Robust Optimization

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Learning objectives

- Describe the basics ideas and methods of robust optimization
- Describe examples in which robust optimization leads to a new quality of the treatment plans (better than margins)

Uncertainties in Radiation Therapy

- Geometric, physical, technical
  - Patient setup
  - Location of tumor & inner organs ("motion")
  - Dose calculation
  - Beam delivery system
- Biologic, clinical
  - Volume definition (targets and OARs)
  - Dose prescription (uniform or dose painting)
  - Tolerance dose
  - EUD, NTCP, TCP models (if used)

Uncertainty and Motion

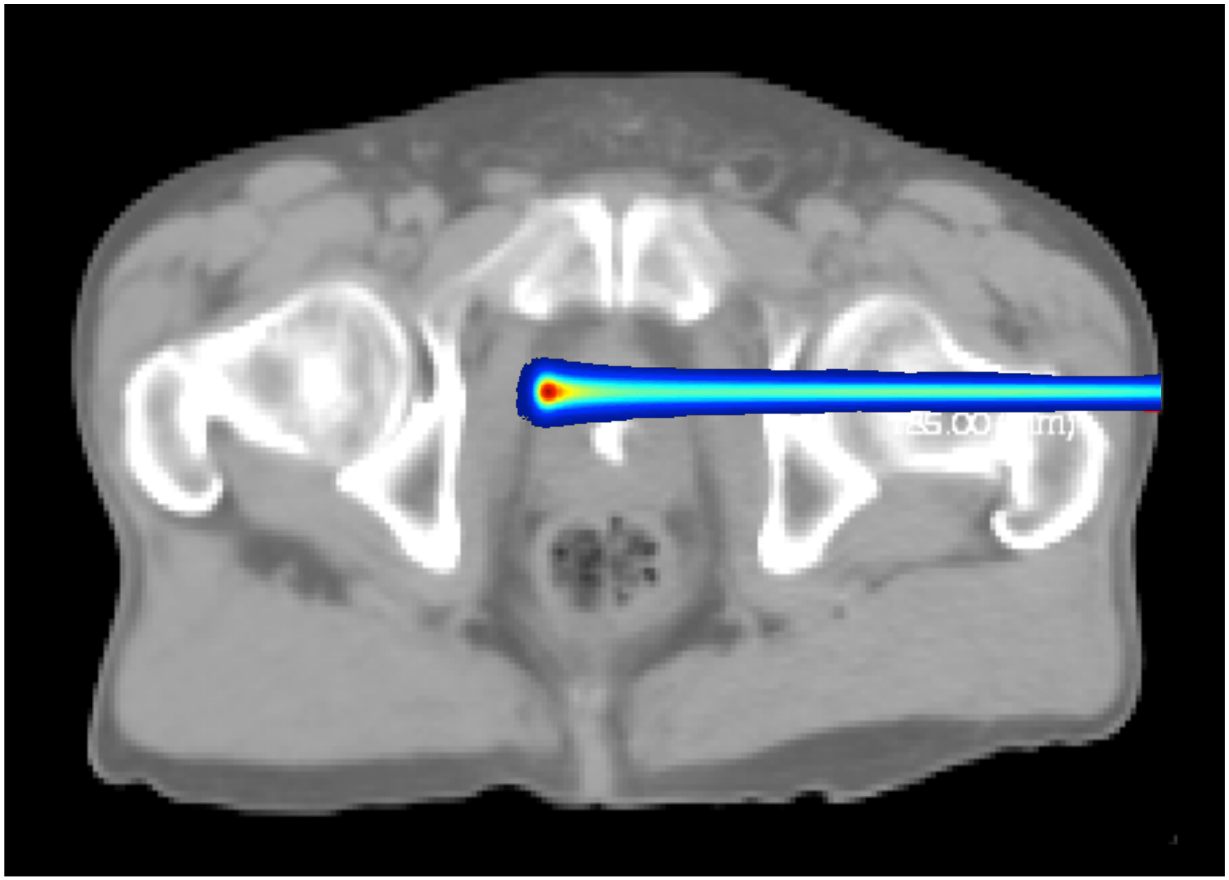
- Motion does not <u>necessarily</u> imply uncertainty
  - If motion is perfectly known, then there is no uncertainty. This case is “easy” to deal with.
- But, when there is motion (e.g., breathing), there are typically more potential sources of uncertainty:
  - Uncertainties in the motion characteristics such as frequency, amplitude, shape of trajectory, irregularity of the motion.

Additional uncertainties in **proton** therapy:

Range uncertainties

- Differences between treatment preparation and treatment delivery (~ 1 cm)
  - Daily setup variations
  - Internal organ motion
  - Anatomical/ physiological changes during treatment
- Dose calculation errors (~ 3-5 mm)
  - Conversion of CT number to stopping power
  - Inhomogeneities, metallic implants
  - CT artifacts
- Biological effect uncertainties

Proton range uncertainties:
Range uncertainties due to setup



Jan 08

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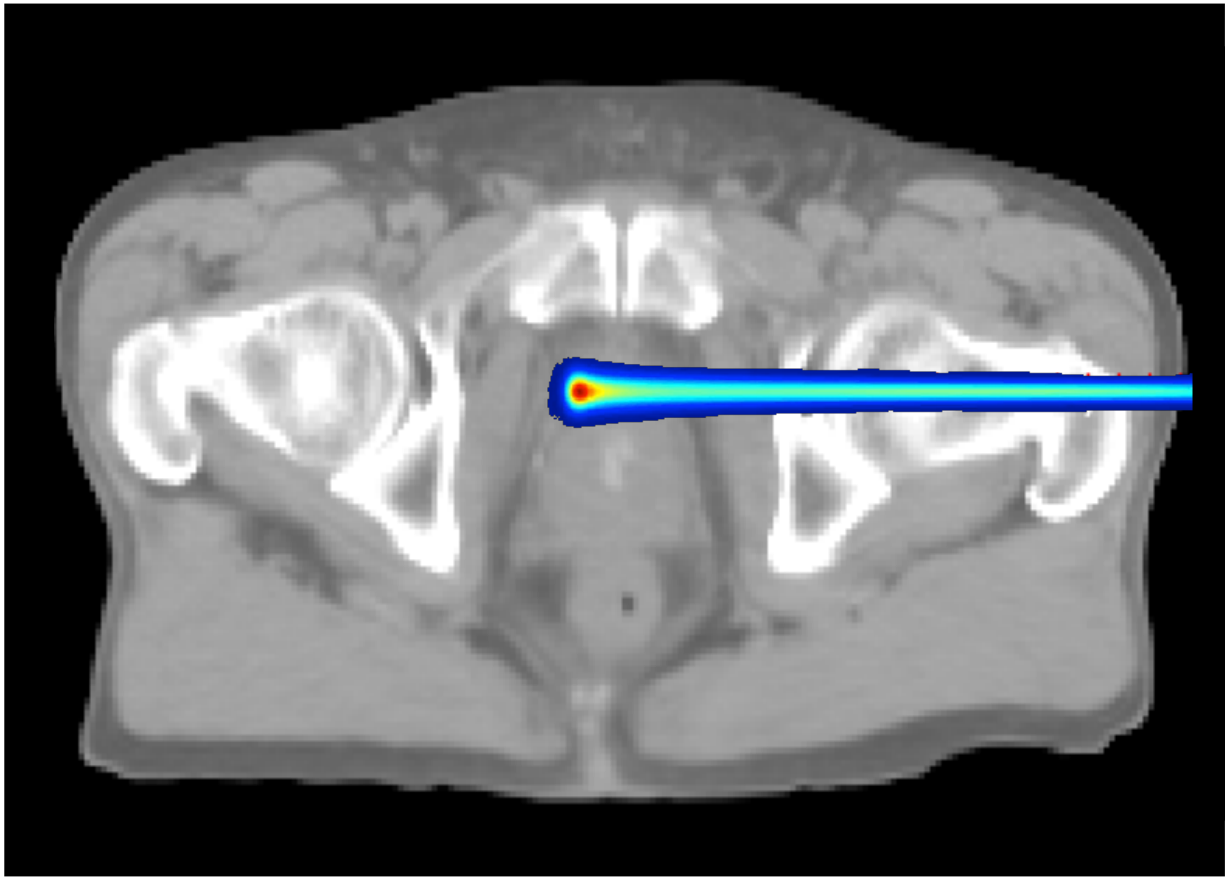
Chen, Rosenthal, et al., IJROBP 48(3):339, 2000

Proton range uncertainties: Range uncertainties due to setup



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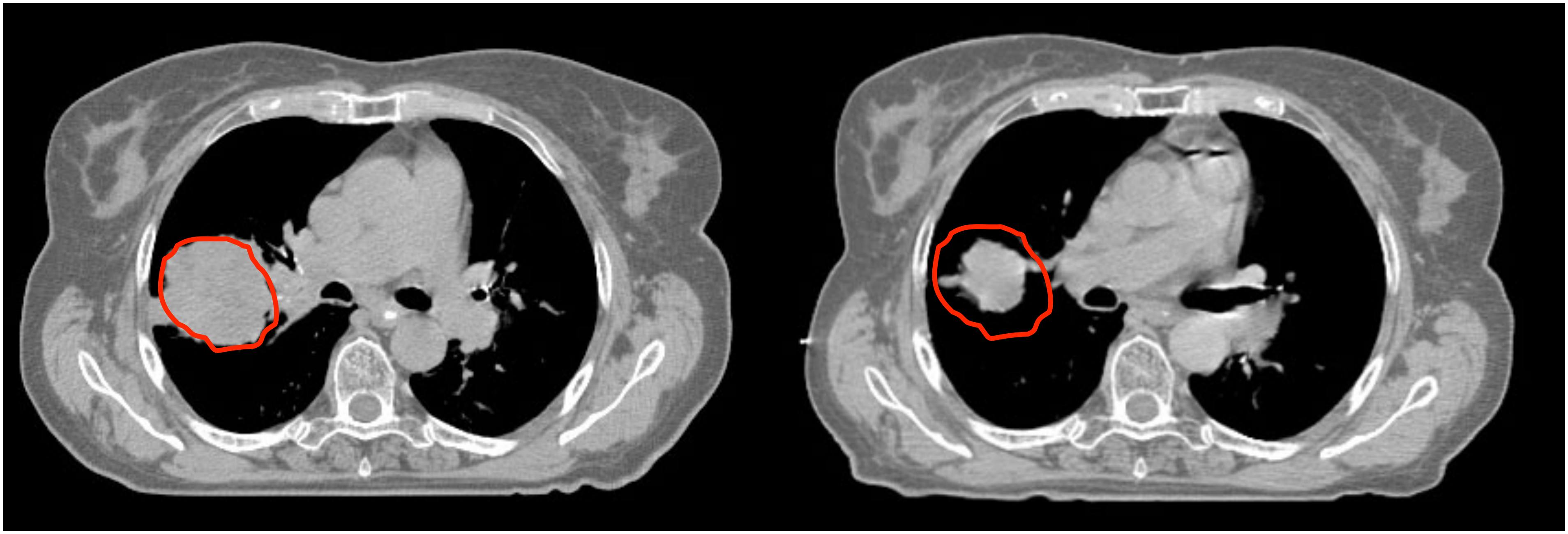
Chen, Rosenthal, et al., IJROBP 48(3):339, 2000

Proton range uncertainties: Tumor motion and shrinkage

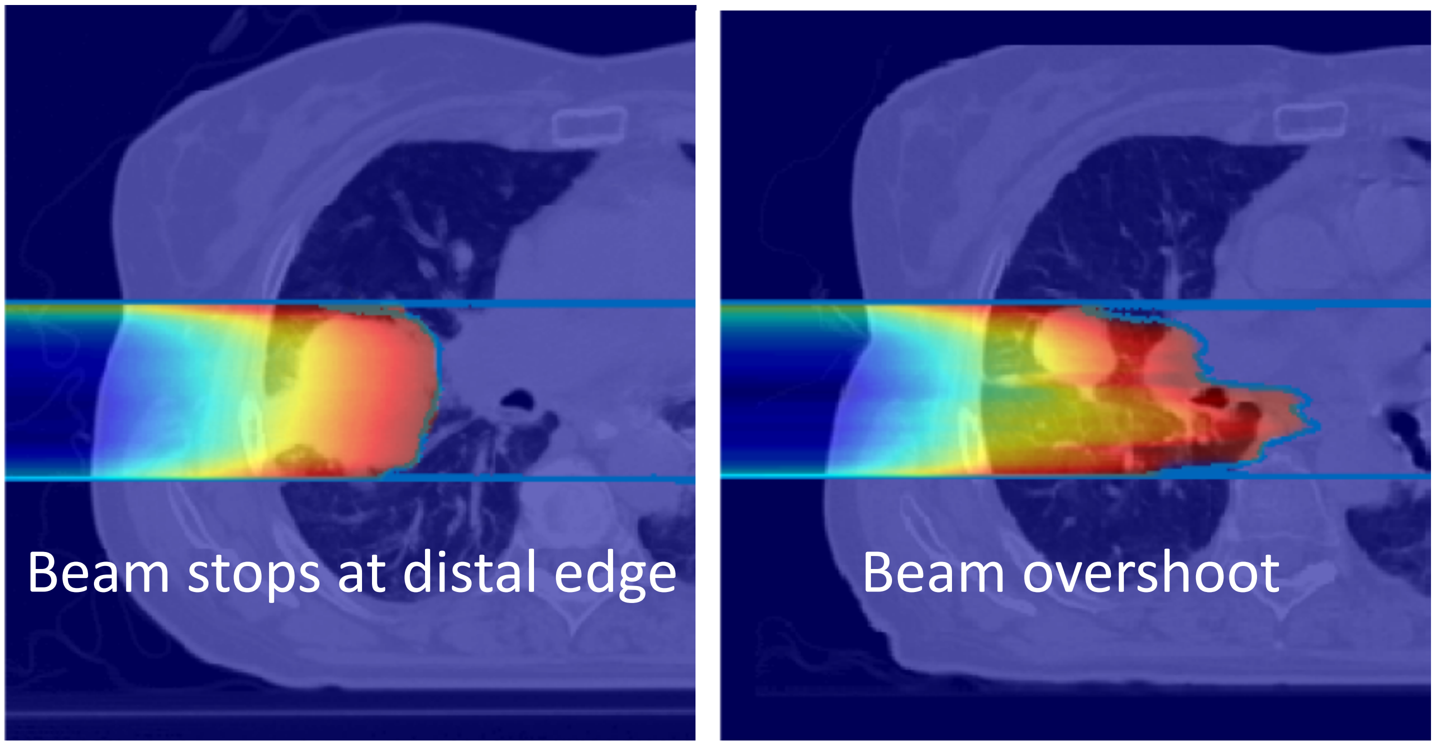
Initial Planning CT	5 weeks later
GTV 115 cc	GTV 39 cc



S. Mori, G. Chen

Proton range uncertainties: Tumor motion and shrinkage

What you see in the plan… is not always what you get.

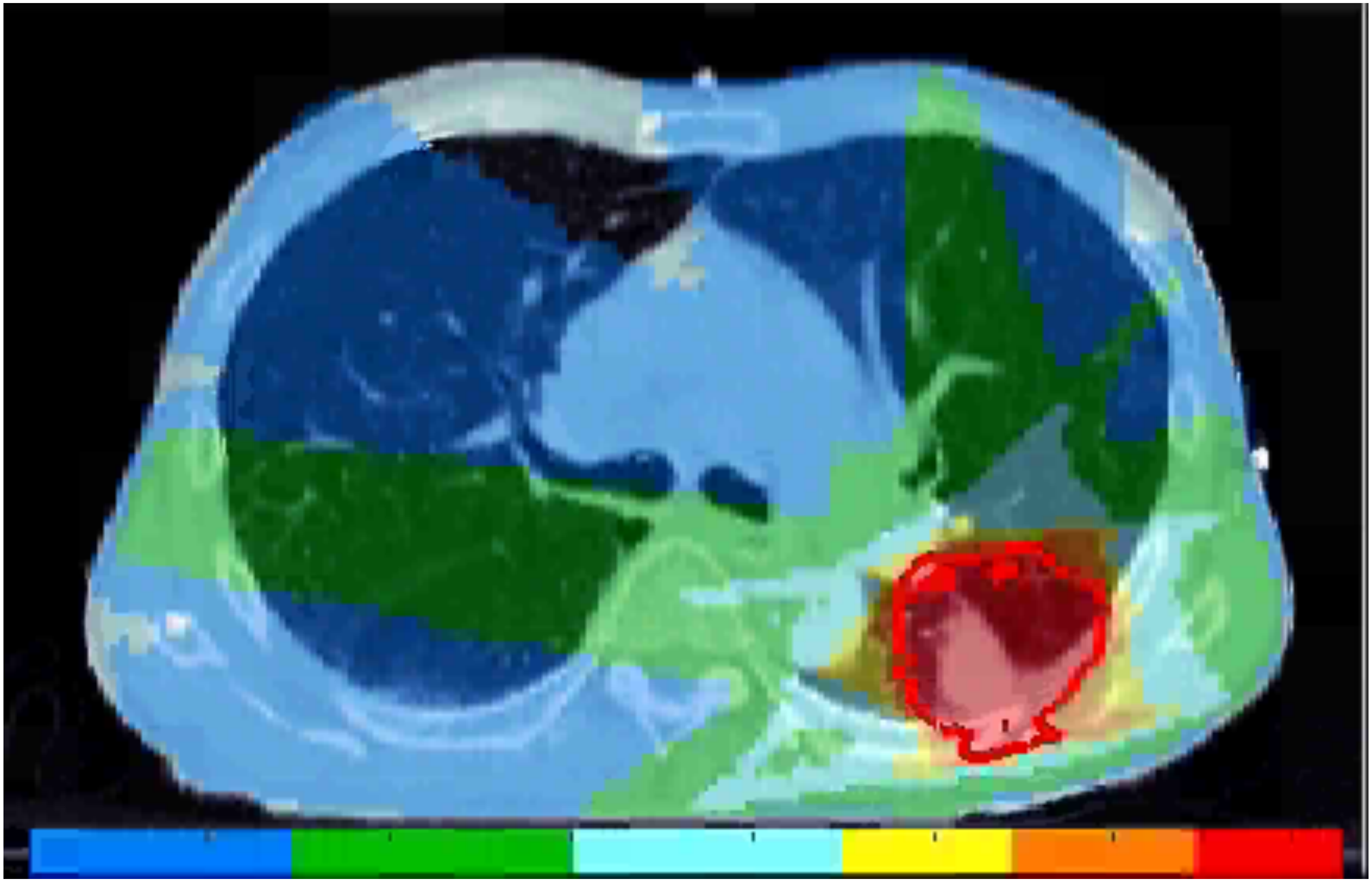


S. Mori, G. Chen

Margins to counteract uncertainties

- Margins around target volumes lead to higher dose to normal tissue
- PTV margins rely on "static dose cloud" assumption – not always justified
- Margins can overlap (PTV, PRV), what then?

The "static dose cloud" assumption – ok for photons, not for protons –



- A potentially better way to deal with uncertainties:

➢ Robust Optimization.

Robust Optimization – Outline

1. Uncertainties, motion, and margins ✓
2. Robust optimization principles
3. Examples of application

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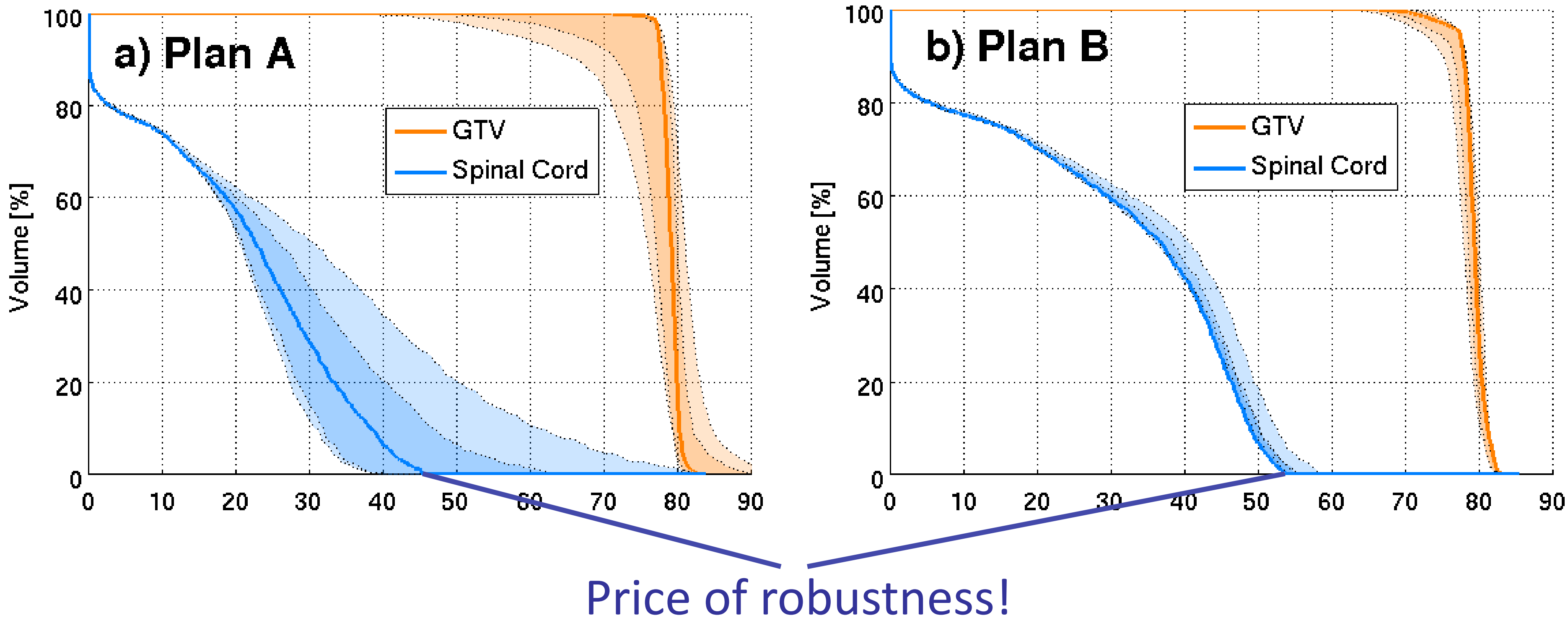
Robustness definition

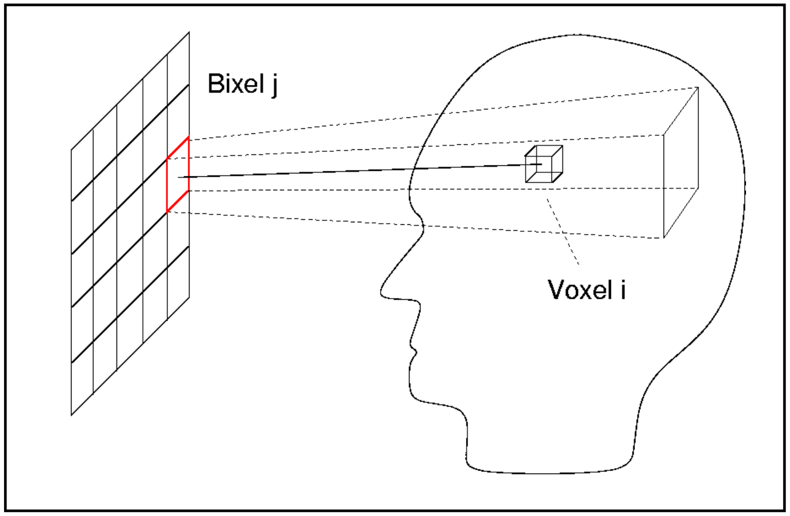
- Robustness = immunity to uncertainty

Examples:
non-robust (Plan A) and robust (Plan B)



Visualize uncertainties: DVH bands, Trofimov 2011

The "standard model" of IMRT optimization



Dose is a linear function of Bixel weights

$$d_i(x) = \sum_j D_{ij} x_j$$

Objective function

$$\underset{x}{\text{minimize}} \quad f(d(x))$$

$$\text{subject to}$$

Dosimetric constraints: $$l_m \leq c_m(d(x)) \leq u_m \qquad \forall m$$

Physical constraints: $$x_j \geq 0 \qquad \forall j$$

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Robust optimization = robustness + optimization

- We want to make a treatment plan as good as possible and at the same time protect it against uncertainties
  - One thing is clear: there is always a **price of robustness**
- How can we do that?

Robust plan optimization, 2 ways:

- Consider different scenarios of treatment delivery (instances of geometry of patient positions, motion trajectories)

1. **"Stochastic programming"**: describe uncertainties with random variables, assume probability density functions (pdf), and optimize expected value of the objective function
2. **The worst case approach** (mathematics, Ben-Tal, Nemirovski) : make sure that constraints are fulfilled in all scenarios, and that we obtain the best plan in the worst case

1. Stochastic programming – the probabilistic approach

For different scenarios *s*: $$d_i^s(x) = \sum_j D_{ij}^s x_j$$

probability of scenario *s*

$$\underset{x}{\text{minimize}} \qquad \langle f \rangle = \sum_s p_s f\left(d^s(x)\right)$$

$$\text{subject to}$$

$$x_j \geq 0 \quad \forall j$$

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1. Stochastic programming – example: quadratic objective function

Objective function:

$$f(d) = \sum_i \left(d_i - d_i^{pres}\right)^2$$

Expected dose:

$$\langle d_i \rangle = \sum_s p_s d_i^s$$

Expected objective function (to be minimized):

$$\langle f \rangle = \sum_i \left[\underbrace{\left(\langle d_i \rangle - d_i^{pres}\right)^2}_{\substack{\text{average deviation} \\ \textbf{Accuracy, bias}}} + \underbrace{\sum_s p_s \left(d_i^s - \langle d_i \rangle\right)^2}_{\substack{\text{Variance} \\ \textbf{Precision}}} \right]$$

Example: setup error (1D)

- Error scenarios defined by shifting to the left or right in steps of 1mm.
- **Random error**: 32 random shifts (for 32 fractions) sampled from a Gaussian with a mean of zero and a set standard deviation σ_{Rand}
- **Systematic error:** single shift with standard deviation σ_{Sys} added to the random shift above
- Objective function:

$$f(d) = w_T \sum_{i \in T} (d_i - D^{pres})^2 + w_{HT} \sum_{i \in HT} (d_i)^2$$

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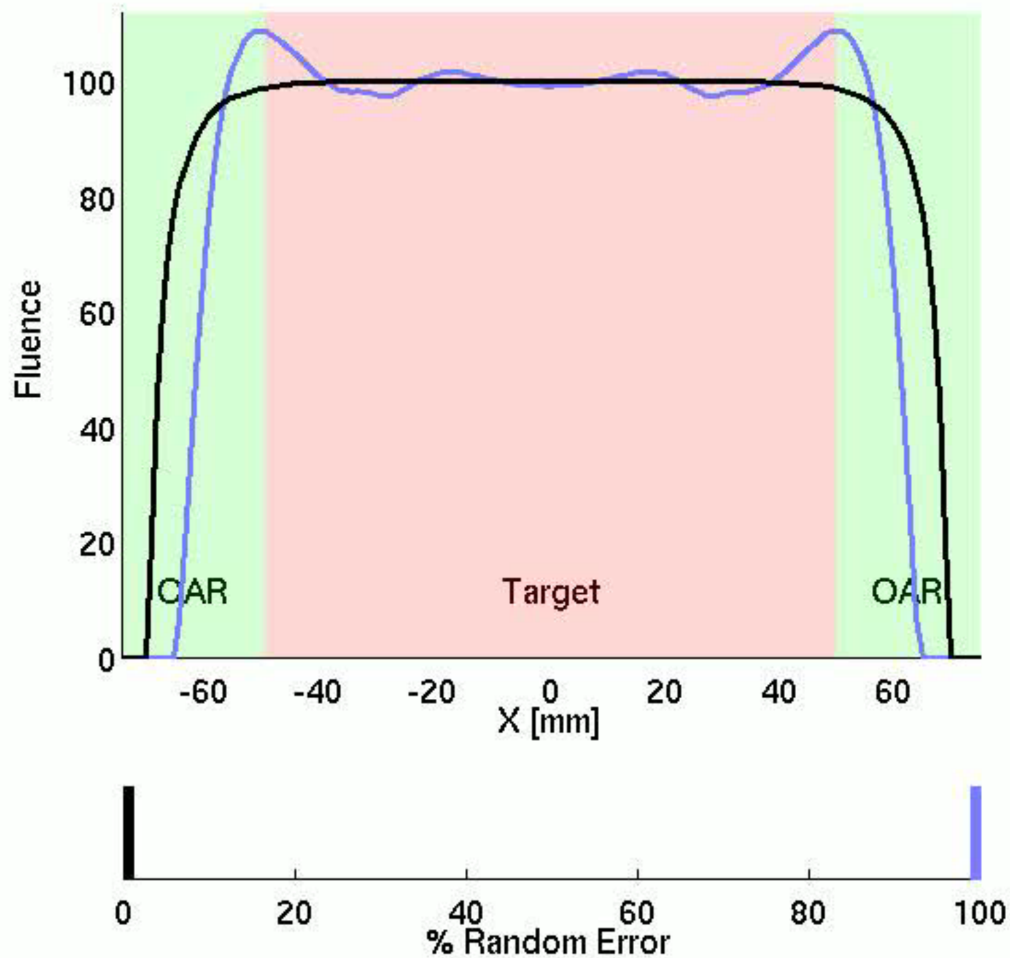
Example: setup error (1D)

$$\overbrace{\sigma^2_{Tot}}^{(10\text{ mm})^2} = \sigma^2_{Rand} + \sigma^2_{Sys}$$



Observations:

- Random errors require smaller margins than systematic errors -> van Herk margin recipe.
- A new type of dose distribution emerges from the probabilistic approach: beam “horns” instead of margins.

Robust plan optimization, 2 ways:

- Consider different scenarios of treatment delivery (instances of geometry of patient positions, motion trajectories)

1. **“Stochastic programming”**: describe uncertainties with random variables, assume probability density functions (pdf), and optimize expected value of the objective function
2. **The worst case approach** (mathematics, Ben-Tal, Nemirovski) : make sure that constraints are fulfilled in all scenarios, and that we obtain the best plan in the worst case

2. Worst case approach

For different scenarios *s*: $$d_i^s(x) = \sum_j D_{ij}^s x_j$$

$$\begin{aligned}
&\underset{x}{\text{minimize}} && \left[\max_s f(d^s)\right] \\
&\text{subject to} && \\
&l_m \leq c_m(d^s(x)) \leq u_m && \forall m, \quad \forall s \\
&x_j \geq 0 && \forall j
\end{aligned}$$

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Robust Optimization – Outline

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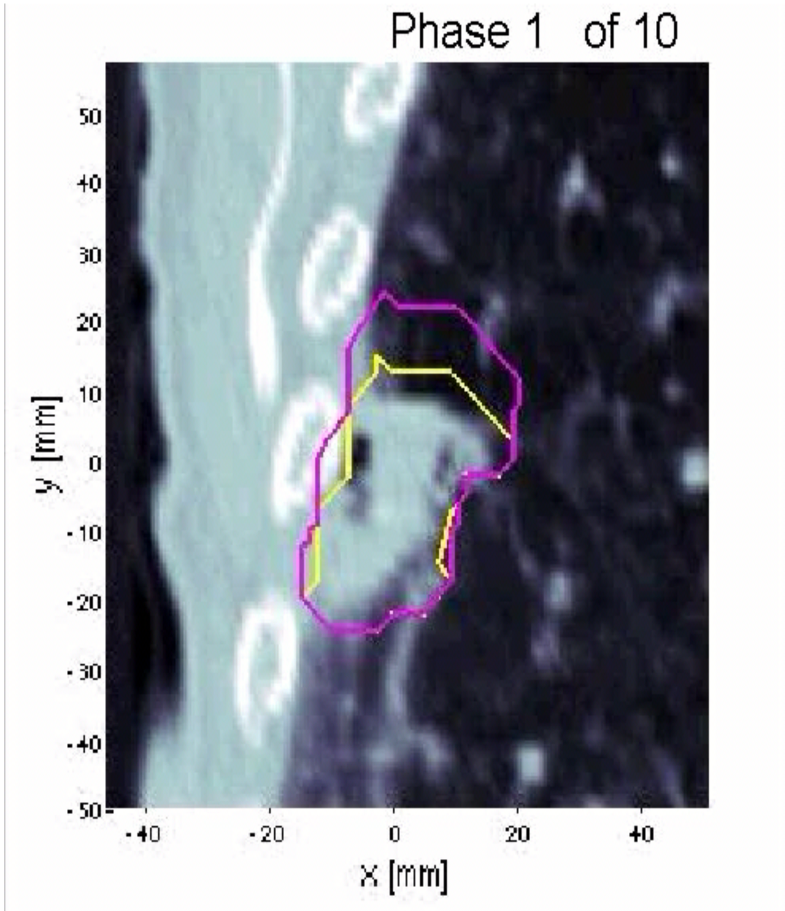
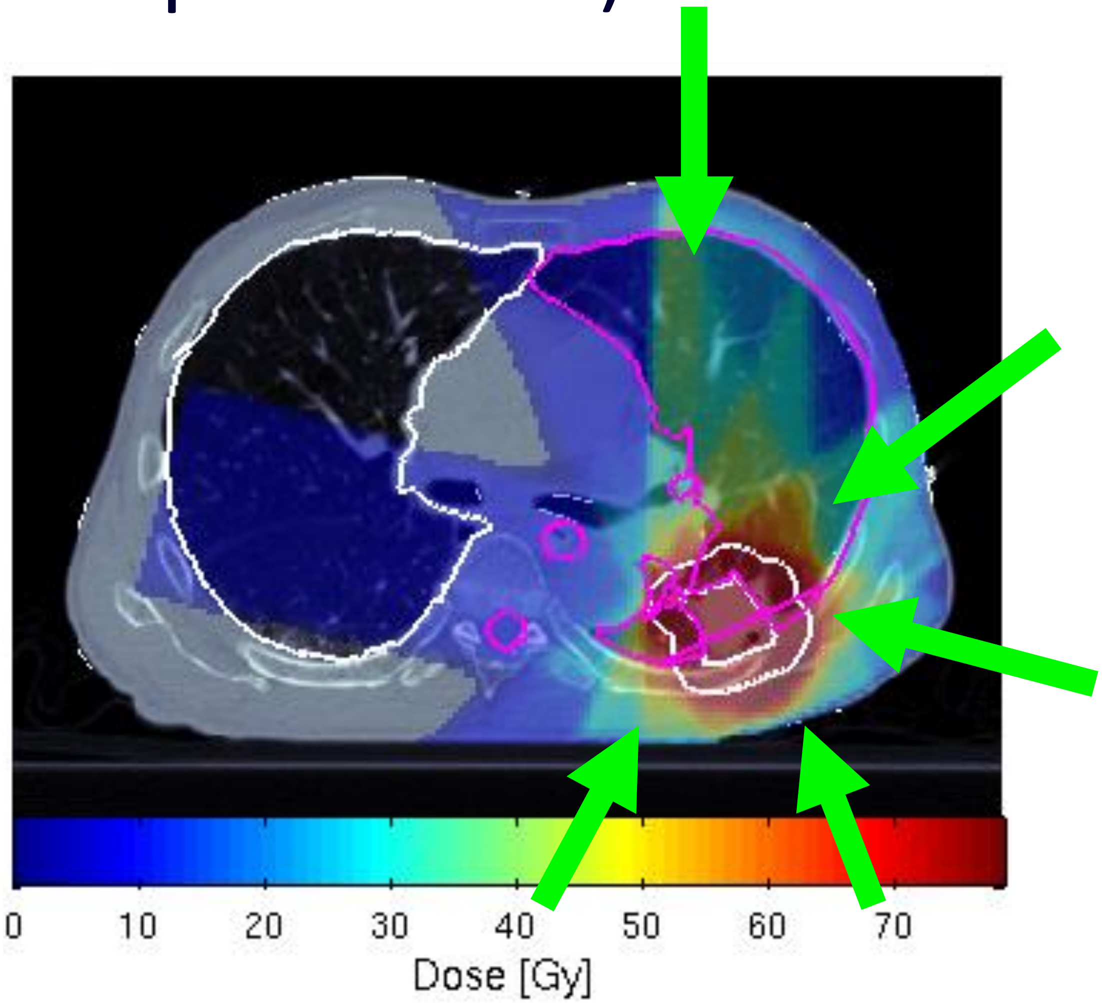
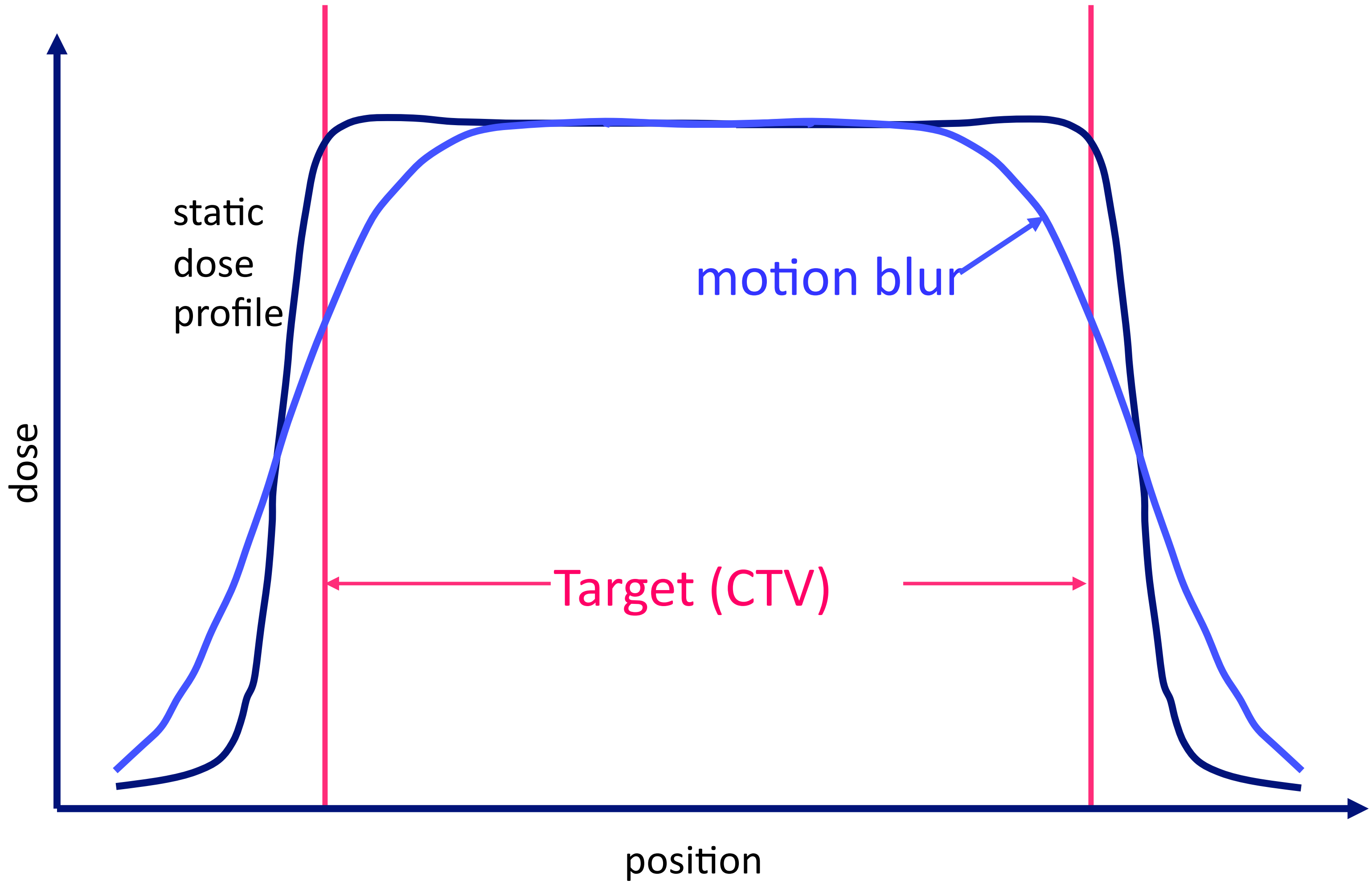
Example 1: Lung, breathing motion
Robust (worst case optimization)

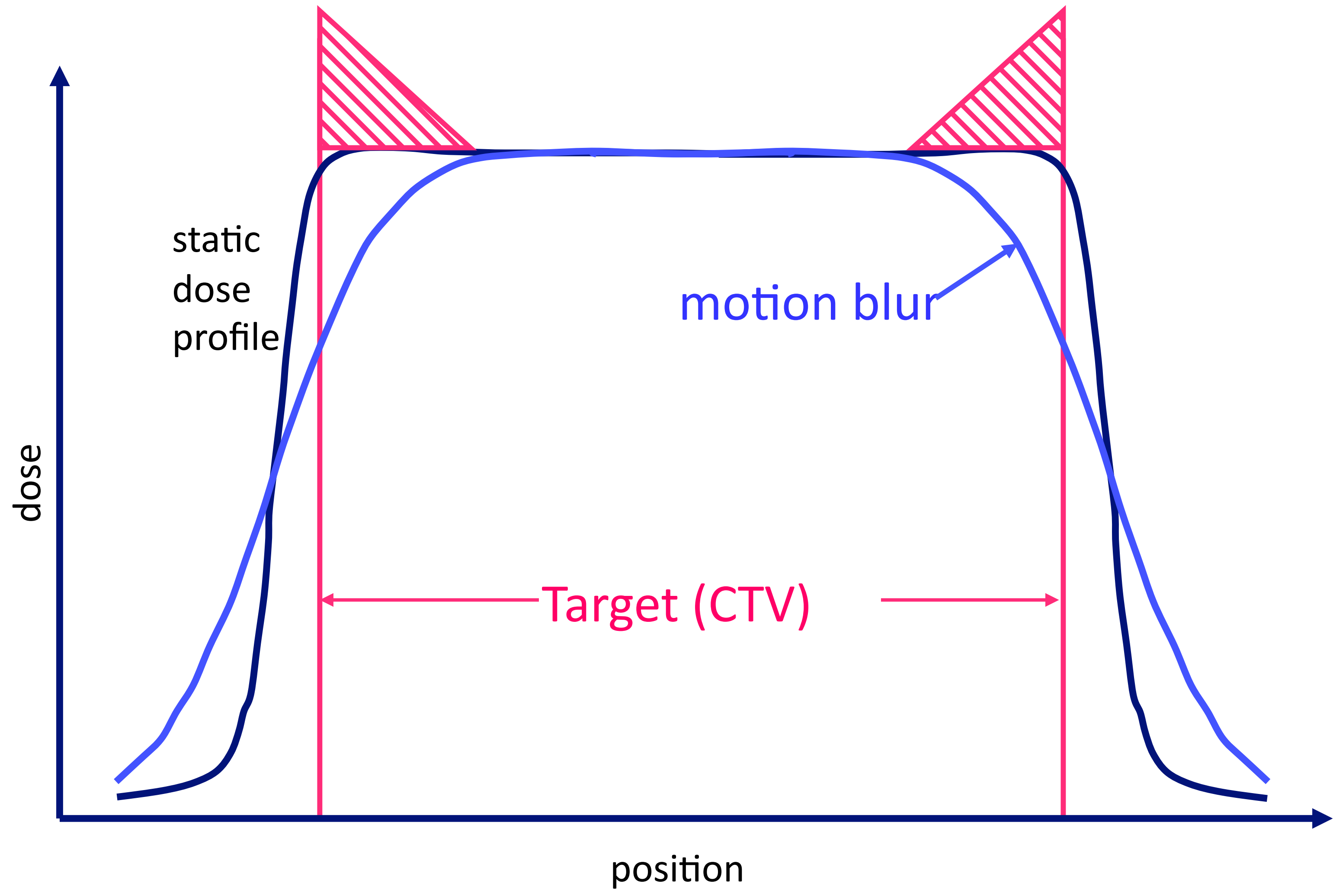




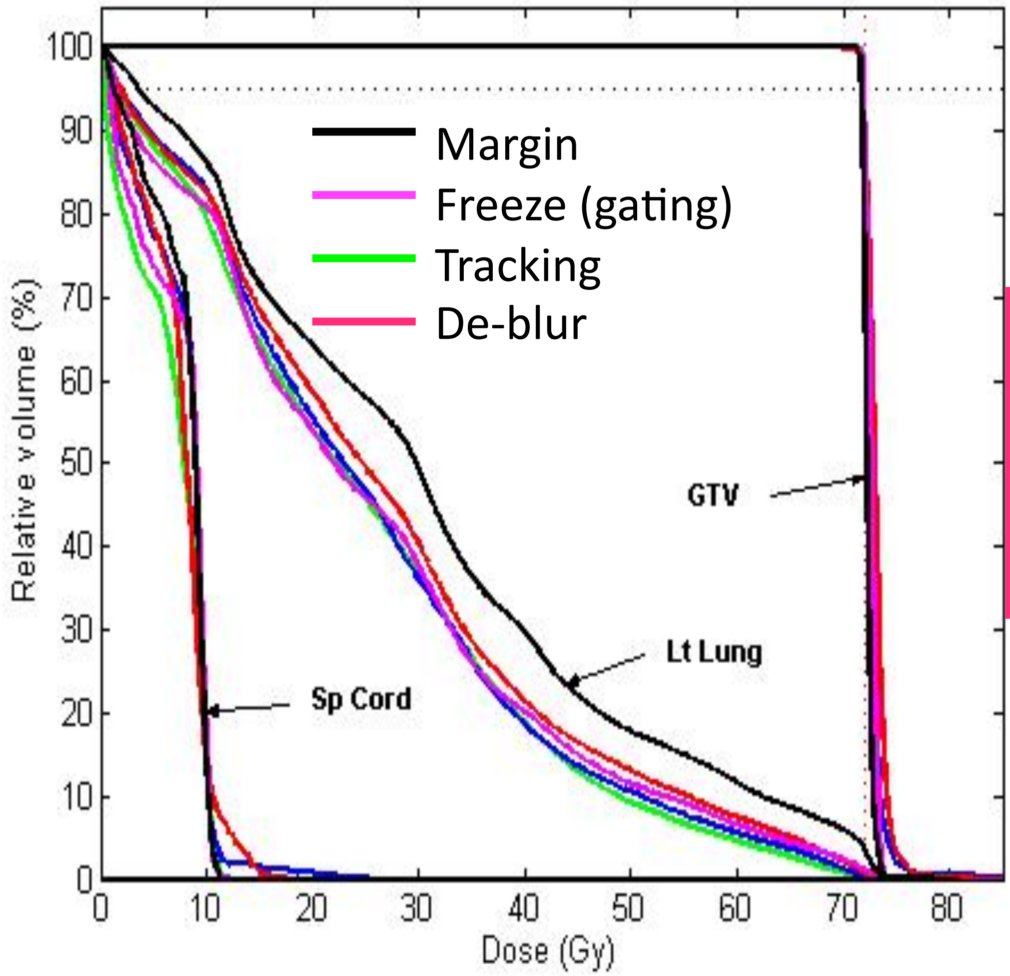
Dose blurring



De-blurring with IMRT -> “horns”



DVH for 4 different techniques



20% reduction of mean dose to left lung compared to margin

Trofimov et al., Phys Med Biol. 50:2779-98, 2005

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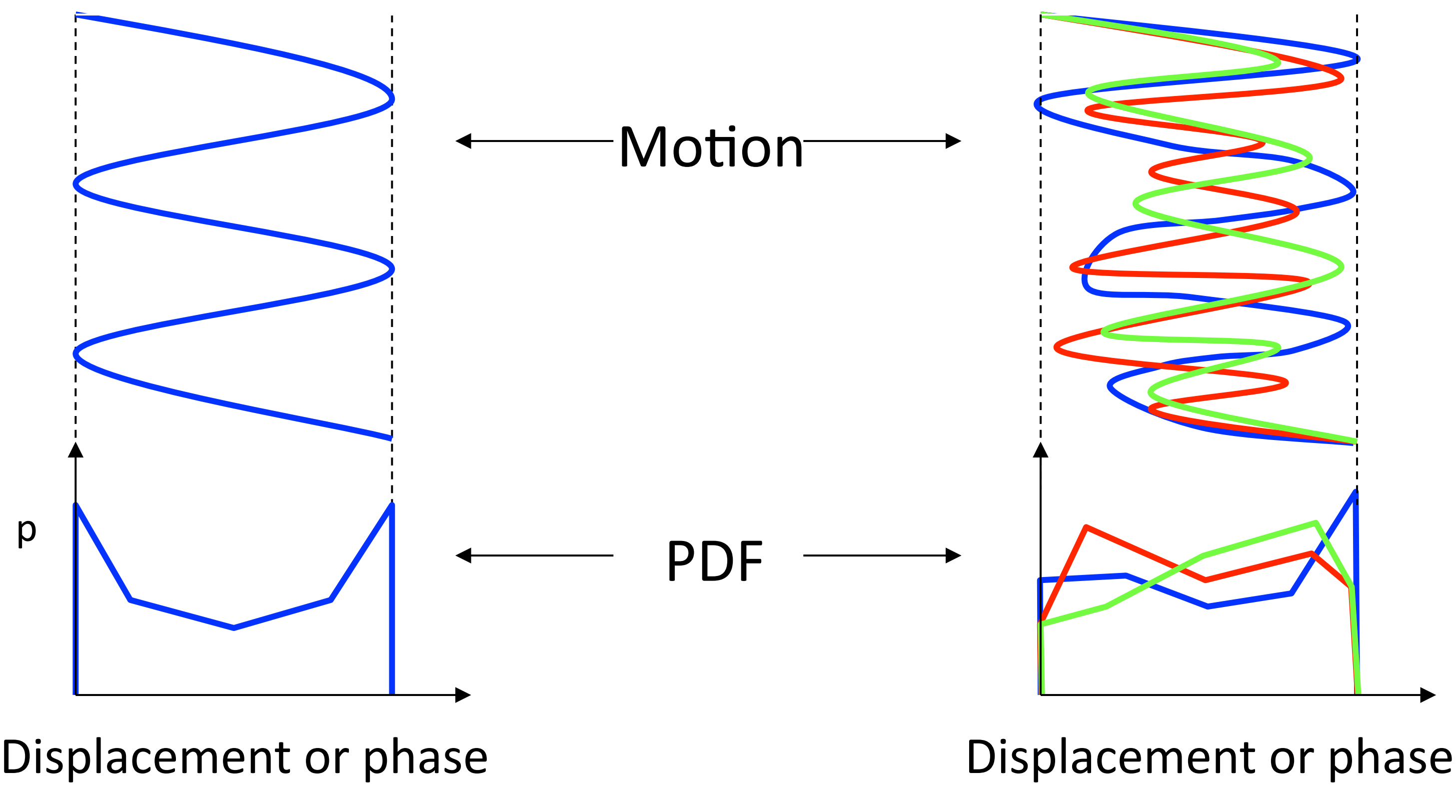
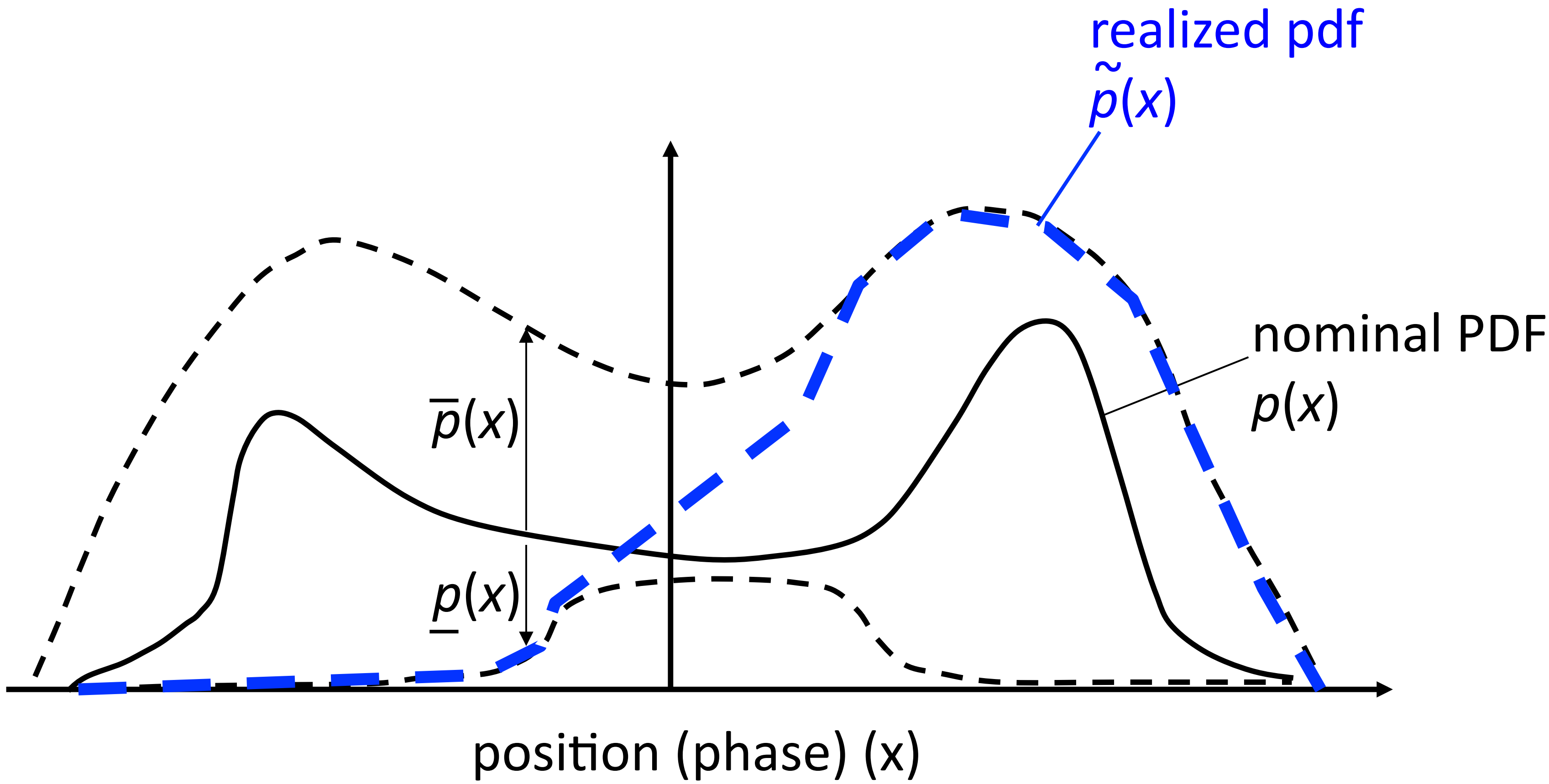
- Dose conformality of edge-enhanced IMRT with “horns” is almost as good as gating or tracking
- Is this too good to be true?

Uncertainty model for de-blurring method

- PDF for regular motion
- Uncertain motion may lead to many PDFs



Uncertainty set – PDF and "error bars"



Tim Chan et al: Phys Med Biol 51:2567 (2006)

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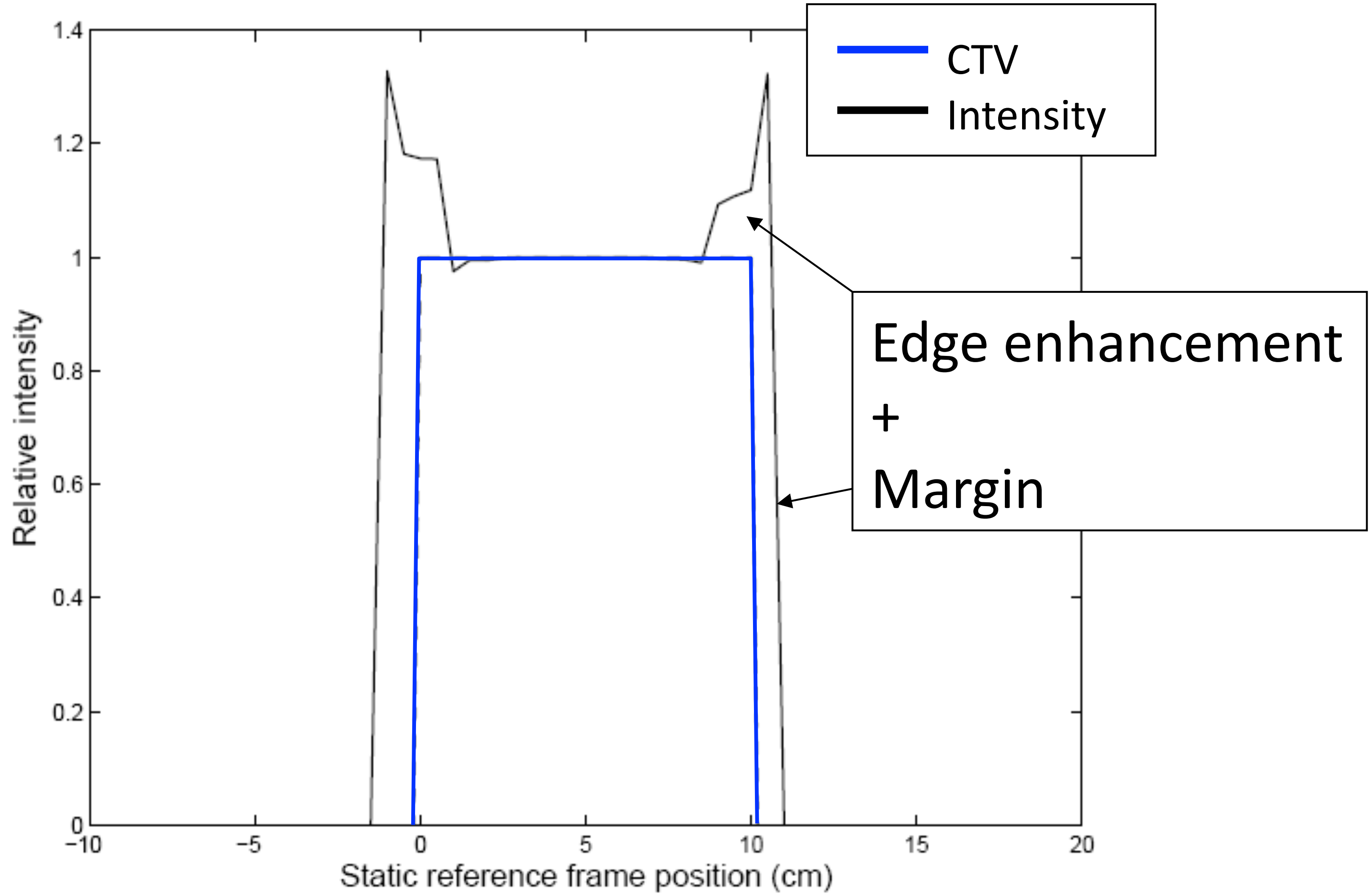
What is the worst case?

- A given **target** voxel gets different dose values for different breathing phases *x*.
- Worst case is when low dose values are more likely ($\overline{p}$) and high dose values are less likely ($\underline{p}$).

- As a <u>consequence</u>, robustification will limit spikes in intensity maps

➢ improved deliverability.

Robust edge enhanced intensity profile



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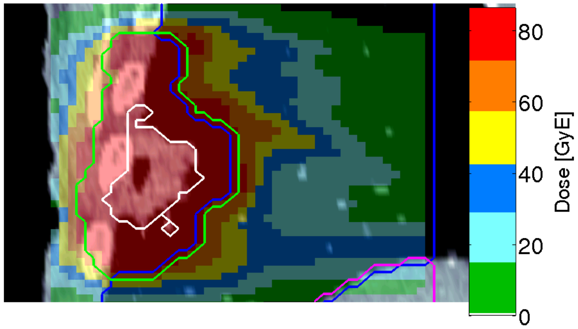
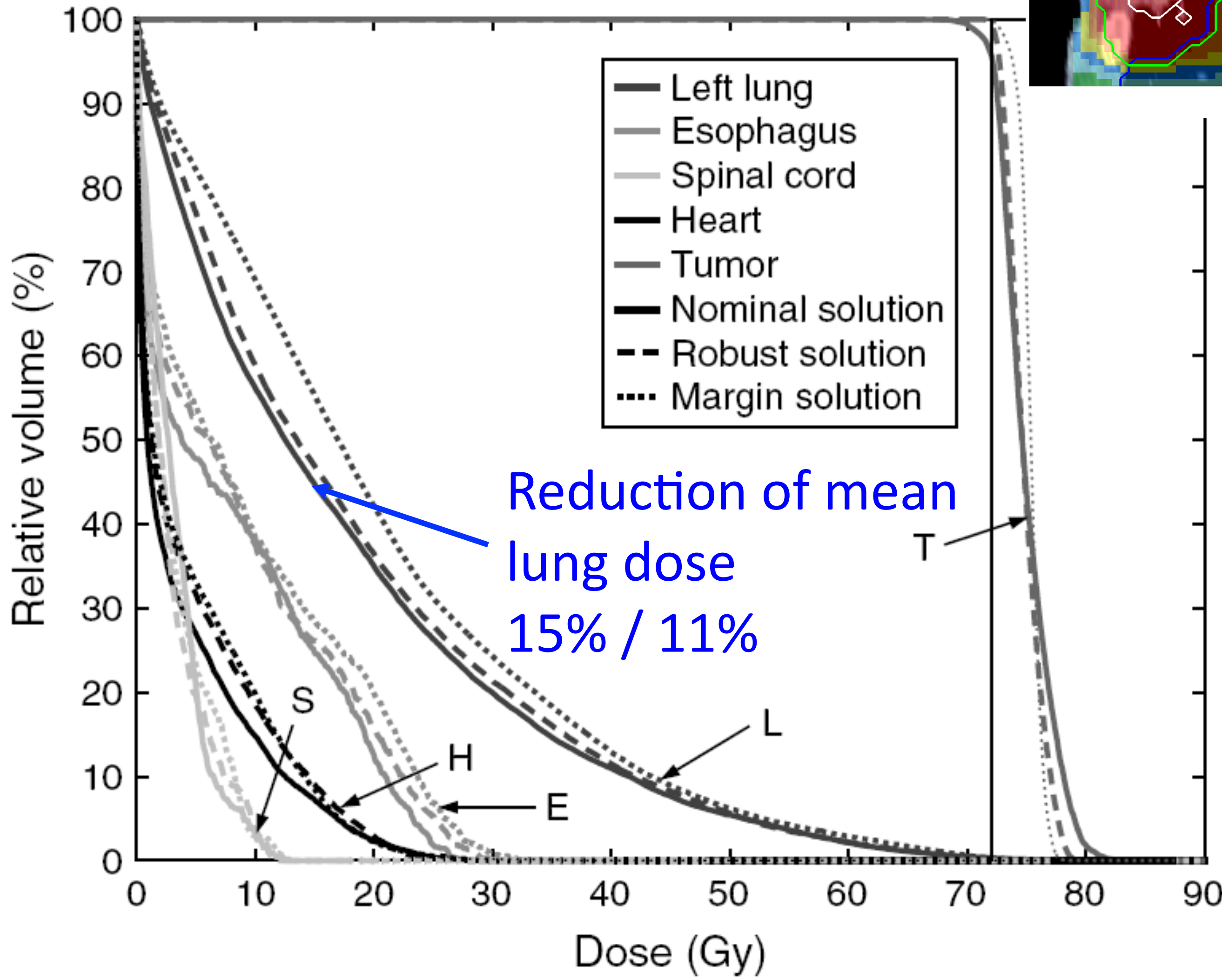
T. Chan et al., PMB 51(2006):2567-2583

Clinical lung case





Reduction of mean lung dose
15% / 11%

Bortfeld, Chan, Trofimov, Tsisiklis, OR 2008

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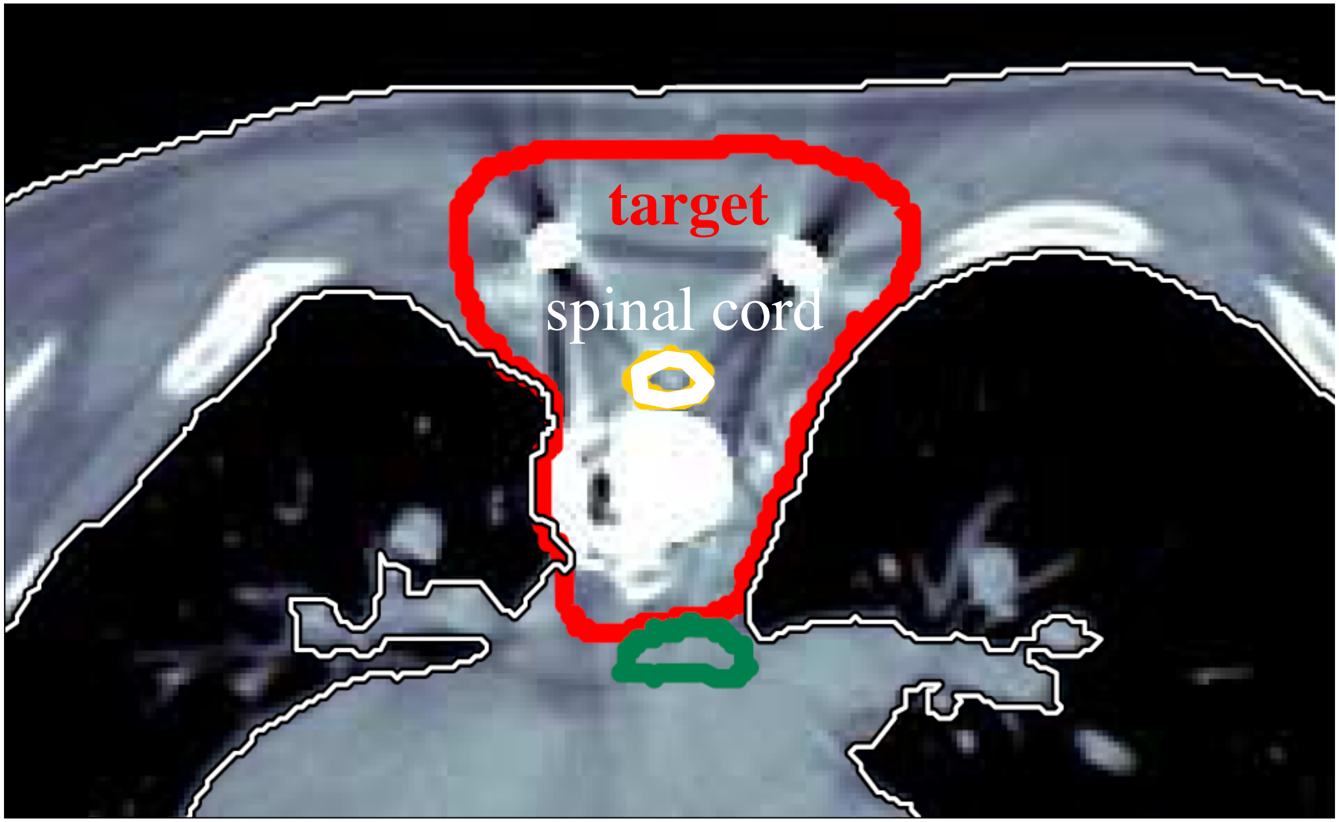
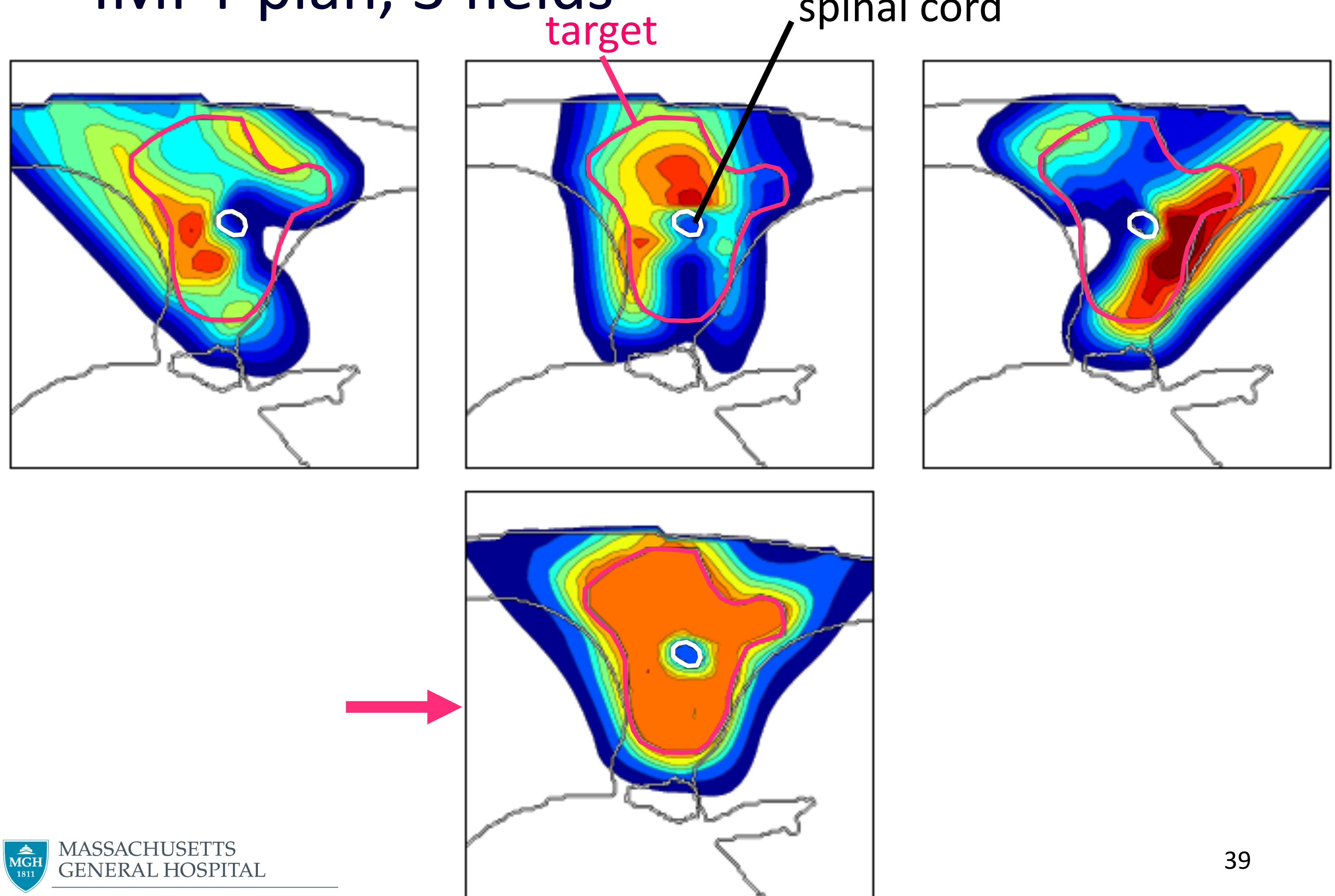
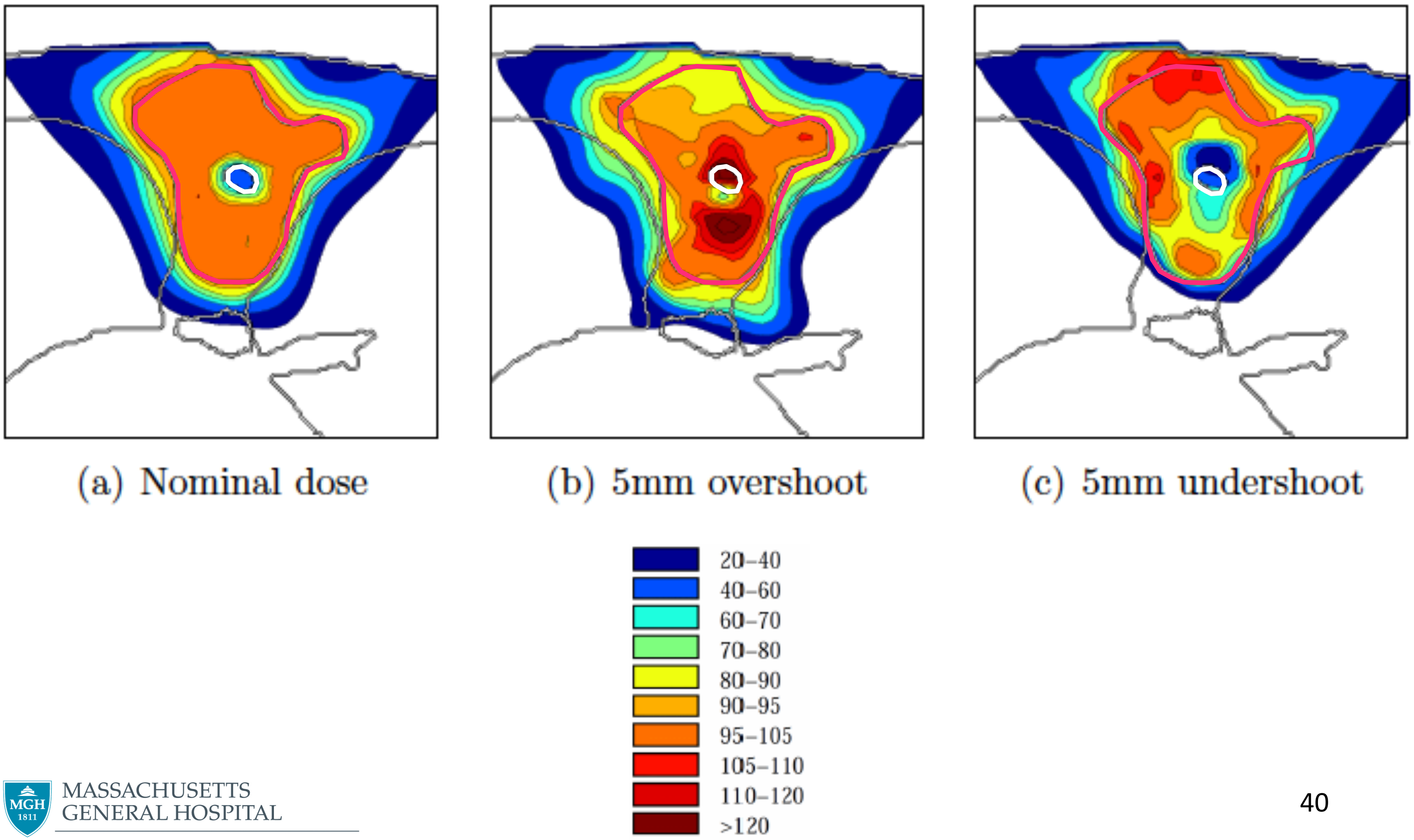
Example 2: Protons, range uncertainties Stochastic programming



IMPT plan, 3 fields



Sensitivity analysis



(a) Nominal dose (b) 5mm overshoot (c) 5mm undershoot

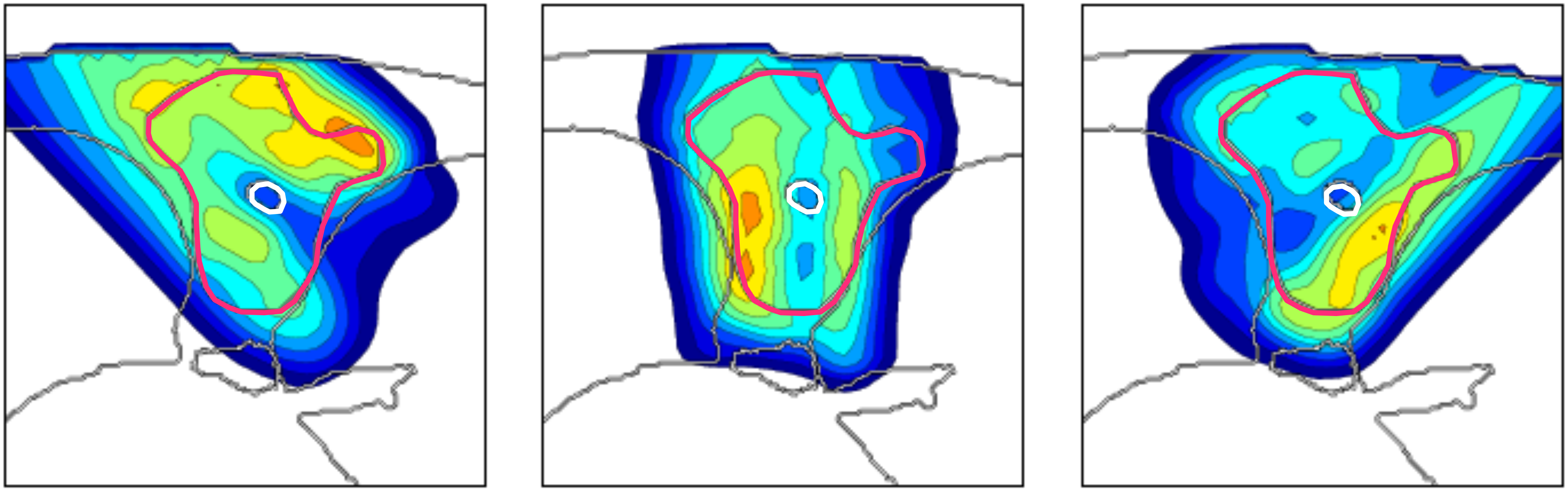
Stochastic programming

$$\underset{x}{\text{minimize}} \quad \sum_s p_s \Bigg[\underbrace{w_T \sum_{i \in T} (d_i^s - D^{pres})^2}_{\text{Target dose deviation}} + \underbrace{w_{SC} \sum_{i \in SC} (d_i^s)^2}_{\text{Spinal cord dose}} \Bigg] + \underbrace{f_{HT}(d^1)}_{\text{healthy tissue dose}}$$

3 scenarios:

- *Scenario 1*: Nominal scenario, $p_1 = 0.5$
- *Scenario 2*: 5 mm range overshoot, $p_2 = 0.25$
- *Scenario 3*: 5 mm range undershoot, $p_3 = 0.25$

Robust IMPT plan



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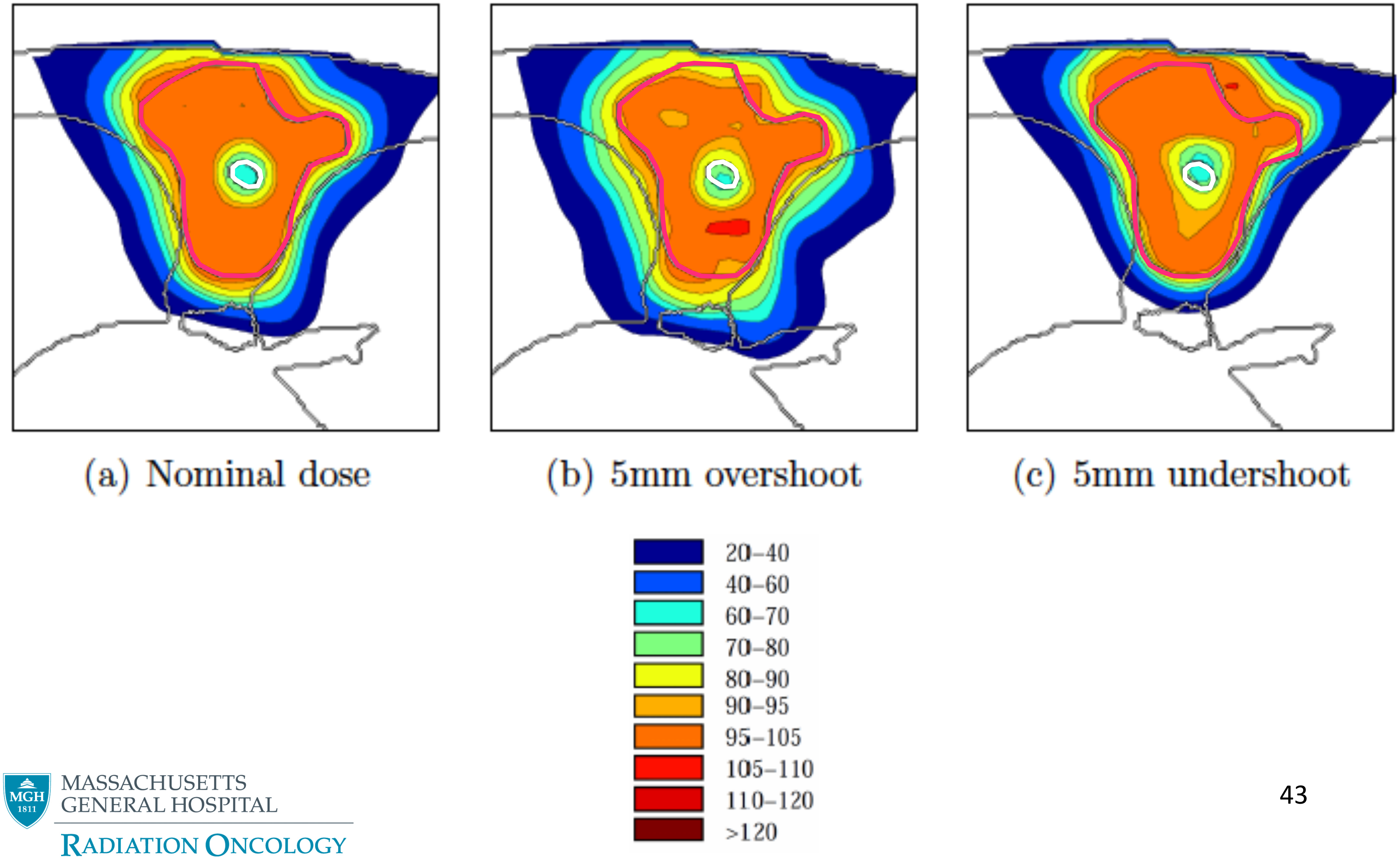
Sensitivity analysis II (robust plan)



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Vision for the future

- No (PTV) margins in treatment planning
- Instead, quantify motion and uncertainties, and let the planning system find a robust solution. This may be a margin-like solution but could also be an advanced intensity-modulated solution (e.g., “horns”).

Main take-home-messages:

- Two ways to include uncertainties in treatment planning:
    1. stochastic programming (optimization of *expected* outcome)
    2. optimize worst case
- Robust optimization can lead to new types of fault-tolerant dose distributions, e.g. beam "horns" for motion, and robust proton dose distributions.
- There is always a price of robustness.