

# Customization of a Model For Knowledge-Based Planning to Achieve Ideal Dose Distributions in Volume Modulated arc Therapy for Pancreatic Cancers

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## Abstract

**Purpose:** To evaluate customizing a knowledge-based planning (KBP) model using dosimetric analysis for volumetric modulated arc therapy for pancreatic cancer. **Materials and Methods:** The first model (M1) using 56 plans and the second model (M2) using 31 plans were created in the first 7 months of the study. The ratios of volume of both kidneys overlapping the expanded planning target volume to the total volume of both kidneys ( $V_{\text{overlap}}/V_{\text{whole}}$ ) were calculated in all cases to customize M1. Regression lines were derived from  $V_{\text{overlap}}/V_{\text{whole}}$  and mean dose to both kidneys. The third model (M3) was created using 30 plans which data put them below the regression line. For validation, KBP was performed with the three models on 21 patients. **Results:**  $V_{18}$  of the left kidney for M1 plans was 7.3% greater than for clinical plans. Dmean of the left kidney for M2 plans was 2.2% greater than for clinical plans. There was no significant difference between all kidney doses in M3 and clinical plans. Dmean of the left kidney for M2 plans was 2.2% greater than for clinical plans. Dmean to both kidneys did not differ significantly between the three models in validation plans with  $V_{\text{overlap}}/V_{\text{whole}}$  lower than average. In plans with larger than average volumes, the Dmean of validation plans created by M3 was significantly lower for both kidneys by 1.7 and 0.9 Gy than with M1 and M2, respectively. **Conclusions:** Selecting plans to register in a model by analyzing dosimetry and geometry is an effective means of improving the KBP model.

**Keywords:** Dosimetric analysis, Knowledge-based planning, model customization, pancreatic cancers

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## INTRODUCTION

Chemoradiotherapy for pancreatic cancer has contributed to improving treatment outcomes.<sup>[1,2]</sup> Late toxicity after chemoradiotherapy for pancreatic cancer includes radiation-induced nephropathy, which can appear months to years after treatment. Radiation-induced nephropathy is recognized as one of the most important dose-limiting factors. Thus, means of minimizing kidney doses are needed to optimize survival benefits.<sup>[3,4]</sup>

Several automatic planning systems have been developed to improve the planning of intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT).<sup>[5-10]</sup> Known advantages of automatic planning over manual planning include less variability of dose distributions, less time required for treatment planning, and more effective sparing of organs at risk (OAR).<sup>[5-8,11,12]</sup>

The performance of a knowledge-based planning (KBP) system (RapidPlan; Varian Medical Systems, Palo Alto, CA, USA), one type of automatic planning system, depends on library plans (LPs) in the model.<sup>[8-11]</sup> KBP models are built by learning the dosimetry and geometry of the OAR and targets of the LPs.<sup>[5-7]</sup> Several studies have reported that RapidPlans are superior to manual plans regarding sparing OAR and planning time.<sup>[5-8,12,13]</sup>

Given that the ability of KBP to spare OAR depends on LPs in the model, selecting LPs is important in creating models that

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are more effective in reducing OAR dose. Wang *et al.* reported achieving interactive improvement of RapidPlan models for rectal VMAT by closed-loop re-optimization.<sup>[13]</sup> Wu *et al.* reported a method for comparing treatment plans that use overlapping planning target volume (PTV) and OAR volumes to estimate potential OAR's dose volumes.<sup>[14]</sup> However, there is no report to construct the KBP model using the dosimetric analysis focused on the overlapping region of PTV and OAR.

We suggested creating a KBP model reducing specific OAR doses by selecting LPs with dosimetric analysis focused on the overlapping volume with PTV and OAR. The aim of this study was to evaluate a method for creating a KBP model the dosimetric analysis focused on the overlapping regions of PTV and OAR in the abdominal region. This method is enabled to create KBP models reducing specific OAR dose and is important for the improvement of KBP models to reduce doses of specific organs as required by the user.

## MATERIALS AND METHODS

### Participants

This study cohort comprised 77 patients who received VMAT for pancreatic cancer at Osaka International Cancer Institute (OICI) from August 2017 to February 2019. Fifty-six patients who received treatment before August 2018 were used to create a KBP model. The remaining 21 patients who were treated after September 2018 were used for KBP model validation. The Ethics Committee of OICI approved the study (review board number: 19068).

### Computed tomography acquisition

All patients were immobilized with a vacuum pillow in a supine position. Image acquisitions were performed with a Revolution HD computed tomography (CT) scanner (GE Medical Systems, Waukesha, WI, USA). The parameters for image acquisition were 2.5-mm slice thickness,  $512 \times 512$  matrix, and 500-mm field of view. Images were acquired by four-dimensional CT, which was performed using the step-and-shoot scanning technique. The step-and-shoot scanning technique was to acquire scan data in axial cine mode, and upon completion, the couch moved to the next scan position and started acquiring scan data again. During acquisition, the patients were instructed to breathe freely and their respiratory waveforms were recorded using a Real-time Position Management system (Varian Medical Systems). The four-dimensional CT images were loaded into a workstation (Advantage Sim; GE Medical Systems) and 0% phase and 50% phase images, average intensity projection (AIP) images, and maximum intensity projection images were generated from 10 respiratory-phase images.

### Contouring

The target volume and OAR were delineated on AIP using the Eclipse treatment planning system (Varian Medical Systems) by radiation oncologists at the OICI institute. The gross pancreatic tumor volume was delineated. The clinical

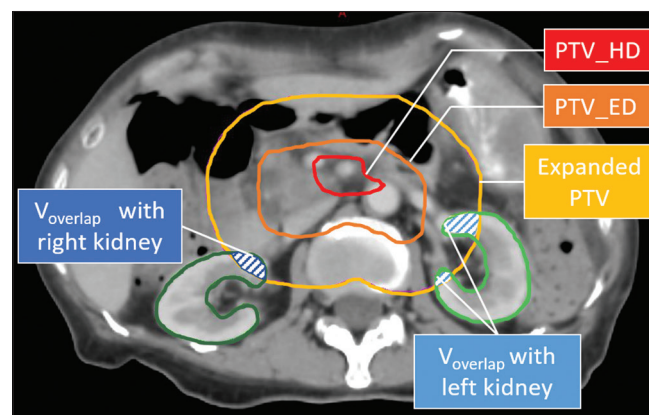
target volume high dose area (CTV\_HD) consisted of the retroperitoneal soft tissue and surrounding regional nodal areas, including the para-aortic region, with a 3 mm margin. The CTV elective dose (ED) area consisted of the primary pancreatic tumor site with a 5–10 mm margin and the CTV\_HD. To define the internal target volume HD area, both CTV\_HDs contoured on 0% and 50% phase images were combined. The internal target volume ED area was defined similarly. Also, the PTV HD area was defined as the area with a 3 mm margin in the internal target volume HD area. A PTV ED area with an omnidirectional 5 mm margin from the internal target volume ED area was then created. The ratio of an OARs' volume that overlapped the volume created with a 2 cm margin from the PTV\_ED to the whole organ volume ( $V_{\text{overlap}}/V_{\text{whole}}$ ) was used as an indicator of the relationship between distance and position of PTV\_ED and OAR. The size of the margin to be expanded from PTV\_ED was determined to enable the expanded PTV to overlap both kidneys in all cases. Figure 1 indicates the relationship between PTV, kidneys, and  $V_{\text{overlap}}$  with the kidney.

### Beam setting

Treatment planning was performed with a Varian Truebeam STx (Varian Medical Systems) linear accelerator equipped with a high definition 120 Multileaf Collimator. VMAT plans used 6-MV photon with a maximum available dose rate of 600 MU/minute. VMAT plans were based on two arcs each at  $179^\circ$ – $181^\circ$  clockwise,  $270^\circ$ – $90^\circ$  counterclockwise. The collimator angles were set to  $340^\circ$ ,  $20^\circ$  for each arc. The plans aimed to deliver 47.5 Gy to 95% of PTV\_ED and 60 Gy to a mean dose of PTV\_HD for prescription dose in 25 fractions.

### Optimization

Optimization for VMAT was performed in Eclipse systems. Photon optimization ver. 13.0 was used with 2.5 mm grid

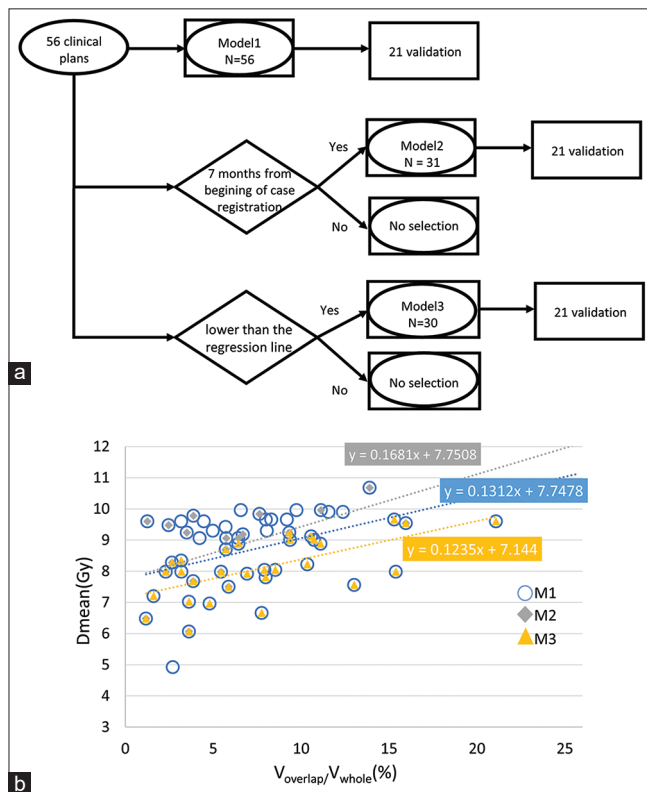


**Figure 1:** The relationship between planning target volume high dose area, planning target volume elective dose area, kidneys, and kidneys' volume that  $V_{\text{overlap}}$  (i.e., overlapped the volume created with a 2 cm margin from the planning target volume high dose). The contour lines of Red, orange, yellow, dark green and light green represent planning target volume\_high dose, planning target volume\_elective dose, expanded planning target volume with 2cm margin from planning target volume\_elective dose, right and left kidneys, respectively. The areas of blue and sky blue stripes represent  $V_{\text{overlap}}$  with right and left kidneys, respectively

size and followed by dose calculation using the Anisotropic Analytical Algorithm ver. 13.7 (Varian Medical Systems). The clinical plans were subjected to multiple optimizations to achieve dose constraints. OAR dose-volume limitations required that the mean dose (Dmean) to each kidney was 10% or less and  $V_{18}$  (i.e., volume ratio that receives a dose exceeding 18 Gy) was 25% or less.  $V_{50}$  (i.e., volumes receiving at least 50 Gy) and maximum dose for the gastrointestinal tracts (e.g., stomach, duodenum, bowel) were 15cc or less and 57 Gy or less, respectively. The maximum dose for the spinal cord was 45 Gy or less.

### Modeling for RapidPlan

The KBP modeling was performed with 56 plans. The procedure for selecting plans by the three models for these 56 plans is shown in Figure 2a. The first model ( $M_1$ ) was created from all 56 plans. The second model ( $M_2$ ) was from the 31 plans treated in the first 7 months of the study. The third model ( $M_3$ ) was created from 30 optimal plans chosen from the 56 plans and included dosimetric analysis of both kidneys. The means for selecting plans for each model were as follows. First, the relationship between doses to both kidneys and  $V_{overlap}/V_{whole}$  was drawn for the 56 plans [Figure 2b] and those that fell below



**Figure 2:** Flow chart showing the procedure for selecting plans for knowledge-based planning models for training and verification (a). The regression line indicates the relationship between Dmean (i.e., average dose received by target) of both kidneys and  $V_{overlap}/V_{whole}$  (i.e., ratio of an organ's volume that overlaps with the volume created by a 2 cm margin from planning target volume\_elective dose to the whole organ volume) (b). Blue circles, gray diamonds and yellow triangles represent M1, M2 and M3, respectively. Blue, gray and yellow dotted lines indicate the regression lines of M1, M2 and M3, respectively

the M2 regression line were allocated to  $M_3$ . One plan that fell far below was excluded. Tables 1 and 2 show  $V_{overlap}/V_{whole}$  and dosimetric parameters in LPs for each model.

### Creating validation plan

The performances of all three models were tested on the 21 validation cases, a single optimization being performed. Validation planning was performed with the same beam setting as in the treatment planning. The clinical plans and the three model plans were all compared. Upper and lower objectives were added to make the PTV dose equal to that of the clinical plans. OARs were added as line objectives. Upper objectives were added at 57 and 45Gy to reduce maximum doses for all gastrointestinal tract and spinal cord.

### Data analysis

Several dose parameters for PTV and OAR of clinical plans and the three model plans were evaluated. In the PTV<sub>HD</sub> and PTV<sub>ED</sub>,  $D_{95}$  and  $D_2$  (i.e., the doses received by 95% and 2% of the volume) were compared. The conformity and homogeneity of each plan were evaluated, the target conformity index (CI<sub>PTV<sub>HD</sub></sub> and CI<sub>PTV<sub>ED</sub></sub>) and the target homogeneity index (HI<sub>PTV<sub>HD</sub></sub> and HI<sub>PTV<sub>ED</sub></sub>) being defined as below.

$$CI = V_{95\%} / PTV \text{ volume}$$

( $V_{95\%}$  = volume of the isodose of 95% of the prescribed dose)

$$HI = D_{2\%} / D_{98\%}$$

( $D_{2\%}$  = minimum dose to 2% of the PTV,  $D_{98\%}$  = minimum dose to 98% of the PTV)

In OAR  $V_{50}$  (i.e., the volume receiving at least 50 Gy), and  $D_2$  (i.e., the dose received by 2% of the volume) for gastrointestinal tract (e.g., stomach, duodenum, bowel), Dmean and  $V_{18}$  (i.e., volume receiving at least 18 Gy) for each kidney, and  $D_1$  (i.e., the dose received by 1% of the volume) for the spinal cord were extracted.

### Statistical analysis

All statistical analyses were performed using the SPSS 8.0 software package (SPSS, Inc., Chicago, IL, USA). In analysis among model and clinical plans with validation cases, the paired Wilcoxon signed-rank test was used to calculate and evaluate the differences in dosimetric parameters.

## RESULTS

Table 3 summarizes selected dosimetric parameters for the PTV and the OAR in the clinical and validation plans with each model. In PTV<sub>60</sub>,  $D_2$  was significantly different between M3 plans and clinical plans ( $P < 0.05$ ), although the differences were small. The other parameters for PTV<sub>60</sub> did not differ between the clinical and model plans ( $P > 0.201$ ). In PTV<sub>50</sub>,  $D_{95}$  were 1.5%, 1.4%, and 1.2% significantly higher on average in the M1, M2, and M3 plans, respectively, than in the clinical plans ( $P < 0.01$ ).  $CI_{95}$  were significantly different between M2, M3 plans and clinical plans ( $P < 0.05$  and  $P < 0.01$ ), and

**Table 1: Total volume and volume of indicated organs overlapping with expansion of the total volume by a 2 cm margin from the planning target volume for elective dose area (planning target volume elective dose area) to the whole organs (ratio of an organ's volume that overlaps with the volume created by a 2 cm margin from planning target volume for elective dose to the whole organ volume) for registered cases in models 1, 2, and 3**

	Volume type	Volume		
		Model 1	Model 2	Model 3
Left kidney	Total (cm <sup>3</sup> )	151.7±42.2	154.7±42.5	148.9±38.1
	Overlap (%)	13.2±7.4	11.9±7.0	13.2±6.8
Right kidney	Total (cm <sup>3</sup> )	145.5±40.4	147.9±40.4	145.0±35.1
	Overlap (%)	2.8±4.6	3.3±5.4	2.0±3.0
Both kidneys	Total (cm <sup>3</sup> )	300.1±81.3	305.4±81.6	293.9±71.2
	Overlap (%)	8.1±5.1	7.7±5.3	8.3±5.0
Duodenum	Total (cm <sup>3</sup> )	78.4±25.6	72.8±27.4	74.2±28.1
	Overlap (%)	67.9±22.8	67.2±22.7	61.5±21.5
Stomach	Total (cm <sup>3</sup> )	253.6±92.2	242.8±98.4	237.5±88.0
	Overlap (%)	25.6±15.9	24.2±13.7	26.2±14.7
Bowel	Total (cm <sup>3</sup> )	664±360.9	671.6±377.9	641.7±333.8
	Overlap (%)	18.7±12.0	18.1±12.4	21.5±10.9
Spinal cord	Total (cm <sup>3</sup> )	30.0±11.4	21.4±10.7	23.0±11.3
	Overlap (%)	0.09±0.4	0.04±0.1	0.2±0.7

**Table 2: Dosimetric comparison of models 1, 2, and 3**

Structures	DP	Mean±SD		
		Model 1	Model 2	Model 3
PTV <sub>60</sub>	D <sub>2</sub>	104.2±0.7	104.0±0.7	104.0±0.6
	D <sub>98</sub>	91.6±1.2	91.7±1.2	91.8±1.1
	D <sub>95</sub>	93.7±0.6	93.8±0.7	93.8±0.5
PTV <sub>50</sub>	D <sub>2</sub>	103.5±0.7	103.3±0.6	103.1±0.5
	D <sub>98</sub>	76.1±1.5	76.3±1.4	76.0±1.1
	D <sub>95</sub>	79.1±1.1	79.1±1.0	78.9±0.9
Left kidney	D <sub>mean</sub>	10.5±1.5	10.1±1.6	9.8±1.4
	V <sub>18</sub>	15.6±5.2	16.4±5.3	15.5±5.1
Right kidney	D <sub>mean</sub>	6.6±4.7	7.1±1.8	6.3±1.5
	V <sub>18</sub>	6.6±4.7	7.0±5.4	5.7±4.0
Both kidneys	D <sub>mean</sub>	8.8±1.2	8.4±1.7	8.0±1.0
	V <sub>18</sub>	11.5±3.7	12.1±3.9	10.8±3.4
Duodenum	V <sub>50</sub>	5.1±3.5	5.1±3.6	4.1±3.9
	D <sub>2</sub>	50.3±3.5	49.9±4.1	50.2±2.3
Stomach	V <sub>50</sub>	0.8±1.1	0.6±1.1	1.4±1.8
	D <sub>2</sub>	37.7±10.7	36.8±11.0	40.3±8.0
Bowel	V <sub>50</sub>	2.7±3.7	1.9±2.4	3.0±3.3
	D <sub>2</sub>	38.9±6.5	38.0±6.2	40.4±7.2
Spinal cord	D <sub>1</sub>	25.9±4.0	25.4±6.5	23.8±5.1

DP: Dosimetric parameter, SD: Standard deviation, PTV: Planning target volume, D<sub>2</sub>: Doses expressed in grays to 2% of the volume (%), D<sub>98</sub>: Doses expressed in grays to 98% of the volume (%), D<sub>95</sub>: Doses expressed in grays to 95% of the volume (%), D<sub>mean</sub>: Mean dose in gray, V<sub>18</sub>: Volume ratio that receives a dose exceeding 18 Gy (%), V<sub>50</sub>: Volume that receives a dose exceeding 50 Gy (cm<sup>3</sup>), D<sub>1</sub>: Doses expressed in grays to 1% of the volume

HI were significantly different between M1, M2 plans, and clinical plans ( $P < 0.05$  and  $P < 0.01$ ), although the differences were small. There were no differences in average other PTV<sub>50</sub> parameters between the clinical plans and any of the model plans.

As shown in Table 3, all kidney doses did not differ significantly between the clinical and M3 plans ( $P > 0.082$ ). Dmean to the left kidney was 2.2% significantly higher for M2 plans than for clinical plans ( $P < 0.05$ ). V<sub>18</sub> of the left kidney was 7.3% significantly higher for M1 plans than for clinical plans ( $P < 0.05$ ). There were no significant differences between the validation plans in dosimetric parameters for gastrointestinal organs such as stomach, duodenum, and bowel ( $P > 0.136$ ). D<sub>1</sub> to the spinal cord was significantly lower with M1, M2, and M3 plans than with clinical plans, the mean differences being of 8.8, 6.7, and 7.2 Gy, respectively ( $P < 0.01$ ).

Figure 3 shows the relationship between  $V_{\text{overlap}}/V_{\text{whole}}$  and Dmean for both kidneys in the validation and LPs for each model. The dotted lines represent regression lines between Dmean and  $V_{\text{overlap}}/V_{\text{whole}}$  for both kidneys. The slopes represent the rate of change in OAR dose per unit  $V_{\text{overlap}}/V_{\text{whole}}$  in each KBP model. Thus, smaller values were superior at sparing the OAR dose per unit  $V_{\text{overlap}}/V_{\text{whole}}$ . The slopes for LPs were 0.13, 0.25, and 0.12 for M1, M2, and M3, respectively, and the slopes for the validation plans were 0.13, 0.15, and 0.08, respectively. The smaller the slope for LPs, the more Dmean for both kidneys for the validation plans dose was reduced. In the LPs and validation plans, M3 has the smallest slope of all models.

Figure 4 is a box plot of Dmeans for both kidneys in each model. The validation patients ( $n = 21$ ) were categorized into two groups based on overlap volume (one group of 10 and the other of 11 patients). One of these groups (Group A), as shown in part (a), had smaller than average volume, whereas the other (Group B), as shown in part (b), had greater than average volume. Dmeans of both kidneys were not significantly different than average doses in group A ( $P = 0.33$  and  $P = 0.24$ ). In Group B, Dmeans of both kidneys were

**Table 3: Dosimetric comparison of clinical and validation models (models 1, 2, and 3)**

Structures	DP	Mean±SD				P value versus clinical		
		Clinical	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
PTV <sub>60</sub>	D <sub>2</sub>	104.1±0.5	104.2±0.6	104.1±0.5	104.4±0.5	0.230	0.357	<0.05
	D <sub>95</sub>	93.1±2.2	93.6±0.5	93.6±0.6	93.3±0.8	0.522	0.408	0.778
	CI <sub>95</sub>	1.0±0.0	1.0±0.1	1.0±0.1	1.0±0.1	0.852	0.848	0.422
	HI	1.2±0.1	1.1±0.0	1.1±0.0	1.1±0.0	0.931	0.543	0.332
PTV <sub>50</sub>	D <sub>2</sub>	103.5±0.8	103.3±0.6	103.3±0.6	103.8±0.4	0.848	0.170	0.063
	D <sub>95</sub>	78.5±1.1	79.9±0.8	80.0±0.8	79.7±0.7	<0.01	<0.01	<0.01
	CI <sub>95</sub>	1.1±0.0	1.1±0.1	1.1±0.2	1.1±0.1	<0.01	0.259	<0.01
	HI	1.4±0.1	1.3±0.0	1.3±0.0	1.4±0.0	<0.05	<0.01	0.149
Left kidney	D <sub>mean</sub>	9.5±2.3	10.5±2.7	11.7±3.5	9.4±2.1	0.274	<0.05	0.614
	V <sub>18</sub>	14.2±7.7	21.5±10.1	19.6±12.5	16.1±8.6	<0.05	0.173	0.626
Right kidney	D <sub>mean</sub>	6.5±2.3	6.1±1.2	6.4±1.1	6.0±1.1	0.556	0.321	0.339
	V <sub>18</sub>	4.9±5.1	3.3±2.5	2.6±2.8	2.7±3.1	0.532	0.097	0.082
Both kidneys	D <sub>mean</sub>	7.9±1.5	8.3±1.4	8.8±1.7	7.7±0.9	0.414	0.274	0.274
	V <sub>18</sub>	10.2±4.7	13.3±4.7	10.7±5.9	10.4±4.6	0.065	0.955	0.808
Duodenum	V <sub>50</sub>	3.8±2.6	6.4±6.5	4.9±3.6	6.7±6.7	0.469	0.421	0.212
	D <sub>2</sub>	48.6±4.8	49.2±5.9	49.2±5.9	49.3±5.9	0.421	0.398	0.136
Stomach	V <sub>50</sub>	1.4±2.4	1.7±3.0	1.6±2.5	1.7±2.6	0.778	0.535	0.702
	D <sub>2</sub>	37.9±11.1	38.1±12.0	38.0±11.9	37.6±12.2	0.821	0.754	0.768
Bowel	V <sub>50</sub>	4.5±5.3	5.8±6.3	5.6±6.1	5.8±6.1	0.455	0.639	0.689
	D <sub>2</sub>	40.7±5.8	41.1±6.9	40.9±7.1	41.3±7.0	0.808	0.876	0.808
Spinal cord	D <sub>1</sub>	27.3±4.0	18.5±2.3	20.6±3.6	20.1±2.5	<0.01	<0.01	<0.01

DP: Dosimetric parameter, SD: Standard deviation, PTV: Planning target volume, D<sub>2</sub>: Doses expressed in grays to 2% of the volume, D<sub>98</sub>: Doses expressed in grays to 98% of the volume, D<sub>95</sub>: Doses expressed in grays to 95% of the volume, HI: Homogeneity index, CI: Conformity index, D<sub>mean</sub>: Mean dose, V<sub>18</sub>: Volume ratio that receives a dose exceeding 18 Gy, V<sub>50</sub>: Volume that receives a dose exceeding 50 Gy, D<sub>1</sub>: Doses expressed in grays to 1% of the volume

significantly lower, by 0.9 and 1.7 Gy, for M3 than for M1 and M2, respectively ( $P < 0.05$  and  $P < 0.01$ ).

## DISCUSSION

The spatial configuration of the OARs relative to the target determines to a large extent the dose distribution of the OARs. The relationship between overlap volume and organ dose has been reported in several papers.<sup>[6,14,15]</sup> This maenad that it was easy to spare the OAR dose when the overlap volume was small, while it was difficult to spare the OAR dose when the overlap volume was large. However, the overlap volume was not meaningful when the OAR and PTV did not overlap. In the cases used in this study, the PTV and both kidneys often did not overlap. We deliberately created an overlap volume with OAR by extending the PTV and determined the relationship between PTV and positions and doses of OARs. To the best of our knowledge, in no other published study has a model based on this relationship with overlap volume been constructed; the present study is therefore novel in this respect. This enables the selection of LPs according to the user’s intention and is thus an important means for promoting more widespread use of KBP.

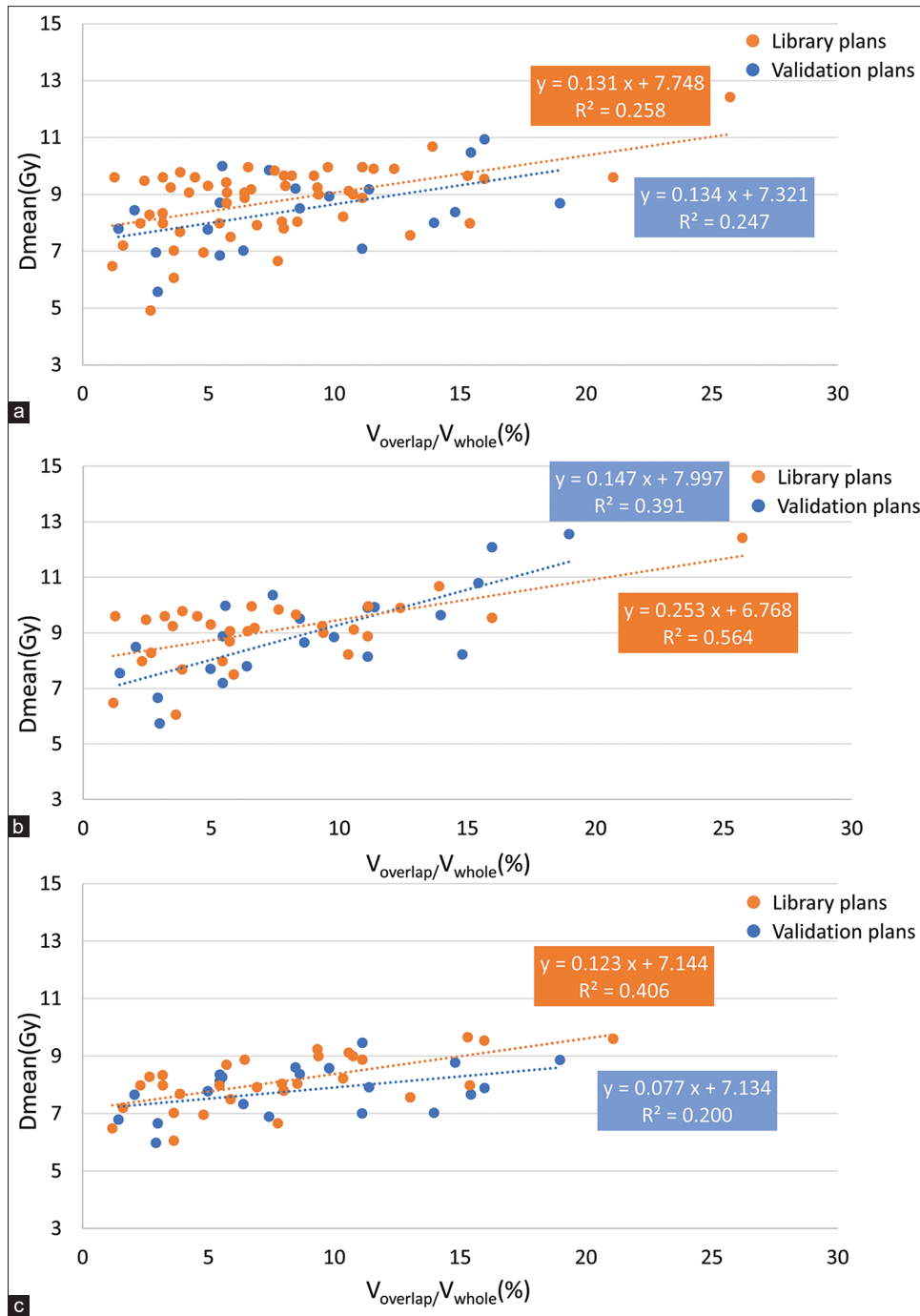
The average dose and V<sub>20</sub> for both kidneys should be less than 18 Gy and 32%, respectively.<sup>[4,16]</sup> The risk of radiotherapy-associated renal injury depends largely on the dose delivered to the volume of each kidney.<sup>[3,4,17]</sup> Therefore, creating a plan to reduce kidney dose is important for reducing renal toxicity. The model created by the method

we here propose was the most capable of the three models of reducing the dose to both kidneys and is therefore the method of selecting LPs for creating a model that delivers minimal doses to both kidneys.

We now treated 77 patients since starting pancreas VMAT. In the early stages of its implementation, kidney doses were not sufficiently smaller than later clinical plans because the planner was not experienced in planning pancreas VMAT. Batumalai *et al.* reported that dosimetrists who were experienced in planning IMRT produced better IMRT plans than dosimetrists who were less experienced.<sup>[18]</sup> Therefore, the M1 and M2 plans included plans with insufficiently low kidney doses and thus had higher average kidney doses than did the clinical plans for validation.

Although M3 initially was created 20 selecting plans, which was the minimum number of plans required for the RapidPlan model, M3 created validation plans that failed to achieve the dose constraint in several cases. This problem was resolved by increasing the number of LPs. The manufacturer’s specialist suggested that more LPs would help to create a more robust model.<sup>[19]</sup> In addition, Zhang *et al.* reported that a minimum of 30 plans was needed to predict DVH of OAR, and hence M3 consisted of 30 selecting plans.<sup>[20]</sup>

Wang *et al.* have proposed a method for creating a better model through a closed-loop evolution process.<sup>[13]</sup> However, the doses delivered by plans created using their model cannot be predicted. M3, which had the lowest slope of the

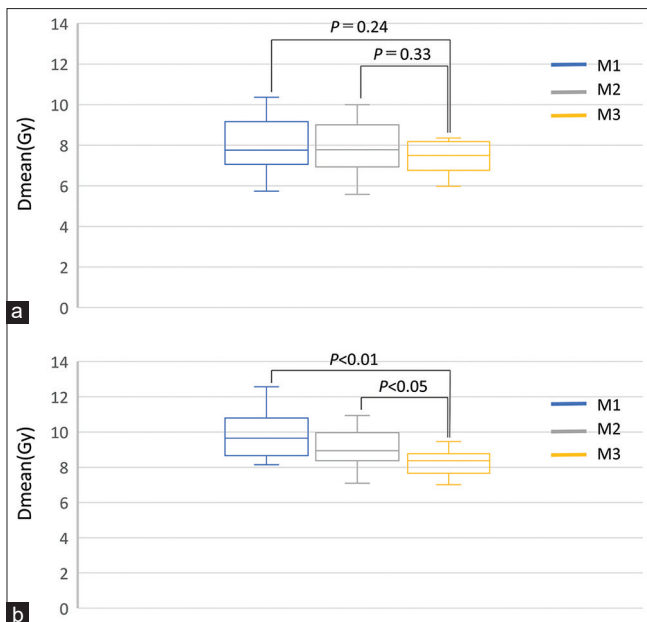


**Figure 3:** The relationships between Dmean (i.e., average dose received by the target) of both kidneys and  $V_{\text{overlap}}/V_{\text{whole}}$  (i.e., ratio of an organ’s volume that overlaps with the volume created by a 2 cm margin from planning target volume\_elective dose to the whole organ volume) in M1, M2 and M3 are shown in parts (a-c), respectively, of this figure. The blue and orange points represent the validation plans and library plans, respectively. Blue and orange dotted lines indicate the regression lines of validation and library plans, respectively

three models, was most successful at reducing kidney doses in the validation plans. We have shown that the ability of our method to reduce the dose of a specific organ can be expressed as a slope, making it possible to customize a model that is capable of reducing the dose to a specific organ.

The method that we here propose requires dose analysis and is laborious. However, information on PTVs and organs

registered in the model is systematically recorded. Model analysis using the website that we used in this study (<https://ModelAnalytics.varian.com>) makes it easy to assess the relationship between dose and organ location.<sup>[15,21]</sup> Another means of managing doses by analyzing dosimetric parameters in LPs is to use a database.<sup>[22]</sup> Our findings indicate the importance of plans being registered in a model and that it is important to perform dose management when creating a



**Figure 4:** Boxplots showing the Dmean (i.e., average dose received at target) of both kidneys. The plots show the group mean of  $V_{\text{overlap}}/V_{\text{whole}}$  (i.e., ratio of an organ's volume that overlaps with the volume created by a 2 cm margin from planning target volume\_elective dose to the whole organ volume). Blue, gray, and yellow lines represent M1, M2, and M3, respectively. In the Group A ( $n = 10$ ) as shown in part (a),  $V_{\text{overlap}}/V_{\text{whole}}$  is 8.1% below average volume, whereas in the Group B ( $n = 11$ ) as shown in part (b),  $V_{\text{overlap}}/V_{\text{whole}}$  is 8.1% larger than the average volume. Each error bar represents the min and max

model to enable optimal selection of the plans to register in the model.

## CONCLUSIONS

Selecting plans to register in a model by analyzing the doses to and locations of specific organs is an effective means of constructing a model that reduces doses to specific organs as required by the user.

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## Conflicts of interest

There are no conflicts of interest.

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