Understanding the Uncertainties in Proton Therapy

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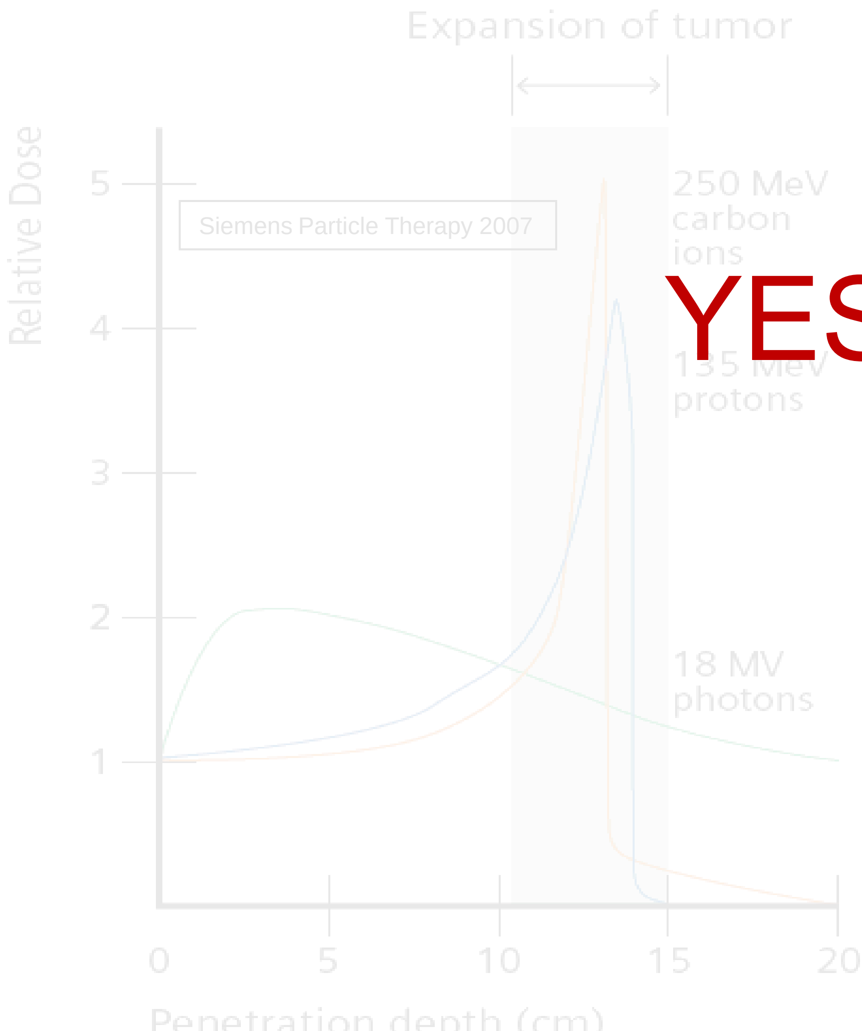
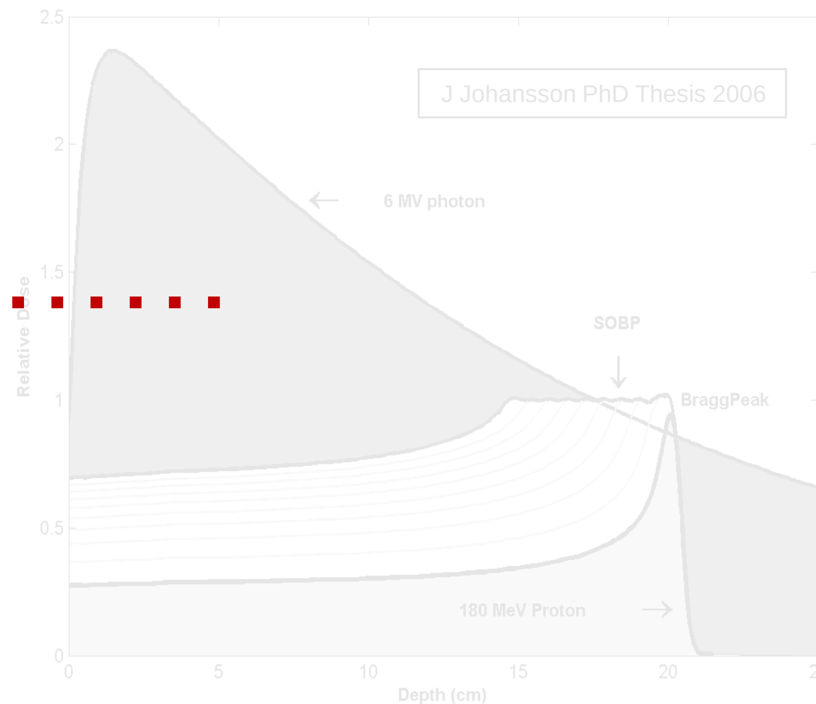
Is there an issue with these illustrations?

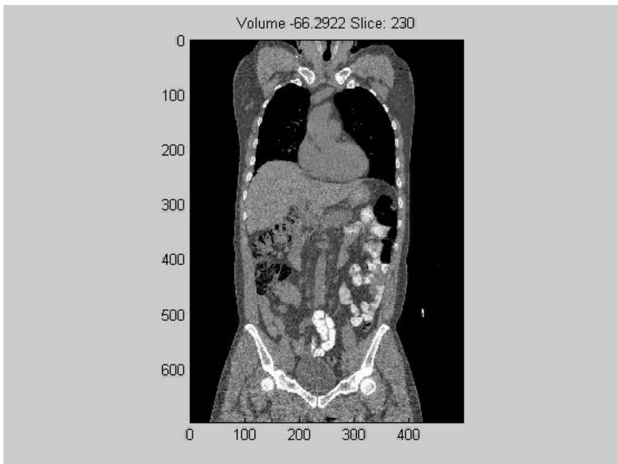


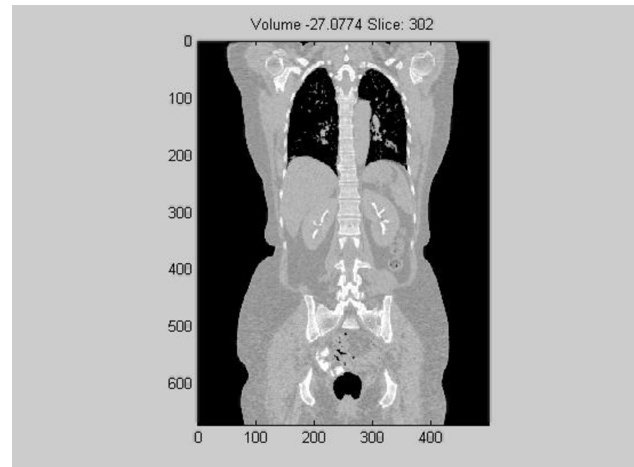
YES……

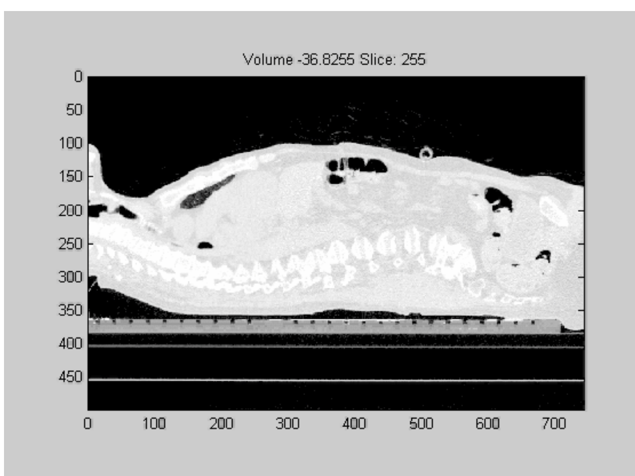


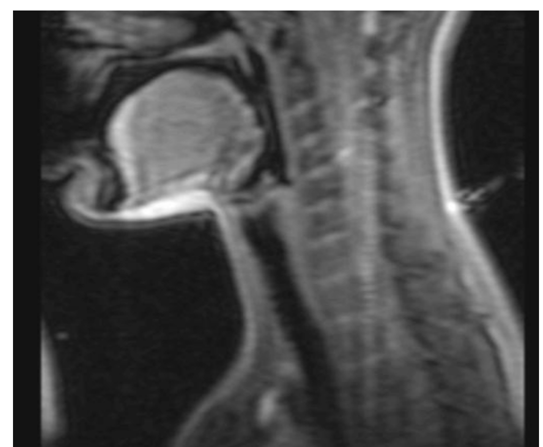
Proton spot scanning (from PSI home page, Pedroni *et al*)

The issue is to accurately deliver proton therapy to a real dynamic patient









Uncertainties in Proton Therapy Delivery

- **Common to conventional photon radiotherapy:**
  - Target definition
  - Target motion
  - Tumor regression/growth during treatment course
- **Range Uncertainties**
  - CT Hounsfield number to stopping power conversion uncertainties
    - HU uncertainties as function of
      - patient size
      - scanning techniques
      - reconstruction algorithms
  - CT artifacts
  - Stopping power measurement/calculation uncertainties
- **Normal organ motion and changes**
  - Bladder filling
  - Rectum gas
  - Amount of lung in beam path for thorax

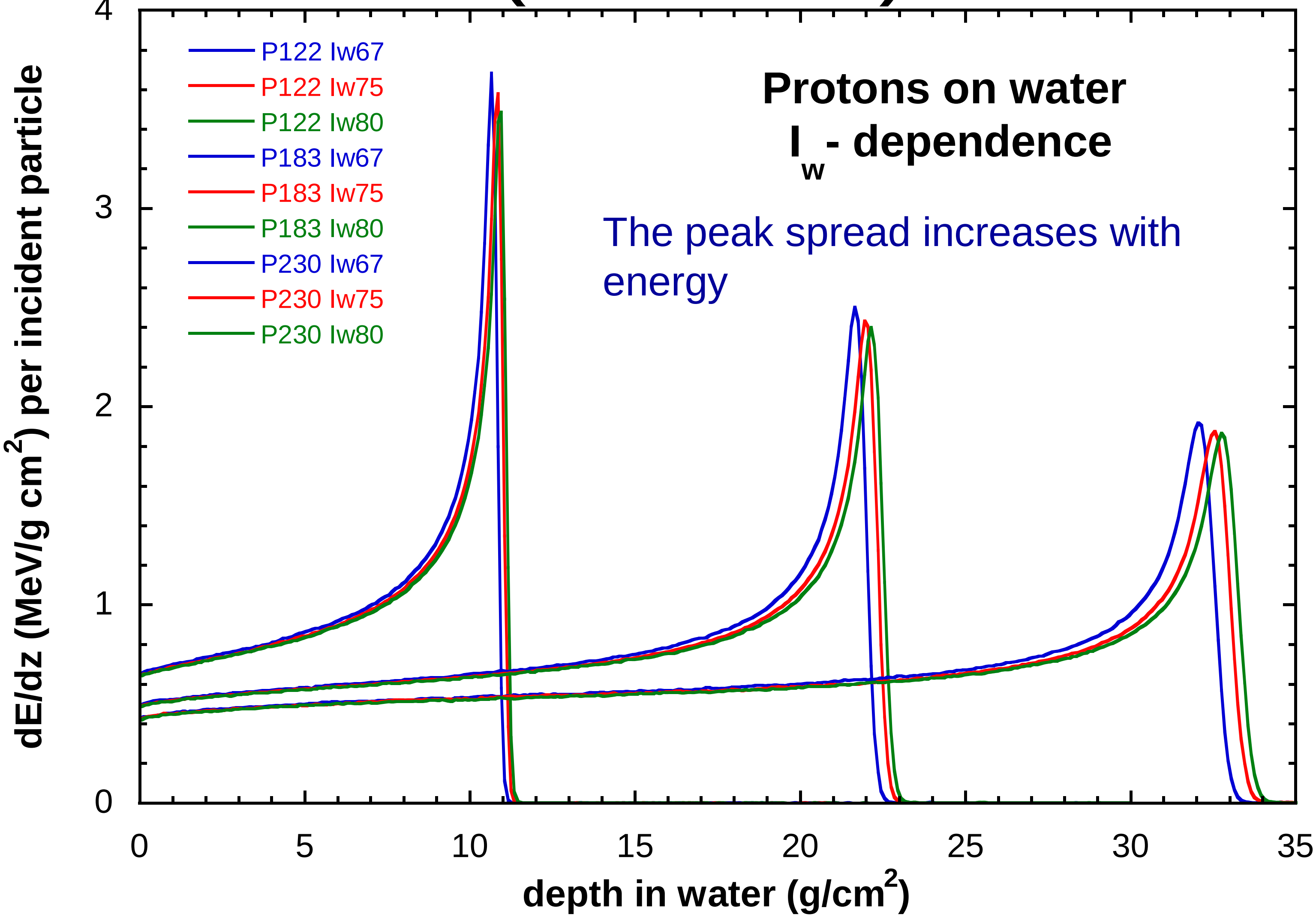
Main differences between **photons** and **protons**

	Factors	Protons	Photons
1	CT # and stopping powers accuracy	Sensitive - affect range, distal target coverage or distal normal tissue sparing	Not sensitive
2	Target motion normal to beam	Affects margin, may affect dose distribution distal to target	Affects margin
3	Normal structure motion orthogonal to beam	Affects range, dose distribution distal to structure	Minimal effect
4	Target motion along beam direction	No effect	Affects margin
5	Normal structure motion along beam direction	No effect	Minimal effect
6	Complex inhomogeneities	Not well characterized, perturb dose distributions, degrade distal edge	Well understood, effect not strong
7	Anatomy changes over course of RT	Affect dose distribution	Minimal effect
8	Plan Evaluation	Impact of uncertainties significant, PTV concept not valid, validity of initial nominal plan questionable	PTV concept valid, dose distributions relatively invariant to uncertainties, initial plan acceptable approximations

Factors that contribute to range uncertainties

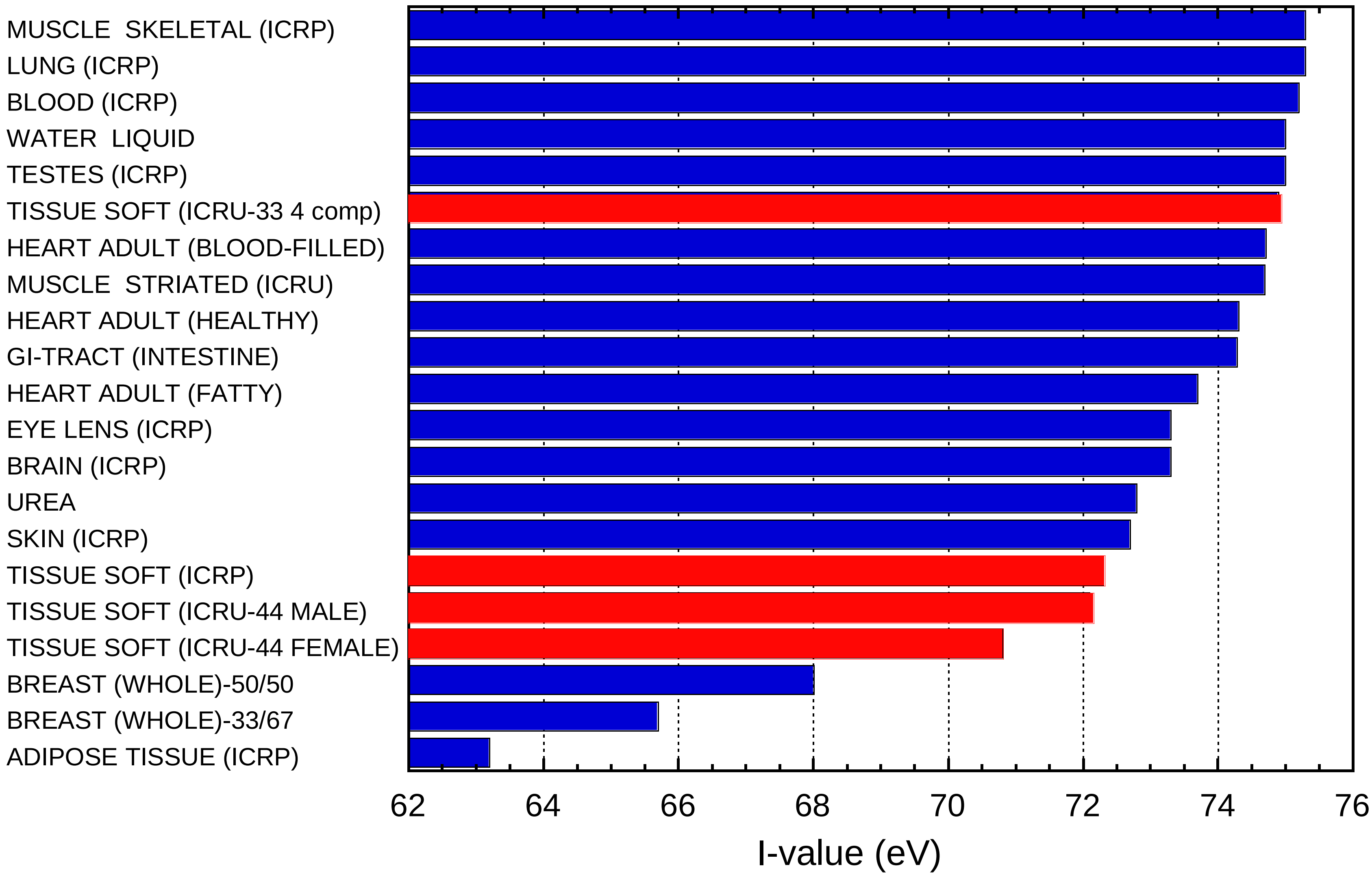
- Inherent uncertainties in linear stopping power
- Uncertainties in the formation of broad clinical proton beams (laterally and in-depth)
- Uncertainties in the determination of radiological thicknesses of bolus/compensator materials and accessories

Intrinsic basic physics uncertainty (I-values)

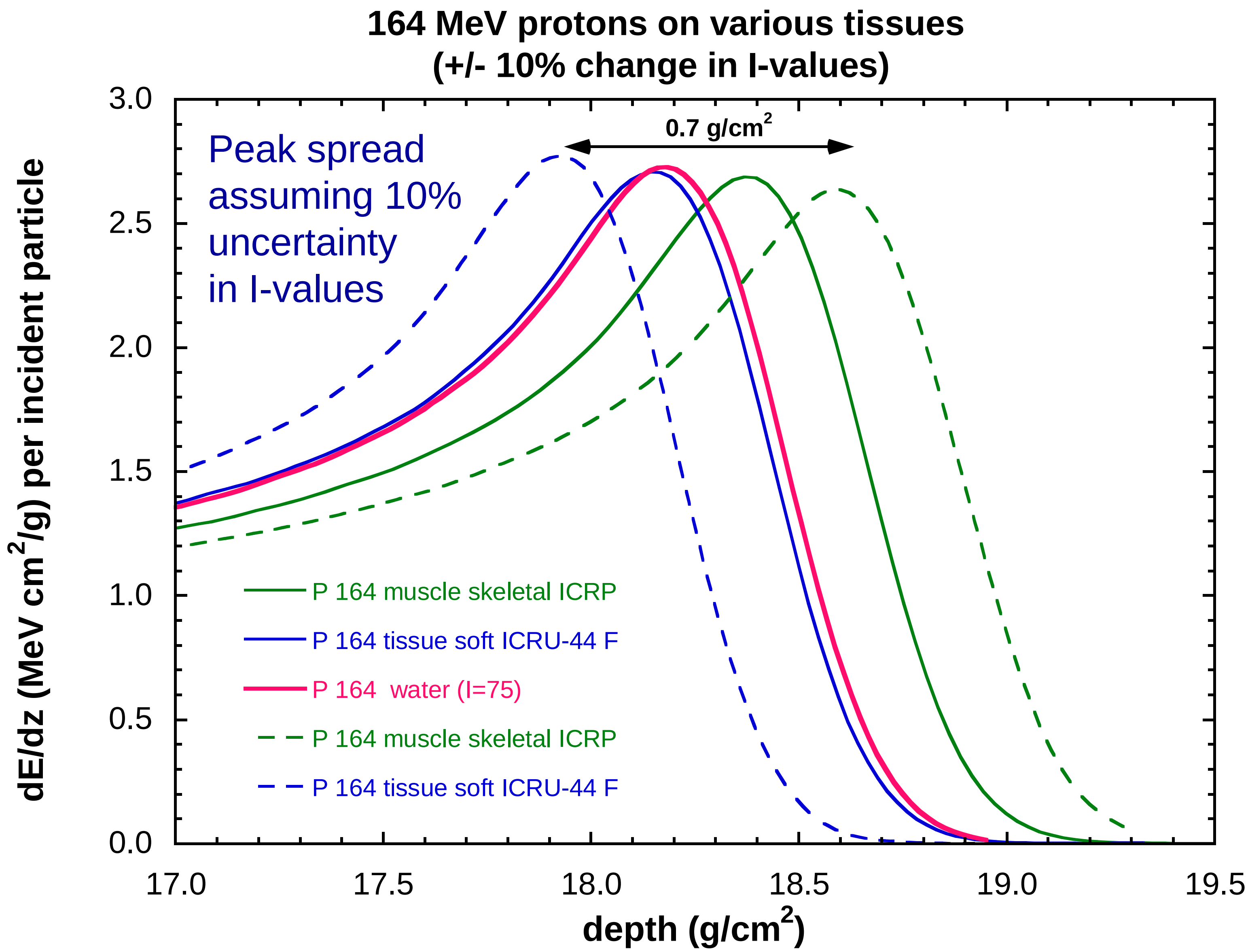


P Andreo, Phys Med Biol, 2009

average I-values of various soft tissues

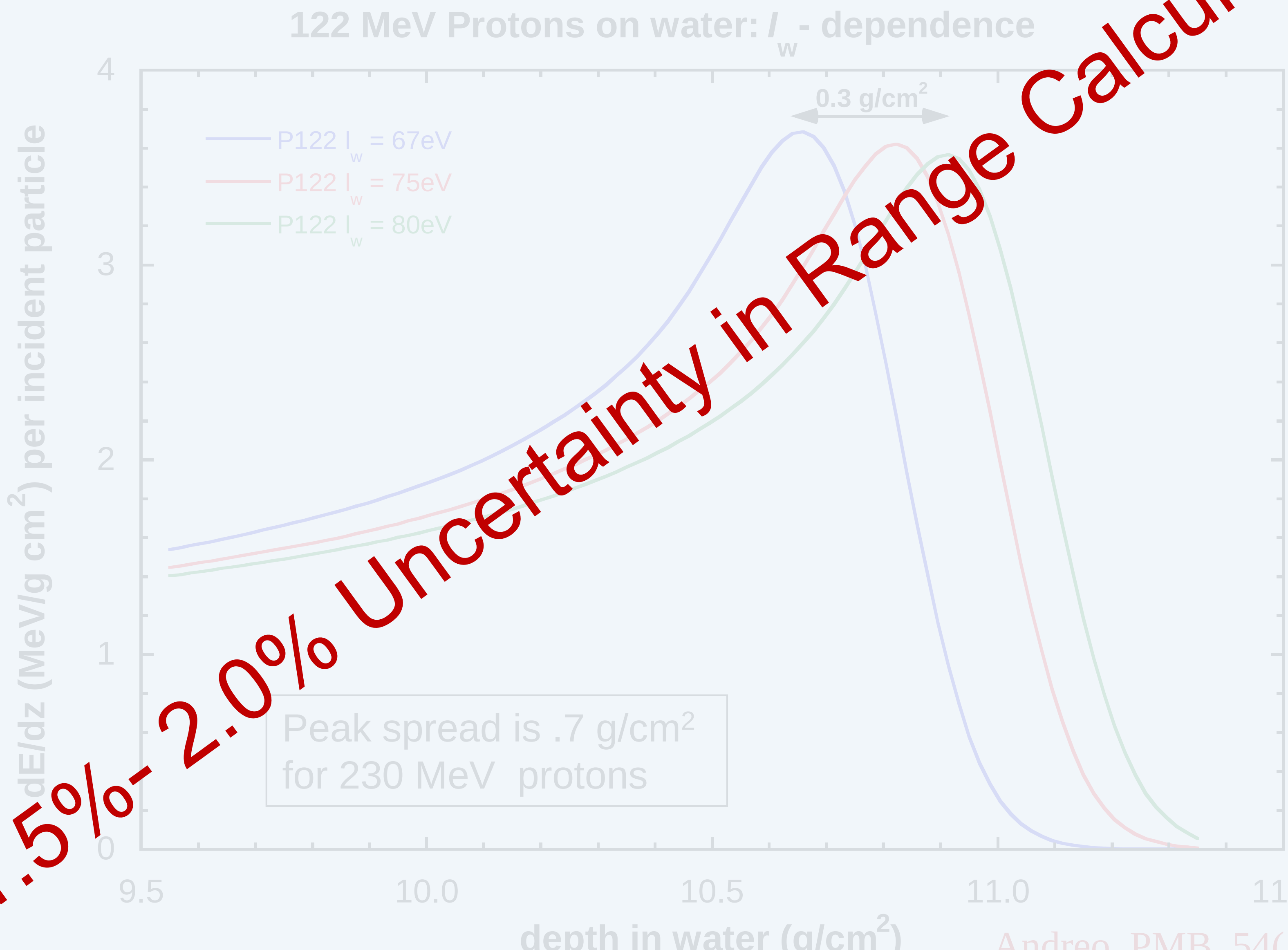


P Andreo, Phys Med Biol, 2009



P Andreo, Phys Med Biol, 2009

Impact of inherent uncertainty in Linear Stopping Power

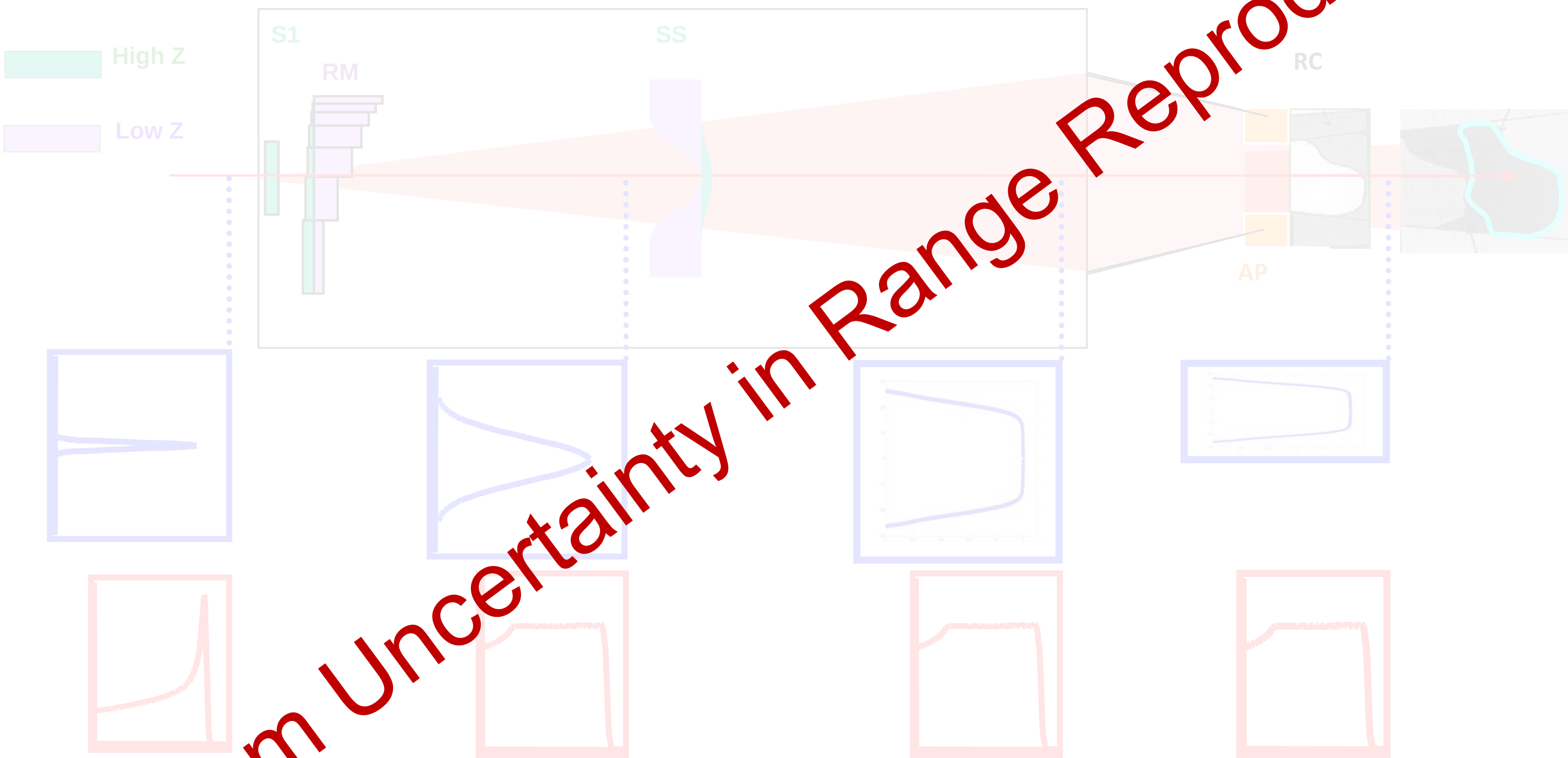


± 1.5%- 2.0% Uncertainty in Range Calculation

Andreo, PMB, 54(1), 2009

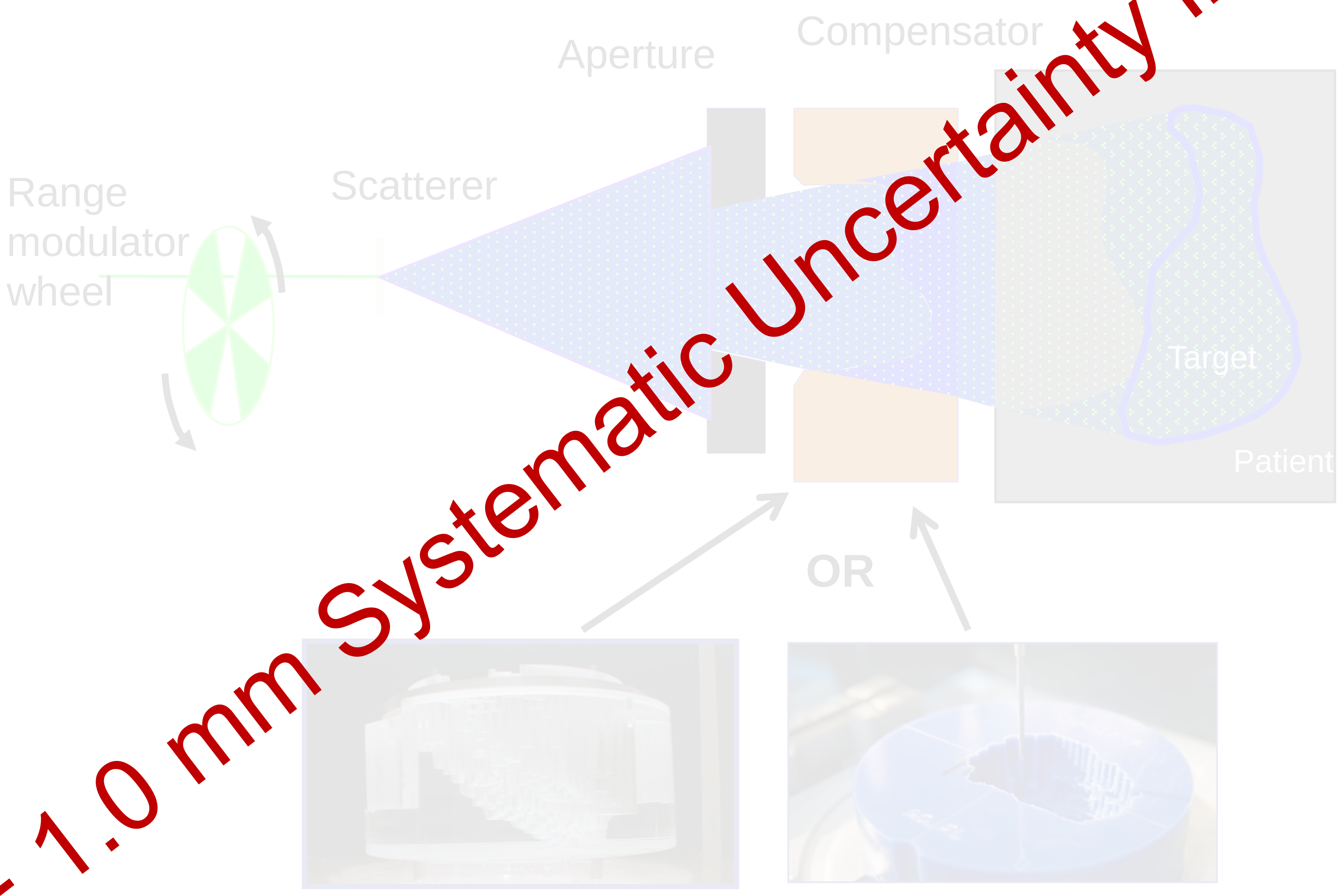
Uncertainties in the formation of Broad clinical beam

± 1.0 mm Uncertainty in Range Reproducibility



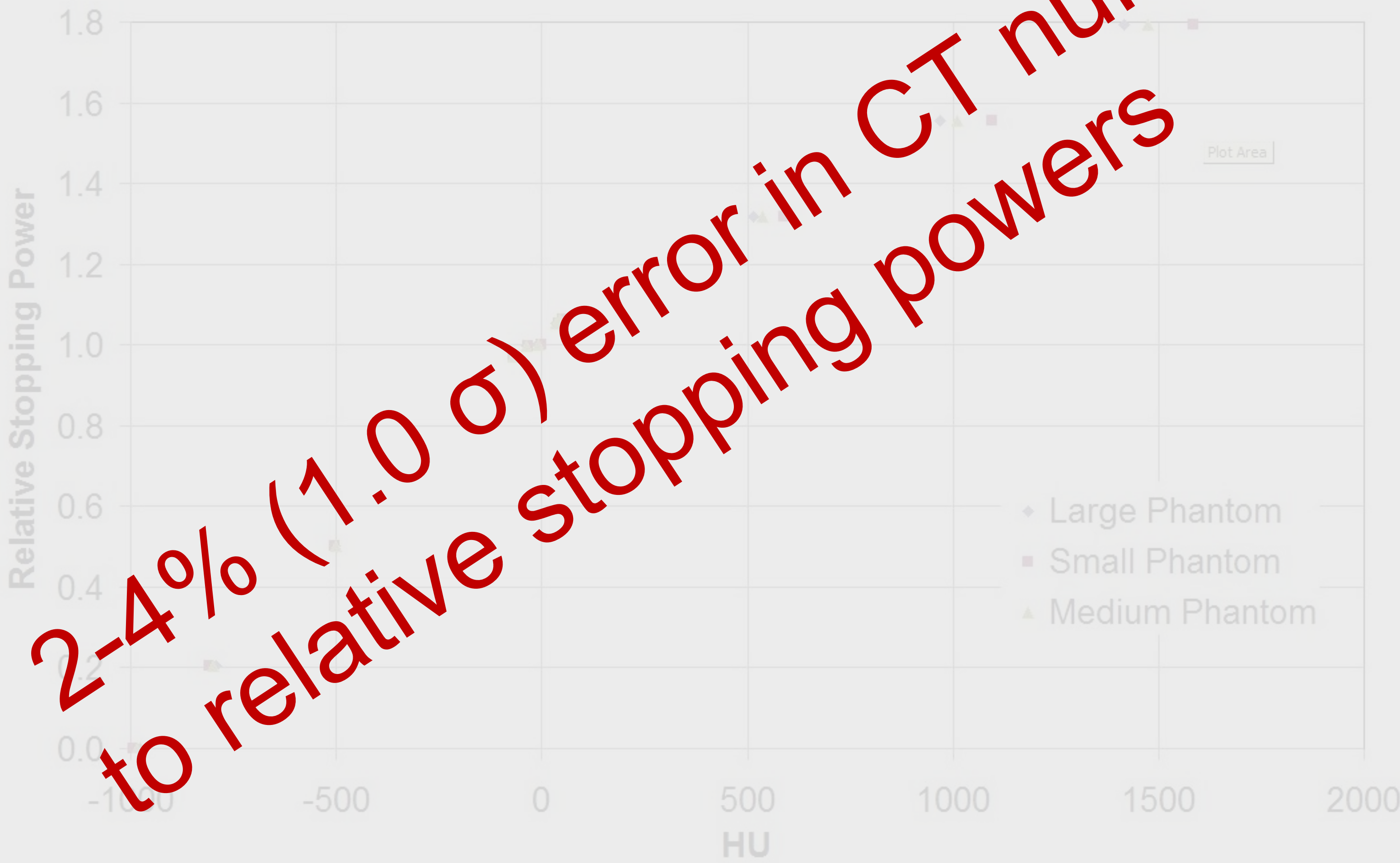
S1 – first scatterer, RM – range modulator, SS – second scatterer, AP – aperture, RC – range compensator.

Uncertainties in the thickness of bolus/compensator materials



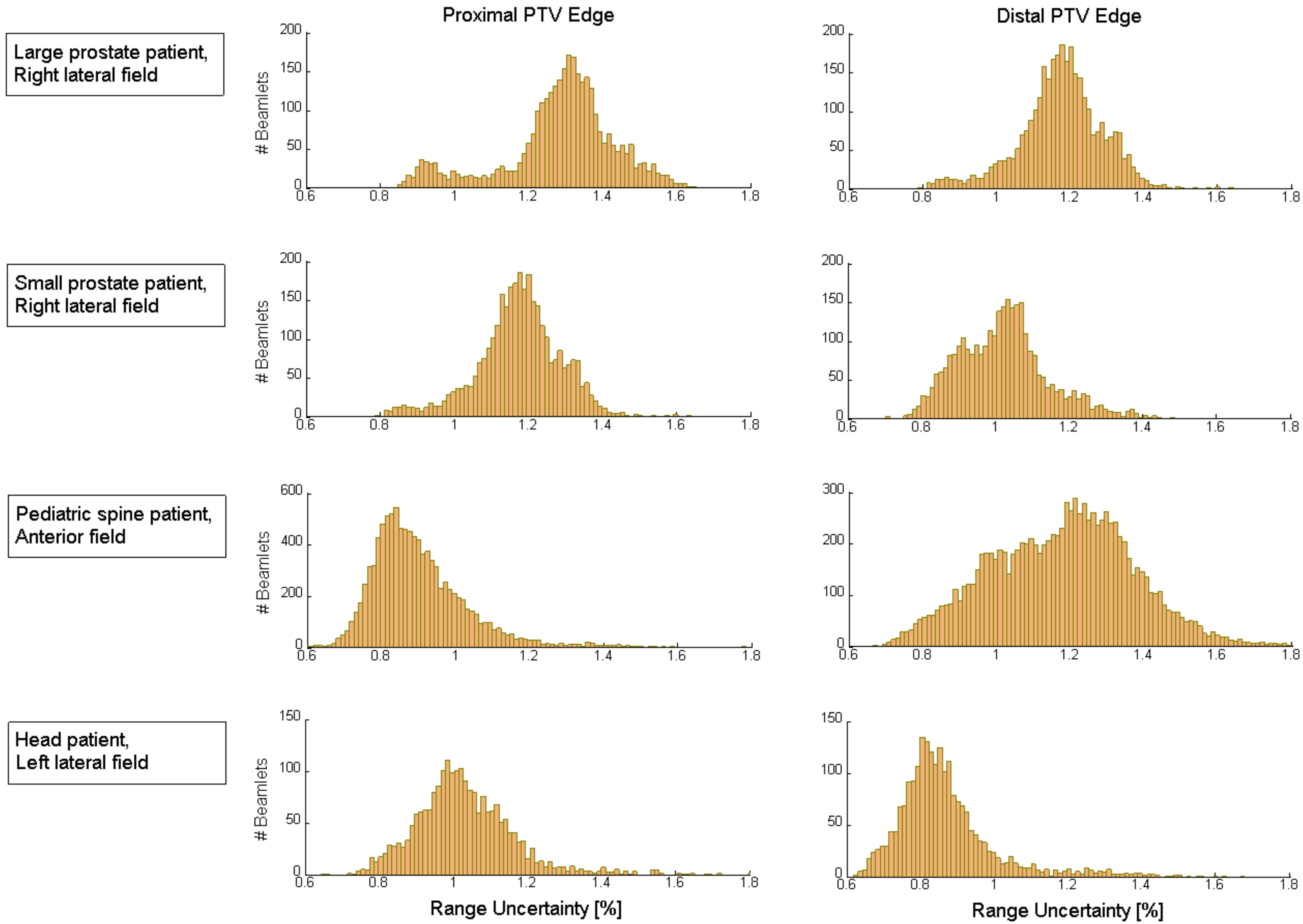
± 1.0 mm Systematic Uncertainty in Range

CT Numbers to Relative Stopping Power Conversion Uncertainties

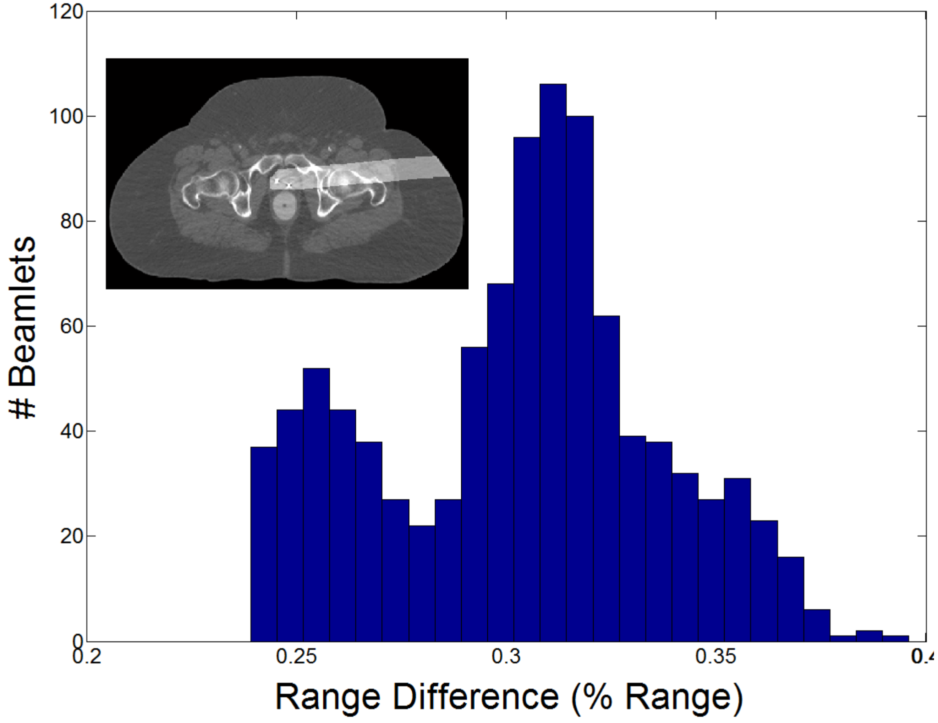


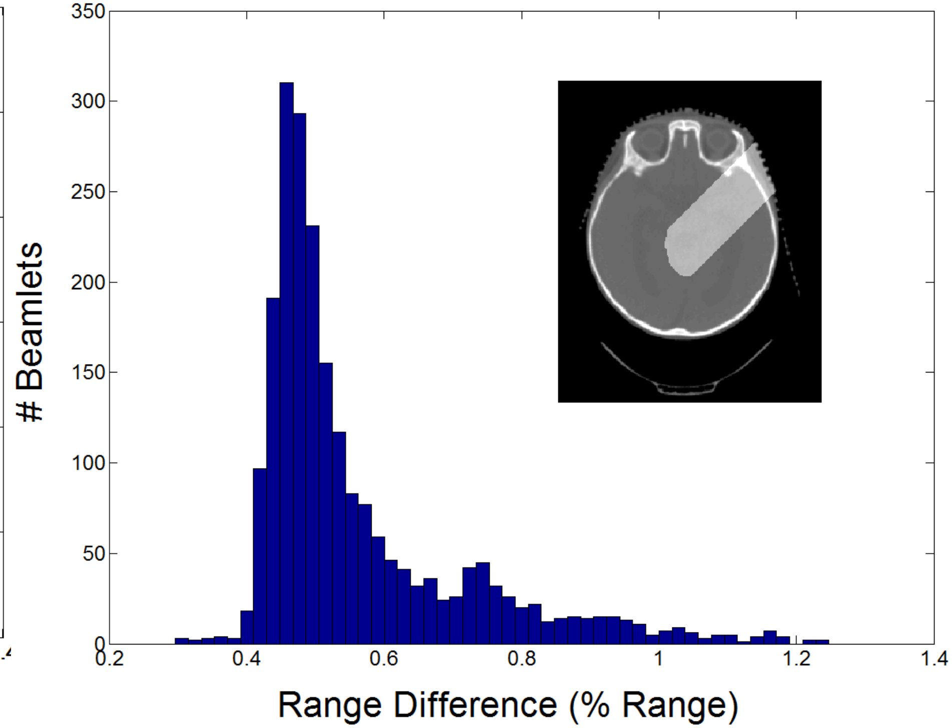
2-4% (1.0 σ) error in CT numbers to relative stopping powers

HU-Stopping Power Conversion Uncertainties Results in Range Uncertainties



S Flampouri, UFPTI

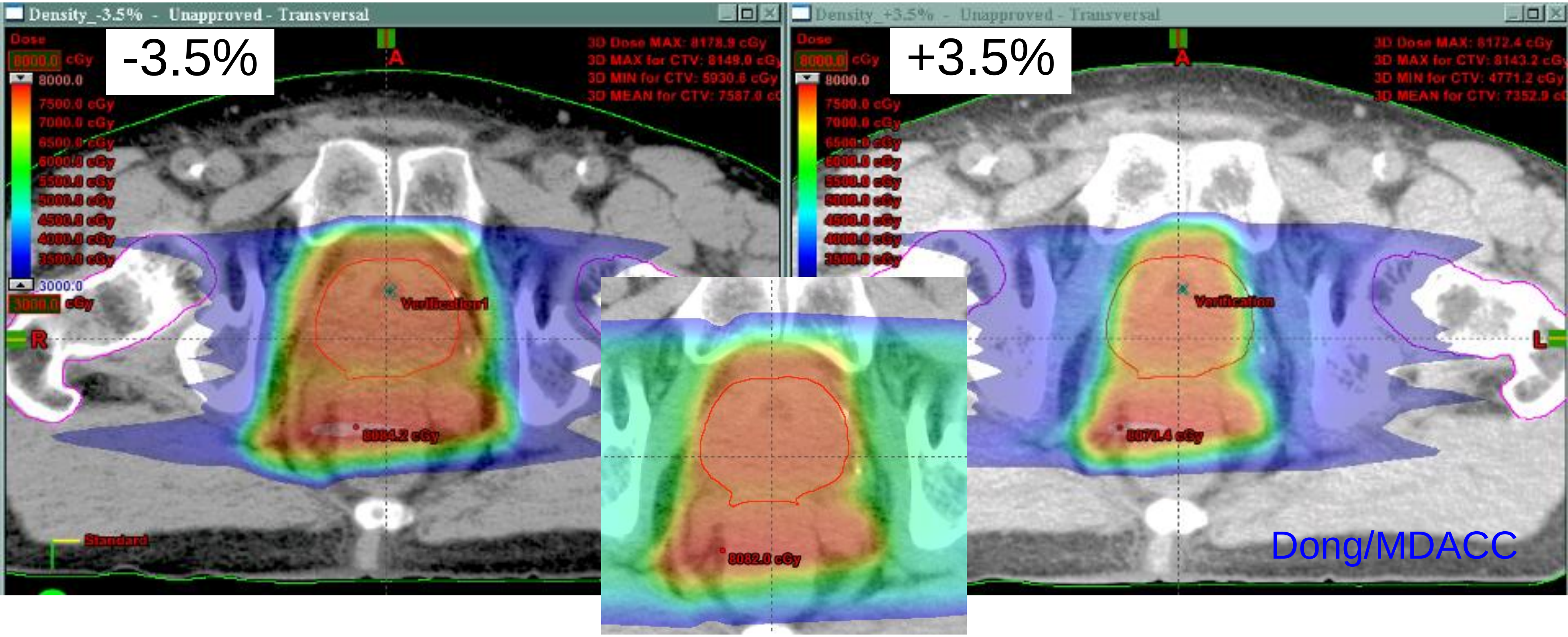




Range uncertainties computed for a small pediatric and a large prostate patient. The discrepancies in the proton range varied .4-.7% and .6-1.2% for prostate and pediatric patient respectively.

Flampouri, UFPTI

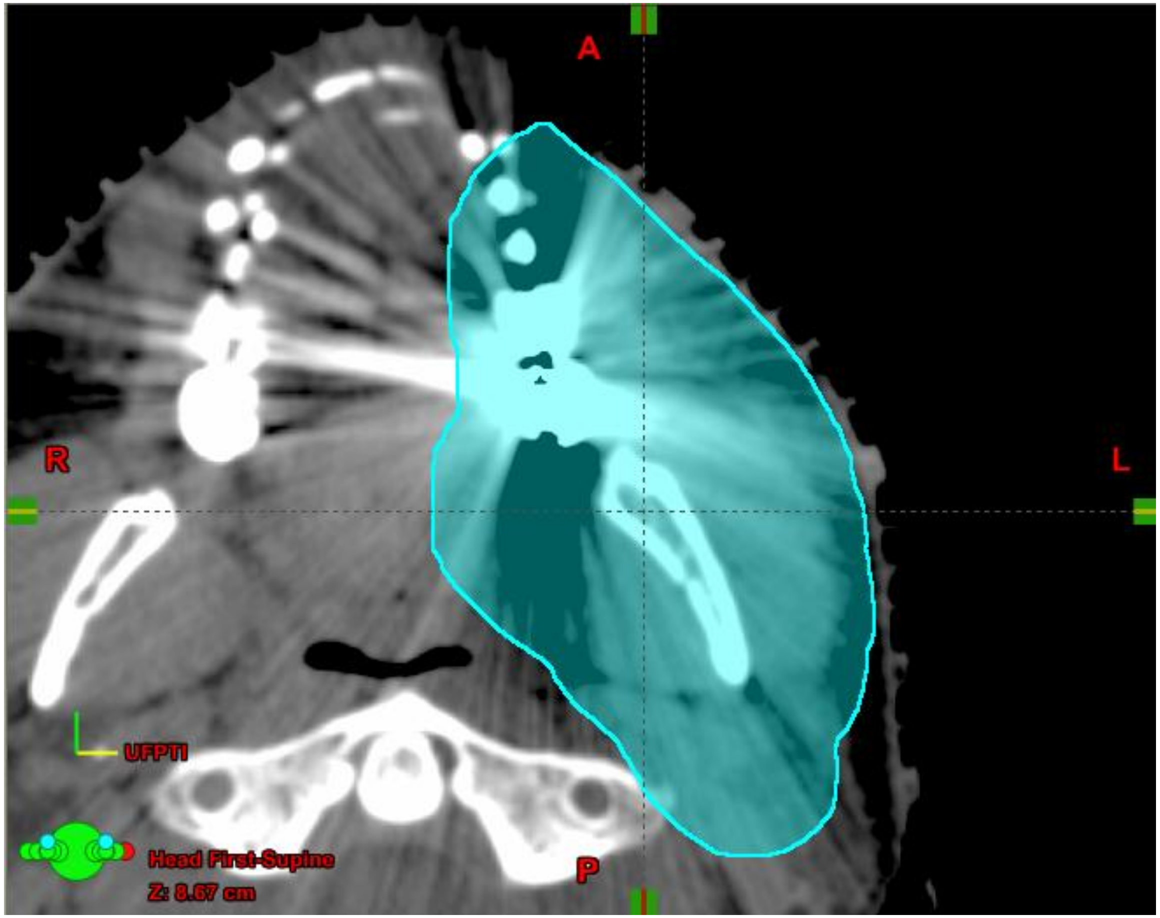
Impact of CT Hounsfield number uncertainties on dose distributions



0% uncertainty

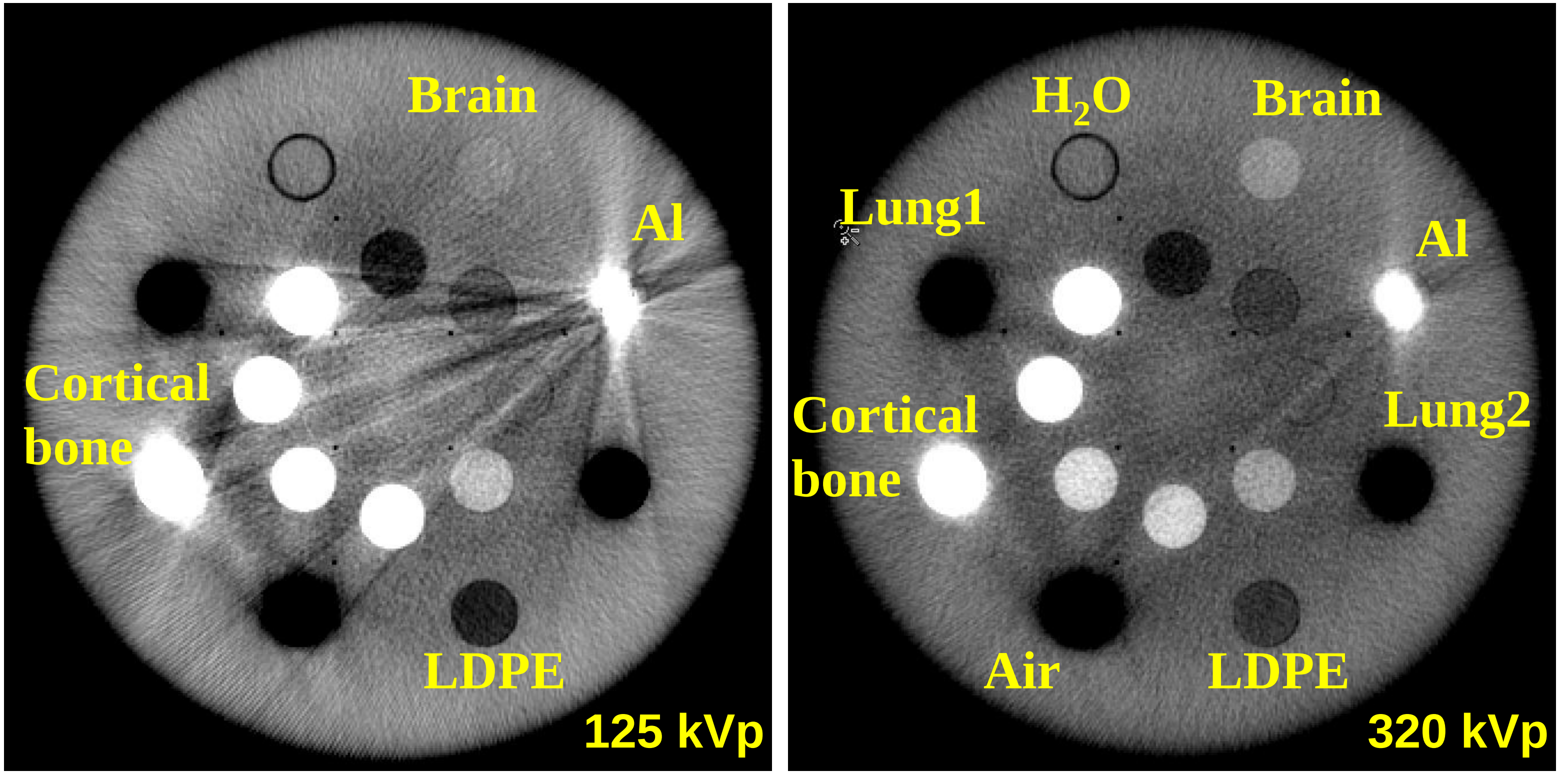
Individualized patient determination of tissue composition along the complete beam path, rather than CT Hounsfield numbers alone, would probably be required even to reach "sub-centimeter precision"

CT Artifacts and Hounsfield Numbers

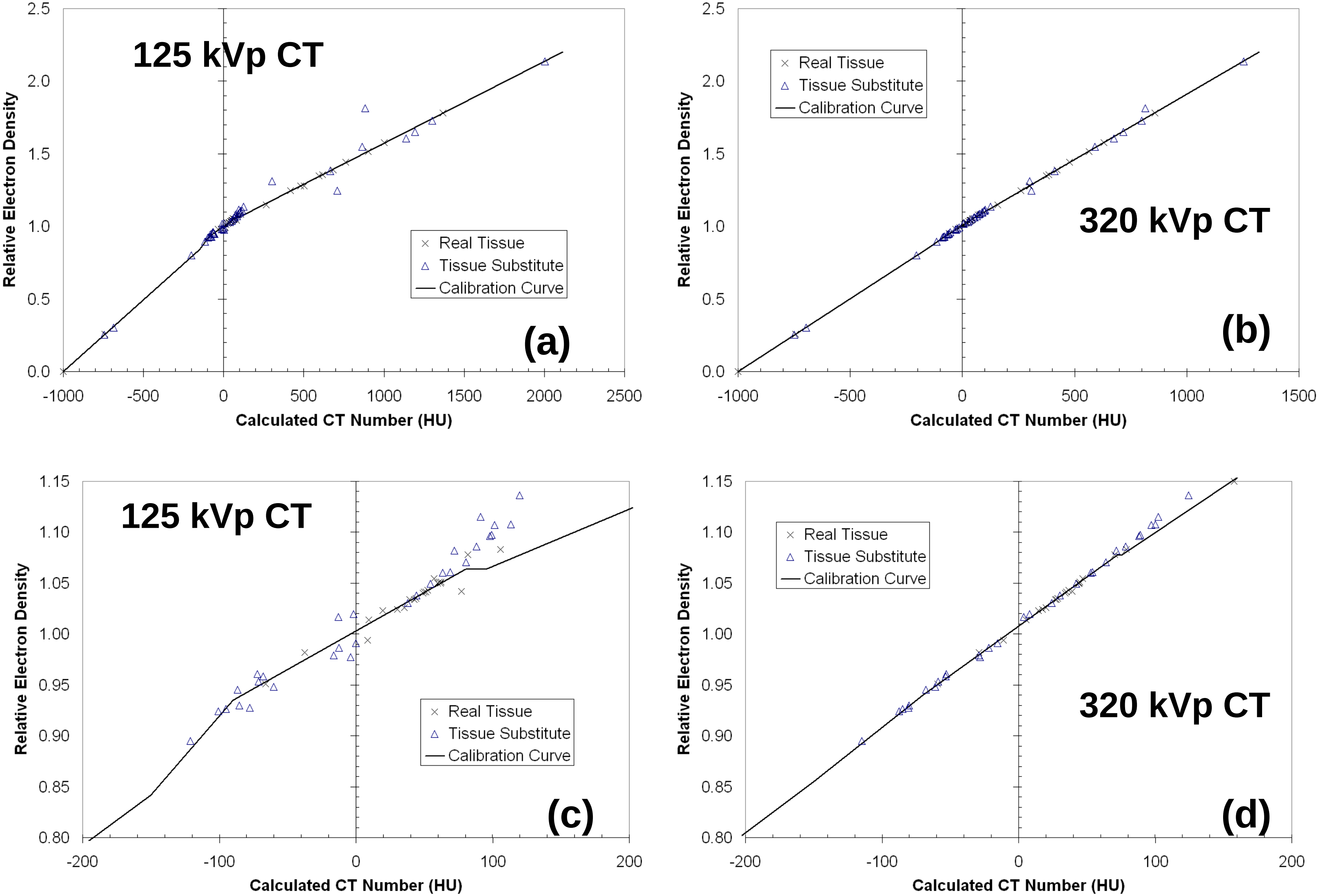


“It is imperative that body-tissue compositions are not given the standing of physical constants and their reported variability is always taken into account” (ICRU-44, 1989).

Improving CT number accuracy and reducing metal artifacts with Orthovoltage CT imaging

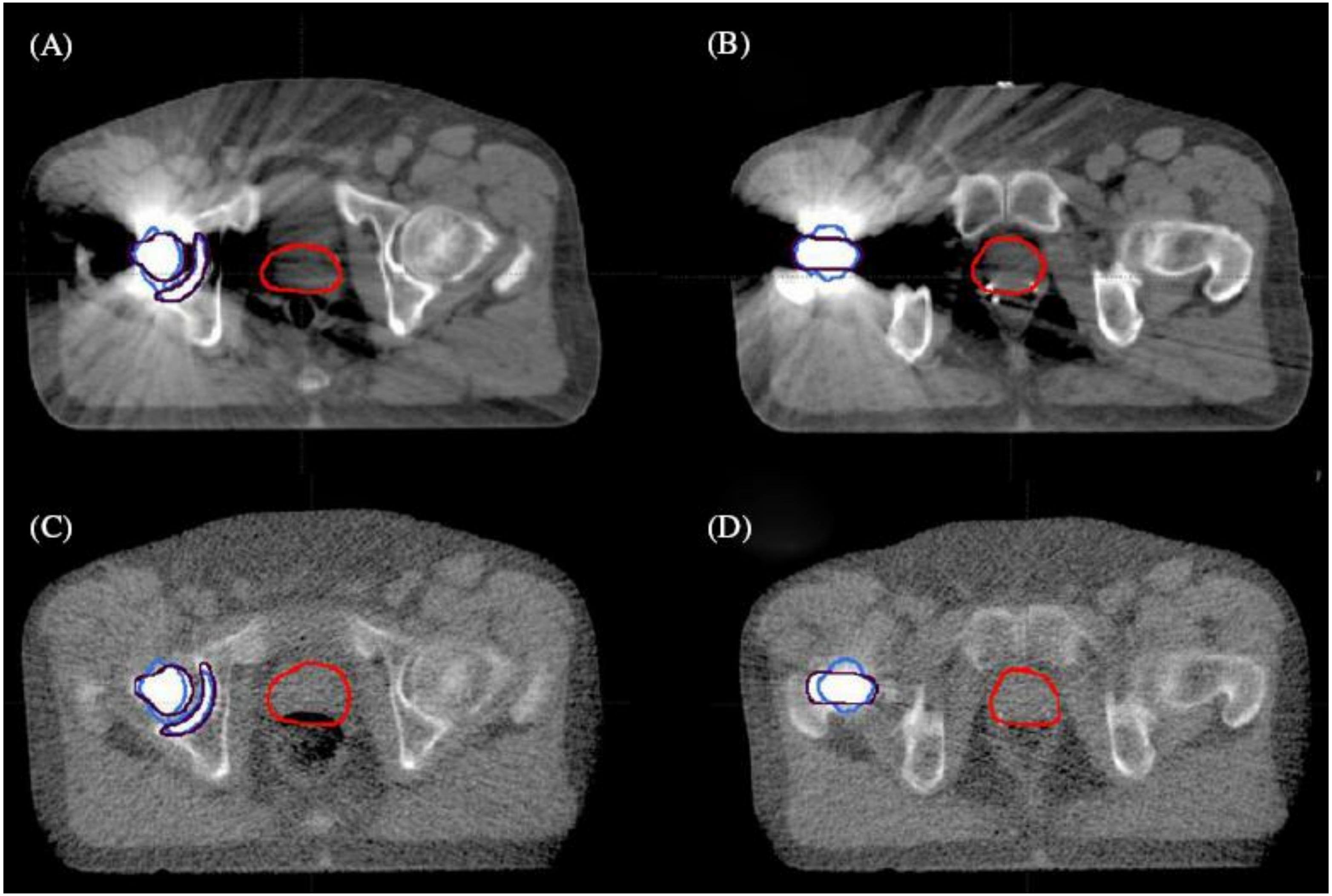


Yang et al. Med Phys 35 (5):1932-1941, 2008



Yang et al. Med Phys 35 (5):1932-1941, 2008

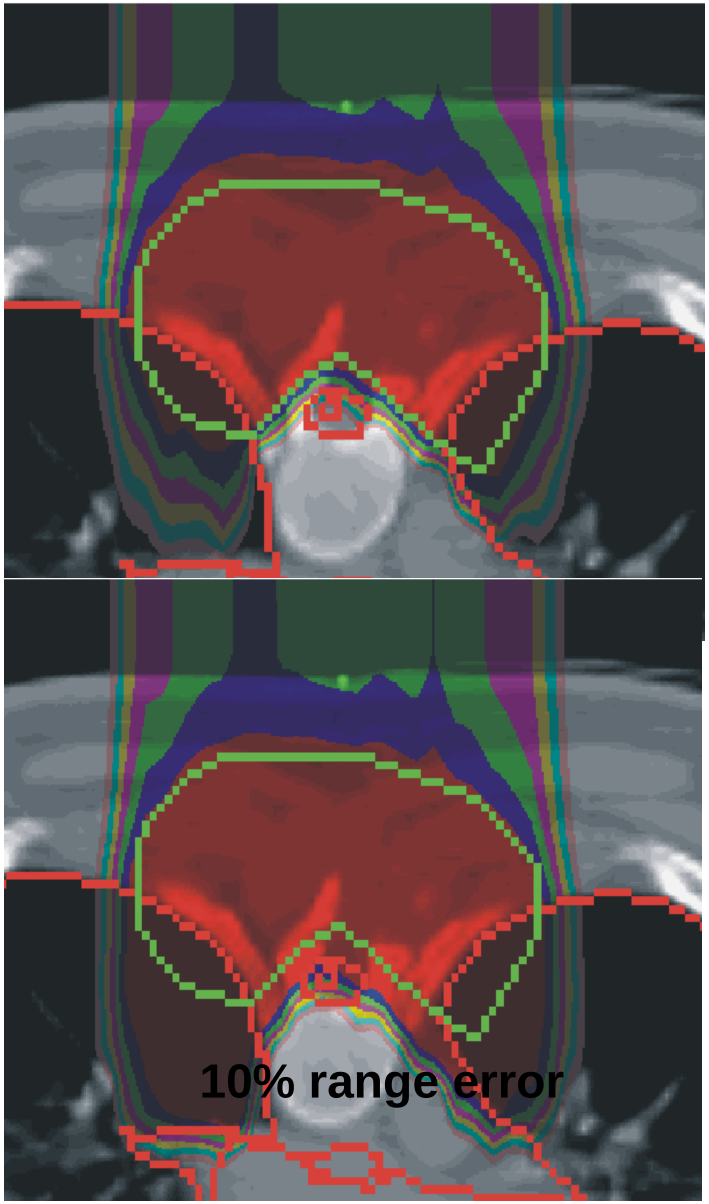
Megavoltage CT for Proton Dose Calculation



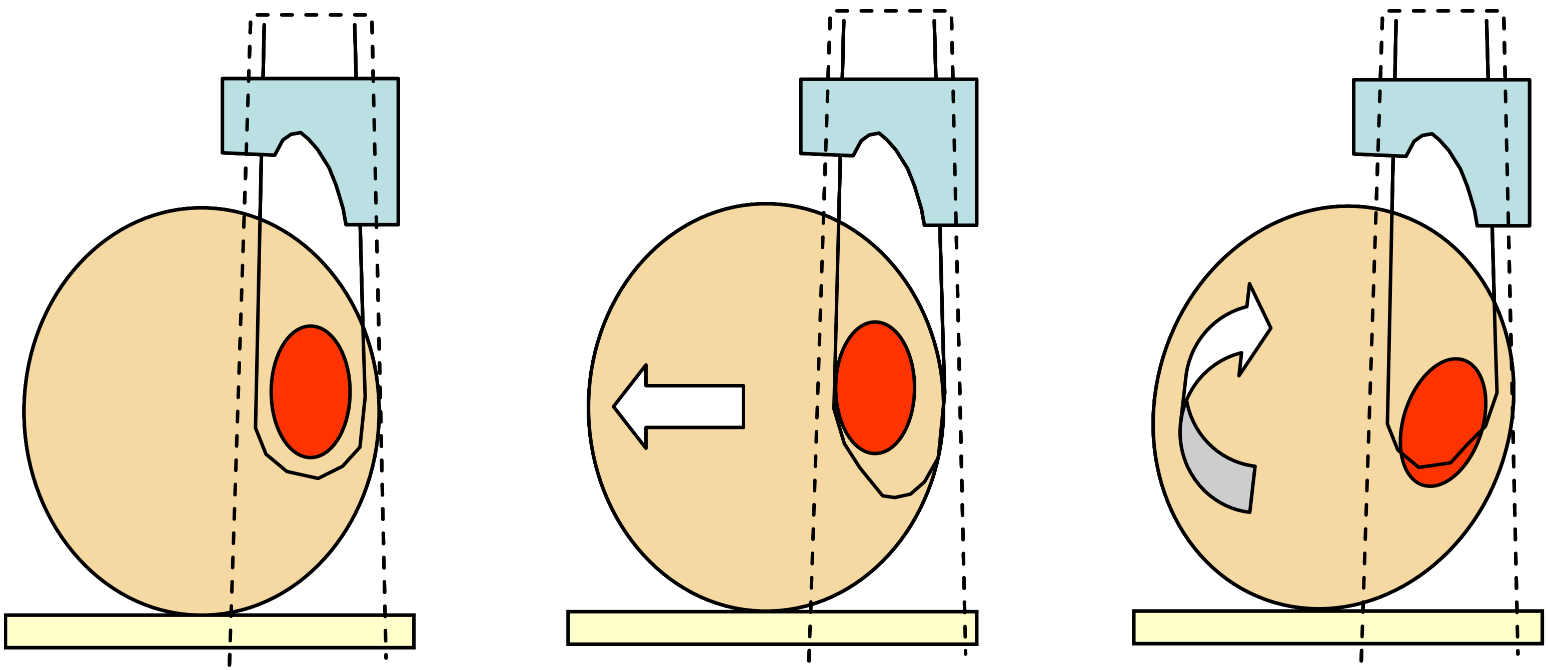
Newhauser et al. PMB 53 (2008) 2327-2344

Range degradation in patients

- patient alignment and setup in the treatment beam
- relative motion of internal structures with respect to the target volume
- misalignment of the apertures and compensator (if present) with the target volume and critical organs



Misalignment of the compensator with target volume



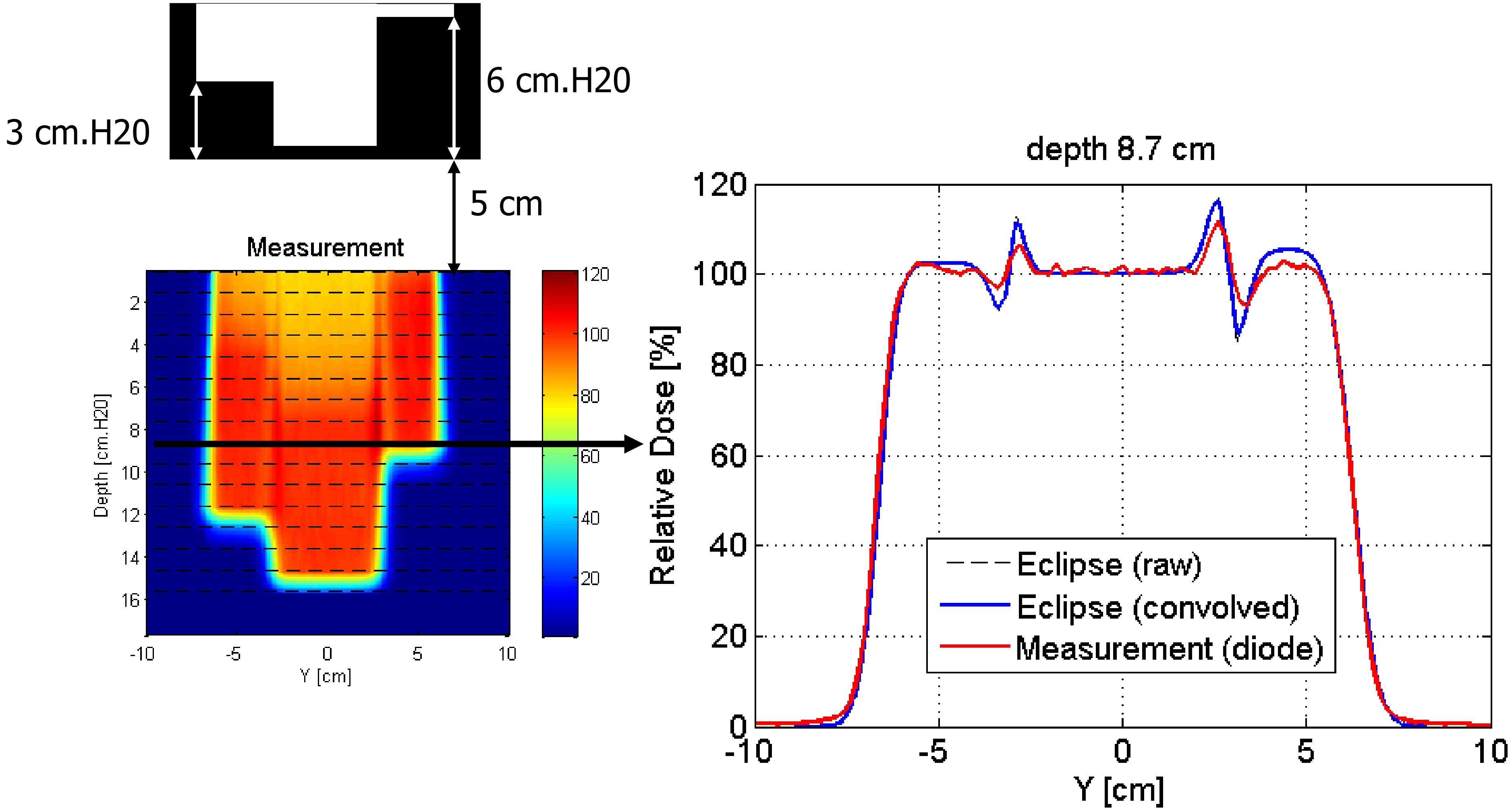
Correct alignment of the compensator and target volume

Patient is shifted left

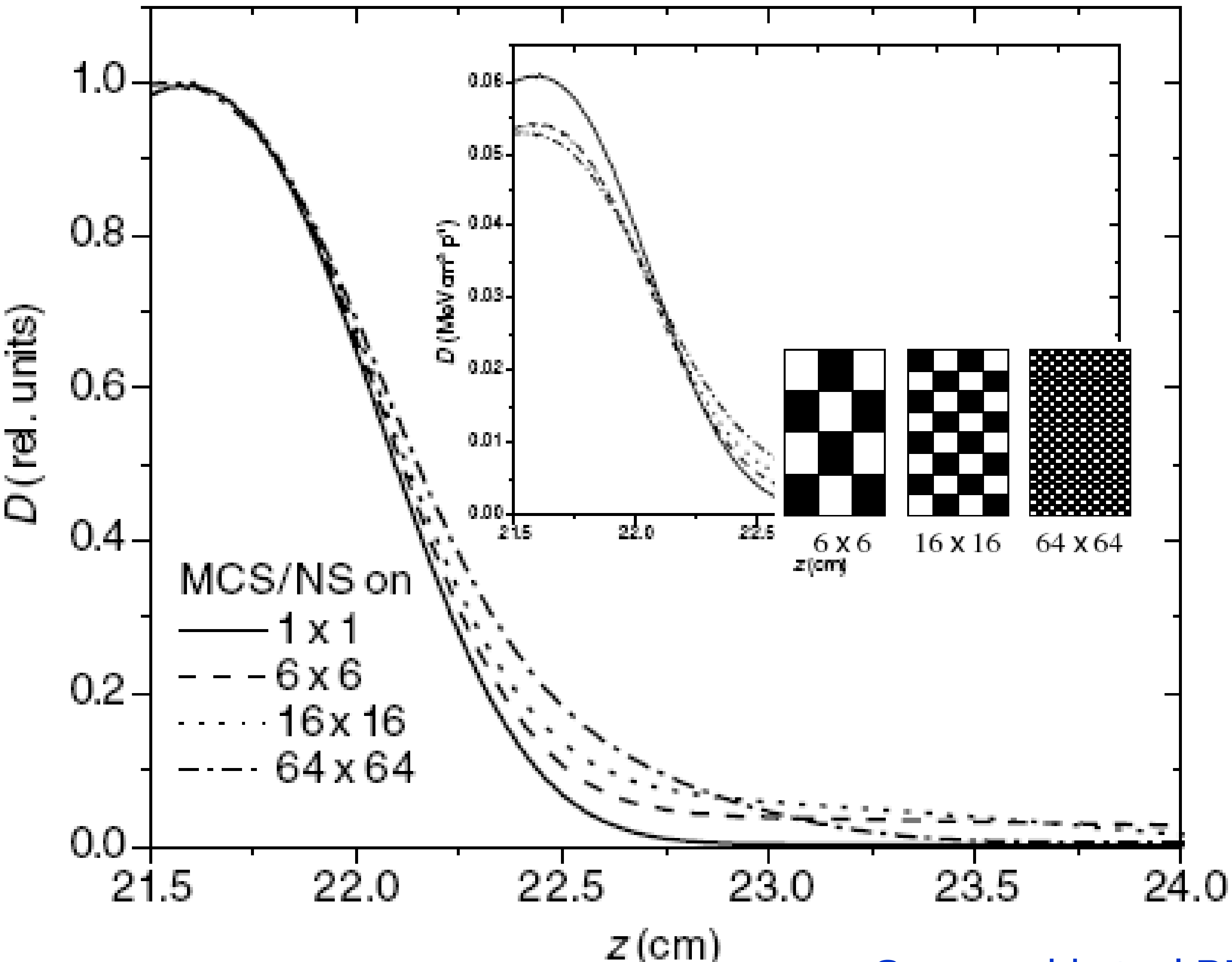
Patient is rotated clockwise

ICRU Report 78

Edge-scattering effect in proton beam is not as significant as in electron beam

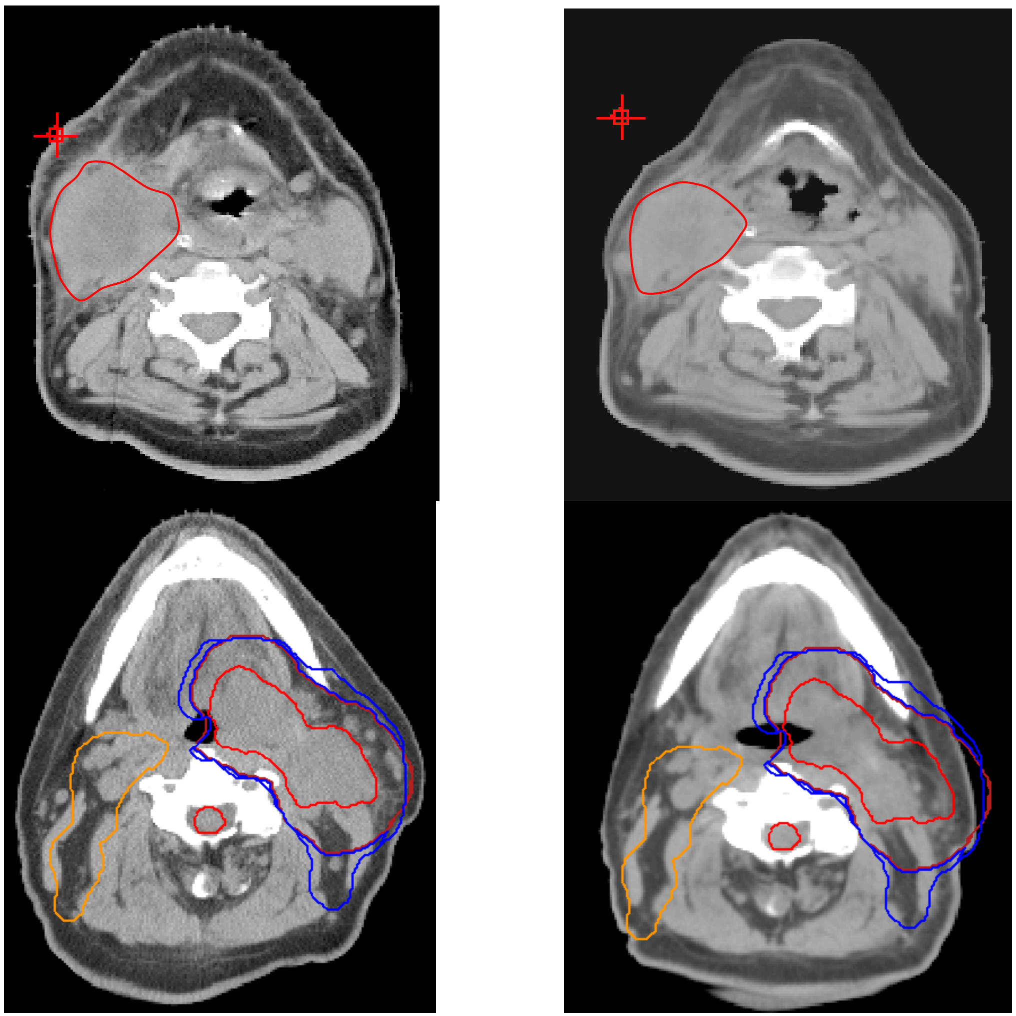


Impact of complexly structured heterogeneities in proton beam



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

Anatomic Variations During Course of Radiotherapy



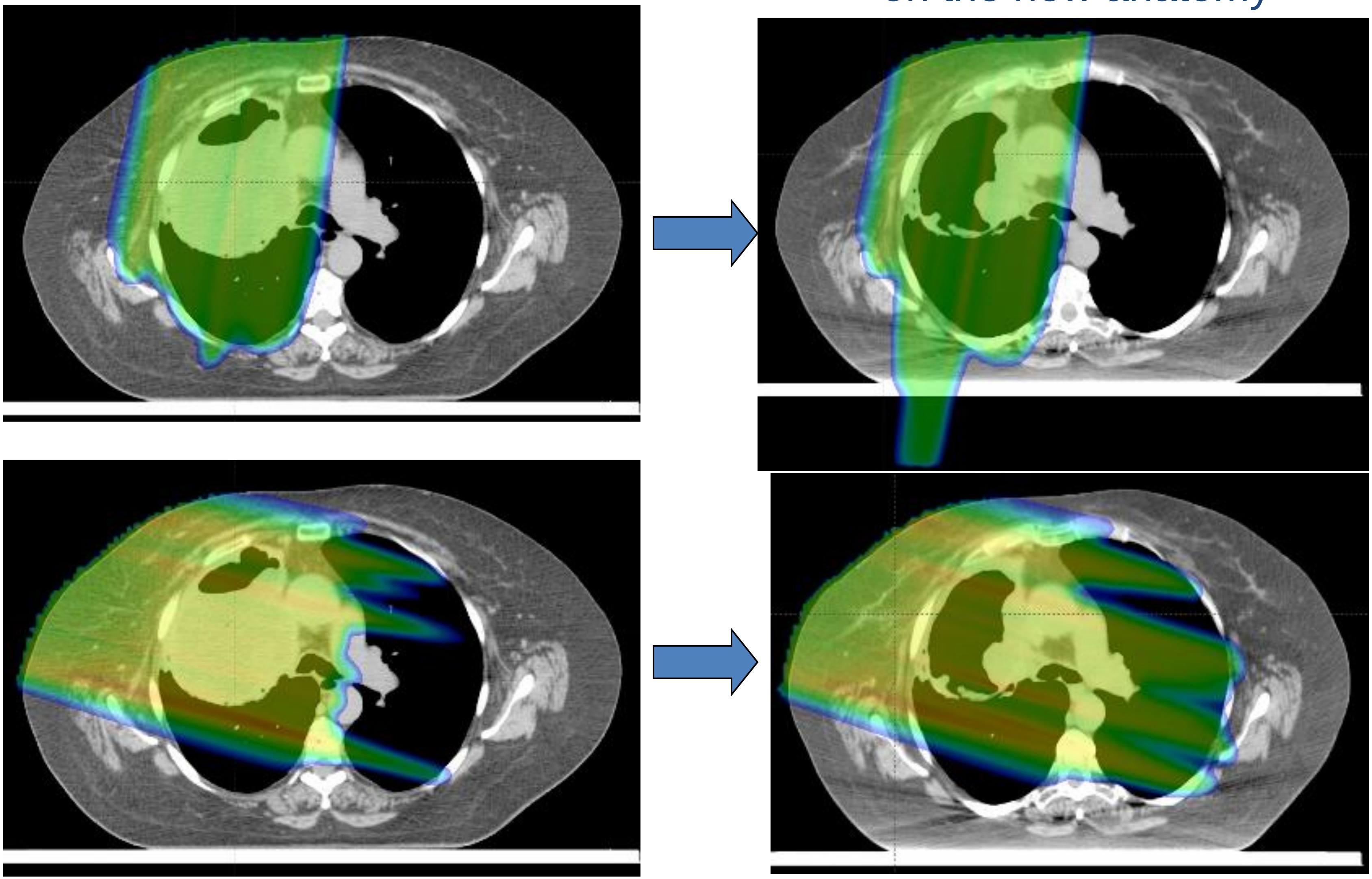
Planning CT | Three Weeks into RT

Barker et al. *Int J Radiat Oncol Biol Phys* 2004;59:960-970.

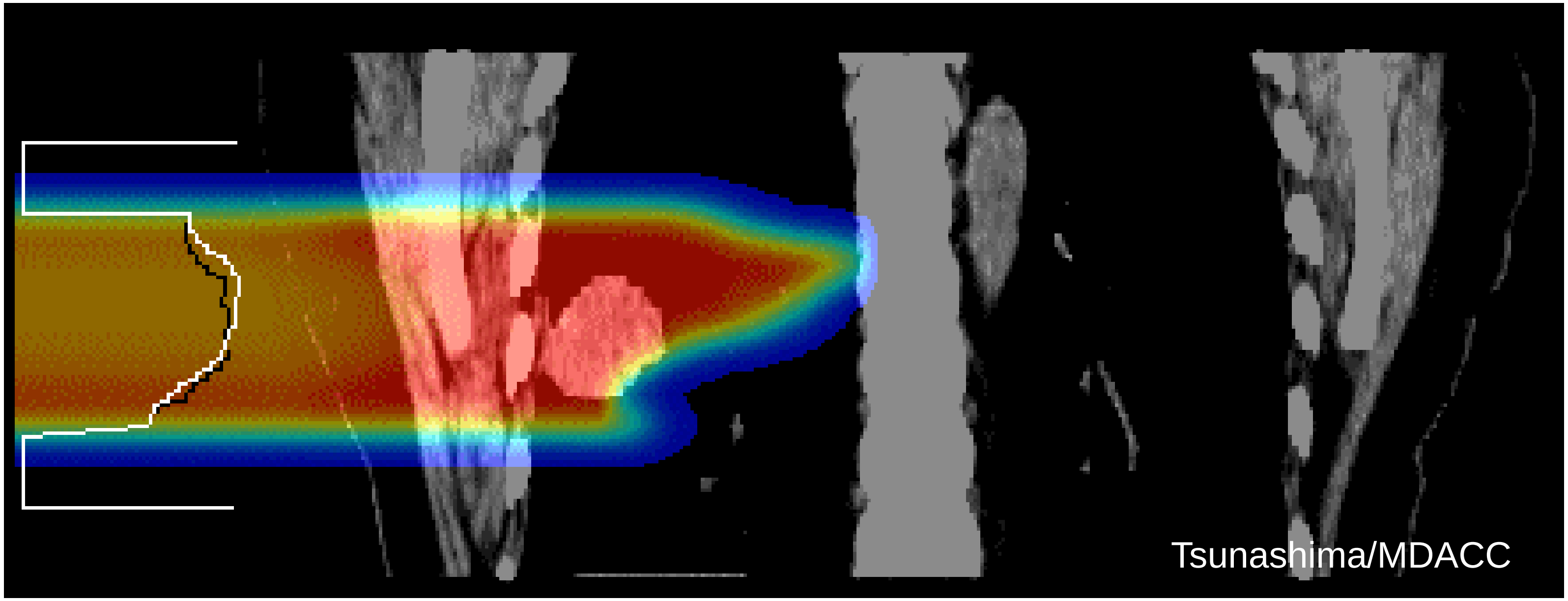
Impact of Tumor Shrinkage on Proton Dose Distribution

Original Proton Plan

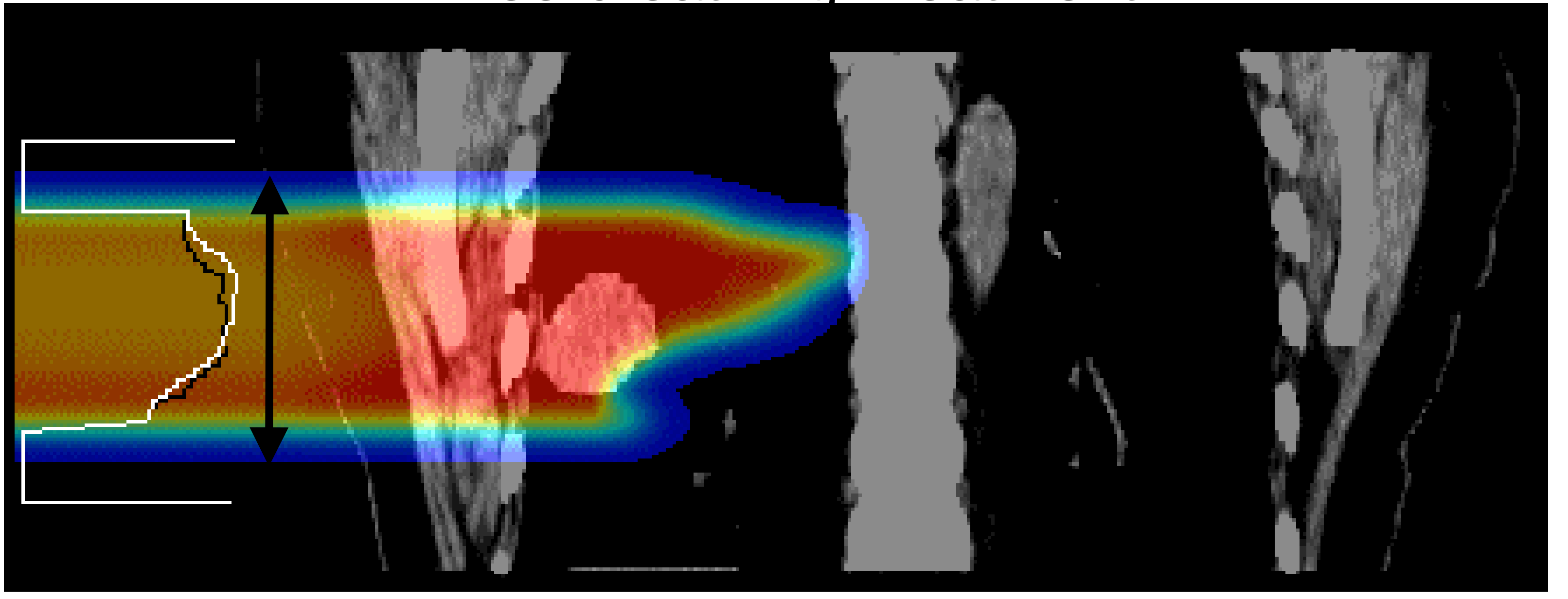
Dose recalculated on the new anatomy



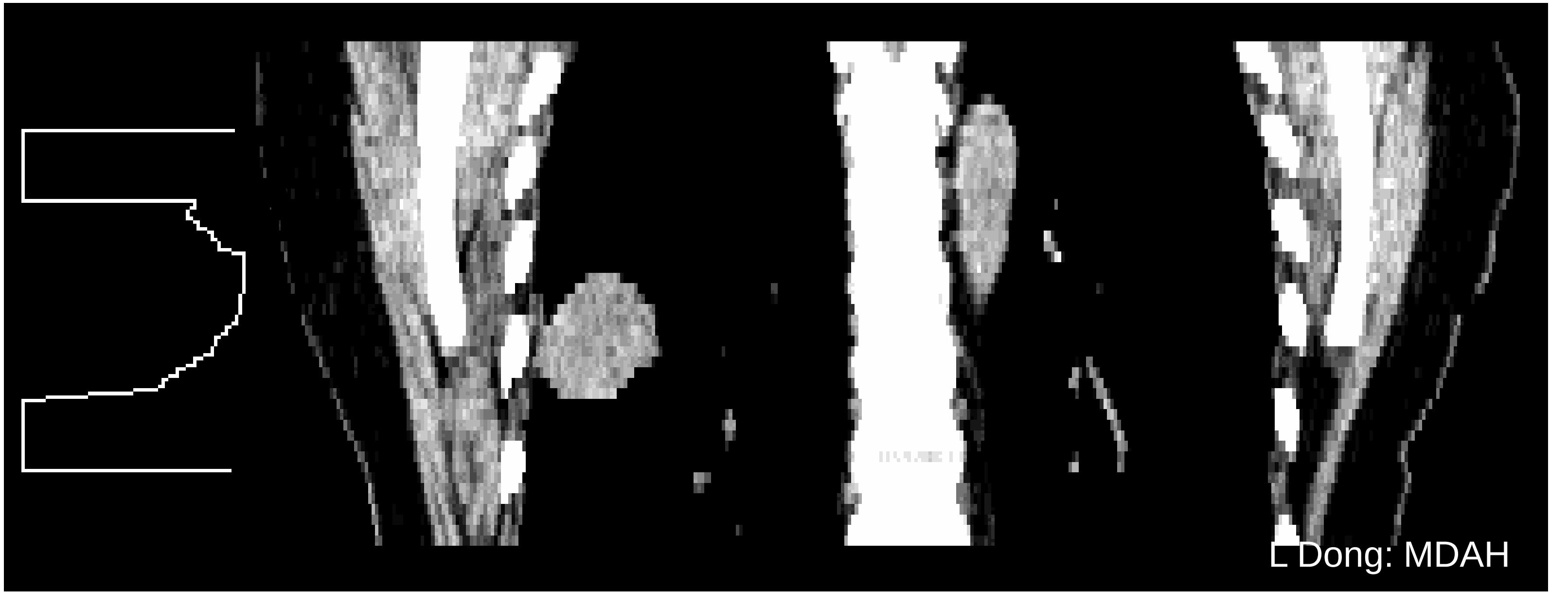
Impact of Organ Motion on Proton Dose Distributions



Free breathing Treatment



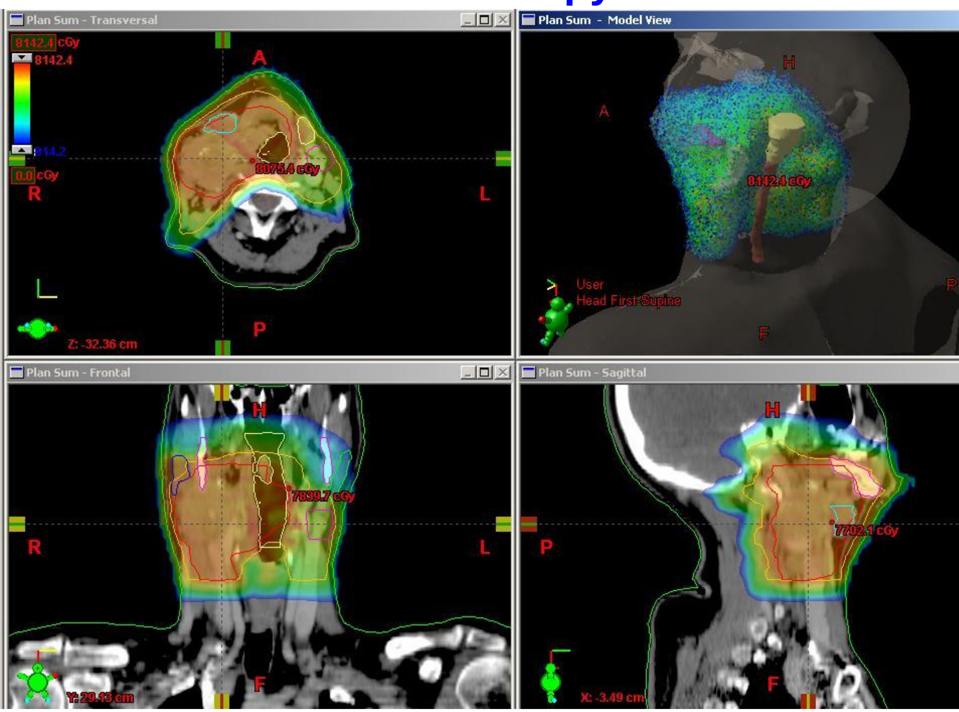
Gated treated on exhale

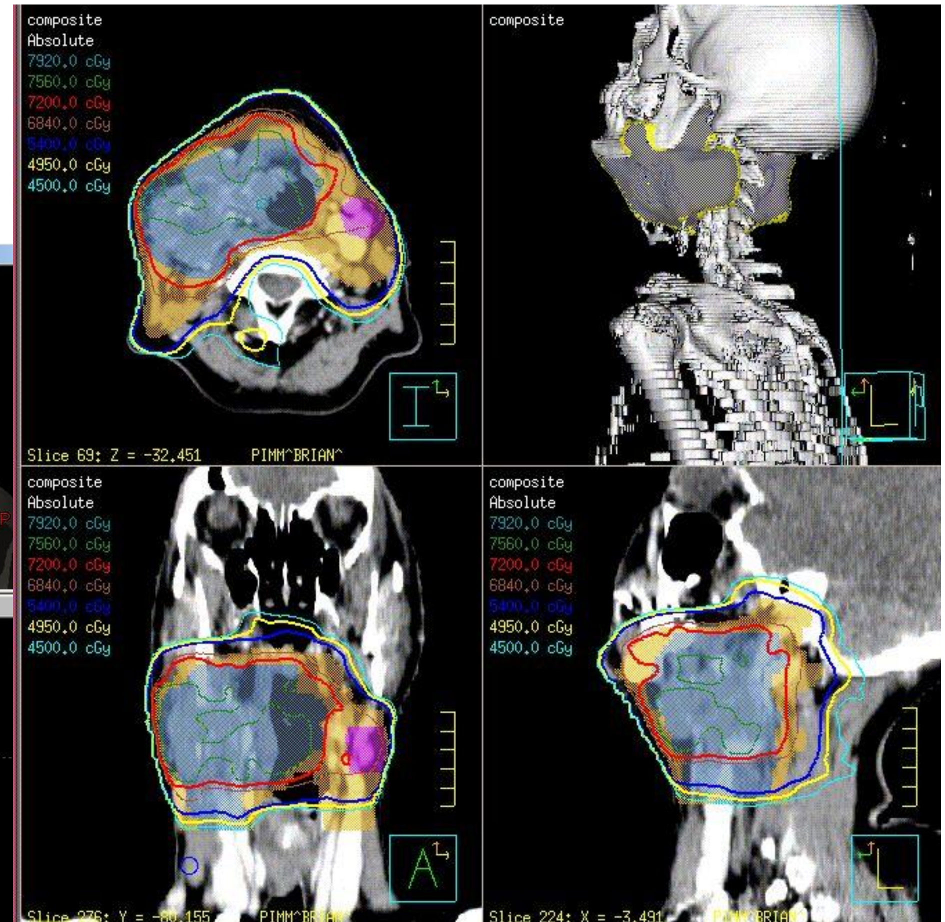


Comparing Proton Therapy with IMRT

It is incontrovertible that dose distributions of protons can be theoretically superior to those of high energy photons

Protons Therapy



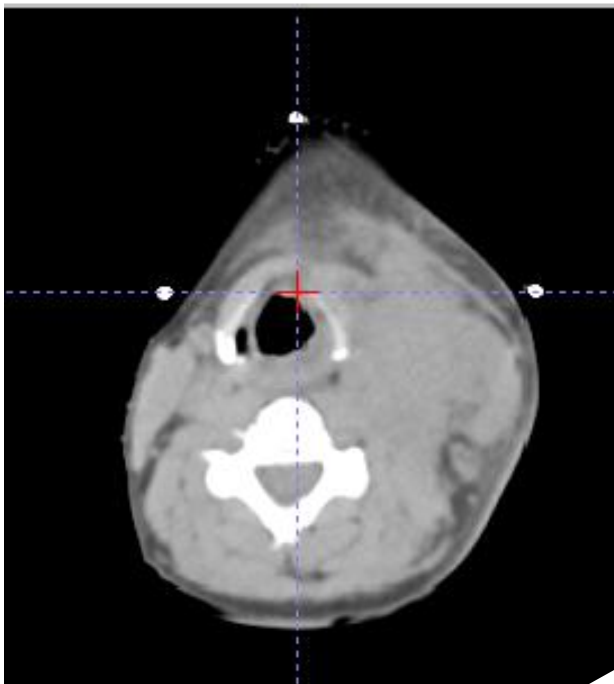


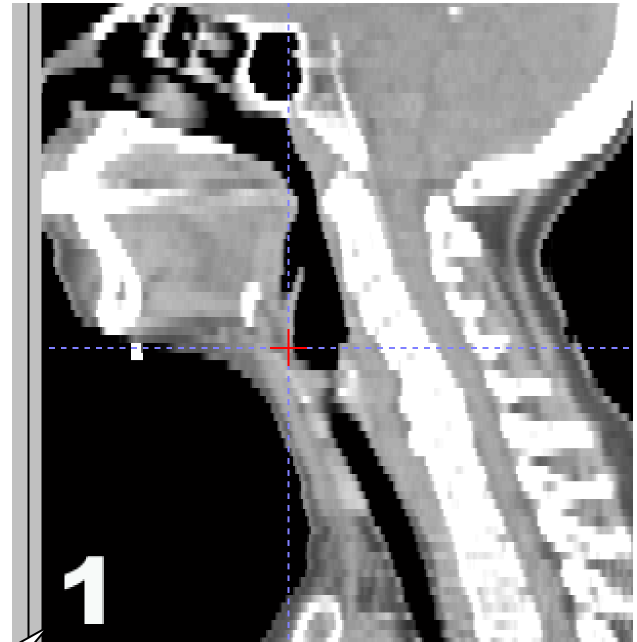
Ca Oropharynx

Photon IMRT

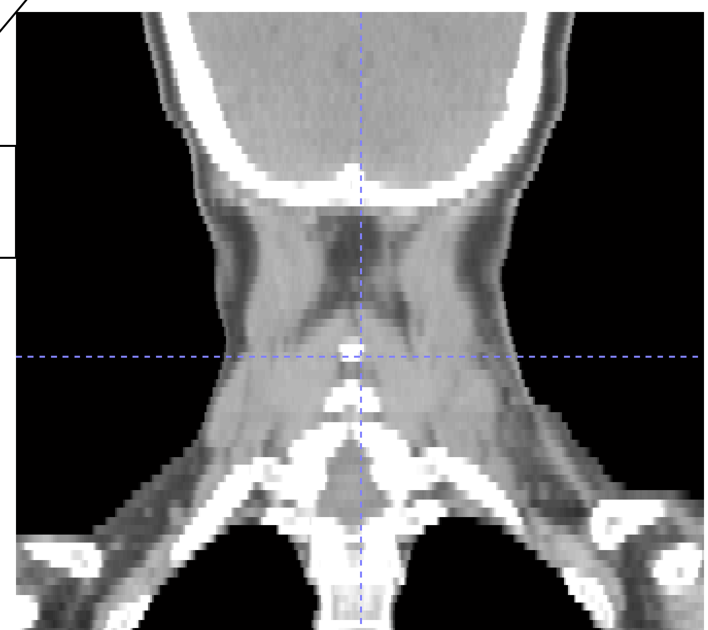
Yeung UFPTI

Inter-Fraction Motion in H &N





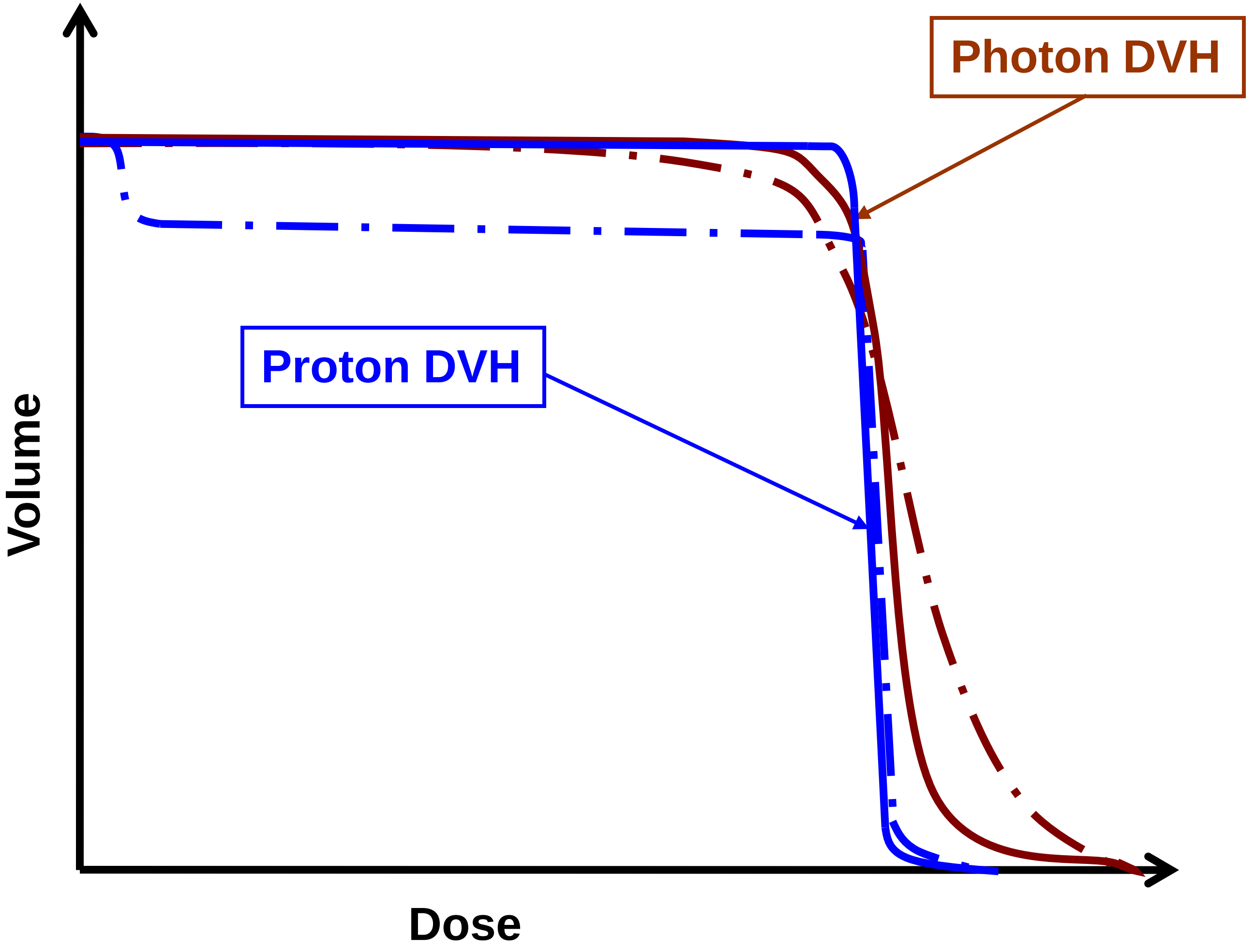
Elapsed Treatment Days



- Setup uncertainty
- Anatomic volume changes
  - Tumor shrinks
  - Parotid glands shrink

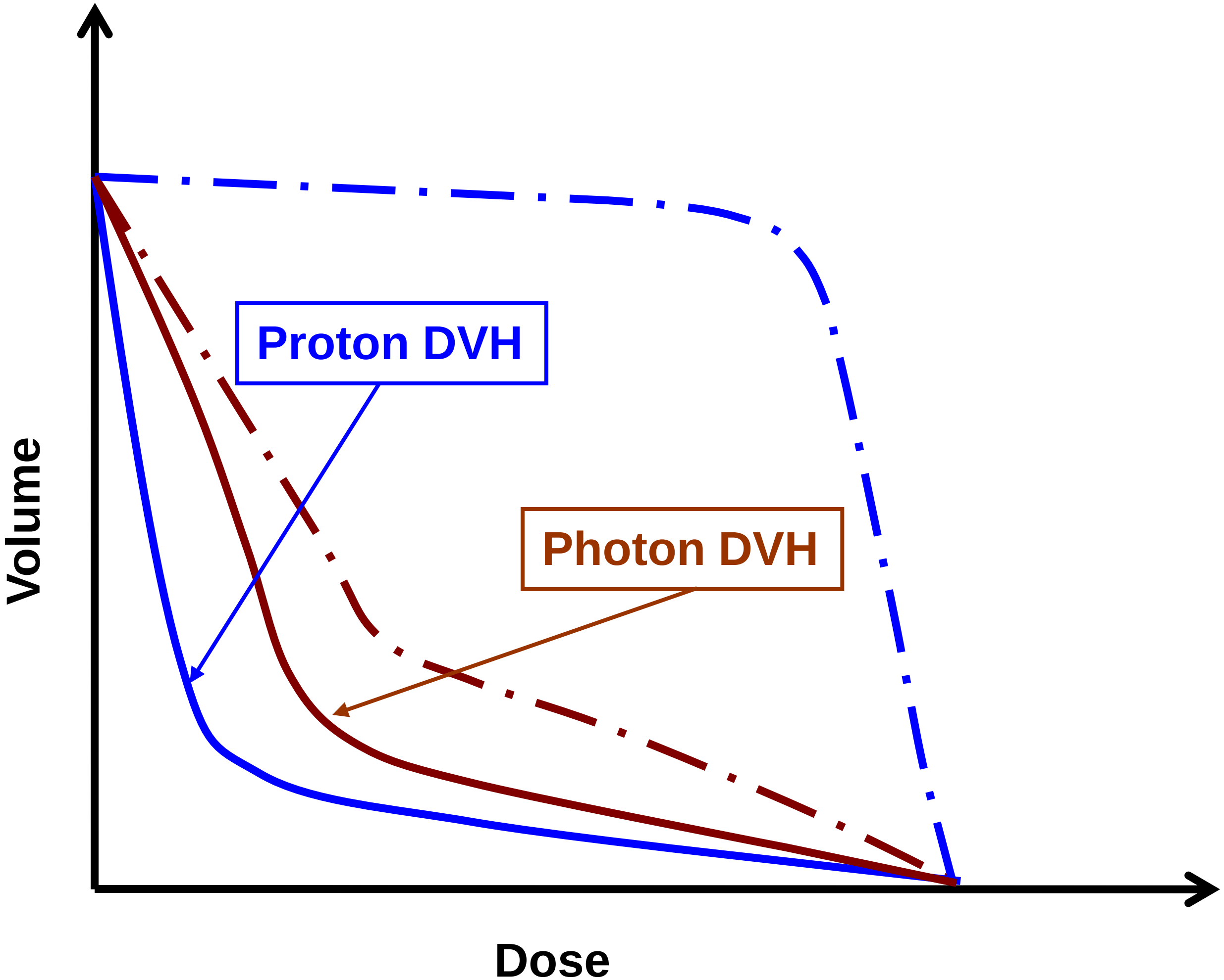
Plan DVH Evaluation (PTV)

What you see is not what you always get….

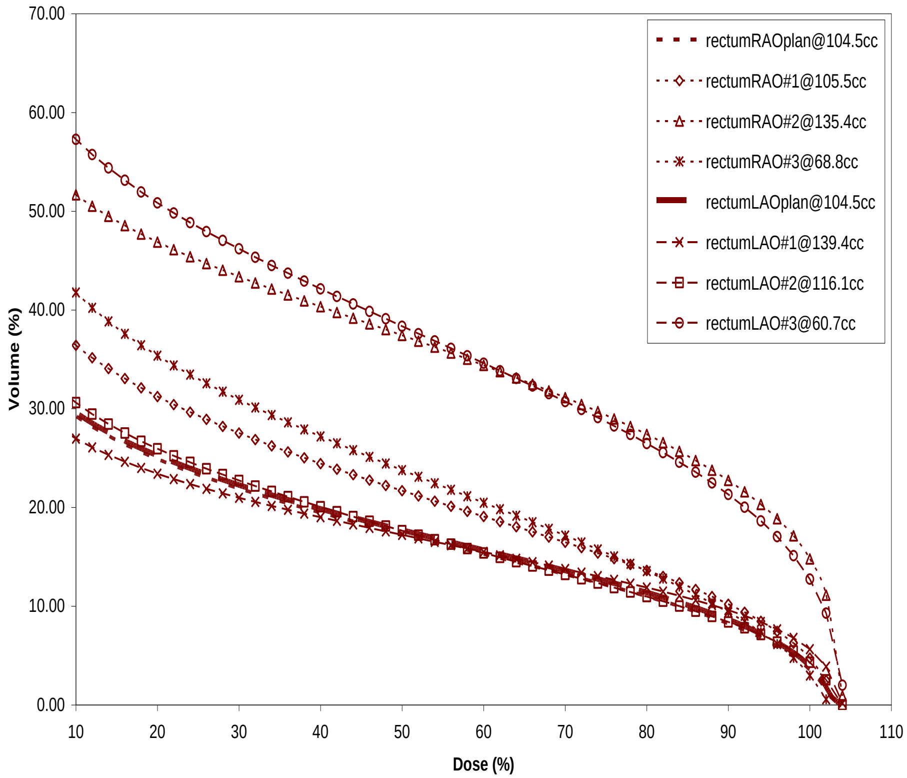


Plan DVH Evaluation (PRV)

What you see is not what you always get..



Rectal DVH from multiple post treatment PET/CT



Uncertainties in Rectal V_{74} and V_{39}

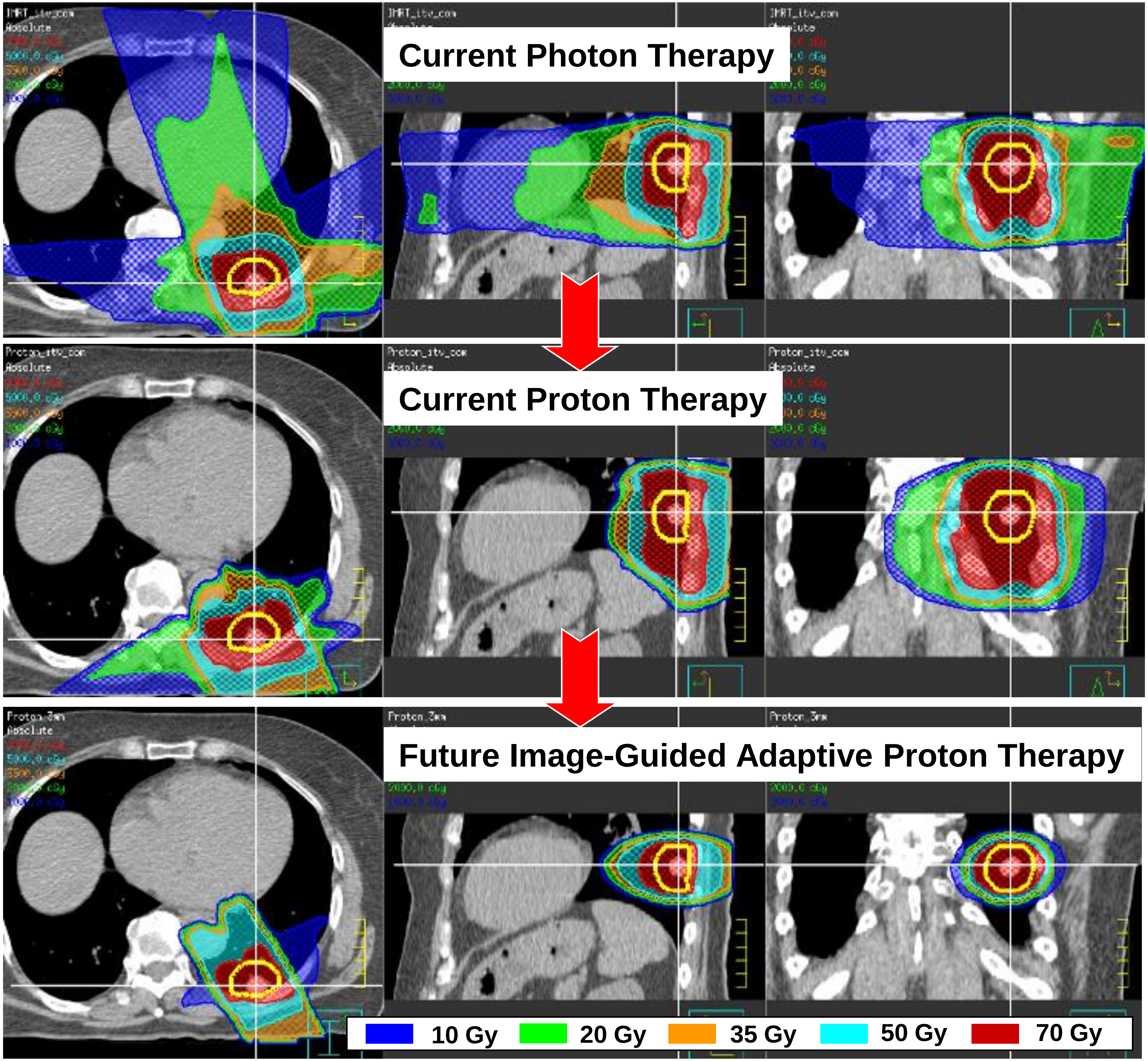
	Mean ± Dev.	Rel. Dev. ± Dev.
V_{74}	9.6%±7.2%	**73.9%±20.5%**
V_{39}	25.2%±11.4%	**42.1%±15.3%**

Yin: UFPTI

Improving Proton Therapy

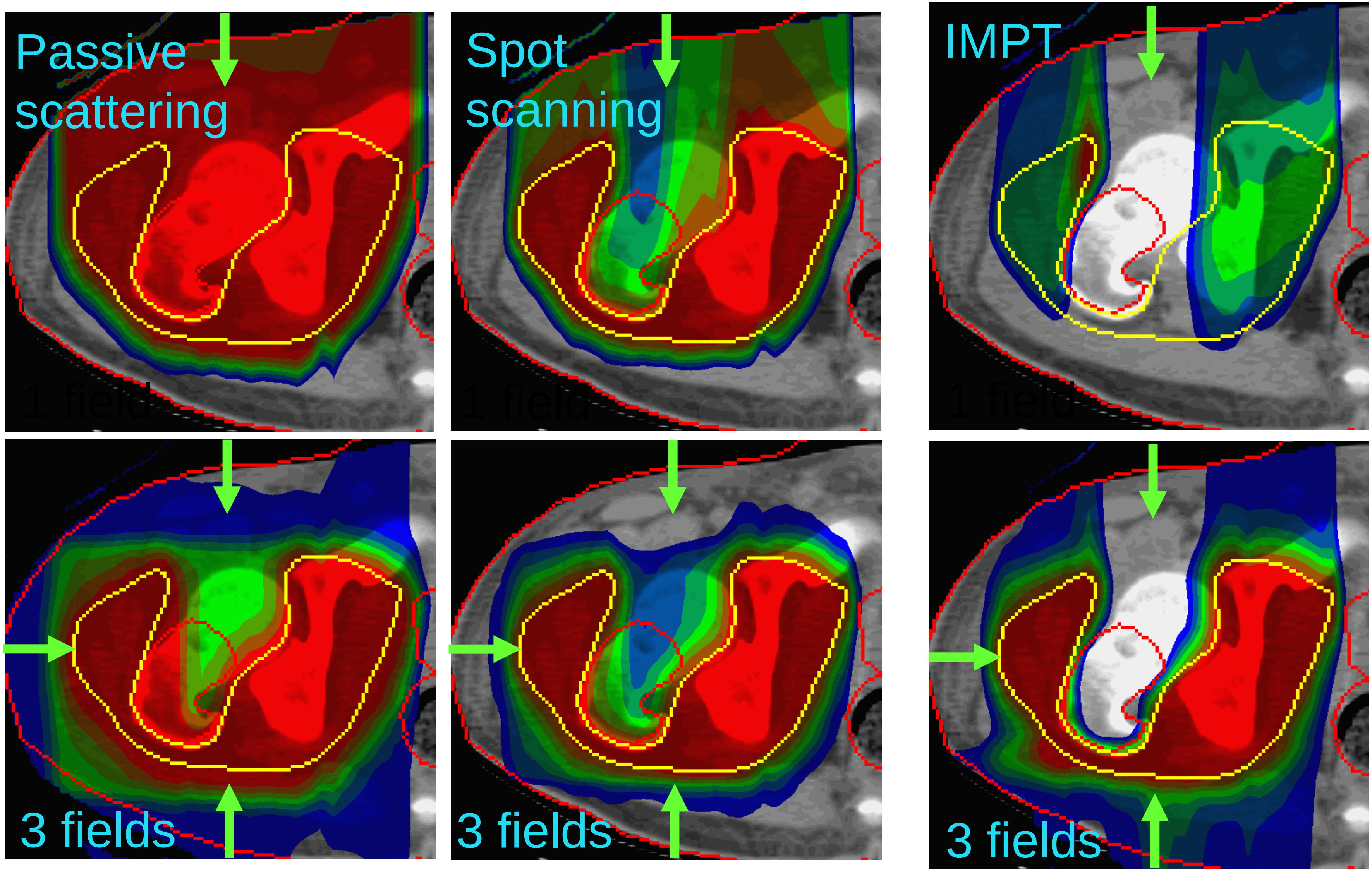
- Anatomy variations
  - IGRT/adaptive radiotherapy
  - Robust optimization
- Intra-fractional motion
  - Gating, coaching, tracking…
- Accurate stopping power ratios (CT number conversion)
- Scanning pencil beams (IMPT)

Research Driven Patient Care



L Dong: ASTRO 2010

Intensity Modulated Proton Therapy (IMPT)



Lomax/PSI

Summary

- **Uncertainties in predicting the proton beam range in patients are in the order of ~3-5%**
  - (Advanced dose calculation methods might reduce this to ~2.5%)
  - Uncertainties can be minimized in (robust) IMPT optimization
- **Proton beams are more sensitive to**
  - CT Hounsfield number/Stopping Power accuracy
  - Organ motion
  - Anatomy changes
- **Proton plans are difficult to evalua**te
  - “What you see is not what is delivered”

Summary

- **Reduction in radiation "dose bath," (by up to ~60% vs. photons) expected to be the principal basis for clinical advantage for protons**
  - IMRT is more conformal in the high dose region immediately around the target than 3D conformal protons
  - IMPT may deliver comparable dose distribution but more research is necessary to ensure optimization and delivery of IMPT
- **Inter/Intra-fractional variations have far more significant consequences in patients treated with proton therapy**
  - Approaches and data to deal with this issue is still lacking
    - Minimize it and develop strategies to deal with the residual motion

Source of Uncertainty	Uncertainty Before Mitigation	Mitigation Strategy	Uncertainty After Mitigation
*Inherent range uncertainty (pristine Bragg peak)	± 1-3 mm	None	± 1-3 mm
*Inherent range uncertainty (spread out Bragg peak)	±.6-1.0mm	None	±.6-1.0mm
Range reproducibility	±1.0mm	Rigorous QA	±.5mm
Compensator	±1.0mm	Rigorous QA of compensator material	±.5mm
Accessories (table top, immobilization jig, etc.)	±1.0mm	Rigorous QA of all accessories	±.5mm

Source of Uncertainty	Uncertainty Before Mitigation	Mitigation Strategy	Uncertainty After Mitigation
CT	± 3.5% of range	Site specific imaging protocols	± 1-2.0% of range
Patient setup	± 1.5mm	Rigorous patient selection criteria	± 1.0mm
Intrafractional patient motion	Variable	Rigorous patient selection criteria	± 1.0mm
Compensator position relative to patient	Variable	Rigorous patient selection criteria	± 1.0mm
Range uncertainty (straggling) due to complex heterogeneities	± 1mm	Rigorous patient selection criteria	±.5mm

Source of Uncertainty	Uncertainty Before Mitigation	Mitigation Strategy	Uncertainty After Mitigation
CT artifacts	Variable	Rigorous patient selection criteria	± 1.0mm
Range computation in water in a TPS	Variable	Rigorous patient selection criteria and image edits	± .5mm
Range computation in tissue of known composition and density in a TPS	± .5mm	None	± .5mm

Source of Uncertainty	Uncertainty Before Mitigation	Mitigation Strategy	Uncertainty After Mitigation
Multi-modality image registration	± 1mm	Better dose computation algorithms	± .5mm
Treatment delivery (target coverage uncertainty)	±1-3mm	Site specific image registration protocols	±1-2mm
Treatment delivery (dosimetric uncertainty)	±1-3mm	Rigorous site specific delivery technique selection	± 1mm
Treatment delivery (dosimetric uncertainty)	± 1-3.0%	Rigorous QA	± 1.0%