Proton Treatment Planning

Stefan Both, PhD

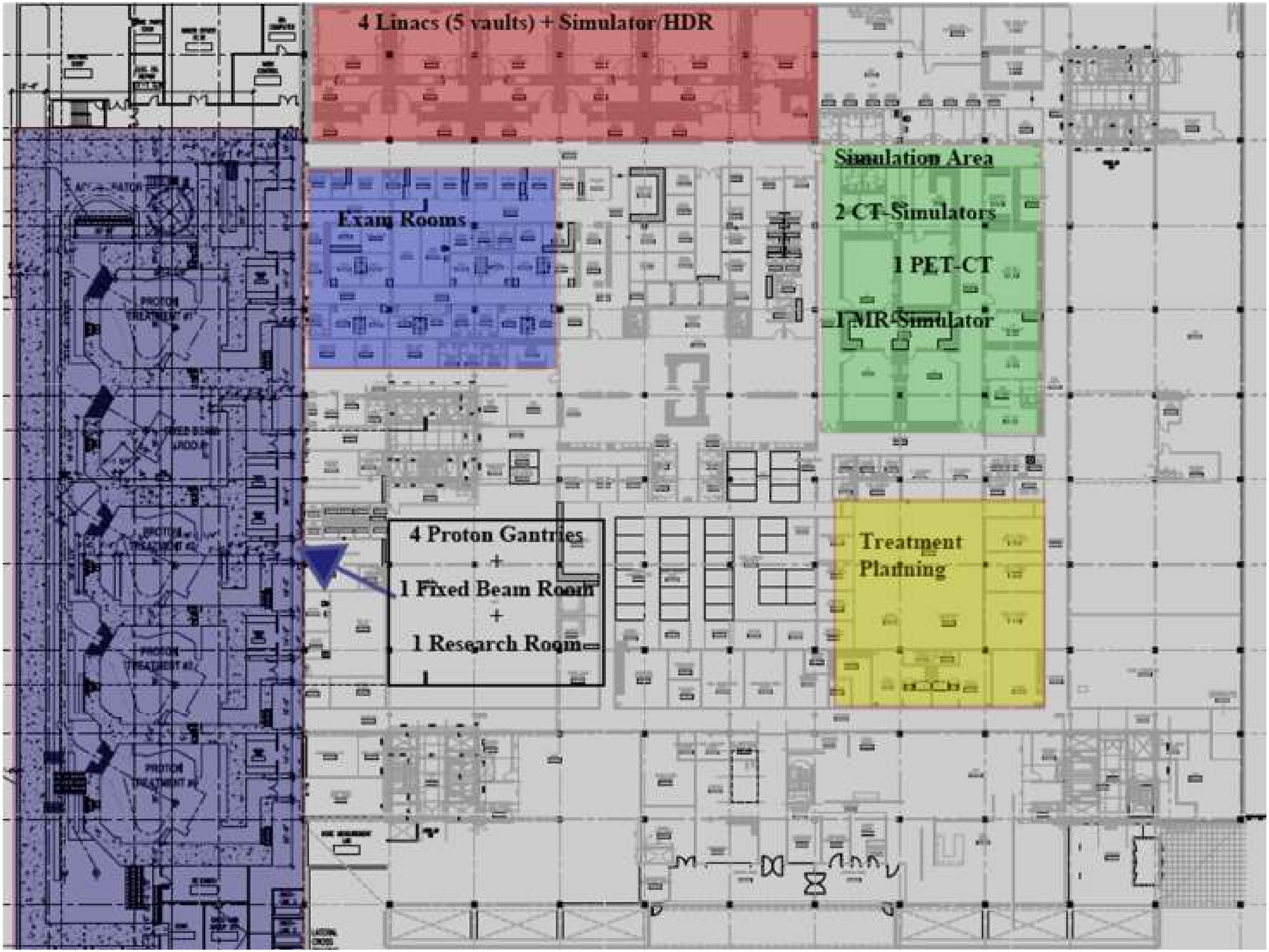
November, 9th, 2012

AAPM GLCM, Flint, MI

Penn Radiation Oncology
Penn Medicine

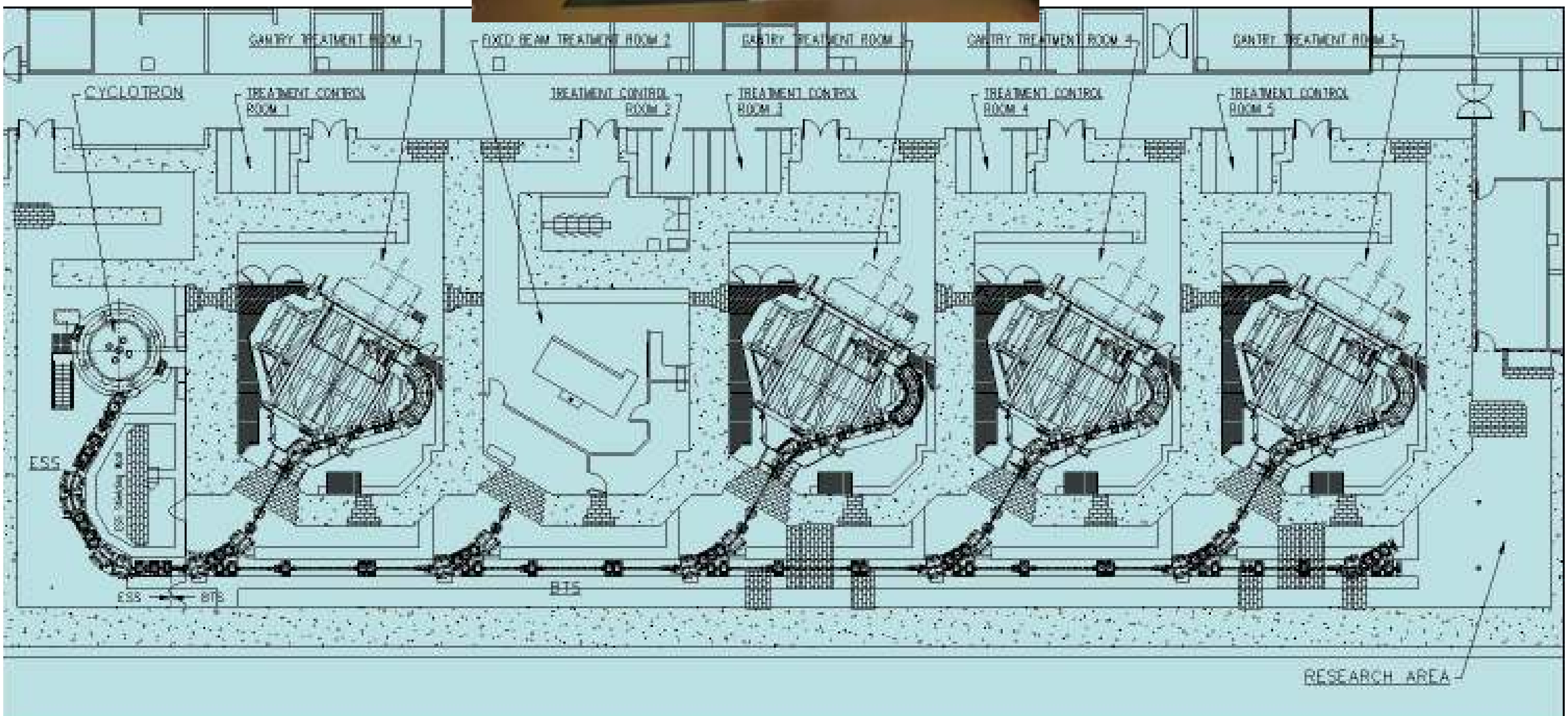
Outline

- Proton Therapy @ UPenn
- Principles of Proton Therapy and Treatment Planning
- PBS Clinical Implementation: Penn Solutions &future work
- Summary



4 Linacs (5 vaults) + Simulator/HDR
Simulation Area
2 CT-Simulators
1 PET-CT
1 MR-Simulator
Exam Rooms
4 Proton Gantries
+
1 Fixed Beam Room
+
1 Research Room
Treatment Planning

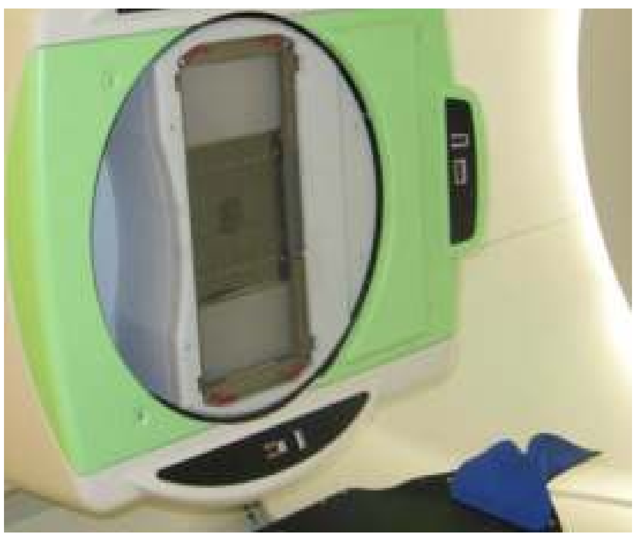

IBA


GANTRY TREATMENT ROOM 1
FIXED BEAM TREATMENT ROOM 2
GANTRY TREATMENT ROOM 3
GANTRY TREATMENT ROOM 4
GANTRY TREATMENT ROOM 5
CYCLOTRON
TREATMENT CONTROL ROOM 1
TREATMENT CONTROL ROOM 2
TREATMENT CONTROL ROOM 3
TREATMENT CONTROL ROOM 4
TREATMENT CONTROL ROOM 5
ESS
ESS
BTS
BTS
RESEARCH AREA

Description of the Roberts Proton Therapy Center

- 4 gantries + 1 fixed-beam room + 1 research room
- 2 gantries have universal nozzles with SS, DS, US, PBS & MLCs
- 2 gantries have universal nozzles with SS, DS, US & MLCs

- Fixed-Beam-Room has dedicated PBS nozzle
- All patients are setup with orthogonal x-ray (G=270 degrees)
- All gantries have MLCs with two compensator mounts

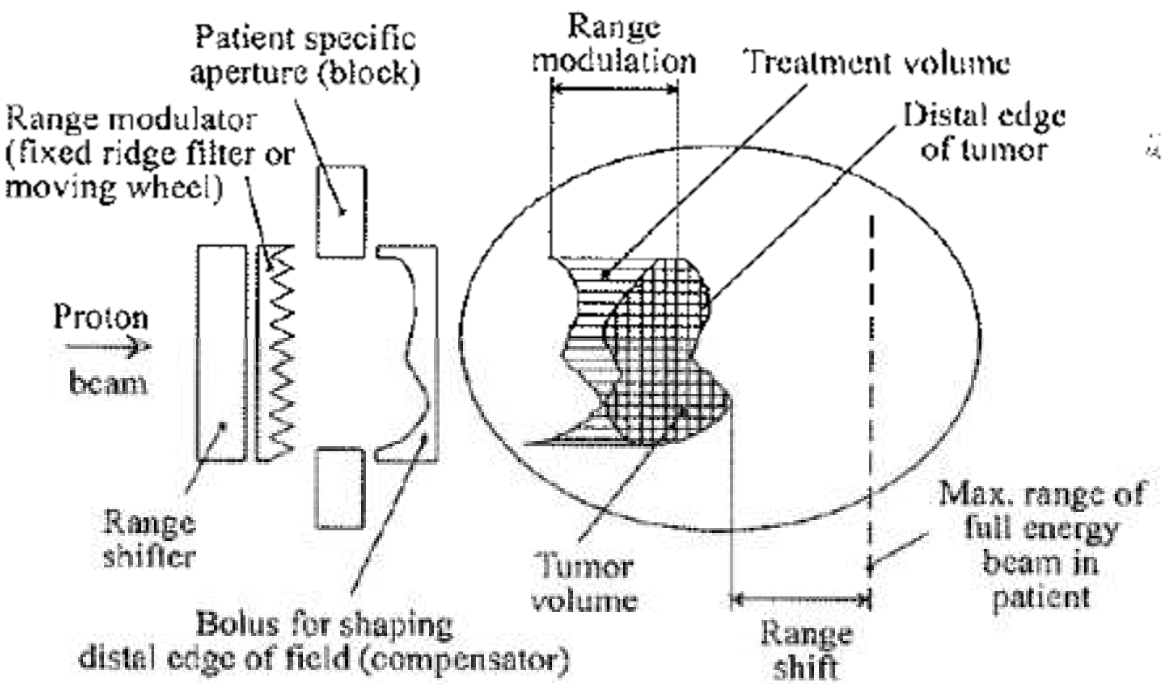


PENN RADIATION ONCOLOGY
Penn Medicine

Delivery Methods- Passive Scattering

- Accelerated protons are near monoenergetic and form a beam of small lateral dimension and angular divergence
- Single Bragg Peak spread out by range modulator
- Field Profile spread laterally by a set of spreaders compensated for the range
- Beam Shaping:

  -Block/MLC Laterally and Compensator in Range(Distally)

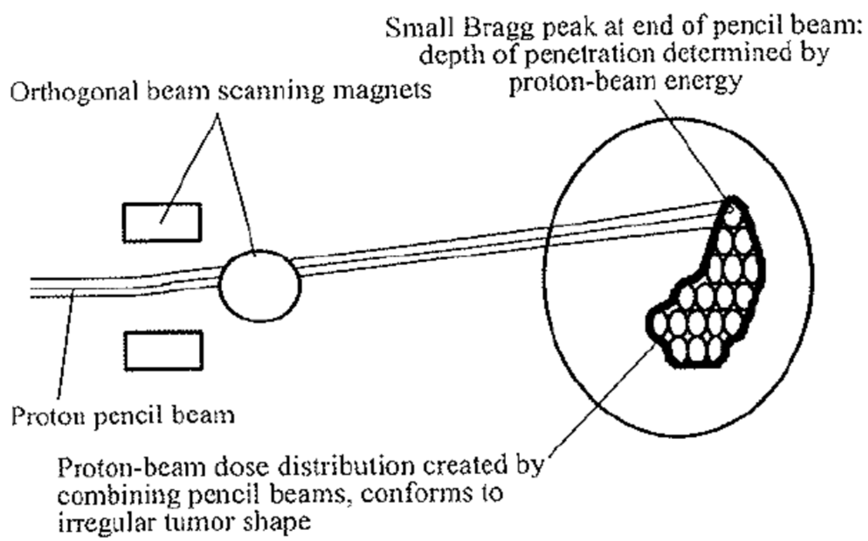


Delivery Methods: Pencil Beam Scanning

A PB is scanned both laterally and in depth (by changing its energy) => in a near arbitrary dose distribution laterally and dose sharpening in depth (Pedroni et al.)

- lateral distribution determined by the lateral positions and weights of each pencil beam of a chosen energy- Isolayers

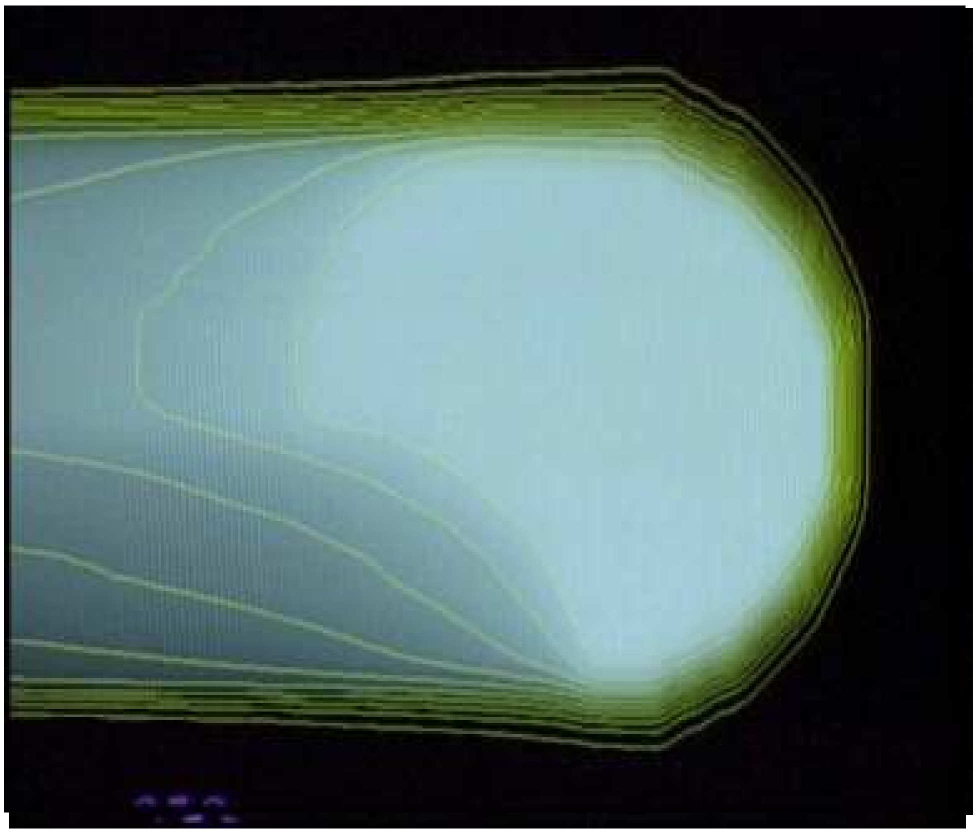
- distribution in depth is determined by weighting the pencil beam at each position within the field.



Pencil-Beam Scanning – PBS

Magnetically scan p beam left / right (X,Y) and control depth with Energy (Z)

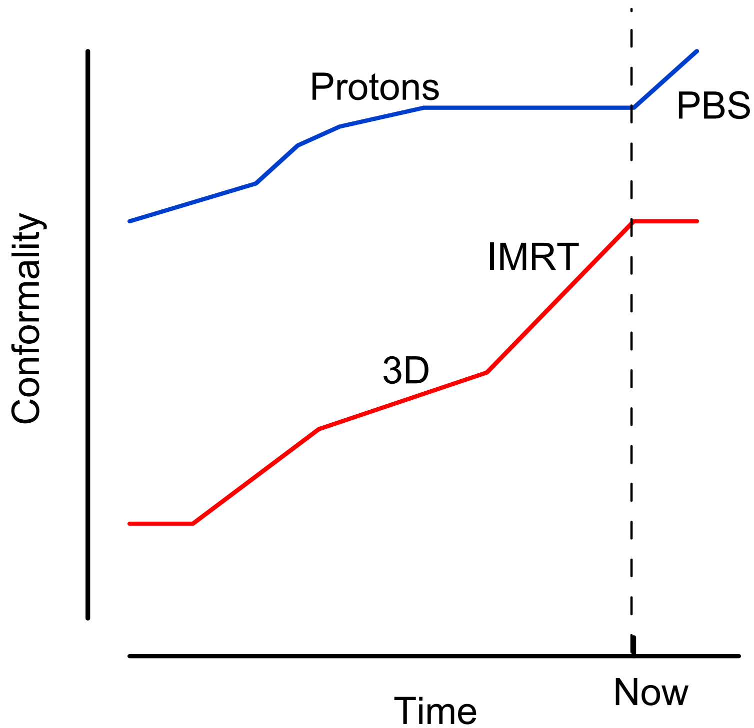
<u>Fully electronic and no mechanical parts!</u>

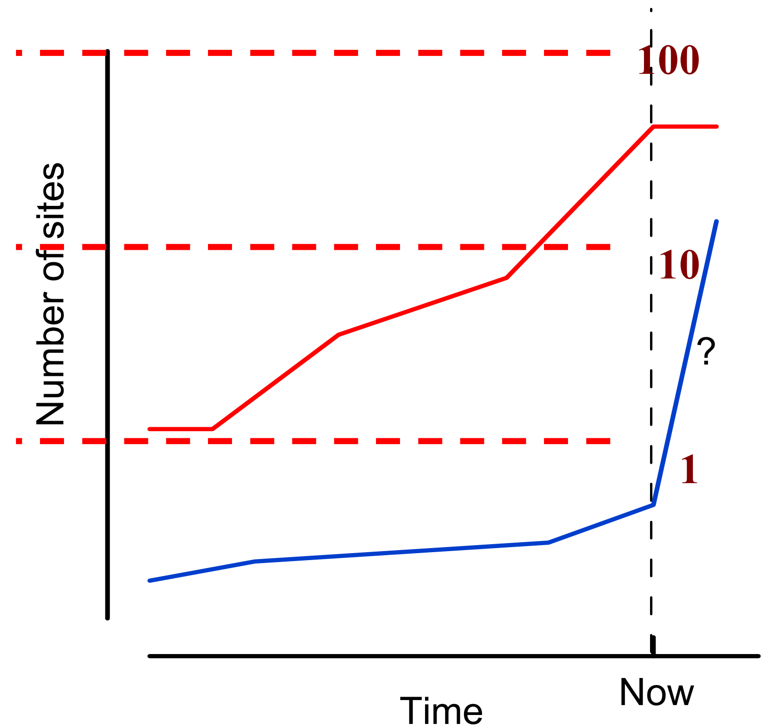


A full set, with a homogenous dose conformed distally <u>*and*</u> proximally

Images courtesy of Eros Pedroni, PSI

Relevance of pRT





- **PT and XRT treatment history is inversely symmetric**
  - Emphasis of XRT was to increase conformality – IMRT
  - Emphasis of PT must be on PBS and promulgate

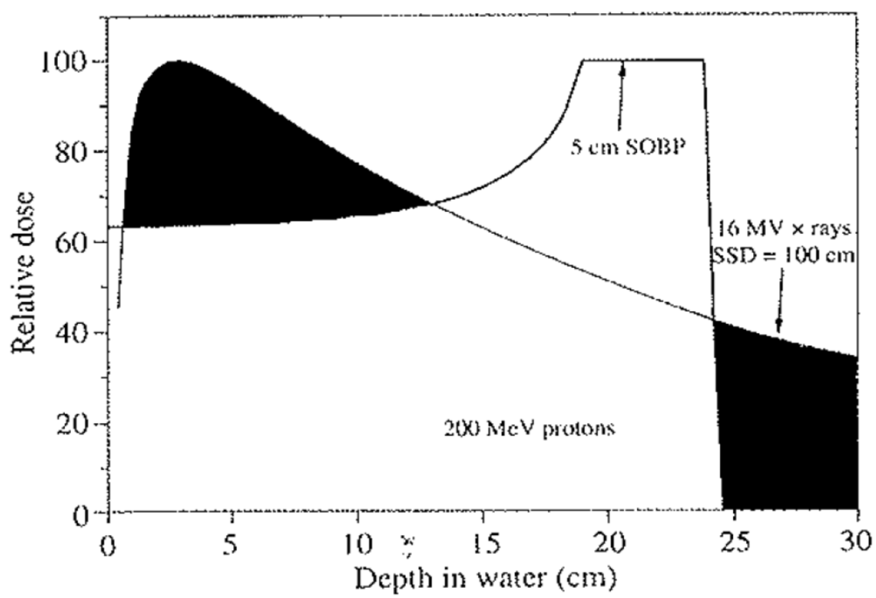
- **p always has "superior" dose distributions**
- **… but does not treat enough sites**
  - Not Quantitatively (< 1%)
  - Not Qualitatively (prostate)

Courtesy of Hanne Kooy

Principals of PROTON Therapy and Planning

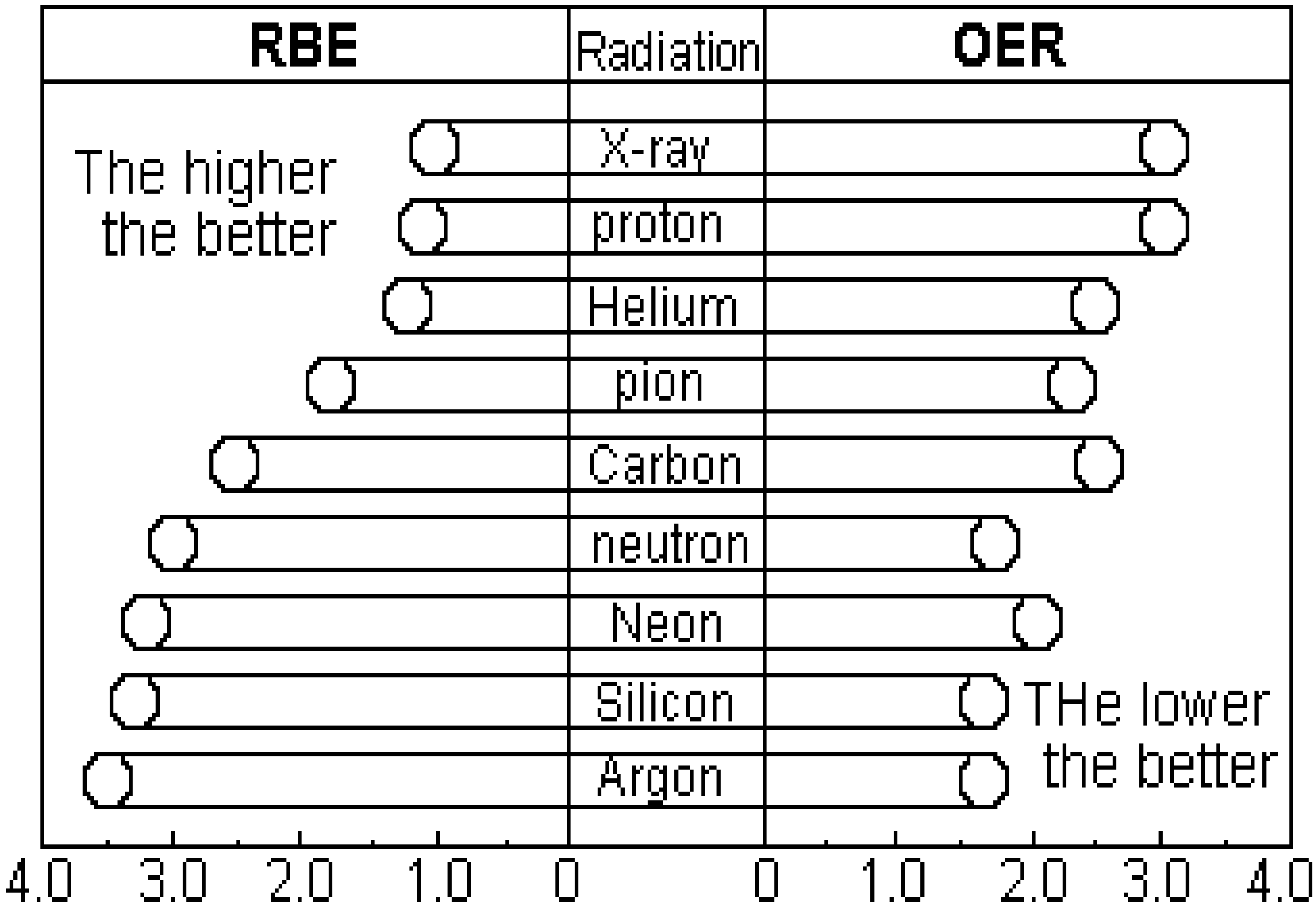
Contrast with photons (x-rays)

- Photons continue to deposit dose beyond target in tissue….



..while normal tissue radiation offers no advantages for the patient

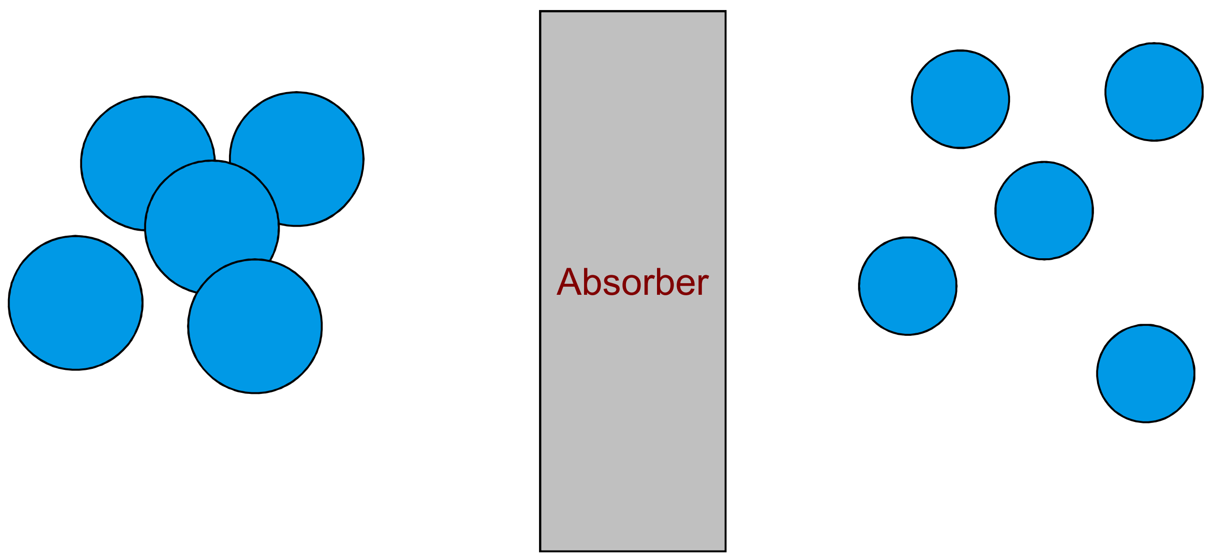
RBE and OER for Protons



Physics of p is understood…

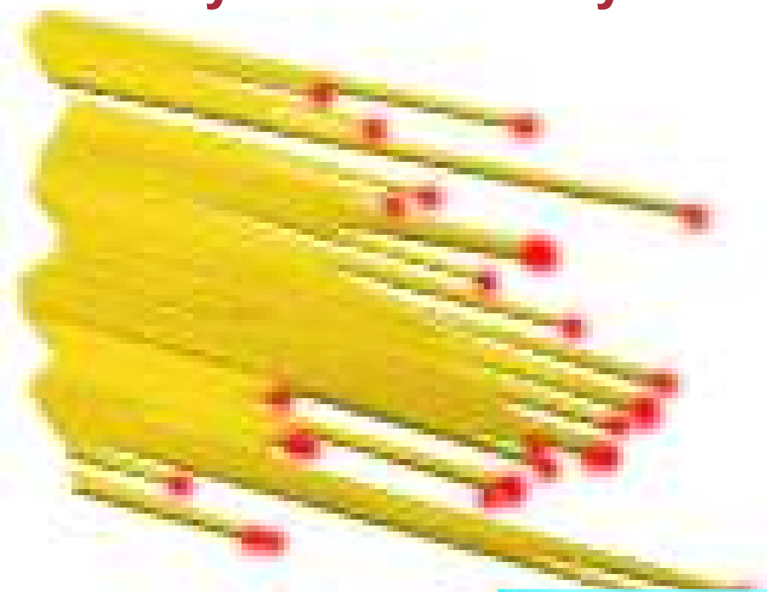
Proton beam could be shaped and manipulated completely by mechanical means- passive scattering, >50 yrs.

- **Passage through an absorber means**
  - Reduction in energy but NOT intensity (number)
  - Dispersion (scatter) of beam



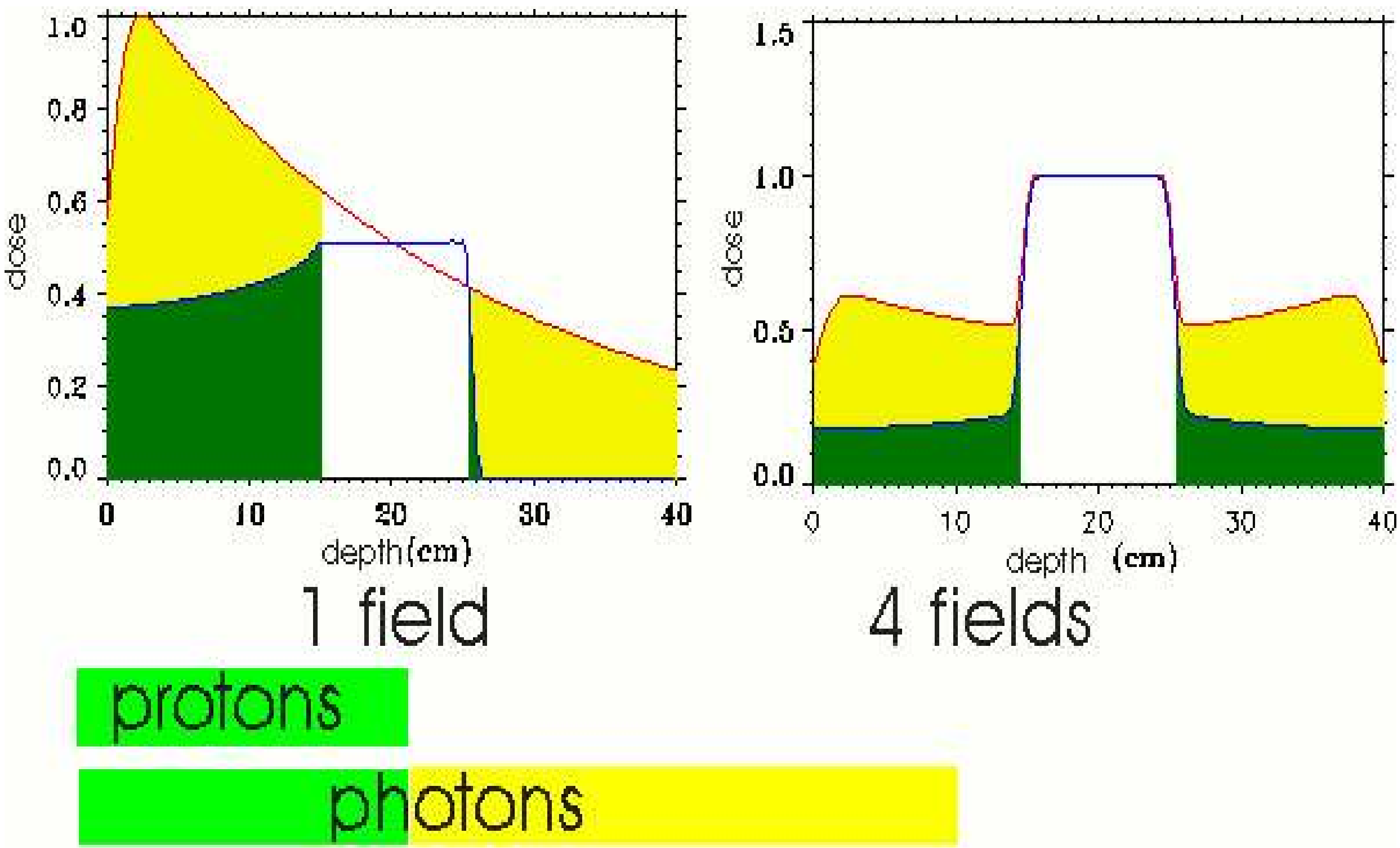
Tracks in Patient

Courtesy of Hanne Kooy



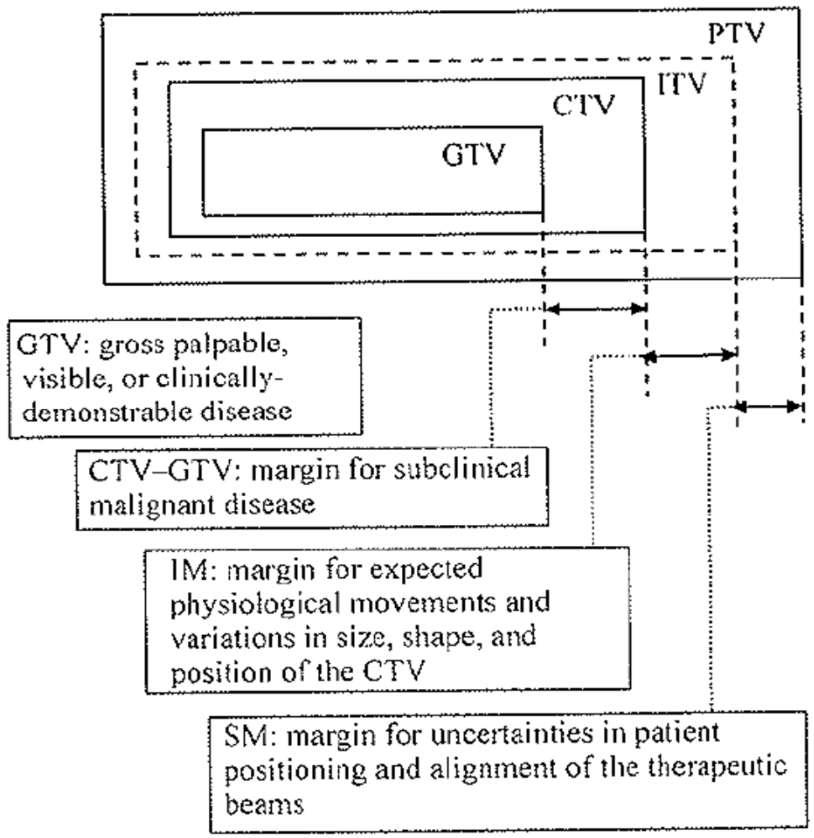
$m_p = 2{,}000\ m_e$

Normal Tissue Exposure to Radiation Dose



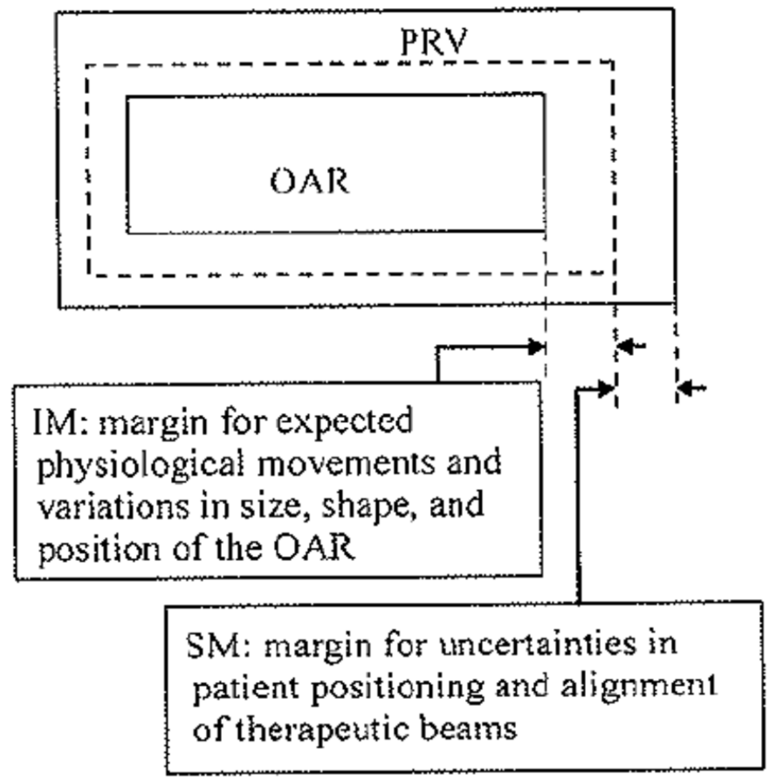
Planning of Proton Therapy

- **Illustration of the volume and margins relating to the definition of the target volume per ICRU 62:**



Planning of Proton Therapy

- **Volumes and margins related to the OARs:**



Planning of Proton Therapy

Proton –specific issues related to the PTV

- **For photon beam the PTV is primarily used to delineate the lateral margin**
- **For protons in addition to lateral margins a margin in depth has to be left to allow for uncertainties in the knowledge where the distal 90% IDL would fall**
- **Proton Beam Energy should be selected in a way that the CTV is within the irradiated volume taking into account both motion and range uncertainties**
- **Since the lateral and the margins in depth solve different problems each beam orientation would need a different PTV**
- **Alternatively the beam parameters are determined based on the CTV adding the lateral and range margins to the TPS alg.**

Planning of Proton Therapy

- In practice the beam parameters are determined based on the CTV adding the lateral and range margins to the TPS alg for *each* beam.
- For scanned Beams and IMPT these margins would influence which pencil beam would be used and each one's depth of penetration. It is much easier to visualize using optimization volumes(PBSTV)
- It is "required" that the dose distribution within the PTV is recorded and reported , therefore a PTV relative to CTV based on lateral uncertainties alone is proposed by ICRU 78
- We can safely do this is we ensure plan robustness first.

Planning of Proton Therapy

Sources of uncertainties:

- **Patient related:** Setup, movements, organ motion, body contour, target definition, etc…
- **Physics related:** CT number conversion, dose calculation, etc…
- **Machine related:** Device tolerances, beam energy, delivery method, etc…
- **Biology related :** Relative biological effectiveness (RBE), etc..

Uncertainties in Proton Therapy

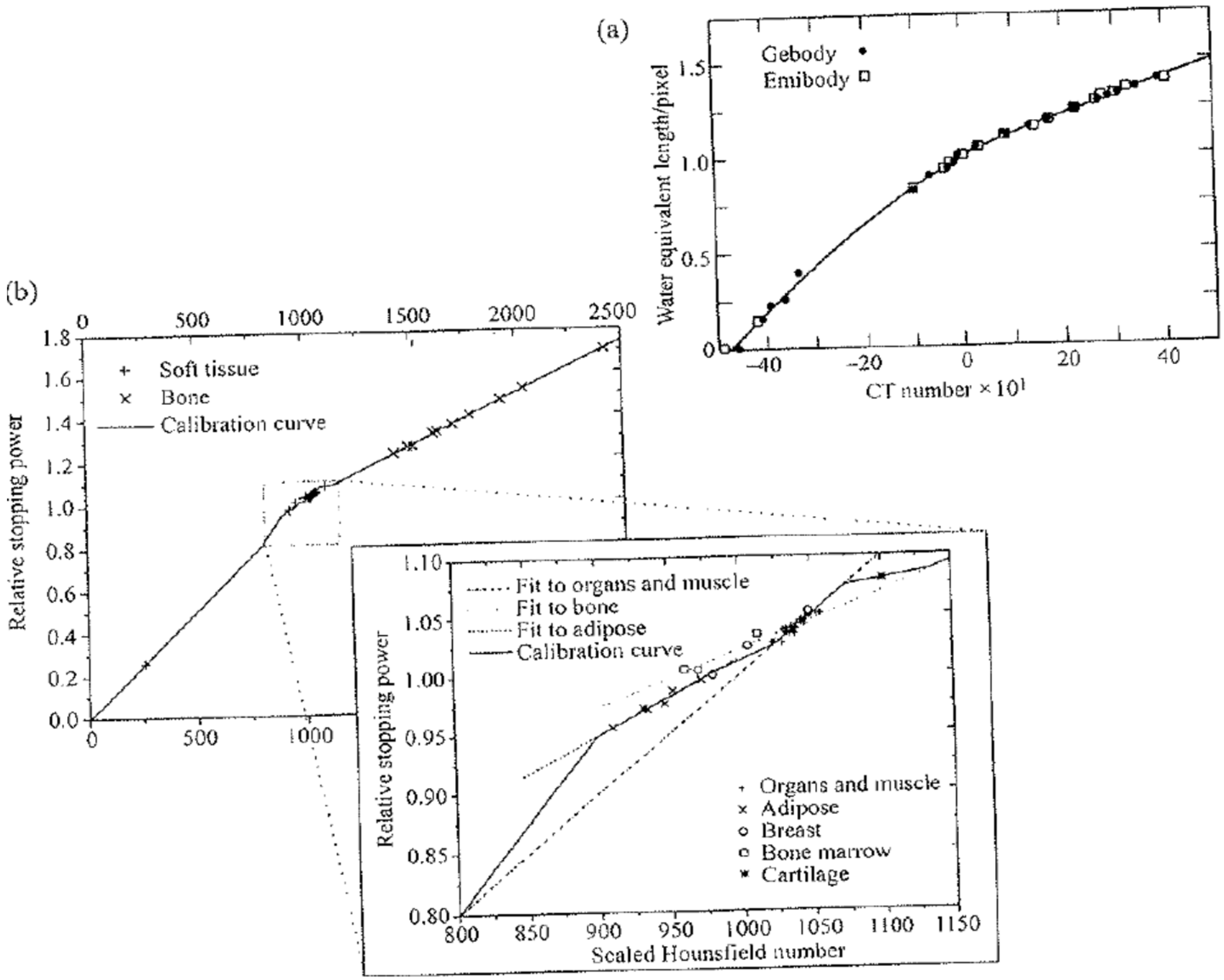
"If something goes wrong in the planning process it starts usually at the CT Simulator …"

Physics Issues:

- **CT Calibration Curve:**
  - Proton interaction ≠ Photon interaction
  - Multisegmental curves are in use
  - No unique SP values for soft tissue HU range
  - Tissue substitutes ≠ real tissues
  - Statistical and systematic variations in CT numbers
  - Image reconstruction artifacts (High Z materials)

Uncertainties in Proton Therapy CT

Calibration Curve Stoichiometric Method



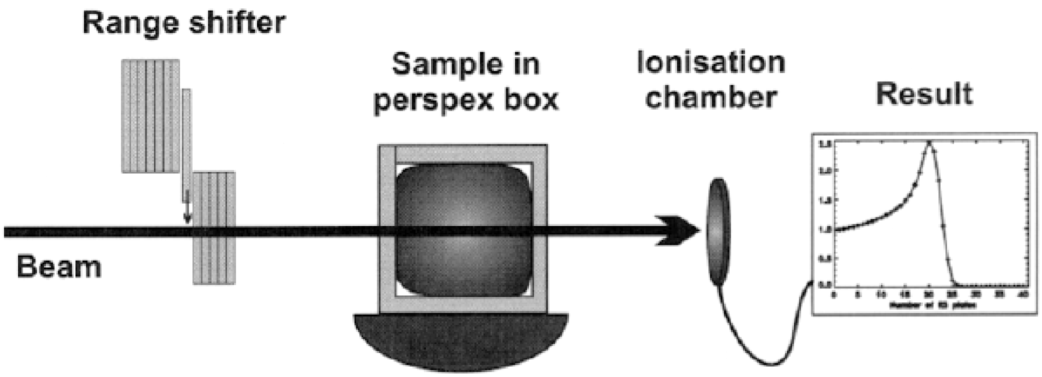
Uncertainties in Proton Therapy

CT Calibration Curve Stoichiometric Method

Is the 3.5% CT# correction for proton range uncertainty conservative?

Experimental evaluation of the relationship between the CT#

and proton stopping power ratio was done at PSI using a stoichiometric method (Schaffner et al 1998, PMB)



Conclusion: There is a 1.1 % uncertainty in soft tissue and 1.8% in bone.

Reality…A decade later it is still NOT the current clinical practice !

3.5% standard…

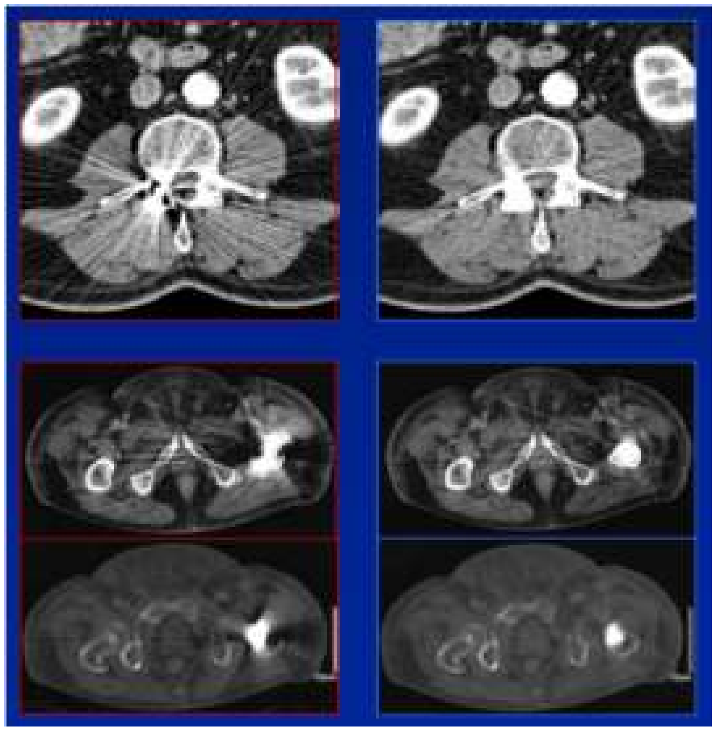
Uncertainties in Proton Therapy CT

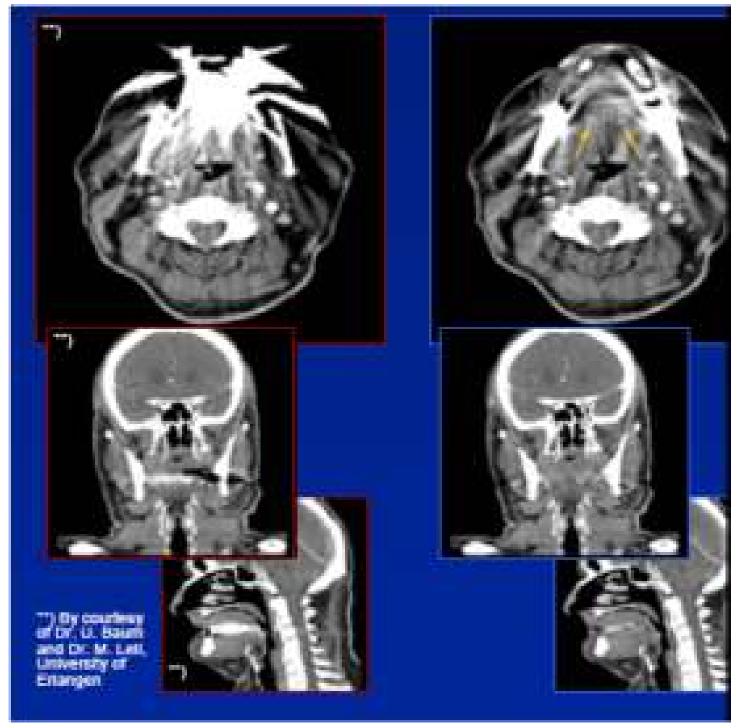
High Z artifacts

- Artifacts due to high Z materials (metal clips, fiducials, Calypso beacons, prosthesis, dental fillings, etc.) are common in RT.
- Avoid beam paths through high Z structures.
- Range uncertantanties in proton therapy due to significant CT reconstruction artifacts require to increase the typical **3.5%** range uncertainty to 5% for the distal margin after manual clean up of the CT image by the planner.

Uncertainties in Proton Therapy CT

High Z artifacts





Note: Image quality improvement for diagnostic purpose do not account for HU corrections at an accuracy level required for calculations in RT

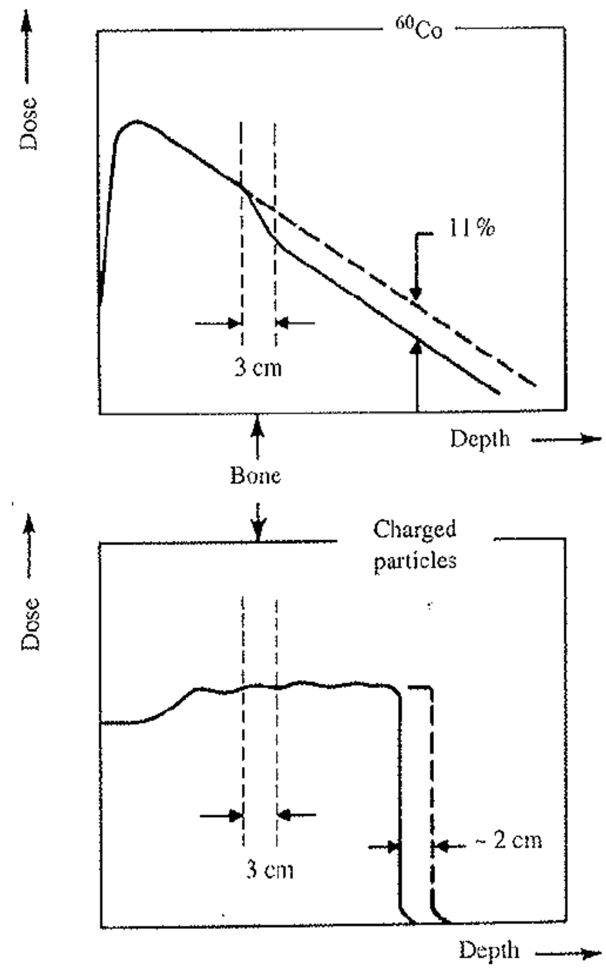
Proton Treatment Planning: Inhomogeneitis

- The effect of tissue inhomogeneity is greater for protons then for photons (ICRU 78)

- Failure to allow for a higher density along the proton path may result in a near zero dose in a distal segment of the target due to the reduced range of the protons.

- Penumbra is minimally affected for the materials limited to the human body, but it changes significantly for other material as it is caused by multiple scattering

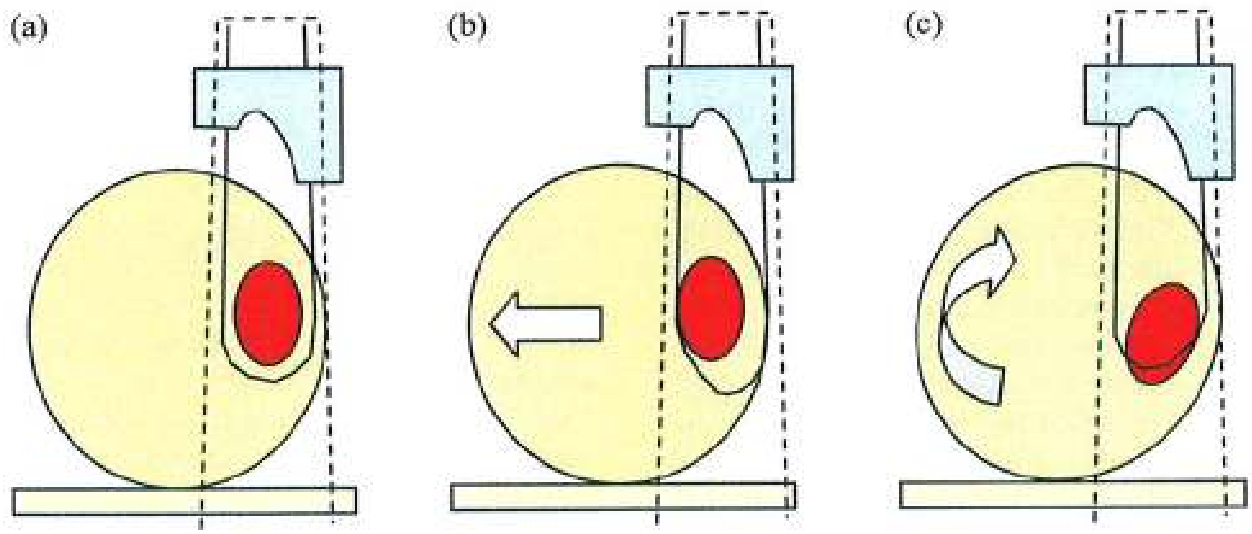
- Conversely neglecting to account for an air cavity upstream of the target => in high dose deposited in distal normal structures.



Uncertainties in Proton Therapy

Motion and Setup uncertainties

- **What happens if the beam is nearly tangential to the target?**



- **Therefore, tangentials fields are avoided in clinical practice**

ICRU 78

Planning of Proton Therapy

RBE Uncertainties

- Clinical RBE: 1 Gy proton dose $\equiv$ 1.1 Gy Cobalt γ dose (RBE = 1.1 in the middle of SOBP)
- RBE weighted dose concept introduced by ICRU 78
- RBE vs. depth (LET) is not constant
- RBE also depends on
  - dose
  - biological system (cell type)
  - clinical endpoint (early response, late effect)

- How do we overcome this uncertainty in clinical practice?

In general, not more then 2/3 of our prescribed dose comes from beams pointed towards a critical structure.

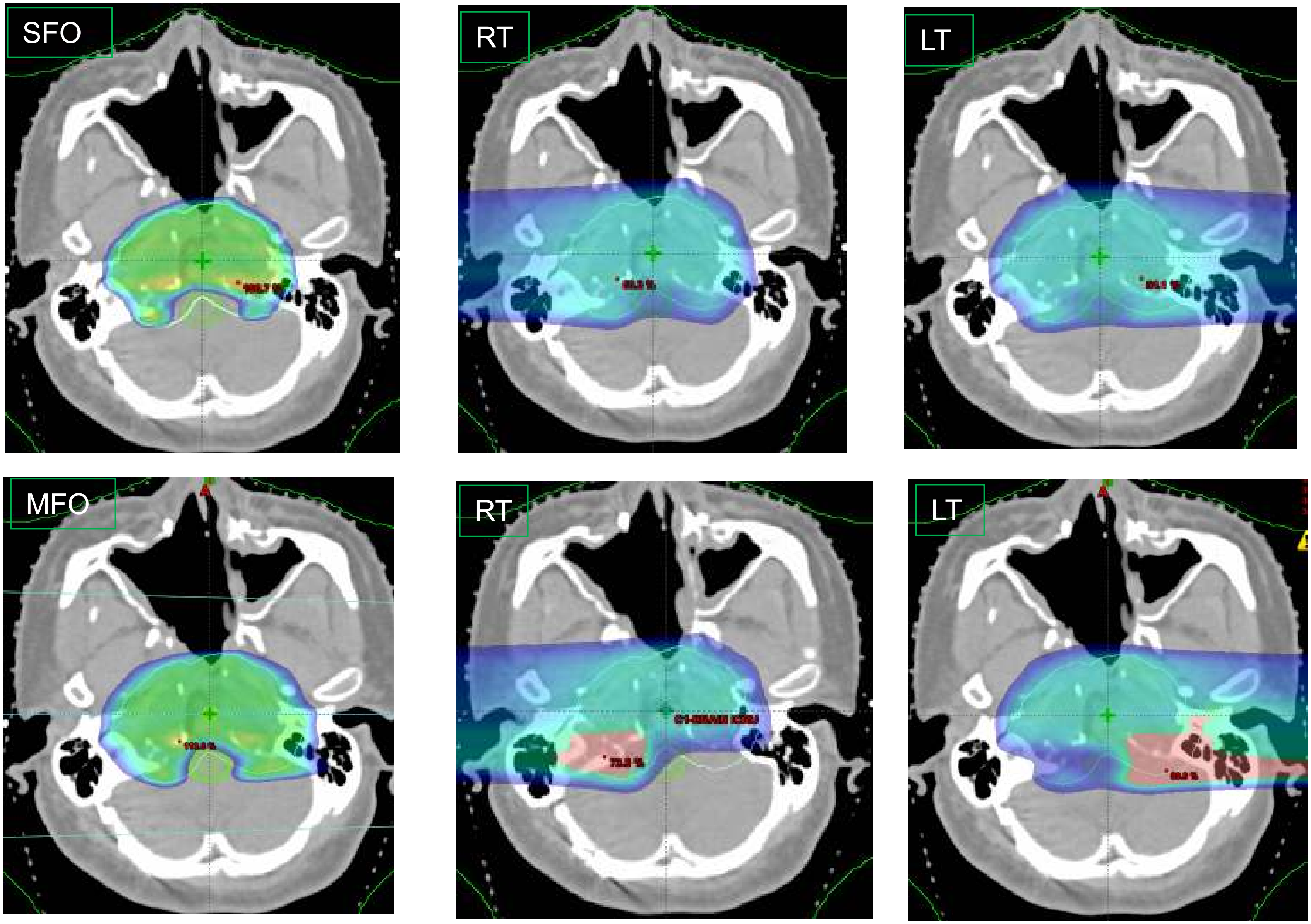
PBS Planning Techniques

- PBS based treatment planning can be performed using two different techniques:

- Single field optimization (SFO)- where single fields are optimized to achieve uniform dose (as known as SFUD).

- Multifield optimization (MFO, IMPT)- where all spots from all fields are optimized simultaneously, and dose in each single field is not uniform (similar to IMRT).

SFO (SFUD) vs. MFO



Optimization Volume-PBSTV

- **<u>Beam specific PTV margins</u> are related to the range uncertainties and incorpoated in the optimization volume-PBSTV.**

Distal and proximal margins are set from CTV:

- DM = (0.035 x CTVdistal) + 1 mm
- PM ≈ (0.035 x CTVproximal) + 1mm

- Lateral margins based on setup, motion, penumbra.

3.5%- uncertainty in the CT# and their conversion to relative proton linear stopping power

1 mm - added to correct for range uncertainty

SFUD vs. MFO vs. Passive Scattering

Conformality			Robustness			Planning		
Best → Worst			Best → Worst			Easiest → Hardest		
MFO	SFUD	PS	PS	SFUD	MFO	MFO	SFUD	PS

- **Double scattering for moving targets**
- **Uniform scanning for sharp penumbra, larger field, deep seated tumor**
- **SFUD for highly conformal dose distribution**
- **MFO is currently not employed at Penn**

Clinical Implementation:Base of Skull RT

Some tumors require high dose of radiation (> 70Gy) while we have:

- Limited dose level tolerances for brainstem, optical chiasm, optical nerves, cochlea , etc..
- To decrease the amount of normal brain irradiated

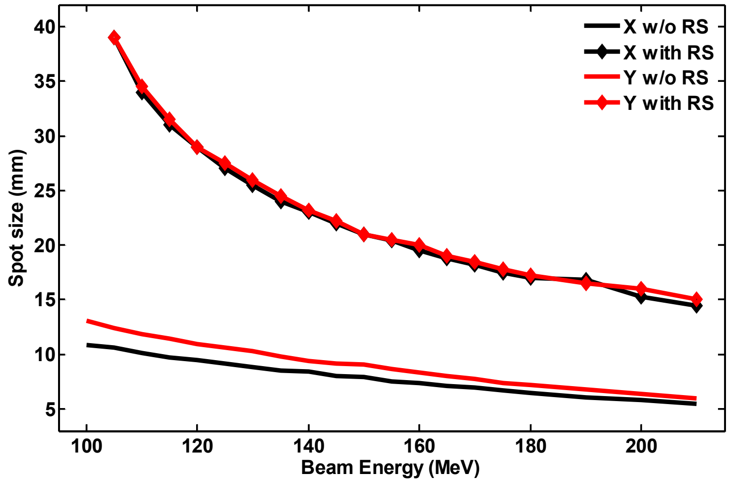
With PBS:

- Rapid dose fall off achievable through small pencil beam size
- Proximal and distal dose conformality
- Reduced integral dose

Range Shifter & Spot Size

- The fix beamline has energy range (100 MeV to 235 MeV)
- For targets <7cm from the surface require the use of energy absorber (range shifter)

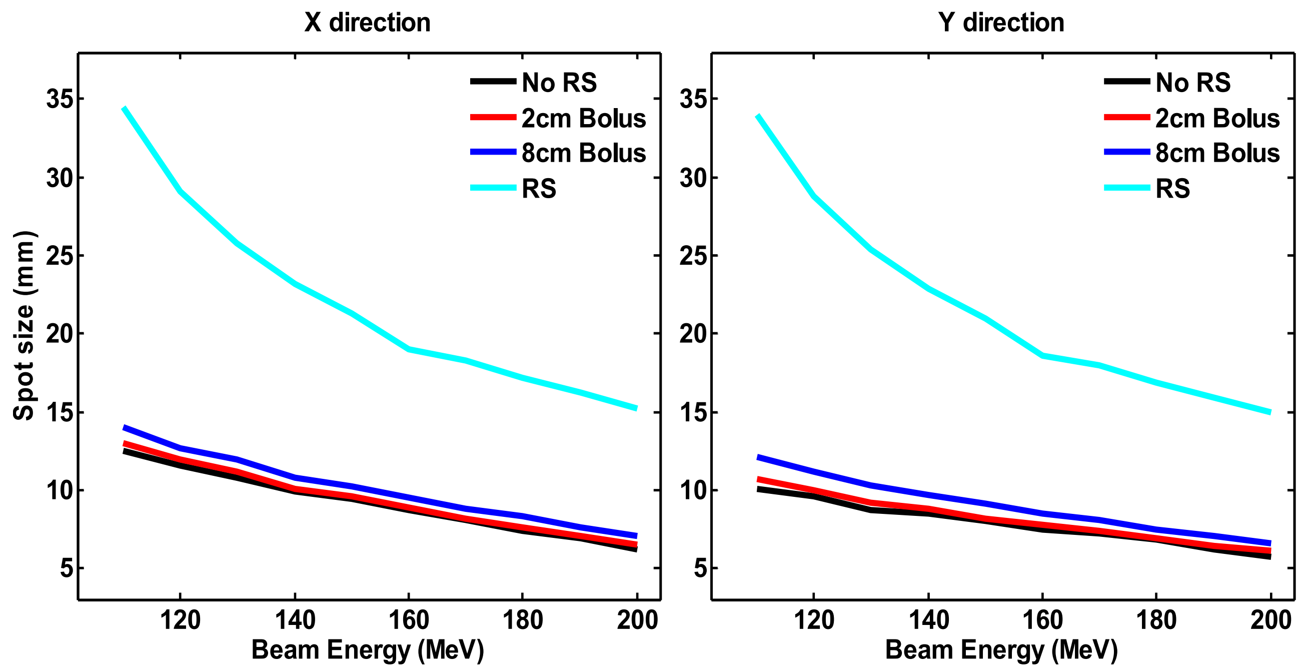
- Range shifter positioned at the surface of the snout with >30cm air gap to ISO



- Pencil beam spot size increases significantly with air gap

Bolus for Brain Tumor

- Maintain the size of the pencil beam
- Minimizing the air gap and the amount of material in the beam
- Range shifter (RS) was replaced with an Universal Patient Bolus



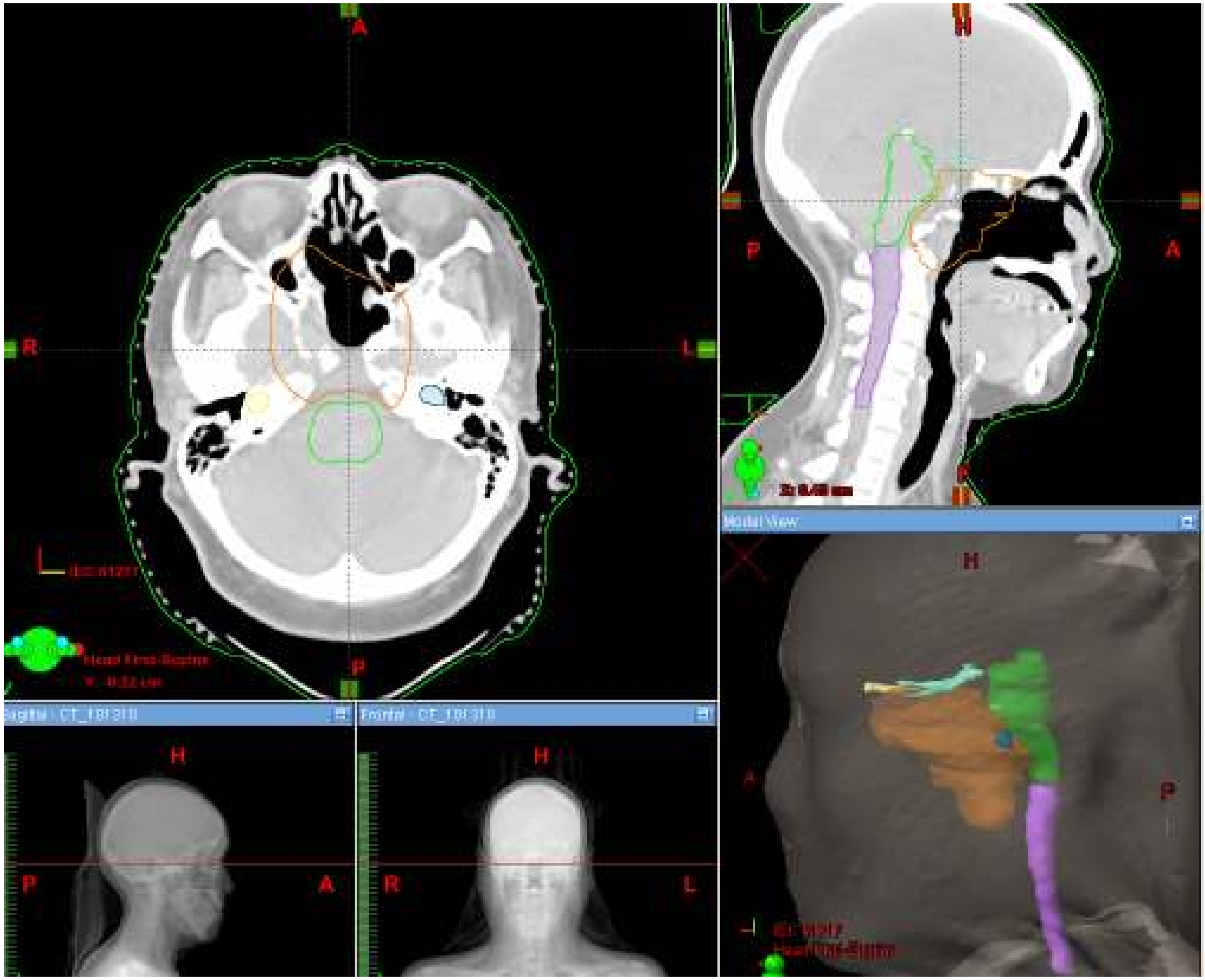
Pencil Beam Scanning Technologies

Spot Size Integrity - Penn Solution

In Room Implementation

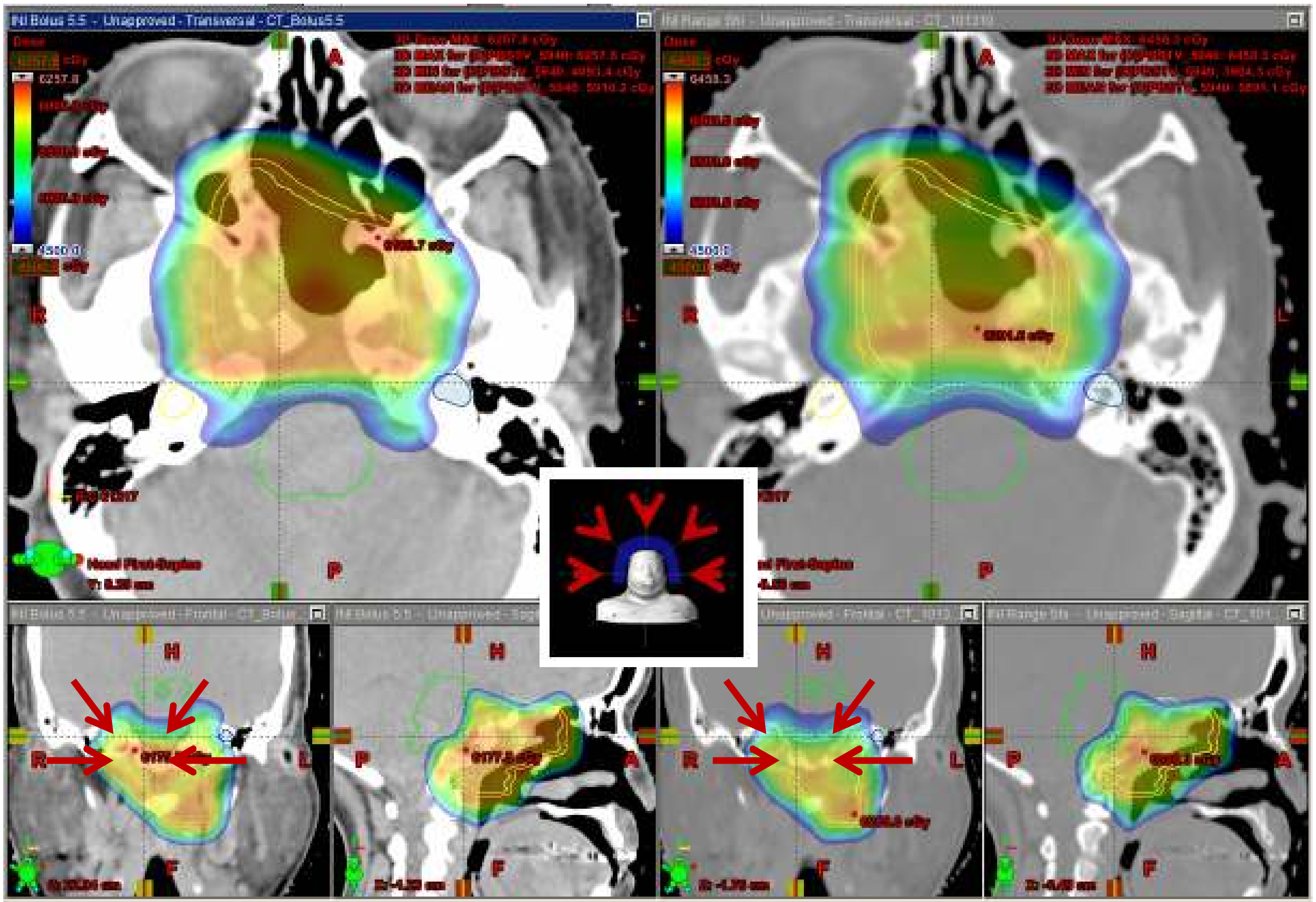
Clinic Example

- Target is close to brainstem, cord, cochlea and optical structures.

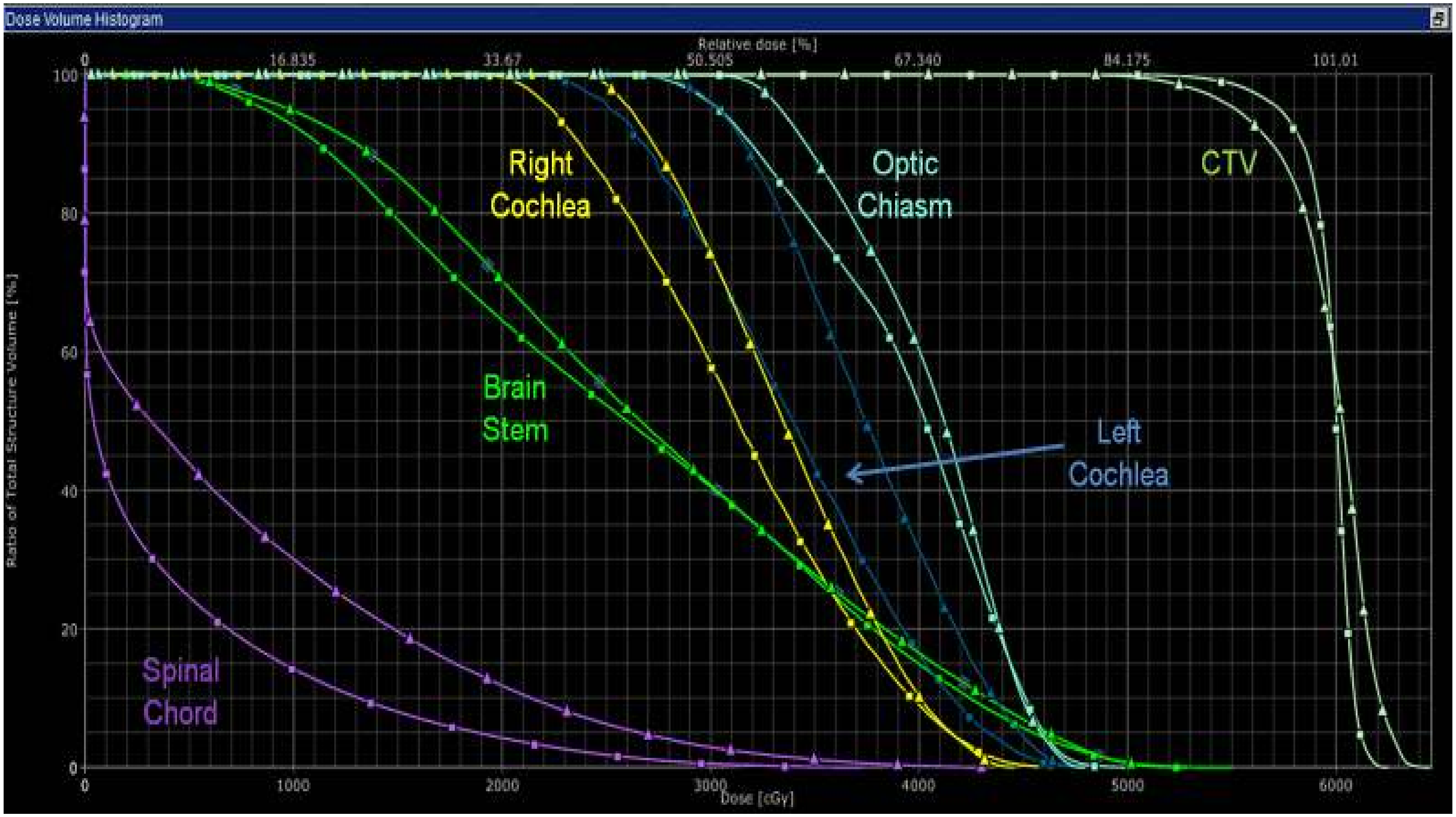


Pencil Beam Scanning Technologies

Eclipse *Bolus vs. Range Shifter*



DVH Comparison: Bolus (■) vs. RS (▲)



- More uniform target coverage and superior conformality
- The biggest differences in dose for the OARs are for the peripheral structures such as the cord and cochlea
- The brainstem and chiasm are similar in the high dose region

Choosing Beam Orientation

- Beam orientation is chosen to have the shortest and the most homogenous distance to the target (for robustness)
- Multiple beams are used for robustness, but less beams than DS due to TPS limitation
- Multiple beams without skin overlap to reduce the skin dose
- Avoid beams point towards critical structure due to range uncertainty

Penn Collision Detection Software

- CAD /MATLAB ray casting algorithm.
- Incorporated during the proton treatment planning phase, to improve clinical efficiency.
- The method could apply to patient collision detection in XRT.

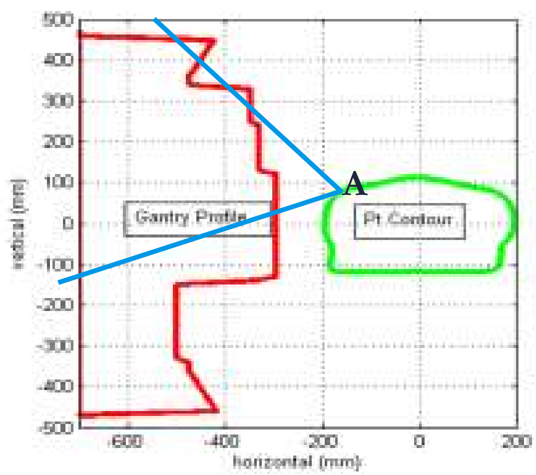


Figure 3

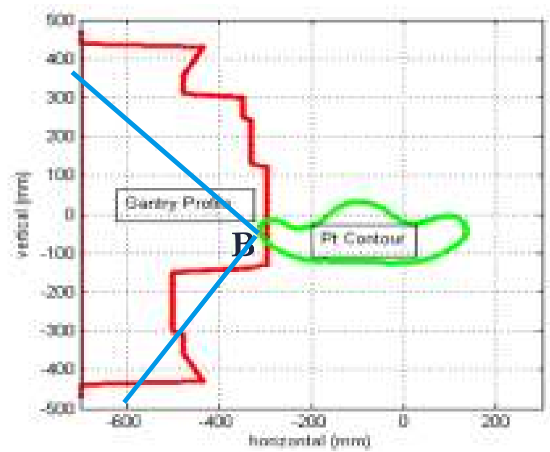


Figure 4

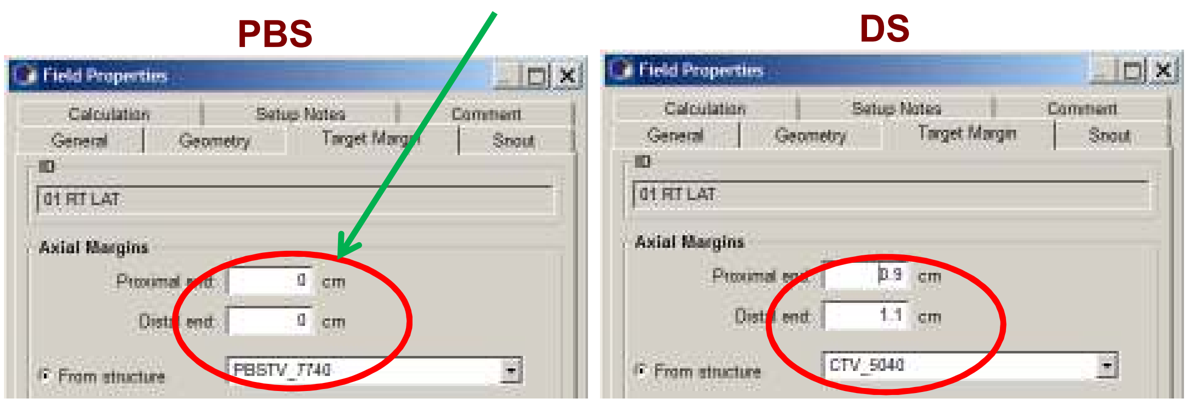
Figures 3 & 4 illustrating the collision detection method (green – body contour points; red – gantry polygon).

W. Zou, S.Both. Et al.“A Clinically Feasible Collision Detection Method for Proton Therapy” (accepted Med Phys J.).

SFUD planning in Eclipse (1) - Volume

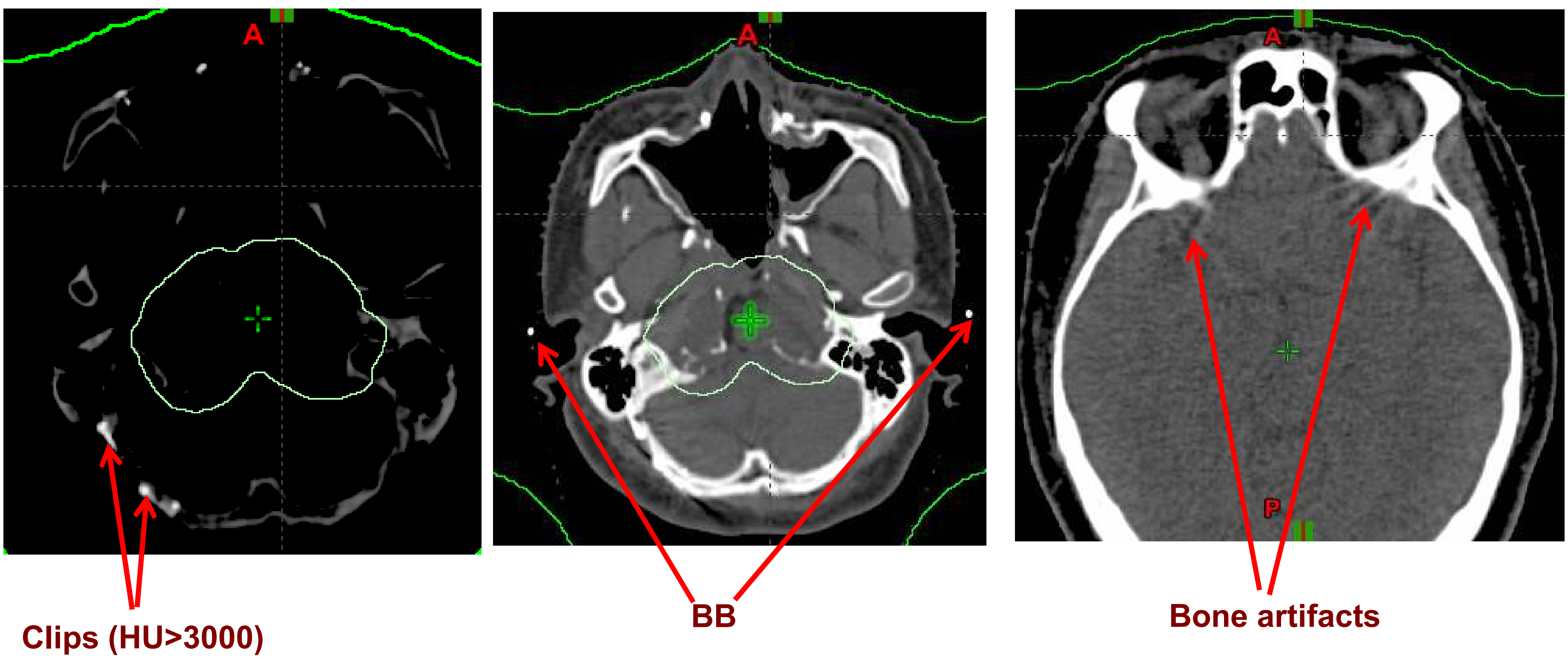
- **PBS plan needs a volume for selection of spot position**
- **Volume for optimization: pencil beam scanning target volume (PBSTV) that includes range uncertainty in beam direction**
- **For brain tumors, PBSTV=CTV+5mm**
- **Eclipse limitation: it could not add late margins in beam direction for PBS optimization**

Eclipse Limitation

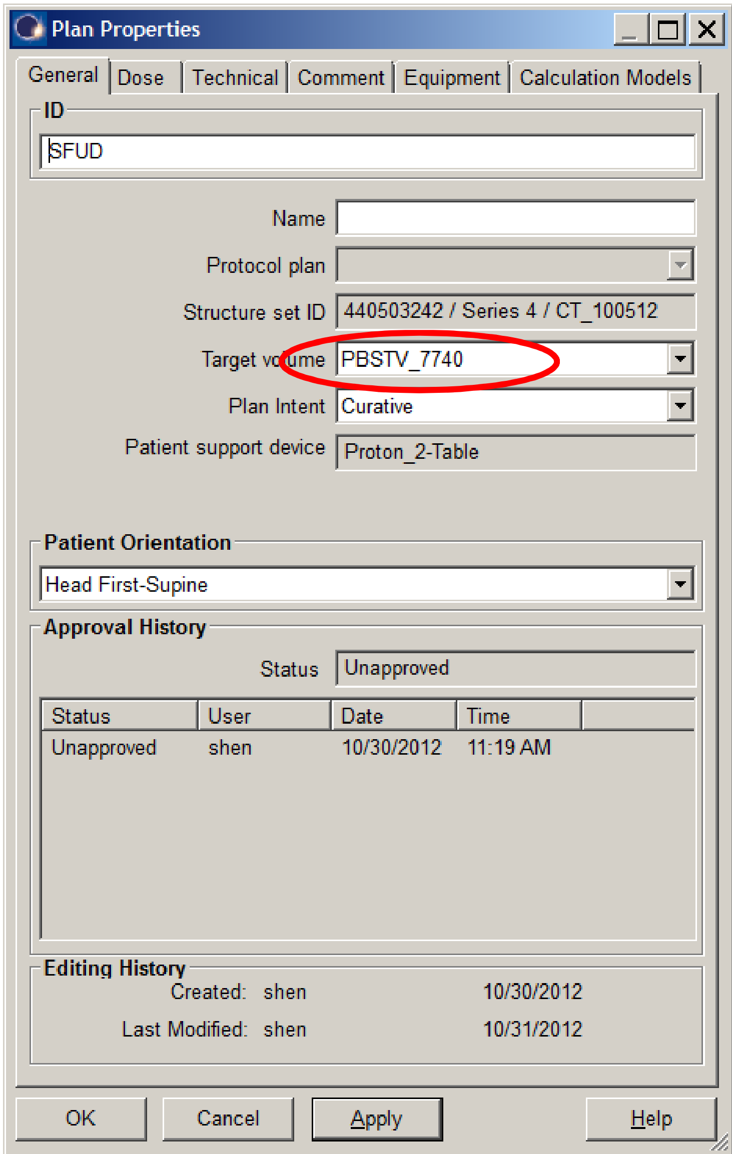


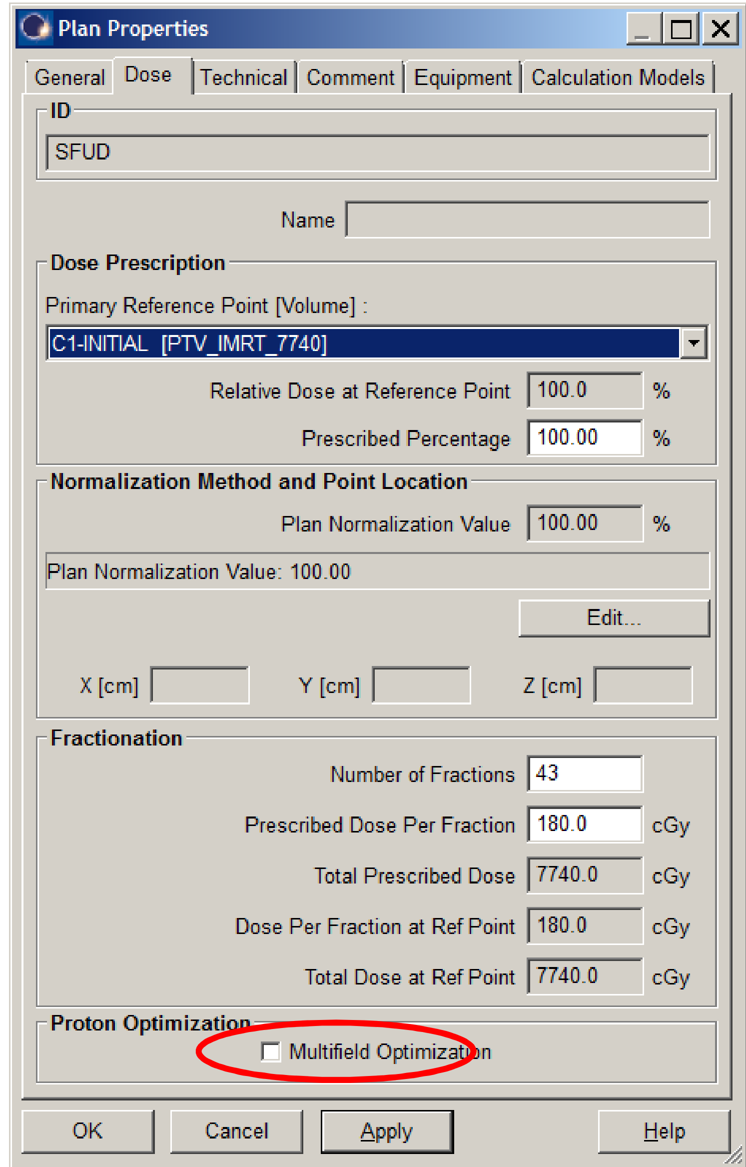
SFUD planning in Eclipse (2) - Artifacts

- **All CT artifacts need to be contoured and overwritten with appropriate HU (e.g. high density clips, BB, bone artifacts).**
- **It will needs to change window and level to identify them.**



SFUD planning in Eclipse (3)

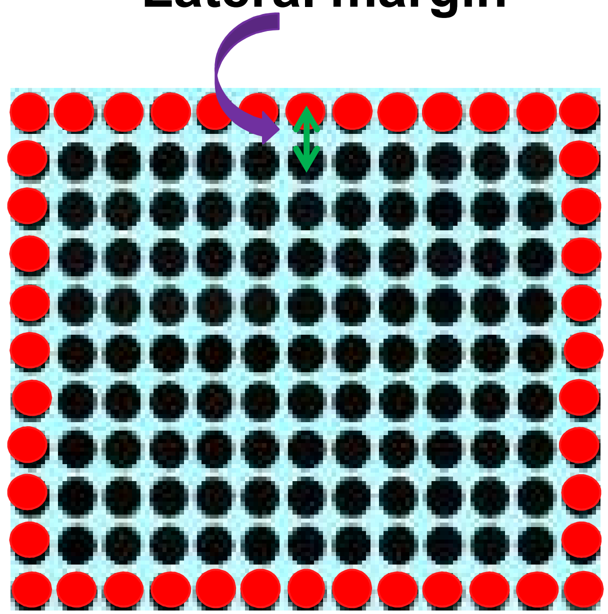


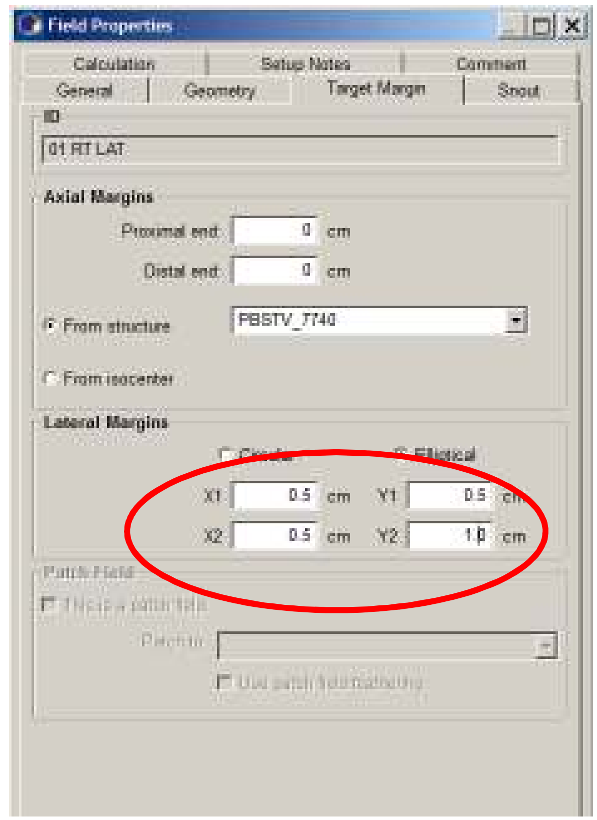


SFUD planning in Eclipse (4)

- **Lateral margins (1-2 spot spacing) are used for extension of dose grid, so spots can deposit outside the PBSTV in order to achieve good coverage**

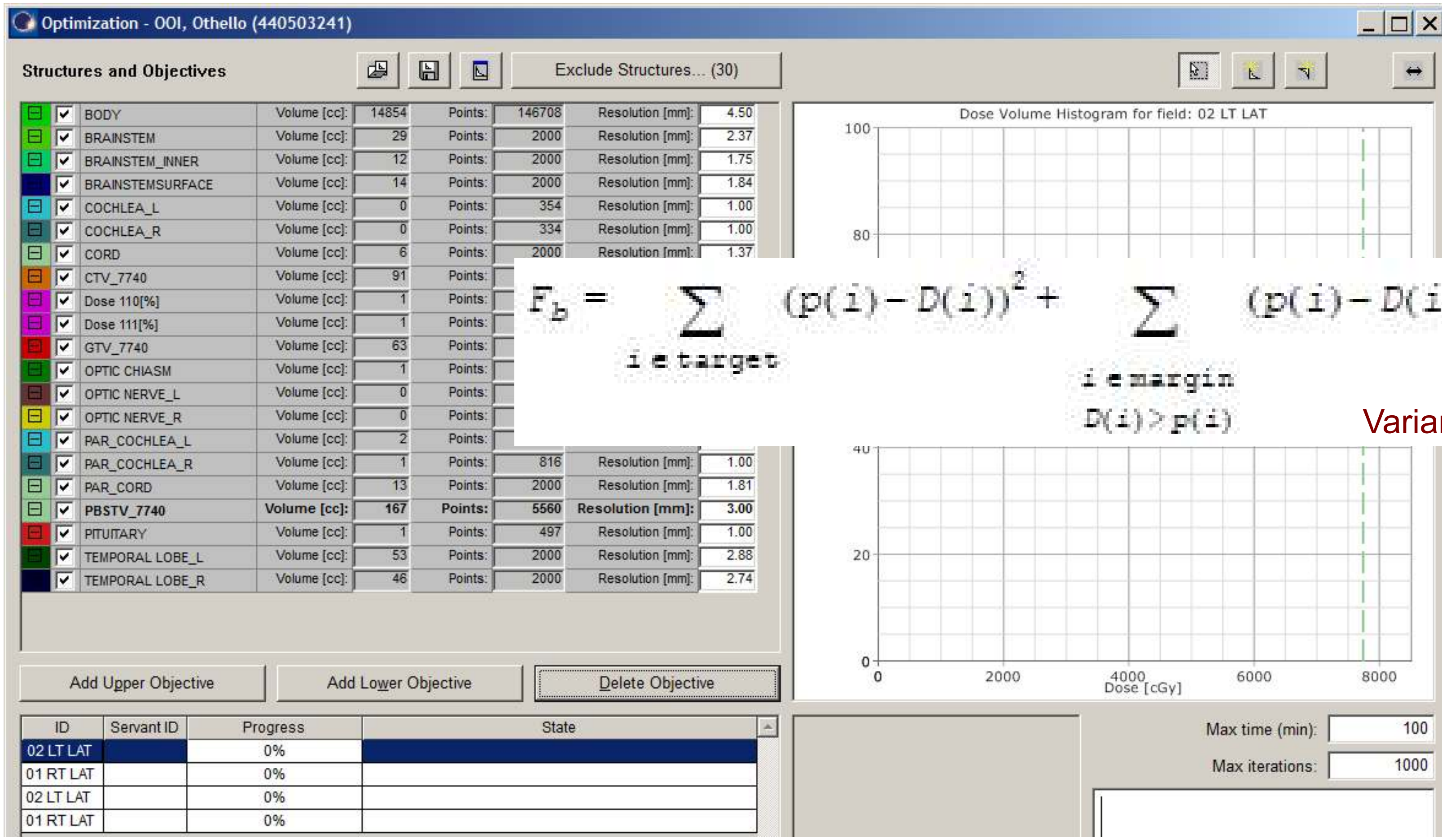
Lateral margin





SFUD planning in Eclipse (5)

- **Simultaneous spot optimization (without OAR constraints)**

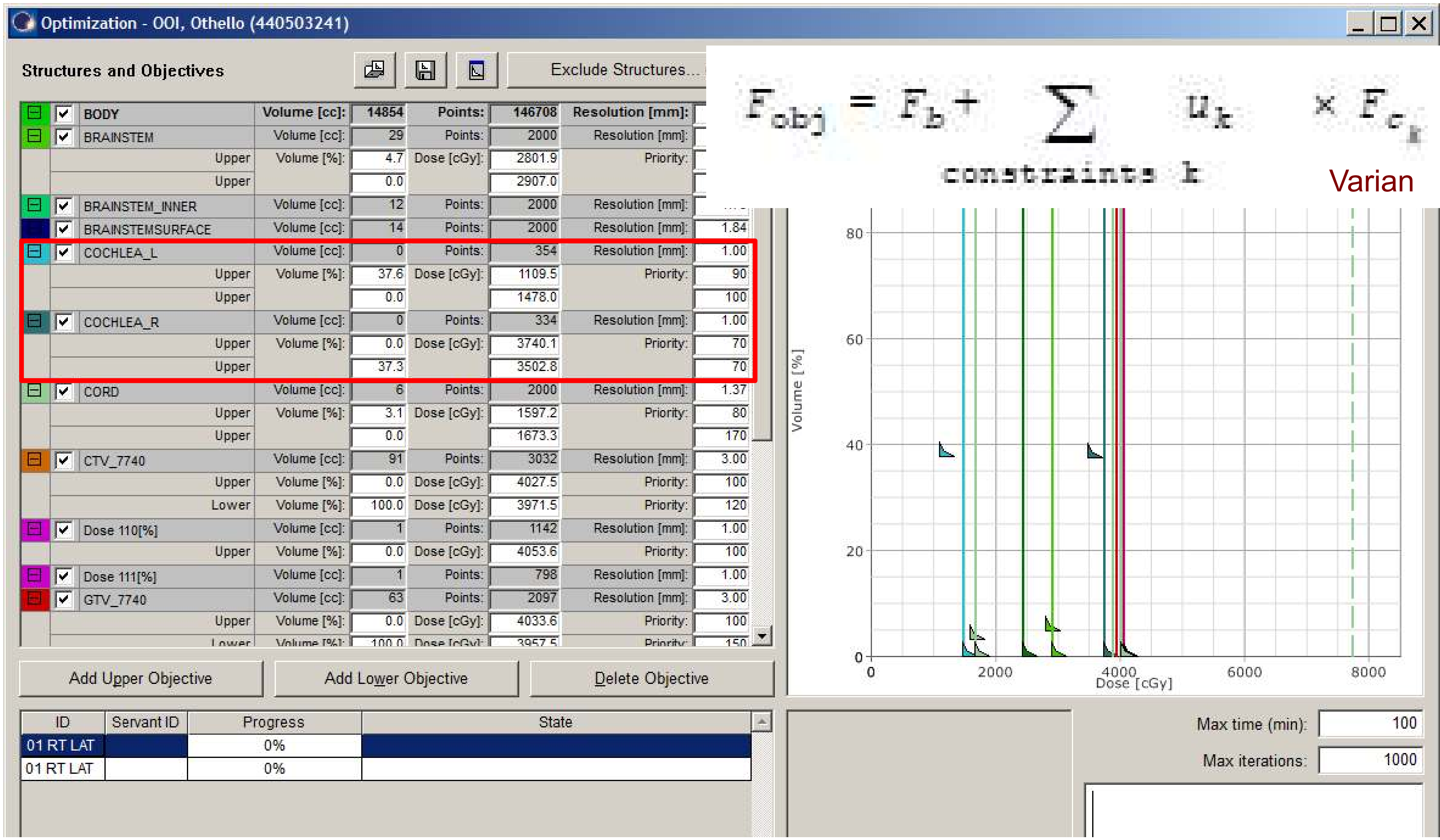


$$F_b = \sum_{i \in target} (p(i)-D(i))^2 + \sum_{\substack{i \in margin \\ D(i) > p(i)}} (p(i)-D(i))^2$$

Varian

SFUD planning in Eclipse (6)

- **OAR optimization (field by field)**



$$F_{obj} = F_b + \sum_{\text{constraints } k} w_k \times F_{c_k}$$

Minimum MU

- **A minimum signal-to-noise ratio is required for reliable spot position measurement**

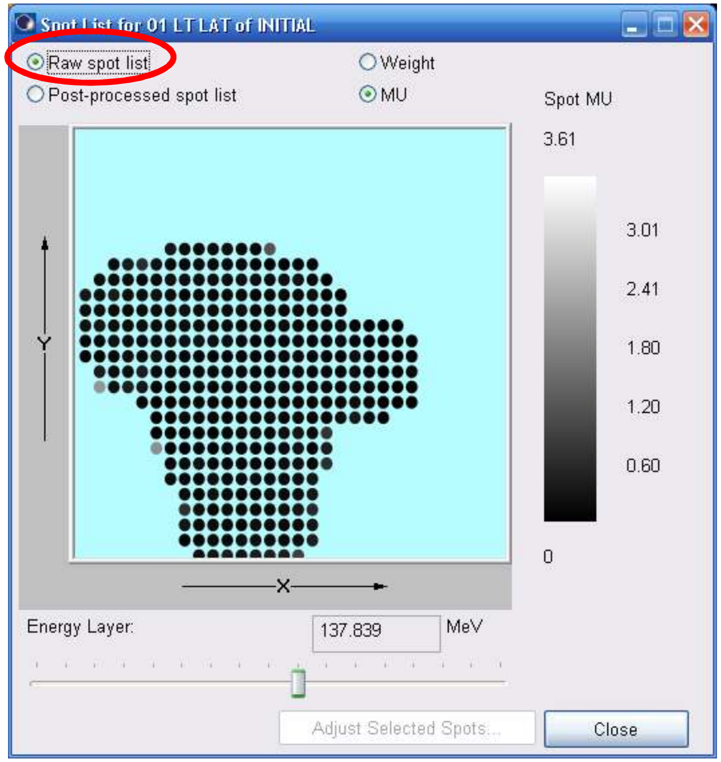
- **The spot does should be greater than the expected delayed dose (the dose delivered after the beam spot termination signal is sent by the main dose monitor)**

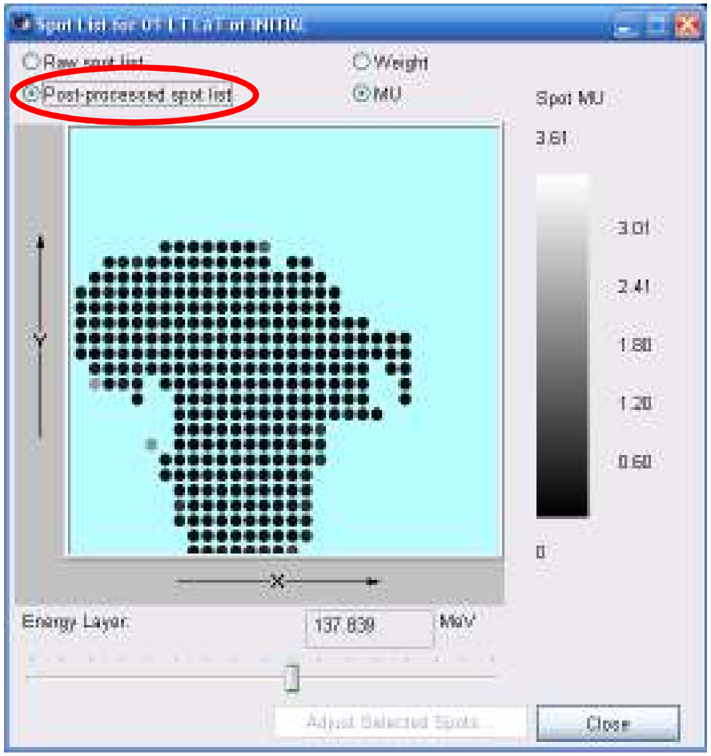
- **Our minimum MU is 0.021MU, ~ 60 pC**

- **Spot post processing**
  - Rounding down: spot is deleted if $MU < 0.5\ MU_{min}$
  - Rounding up: spot is rounded to MU_{min} if $0.5\ MU_{min} \leq MU < MU_{min}$

Spot Post Processing

- **Post-processing runs automatically after the optimization and before dose calculation**
- **Optimal spot weights (raw) changed after post processing**





Rounding Errors – TPS Limitation

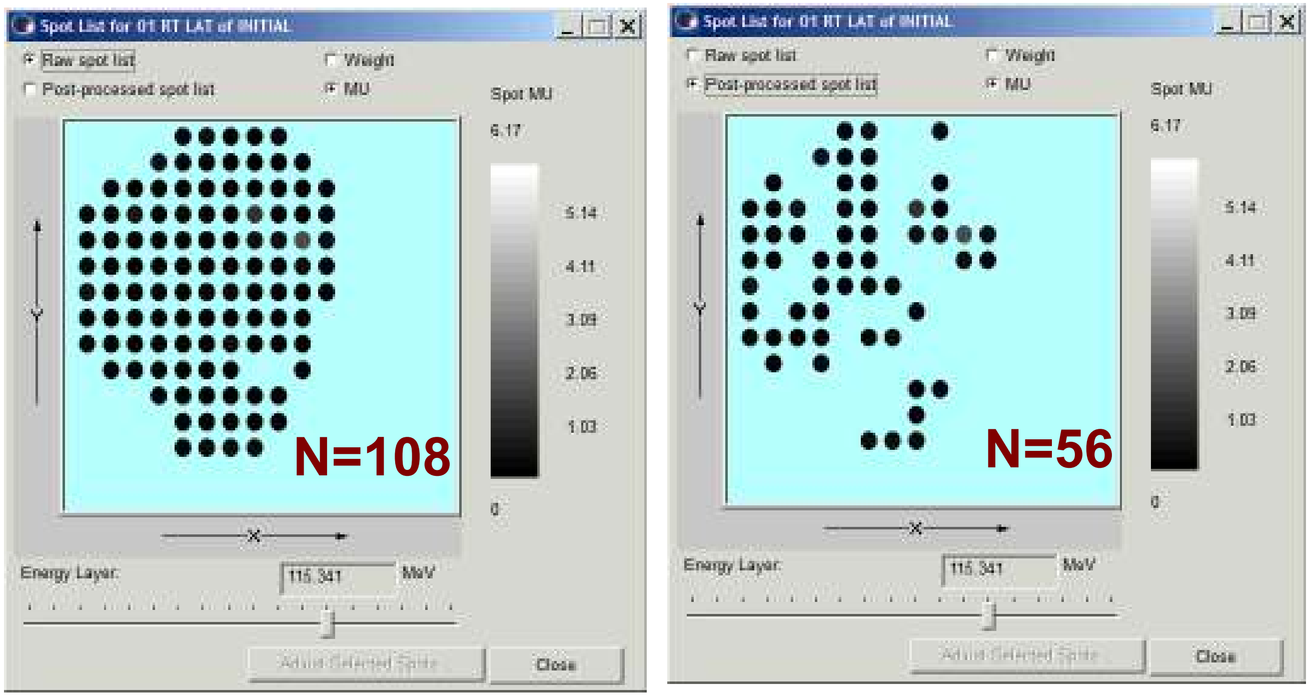
- Since Eclipse does not incorporate minimum MU constraint in optimization, the ideally optimized dose distribution was distorted after post processing due to minimum MU.

- The dose distribution is more distorted the plans with multiple fields because MU for each spot is reduced.

- Do not use too many fields due to this limitation in TPS.

TPS limitation on PBS optimization

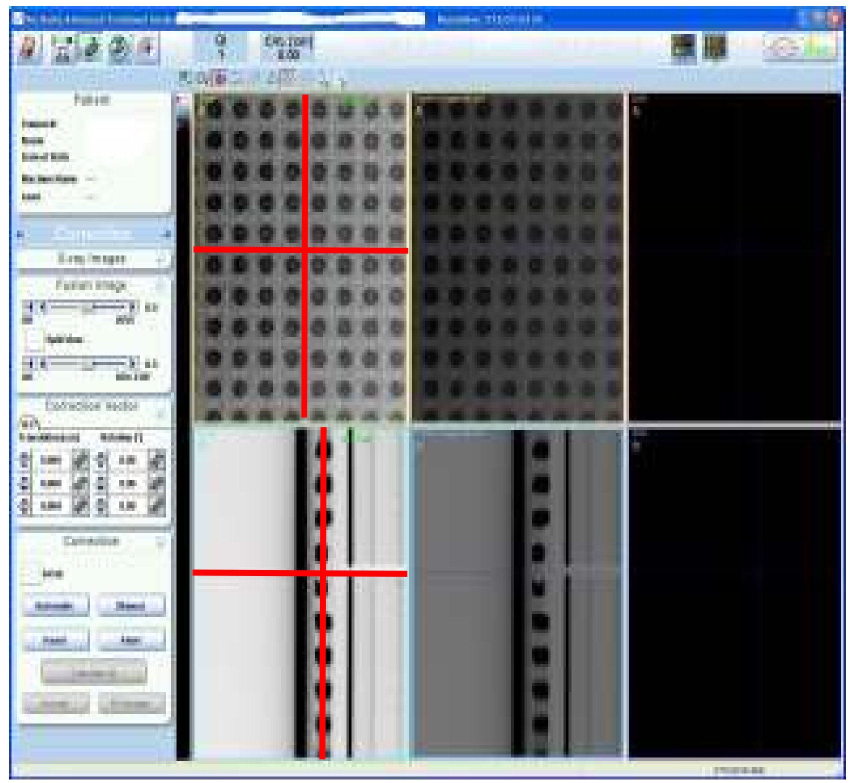
- A BOS case with four equally weighted fields.
- For this specific layer almost half of the spots were deleted after post processing.



- TPS should incorporate MU constraints in the optimization process!

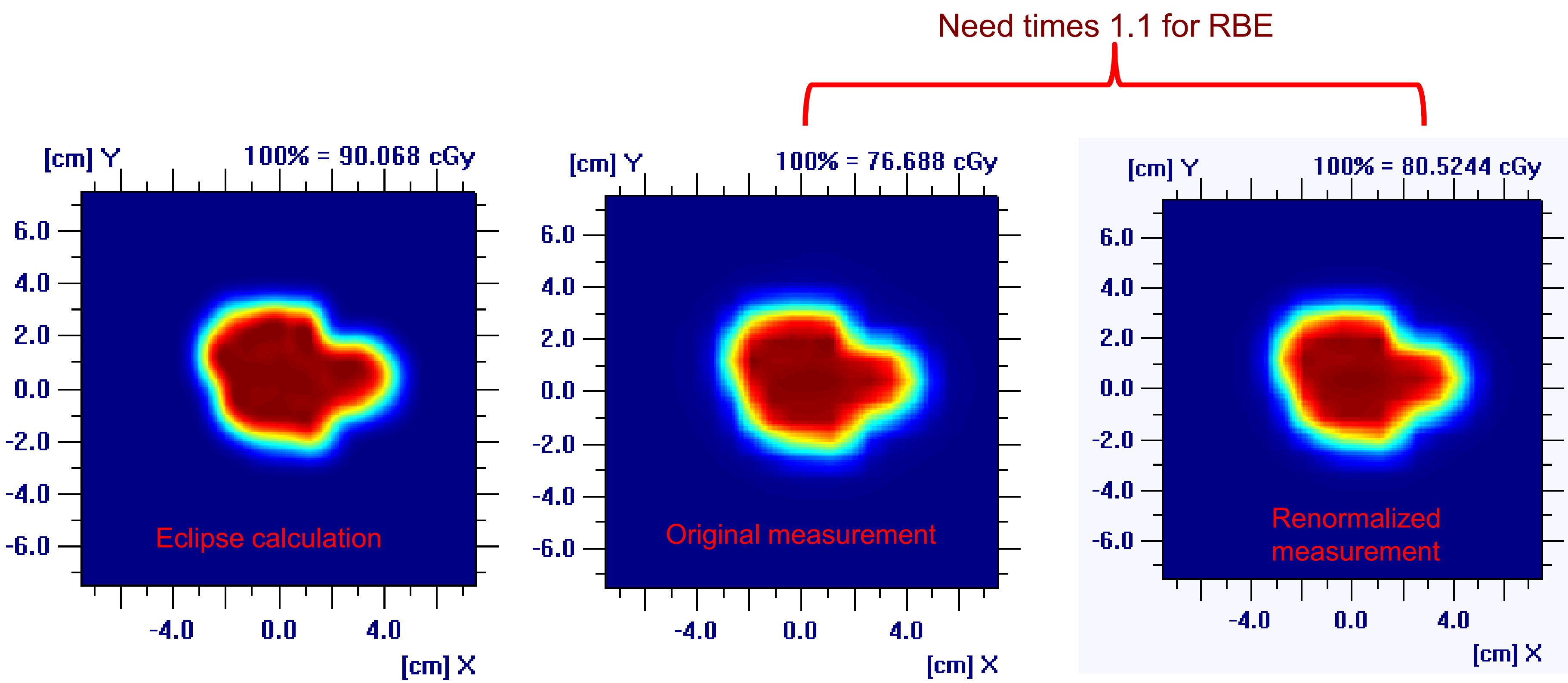
Patient Specific QA

- Geometry: center of SOBP align with ISO, sub mm accuracy of alignment was achieved with IGRT
- Dose maps in four depths were measured
- Absolute point dose comparisons and gamma analysis for 2D dose map



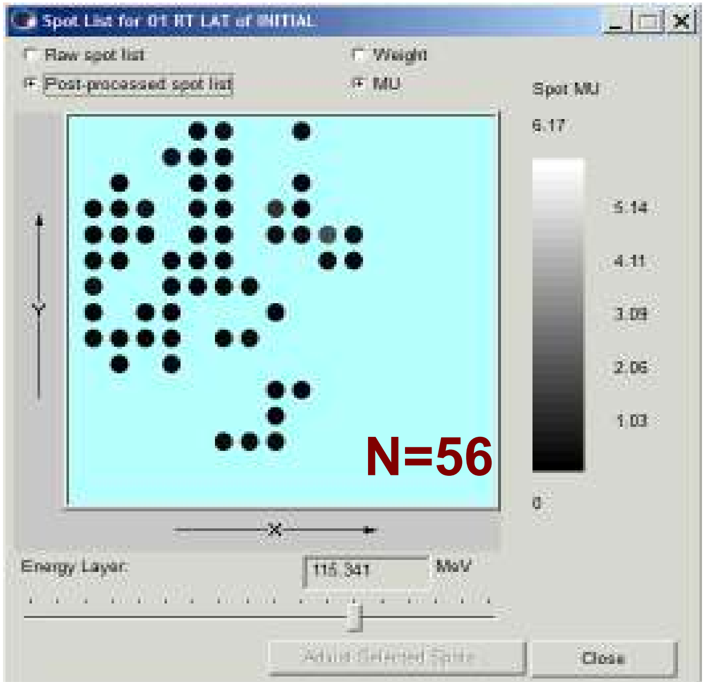
Small Fields Dose Discrepancies

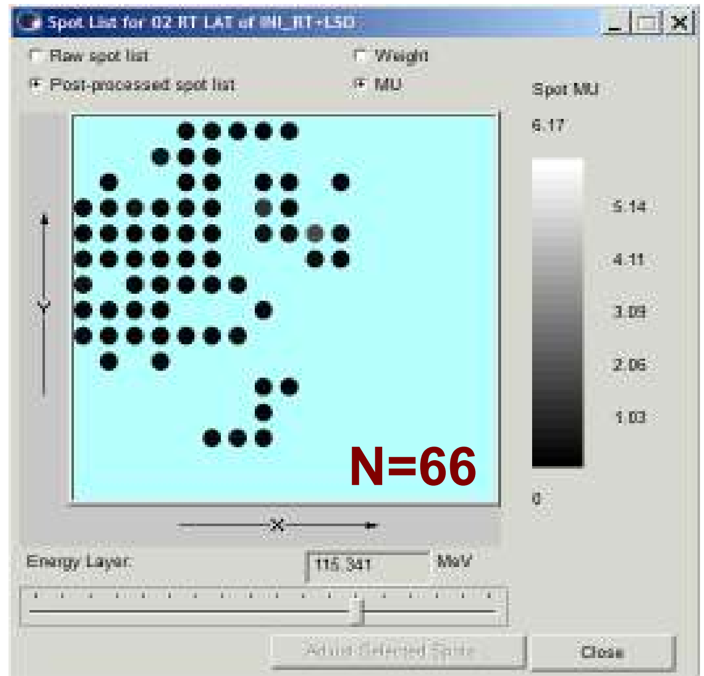
- **Measured output for some brain fields (small field and lower energy) could be 10% less than the Eclipse calculation**
- **Renormalization is made in TPS, and redo QA at center SOBP**



Renormalization - Caveat

- More spot s may appear after renormalization because more spots may be rounded up





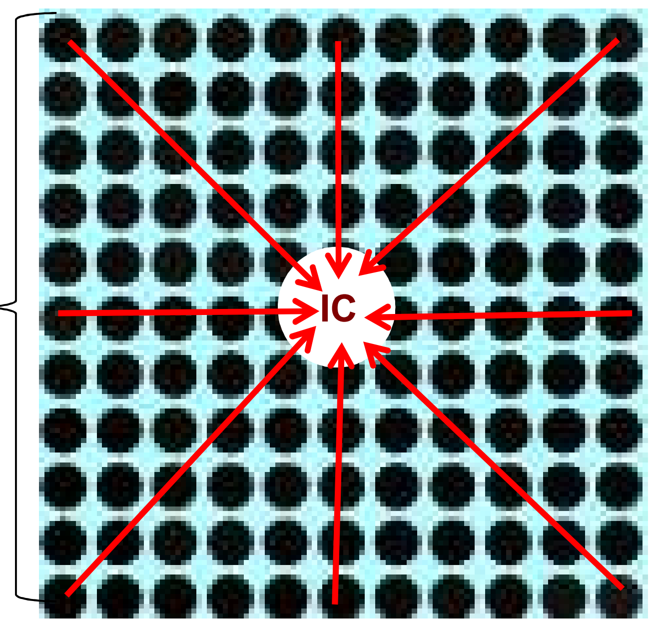
- Renormalized plan ≠ approved plan
- Need to remove additional spots to keep plan integrity
- QA should be performed again for center of SOBP plane

Why Small Field Need Renormalization

- Halo is produced from beam profile monitor in the upstream, which affects more for the low energy beam (e.g. brain cases).
- Halo dose is small, but its FWHM can be more than 10cm.
- With >1000 spots in PBS field, even a low dose tail (0.1%) could accumulate to a significant dose contribution

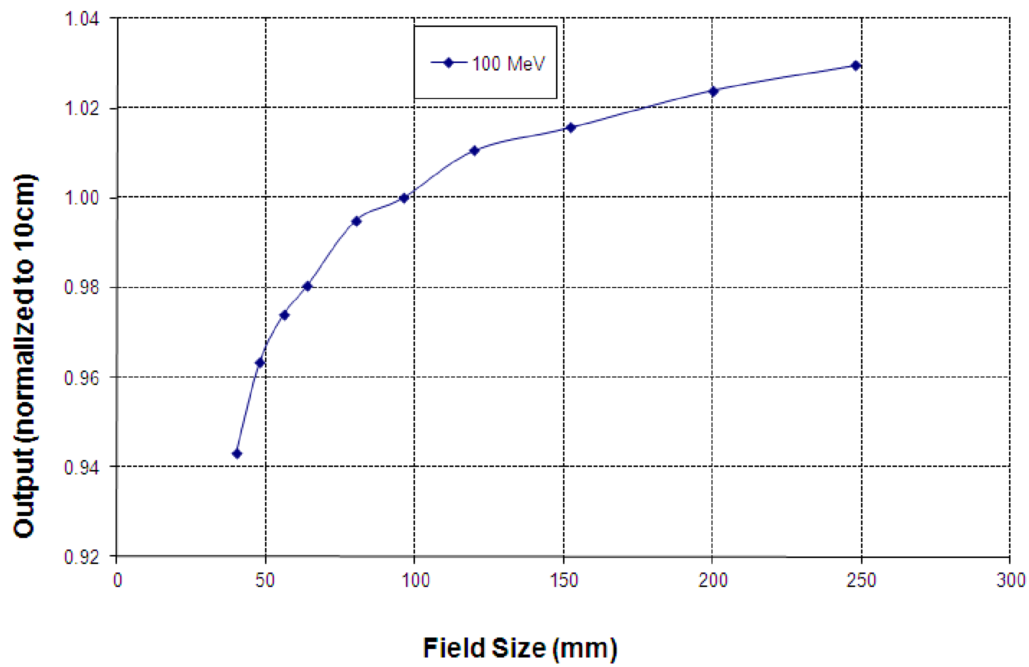
- Primary Gaussian σ_1=1cm, secondary Gaussian (halo) σ_2=5cm.

20 cm



Field Size Factor

- **In air measurement of output varies with field size**

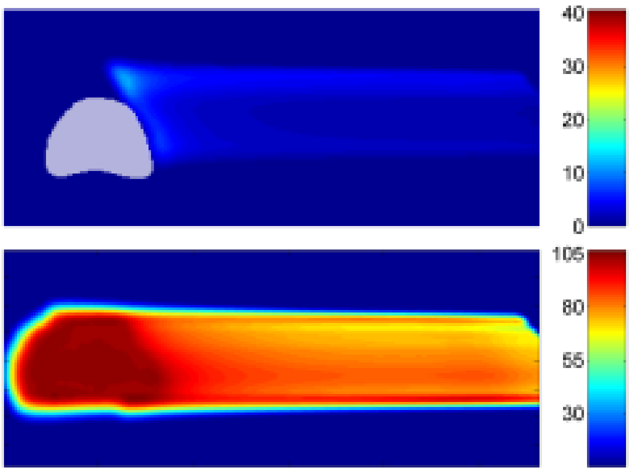


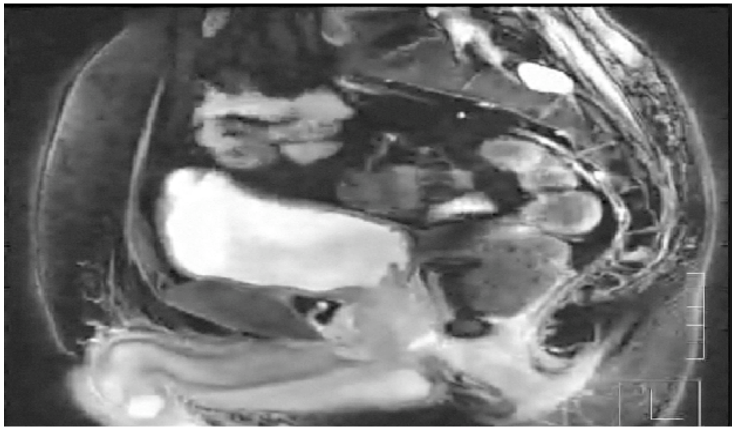
- **With one Gaussian fit for in air profile, output calculated by Eclipse is almost a constant for all field sizes.**
- **Output was matched to field size about 10cmx10cm, which is an overestimation for small fields (e.g. brain fields).**

PBS Treatment Planning-Prostate

Interplay Effect & Prostate Motion

- PBS delivers a plan spots by spots; layers by layers.
- Each layer is delivered almost instantaneously.



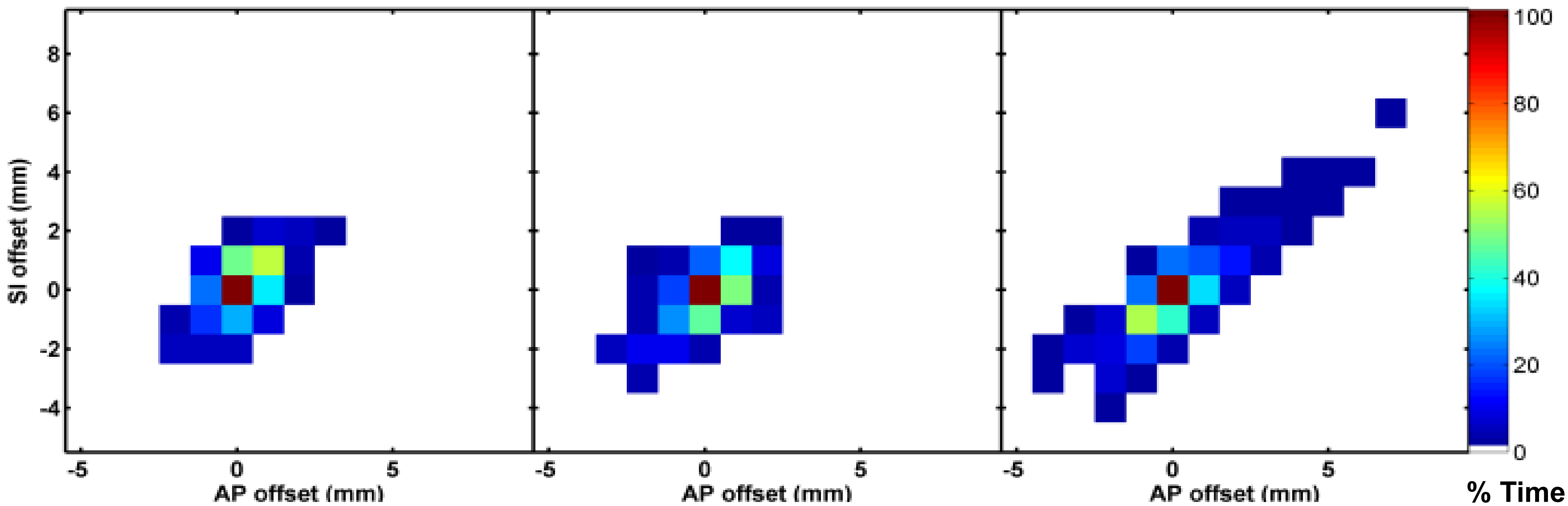


- The switch (beam energy tuning) between layers takes about 7s.
- Prostate motion during beam energy tuning causes an interplay effect.

Pencil Beam Scanning Technologies

Calypso Based SI & AP Prostate Motion

For One Patient



Best scenario

Intermediate scenario

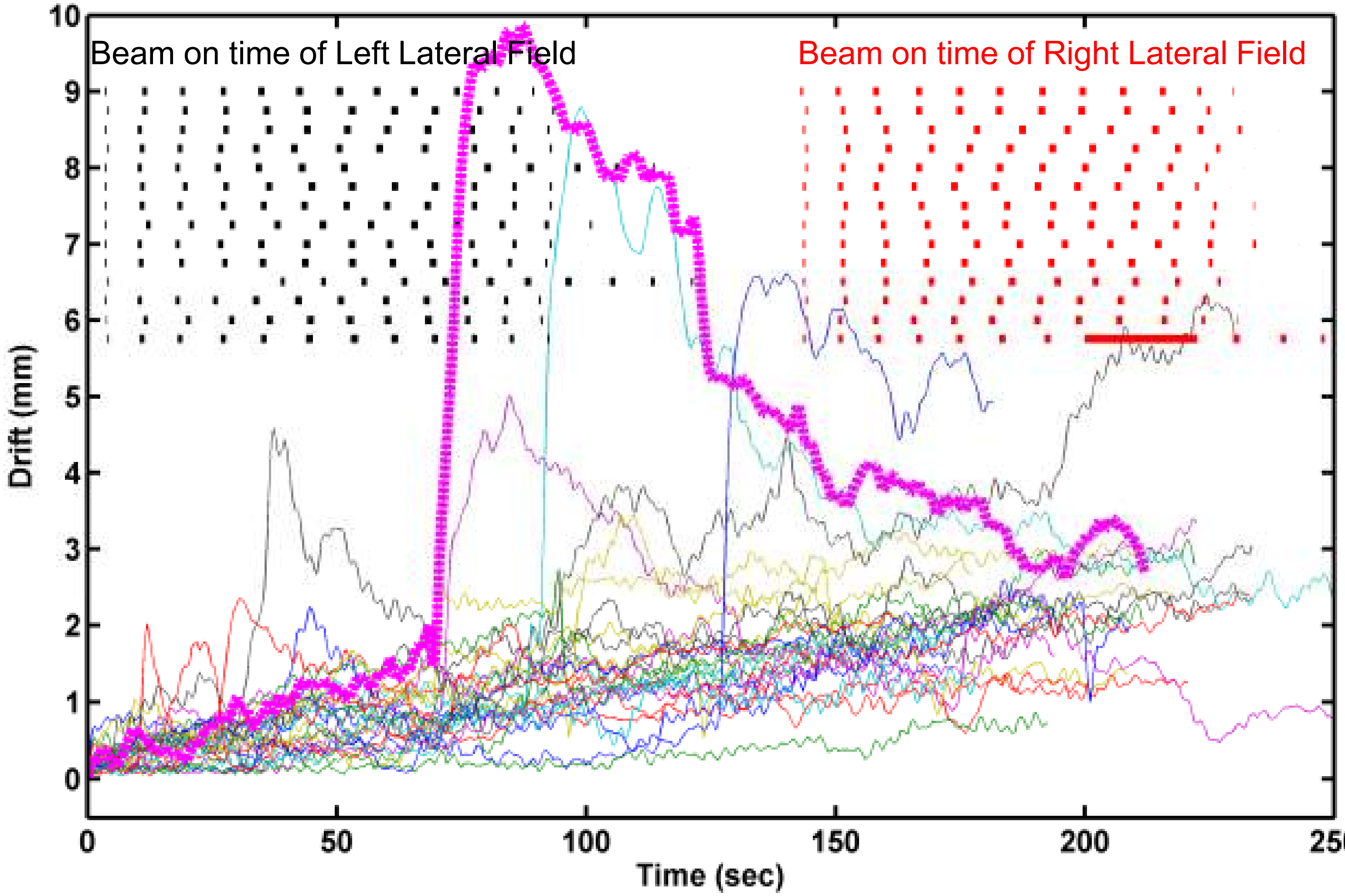
Worst scenario

Both, et. al. IJROBP, 12/2011

Pencil Beam Scanning Technologies

Prostate Drifting and Beam on Time (Calypso)

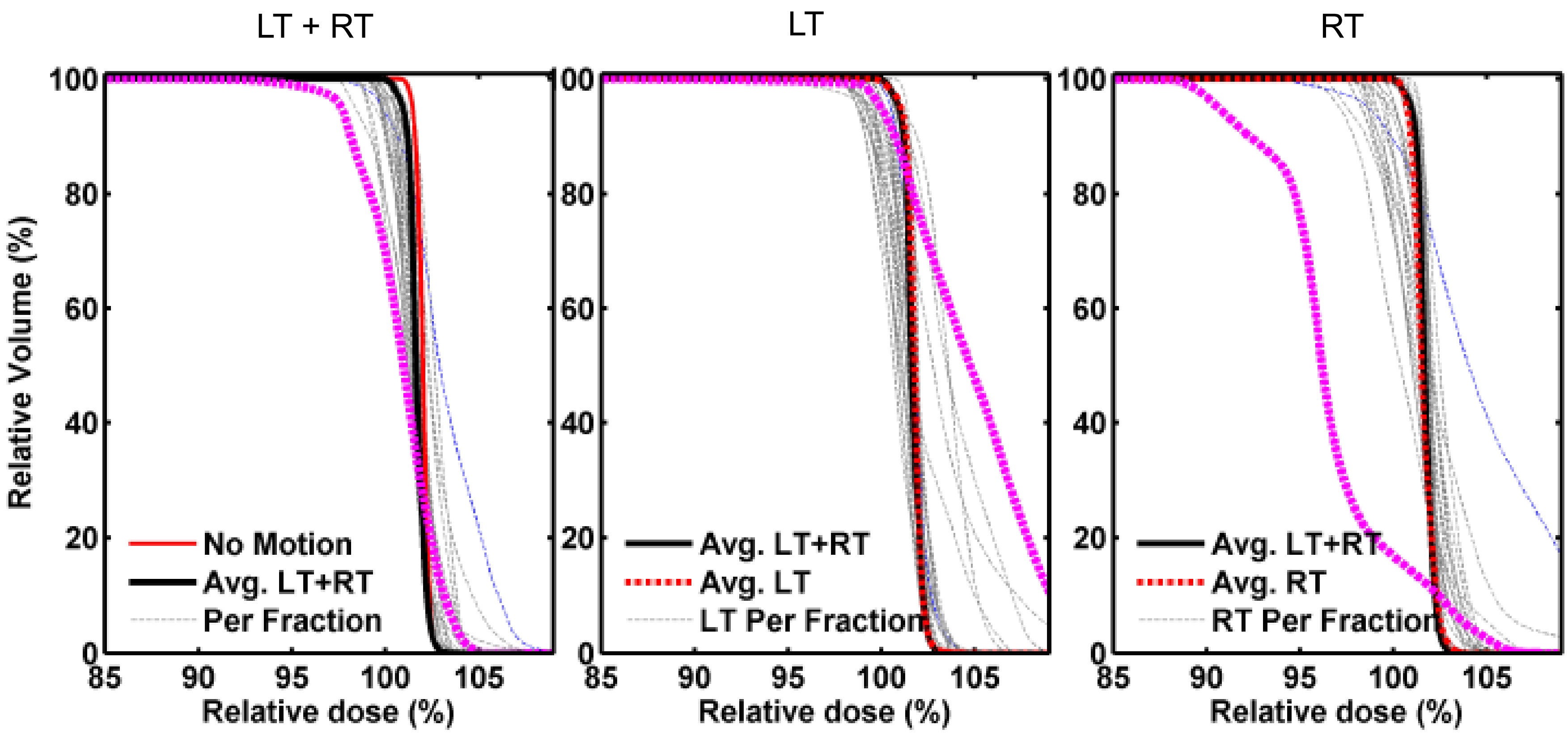
Worst Case Scenario Patient



Pencil Beam Scanning Technologies

DVH of SFUD Plan

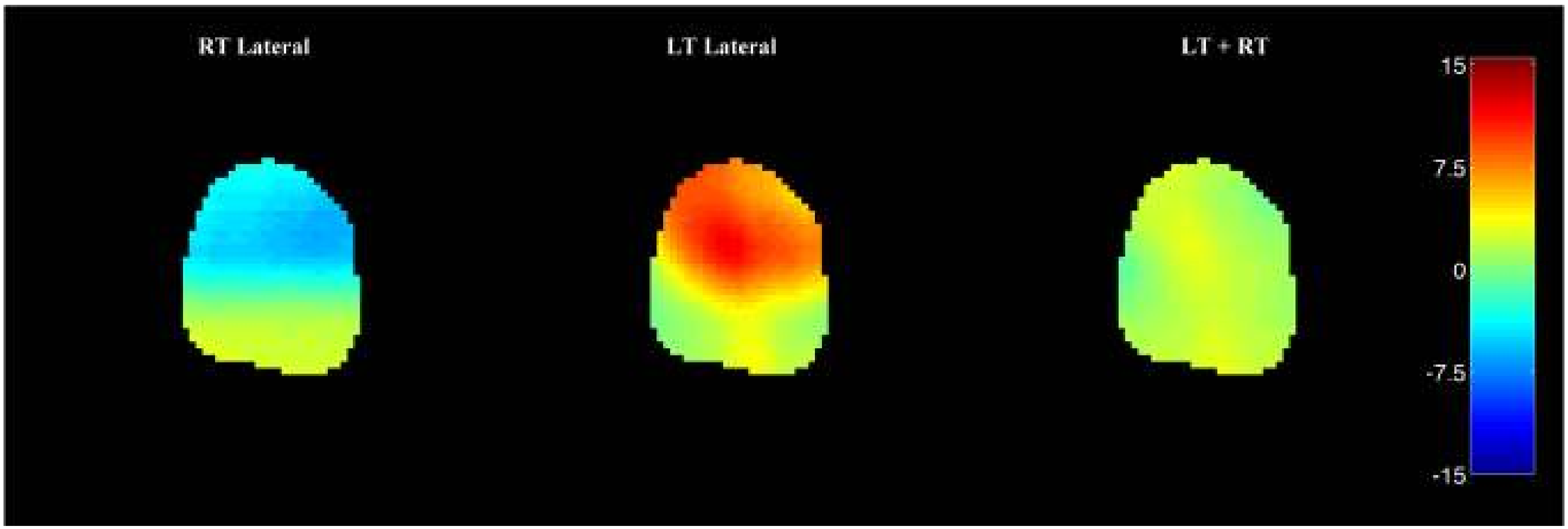
Worst Case Scenario Patient



Pencil Beam Scanning Technologies

Interplay Effect on Dose Distribution

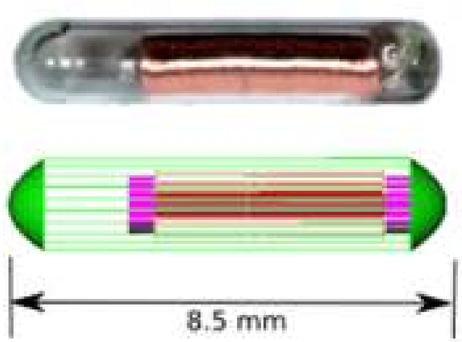
Worst Case Scenario Patient – Worst Fraction

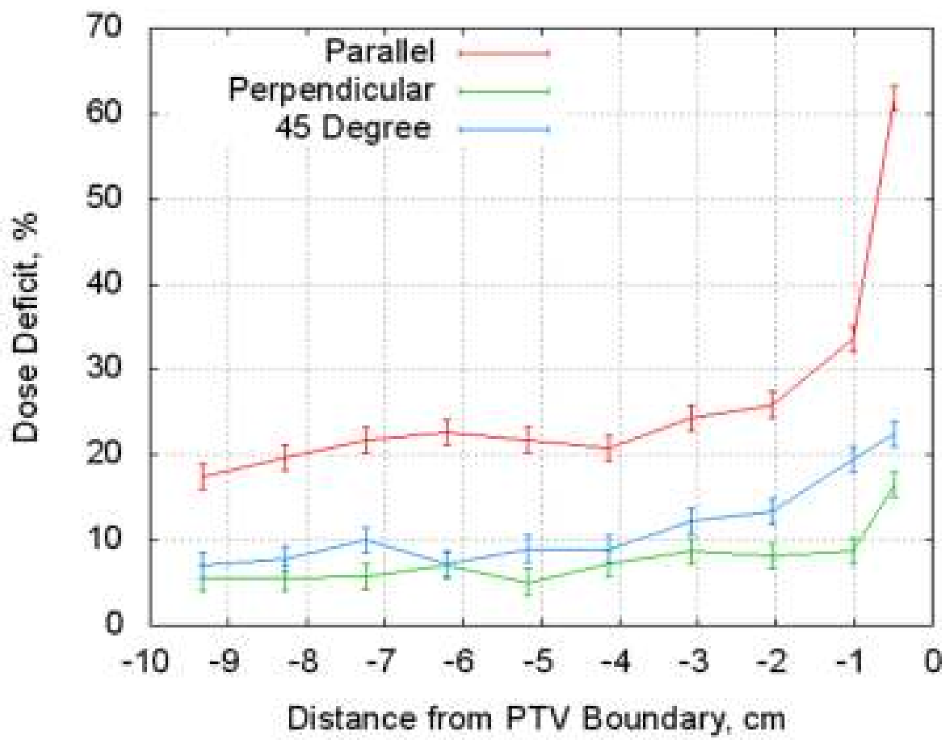


Both S. Proton Treatment Planning, AAPM 2012.
Tang *et al*. Interplay Effect and Prostate PBS Dose Distribution (Manuscript in progress).

Pencil Beam Scanning

Motion management and Tx Delivery: Is Calypso an option?





Max. dose deficit occurring within the PTV from Calypso in a proton beam as a function of the WED from the distal PTV boundary for 3 different beacons orientations with respect to the beam direction.

Dolney D. et al. “Dose Perturbations by Electromagnetic Transponders in the Proton Environment” (submitted manuscript).

Pencil Beam Scanning Technologies

Motion management and Tx Delivery: Calypso

- If a transponder is implanted or migrates to within 5 mm of the PTV boundary, our findings indicate the possibility for greater than 10% dose shadow downstream of the transponder.

- Plan design with multiple beam angles to distribute the shadow over a larger volume, or possibly increasing the dose in the expected shadow region to offset the deficit could work.

- Electromagnetic transponders could be used for patient setup and motion management for proton therapy provided some guidelines regarding their placement and orientation with respect to the beam can be met.

Proton Treatment Planning & Delivery Issues

Summary

- Uncertainties have a significant impact on dose distributions actually delivered and may affect outcome
- It is KEY to educate ourselves about the impact of uncertainties and how we account for them in planning process
- Proton RT is very different from Photon RT, as Proton RT requires site dependent implementation.
- Once we solve the problems related to PBS deployment, it may lead to better outcome in RT.

Thank You

Acknowledgements:

Penn Radiation Oncology