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# Online supplement to “Robust optimization of dose-volume metrics for prostate HDR-brachytherapy incorporating target- and OAR volume delineation uncertainties”

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## 1. Full nominal plan optimization model

The full treatment planning model described by Gorissen et al. (2013) is:

$$\begin{aligned}
 (LDV) \quad & \max \sum_{i \in I_P} v_i \\
 \text{s.t.} \quad & \tilde{d}_i^T t \geq v_i L & \forall i \in I_P & (1) \\
 & \tilde{d}_i^T t \leq L_U + (H_U - L_U)(1 - z_i) & \forall i \in I_U & (2) \\
 & \sum_{i \in I_U} z_i \geq \tau_U |I_U| & & (3) \\
 & t_j \leq T_{max} b_k & \forall j \in J_k, \forall k \in K & (4)
 \end{aligned}$$

$$b_{k_1} \leq 1 - b_{k_2} \quad \forall k_2 \in \Gamma(k_1), \forall k_1 \in K \quad (5)$$

$$\sum_{k \in K} b_k \leq 20 \quad (6)$$

$$t \geq 0$$

$$v_i \in \{0, 1\} \quad \forall i \in I_P$$

$$u_i \in \{0, 1\} \quad \forall i \in I_\diamond, \forall \diamond \in \{R, U\}$$

$$b_k \in \{0, 1\} \quad \forall k \in K.$$

The objective and constraint (1) are discussed in Section 2.1 of the manuscript. Constraint (2) ensures that a calculation point in the urethra does not receive a dose above  $H_U$ . At most a fraction  $\tau_U$  of the calculation points in the urethra may receive a dose above  $L_U$ , as is enforced by constraints (2) and (3). The variable  $b_k$  is binary, and is equal to 1 when catheter  $k$  is used. The set  $K$  is the set of possible catheter locations, and  $J_k$  is the set of dwell positions in catheter  $k$ . At most 20 catheters can be used (constraint (6)). Dwell times within catheter  $k$  can only be positive if the catheter position is used, and they can never exceed a predetermined maximum dwell time  $T_{max}$  (constraint (4)). Two neighboring catheters cannot both be used, as is ensured by constraint (5), where  $\Gamma(k)$  is the set of catheter locations neighboring location  $k$ . The parameter values that were used in our tests are in Table 1. The maximum allowed dwell time is set to 5 seconds.

**Table 1** Model parameters used in the numerical experiments.

	Rectum	Urethra
$L_\diamond$	7.2 Gy	8 Gy
$H_\diamond$	10 Gy	10.6 Gy
$\tau_\diamond$	0.9	0.9

## 2. Algorithm procedures

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### Procedure “Input and initialize”

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Choose values for input parameters:

Optimality gaps  $g_1$  and  $g_2$ ,  $g_1 > g_2$

Fractions of calculation points  $\eta_{100\%}$  and  $\eta_{200\%}$

Set optimality gap to  $g_1$ .

Initialize  $S_{100\%} = \{\text{nom}\}$ ,  $S_{200\%} = \emptyset$

Solve (RC), denote solution by  $t^*$ .

$\tilde{I}_C^n := \{i \in \tilde{I}_C : d^T t^* \geq L\}$

$\tilde{I}_C^f := \{i \in \tilde{I}_C : d^T t^* \leq 2L\}$

**if**  $\arg \min_{s \in S} \{V_{100\%}^s(t^*)\} \neq \text{nom}$  **then**  $S_{100\%} := S_{100\%} \cup \arg \min_{s \in S} \{V_{100\%}^s(t^*)\}$

**end if**

**if**  $\max_{s \in S} \{V_{200\%}^s(t^*)\} > 0.2$  **then**  $S_{200\%} := \arg \max_{s \in S} \{V_{200\%}^s(t^*)\}$

**end if**

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### Procedure “Update $\tilde{I}_C^n$ and $\tilde{I}_C^f$ ”

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Note:  $\dagger = 1$  if catheters a variable, 2 if catheters are fixed.

Calculate the worst case objective value  $V_{\text{true}}$  and  $V_{200\%}$  for the current solution using the complete set  $\tilde{I}_C$ , based on scenario sets  $S_{100\%}$  and  $S_{200\%}$ , respectively.

**if**  $V_{\text{true}} - V^* > g_{\dagger}$  **then** Remove the  $\eta_{100\%} |\tilde{I}_{CTV}|$  calculation points with the lowest dose from  $\tilde{I}_C^n$ .

**end if**

**if**  $V_{200\%} > 0.2$  **then** Remove the  $\eta_{200\%} |\tilde{I}_{CTV}|$  calculation points with the highest dose from  $\tilde{I}_C^f$ .

**end if**

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### Procedure “Update $S_{100\%}$ and $S_{200\%}$ ”

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**if**  $\bar{s} := \arg \min_{s \in S} \{V_{100\%}^s(t^*)\} \notin S_{100\%}$  **then**  $S_{100\%} := S_{100\%} \cup \bar{s}$ .

**end if**

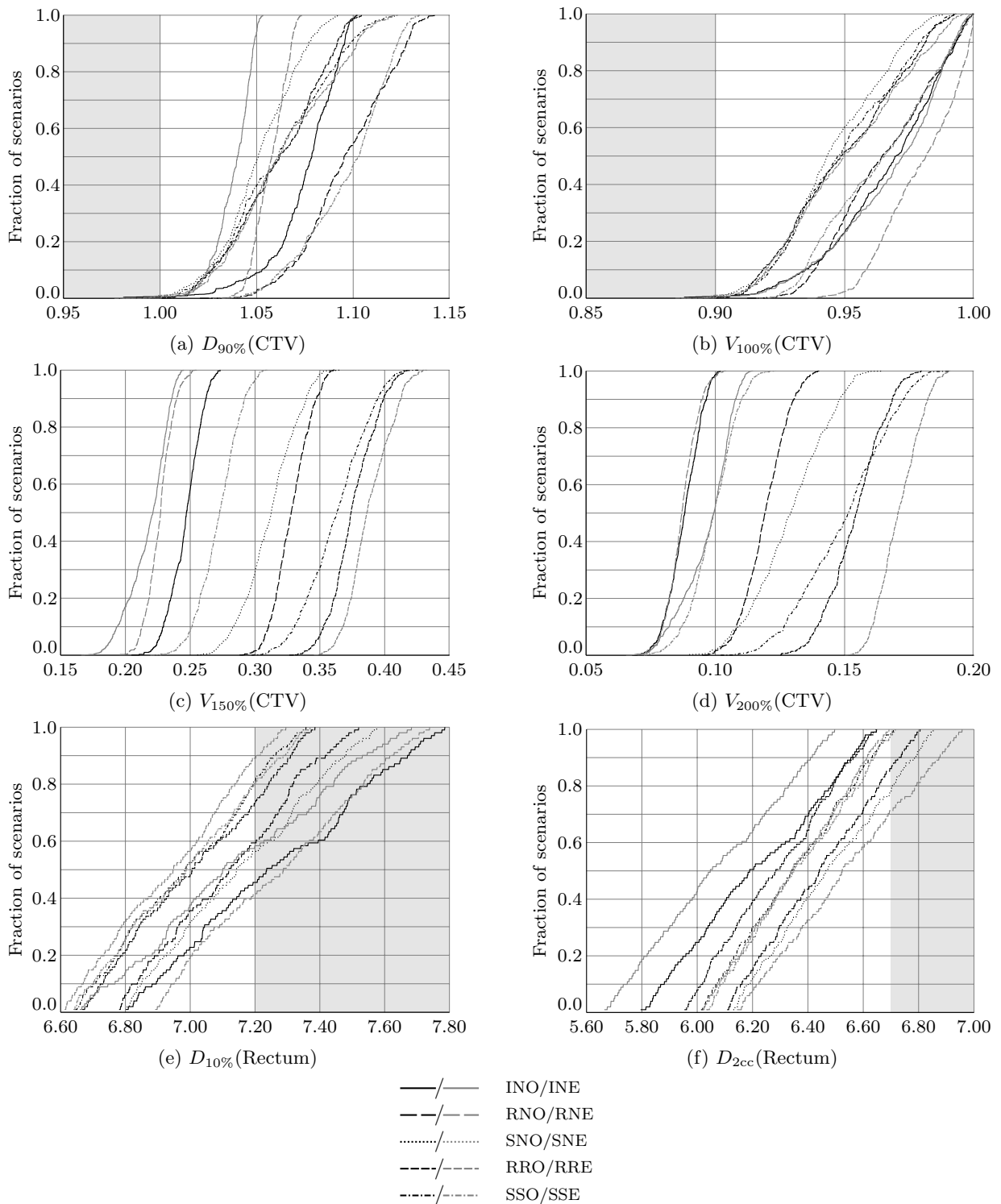
**if**  $\max_{s \in S} \{V_{200\%}^s\} > 0.2$  **then**  $S_{200\%} := S_{200\%} \cup \arg \max_{s \in S} \{V_{200\%}^s\}$ .

**end if**

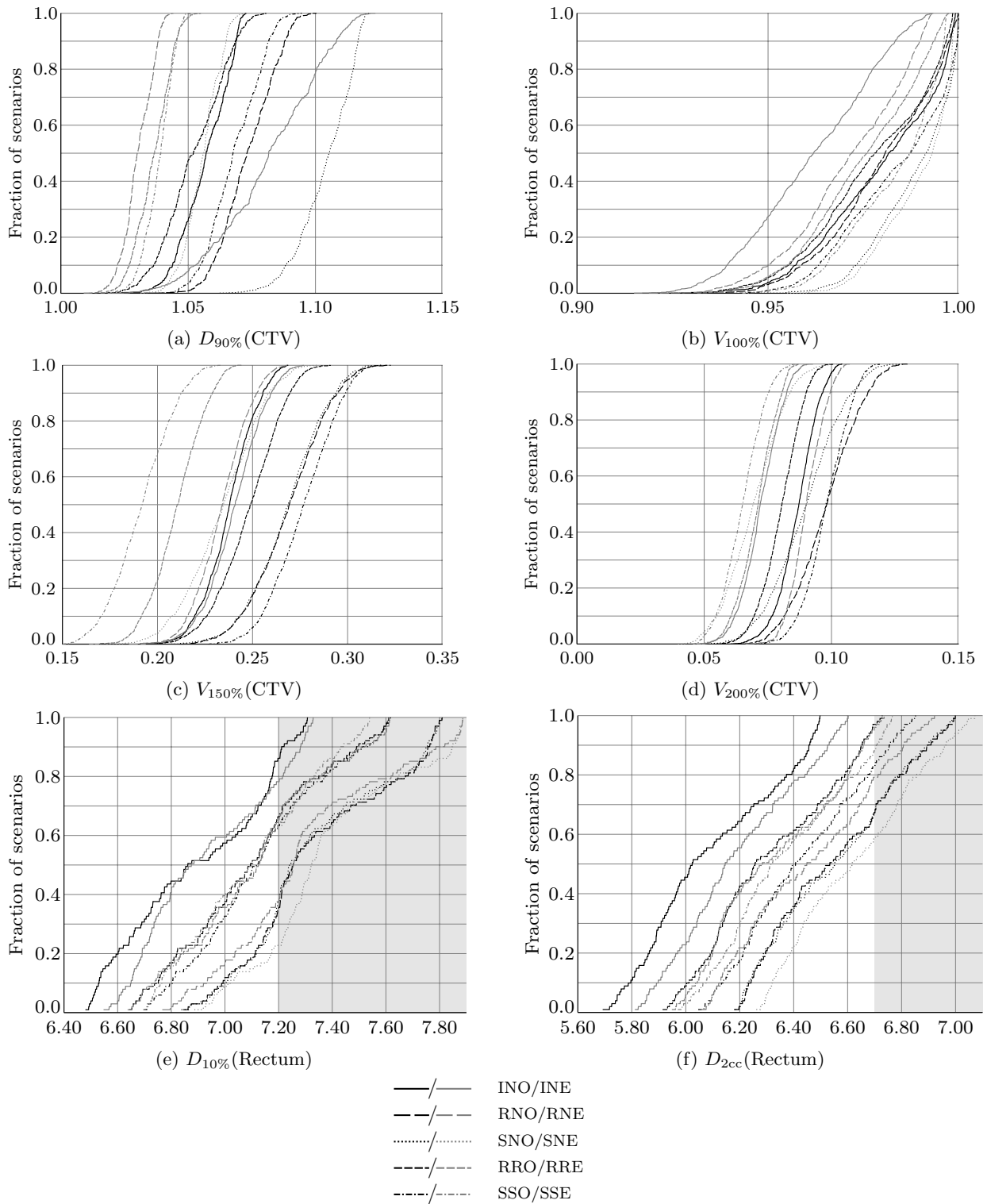
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### 3. Results

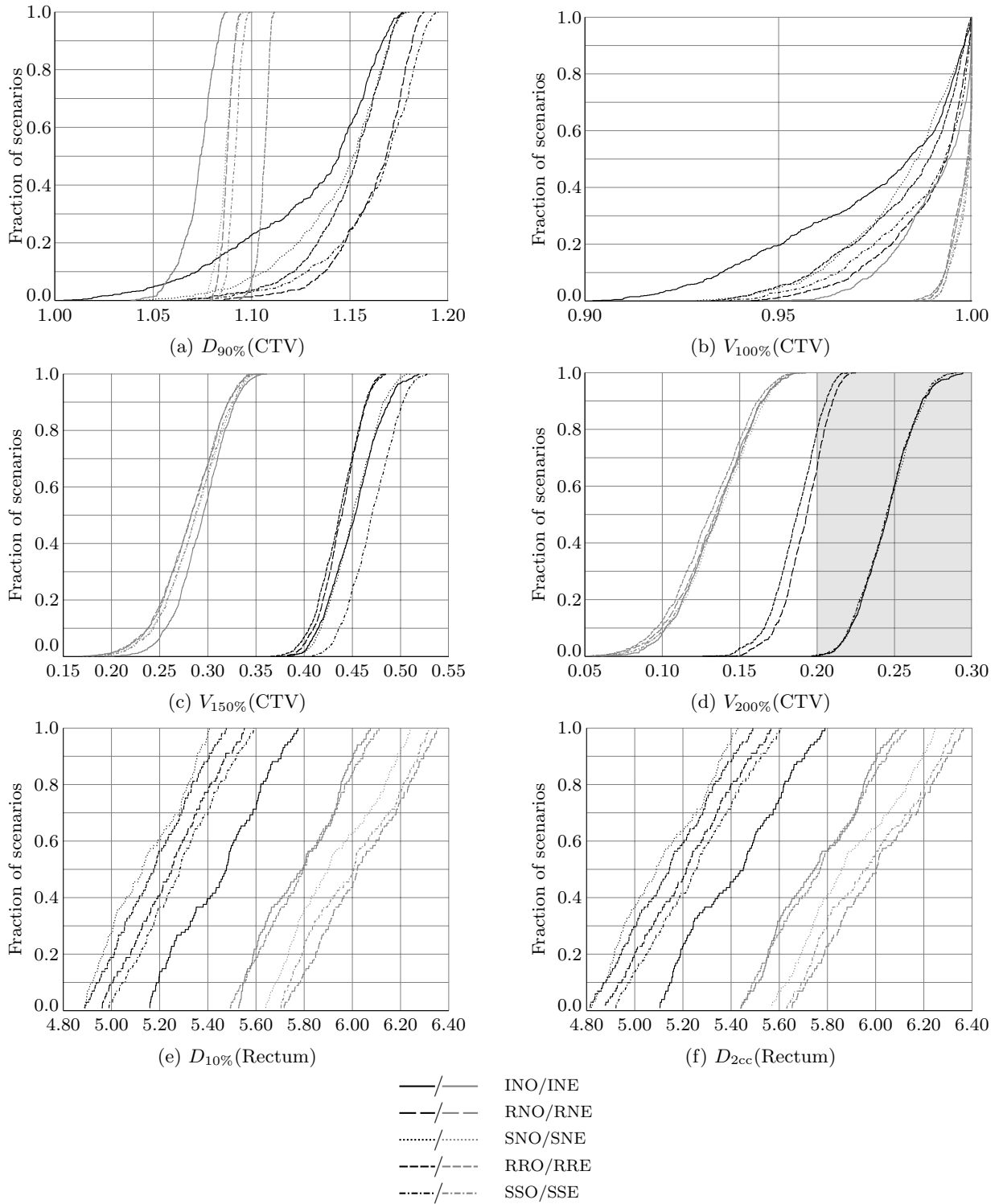
#### 3.1. DVH distributions for patients 2 through 6



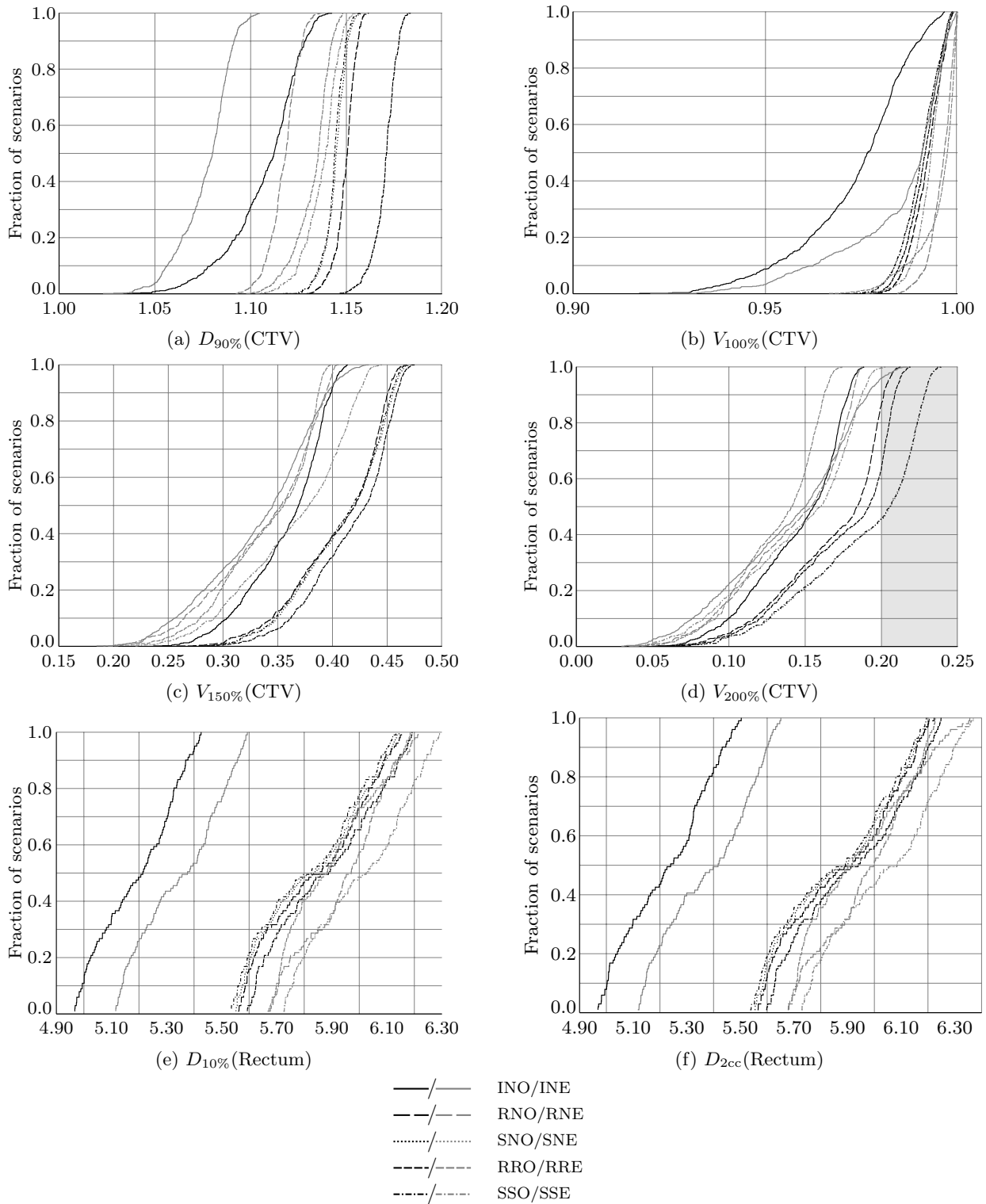
**Figure 1** DVH metrics for patient 2 obtained with various models, evaluated in the evaluation dataset. The curves for SNE and SSE coincide, as the treatment plans are identical. The gray area indicates scenarios where the DVH requirement from Table 1 in the manuscript was not met.



**Figure 2** DVH metrics for patient 3 obtained with various models, evaluated in the evaluation dataset. The gray area indicates scenarios where the DVH requirement from Table 1 in the manuscript was not met.



**Figure 3** DVH metrics for patient 4 obtained with various models, evaluated in the evaluation dataset. The gray area indicates scenarios where the DVH requirement from Table 1 in the manuscript was not met.



**Figure 4** DVH metrics for patient 5 obtained with various models, evaluated in the evaluation dataset. The gray area indicates scenarios where the DVH requirement from Table 1 in the manuscript was not met.

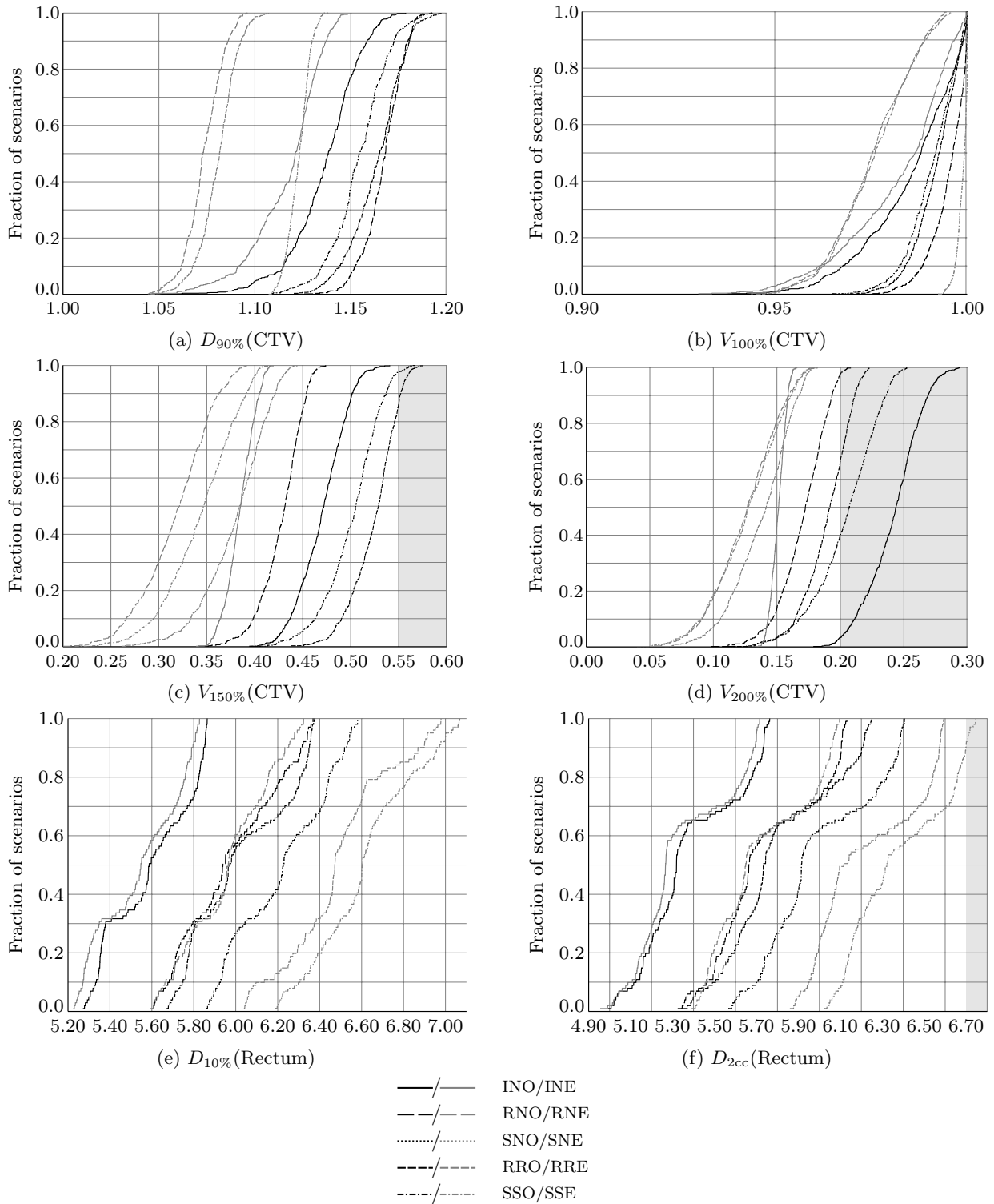


Figure 5 DVH metrics for patient 6 obtained with various models, evaluated in the evaluation dataset. The gray area indicates scenarios where the DVH requirement from Table 1 in the manuscript was not met.

### 3.2. DVH parameters for the urethra

**Table 2 DVH parameters of the urethra for the ten optimization models, measured in Gy.**

Model	DVH parameter and constraint	Patient					
		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
INO	$D_{10\%}(\text{Urethra}) \leq 10$	9.9	9.8	9.5	9.8	9.8	9.7
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.4	10.8	10.3	10.1	10.2	9.8
RNO	$D_{10\%}(\text{Urethra}) \leq 10$	10.0	9.9	9.9	10.0	10.0	10.0
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.5	10.4	10.6	10.3	10.6	10.2
RRO	$D_{10\%}(\text{Urethra}) \leq 10$	10.0	10.0	9.8	10.0	10.0	9.9
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.4	10.5	10.6	10.5	10.5	10.1
SNO	$D_{10\%}(\text{Urethra}) \leq 10$	9.9	10.0	9.9	10.0	10.0	10.0
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.3	10.5	10.5	10.2	10.4	10.3
SSO	$D_{10\%}(\text{Urethra}) \leq 10$	9.9	10.0	10.0	10.0	10.0	10.0
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.3	10.5	10.6	10.2	10.4	10.3
INO	$D_{10\%}(\text{Urethra}) \leq 10$	9.9	9.8	9.8	9.8	9.6	9.6
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.4	10.6	10.5	9.9	10.0	9.7
RNO	$D_{10\%}(\text{Urethra}) \leq 10$	9.9	9.8	9.4	10.0	10.0	9.9
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.6	10.3	10.2	10.2	10.4	10.1
RRO	$D_{10\%}(\text{Urethra}) \leq 10$	10.0	9.8	9.6	10.0	10.0	9.9
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.5	10.0	10.5	10.2	10.4	10.2
SNO	$D_{10\%}(\text{Urethra}) \leq 10$	10.0	9.9	9.8	10.0	10.0	10.0
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.3	10.5	10.6	10.2	10.5	10.3
SSO	$D_{10\%}(\text{Urethra}) \leq 10$	10.0	9.9	9.7	9.9	10.0	10.0
	$D_{0.1cc\%}(\text{Urethra}) \leq 10$	10.3	10.5	10.6	10.0	10.5	10.3

## 4. Changing the algorithm's parameters - detailed results

**Table 3 The effect of the allowed optimality gap  $g_2$  on solution time, objective function value, and worst case  $V_{100\%}(\text{CTV})$ , both for the optimization scenarios and for the simulations.**

	Gap (%)	Solution time	Objective value	Worst case $V_{100\%}(\text{CTV})$	
				over scenarios	over simulations
Patient 1	0.3	2389	98.9	88.1	86.4
	0.4	571	98.9	87.2	85.8
	0.5	444	98.6	85.2	84.9
	0.75	310	98.6	86.0	84.8
Patient 3	0.025	176	99.8	96.1	92.7
	0.05	175	99.8	96.1	92.7
	0.1	165	99.7	95.8	92.2
	0.2	138	99.7	95.6	92.1
	0.3	112	99.7	95.6	92.1
	0.4	74	99.4	90.0	87.8

**Table 4** The effect of different values for  $\eta_{100\%}$  and  $\eta_{200\%}$  on the solution times, objective function value and the worst case  $V_{100\%}$ (CTV), both for the optimization scenarios and for the simulations. The results shown are for patient 1.

$\eta_{100\%}$	$\eta_{200\%}$	Worst case $V_{100\%}$ (PTV)			
		Solution time	Objective value	over scenarios	over simulations
0.05	0.05	1274	98.8	87.9	85.7
0.05	0.10	915	98.9	87.3	86.0
0.05	0.15	904	98.9	87.3	86.0
0.10	0.05	481	98.7	86.4	85.0
0.10	0.10	571	98.9	87.2	85.8
0.10	0.15	1811	98.9	87.3	85.9
0.15	0.05	472	98.7	86.4	85.0
0.15	0.10	1819	98.9	87.3	85.9
0.15	0.15	1798	98.9	87.3	85.9

## References

- Gorissen, B, D den Hertog, A Hoffmann. 2013. Mixed integer programming improves comprehensibility and plan quality in inverse optimization of prostate HDR brachytherapy. *Physics in Medicine and Biology* **58** 1041–1057.