Treatment Planning and Delivery for Proton Thoracic Therapy

An European Center's Experience

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Disclosures

umcg

	COI status	Names of companies / organizations
① Post of executive / consultant	No	
② Stocks	No	
③ Patent royalties	No	
④ Stage moneys	No	
⑤ Manuscript fees	No	
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⑦ Other rewards	No	

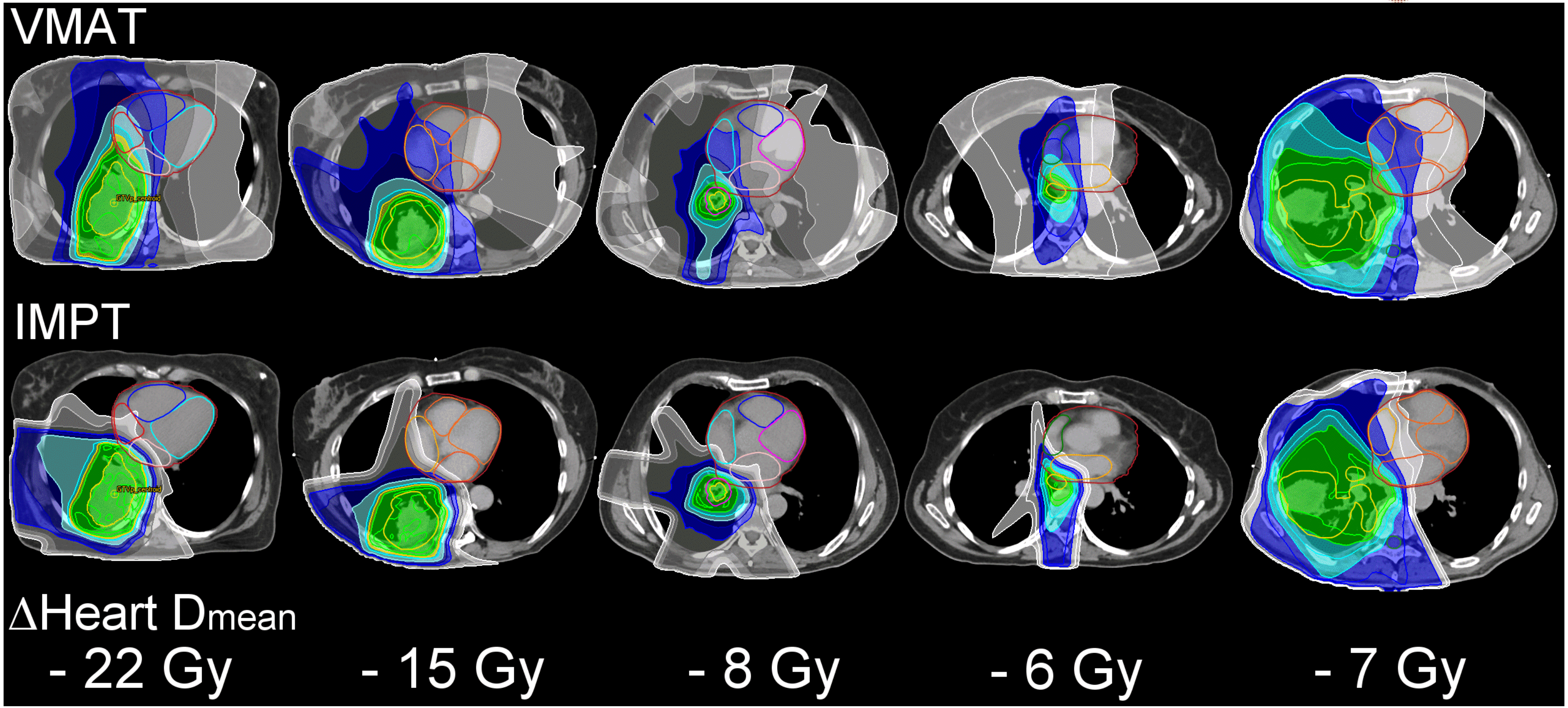
Outline

- Introduction
- Motion assessment
- Robust planning
- Robustness evaluation
- Retrospective 4D dose reconstruction
- Future Developments

IMPT Thoracic indications@UMCG

- **Lung**
- **Lymphoma**
- Esophagus
- Breast

Lung IMPT: Reduced Heart & Lung Dose



vd Laan, HP et al. (2019) Acta Oncol. ***Organ sparing potential and inter-fraction robustness of adaptive intensity modulated proton therapy for lung cancer***

Patient qualifies for protons?

Decision Support System

Result	Protons

Yes

☺

	Photon plan	Proton plan
	Mean Dose (Gy)	Mean Dose (Gy)
Heart	11.6	1.0
Lung	15.3	10.9
Esophagus	18.5	12.3

GRADE 2 Complications	NTCP Photons	NTCP protons	ΔNTCP DSS	Threshold
Radiation Pneumonitis	36.9%	24.2%	12.8%	>10%
Dysphagia	44.5%	30.3%	14.2%	>10%
ΣΔNTCP Grade 2 complications			27.0%	>15%

Grade 5 complications	NTCP Photons	NTCP protons	ΔNTCP DSS	
2-year mortality	55.8%	40.2%	15.7%	>2%
ΣΔNTCP all complications			42.6%	

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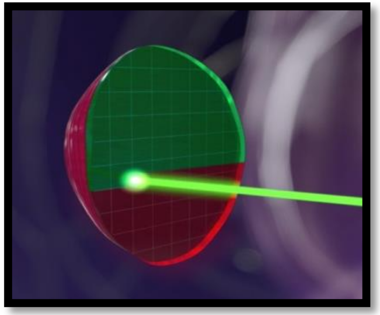
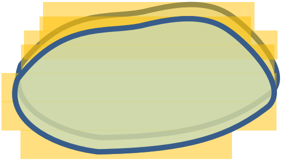
Motion induced dose variations
Interplay effect

- Dynamic treatment

  ‘interplay’ dynamic beam & patient geometry



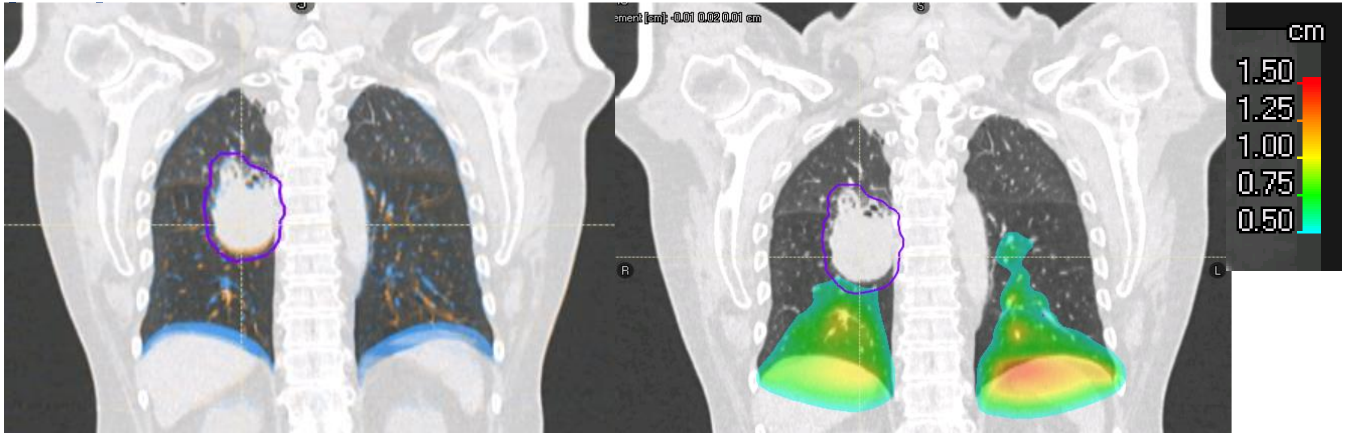
Static target
Dynamic treatment



Dynamic target
Dynamic treatment

Target Motion Evaluation: 4DCT

Coregistered INHALE+EXHALE | **Exhale Def. Field Vector , target**



Clinical Pt
NSCLC 05
DIR

- Max inhale vs. max exhale
- Superimposed on max exhale

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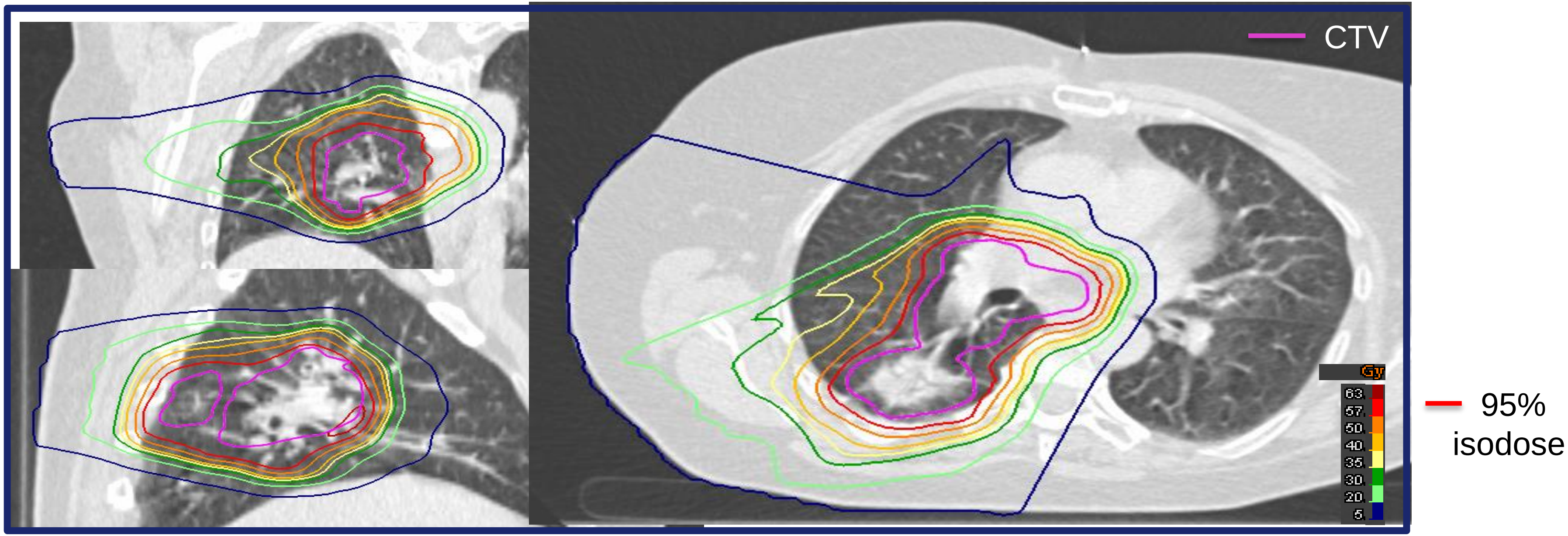
Robust planning

AveCT robust clinical plan recalculated on the 4DCT to check robustness

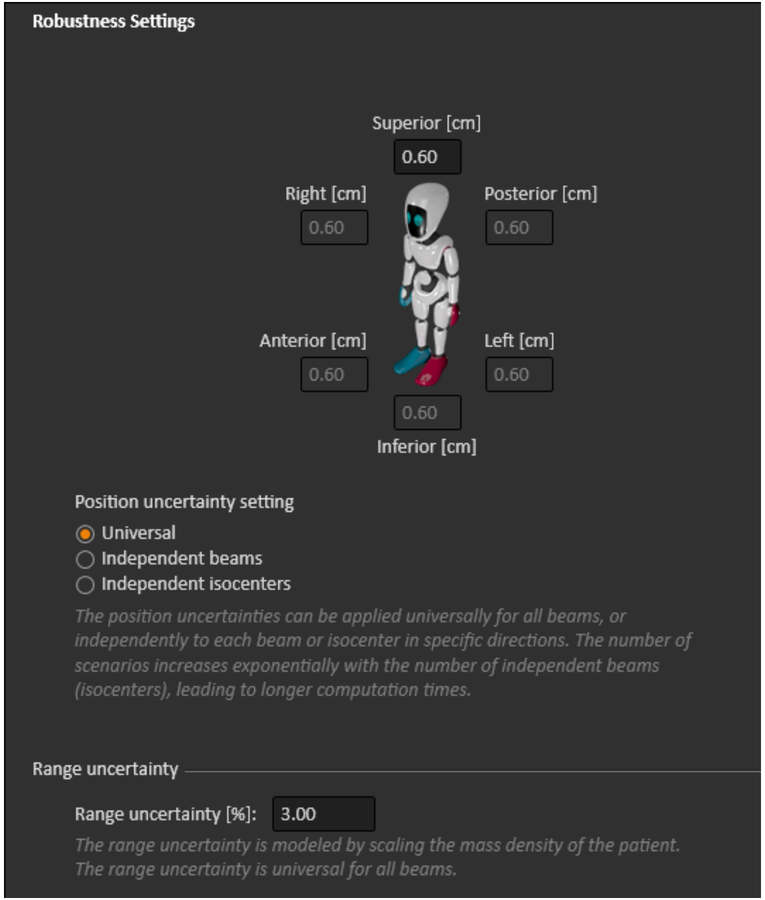
ROBUST planned protons



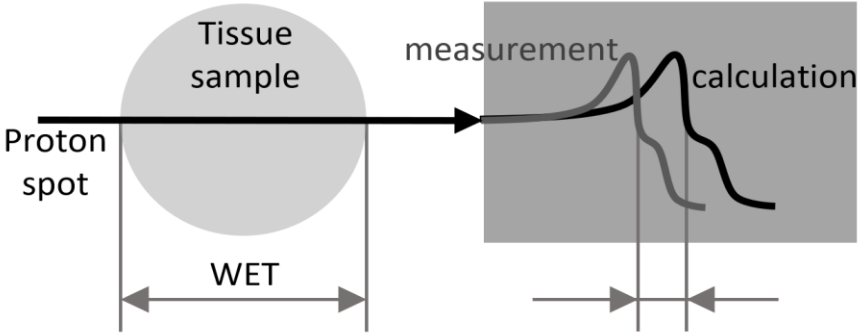
Inoue T et al. 2016 *Limited Impact of Setup and Range Uncertainties, Breathing Motion & Interplay …* IJROB

Robust planning

- LUNG : 25 x 2.4 Gy(RBE)
- 3 beams
- Monte Carlo(Raysearch)
- Planning on ITV & average of 4DCT
- Density override ITV(muscle density)
- Robustness Settings(setup/**range**)



Relative residual range errors



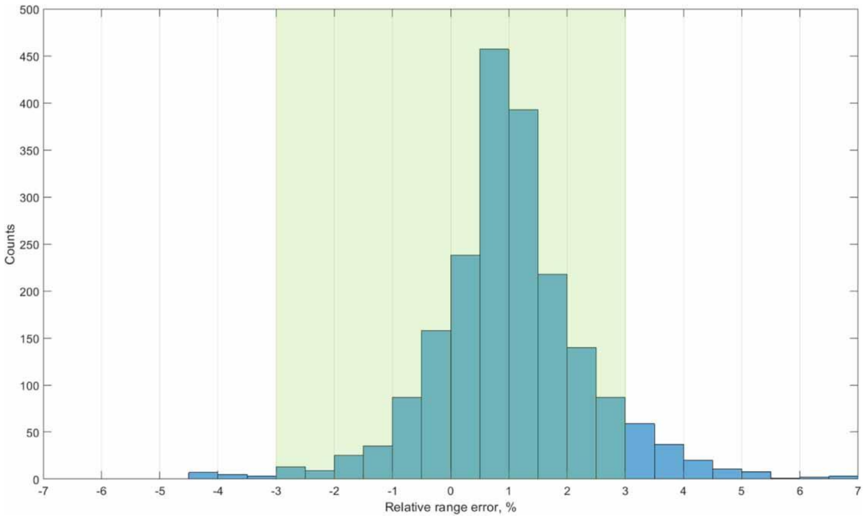
Corresponding phase
Average CT

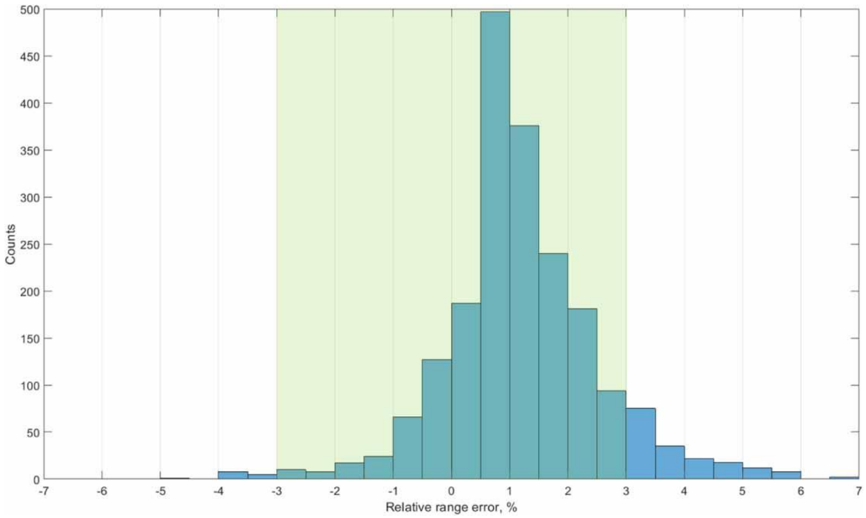
$$(\text{Rel. range error})^{-1} = \text{WET} \, / \, \text{Residual range error}$$

A Meijers et al: Assessment of range uncertainty in lung-like tissue using a porcine lung phantom and proton radiography, PMB, Vol.65, 2020

Average 4DCT

Phase 4DCT





Mean rel. range error 1.0 %
(1.5SD 2.2%)

Mean rel. range error 1.2 %
(1.5SD 2.3%)

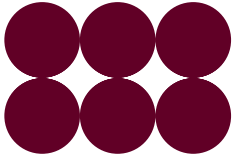
A Meijers et al: Assessment of range uncertainty in lung-like tissue using a porcine lung phantom and proton radiography, PMB, Vol.65, 2020

Robust planning

- Repainting of Pencil Beam spots Energy Layer wise

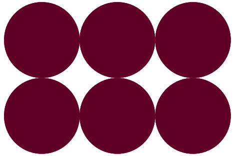
BEV

1 in layer rescanning

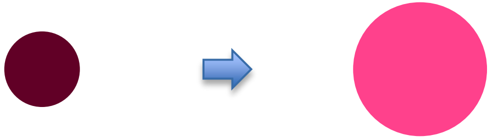


BEV

5 in layer rescanning

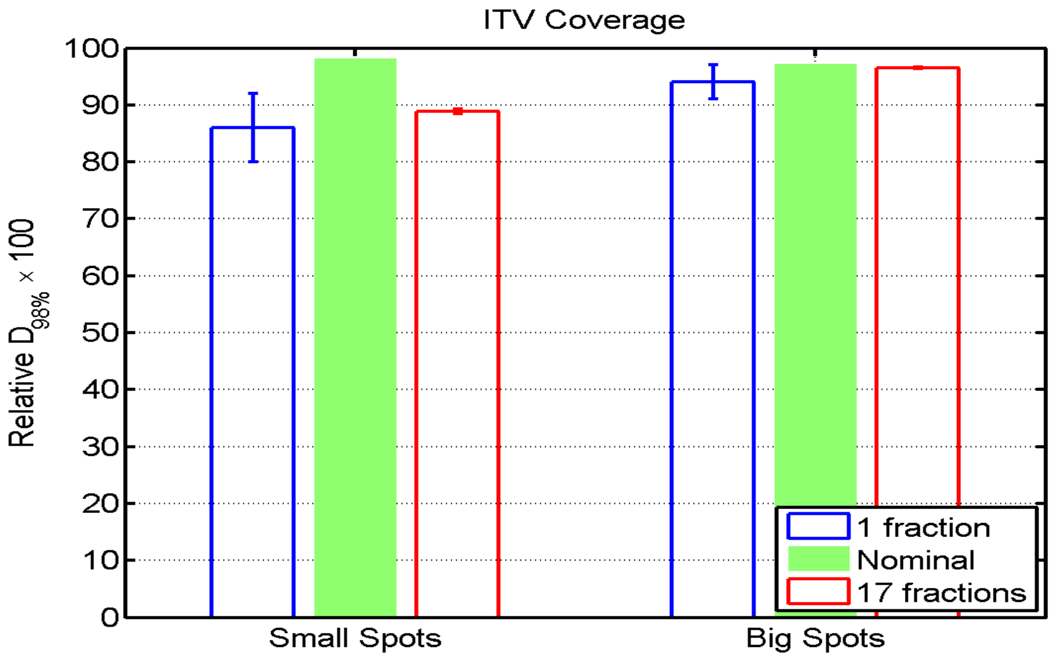


- Optional: enlargement of the spot size



Spot size&Interplay

- Small spots: $\sigma \sim 5$ mm vs. Big spots: $\sigma \sim 10$ mm

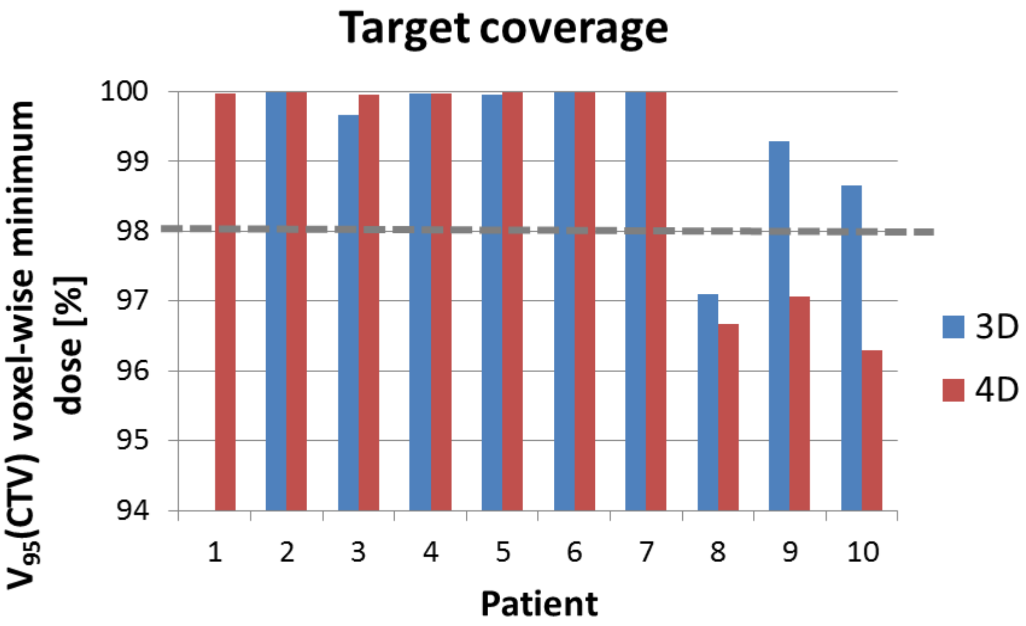


Bigger spots can correct for Interplay.

Zeng C et al.:Proton pencil beam scanning for mediastinal lymphoma: the impact of interplay between target motion and beam scanning, *PMB60(2015)*

3D vs. 4D Robust planning optimization

Preclinical study



*Comprehensive 4D Robustness evaluation

+ Setup errors
+ Proton range uncertainty
+ Breathing motion
+ Interplay effect
+ Beam delivery accuracy
+ Fractionation
+ Anatomical variations

4D rCT

*Ribeiro, CO et al. (2019) Radiother Oncol *Comprehensive 4D Robustness Evaluation ..*
Ribeiro, CO et al. (2019) IJROBP *Towards the Clinical Implementation of Pencil Beam Scanned Proton ..*

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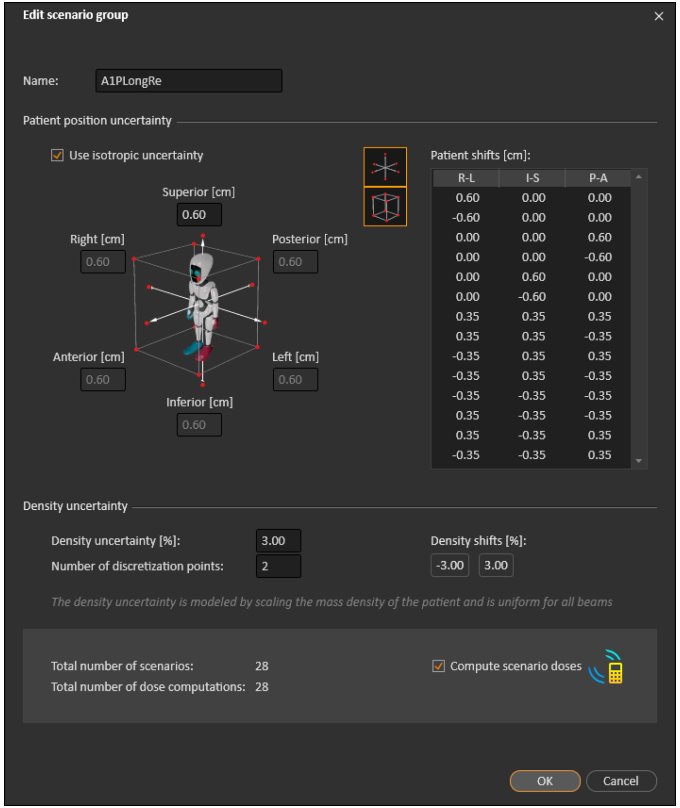
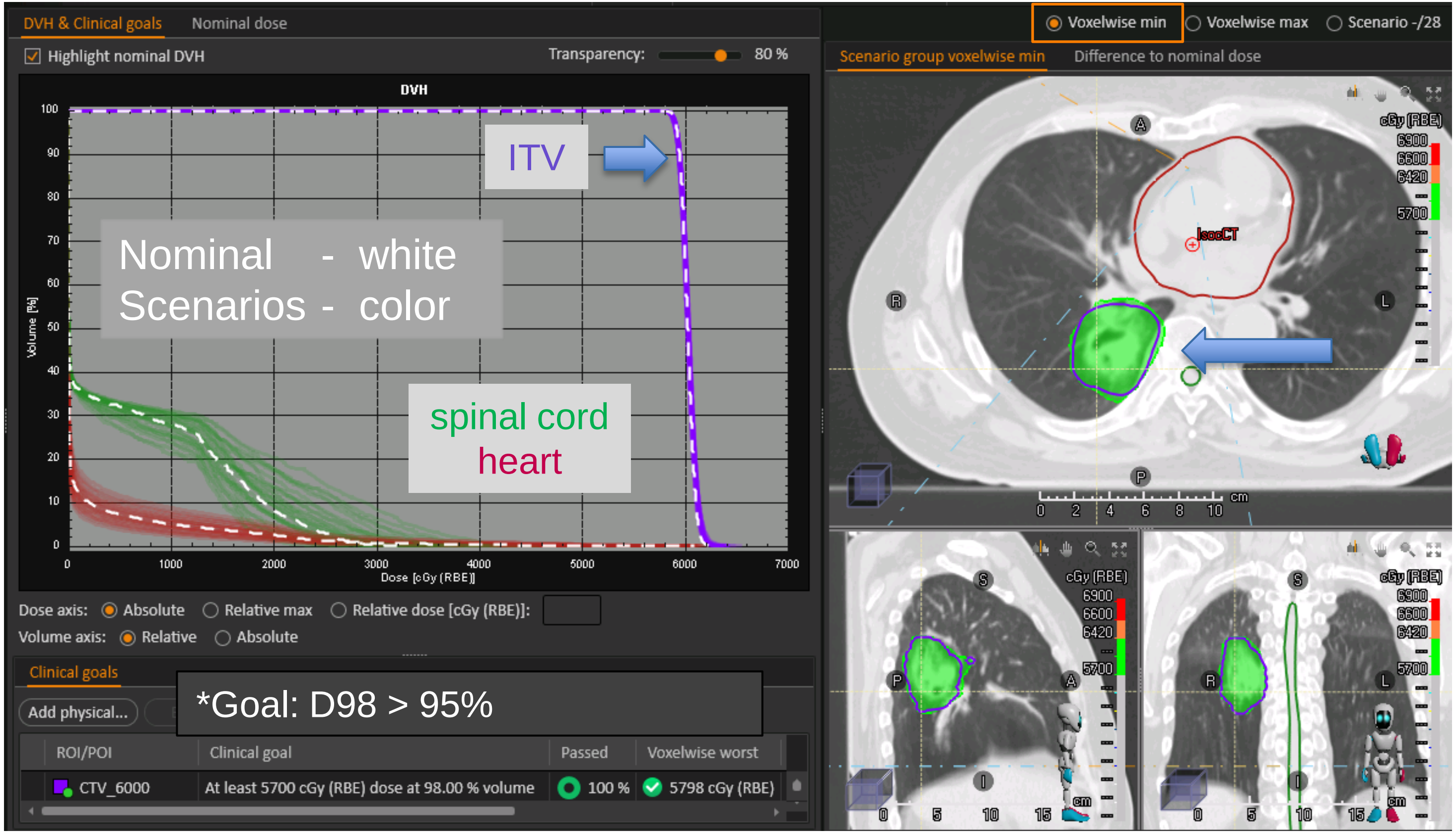
Pre-treatment robustness evaluation

Setup errors
Proton range uncertainty

Planning CT



Pre-treatment robustness evaluation 6mm/3%



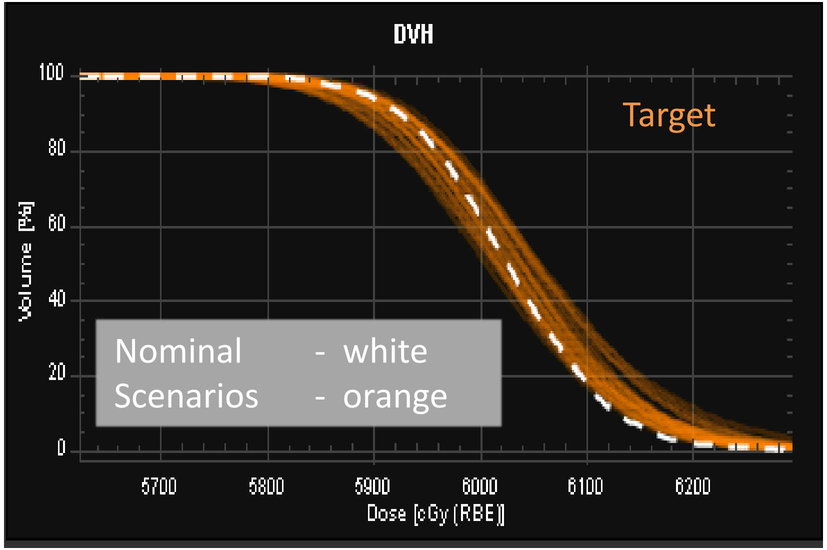
Clinical Pt
NSCLC 05

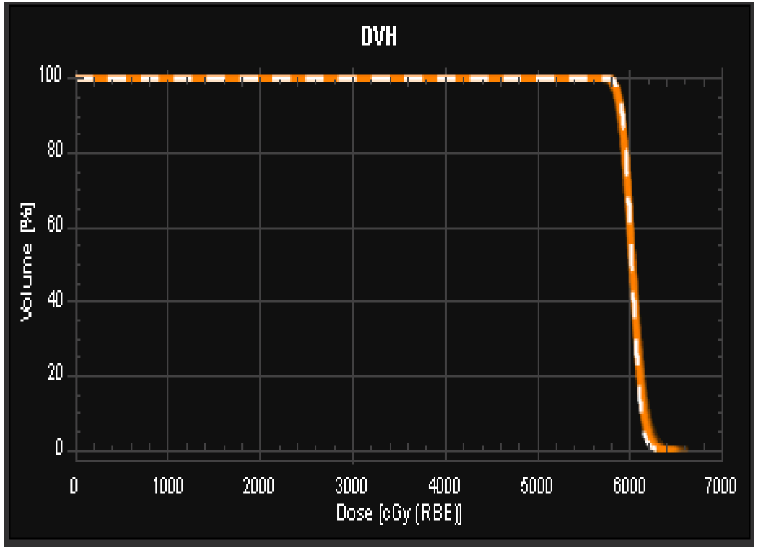
95% isodose

*Korevaar, EW et al. (2019) Radiother Oncol Practical robustness evaluation in radiotherapy ..

Pre-treatment robustness evaluation

Patient position errors	0.6 cm
Proton range uncertainty	3%

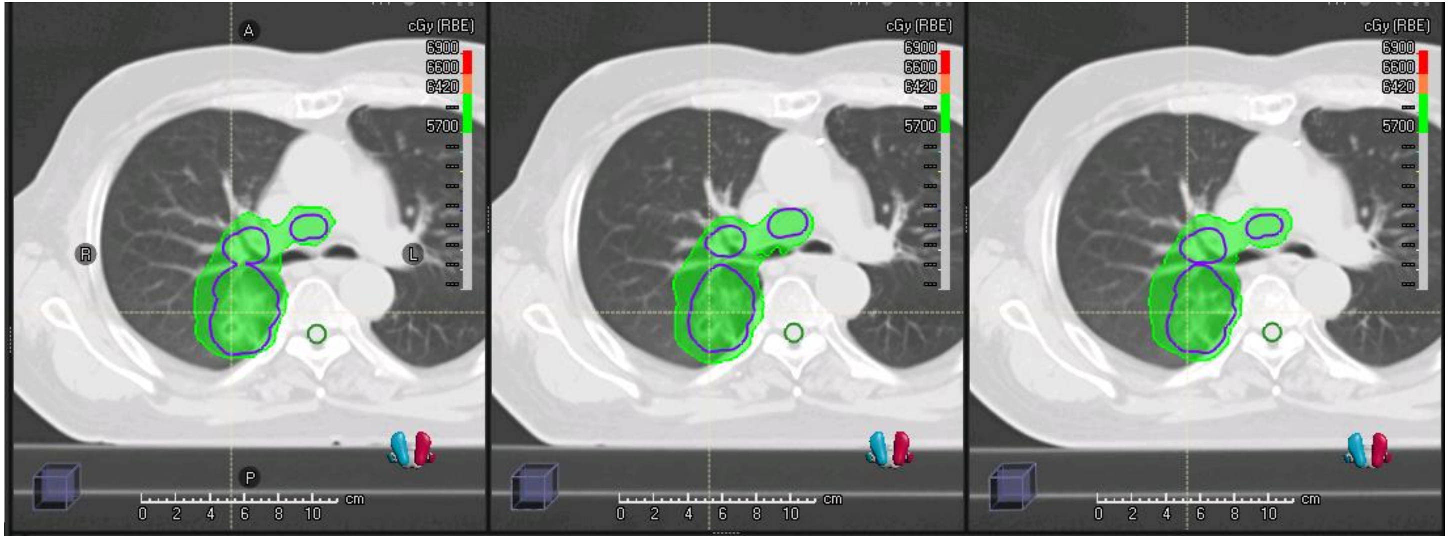




**Korevaar, EW et al. (2019) Radiother Oncol Practical robustness evaluation in radiotherapy ..*

On treatment robustness evaluation on AVECT with Vox$_{min}$ and Voxmax eval(3%/2mm)

Fraction 08 | Fraction 13 | Fraction 22



Clinical Pt NSCLC 5

Voxel-wise min

95% isodose

Goal: D98 > 95%

Frct	Dose	ROI/POI	Clinical goal	Value	Result
08	Perturbed dose (RBE):...	CTV_6000	At least 5700 cGy (RBE) dose at 98.00 % volume	5790 cGy (RBE)	✓
13	Perturbed dose (RBE):...	CTV_6000	At least 5700 cGy (RBE) dose at 98.00 % volume	5761 cGy (RBE)	✓
22	Perturbed dose (RBE):...	CTV_6000	At least 5700 cGy (RBE) dose at 98.00 % volume	5774 cGy (RBE)	✓

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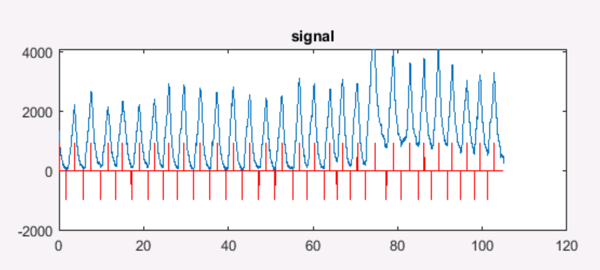
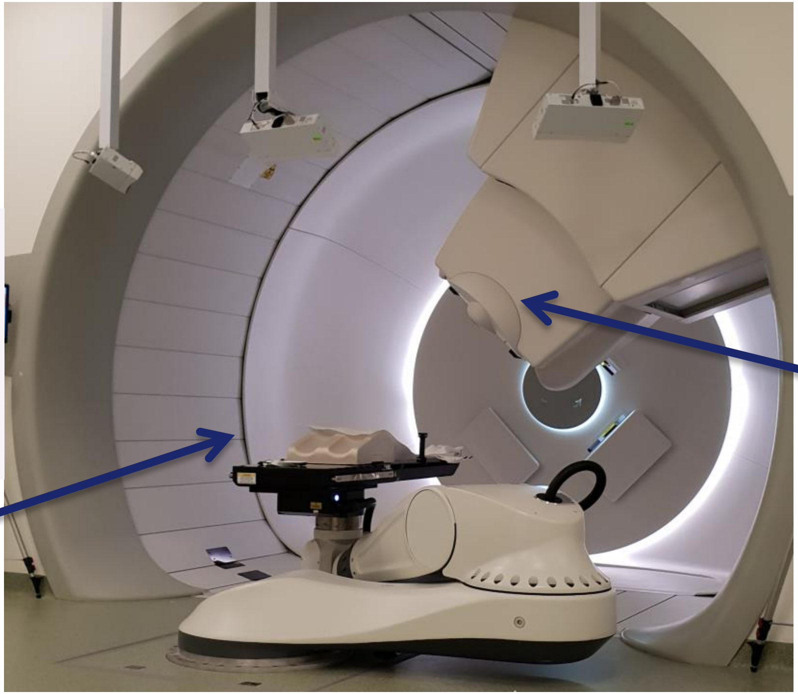
Daily 4D dose reconstruction

ANZAI
breathing signal

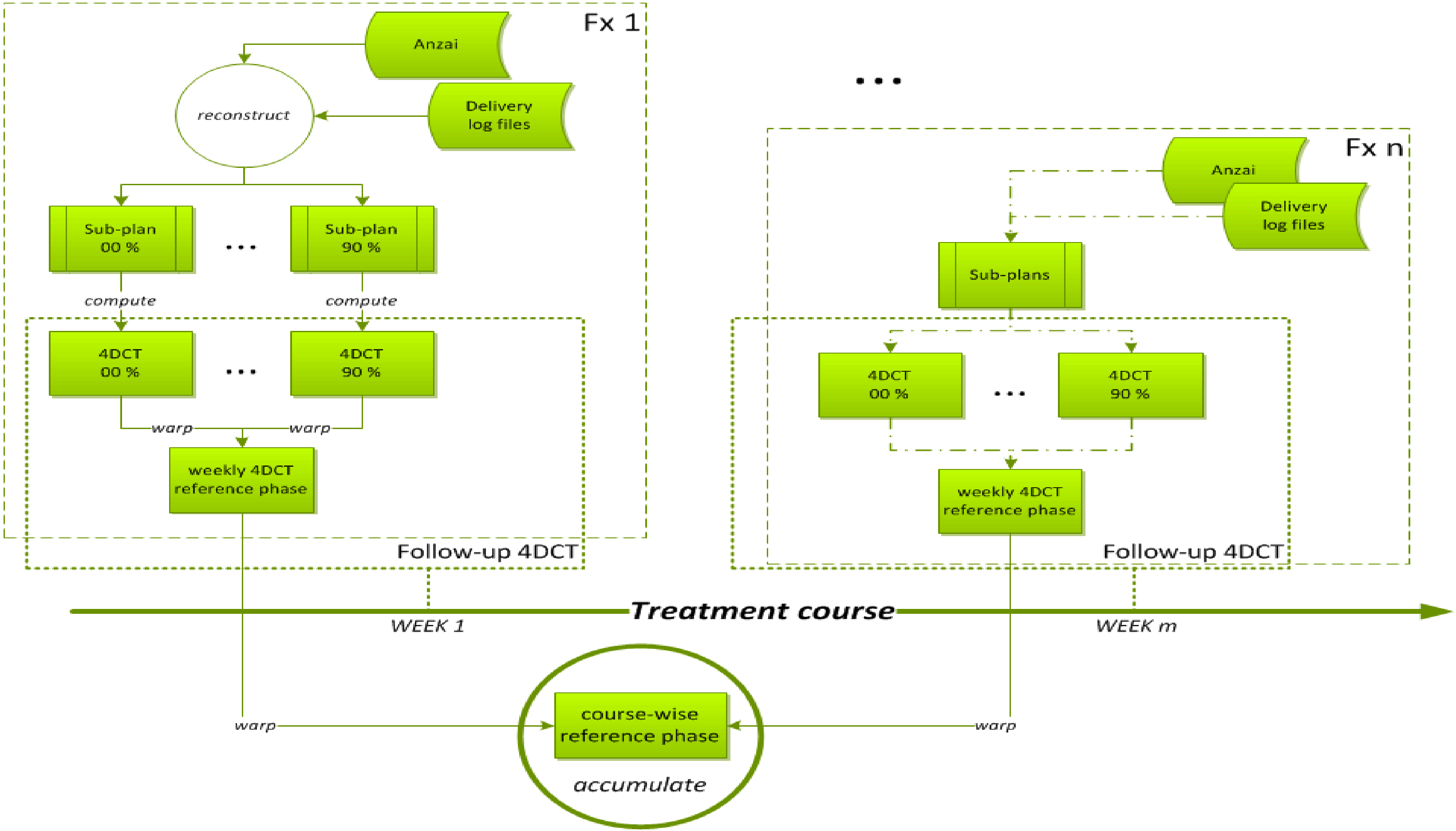




Delivery
log files

```
21:33:04.679,5.81,4.26,-6.32,
21:33:04.679,5.81,4.26,-6.32,
21:33:04.679,5.81,4.26,-6.31,
```

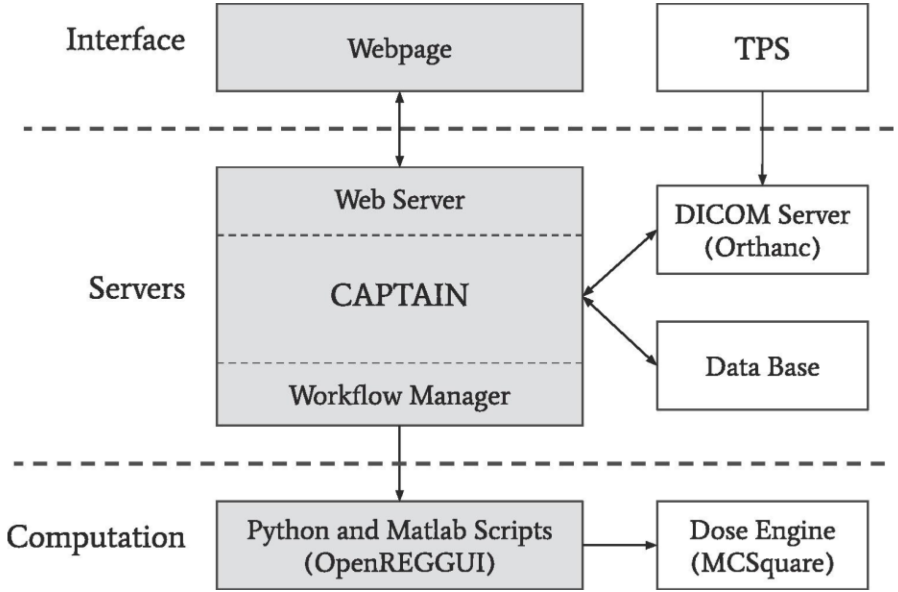
Meijers A et al., Log file-based dose reconstruction and accumulation for 4D adaptive pencil beam scanned proton therapy in a clinical treatment planning system: Implementation and proof-of-concept. Med Phys. 2019 Mar;46(3):1140-1149



Meijers, A et al. Evaluation of interplay and organ motion effects by means of 4D dose reconstruction and accumulation", Radiotherapy and Oncology 150 (2020) 268-274

On treatment robust evaluation

Clinical Control Infrastructure



The platform architecture: core units (in grey) and external components (in white).

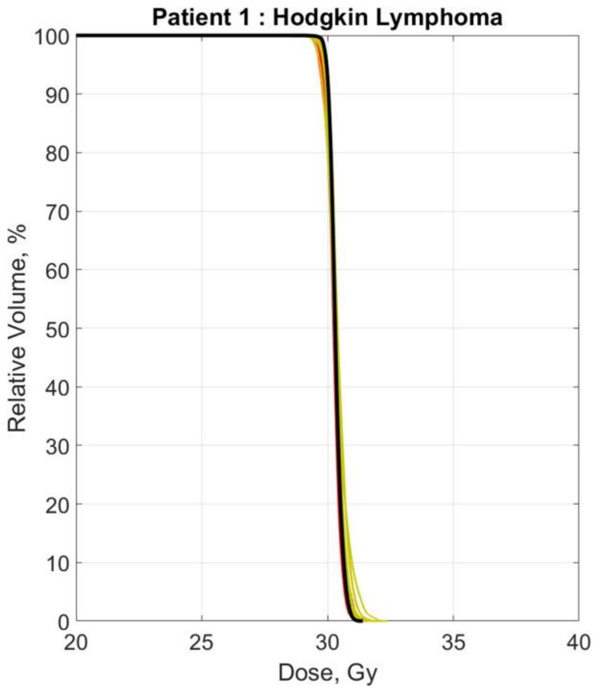
G. Guterres Marmitt et al: Platform for automatic patient quality assurance via Monte Carlo simulations in proton therapy;PM, Vol.70 2020

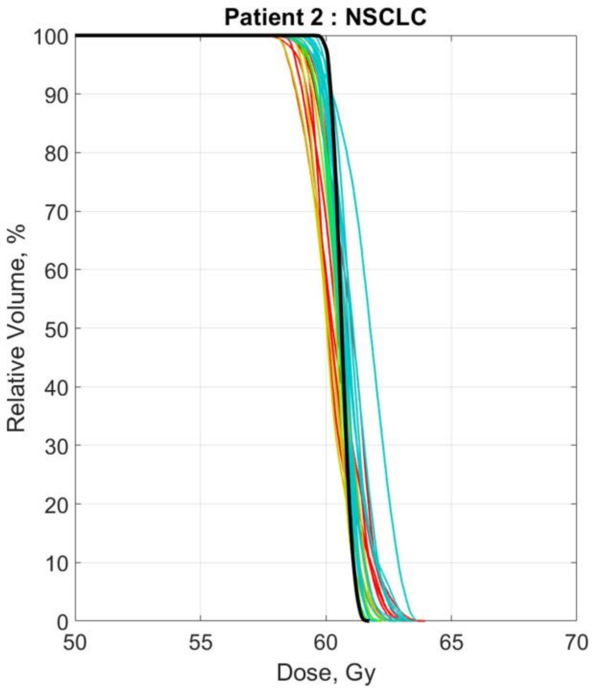
Characteristics of treatmeant course preparation 10 consecutive patients treated with IMPT@UMCG

Pat. #	Indication	Prescription	ITV volume, cm^3	Mean motion, mm	Point-max motion mm	ITV $V95_{vox\text{-}min}$, %
01	Lymphoma	$15 \times 2.0\ Gy_{RBE}$	166	0.9	<5	98.13
02	NSCLC	$25 \times 2.4\ Gy_{RBE}$	44	2.2	<6	99.42
03	NSCLC	$25 \times 2.4\ Gy_{RBE}$	243	0.9	<6	99.77
04	NSCLC	$25 \times 2.4\ Gy_{RBE}$	131	0.7	<5	99.82
05	NSCLC	$25 \times 2.4\ Gy_{RBE}$	357	0.7	<7	99.06
06	NSCLC	$25 \times 2.4\ Gy_{RBE}$	217	1.1	<5	99.74
07	NSCLC	$25 \times 2.4\ Gy_{RBE}$	298	1.2	<9	98.41
08	NSCLC	$25 \times 2.4\ Gy_{RBE}$	202	1.4	<8	98.41
09	NSCLC	$25 \times 2.4\ Gy_{RBE}$	336	0.6	<6	99.49
10	Lymphoma	$15 \times 2.0\ Gy_{RBE}$	339	2.1	<20	99.67

A. Meijers, et al. Evaluation of interplay and organ motion effects by means of 4D dose reconstruction and accumulation", Radiotherapy and Oncology 150 (2020) 268-274

Daily 4D Dose reconstruction





Lung&Mediastinal Lymphoma:

- Similar motion
- Different Target Volumes
- Small vs. Enlarged Spots
- Larger hot/cold spots
- Similar cummulative dose

A. Meijers, et al. Evaluation of interplay and organ motion effects by means of 4D dose reconstruction and accumulation", Radiotherapy and Oncology 150 (2020) 268-274

Lung Big Movers Study

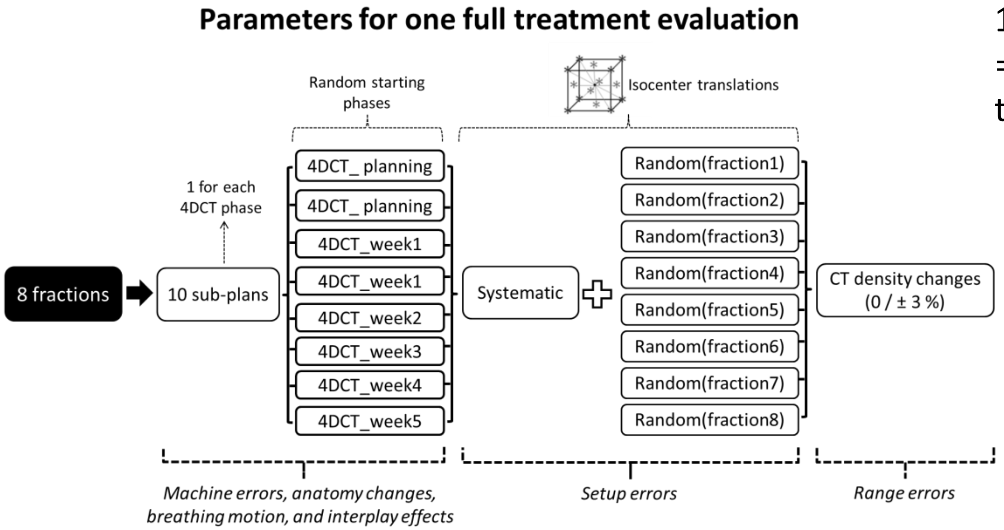
- Thoracic indications
  - 9 lung + 1 thymoma cancer
    - Large CTV motion amplitudes (> 10 mm)
  - IMPT_3D plans
    - Clinically approved
    - 4DREM
      - Machine log files
      - Patient weekly repeated 4DCTs
      - End-exhale planning CT phase

	Primary tumour	Point maximum CTV motion [mm]	Mean CTV motion [mm]	
Patient	**Location**	**Planning 4DCT**	**Planning 4DCT**	**Verification 4DCTs**
1	Lung (right-lower)	< 12	5.1	3.9 ± 0.4
2	Lung (right-middle)	< 12	8.9	7.0 ± 0.5
3	Anterior mediastinum	< 15	9.7	8.9 ± 1.0
4	Lung (right-upper)	< 12	1.5	1.8 ± 0.4
5	Lung (right-middle)	< 16	5.0	4.1 ± 0.8
6	Lung (left-lower)	< 15	9.0	8.2 ± 0.8
7	Lung (right-middle)	< 11	10.9	7.7 ± 1.6
8	Lung (right-middle)	< 12	5.9	7.6 ± 0.3
9	Lung (left-upper)	< 12	4.9	4.4 ± 0.8
10	Lung (right-upper)	< 12	5.4	5.0 ± 0.1

C.O. Ribeiro :Patient and machine specific evaluation of intensity-modulated proton therapy (IMPT) for thoracic indications with large motion. PTCOG 2021

Big Movers Study

- 4DREM (with dose-fraction-smoothening effect)



14 4D accumulated scenario dose distributions = 14 possible fractionated treatment courses of the nominal plan

Target coverage → $4DVwa_{min}$

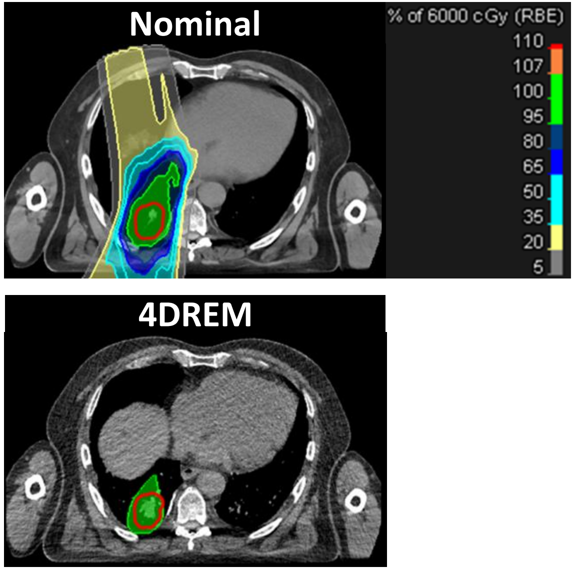
OARs → scenarios

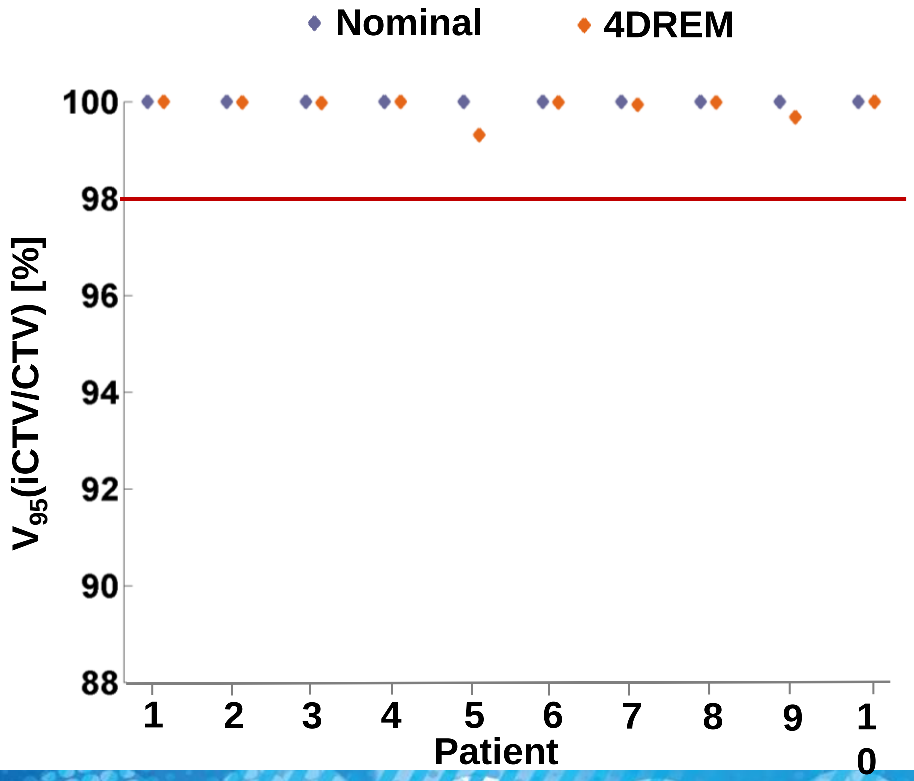
Ribeiro, *et al.*, "Comprehensive 4D robustness evaluation for pencil beam scanned proton plans", 2019.

Results – Target coverage

4DREM → 4DVw$_{min}$

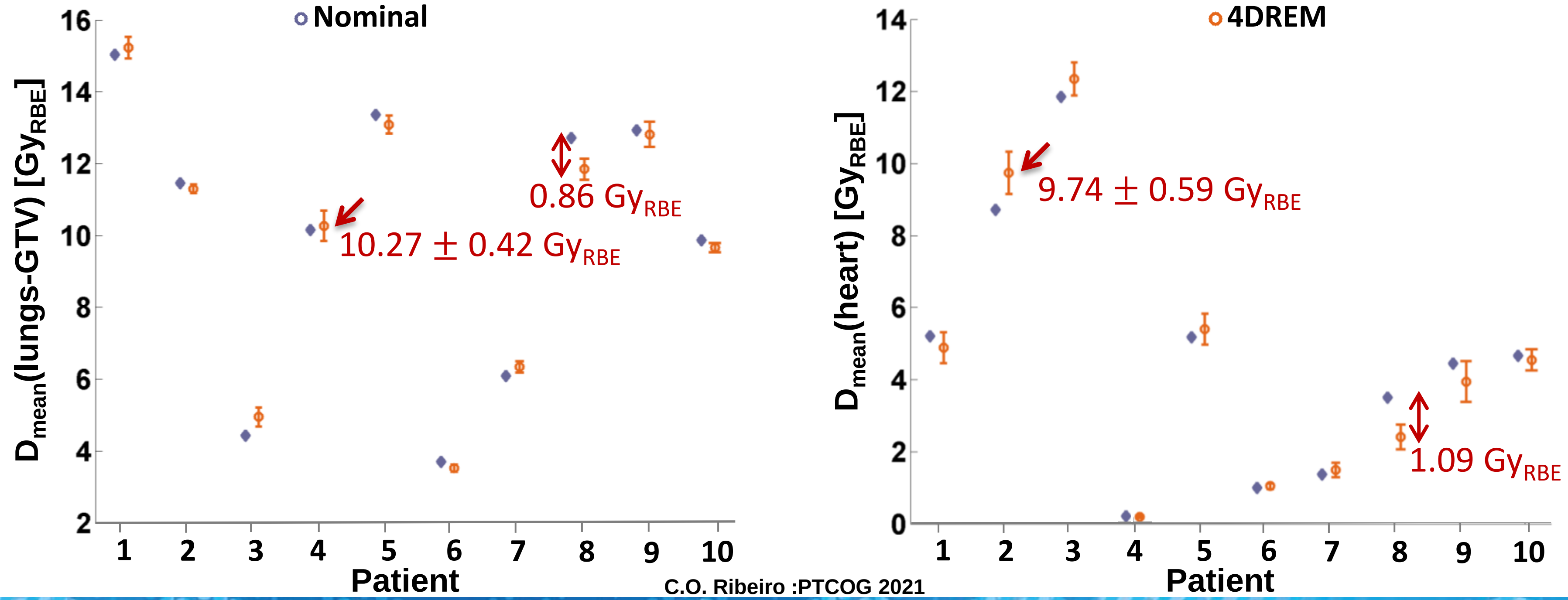
Lung cancer patient 5





OARs (lungs and heart)

4DREM = scenarios



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FUTURE :

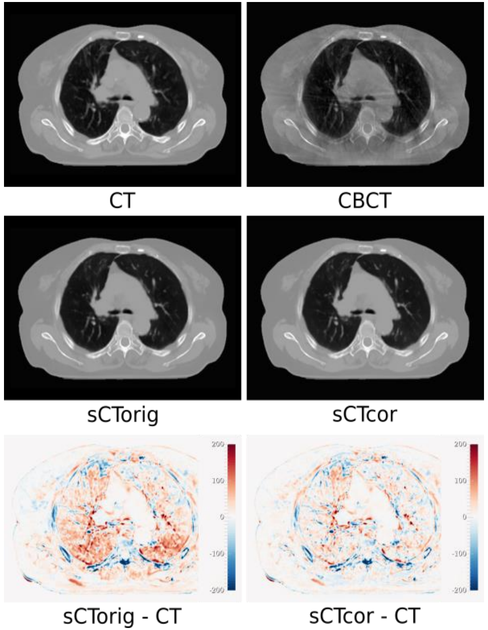
Automatize treatment planning and QA processes on our clinical control platform for daily treatment monitoring and model based adaptive proton therapy workflows based on :

- **Quality of Life based robust optimized planning**

- **daily 3D /4D synthetic CT generated from 3D /4D CBCT**

- **patient treatment log File / machine File**

- **“end to end “ treatment verification such as proton radiography measurements**



Thummerer A.: Neural Network Based Synthetic CTs for Adaptive Proton Therapy of Lung Cancer, Oral Presentation, ESTRO 2021

Conclusions:

- Rescanned delivered 3D robustly optimized and evaluated IMPT based on 4DCT can treat moving targets in free breathing for an increasing range of motion.

- Use of enlarged spots further robustify IMPT.

- Treatment adaptations are mostly due to anatomical changes.

- 4D dose reconstructions are a good predictor for plan robustness assesing the delivered dose considering patient anatomy and breathing pattern changes as the treatment progresses.

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www.umcg.nl

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