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	Planned dose (mean)			Delivered dose (mean)		
	t-test p (95% CI)	OR (95% CI)	AUC (95% CI)	t-test p (95% CI)	OR (95% CI)	AUC (95% CI)
<b>OARs</b>						
CTCAE v4.03 Grade 2+ Xerostomia						
IPG	0.70 -4.1 to 2.8	1.007 0.972 to 1.044	0.54 0.48 to 0.64	0.77 -4.0 to 3.0	1.005 0.971 to 1.041	0.53 0.43 to 0.63
CPG	0.018 -9.4 to -0.9	1.033 1.006 to 1.063	0.61 0.51 to 0.71	0.012 -10.0 to -1.2	1.034 1.007 to 1.063	0.62 0.52 to 0.71
ISMG	0.066 -8.7 to 0.3	1.039 0.999 to 1.108	0.65 0.54 to 0.76	0.058 -9.1 to 0.2	1.040 1.000 to 1.107	0.66 0.56 to 0.77
CSMG	<0.001 -16.7 to -4.8	1.035 1.015 to 1.058	0.64 0.54 to 0.73	<0.001 -17.0 to -4.8	1.034 1.014 to 1.056	0.64 0.54 to 0.73
CTCAE v4.03 Grade 2+ Salivary duct inflammation						
IPG	0.75 -4.14 to 3.0	1.006 0.969 to 1.046	0.55 0.45 to 0.65	0.75 -4.2 to 3.1	1.006 0.970 to 1.045	0.55 0.45 to 0.65
CPG	0.038 -9.2 to -0.3	1.031 1.002 to 1.063	0.61 0.51 to 0.70	0.020 -10.1 to -0.9	1.034 1.005 to 1.065	0.62 0.52 to 0.71
ISMG	0.38 -6.8 to 2.7	1.019 0.982 to 1.079	0.56 0.45 to 0.68	0.37 -7.1 to 2.7	1.019 0.983 to 1.078	0.57 0.48 to 0.69
CSMG	0.011 -14.7 to -1.9	1.031 0.979 to 1.047	0.60 0.51 to 0.70	0.011 -14.9 to -1.9	1.030 1.007 to 1.058	0.61 0.51 to 0.70
CTCAE v4.03 Grade 2+ Dysphagia						
SPC	0.012 -11.2 to -1.4	1.148 1.045 to 1.311	0.69 0.58 to 0.79	0.009 11.6 to -1.7	1.161 1.053 to 1.338	0.70 0.66 to 0.80
MPC	0.039 -10.9 to -0.3	1.113 1.023 to 1.259	0.65 0.53 to 0.76	0.035 -11.4 to -0.4	1.106 1.023 to 1.237	0.66 0.54 to 0.77
OC	0.049 -10.2 to 0	1.063 1.006 to 1.145	0.58 0.48 to 0.68	0.048 -10.5 to -0.1	1.063 1.007 to 1.142	0.58 0.47 to 0.68
SGL	0.059 11.3 to 0.2	1.079 1.010 to 1.187	0.61 0.50 to 0.73	0.052 -11.9 to 0.1	1.079 1.012 to 1.182	0.62 0.51 to 0.74

Table 1: Univariate analysis of late toxicity (1 year point prevalence) as a function of planned (D<sub>p</sub>) and delivered (D<sub>a</sub>) dose parameters to OARs (ipsilateral - I and contralateral - C parotid glands - PG and submandibular glands - SMG, superior - S and middle - M pharyngeal constrictor muscles PC, oral cavity - OC and supraglottic larynx - SGL) . ORs indicate % increase in odds of Gr2+ toxicity/Gy increase to OAR. No relationship found - cells clear. No relationship between dose to OAR and toxicity endpoint - cells clear. Relationship stronger - cells green (D<sub>a</sub> stronger = 15). Relationship weaker - cells red (D<sub>a</sub> weaker = 2). Relationship equivalent or equivocal - cells blue (7).

**Conclusion**

Clear associations with concomitant SACT, pre-treatment symptoms and toxicity were seen. D<sub>A</sub> was higher than D<sub>P</sub> to all OARs. Differences were small in most patients. Despite this, a trend for marginally stronger univariate associations between D<sub>A</sub> parameters, compared to D<sub>P</sub>, and toxicity was seen. Results should be interpreted with caution due to multiple testing, and comparison with multivariate models is required as a next step. Nonetheless, this data is the first to compare relationships between both D<sub>P</sub> & D<sub>A</sub> and toxicity in HNC, and to suggest stronger links with the latter.

**PO-0985 Online-adaptive proton therapy: assessing accuracy of robust dose restoration in lung patients.**  
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**Purpose or Objective**

Intensity-modulated proton therapy (IMPT) offers excellent dose conformity and reduces the integral dose in the OAR compared to conventional radiotherapy. During the treatment, density changes may alter planned proton ranges in the patient and compromise the accuracy of the plan. To take into account this effect, isovolume dose restoration (iDR) uses isodose contours generated from the initial dose distribution and their associated weighted objectives (maximum and minimum) to reoptimize the plan and reproduce the initial dose in repeated CTs. The objective of this work was to test the performance of iDR in lung cancer patients.

**Material and Methods**

The provided database included planned and two repeated 4D-CTs (every two weeks) for fourteen patients. Twelve of them present lymph nodes in addition to the primary tumour. iDR was performed in the first series of repeated 4D-CTs. The prescribed dose (D<sub>p</sub>) to target was 66 Gy (33 fractions of 2 Gy). Robust optimization was used for the targets, with setup errors of 5mm, range errors of 3%, and

three phases of the respiratory cycle (end-exhale, end-inhale, and midV). Plans were optimized based on CTV coverage criteria (worst-case D95%>95%Dp and D5%<105%Dp) in RayStation (RaySearch Laboratories, Sweden). For the evaluation of the results, two different metrics were calculated: 1) D95% and D5% dose values for the CTV in the nominal case; 2) dose differences between restored/distorted and initial dose distributions reported by DE(vol=2%) values in four different volumes (prescribed, high, medium and low dose regions). DE(vol=2%) represents the absolute dose errors (evaluation-initial dose) in at most 2% of the analysed region.

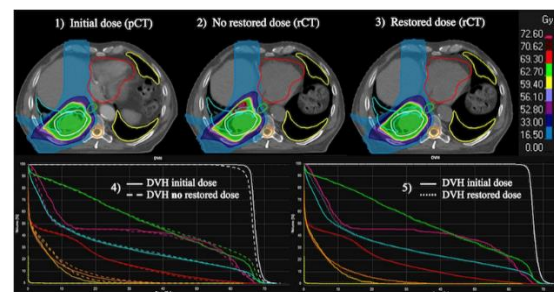
**Results**

The evaluation of initial plans on repeated CTs showed large dose distortions, which were substantially reduced after restoration. No target underdosage was observed after restoration, whereas for 28% (4/14) of the patients, the CTV coverage criteria were not accomplished before restoration. In limit cases (21% or 3/14 patients), where D95%/D5% levels were reached (only ± 1Gy), iDR improved considerably the DVH metrics (see Table 1). In the analysis of local dose differences, median DE(vol=2%) decreased from 10.06 Gy in distorted plans to 3.23 Gy in the restored plans.

Patient	INITIAL		RESTORED		DISTORTED	
	D95% (Gy)	D5% (Gy)	D95% (Gy)	D5% (Gy)	D95% (Gy)	D5% (Gy)
1	65.74	67.99	65.85	67.91	65.55	68.60
2	65.26	70.02	65.42	70.08	63.10*	69.45*
3	65.24	68.79	65.35	68.85	64.52	69.73*
4	65.76	68.57	65.81	68.69	65.11	69.25*
5	65.74	68.14	65.03	67.83	65.41	67.62
6	65.48	68.62	65.45	68.94	62.26*	70.10*
7	65.36	68.04	65.57	68.10	60.68*	67.74
8	65.30	68.57	65.61	68.76	64.73	68.84
9	65.71	68.51	65.46	69.08	64.05	67.94
10	65.89	68.76	65.73	68.60	65.34	69.29
11	65.76	68.07	65.44	68.62	65.56	67.89
12	65.63	69.61	65.63	69.73	63.42*	68.84
13	65.79	68.30	65.63	68.52	65.67	68.55
14	65.58	68.97	65.57	69.18	64.54	68.78

**Conclusion**

Restoring clinically-approved dose distribution on repeated CTs does not require new ROI segmentation and is compatible with an online adaptive workflow. With iDR, we are able to accurately reproduce the initial dose, despite density changes, maintaining stable the DVH-based parameters (see Figure.1). Hot spots and underdosage in the CTV can be corrected by implementing iDR in the clinical workflow.



**PO-0986 Inter-fraction anatomical changes in pediatric abdominal tumors during photon and proton therapy**

F. Guerreiro<sup>1</sup>, E. Seravalli<sup>1</sup>, G.O. Janssens<sup>2</sup>, J.H. Maduro<sup>3</sup>, C.L. Brouwer<sup>3</sup>, E.W. Korevaar<sup>3</sup>, A.C. Knopf<sup>3</sup>, B.W. Raaymakers<sup>1</sup>

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### Purpose or Objective

During radiotherapy treatment (RT) of abdominal pediatric tumors, inter-fraction anatomical changes such as patient's diameter variations due to weight loss/gain and different gastrointestinal gas volumes might occur. The goal of this study was to investigate the dosimetric impact of daily anatomical changes based on cone-beam computed tomography (CBCT) information in robust optimized photon and proton RT dose distributions.

### Material and Methods

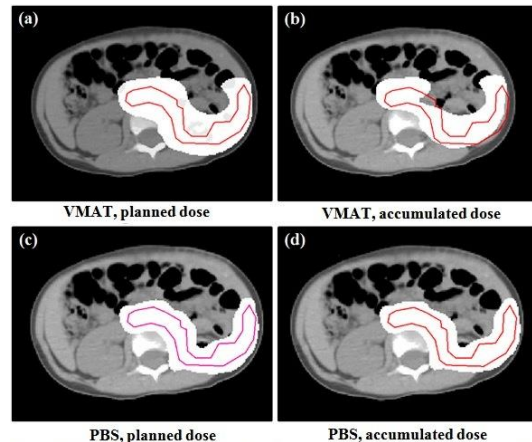
Volumetric modulated arc therapy (VMAT) and pencil beam scanning proton therapy (PBS) dose distributions were calculated using the original planning-CT scan for 20 pediatric patients (average 3, range 1-8 years) treated for neuroblastoma (n=11) and Wilms' tumor (n=9). VMAT plans were based on a 6 MV full-arc while PBS plans on 2-3 posterior-oblique fields with prescribed doses (PD) ranging between 14.4-36 Gy. Treatment plans were robust optimized on the patient-specific internal target volume (ITV) using a uniform 5 mm set-up uncertainty. Moreover, for the PBS plans a 3% proton range uncertainty was accounted for. The plan robustness was evaluated using multiple dose distributions associated with various error scenarios: set-up (with the magnitude of 5 mm in 26 directions per VMAT and PBS plans) and range errors ( $\pm 3\%$  density scaling, resulting in 52 scenarios per PBS plan). Plans were accepted if the V95% of the ITV > 98% in the voxel-wise minimum evaluation dose. Fractional dose re-calculations were performed using clinical CBCT images. For the estimation of Hounsfield units (HUs) from the daily CBCT data, the gas volumes on the planning-CT were filled with a water equivalent density and the planning-CT was deformably registered to each CBCT. Gas volumes were delineated on the CBCTs and copied rigidly to the deformed CTs (dCTs). Fractional doses were re-calculated on the dCTs and accumulated rigidly. To compare planned and accumulated doses, dose-volume histogram (DVH) parameters were calculated for the clinical ITV and organs at risk (OARs).

### Results

For both techniques, the ITV coverage was fulfilled for the original planned dose distributions. For the ITV, mean differences between planned and accumulated doses ranged between [-0.1% - 0.8%] and [-0.1% - 0.1%] for the VMAT and PBS plans (Table 1), respectively. On the accumulated doses, the ITV coverage was not reached (V95% < 99%) for 2 patients, for the VMAT plans (Figure 1). For the OARs, mean differences between planned and accumulated doses ranged between [-0.4% - 0.2%] and [-0.2% - 0.0%] for the VMAT and PBS plans (Table 1), respectively.

**Table 1.** Mean  $\pm$  standard deviation (SD) differences (%) between planned and accumulated doses for selected DVH parameters for VMAT and PBS dose distributions.

Structure	Parameter	Planned - Accumulated Dose (%)			
		VMAT		PBS	
		Mean $\pm$ SD	Range	Mean $\pm$ SD	Range
ITV	D <sub>95%</sub>	0.8 $\pm$ 1.7	[-1.9; 7.2]	0.1 $\pm$ 0.5	[-0.5; 1.9]
	D <sub>mean</sub>	0.2 $\pm$ 0.9	[-2.4; 2.2]	0.1 $\pm$ 0.1	[-0.1; 0.3]
	D <sub>2%</sub>	-0.1 $\pm$ 1.0	[-2.8; 2.3]	-0.1 $\pm$ 0.6	[-1.7; 0.5]
	V <sub>95%</sub>	0.4 $\pm$ 1.5	[0.0; 6.8]	0.1 $\pm$ 0.3	[0.0; 0.7]
Kidney R		-0.4 $\pm$ 2.3	[-5.4; 3.1]	-0.1 $\pm$ 0.4	[-1.0; 0.9]
Kidney L		-0.2 $\pm$ 1.7	[-5.2; 3.8]	0.0 $\pm$ 0.6	[-1.1; 1.6]
Liver	D <sub>mean</sub>	0.2 $\pm$ 0.7	[-0.9; 2.5]	-0.2 $\pm$ 0.7	[-2.3; 1.1]
Spleen		0.0 $\pm$ 1.7	[-5.6; 4.0]	0.0 $\pm$ 0.5	[-1.0; 1.5]



**Figure 1.** VMAT (a,b) and PBS (c,d) planned and accumulated dose distributions for one of the patients failing the ITV coverage (V<sub>95%</sub> < 99%) in the accumulated VMAT dose distribution (b). Dose distributions are overlaid on the planning-CT and the 95% isodose line is shown in white and the ITV in red.

### Conclusion

In this study, the need of performing re-planning during RT was evaluated for children treated for abdominal tumors. RT using PBS with posterior-oblique irradiation fields proved to be highly robust against anatomical inter-fraction changes. In photon therapy using a VMAT delivery, daily anatomical changes proved to affect the target coverage to a higher extent when compared to PBS.

### PO-0987 Rotational setup errors in breast cancer radiotherapy: the effect on treatment margins.

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### Purpose or Objective

Rotational errors might have a significant effect on radiotherapy (RT) target coverage if not considered in PTV margins. In this work, we investigated the residual rotational errors in breast cancer RT.

### Material and Methods

Daily low dose CBCT setup images of 93 breast cancer patients treated with RT were retrospectively investigated for rotational errors in patient setup. Patients were imaged with CT in supine position arms above the head on a breast board (C-Qual™ Breastboard, Civco, USA). 20 of the patients were imaged in deep inspiration breath hold (DIBH). With 50 patients, the treatment area included the whole breast and with 43 patients, the treatment area included also the axillary lymph nodes. A 3D image co-registration was conducted between 1731 CBCT images and the respective planning CT images (Mosaic system v2.62, Elekta AB) and image translation and rotations in coronal (COR), sagittal (SAG) and transversal (TRA) planes were recorded (Fig 1). Pearson correlation coefficient was used to determine the relation between the magnitude of rotational error and body mass index (BMI), age, side of a treatment, use of DIBH, chemotherapy, time between surgery and RT and the number of fractions (either 15 or 25).