

ROCOCO: Radiation Oncology Collaborative Comparison

Results of a Multicenter In Silico Trial Comparing Photons and Protons for Radiotherapy of Non-small Cell Lung Cancer

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estro 2009 maastricht

Partners

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University Hospital Aachen, Germany.

Centre de Protontherapie d'Orsay (CPO), France.

Massachusetts General Hospital and Harvard Medical School (MGH/HMS), USA.

National Institute of Radiological Sciences (NIRS), Japan.

Gesellschaft für Schwerionenforschung (GSI), Germany.

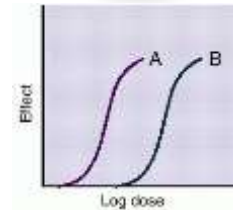
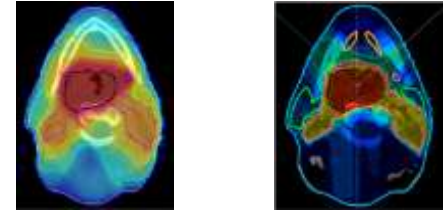
Heidelberger Ionenstrahl-Therapie (HIT), Germany.



In Silico planning study

What is ROCOCO?

- Emulation of phase III clinical trial
- Lung, Prostate, H&N
- Calculate optimal dose distr.
- Predict outcome (TCP/NTCP)



Input for Cost Effectiveness study

- Markov modeling
- Quality of Life Years (QALY)

ROCOCO protocol

- non-selected patients (25 per tumour type)
- images same patients for comparison of different treatment modalities
- every patient is its own control
- given delineation of volumes (CTV, GTV, OAR)
- same radiation schedule: 70 Gy in 2 Gy fr.
- pre-defined planning criteria

Study endpoints

Part I: iso-effective tumor control

- Less dose to normal tissue, same to the tumour

Part II: dose-escalation

- Same to normal tissue, more to tumour

Part III: hypo-fractionation

- Increase dose per fraction, less fractions, less costs

Part IV: expanding project

- More indications
- More modalities
- Validation dataset for future studies

Dataset

- 25 consecutive patients (no selection)
- Stage IA to IIIB NSCLC
- Mean CTV volume 180cc (s.e. 35cc)
- Individ. margins based on 4D CT/PET datasets
- PTV margins different for 3D-CRT
 - 95% isodose around CTV
 - range uncertainties 3.5% and 1 mm*
 - aperture expansion, range compensator smearing**

*Methodologies and tools for proton beam design for lung tumors.

Moyers MF, Miller DW, Bush DA, Slater JD. Int J Radiat Oncol Biol Phys. 2001 Apr

**Target volume dose considerations in proton beam treatment planning for lung tumors.

Engelsman M, Kooy HM. Med Phys. 2005 Dec

Planning criteria

- PTV coverage 95%-107% (ICRU50/62)
- Spinal cord: max. $< 54\text{Gy}$
- Lungs: MLD $< 19\text{ Gy}$
- Esophagus: max. $< 80\text{ Gy}$
- Heart: $V60 < 33\%$, $V45 < 67\%$, $V40 < 100\%$

Results

Lung data available

- 25 3D-CRT (photons)
- 22 IMRT (photons)
 - technical issues (?)
- 23 3D-CPT protons
 - cranial tumours
 - setup uncertainty too big

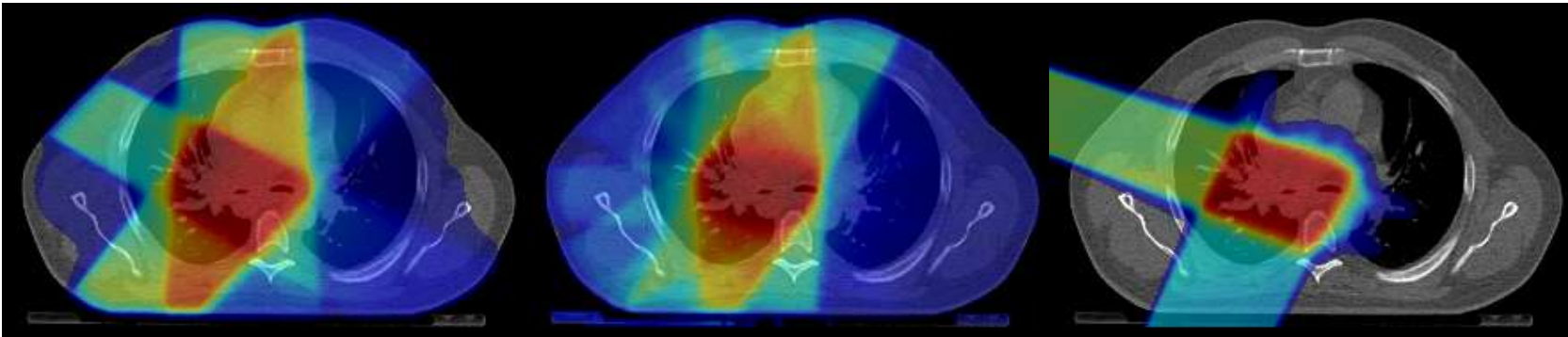
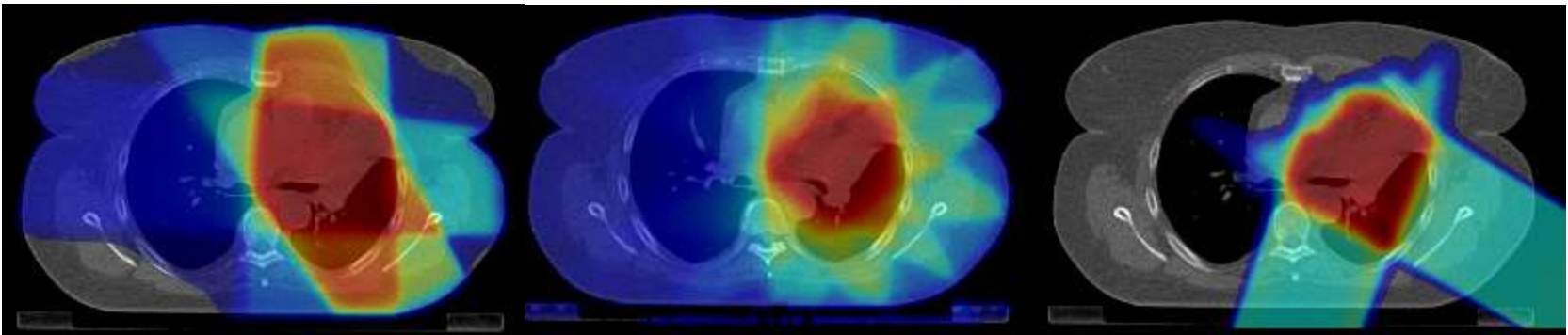


Results: # 12 & 13

3D-CRT

IMRT

3D-CPT

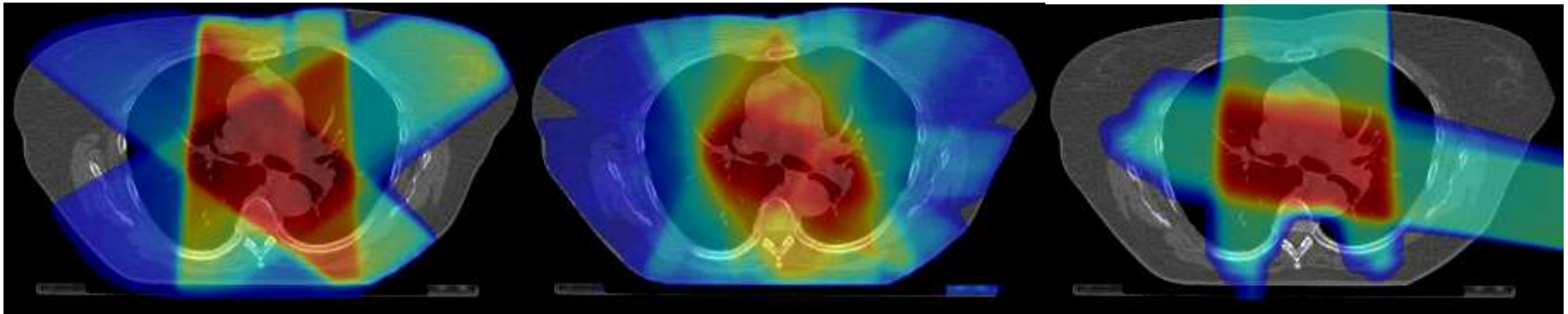
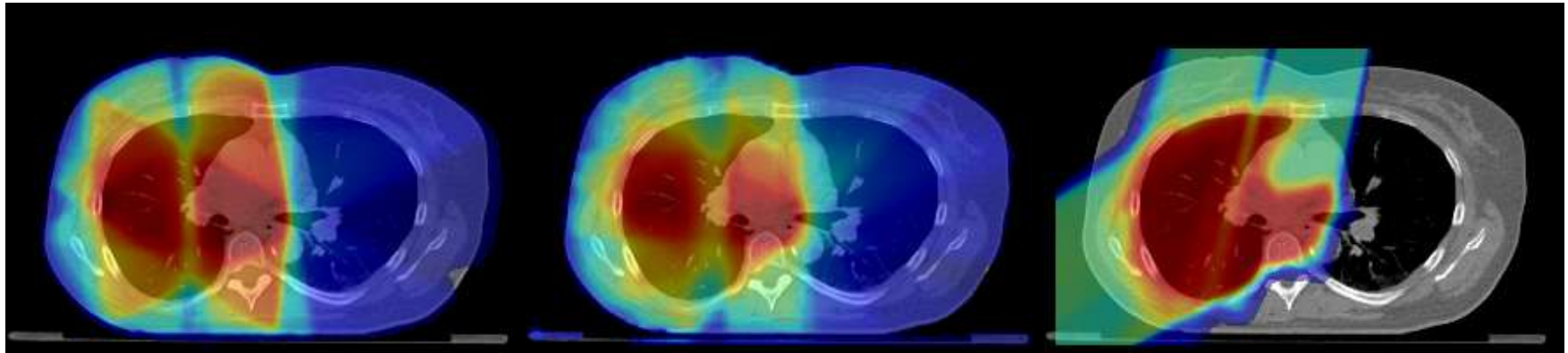


Results: # 17 & 33

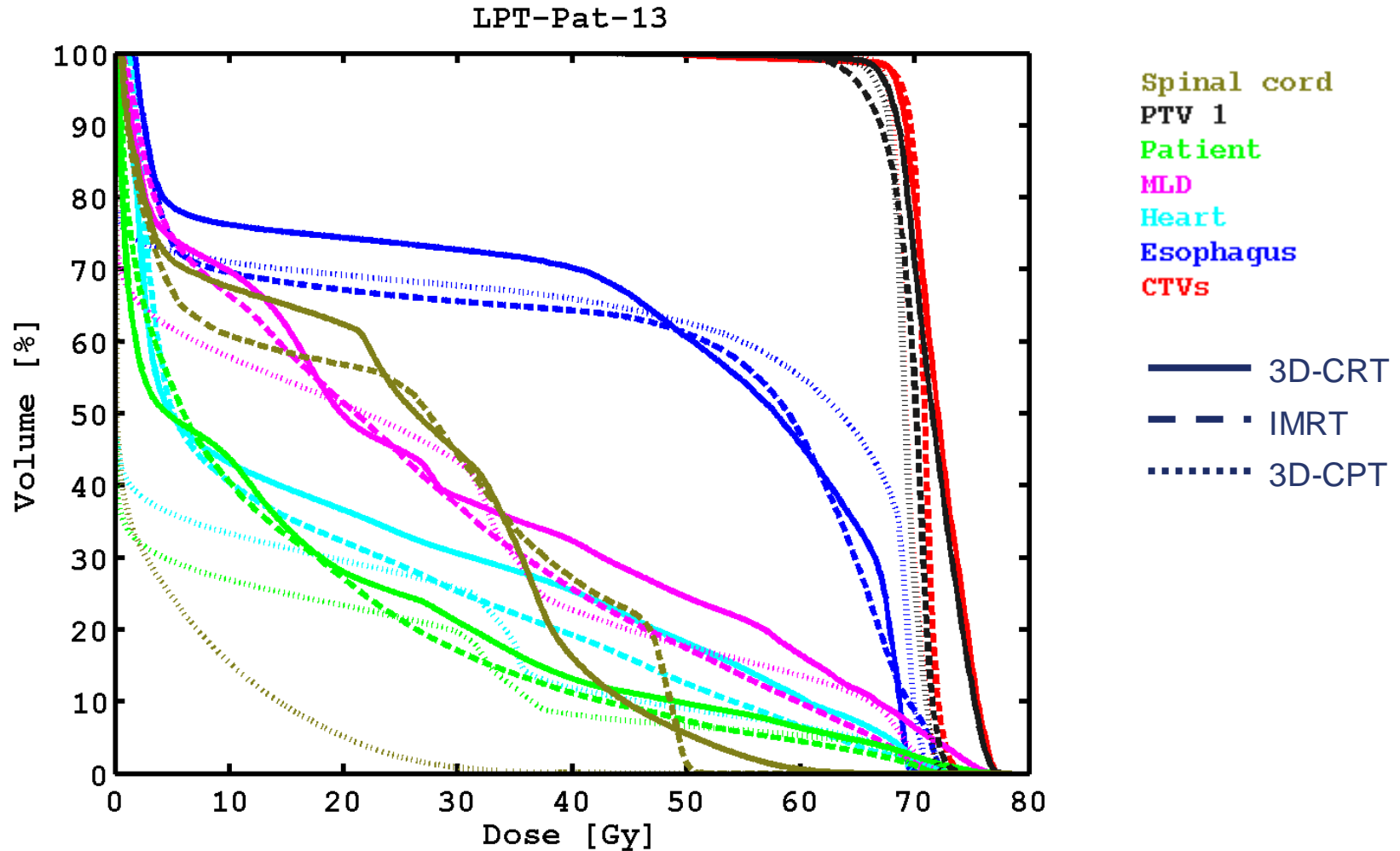
3D-CRT

IMRT

3D-CPT



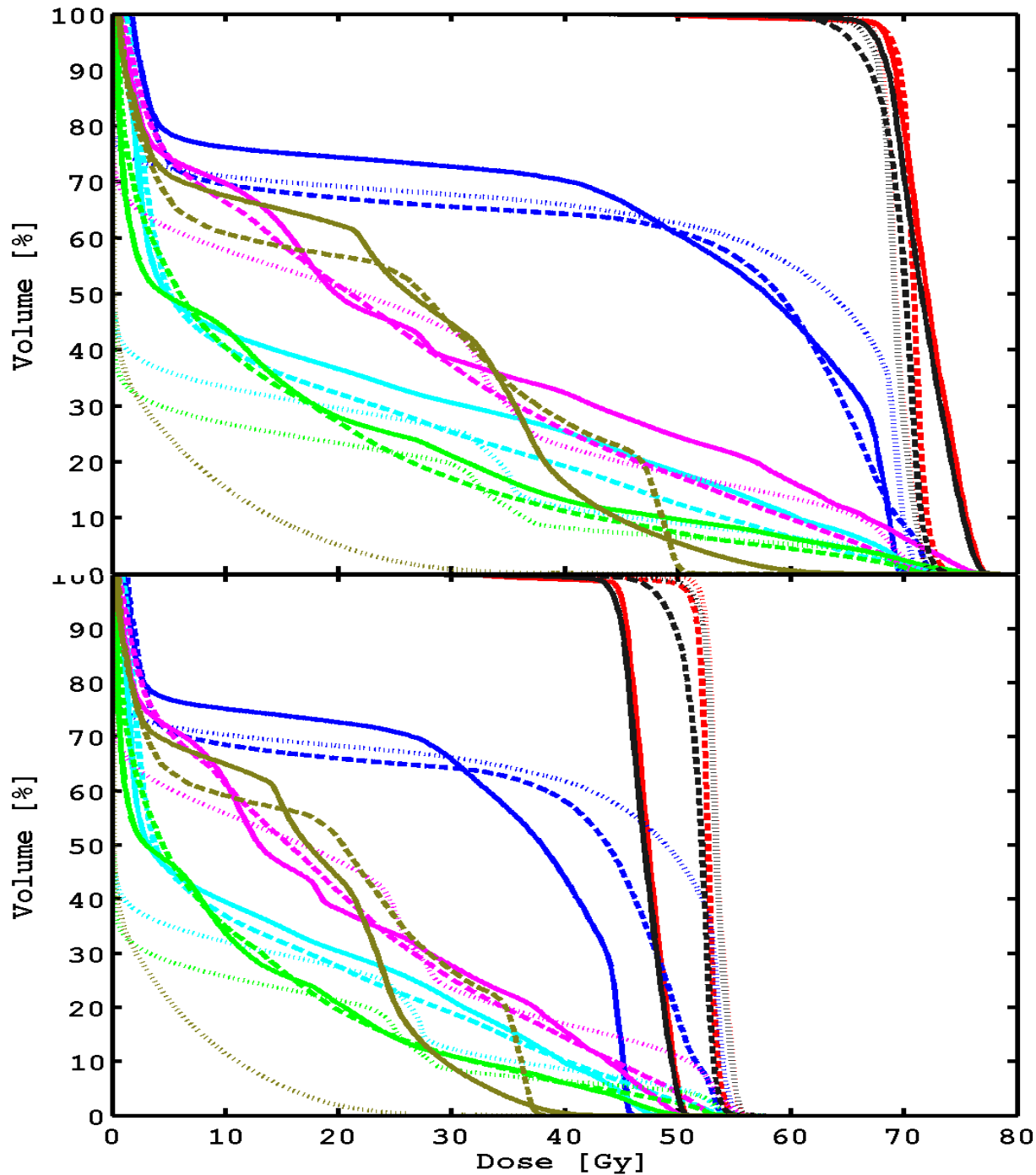
DVH results #13



Limiting OAR

- Prescribed Dose (PD=70Gy) not always reached
 - MTD: Max. Tolerated Dose (in 2 Gy fr.)

	3D-CRT	IMRT	3D-CPT
Limited cases	10 (50%)	6 (30%)	9 (45%)
Mean MTD (se)	62 (2.2)	67 (1.3)	64 (1.7)



Statistics

Modality	MTD [Gy]	Mean Dose [Gy]			Max Dose [Gy]		V40 [%]	V65 [%]
		CTV	MLD	Patient*	Spinal	Esophagu	Heart	
3D-CRT	62	63.2	14.9	8.3	38.2	57.4	10.2	1.1
IMRT	67	67.8	14.6	8.6	42.7	63.1	9.1	1.1
3D-CPT	64	64.6	11.1	5.6	34.5	60.6	6.5	1.6

Friedman	0.462	0.000	0.000	0.000	0.010	0.000	0.184
Wilcox: PR vs PH	-	0.000	0.000	0.010	0.062	0.001	-
Wilcox: PR vs IM	-	0.000	0.000	0.000	0.005	0.003	-
Wilcox: PH vs IM	-	0.279	0.126	0.015	0.255	0.070	-

*integral dose

“Therapeutic Index”

Modality	MTD [Gy]	Mean Dose [Gy]			Max Dose [Gy]		V40 [%]	V65 [%]
		CTV	MLD	Patient*	Spinal	Esophagu	Heart	
3D-CRT	62	63.2	14.9	8.3	38.2	57.4	10.2	1.1
IMRT	67	67.8	14.6	8.6	42.7	63.1	9.1	1.1
3D-CPT	64	64.6	11.1	5.6	34.5	60.6	6.5	1.6

- Surrogate Therapeutic Index

- e.g. $Ti_{\text{heart}} = D_{\text{CTV}} / V40_{\text{heart}}$

Modality	TI					
	MLD	Patient	Spinal cord	Esophagus	V40heart	V65heart
3D-CRT	4.2	7.6	1.7	1.1	6.2	57.2
IMRT	4.6	7.9	1.6	1.1	7.5	62.8
3D-CPT	5.8	11.5	1.9	1.1	9.9	40.5

Conformity

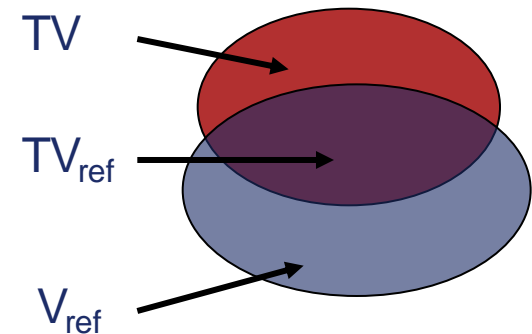
- Lomax: only consider tumour
- Van 't Riet: include surrounding

$$CN = \frac{TV_{ref}}{TV}$$

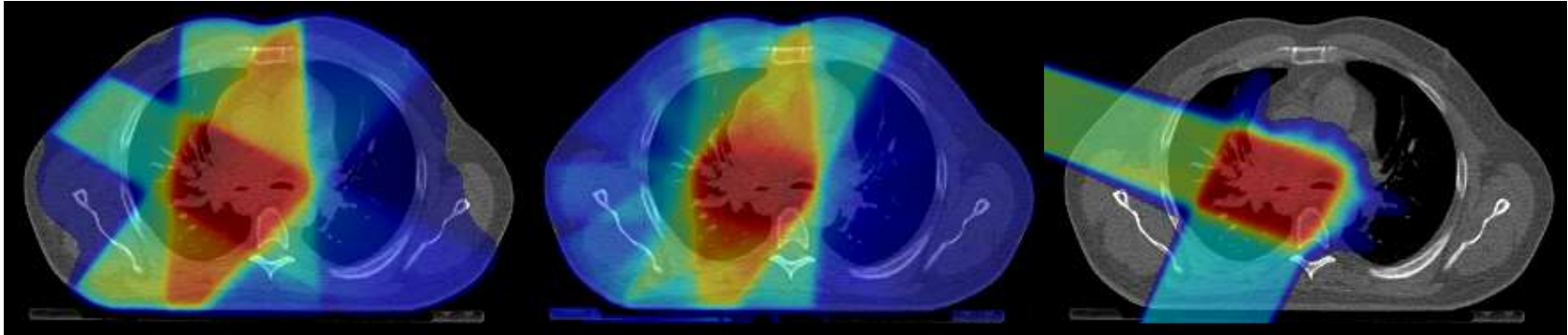
$$CN = \frac{TV_{ref}}{TV} \times \frac{TV_{ref}}{V_{ref}}$$

PTV	Mean (s.e.)	CNlomax100	CNvhRiet100
	3D-CRT	0.71 (0.03)	0.48 (0.03)
	IMRT	0.95 (0.02)	0.45 (0.03)
	3D-CPT	0.69 (0.03)	0.42 (0.04)

CTV	Mean (s.e.)	CNlomax100	CNvhRiet100
	3D-CRT	0.34 (0.02)	0.26 (0.02)
	IMRT	0.60 (0.02)	0.41 (0.03)
	3D-CPT	0.30 (0.02)	0.19 (0.02)

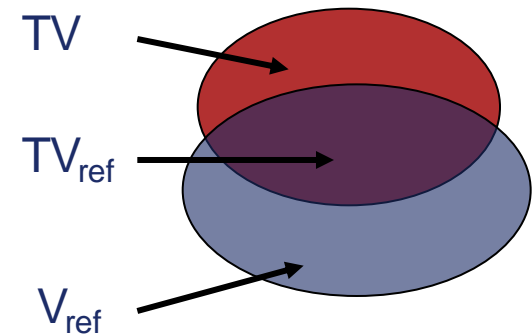


Conformity



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	3D-CPT	0.30 (0.02)	0.19 (0.02)



Conclusions

- Conformity lower for protons
 - close around tumour
- Protons support ALARA principle
 - further away from tumour
 - secondary tumour ind.?
- Dose-escalation possible
 - Mean MLD ~11Gy (max = 19Gy)
 - Mean Spinal cord ~35Gy (max = 54Gy)

Future work

- TCP / NTCP modelling
 - Collab. with ALLEGRO project
 - Collab. with Alan Nahum
- Hyperfractionation
 - Safe to reduce costs?
- Expansion
 - Modalities
 - Tumour sites

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Pro-Tones : real Music Guided Radiation Therapy



ESTRO social event
Tonight : 20:00
La Caverne de Geulhem
(transport provided)