

# Treatment planning optimization and validation

E. Sterpin

Katholieke Universiteit Leuven  
Université catholique de Louvain  
ParTICLE project



# ParTICLe

## Particle Therapy Interuniversity Center Leuven

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

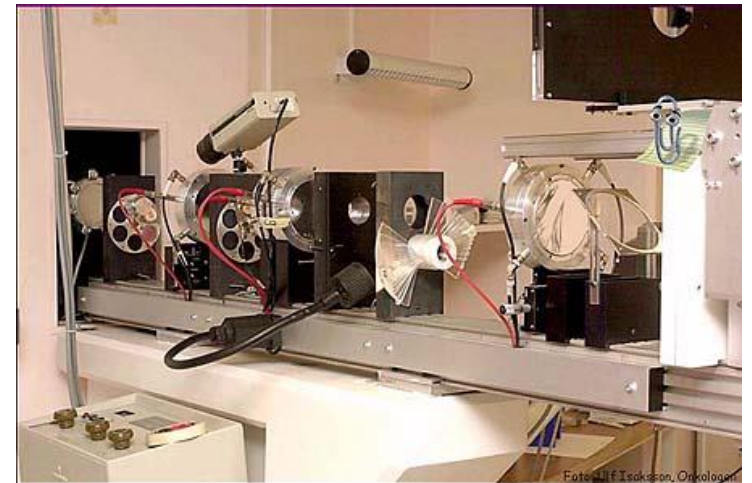


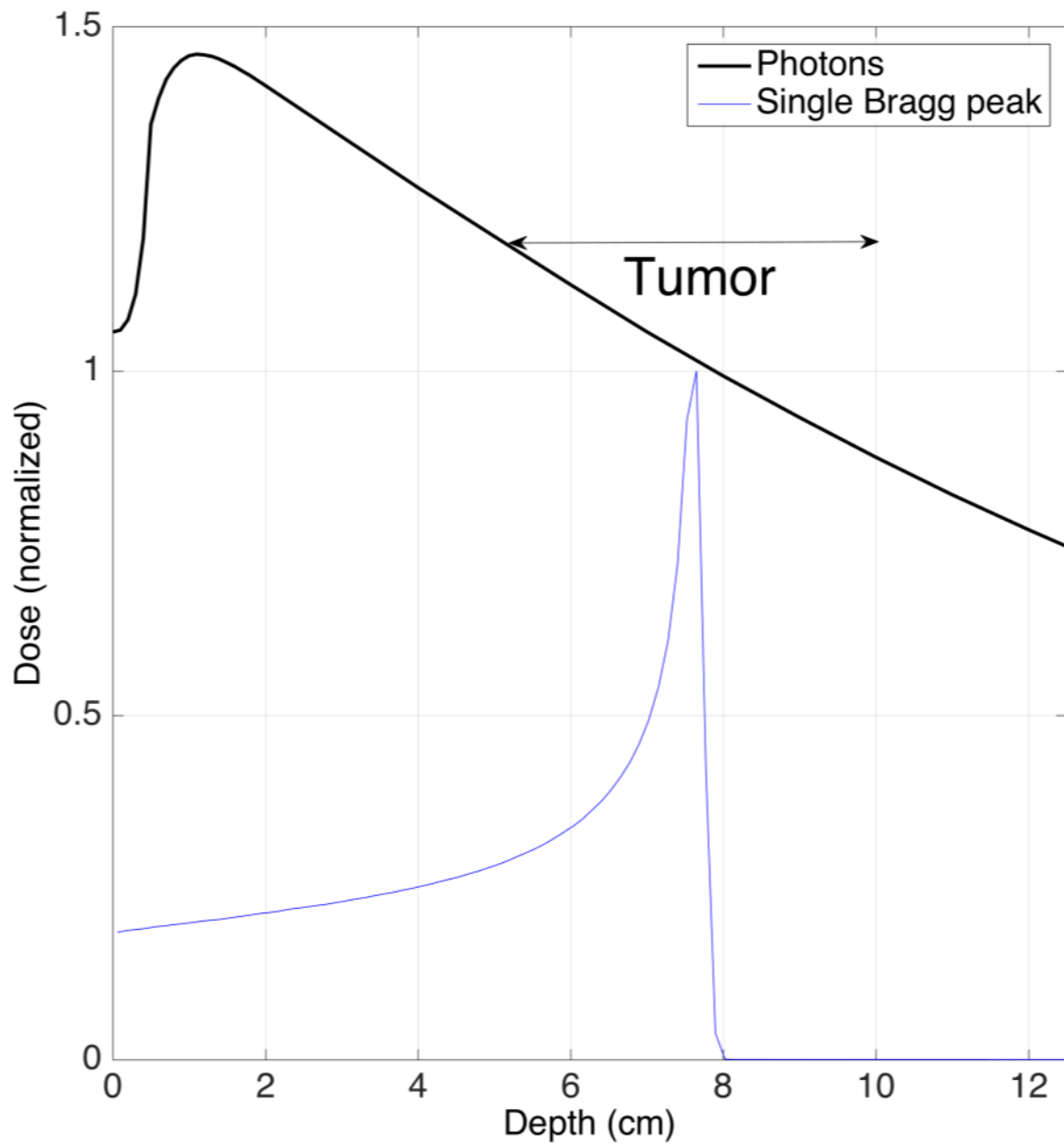
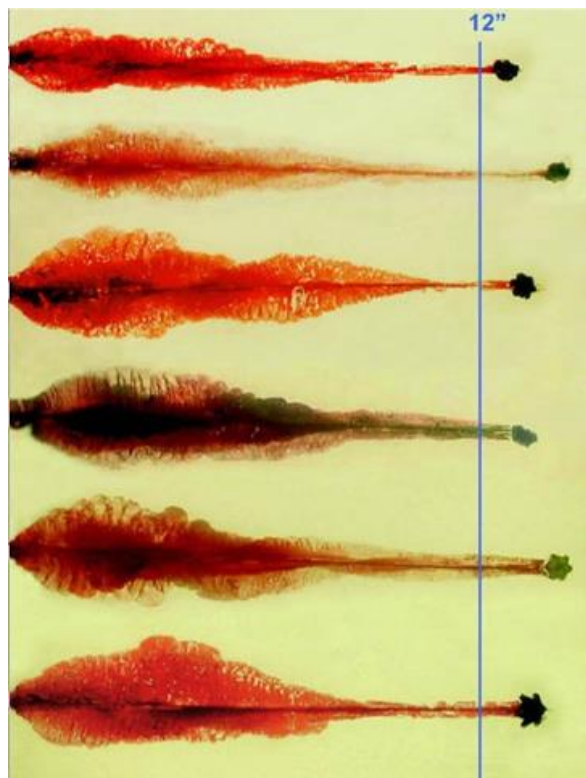
# Facility setup

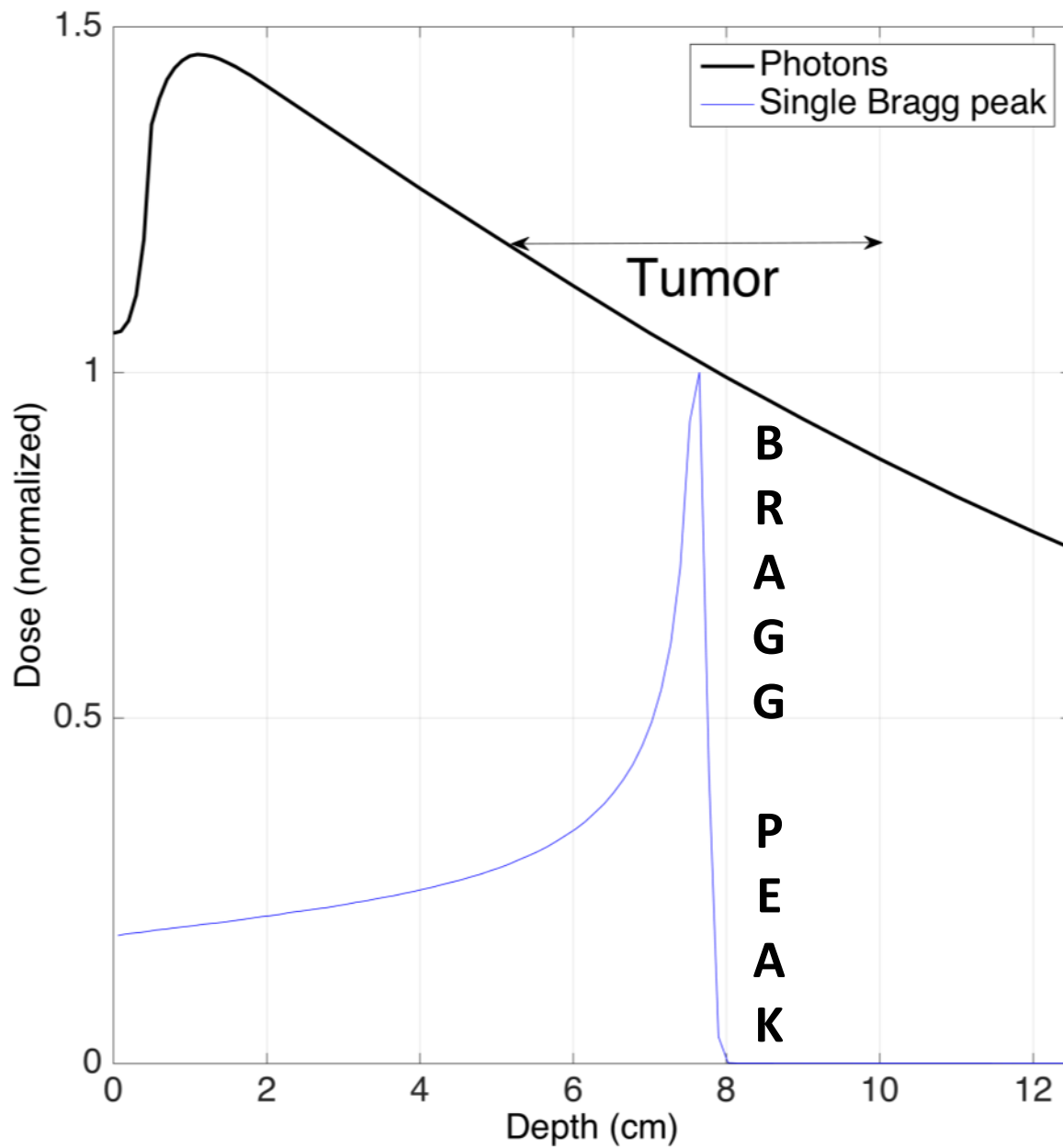
## Clinical beam line

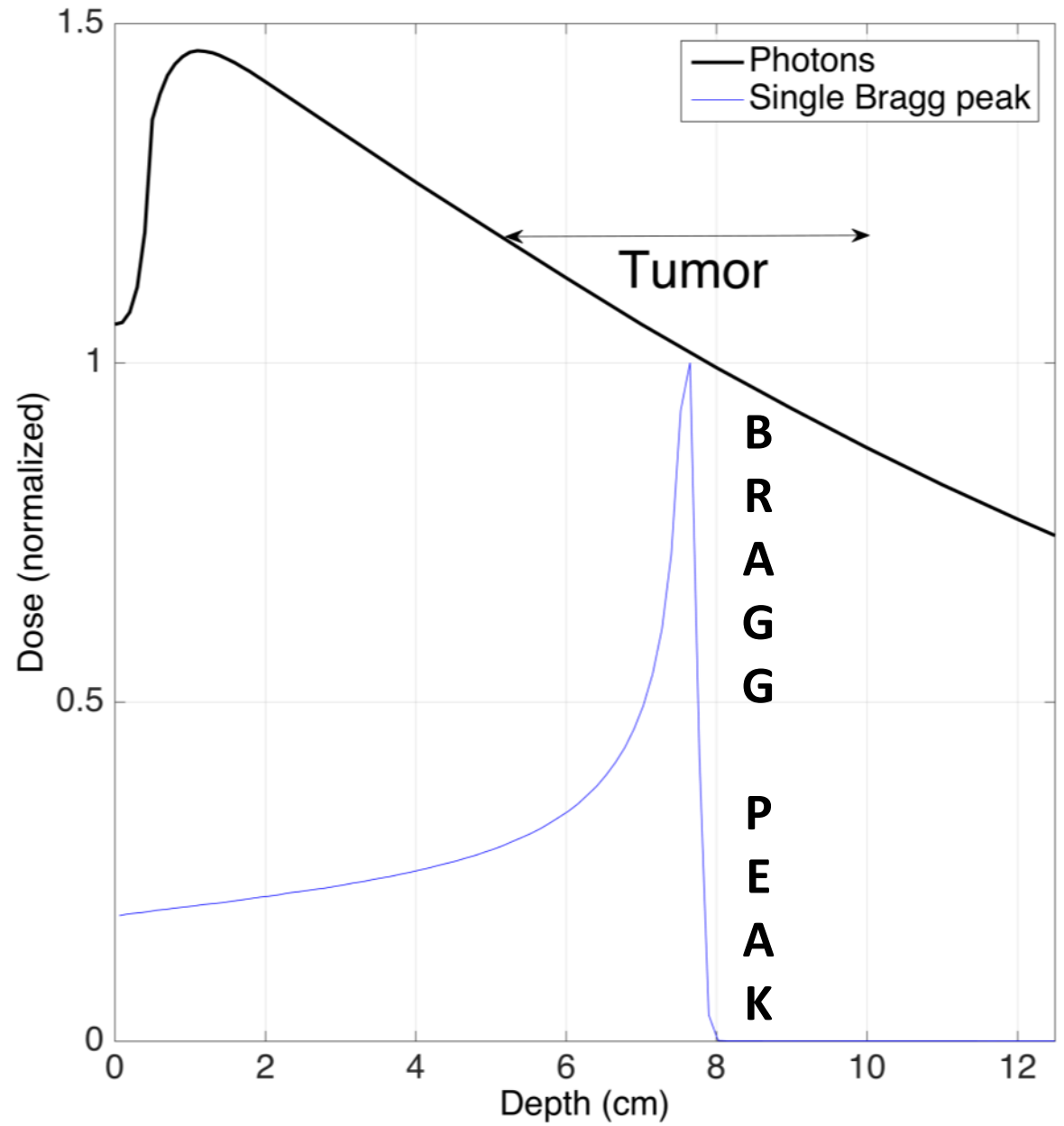
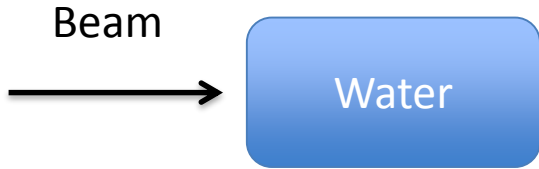


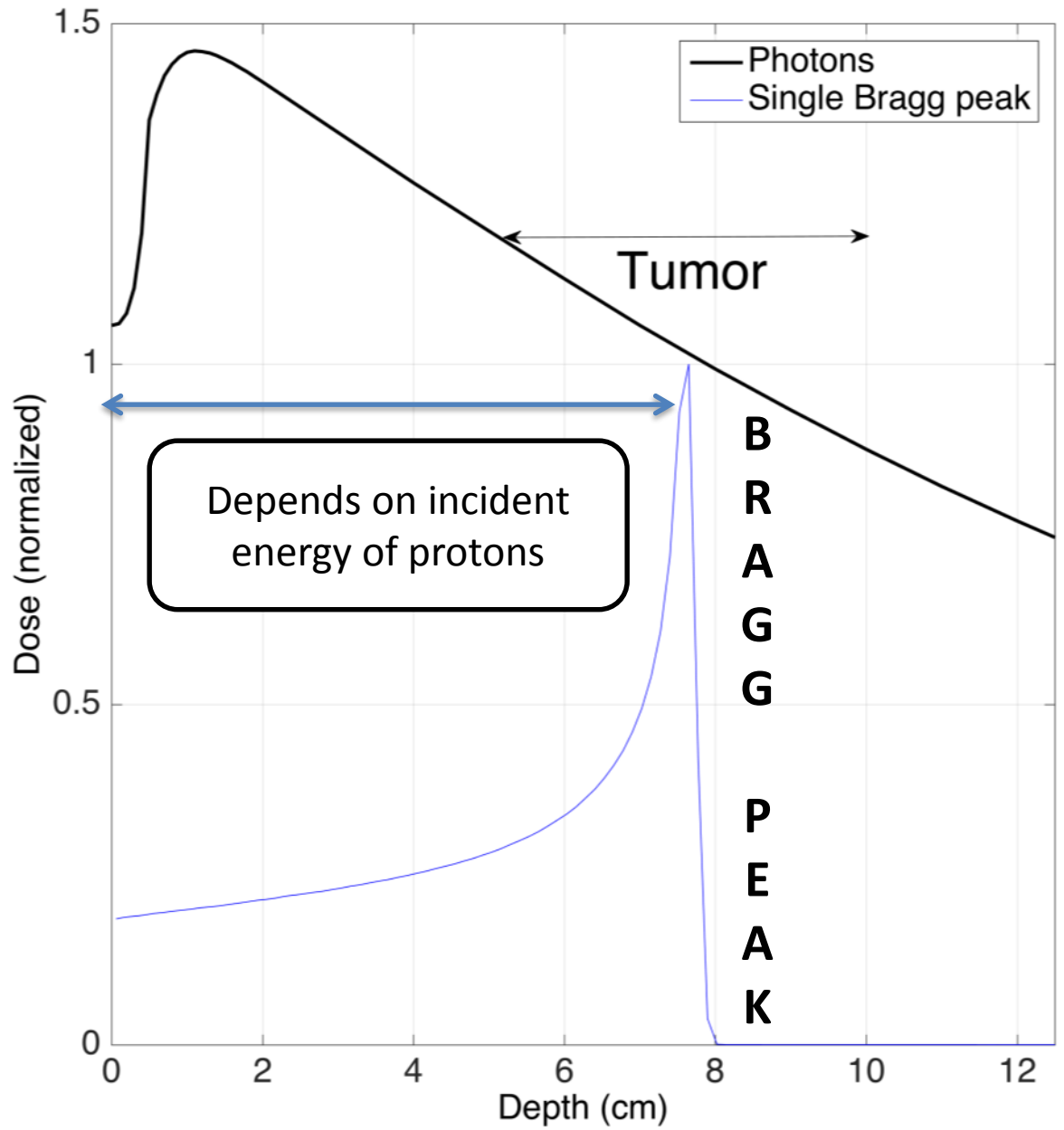
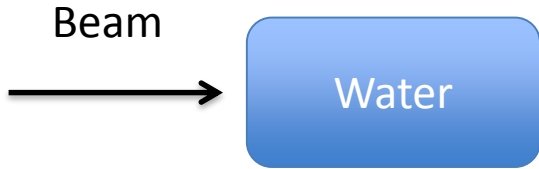
## Research beam line

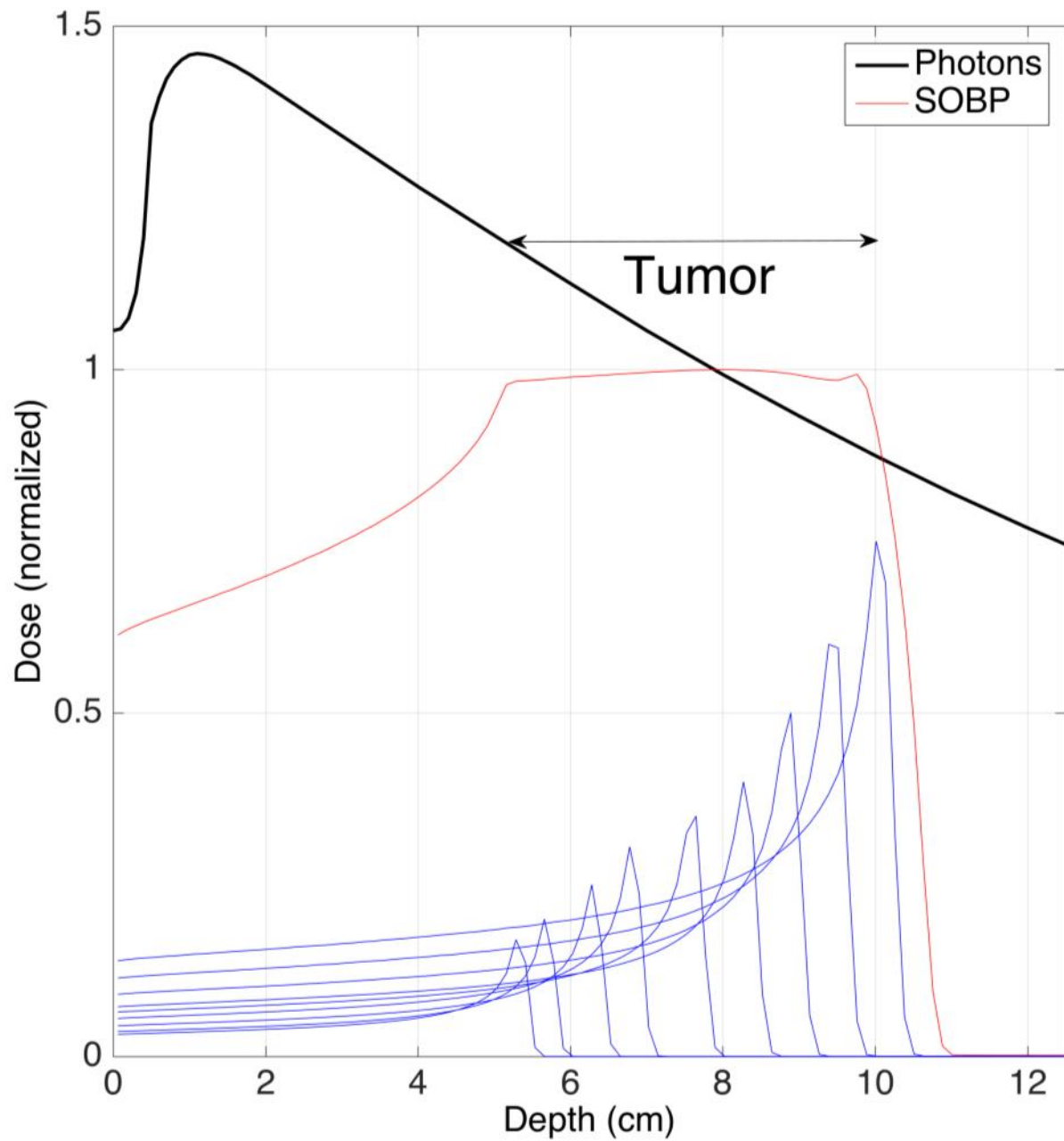




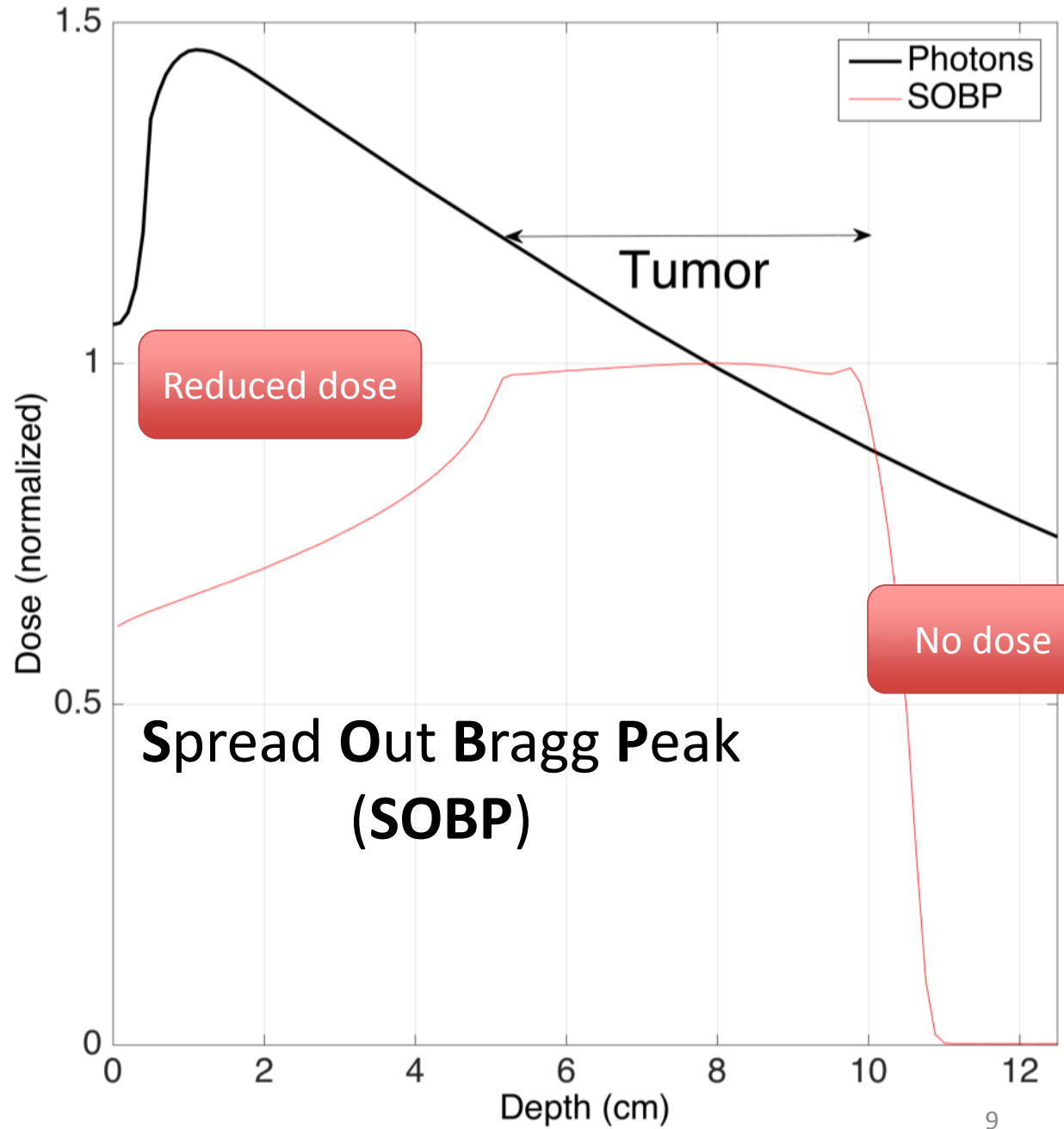
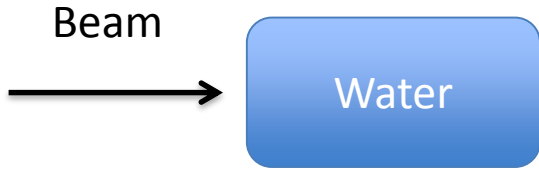




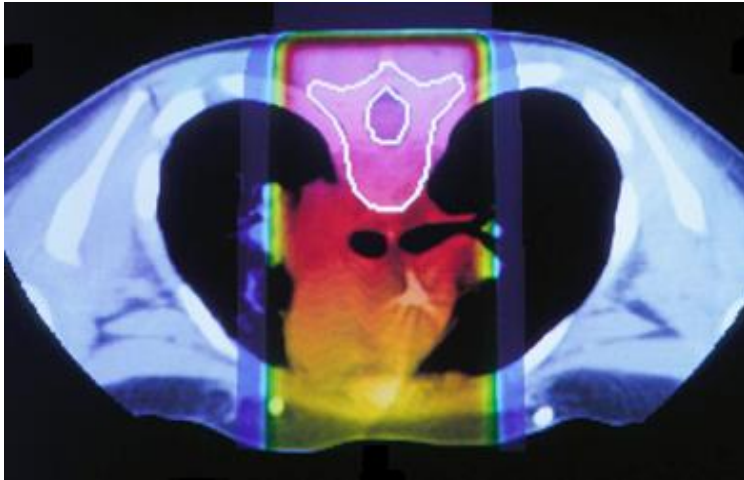




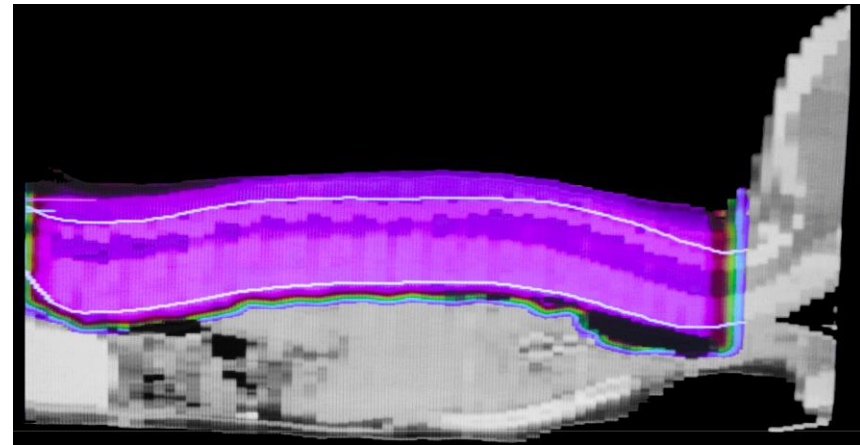
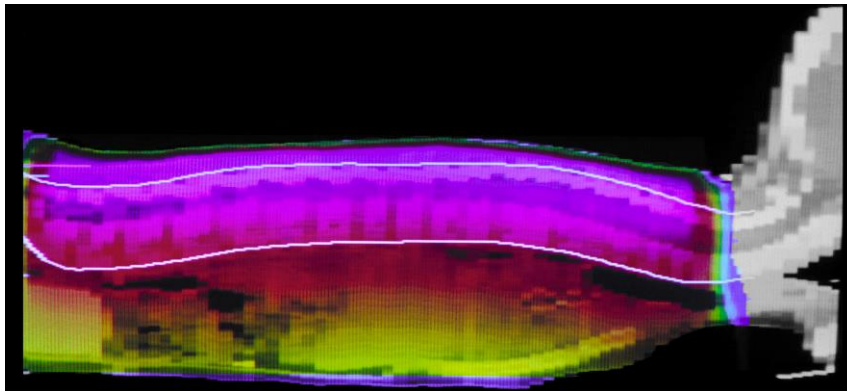
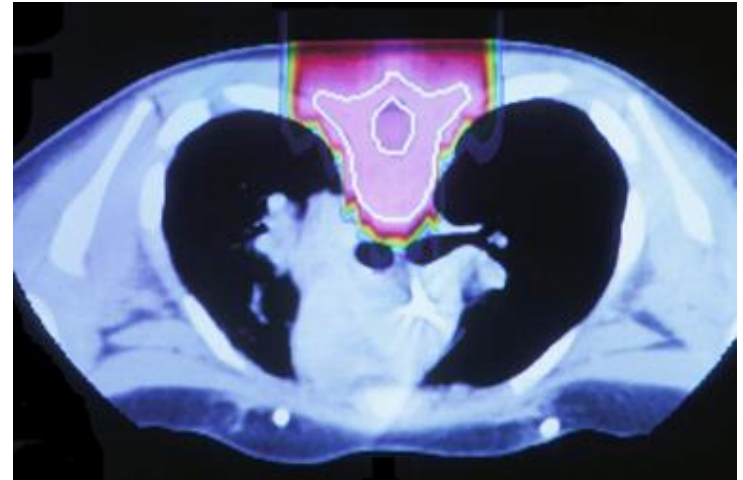


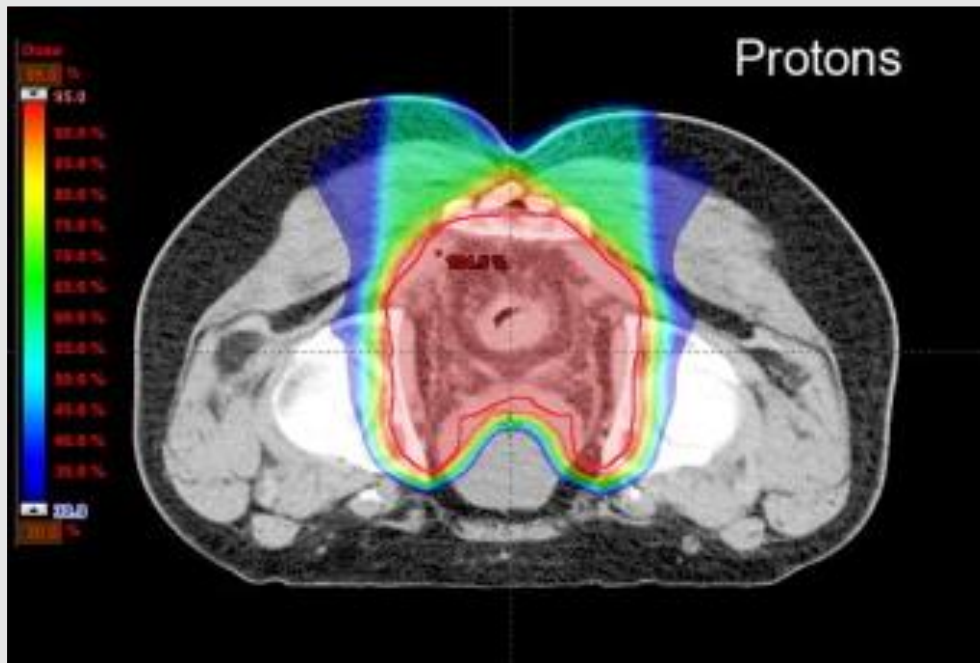
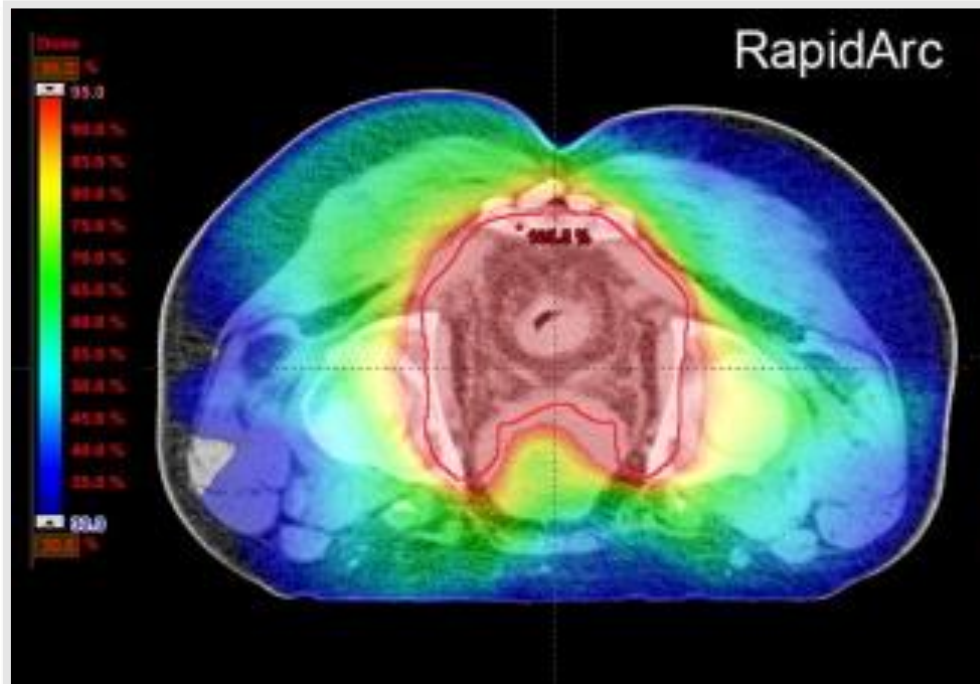


# Radiotherapy



# Proton therapy





**How do we DELIVER protons?**

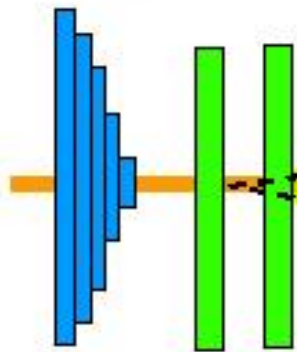
**Broad beam (double scattering)**

Pencil beam scanning

Energy modulation

Beam shaping

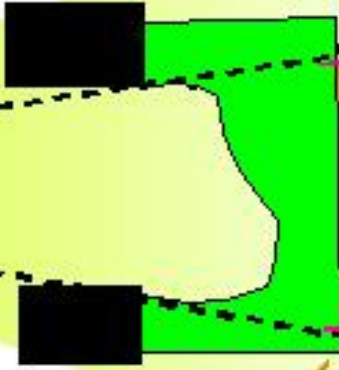
Range-shifter wheel



scatter foils

Scattering

collimator

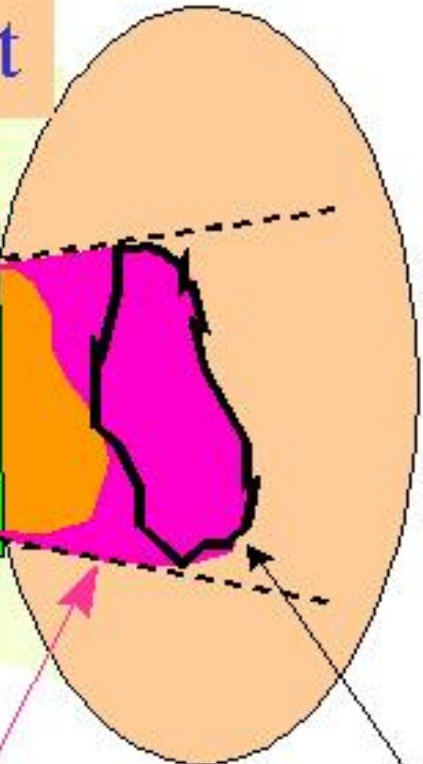


compensator

entrance dose

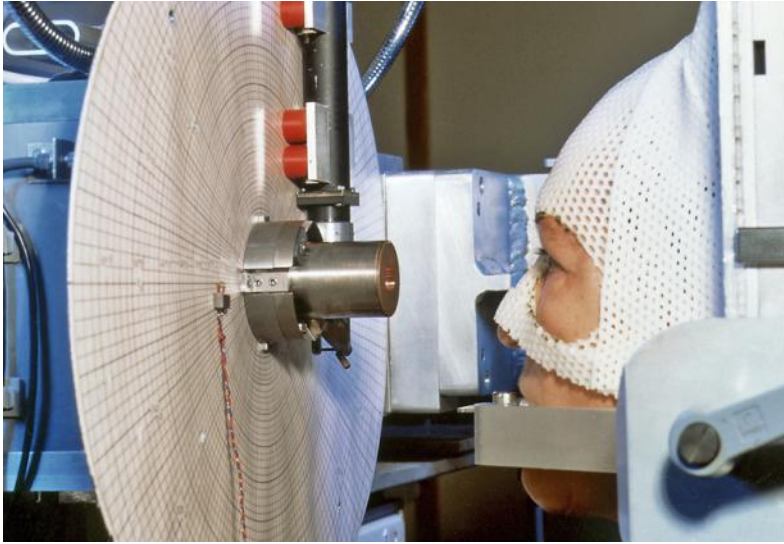
max dose

patient



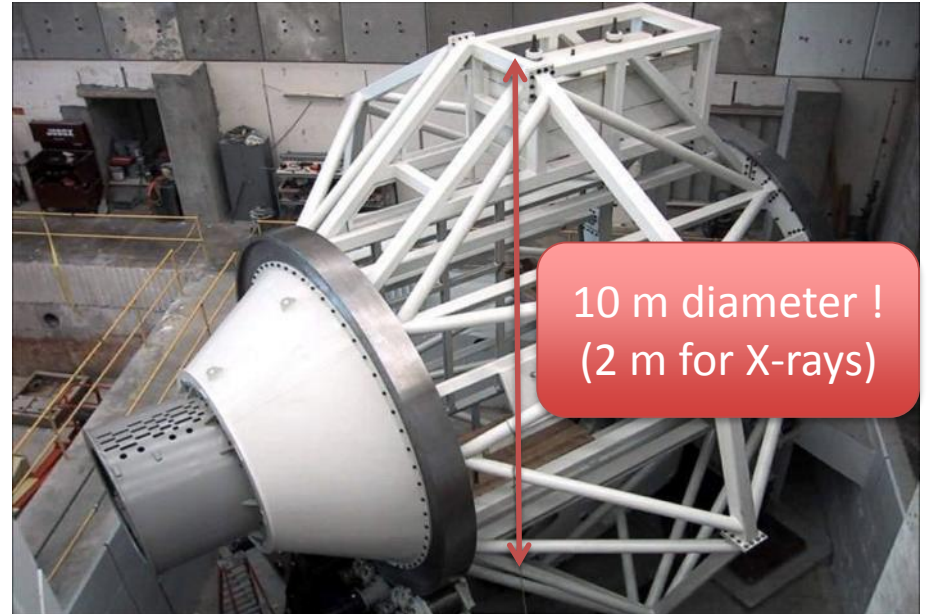
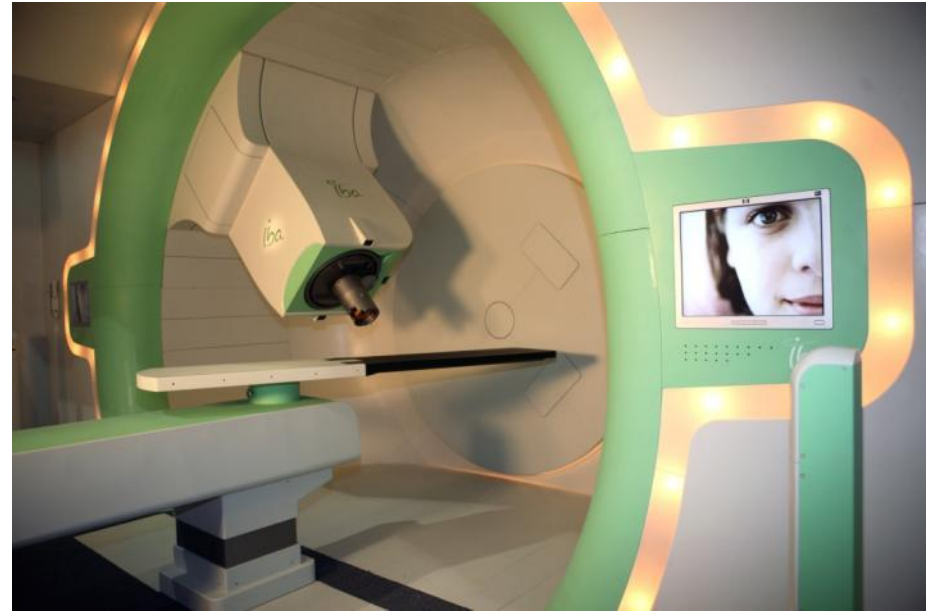
Target volume

# Fixed beam line



[http://www.psi.ch/ImageBoard/ig\\_p\\_1024x640%3E\\_ba192.007.jpg](http://www.psi.ch/ImageBoard/ig_p_1024x640%3E_ba192.007.jpg)

# Gantry



# How do we DELIVER protons?

Broad beam (double scattering)

**Pencil beam scanning**

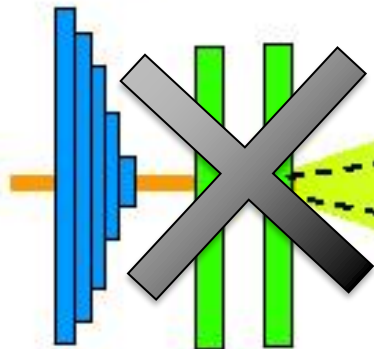
Energy modulation

Beam shaping

Range-shifter wheel

patient

collimator



scatter foils

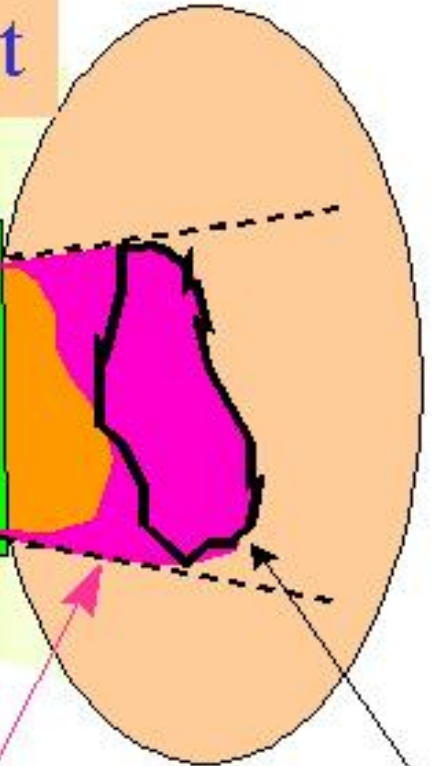
Scattering

compensator

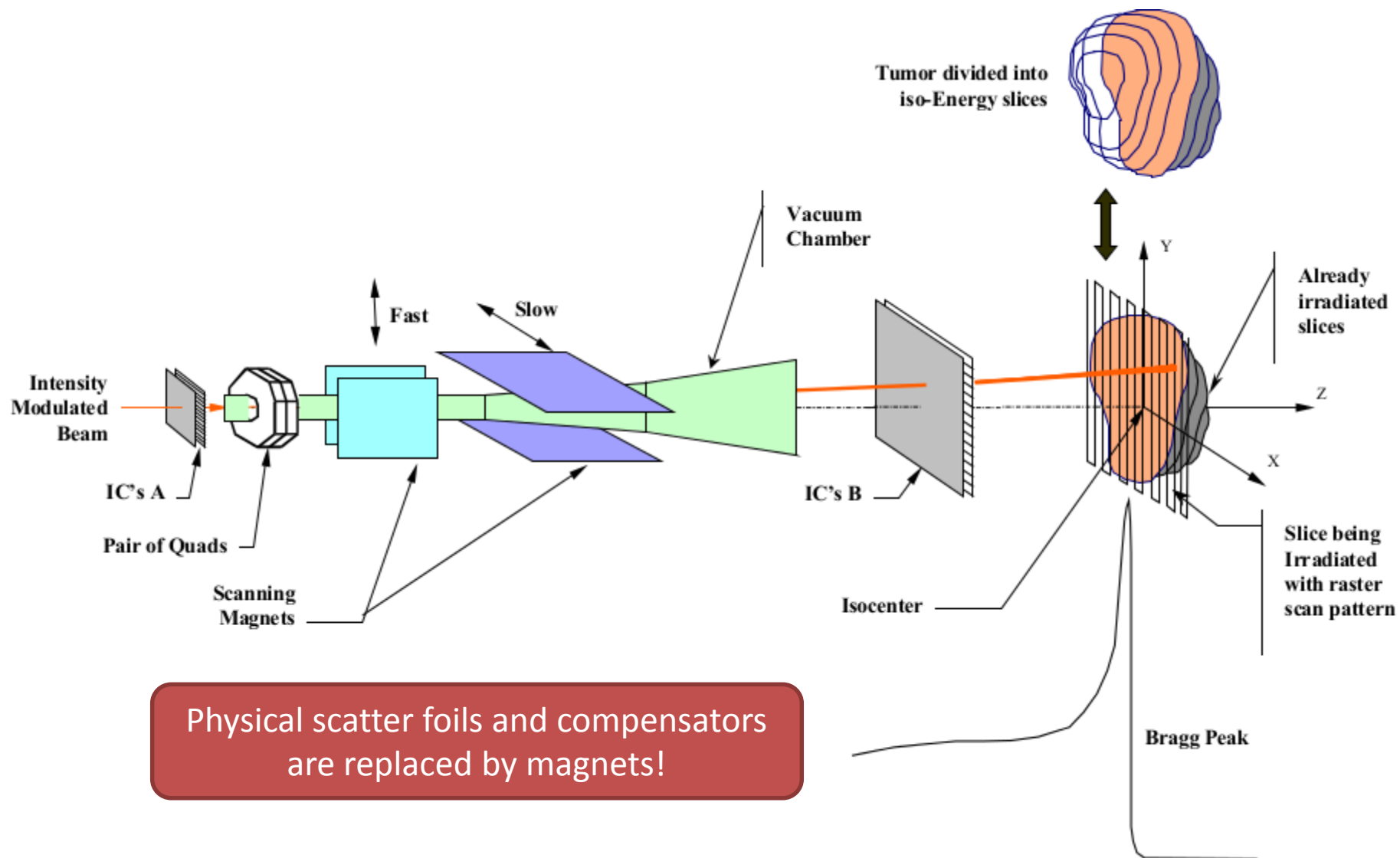
entrance dose

max dose

Target volume









# Generalities on treatment preparation and delivery workflow

Image acquisition



Manual contouring



Treatment optimization



Treatment validation



Treatment delivery



Follow-up

# Various imaging modalities

Image acquisition

Manual contouring

Treatment optimization

Treatment validation

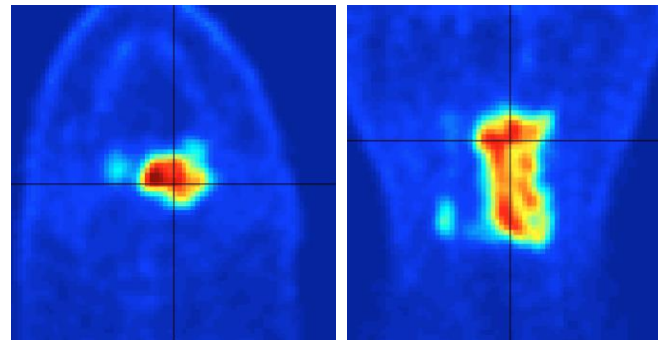
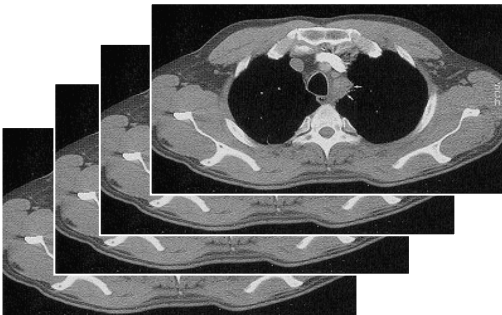
Treatment delivery

Follow-up

CT

PET

MRI



# Contouring of target volumes and organs-at-risk

Image acquisition



Manual contouring



Treatment optimization



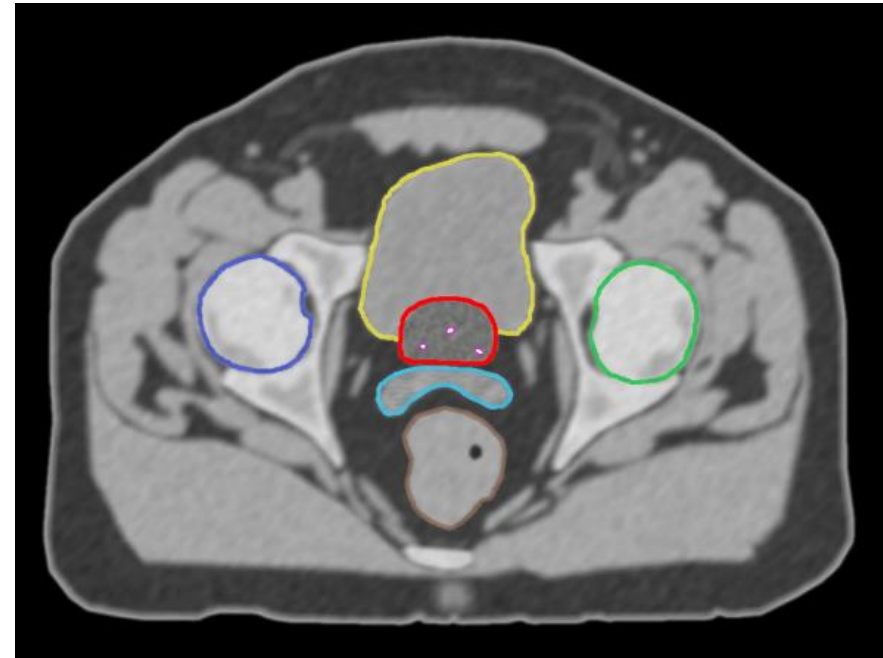
Treatment validation



Treatment delivery



Follow-up



# Treatment optimization

Image acquisition



Manual contouring



Treatment optimization



Treatment validation



Treatment delivery



Follow-up

RayStation - v3.7.0.47 - Prostate ASTRO Proton Prostate, Composite Planning\* - Not for Clinical Use

Patient Data Management Patient Modeling Plan Design Plan Optimization Plan Evaluation QA Preparation Fallback Planning Treatment Adaptation

Plan Setup 3D-CRT Beam Design Electron Beam Design Proton Beam Design Patient: Prostate ASTRO Proton Prostate Plan: Composite Planning Beam Set: IMRT Boost Beam Set Dose

34.20 Gy to 95% of dose at 95.00% volume in PTV Prescription fulfilled

PLAN PREPARATION DOSE COMPUTATION FINAL DOSE PRESCRIPTION

Treatment plan Plan: Composite Planning

Beam Sets:

Name	Machine	Fractions	Modality	Treatment technique
3D Plan	Varian 2100	25	Photons	3D-CRT
IMRT Boost	Varian 2100	19	Photons	SMLC

2D Beam set dose: IMRT Boost (Composite Planning, CT1) [Clinical: Collapsed Cone v2.3] Position: 12.73 -1.16 29.67 cm CT - HU Density: Dose: % of 34.20 Gy

3D Setup DRR Plan: Composite Planning / Beam set: IMRT Boost Position: 12.73 -1.16 29.67 cm % of 34.20 Gy

2D Beam set dose: IMRT Boost (Composite Planning, CT1) [Clinical: Collapsed Cone v2.3] Position: 8.11 12.52 0.32 cm CT - HU Density: Dose: % of 34.20 Gy

BEV DRR Weighted sum of energy (MeV) X1 X2 Y1 Y2

Beams Control points Jaw assignment Setup beams Beam Dose Specification Points

No.	Name	Isocenter [cm]			SSD [cm]	To surface	To skin	Energy [MV]	Gantry angle [deg]	Coll. angle [deg]	Couch angle [deg]	Number of segments	MU/fx	Bolus	Jaw max aperture [cm]			
		R-L	I-S	P-A											X1	X2	Y1	Y2
1	0	0.11	-1.48	-3.41	86.64	86.64	6	0.0	0.0	0.0	0.0	6	40.82	(None)	-4.96	4.98	-5.50	5.50
2	40	0.11	-1.48	-3.41	85.17	85.17	6	40.0	0.0	0.0	0.0	4	35.40	(None)	-5.00	5.50	-5.50	5.50
3	80	0.11	-1.48	-3.41	81.71	81.71	6	80.0	0.0	0.0	0.0	6	59.12	(None)	-4.85	4.65	-5.50	5.50
4	120	0.11	-1.48	-3.41	79.63	79.63	6	120.0	0.0	0.0	0.0	7	55.30	(None)	-4.84	4.62	-5.50	5.50
5	160	0.11	-1.48	-3.41	87.79	87.79	6	160.0	0.0	0.0	0.0	5	37.02	(None)	-4.82	4.93	-5.50	5.50
6	200	0.11	-1.48	-3.41	87.78	87.78	6	200.0	0.0	0.0	0.0	4	34.54	(None)	-5.50	5.00	-5.50	5.50
7	240	0.11	-1.48	-3.41	79.37	79.37	6	240.0	0.0	0.0	0.0	5	45.96	(None)	-4.90	4.83	-5.50	5.50

# How to assess the clinical quality of the dose distribution?

Image acquisition

Manual contouring

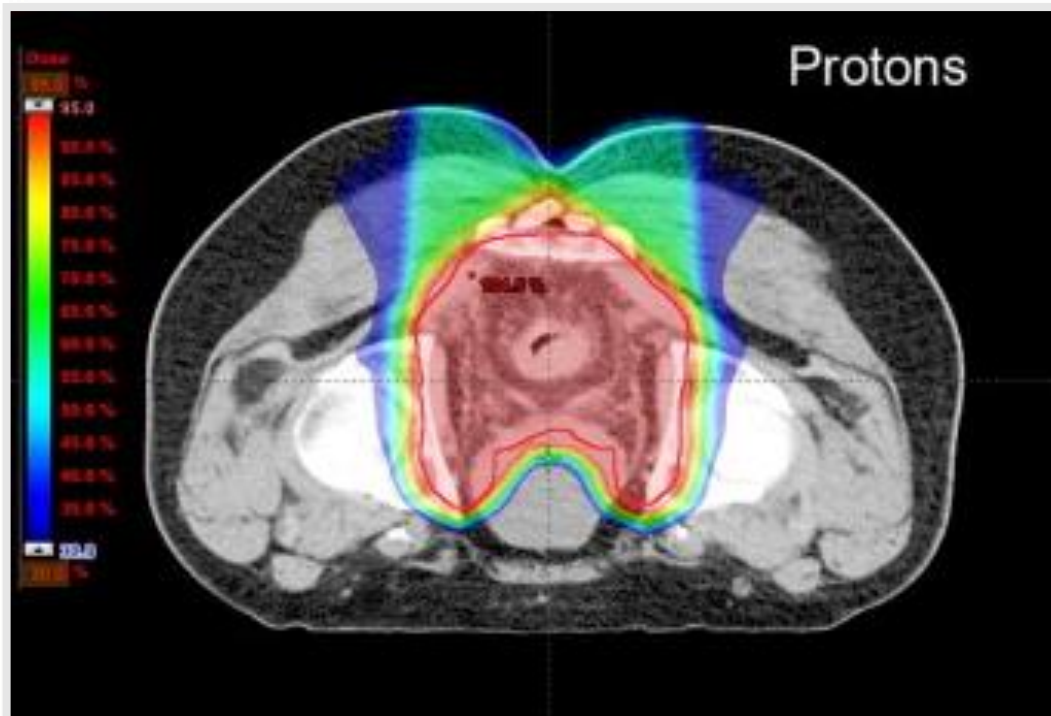
Treatment optimization

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

# How to assess the clinical quality of the dose distribution?

Image acquisition

Manual contouring

Treatment optimization

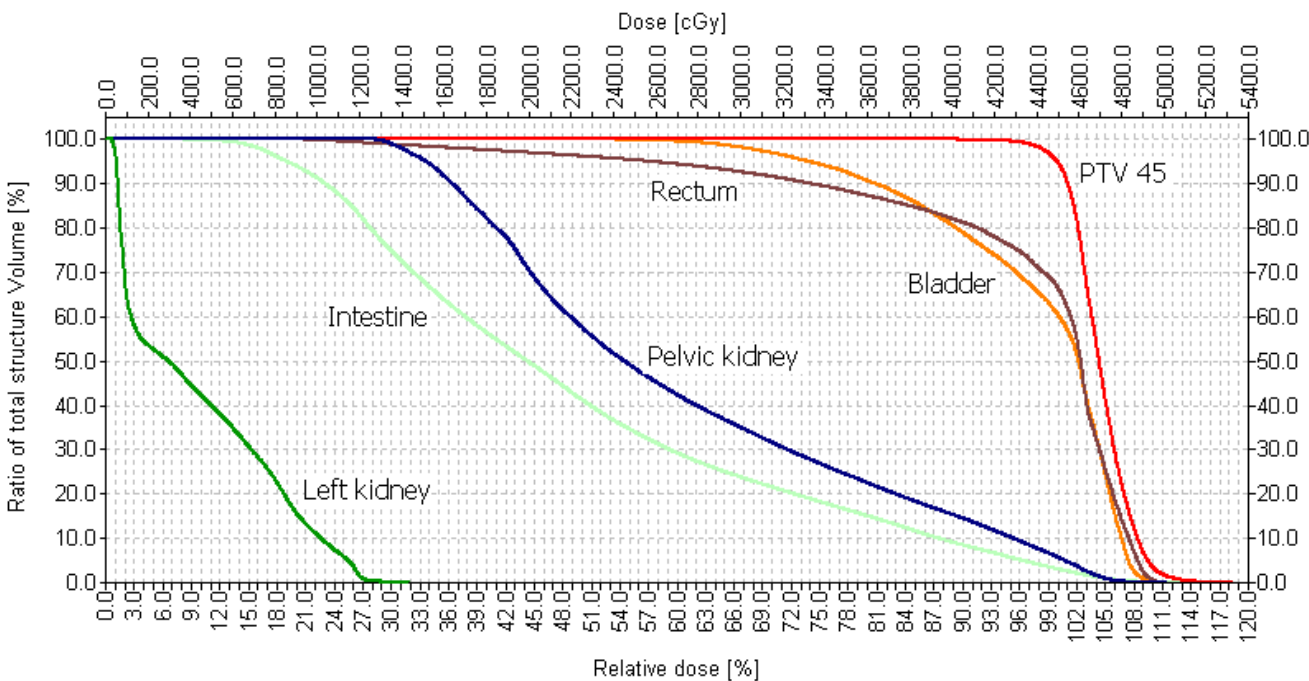
Treatment validation

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



# Treatment optimization: manual versus computerized

Image acquisition

Manual contouring

Treatment optimization

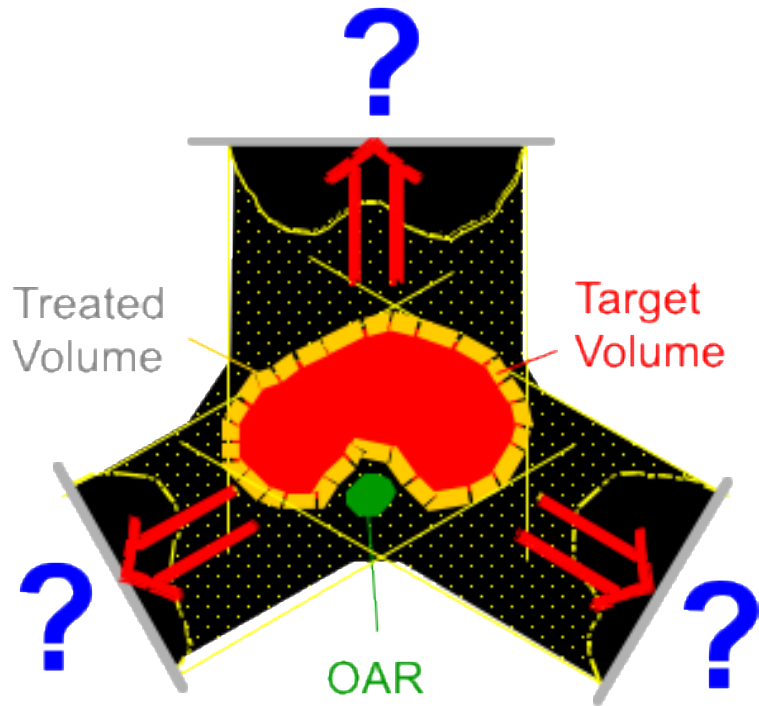
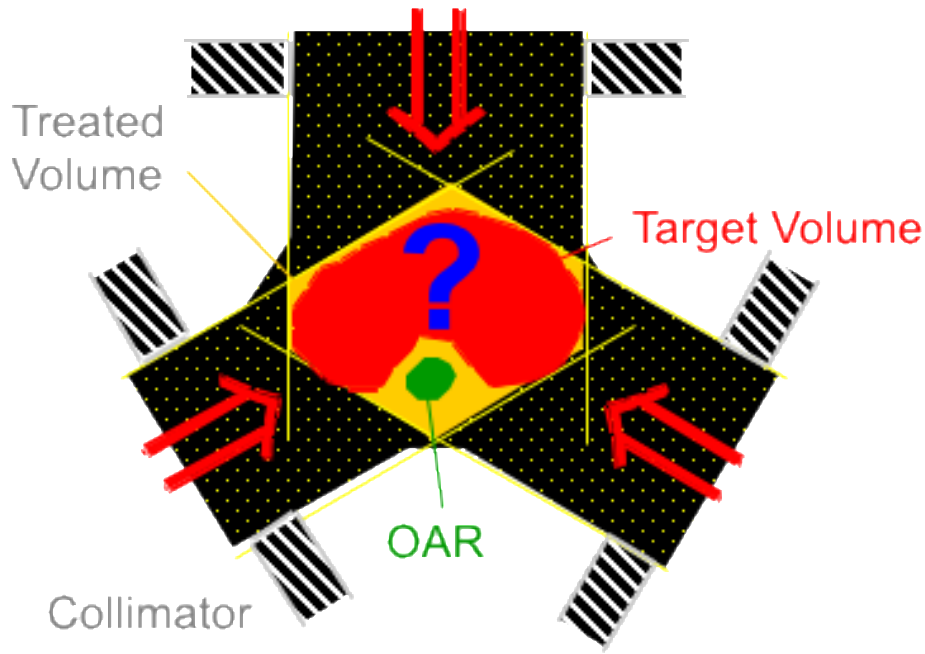
Treatment validation

Treatment delivery

Follow-up

## Forward Planning

## Inverse Planning



Human iterative improvement ...  
based on human experience

Computerized process

# Inverse treatment planning

Image acquisition

Manual contouring

Treatment optimization

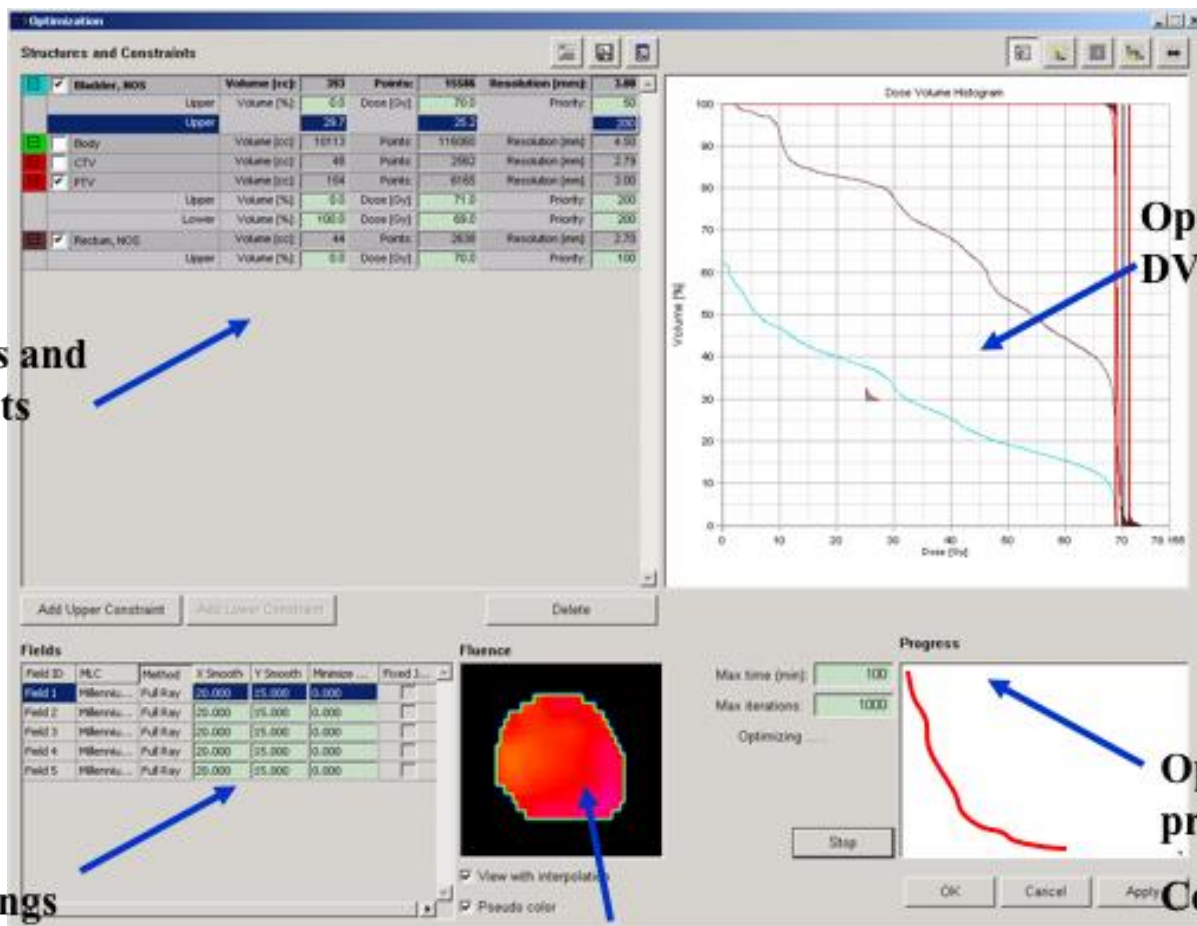
Treatment validation

Treatment delivery

Follow-up

Structures and Constraints

Field settings

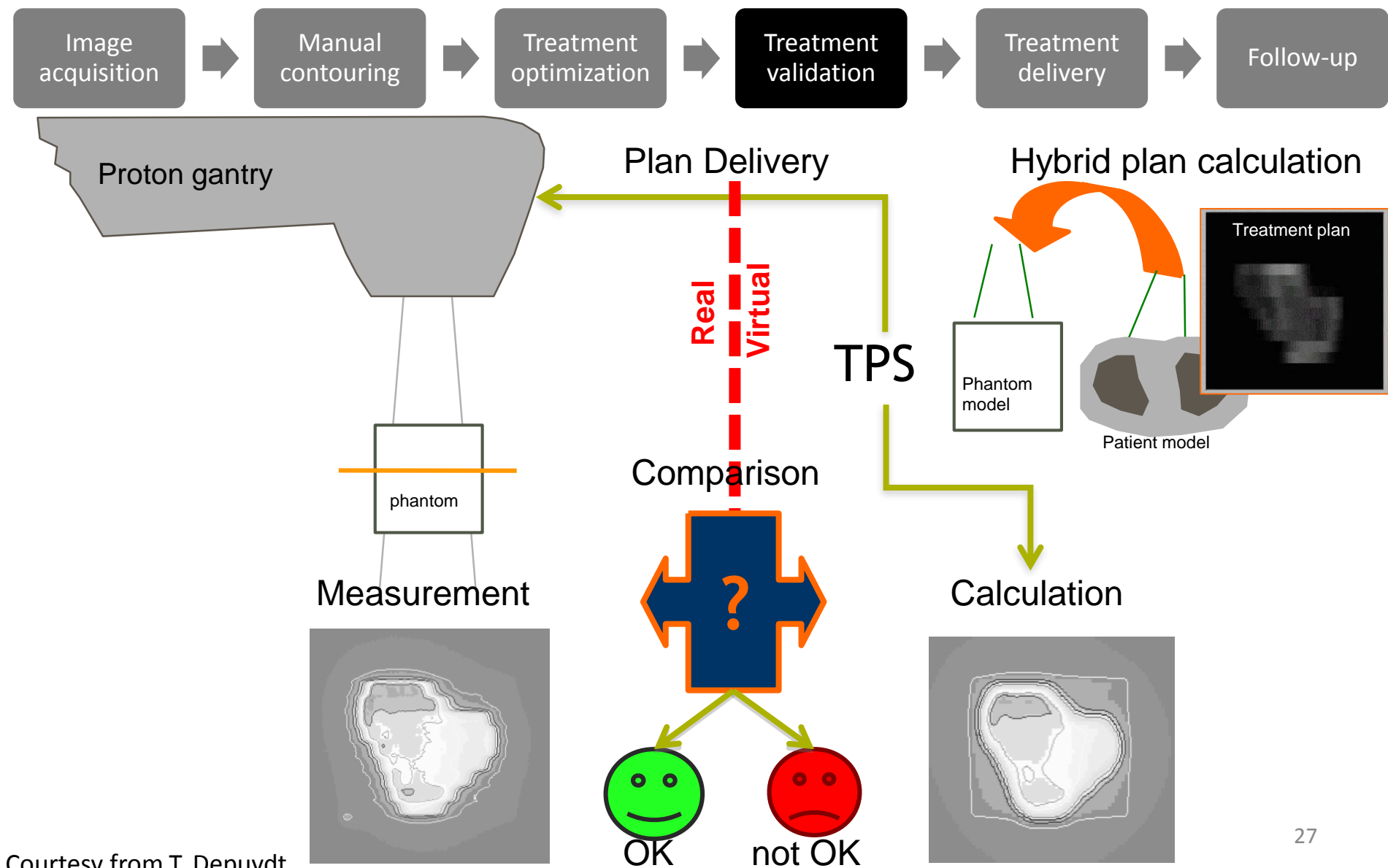


Optimization DVHs

Optimization progress, Cost-function

Field Intensity Map

# Treatment preparation and delivery workflow



# Treatment preparation and delivery workflow

Image acquisition

Manual contouring

Treatment optimization

Treatment validation

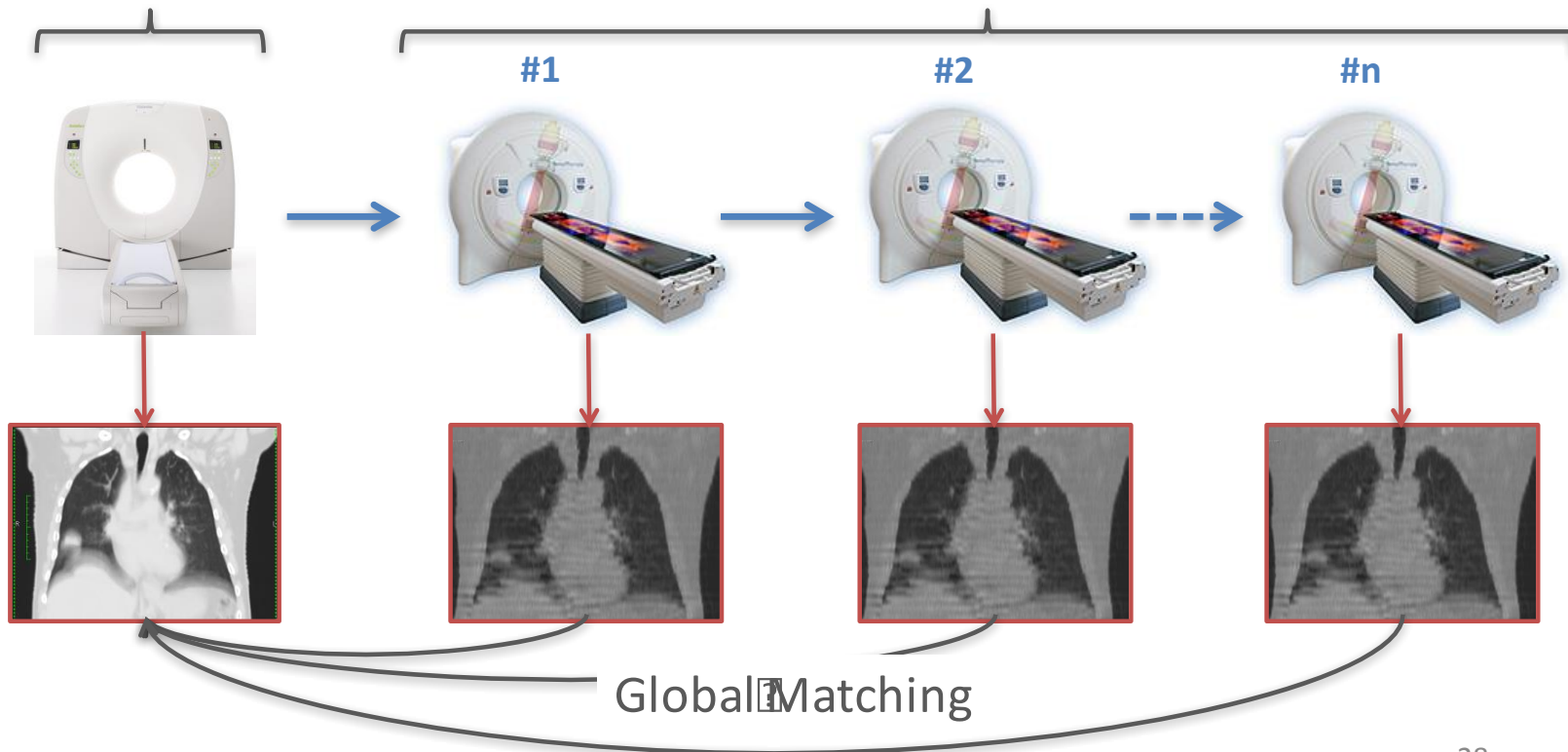
Treatment delivery

Follow-up

Positioning

Simulation

Treatment



# Treatment preparation and delivery workflow

Image acquisition

Manual contouring

Treatment optimization

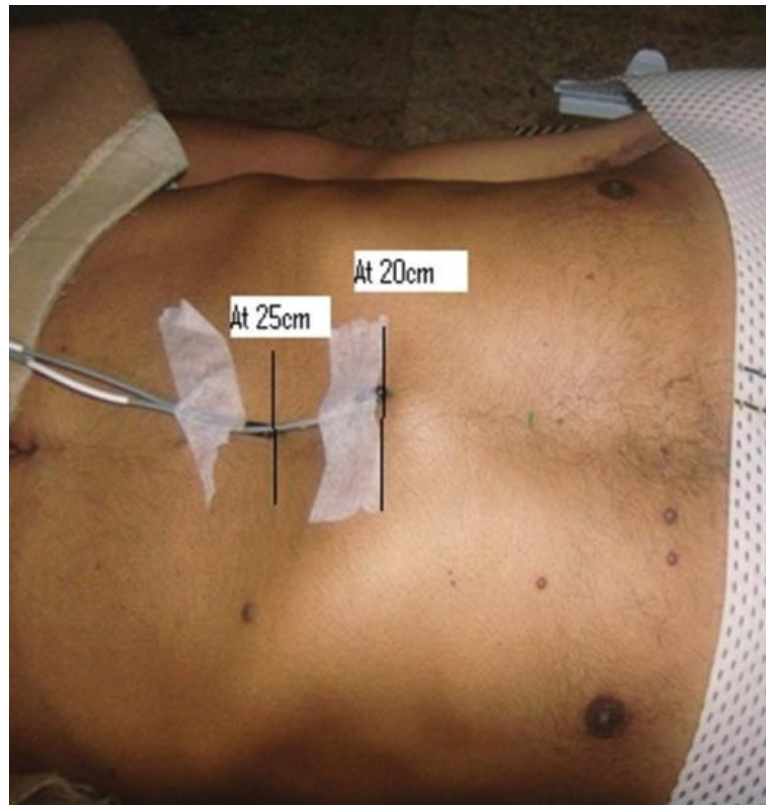
Treatment validation

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

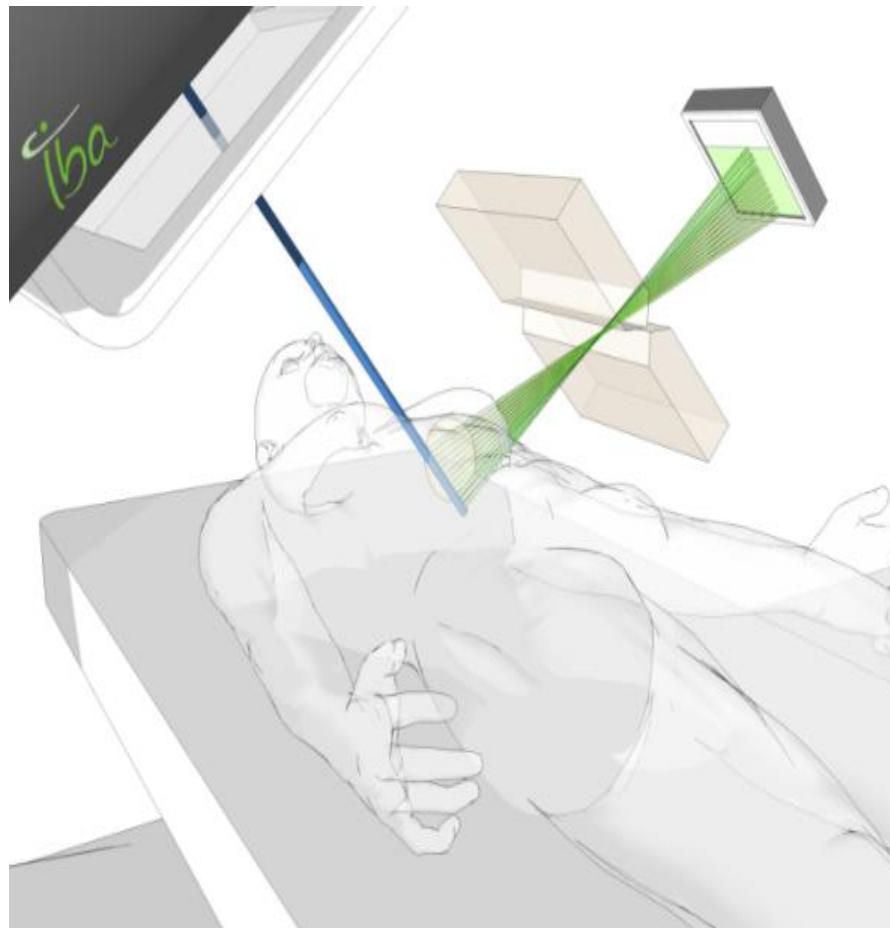
Treatment optimization

Treatment validation

Treatment delivery

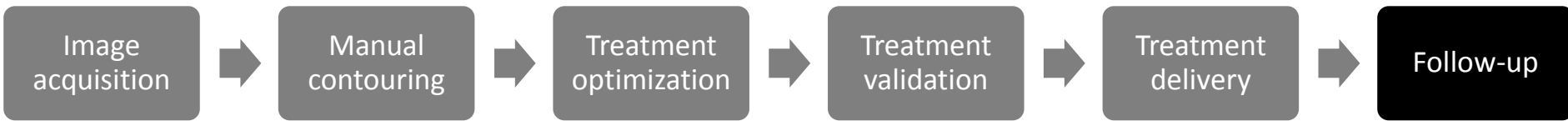
Follow-up

Range verification



Prompt gamma imaging

# Treatment follow-up



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

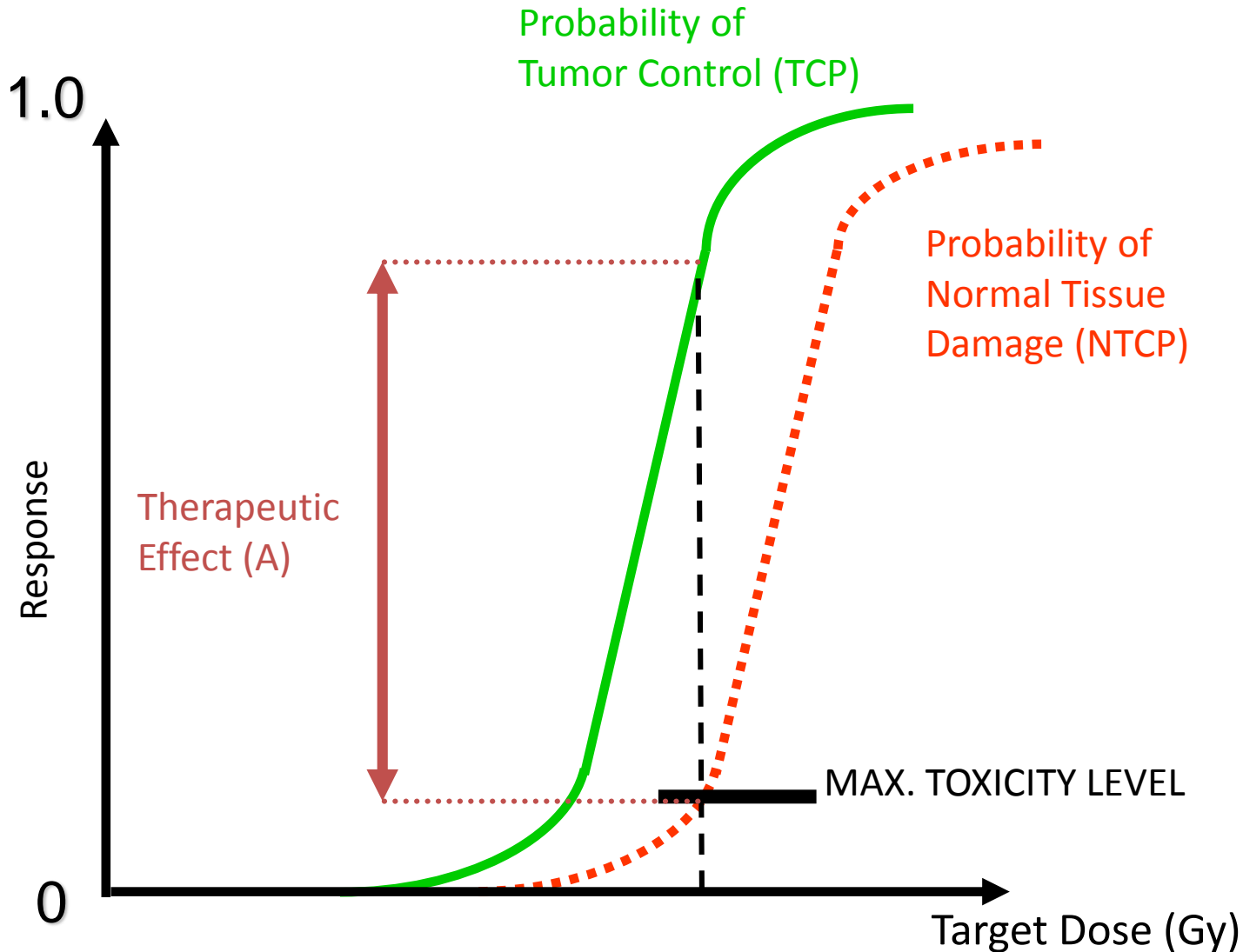


# Treatment plan optimization

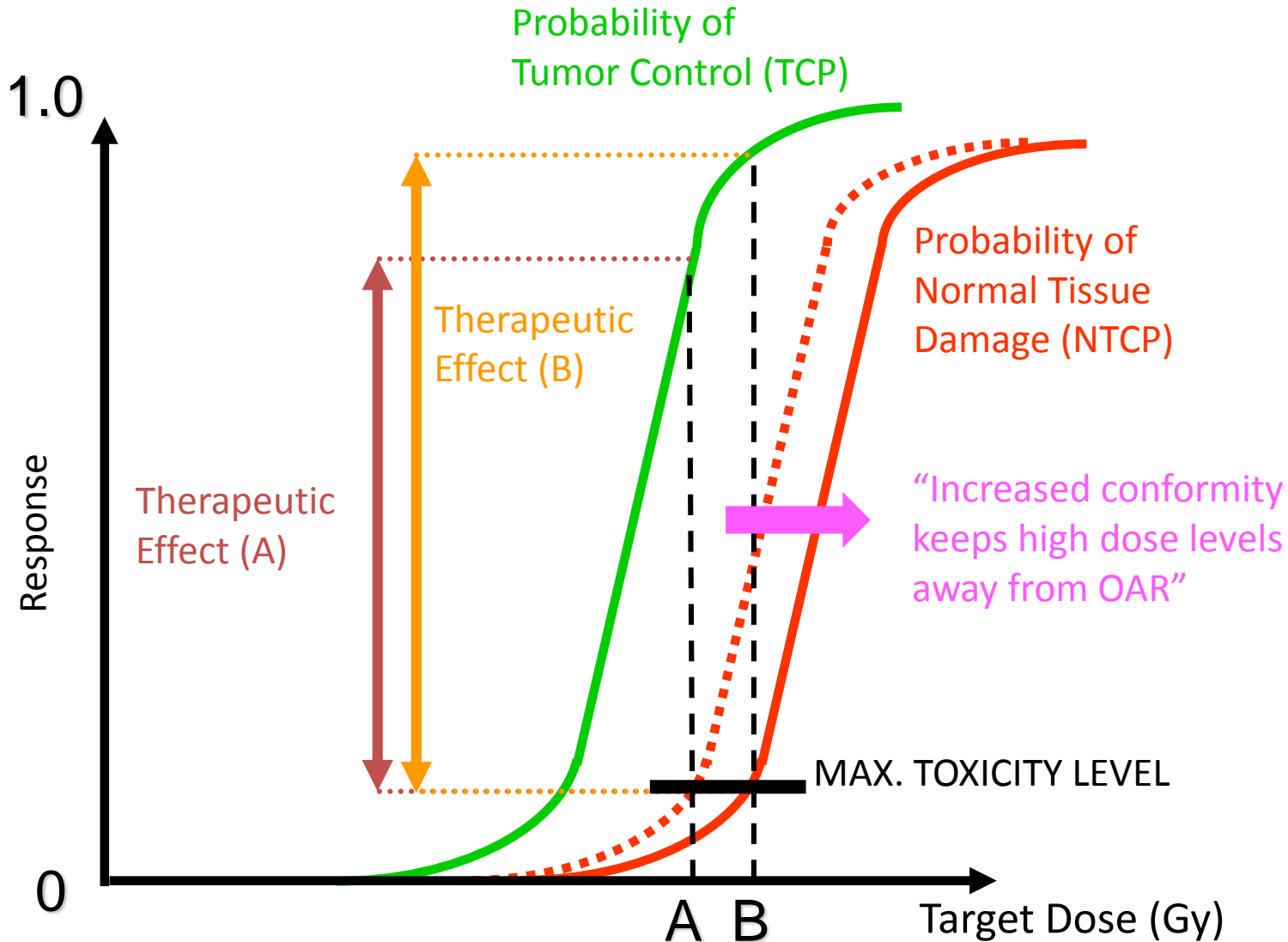
## Objectives

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

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

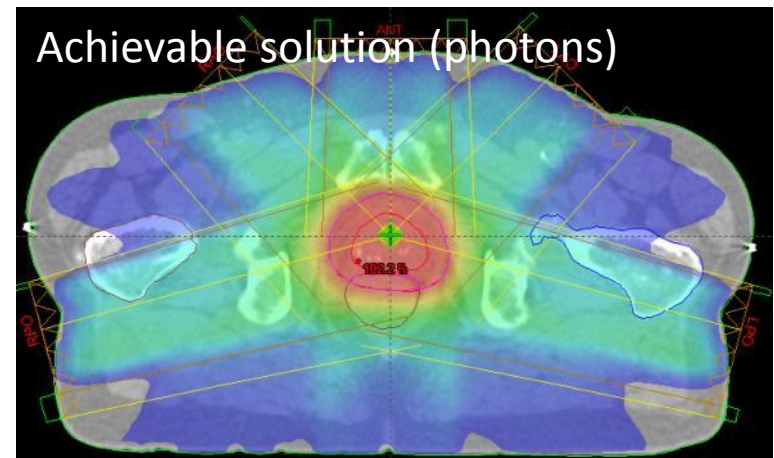
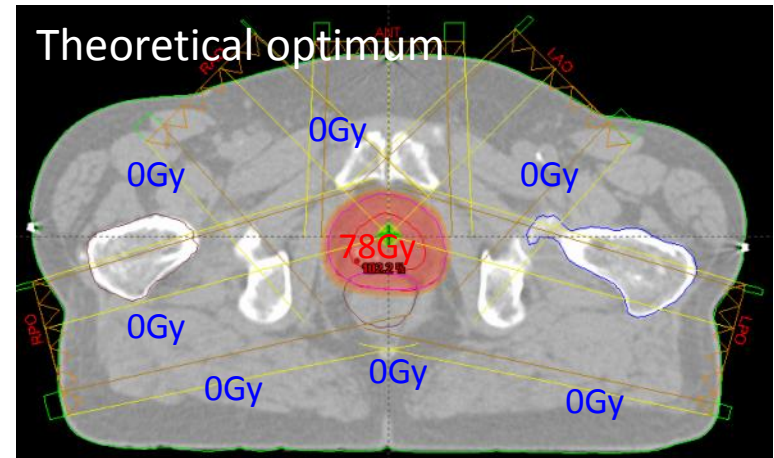


# Best trade-off between target coverage and organs-at-risk sparing



# The inverse problem

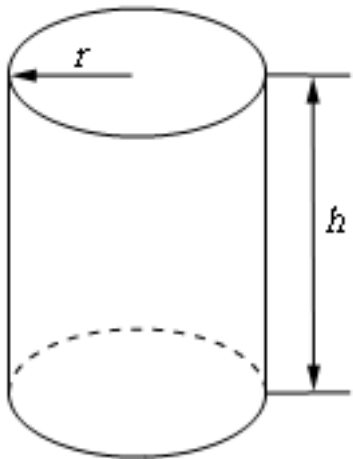
- The ideal dose distribution might be unreachable ...
- So, the best clinical result might not be possible
- So, compromise ...  
**(with OPTIMIZATION)**
- Try and get the best approximation to the ideal dose distribution
- Define treatment goals mathematically with a function whose minimum corresponds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



# 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.”*



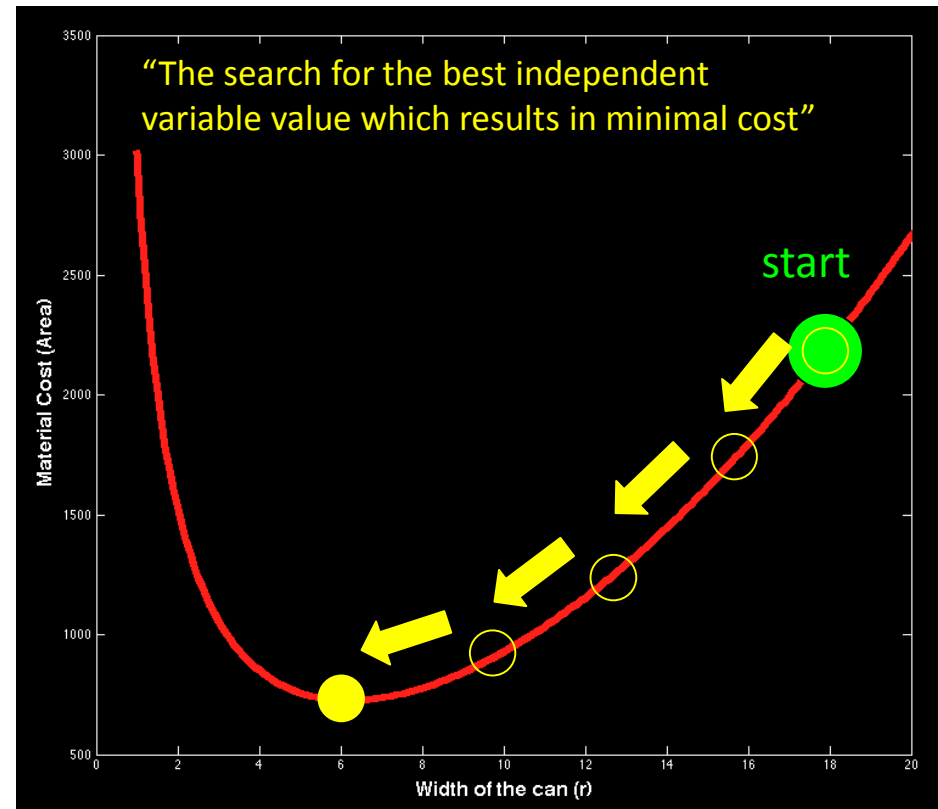
$$V = (\pi r^2)(h) = \pi r^2 h$$

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

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

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

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



# 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”*

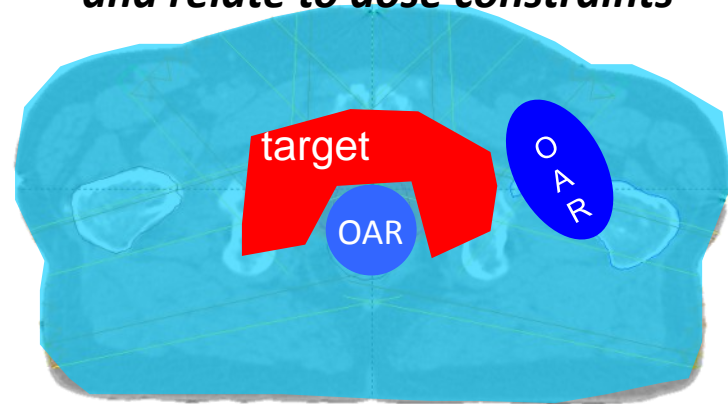
### Physical dose

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

### Biological effect

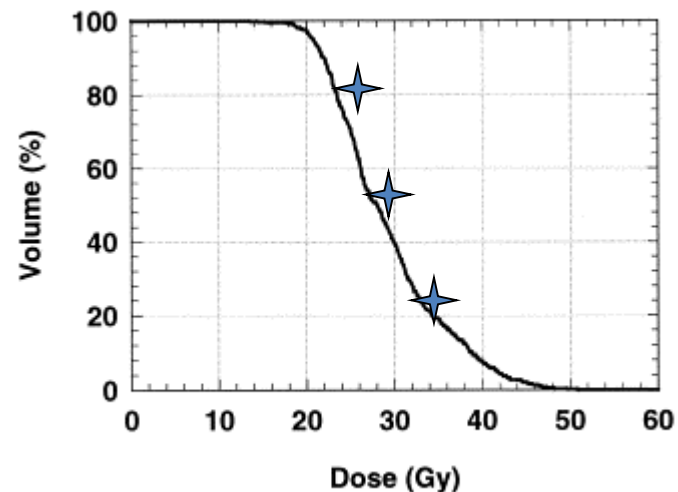
- TCP, NTCP
- EUD
- ...

*“Subdivide into different preferably non-overlapping volumes and relate to dose constraints”*



Desired/limiting dose

### DVH constraints



# Cost function

**“Combining all sometimes competing goals in one cost function ...”**

$\beta$  is the relative weight factor

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

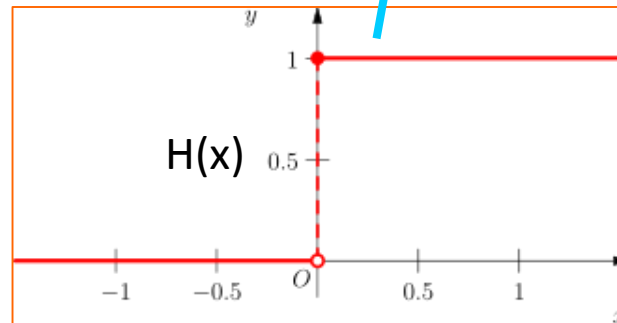
Penalty for not having uniform dose  $d_0$   
(optimising uniformity in target)

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

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

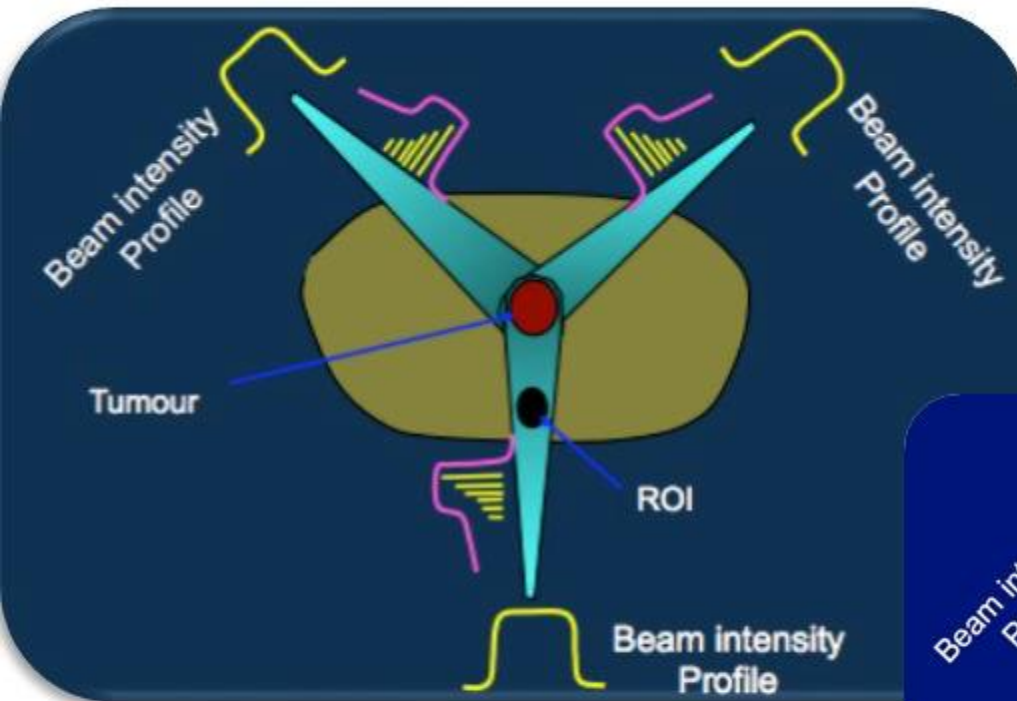
$$\beta_{OAR2} \frac{1}{n_{OAR2}} \sum_{i \in OAR2} H(d_i - d_0)(d_i - d_0)$$

Penalty for dose above “tolerance dose  $d_0$ ” in OAR (keeping max dose below  $d_0$ )

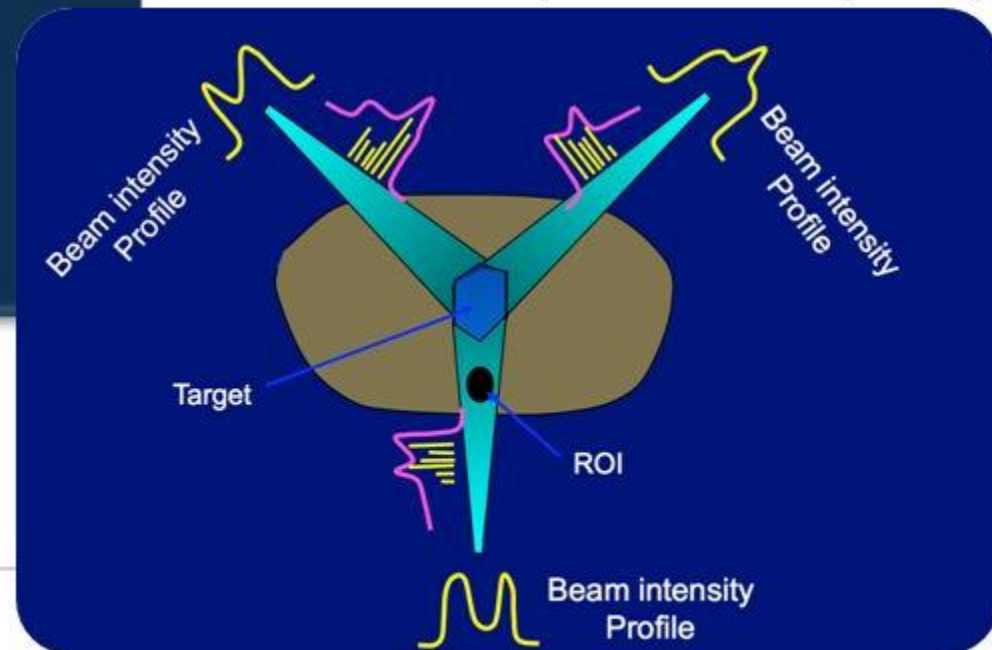


# Optimization of spot weights

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

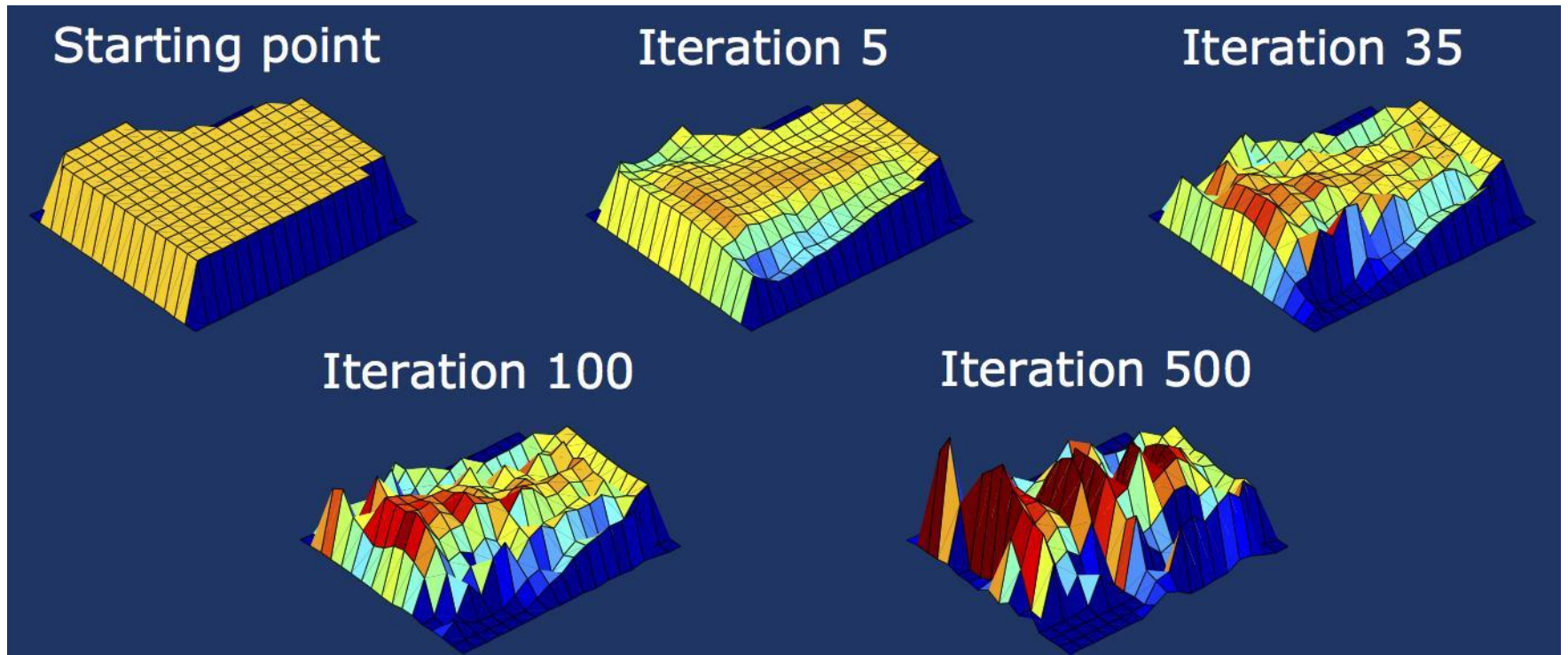


*Pencil Beam Scanning – Multi Field Optimization (MFO)*

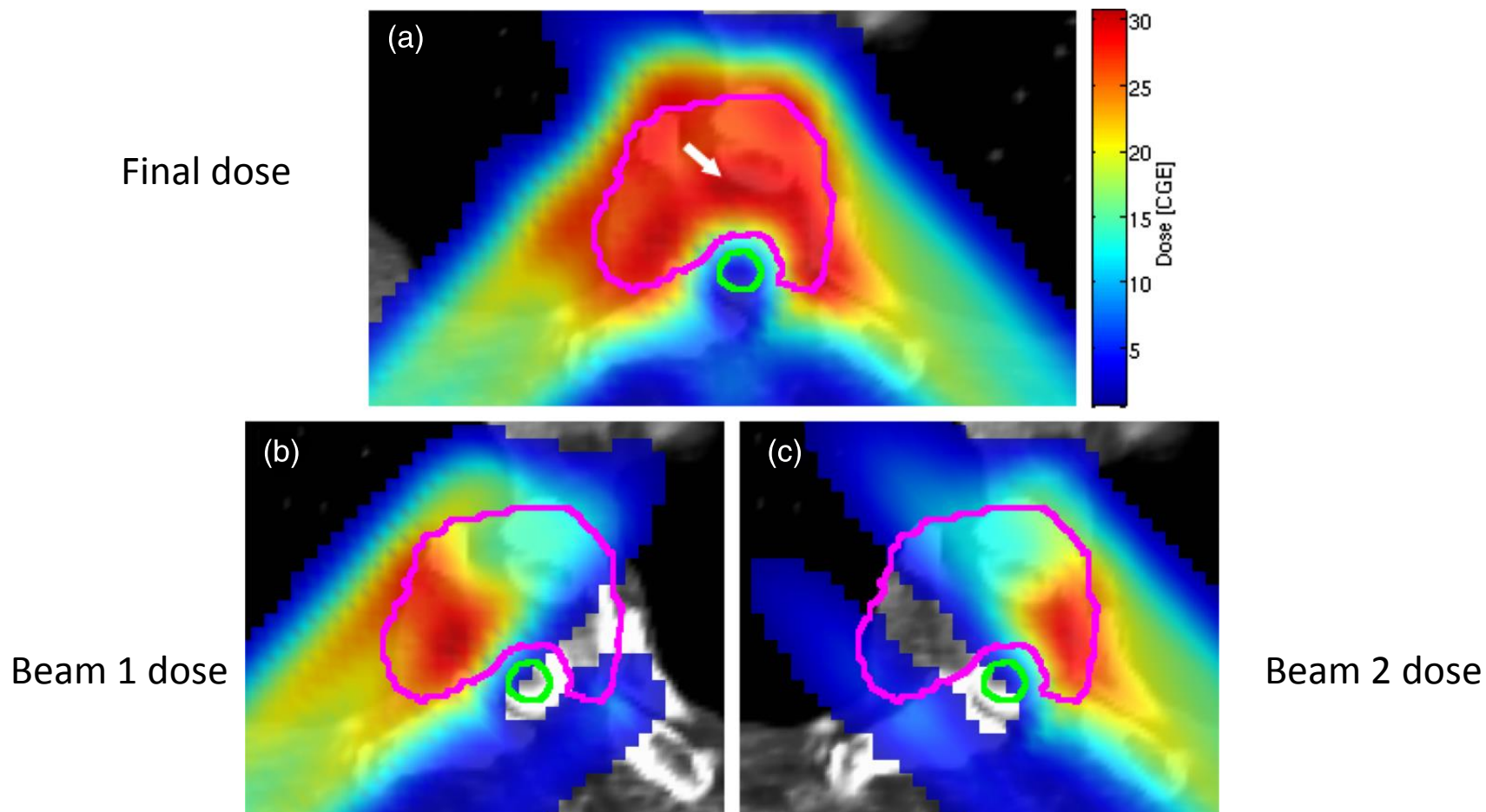




# Optimization of spot weights



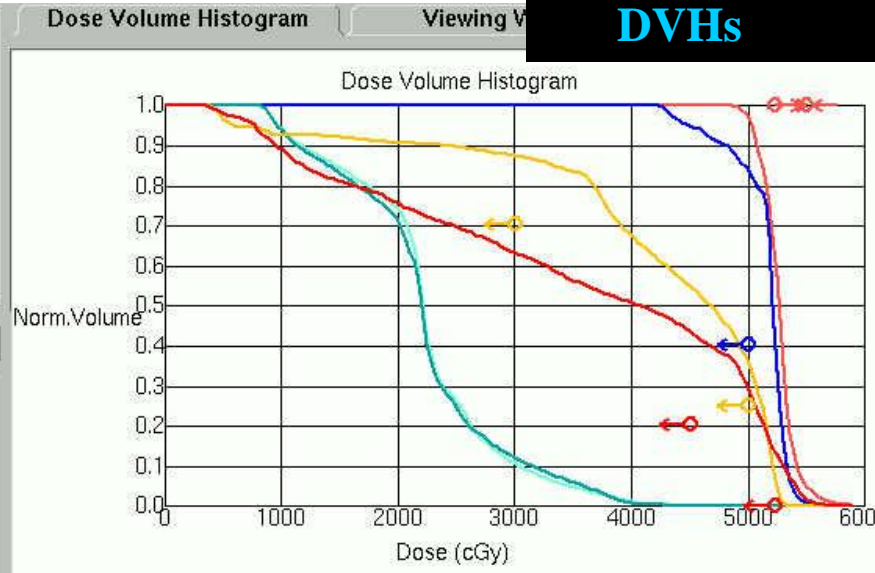
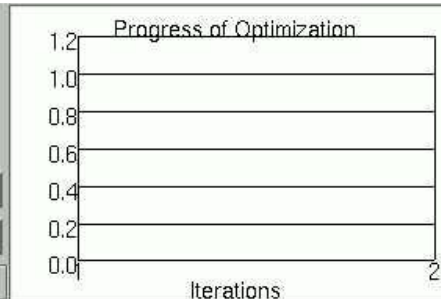
# Optimization of spot weights



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

# Optimization DVHs

Optimization progress, Cost-function



Field Intensity Map



Structures and Constraints

ROI	Type	Constrain	Target cGy	% Volume	% Variation	Weight	Objective Value	a	gEUD
AIPTVs	Uniform Dose		5500			1	0.00267438		
Rectum-PTVs	Max Dose		5225			1	1.35472e-07		
Rectum	Max DVH		3000	70		1	0.00820967		
Rectum	Max DVH		5000	25		1	2.39142e-05		
Bladder-PTVs	Max Dose		5225			1	0.0001509		
Bladder	Max DVH		5000	40		1	0.00055784		
Total_Bowel	Max Dose		5225			1	0.000151849		
Total_Bowel	Max DVH		4500	20		1	0.00226715		
AIPTVs	Min Dose		5225			1	0.000255507		

Highest cost

Change of weights  
change the  
optimisation

The screenshot displays a radiotherapy optimization software interface. At the top left, a 'Progress of Optimization' graph shows the objective value decreasing from approximately 0.0185 to 0.0155 over 50 iterations. The top right shows a 'Dose Volume Histogram' (DVH) with 'Norm. Volume' on the y-axis (0.0 to 1.0) and 'Dose (cGy)' on the x-axis (0 to 6000). Multiple colored curves represent different constraints, with red circles and blue diamonds marking specific points. The bottom section is a table of constraints with columns for ROI, Type, Constrain, Target cGy, % Volume, % Variation, Weight, Objective Value, a, and gEUD. A red arrow points from the text 'Change of weights' to the 'Weight' column of the second row. Another red arrow points from the text 'Add a constraint' to the 'Weight' column of the last row.

ROI	Type	Constrain	Target cGy	% Volume	% Variation	Weight	Objective Value	a	gEUD
AllPTVs	Uniform Dose	<input type="checkbox"/>	5500			50	0.0111425		
Pectum	Max Dose	<input type="checkbox"/>	5225			50	0.00100769		
Pectum	Max DVH	<input type="checkbox"/>	3000	70		1	8.33593e-06		
Pectum	Max DVH	<input type="checkbox"/>	5000	25		1	1.40611e-05		
Bladder-PTVs	Max Dose	<input type="checkbox"/>	5225			1	0.000154987		
Bladder	Max DVH	<input type="checkbox"/>	5000	40		10	0.000495085		
Total_Bowel	Max Dose	<input type="checkbox"/>	5225			50	0.00167087		
Total_Bowel	Max DVH	<input type="checkbox"/>	4500	20		1	0.000557206		
Bladder	Max DVH	<input type="checkbox"/>	4000	80		10	0.000686764		

Composite objective value: 0.0157375    Recompute Values

Add a  
constraint

# This is all nice but...

Image acquisition

Manual contouring

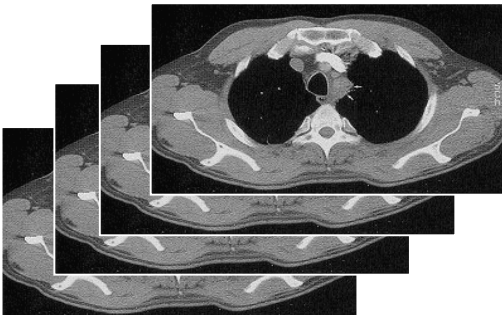
Treatment optimization

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

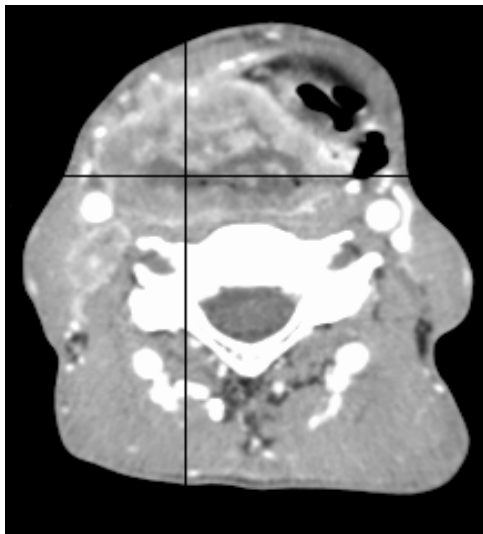
Manual contouring

Treatment optimization

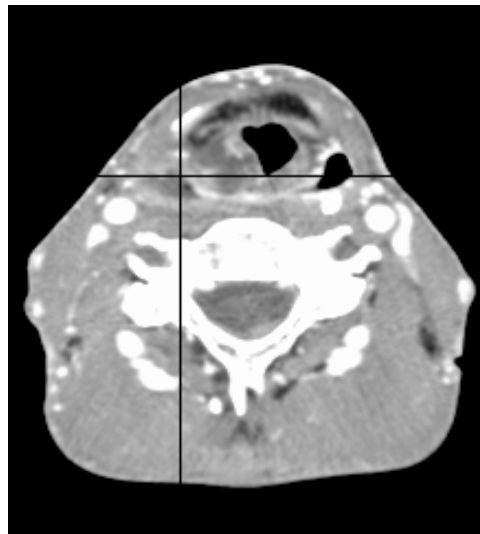
Treatment validation

Treatment delivery

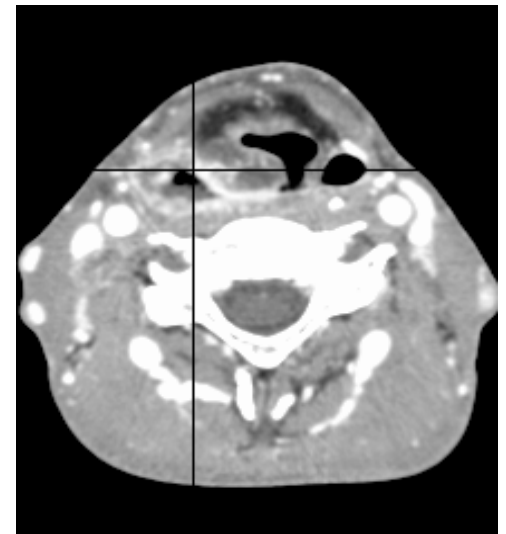
Follow-up



**Pre-RT**



**Week 3**



**Week 5**

# Breathing

Image acquisition

Manual contouring

Treatment optimization

Treatment validation

Treatment delivery

Follow-up

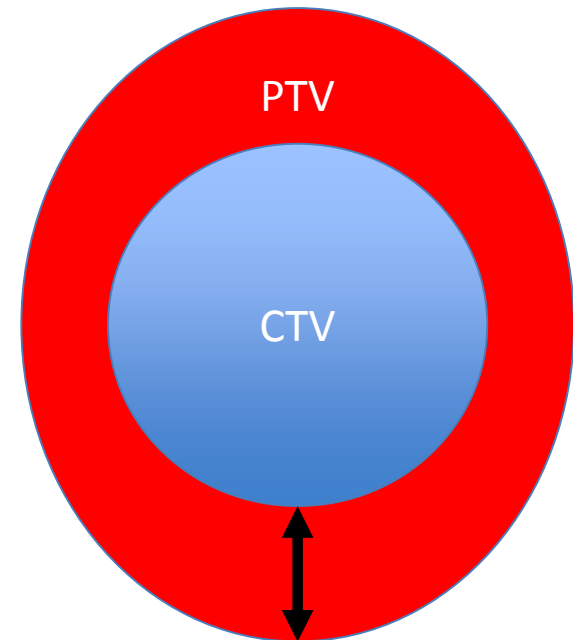


# How to ensure that the target is covered *despite* geometric uncertainties?

To make sure we irradiate the Clinical Target Volume...



We irradiate a larger volume, the Planning Target Volume



PTV safety margin



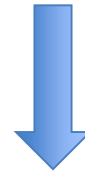
## CTV-PTV margin?

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

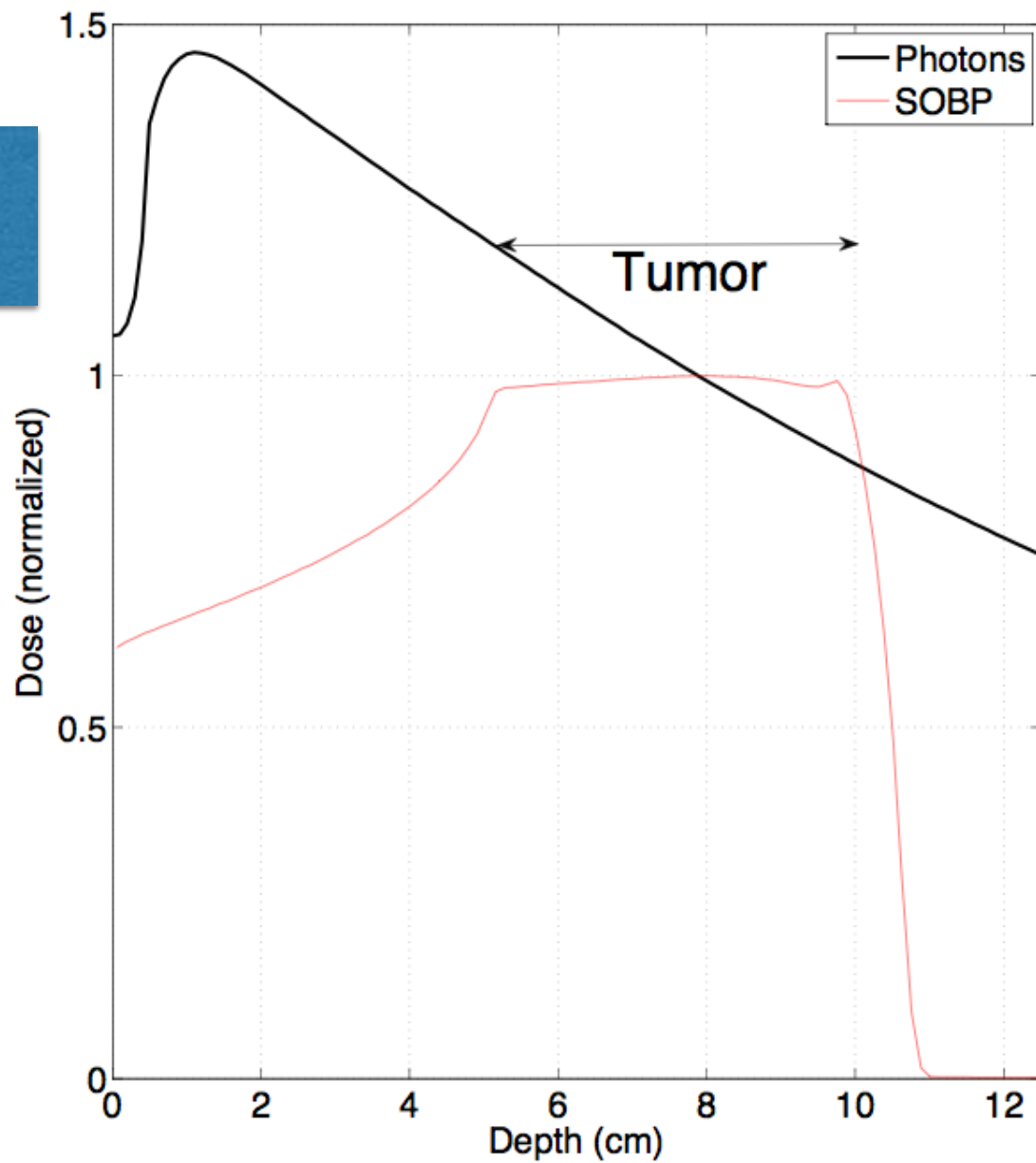
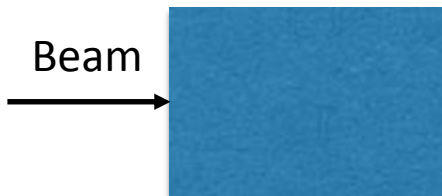
Systematic errors

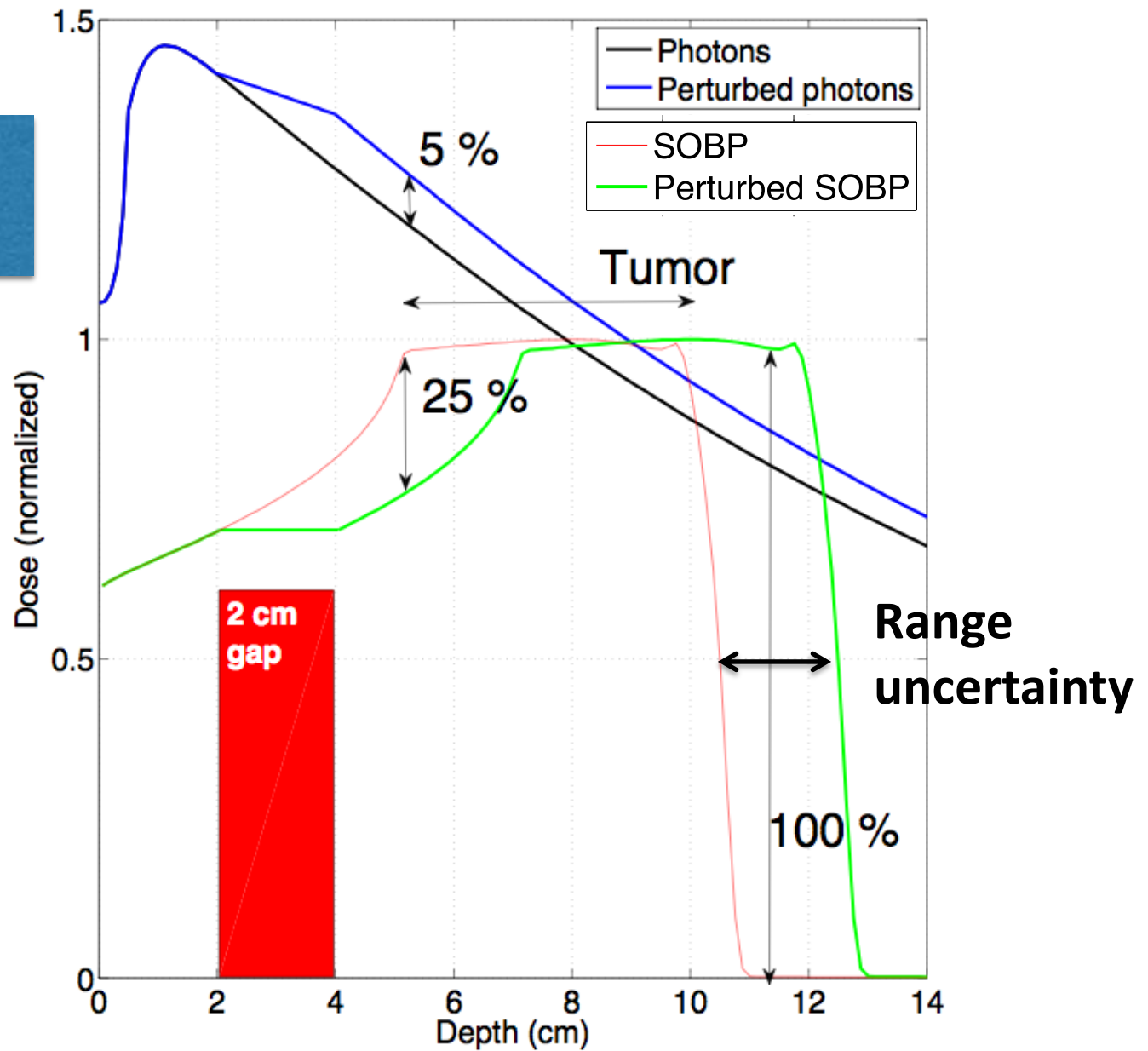
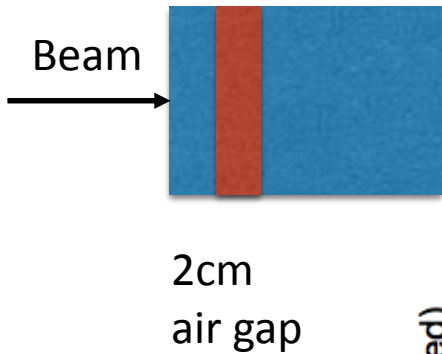
Random errors

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

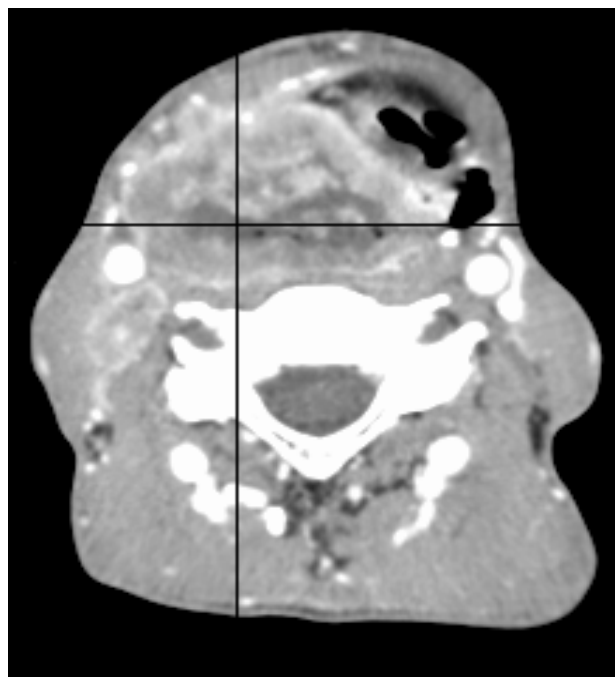


The CTV “navigates” in a stable dose distribution



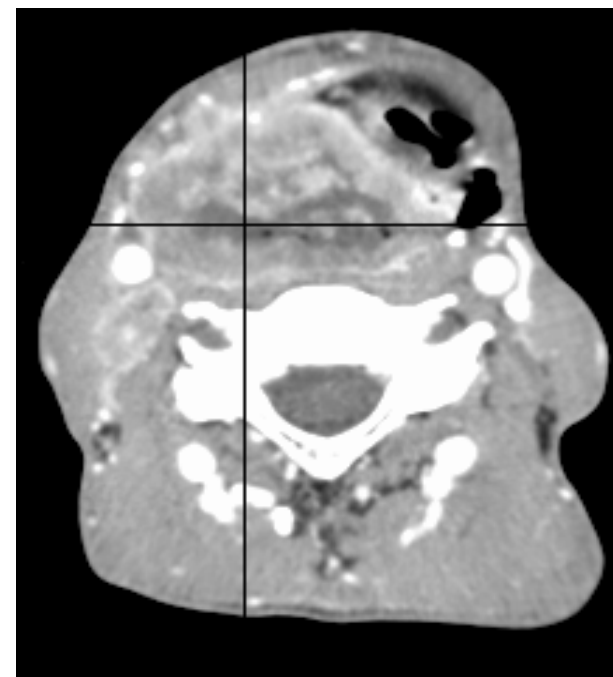


# Range uncertainties due to image conversion into stopping powers



**Hounsfield Units  
(photon attenuation)**

Conversion



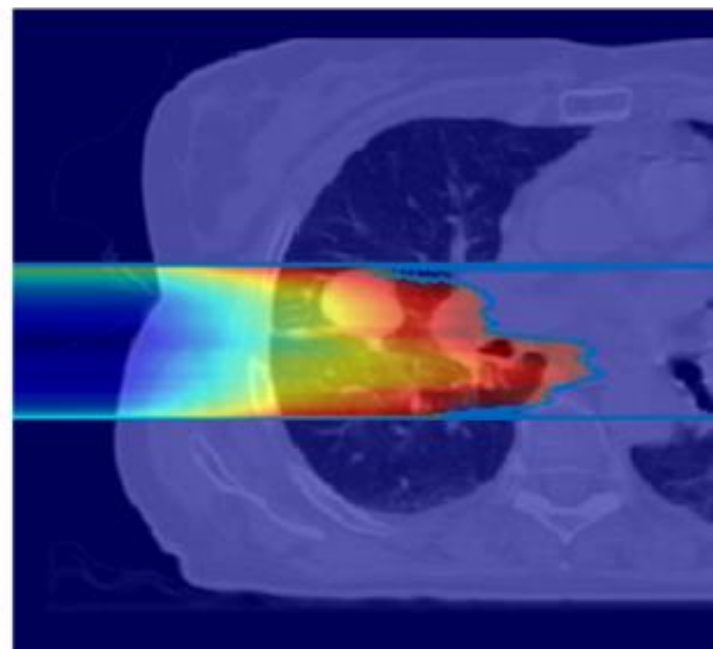
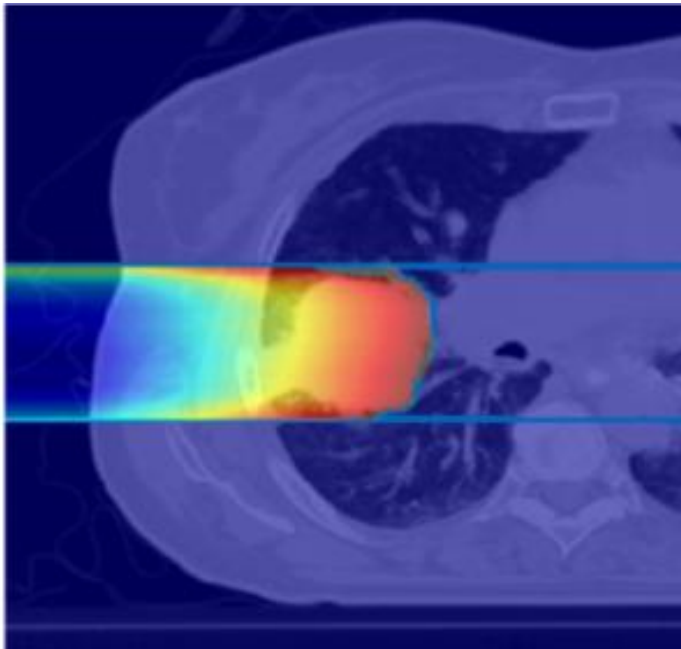
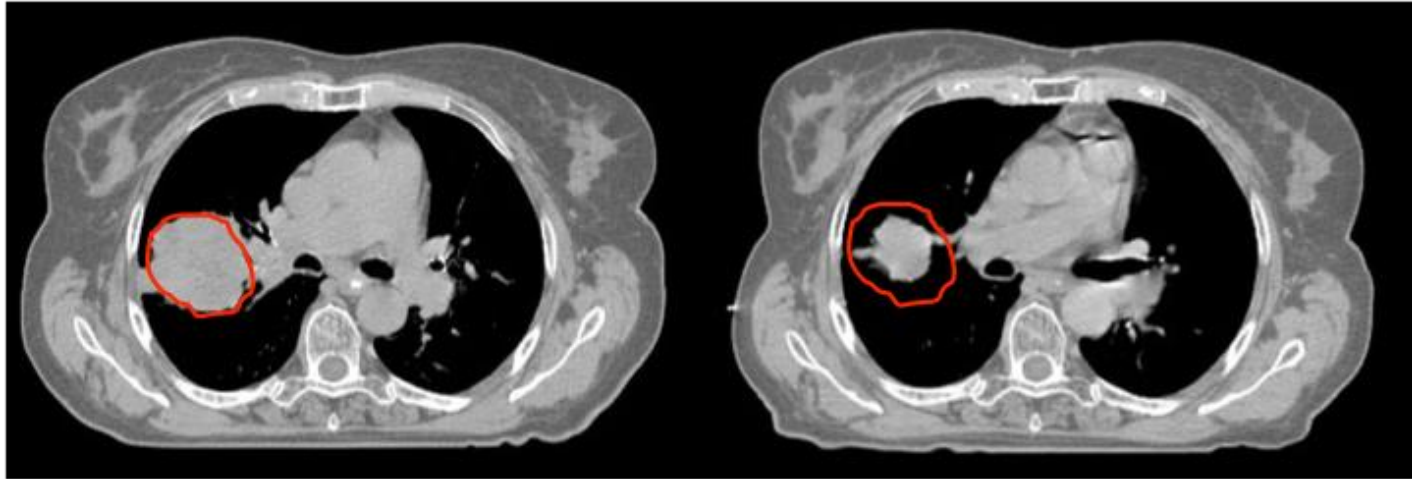
**Map of stopping powers**

## 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



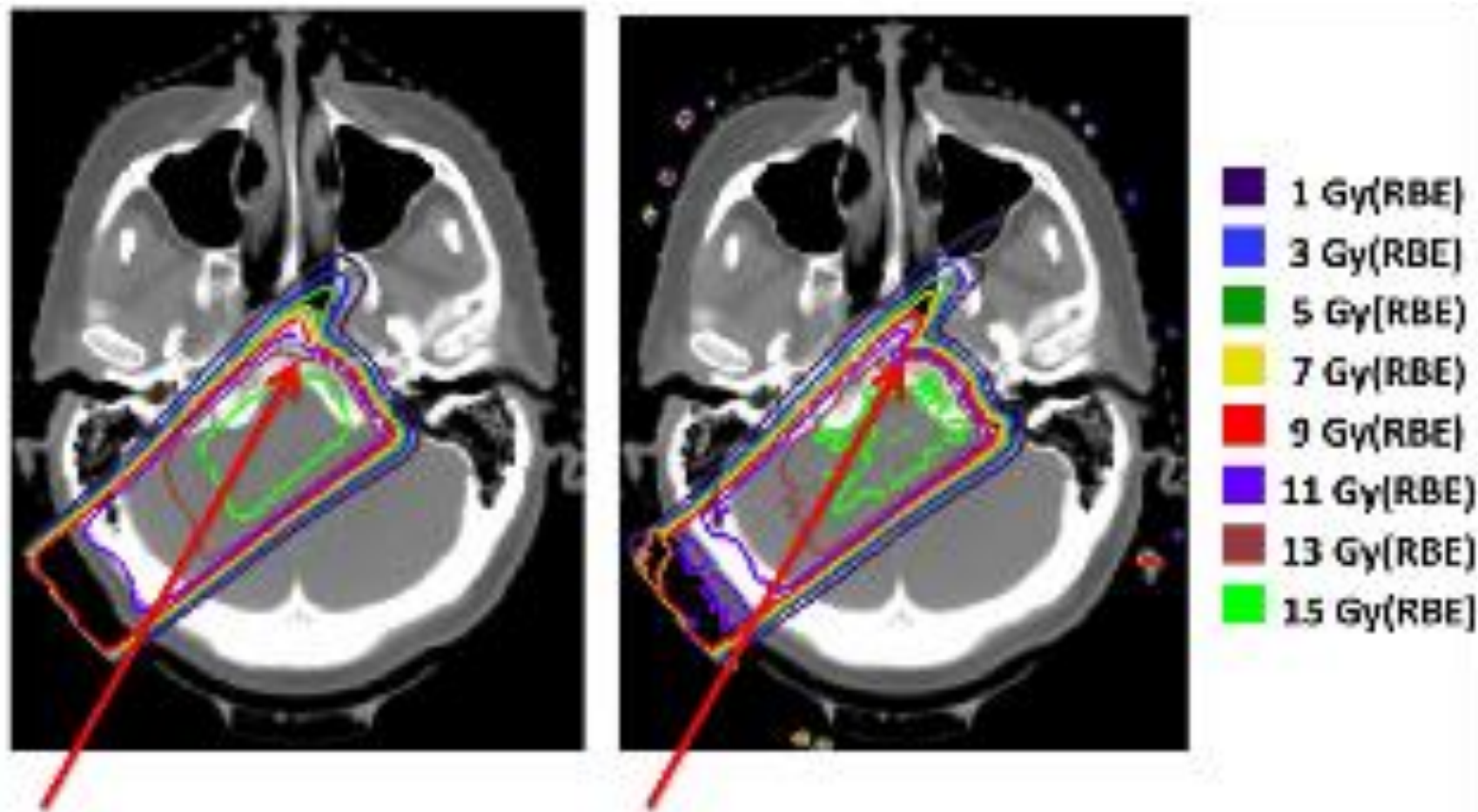
Day 0

Day 35

# Range uncertainties due to breathing



# Range uncertainties due to dose calculation errors



Bad algorithm

Good algorithm

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

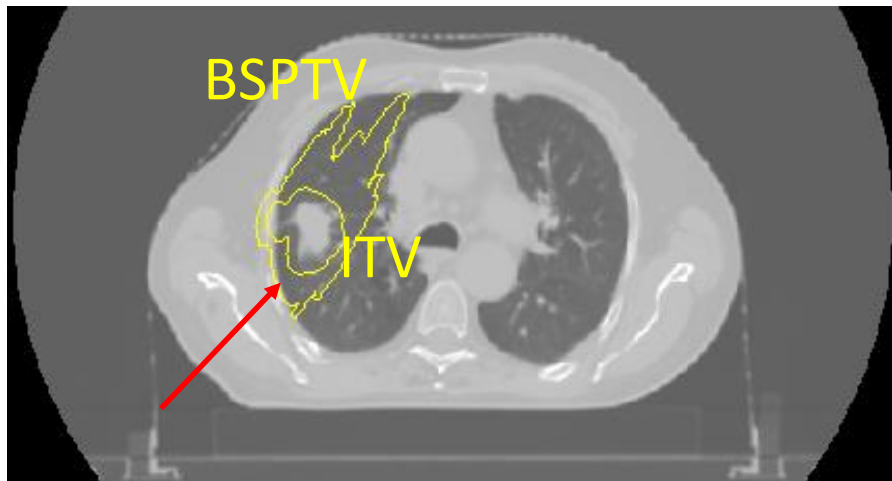
In proton therapy, the dose distribution is not *stable*

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



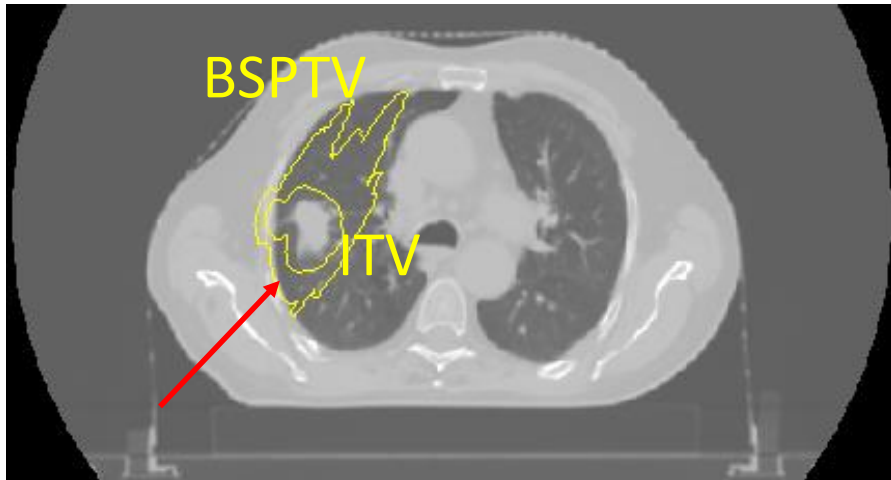
210°



150°

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

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

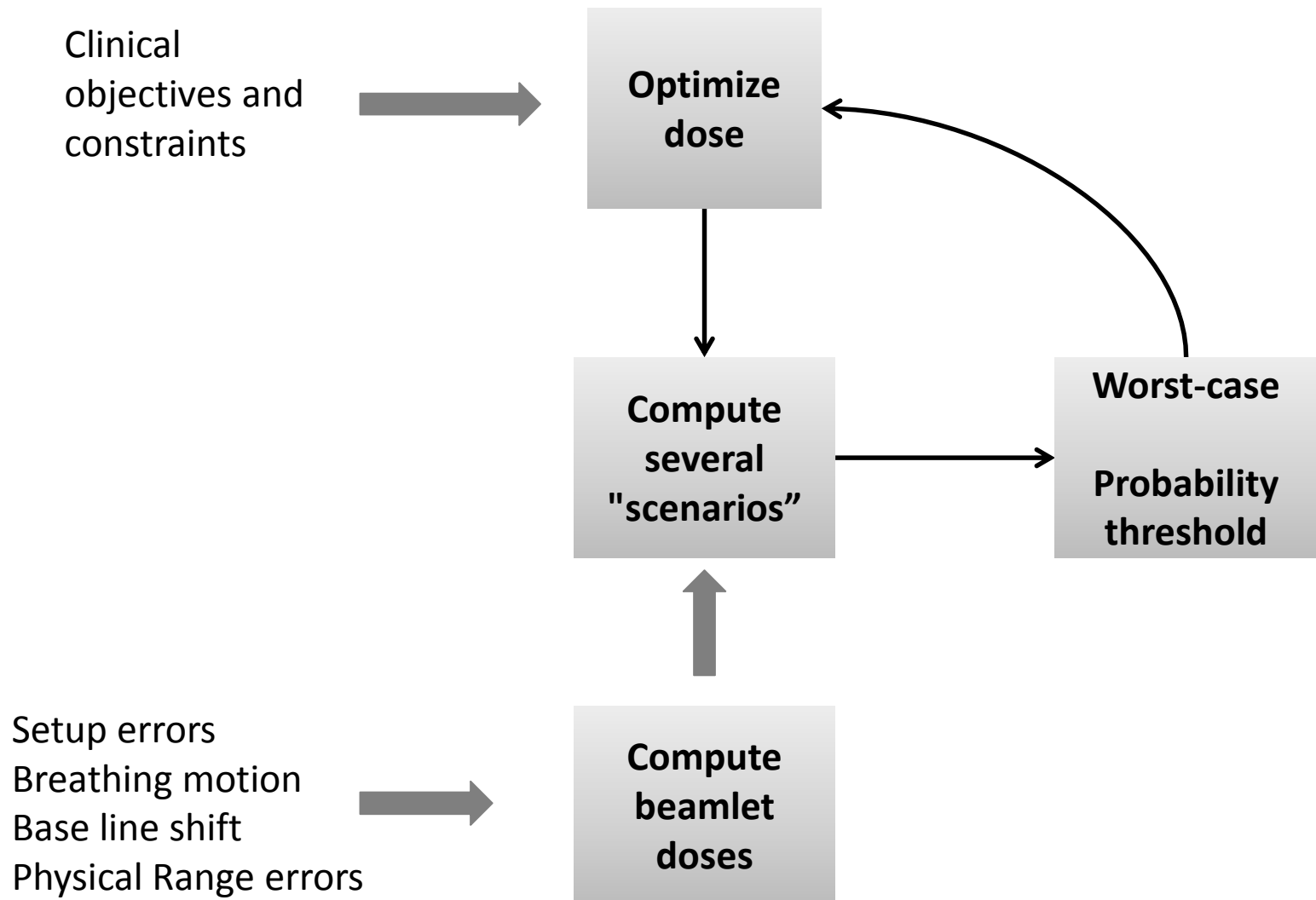


**210°**

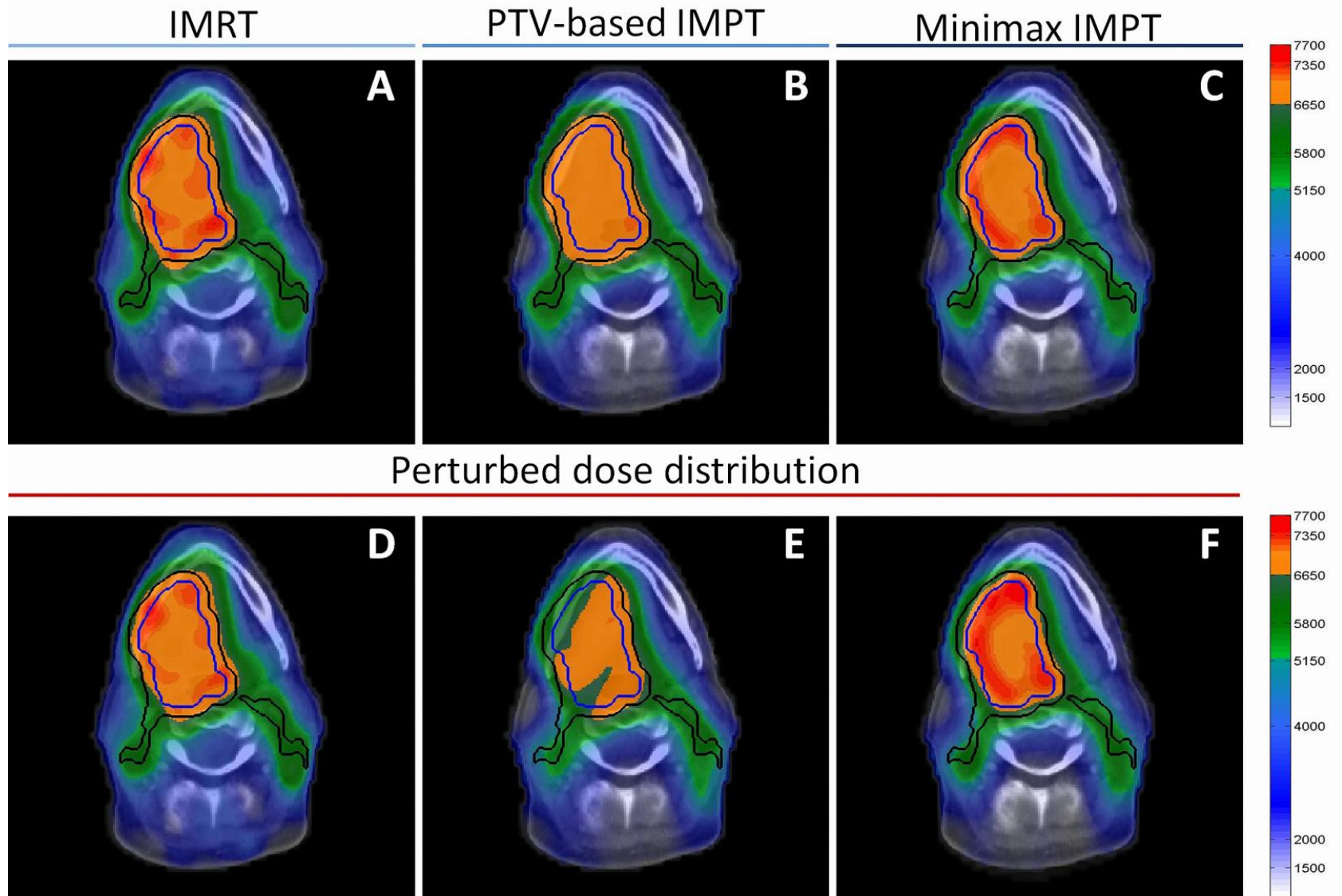


**150°**

# IMPT (PBS) → robust optimization

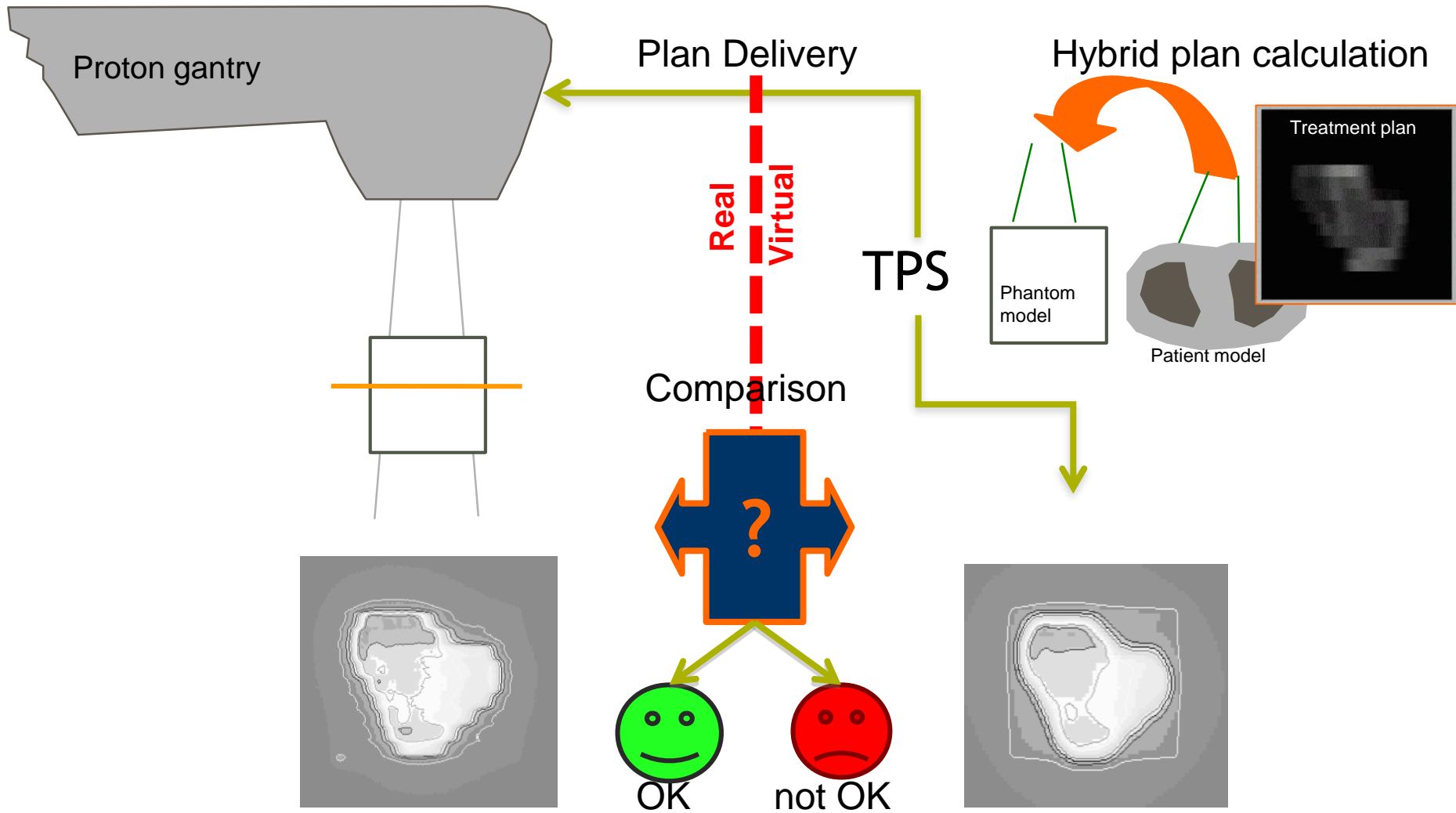


# Effectiveness of robust optimization



From Van Dijk et al (Plos One 2016)

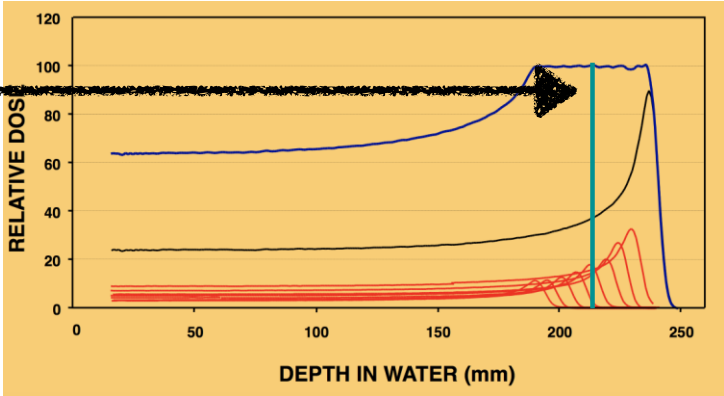
# Treatment verification



Experiment



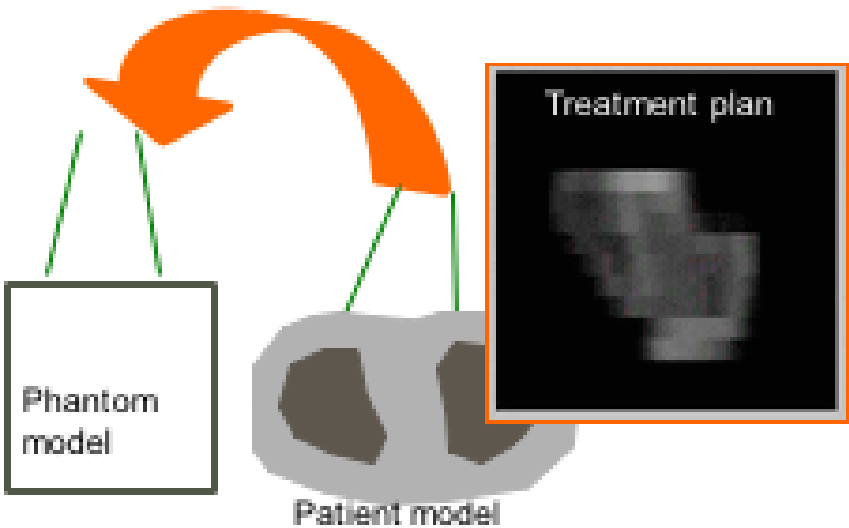
Horizontal Proton beam



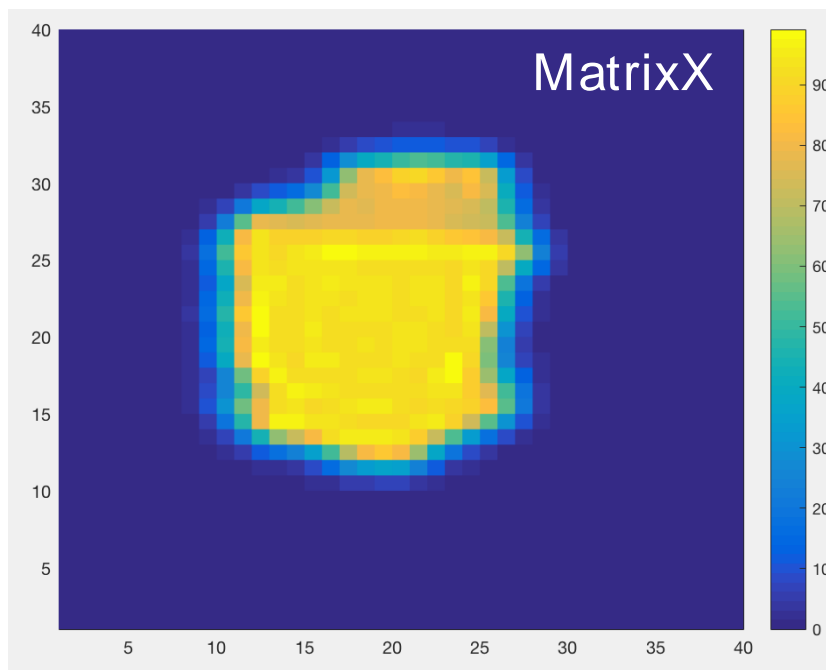
- One measurement per field (2 fields = 2 measurements)
- Depth of the detector at Mid-SOBP.

Dose calculation

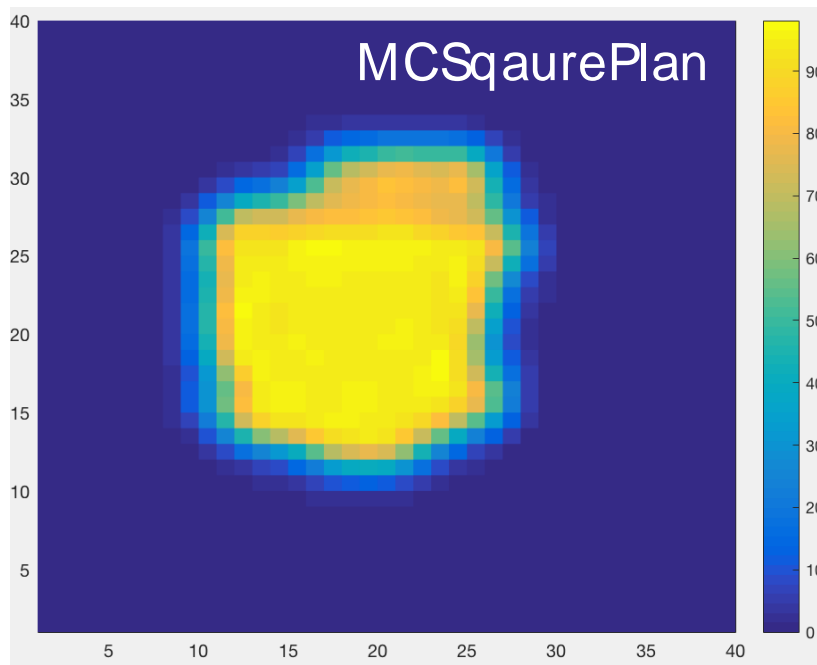
Hybrid plan calculation



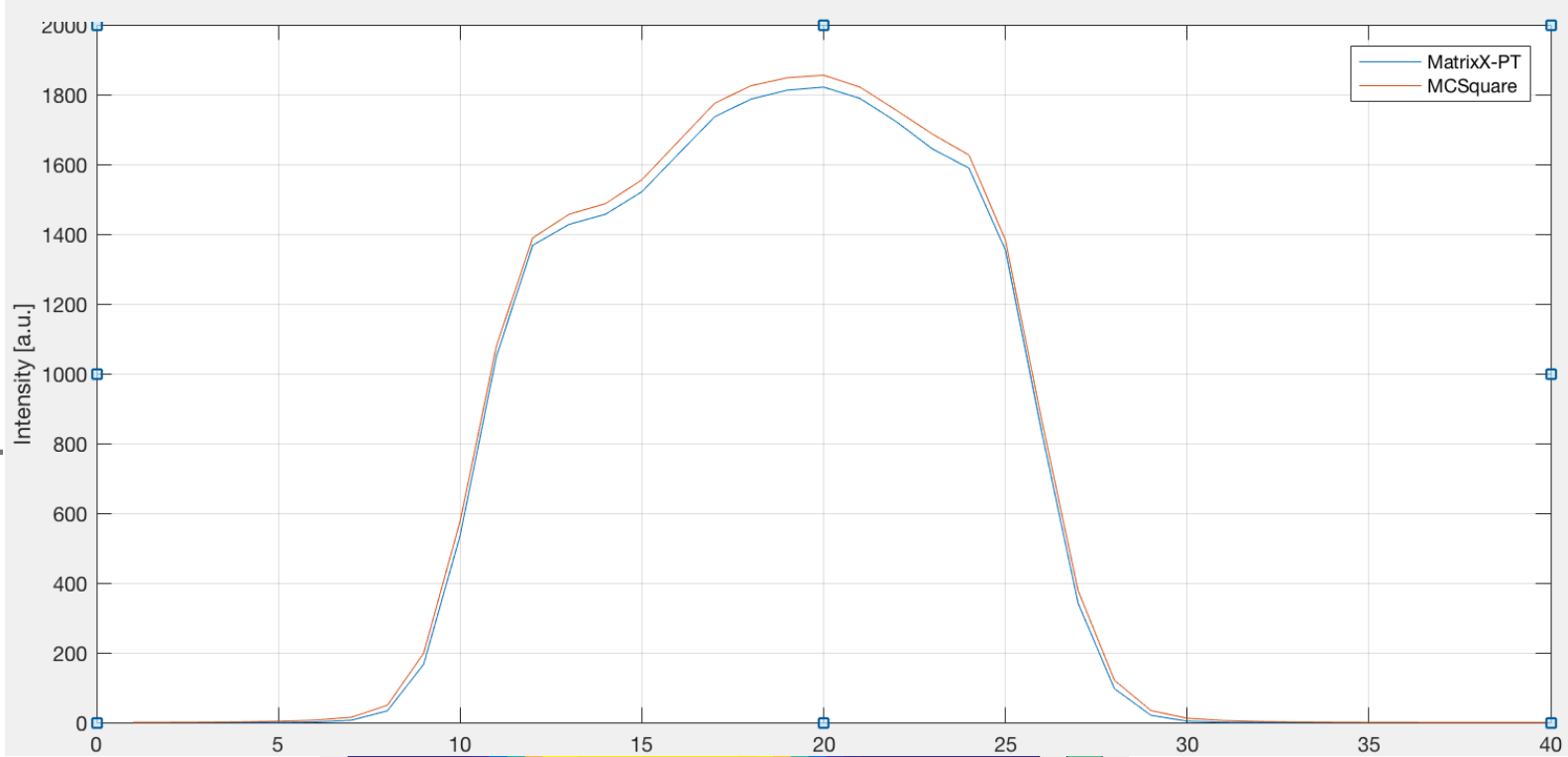
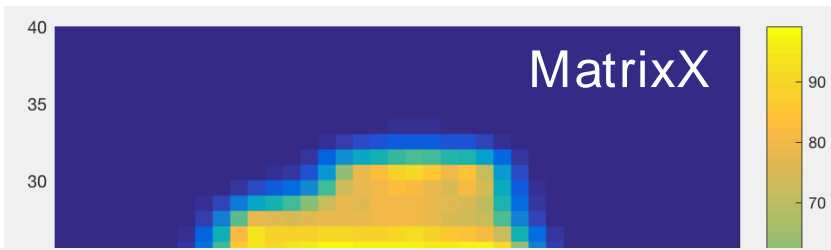
Experiment



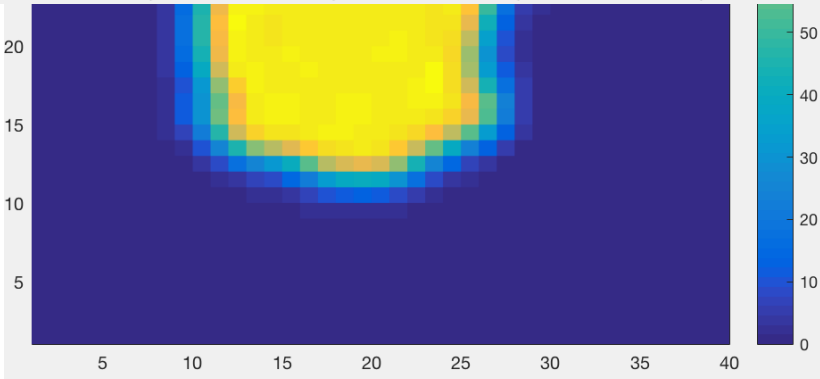
Dose calculation



Experiment



Dose calculation

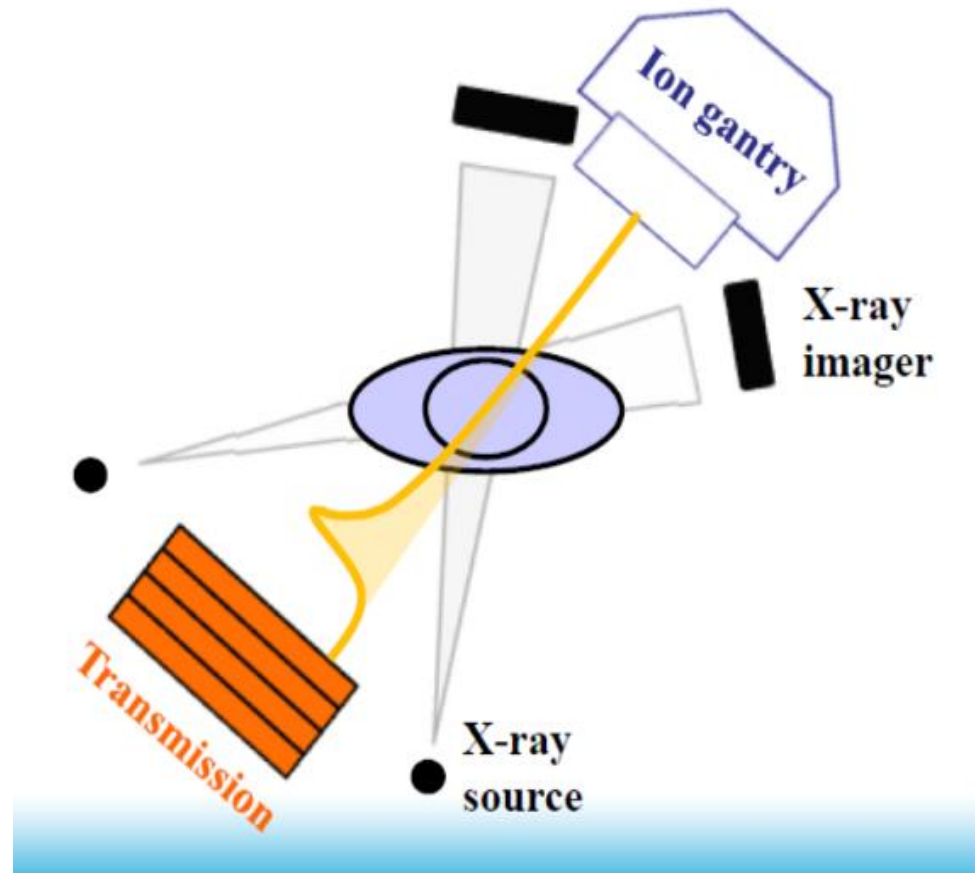




# In vivo range verification

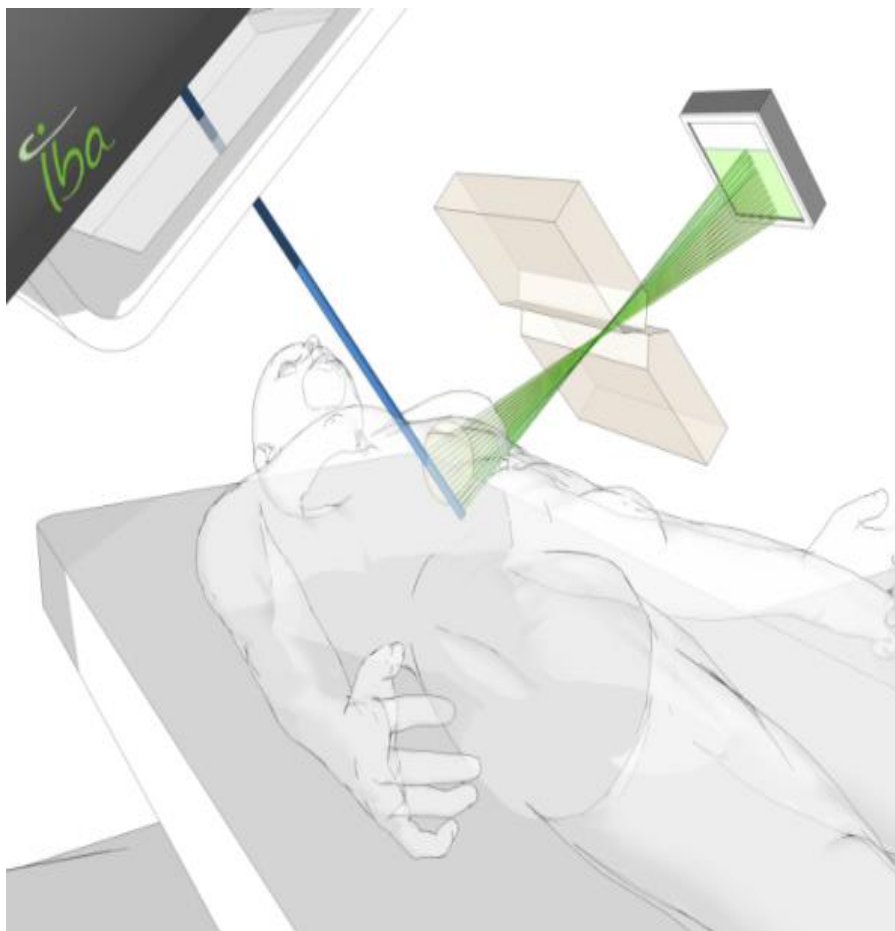
# Proton radiography

- 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**

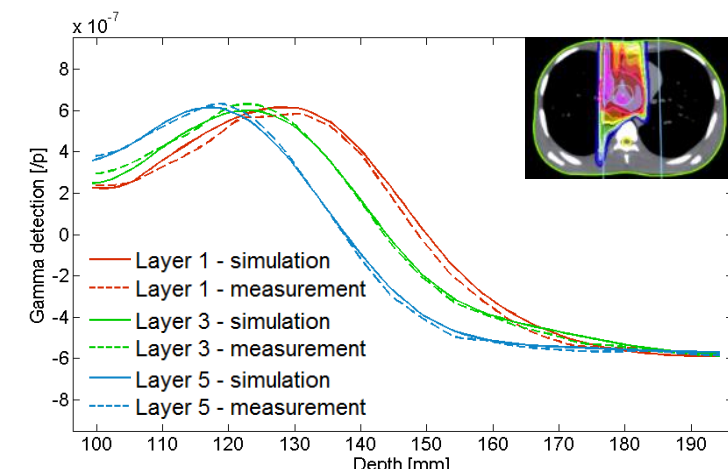
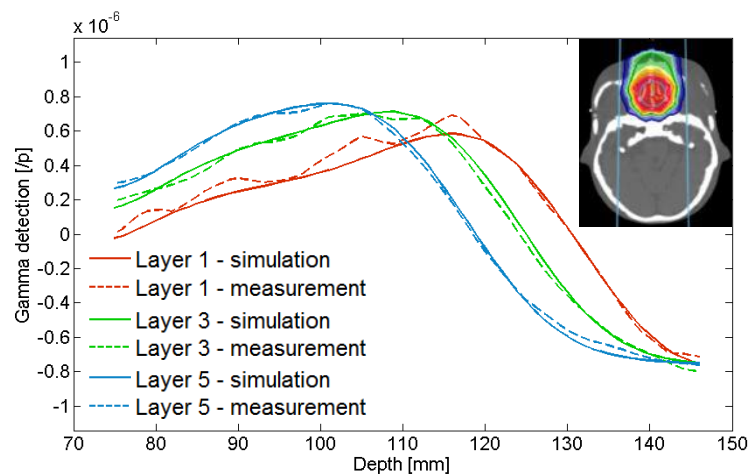
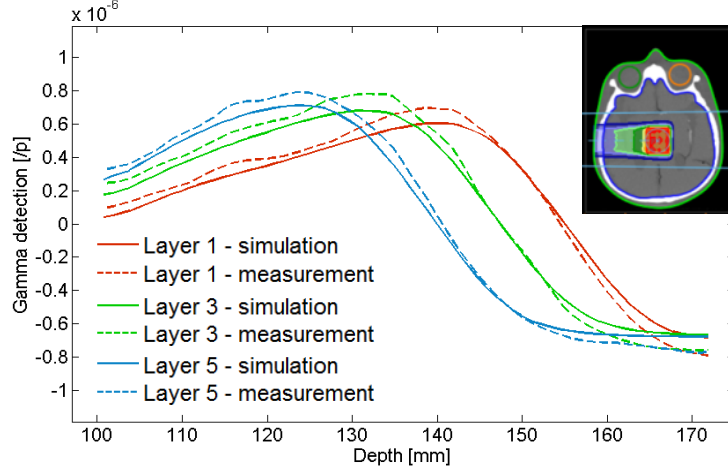
Target performance:

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

Points of attention:

Simplicity, cost effectiveness





# 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:**

Yunhe Xie<sup>1</sup>, Hassan Bentefour<sup>2</sup>, Guillaume Janssens<sup>2</sup>, Julien Smeets<sup>2</sup>, François Vander Stappen<sup>2</sup>, Lucian Hotoiu<sup>2</sup>, Lingshu Yin<sup>1</sup>, Derek Dolney<sup>1</sup>, Stephen Avery<sup>1</sup>, Fionnbarr O'Grady<sup>1</sup>, Damien Prieels<sup>2</sup>, James McDonough<sup>1</sup>, Timothy D. Solberg<sup>3</sup>, Robert Lustig<sup>1</sup>, Alexander Lin<sup>1</sup>, Boon-Keng K. Teo<sup>1</sup>

**Affiliations:**

<sup>1</sup>Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA

<sup>2</sup>Advanced Technology Group, Ion Beam Applications SA, Louvain-la-Neuve, Belgium

<sup>3</sup>Department of Radiation Oncology, University of California, San Francisco, CA

# Conclusions

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

Thank you!