

PAUL SCHERRER INSTITUT



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

## Special techniques II: Proton therapy

FMH physics training 2022

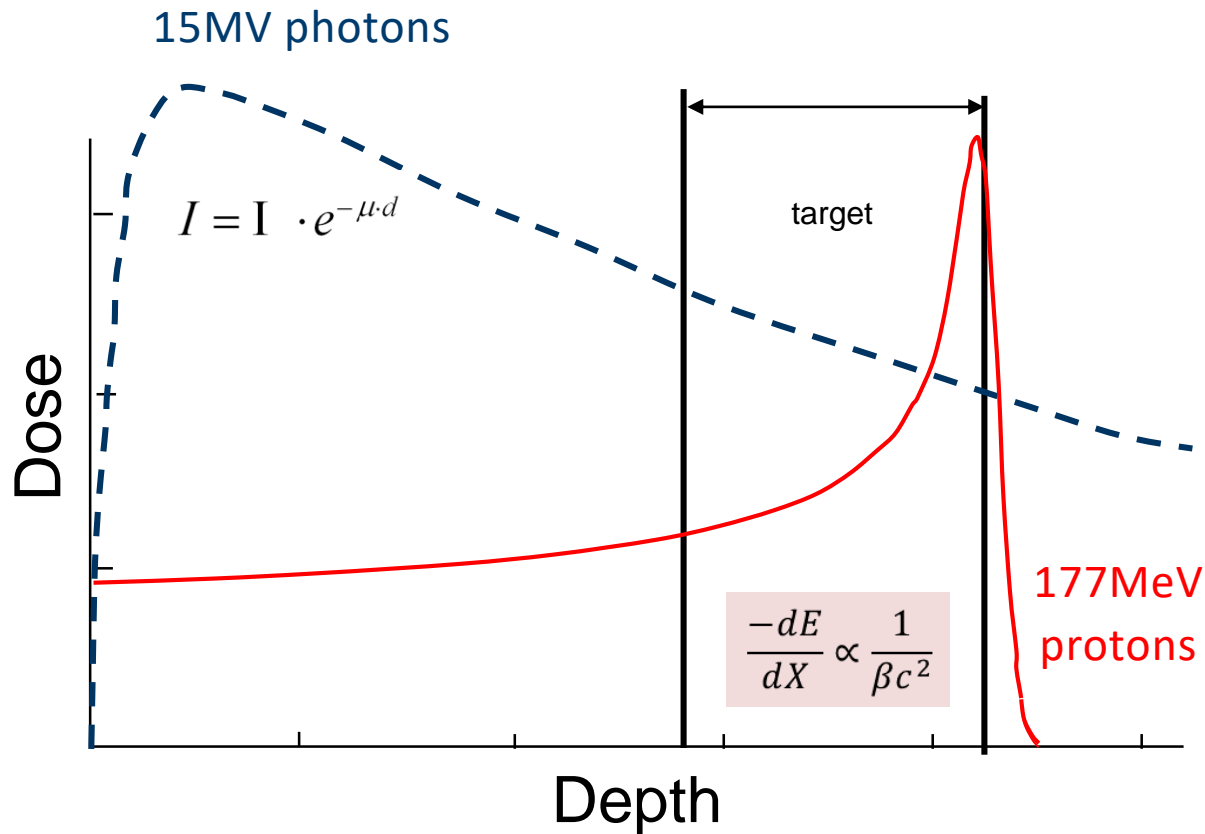
# Overview

- 1. The principles of proton therapy**
2. The potential of proton therapy
3. The challenges of proton therapy
4. Proton therapy at PSI

# The principles of proton therapy

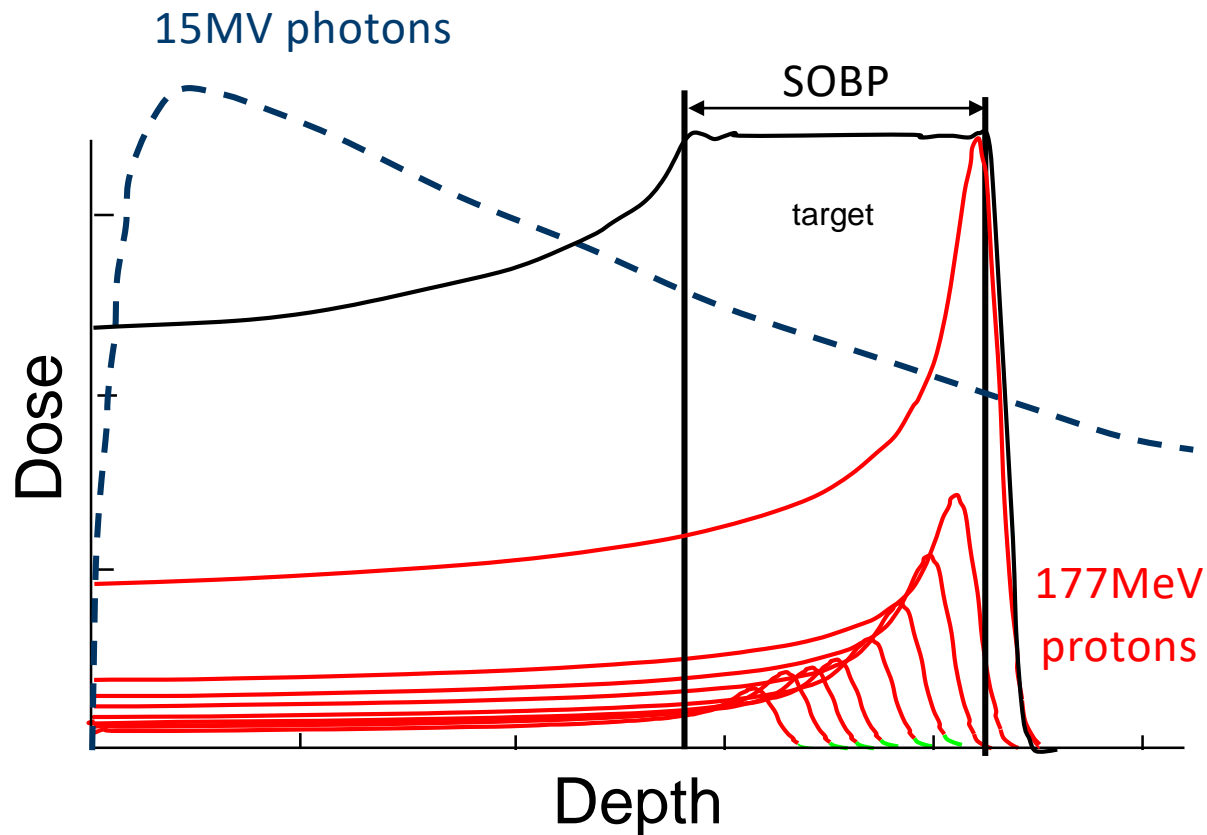
## Interactions of protons

### The proton depth-dose curve



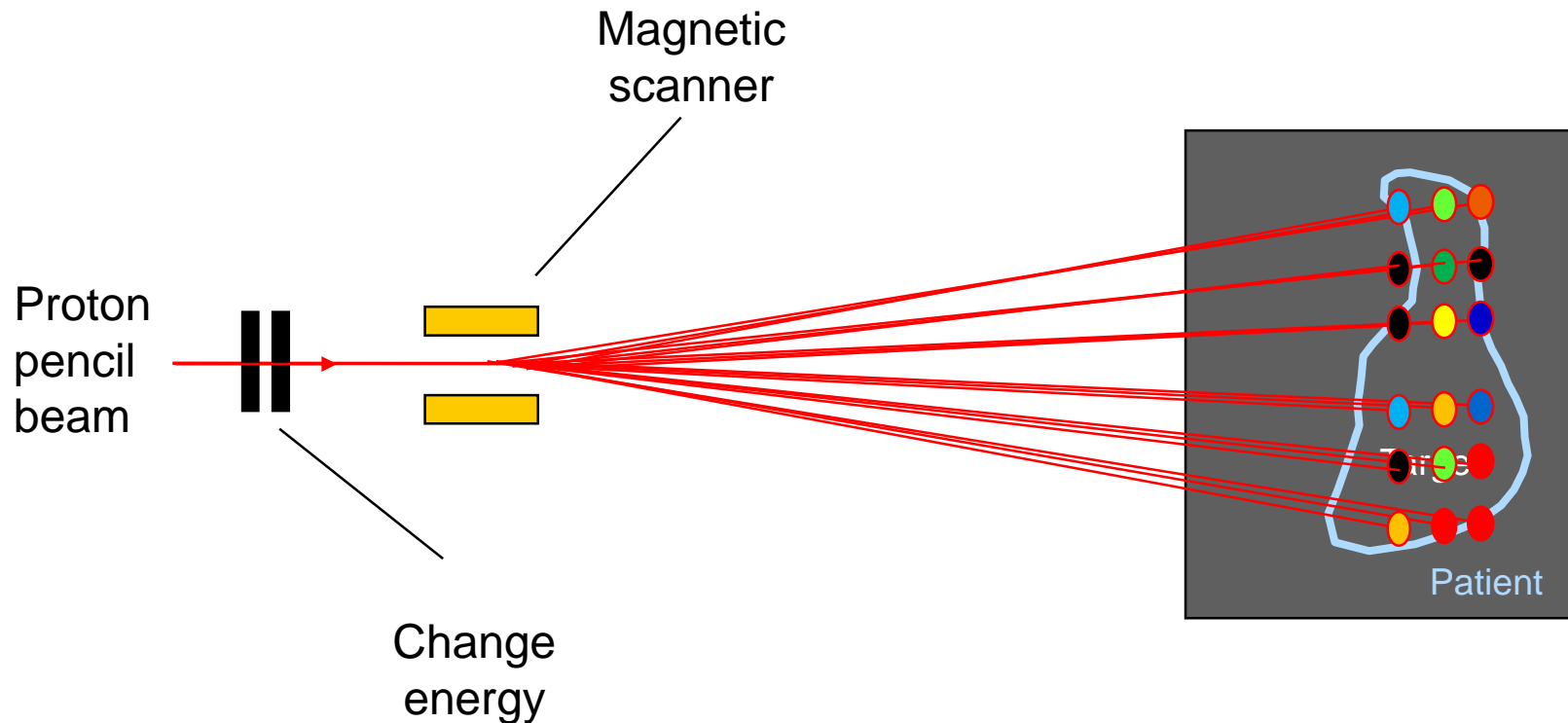
# The principles of proton therapy

## Modulating protons in depth.



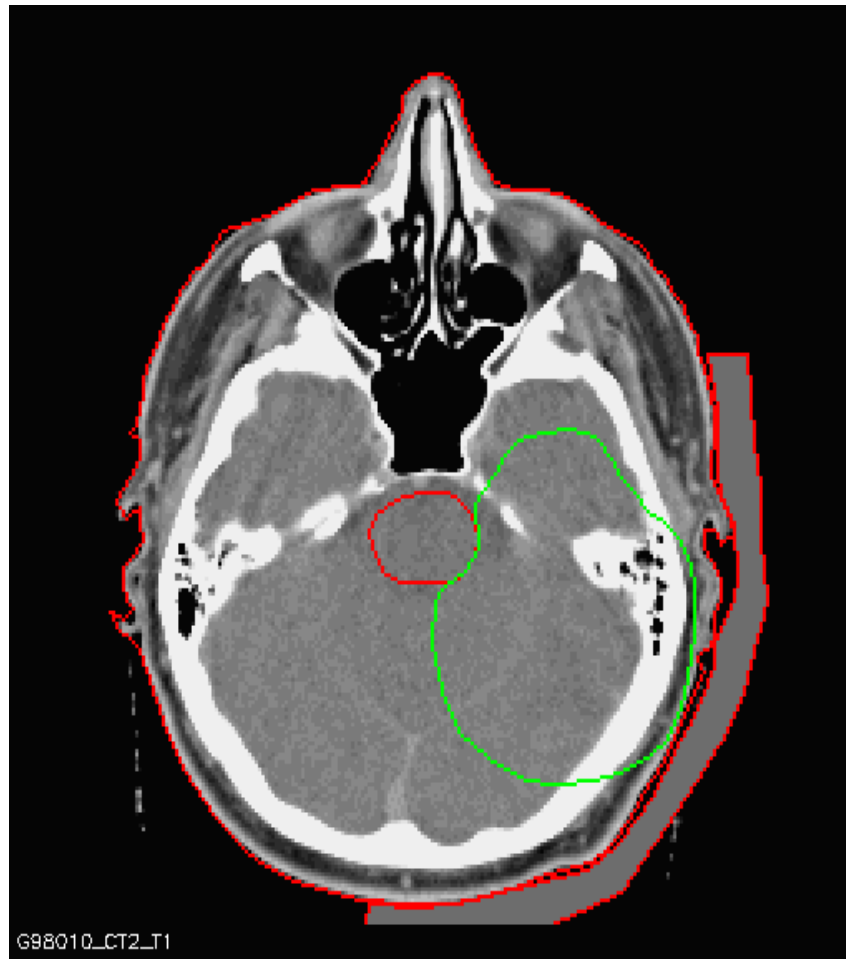
# The principles of proton therapy

## Modulating protons laterally Pencil Beam Scanning (PBS).



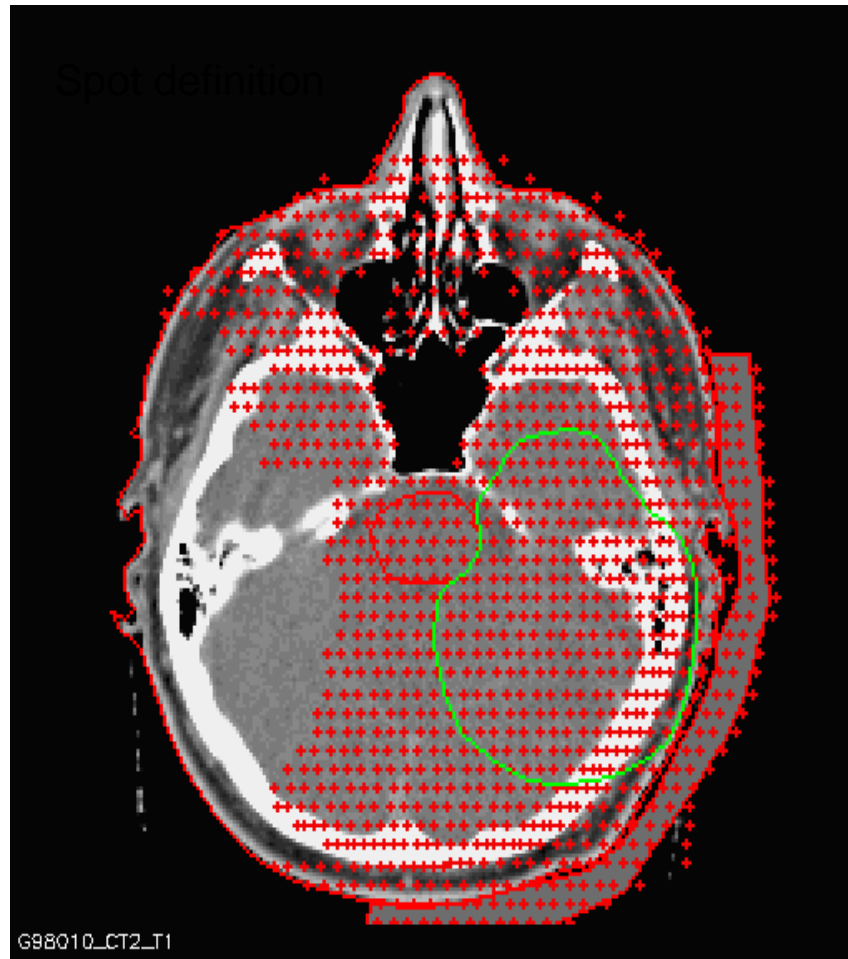
# The principles of proton therapy

## Treatment planning for protons



# The principles of proton therapy

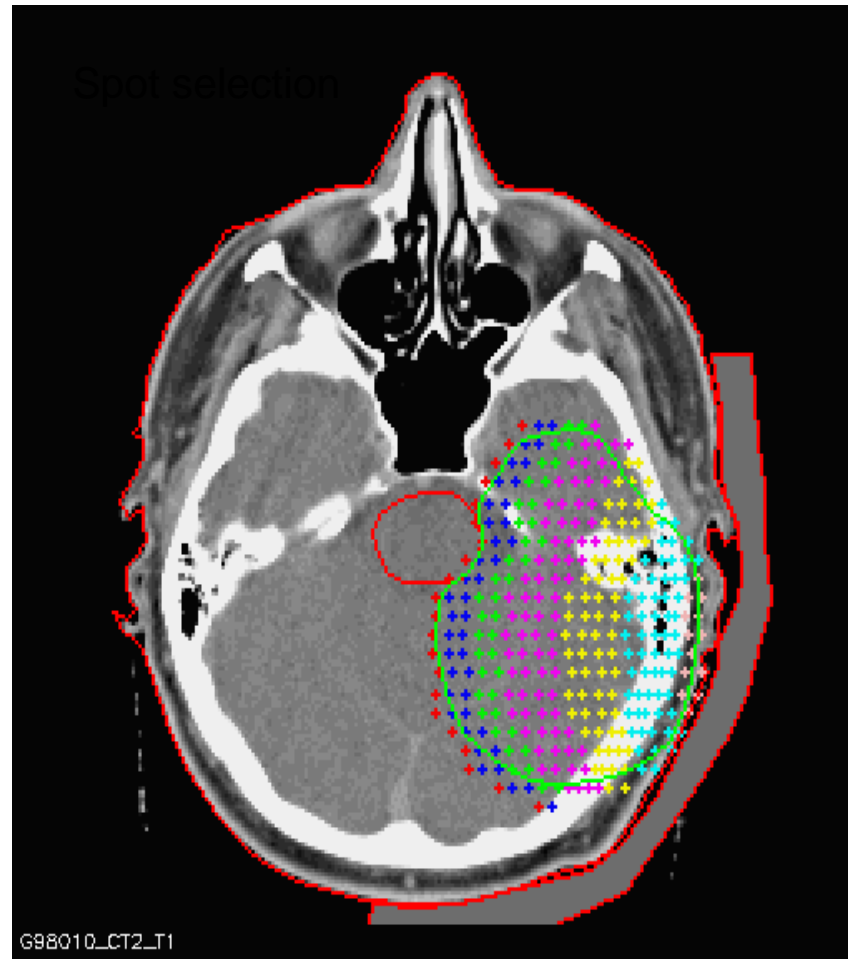
## Treatment planning for protons



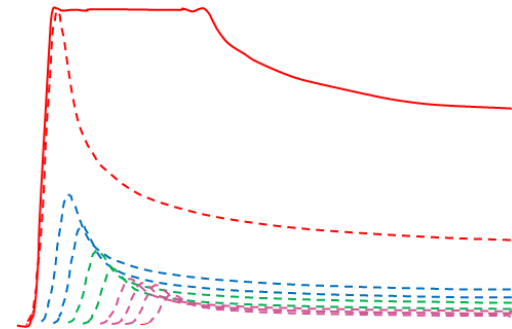
Incident field  
←

# The principles of proton therapy

## Treatment planning for protons

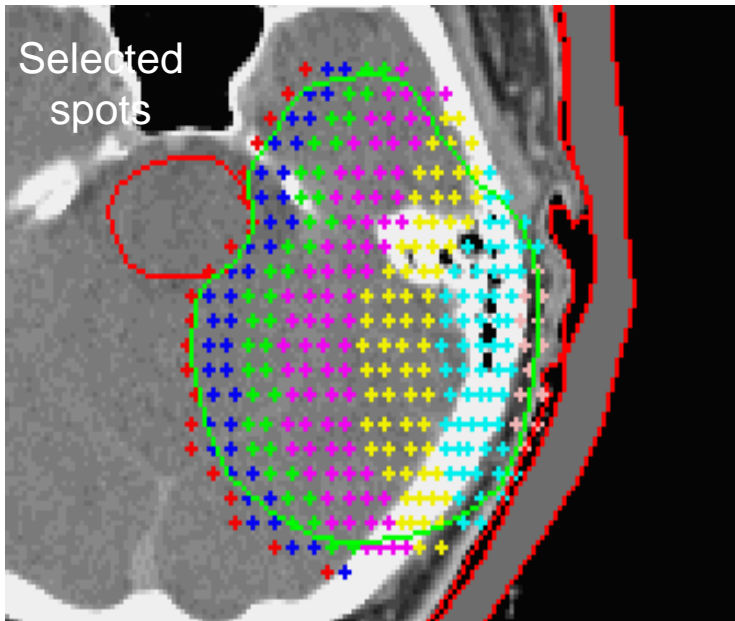


Incident field

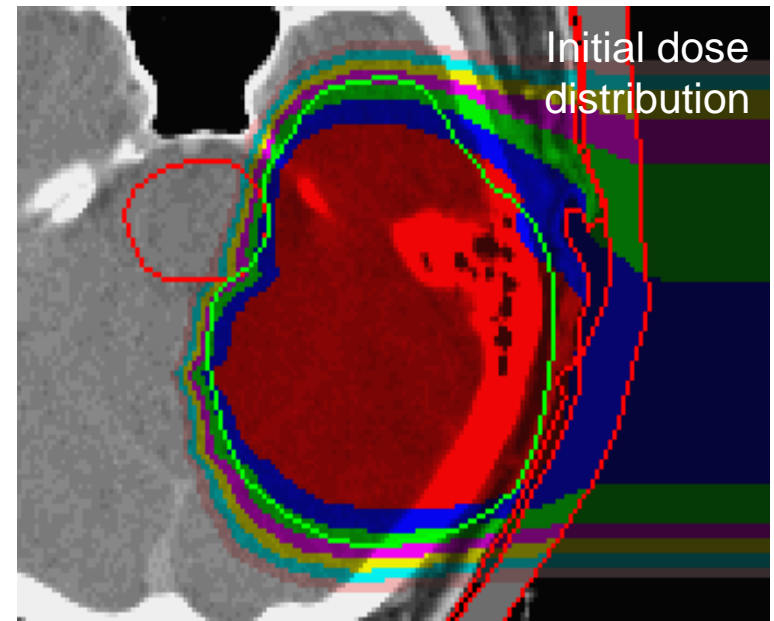




## Treatment planning for protons

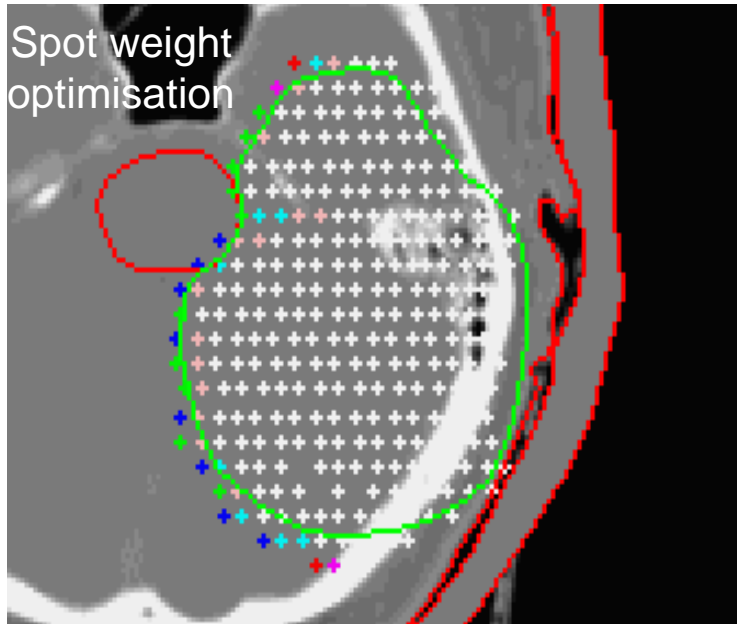


Dose calculation  
➔

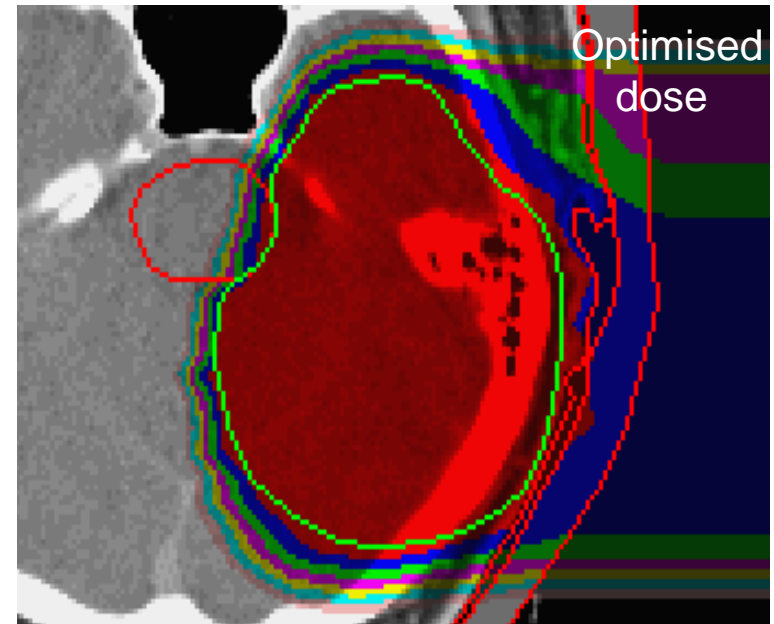


# The principles of proton therapy

## Treatment planning for protons

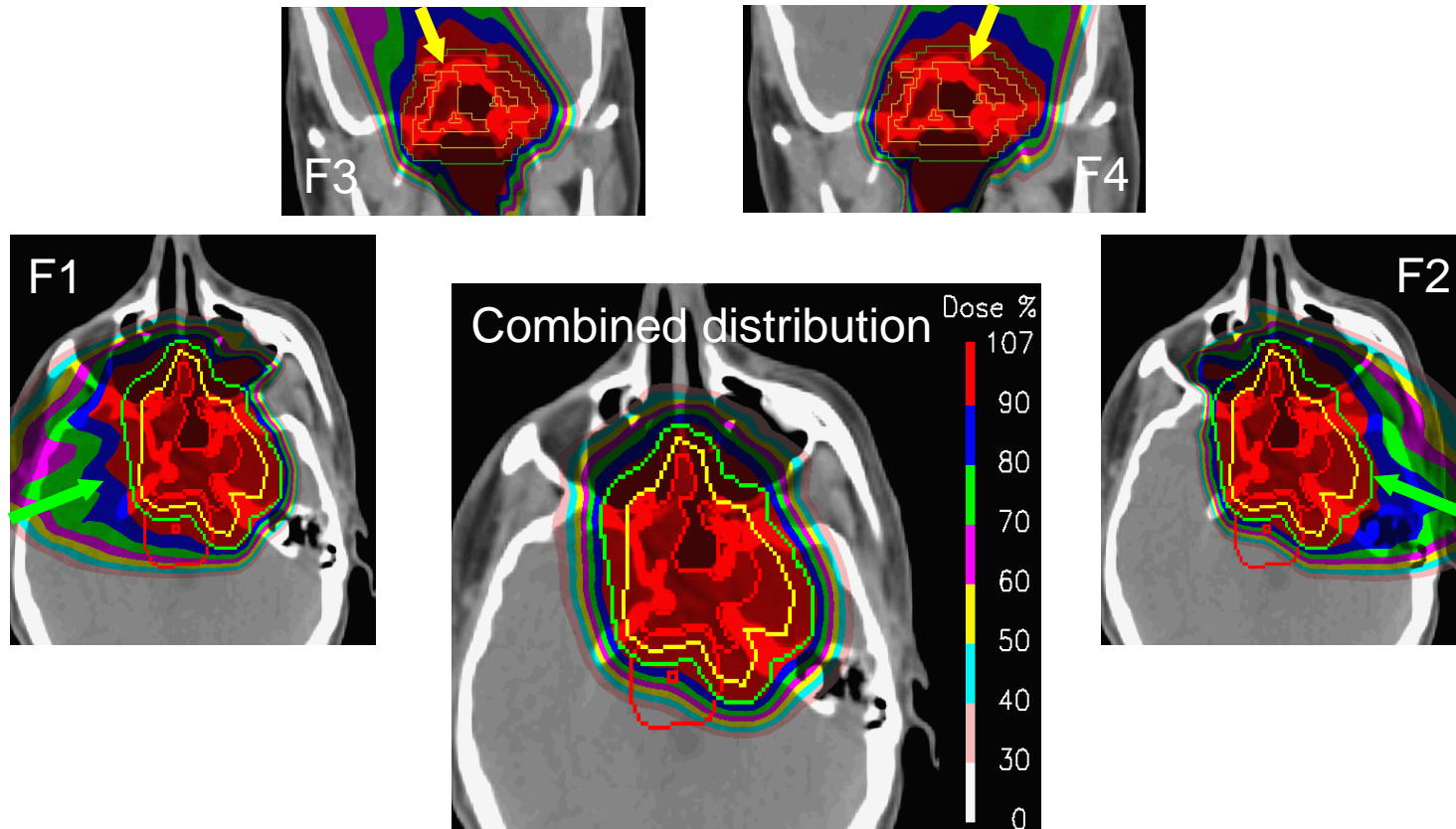


Dose calculation  
➔



# The principles of proton therapy

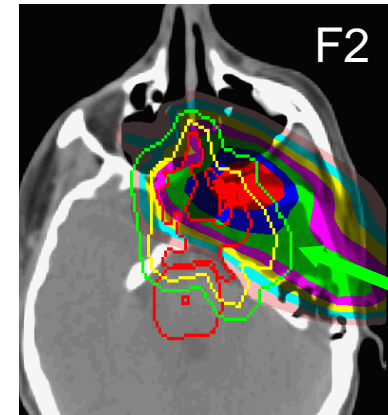
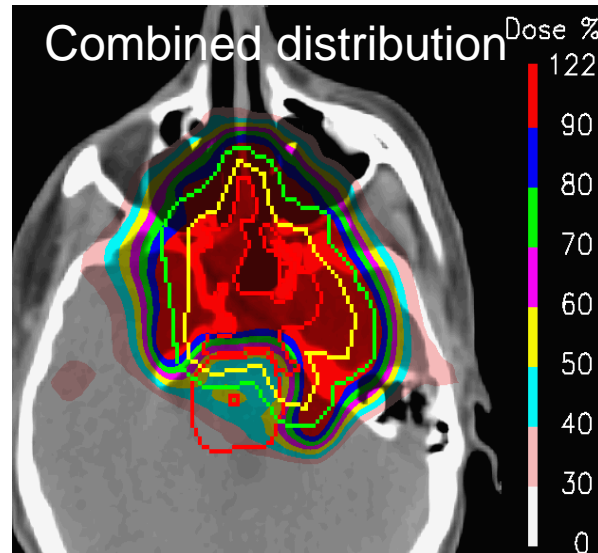
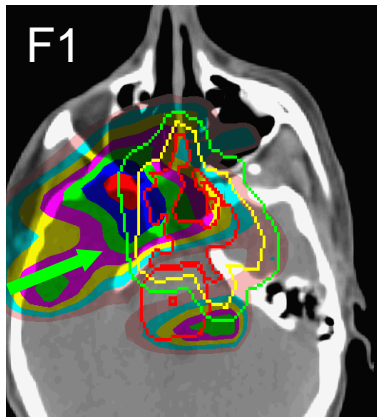
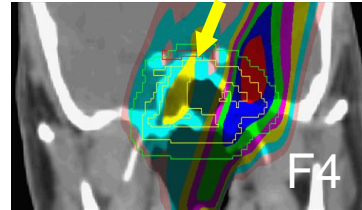
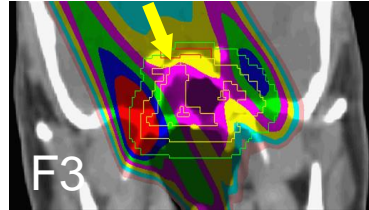
## A multi-field plan (SFUD).



Note, each individual field is (more or less) homogenous across the target volume

# The principles of proton therapy

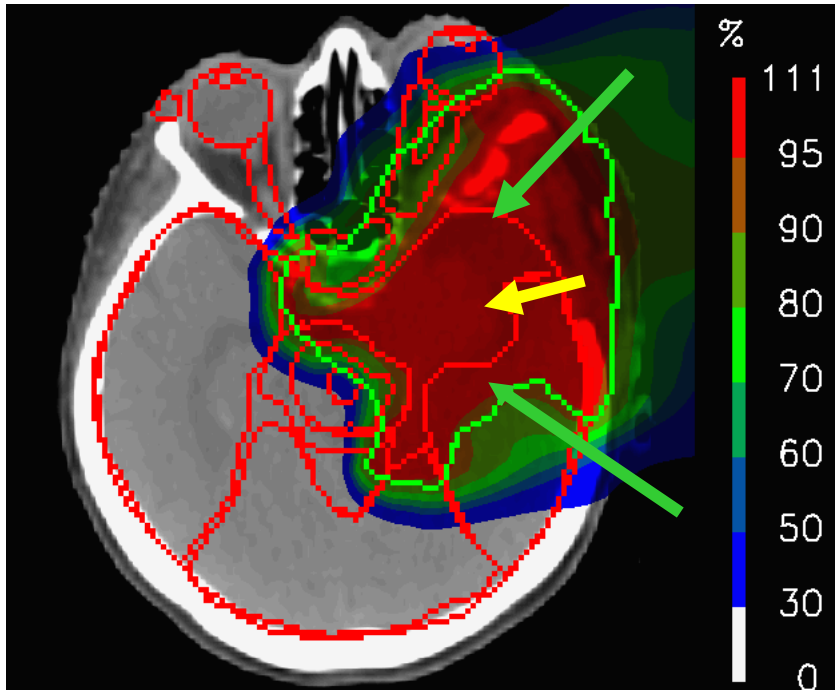
## An multi-field plan (IMPT)



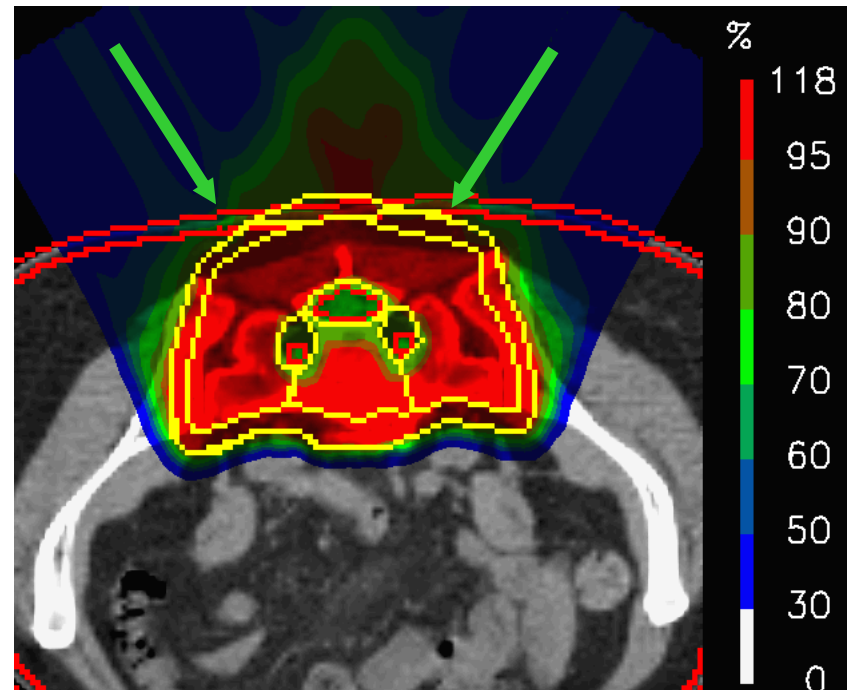
Note, each individual field is highly in-homogenous (in dose) across the target volume (c.f. SFUD plans)

# The principles of proton therapy

## Example clinical IMPT plans delivered at PSI



Meningioma ( 3 fields)

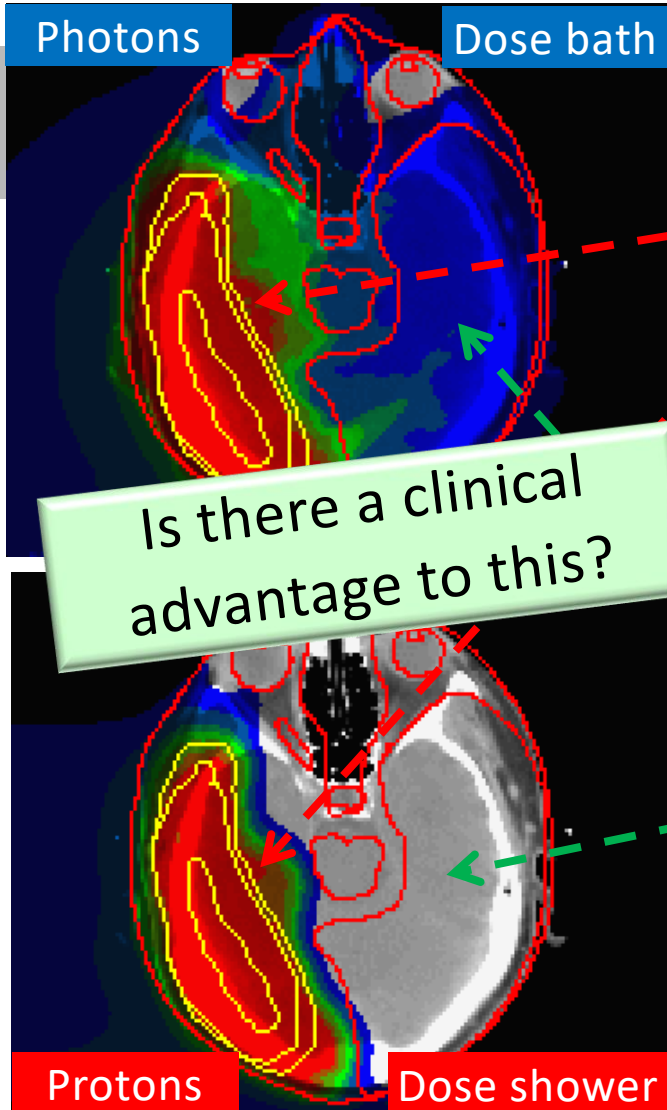


Sacral Chordoma (2 fields)

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# The potential of proton therapy

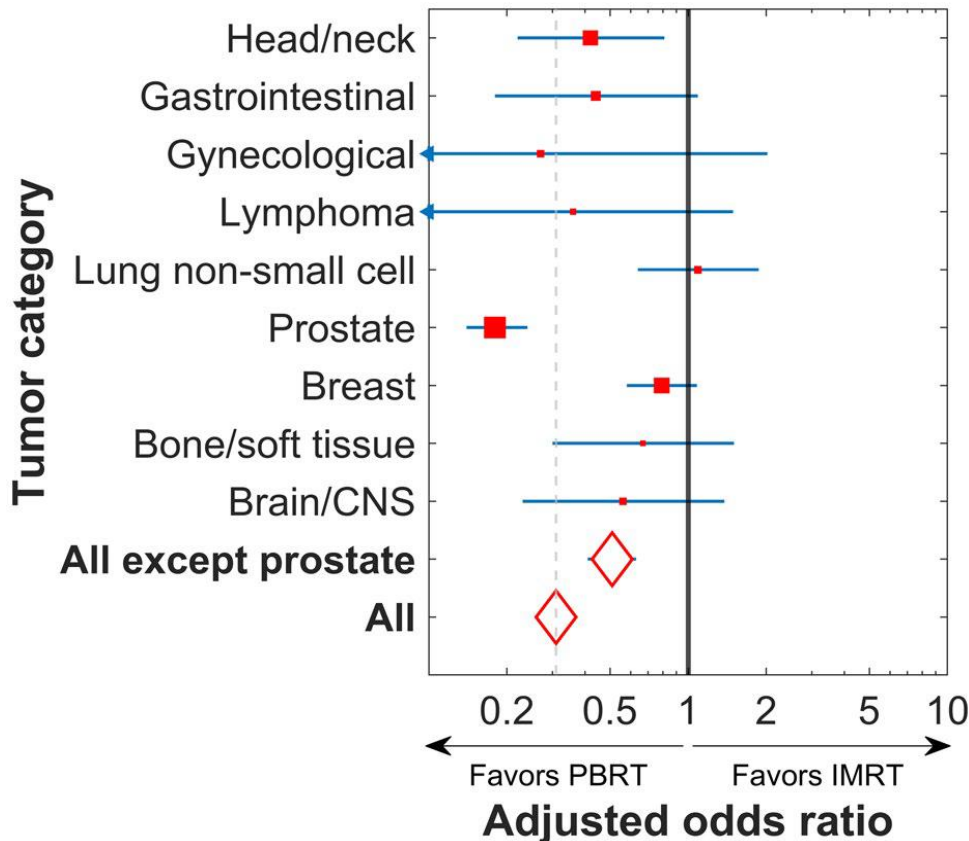


- The advantage of protons is NOT in high dose conformation
- Their advantage is mainly in reducing the mid-to-low dose levels in comparison to photons

# Reduced secondary cancer risk

A recent retrospective study from Stanford\*

- >450000 RT patients identified from National Database (US)
- 9 tumour types, 35% 3DCRT, 65% IMRT, 1.3% Protons
- Median F/U 5.1 Yrs



Incidence per 100 patient-years

- Protons 0.44
- IMRT 1.55
- Hazard ratio 0.31!

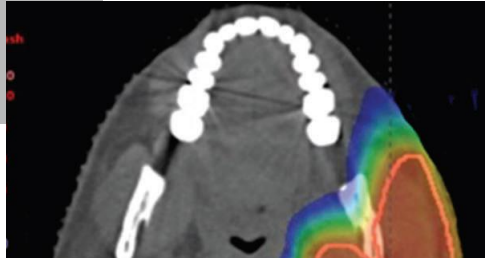
\*Xiang et al. Cancer. 2020 126:3560-3568.



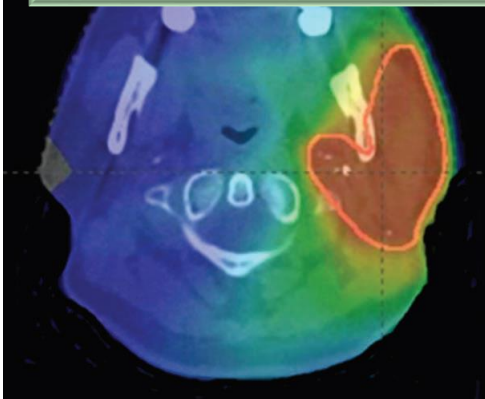
# Improved tolerance to treatments

A recent retrospective study from the University of Pennsylvania

- Comparison of 391 *proton* and 1092 *photon* patients treated with concurrent chemotherapy
- Endpoint – number of unplanned hospitalizations due to adverse events

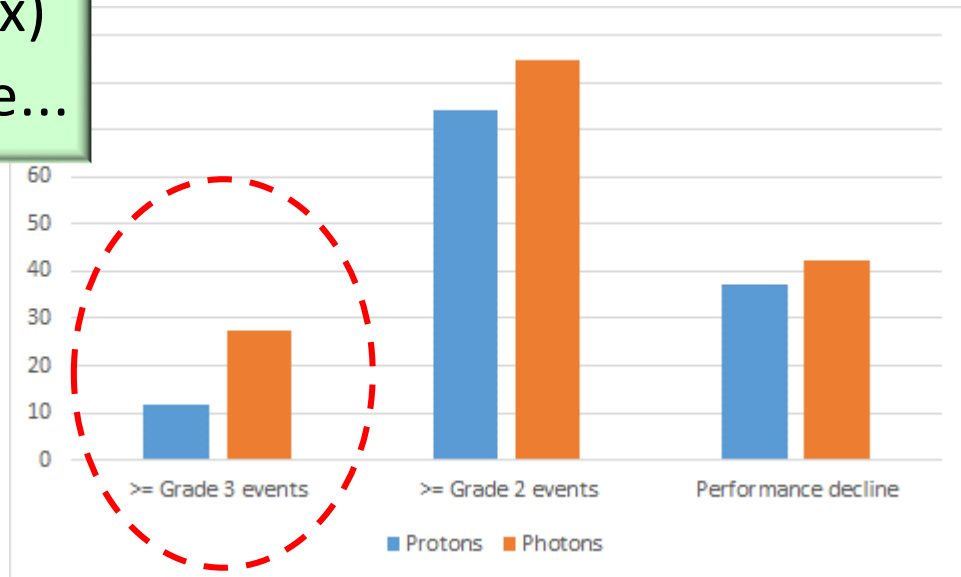


Nearly 3 times decrease in severe adverse events, despite a moderate (1.3x) reduction in integral dose...



patients include those also treated with a combination of *protons* and *photons*.

Integral dose ratio *protons/photons* ~0.7

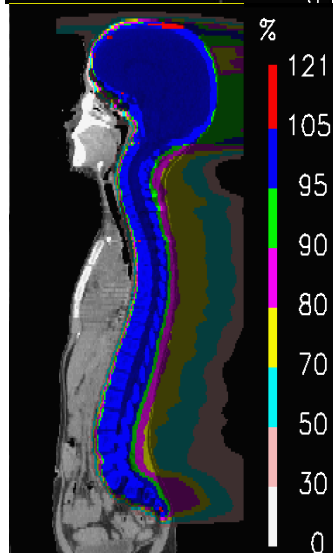
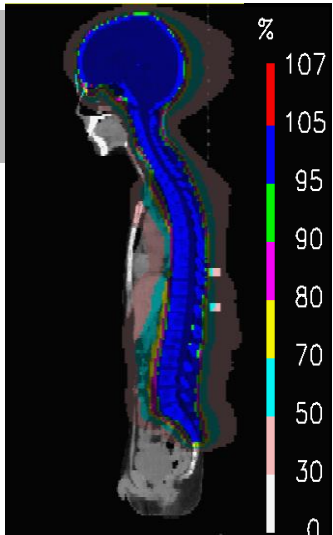


# Reduced late toxicities (1)

## A comparative study from MGH/Emory

- 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... total CSI dose,  $p < 0.01$
- Me...  $p < 0.01$

1.5-6 times reduction of frequent (>19% incidence) radiation induced side effects

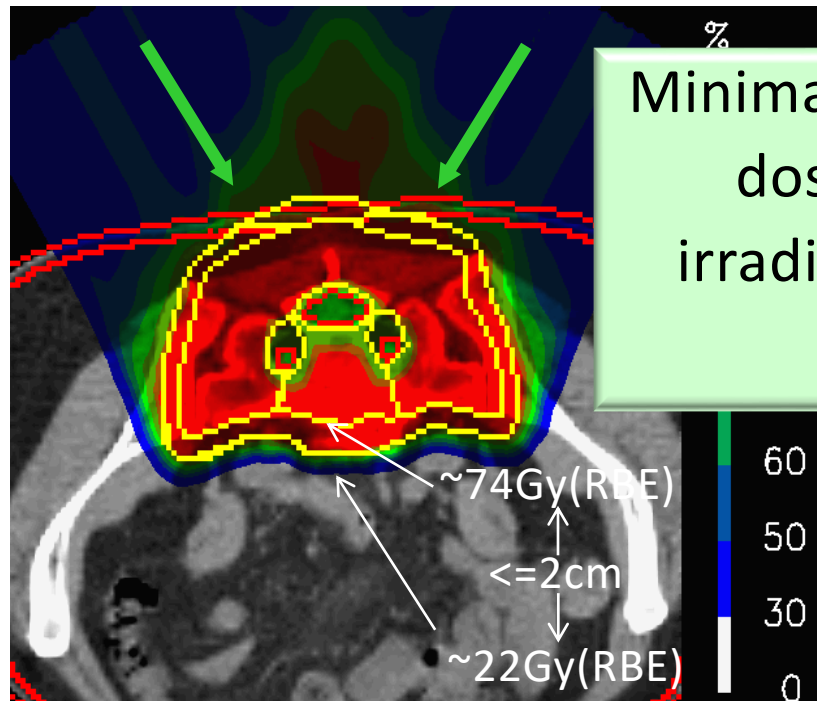


Outcome	Modality	Events	Reduction	P-value
Hypothyroidism	Protons	23%	<b>2.8</b>	<0.001
	X-rays	65%		
Sex hormone deficiency	Protons	3%	<b>6.3</b>	0.025
	X-rays	19%		
Endocrine replacement therapy	Protons	55%	<b>1.4</b>	0.030
	X-rays	78%		

# Reduced late toxicities (2)

## Bowel toxicity after high dose, large volume irradiations at PSI

- 31 mesenchymal tumours treated with PBS *proton* therapy



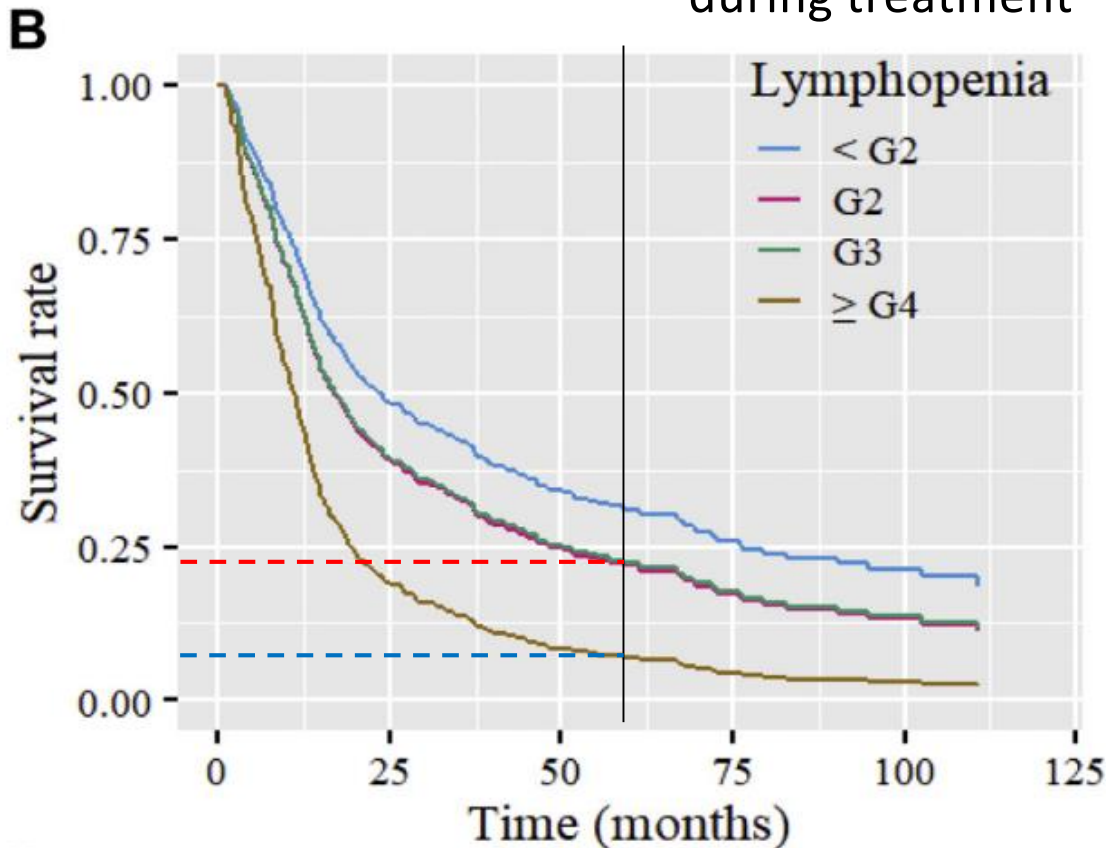
Minimal toxicity after high dose, high volume irradiation close to the bowel.

OS @ 7 years	72%
Mean V60 (small bowel)	7ml
Mean V5 (small bowel)	87ml
Grade 1 toxicities	3%
>= Grade 2 toxicities	0%

# Improved overall survival?

## Reduced treatment induced lymphopenia

- 305 Esophageal cancer patients
  - Dose 52Gy
- Overall survival as function of lymphopenia grade recorded during treatment



5y OS (G3/G2) ~22%

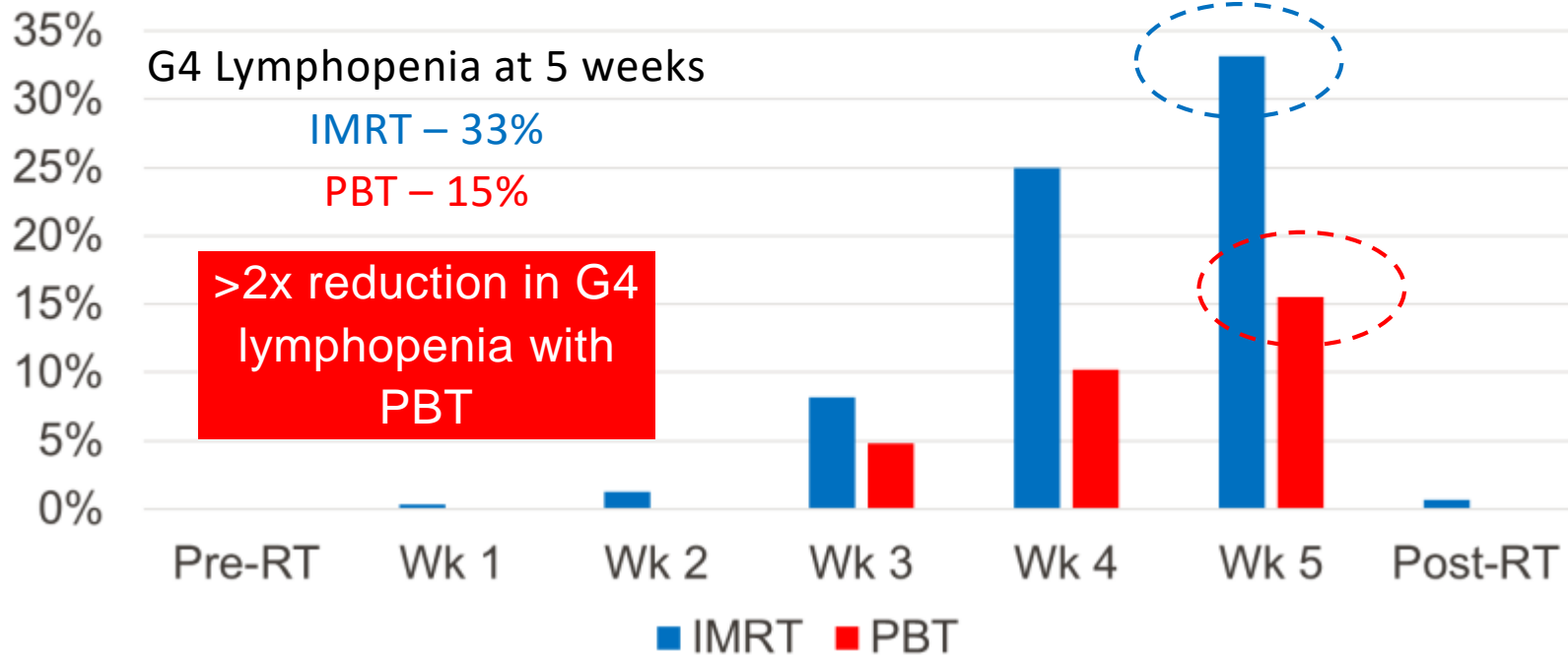
5y OS ( $\geq$ G4) ~7%

~ 3x decreased OS if patient suffers G4 lymphopenia during therapy

# Improved overall survival?

## Reduced treatment induced lymphopenia

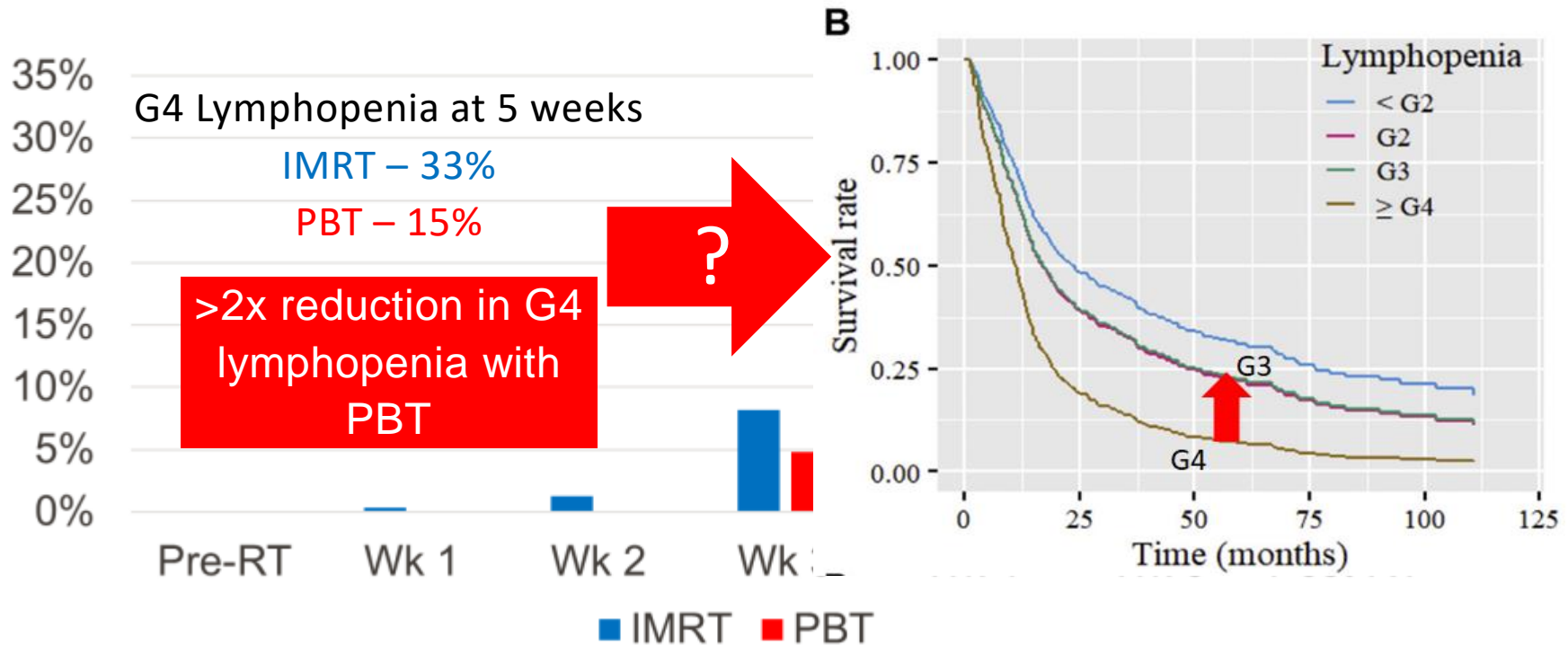
504 esophageal cancer patients treated with CRT  
**Incidence of Grade 4 lymphopenia**



# Improved overall survival?

## Reduced treatment induced lymphopenia

504 esophageal cancer patients treated with CRT  
**Incidence of Grade 4 lymphopenia**



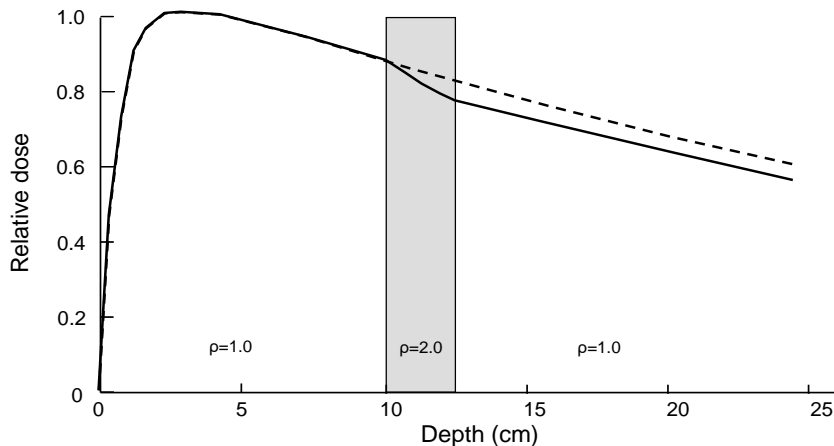
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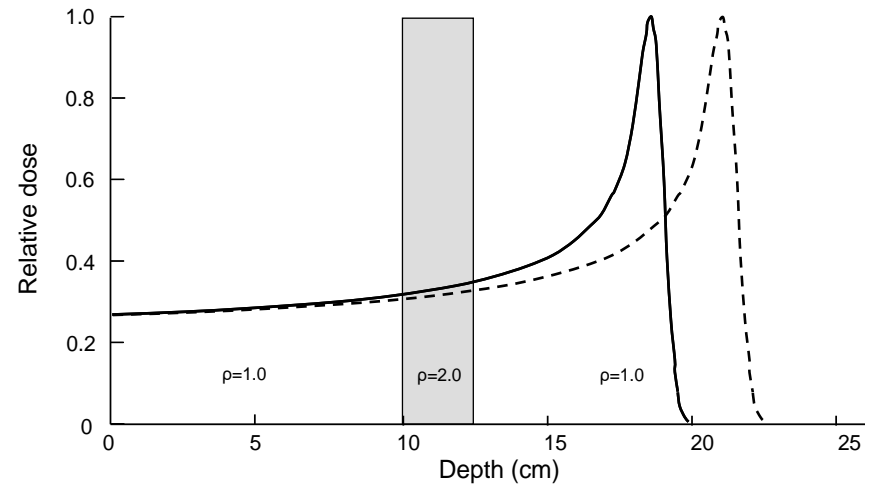
# Range uncertainty

The effect of (unplanned) density heterogeneities on  
photons and protons

Photons...



... and protons.



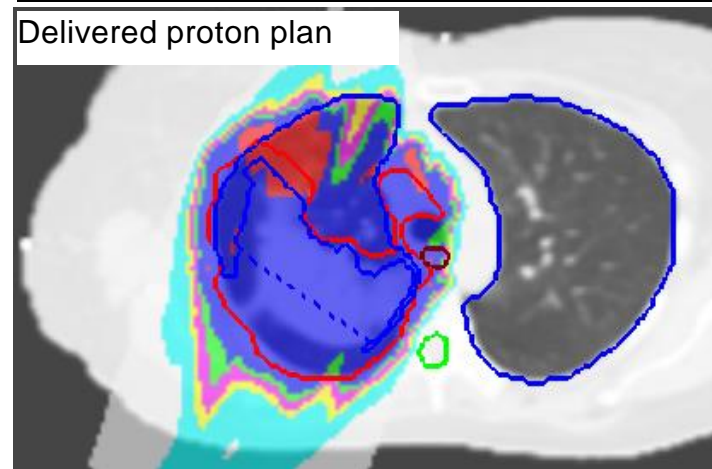
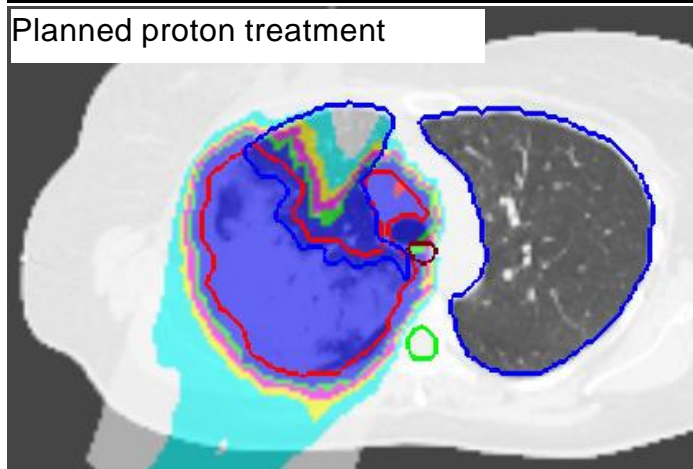
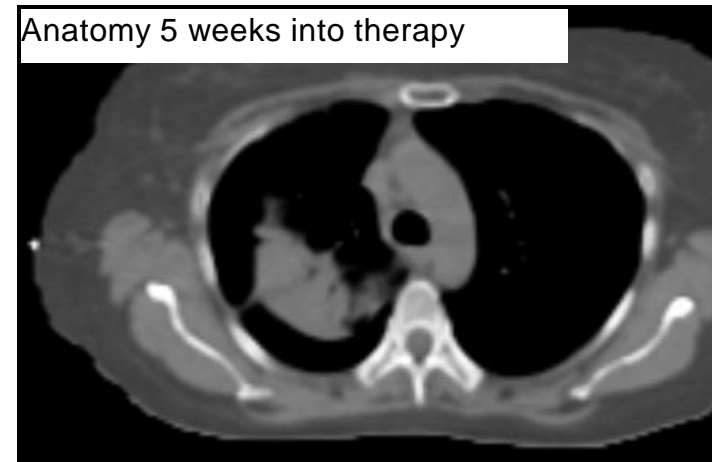
The advantage of protons is that they stop 😊

The disadvantage of protons is that we don't always know where... 😞



# Range uncertainty

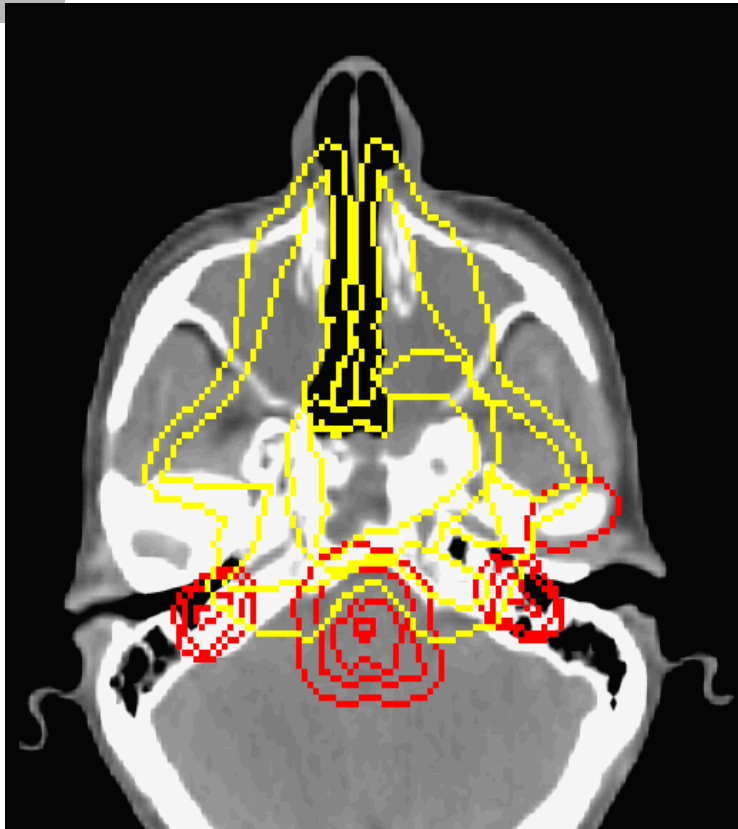
E.g. the effect of anatomical changes



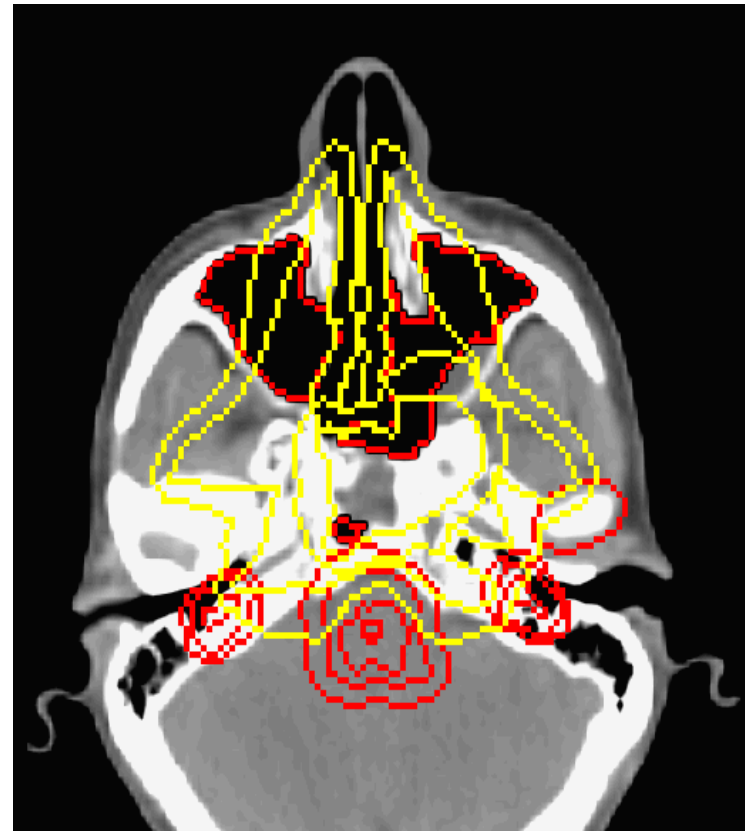
# Range uncertainty

## Cavity filling and range changes

E.g. Skull base Chondrosarcoma



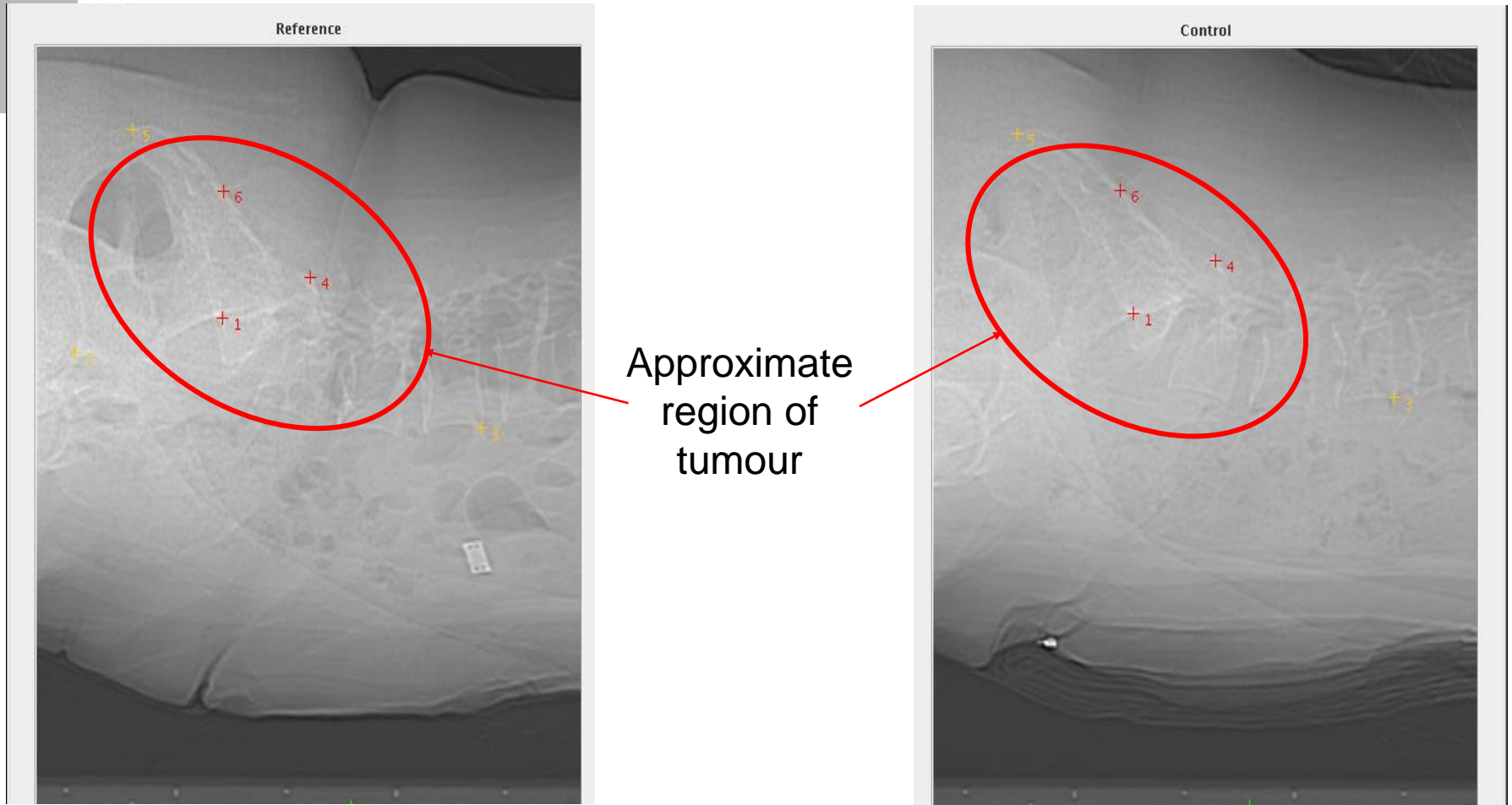
Planning CT



Repeat CT after 2 weeks

# Range uncertainty

## A case of the wrong trousers...

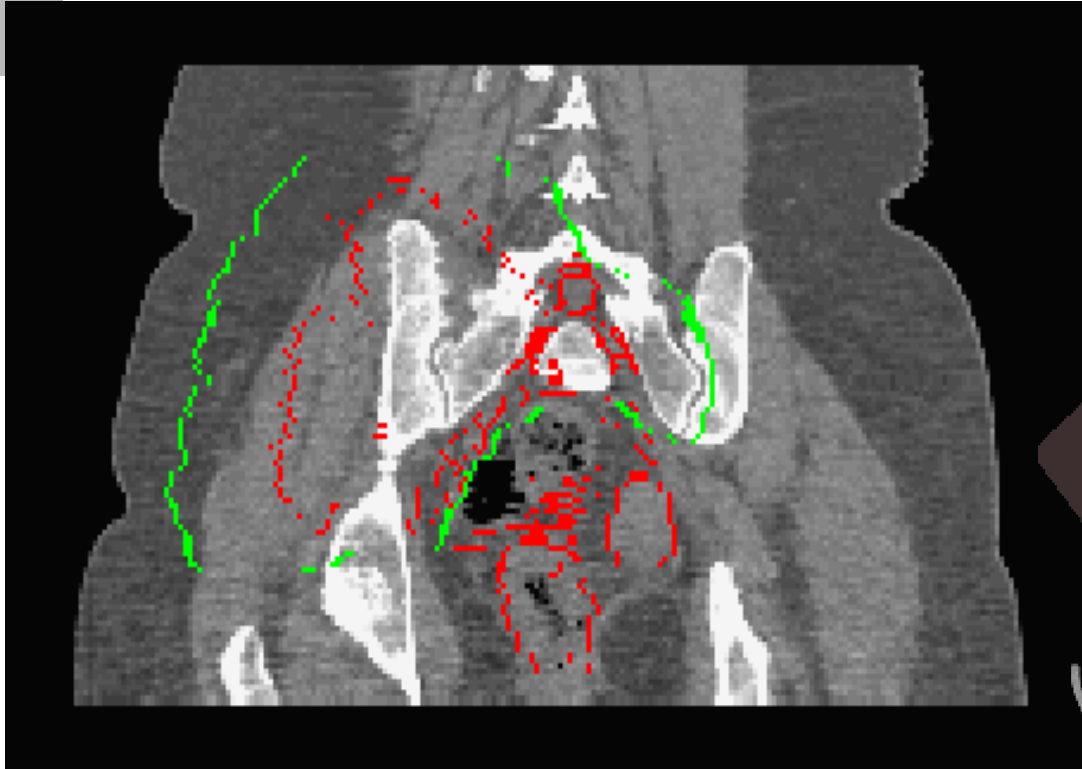


Reference simulation image

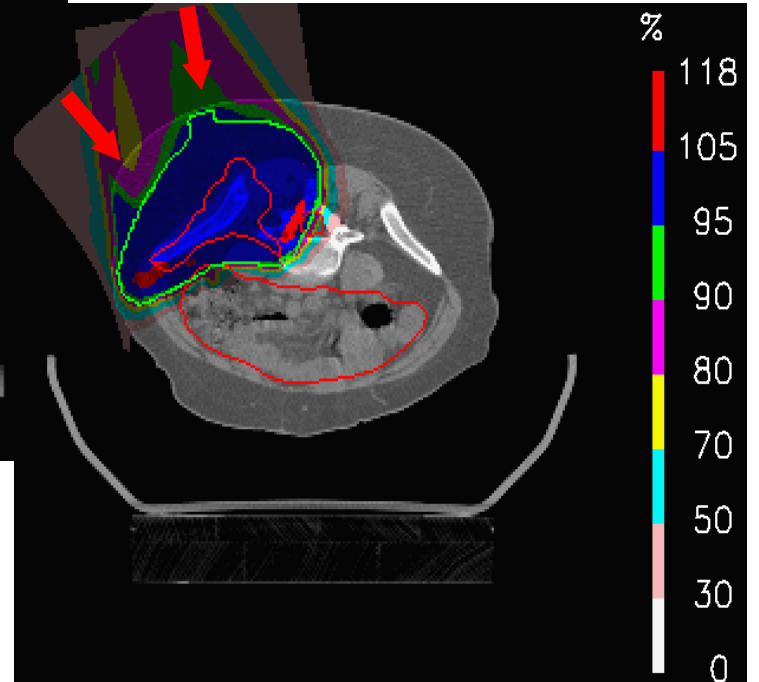
Simulation image – 1st fraction

# Range uncertainty

## A case of the wrong trousers...



Original planning  
CT and plan



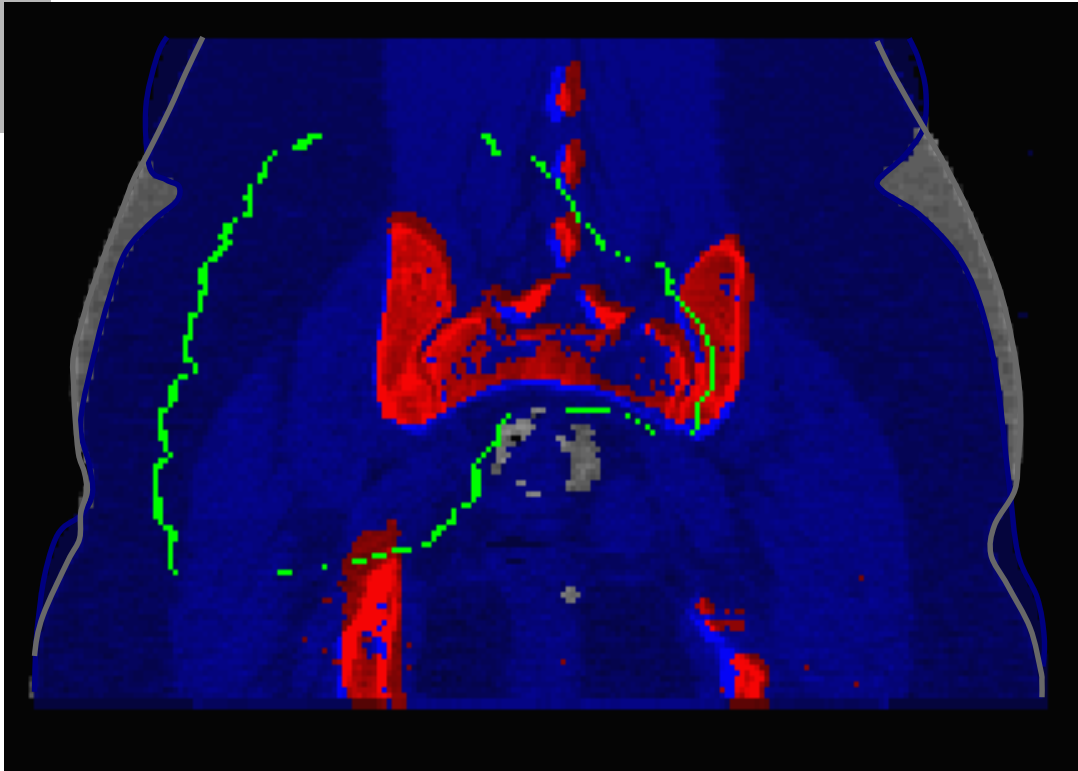
Francesca Albertini, PSI

The problem with the patient...

Heidelberg summer school 2017

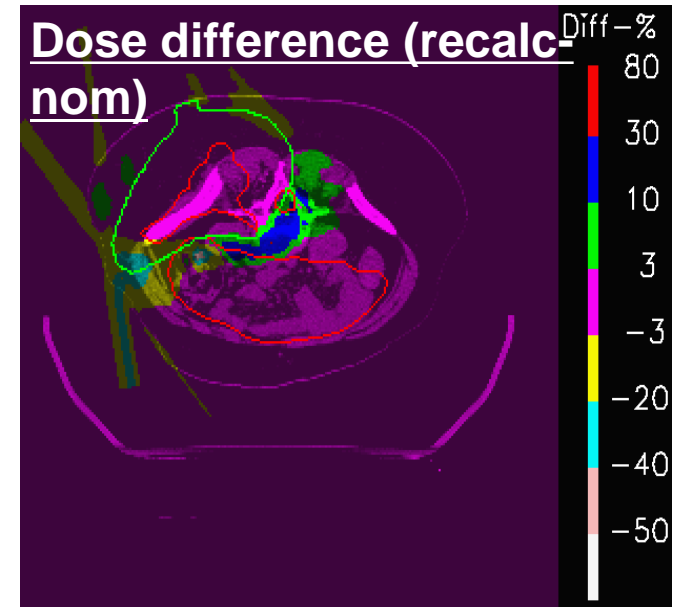
# Range uncertainty

## A case of the wrong trousers...



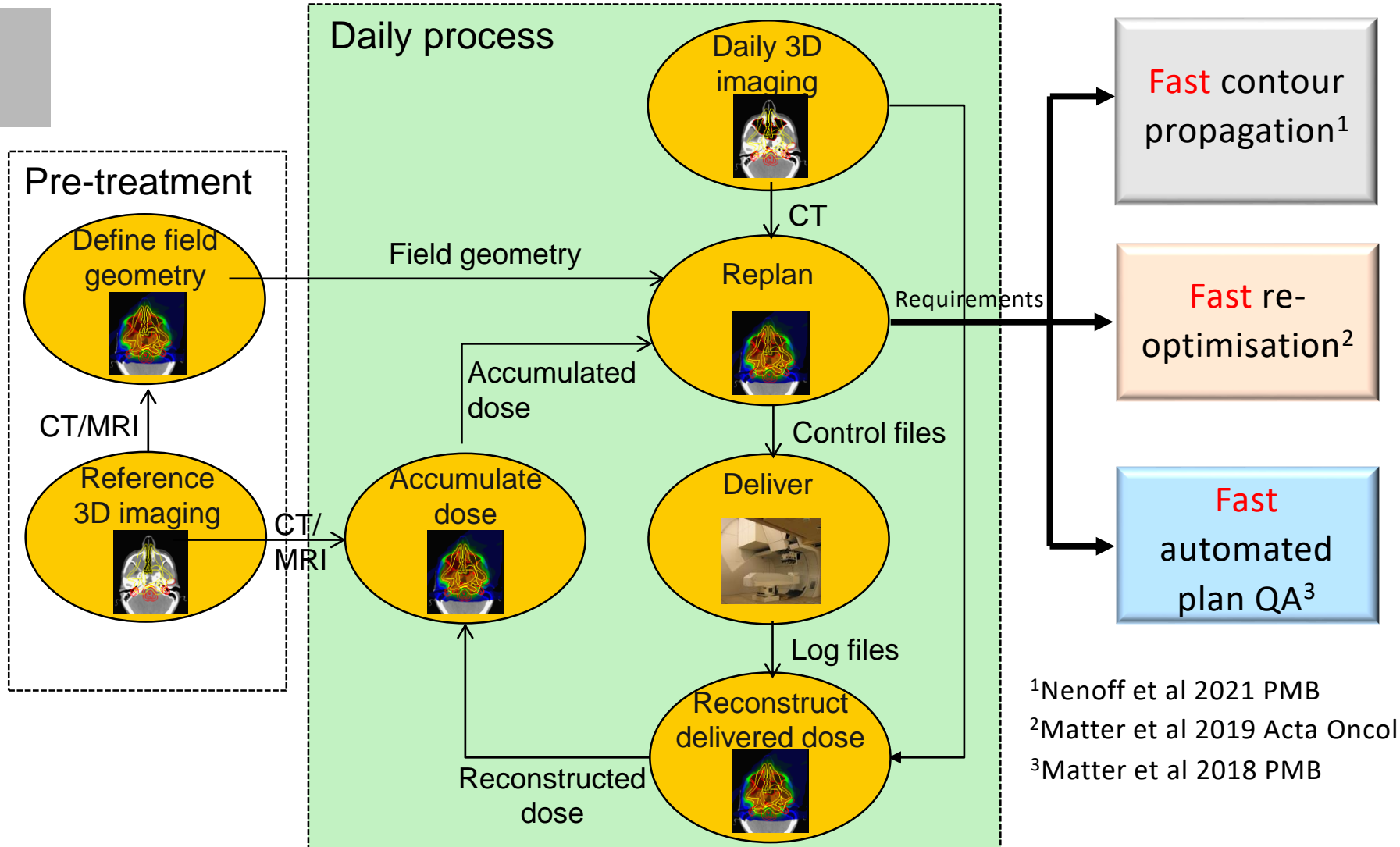
Max range differences:  
**3.6 cm**

Planning and repet  
CT overlaid



# Range uncertainty

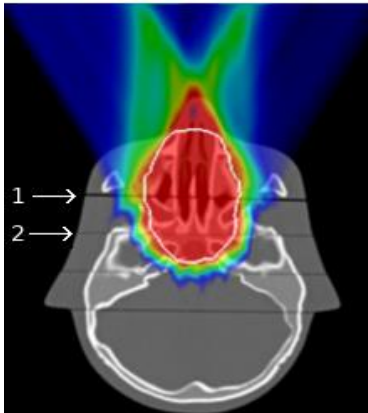
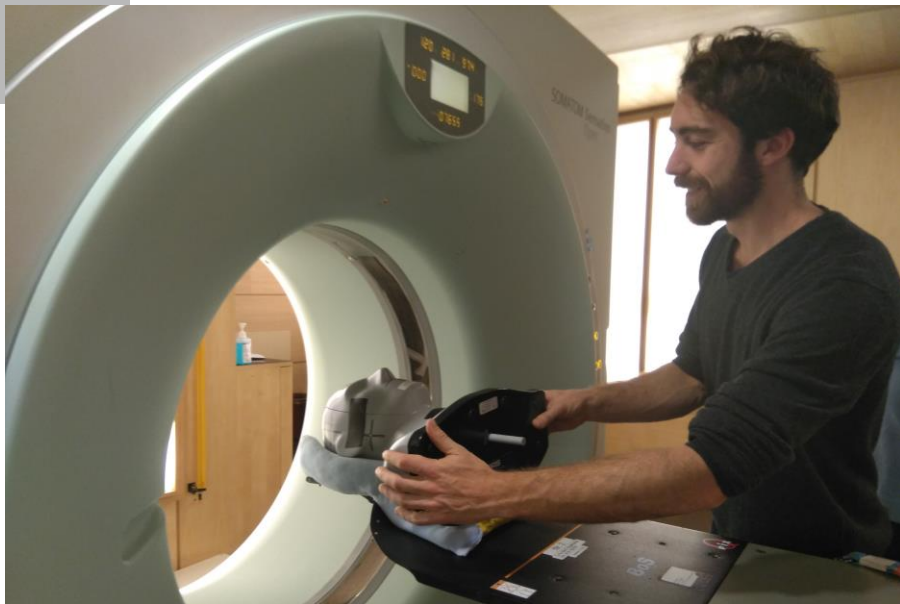
## Daily Adaptive Proton Therapy



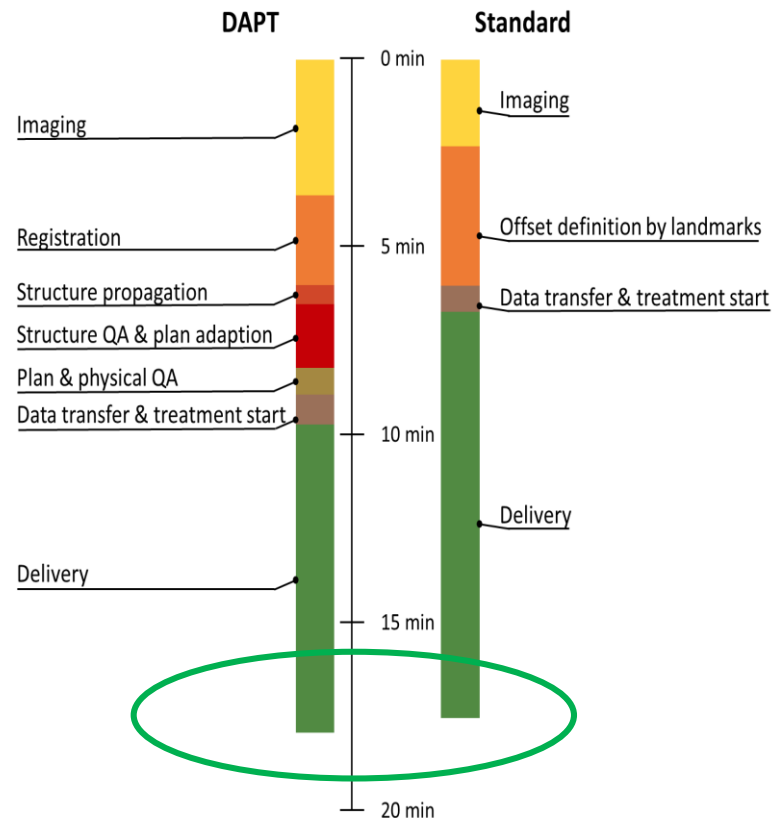
<sup>1</sup>Nenoff et al 2021 PMB  
<sup>2</sup>Matter et al 2019 Acta Oncol  
<sup>3</sup>Matter et al 2018 PMB

# Range uncertainty

## Daily Adaptive Proton Therapy in practice (almost...)



Timings of conventional and full DAPT deliveries



Almost the same time for a DAPT and conventional fraction (<20mins)

# Size and costs

$$m_p = 1800 \times m_e$$

An electron



My bike ~ 6.5kg

A proton



A M113 Tank ~ 12500kg



# Size and costs

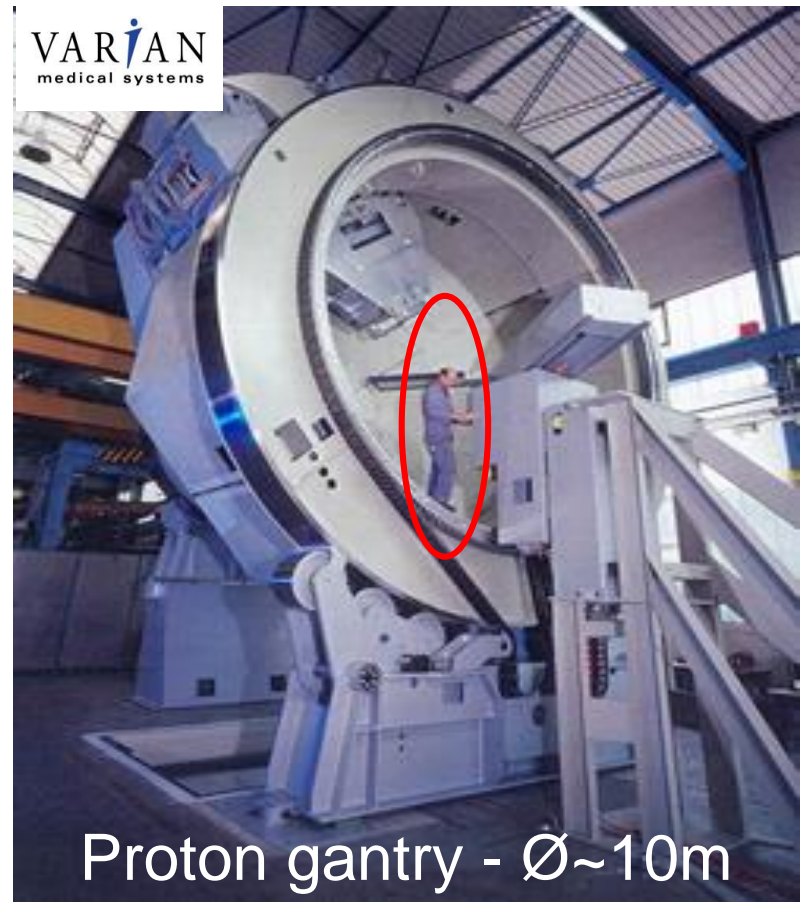
## Photon and proton gantries

VARiAN  
medical systems



Photon LINAC -  $\varnothing \sim 2\text{m}$

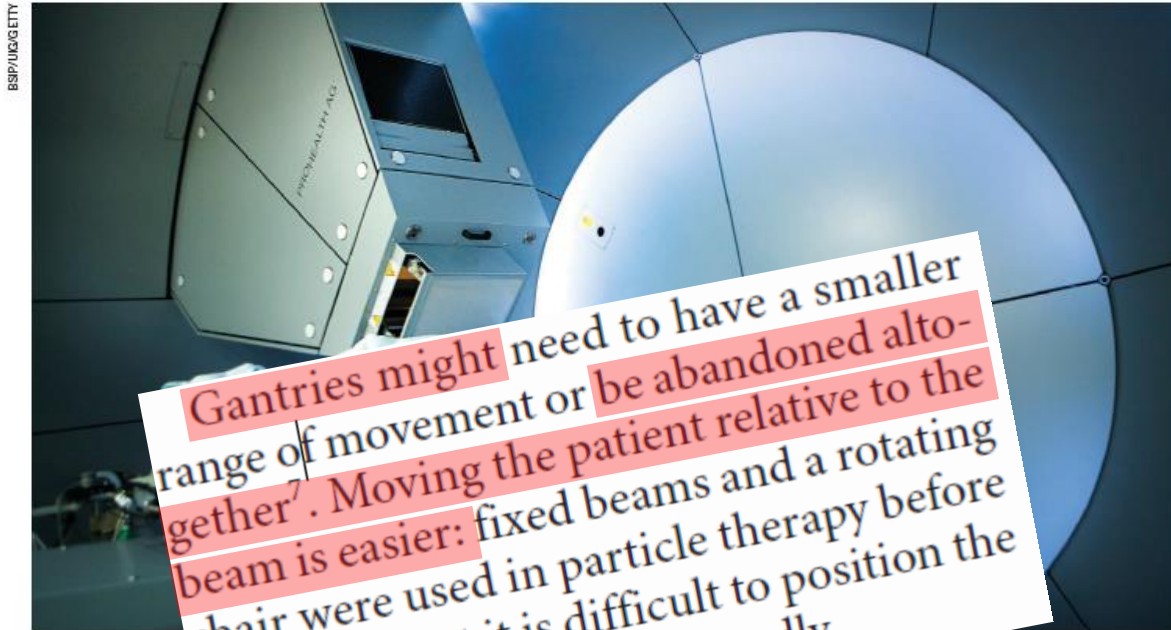
VARiAN  
medical systems



Proton gantry -  $\varnothing \sim 10\text{m}$

# Size and costs

## The return of gantry-less systems?



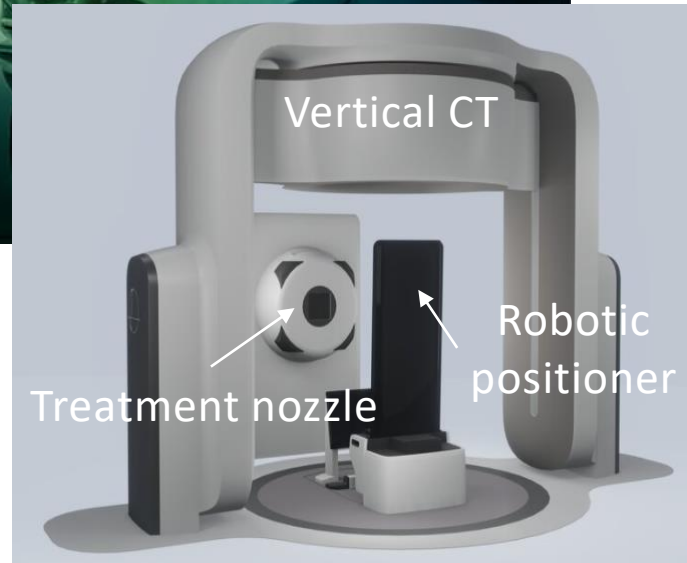
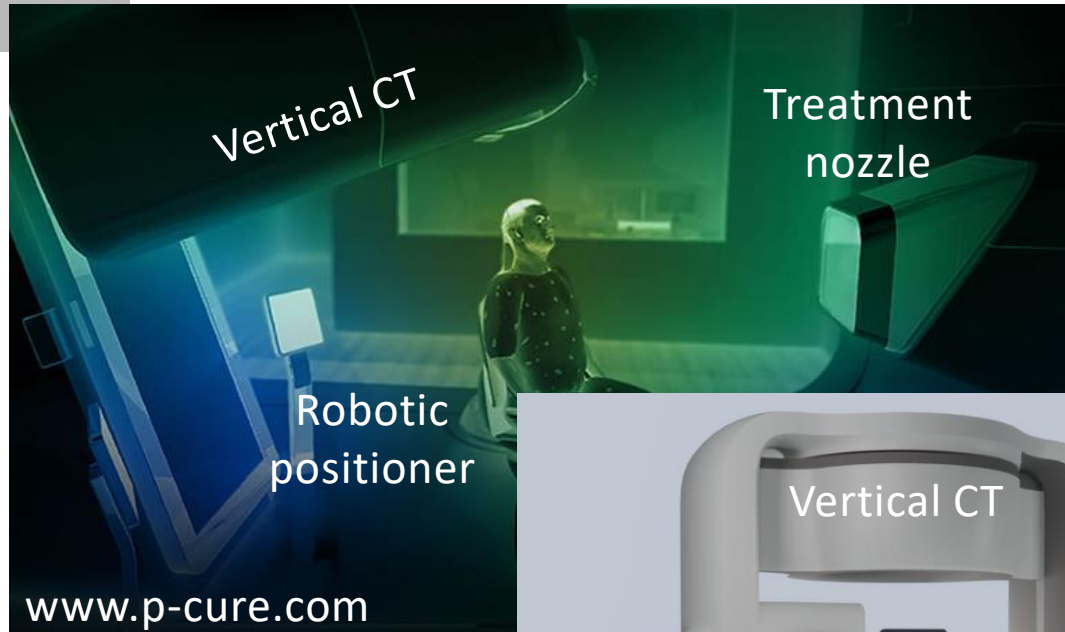
A proton-therapy machine

## ways to make proton therapy affordable

Shrink accelerators, sharpen beams and broaden health-care coverage so more people can get this type of radiation treatment, argue Thomas R. Bortfeld and Jay S. Loeffler.

# Size and costs

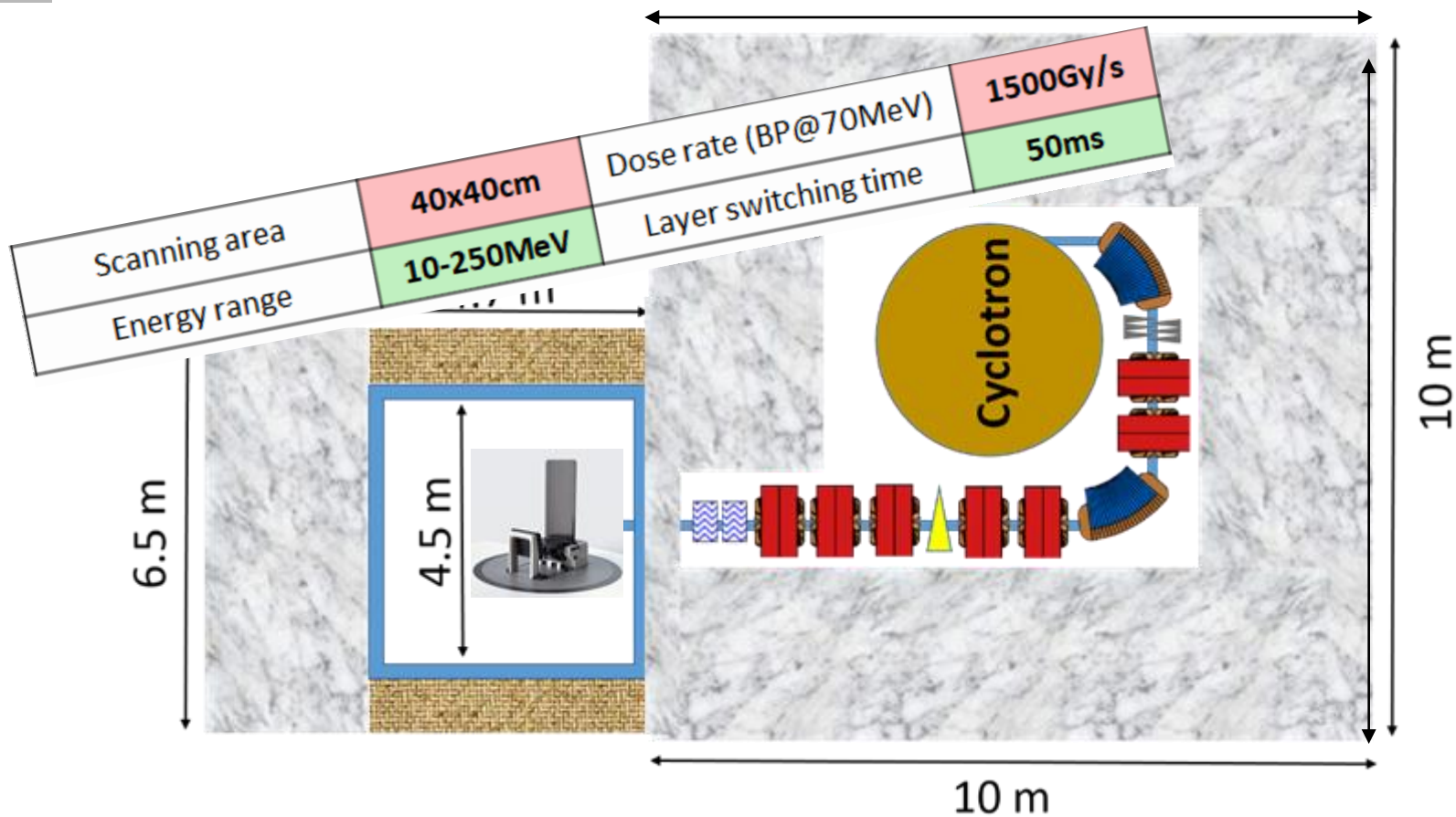
## The return of gantry-less systems?



# Size and costs

## What could be possible without a Gantry...?

An ultra-compact single room, PBS proton therapy system

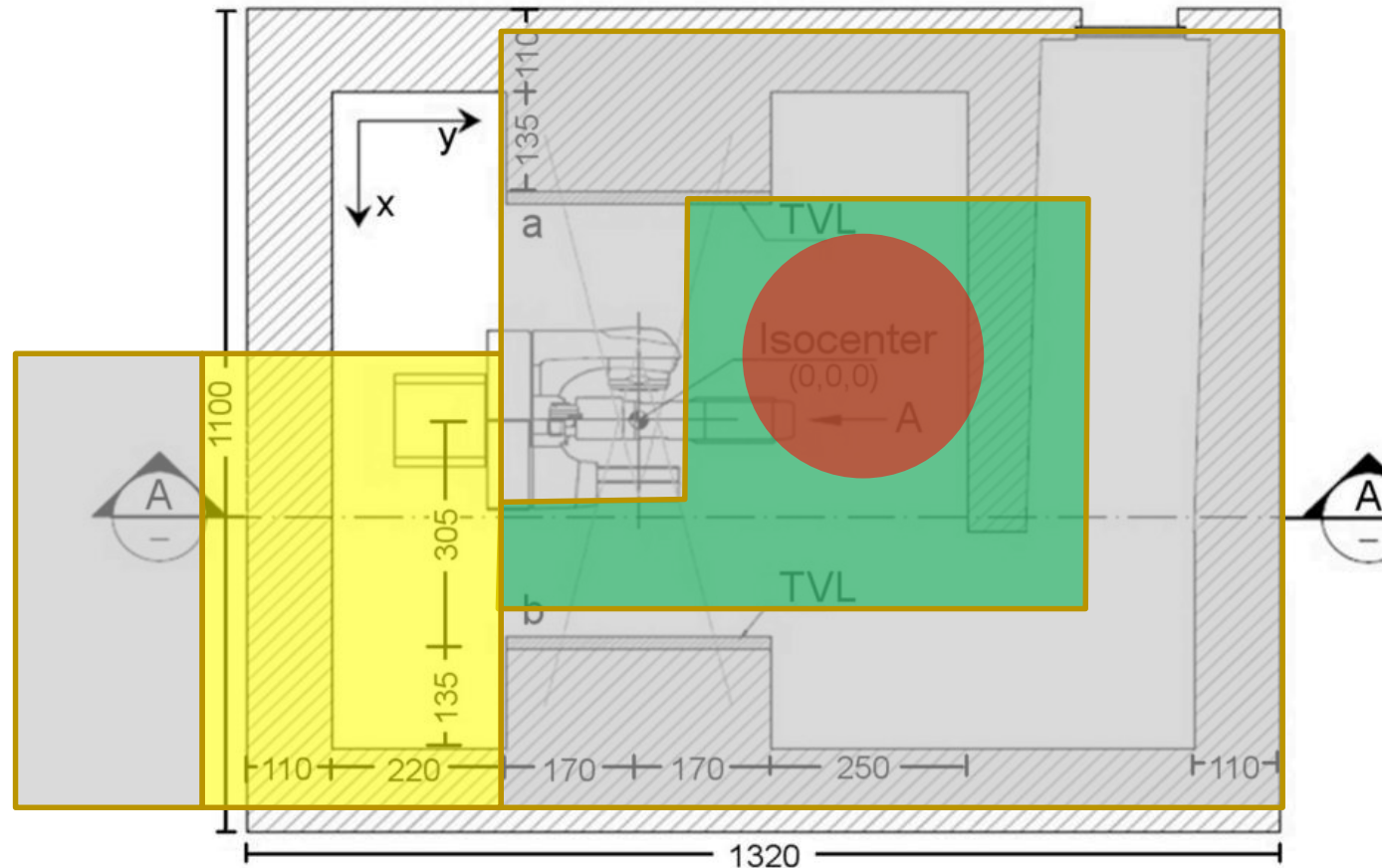


# Size and costs

## PBS proton therapy in a Linac bunker?

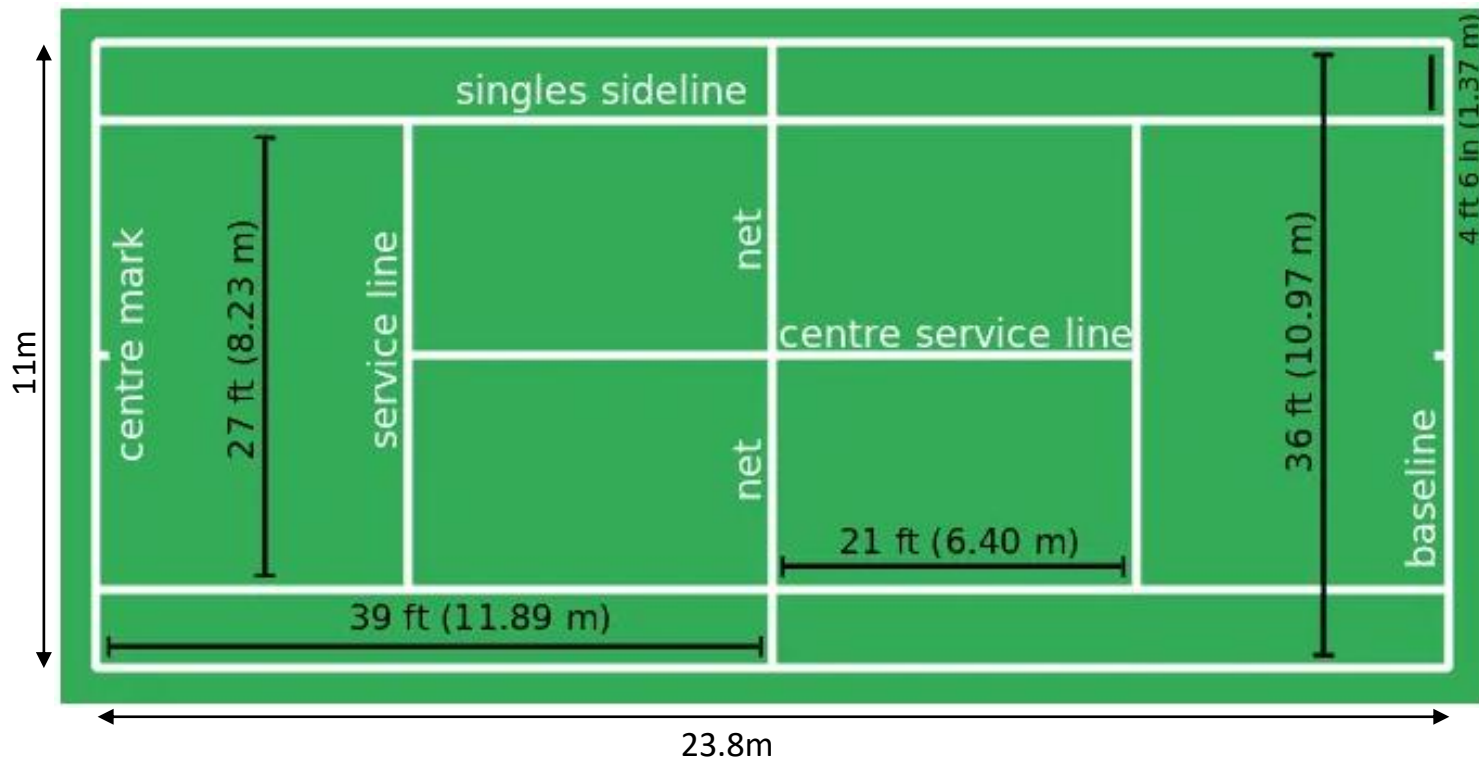
A typical Linac Bunker

The ultra-compact proton design



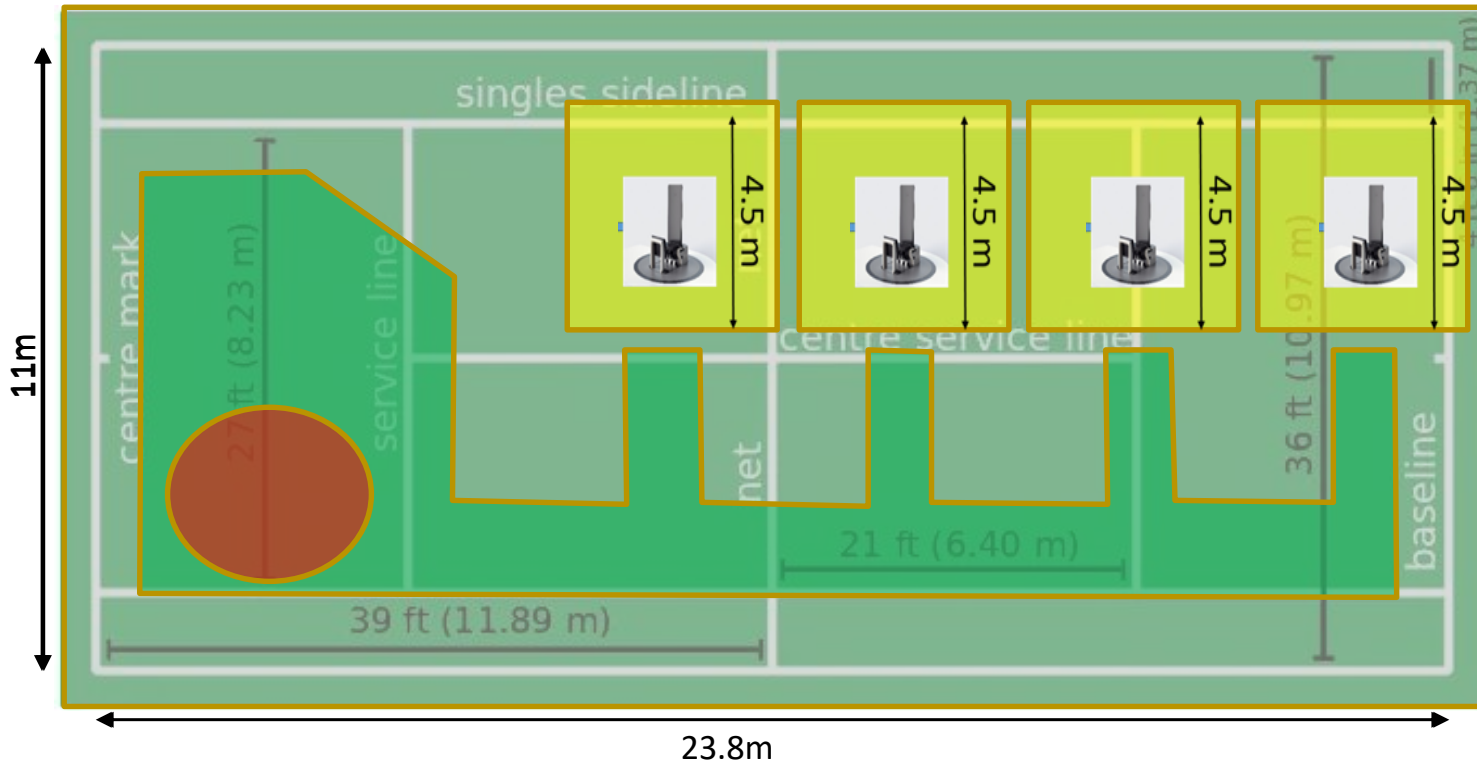
# Size and costs

Or a 4 room facility on the area of a tennis court?



# Size and costs

Or a 4 room facility on the area of a tennis court?



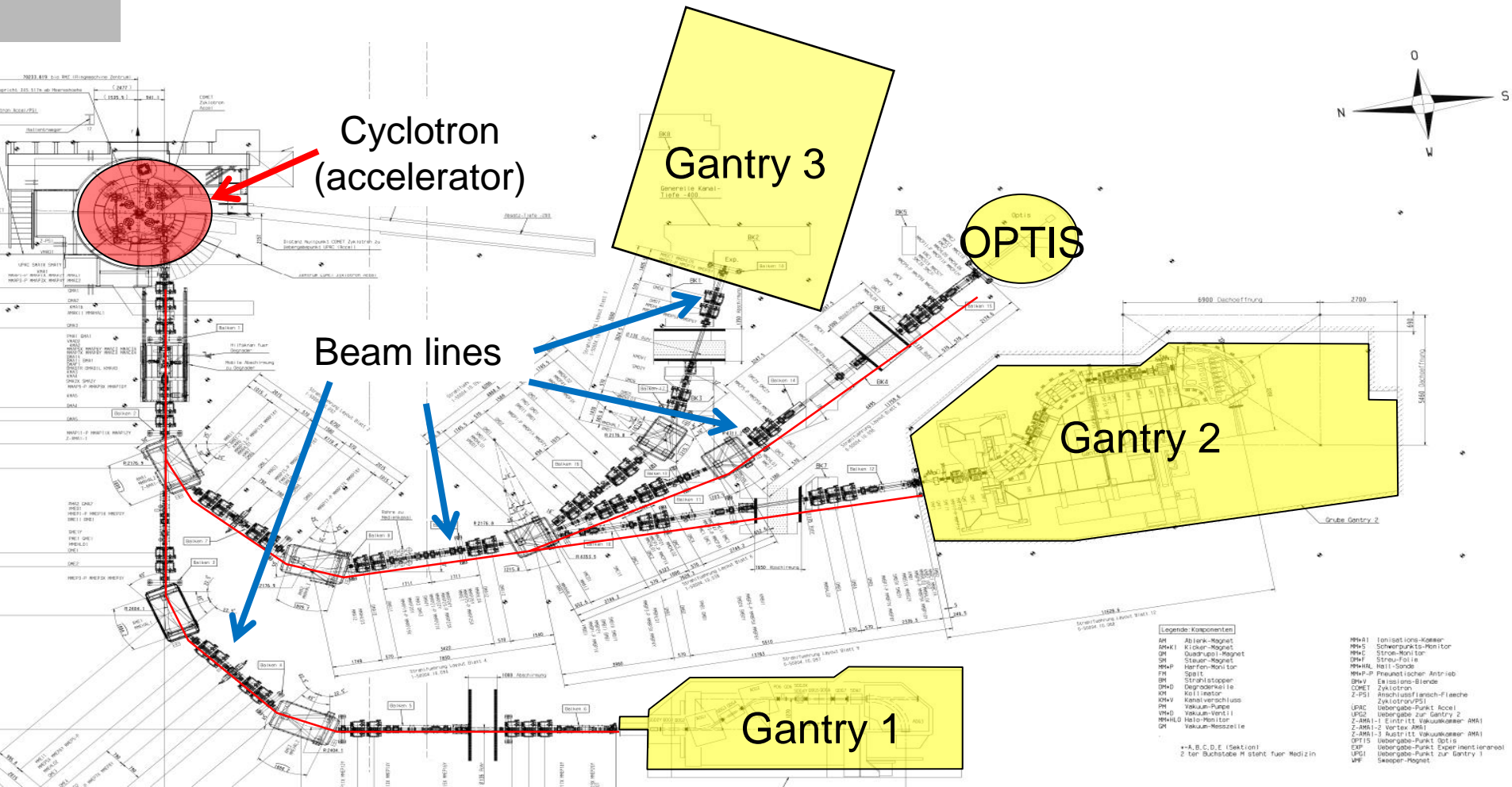
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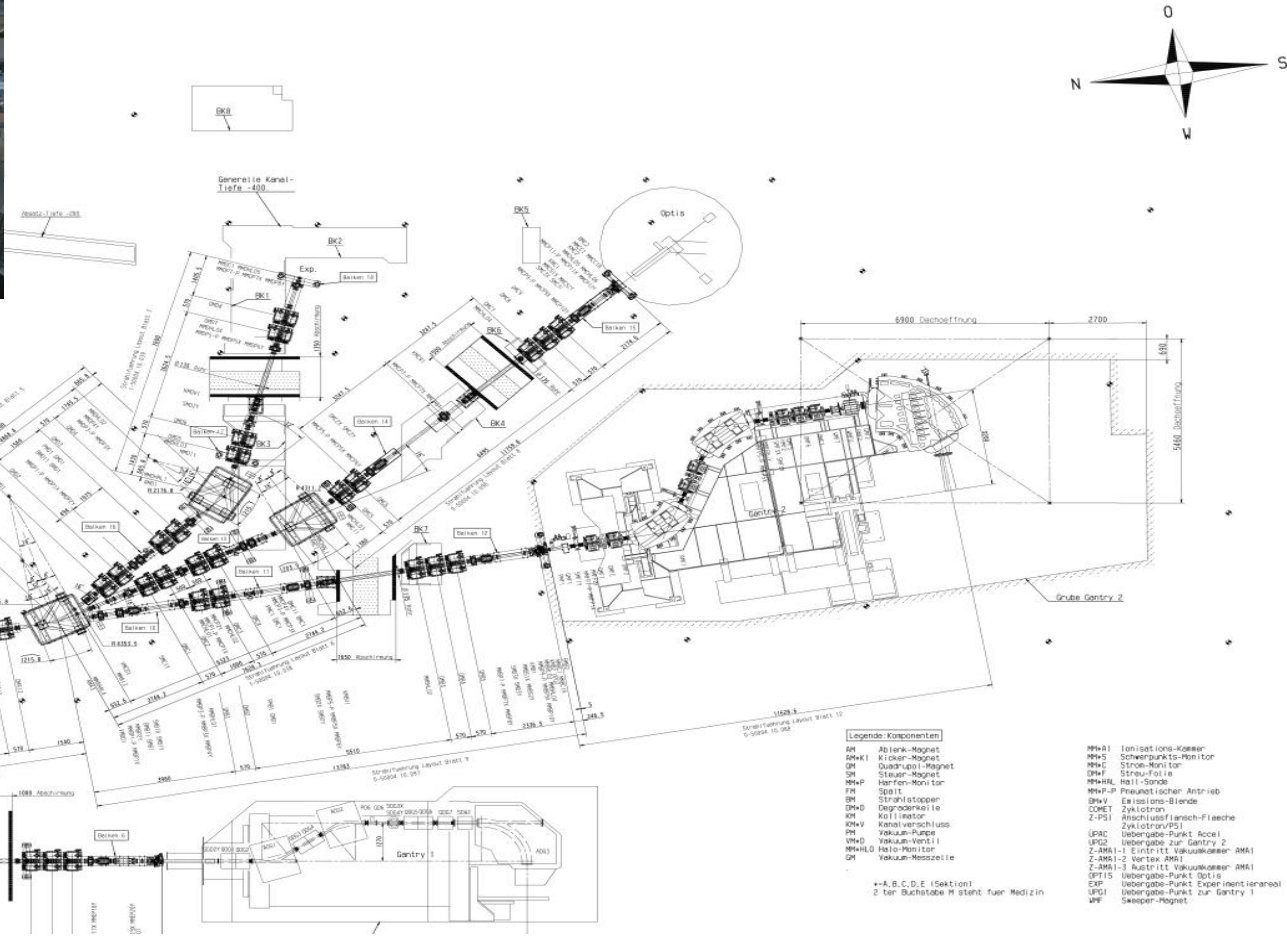
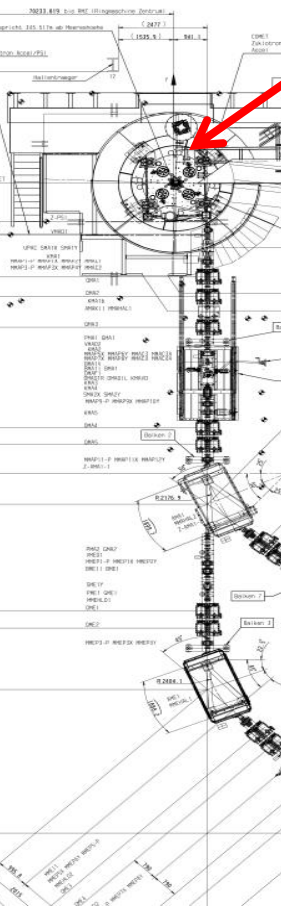


# Proton therapy at PSI

## The proton therapy facility at PSI

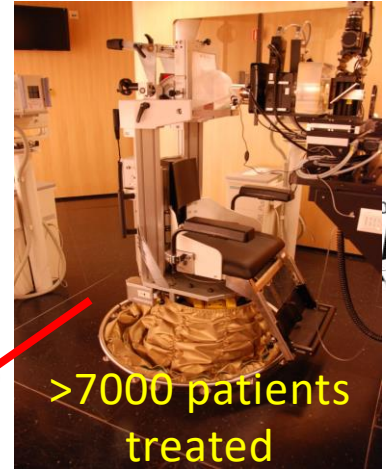


# Proton therapy at PSI

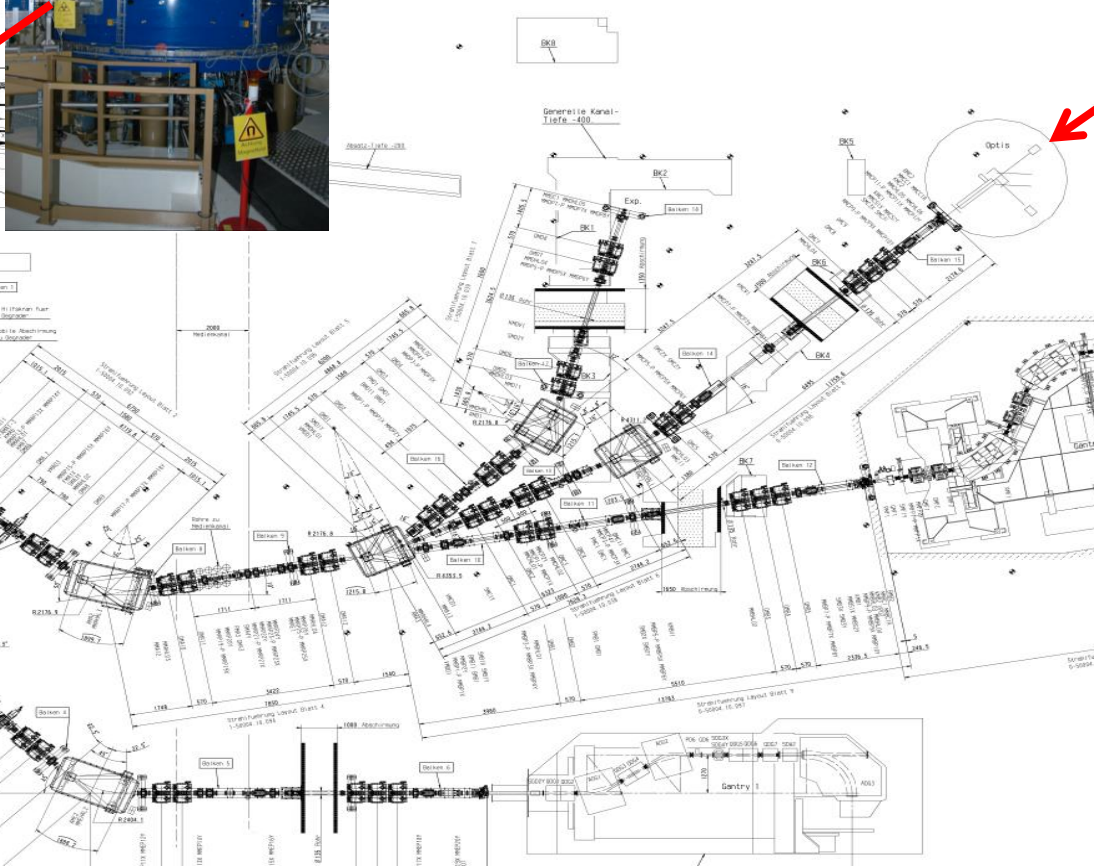
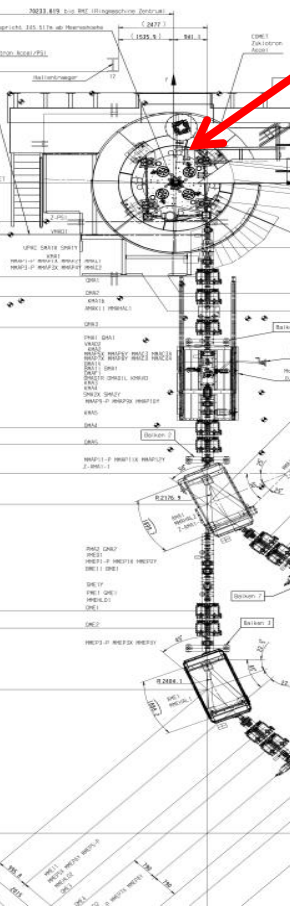


- Legende Komponenten**
- AM Ablenk-Magnet
  - BMK1 Kick-Magnet
  - DM Quasidipol-Magnet
  - SM Strahl-Magnet
  - SMSP Harfen-Monitor
  - SP Split
  - SM Strahlstopper
  - DMO Dipolmagnete
  - KH Kollimator
  - RPV Kanalventil
  - PM Vakuum-Pumpe
  - VMD Vakuum-Ventil
  - MH4LO Halo-Monitor
  - DM Vakuum-Messzelle
- MH4I Ionisat-Ionen-Kammer
  - MH5 Schwertpunkt-Monitor
  - MH6 Strahl-Monitor
  - DMF Streufolie
  - MH4HL Hall-Sonde
  - MSP-II Präzisionscher Antrieb
  - BWV Eis-Ionen-Blenne
  - COMET Zählrohr
  - RIKUS Luft-Ionen-Flechte
  - Z-PSI Zählrohr
  - UPAC Übergabe-Punkt Accel
  - UPG2 Übergabe-Punkt Gantry 2
  - Z-AMA-1 Einleit. Vakuumkammer AMA
  - Z-AMA-2 Vert. Vak.
  - Z-AMA-3 Austritt. Vakuumkammer AMA
  - OPTIS Übergabe-Punkt Optis
  - EZP Übergabe-Punkt Experimentierinsel
  - UPG1 Übergabe-Punkt zur Gantry 1
  - WVF Wecker-Magnet
- +A, B, C, D, E (Sektion)  
 2 ter Buchstabe M steht fuer Medizin

# Proton therapy at PSI



>7000 patients treated



- Legende Komponenten
- AM Ablenk-Magnet
  - BK1 Kicker-Magnet
  - DM Quasigap-Magnet
  - SM Strahl-Magnet
  - MSP Harfen-Monitor
  - EM Spalt
  - SM Strahlstopper
  - DMD Diagnostikdiode
  - KM Kollimator
  - SMV Kamerasystem
  - PM Vakuum-Pumpe
  - VMD Vakuum-Ventil
  - MH40 Halo-Monitor
  - DM Vakuum-Messzelle
  - MH41 Ionisat-Ionen-Kammer
  - MH45 Schwerpunkts-Monitor
  - MH4C Strahl-Monitor
  - DMF Streufolie
  - MH4HL Hall-Sonde
  - MH4F Piezoelektrischer Antrieb
  - BWV Eisassians-Blennde
  - COMET Zyklotron
  - Z-PSI Röhrenluftfrisch-Flechte
  - UPAC Übergabe-Punkt Accel
  - UPG2 Übergabe zur Gantry 2
  - Z-AMA-1 Einleit. Vakuumkammer AMA
  - Z-AMA-2 Vertik. AMA
  - Z-AMA-3 Austritt. Vakuumkammer AMA
  - OPTIS Übergabe-Punkt Optis
  - EZF Übergabe-Punkt Experimentierinsel
  - UPG1 Übergabe-Punkt zur Gantry 1
  - WFF Sleeper-Magnet
- ++A, B, C, D, E (Sektion)  
2 ter Buchstabe M steht fuer Medizin

# Proton therapy at PSI

## OPTIS - Treatment of ocular tumours

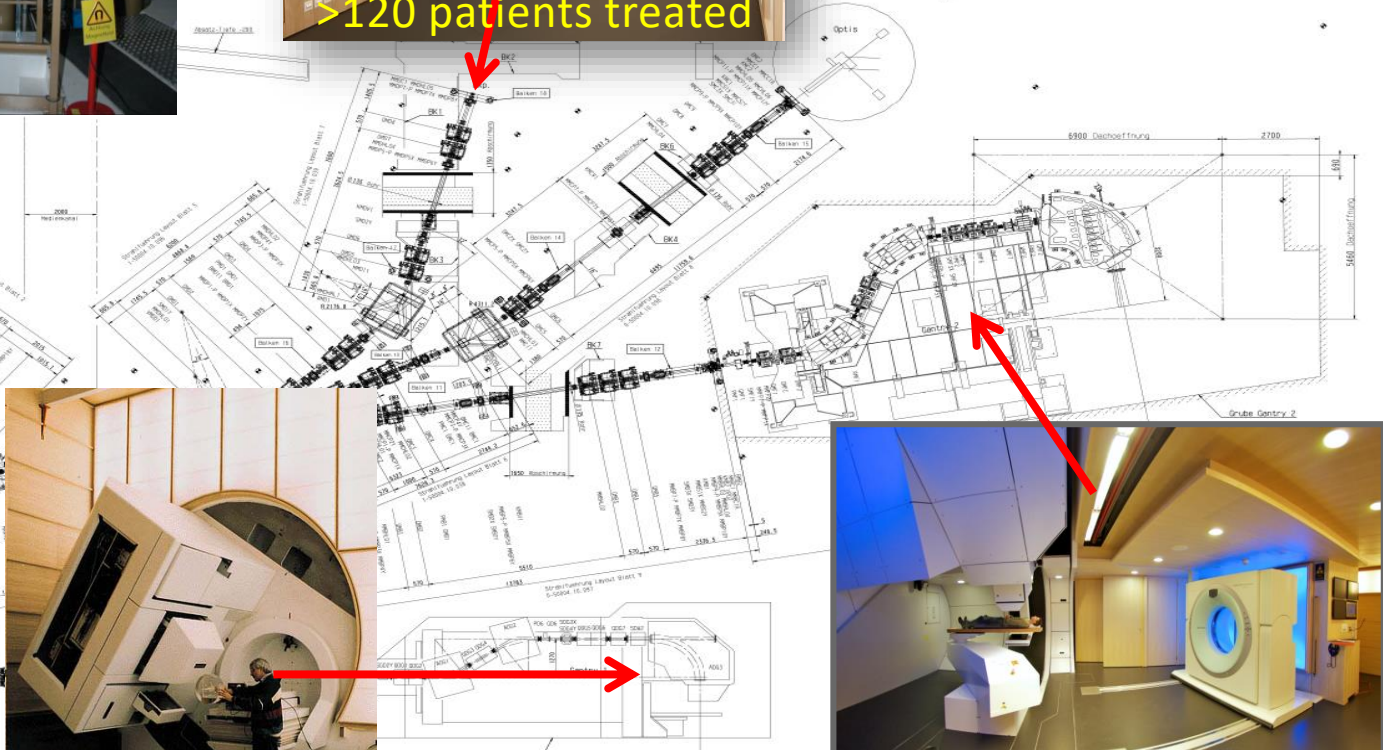
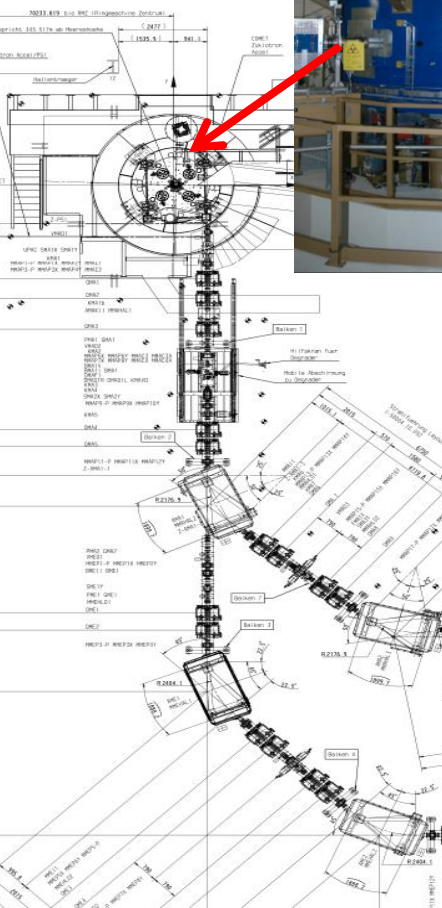
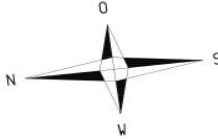


- Eye irradiations of uveal melanomas at PSI since 1984 with more than 7000 patients treated
- Typically 4-8 patients a day under treatment, ~200-220 a year
- Tumour control rate of 98%, eye retention rate ~90%

# Proton therapy at PSI



>120 patients treated



>1300 patients treated

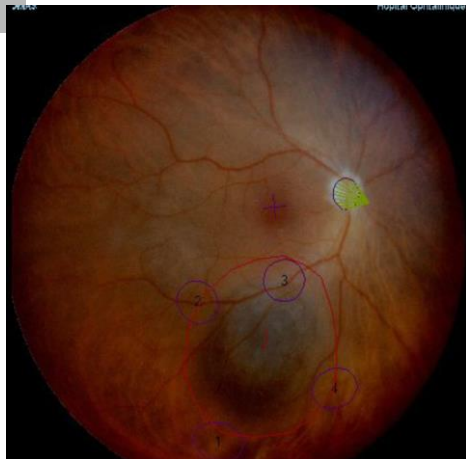


>330 patients treated

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# Proton therapy at PSI

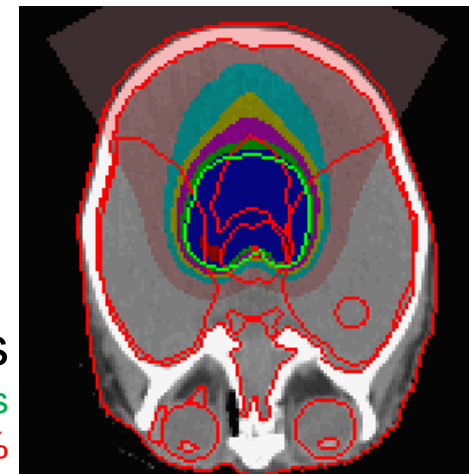
## The power of the proton (1). Clinical results from PSI



### Uveal melanomas

>7000 Patients

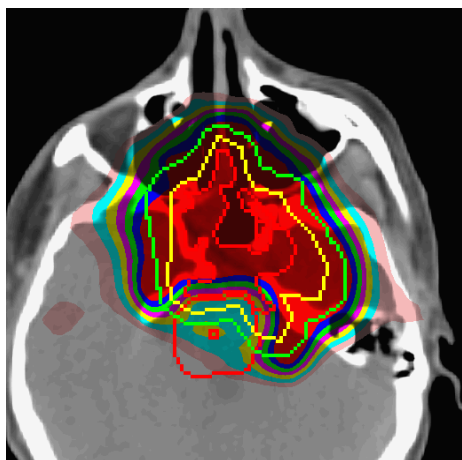
5y Local control: 98%



### Ependymomas

50 Patients

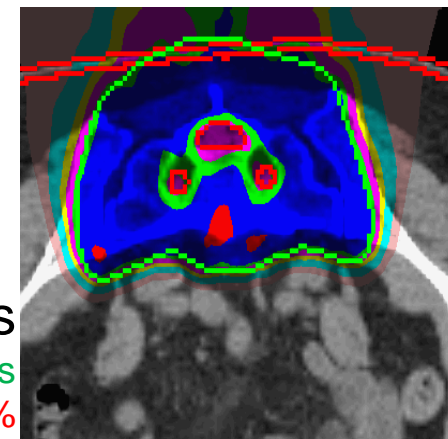
5y Local control: 78%



### Skull base tumours

222 Patients

7y Local control: 80%



### Sacral chordomas

36 Patients

5y Local control: 66%

# Summary

- The proton Bragg peak can substantially reduce mid-to-low doses delivered to normal tissues...
- ... but makes proton therapy more sensitive to anatomical changes and motion
- Nevertheless, studies indicate that reduced normal tissue could result in substantial reductions in secondary tumour incidence (factor 2-3)...
- ... and also to improved tolerance to radio-chemo therapy regimes
- In addition, substantial reductions in late normal tissue side effects are also being observed.
- Costs however remain high, making patient selection an important topic

# Proton therapy in Switzerland

Any questions?

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