University of Miami Miller School of Medicine, Prostate with Lymph Nodes RapidPlan PT Model Description

Created at Sylvester Comprehensive Cancer Center

Note: *The University of Miami does not take any responsibility for improper use of their RapidPlanPT models. RapidPlanPT knowledge-based planning and its models are not intended to replace clinical decisions, provide medical advice, or endorse any particular radiation plan or treatment procedure. The patient's medical professionals are solely responsible for and must rely on their professional clinical judgment when deciding how to plan and provide radiation therapy. You should validate every DVH estimation model before implementing it clinically.*

Purpose:

This document describes the context in which the SCCC Prostate (or Prostate bed) with Pelvic Lymph Nodes RapidPlanPT model should be used, as well as how the model was configured and validated.

The SCCC Prostate with Lymph Nodes RapidPlanPT model was created by the Radiation Oncology Department, University of Miami Miller School of Medicine at Sylvester Comprehensive Cancer Center. This model is designed to be used for intensity modulated proton treatment (IMPT) plans with two to three Clinical Target Volumes (CTVs) and optional Gross Tumor Volumes (GTVs) for boost. The model also includes prostate bed plans for patients who have undergone prostatectomy. CTV_Prostate is the prostate + proximal seminal vesicles or prostate bed.

The second CTV (CTV_LN) will consist of the pelvic lymph nodes. The third optional CTV (CTV SVs Dist) is the distal seminal vesicles. The optional boost GTV (GTVp) can be either the primary lesion or nodule included in the CTV_Prostate or CTV LN. The model estimates DVHs for all targets (GTVp, CTV_Prostate and CTV LNs), as well as surrounding OARs including rectum (anus and rectum combined), bladder, bowel, cauda equina, each femoral head, both kidneys, penile bulb, and spinal cord.

The SCCC Prostate with Lymph Nodes RapidPlanPT model is intended to be used for DVH estimates of prostate with lymph nodes treatments. The model is ideal for treating prostate with pelvic lymph nodes to two different dose prescriptions. For example, this model would be ideal for treating CTV_Prostate to 80 Gy in 40 fractions and treating CTV_LNs to 56 Gy in 40 fractions, with simultaneously treating GTVp to 86 Gy in 40 fractions.

Target and OAR contouring guidelines:

The SCCC Prostate (or Prostate bed) with Lymph Nodes RapidPlanPT model was created using the following contouring guidelines. Model performance may vary depending on institutional guidelines for contouring and planning. The model should be validated with your institutions' contouring and planning guidelines.

CTV/ Control structure contouring guidelines:

CTV_Prostate	Prostate + proximal seminal vesicles, or prostate bed for post prostatectomy patient
CTV LN:	CTV_LNs are composed of only the pelvic lymph node vessels including the lymph nodes.
GTVp	Primary lesion in prostate or lymph nodule
OV_LN	CTV LN + CTV SVs Dist (when necessary) cropped away from higher dose CTVs or GTV, using a 5% dose fall off per mm rule of thumb estimate.
OV_Prostate	CTV_Prostate cropped away from higher dose CTVs or GTVs, using a 5% dose fall off per mm rule of thumb estimate.
Ring_Bst	Outer wall margin of 1cm and an inner wall margin of 0cm from GTVp, and crop away lower dose rings 1cm from higher dose target volumes.
Ring_LN	Outer wall margin of 1cm and an inner wall margin of 0cm from CTV LN, and crop away lower dose rings 1cm from higher dose target volumes.
Ring_Prostate	Outer wall margin of 1cm and an inner wall margin of 0cm from CTV_Prostate, and crop away lower dose rings 1cm from higher dose target volumes.

OAR Contouring Guidelines:

Rectum: Anus plus rectum. The anus is entire rectum from bottom of ischial tuberosities to 15 cm superiorly or to rectosigmoid junction. The rectum is entire contents from 3 cm superior to ischial tuberosities to sigmoid flexure.

Bladder: Bladder wall and lumen.

Bowel[2]: Volume in which the small and large bowel may occupy are outlined by abdominal wall anteriorly, pelvic sidewalls laterally (excluding the pelvic lymph node regions), superiorly to one slice above last axial CT image on which the lymph nodes are outlined, and inferiorly from the

top level of the CTV, and posteriorly extended to in front of sacrum, abutting anterior presacral nodal contours.

Femoral Heads: Each femoral head should be contoured superiorly to the top of the ball of the femur including the trochanters through the lesser trochanter.

For other OAR structures contouring guidelines, please refer to RTOG 0534[2].

Treatment planning guidelines:

70 patients treated to prostate (or prostate bed) and pelvic lymph nodes with IMPT technique were. All cases used to train and validate this model were planned using head-first supine position IMPT technique. The number of fields used varied from three to four depending upon each patient. Multi-field optimization (MFO) was used. For each field, a field-specific target encompassing all CTVs was created. IMPT plans were generated using robust optimization to the clinical target volume (CTV) but not to gross tumor volume (GTV). Planners generally only add robust objectives to targets but may opt to add robustness on critical organ-at-risk (OARs). For CTVs, 3mm or 5mm setup uncertainties in all directions coupled with proton range uncertainties of ±3.5% are used resulting in 12 uncertainty scenarios.

The following dose prescription and planning guidelines below were used to train and to validate the SCCC Prostate (or Prostate Bed) with pelvic Lymph Nodes model.

Prostate with pelvic lymph nodes:

Treatment strategy: CTV includes prostate + seminal vesicles and pelvic lymph nodes with optional GTV boost in 40 fractions.

Commonly used prescription for

GTVp (optional):	86Gy or 88Gy for primary prostate lesion GTV, and 72Gy, 74Gy or 76Gy for lymph nodule GTV
CTV_Prostate:	80Gy
CTV SV Dist:	56Gy
CTV LN:	56Gy

Other specific prescriptions:
For one patient, 65Gy to lymph nodule GTVp, 70.2Gy to prostate, and 46.8Gy to CTV LN and CTV SV Dist in 26 fractions

For one patient, 74.1Gy to primary prostate lesion GTVp, 70.2Gy to prostate, and 49.4Gy to CTV LN and CTV SV Dist in 26 fractions

Target coverage constraints for CTV

Nominal plan:	100% dose covers 95% of target volume.
The worst-case scenario:	95% dose covers 95% of target volume.

Target coverage constraints for GTVp

Nominal plan: 100% dose covers 95% of target volume.

Prostate bed with pelvic lymph nodes:

Treatment strategy: CTV includes prostate bed and pelvic lymph nodes with optional GTV boost in 34 fractions.

Commonly used prescription for:
Lymph nodule GTVp: 73.1Gy or 74.8Gy or 76Gy for GTV
CTV_Prostate: 68Gy
CTV LN: 52.7Gy

Other specific prescriptions:
For one patient, 69.3Gy to lymph nodule GTVp, 66Gy to prostate bed, and 49.5Gy to CTV LN in 33 fractions

For one patient, 60Gy to lymph nodule GTVp, 57.5Gy to prostate bed, and 50Gy to CTV LN in 25 fractions

Target coverage constraints for CTV
Nominal plan: 100% dose covers 95% of target volume.
The worst-case scenario: 95% dose covers 95% of target volume.

Target coverage constraints for GTVp
Nominal plan: 100% dose covers 95% of target volume.

OARs:
The following OAR guidelines were used for all cases used for model training and validation.
Table 1: Constraints for OARs

	Dose-Volume Constraints
Body	Dmax < 115%
Bowel	V40Gy < 150 cc
Rectum	V40Gy < 34%
	V65Gy < 17%
	V75Gy < 10%
Bladder	V40Gy < 50%
	V65Gy < 25%
	V75Gy < 15%
Femoral Head	D0.03cc < 45 Gy
Penile Bulb	Dmean < 60 Gy
Spinal Cord	D0.03cc < 45 Gy
Cauda equina	D0.03cc < 66 Gy

References for planning guidelines:

1. Pollack A, Hanlon AL, Horwitz EM, Feigenberg SJ, Konski AA, Movsas B, et al. Dosimetry and preliminary acute toxicity in the first 100 men treated for prostate cancer on a randomized hypofractionation dose escalation trial. *Int J Radiat Oncol Biol Phys* 2006;64(2):518-26.
2. Pollack A, Karrison TG, Balogh A, Gomella LG, et al. The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy (NRG Oncology/RTOG 0534 SPPORT): an international, multicentre, randomised phase 3 trial. Lancet 2022; DOI: 10.1016/S0140-6736(21)01790-6

Structure codes:

In order to ensure proper structure matching between cases and the structures defined in the model, the following structure code assignments are recommended (note: OV_LN and OV_Prostate are assigned as target):

Structure name example	Structure name in model
CTV_Prostate:	CTV_High
CTV LN:	CTV_Intermediate
CTV SVs Dist:	CTV_Intermediate
GTVp:	GTVp
OV_LN:	Control
OV_Prostate:	Control
Bladder:	15900 (FMA)
Bowel:	7199 (FMA)
CaudaEquina	52590 (FMA)
FemHeadNeck_L:	32843 (FMA)
FemHeadNeck_R:	32842 (FMA)
Kidney_L:	7205 (FMA)
Kidney_R:	7204 (FMA)
PenileBuilb:	19614 (FMA)
Rectum:	14544 (FMA)
Ring_Bst:	Ring
Ring_LN:	Ring
Ring_Prostate:	Ring
Skin:	7163 (FMA)
SpinalCord:	7647 (FMA)

Optimization objectives and optimization settings:

In addition to the DVH estimates, the following optimization objectives will be generated when the model is applied to a new case:

Table 2: Final Optimization Objectives

Structure	Objective type	Relative volume (%)	Dose	Priority
CTV_Prostate	Upper	0.0	105.0%	0
	Lower	99.9	101.0%	175
	Lower*	98.0	99.0%	210
	Lower	95.0	100.0%	0
	Lower gEUD		100.0	200
CTV LN	Lower	99.9	102.0%	175
	Lower*	98.0	99.0%	210
	Lower	95.0	100.0%	0
	Lower gEUD		100.0%	200
CTV SVs Dist	Lower	99.9	101.0%	150
	Lower*	98.0	99.0%	175
	Lower gEUD		100.0%	200
GTVp	Upper	0.0	101.0%	175
	Lower	97.0	101.0%	200
	Lower	100.0	97.0%	175
OV_LN	Upper	0.0	105.0%	250
OV_Prosate	Upper	0.0	105.0%	250
Bladder	Upper	15.0	87.0%	50
	Upper	25.0	75.0%	50
	Upper	50.0	44.0%	50
	Upper (fixed vol., generated dose)	0.0	Generated	119
	Line (pref. target)	Generated	Generated	140
Bowel	Upper	0.0	56.00 Gy	200
	Upper	1.0	40.00 Gy	120
	Upper (fixed vol., generated dose)	0.0	Generated	99

	Mean		Generated	99
	Line (pref. target)	Generated	Generated	150
CaudaEquina	Upper	0.0	66.0%	200
	Upper (fixed vol., generated dose)	0.0	Generated	99
	Line (pref. target)	Generated	Generated	100
FemHeadNeck_L	Upper*	0.0	37 Gy	200
	Upper (fixed vol., generated dose)	0.0	Generated	150
	Mean		Generated	99
	Line (pref. target)	Generated	Generated	100
FemHeadNeck_R	Upper*	0.0	37 Gy	200
	Upper (fixed vol., generated dose)	0.0	Generated	150
	Mean		Generated	99
	Line (pref. target)	Generated	Generated	100
Kidney_L	Mean		2.00 Gy	100
Kidney_R	Mean		2.00 Gy	100
PenileBulb	Upper	0.0	80.0%	100
	Upper (fixed vol., generated dose)	0.0	Generated	99
	Mean		25.00 Gy	100
	Line (pref. target)	Generated	Generated	100
Rectum	Upper	5.0	87.0%	200
	Upper	15.0	75.0%	200
	Upper	30.0	50.0%	200
	Upper	0.0	100.0%	200
	Line (pref. target)	Generated	Generated	140
Ring_Bst	Upper	0.0	88.25 Gy	150
	Upper (fixed vol., generated dose)	0.0	Generated	250
	Line (pref. target)	Generated	Generated	100
Ring_LN	Upper	0.0	56.25 Gy	150
	Upper (fixed vol., generated dose)	0.0	Generated	250
	Line (pref. target)	Generated	Generated	100

Ring_Prostate	Upper	0.0	80.25 Gy	150
	Upper (fixed vol., generated dose)	0.0	Generated	250
	Line (pref. target)	Generated	Generated	100
Skin	Upper	0.0	30.0%	100
	Upper	0.0	50.00 Gy	100
	Upper (fixed vol., generated dose)	0.0	Generated	99
	Line (pref. target)	Generated	Generated	50
SpinalCord	Upper	0.0	37.00 Gy	250
	Upper	0.0	25.00 Gy	50

* Robust optimization was enabled for these objectives

The model is set with the following manual Normal Tissue Objective (NTO) parameters:

NTO Priority	100
Distance from Target Border	0.7cm
Start Dose	98.0%
End Dose	30.0%

Model Description and Training:

The training cases were extracted from the pool of already treated prostate (or prostate bed) with Pelvic Lymph Nodes on ProBeam at SCCC that satisfied the contouring and planning guidelines described above. The SCCC RapidPlanPT prostate model was created with the previous 50 IMPT cases in total using RapidPlanPT (ver. 16.1).

The prescribed dose to intact prostate patient with nodal involvement (totally 34 plans) and its corresponding number of patients are as follows:

CTV_Prostate	CTV LN	Lymph Nodule GTVp	Primary prostate lesion GTVp	Number of patients
80Gy	56Gy	nan	nan	2
80Gy	56Gy	74Gy	nan	1
80Gy	56Gy	72Gy	nan	1
80Gy	56Gy	nan	86Gy	15
80Gy	56Gy	nan	88Gy	9

80Gy	56Gy	72Gy	86Gy	2
80Gy	56Gy	76Gy	88Gy	1
80Gy	56Gy	72Gy	88Gy	1
70.2Gy	46.8Gy	65Gy	nan	1
70.2Gy	56Gy	nan	74.1Gy	1

The prescribed dose to prostatectomy patient prostate bed with nodal involvement (totally 16 plans) and its corresponding number of patients are as follows:

CTV Prostate (prostate bed)	CTV LN	Lymph Nodule GTVp	Number of patients
68Gy	52.7Gy	nan	4
68Gy	52.7Gy	74.8Gy	5
68Gy	52.7Gy	73.1Gt	5
66Gy	49.5Gy	69.3Gy	1
57.5Gy	50Gy	60Gy	1

The dose distributions and geometric parameters were analyzed using the machine learning algorithm tools. After the completion of initial training, outliers were identified by visually comparing the estimated DVH range and the actual DVH curves.

During development of the model, the user sets optimization objectives that act as a template for every model-generated plan. A subset with 20 patients from the training cohort were employed to iteratively tune the model. The iterative tuning process includes creating plans using the initial RapidPlanPT, comparing the achieved DVH with clinical plan, adjusting the model objective list as needed and exclusion of some outliers as needed. As a result, 12 cases for bowels were excluded from the model when the model significantly overestimated or underestimated the DVH for bowel. As the bowel has a very large volume, even small misestimation on the relative volume can make a big difference on the absolute volume (e.g., for an 8000cc bowel, the increase of V40Gy from 1.5% to 2.5% would result in absolute volume increase from 120cc to 200cc).

Aggregate differences between the manual (clinical) and KBP-model generated plans are used to iteratively adjust the optimization objectives. This recursive method was used until a paired t-test ($p<0.05$) showed no statistically significant differences between KBP model generated and manual plans and the optimization objectives were finalized. Table 3 shows the final training results for this model

Table 3. Summary of the final training results

Structure	Trained	R^2	χ^2	Matched	In-field
GTVp	N/A			50	
CTV LN	N/A			49	
CTV SVs Dist	N/A			18	
CTV_Prostate	N/A			50	
OV_LN	N/A			49	
OV_Prostate	N/A			35	
Bladder	Yes	0.80	1.12	50	50
Bowel	Yes	0.82	1.16	38	38
FemHeadNeck_L	Yes	0.68	1.07	50	50
FemHeadNeck_R	Yes	0.74	1.15	50	50
PenileBulb	Yes	0.63	1.04	43	43
Rectum	Yes	0.69	1.12	50	50
Ring_Bst	Yes	0.70	1.16	50	50
Ring_LN	Yes	0.41	1.01	50	50
Ring_Prostate	Yes	0.48	1.07	49	49
Skin	Yes	0.90	1.28	25	25
CaudaEquina	Yes	0.92	1.29	40	39
Kidney_L	Yes	0	0	30	11
Kidney_R	Yes	0	0	31	13
SpinalCord	No			13	8

Model validation:

The SCCC Prostate (or Prostate Bed) with Pelvic Lymph Nodes model was validated by re-planning of an independent set of 20 cases which were not included in the KBP model library. The details of the validation cases were given in Tables below.

The prescribed dose to intact prostate patient with nodal involvement (totally 13 plans) and its corresponding number of patients are as follows:

CTV Prostate	CTV LN	Lymph Nodule GTVp	Primary prostate lesion GTVp	Number of patients
80Gy	56Gy	nan	86Gy	6
80Gy	56Gy	nan	88Gy	5
70.2Gy	49.4Gy	nan	75.4Gy	1
63Gy	49Gy	nan	70Gy	1

The prescribed dose to prostatectomy patient prostate bed with nodal involvement (totally 7 plans) and its corresponding number of patients are as follows:

CTV Prostate (prostate bed)	CTV LN	Lymph Nodule GTVp	Number of patients
68Gy	52.7Gy	nan	3
68Gy	52.7Gy	74.8Gy	2
68Gy	52.7Gy	73.1Gt	1
68Gy	52.7Gy	76.5Gt	1

The model was validated in a single phase. The purpose of the validation was to demonstrate that the model would produce plans comparable to expert plans with minimal user interference. Model performance was validated by optimizing and calculating 20 previously treated prostate (or prostate bed) with lymph nodes cases. The DVHs produced by the model were compared against DVHs of an expert's plan that were deemed clinically acceptable for treatment at SCCC. Plans created using the model library were only optimized once for this validation. During validation, all priorities were generated, Automatic NTO was employed, and all plans normalized to meet the target constraints. In addition to DVH comparison, the dose-volume indices to targets and OARs were compared.

Please refer to Annexes A, B, and C for library validation and optimization results and an example case.

Annex A

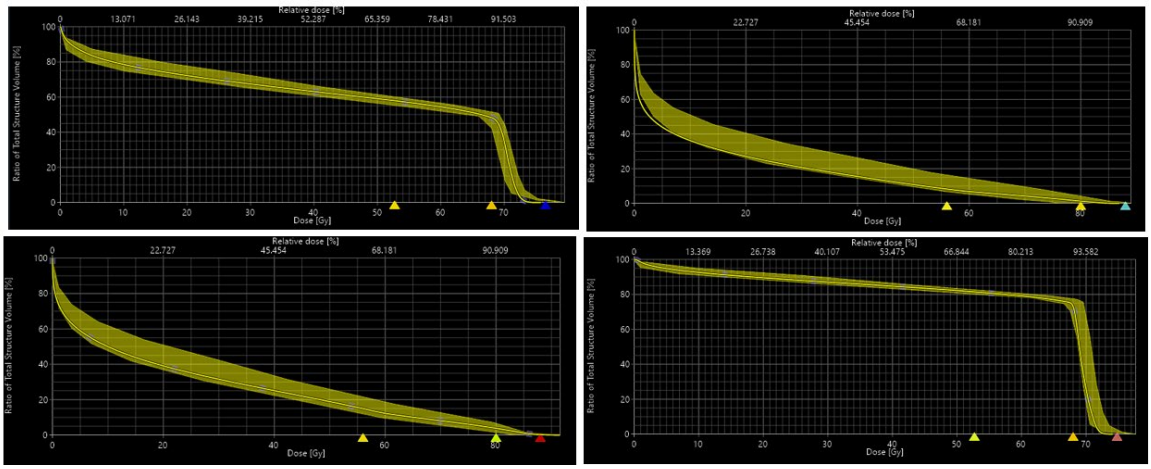

Figure A1: DVH estimate bands shown along with achieved DVHs for bladder. Triangles represent the prescription dose to the CTV. Dose is presented on the X-axis in % and the relative volume is on the Y-axis (%).

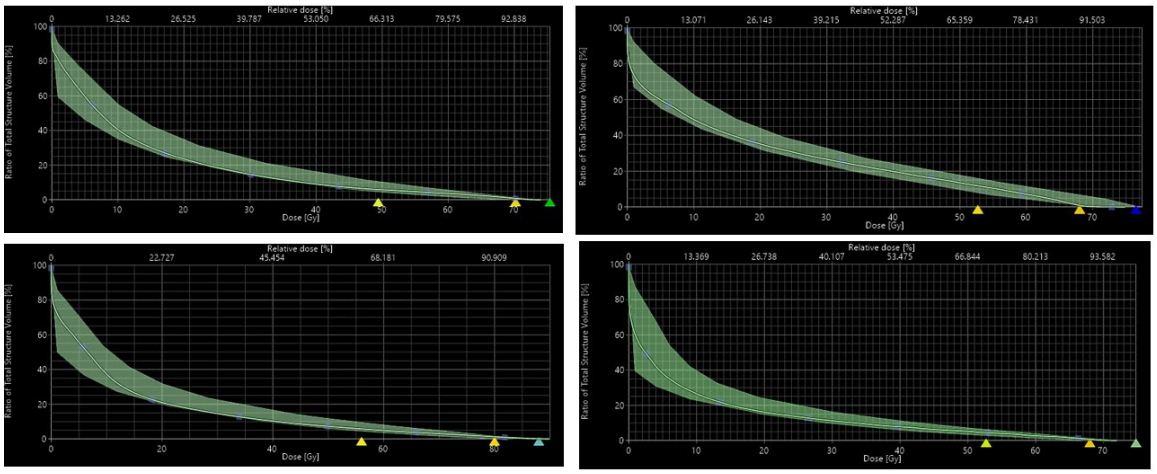

Figure A2: DVH estimate bands shown along with achieved DVHs for rectum. Triangles represent the prescription dose to the CTV. Dose is presented on the X-axis in % and the relative volume is on the Y-axis (%).

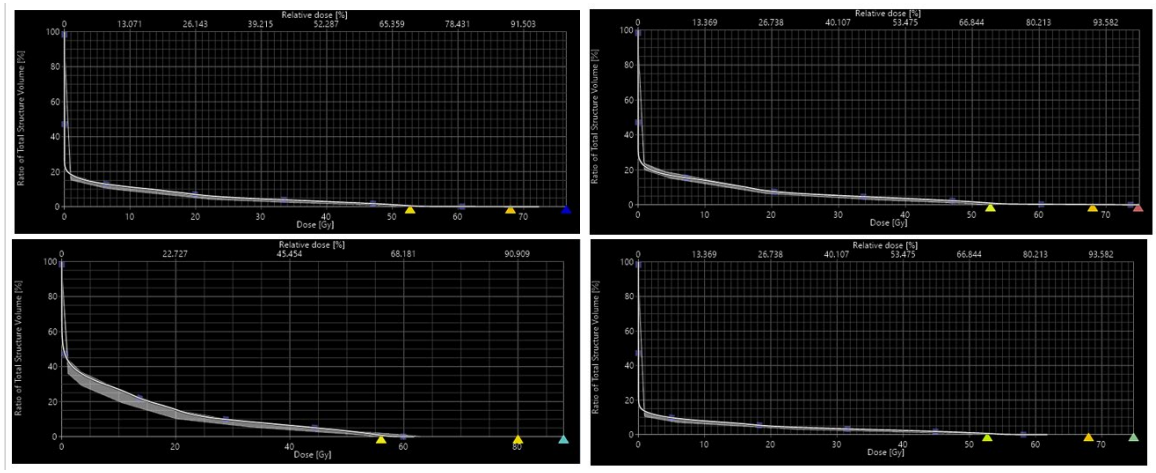

Figure A3: DVH estimate bands shown along with achieved DVHs for bowel. Triangles represent the prescription dose to the CTV. Dose is presented on the X-axis in % and the relative volume is on the Y-axis (%).

Annex B

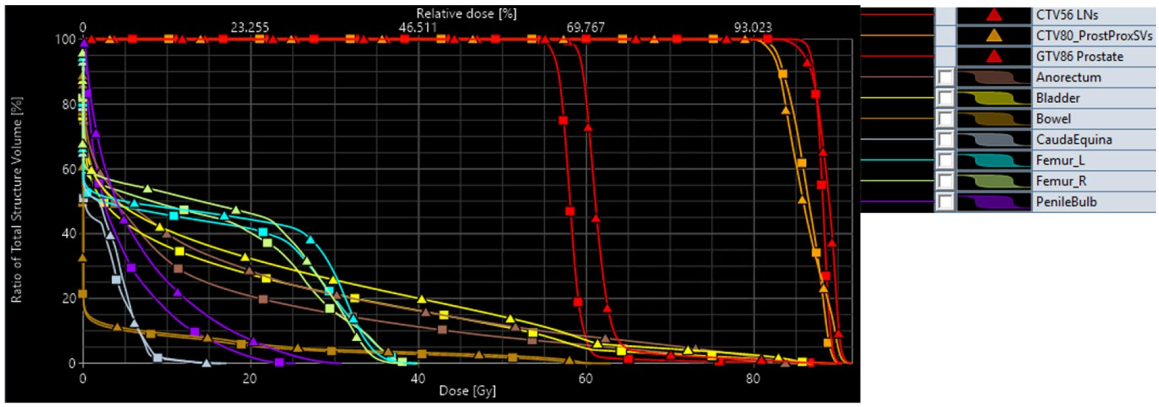

Figure B1: Model validation DVH comparison results for an example case: DVHs produced by the model-based library (squares) and the corresponding expert plan (triangles). Dose is presented on the X-axis in Gy and the relative volume is on the Y-axis (%).

Annex C:

Table C1: Overview of dosimetric parameters for 20 validation patients. Table lists mean dose and standard deviation across 20 patients for clinical manual reference plans, model-created plans, difference in mean values and p-values from paired t-test. Significant values highlighted in red.

	Clinical	Validation	Validation - Clinical	P-value
Dmax (%)	104.85 ± 1.69	104.95 ± 2.9	0.11 ± 3.05	0.87
GTV_Prostate V100 (%)	96.57 ± 2.02	98.91 ± 1.76	2.34 ± 1.91	< 0.01
CTV Prostate V100 (%)	99 ± 1.56	99.15 ± 1.39	0.14 ± 1.6	0.69
CTV Prostate V95 (worst case scenario) (%)	97.39 ± 2.79	96.78 ± 1.27	-0.61 ± 2.78	0.34
CTV Distal SV V100	99.99 ± 0.03	99.97 ± 0.07	-0.02 ± 0.08	0.60
CTV Distal SV V95 (worst case) (%)	98.34 ± 0.65	98.25 ± 1.59	-0.09 ± 2.17	0.91
CTV LN V100 (%)	97.75 ± 1.54	96.65 ± 1.43	-1.1 ± 2.71	0.09
CTV LN V95 (worst case scenario) (%)	96.07 ± 1.88	96.9 ± 0.91	0.82 ± 1.95	0.07
Rectum V40Gy<35%	18.83 ± 5.68	14.57 ± 6.52	-4.26 ± 3	< 0.01
Rectum V65Gy<17%	6.94 ± 2.85	4.33 ± 2.1	-2.61 ± 1.85	< 0.01
Rectum V75Gy<10%	2.29 ± 2.48	1.28 ± 1.37	-1.01 ± 1.26	< 0.01
Bladder V40Gy<50%	32.09 ± 19.35	25.73 ± 20.24	-6.36 ± 4.34	< 0.01
Bladder V65Gy<25%	17.81 ± 18.43	15.63 ± 19.23	-2.18 ± 5.31	0.08
Bladder V75Gy<15%	2.98 ± 3.6	1.65 ± 2.1	-1.32 ± 1.68	< 0.01
Bowel V40Gy<150cc	114.71 ± 31.73	123.46 ± 39.39	8.75 ± 27.3	0.17
Bowel D0.03cc (Gy)	60.16 ± 5.37	61.56 ± 4.77	1.4 ± 5.18	0.24
Femur_L D0.03cc<45Gy	35.99 ± 6.18	38.49 ± 5.74	2.5 ± 3.69	0.01
Femur_R D0.03cc<45Gy	37.31 ± 4.14	38.62 ± 6.26	1.31 ± 6.23	0.36
Cauda Equina D0.03cc (Gy)	15.57 ± 4.85	19.01 ± 7.62	3.44 ± 6.09	0.02
Penile Bulb Dmean (Gy)	24.13 ± 17.81	12.52 ± 8.55	-11.61 ± 9.76	< 0.01
Kidney_L Dmean (Gy)	0.01 ± 0.05	0.02 ± 0.06	0 ± 0.01	0.12
Kidney_R Dmean (Gy)	0.03 ± 0.1	0.03 ± 0.13	0.01 ± 0.04	0.54

GTV_Prostate: primary prostate lesion GTV for boost; GTV_LN: primary lymph nodule GTV for boost

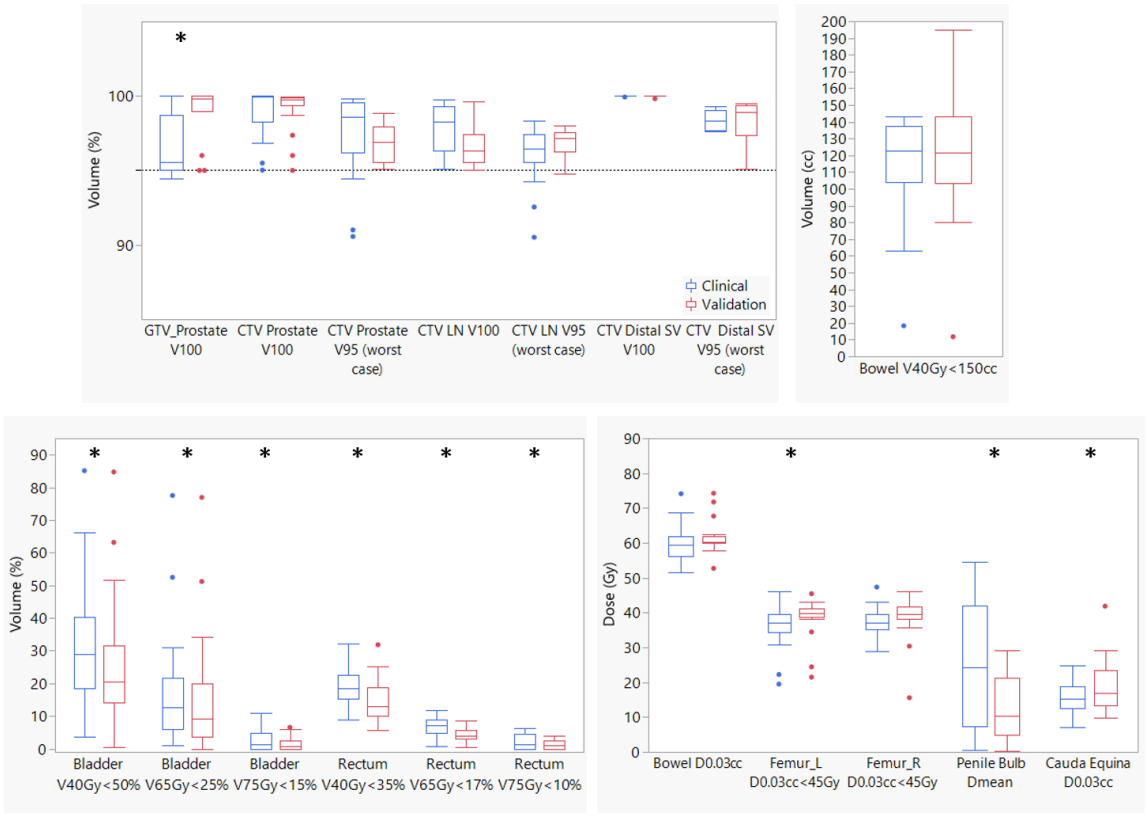

Figure C1: Boxplots of dosimetric parameters for the target and organs-at-risk, with the blue box representing the clinical manual plans and red boxes showing model-generated plans. Boxes represent 2nd and 3rd quartiles, whiskers denote data range within 1.5 interquartile range, outliers shown as crosses. Asterisk (*) highlights significance ($p<0.05$).

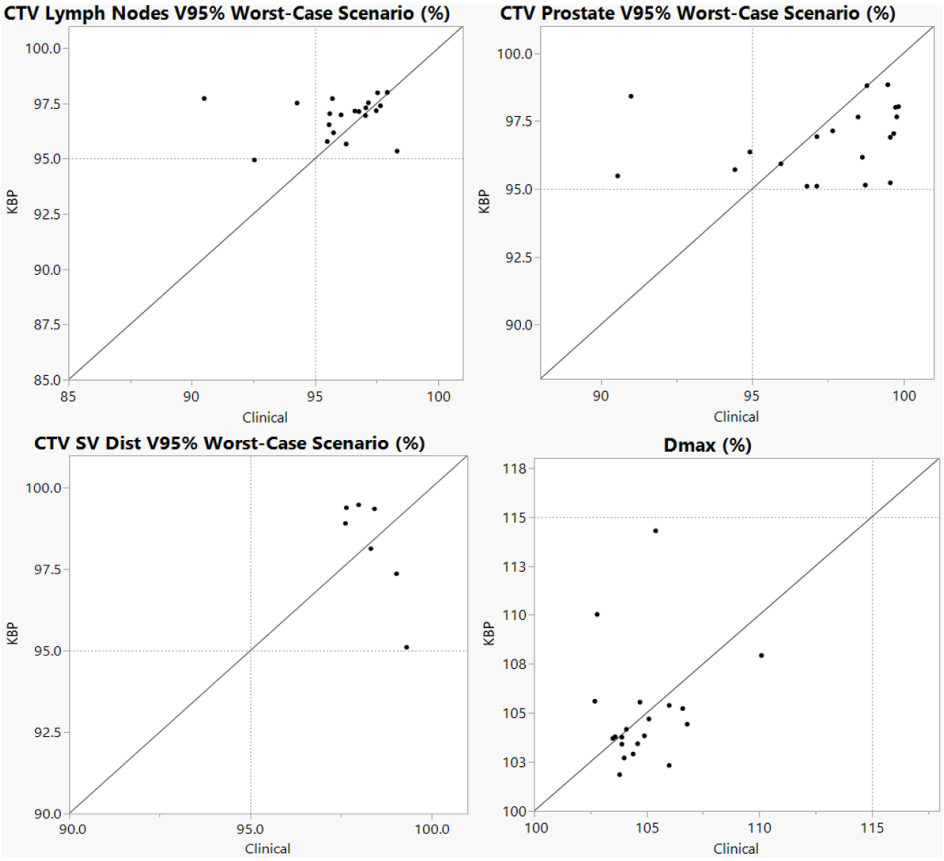

Figure C2: CTV parameters where each point is one plan with the x-coordinate being the manual clinical plan and the y-coordinate the KBP value. Points above the equality line thus indicate a higher value of the model-generated (validation) plan compared to the clinical plan and vice versa. The gray dashed line represents the value of dose-volume used in our institution.

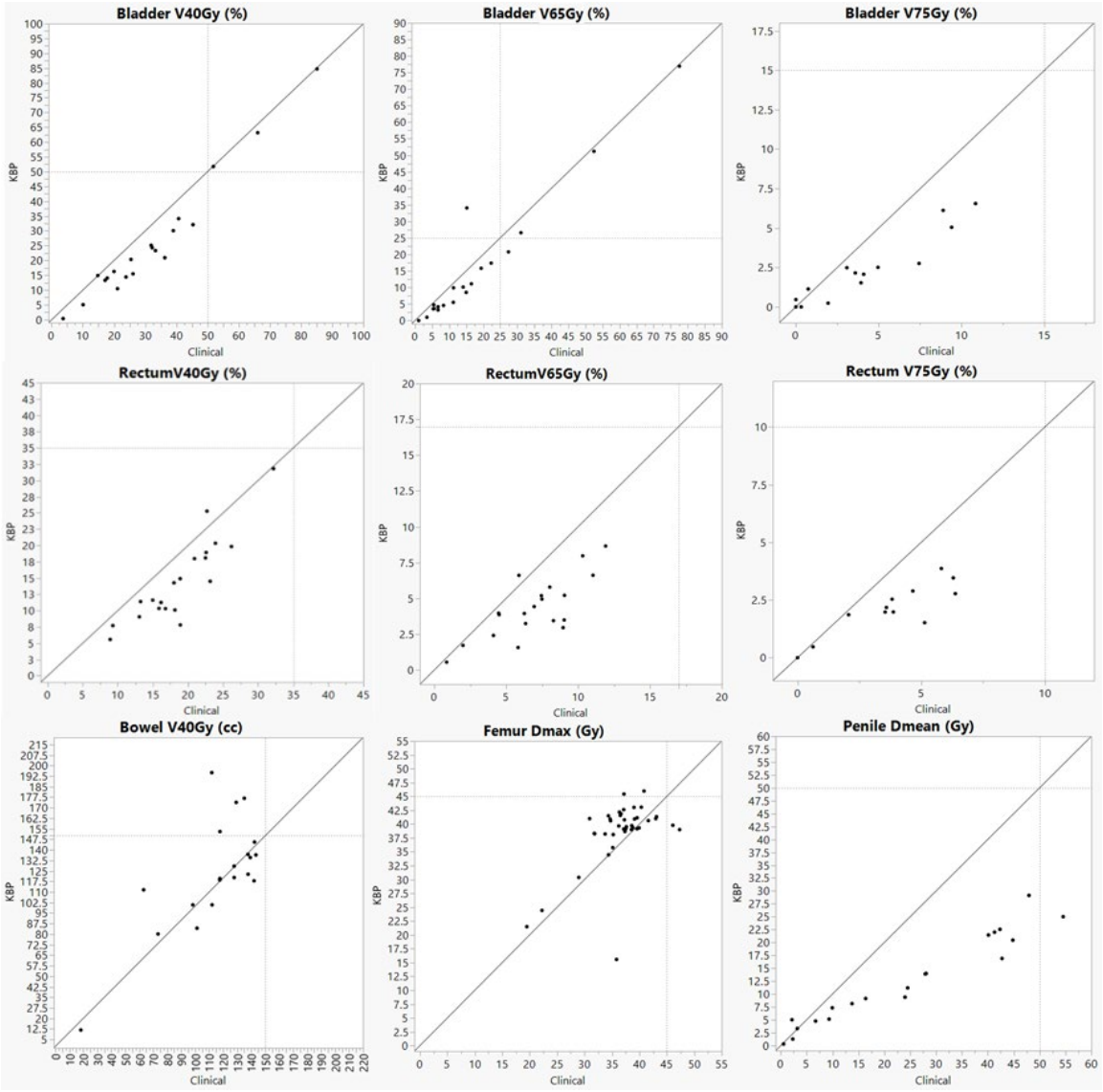

Figure C3: OAR parameters where each point is one patient with the x-coordinate being the clinical plan value and the y coordinate the model-generated (validation) plan value. The gray dashed line represents the value of dose-volume used in our institution.