Supplementary material

Table 1: Patient characteristics

Characteristics			**AMC cohort**	**AUH cohort**
Strategy			CT strategy	CBCT strategy
Age (yr)	Median		79	76
	Interquartile range		71 - 84	68 - 78
Sex	Female		1	0
	Male		9	10
GTV volume (cm^3)	Median		21.5	10.9
	Interquartile range		11.8 – 35.8	7.1 – 27.5
Actual treatment	Fractionation scheme	Tumor	55 Gy in 20 fractions	70 Gy in 35 fractions
		High-risk $PTV_{elective}$	40 Gy in 20 fractions	60 Gy in 30 fractions
		Low-risk $PTV_{elective}$	40 Gy in 20 fractions	48 Gy in 30 fractions
	ART		Adaptive plan selection, CT strategy	Non-adaptive treatment
Treatment period			March 2013 – September 2014	May 2008 – August 2013

Table 2: Used dose constraints for the organs at risk.

	CBCT strategy	**CT strategy**
Rectum	V40Gy ≤ 50%	V50Gy ≤ 50%
Bowel cavity	V35Gy ≤ 40%	V60Gy < 3 cc V44Gy < 5%
Femoral heads	D_{max} < 52 Gy	D_{max} < 52 Gy
Body contour	D_{max} < 107% of prescribed dose	D_{max} < 107% of prescribed dose

D_{max} = Maximum dose

Table 3: Equations for the calculation of $TCP_{bladder}$. Linear-Quadratic model obtained from Wright et al. [8]

Survival fraction (SF):

$$SF_i = \prod_{j=1}^{n} SF_{i,j} = e^{-\sum_{j=1}^{n}(\alpha d_{i,j} + \beta {d_{i,j}}^2)} \quad (1)$$

, where

i = voxel

j = fraction

n = total number of fractions

α and β = radiosensitivity parameters

Voxel control probability (VCP):

$$VCP_i = e^{-V_{vox}\rho_i SF_i} \quad (2)$$

, where

V_{vox} = voxel volume

ρ_i = clonogenic cell density in voxel

Tumor control probability (TCP):

$$TCP = \prod_i VCP_i = e^{-V_{vox}\sum_i \rho_i SF_i} \quad (3)$$

Convolving Equation 3 with a Gaussian distribution for α to include interpatient variations in radiosensitivity :

$$TCP = \int_0^{\infty} e^{-V_{vox}\sum_i \rho_i SF_i}\, g(\alpha) d\alpha \quad (4)$$

Incorporating a different clonogenic cell density for tumor and bladder wall:

$$TCP_{bladder} = \left(\int_0^{\infty} e^{-V_{vox}\rho_{tumor}\sum_i SF_i} \times e^{-V_{vox}\rho_{wall}\sum_{k\neq i} SF_k} \right) g(\alpha) d\alpha \quad (5)$$

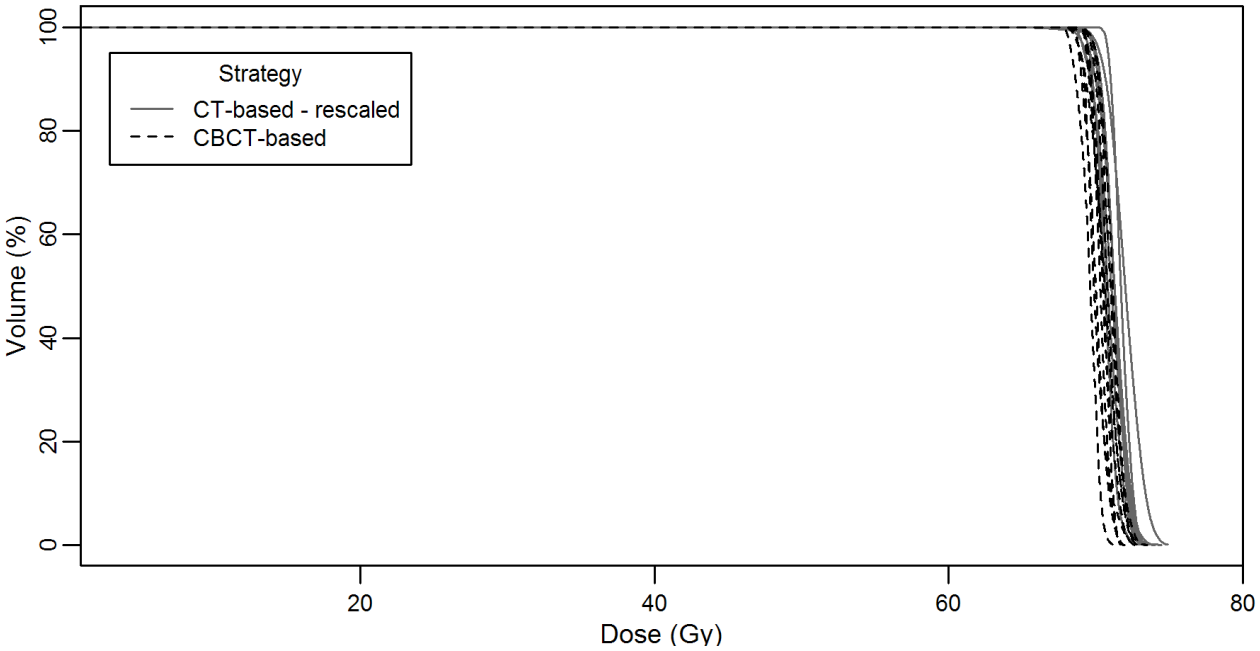

Figure 1: Dose volume histograms (DVHs) of GTV for each patient, derived from summated dose distributions. The black dotted lines show the DVHs for the CBCT-based strategy. The grey lines show the CT-based strategy DVHs, rescaled to a dose of 70 Gy in 35 fractions.

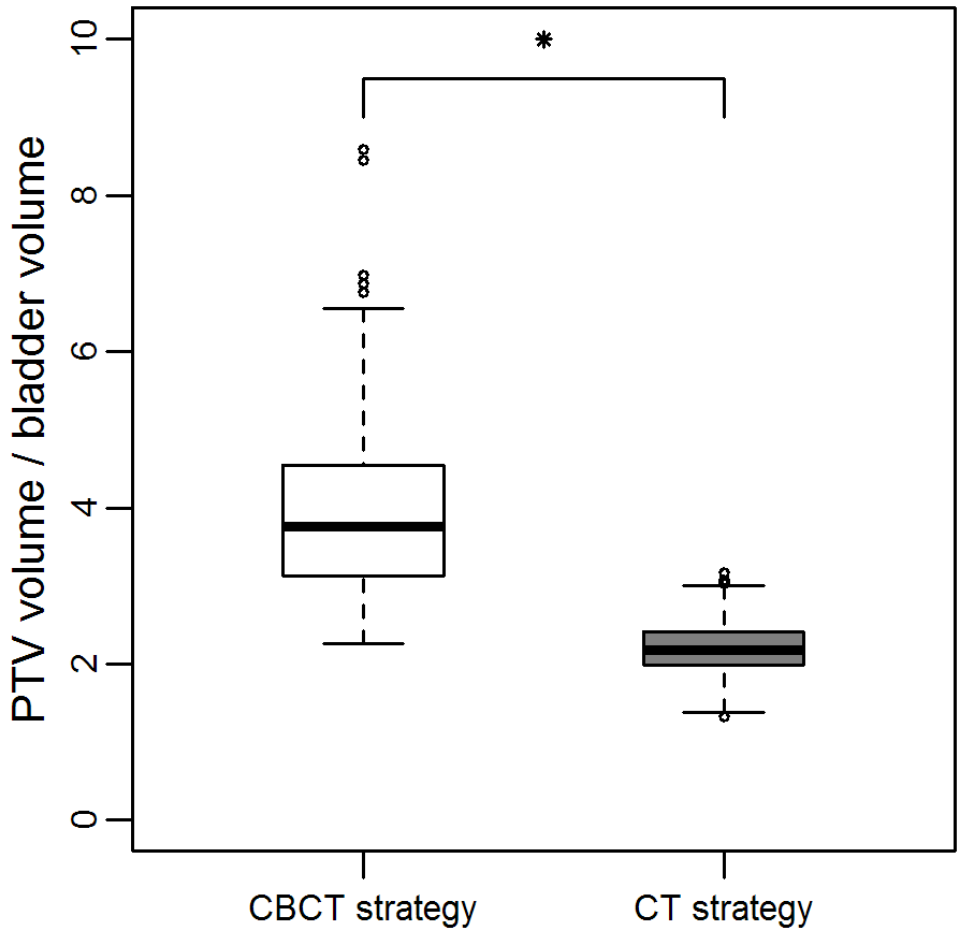

Figure 2: Daily $PTV_{elective}$ volume (excluding the lymph nodes) divided by the daily bladder volume. Data is on all separate fractions.

The PTV is on average 3.9 times larger than the daily bladder volume for the CBCT-based strategy, compared to 2.2 times for the CT-based strategy ($p<0.01$, calculated using the t-test).

This difference is caused by how well each strategy deals with shape changes and the distribution of target volumes between the different plans. For the CT-based strategy, due to the equal distribution of volumes between full and empty, a certain shape change will usually be matched by one of the target volumes. Therefore, generally, a well-fitting PTV for a certain bladder volume is found, reflected in the low values of PTV/bladder. For the CBCT-based strategy however, a small shape change can require the selection of the large plan, which is created using large PTV margins (see table 1). This results in PTV-volumes that do not fit the bladder volume well, which leads to limited sparing.