PAUL SCHERRER INSTITUT

PSI

Tony Lomax :: Head of Medical Physics :: Paul Scherrer Institute
Department of Physics :: ETH-Zurich

Physics against cancer: Proton therapy at PSI.

PSI summer school 2024

Overview

1. Principles of radiotherapy
2. The physics of proton therapy
3. Proton therapy at PSI
4. Clinical advantages of protons
5. Current research at PSI

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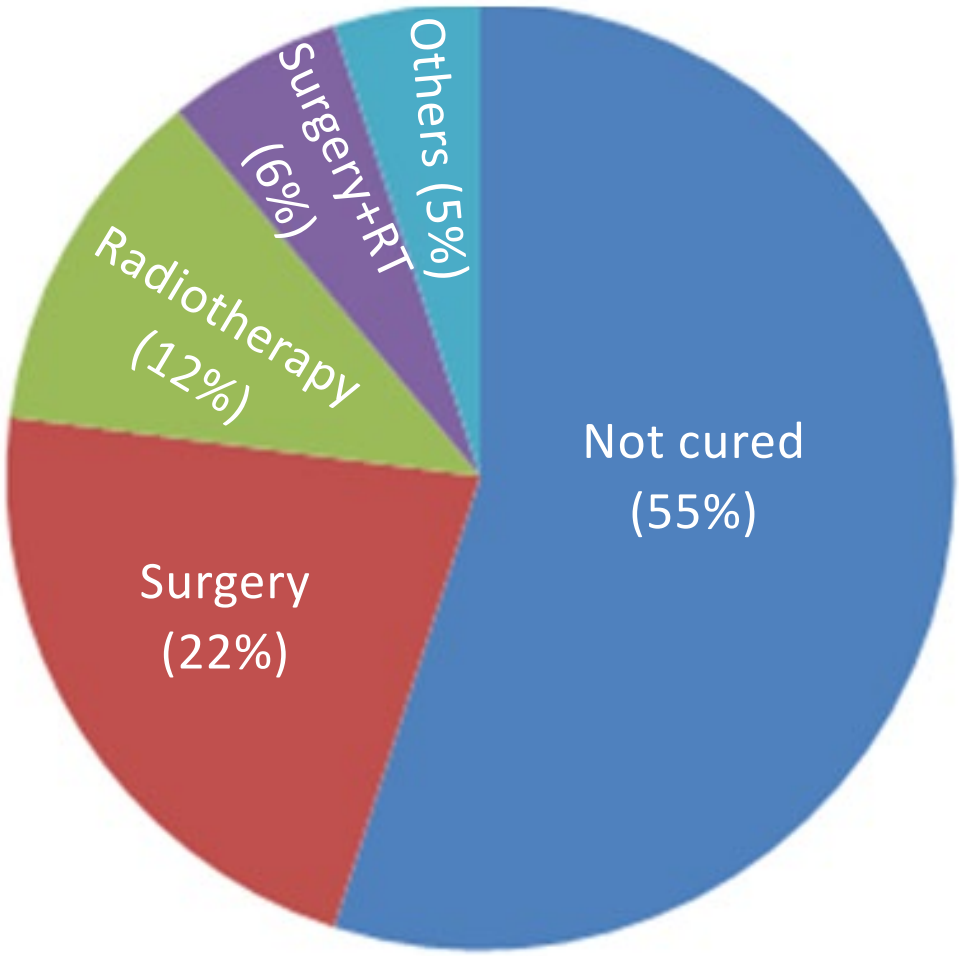
Cancer treatments and their cure* rates



*Cure - survival >5 years after diagnosis

The principle of radiation therapy.

• Energy deposited by radiation (dose = J/kg or Gray) can damage DNA and thus sterilise cells

•The higher the delivered dose to the whole tumour, the higher the probability of controlling it.

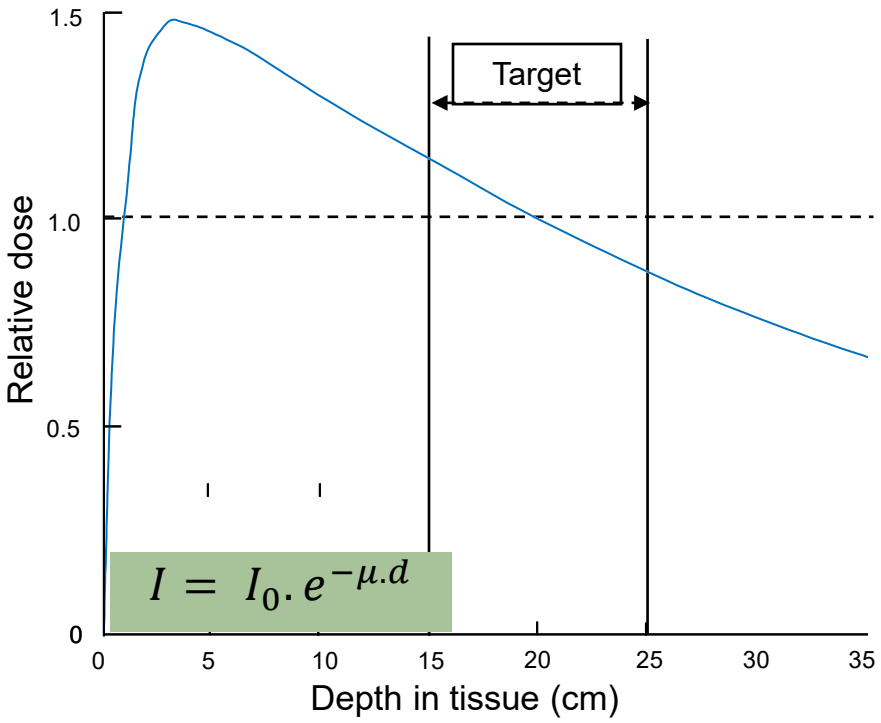
BUT…

• Normal tissues will also be damaged and sterilized by irradiation in a similar way.

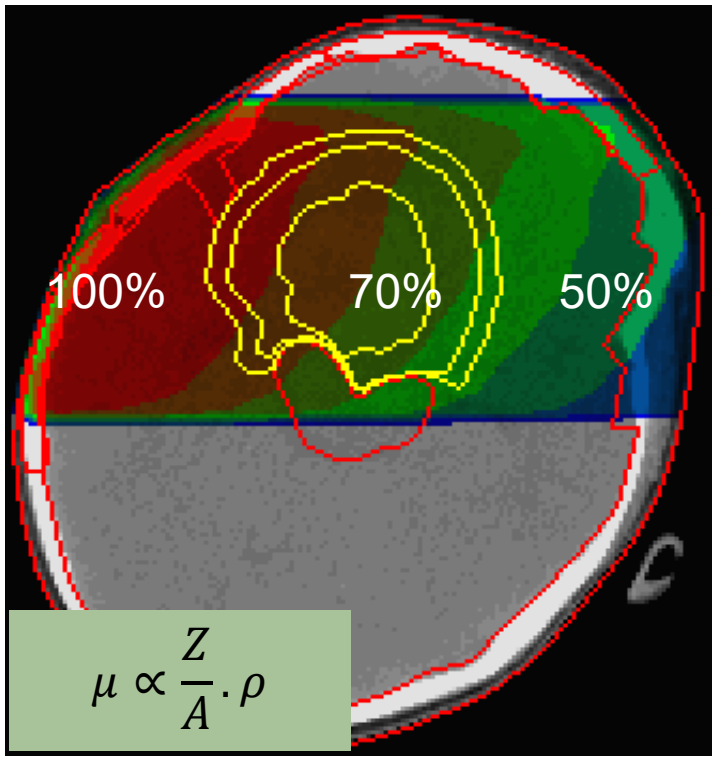
The science of radiotherapy then, is to concentrate the dose in the tumour whilst sparing the surrounding normal tissues as much as possible.

Principle interactions of photons.

Depth-dose curve for 15 MeV photons



Dose distribution for 15 MeV photons



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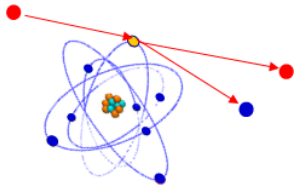
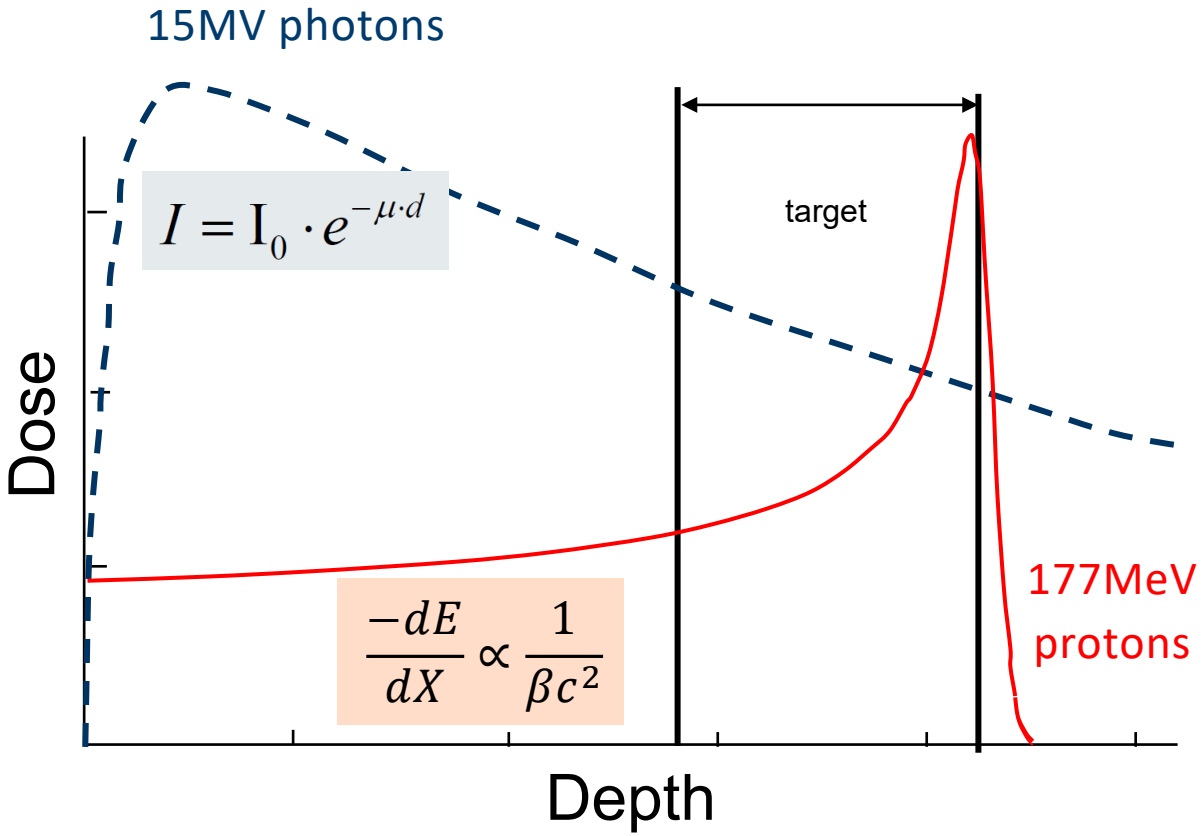
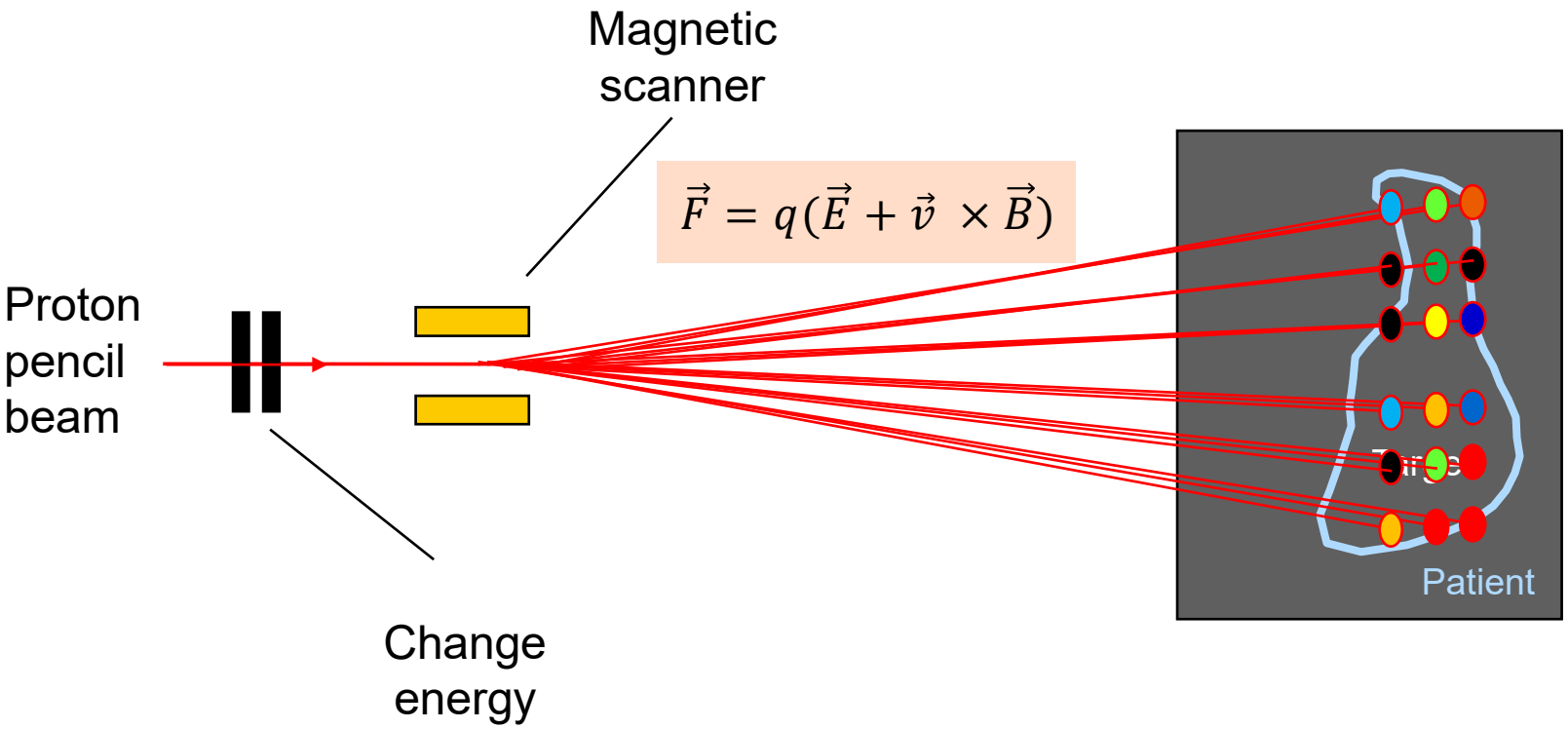
Interactions of protons



Energy loss



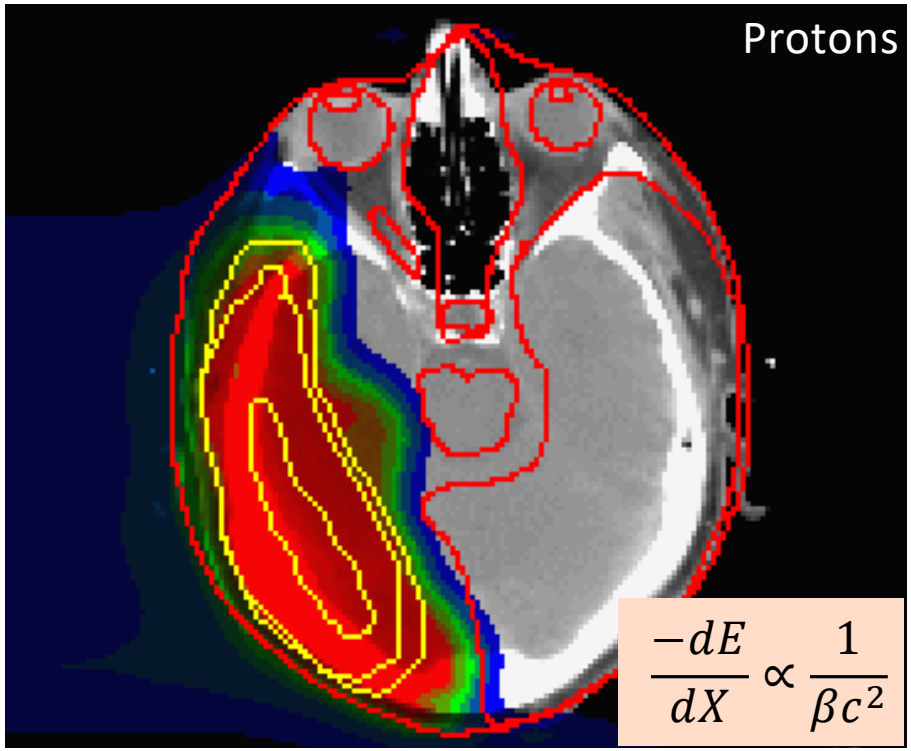
Modulating protons for therapy Pencil Beam Scanning (PBS).



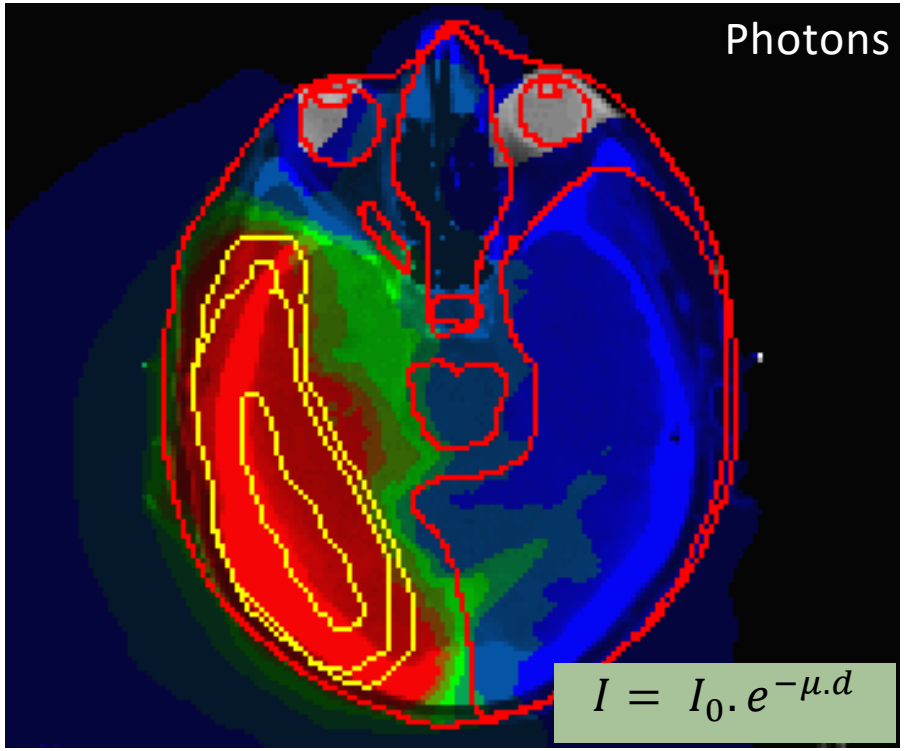
Pedroni et al 1995, Med. Phys. 22:37-53.

The advantage of proton physics.

Proton physics



Photon physics



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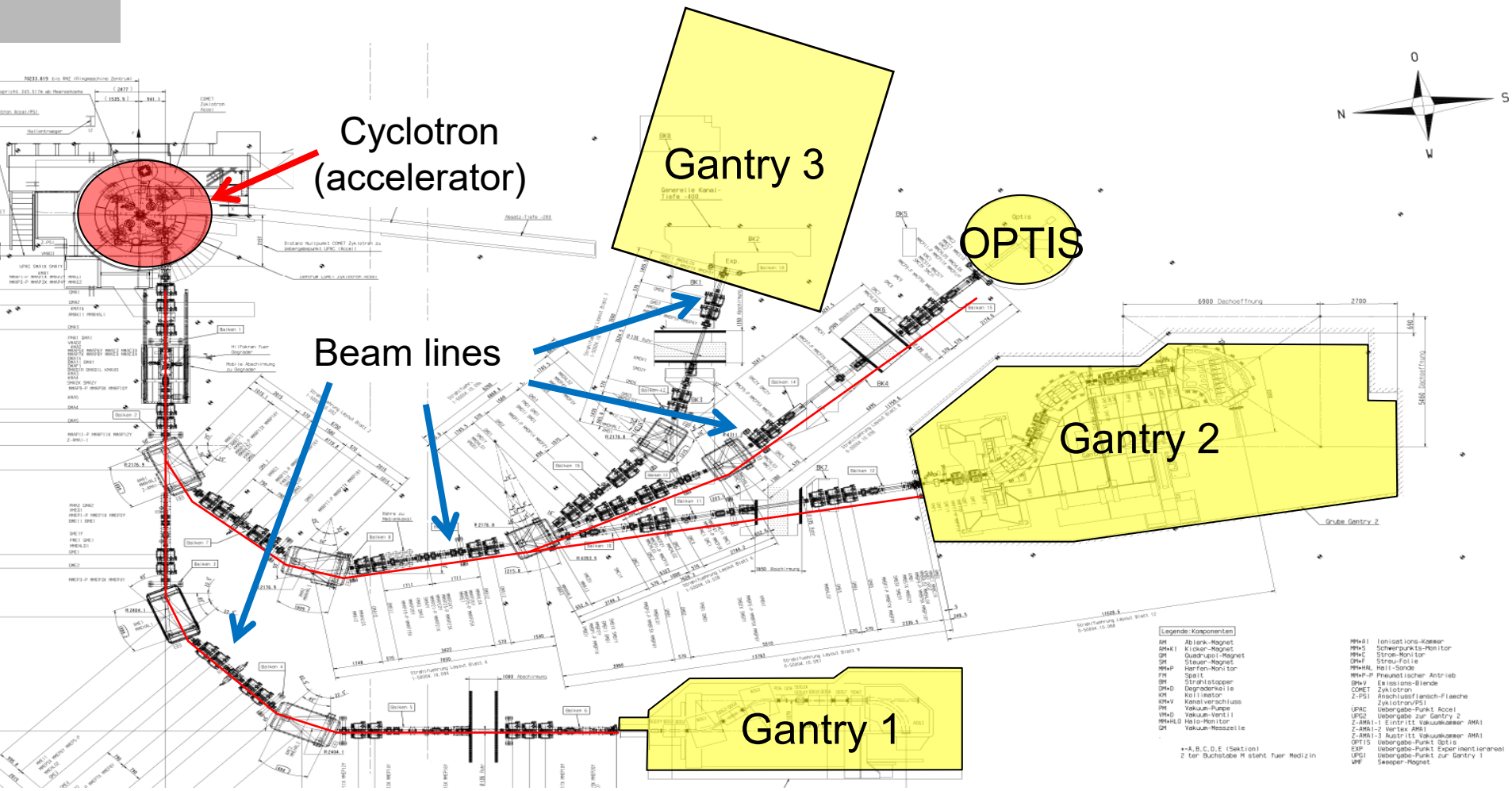
The proton therapy facility at PSI



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Clinical proton therapy at PSI

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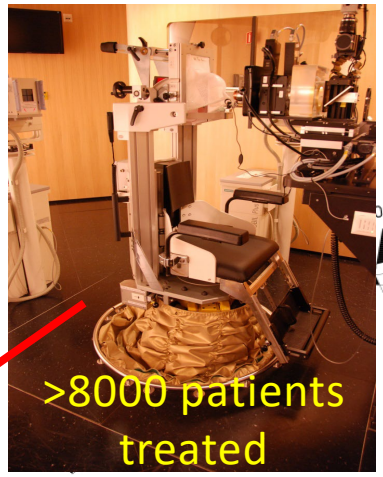
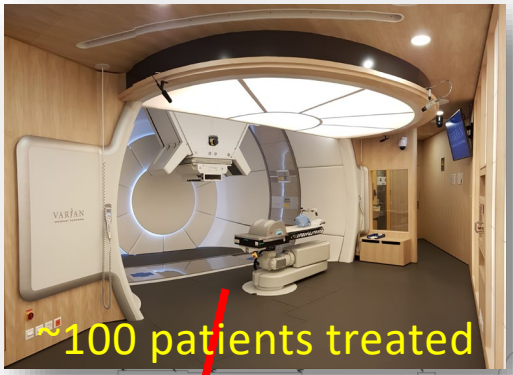
Clinical proton therapy at PSI



OPTIS - Treatment of ocular tumours

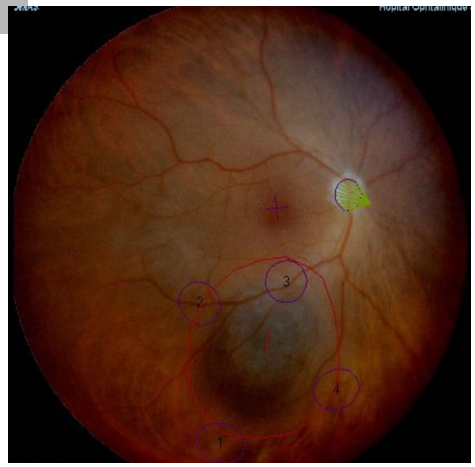
- Eye irradiations of uveal melanomas at PSI since 1984 with more than 8000 patients treated
- Typically 4-8 patients a day under treatment, ~150-200 a year
- Tumour control rate of 98%, eye retention rate ~90%

Clinical proton therapy at PSI

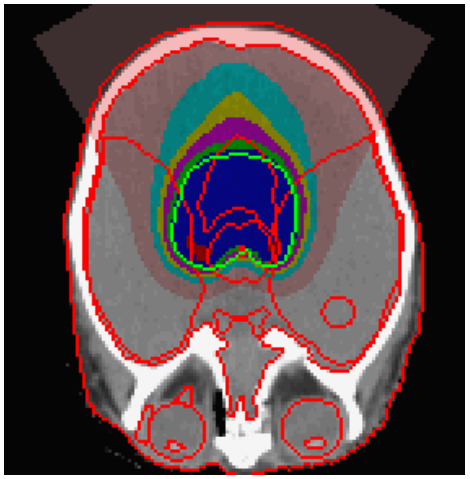


The power of the proton (1).

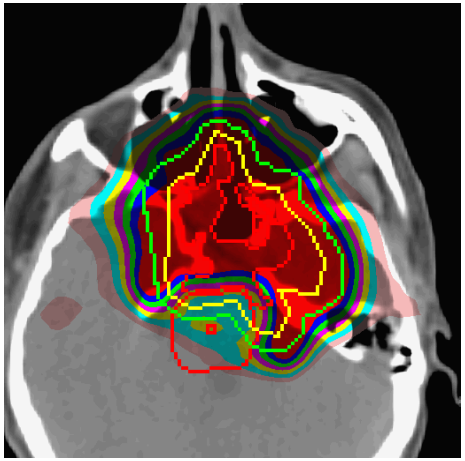
Clinical results from PSI



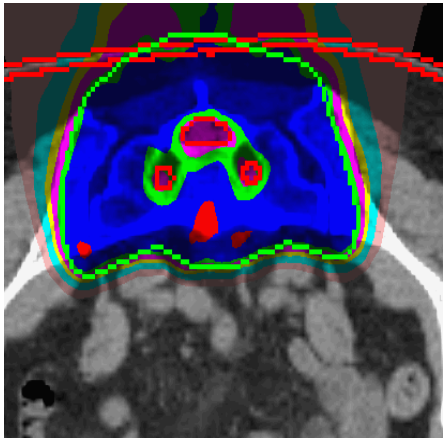
Uveal melanomas
>8000 Patients
5y Local control: 98%



Ependymomas
50 Patients
5y Local control: 78%



Skull base tumours
222 Patients
7y Local control: 80%



Sacral chordomas
36 Patients
5y Local control: 66%

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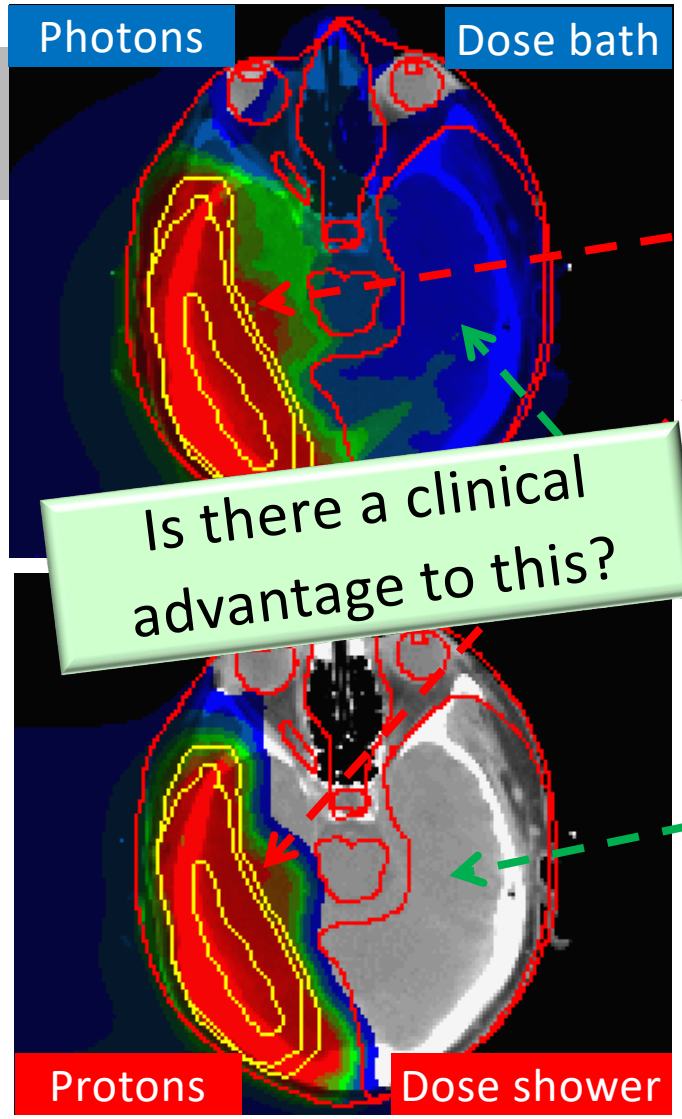
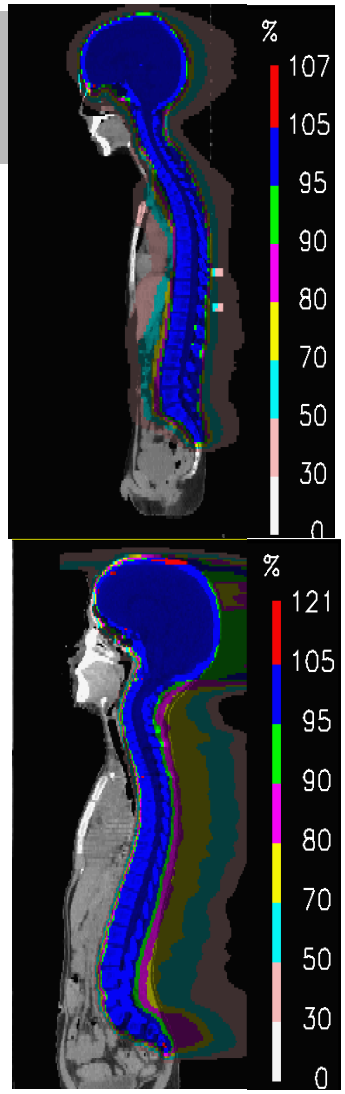
Clinical advantages of protons



- The advantage of protons is NOT in high dose conformation
- Their advantage is mainly in reducing the mid-to-low dose levels in comparison to photons

Can showering reduce side effects



- *Comparison of CSI patient cohorts treated with protons (MGH) and photons (Emory)*
- Median age: PRT 6.2 and XRT 8.3 years (p<0.01).
- Co… CSI dose, tot…
- Me… p<0.01)

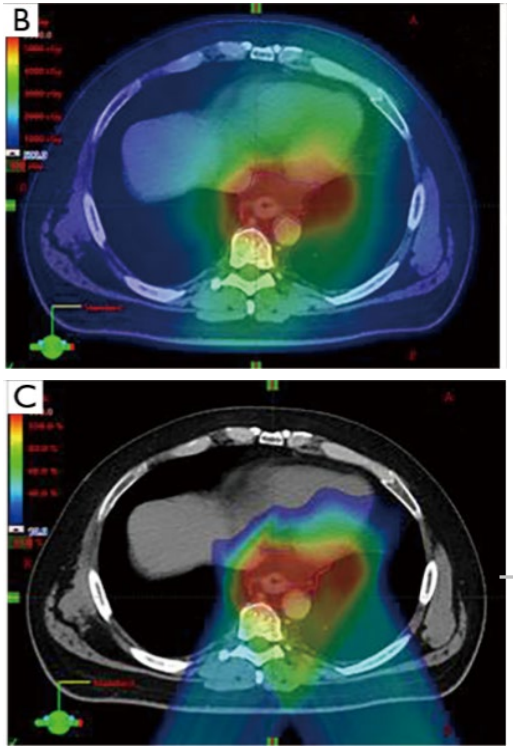
1.5-6 times reduction of *frequent* (~>20% incidence) radiation induced side effects

Outcome	Modality	Events	Reduction	P-value
Hypothyroidism	Protons	23%	2.8	<0.001
	Photons	65%		
Sex hormone deficiency	Protons	3%	6.3	0.025
	Photons	19%		
Endocrine replacement therapy	Protons	55%	1.4	0.030
	Photons	78%		

Eaton et al Neuro. Oncol. 2016 18: 881-7

Can showering reduce side effects

- MD Anderson phase IIB randomised trial for Esophageal cancer.
  - N=107 patients (61 IMRT and 46 PT)



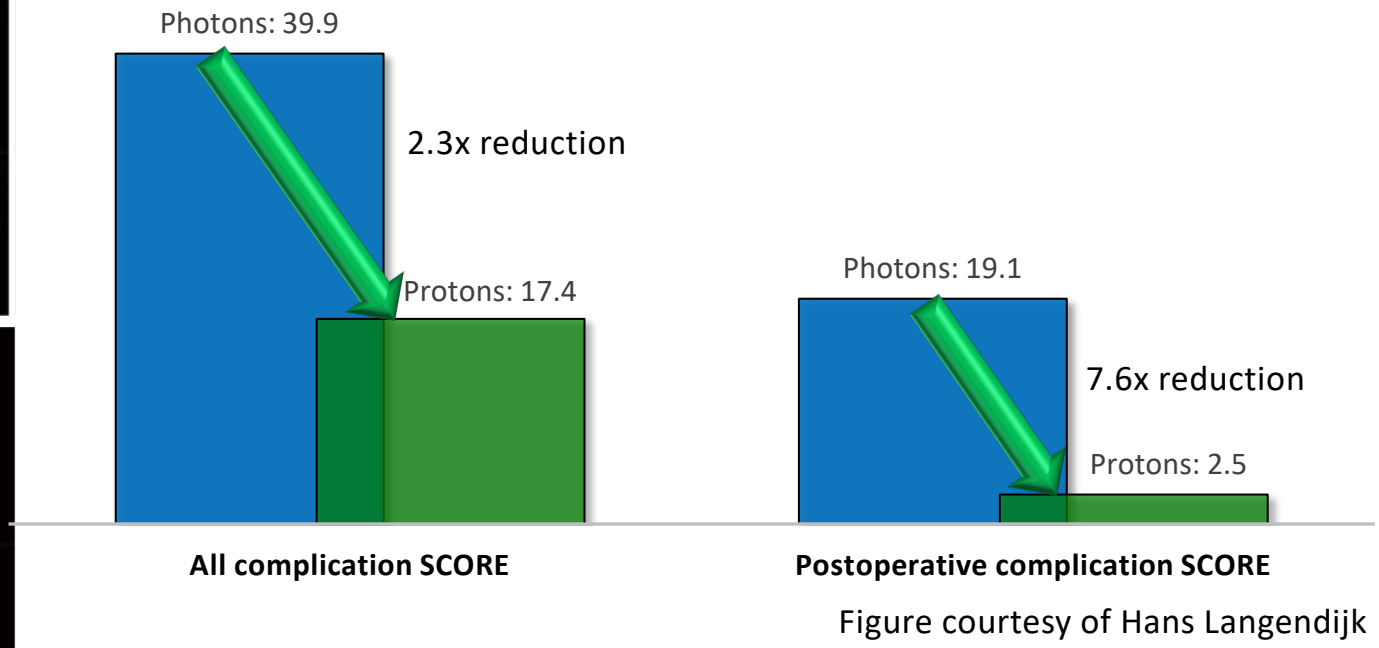
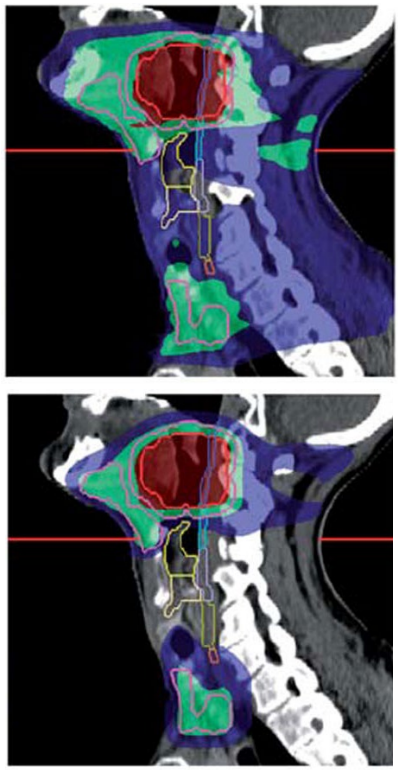


Figure courtesy of Hans Langendijk

Lin et al, J. Clin. Oncol., 2020 38:1569.

Can showering reduce side effects

- Nasopharnyx carcinomas, University of Groningen
  - 141 Nasopharynx patients (42 IMRT, 99 PT)



Total Toxicity Burden (grade 2+ and grade 3+)

Toxicity endpoints	Photons (n=42)												
	T0	W1	W2	W3	W4	W5	W6	W7	W12	M6	M12	M18	M24
Dysphagia Gr2+	16%	17%	31%	60%	70%	91%	97%	97%	77%	29%	16%	16%	17%
Dysgeusia Gr2+	7%	8%	8%	42%	73%	92%	92%	100%	46%	13%	17%	14%	32%
Mucosal reactions Gr2+	0%	0%	0%	28%	59%	79%	83%	88%	34%	3%	19%	12%	21%
Dry mouth Gr2+	0%	3%	8%	8%	53%	71%	75%	74%	49%	56%	48%	39%	48%
Dysphagia Gr3+	8%	11%	25%	34%	55%	71%	81%	79%	71%	9%	0%	0%	0%
Tube feeding	5%	6%	17%	31%	46%	62%	69%	77%	69%	3%	0%	0%	0%
Salivary duct inflammation Gr2+	0%	0%	13%	23%	43%	59%	70%	79%	30%	12%	10%	7%	10%
Dermatitis Gr2+	0%	0%	0%	0%	8%	17%	42%	58%	0%				
Sore mouth Gr2+	5%	0%	6%	11%	18%	24%	24%	38%	6%	0%	0%	0%	0%
Mucosal reactions Gr3+	0%	0%	0%	3%	3%	27%	39%	39%	3%	0%	0%	0%	0%
Sore throat Gr2+	3%	0%	0%	7%	11%	14%	13%	18%	13%	0%	0%	0%	0%
Laryngeal voice Gr2+	2%	3%	8%	10%	14%	3%	11%	18%	29%	2%	0%	0%	0%
Aspiration Gr2+	0%	0%	0%	7%	8%	8%	17%						
Dry mouth Gr3+	0%	0%	0%	5%	5%	6%	8%						
Laryngeal edema Gr2+	0%												

1.3 late toxicities per patient

Acute toxicity | Late toxicity

Can showering reduce side effects

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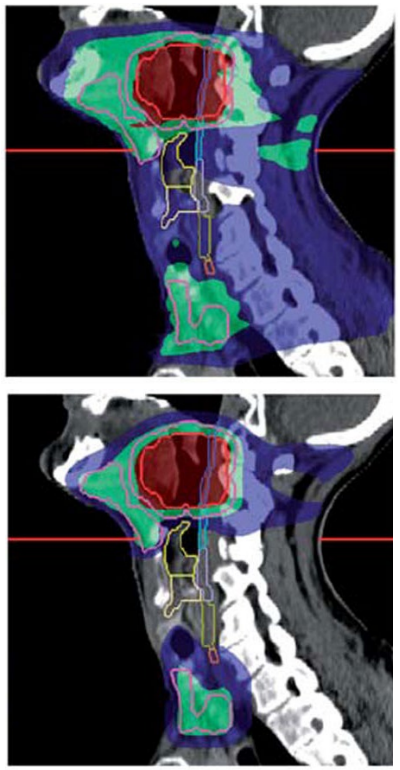

Total Toxicity Burden (grade 2+ and grade 3+)

Toxicity endpoints	Photons (n=42)												Protons (n=99)											
	T0	W1	W2	W3	W4	W5	W6	W7	W12	M6	M12	M18	M24	T0	W1	W2	W3	W4	W5	W6	W7	W12	M6	M12	M18	M24
Dysphagia Gr2+	16%	17%	31%	60%	70%	91%	97%	97%	77%	29%	16%	16%	17%	7%	6%	7%	19%	28%	40%	51%	68%	19%	5%	0%	0%	0%
Dysgeusia Gr2+	7%	8%	8%	42%	73%	92%	92%	100%	46%	13%	17%	14%	32%	7%	7%	12%	19%	36%	44%	47%	50%	17%	0%	0%	0%	0%
Mucosal reactions Gr2+	0%	0%	0%	28%	59%	79%	83%	88%	34%	3%	19%	12%	21%	0%	0%	0%	7%	17%	33%	58%	75%	0%	5%	11%	10%	7%
Dry mouth Gr2+	0%	3%	8%	8%	53%	71%	75%	74%	49%	56%	48%	39%	48%	2%	0%	0%	0%	3%	7%	11%	14%	15%	12%	13%	10%	13%
Dysphagia Gr3+	8%	11%	25%	34%	55%	71%	81%	79%	71%	9%	0%	0%	0%	3%	3%	5%	10%	14%	26%	35%	45%	9%	2%	0%	0%	0%
Tube feeding	5%	6%	17%	31%	46%	62%	69%	77%	69%	3%	0%	0%	0%	2%	2%	4%	5%	12%	19%	28%	34%	8%	2%	0%	0%	0%
Salivary duct inflammation Gr2+	0%	0%	13%	23%	43%	59%	70%	79%	30%	12%	10%	7%	10%	2%	2%	0%	2%	5%	9%	18%	16%	9%	5%	7%	5%	6%
Dermatitis Gr2+	0%	0%	0%	0%	8%	17%	42%	58%	0%					0%	0%	0%	0%	9%	28%	63%	84%	0%				
Sore mouth Gr2+	5%	0%	6%	11%	18%	24%	24%	38%	6%	0%	0%	0%	0%	2%	2%	2%	6%	6%	12%	12%	14%	2%	0%	0%	0%	0%
Mucosal reactions Gr3+	0%	0%	0%	3%	3%	27%	39%	39%	3%	0%	0%	0%	0%	0%	0%	0%	0%	2%	5%	14%	32%	0%	0%	0%	0%	0%
Sore throat Gr2+	3%	0%	0%	7%	11%	14%	13%	18%	13%	0%	0%	0%	0%	0%	0%	0%	3%	5%	9%	12%	18%	0%	0%	0%	0%	0%
Laryngeal voice Gr2+	2%	3%	8%	10%	14%	3%	11%	18%	29%	2%	0%	0%	0%	0%	0%	5%	10%	7%	0%	2%	0%	4%	0%	0%	0%	0%
Aspiration Gr2+	0%	0%	0%	7%	8%	8%	17%							0%							13%					
Dry mouth Gr3+	0%	0%	0%	5%	5%	6%	8%																			
Laryngeal edema Gr2+	0%																									

1.3 late toxicities per patient

4.3x reduction

0.3 late toxicities per patient

Acute toxicity | Late toxicity | Acute toxicity | Late toxicity

Figure courtesy of Hans Langendijk

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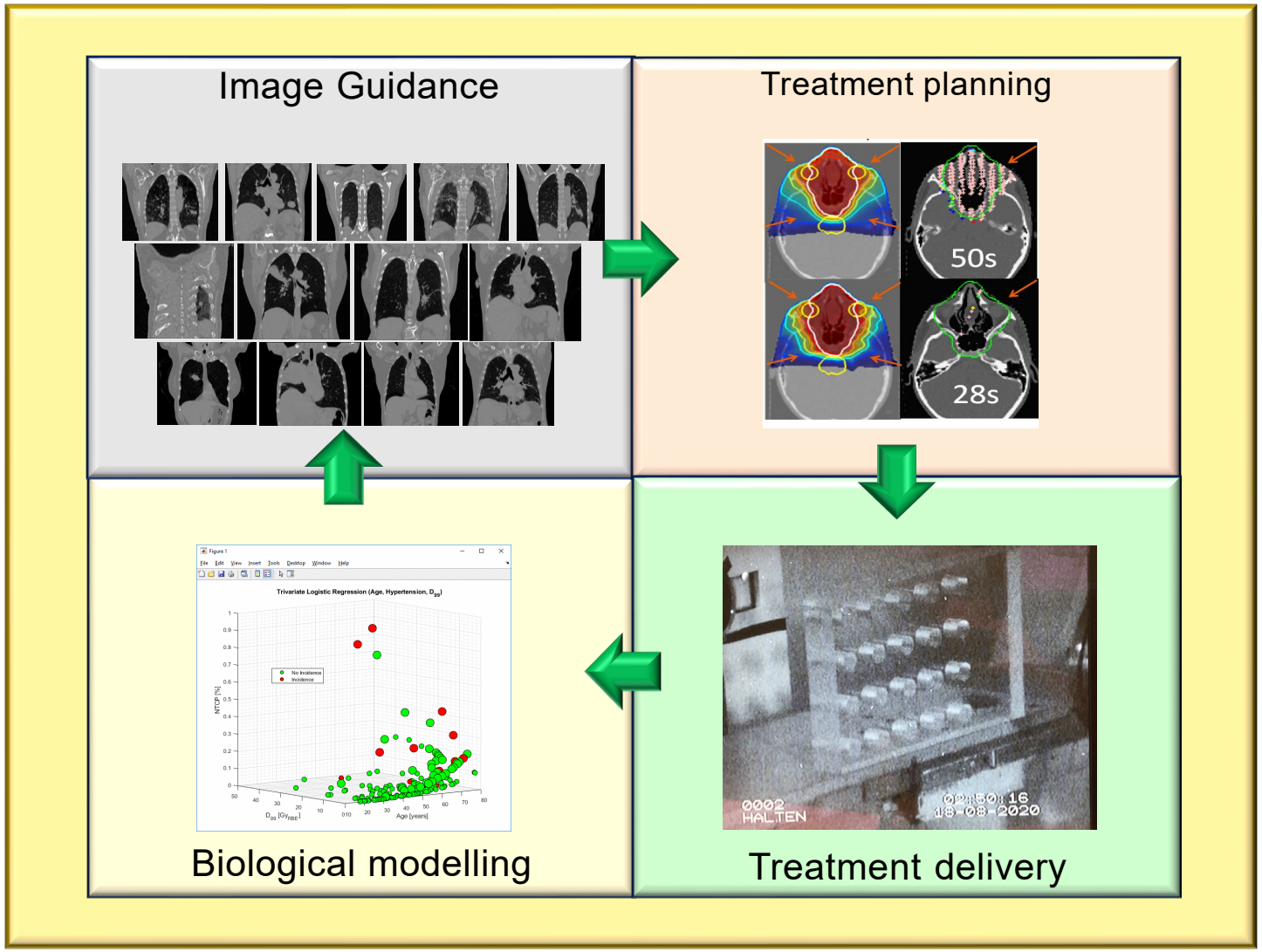
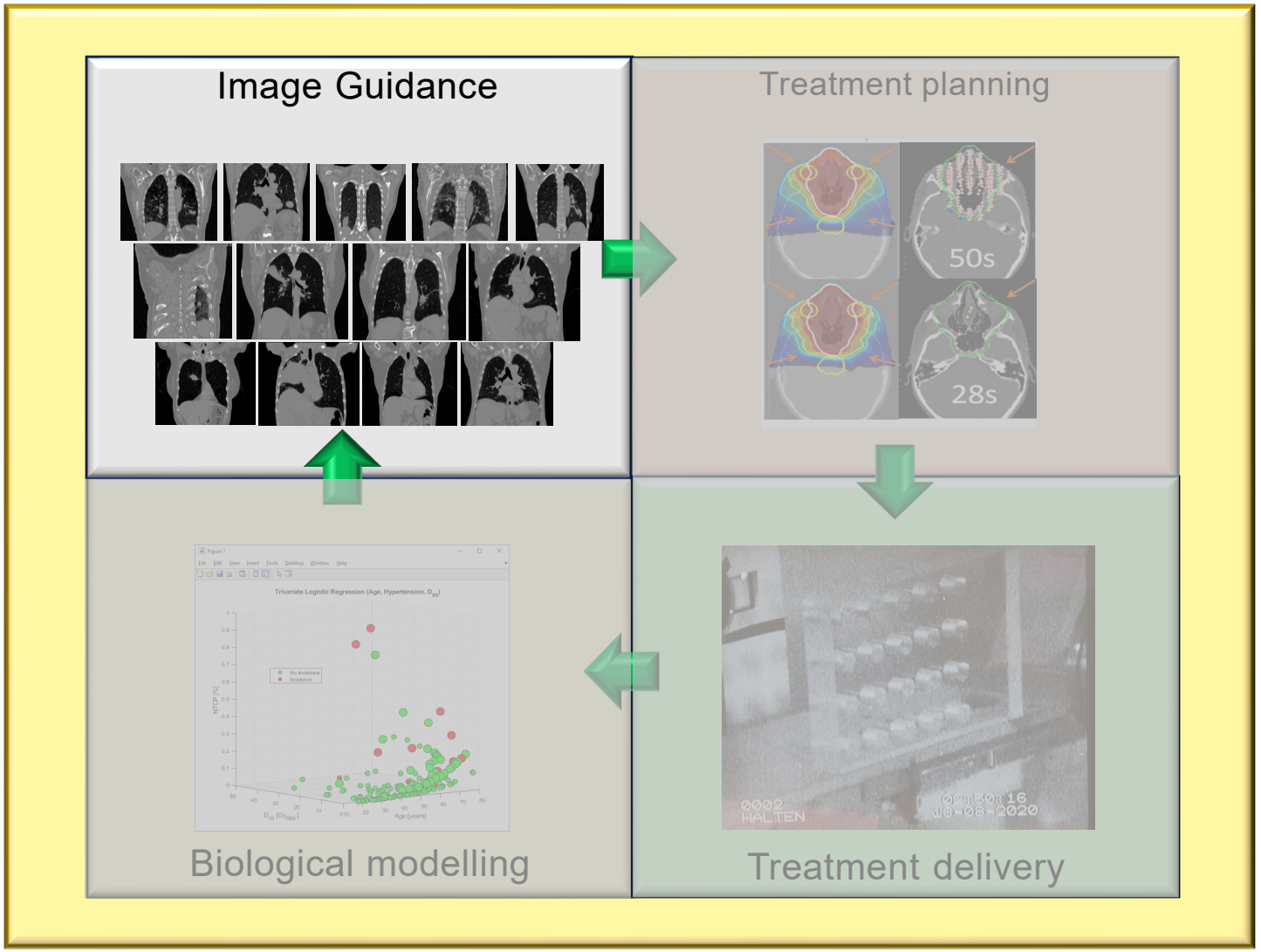
Current R&D themes



Current R&D themes



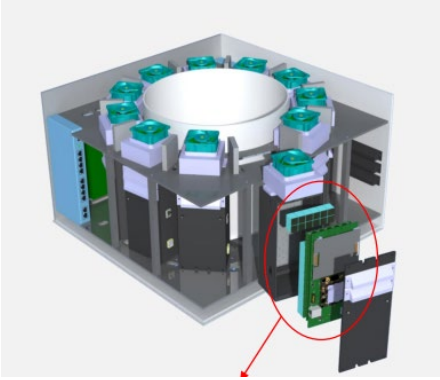
PETiTiON

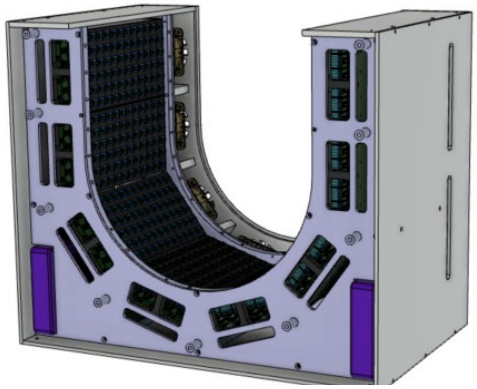
Swiss National Science Foundation

PET for InTensive Care units and Innovative protON therapy

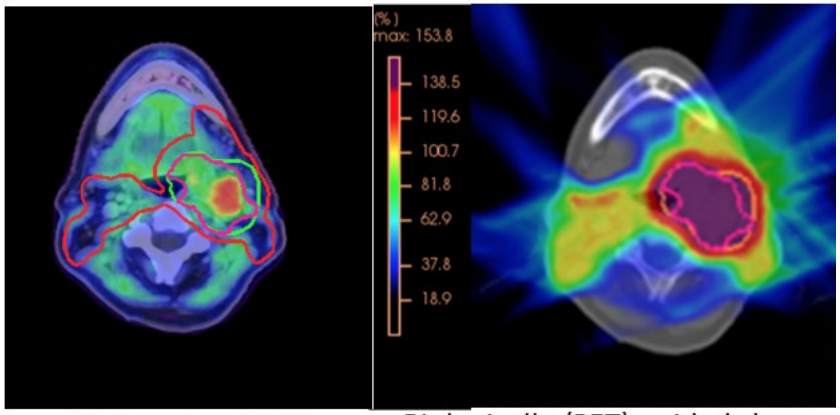
ETH zürich IPA

PAUL SCHERRER INSTITUT PSI

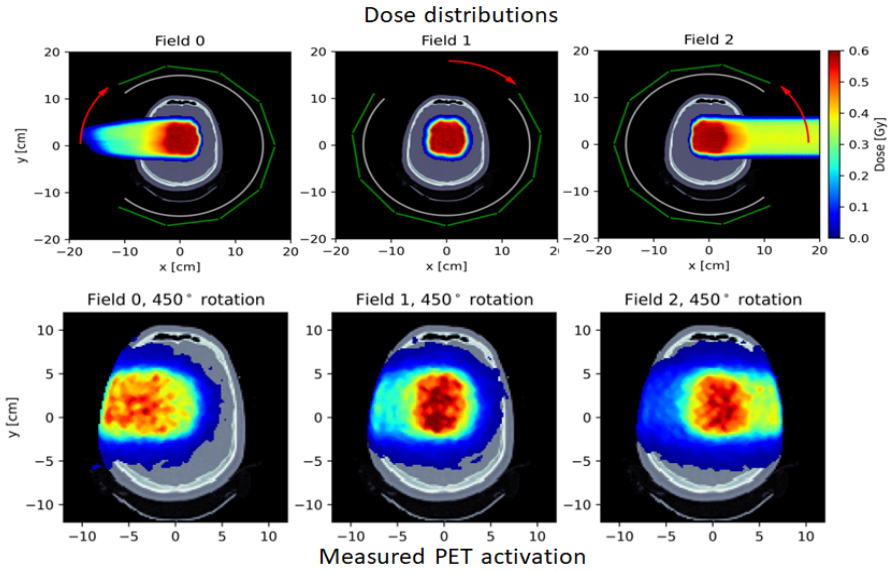




CHUV Service de médecine nucléaire et imagerie moléculaire



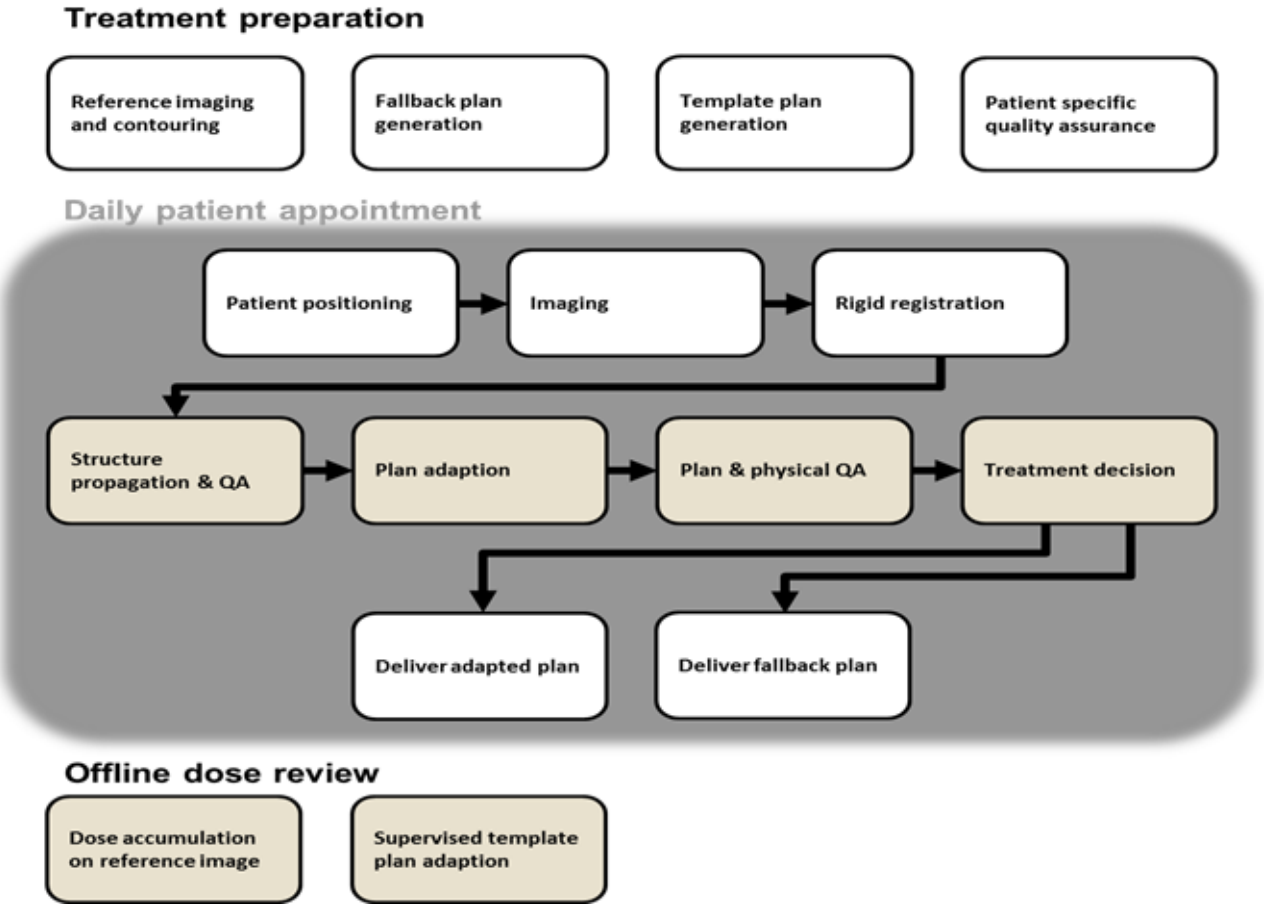
PET imaging (HX4) | Biologically (PET) guided dose boosting



Shubhangi Makkar, Keegan MacNamara, Carla Winterhalter

The RAPTOR project – Real-Time Adapted Proton Therapy

Image, plan and deliver on a daily basis

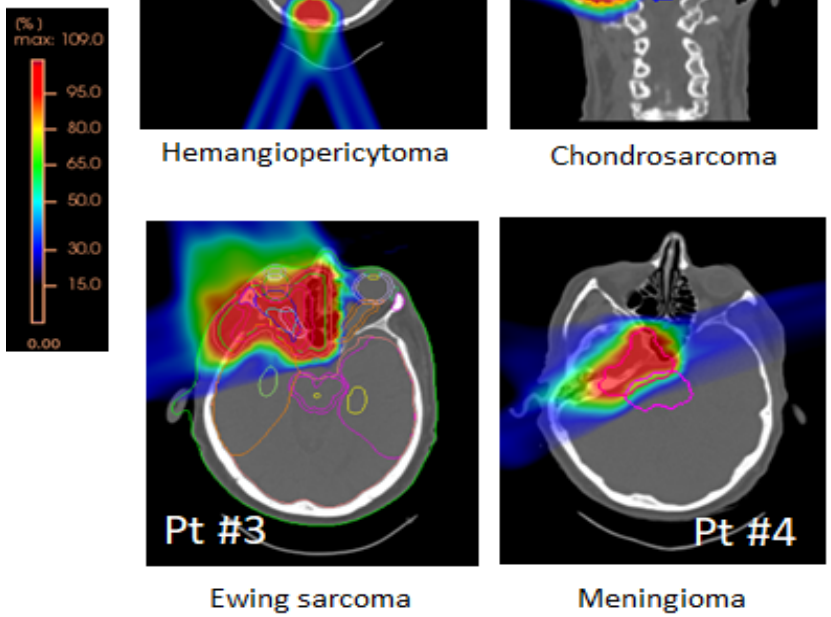


Andreas Smolders, Eva Choulilitsa, Kasia Czerska, Francesca Albertini

The RAPTOR project – Real-Time Adapted Proton Therapy

Daily adapted proton therapy at PSI – A world first!

1st four DAPT patients at PSI



Hemangiopericytoma | Chondrosarcoma

Ewing sarcoma | Meningioma

Delivery times

		Average duration [range] (min)
	Set-up and CT acquisition	2:50 [2:30-3:10]
Online adaptive steps	Registration	3:10 [2:10-4:50]
	Initial integrity checks	1:10 [0:50-1:40]
	Daily structure approval	2:30 [1:10-3:50]
	Daily Plan clinical evaluation & approval	2:20 [1:10-3:40]
	Plan QA (incl. check of secondary dose)	0:50 [0:30-1:00]
	Delivery	9:00 [7:00-11:10]
	Total	22:20 [17:30-25:50]

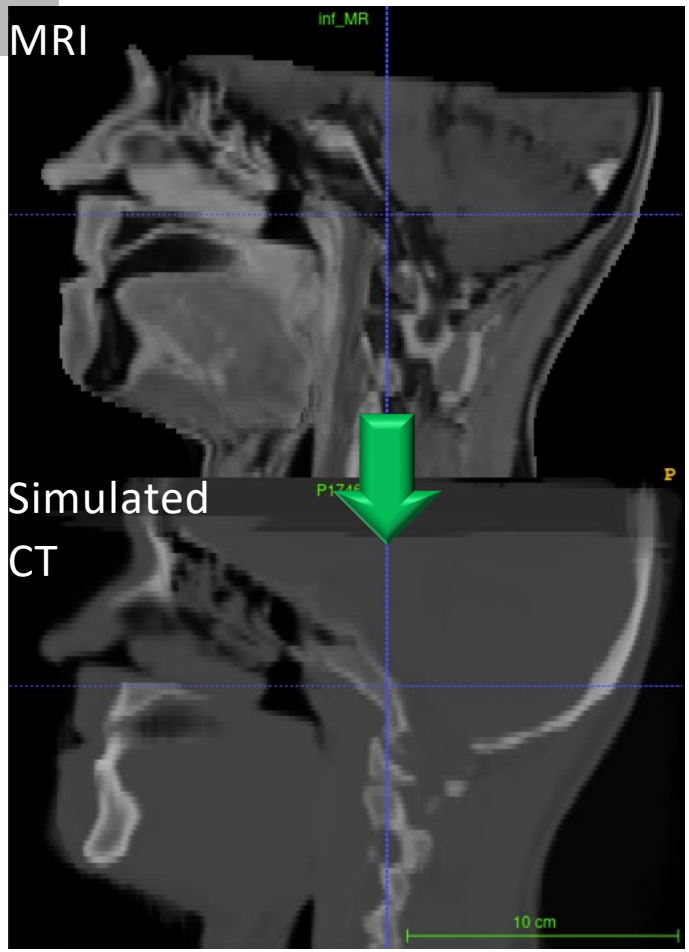
Online steps:
6:50 mins

DAPT fraction times:
22:20 (17:30-25:50) mins

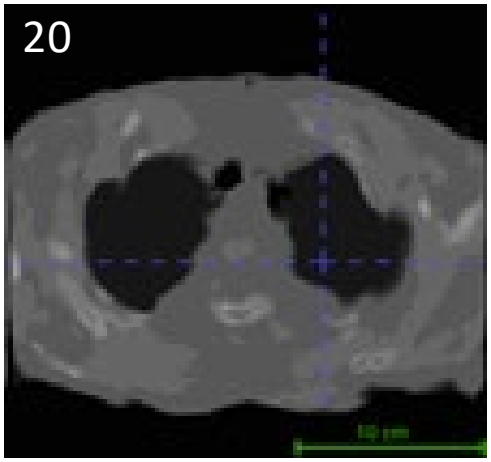
Andreas Smolders, Eva Choulilitsa, Kasia Czerska, Francesca Albertini

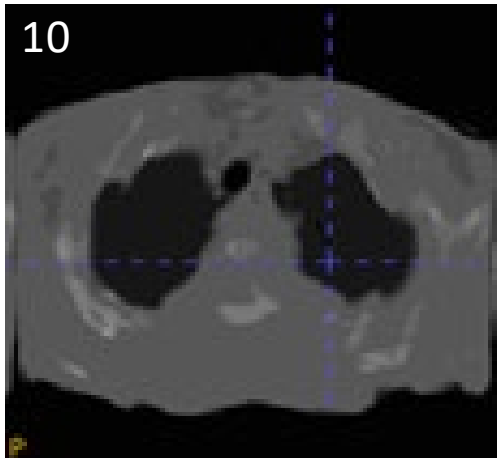
Towards low-dose adaptive therapy

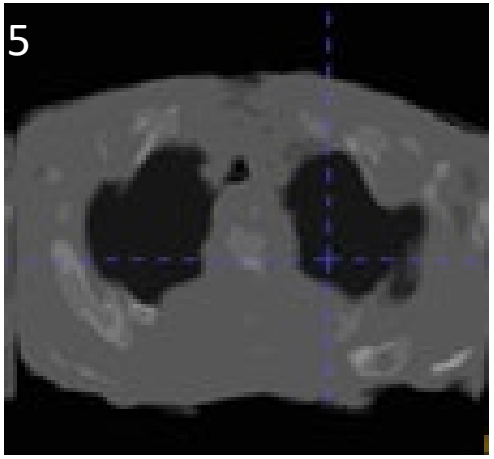
AI based MRI to CT prediction

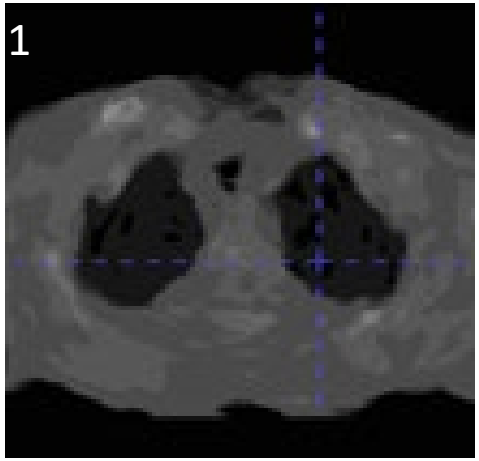


CT reconstruction from sparse projections



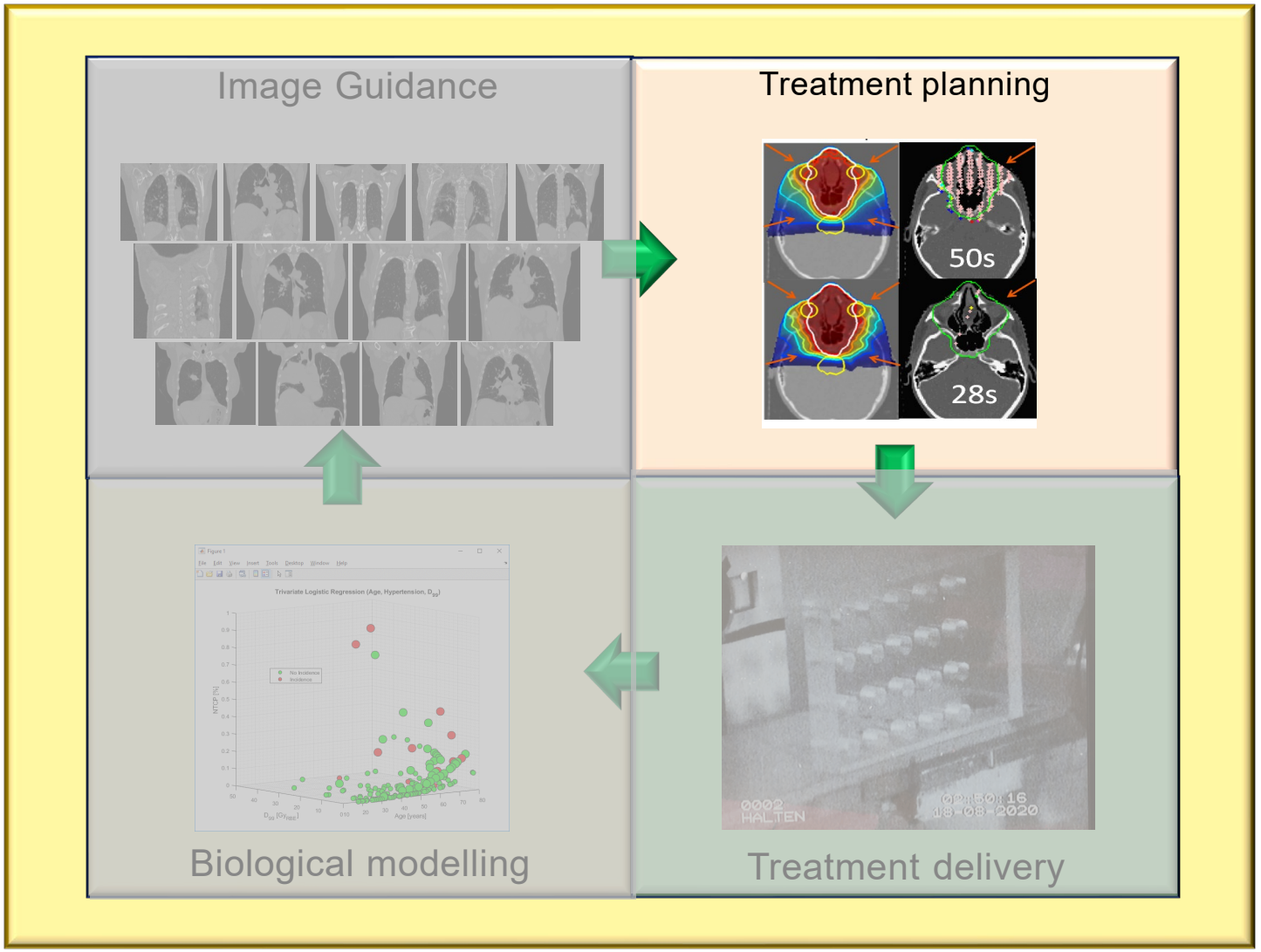






Xia Li, Muheng Li, Ye Zhang

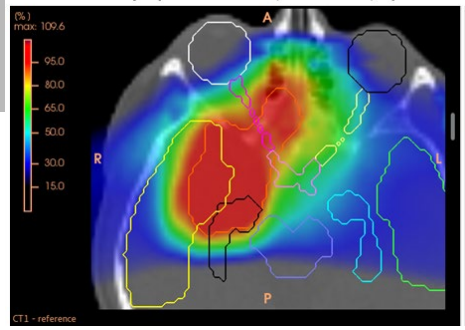
Current R&D themes



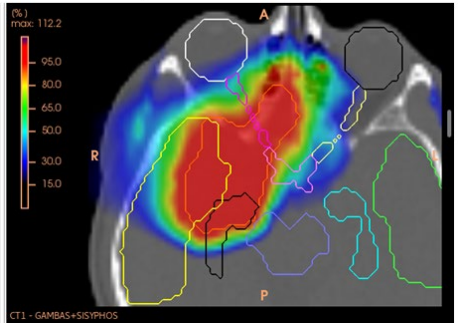
Treatment planning

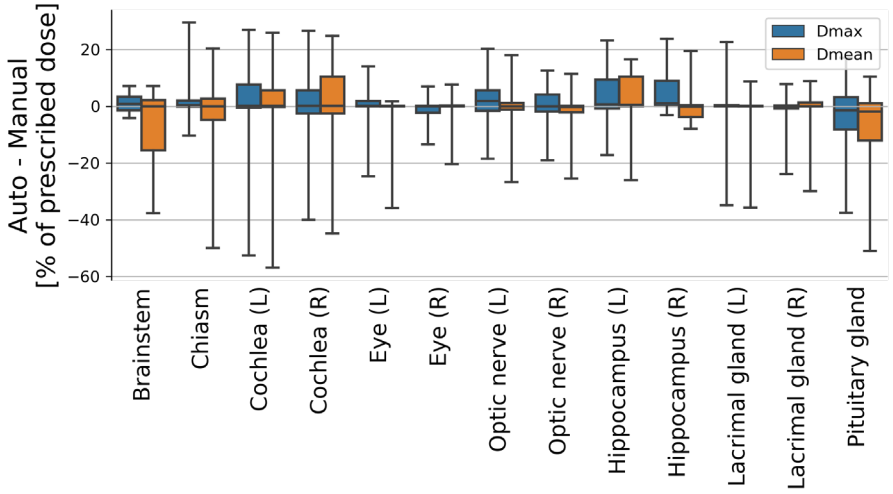
Fully automated treatment planning

Manually planned (clinical) plan



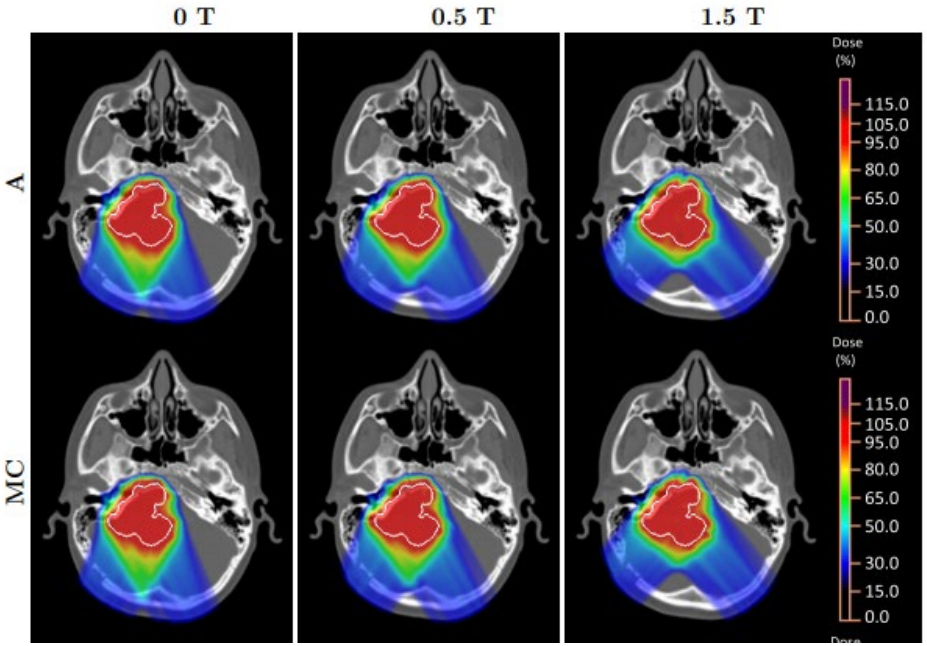
Fully automated plan





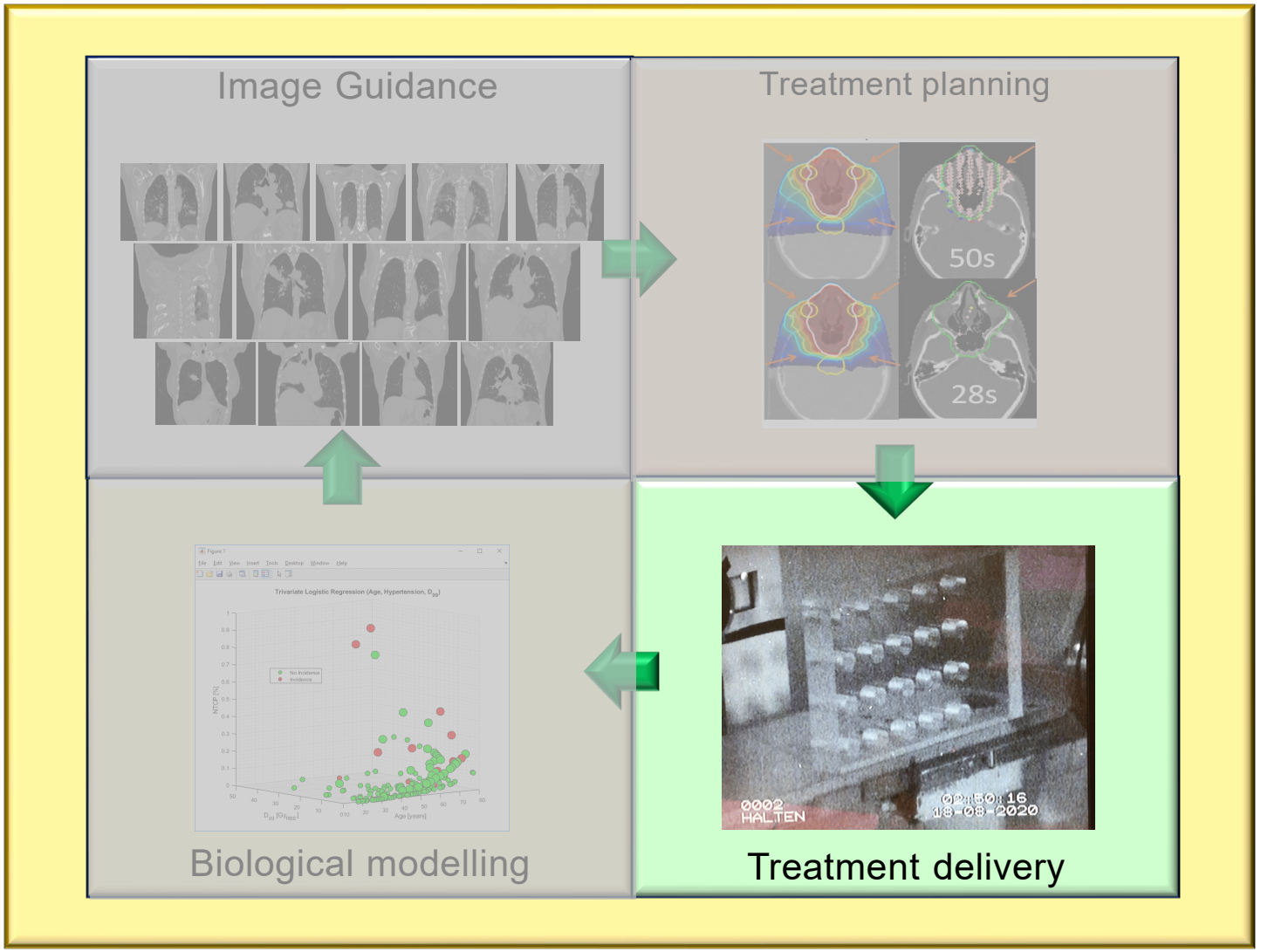
Renato Belotti, Jan Hrbacek

Dose calculations in magnetic fields



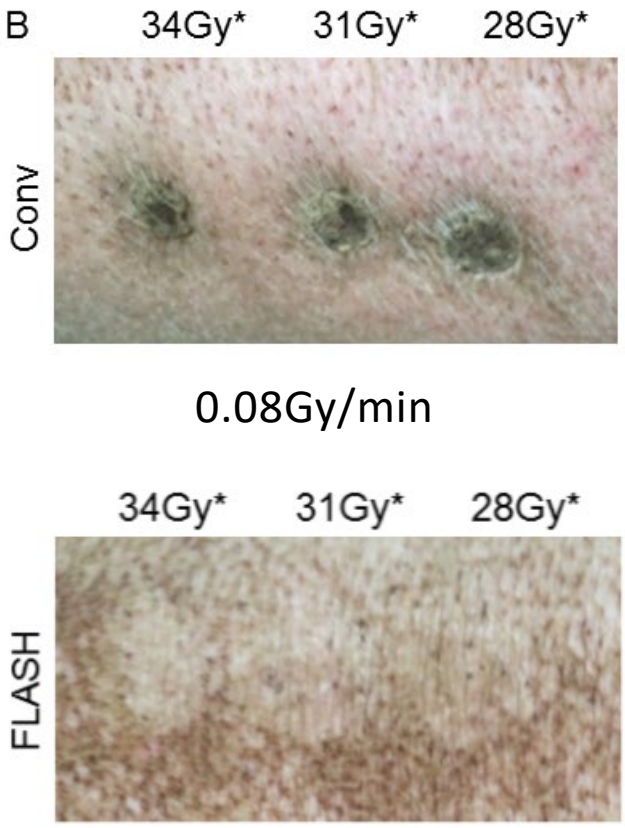
Alisha Deutschler, Muheng Li, Ye Zhang

Current R&D themes

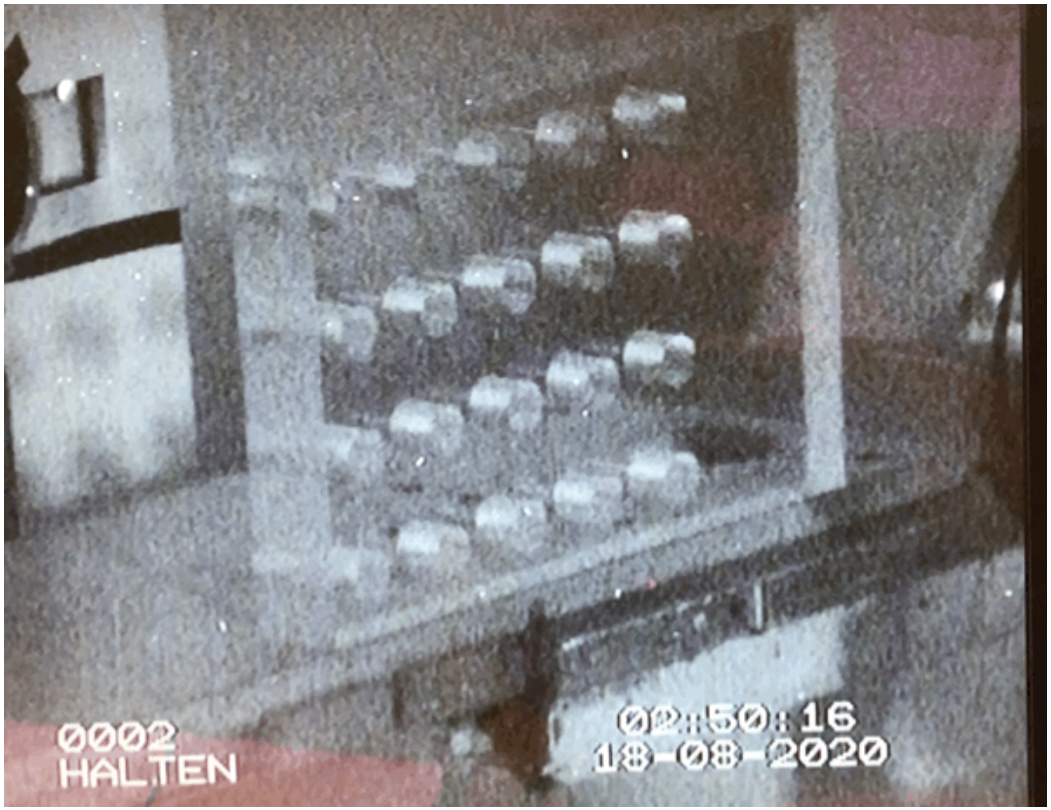


Ultra-high dose rate delivery (FLASH)

The FLASH effect with electrons



Ultra high proton dose rates for FLASH on Gantry 1 at PSI



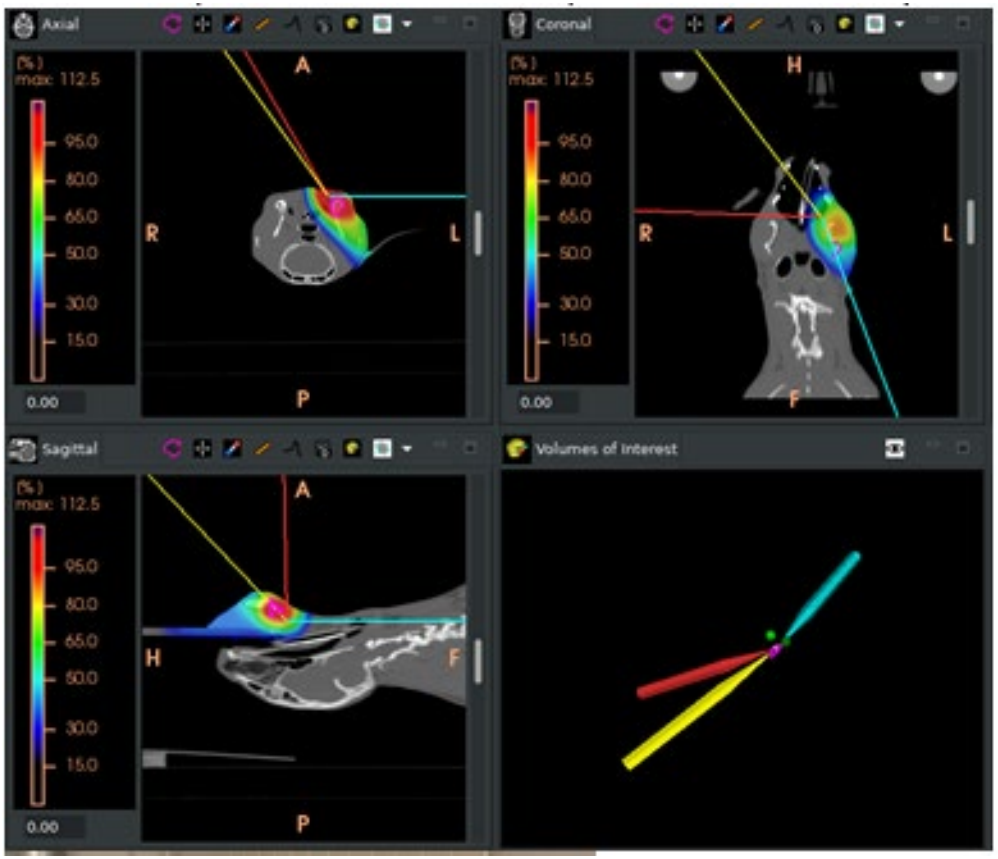
~ 1400Gy/s in high dose region

Isabella Collizzi, Gaia Dellepiane, Robert Schaeffer, David Meer

Ultra-high dose rate delivery (FLASH)

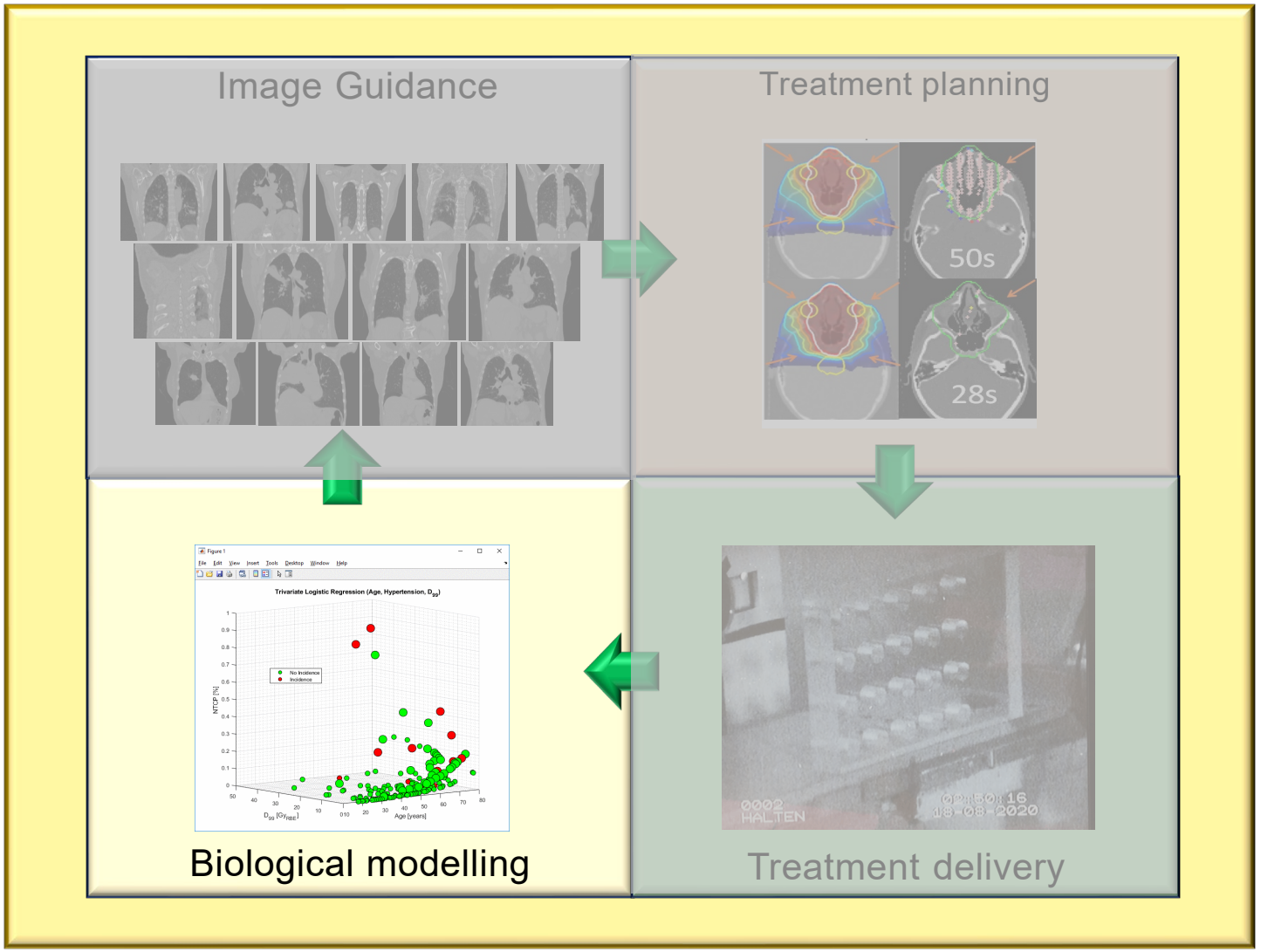
The FEATHER trial – FLASH irradiations of cat patients

CPT and Tierspital Zurich (Prof Carla Rohrer Bley)

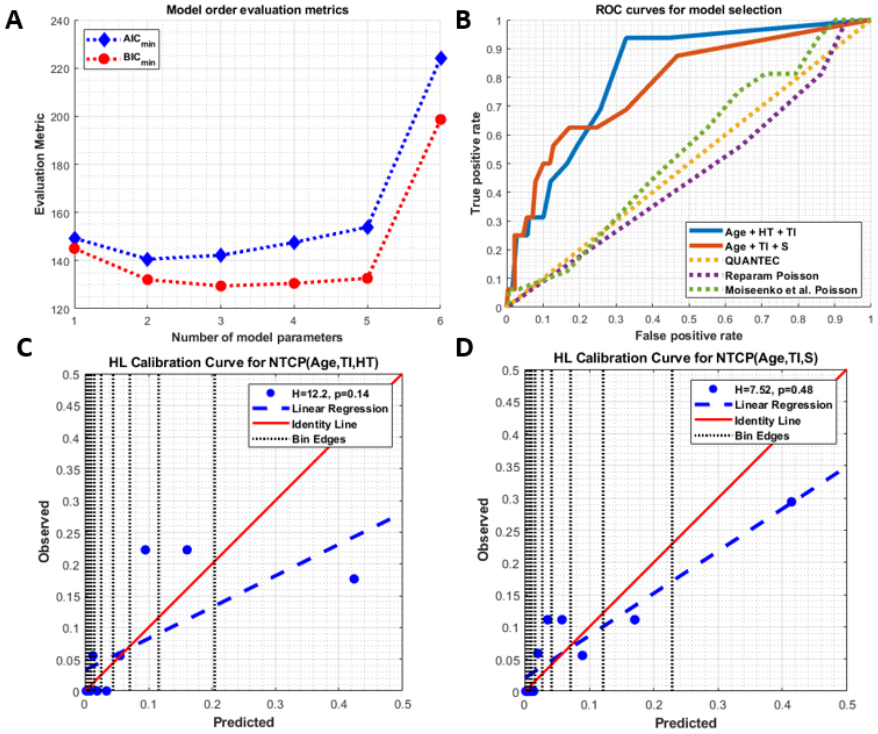


Isabella Colizzi, Gaia Dellepiane, Robert Schaeffer, David Meer

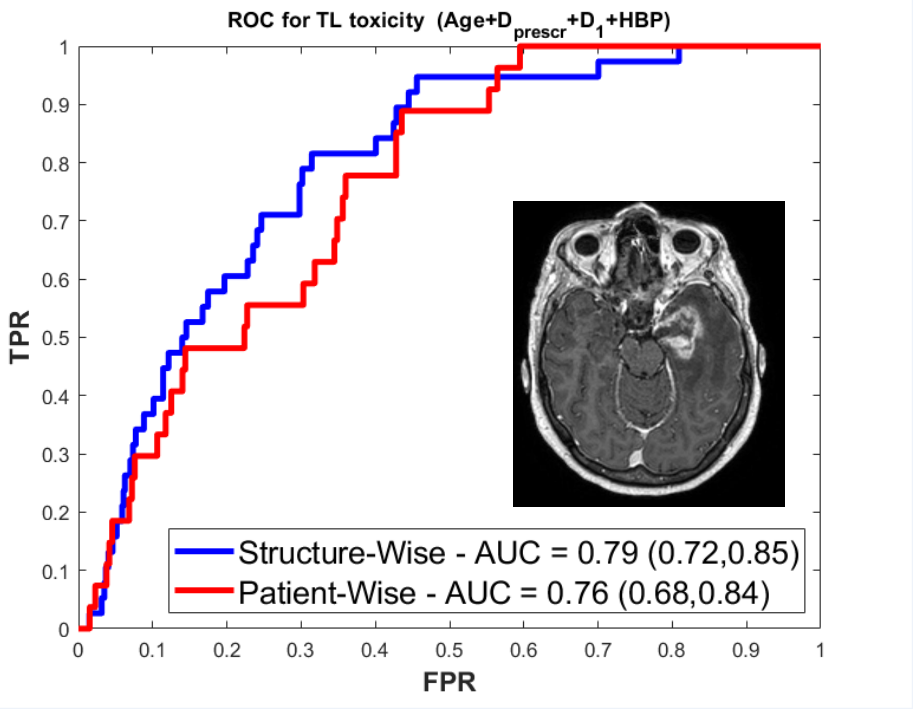
Current R&D themes



Outcomes analysis and NTCP modelling



NTCP modeling of optical neuropathy



NTCP modeling of temporal lobe necrosis

Bastien Gollomer, Giovanni Fattori

PAUL SCHERRER INSTITUT

Summary

- Radiation therapy is a very successful weapon against cancer
- Protons can better focus dose to the target, while reducing dose to normal tissues
- Increasing clinical evidence of the advantages of this (radiation dose is NOT benign)
- PSI has been a pioneer in the development of proton therapy, and continues to have an active, and innovative clinical and research program