scripting API (ESAPI) was first released with Eclipse v11 as a read-only API that provided access to external beam workspace data with an emphasis on allowing extraction of external beam photon treatment planning data, structure sets, 3D dose and image matrices, and dose–volume histogram (DVH) data. Later versions included major supports like automated plan and dicom file pushing. This is a toolbox based on the C#.Net programming language with .NET framework Common Language Runtime (CLR). External binaries were granted authorization to host ESAPI through .NET command-line interface (CLI) in Eclipse version 15.5, allowing for read-only access in clinical mode and read/write access in research mode. ESAPI can be used in two different modes of interaction with plugin scripts, and with standalone executable scripts. A new Python for .NET implements such a CLR host in Python. This script allows “direct” access to the .NET objects in ESAPI through native Python (PyESAPI). Jupiter notebook tool enables us to do real-time interactive access to the Python runtime in a user-friendly notebook-style web interface. Jupyter notebook allows us to browse the ESAPI data model, draft and debug code, and results in real time. This does not require re-compile and re-start of Eclipse to update/re-run the new code. It is recommended to install PyESAPI and Eclipse database in TBox was set to research mode and PyESAPI was installed to pull the patients’ CT images, RT prescriptions, and RT dose “directly” without the need for import and export filter. A sample script with highlighted code to recall the dose distribution in region of interest of patient image dataset is shown in Figure 1.

Research has been carried out in automation process of treatment planning which resulted in the concept of

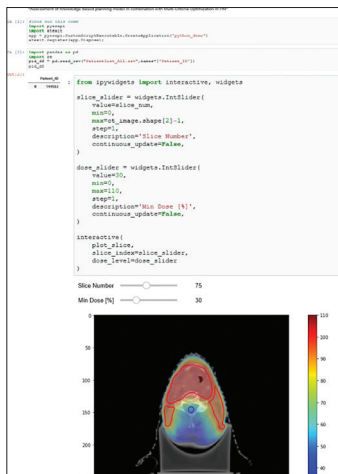


Figure 1: Sample script with coding that recalls the dose distribution in the patient image dataset

KBPM.^[8,9] Optimal treatment plans generated based on the dose constraints and trade-offs are used as input to build and train the model. This model can predict the DVH of the OARs of new patients. RapidPlan (RP) is a KBPM model incorporated in Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA, USA). As there were few literatures relevant to RP model in head and neck^[10,11] and also to further understand the model configuration process, we conducted this study as an extension of our previous work.^[12] The main objectives of the study were to (i) select a cohort of clinical RA treatment plans by expert planners and to explore trade-off to improve plan quality with MCO-RA plan, (ii) compare the high-quality plans with in-house developed Python script to generate and analyze dose–volume metric automatically from Eclipse planning, (iii) selected quality plans were used to build KBP model to automate planning and evaluate with Model Analytics (MA), and (iv) dosimetric comparison of KBPM with clinical plans (CP) to validate KBPM plans to be used in Clinic.

MATERIALS AND METHODS

Patient selection

Two hundred previously treated simultaneously integrated boost (SIB) HN patients with volumetric-modulated arc therapy (VMAT) technique planned by expert planners were selected for this study. The dose to SIB targets, PTV high risk, PTV intermediate risk, and PTV low risk ranges from 54Gy to 70Gy with dose per fraction ranging between 1.63Gy to 2.12Gy. Clinical goals for all target coverage were normalized based on RTOG protocol #0225 and #0522. The OAR constraints are listed in Table 1.

All the treatment plans were optimized using RapidArc, with two full coplanar arcs and collimator angles 30° and 330° using 6 MV photon beams in TrueBeam equipped with Millennium 120-MLC. Inverse planning optimizer used was

Table 1: Planning goals for planning target volumes and organs at risk with dose-volume constraints

PTV/OAR	Dose-volume constraints
PTV HR	$D_{95\%} \geq 95\%$
	$D_{98\%} \geq 93\%$
	$D_{2\%} < 107\%$
PTV IR	$D_{95\%} \geq 95\%$
PTV (IR-HR)	$V_{HRDose} < 20\%$
PTV LR	$D_{95\%} \geq 95\%$
PTV (LR-IR)	$V_{LRDose} < 20\%$
Spinal cord	$D_{max} < 45$ Gy
Brainstem	$D_{max} < 48$ Gy
Parotids	$D_{mean} < 26$ Gy
Larynx	$D_{mean} < 45$ Gy
Mandible	$D_{max} < 70$ Gy
Lips	$D_{mean} < 20$ Gy
Oral cavity	$D_{mean} < 35$ Gy

PTV: Planning target volume, OAR: Organ at risk, HR: High risk, IR: Intermediate risk, LR: Low risk

The target upper and lower objectives were manually defined for model-based plans, whereas the OAR line integrals were derived by model estimate. Additionally to control spill-off, normal tissue objective was used with fall-off 0.1, from a start dose of 100% to 50% from target border of 1 mm.

RapidPlan-knowledge-based planning validation

Published KBP models were then validated for a new set of 35 HN-SIB patients with VMAT CPs. Model plans were created and compared with clinical RA plans (CP). Plans were compared and analyzed individually and using Python script to quantify plan metrics. Statistical analysis was performed to compare the dosimetric differences between CP and RP plans. Paired *t*-test was used to compare the different dosimetric parameters. *P* < 0.05 was considered statistically significant.

RESULTS

RapidPlan versus multi-criteria optimization–RA plans

Clinical RA plans selected for model creation were further tuned with MCO trade-off exploration. While both the sets of plans achieved the clinical objectives, MCO-RA plans were better in sparing the bilateral parotids, spinal cord, etc., Figure 4 compares the OAR dosimetric parameters between RA and MCO-RA plans by five expert planners extracted using in-house developed Python script. Figure 5 compares the overall OAR sparing by RA and MCO-RA plans for the set of 200 patient plans. It is observed except few potential outliers; MCO-RA plans were able to improve OAR sparing, especially for bilateral parotids and spinal cord.

Knowledge-based planning model analysis

Table 2 summarizes the evaluation of the published model quality. For each structure in the model, goodness of fit was evaluated with coefficient of determination (*R*²) and the average Pearson’s Chi-square (χ^2). Potential outliers in the model OAR are also listed in Table 2. These together with MA helped in improving the model prediction power.

RapidPlan-knowledge-based planning model validation

RP-KBP model was validated against the CP.

Target coverage

The dose distributions for one representative HN cancer (HNC) patient on all planes of CP and RP plans are shown in Figure 6. Table 3 shows the detailed statistical analysis of PTVs, which are averaged over 35 patients. Statistically significant differences are observed between CP and RP plans in terms of PTV high risk, PTV intermediate risk, and HI. With better sparing of OARs, the target homogeneity was slightly compromised in RP plans.

Organ at risk sparing

Figure 7 shows the DVHs of OARs for one representative patient which shows that RP plans significantly reduce dose to OARs in comparison with CP plans. The MD results for the OARs are summarized in Table 3. When looking at

Table 2: Summary of model evaluation statistics of trained knowledge-based planning model

Structure	<i>R</i> ²	χ^2	Outliers
Brainstem	0.690	1.019	34
Spinal cord	0.294	1.026	5
Parotid-contra	0.328	1.026	7
Parotid-ipsi	0.355	1.026	4
Larynx	0.549	1.045	17
Lips	0.884	1.082	0
Oral cavity	0.682	1.038	15
Mandible	0.810	1.020	7
Pharyngeal constrictors	0.895	1.215	0

Table 3: Dosimetric results of planning target volumes and organs at risk between clinical plan and RapidPlan

PTV/OARs	Parameter	CP	RP	<i>P</i>
PTV				
PTV HR	D _{98%} (%)	96.89±2.21	98.01±1.83	<0.001*
	D _{2%} (%)	105.13±1.12	106.92±1.13	0.142
	HI	1.06±0.04	1.07±0.06	0.020*
PTV IR	D _{95%} (%)	97.03±1.68	99.76±0.82	0.004*
PTV _{IR-HR}	V _{HRD} (%)	17.77±1.28	19.33±2.56	
PTV LR	D _{95%} (%)	98.14±0.76	98.81±2.33	0.943
PTV _{LR-IR}	V _{IRD} (%)	12.34±2.05	14.25±1.83	
OARs				
Brainstem	D _{0.03cc} (Gy)	27.23±12.14	22.84±12.76	<0.001*
Spinal cord	D _{0.03} (Gy)	34.12±8.06	33.01±2.15	0.073
Left parotid	D _{mean} (Gy)	29.38±6.44	26.33±5.81	0.014*
Right parotid	D _{mean} (Gy)	28.65±8.88	26.56±9.44	<0.001*
Oral cavity	D _{mean} (Gy)	29.83±5.81	29.11±12.02	0.190
Larynx	D _{mean} (Gy)	35.64±12.41	33.59±13.79	0.204
Lips	D _{0.1cc} (Gy)	49.11±7.53	41.78±5.83	<0.001*
Mandible	D _{0.1cc} (Gy)	61.93±11.32	61.01±11.89	0.152
MU		612±86	558±71	0.039*

**P*<0.05 was considered statistically significant. PTV: Planning target volume, OAR: Organ at risk, HR: High risk, IR: Intermediate risk, LR: Low risk, CP: Clinical plan, RP: RapidPlan, MU: Monitor unit, HI: Homogeneity index

each organ separately, the brainstem maximum dose was significantly lower with RP (22.84 ± 12.76 Gy) compared to CP (27.23 ± 12.14 Gy), *P* < 0.001. No statistical difference was found in spinal cord doses between two plans. Relatively remarkable decreases were observed in D_{mean} of both parotids. MD was significantly lesser in RP plans (*P* = 0.014, <0.001). There were no significant differences in OARs sparing of larynx, oral cavity, and mandible.

Plan MUs

To achieve a balanced plan between multiple PTVs and OARs in HNC treatment is a time-consuming task. The mean number of MUs for CP plans was 612 compared to 558 for RP plans (*P* < 0.05). A statistically significant reduction of MUs was observed in RP plans.

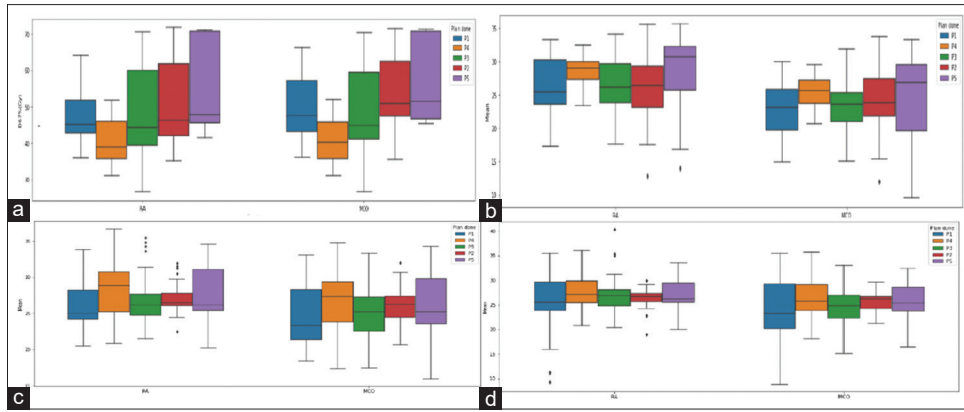


Figure 4: Comparing each of five expert planner plans (RA) and multi-criteria optimization-RA plans for few representative organs at risk. Number of samples for each planner 30 RA and 30 multi-criteria optimization-RA plans. In-house Python script helps with data informatics to segregate plans based on planner, organs at risk, etc., (a) Box and whisker plot of oral cavity ($D_{67\%}$). (b and c) Box and whisker plot of mean dose to left and right parotids. (d) The box and whisker plot for $D_{0.03cc}$ of spinal cord

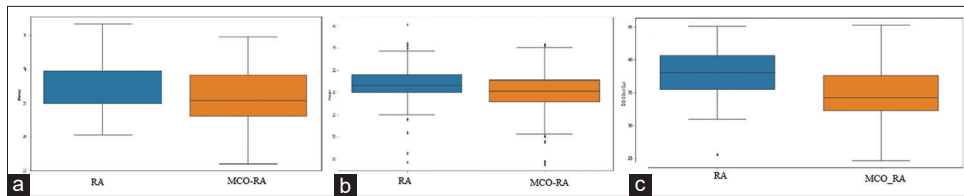


Figure 5: Comparing the RA plans with multi-criteria optimization-RA plans for representative organs at risk for 200 sets of plans. (a and b) Comparing mean dose to left and right parotids, respectively, for RA vs. multi-criteria optimization-RA plans. (c) comparing the maximum dose $D_{0.03cc}$ to spinal cord

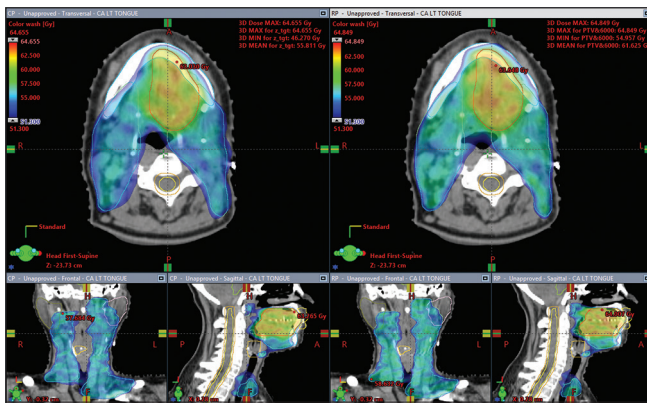


Figure 6: The dose distribution of representative HN cancer patient with cancer tongue. Use of normal tissue objective in RP plan improved the conformity of dose distribution better than clinical plan plans

Treatment time efficacy

The time taken to return the clinically deliverable plans were individually assessed. While CP plans required several iterations to reach the desired plan outcome, RP plans required one or two iterations only. RP plans consumed lesser time by 50% to return the desirable clinically deliverable plans compared to user CPs.

DISCUSSION

In this study, we evaluated the performance of RP model on HNC radiotherapy based on RA planning. The analyzed results

showed that RP plans provided comparable and improved plan quality over the CPs. The superiority of RP plans over the CP could be due to the challenging nature of optimally and consistently performing interactive planning for plans which contain many OARs, within a limited number of iterations. Caution should be used when applying RP models to patients whose geometry falls outside the range of the constituent plans in the model.

Optimization of RA plans can be a time-consuming trial and error process, as many planning objectives are contradictory to each other and cannot reach their individual optimum at the same time. MCO combined with interactive plan navigation is a promising approach to overcome these problems.^[14] Literatures have reported that the use of RP and MCO in clinical practice has reduced the treatment planning time.^[15] MCO-based treatment planning can be used as a tool for educational purposes for emerging clinical physicists. It is promising to combine MCO with KBPM. The combination of KBP and MCO is synergistic as the knowledge-based system provides the templates and beam orientations, as well as the starting point for the interactive navigation. If in any case with gross deviation in OAR overlaps with target, or the volume deviates grossly with the cohort of plans in model, it will reduce the efficiency of DVH estimate by our KBPM, with a warning of potential outlier that requires manual iterations. One of the advantages of KBPM is that the ongoing CPs can be added to the existing model to better train the model to improve its power of DVH estimate. Planners’ expertise is of least concern

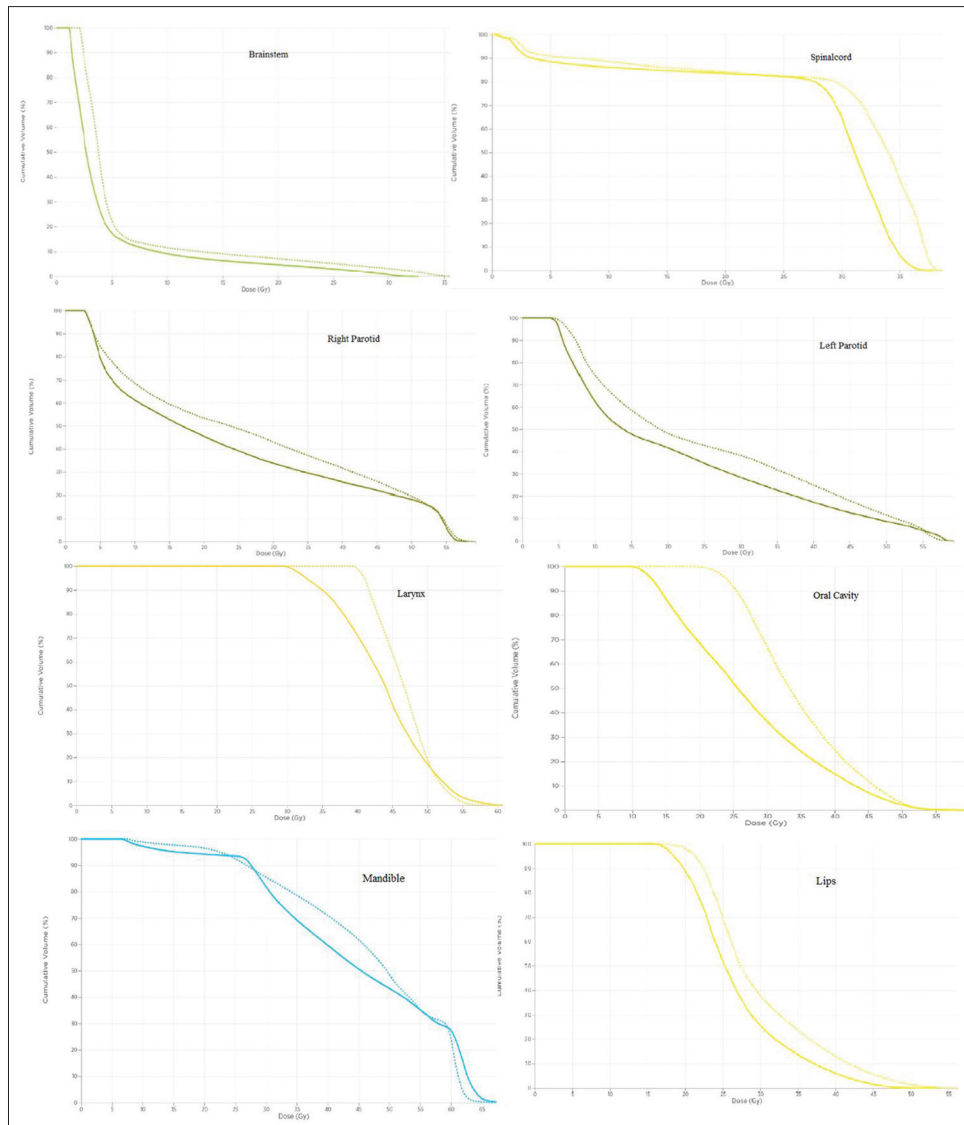


Figure 7: The organ at risk sparing comparison dose–volume histogram between RP (solid line) and clinical plan (dotted lines) for brainstem, spinal cord, larynx, oral cavity, mandible, and lips

and it empowers the confidence in young planners to improve their planning skills. Furthermore, with DVH estimates, KBPM could help the clinician to judge plan outcome beforehand what could be the expected lines of clinical outcome with their contouring input.

CONCLUSION

The KBP model published with our institute data using the MCO-RA plans delivers the best DVH estimate of OAR sparing for the given geometry of the patient. The treatment planning process was well streamlined with DVH estimate model to return highly efficient plans and avoid the need for multiple iteration process. Expertise of the planner is of least concern as KBP delivers highly efficient and consistent plans with lesser time spent on treatment planning. The in-house developed Python ESAPI script is a great tool for clinician to quickly evaluate whether plan clinical goals are met.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Langendijk JA, Doornaert P, Verdonck-de Leeuw IM, Leemans CR, Aaronson NK, Slotman BJ. Impact of late treatment-related toxicity on quality of life among patients with head and neck cancer treated with radiotherapy. *J Clin Oncol* 2008;26:3770-6.
- Müller BS, Shih HA, Efstathiou JA, Bortfeld T, Craft D. Multicriteria plan optimization in the hands of physicians: A pilot study in prostate cancer and brain tumors. *Radiat Oncol* 2017;12:168.
- Voet PW, Dirx ML, Breedveld S, Fransen D, Levendag PC, Heijmen BJ.

- Toward fully automated multicriterial plan generation: A prospective clinical study. *Int J Radiat Oncol Biol Phys* 2013;85:866-72.
4. McNutt T, Wu B, Moore J, Petit S, Kazhdan M, Taylor R. TH-E-BRCD-02: Automated Treatment Planning Using a Database of Prior Patient Treatment Plans. *Med Phys* 2012;39:4008.
 5. Craft DL, Hong TS, Shih HA, Bortfeld TR. Improved planning time and plan quality through multicriteria optimization for intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2012;82:e83-90.
 6. Craft D, Süß P, Bortfeld T. The tradeoff between treatment plan quality and required number of monitor units in intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;67:1596-605.
 7. Cotrutz C, Lahanas M, Kappas C, Baltas D. A multiobjective gradient-based dose optimization algorithm for external beam conformal radiotherapy. *Phys Med Biol* 2001;46:2161-75.
 8. Yuan L, Ge Y, Lee WR, Yin FF, Kirkpatrick JP, Wu QJ. Quantitative analysis of the factors which affect the interpatient organ-at-risk dose sparing variation in IMRT plans. *Med Phys* 2012;39:6868-78.
 9. Moore KL, Brame RS, Low DA, Mutic S. Experience-based quality control of clinical intensity-modulated radiotherapy planning. *Int J Radiat Oncol Biol Phys* 2011;81:545-51.
 10. Tol JP, Delaney AR, Dahele M, Slotman BJ, Verbakel WF. Evaluation of a knowledge-based planning solution for head and neck cancer. *Int J Radiat Oncol Biol Phys* 2015;91:612-20.
 11. Chang AT, Hung AW, Cheung FW, Lee MC, Chan OS, 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.
 12. Anchineyan P, Amalraj J, Jayaraman P, Krishnan B, Ca M, Balaji B. Assessment of Knowledge based planning model in combination with Multi-Criteria Optimization in HN. *Radiat Oncol J* 2019;141:S33-4.
 13. Pyyry J, Keranen W. Varian APIs: A Handbook for Programming in the Varian Oncology Software Ecosystem. 1.0.; 2018. Available at: <https://varianapis.github.io/VarianApiBook.pdf>. [Last accessed on 2019 May 30].
 14. Thieke C, Küfer KH, Monz M, Scherrer A, Alonso F, Oelfke U, *et al.* A new concept for interactive radiotherapy planning with multicriteria optimization: First clinical evaluation. *Radiother Oncol* 2007;85:292-8.
 15. Yuan L, Wu Q, Sheng Y, Liu J, Benitez A, Yin F, *et al.* SU-E-T-537: Local Multi-Criteria Optimization for Clinical Tradeoff Decision Guidance in RT Planning. *Med Phys* 2015;42:3459.