Heavy Ion Therapy Research Integration

Impact and mitigation of uncertainties in particle therapy treatment planning

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Heavy Ion Therapy
Masterclass school

Impact and mitigation of uncertainties in particle therapy treatment planning

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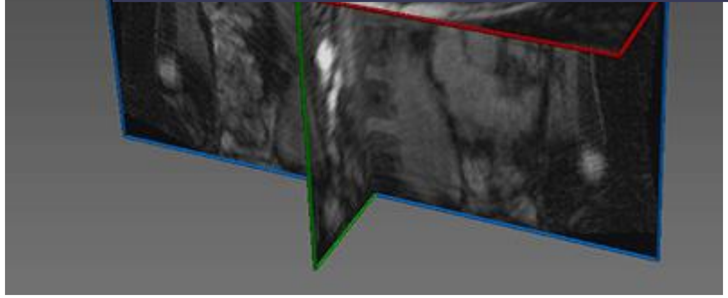
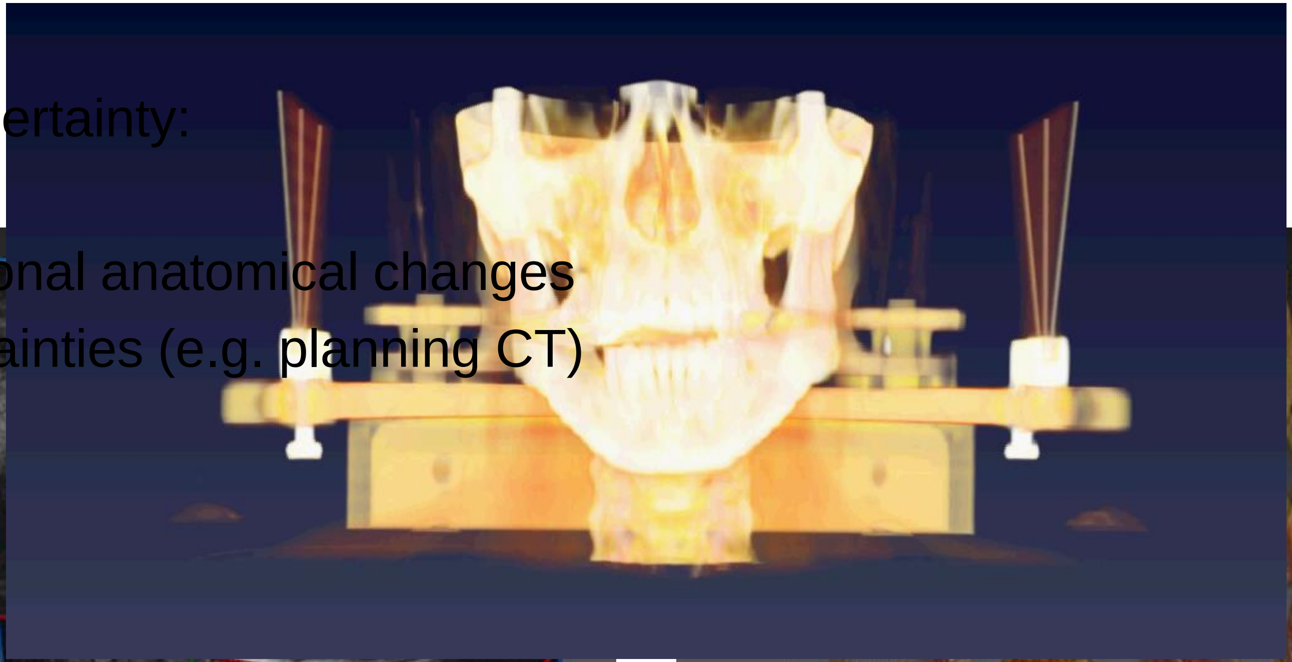
Recap: Dealing with uncertainties

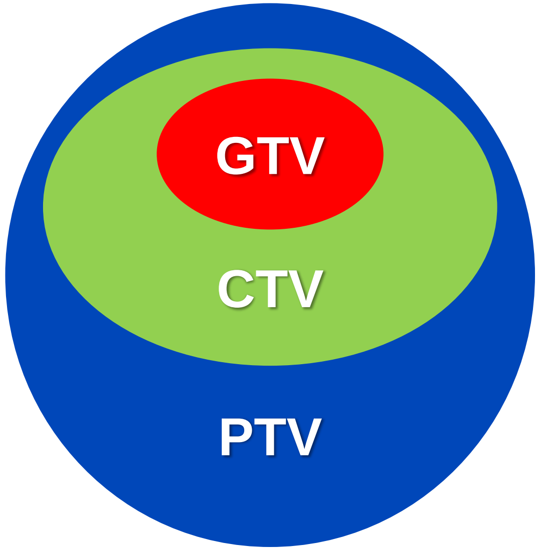
- Possible sources of Uncertainty:
  - Daily patient set-up
  - Inter- and intraffractional anatomical changes
  - Preparational uncertainties (e.g. planning CT)
  - machine set-up
  - etc.





Animations courtesy of Paul Merca & Markus Stoll

Recap: Margins in treatment planning



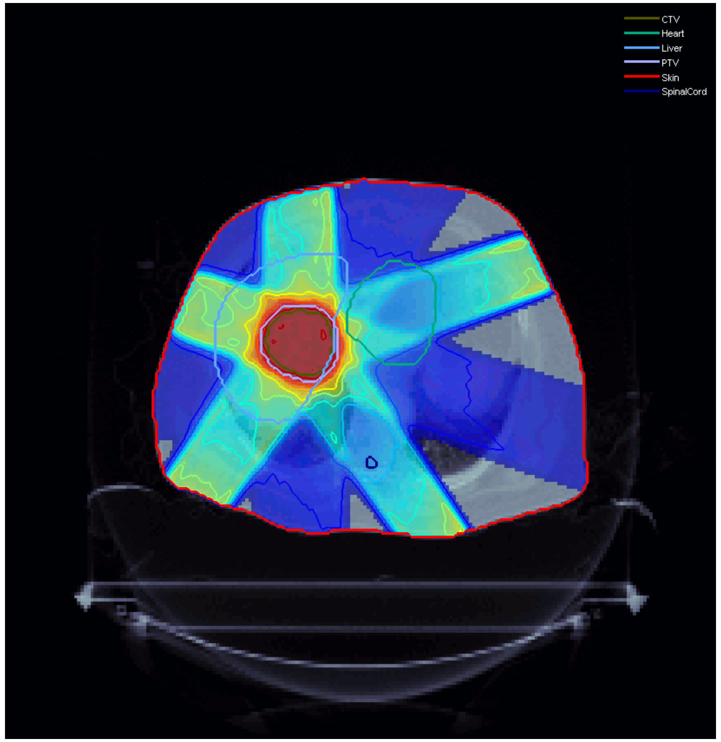
- GTV = Gross tumor volume
  tumor volume that is visible on the images
- CTV = Clinical target volume
  includes the GTV and regions where invisble tumor tissue is expected
- PTV = Planning target volume
  safety margin to take uncertainties into account

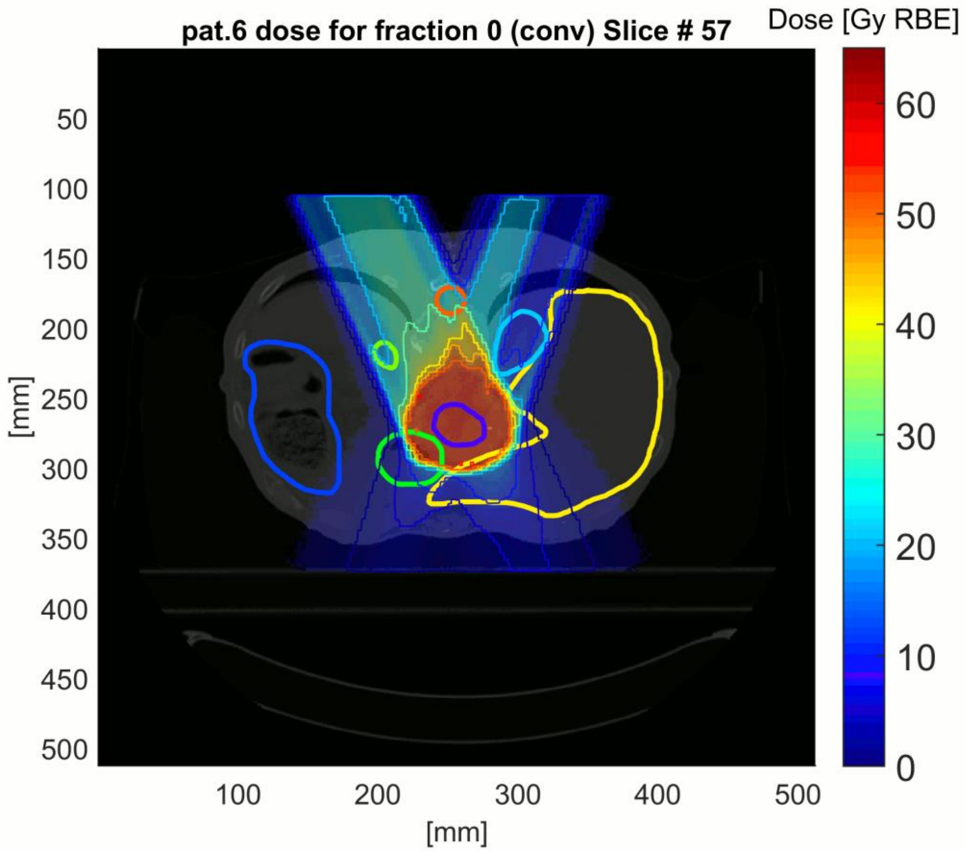
W. Schlegel & A. Mahr: 3D Conformal Radiation Therapy Springer Multimedia DVD

ICRU report 50

Recap: Margins, really?

- The “original” margin recipe for photon therapy:
  “**Minimum dose to CTV is 95% for 90% of population**” $2.5\,\sigma_{\mathrm{sys}} + 0.7\sigma_{\mathrm{rand}} - 3\mathrm{mm}$





→ Not applicable for protons / ions!

Steitz et al., *Radiation Oncology 2016,* **11**:134

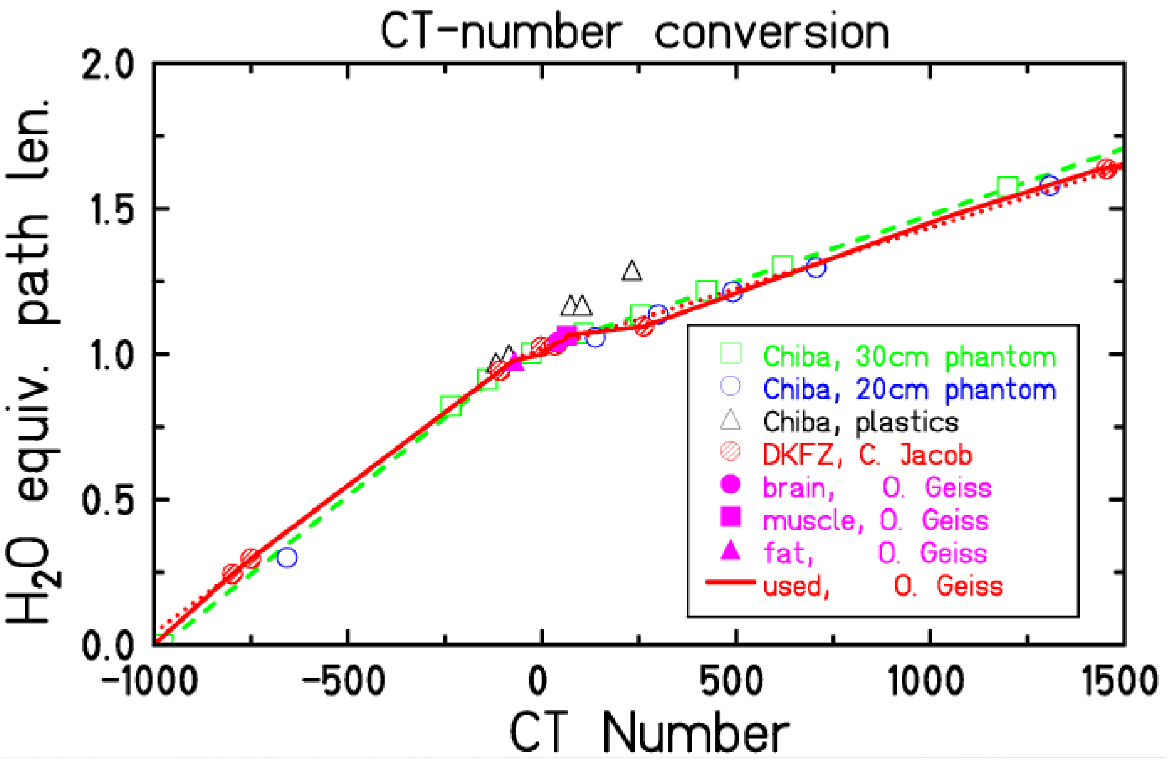
van Herk et al., *IJRBOP 2000,* **57**(4):1121

Range Uncertaintes: HU → RSP Conversion

- CT Image in Hounsfield Units
  → Attenuation of photon beam in medium
  → relevant ion quantities: $S \rightarrow I, n_e$

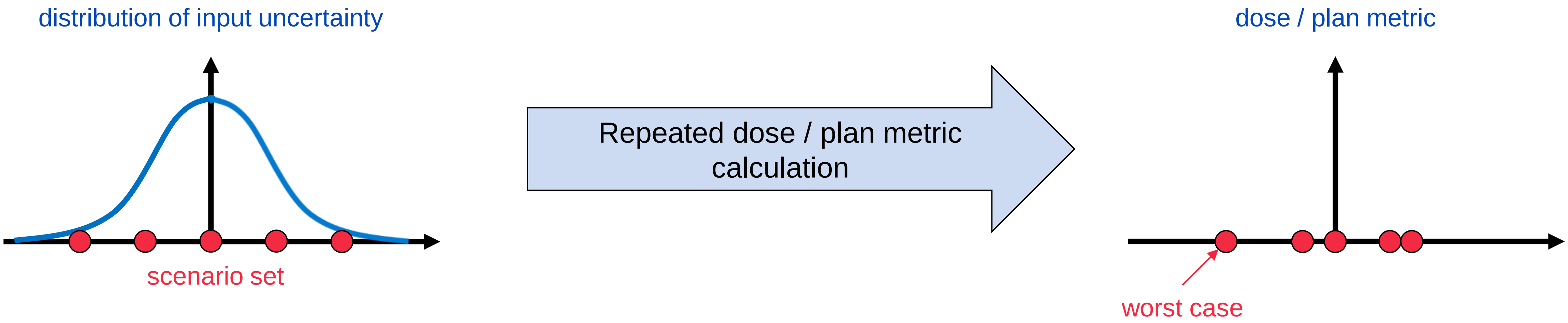
- Dose calculation algorithms require
  - Deterministic algorithms:
    Water-equivalent path length (WEPL) / relative stopping power
  - Monte Carlo:
    Material properties/ Material density

→Uncertainties in calibration!
(compare previous talk by Joao Seco: Dual energy CT)



Quantification & mitigation techniques in planning: Robust / worst-case approach

- Robust / worst-case approach:



- Optimization:
  minimax, voxel-wise worst-case, etc.
- Limitations:
  - Robustness enforced, but is the output worst case really among the input worst cases?
  - Complexity depends heavily on number of uncertain variables

Robust/worst case optimization: Example 1

- Describe uncertainty with scenarios π from a discrete uncertainty set
- During optimization, evaluate all objective functions and “act” on the worst case / maximum

Optimization problem

$$\boldsymbol{w}^* = \arg\min \max_{\pi} F(\boldsymbol{d}^{\pi})$$

s. t.

$$\boldsymbol{c}^l \leq C(\boldsymbol{d}^{\pi}) \leq \boldsymbol{c}^u$$

„while the minimum PTV dose is above 56 Gy in all scenarios“

„Minimize the maximum mean lung dose from all scenarios....“

Robust/worst case optimization: Example 2

- Describe uncertainty with scenarios π from a discrete uncertainty set
- All scenarios may contribute to a voxel-wise combination of a worst case dose distribution

$$d_i^{WC} = \begin{cases} \min(d_i^{\pi}), i \in target \\ \max(d_i^{\pi}), i \in rest \end{cases}$$

Optimization problem

$$\boldsymbol{w}^* = \arg\min \ F(\boldsymbol{d}^{WC})$$

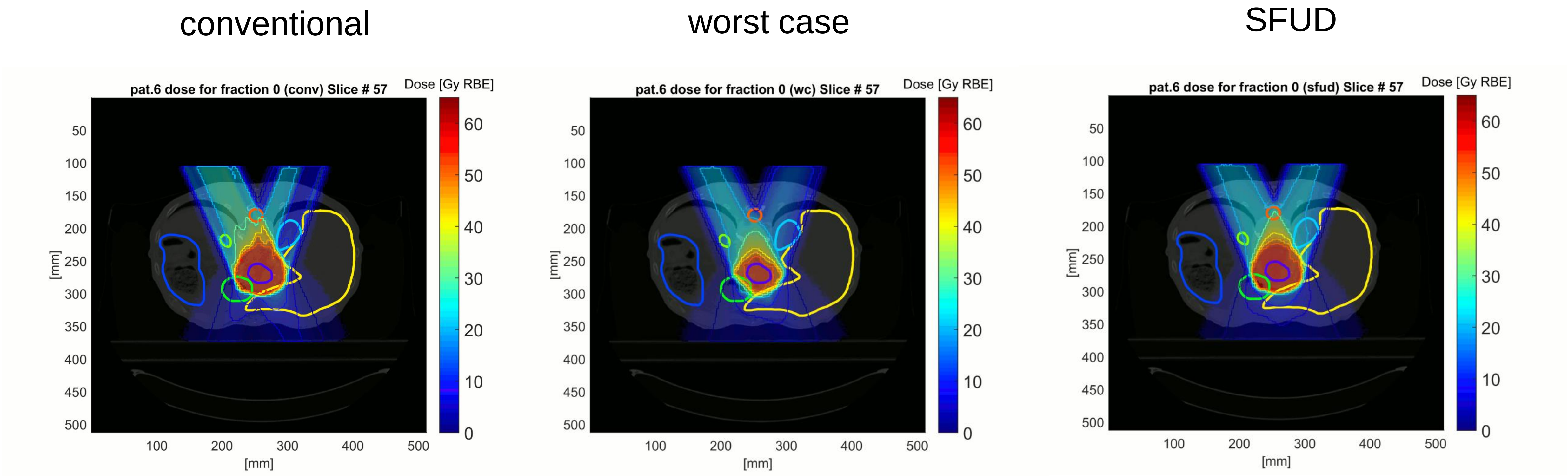
s. t.

$$\boldsymbol{c}^l \leq C(\boldsymbol{d}^{WC}) \leq \boldsymbol{c}^u$$

„while the minimum PTV dose is above 56 Gy in all scenarios“

„Minimize the mean of maximum voxel doses from all scenarios....“

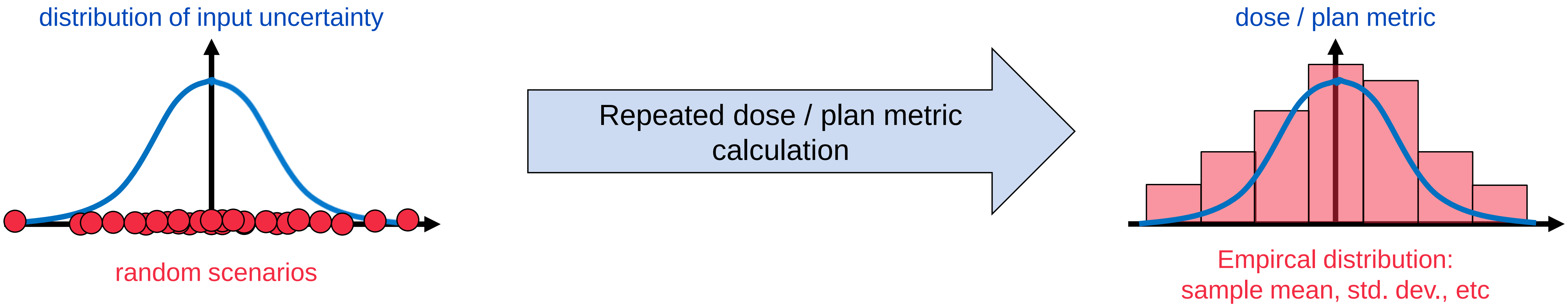
Robust/worst case optimization: Patient case



J Steitz, et al (2016). Worst case optimization for interfractional motion mitigation in carbon ion therapy of pancreatic cancer. *Radiation Oncology* **11**(1):134

Quantification & mitigation techniques in planning: stochastic / probabilistic optimization

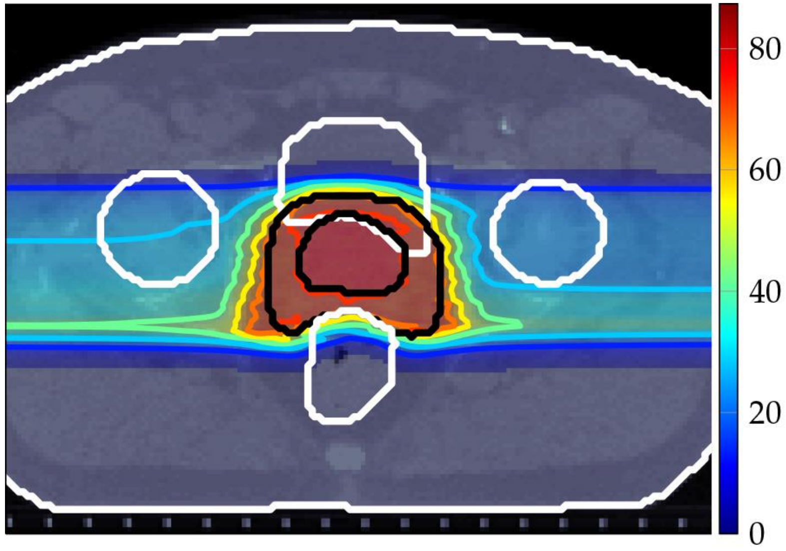
- Stochastic approach



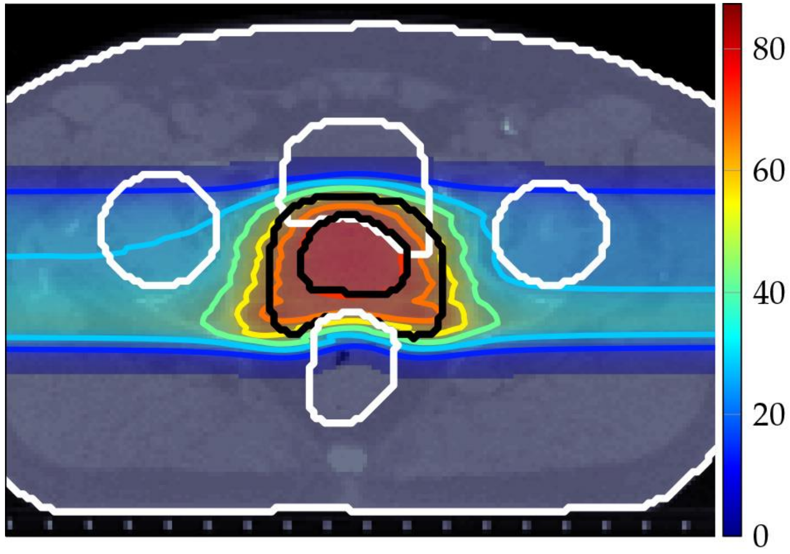
- Optimization:
  - Expected value / statistical mean of objective function
- Limitations:
  - statistical accuracy depends on number of samples (→ computational complexity)
  - no classical „robustness“ enforced

Quantification & mitigation techniques in planning: stochastic / probabilistic optimization

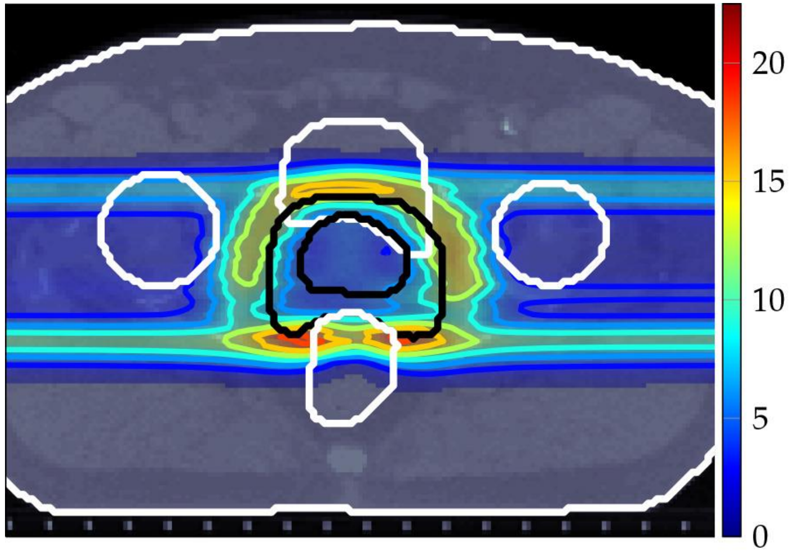
nominal dose



expected dose

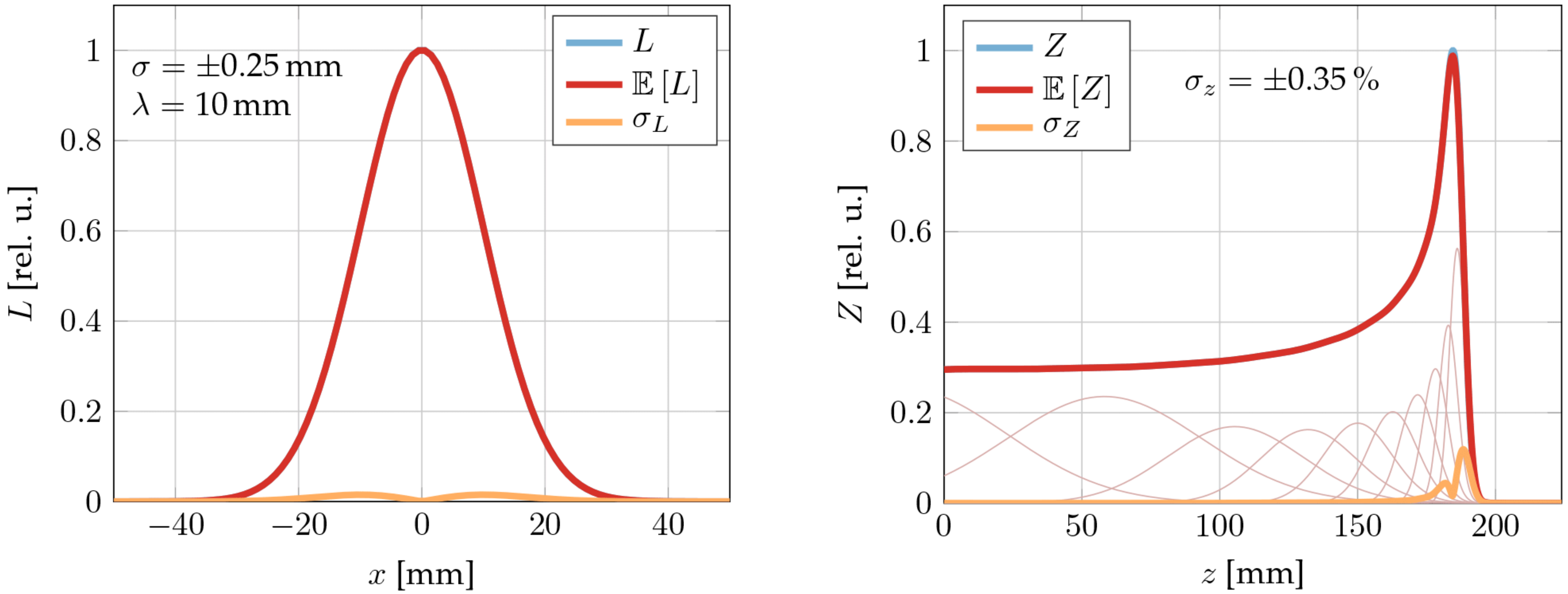


std. dev. of dose



Excursion: Probabilistic Interpretation

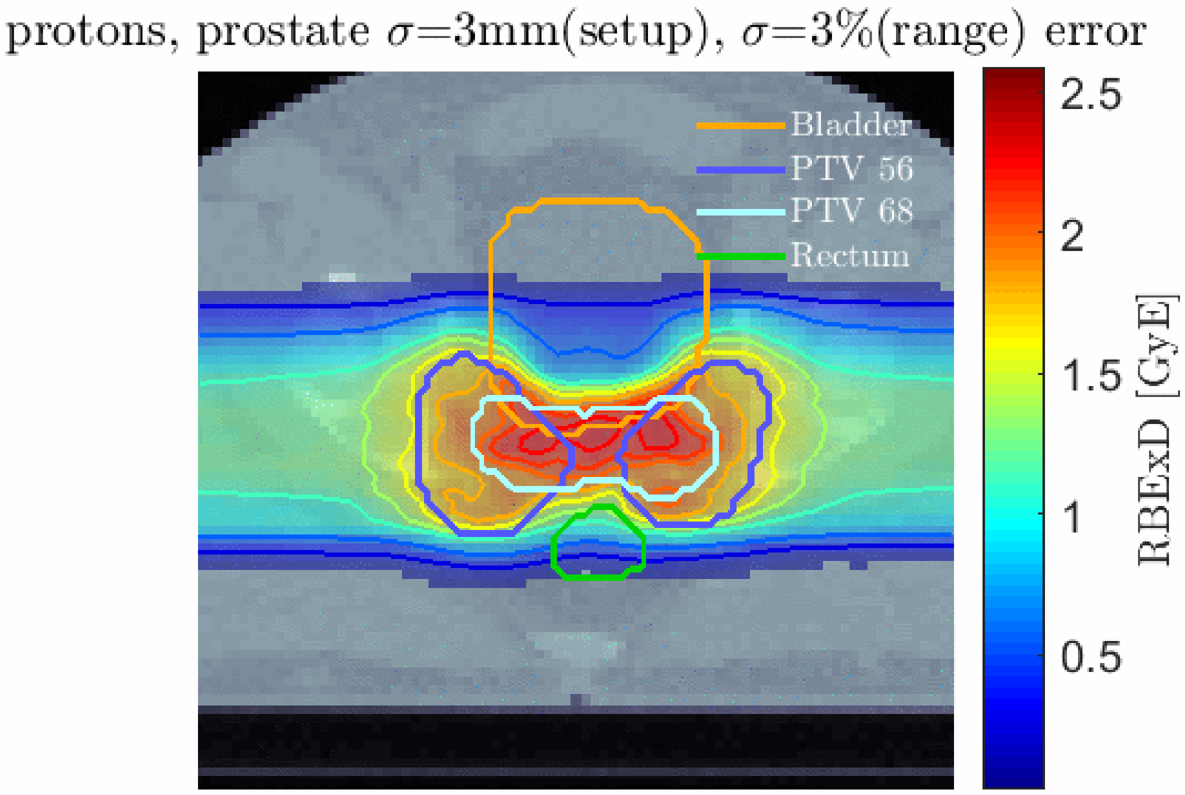
- Thinking about the individual beamlet dose as a probabilistic quantity illustrates "degradation"

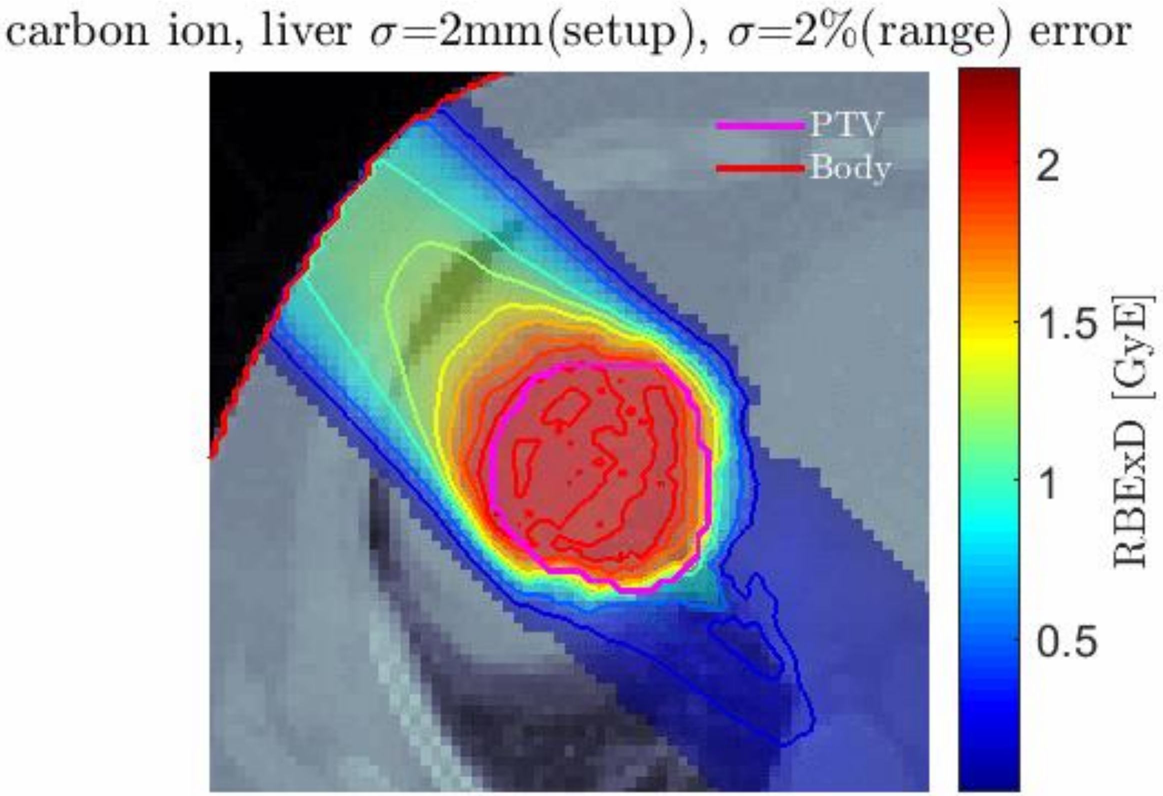


Bangert et al (2013), DOI: 10.1088/0031-9155/58/16/5401
Wahl (2018), DOI: DOI: 10.11588/heidok.00025127

Excursion: Probabilistic Interpretation

- Illustration of uncertainty space of treatment plans





Stochastic optimization

- Describe uncertainty with scenarios π from a sampled uncertainty set
- During optimization, evaluate all objective functions and optimize the expected value / the sample mean

Optimization problem

$$\boldsymbol{w}^* = \mathrm{E}[F(\boldsymbol{d})] \approx \frac{1}{n_\pi}\sum_{\pi} F(d_\pi)$$

s. t.

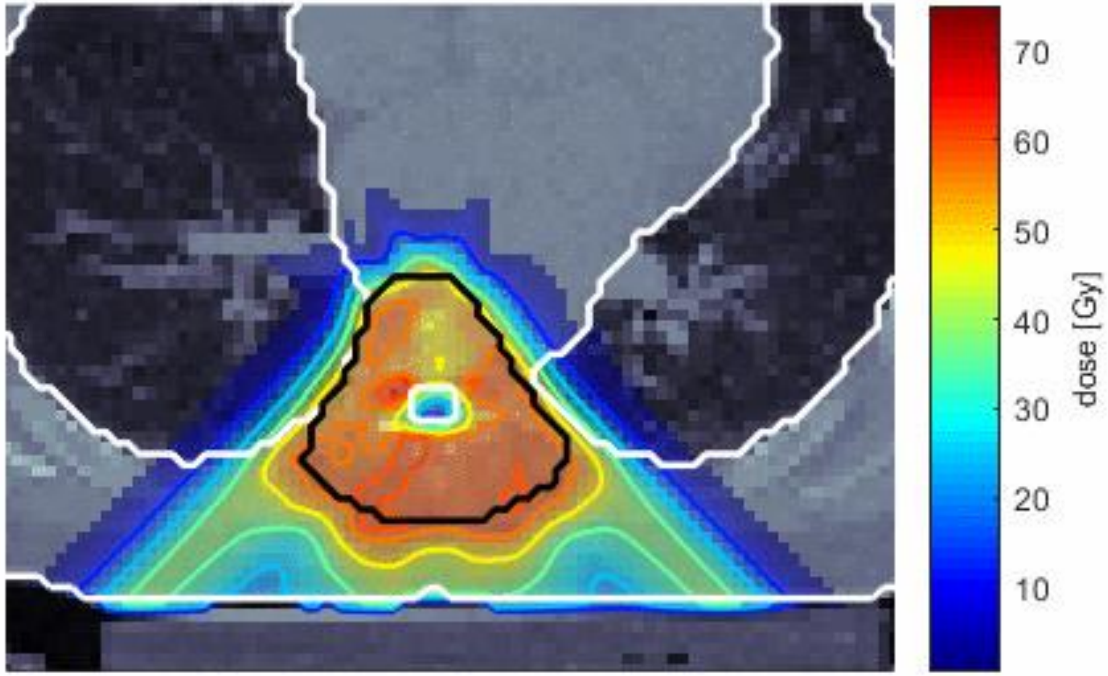
$$\boldsymbol{c}^l \leq C(\boldsymbol{d}^\pi) \leq \boldsymbol{c}^u$$

„while the minimum PTV dose is above 56 Gy in all scenarios“

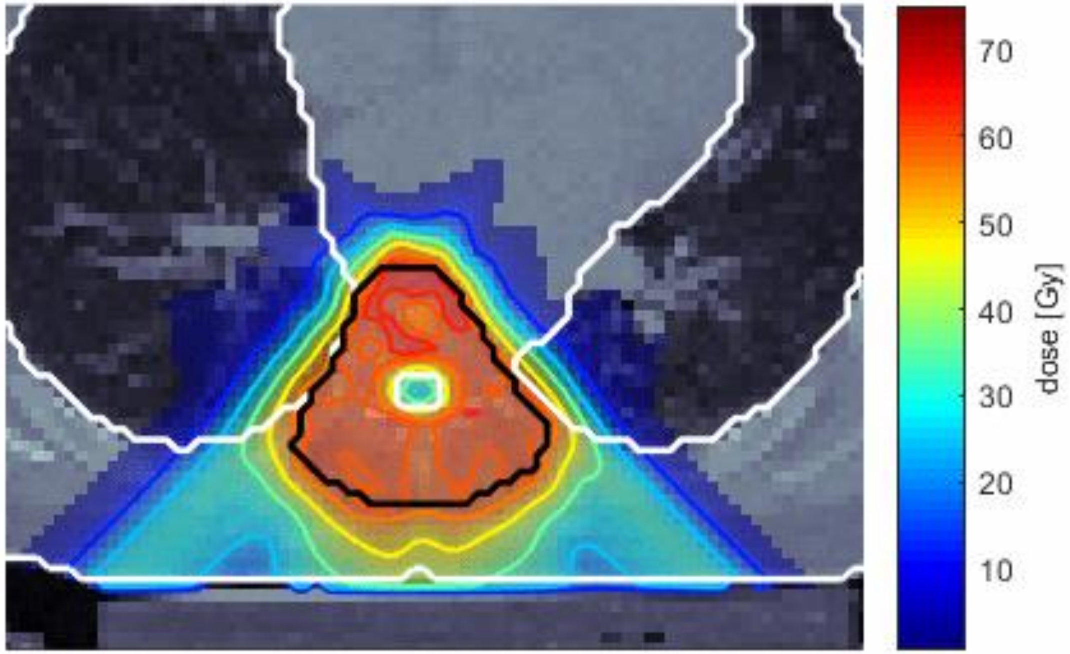
„Minimize the expected mean lung dose from all scenarios....“

Samples from nominal and probabilistic plan

Nominal plan



Probabilistic plan

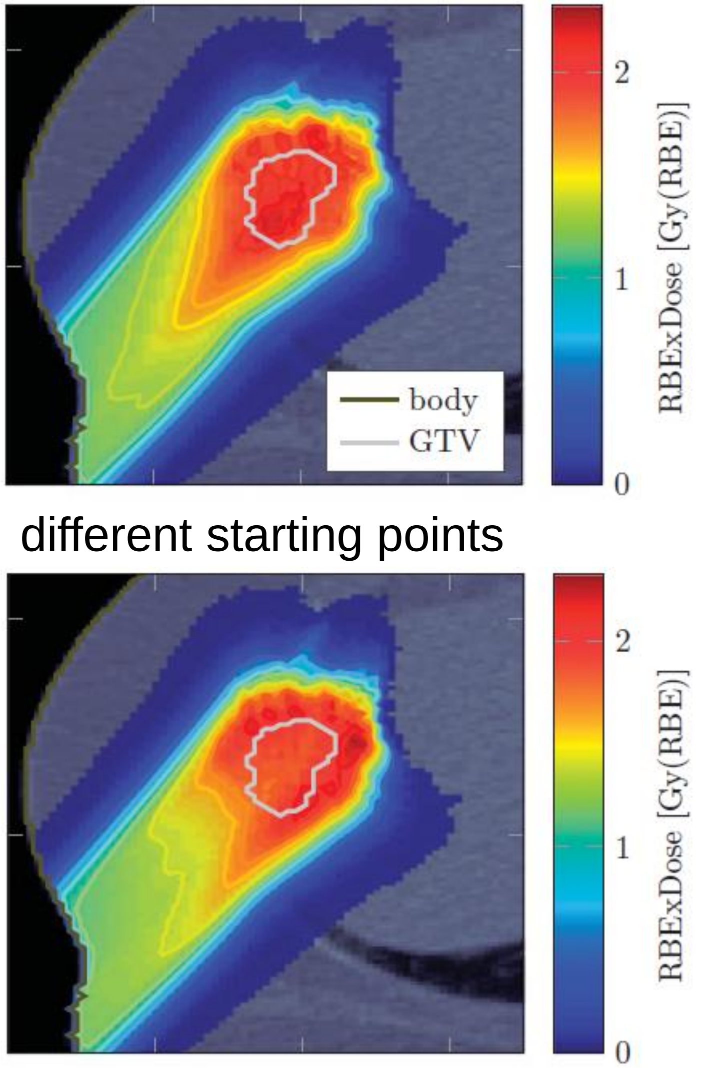


Uncertainty due to delivery during motion – Interplay effects

- Scanning methods deliver spots in (uncertain) time sequence:
  - Starting point?
  - Duration for energy level switch
  - Scanning pattern

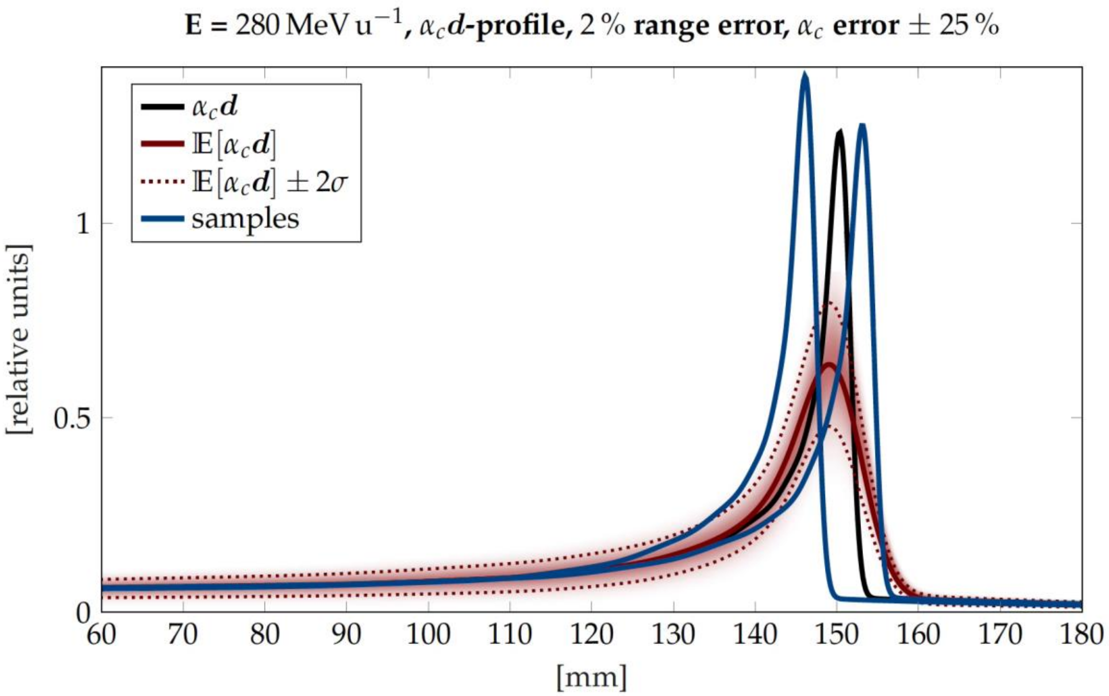
→Interplay effect

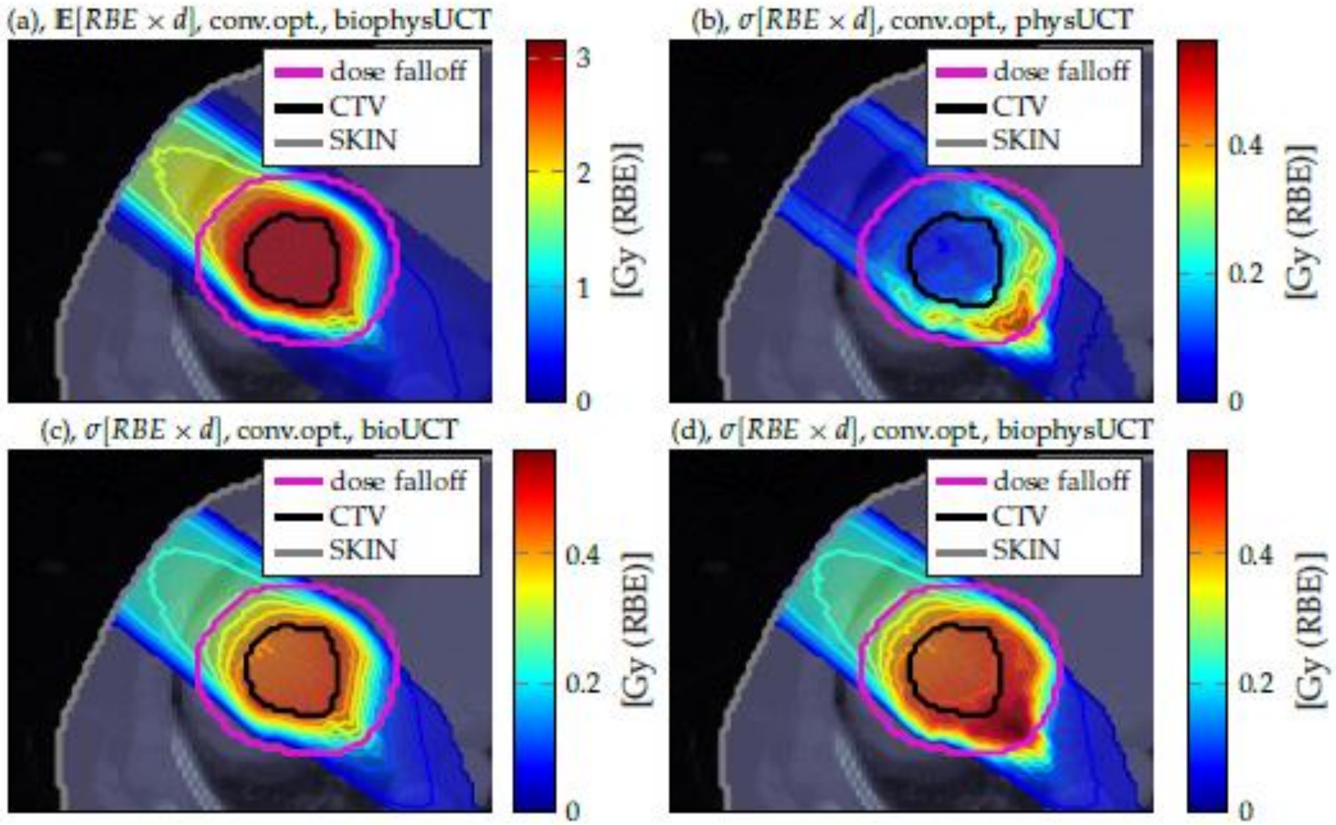
- Mitigation techniques (also check previous talk):
  - Fixation techniques to minimize motion during treatment
  - Daily adaptation
  - Rescanning
  - Robust Optimization



Ulrich et al., *Acta Oncologica, 2017,* **56**:1420

Not to forget: Uncertainty due to biology (example for carbon ions)





- Biological uncertainty in model parameters can be large and affect the whole dose profile!

HP Wieser, *PhD thesis*, University of Heidelberg, 2020

Summary

- Ion therapy is particularly sensitive to uncertainties
  - CT Hounsfield Units to rSP conversion
  - Patient set-up
  - Inter & intra-fractional motion, interplay
  - Biological model
  - etc.

- Ion therapy requires a *personalized* consideration of uncertainties, generic margin principles mostly don’t work!

- In planning, the problem is often approached by robust/stochastic optimization techniques

- Consider the other talks: due to the uncertainties ion therapy needs better fixation, better/more imaging, range verification, etc.

THANK YOU

This presentation was prepared for the HITRIplus Heavy Ion Therapy Masterclass School 2021.
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