

# Dosimetric Evaluation of Simplified Knowledge-Based Plan with an Extensive Stepping Validation Approach in Volumetric-Modulated Arc Therapy-Stereotactic Body Radiotherapy for Lung Cancer

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## Abstract

**Purpose:** We investigated the performance of the simplified knowledge-based plans (KBPs) in stereotactic body radiotherapy (SBRT) with volumetric-modulated arc therapy (VMAT) for lung cancer. **Materials and Methods:** For 50 cases who underwent SBRT, only three structures were registered into knowledge-based model: total lung, spinal cord, and planning target volume. We performed single auto-optimization on VMAT plans in two steps: 19 cases used for the model training (closed-loop validation) and 16 new cases outside of training set (open-loop validation) for TrueBeam (TB) and Halcyon (Hal) linacs. The dosimetric parameters were compared between clinical plans (CLPs) and KBPs: CLP<sub>closed</sub>, KBP<sub>closed</sub>-TB and KBP<sub>closed</sub>-Hal in closed-loop validation, CLP<sub>open</sub>, KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal in open-loop validation. **Results:** All organs at risk were comparable between CLPs and KBPs except for contralateral lung: V<sub>5</sub> of KBPs was approximately 3%–7% higher than that of CLPs. V<sub>20</sub> of total lung for KBPs showed comparable to CLPs; CLP<sub>closed</sub> vs. KBP<sub>closed</sub>-TB and CLP<sub>closed</sub> vs. KBP<sub>closed</sub>-Hal: 4.36% ± 2.87% vs. 3.54% ± 1.95% and 4.36 ± 2.87% vs. 3.54% ± 1.94% (*P* = 0.54 and 0.54); CLP<sub>open</sub> vs. KBP<sub>open</sub>-TB and CLP<sub>open</sub> vs. KBP<sub>open</sub>-Hal: 4.18% ± 1.57% vs. 3.55% ± 1.27% and 4.18% ± 1.57% vs. 3.67% ± 1.26% (*P* = 0.19 and 0.27). CI<sub>95</sub> of KBPs with both linacs was superior to that of the CLP in closed-loop validation: CLP<sub>closed</sub> vs. KBP<sub>closed</sub>-TB vs. KBP<sub>closed</sub>-Hal: 1.32% ± 0.12% vs. 1.18% ± 0.09% vs. 1.17% ± 0.06% (*P* < 0.01); and open-loop validation: CLP<sub>open</sub> vs. KBP<sub>open</sub>-TB vs. KBP<sub>open</sub>-Hal: 1.22% ± 0.09% vs. 1.14% ± 0.04% vs. 1.16% ± 0.05% (*P* ≤ 0.01). **Conclusions:** The simplified KBPs with limited number of structures and without planner intervention were clinically acceptable in the dosimetric parameters for lung VMAT-SBRT planning.

**Keywords:** Knowledge-based plan, non-small cell lung cancer, plan quality, stereotactic body radiotherapy

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## INTRODUCTION

Stereotactic body radiotherapy (SBRT) is an effective and noninvasive treatment for early-stage non-small cell lung cancer in patients who are medically inoperable or refuse surgery.<sup>[1]</sup> The local control rate at 3 years exceeds 90% with mild toxicity.<sup>[2-4]</sup> Intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT) can achieve higher conformity and have greater sparing of normal organs than conventional three-dimensional conformal radiotherapy (3D-CRT) with multiple noncoplanar beams.<sup>[5-9]</sup> The use of SBRT with IMRT/VMAT techniques is also well-tolerated and effective for lung tumors.<sup>[4,10]</sup> However,

differences in the skill and experience levels of planners and institutions can cause large variations in IMRT/VMAT plan quality.<sup>[11-13]</sup>

The use of a knowledge-based plan (KBP) can improve the consistency of treatment planning and reduce the variation of plan quality between planners or institutions.<sup>[14]</sup> A KBP

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model is devised to create KBPs based on previously delivered clinical plans (CLPs), including dose distributions and geometric characteristics such as the anatomical features of the target and organs at risk (OARs) and beam arrangement. This model trains the geometric characteristics and associated dose-volume histogram (DVH) of the plans included in the model using the combination of principal component analysis and regression techniques to predict the achievable DVH range for OARs of new patients. This range is produced by the mean estimated DVH  $\pm$  one standard deviation (SD). Then, the KBP model generates dose-volume objectives below the lower boundary of the estimated DVH automatically, and the auto-optimization is performed.

The utility of KBP with IMRT/VMAT has been reported at various treatment regions (e.g., head and neck, breast, prostate, and hepatocellular cancer).<sup>[14-28]</sup> In SBRT of lung cancer, the doses to the lungs and heart can be reduced more in KBPs than CLPs.<sup>[29]</sup> However, some reports have trained KBP models using 9 or 10 structures.<sup>[10,30]</sup> The use of many structures can cause large variations between planners because exact delineation of the same structures by different planners is challenging.<sup>[31]</sup> Thus, simplified KBPs to include only a limited number of structures and generating the plans with a single auto-optimization are crucial for the elimination of large between-planners' variation. The aim of this study was to investigate whether the simplified KBPs could be produced by a single auto-optimization and then used for lung SBRT in the clinical situations. We validated both closed- and open-loop KBP models to verify their usability and employed two different radiotherapy machines to compare their effects on plan quality.

## MATERIALS AND METHODS

This study was approved by the Institutional Review Board (Approval No. 29-133) of the Kindai University Faculty of Medicine, in accordance with the Declaration of Helsinki. The requirement for informed consent was waived for all analyzed patients.

### Clinical plans for training of the knowledge-based plan model

The computed tomography (CT) images and treatment plans of 50 sequential cases in which patients underwent SBRT for lung cancer at our institution between October 2013 and November 2018 were enrolled to train the KBP model. The patients' characteristics are shown in Table 1. The number of CLPs that employed 3D-CRT, IMRT, and VMAT were 9, 16, and 25, respectively. The locations of the lung tumors (e.g., left or right lung, central or peripheral) were not classified in the database. All patients received four-dimensional CT with 10 respiration phases for planning. The internal tumor volume (ITV) was evaluated on CT images in the every phase and delineated. The planning target volume (PTV) was defined as an automatic expansion by 5 mm from the ITV. The OARs of the total lung, ipsilateral lung for tumor, contralateral lung

**Table 1: Patients' characteristics in the training set, closed-loop validation group, and open-loop validation group**

Characteristics	Database ( <i>n</i> =50)	Closed-loop ( <i>n</i> =19)	Open-loop ( <i>n</i> =16)
Age, years			
Median (range)	76 (64-91)	77 (66-91)	78 (64-90)
Gender			
Male	35	9	9
Female	15	10	7
Tumor location			
Right	31	10	12
Upper lobe	10	4	6
Middle lobe	5	1	1
Lower lobe	12	4	5
Resection stump	4	1	0
Left	19	9	4
Upper lobe	12	7	3
Middle lobe	2	1	0
Lower lobe	3	1	1
Resection stump	2	0	0
Stage			
Primary lung cancer			
T1a	4	2	0
T1b	20	9	6
T1c	5	2	4
T2a	7	1	5
T2b	2	2	0
Postoperative recurrence	9	1	0
Metastasis	3	2	1
PTV volume (cm <sup>3</sup> )			
Median	37.2	29.5	31.3
Range	11.2-190.7	12.2-190.7	10.7-97.3

PTV: Planning target volume

for tumor, heart, and esophagus, and planning organ at risk volume (PRV) added to the spinal cord were delineated by experienced radiation oncologists.

The CLPs prescribed 40–52 Gy in 4–5 fractions were mixed in the model; a higher priority assigned to homogeneity between October 2013 and April 2018 and a relatively high acceptable maximum dose to the PTV (up to 140% of the prescribed dose) between May 2018 and February 2020. Therefore, all plans were re-normalized to the prescribed dose of 48 Gy in 4 fractions covering 95% of the PTV using the Eclipse treatment planning system ver. 15.0 (Varian Medical Systems, Palo Alto CA, USA). All CLPs used Varian anisotropic analytical algorithm (AAA) for lung treatment planning clinically. This purpose is to unify the prescribed dose. The most CLPs were created by coplanar technique, and the all KBPs were created by coplanar technique. The CLPs were optimized for the TrueBeam linear accelerator (linac) (Varian Medical Systems, Palo Alto CA, USA), and the KBPs were optimized automatically for the TrueBeam and Halcyon linacs (Varian Medical Systems, Palo Alto CA, USA). The dose distributions in CLPs and KBPs were calculated with

the AAA for the comparison with CLPs to eliminate any effect of the calculation algorithm.<sup>[32]</sup> The KBPs with both the TrueBeam and Halcyon used 6-MV flattening filter free beams. The beam and collimator angles of the CLPs were arranged to decrease the doses to the OARs. In contrast, to eliminate the subjectivity of the planners, the beam angles for the KBPs were determined using two full arcs for the TrueBeam (gantry angles: clockwise [181°–179°] and counterclockwise [179°–181°]; collimator angles: 30° and 330° for each arc) and four full arcs for the Halcyon (gantry angles: clockwise [181°–179°], counterclockwise [179°–181°], clockwise [181°–179°], and counterclockwise [179°–181°]; collimator angles: 281°, 326°, 11°, and 56° for each arc). The irradiation time with 4 arcs for Halcyon is almost equal to that with 2 arcs for the TrueBeam. The dose constraints for the PTV and OARs were based on the previous report, as shown in Table 2.<sup>[33]</sup>

### Closed- and open-loop knowledge-based plan model validations

The closed- and open-loop KBP model validations<sup>[34]</sup> were performed, as shown in Figure 1:

- a. Closed-loop validation: 19 VMAT plans in the database performed between August 2017 and November 2018 were used to generate the KBP. This step aimed to evaluate the ability to reproduce or improve the plans used for model training retrospectively.<sup>[34]</sup> The KBPs calculated with the TrueBeam and Halcyon linacs were denoted as KBP<sub>closed</sub>-TB and KBP<sub>closed</sub>-Hal, respectively
- b. Open-loop validation: 16 VMAT plans performed between January 2019 and February 2020 were enrolled. These were new cases that were not used in the database. This step aimed to test the capability of the KBP model to generate high-quality plans for new patient cases prospectively.<sup>[34]</sup> The KBPs calculated with the TrueBeam and Halcyon linacs were denoted as KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal, respectively.

All KBPs were generated with a single auto-optimization using the KBP model. The patients' characteristics in each group are shown in Table 1. Only three structures were registered into the KBP model: the PTV, the total lung, and the PRV of the spinal cord. The objectives for all OARs were generated automatically [Table 3].

The following parameters were compared between the CLPs and KBPs in the closed- and open-loop validations;

1. Dose to 2% ( $D_{2\%}$ ), 50% ( $D_{50\%}$ ), and 98% ( $D_{98\%}$ ) of the PTV
2. Homogeneity index (HI) defined as the indicators of dose uniformity for the PTV ( $HI = 100 \times [D_{2\%} - D_{98\%}] / D_{50\%}$ )<sup>[35]</sup>
3. Conformity index ( $CI_{95}$ ) defined as the indicators of dose convergence for the PTV ( $CI_{95} = V_{95\%} / V_{PTV}$ )<sup>[36]</sup>
4.  $D_{mean}$  and the volumes receiving 40 Gy ( $V_{40}$ ), 20 Gy ( $V_{20}$ ), 15 Gy ( $V_{15}$ ), and 5 Gy ( $V_5$ ) of the total lung
5.  $D_{mean}$  and the volume receiving 20 Gy ( $V_{20}$ ) and 5 Gy ( $V_5$ ) of the ipsilateral and contralateral lungs
6. Maximum dose ( $D_{max}$ ) to the spinal cord

7. Volume receiving 30 Gy ( $V_{30}$ ) of the heart
8. Volumes receiving 35 Gy ( $V_{35}$ ) and 40 Gy ( $V_{40}$ ) of the esophagus
9. Ratio of the volume of the 50% of prescription isodose curve to PTV ( $R_{50}$ )<sup>[37]</sup>
10. Total monitor units (MU).

### Statistical analysis

Data are reported as mean values ± one SD. The Mann–Whitney U-test was used to make the comparisons between the CLPs and KBPs. Statistical analysis was performed using StatFlex ver. 7 (Artec Inc., Osaka, Japan), and differences were considered statistically significant at  $P < 0.05$ .

## RESULTS

### Closed-loop knowledge-based plan model validation

Table 4 compares the parameters between the CLPs and KBPs in closed-loop validation. The HI of the PTV for the KBP<sub>closed</sub>-Hal was significantly higher than those of the CLP, but there was no significant difference between the KBP<sub>closed</sub>-TB and CLP. The  $CI_{95}$  of the KBP<sub>closed</sub>-TB and KBP<sub>closed</sub>-Hal was significantly lower than that of the CLP. For the OARs, almost all dose-volume parameters

**Table 2: Dosimetric constraints of planning target volume and organs at risk based on Japan clinical oncology group trial 1408**

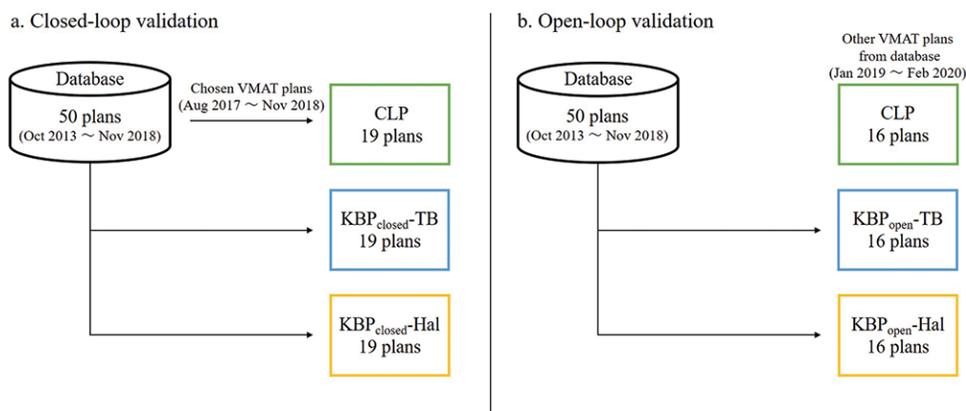
Dose-volume parameter	Constraint
PTV	
$D_{max}$	≤120%-140%
$D_{mean}$	≈ 108%
$D_{min}$	≥94%
Total lung	
$D_{mean}$	≤18 Gy
Volume receiving ≥15 Gy ( $V_{15 Gy}$ )	≤25%
Volume receiving ≥20 Gy ( $V_{20 Gy}$ )	≤20%
Volume receiving ≥40 Gy ( $V_{40 Gy}$ )	≤100 cm <sup>3</sup>
Spinal cord (PRV)	
$D_{max}$	≤25 Gy
Esophagus	
Volume receiving ≥40 Gy ( $V_{40Gy}$ )	≤1 cm <sup>3</sup>
Volume receiving ≥35 Gy ( $V_{35Gy}$ )	≤10 cm <sup>3</sup>
Heart	
Volume receiving ≥30 Gy ( $V_{30Gy}$ )	≤15 cm <sup>3</sup>

PTV: Planning target volume, PRV: Planning organ at risk volume, Dmax: Maximum dose, Dmean: Mean dose, Dmin: Minimum dose

**Table 3: Model objectives and priorities**

Structure	Objective type	Relative volume (%)	Relative dose (%)	Priority
PTV	Upper	0	120	100
	Lower	100	94	100
Total lung–PTV	Line	Generated	Generated	Generated
Spinal cord	Line	Generated	Generated	Generated

PTV: Planning target volume



**Figure 1:** Schema of the validation method. (a) Closed-loop validation based on 19 volumetric-modulated arc therapy plans: clinical plan (CLP) vs. knowledge-based plan using the TrueBeam (KBP<sub>closed</sub>-TB) vs. Halcyon (KBP<sub>closed</sub>-Hal) for the cases enrolled in the database. (b) Open-loop validation based on 16 volumetric-modulated arc therapy plans: CLP vs. knowledge-based plan using the TrueBeam (KBP<sub>open</sub>-TB) vs. Halcyon (KBP<sub>open</sub>-Hal) for the cases not enrolled in the database

**Table 4: Comparison of dose-volume parameters of the planning target volume, lung, spinal cord (PRV), and monitor unit between the clinical plan, knowledge-based plan<sub>closed</sub>-TrueBeam, and knowledge-based plan<sub>closed</sub>-Halcyon**

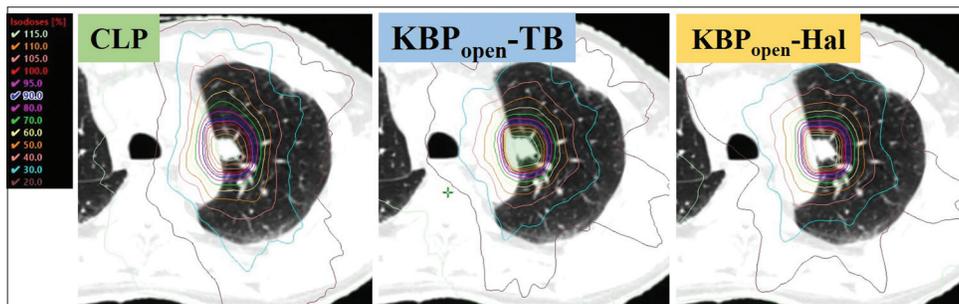
	CLP	KBP <sub>closed</sub> -TB	KBP <sub>closed</sub> -Hal	P		
				CLP vs. KBP <sub>closed</sub> -TB	CLP vs. KBP <sub>closed</sub> -Hal	KBP <sub>closed</sub> -TB vs. KBP <sub>closed</sub> -Hal
<b>PTV</b>						
D <sub>2%</sub> (Gy)	57.01±2.28	58.50±1.51	59.12±1.72	0.08	0.004	0.34
D <sub>50%</sub> (Gy)	51.97±1.02	53.25±0.78	53.87±1.08	<0.001	<0.001	0.02
D <sub>98%</sub> (Gy)	47.39±0.45	47.26±0.45	47.10±0.19	0.01	0.002	0.29
HI	18.49±4.29	21.09±2.83	22.27±3.14	0.07	0.004	0.19
CI <sub>95</sub>	1.32±0.12	1.18±0.09	1.17±0.06	<0.001	<0.001	0.88
<b>Total lung</b>						
D <sub>mean</sub> (Gy)	3.33±1.55	3.31±1.44	3.34±1.43	0.90	0.99	0.93
V <sub>40</sub> (cm <sup>3</sup> )	22.25±15.89	13.64±6.58	13.27±6.27	0.04	0.04	0.98
V <sub>20</sub> (%)	4.36±2.87	3.54±1.95	3.54±1.94	0.54	0.54	0.99
V <sub>15</sub> (%)	6.40±3.97	5.45±2.78	5.68±3.01	0.70	0.87	0.80
V <sub>5</sub> (%)	15.57±7.11	19.41±9.68	19.25±9.39	0.27	0.30	0.88
<b>Ipsilateral lung</b>						
D <sub>mean</sub> (Gy)	5.73±2.68	5.16±2.01	5.23±2.06	0.68	0.74	0.82
V <sub>20</sub> (%)	9.32±6.34	7.36±3.98	7.37±4.05	0.46	0.40	0.99
V <sub>5</sub> (%)	28.94±11.54	28.25±10.56	28.75±10.79	0.77	0.93	0.84
<b>Contralateral lung</b>						
D <sub>mean</sub> (Gy)	1.13±0.65	1.55±0.96	1.53±0.92	0.15	0.13	0.95
V <sub>20</sub> (%)	0.0	0.0	0.0	1	1	1
V <sub>5</sub> (%)	2.43±4.19	10.41±10.81	9.43±10.13	0.002	0.007	0.73
<b>Spinal cord (PRV)</b>						
D <sub>max</sub> (Gy)	11.78±6.45	11.99±3.71	11.62±4.61	0.34	0.90	0.35
<b>Heart</b>						
V <sub>30</sub> (cm <sup>3</sup> )	1.32±4.14	1.61±5.93	1.48±5.39	0.65	0.87	0.99
<b>Esophagus</b>						
V <sub>35</sub> (cm <sup>3</sup> )	0.0	0.0	0.0	1	1	1
V <sub>40</sub> (cm <sup>3</sup> )	0.0	0.0	0.0	1	1	1
R <sub>50</sub>	5.03±0.91	4.31±0.72	4.27±0.66	0.007	0.003	0.95
MU	3067.10±511.80	4285.60±608.97	3295.02±323.71	<0.001	0.18	<0.001

PTV: Planning target volume, PRV: Planning organ at risk volume, MU: Monitor unit, CLP: Clinical plan, KBP: Knowledge-based plan, TB: TrueBeam, Hal: Halcyon, D<sub>mean</sub>: Mean dose, D<sub>max</sub>: Maximum dose

**Table 5: Comparison of dose-volume parameters of the planning target volume, lung, spinal cord (PRV), and monitor unit between the clinical plan, knowledge-based plan<sub>open</sub>-TrueBeam, and knowledge-based plan<sub>open</sub>-Halcyon**

	CLP	KBP <sub>open</sub> -TB	KBP <sub>open</sub> -Hal	P		
				CLP vs. KBP <sub>open</sub> -TB	CLP vs. KBP <sub>open</sub> -Hal	KBP <sub>open</sub> -TB vs. KBP <sub>open</sub> -Hal
PTV						
D <sub>2%</sub> (Gy)	59.63±2.77	58.98±0.93	59.44±1.07	0.34	0.85	0.17
D <sub>50%</sub> (Gy)	52.84±1.20	53.55±0.53	53.83±0.47	0.02	0.007	0.13
D <sub>98%</sub> (Gy)	46.91±0.70	47.21±0.14	47.20±0.12	0.36	0.40	0.82
HI	23.98±5.40	21.96±1.71	22.72±1.97	0.16	0.36	0.24
CI <sub>95</sub>	1.22±0.09	1.14±0.04	1.16±0.05	0.003	0.01	0.56
Total lung						
D <sub>mean</sub> (Gy)	3.08±0.69	3.12±0.66	3.17±0.71	0.75	0.78	0.72
V <sub>40</sub> (cm <sup>3</sup> )	17.70±12.38	13.46±6.75	14.05±6.48	0.22	0.40	0.58
V <sub>20</sub> (%)	4.18±1.57	3.55±1.27	3.67±1.26	0.19	0.27	0.81
V <sub>15</sub> (%)	6.36±2.17	5.73±1.89	5.84±1.86	0.35	0.58	0.65
V <sub>5</sub> (%)	15.03±3.70	17.03±3.43	17.36±3.87	0.09	0.08	0.52
Ipsilateral lung						
D <sub>mean</sub> (Gy)	5.02±1.22	4.72±1.17	4.85±1.19	0.51	0.73	0.66
V <sub>20</sub> (%)	7.81±2.83	6.58±2.23	6.80±2.20	0.17	0.25	0.69
V <sub>5</sub> (%)	26.63±7.27	26.13±7.28	26.61±7.68	0.78	0.99	0.72
Contralateral lung						
D <sub>mean</sub> (Gy)	0.82±0.31	1.23±0.40	1.26±0.39	0.006	0.004	0.76
V <sub>20</sub> (%)	0.0	0.0	0.0	1	1	1
V <sub>5</sub> (%)	1.50±2.32	6.08±5.73	6.33±6.18	0.006	0.005	0.92
Spinal cord (PRV)						
D <sub>max</sub> (Gy)	11.26±5.57	12.19±4.13	12.32±4.51	0.45	0.24	0.75
Heart						
V <sub>30</sub> (cm <sup>3</sup> )	0.0	0.0	0.0	1	1	1
Esophagus						
V <sub>35</sub> (cm <sup>3</sup> )	0.0	0.03±0.11	0.03±0.10	0.35	1	0.99
V <sub>40</sub> (cm <sup>3</sup> )	0.0	0.002±0.01	0.004±0.01	0.35	1	0.99
R <sub>50</sub>	4.79±0.71	4.16±0.53	4.35±0.72	0.008	0.09	0.49
MU	3527.94±655.43	4176.44±466.55	3311.17±290.15	0.003	0.57	<0.001

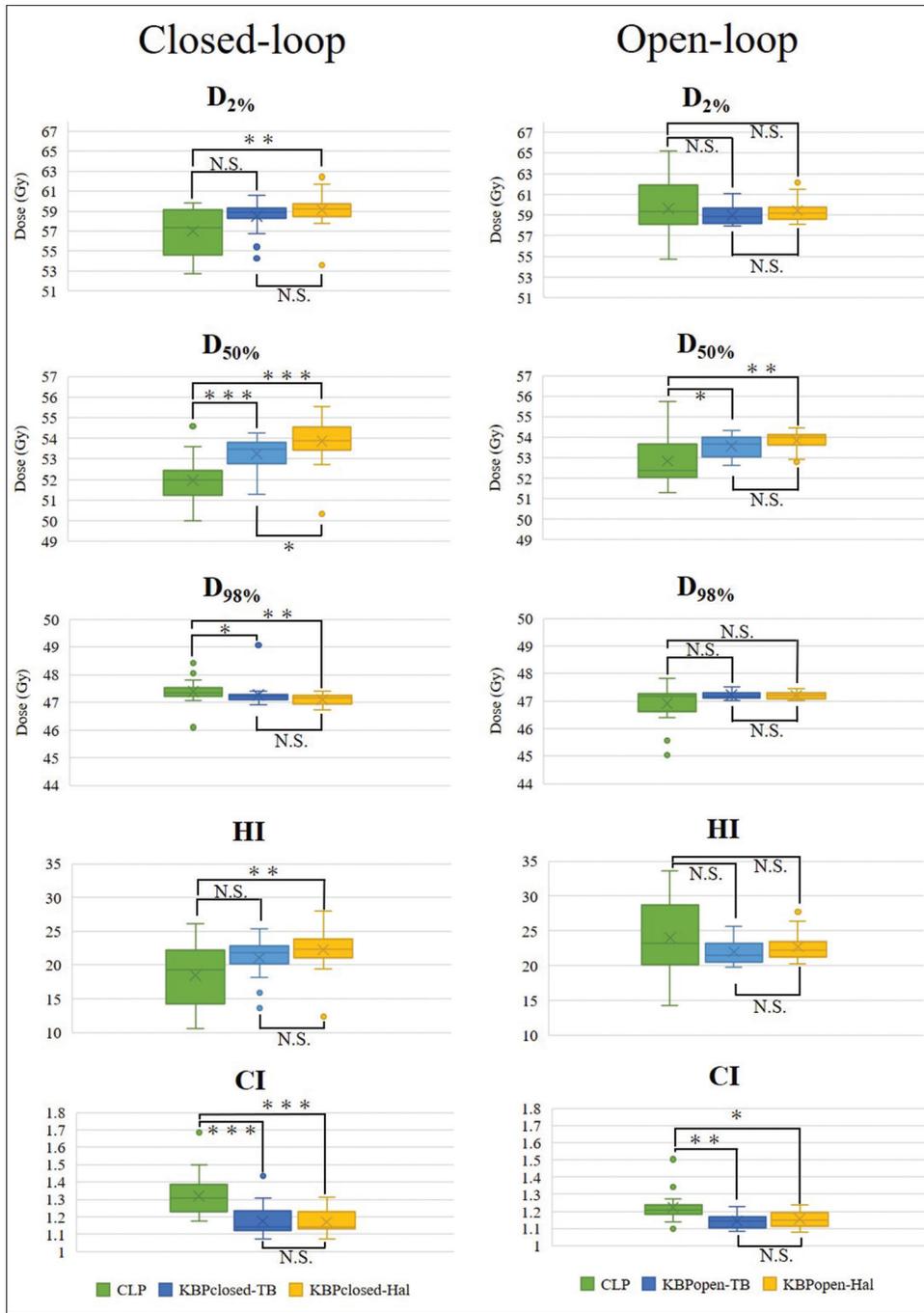
PTV: Planning target volume, PRV: Planning organ at risk volume, MU: Monitor unit, CLP: Clinical plan, KBP: Knowledge-based plan, TB: TrueBeam, Hal: Halcyon, D<sub>mean</sub>: Mean dose, D<sub>max</sub>: Maximum dose



**Figure 2:** Example dose distributions for the clinical plan (CLP) and knowledge-based plans using the TrueBeam and Halcyon in open-loop validation (KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal). Compared with the clinical plans, both the KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal had more extended low-dose distribution but higher conformity to the planning target volume

were comparable between the CLP, KBP<sub>closed</sub>-TB, and KBP<sub>closed</sub>-Hal, whereas the V<sub>5</sub> of the contralateral lung in the both KBP<sub>closed</sub>-TB and KBP<sub>closed</sub>-Hal was higher than those of the CLP. The R<sub>50</sub> of KBP<sub>closed</sub>-TB and KBP<sub>closed</sub>-Hal

was significantly lower than that of the CLP. The MU of the KBP<sub>closed</sub>-TB was significantly higher than that of the CLP, while that of the KBP<sub>closed</sub>-Hal was not significantly different from that of the CLP.



**Figure 3:** Comparisons of dose-volume parameters of the planning target volume between the clinical plans (CLPs) and knowledge-based plans (KBPs) using the TrueBeam and Halcyon in closed- and open-loop validations (KBP<sub>closed</sub>-TB, KBP<sub>closed</sub>-Hal, KBP<sub>open</sub>-TB, and KBP<sub>open</sub>-Hal, respectively). Central line of each box: median line; lower line: first quartile; upper line: third quartile. Whisker ranges do not contain outliers, which are plotted as individual points. N.S.; not significant, \**P* < 0.05, \*\**P* < 0.01, \*\*\**P* < 0.001

**Open-loop knowledge-based plan model validation**

Table 5 compares the parameters between the CLPs and KBPs in open-loop validation. Figure 2 shows the dose distributions of the CLP, KBP<sub>open</sub>-TB, and KBP<sub>open</sub>-Hal for one selected patient. There were no significant differences in the HI of the PTV between the CLP, KBP<sub>open</sub>-TB, and KBP<sub>open</sub>-Hal. The CI<sub>95</sub> of the KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal was significantly lower than that

of the CLP. Most dose-volume parameters of the OARs were comparable between the CLP, KBP<sub>open</sub>-TB, and KBP<sub>open</sub>-Hal, but D<sub>mean</sub> and V<sub>5</sub> of the contralateral lung were higher in both the KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal than that in the CLP (shown in Figure 2 as the extent of the low-dose distribution in both KBPs). In this patient, V<sub>5</sub> of the contralateral lung in the CLP, KBP<sub>open</sub>-TB, and KBP<sub>open</sub>-Hal were 0.6%, 4.8%, and 6.4%, respectively. The CI<sub>95</sub> of the CLP, KBP<sub>open</sub>-TB, and KBP<sub>open</sub>-Hal

were 1.34, 1.16, and 1.19, respectively. The  $R_{50}$  of KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal were significantly lower than that of the CLP. The MU of the KBP<sub>open</sub>-TB was significantly higher than that of the CLP, but there was no significant difference between the KBP<sub>open</sub>-Hal and CLP. A significant difference was observed only in the MU value between KBP<sub>open</sub>-TB and KBP<sub>open</sub>-Hal.

Figure 3 compares the dose-volume parameters of the PTV between the CLPs and KBPs in closed- and open-loop validations. Many dose-volume parameters of the PTV showed significant differences between the CLPs and KBPs in closed-loop validation. The CLPs had significantly lower  $D_{50}$  and higher  $CI_{95}$  than the KBPs had in open-loop validation.

## DISCUSSION

In this study, we investigated whether the simplified KBPs using only three structures and a single auto-optimization could be used clinically to create lung VMAT-SBRT plans. Three structures (the PTV, peripheral lung region of the target, and spinal cord as serial organ) were employed for optimization of the KBPs to control the peripheral dose distribution of the target and decrease the maximum dose to the OARs.<sup>[22]</sup> The simplified KBPs were able to generate comparable plan quality to the CLPs, and the dosimetric parameters showed no major differences between the closed- and open-loop KBP model validations. In addition, the dose distribution with coplanar technique using the simplified KBPs for Halcyon linac could be applied to clinical practice as shown Tables 4 and 5 and Figure 2. The locations of the lung tumors (e.g., left or right lung, central or peripheral) were not classified to simplify the KBP model in this study, although several KBP models have been created to perform classification by the location in some studies.<sup>[10]</sup> The dose distributions of the KBPs were not dependent on the linac for any parameters except for MU. Thus, the simplified KBPs using both radiotherapy machines in both loop validations could generate high-quality plans without any intervention by planners, as SBRT for lung cancer has few complex anatomical characters, such as almost no proximity or overlap between the PTV and OARs.<sup>[13,15]</sup> We clarified that the simplified KBPs may have advantages in cases of treatment plans with few or no overlapping structures. KBP models that do not classify the ipsilateral and contralateral OARs or right and left target separately could be trained and established with little or no overlapping structures in SBRT or other precision treatments. Such simplified KBPs could be used clinically to create lung VMAT-SBRT plans.

The variations of the dose-volume parameters of the PTV in the KBPs produced in closed- and open-loop validation groups were lower than those in the CLPs, and the dose-volume parameters of the KBPs were similar between both validations. The planning policy regarding SBRT for lung cancer was not unified between the CLPs in this model, whereas all KBPs employed the same objective parameters in both validations. This suggests that the simplified KBPs minimized the variation

in VMAT-SBRT plan quality. The HI of the PTV for the KBP<sub>closed</sub>-Hal was significantly higher than those of the CLP; however, there was no significant difference between the KBP<sub>closed</sub>-TB and CLP. The number of arcs could affect the plan quality. The numbers of arcs were 2-arcs and 4-arcs were used for TrueBeam and Halcyon in this study, respectively. Michiels *et al.* described the DVH parameters for the Halcyon with 3 arcs were superior to those for the TrueBeam with 2 arcs significantly.<sup>[38]</sup>

The  $V_5$  of the contralateral lung in the KBPs produced using both closed- and open-loop validations were higher than that of the CLPs because full arc VMAT was employed in the KBPs to eliminate planner subjectivity in the beam arrangement. Previous reports showed that the  $V_5$  of the lungs is unlikely to affect the grade of radiation pneumonitis.<sup>[39,40]</sup>  $V_{20}$  is a more well-known risk factor for symptomatic radiation pneumonitis than  $V_5$ .<sup>[41]</sup> The KBPs generated lower  $V_{20}$  than the CLPs in both the closed- and open-loop validations, although there was no significant difference.  $R_{50}$  is commonly used to evaluate the intermediate-to-low dose spread and dose falloff outside the target. The  $R_{50}$  of the KBPs was superior or comparable to that of the CLPs in closed- and open-loop validations, which indicated the KBPs were enough to suppress the spread of dose distribution.<sup>[37]</sup> Therefore, the simplified KBPs are considered to be applicable clinically even if full arc VMAT is employed.

The MU of the KBPs-TB was significantly higher than that of the CLPs and KBPs-Hal. The difference in the number of arcs (two- and four-arc VMAT for the TrueBeam and Halcyon linacs, respectively) and multi-leaf collimator type between the radiotherapy machines could increase the MU and the complexity of multi-leaf collimator motion. These have been described as the characteristics of KBP in several reports.<sup>[14,42]</sup> On the other hand, the reduced MU ensures plan deliverability.<sup>[43]</sup> Thus, the increase of MU should be noted carefully when using KBP.

The simplified approach of KBP with minimized effects of planners' subjectivity (e.g., limited number of structures, no classification of lung tumor location, single auto-optimization, and full arc VMAT without beam arrangement) is crucial to reduce variation caused by differences in planners' or institutions' skill and experience levels. Snyder *et al.* showed the KBP with a full set of OARs could generate the superior or comparable plan quality to the CLP.<sup>[10]</sup> In this study, the simplified KBP can generate the comparable plans to the CLP without a full set of OARs in the model. This approach is expected to increase the ease of KBP model sharing and standardize plan quality between many institutions, including community medical organizations.

## CONCLUSIONS

In SBRT with full arc VMAT for lung cancer, the proposed simplified KBPs with a single auto-optimization are comparable or better than the corresponding CLPs. The simplified KBPs had low  $V_{20}$  of the total lung without deterioration of the dose

to the PTV. The simplified KBPs can be employed effectively for the clinical use in many institutions because of their low variation of plan quality.

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### Conflicts of interest

There are no conflicts of interest.

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