Treatment Planning Techniques in PBS

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Disclosure

- None

Outline

- Uncertainties in PBS
  - Range
  - Setup
  - RBE
  - Motion
  - Anatomy
- Mitigation techniques in treatment planning
  - bsPTV (margin)
  - Beam selection
  - Robust optimization
  - Adaptive RT
  - Re-painting
  - RBE/LET optimization

Introduction

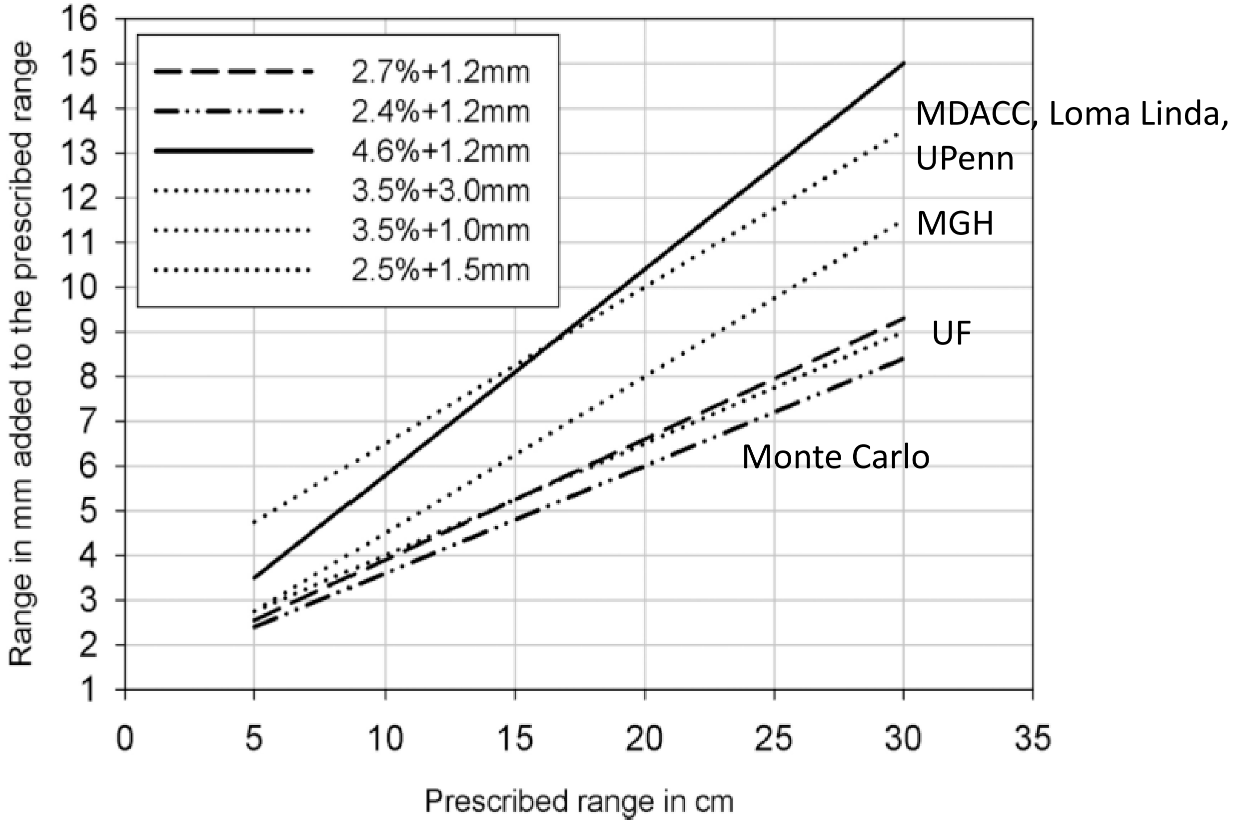
- Uncertainties in PT:

Proton Range

Patient Setup

Range Uncertainty

- CT HU to stopping power ratio (SPR)
  - Both are dominated by electron density ratio
  - But elemental composition matters
  - Various among facilities
  - Typically 2.5-3.5% with additional 1-3mm



3.5 mm at a range of 10 cm

7 mm at a range of 20 cm

Depends on depth !

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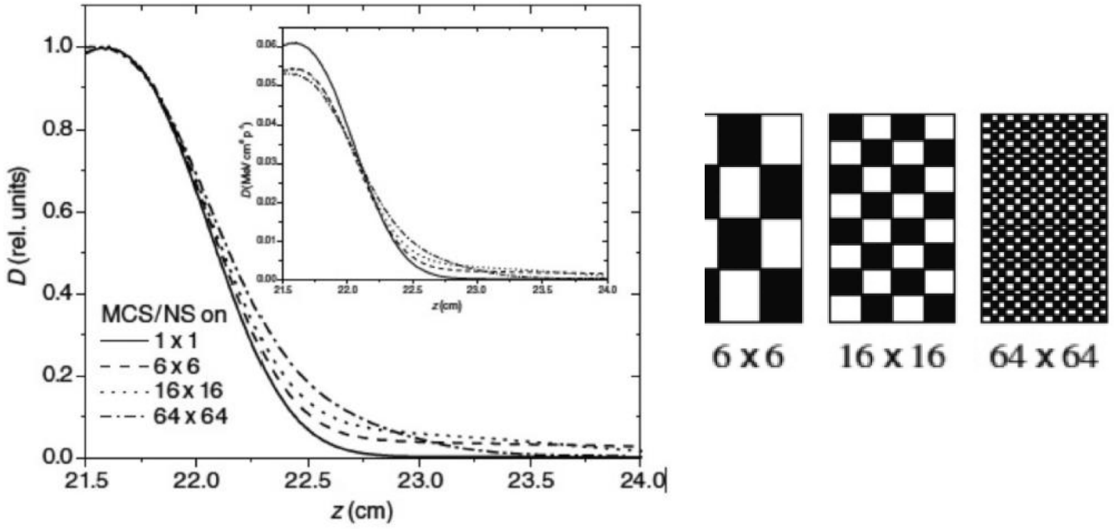
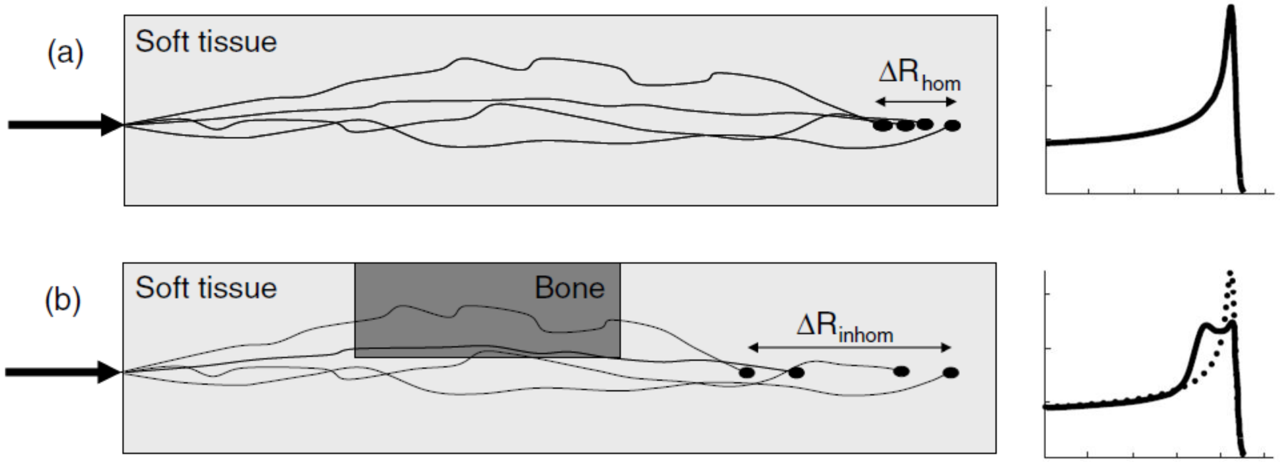
Paganetti, PMB 57(11), 2012

Range Uncertainty

- Tissue heterogeneities
  - Bragg peak degradation



Sawaguchi, *et al.*, PMB, 53(17) 2008



Lomax 2008, PMB, 53

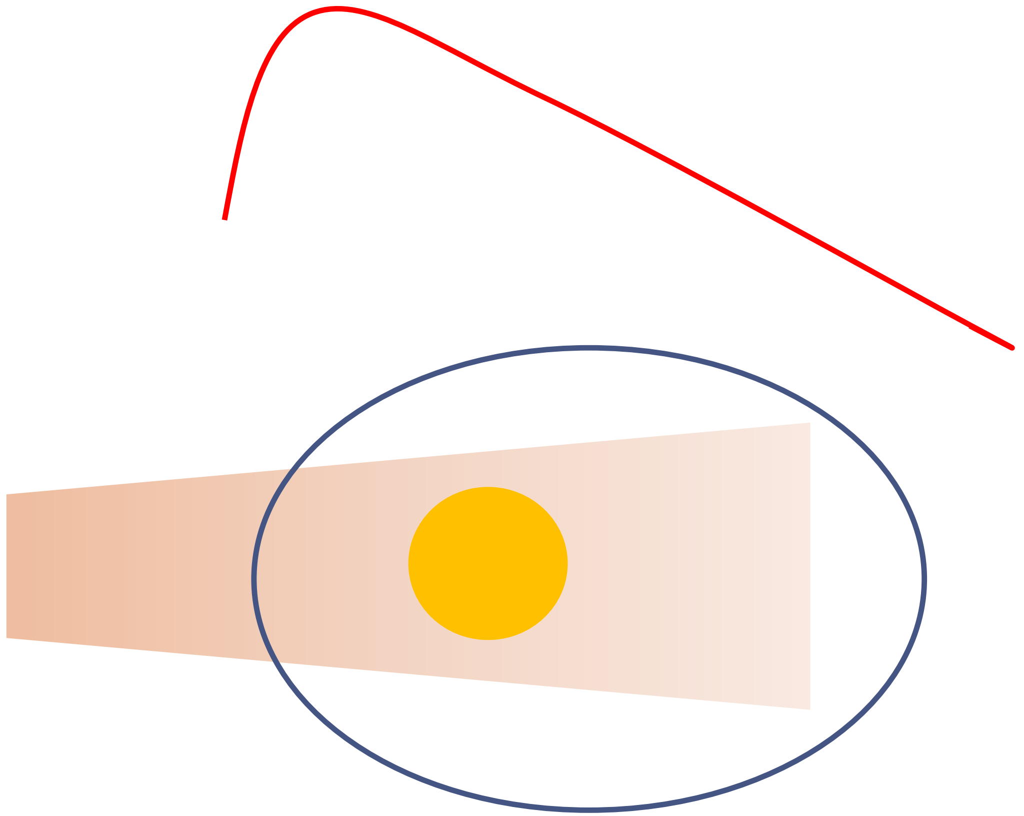
Solution—Margin

- PTV concept: accounts for setup and all geometric uncertainties to ensure dosimetric coverage of CTV

- PTV for proton planning needs to account for range uncertainties too.

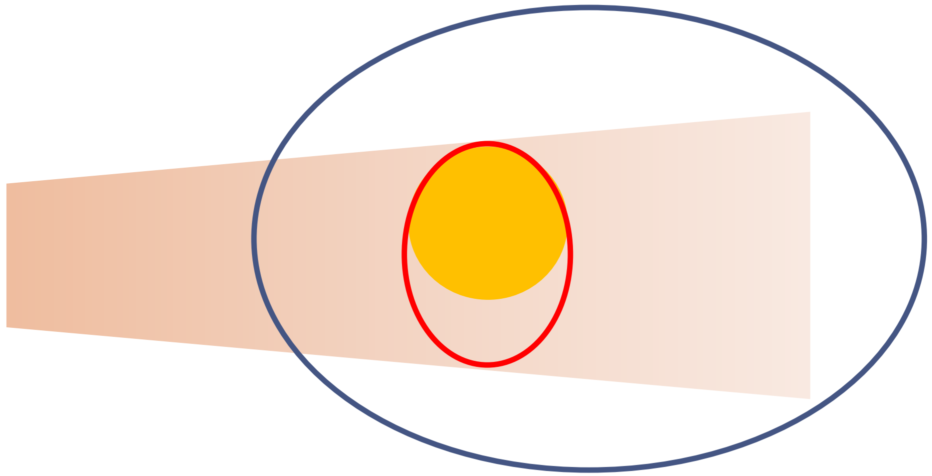
- Beam specific PTV (bsPTV) expansion

Photon PTV margin



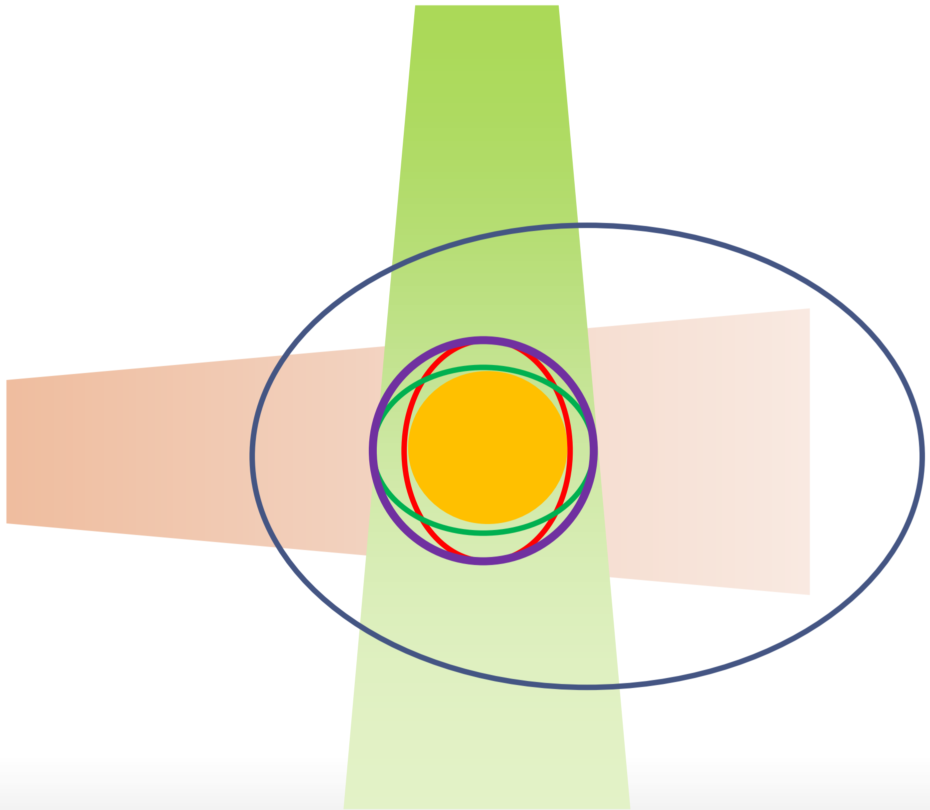
Setup up uncertainties in the direction parallel to beam's central axis has minimal effect (inv. Sq.) and can't be accounted for by margin.

Photon PTV margin



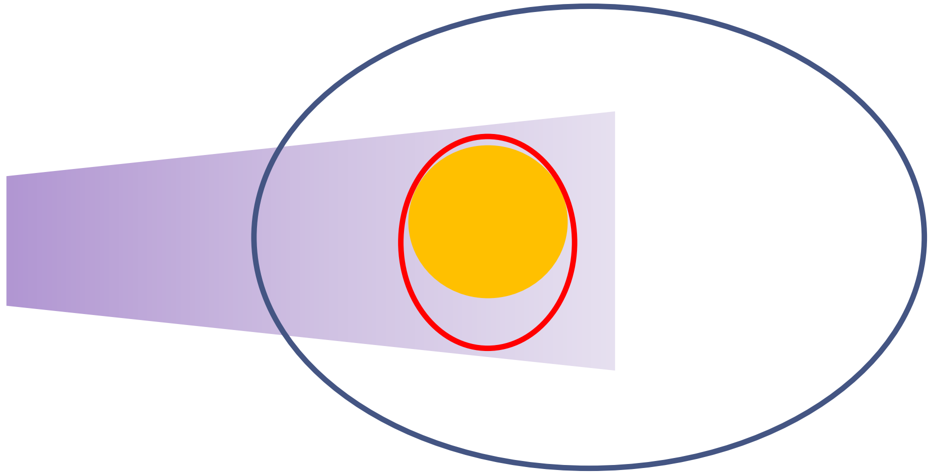
In the beam's eye view, only "lateral" margin is needed to account for setup up uncertainties in the direction perpendicular to beam's central axis

Photon PTV margin



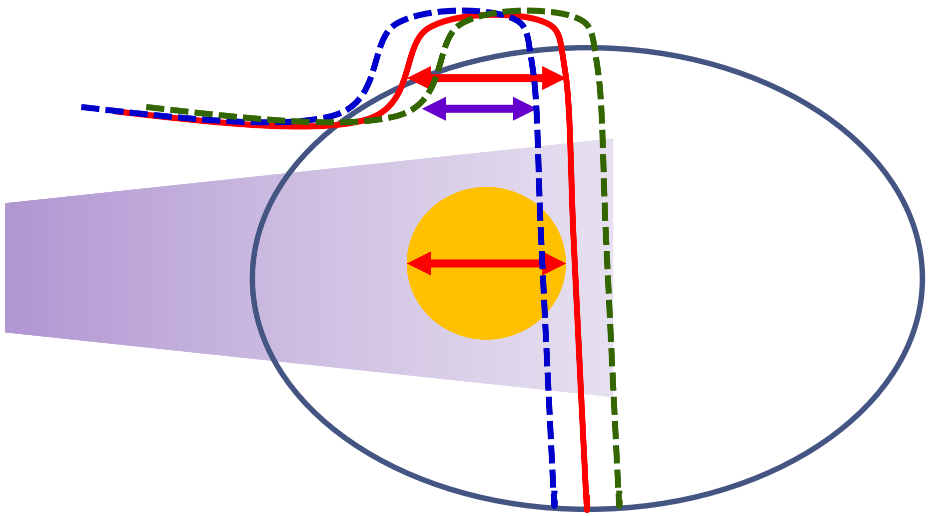
Using multiple beams requires margin in multiple directions

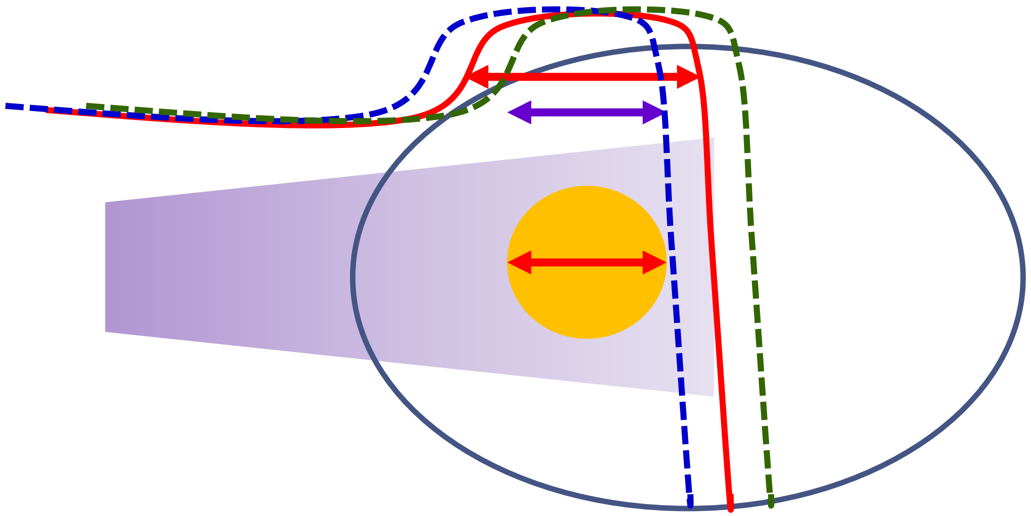
Proton PTV margin



In the beam's eye view, "lateral" margin is needed to account for setup up uncertainties in the direction perpendicular to beam's central axis

Proton PTV margin





Along the beam's central axis, distal and proximal margin are needed to account for Range Uncertainties!

Beam-specific proton PTV

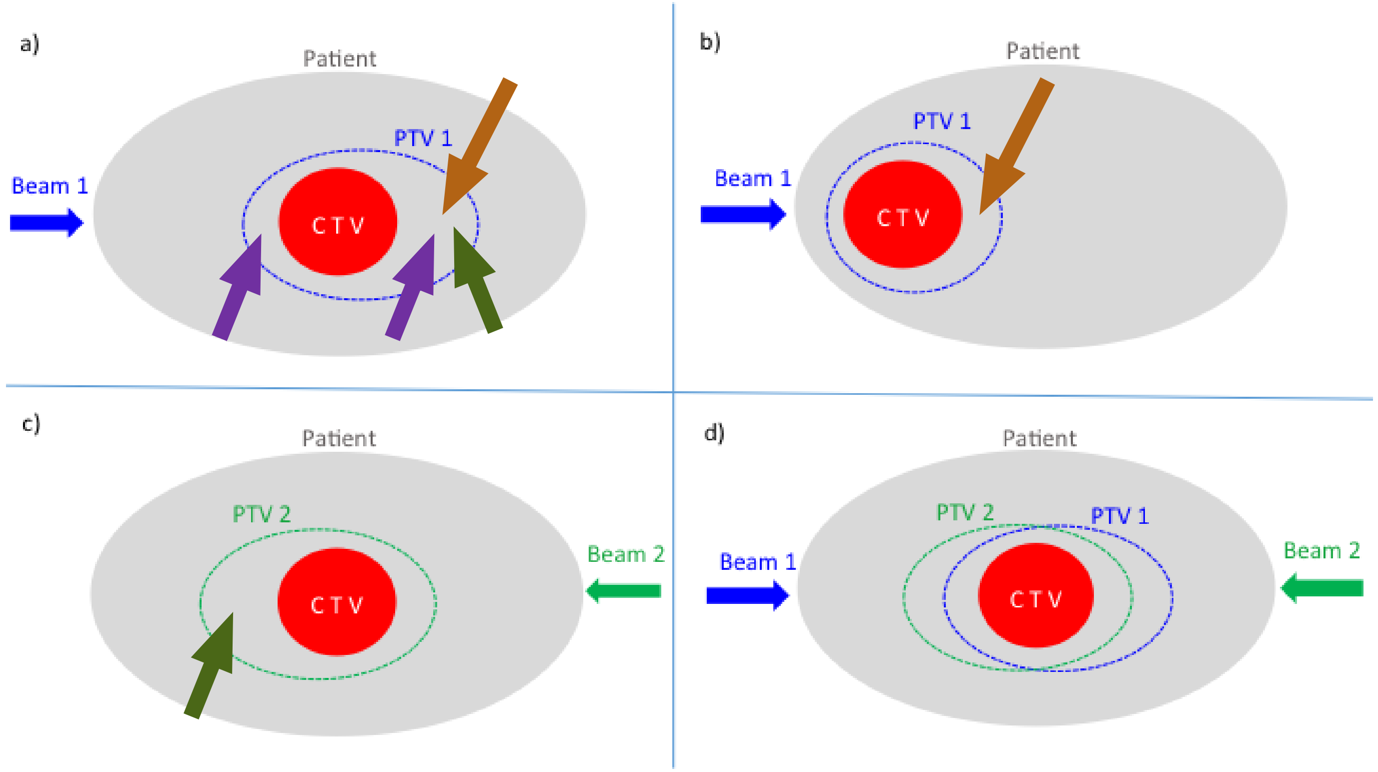


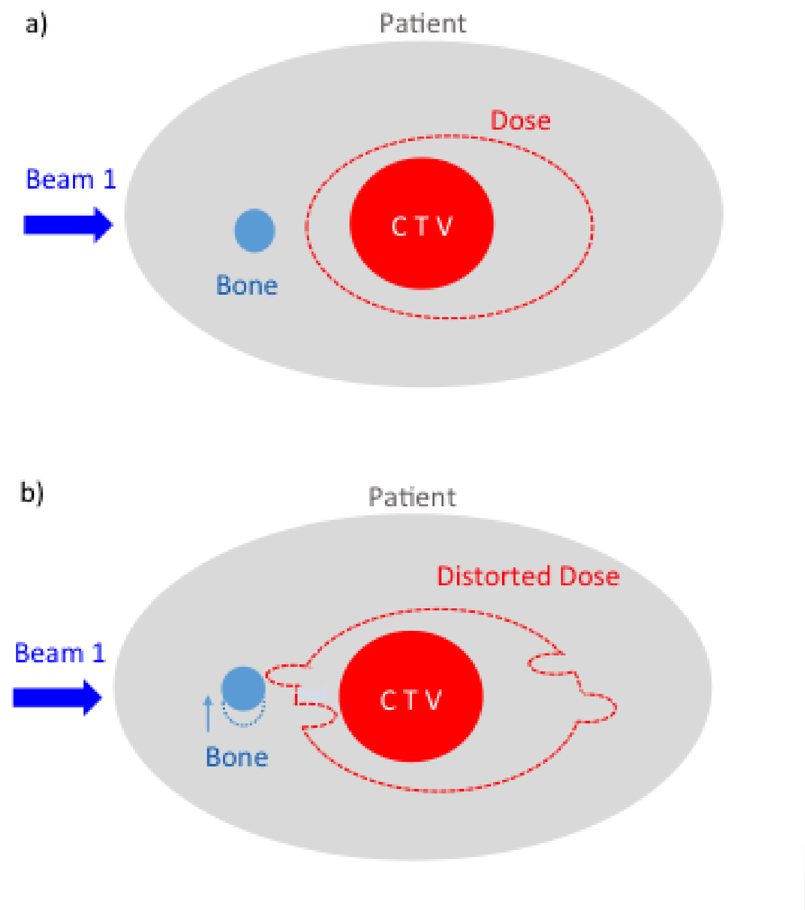
Figure 1 Figures A and B illustrate distal and proximal PTV margins for an identical target located at different depth. Margins are also a function of beam direction (C). The concept of a PTV that is common for all beams does not fulfill the PTV requirement for proton planning (D). (Color version of figure is available online.)

- **Deeper target → larger margin**
- **Distal margin > proximal margin**
- **Beam angle dependent**

Langen and Zhu, Semin. Rad. Onc. 2018

Patient Setup

- Lateral margin is used to account for motion perpendicular to the beam direction;
- However, lateral motion also affect proton dose deposition along the beam direction



Langen and Zhu, Semin. Rad. Onc. 2018

Beam specific PTV

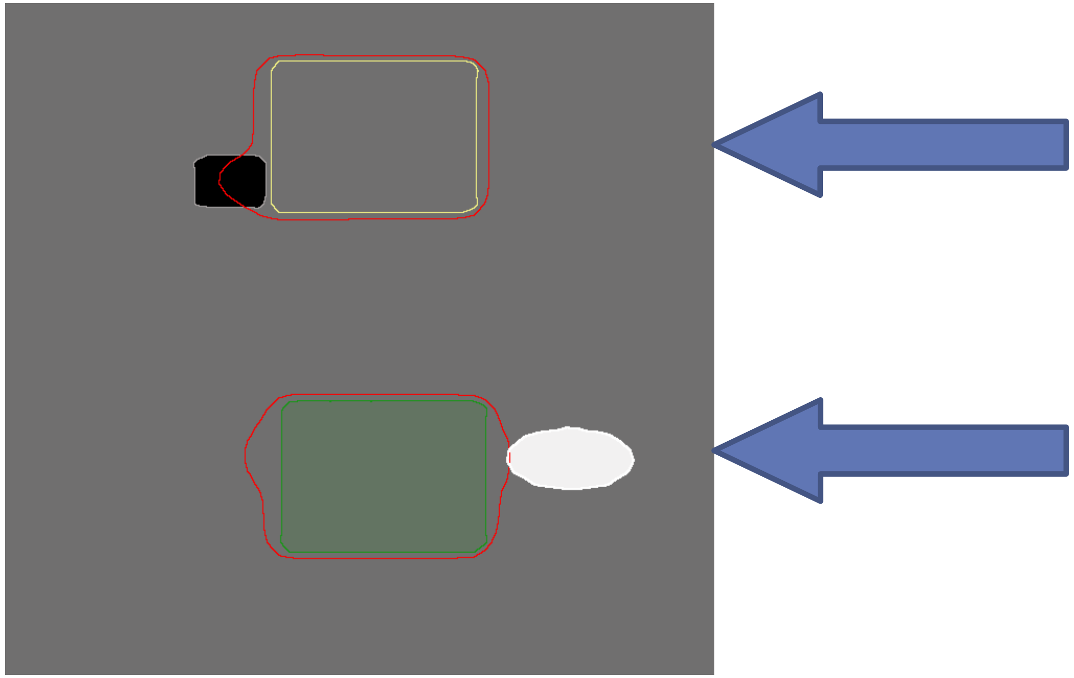
- bsPTV: based on water-equivalent thickness (WET) ray-tracing accounting for
  - Range uncertainties calculated at distal and proximal surface;
  - Patient setup error;
  - Organ motion;

- bsPTV properties:
  - Beam angle dependent;
  - Affected by surrounding tissue density
  - Shape can be unintuitive
  - Can be used for planning and evaluation

Park, et al., Int. J Radiat Oncol Biol Phys. 2012

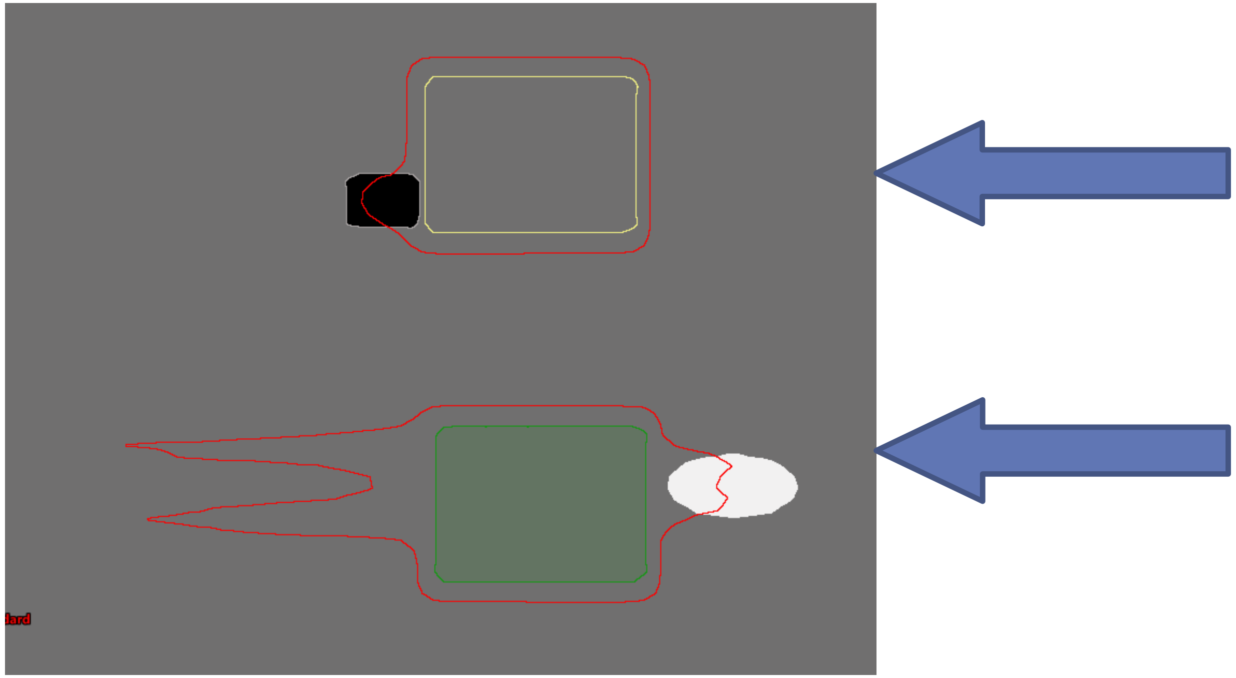
Beam specific PTV

3.5% range uncertainty



- Larger distance in lower density tissue;
- Larger margin with higher density tissue

3.5% range uncertainty **+ 3mm** isocenter shift



- Lateral shift changes distal/proximal margin
- Ideal PTV shape may be very un-intuitive

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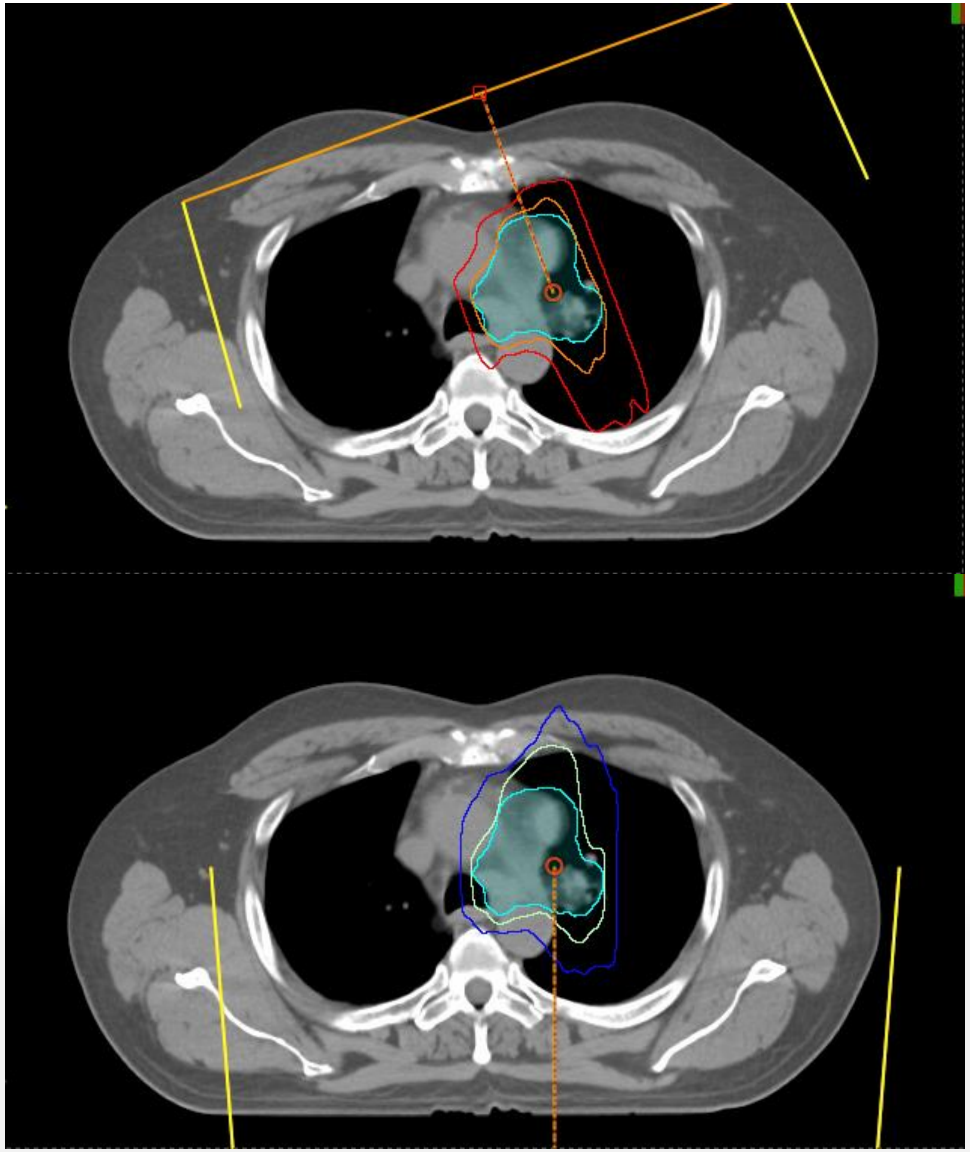
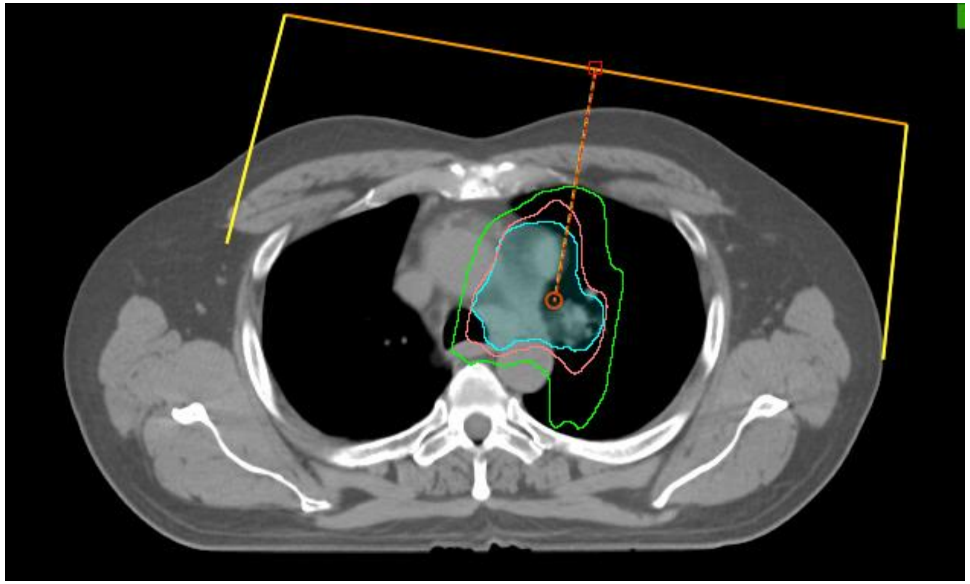
Beam specific PTV for lung tumor





Beam specific PTV calculated for each beam angle based on **CTV**

– Range uncertainty alone

– Range + Setup uncertainty

Setup error→ much bigger margin

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Introduction

- Uncertainties in PT:

Proton Range

Patient Setup

Margin

Beam selection

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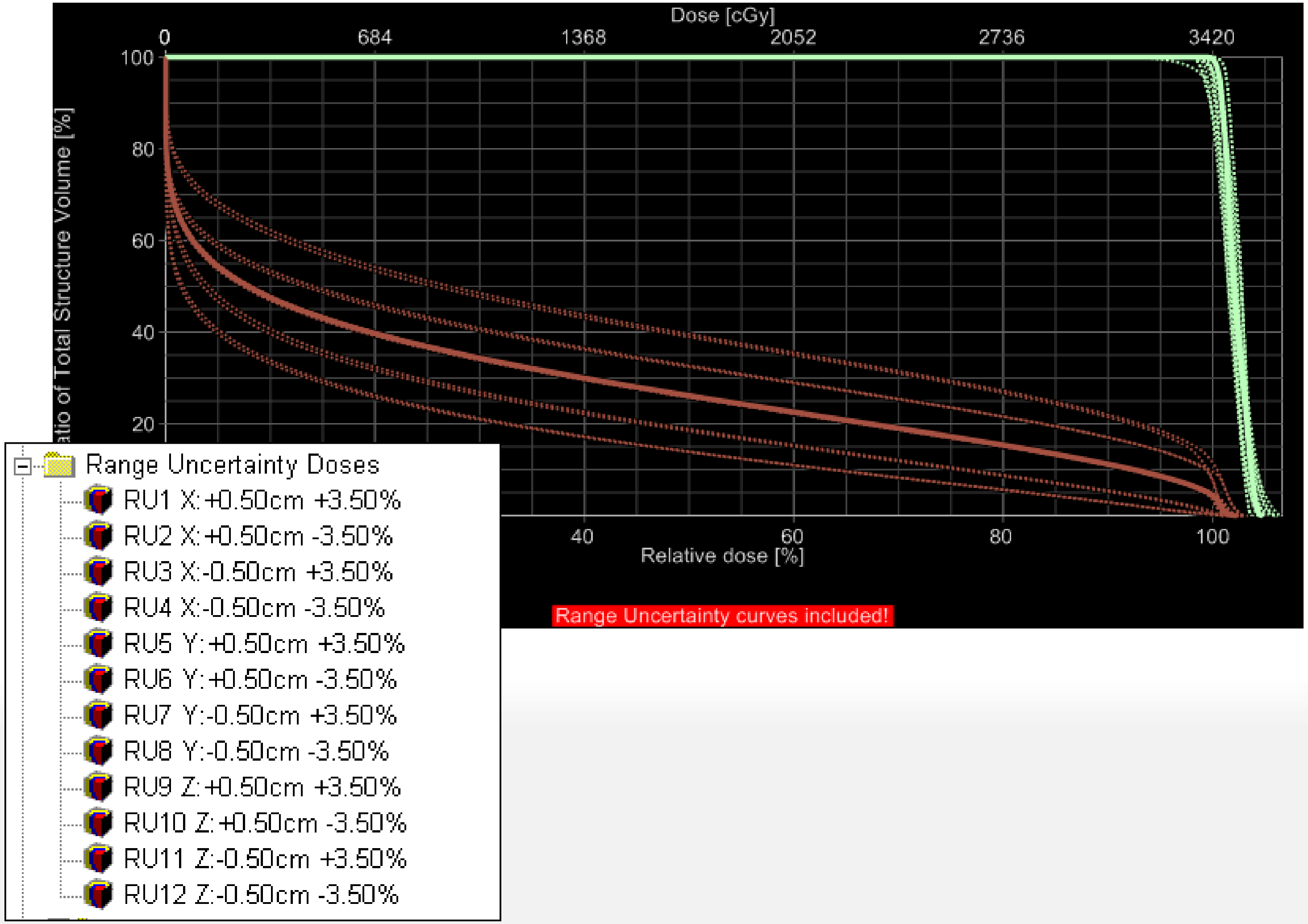
IMPT—Plan robustness

- BS-PTV does not guarantee robustness for inversely optimized IMPT plans;
- Plan robustness is a plan quality metric and needs to be evaluated;
- Ask: what happens to dose distribution if patient shifts and if range is incorrect?



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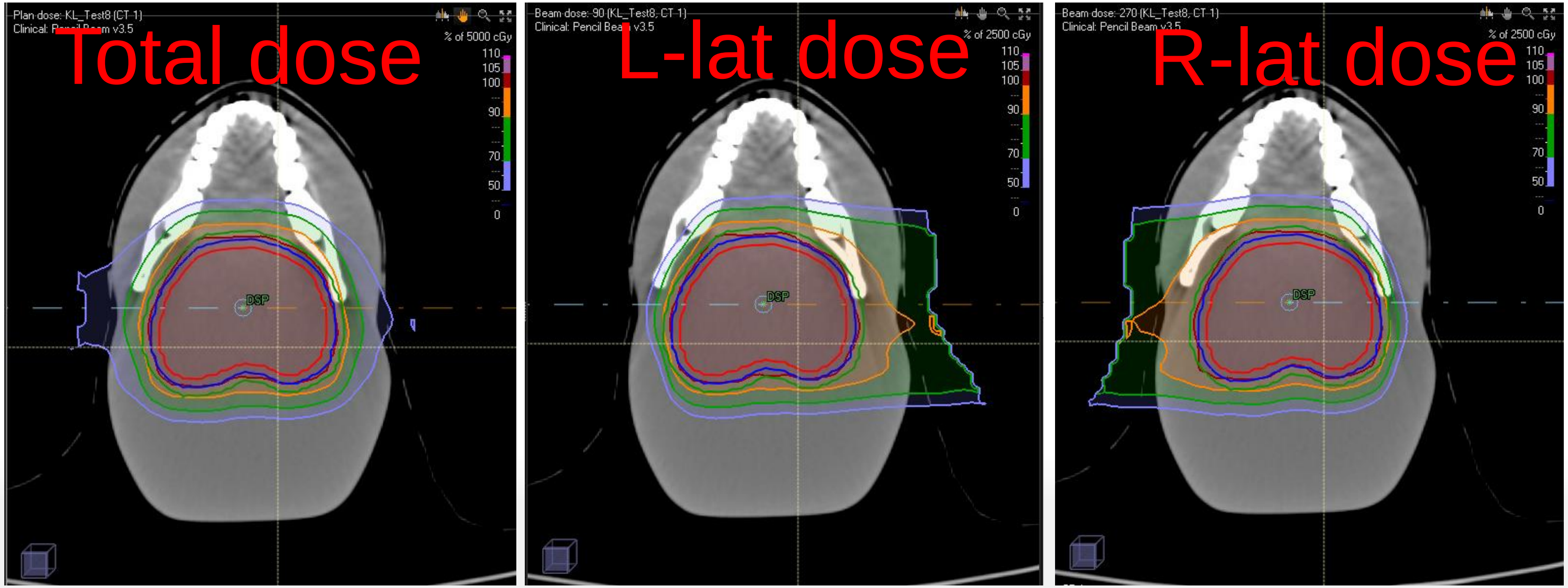
Two basic planning techniques: SFO & MFO

SFO (Single field optimization)
Fields are optimized independently of each other
or: Right hand does not know what the left is doing



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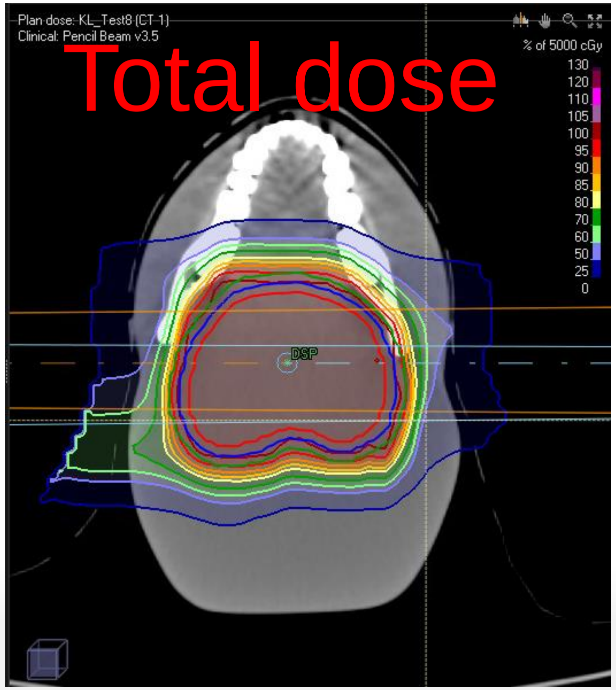
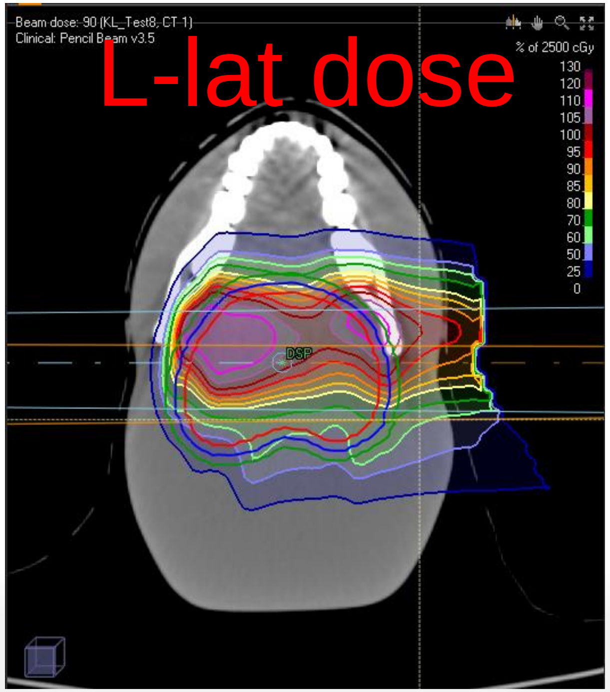
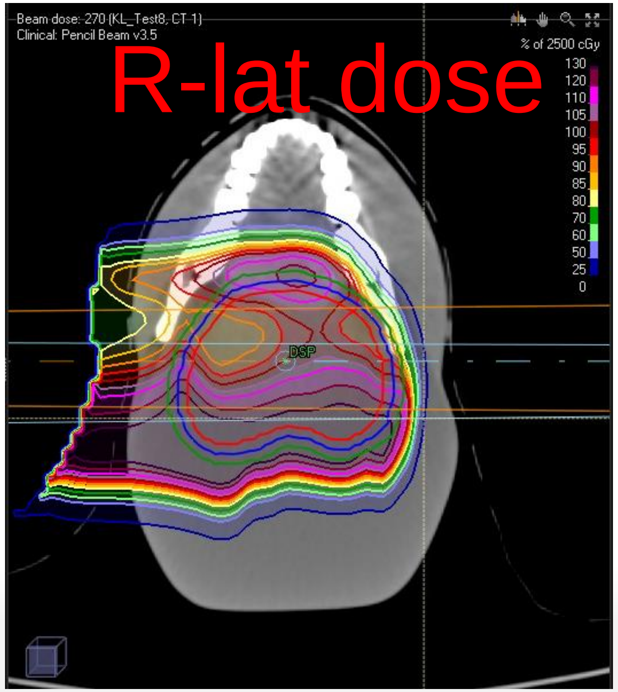
Katja Langen

Two basic planning techniques: SFO & MFO

MFO (Multiple field optimization)
Fields are optimized in unison, they are a team
individual fields can have non-uniform dose

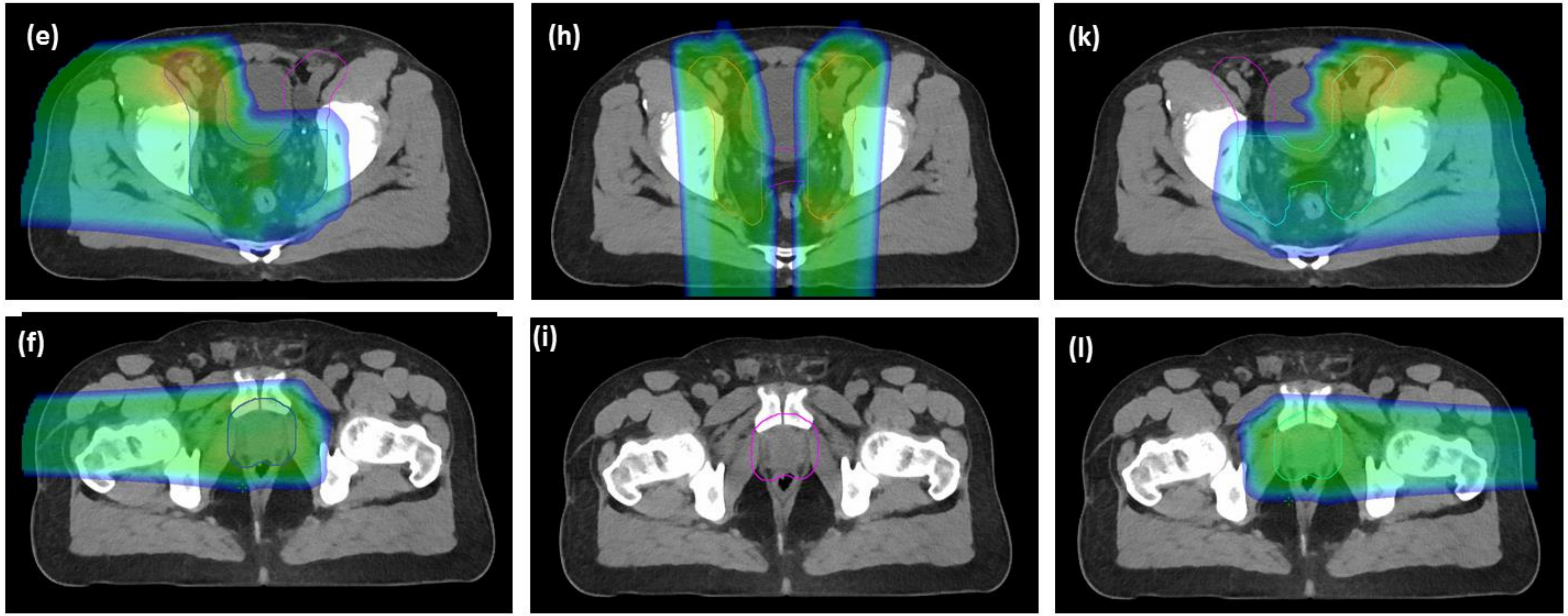






Katja Langen

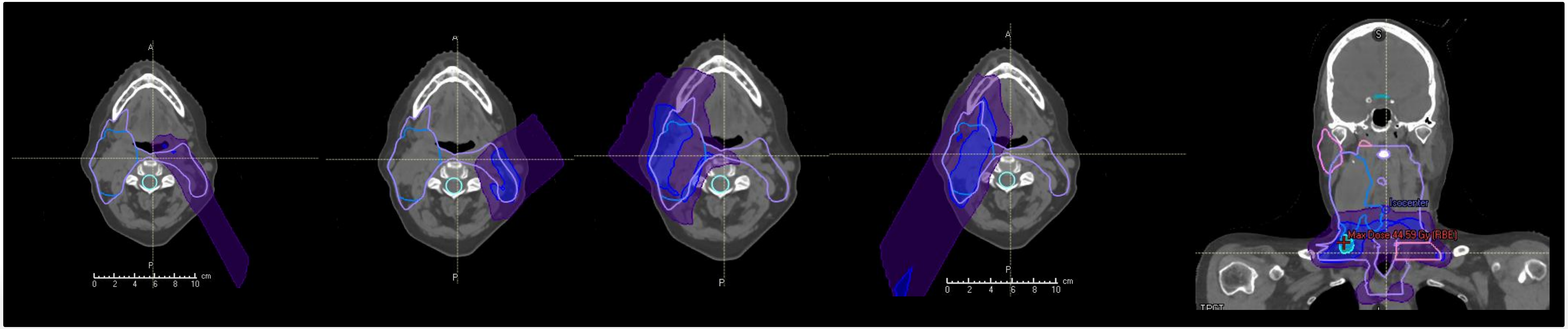
Split targets—by design MFO



3-field prostate+LN

Zhu, *et al*, ARO, in press

Split targets—by design MFO



5-field HN plan

Katja Langen

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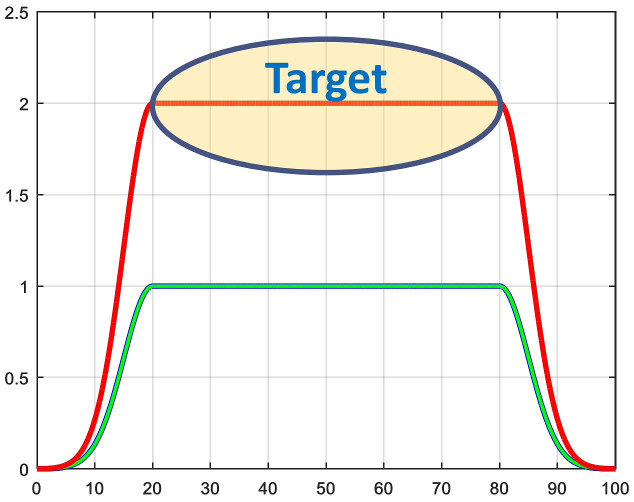
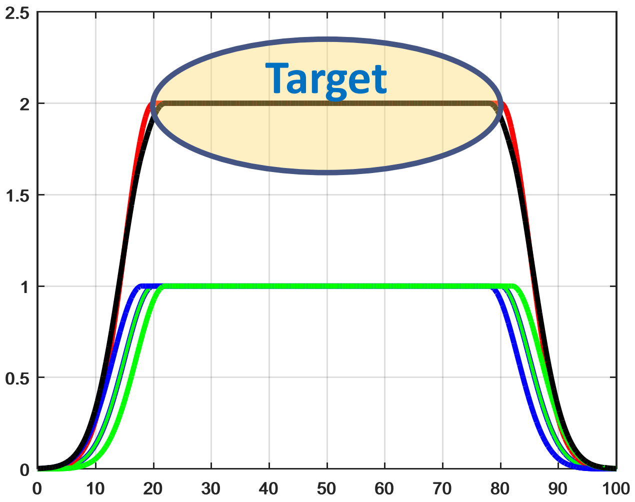
SFO vs. MFO

- In general:
  - SFO is more robust than MFO;
  - MFO can spare normal tissue better for more complicated target shapes
- Use SFO if possible
  - For convex shaped target: SFO is usually good enough
- Use MFO only when needed
  - Concave shaped target, e.g. bi-lat HN
  - OAR surrounded by target,
  - If split the field-target

SFO with uncertainty





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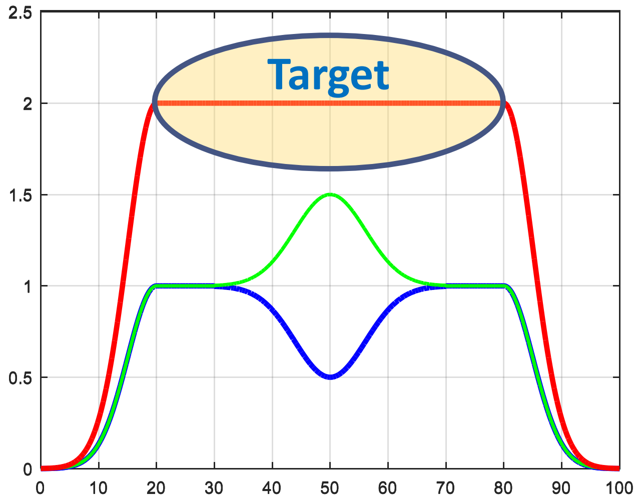
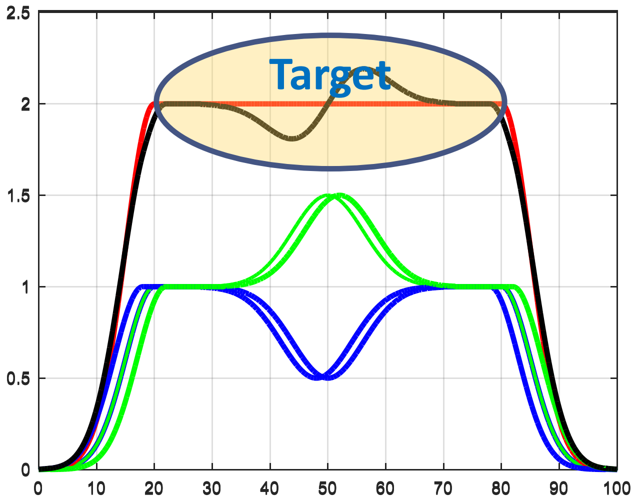
MFO with uncertainty

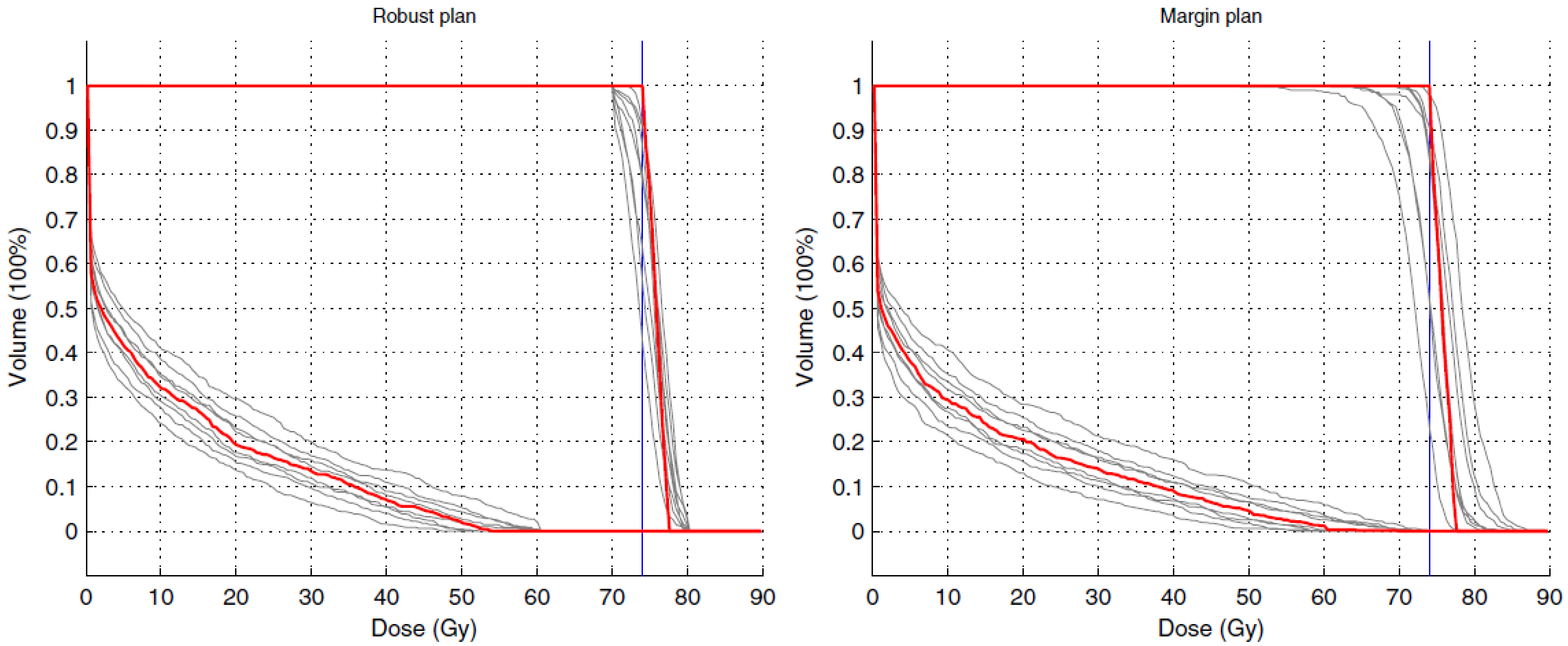




Dose gradient within target!

Robust Optimization

- Include robustness as an objective in optimization



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Chen *et al.*, PMB, 57 (2012), 591

Introduction

- Uncertainties in PT:

Proton Range

Patient Setup

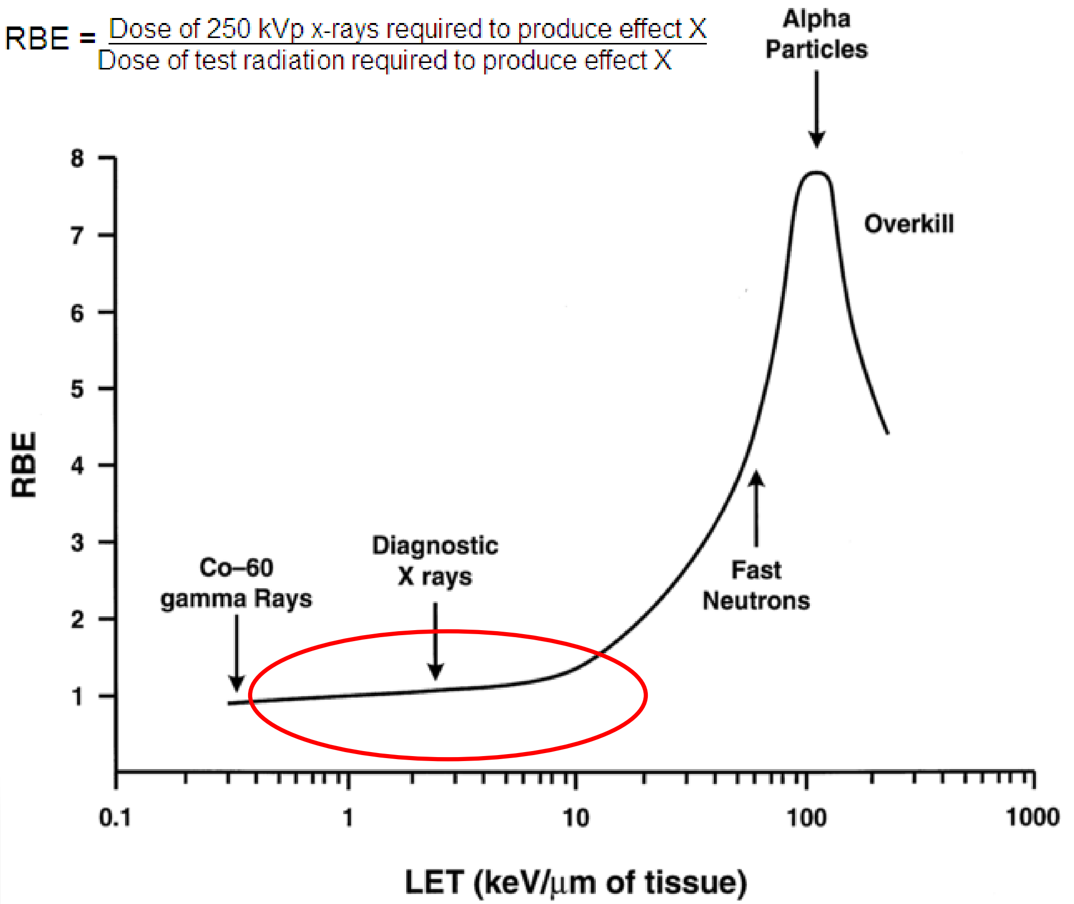
RBE

Margin

Beam selection

Robust optimization

Proton RBE



Protons are NOT high LET particles

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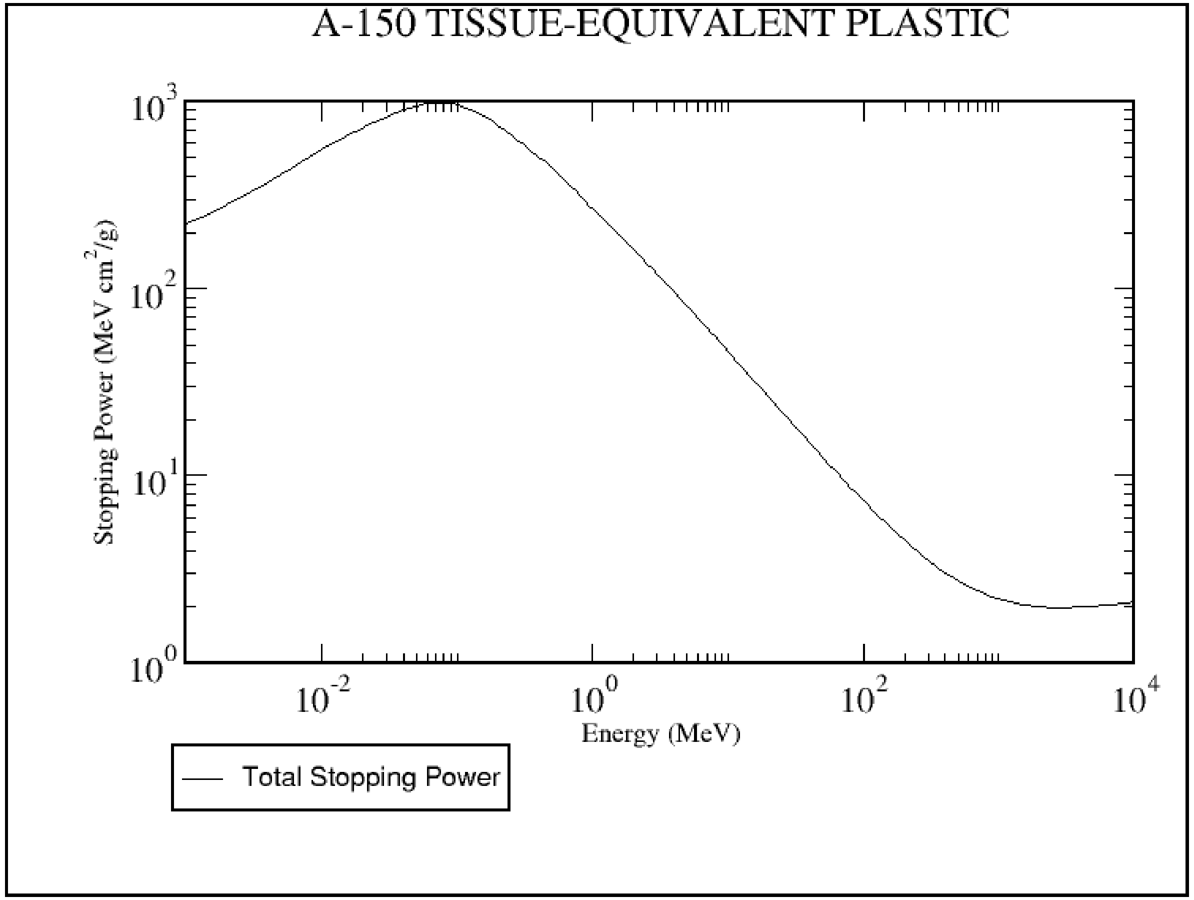
Bushberg, Essentials of Medical imaging, 2nd Ed.

Proton RBE



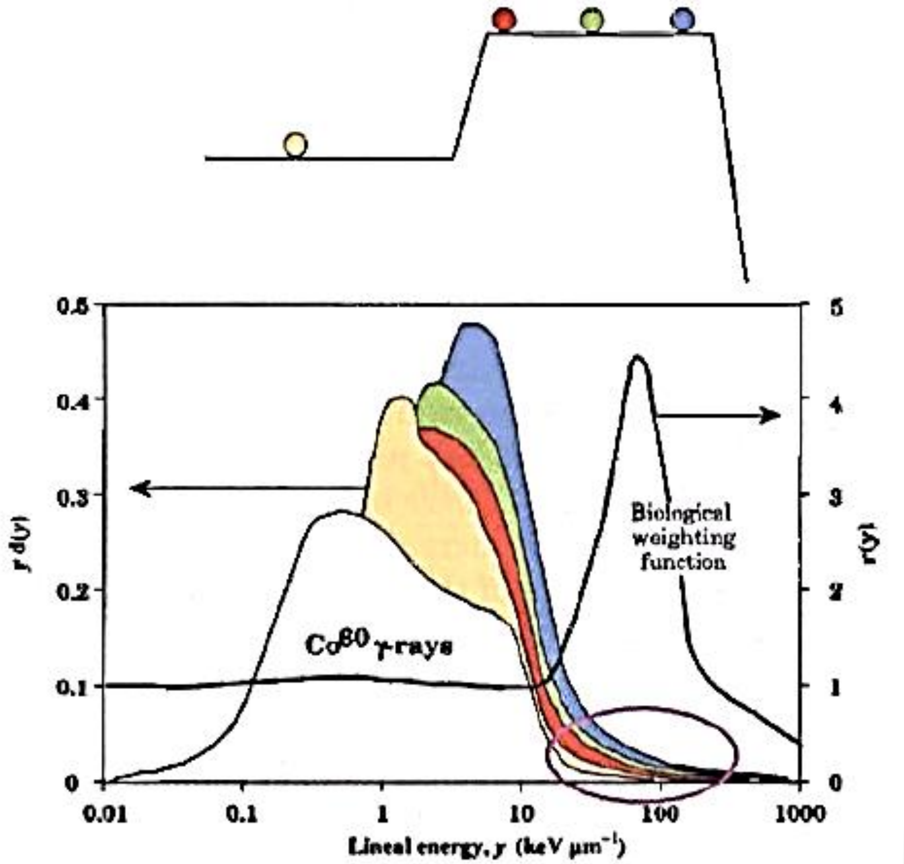
@ 250 MeV: 3 MeV cm^2/g

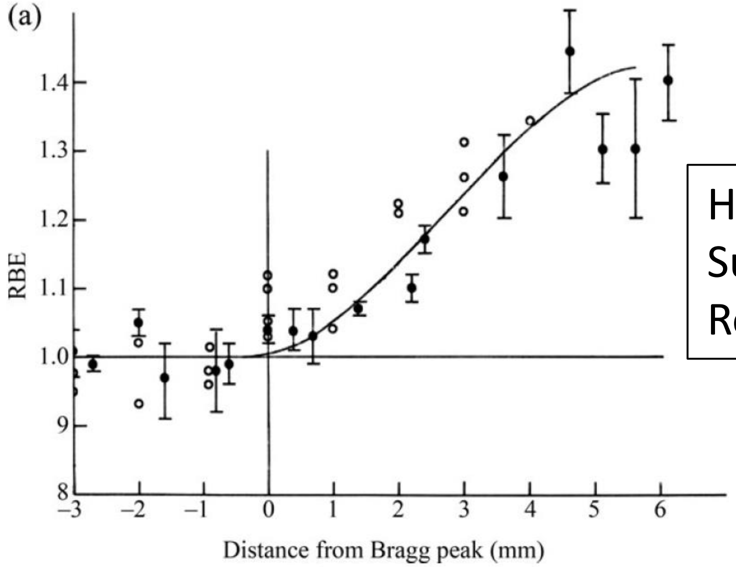
3 MeV/cm= 0.3 keV/μm

@ 10 MeV: 5 keV/μm

@ 1 MeV: 20 keV/μm

RBE uncertainty—distal edge





H4 cell
Survival fraction 0.1
Relative to mid-SOBP

1 physical proton Gy = 1.1 equivalent Gy or
1.1 cobalt-equivalent Gy

Units: CGy, GyE, Gy(E), **Gy(RBE)**

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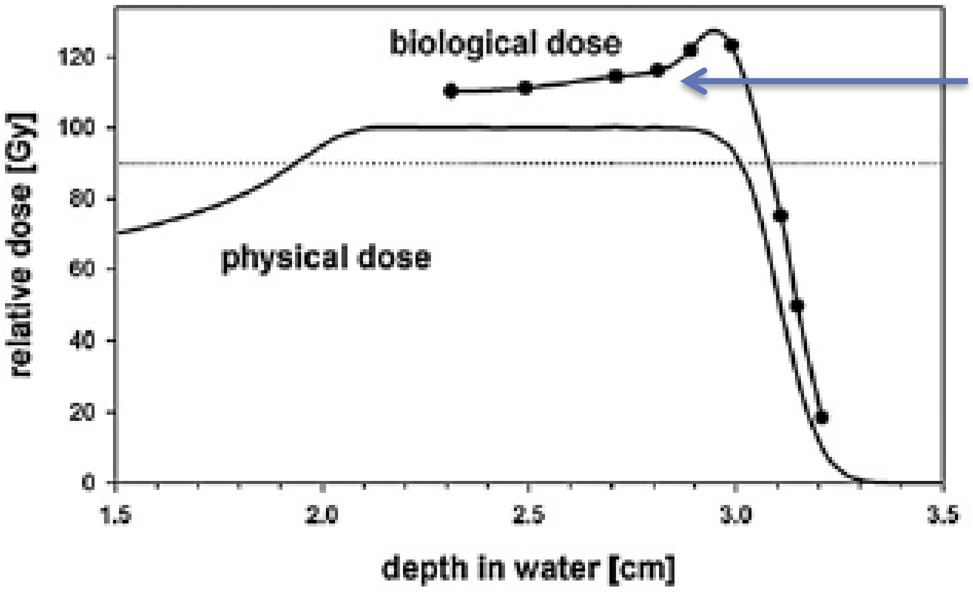
ICRU Report 78: use of generic RBE value of 1.1 is recommended

RBE uncertainty—distal edge



Choose generic RBE value of 1.1

Paganetti, PMB, 57 (2012) R99

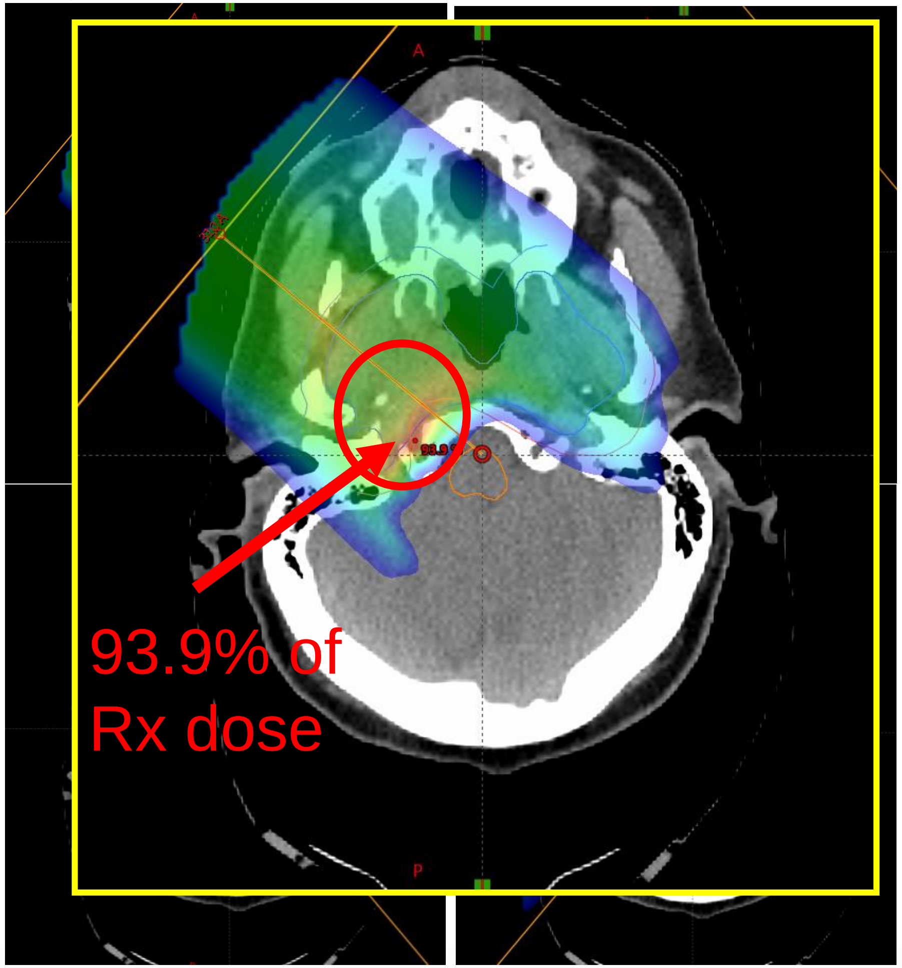
- Use a generic RBE value adds uncertainty to the distal edge RBE dose;
- Biological dose is deeper/higher than physical distal edge dose;
- Real RBE value depends on multiple factors
  - Treatment technique
  - Dose
  - Cell/tissue type
  - End point
  - Radiosensitivity
  - Etc.

RBE uncertainty management

- Use multiple beams
  - Spread uncertainty geometrically
  - Avoid stopping before critical OARs

- Robust optimize and evaluate beam dose

- Variable RBE in plan optimization
  - Not currently available
  - LET_d distribution



The current clinical practice of using a constant RBE for protons should generally be maintained but specific clinical scenarios warrant a change in current practice.

Report of AAPM TG-256 (2019)

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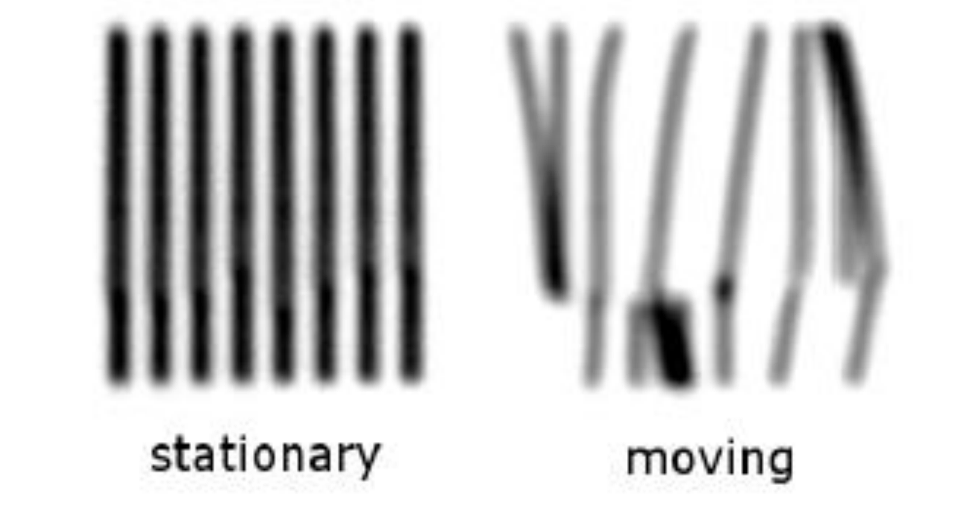
Robust optimization

RBE/LET opt

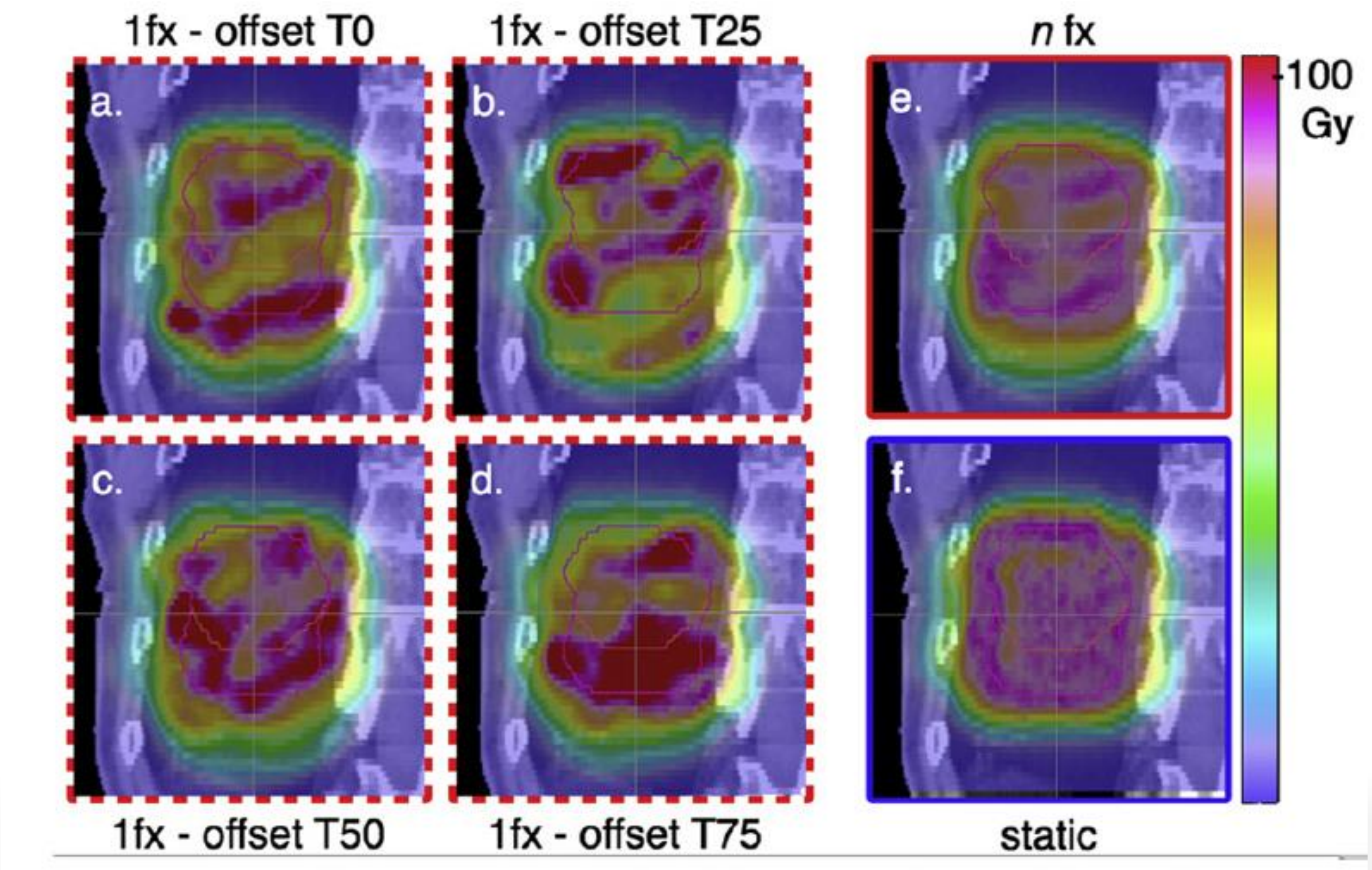
Motion during treatment

- If tumor and beam move independently, spot positions differ from planned positions;
- Similar to interplay between IMRT/VMAT and tumor motion
- Can leads to hot or cold spots in target
- Spot scanning is more sensitive to intra-fraction target motion since it is more dynamic



Groezinger, Thesis, TU Darmstadt

Motion during treatment



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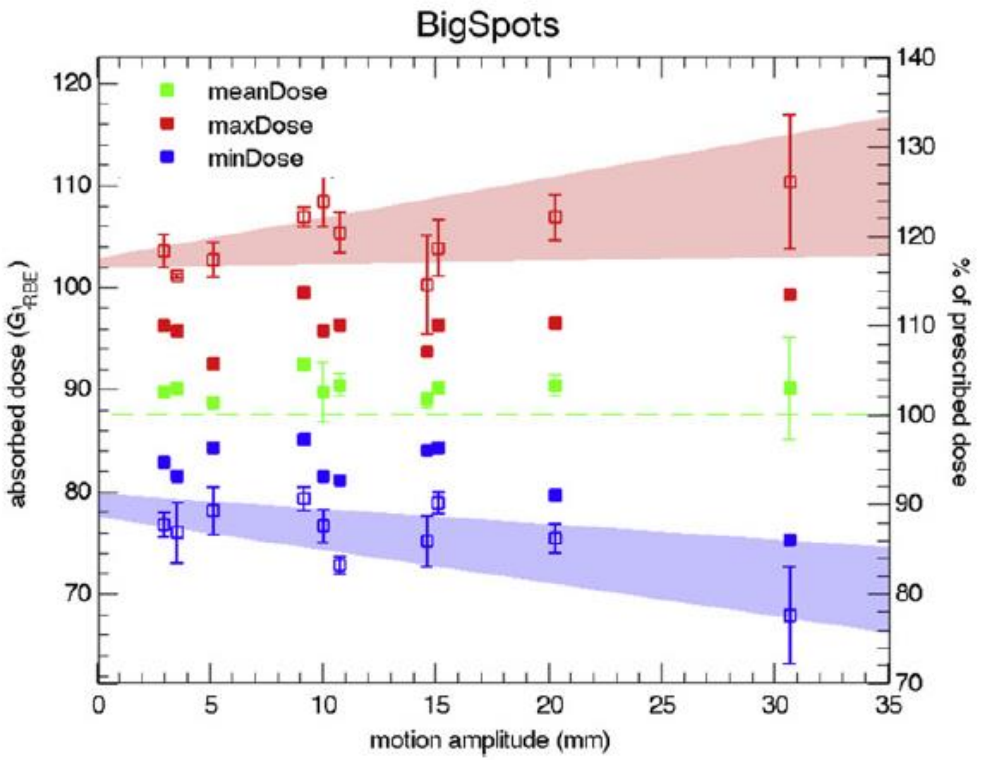
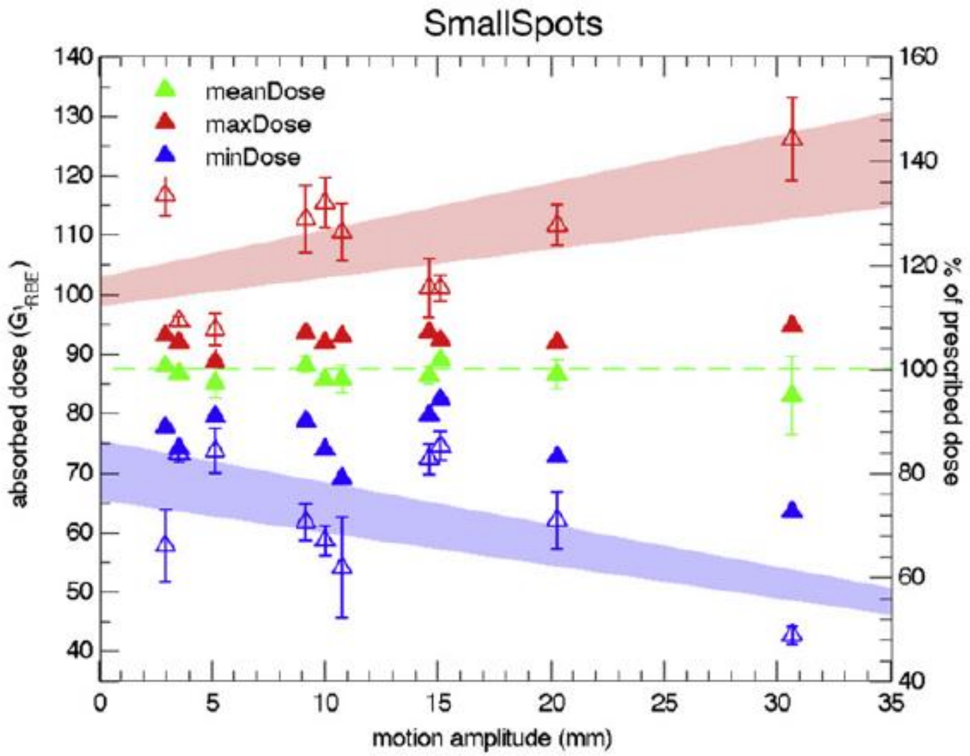
Grassberger et al, IJROBP (86) 2, 380, 2013

Motion during treatment





Open symbols: n=1
Solid symbols: n=4

Grassberger et al, IJROBP (86) 2, 380, 2013

Motion during treatment

- Motion during treatment is important for spot scanning
- Possible approaches:
  - Restrict motion
  - Beam gating
  - Re-scan or re-painting
  - Use big spot
- Be aware, but don't be discouraged!

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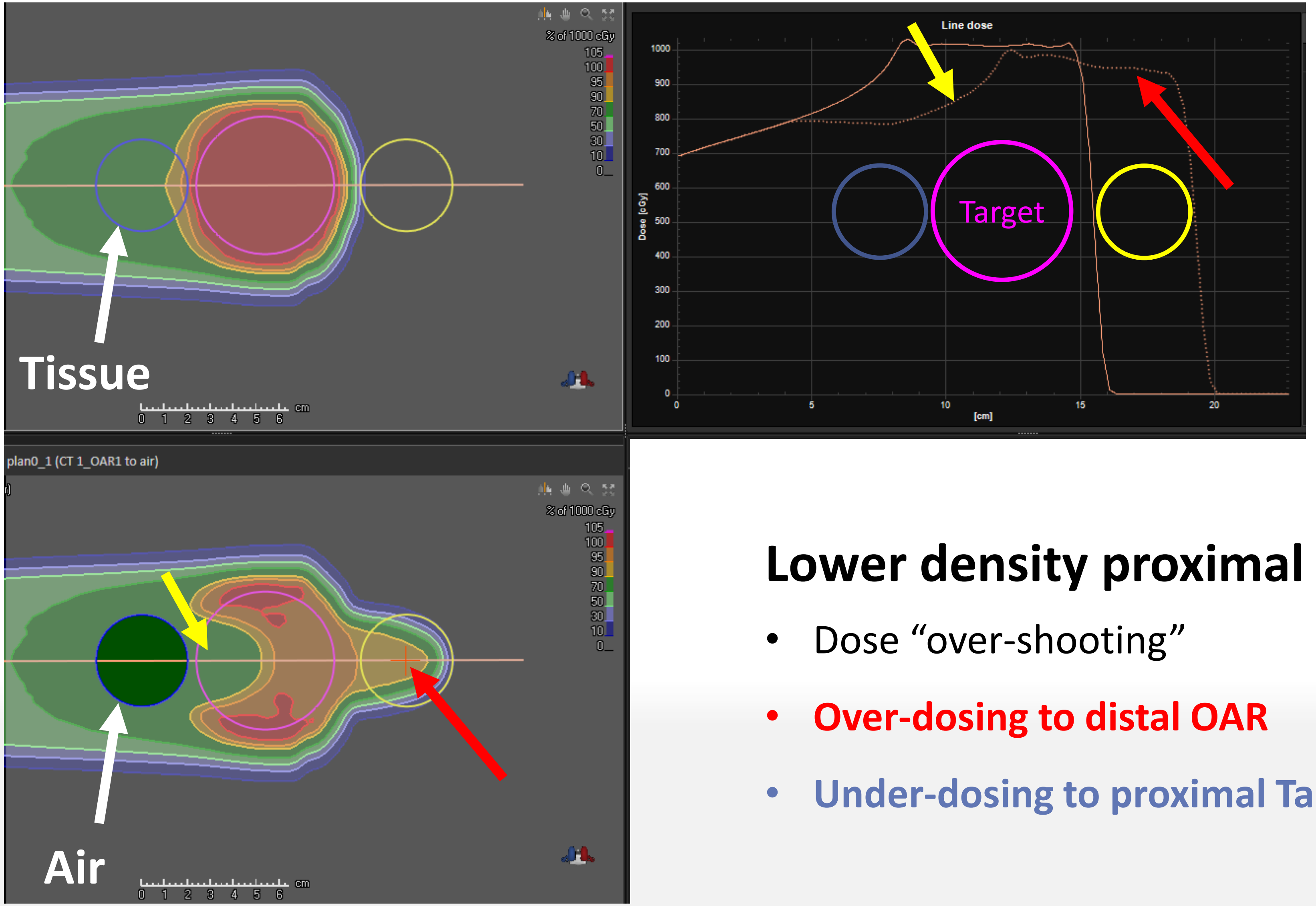
Proton is sensitive to anatomy changes

Proton is sensitive to anatomy changes



Lower density proximal to target:

- Dose "over-shooting"
- **Over-dosing to distal OAR**
- **Under-dosing to proximal Target**

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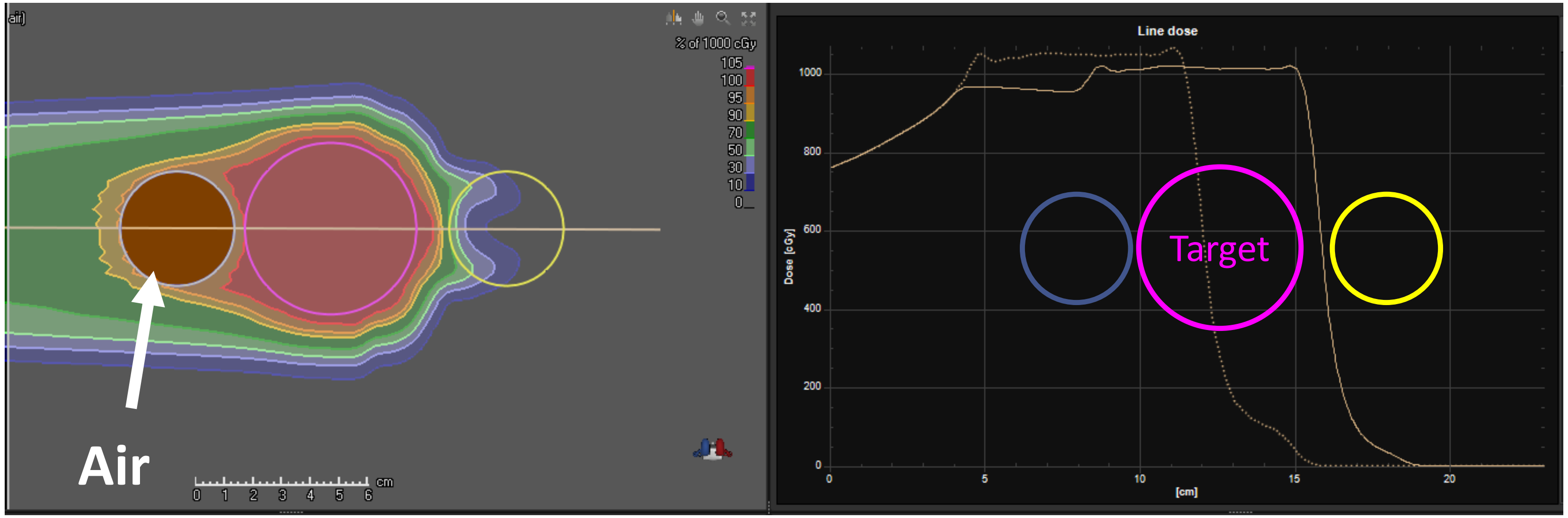
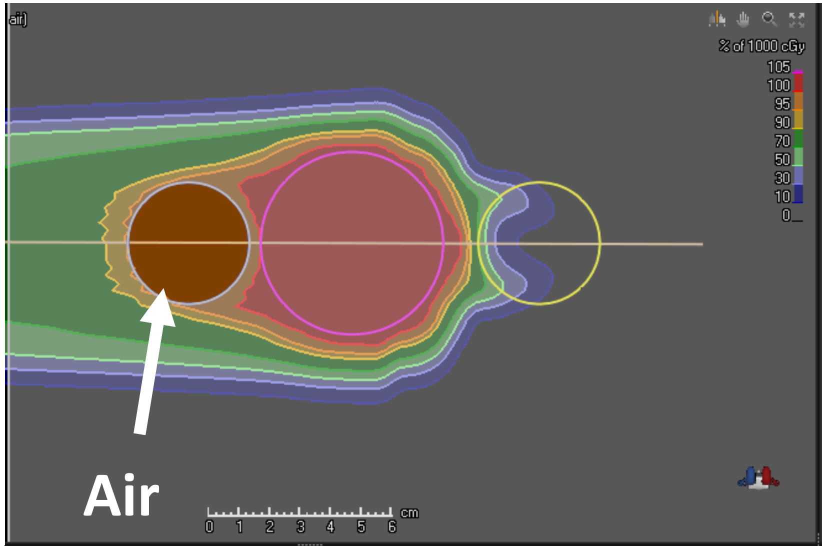
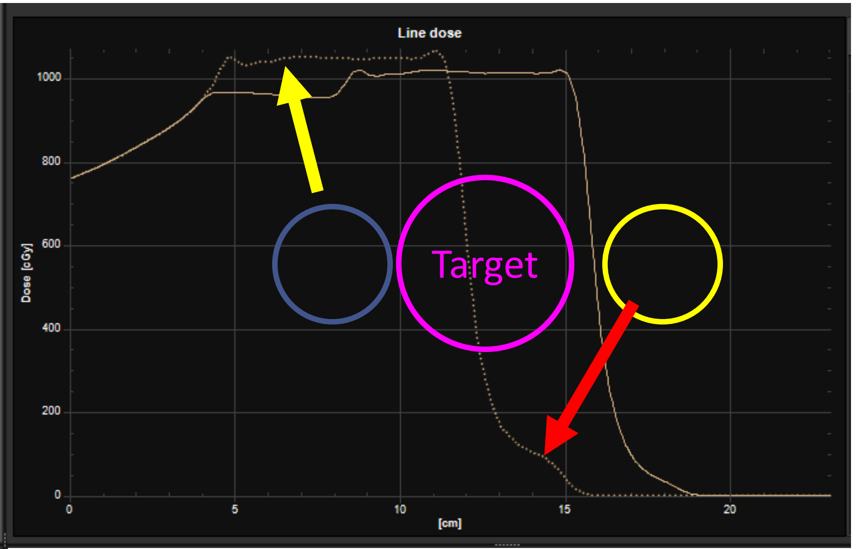
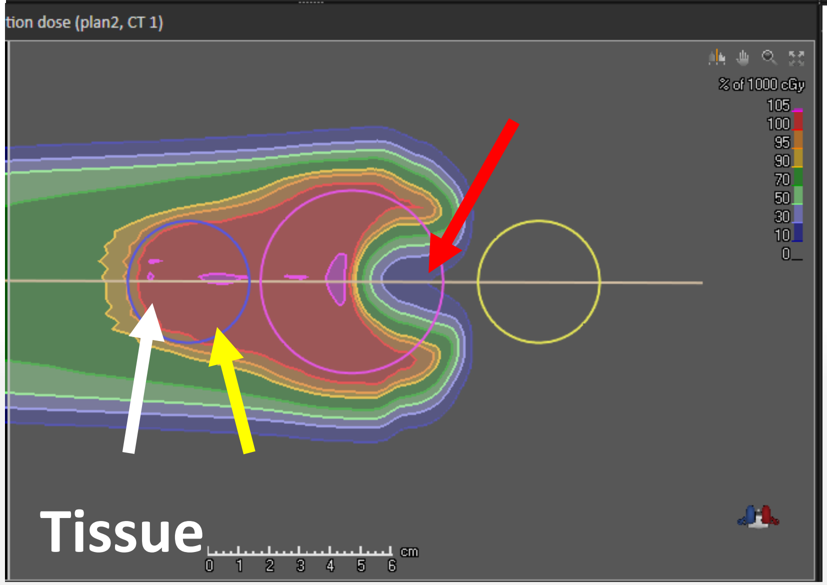
Proton dose is sensitive to anatomy changes



Proton dose is sensitive to anatomy changes







Higher density proximal to target:

- Dose "pulling-back"
- Under-dosing to distal Target
- Over-dosing to proximal OAR

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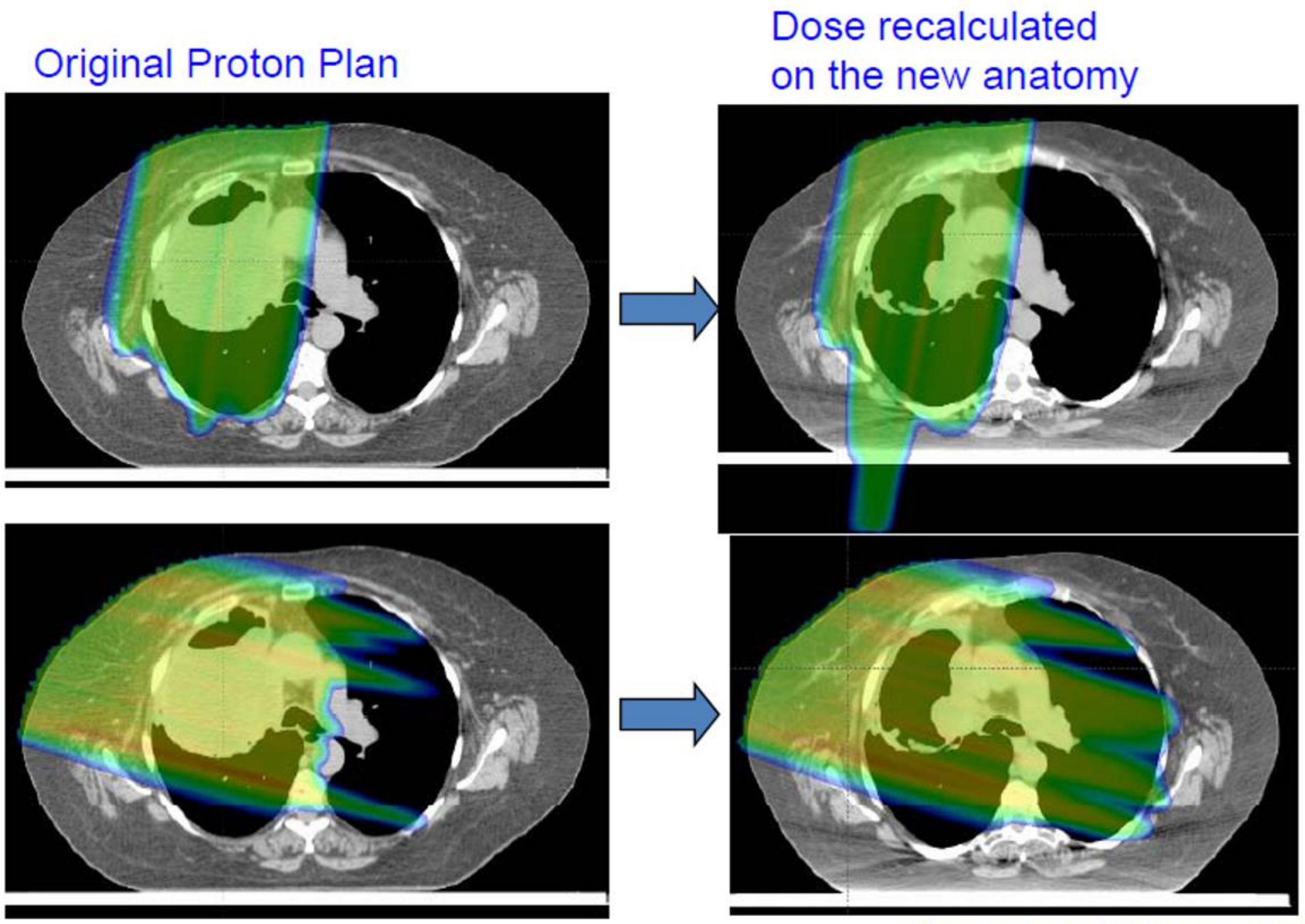
Lung IMPT: anatomy changes dramatically



Bucci et al. ASTRO Abstract, 2007

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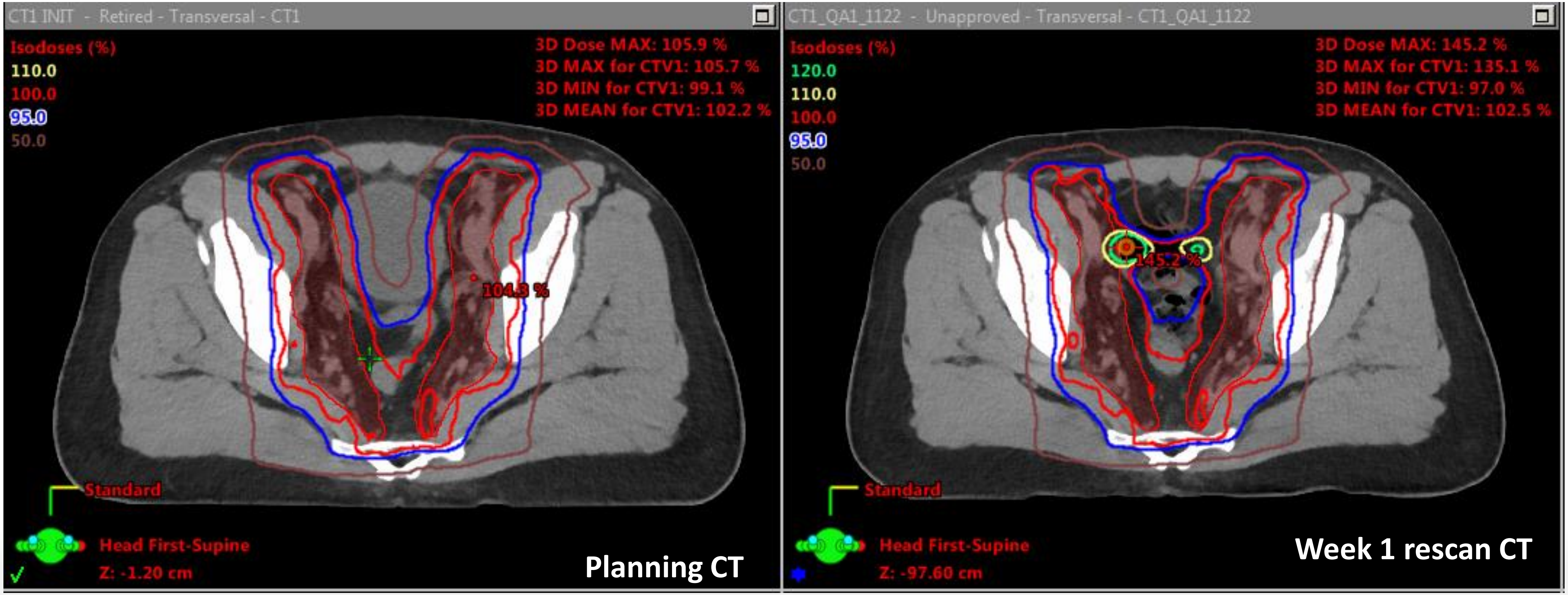
Pelvic IMPT



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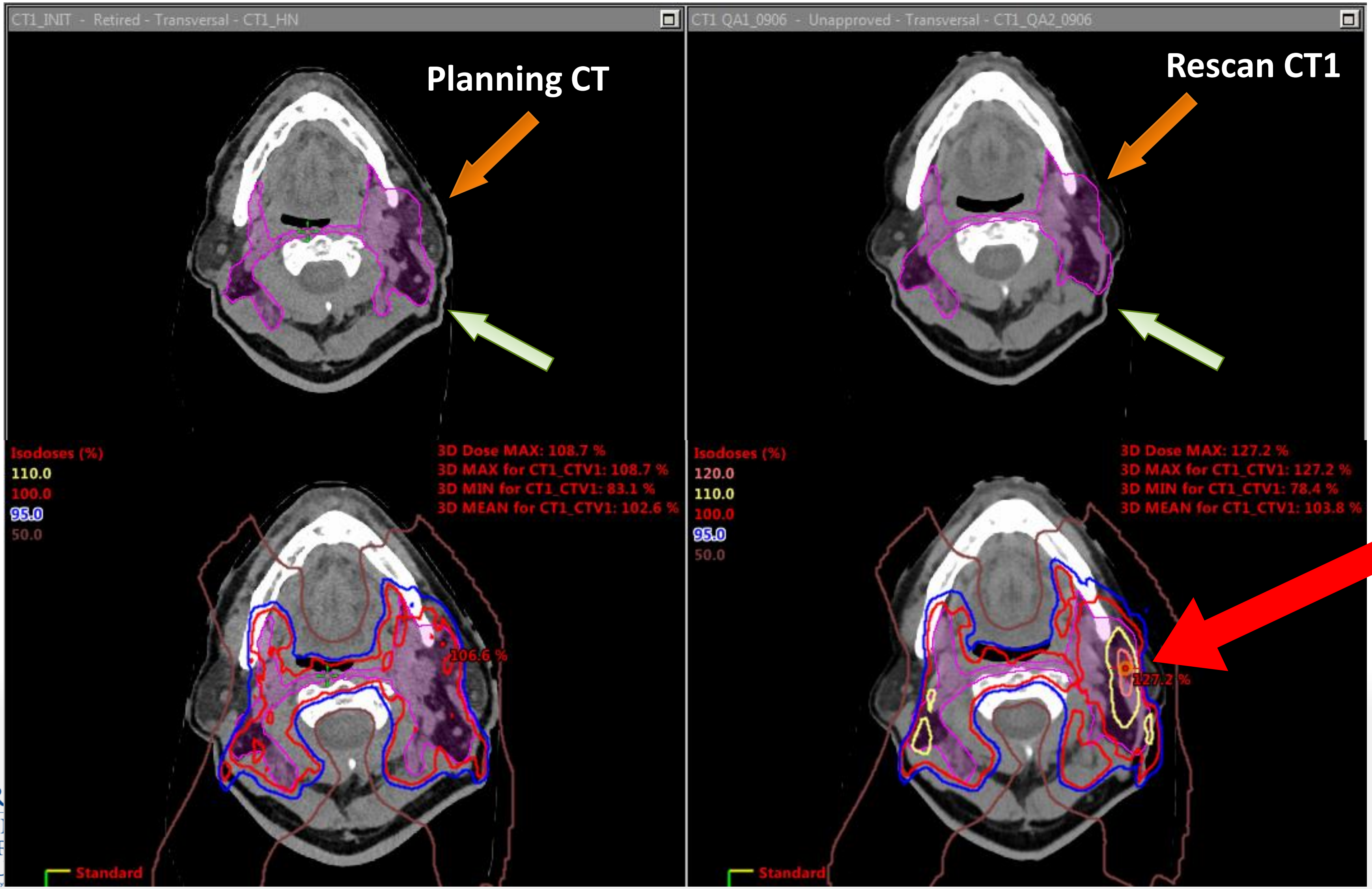
Zhu, ASTRO 2017

Head and neck IMPT



127% hot spot

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Patient anatomy change

- Undesired dosimetric consequence
- Unpredictable dosimetric consequence
- Mitigation strategy:
  - Adaptive RT: frequent re-scan and re-plan
    - Resource intensive
    - Suboptimal treatment

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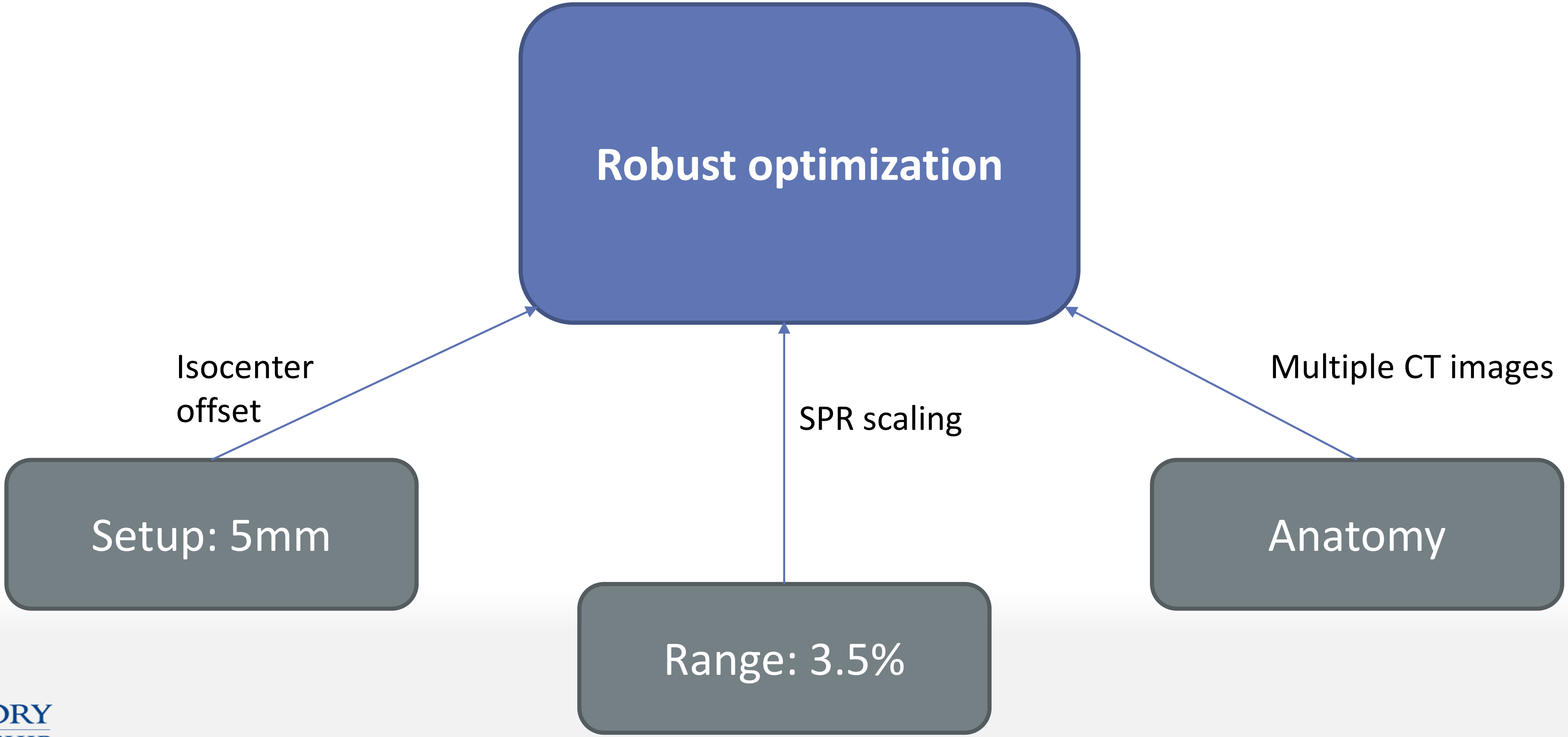
Anatomical robust optimization

Anatomical robust optimization



Types of multiple CT Robust Optimization

Planning CT

+

Adaptive CT

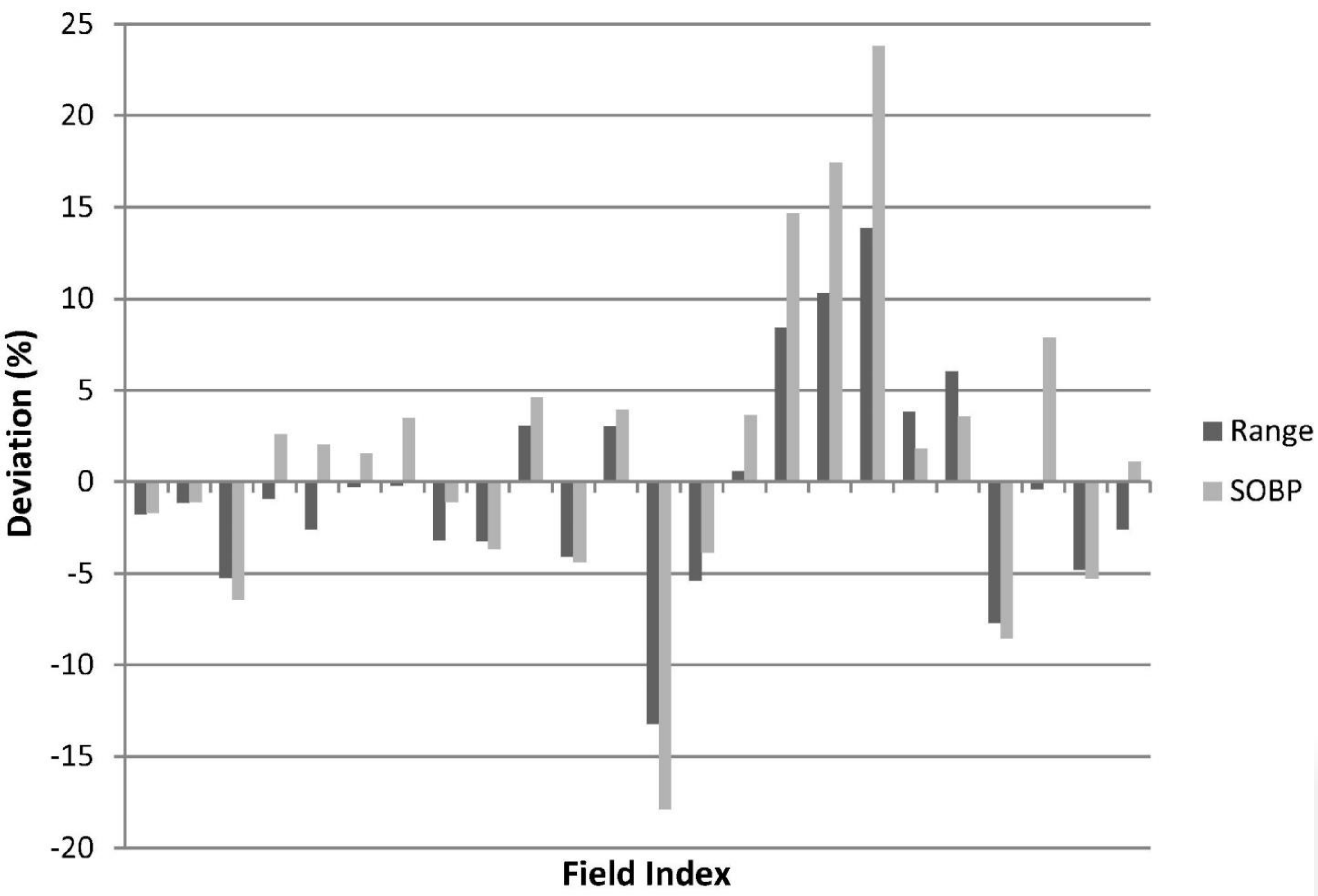
Synthetic CT

mCT RO for Lung IMPT

Planning CT + Adaptive CT

Wang, *et al.*, Radiother Oncol. (2018)

Lung IMPT: anatomy change dramatically



30% re-planning

Between PCT and ACT:

- Negligible variation of CTV volume
- **Large difference of Range and SOBP**

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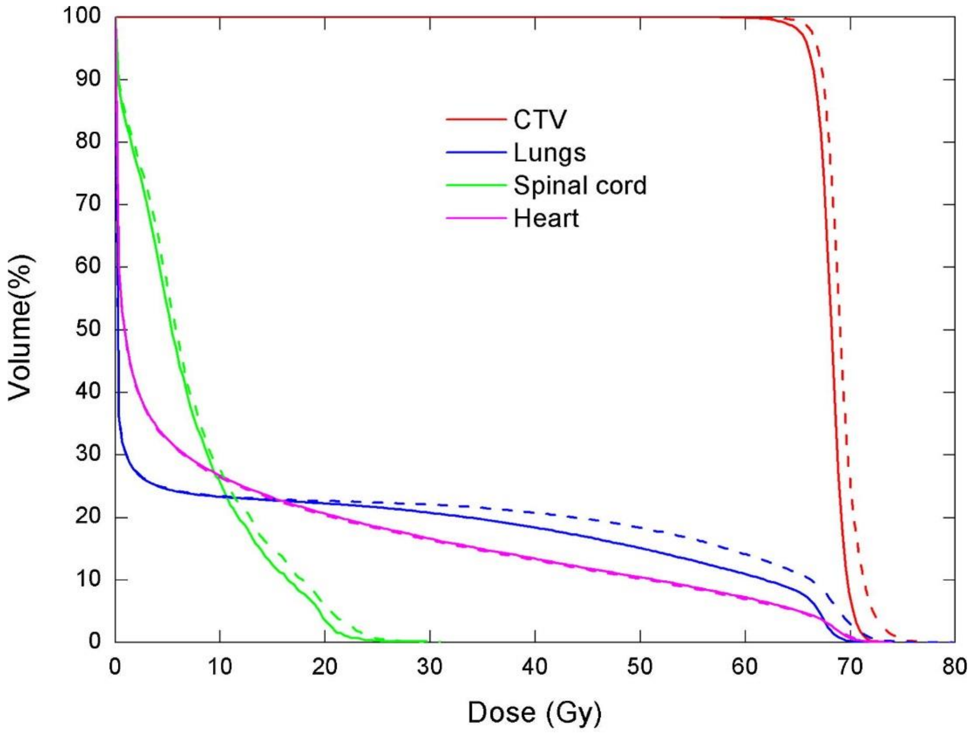
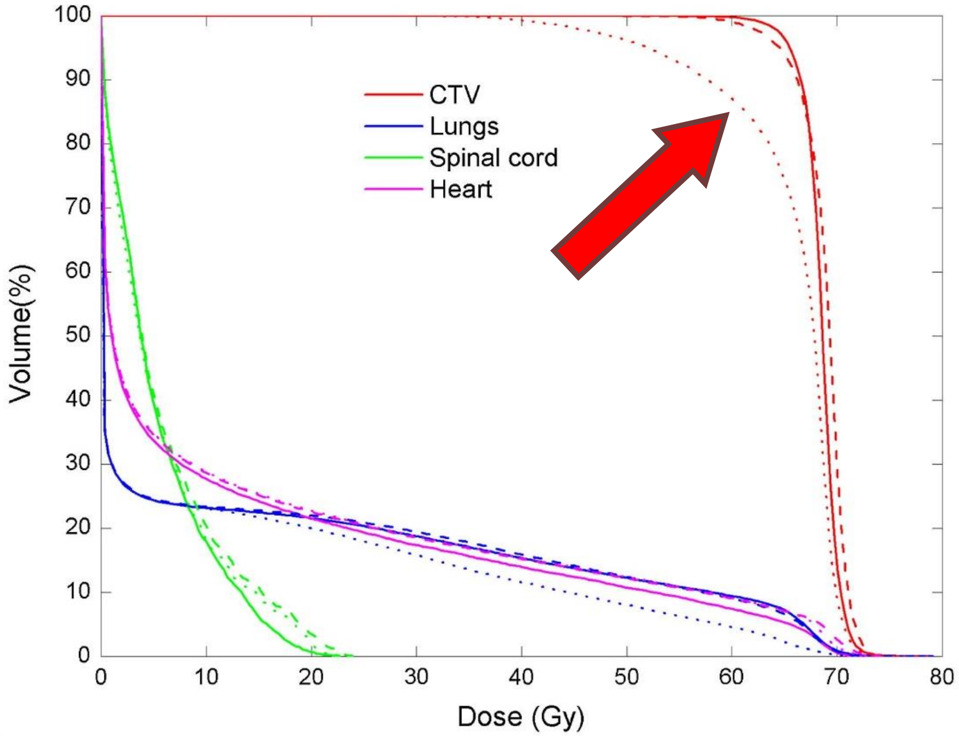
Wang, *et al.*, Radiother Oncol. (2018)

DVH comparison





Solid: P-PCT
Dashed: M-PCT

Solid: A-ACT
Dashed: M-ACT
Dotted: P-ACT

Wang, *et al.*, Radiother Oncol. (2018)

mCT RO for lung IMPT

- Using 2 patient scans: PCT and ACT
  – Include both CTs in optimization
- On PCT:
  – Similar coverage
  – Slightly higher lung dose
  – Similar robustness
  – No statistically difference in heart or spinal cord dose
- **On ACT:**
  – **Reduced cold spot—improve tumor control**
  – **Could potentially reduce re-planning frequency**

mCT RO for lung IMPT is feasible!

Wang, *et al.*, Radiother Oncol. (2018)

mCT RO for head and neck IMPT

Planning CT + Adaptive CT

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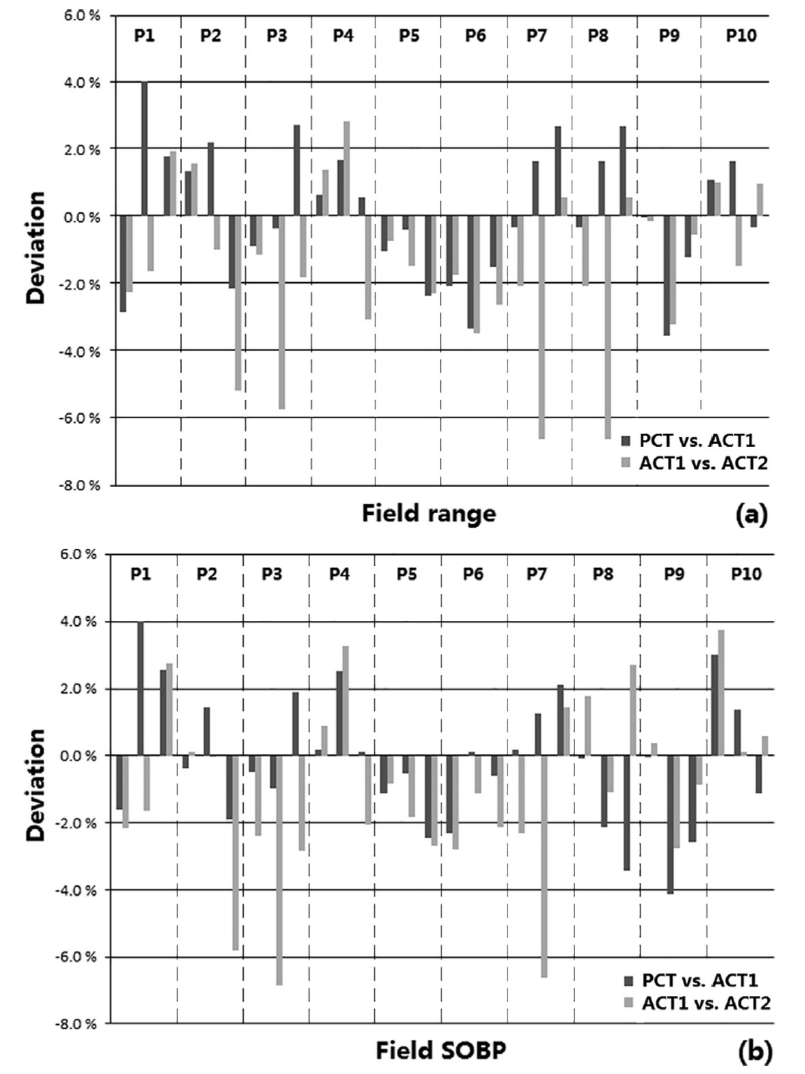
Yang, *et al.*, Radiother Oncol. (2020)

mCT RO for head and neck IMPT



40% re-planning

Between PCT and ACTs:

- Negligible variation of CTV volume
- **Large difference of Range and SOBP**

Yang, *et al.*, Radiother Oncol. (2020)

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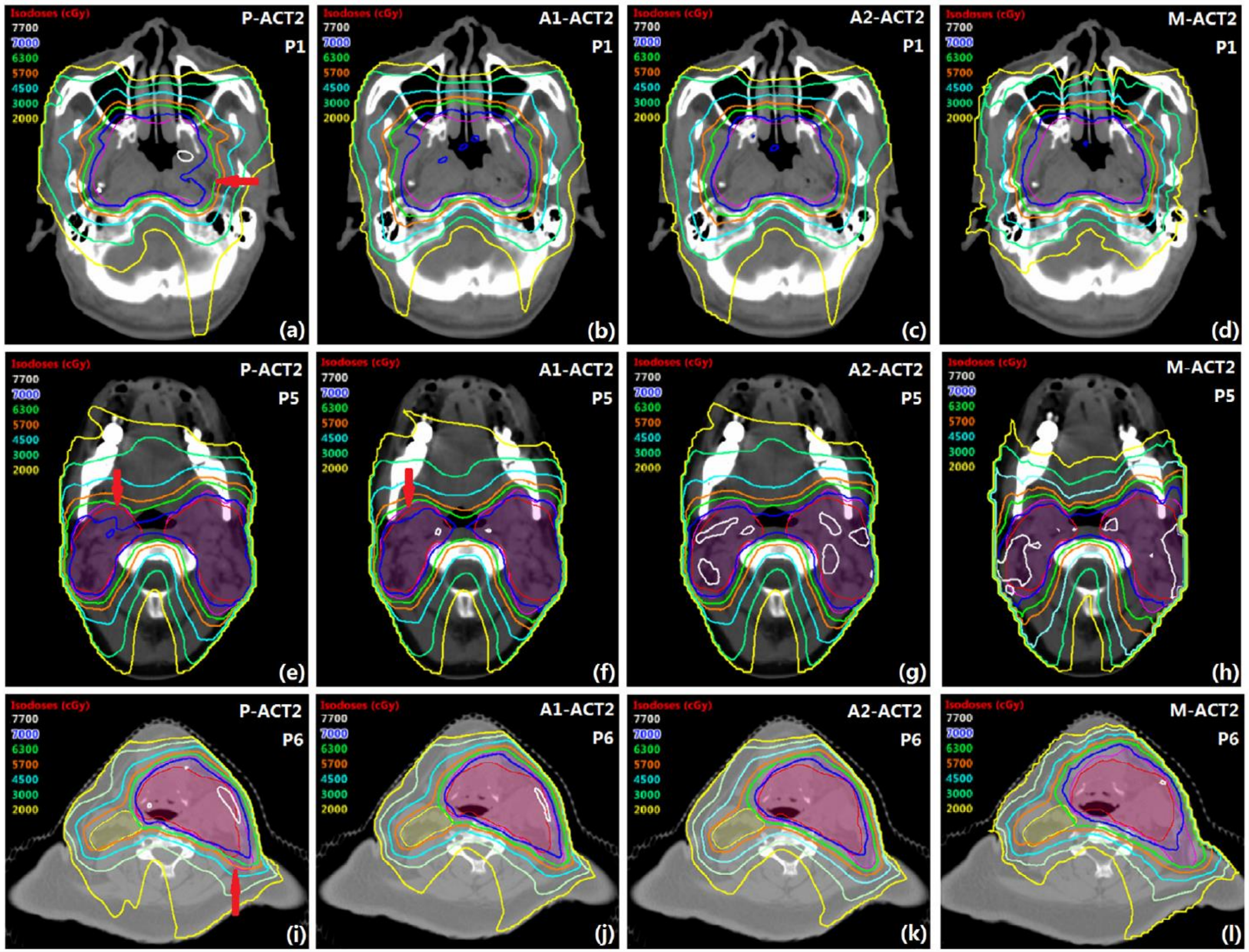
mCT RO for head and neck IMPT



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Yang, *et al.*, Radiother Oncol. (2020)

mCT RO for head and neck IMPT

- Using 2 patient scans: PCT and ACT1
  - Include both CTs in optimization

- For patients with large anatomical changes
  - mCT plan provide more robust target coverage
  - Slightly sacrificed dose conformity

mCT RO for HN IMPT can reduce the need of adaptive planning!

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Yang, *et al.*, Radiother Oncol. (2020)

mCT RO for sinonasal IMPT

Planning CT + Synthetic CTs

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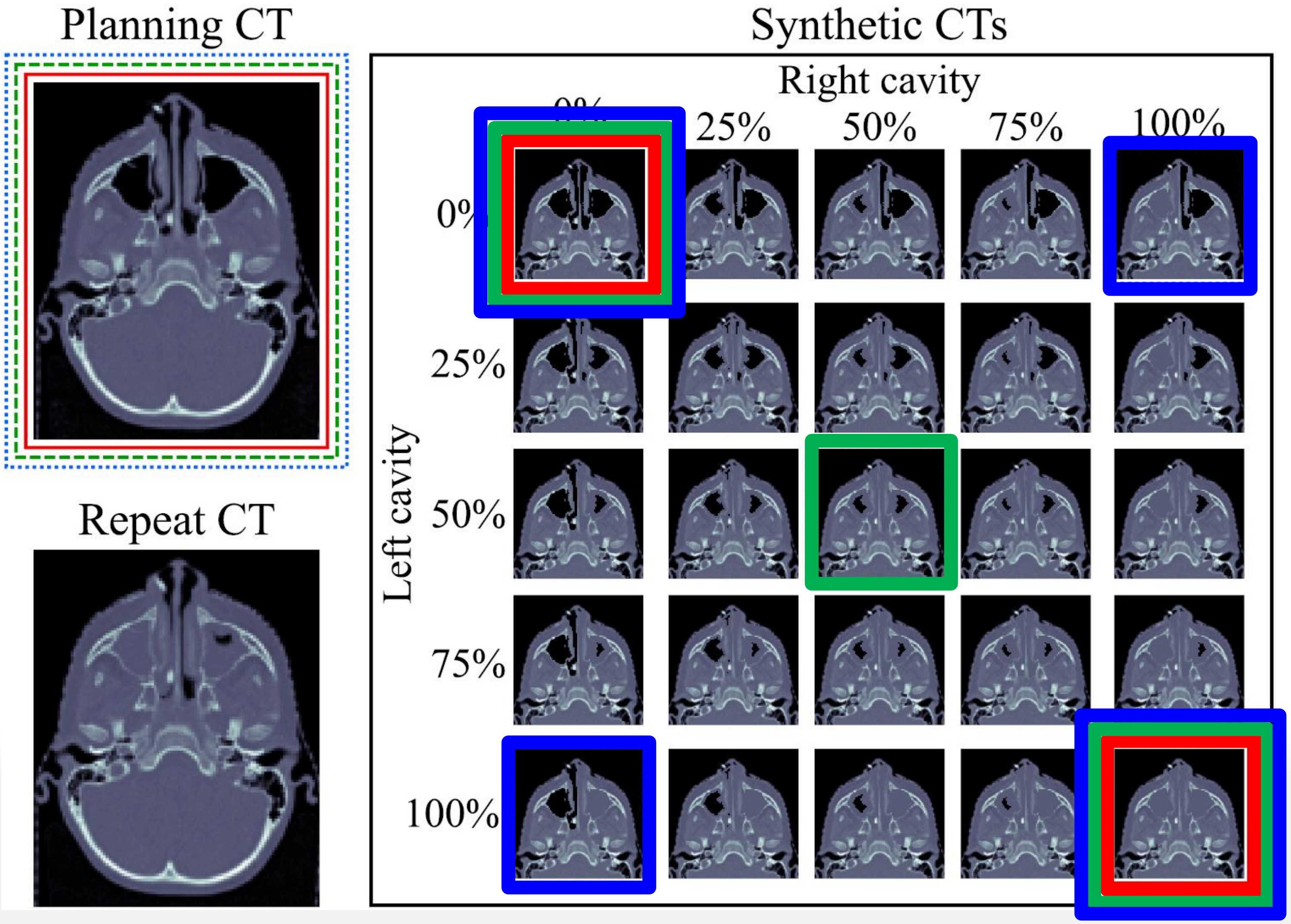
van de Water, *et al.*, Phys. Med. Biol. **63** 025020 (2018)

mCT RO for sinonasal IMPT



Planning CT +

2 synthetic CTs

3 synthetic CTs

4 synthetic CTs

van de Water, *et al.*, Phys. Med. Biol. **63** 025020 (2018)

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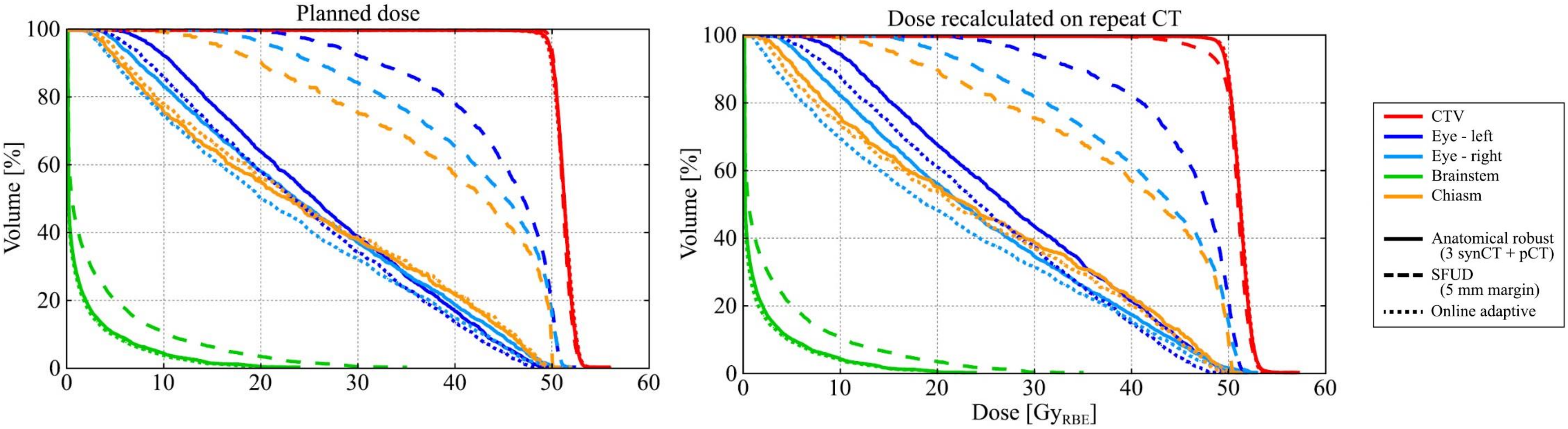
mCT RO for sinonasal IMPT



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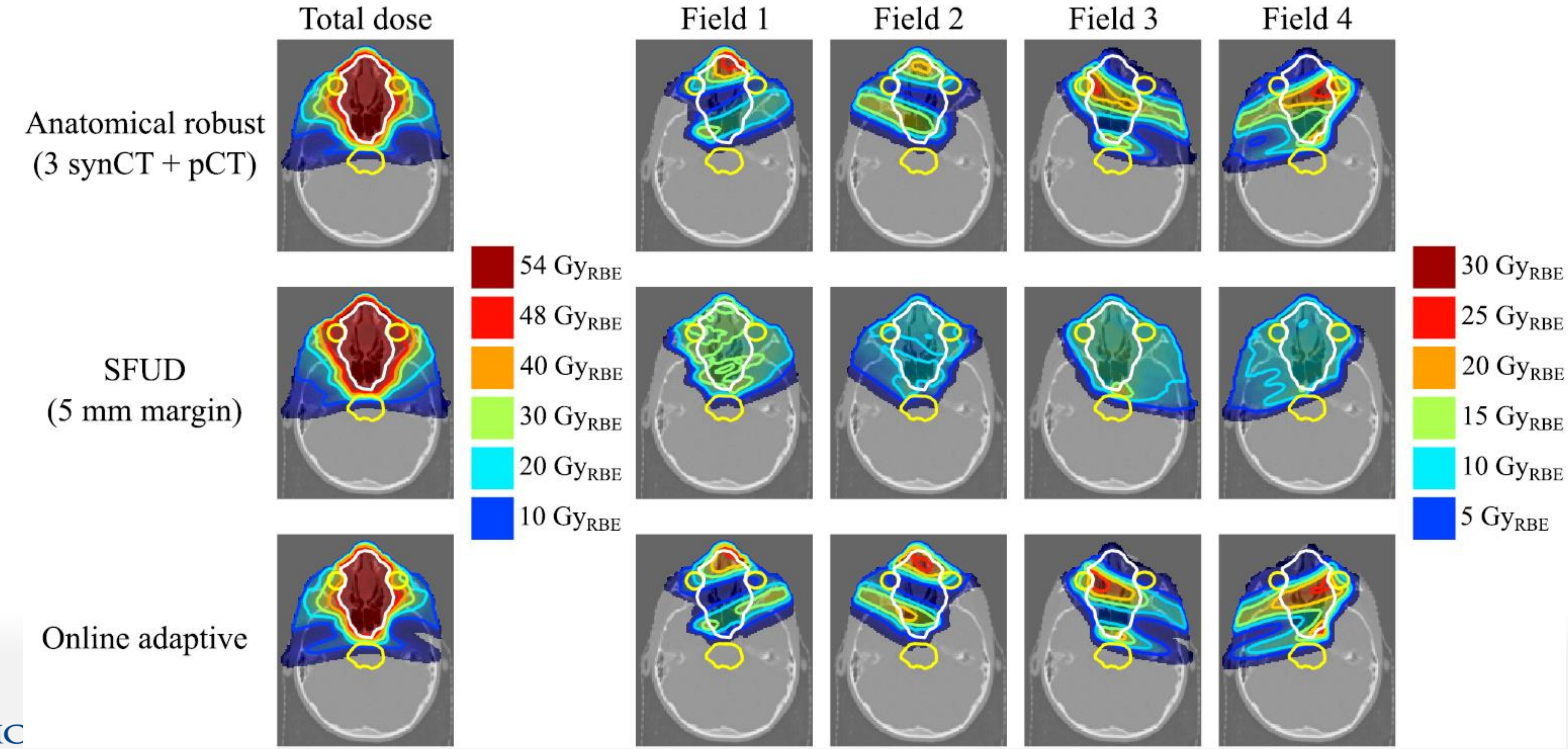
van de Water, *et al*., Phys. Med. Biol. **63** 025020 (2018)

mCT RO for sinonasal IMPT



van de Water, *et al.*, Phys. Med. Biol. **63** 025020 (2018)

mCT RO for sinonasal cancer

- Better target coverage than SFUD (+ margin);
- Lower OAR dose than SFUD (+ margin);

- Online adaptation is the best, but implementation is not realistic;

- mCT RO plans are anatomically robust under conditions of large cavity filling variation, therefore can be an alternative to the online adaptation;

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van de Water, *et al*., Phys. Med. Biol. **63** 025020 (2018)

mCT RO for Pelvic IMPT

Planning CT + Synthetic CTs

Zhu, *et al*, ARO, in press

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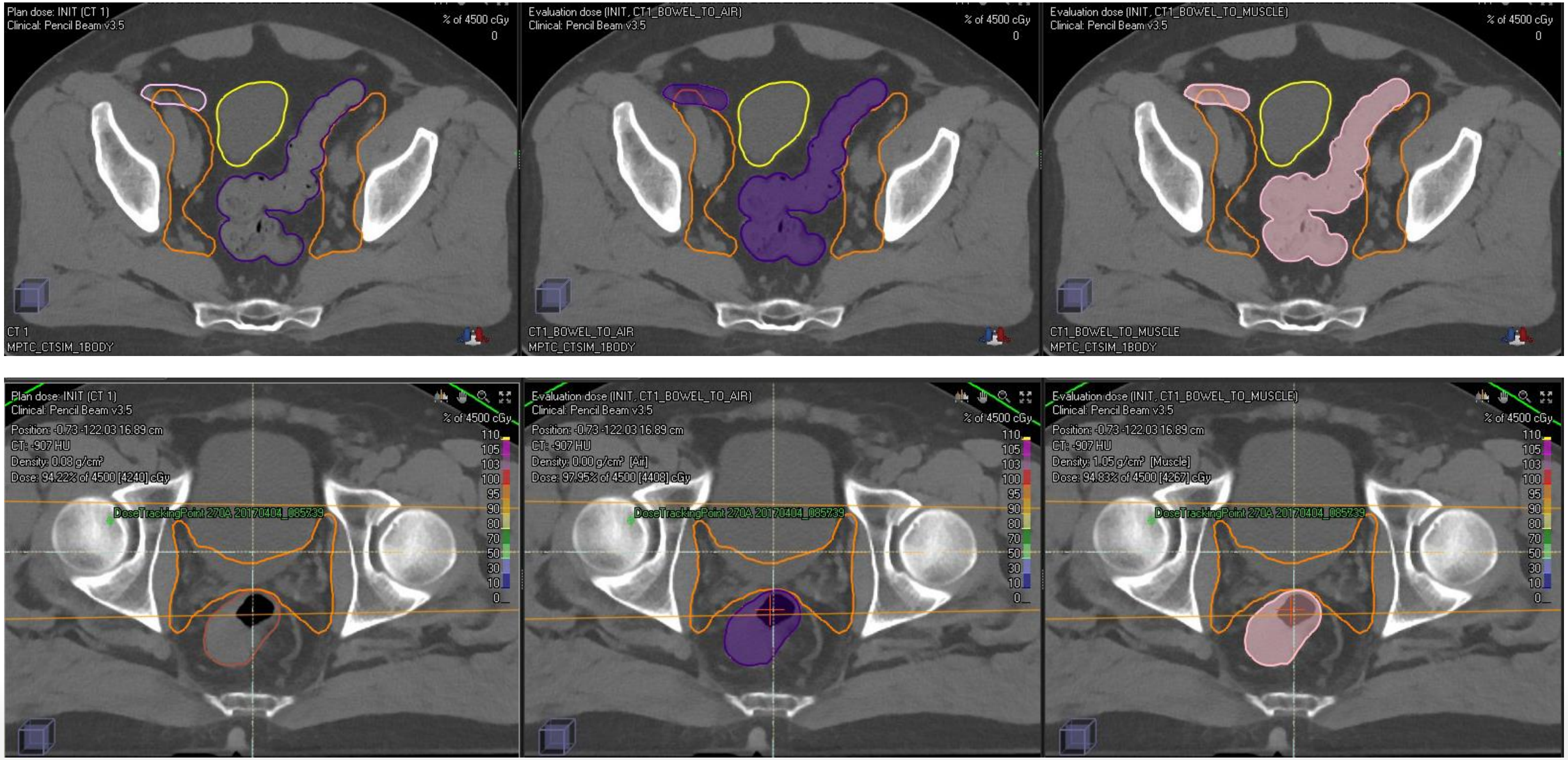
Bowel filling variation simulation



Native CT # and density

Purple: Override to Air

Pink: Override to Muscle

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mCT RO for pelvic IMPT

- Patient position:

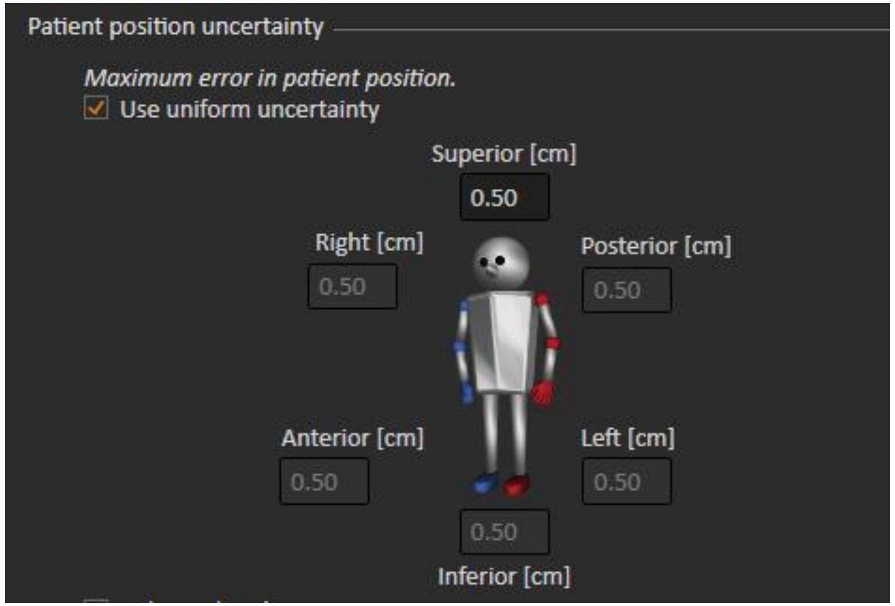
  5 mm

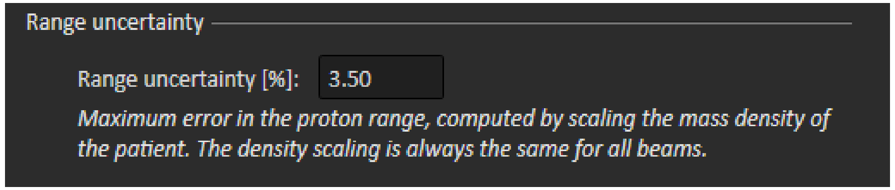
- Range Uncertainty:

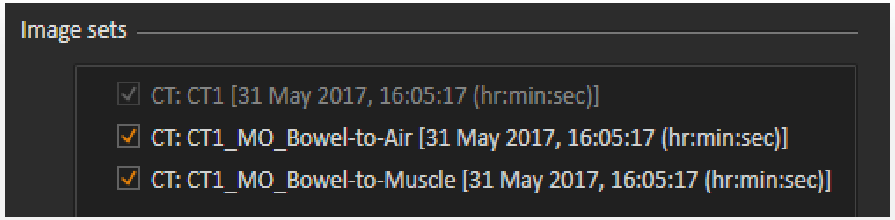
  3.5%

- Image sets:

  3 CTs







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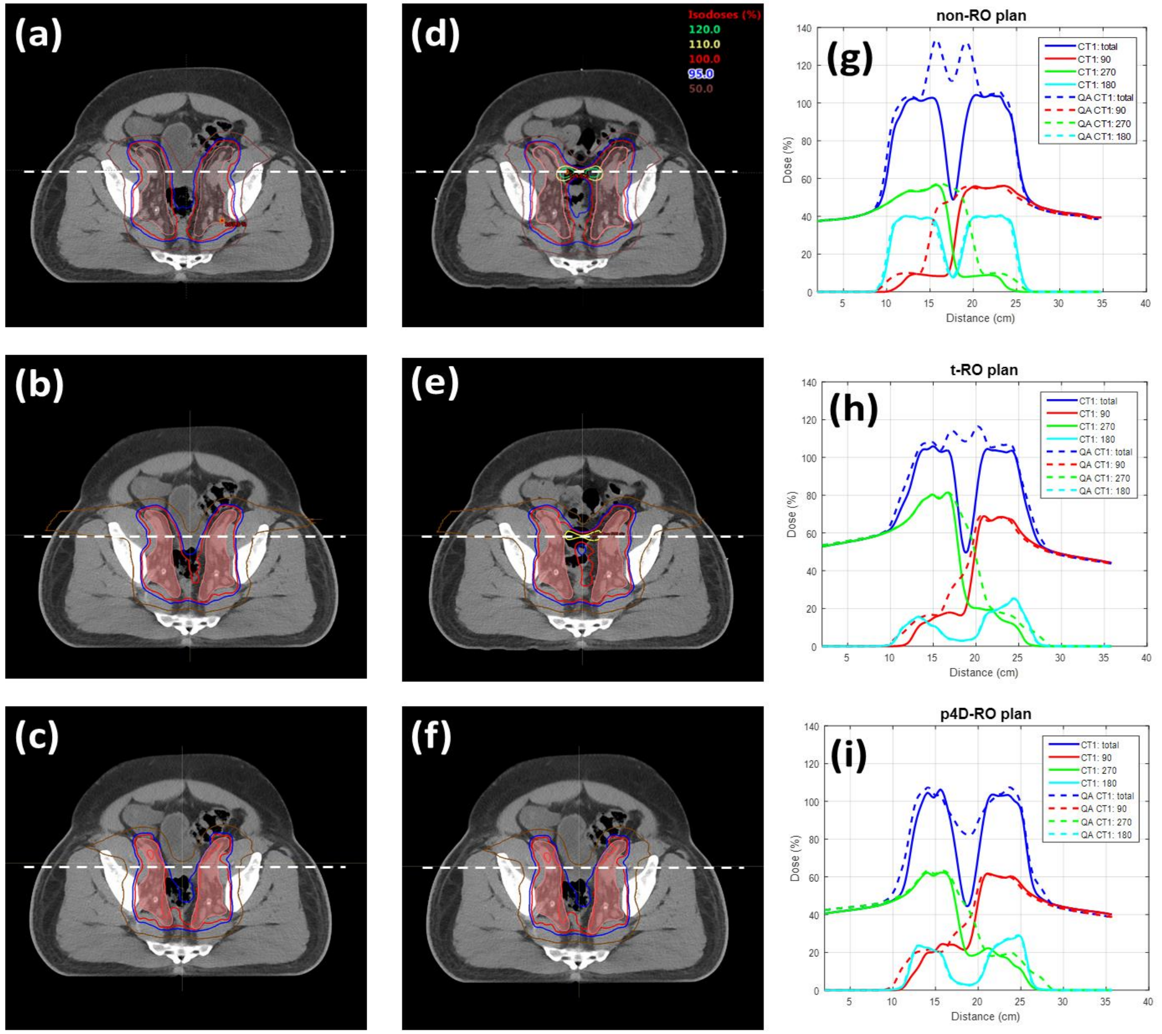
mCT RO for Pelvic IMPT



- 15 patients with pelvic LN irradiation
- Similar target coverage and critical OAR doses
  - On pCT
  - On QACTs
- mCT RO further reduced hot-spot on normal tissue
  - On QACTs

Zhu, *et al*, ARO, in press

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mCT RO Clinical implementation

- All prostate patients are planned with this method at MPTC;
- The frequency of re-scan reduced substantially:
  - From weekly scans to 2 scans through out the treatment course;
- Haven’t observe concerning hot spots on the re-scan CTs so far;
- This method can be used for other disease sites
  - GYN
  - Bladder
  - Anal/rectal
  - Head and neck
  - etc…

Summary

- Uncertainties in PT:

Proton Range

Patient Setup

RBE

Motion

Anatomy variation

Margin

Beam selection

Robust optimization

Re-painting

Adaptive RT

RBE/LET opt

Questions?

Thank you!

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