Treatment planning optimization and validation

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ParTICLe project

ParTICLe

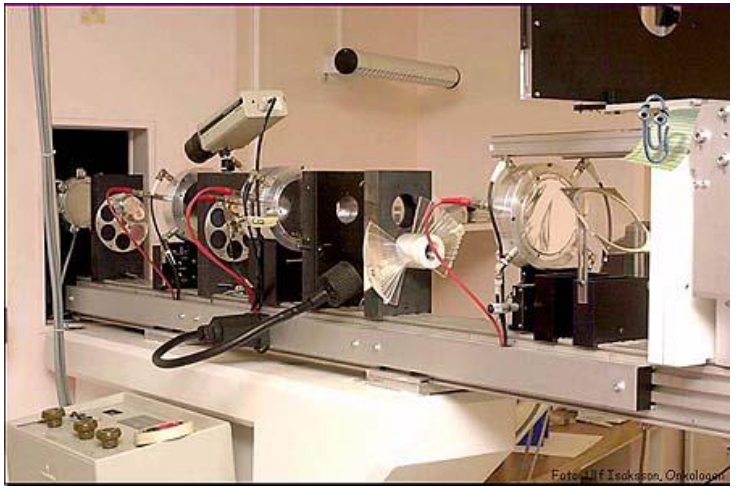
Particle Therapy Interuniversitary Center Leuven

Collaboration between UZL, UCL/CSL, UZG, UZA and UZB

Facility setup

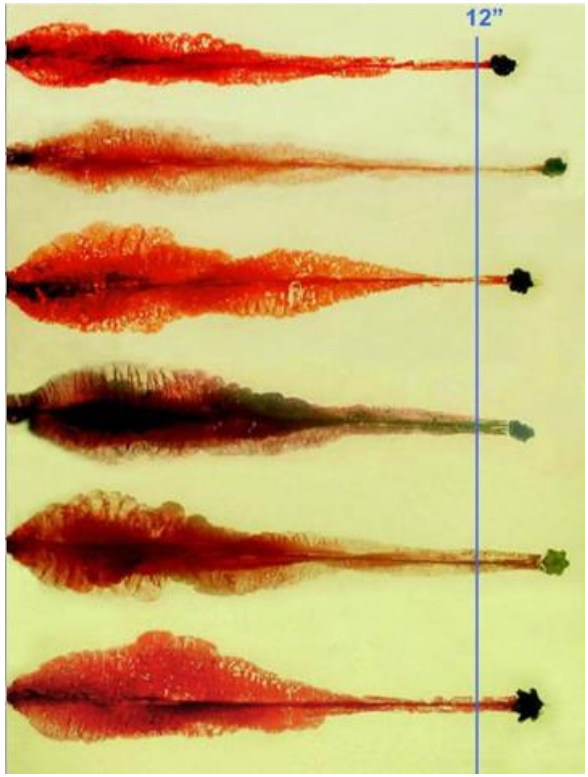
Clinical beam line

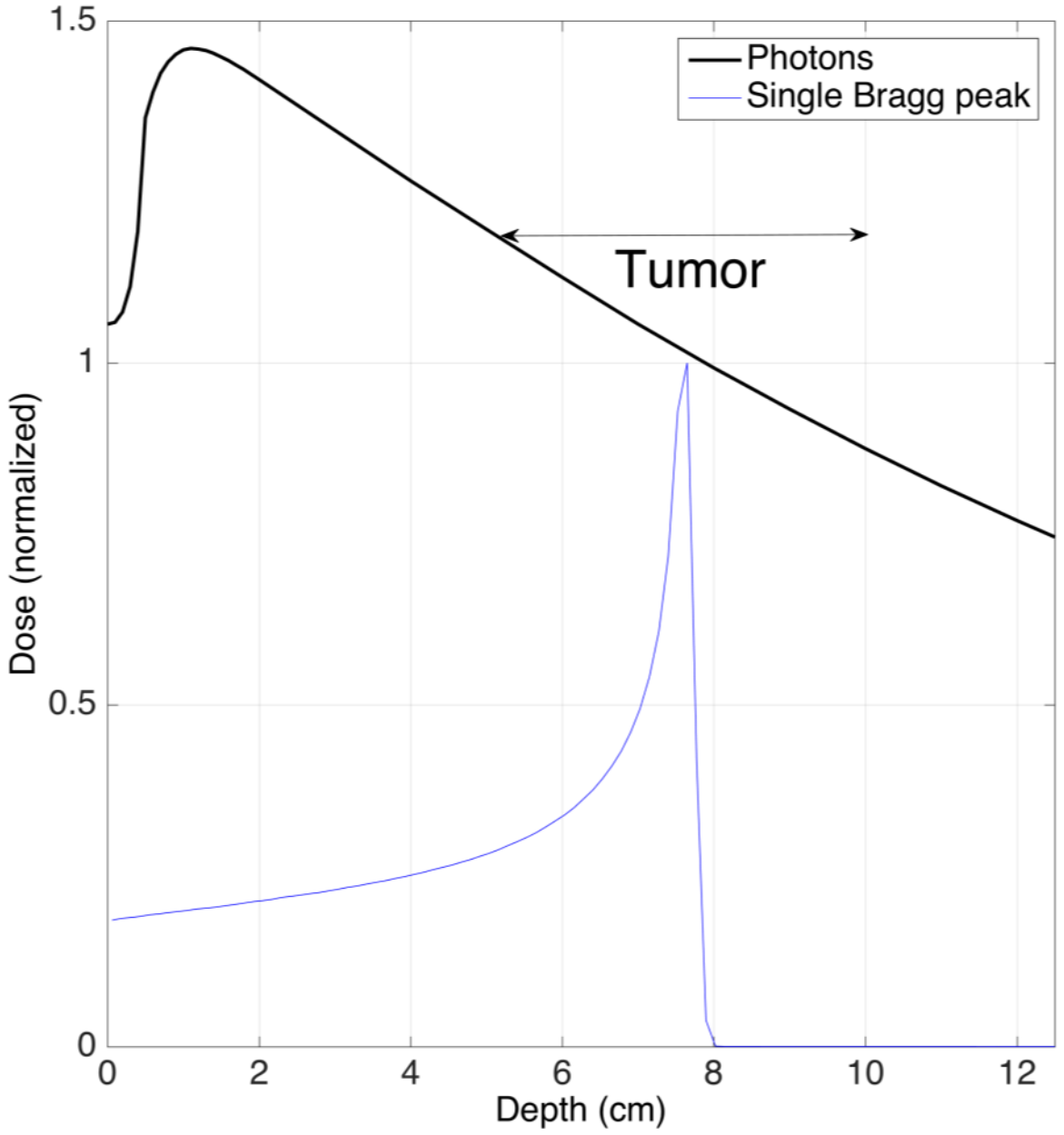
Research beam line



Beam

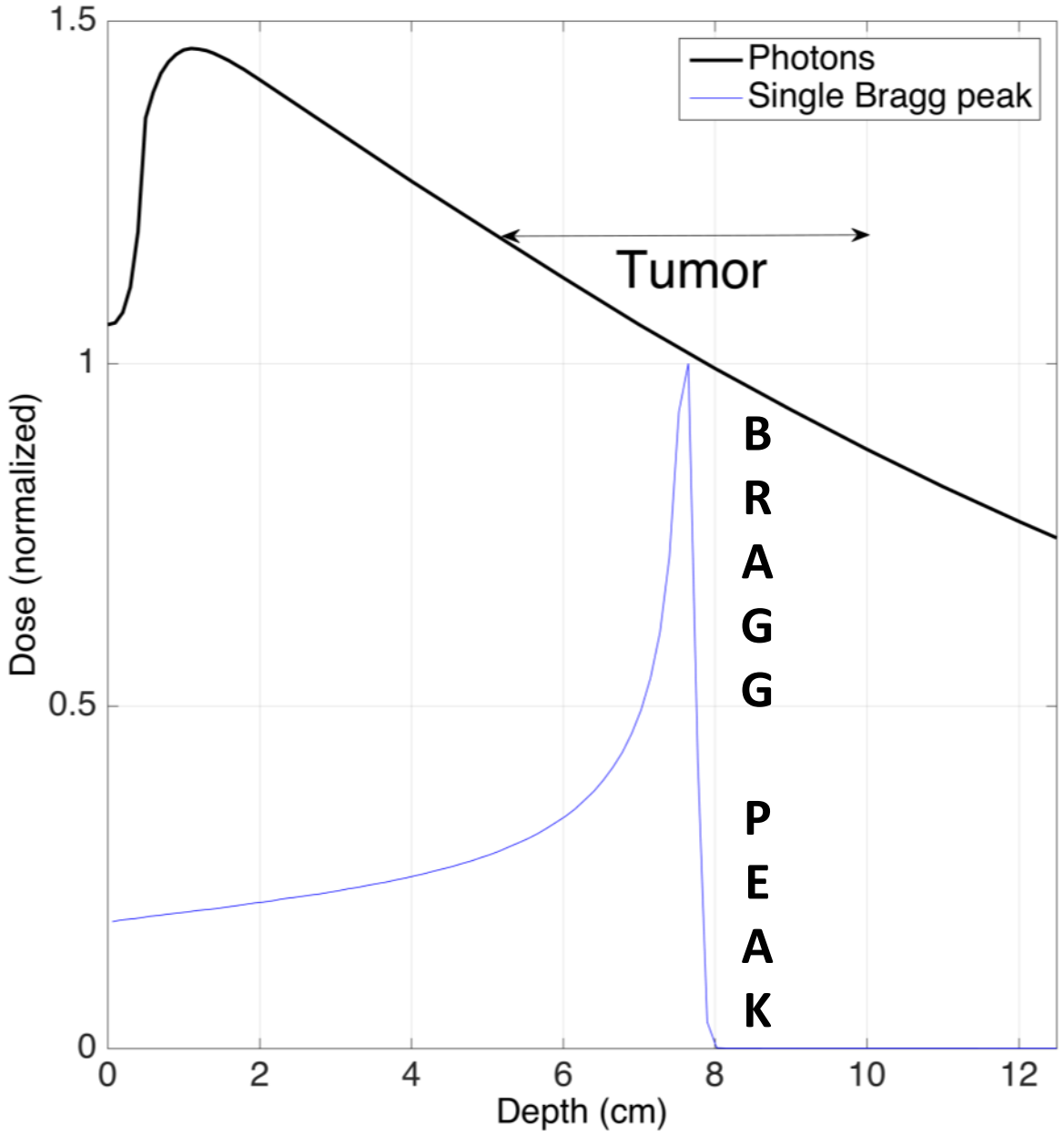
Water


12”


Photons
Single Bragg peak
Tumor
Dose (normalized)
Depth (cm)
0
0.5
1
1.5
0
2
4
6
8
10
12

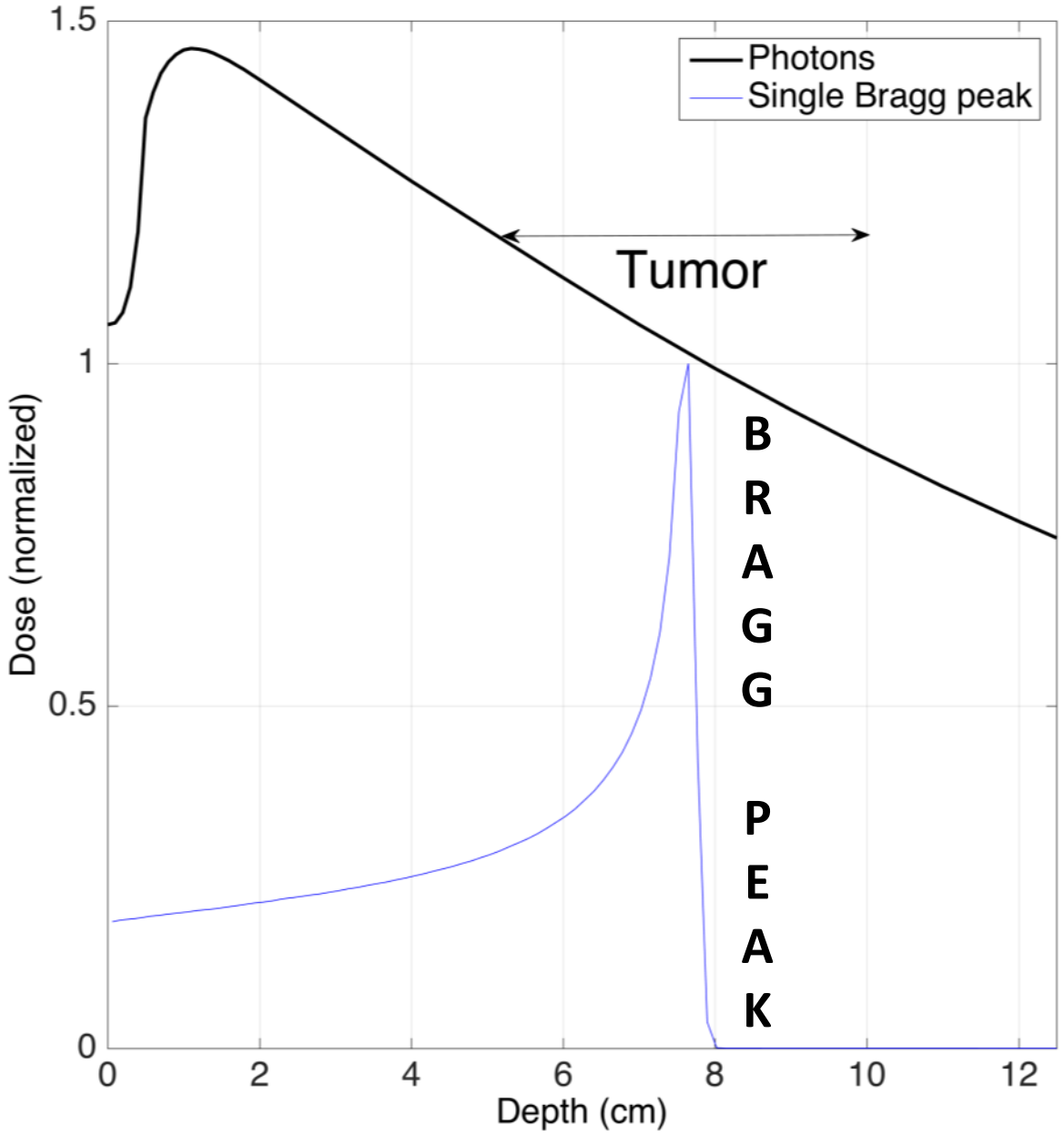
Beam

Water


Photons
Single Bragg peak
Tumor
BRAGG PEAK
Dose (normalized)
Depth (cm)
0
0.5
1
1.5
0
2
4
6
8
10
12

Beam

Water


Photons
Single Bragg peak
Tumor
BRAGG PEAK
Dose (normalized)
Depth (cm)
0
0.5
1
1.5
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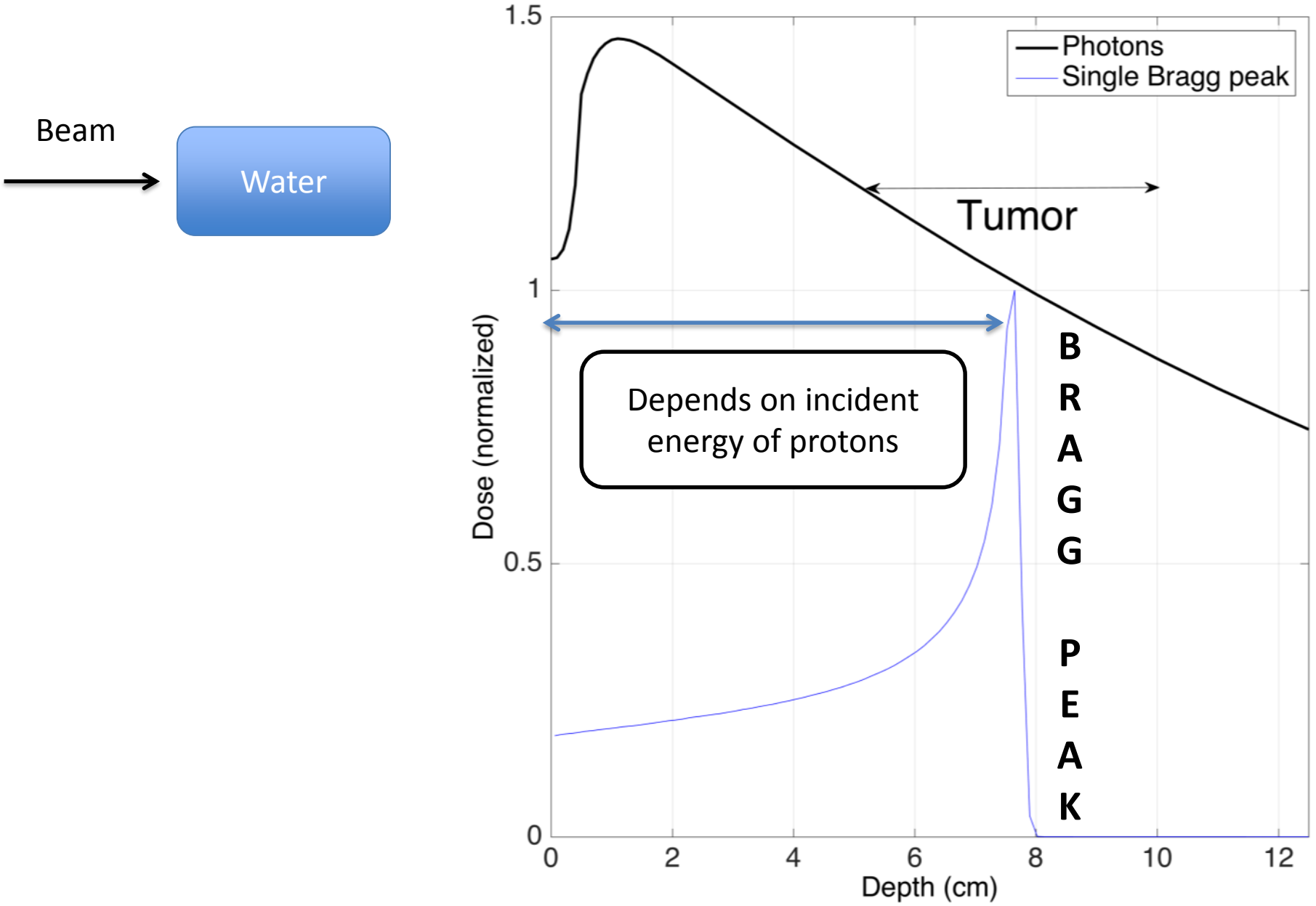
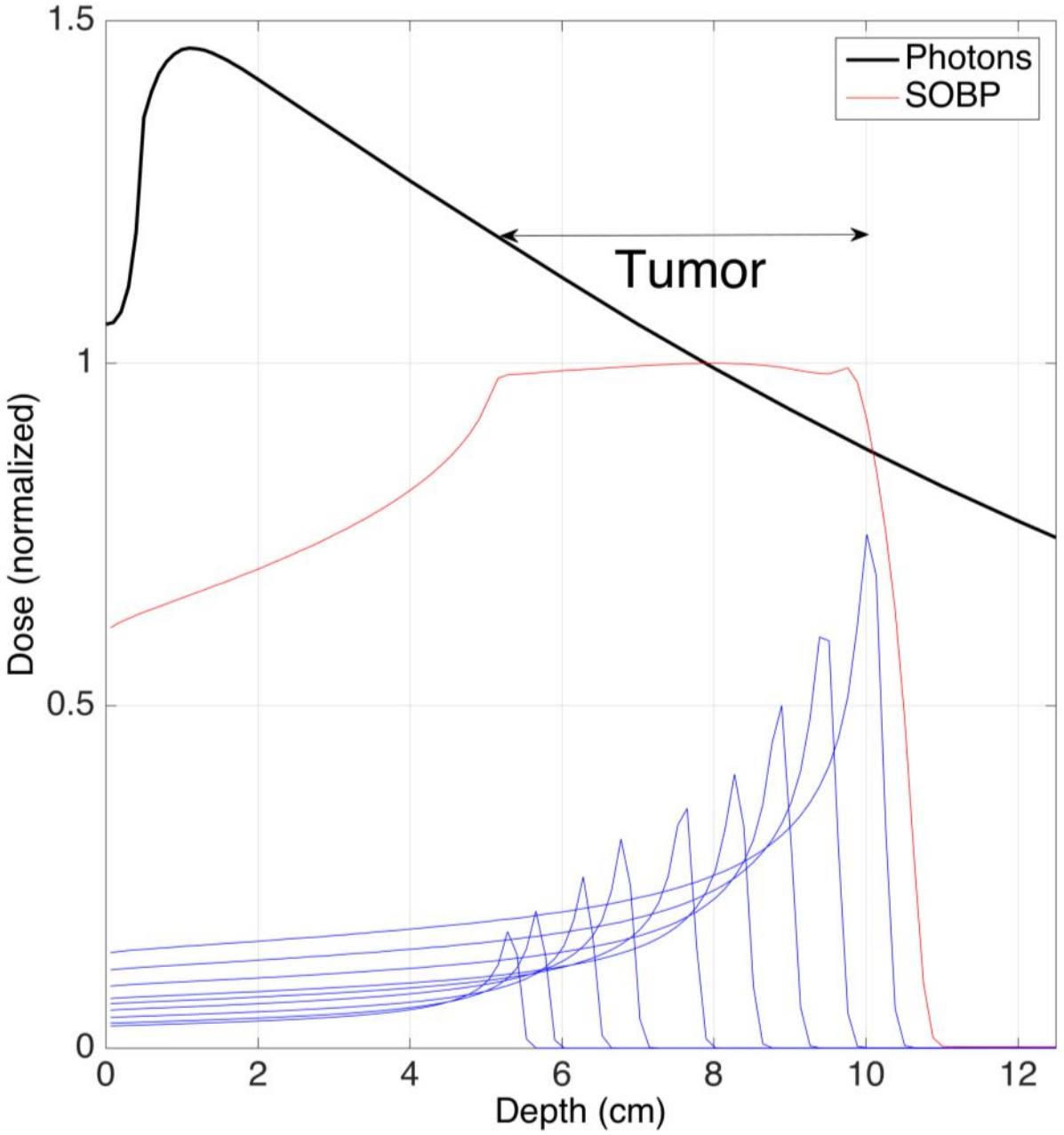
2
4
6
8
10
12


Beam
Water
Photons
Single Bragg peak
Tumor
Depends on incident energy of protons
BRAGG PEAK
Dose (normalized)
Depth (cm)
1.5
1
0.5
0
0
2
4
6
8
10
12

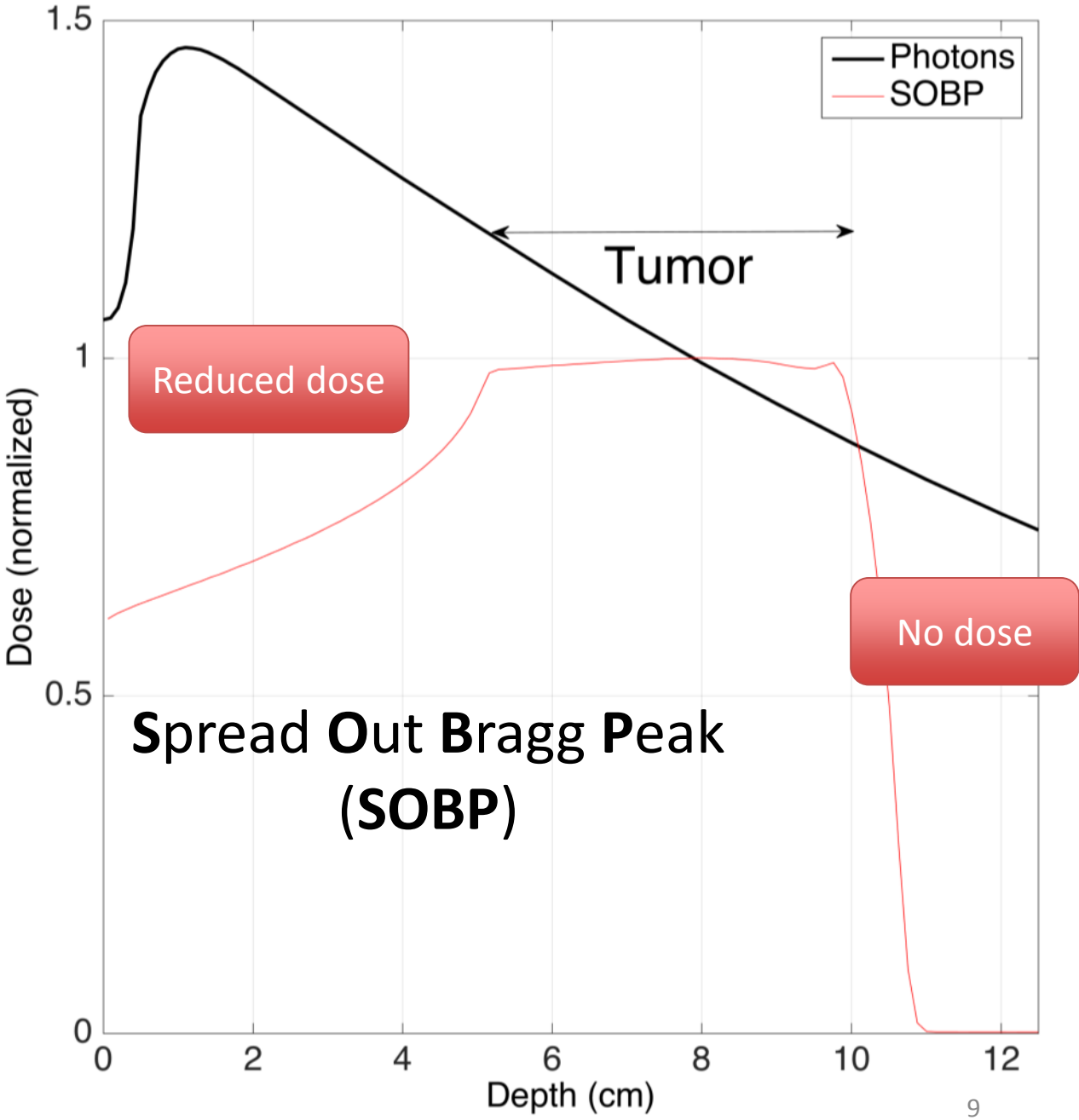
Beam

Water


Photons
SOBP
Tumor
Dose (normalized)
Depth (cm)
0
0.5
1
1.5
0
2
4
6
8
10
12

Beam

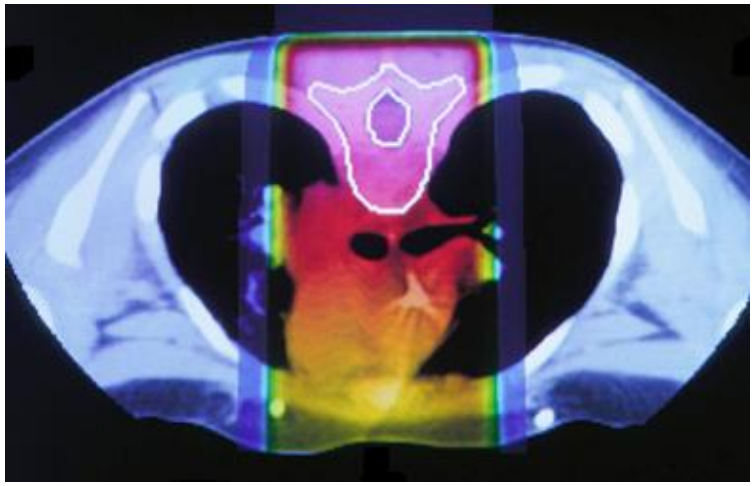
Water

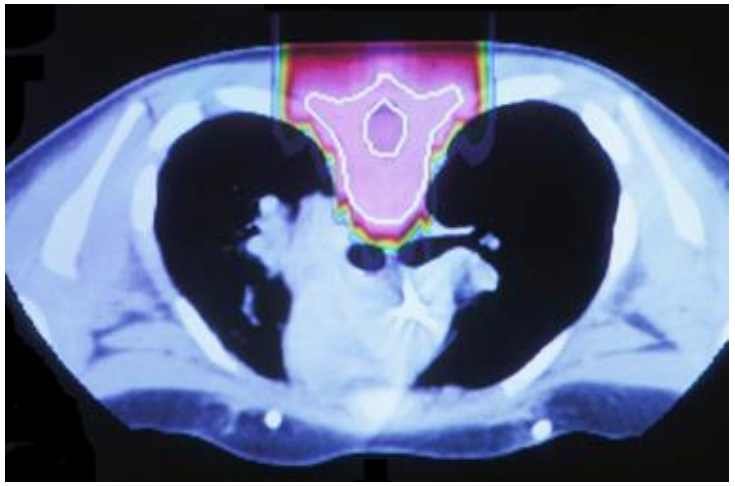


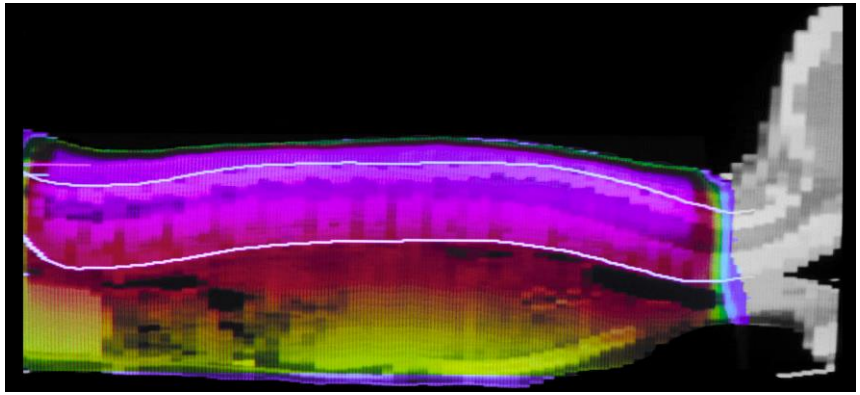
Spread **O**ut **B**ragg **P**eak (**SOBP**)

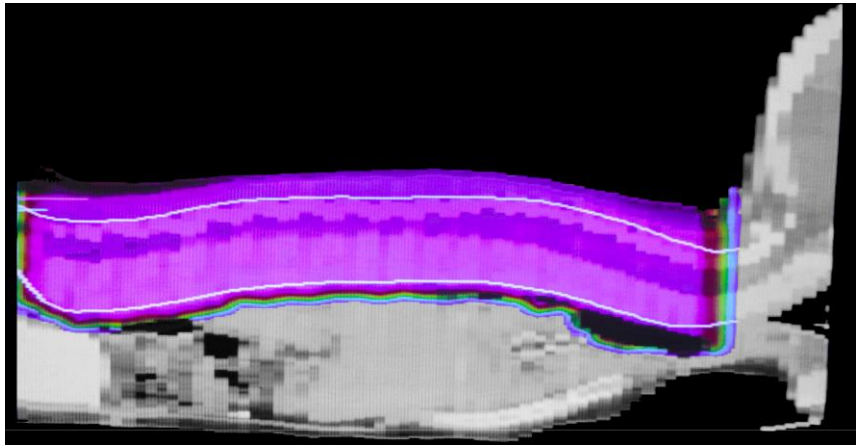
Radiotherapy

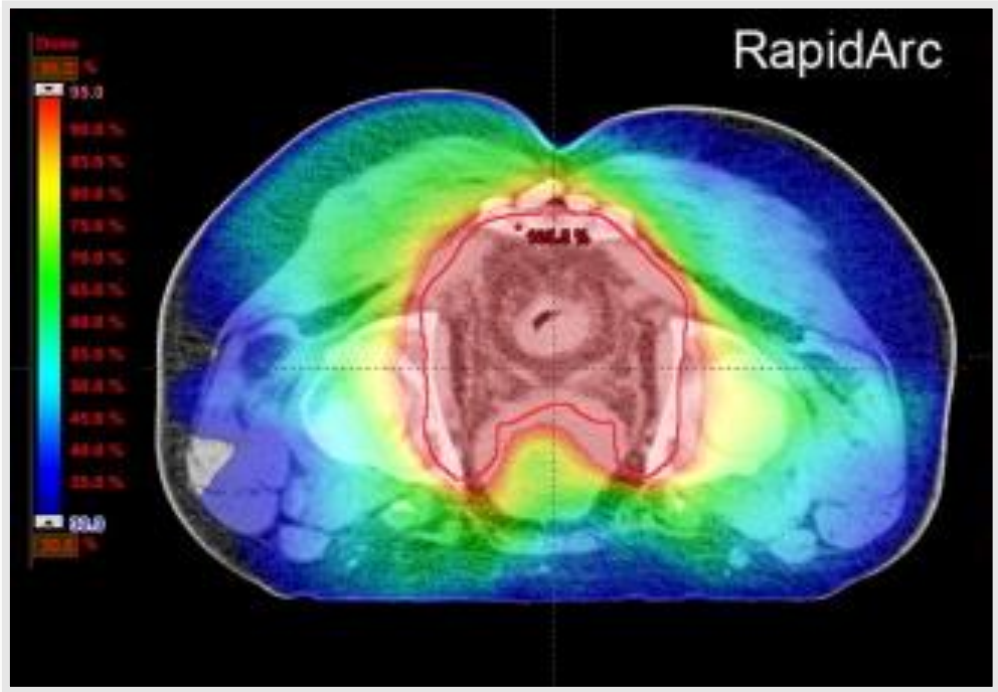
Proton therapy

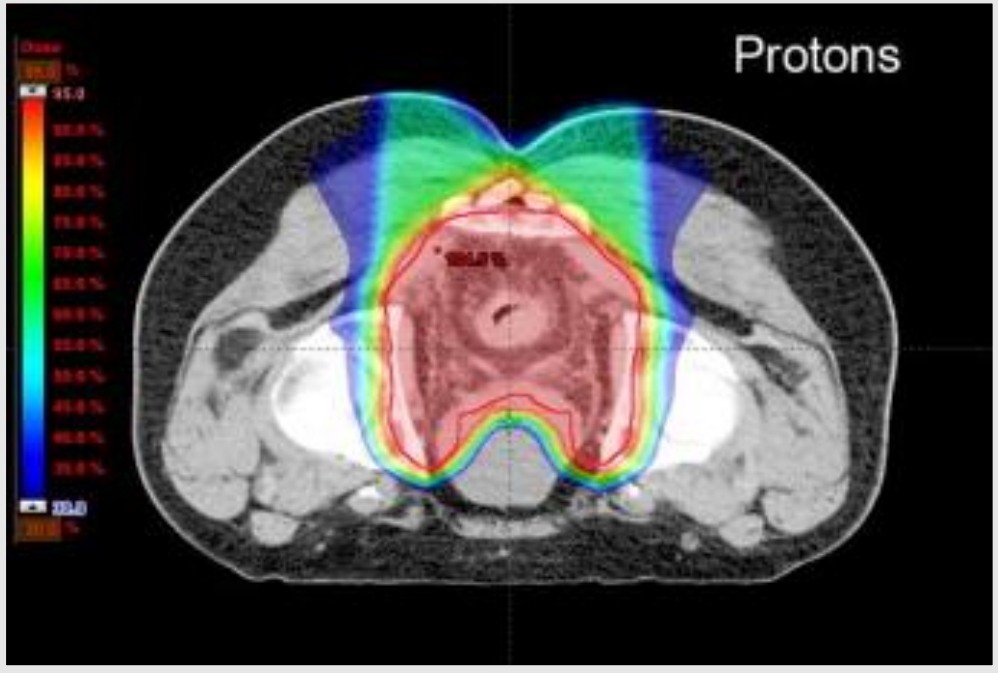








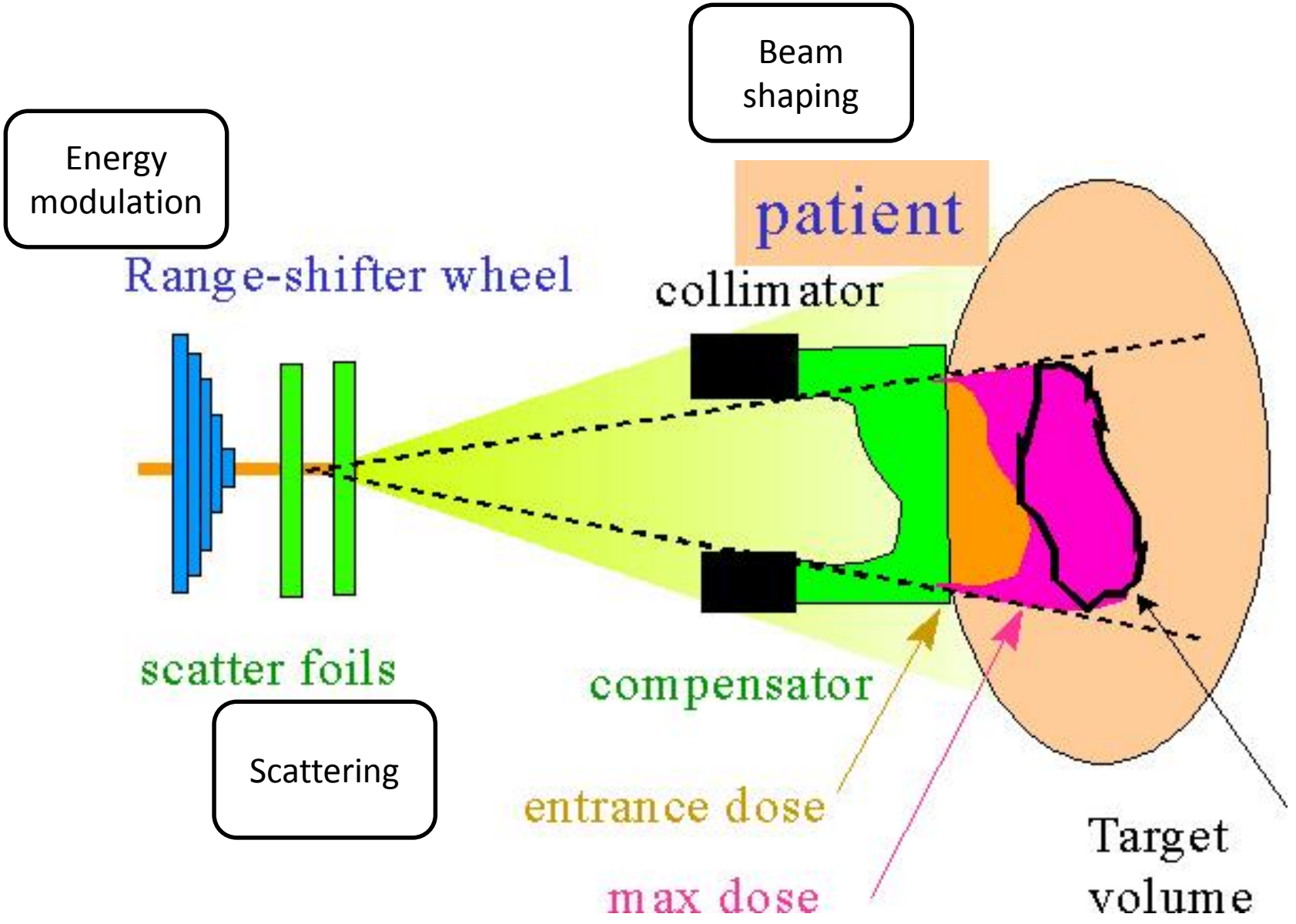

RapidArc


Protons

How do we DELIVER protons?

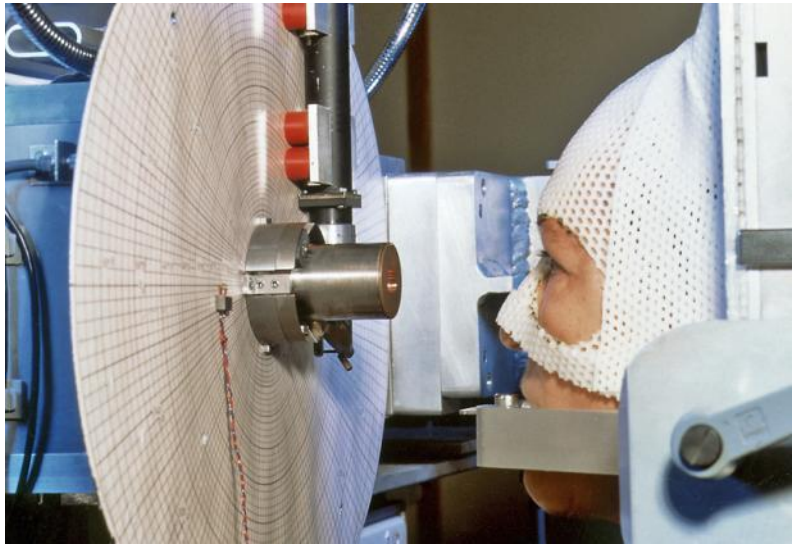
Broad beam (double scattering)

Pencil beam scanning



http://brenthuisman.net/msc/images/passive-beamshaping.jpg

Fixed beam line



http://www.psi.ch/ImageBoard/ig
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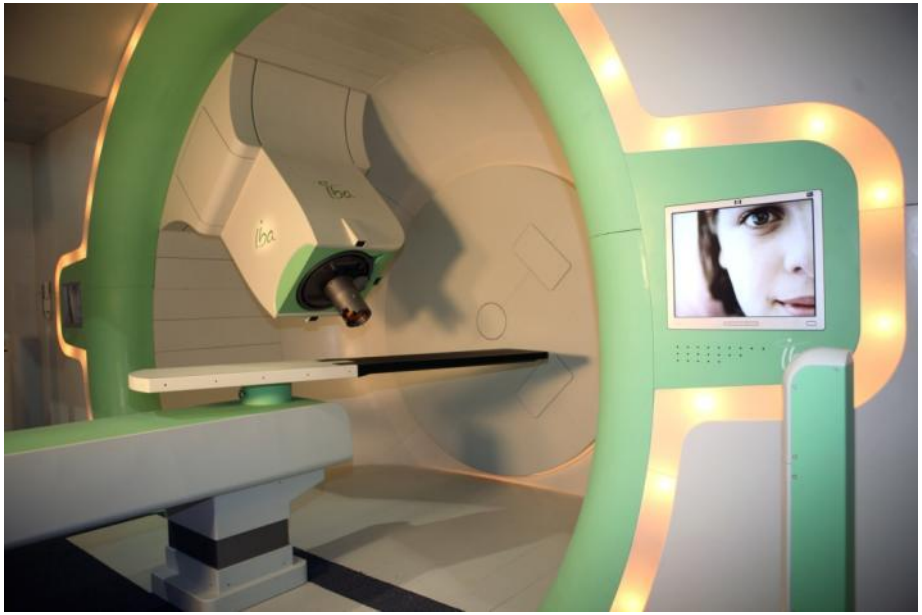
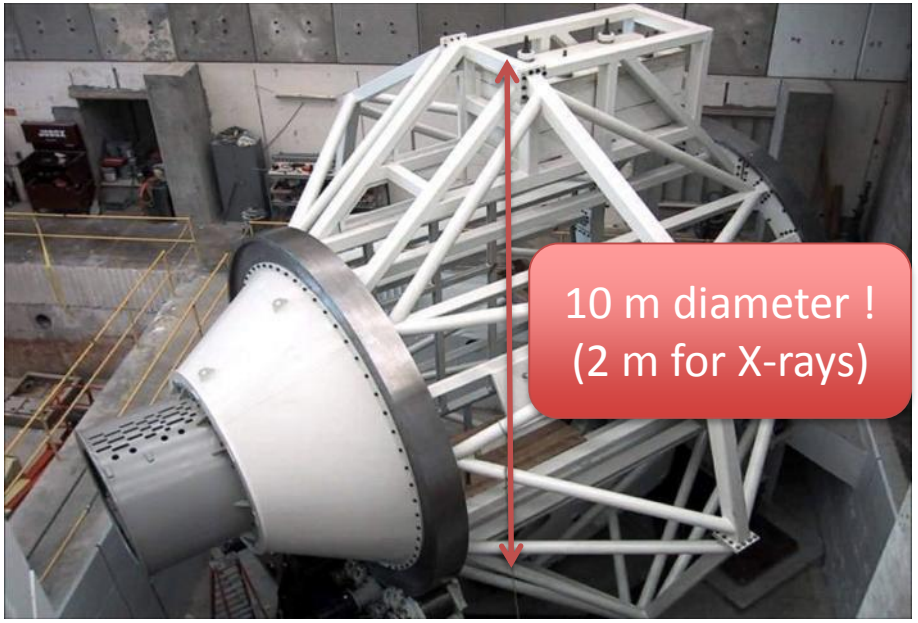
Gantry





How do we DELIVER protons?

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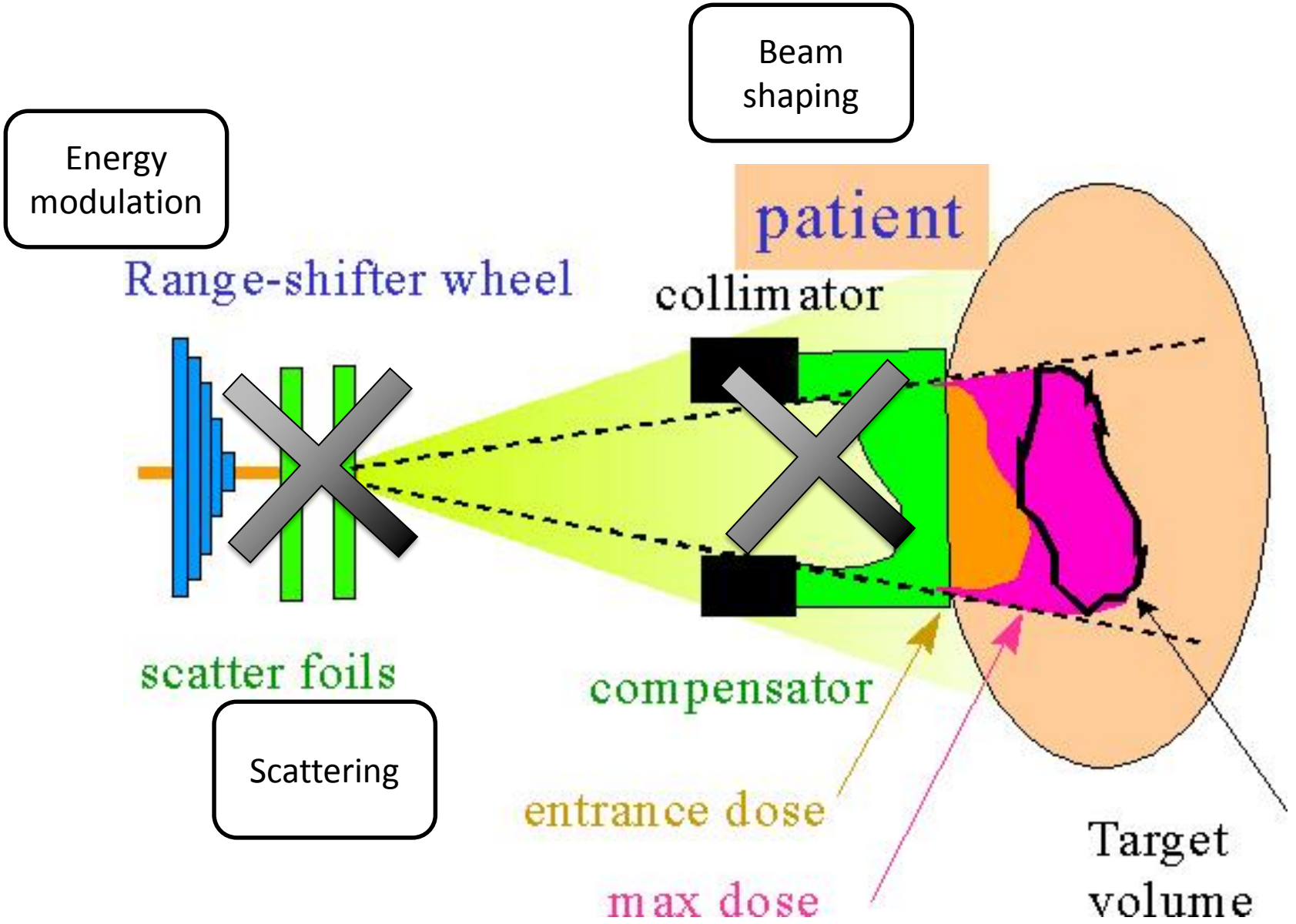
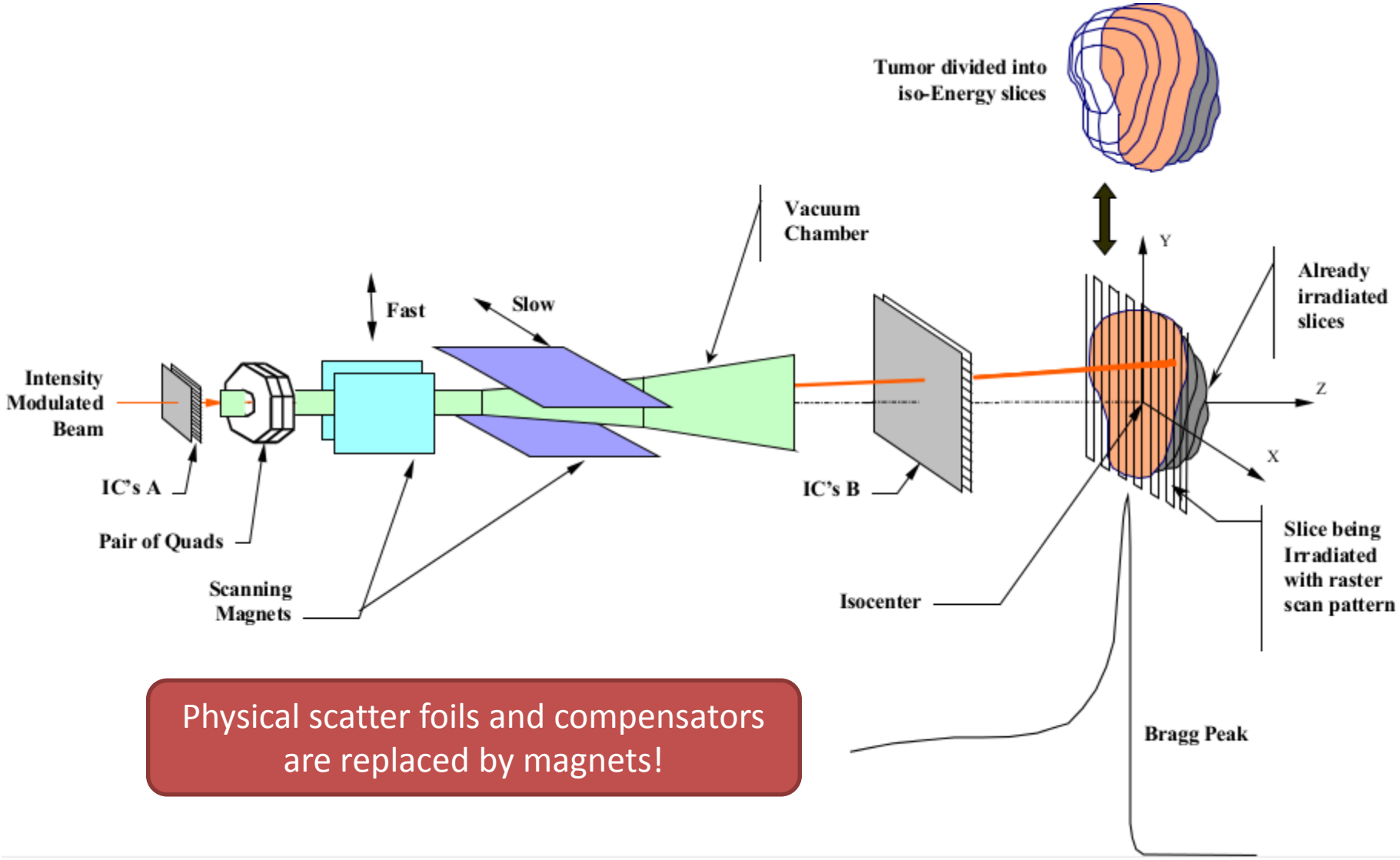
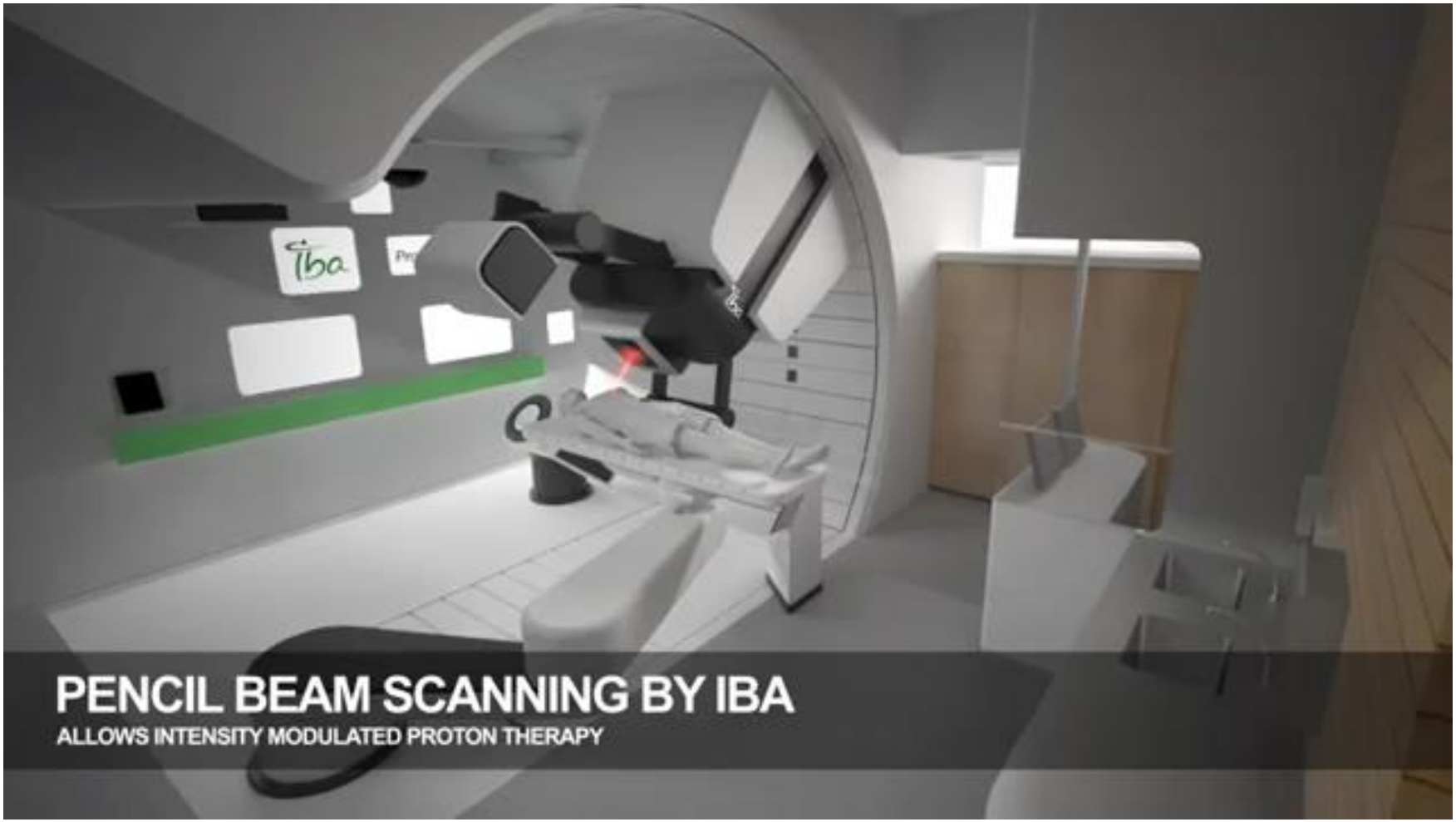


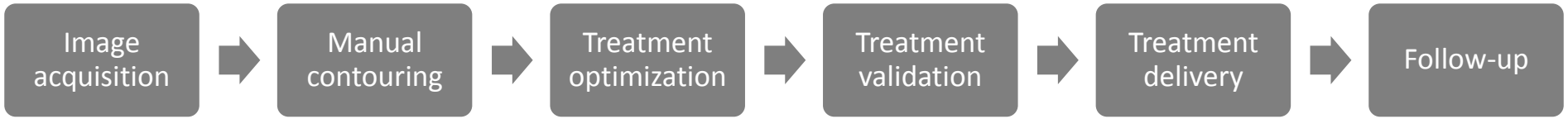
http://brenthuisman.net/msc/images/passive-beamshaping.jpg



Physical scatter foils and compensators are replaced by magnets!


PENCIL BEAM SCANNING BY IBA
ALLOWS INTENSITY MODULATED PROTON THERAPY

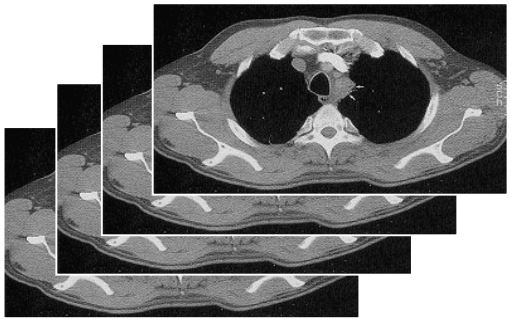
Generalities on treatment preparation and delivery workflow



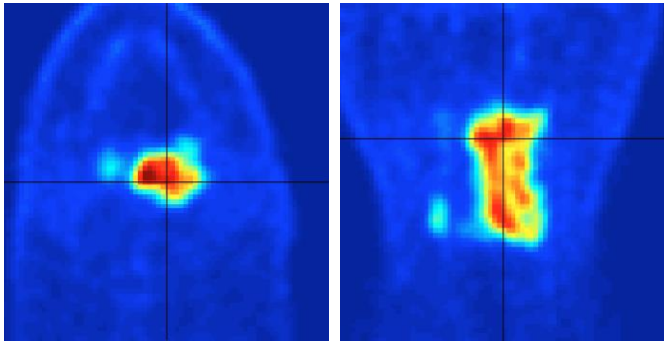
Various imaging modalities

Image acquisition → Manual contouring → Treatment optimization → Treatment validation → Treatment delivery → Follow-up

CT



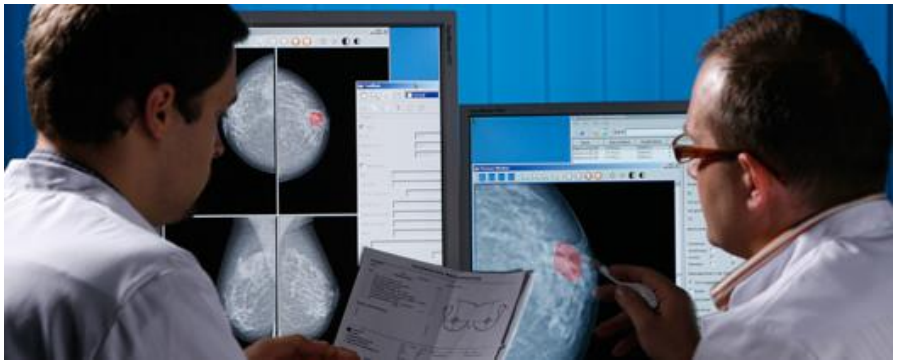
PET

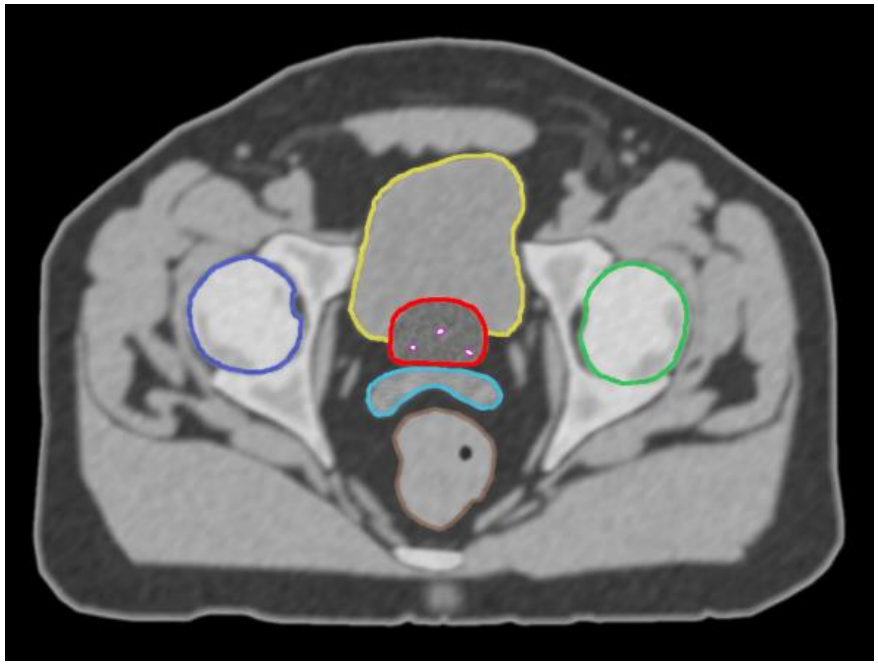


MRI

Contouring of target volumes and organs-at-risk

Image acquisition → **Manual contouring** → Treatment optimization → Treatment validation → Treatment delivery → Follow-up





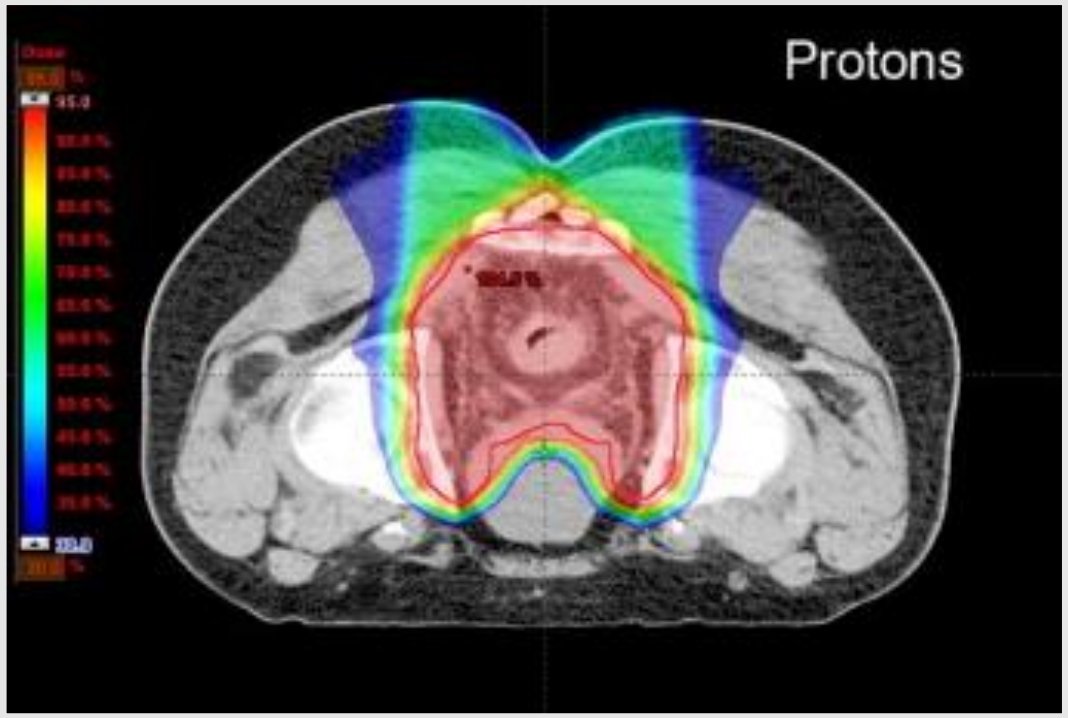
Treatment optimization

Image acquisition → Manual contouring → **Treatment optimization** → Treatment validation → Treatment delivery → Follow-up

How to assess the clinical quality of the dose distribution?

Image acquisition → Manual contouring → **Treatment optimization** → Treatment validation → Treatment delivery → Follow-up

Visual inspection of 3D dose maps



Pitfalls

- Huge amount of data to visualize
- Hard to think in 3 dimensions
- Hard to quantify the clinical effect

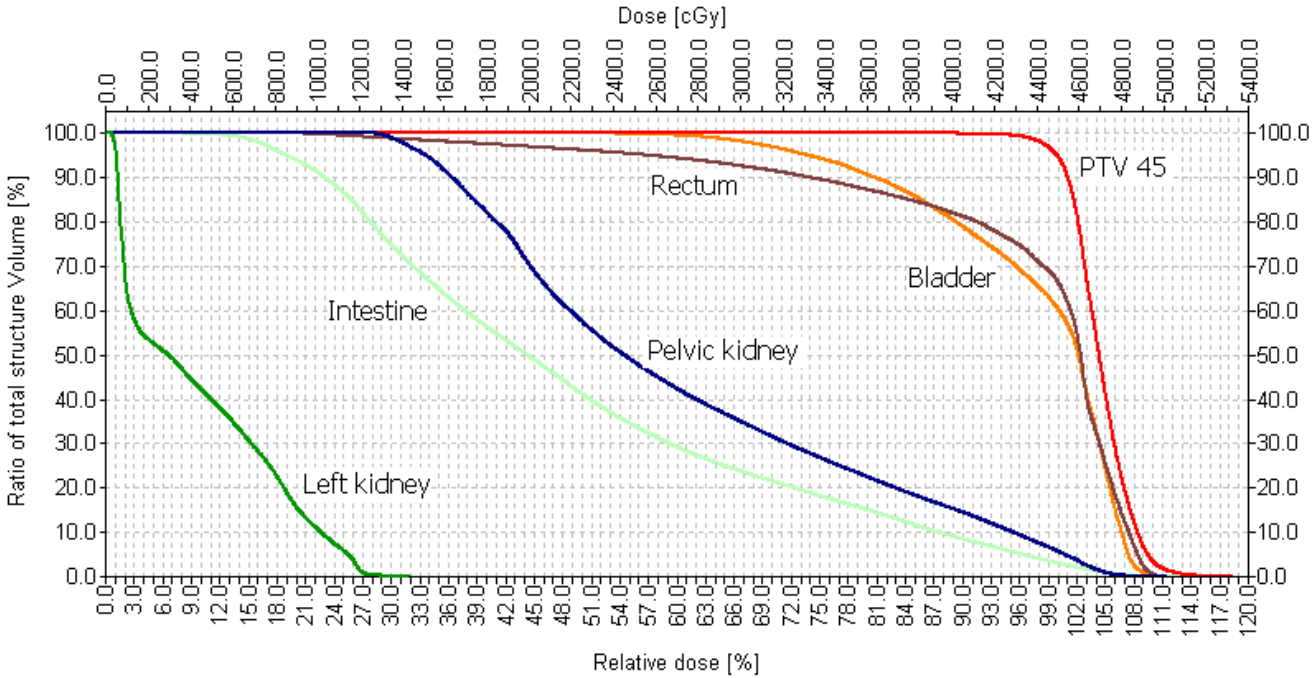
Zhang et al (IJROBP 2010)

How to assess the clinical quality of the dose distribution?

Image acquisition → Manual contouring → **Treatment optimization** → Treatment validation → Treatment delivery → Follow-up

Cumulative dose-volume histograms

= Volumes receiving *at least* a given dose



Pitfalls

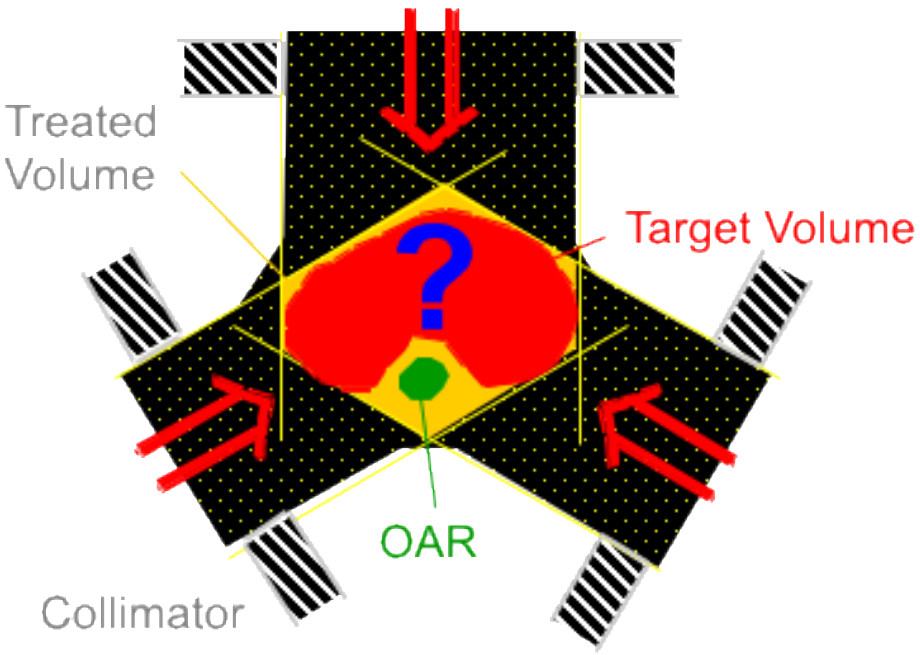
- Small hot and cold spots hardly visible
- No spatial information
- Dose distributions out of pre-contoured structures cannot be represented by DVHs

Castilho et al (Rad. Oncol. 2006)

Treatment optimization: manual versus computerized

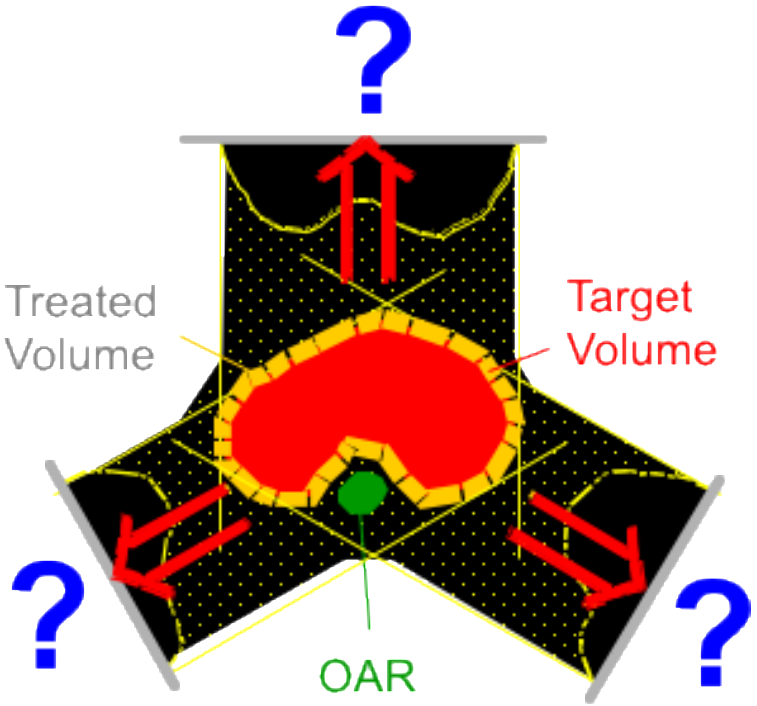
Image acquisition → Manual contouring → **Treatment optimization** → Treatment validation → Treatment delivery → Follow-up

Forward Planning



Human iterative improvement …
based on human experience

Inverse Planning



Computerized process

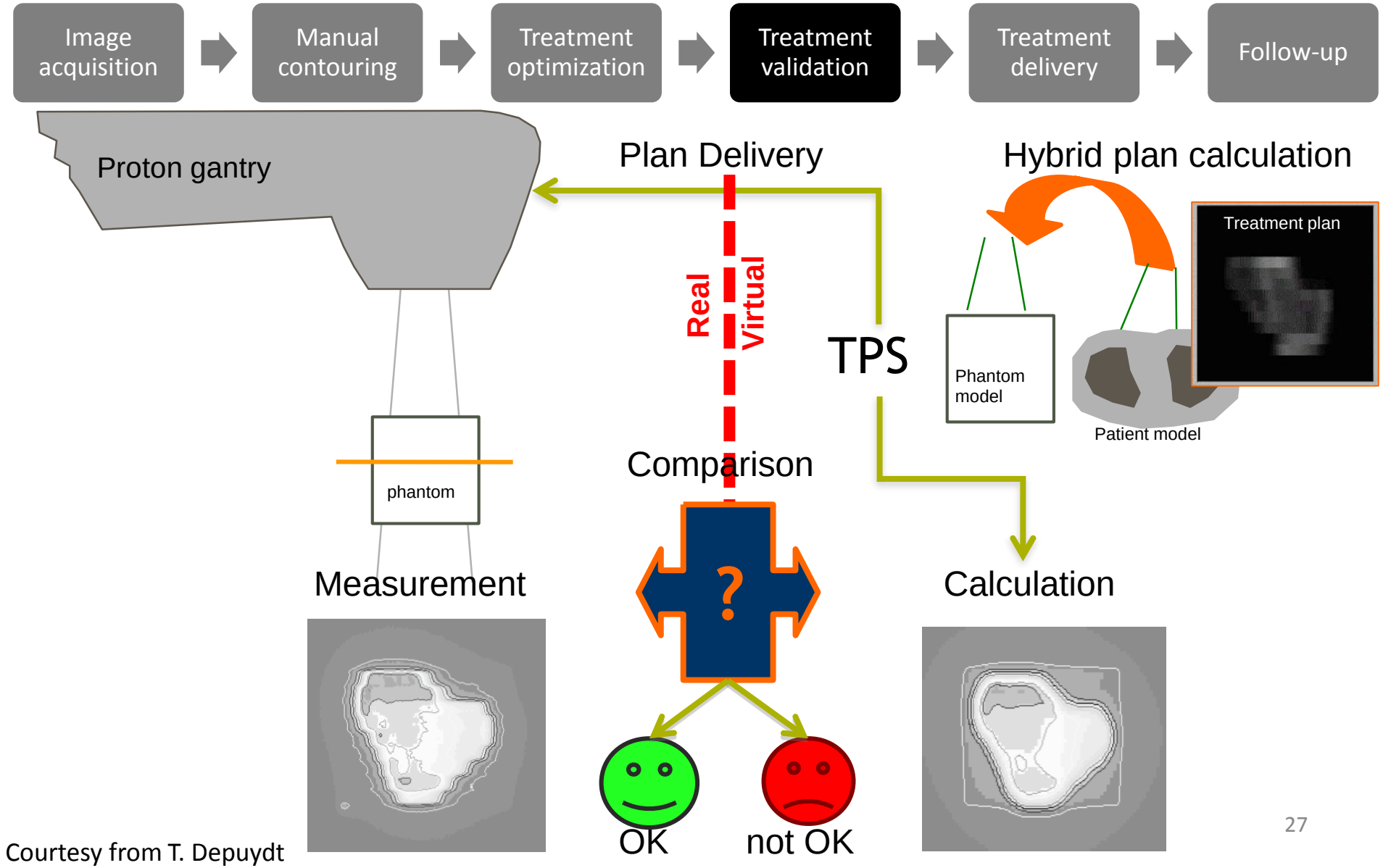
Courtesy from T. Depuydt

Inverse treatment planning

Image acquisition → Manual contouring → **Treatment optimization** → Treatment validation → Treatment delivery → Follow-up

Courtesy from T. Depuydt

Treatment preparation and delivery workflow

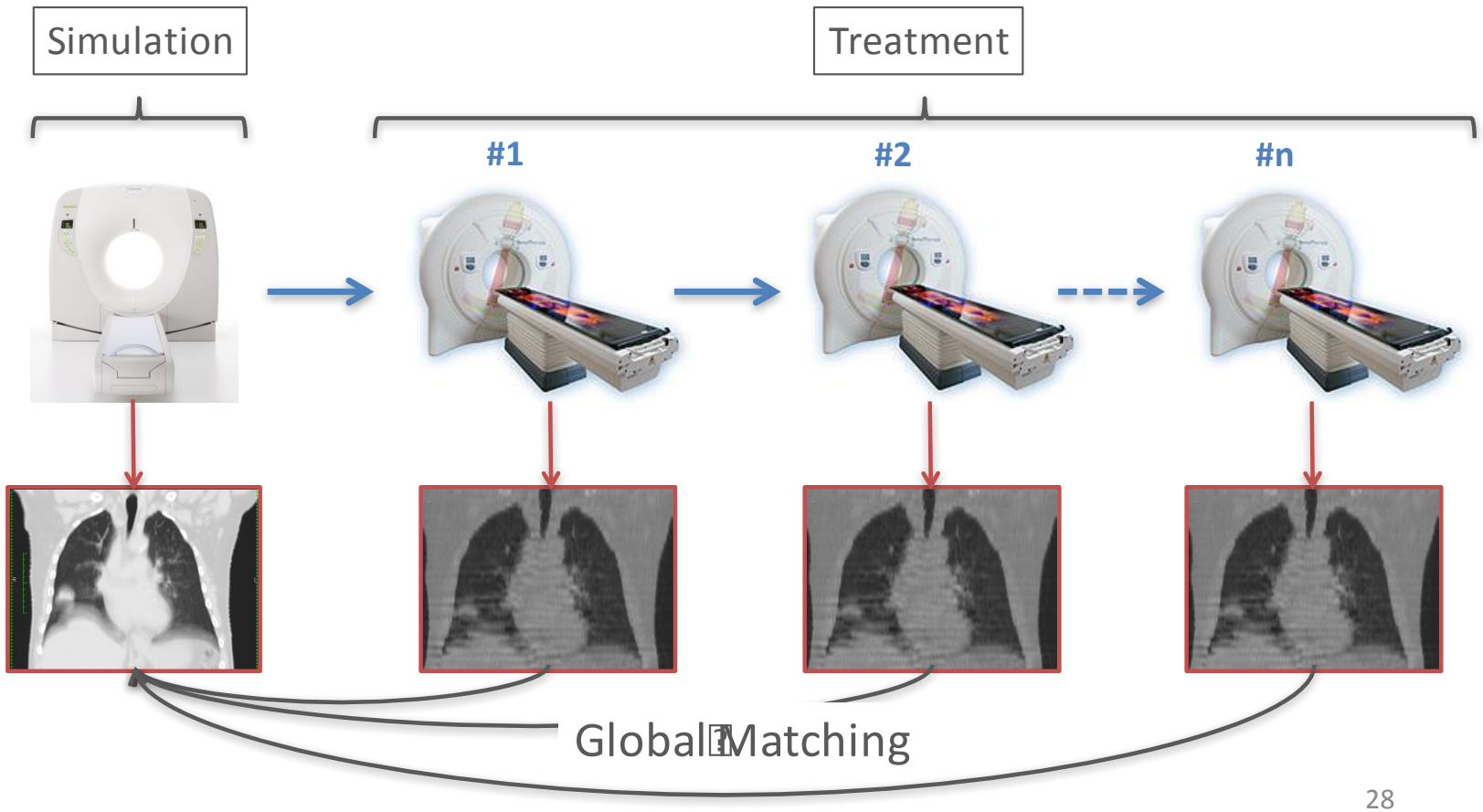


Courtesy from T. Depuydt

Treatment preparation and delivery workflow

Image acquisition → Manual contouring → Treatment optimization → Treatment validation → **Treatment delivery** → Follow-up

Positioning



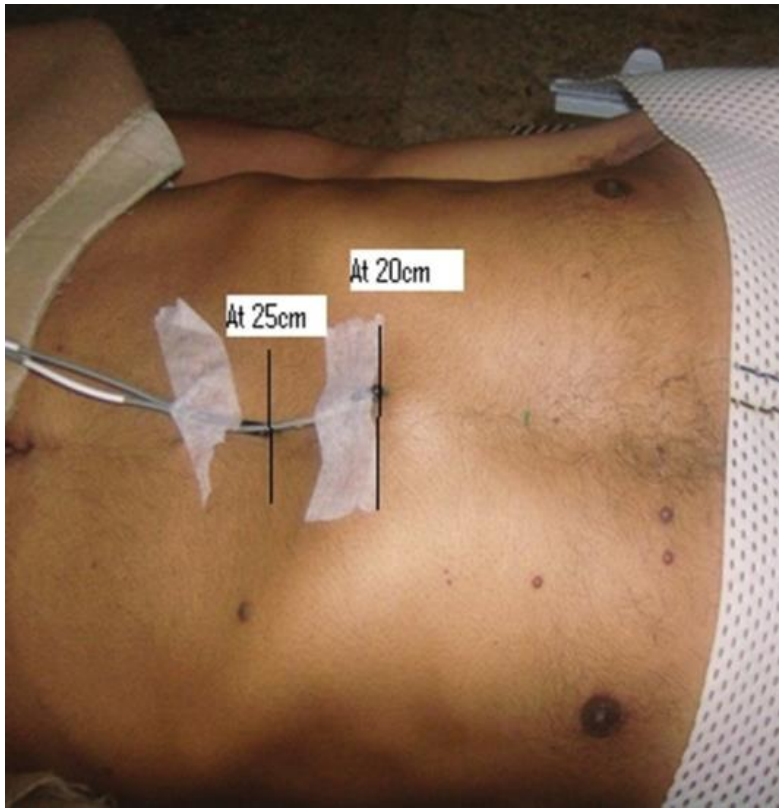
Courtesy from X. Geets

Treatment preparation and delivery workflow

Image acquisition → Manual contouring → Treatment optimization → Treatment validation → **Treatment delivery** → Follow-up

In-vivo dosimetry

Measure the dose in the patient directly during treatment delivery (generally on the surface)



Treatment preparation and delivery workflow

Image acquisition → Manual contouring → Treatment optimization → Treatment validation → **Treatment delivery** → Follow-up

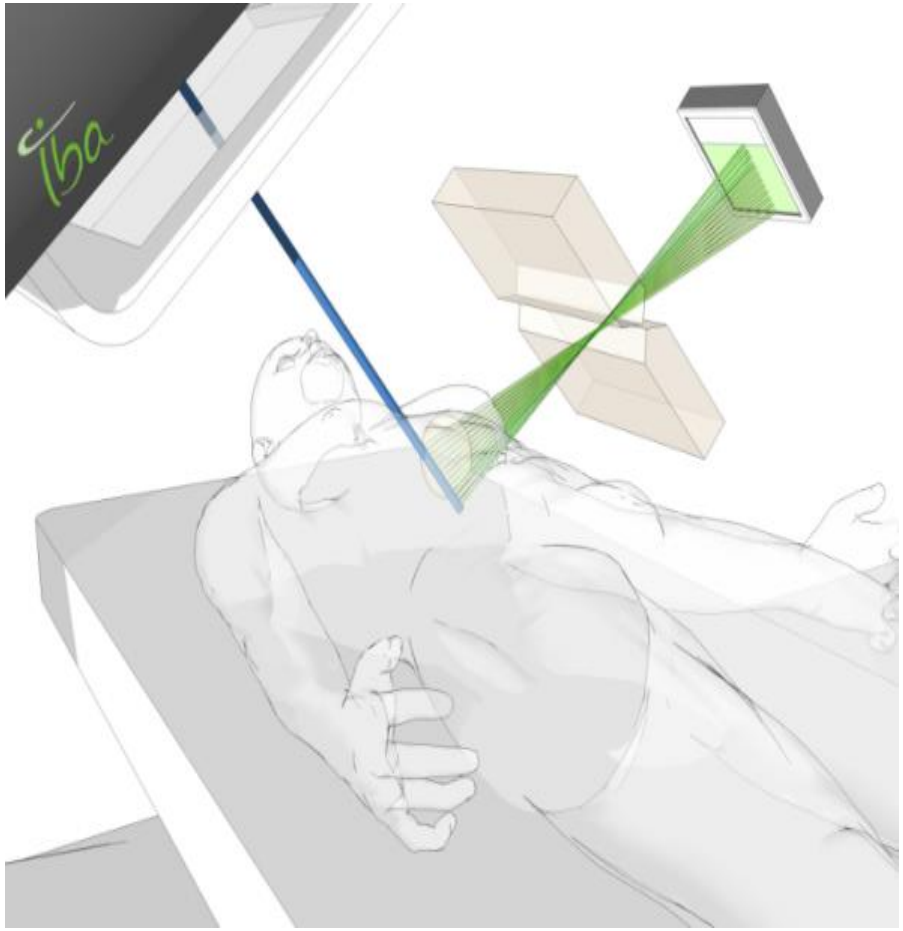
Machine log-files

Use measurements made by embedded detectors in the treatment nozzle!
Stored in so-called “machine log-files”

Treatment preparation and delivery workflow

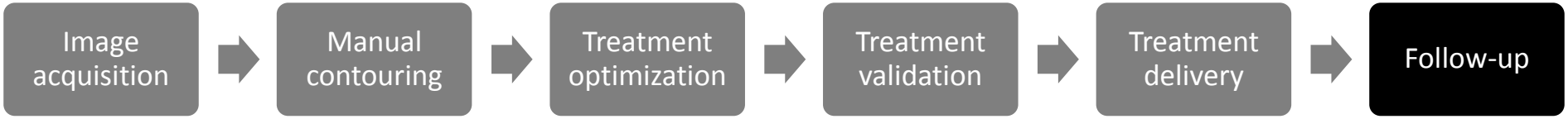
Image acquisition → Manual contouring → Treatment optimization → Treatment validation → **Treatment delivery** → Follow-up

Range verification



Prompt gamma imaging

Treatment follow-up



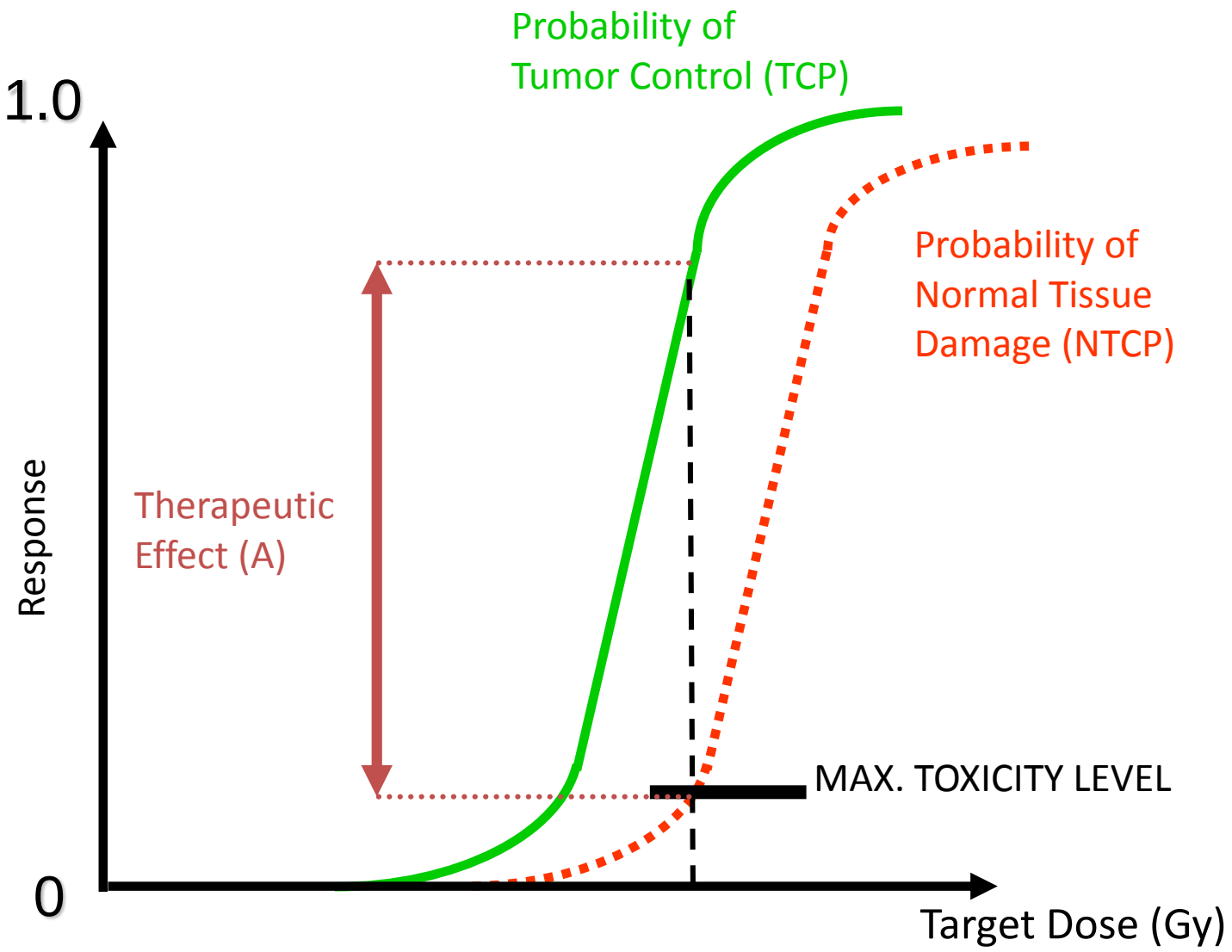
- Unacceptable anatomical changes → treatment adaptation
- Early toxicity assesment
- Tumour response
- …

Treatment plan optimization

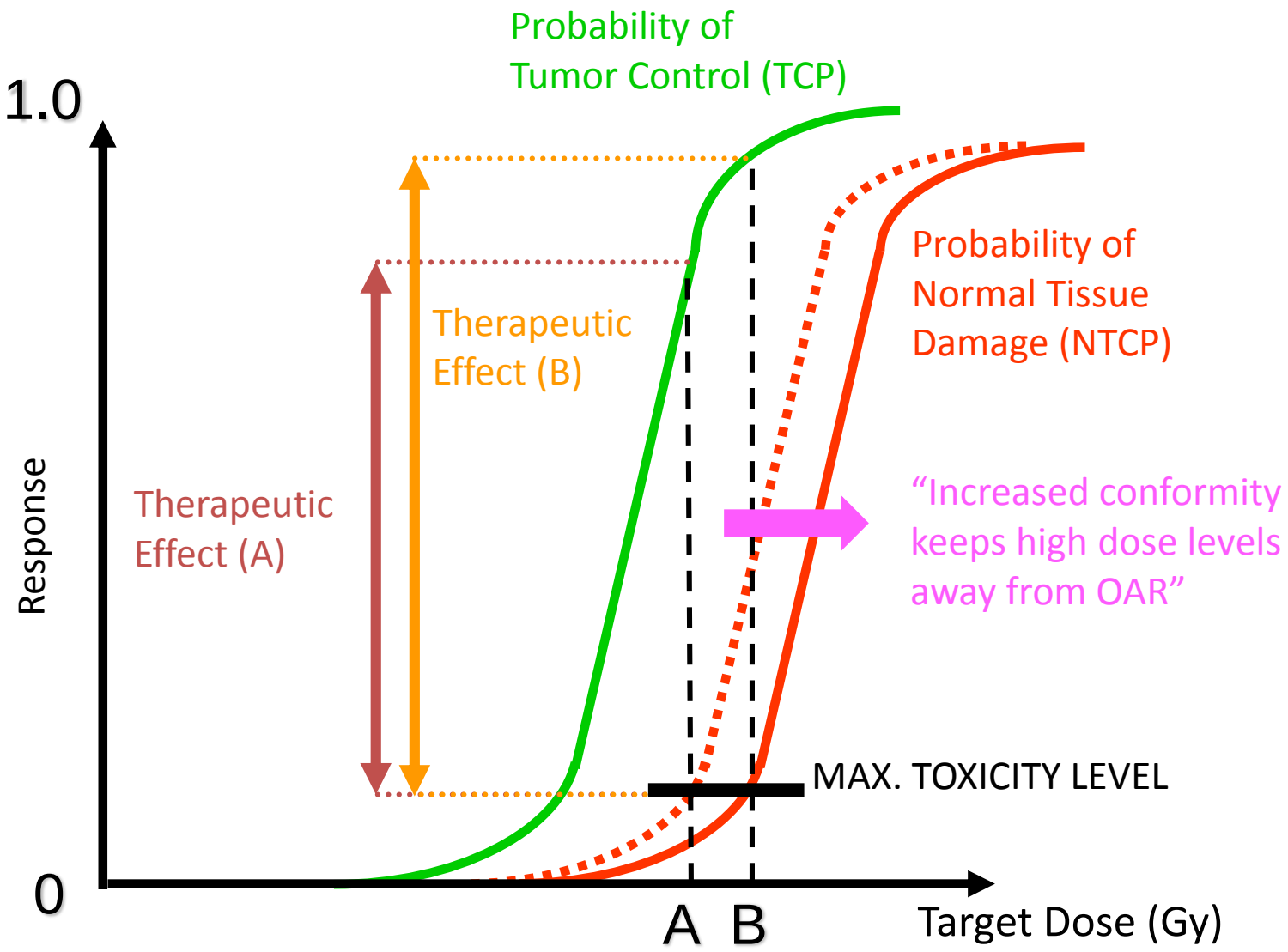
Objectives

- Best trade-off between target coverage and organs-at-risk sparing
- Robustness again geometrical and anatomical uncertainties
- Limited treatment time

Best trade-off between target coverage and organs-at-risk sparing

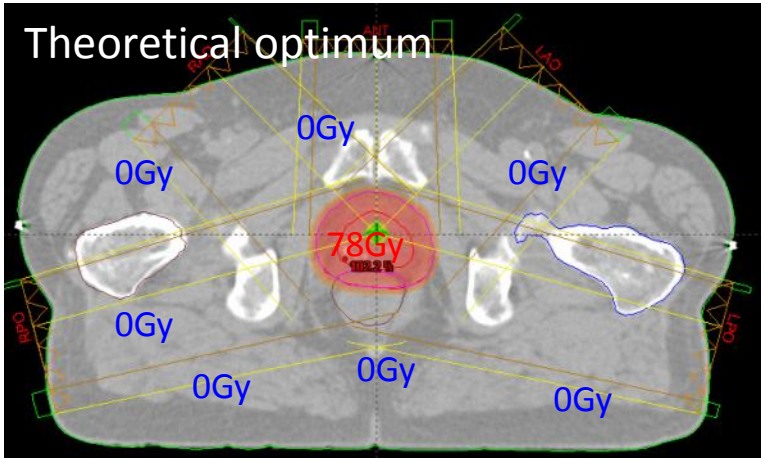


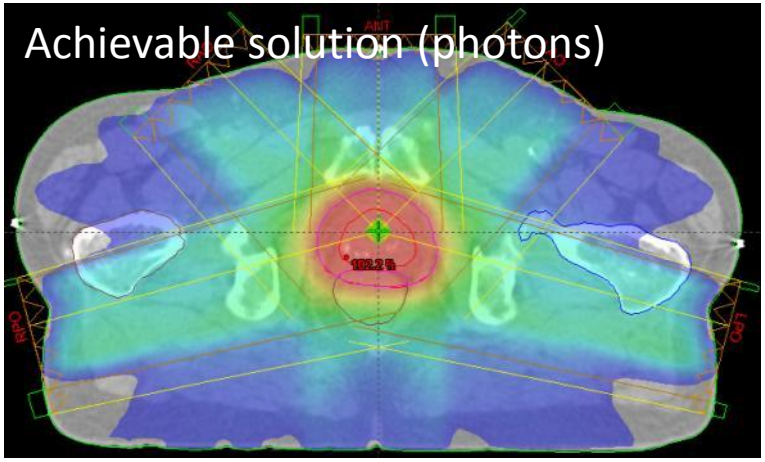
Best trade-off between target coverage and organs-at-risk sparing



The inverse problem

- The ideal dose distribution might be unreachable …
- So, the best clinical result might not be possible
- So, compromise …
  (with OPTIMIZATION)
- Try and get the best approximation to the ideal dose distribution
- Define treatment goals mathematically with a function whose minimum corresponds to our definition of the best plan. The name of such a mathematical function is
  COST FUNCTION
  OBJECT FUNCTION
  SCORE FUNCTION



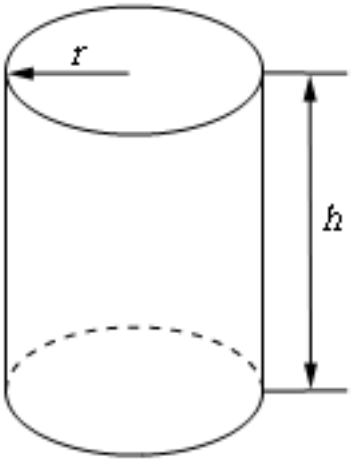


Courtesy from T. Depuydt

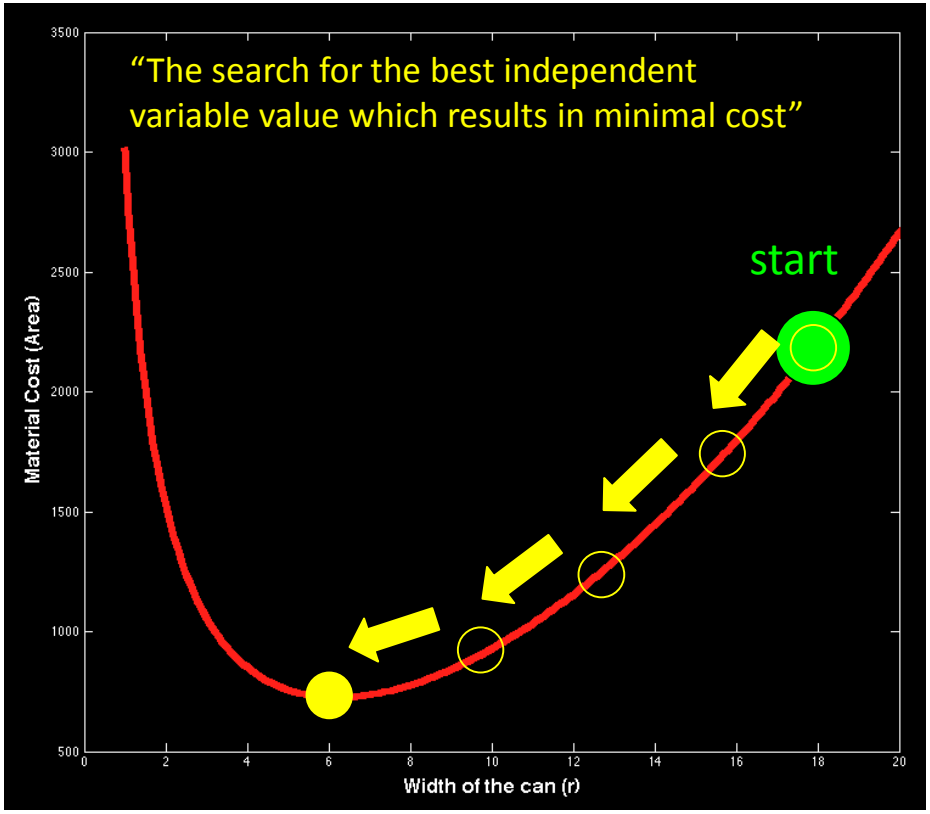
An optimization problem

A simple optimization problem:

"A manufacturer needs to make a cylindrical can that will hold 1.5 liters of liquid. Determine the dimensions of the can that will minimize the amount of material used and as such the ***COST*** *of its construction."*



$$V = (\pi r^2)(h) = \pi r^2 h$$
$$A = (2\pi r)(h) = 2\pi r h$$



$$\text{Minimize} : A = 2\pi rh + 2\pi r^2$$

$$\text{Constraint} : 1500 = \pi r^2 h$$

$$Minimise\ A = \frac{3000}{r} + 2pr^2$$

Courtesy from T. Depuydt

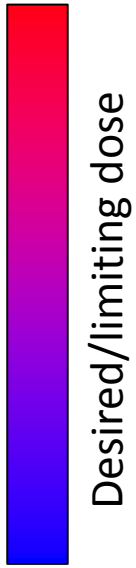
Describe the inverse problem to a computer

Constraints/Goals

"… are constraining the optimization"

"Non-constrained tissue means freedom for the optimizer to put undesired dose there"

"Subdivide into different preferably non-overlapping volumes and relate to dose constraints"



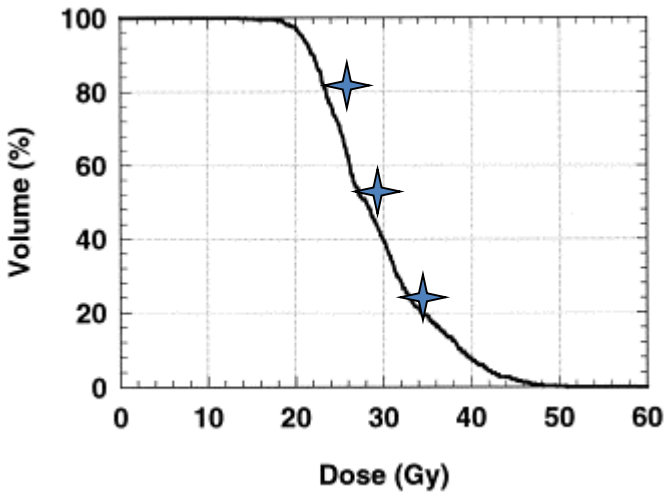
Physical dose

- Target coverage (min, max, …)
- Target homogeneity
- OAR exposure (max, …)
- Surrounding tissues
- …

Biological effect

- TCP, NTCP
- EUD
- …

DVH constraints



Courtesy from T. Depuydt

Cost function

"Combining all sometimes competing goals in one cost function …"

Penalty for not having uniform dose d_0

(optimising uniformity in target)

β Is the relative weight factor

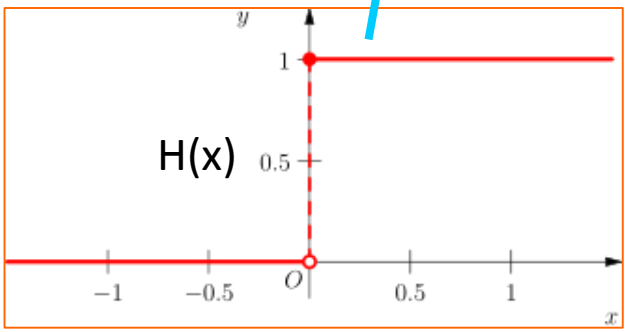
$$C = \beta_T \frac{1}{n_T} \sum_{i \in T} (d_i - d_0)^2 \quad +$$

Penalty for any dose to OAR (minimising the mean of the OAR)

$$\beta_{OAR1} \frac{1}{n_{OAR1}} \sum_{i \in OAR1} d_i \quad +$$

$$\beta_{OAR2} \frac{1}{n_{OAR2}} \sum_{i \in OAR2} \mathrm{H}(d_i - d_0)(d_i - d_0)$$

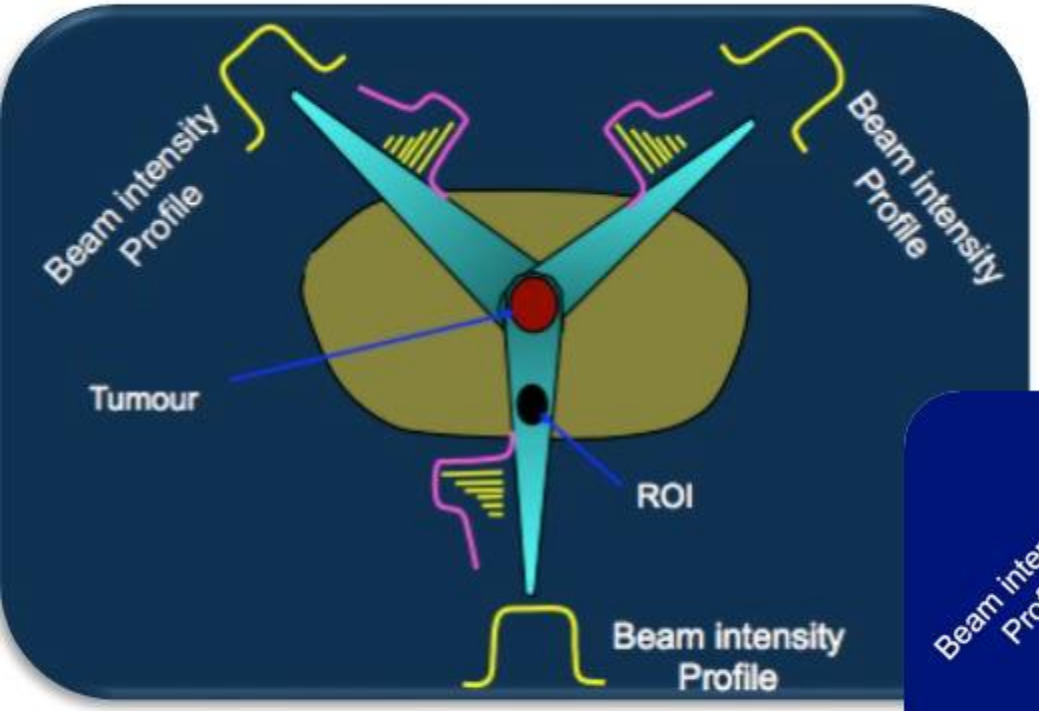
Penalty for dose above "tolerance dose d_0 " in OAR (keeping max dose below d_0)



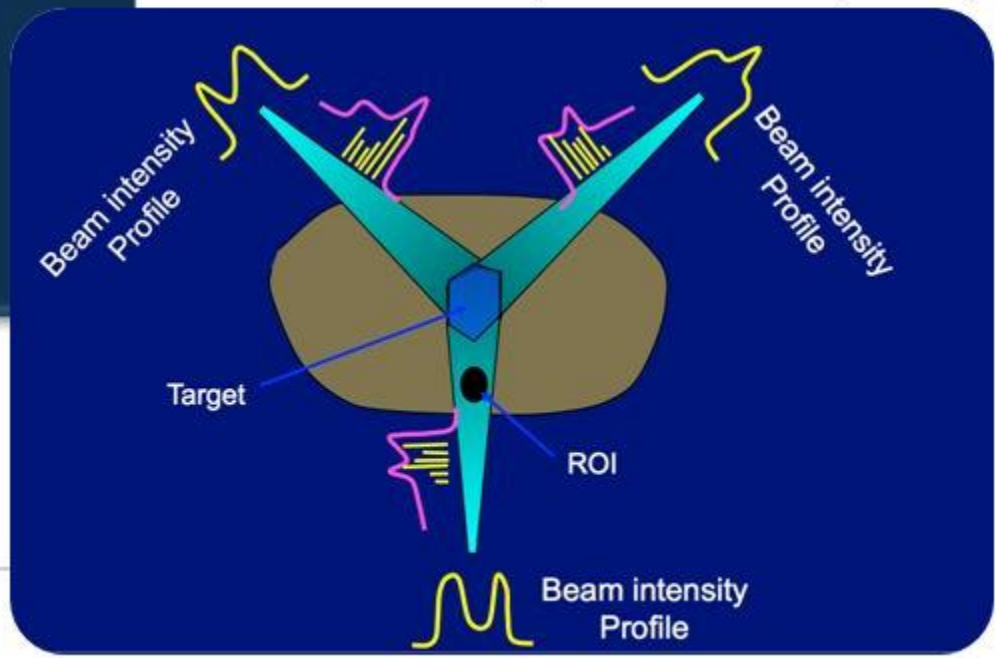
Courtesy from T. Depuydt

Optimization of spot weights

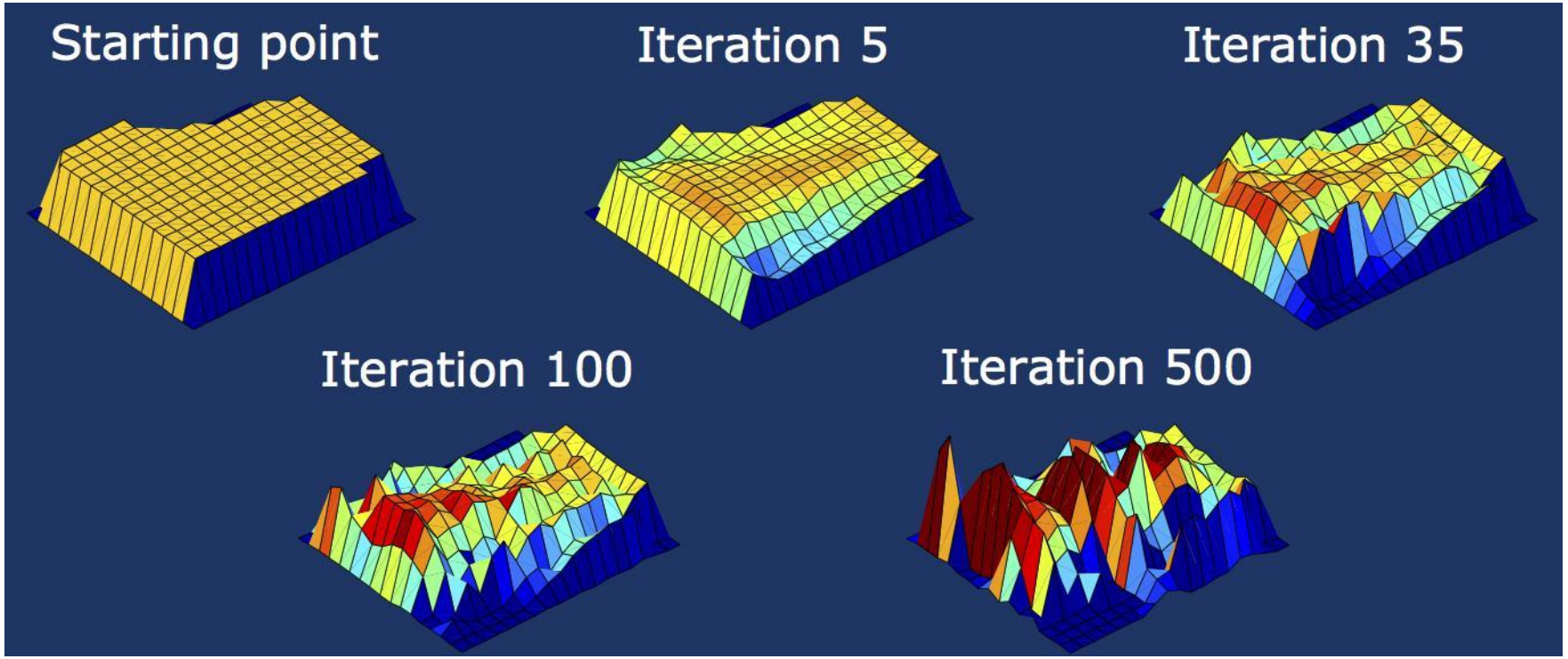
Classical Proton Therapy → DS/US + Single Field Optimization (SFO)



Pencil Beam Scanning – Multi Field Optimization (MFO)



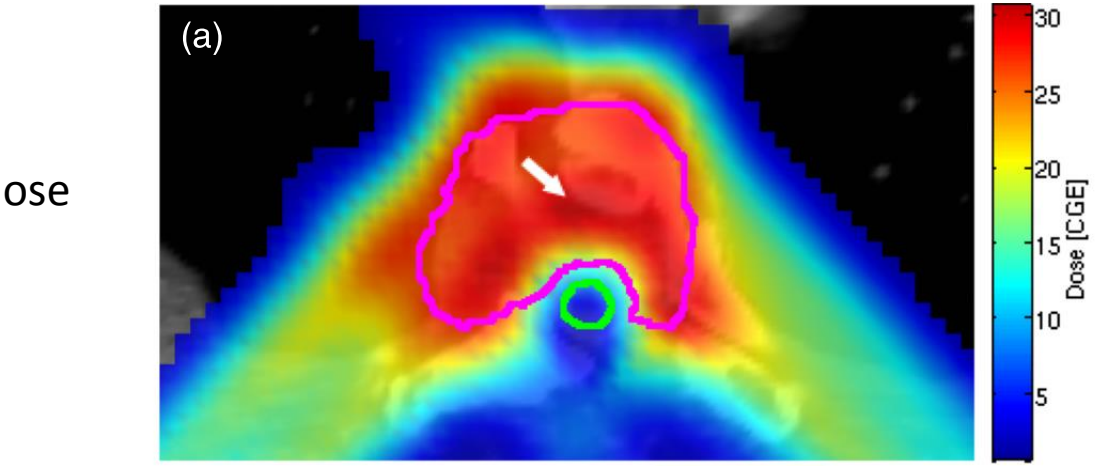
Optimization of spot weights



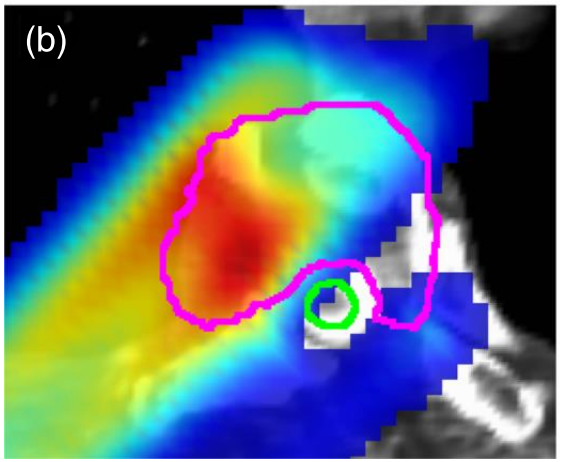
Courtesy from T. Depuydt

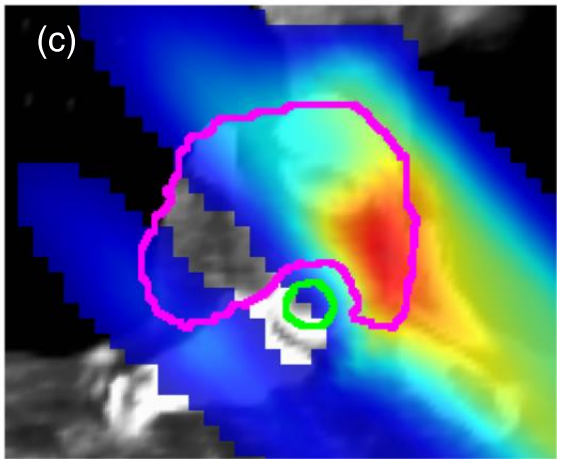
Optimization of spot weights

Final dose



Beam 1 dose





Beam 2 dose

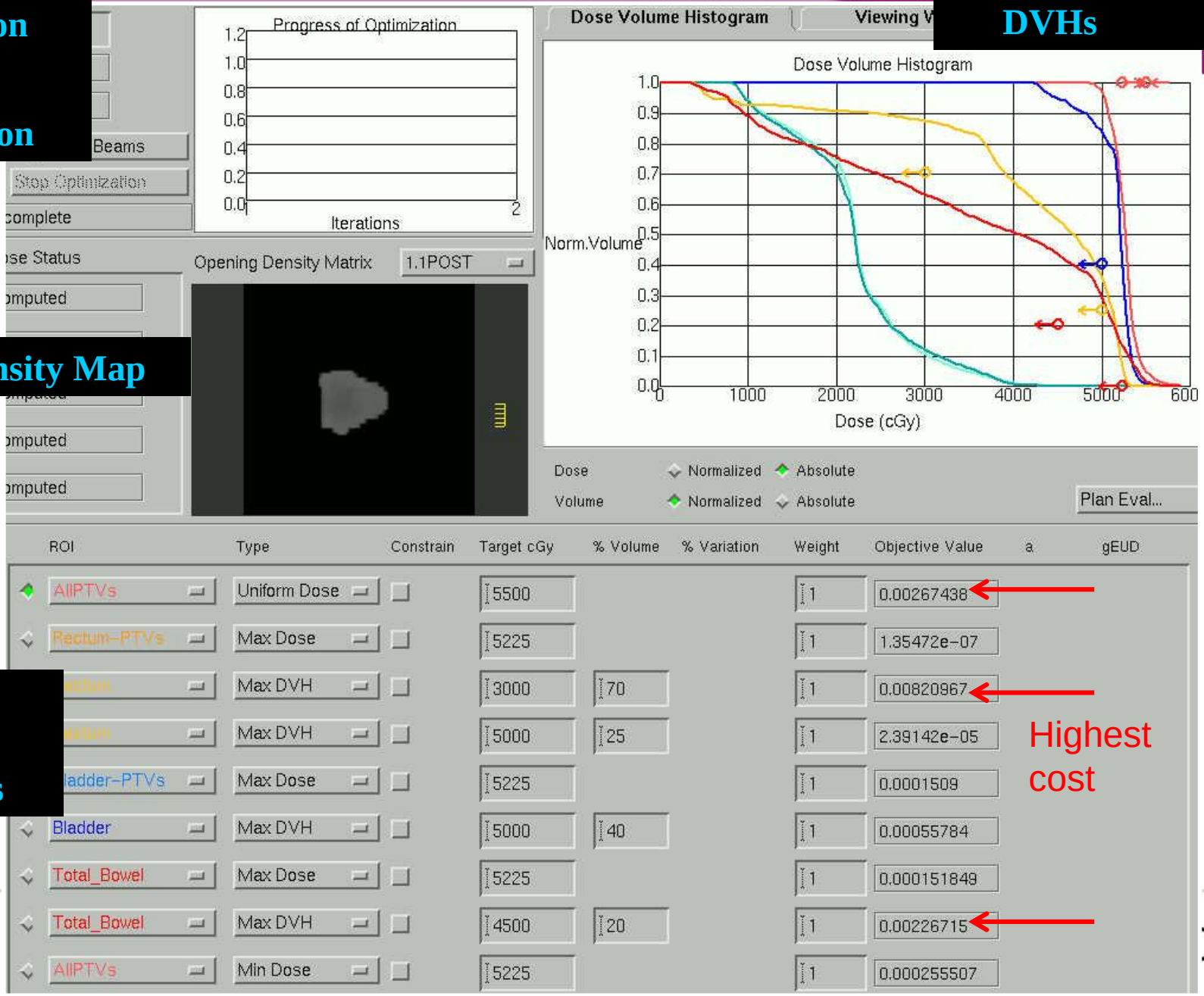
Figure 6. IMPT plan for the paraspinal case using a 5mm (σ) pencil beam. (a) Total dose. (b) Dose from posterior-right lateral beam. (c) Posterior-left lateral beam.

Safai et al (PMB 2013)

Optimization progress,

Cost-function

Optimization DVHs



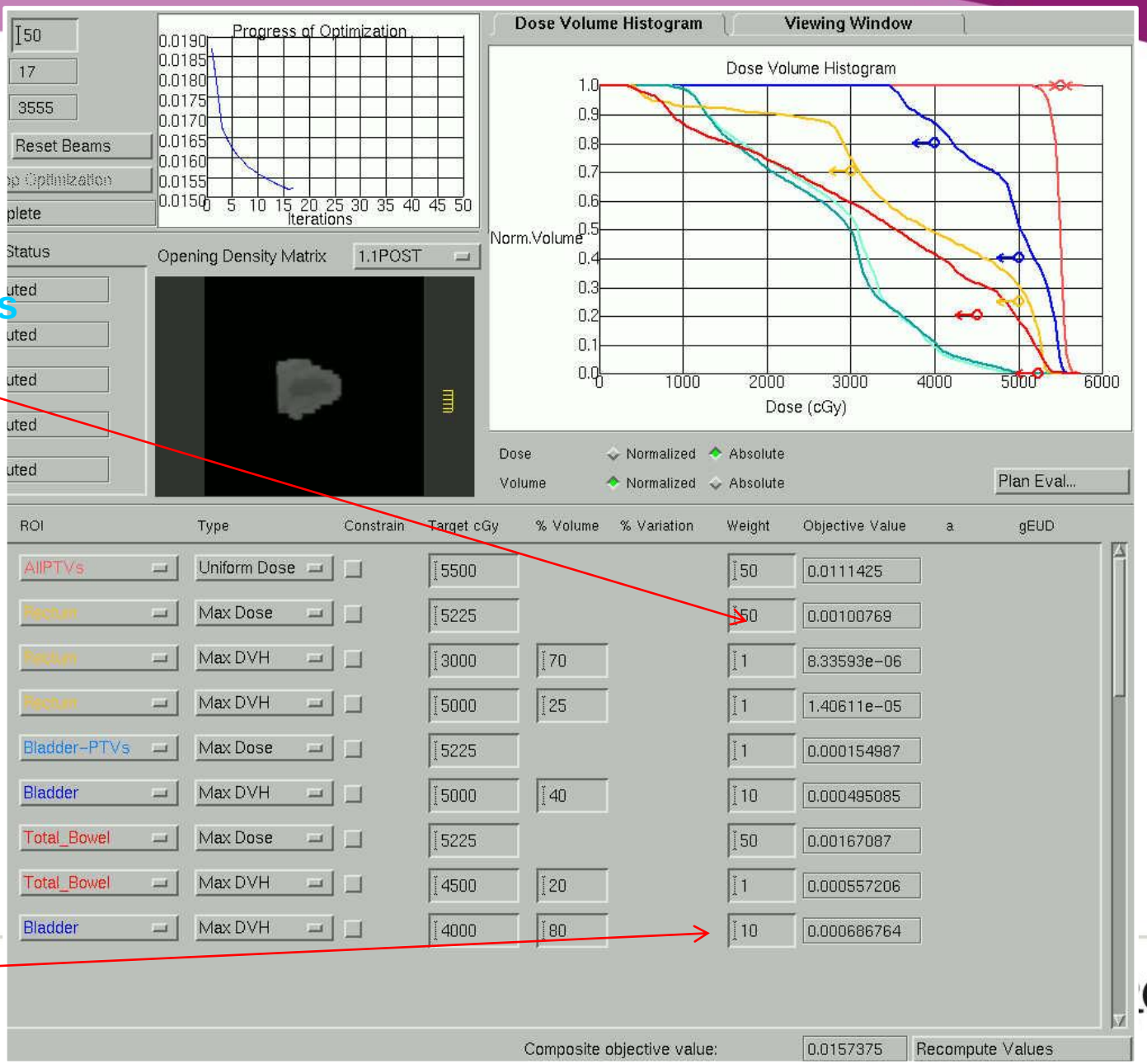
Field Intensity Map

Structures and Constraints

Highest cost

Change of weights change the optimisation

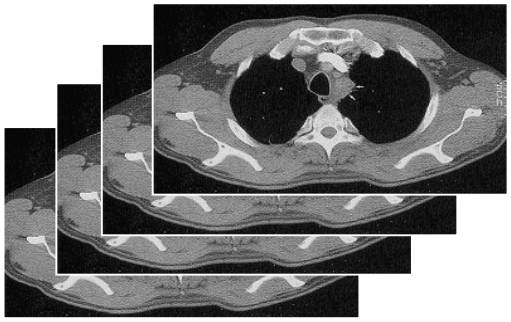
Add a constraint



This is all nice but...

Image acquisition → Manual contouring → Treatment optimization → Treatment validation → Treatment delivery → Follow-up

CT



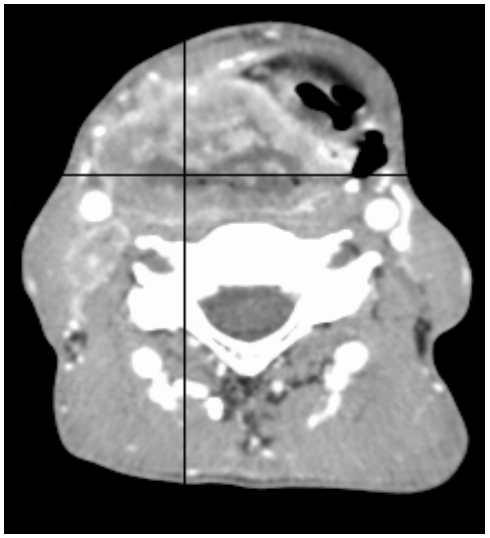
The whole process assumes that the images acquired are a faithful representation of the anatomy during the entire course of the treatment

This is not true:

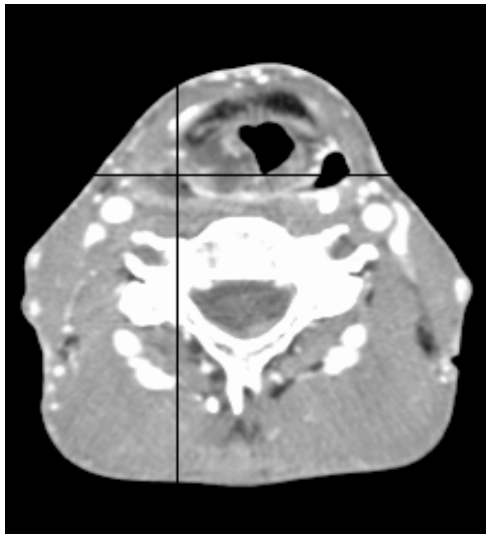
- Patients are not positioned all the time the same way
- Breathing motion is not stable
- The position of the targets and the organs-at-risk may change one relative to another (organ filling)
- The morphology of the patient may change in general (weight loss, tumour shrinkage)

Morphological modifications

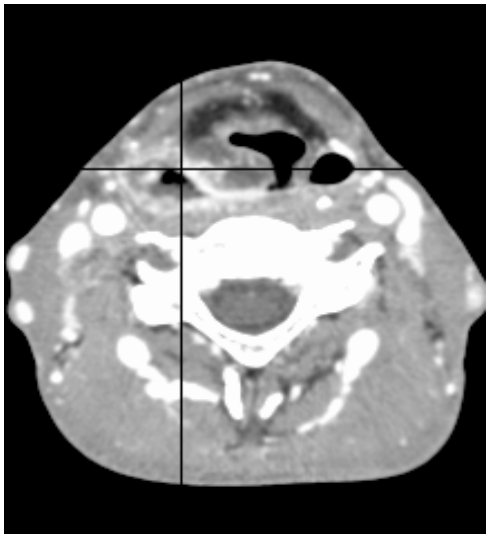
Image acquisition → Manual contouring → Treatment optimization → Treatment validation → Treatment delivery → Follow-up



Pre-RT



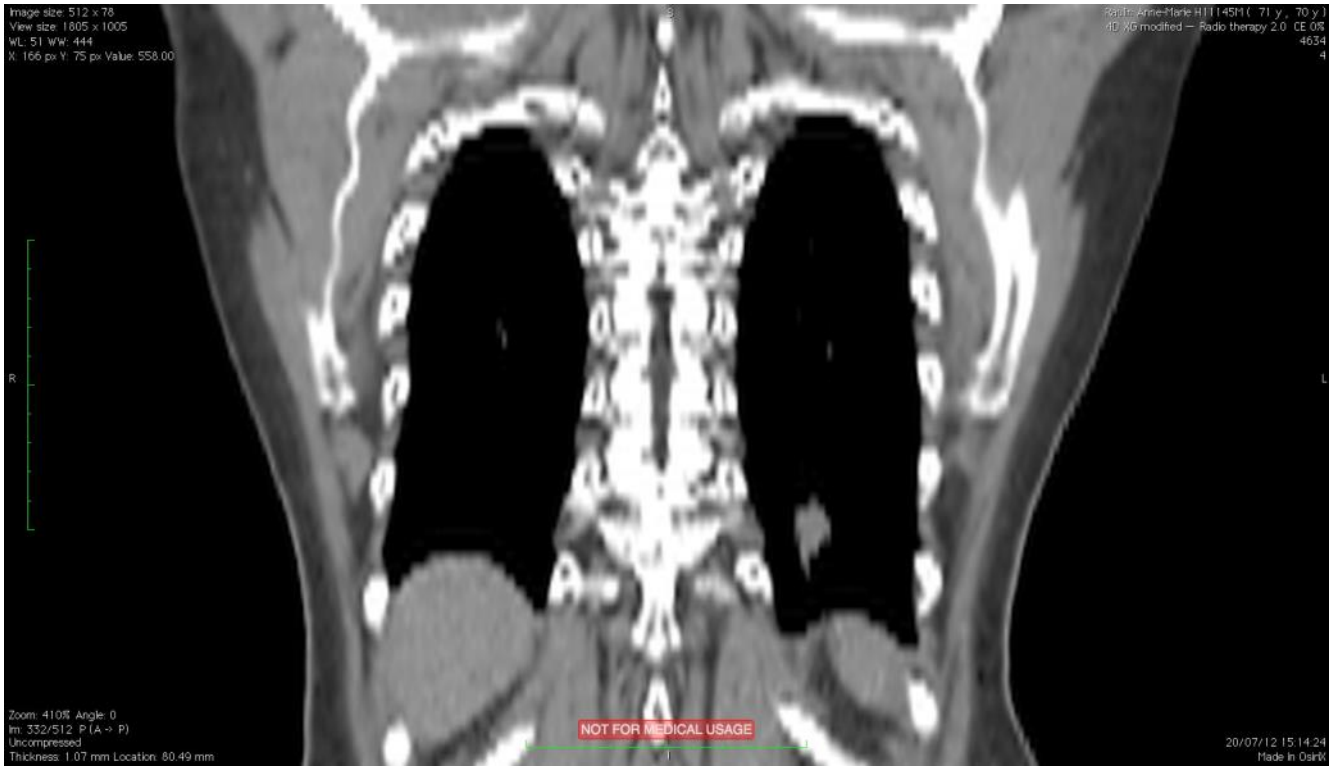
Week 3



Week 5

Breathing

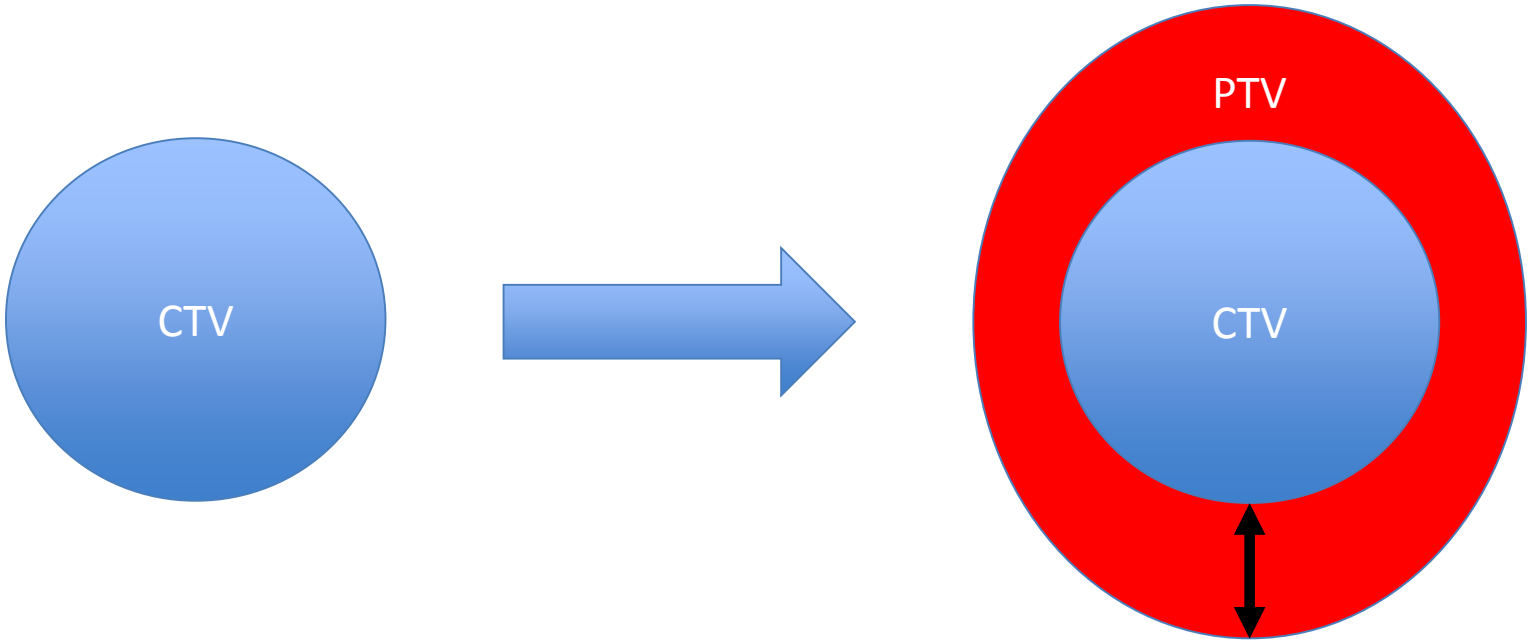
Image acquisition → Manual contouring → Treatment optimization → Treatment validation → Treatment delivery → Follow-up



How to ensure that the target is covered *despite* geometric uncertainties?

To make sure we irradiate the Clinical Target Volume…

We irradiate a larger volume, the Planning Target Volume



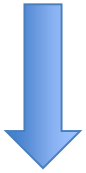
CTV-PTV margin?

$$m_{PTV} = 2.5\Sigma + 0.7\sigma$$

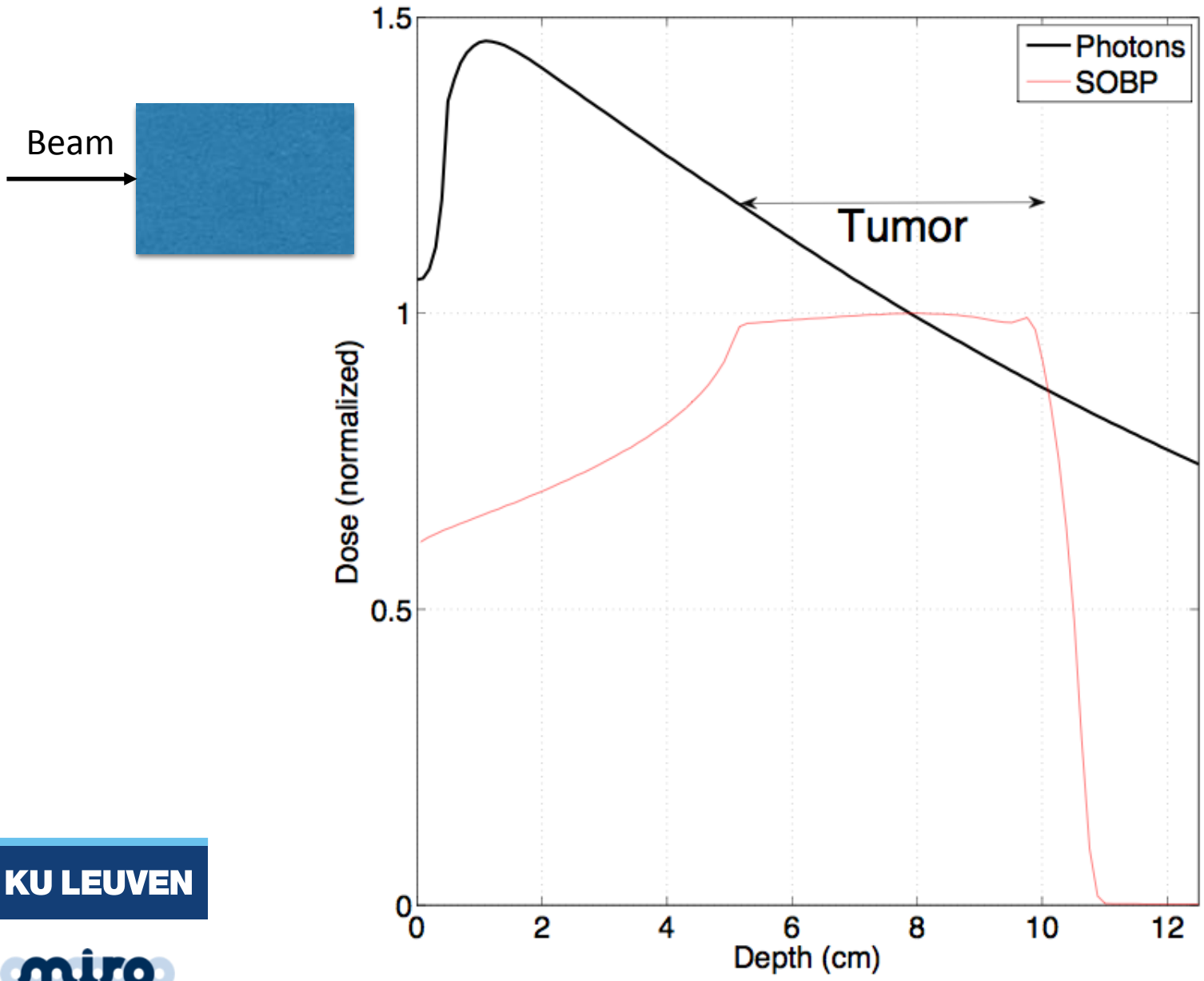
Systematic errors

Random errors

Assumes shift invariance of the dose distribution in ALL directions!!!



The CTV “navigates” in a stable dose distribution



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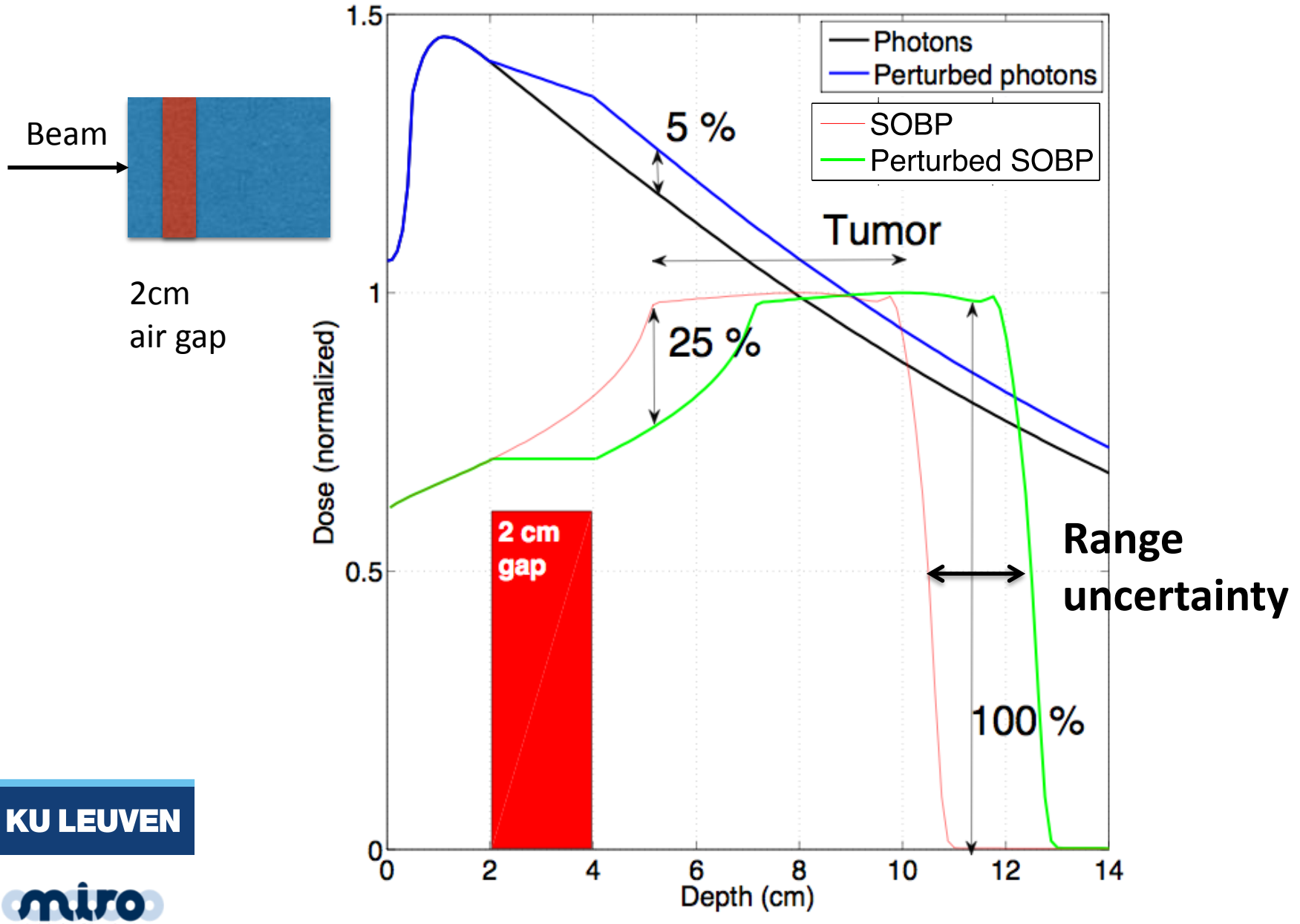
molecular imaging, radiotherapy & oncology



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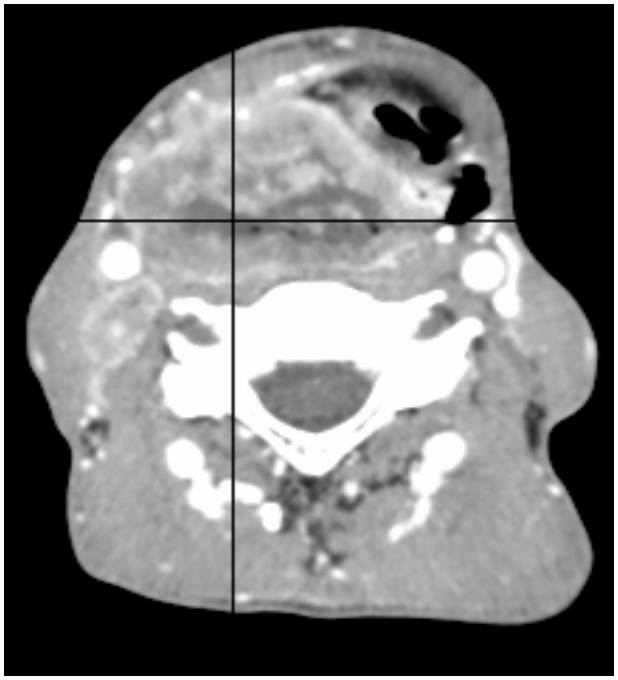
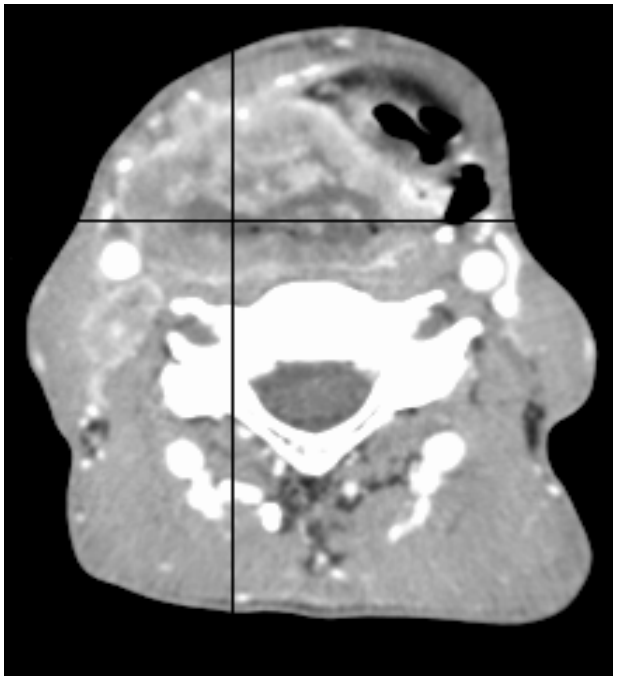
Range uncertainties due to image conversion into stopping powers



Hounsfield Units (photon attenuation)

Conversion



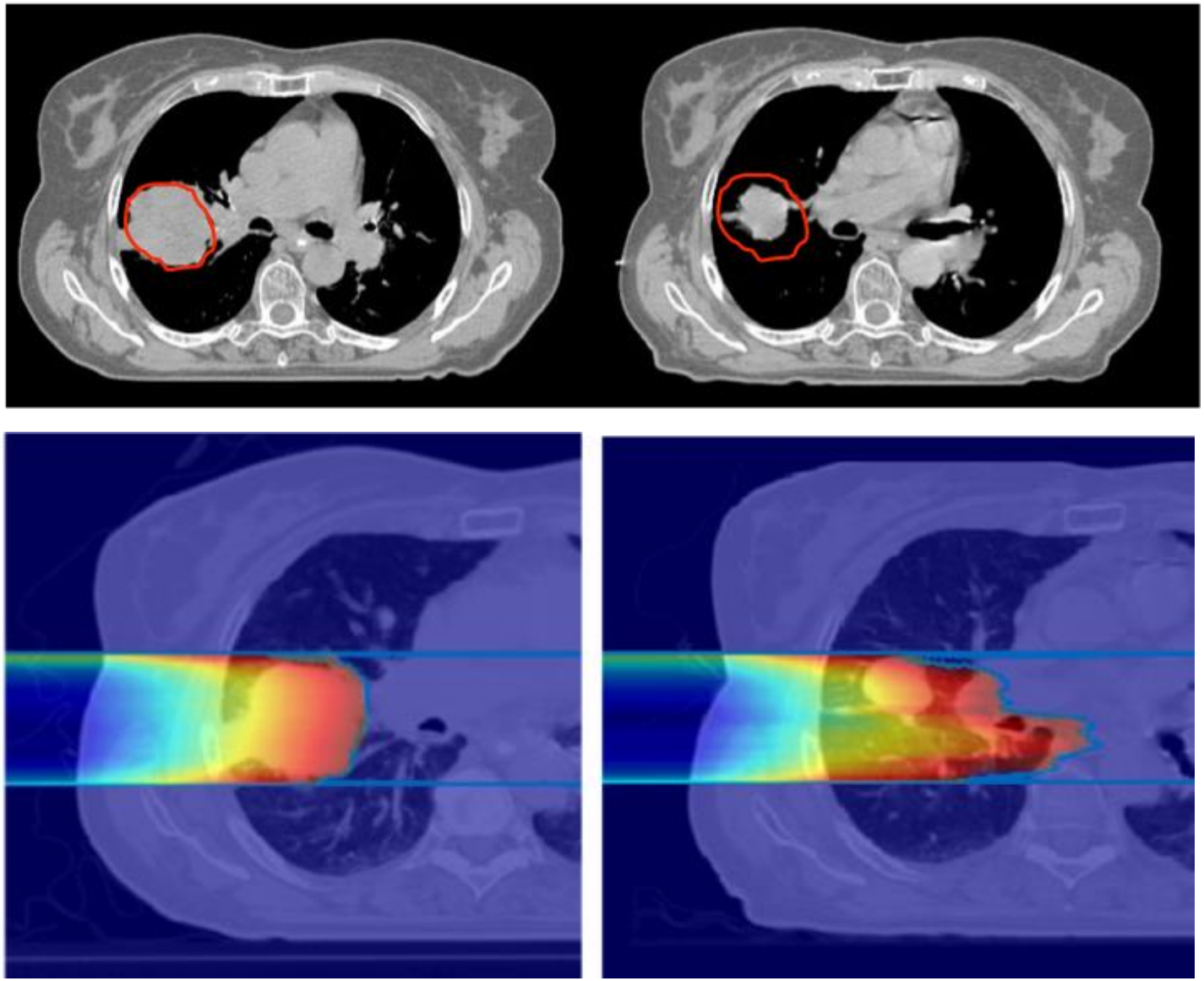
Map of stopping powers

Uncertainties

- Image noise
- Tissue assignment? (Fat, bone, muscle, skin…)
- Tissue composition
- Conversion of a known composition to stopping powers

Total uncertainty of **a few % !**

Range uncertainties due to anatomical changes

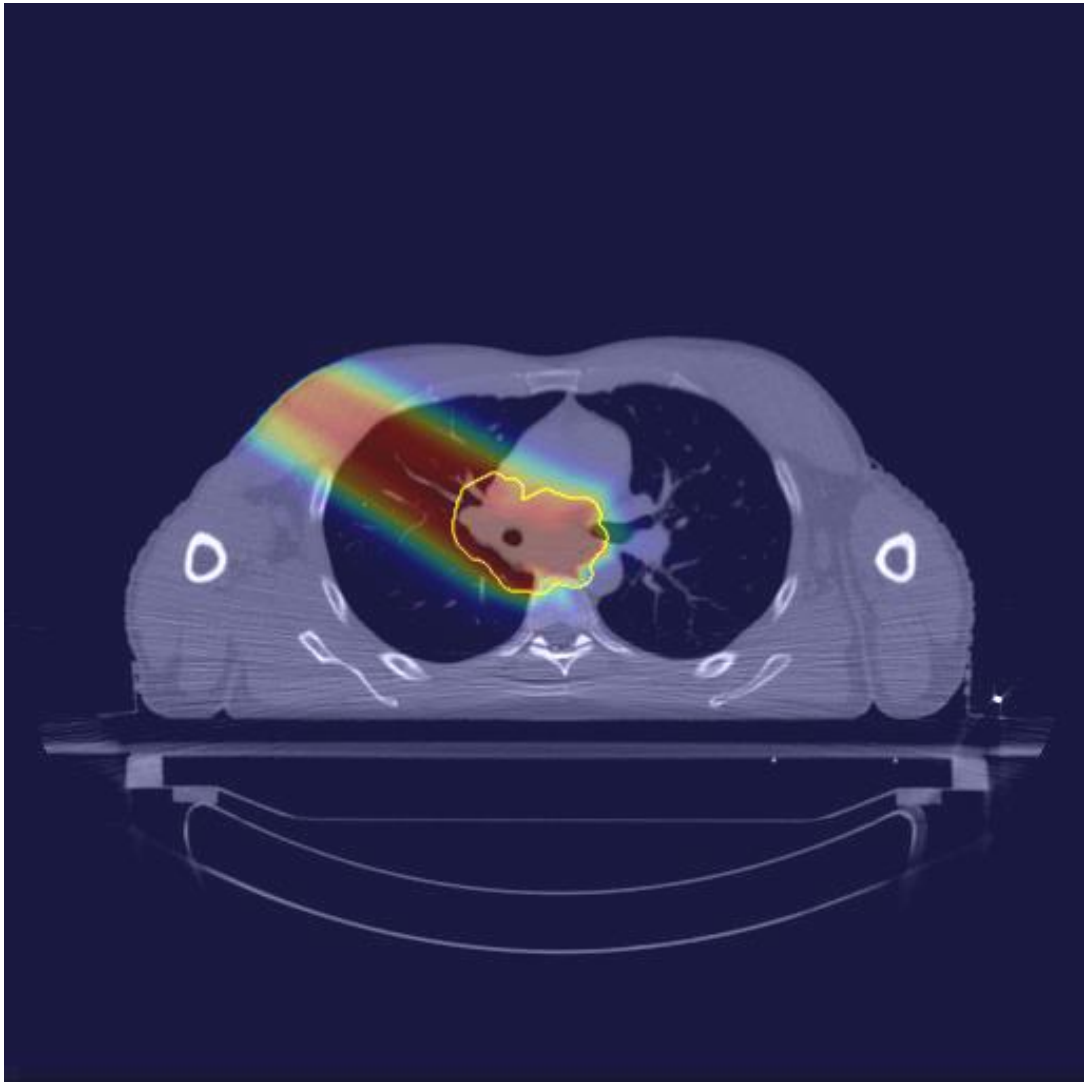


Day 0

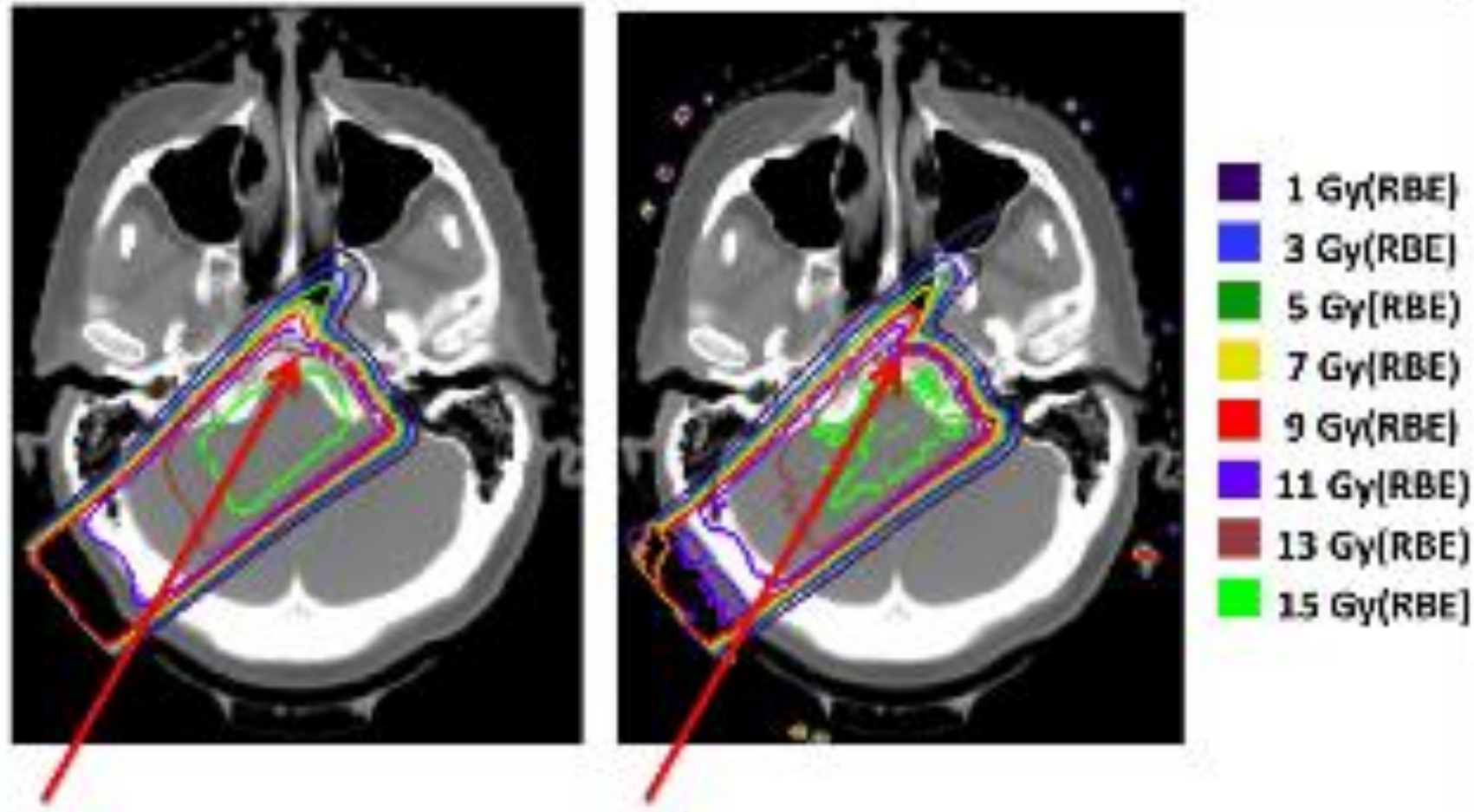
Day 35

From Lomax

Range uncertainties due to breathing



Range uncertainties due to dose calculation errors



Bad algorithm

Good algorithm

Paganetti (2012)

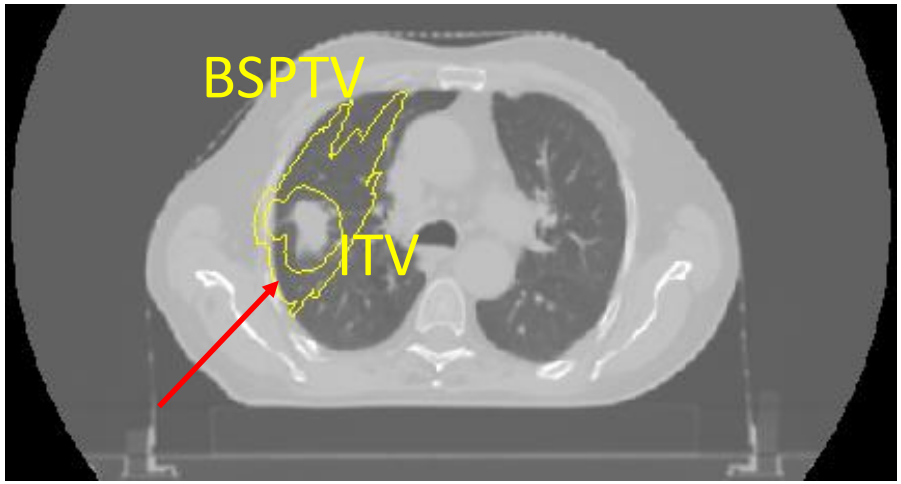
How do we account for range uncertainties in proton therapy treatment planning?

In proton therapy, the dose distribution is not *stable*

Thus the fundamental hypothesis of PTV margin recipes are *not* valid

Beam specific PTV (Single Field Uniform Dose (SFUD))

- **Lateral margin** is calculated similarly to photon PTV
- **Proximal/distal margin** are calculated to compensate for range variations:
  - Motion
  - Setup error
  - Stopping power uncertainties



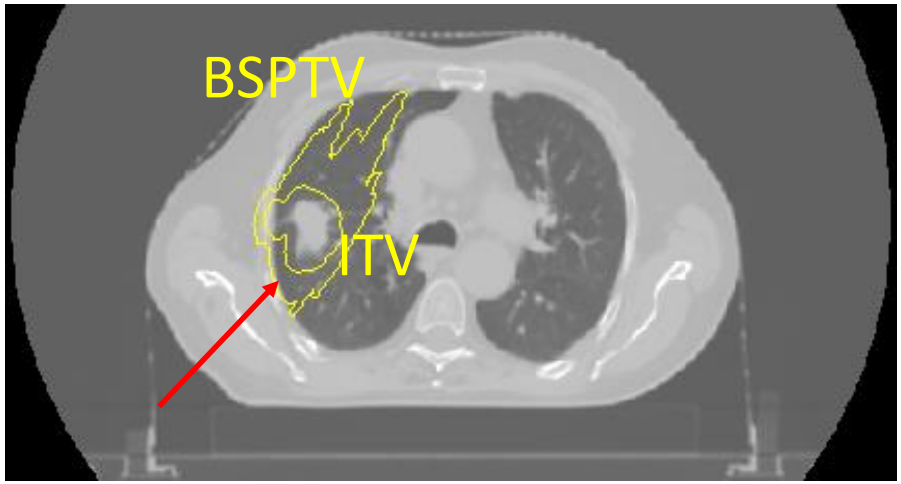
210°

150°

From Souris

Beam specific PTV (Single Field Uniform Dose (SFUD))

DOES NOT WORK for multi-field optimization !
(IMPT - pencil beam scanning)

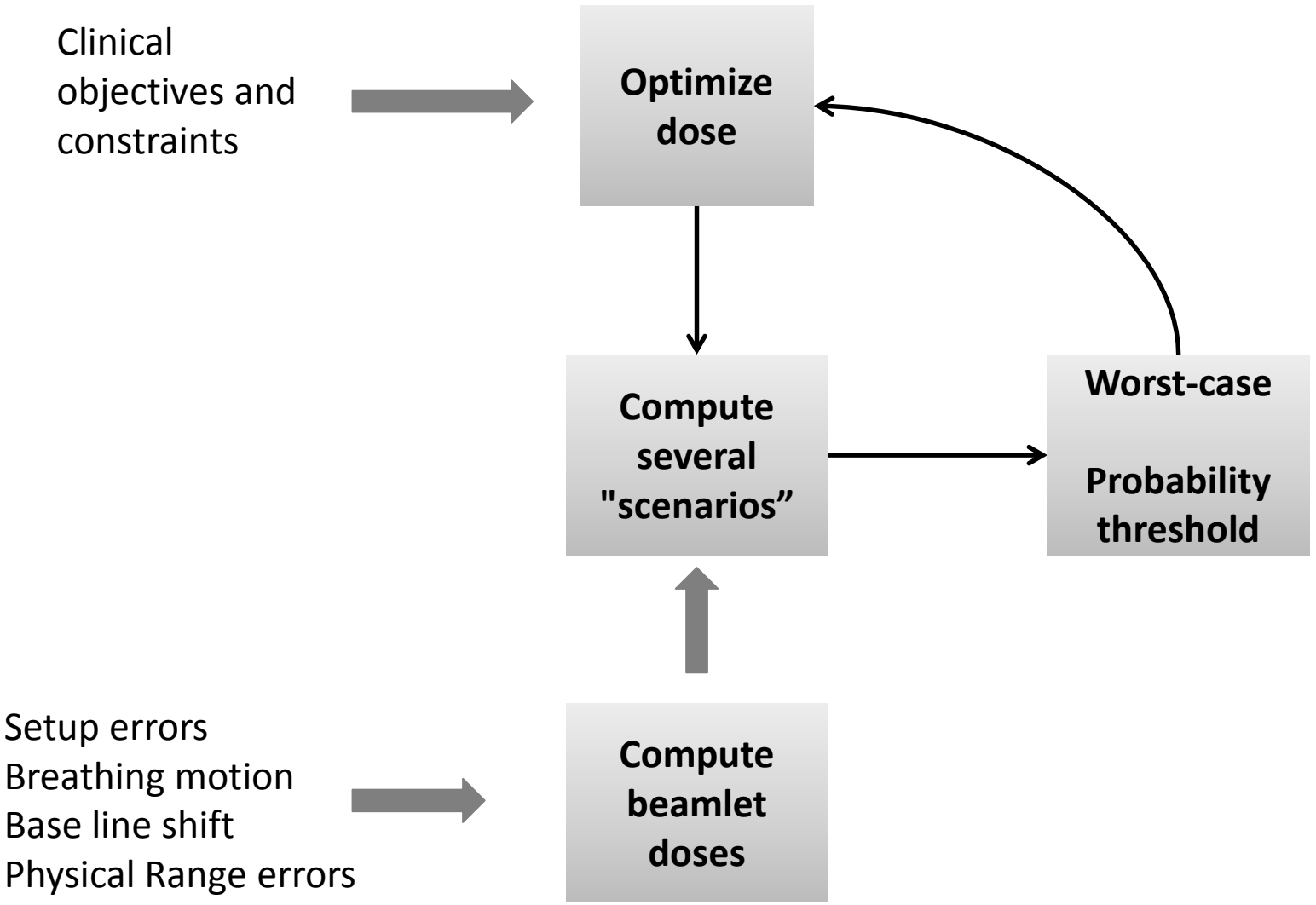


210°

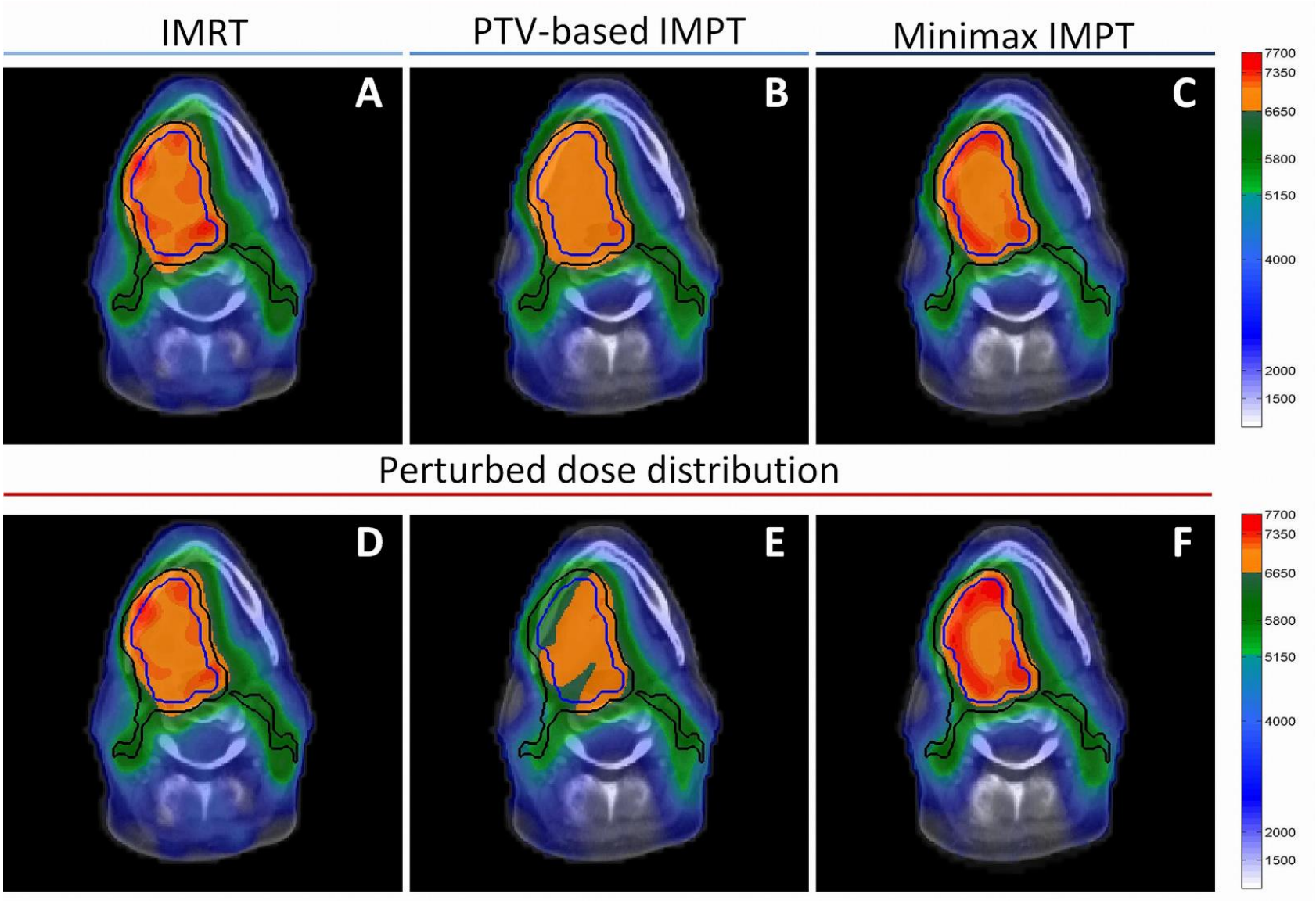
150°

From Souris

IMPT (PBS) → robust optimization

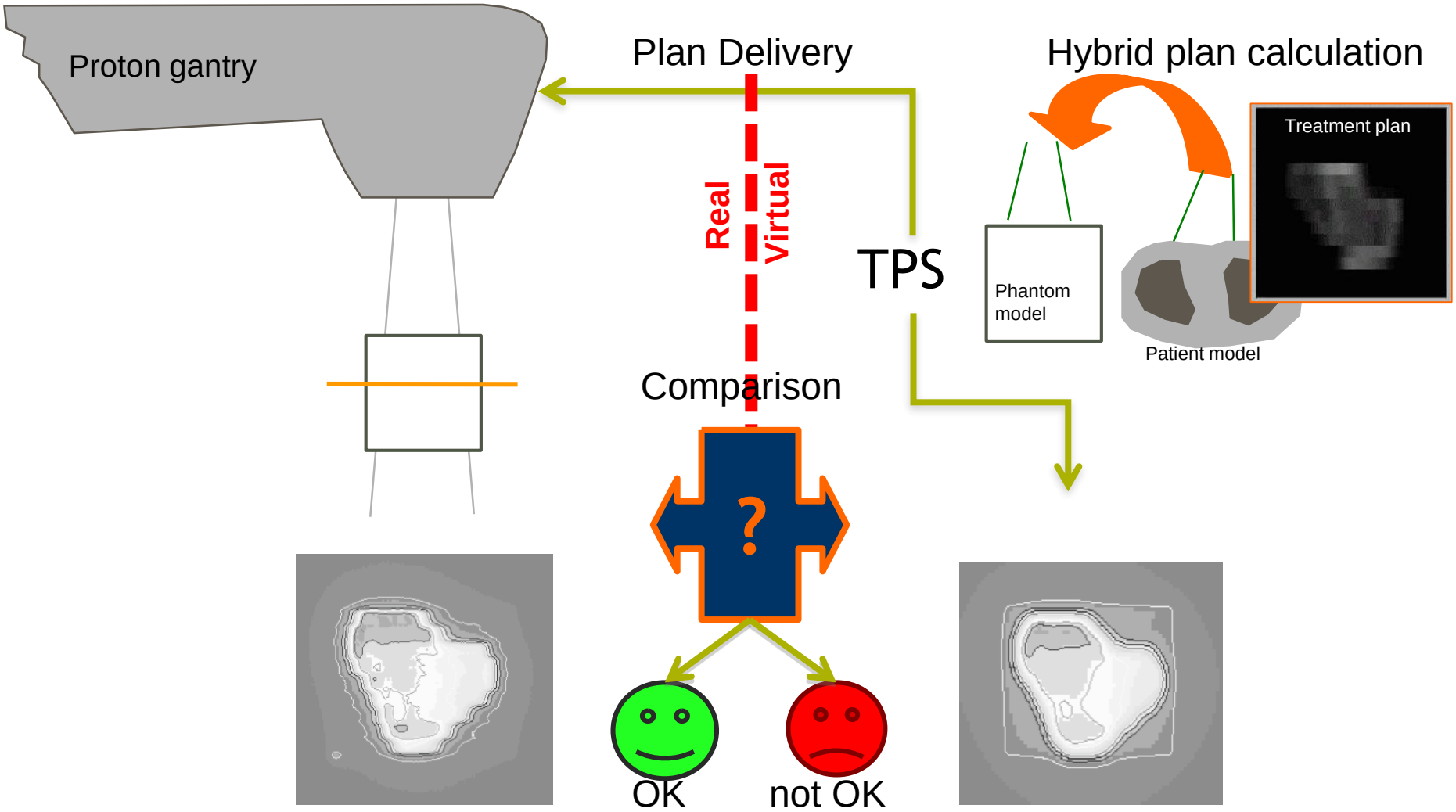


Effectiveness of robust optimization



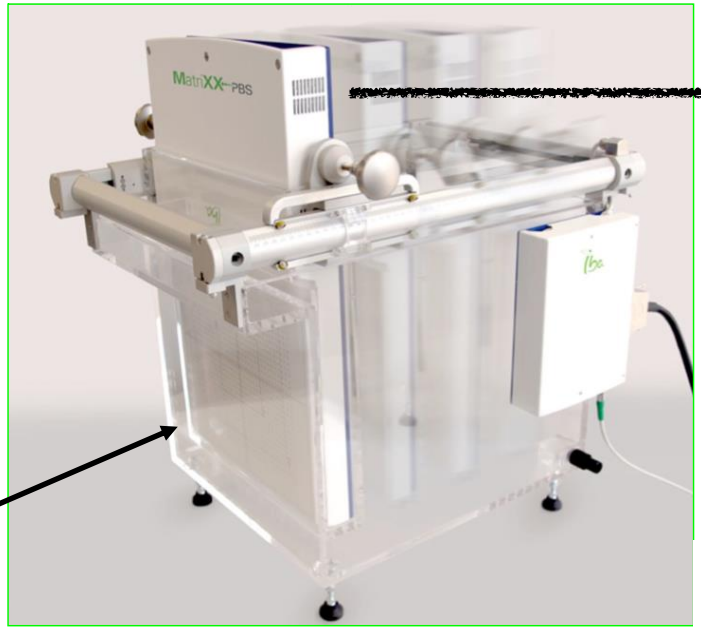
From Van Dijk et al (Plos One 2016)

Treatment verification

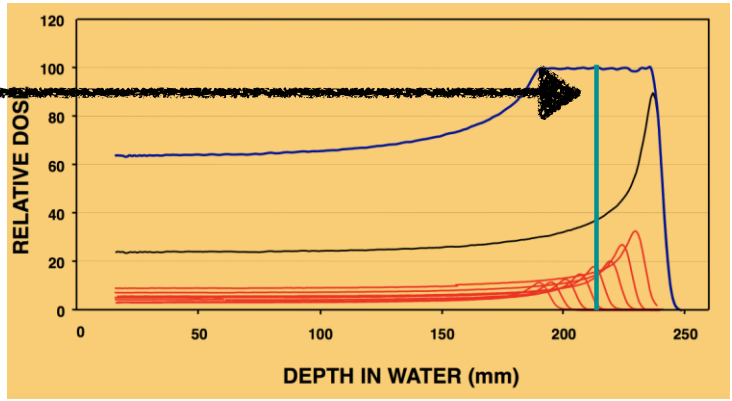


Courtesy from T. Depuydt

Experiment



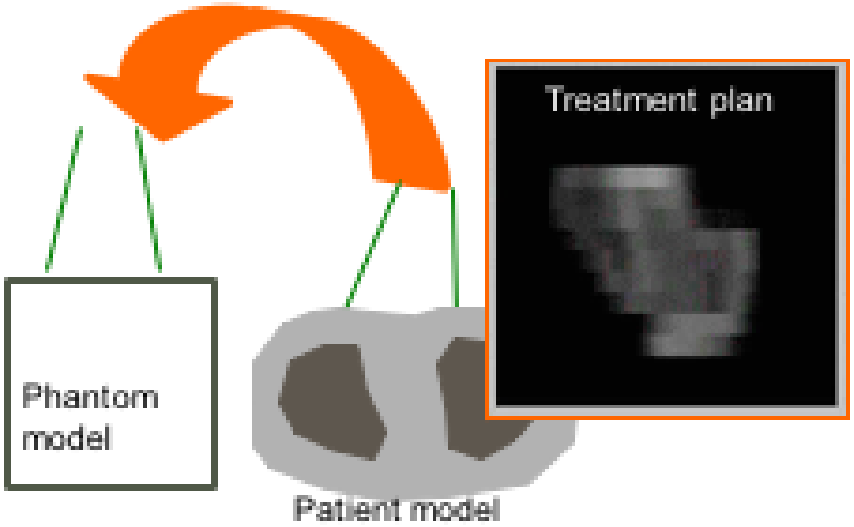
Horizontal Proton beam



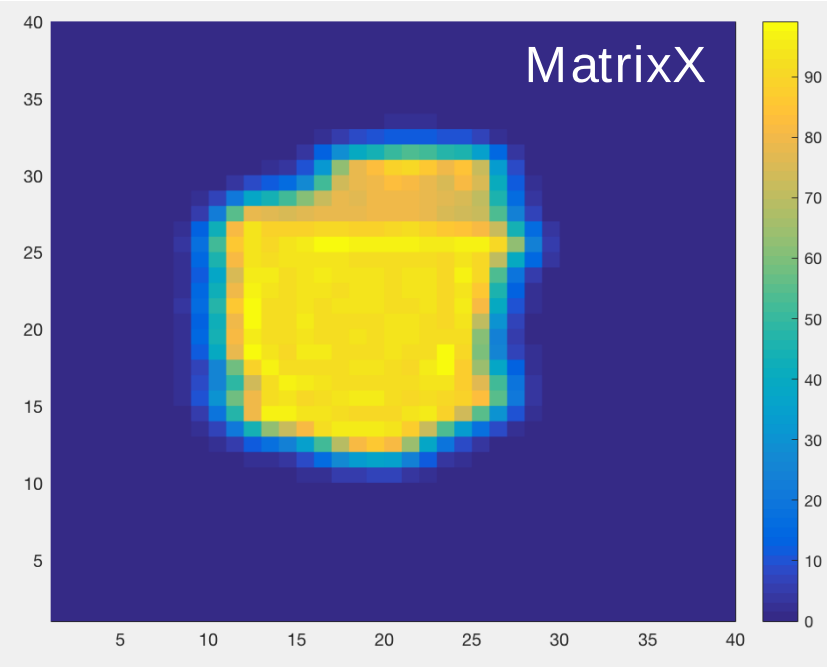
- One measurement per field (2 fields = 2 measurements)
- Depth of the detector at Mid-SOBP.

Dose calculation

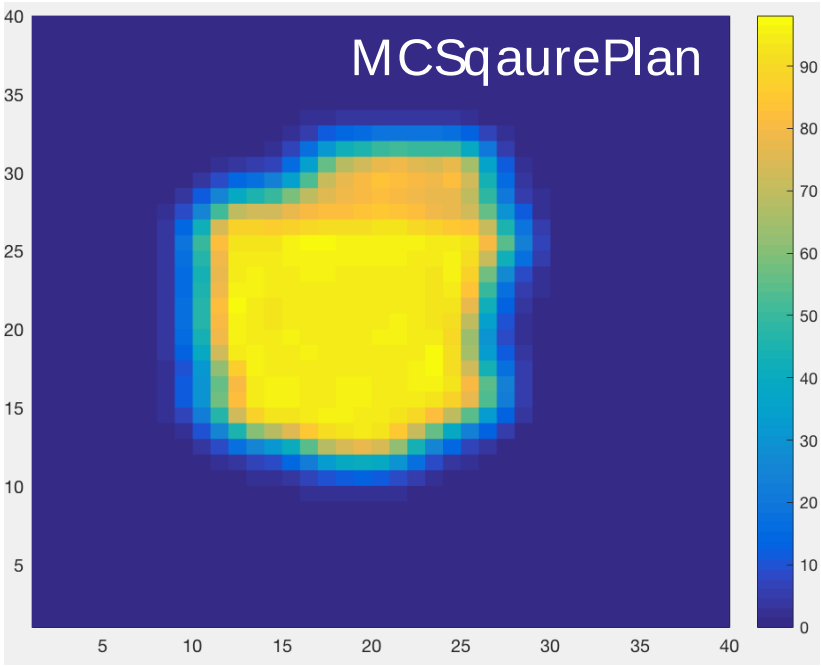
Hybrid plan calculation



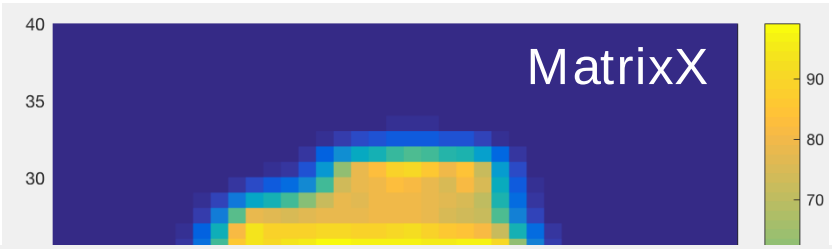
Experiment

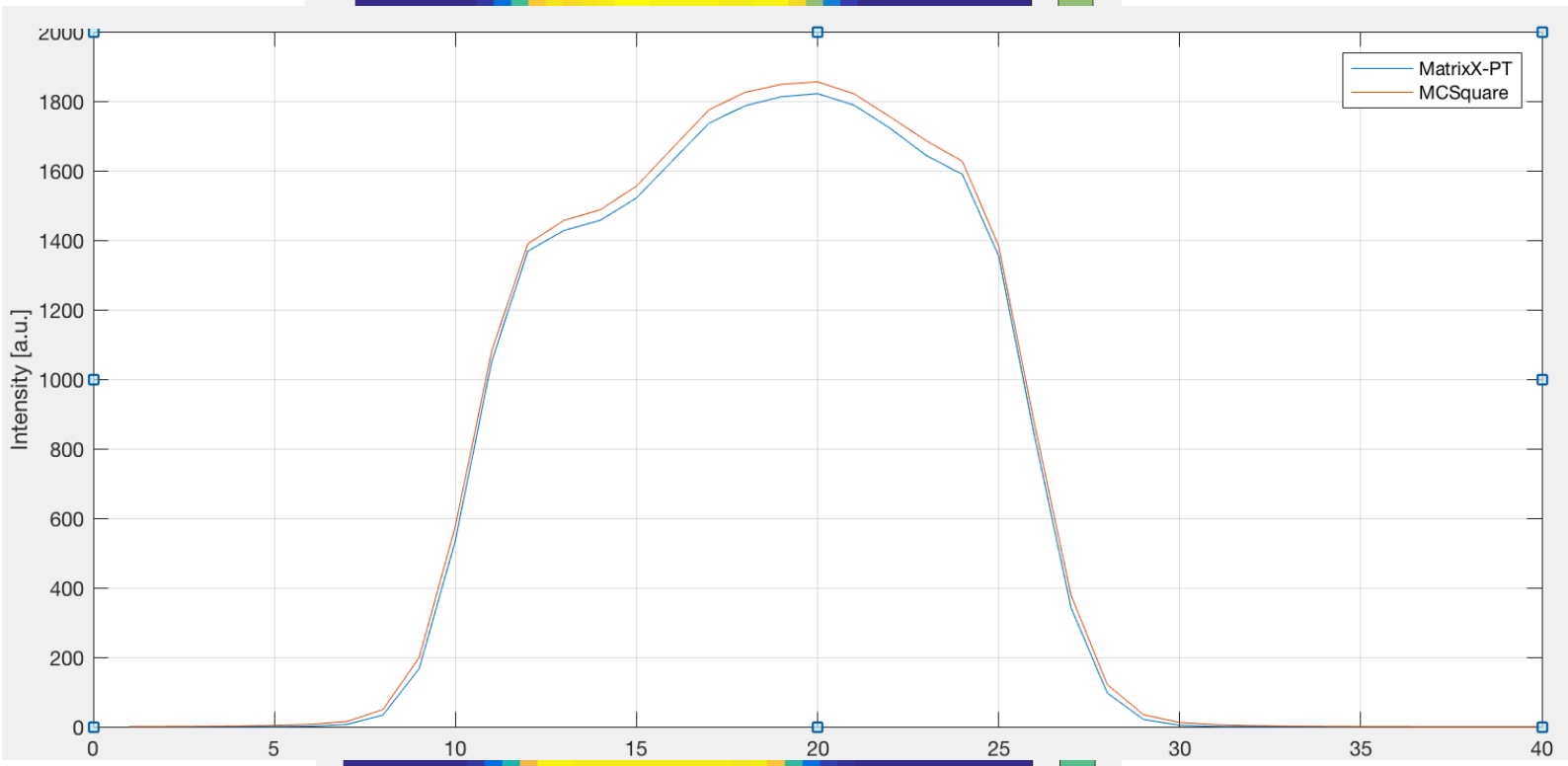


Dose calculation

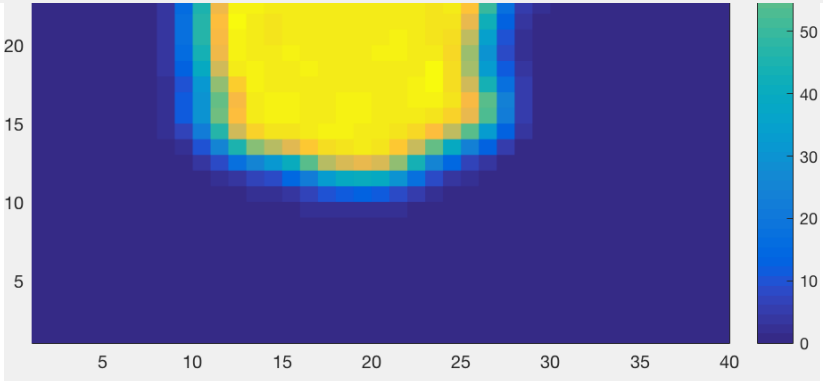


Experiment





Dose calculation



In vivo range verification

Proton radiography

- Most direct verification of the stopping power values of the tissue

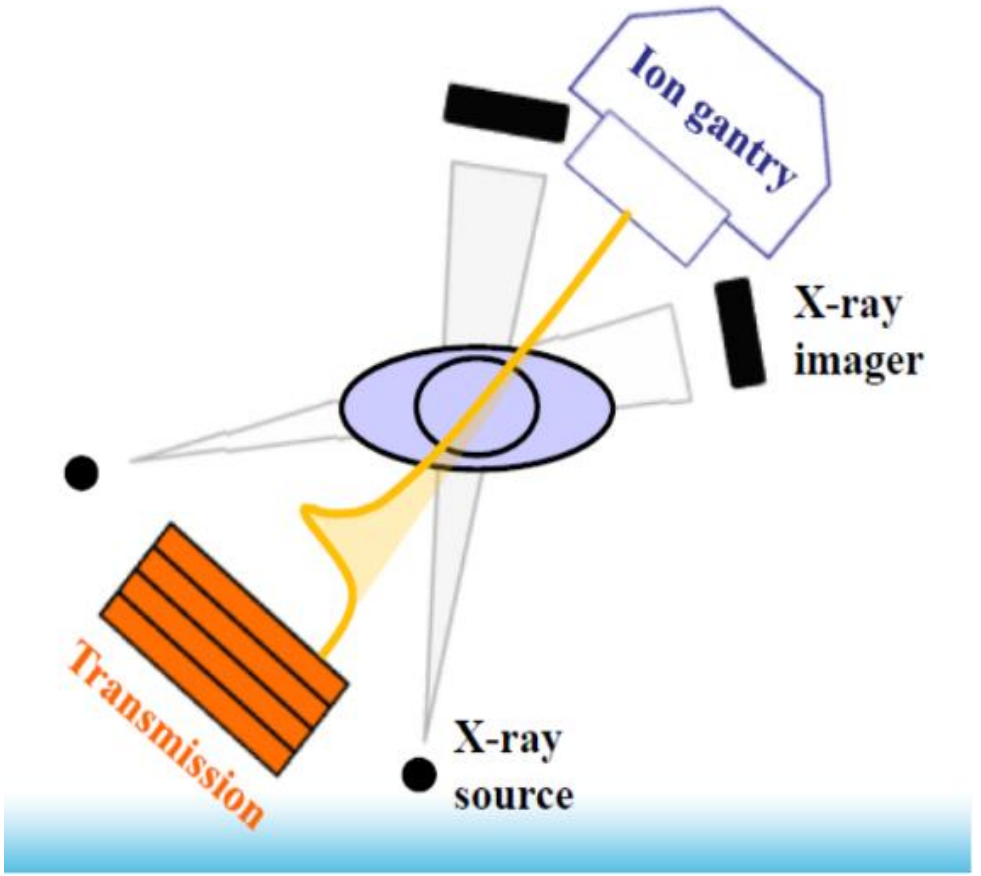
- Compared to x-rays:

  better contrast,

  lower dose

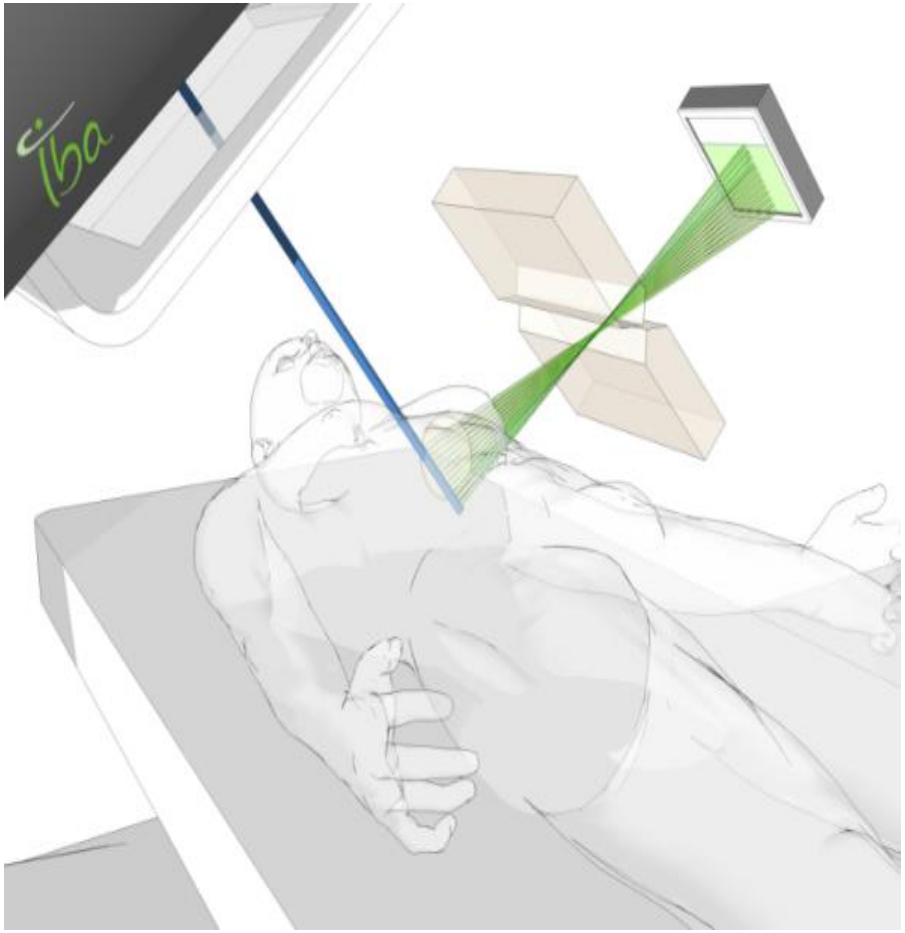
  but poorer spatial resolution (due to MCS)

- Investigated since late 1960s (Koehler 1968), but both technical and financial challenges



K. Parodi (2015).

Prompt gamma imaging (IBA solution)



Intended application:

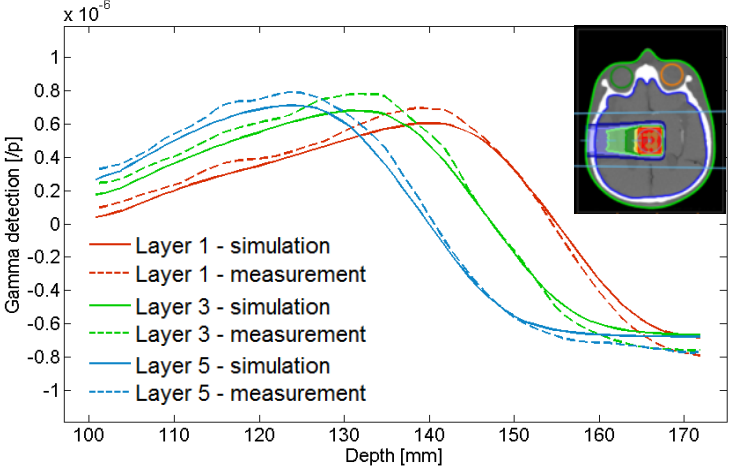
Measurement of the position at which the proton beam stops in the patient in PBS mode

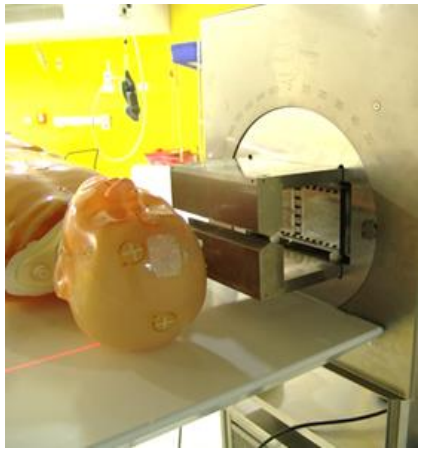
Target performance:

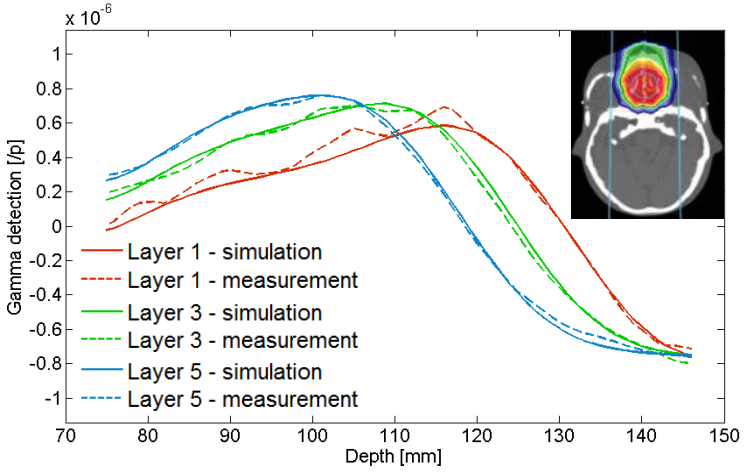
Instantaneous verification with an accuracy better than half the distal margin for a selection of critical spots

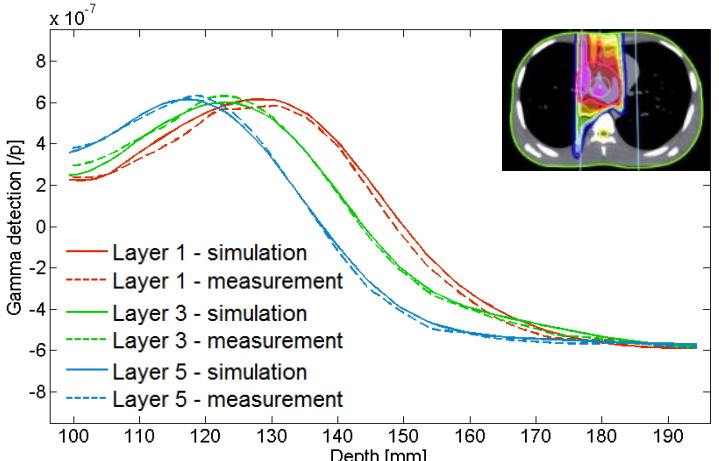
Points of attention:

Simplicity, cost effectiveness


x 10^-6
Gamma detection [/p]
Depth [mm]
Layer 1 - simulation
Layer 1 - measurement
Layer 3 - simulation
Layer 3 - measurement
Layer 5 - simulation
Layer 5 - measurement




x 10^-6
Gamma detection [/p]
Depth [mm]
Layer 1 - simulation
Layer 1 - measurement
Layer 3 - simulation
Layer 3 - measurement
Layer 5 - simulation
Layer 5 - measurement


x 10^-7
Gamma detection [/p]
Depth [mm]
Layer 1 - simulation
Layer 1 - measurement
Layer 3 - simulation
Layer 3 - measurement
Layer 5 - simulation
Layer 5 - measurement

First report of clinical usage of prompt gamma imaging for PBS

Title: Prompt gamma imaging for *in vivo* range verification of pencil beam scanning proton therapy

Running title: Prompt gamma imaging for *in vivo* proton range verification

Authors:
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Conclusions

- Proton therapy (and hadron therapy) is promising
- There are planning and verfication tools to help fulfilling their potential
- Their integration in clinical practice requires multidisciplinary research and streamlined workflows

Thank you!

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