Unveiling pencil beam proton therapy

Jan 8, 2024

Chengzhu Zhang

Acknowledgement

RWJBarnabas HEALTH

Dr Yue (Chief)

Dr Ke Nie (PD)

Rihan Davis (Mentor)

Dr Xiao Wang (Mentor)

NEW YORK PROTON CENTER

Dr Haibo Lin (Chief)

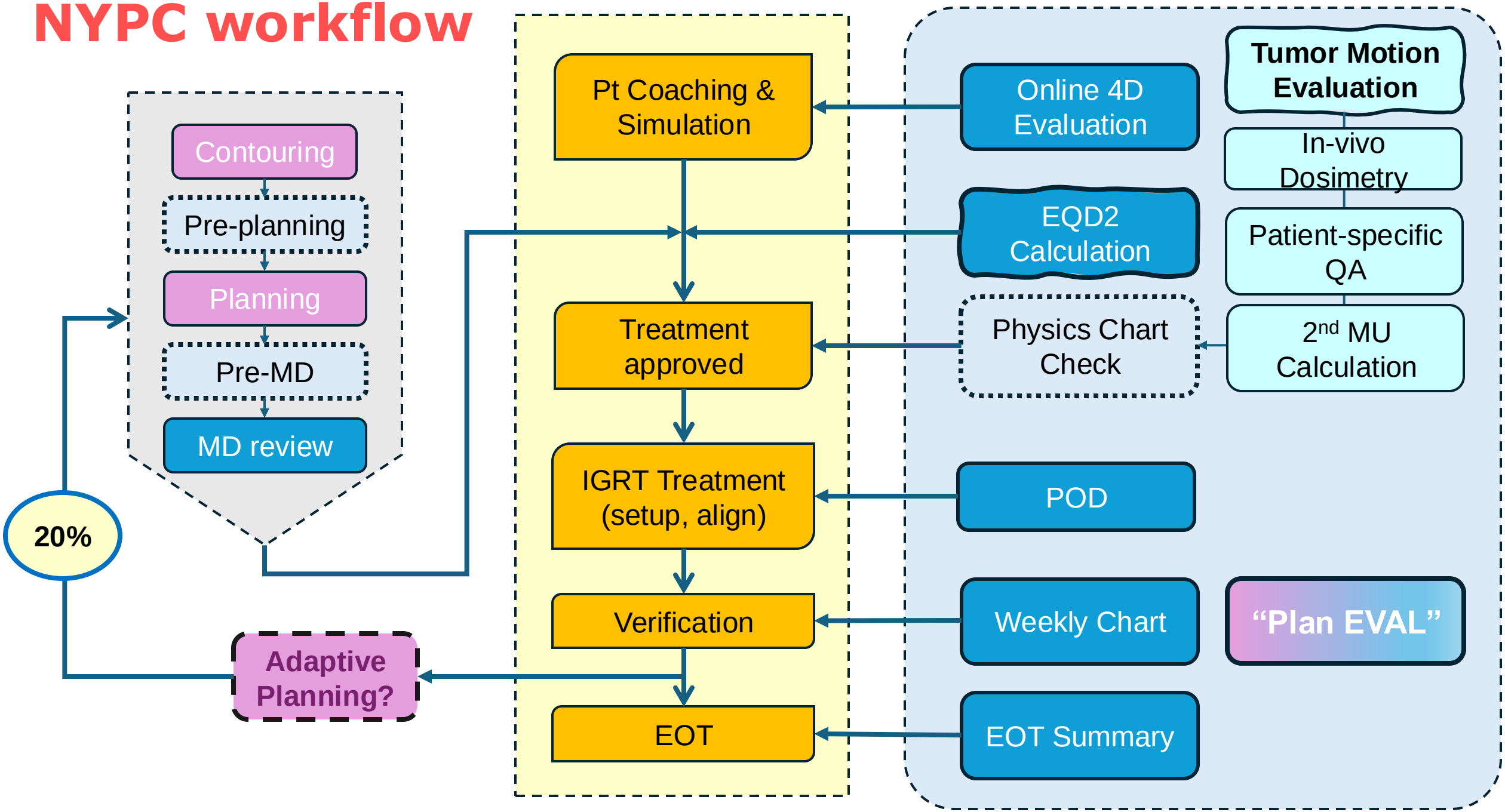
Dr Alex Shouyi Wei (Mentor)

Lee Xu (Planning Physicist)

Peter Park (Dosimetrist)

Treatment room (TR1) @ NYPC

NYPC workflow



Why proton therapy?

The superiority of proton therapy is in question.

No significant improvement in treating prostate cancer (COMPPARE trial)

No significant improvement in treating NSCLC (10-year follow up)

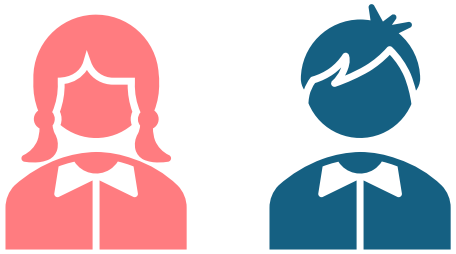
Proton beams have physical limitation.

9-field IMRT is the gold standard for spine SBRT to spare the cord.

Large uncertainty and potential adverse effect.

Expensive!!!

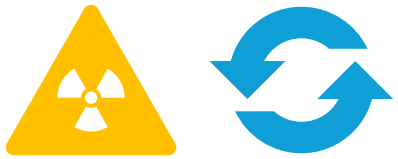
Proton therapy territory



Pediatric Patients

Bone growth
Symmetry
Lower dose

TL SPINE – 18~20 Gy
C spine not much of concern



Reirradiation

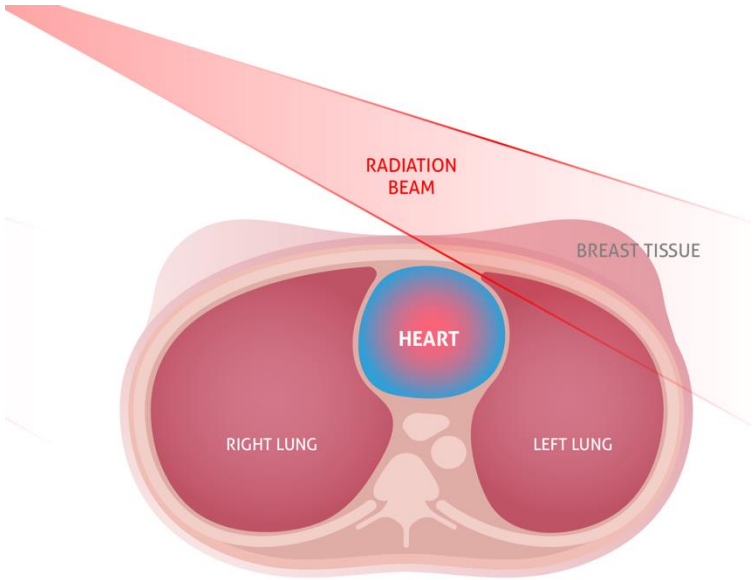
Image registration
Dose deformation
EQD2 evaluation

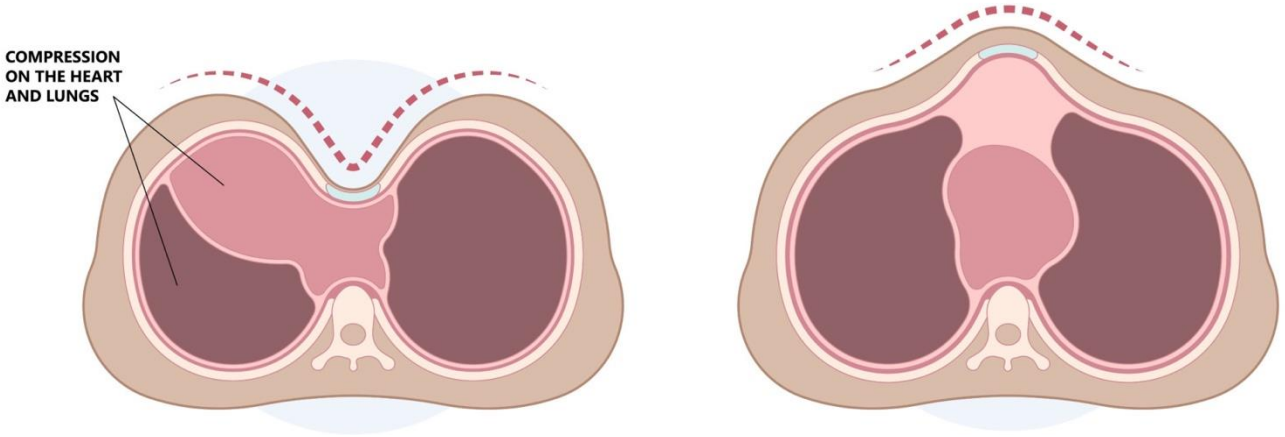
>40% patients have prior RT

Challenging anatomy

Mesothelioma
Cranial-spinal
Pectus Excavatum

Challenging anatomy: pectus excavatum

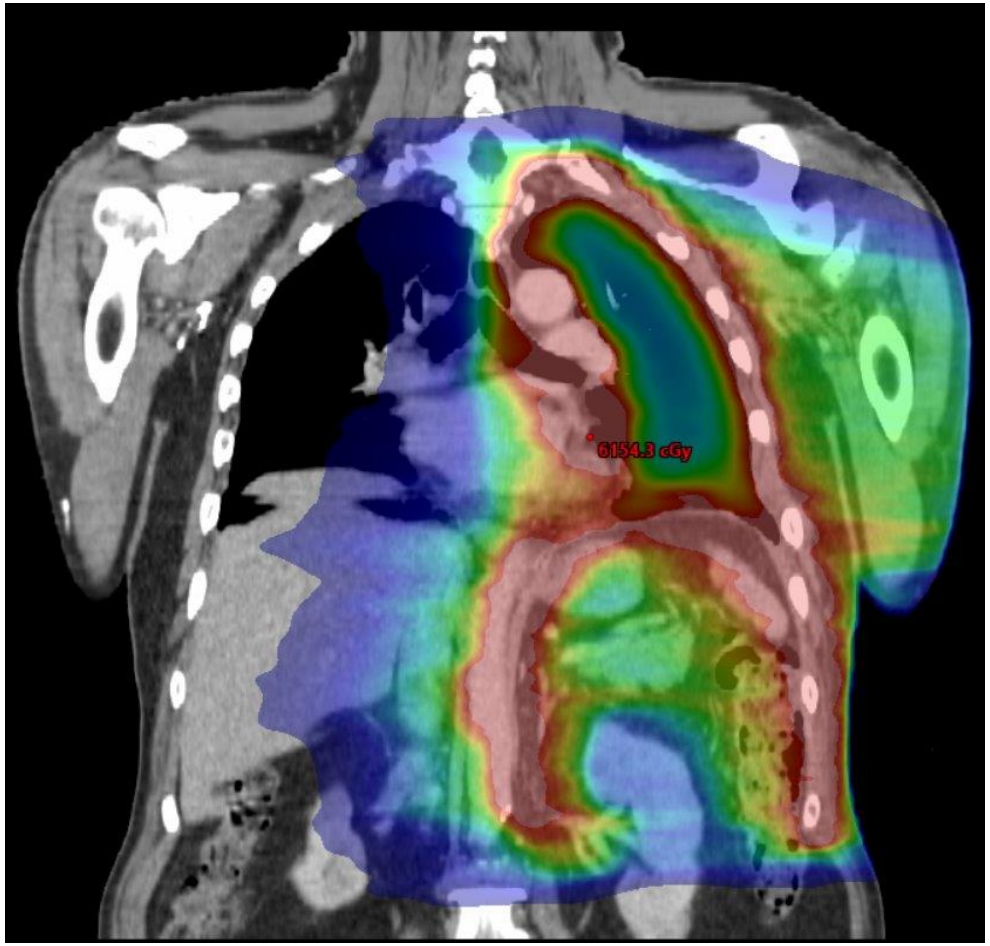




pectus excavatum **pectus carinatum**

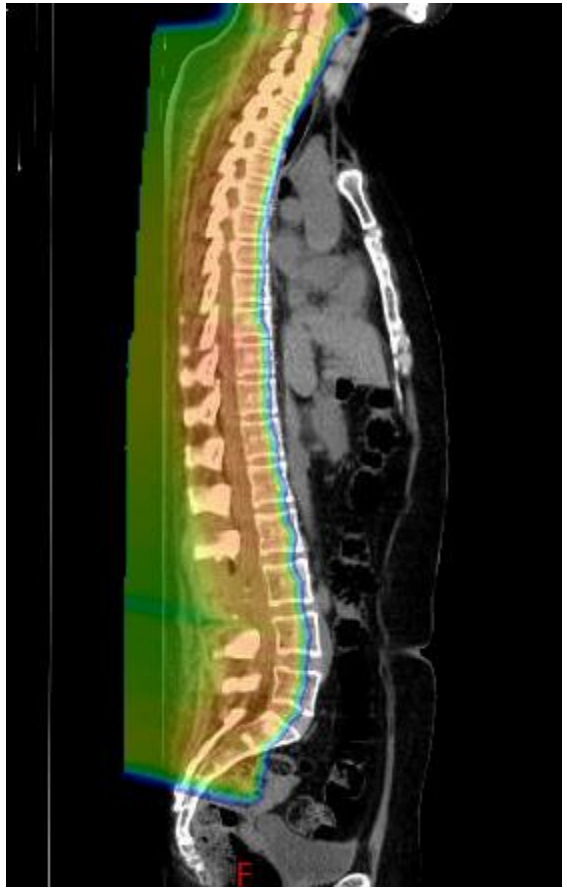
Challenging anatomy: Mesothelioma

Proton

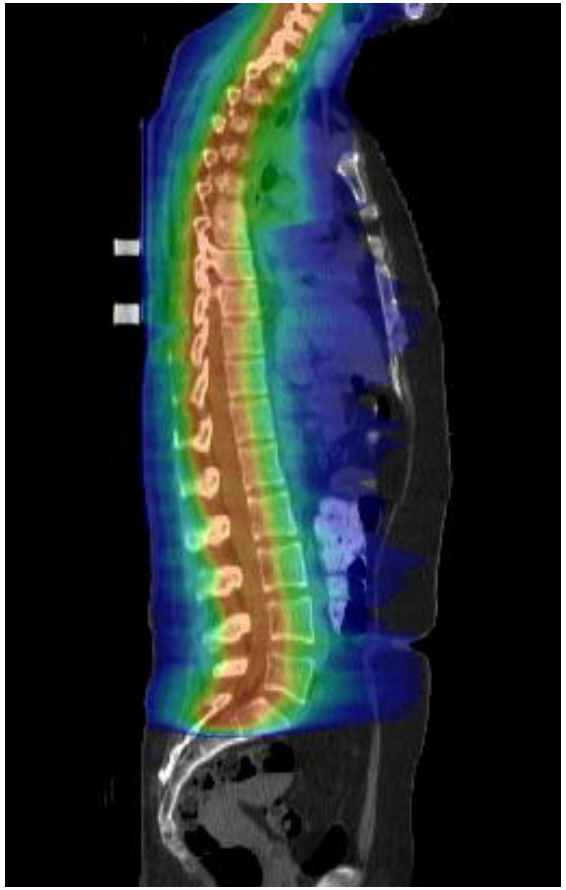


Photon

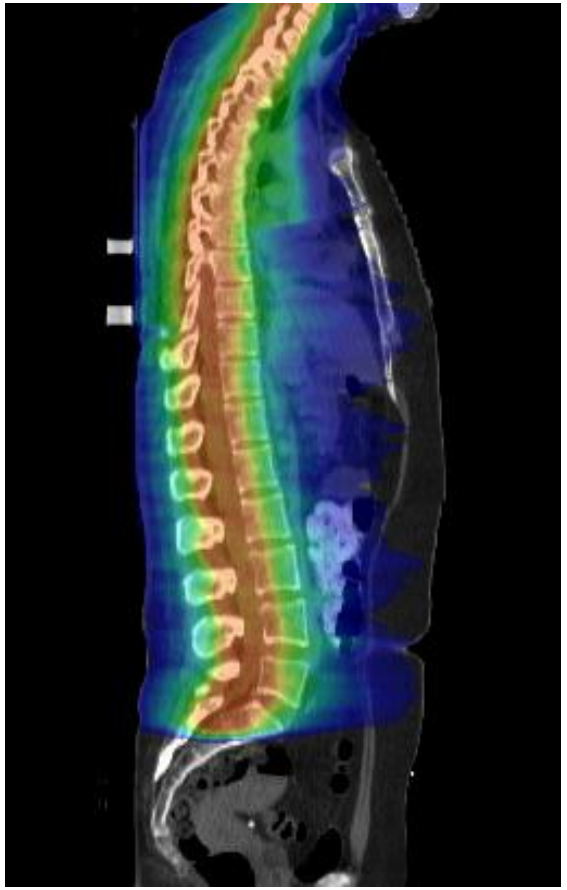
Challenging anatomy: CSI



Proton

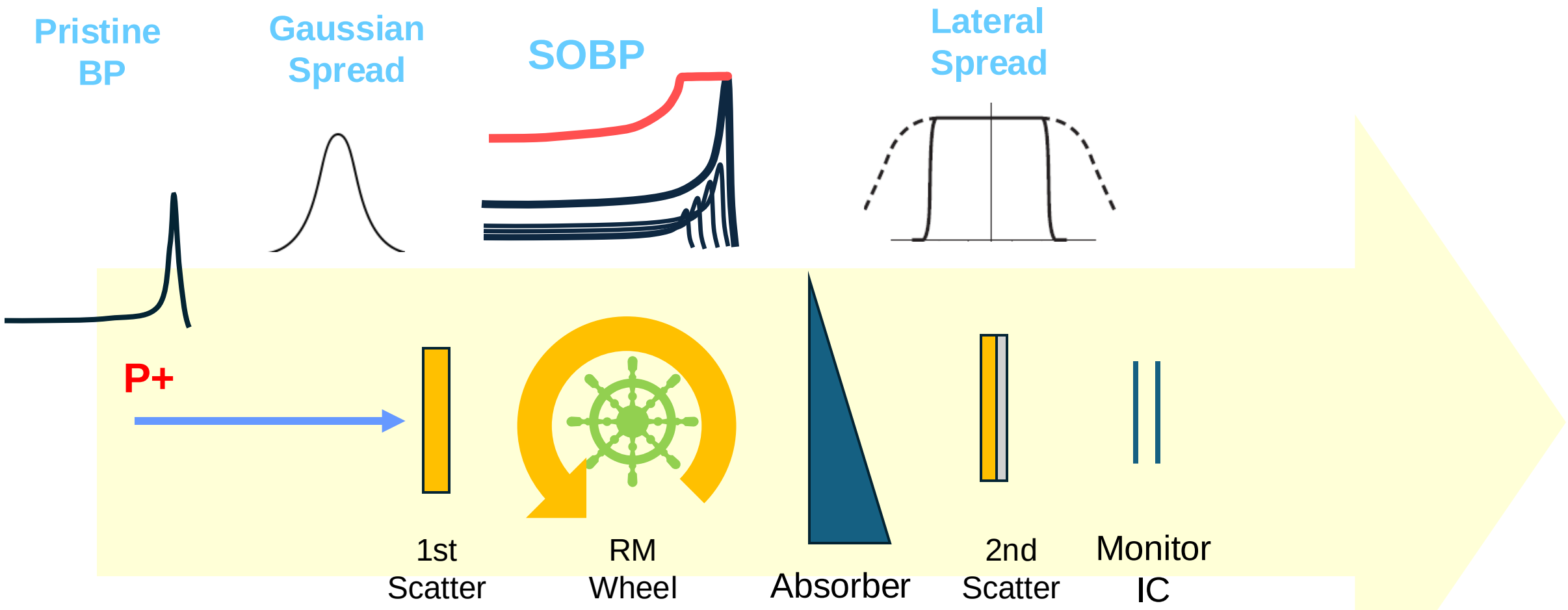


Auto Planning

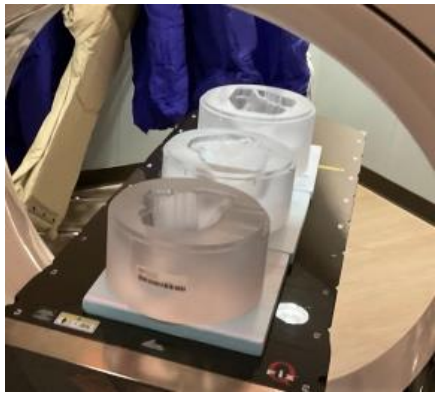


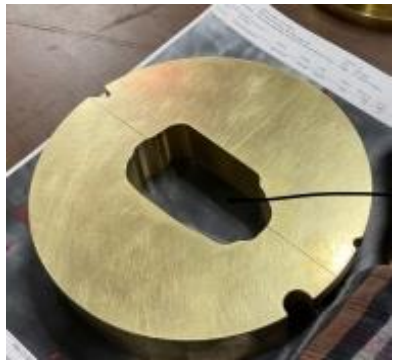
Mannual Plan

Passive Scattering Proton Upstream Beamline

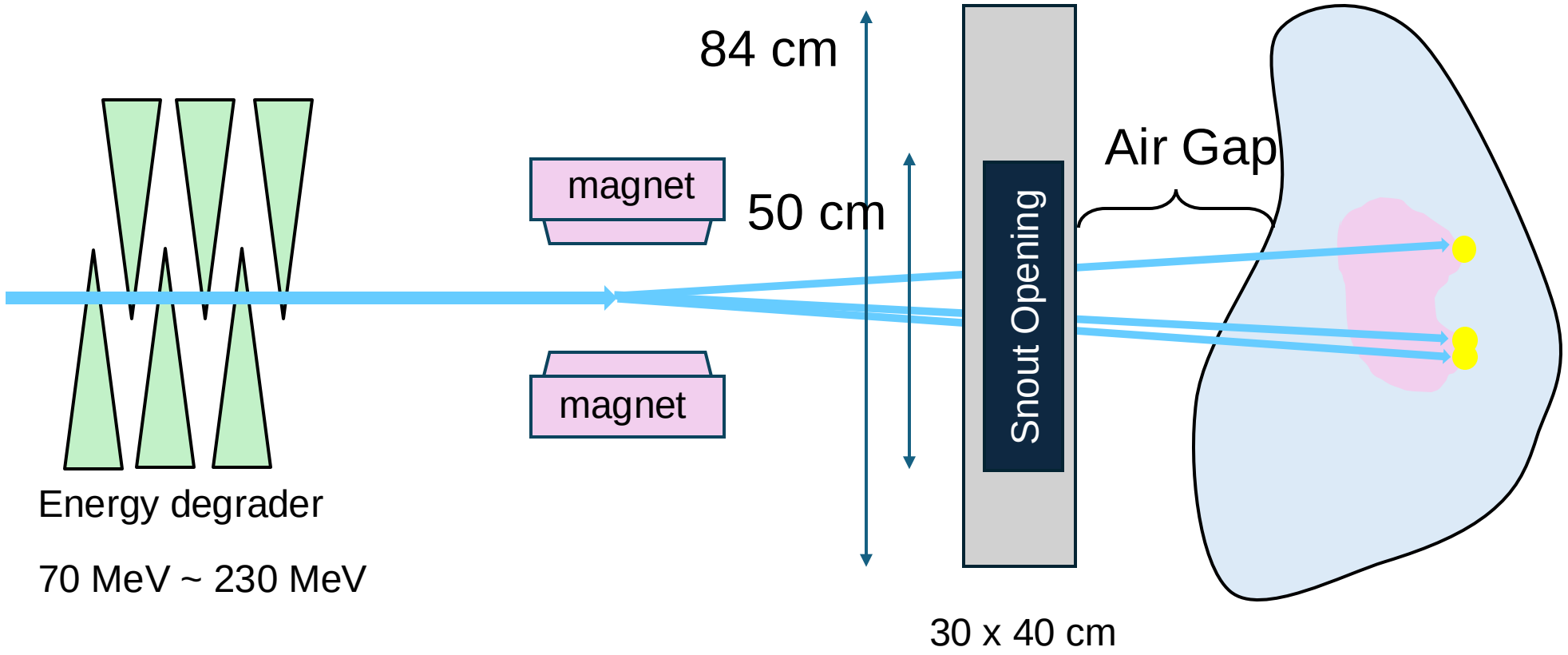


Passive Scattering Proton Downstream Beamline

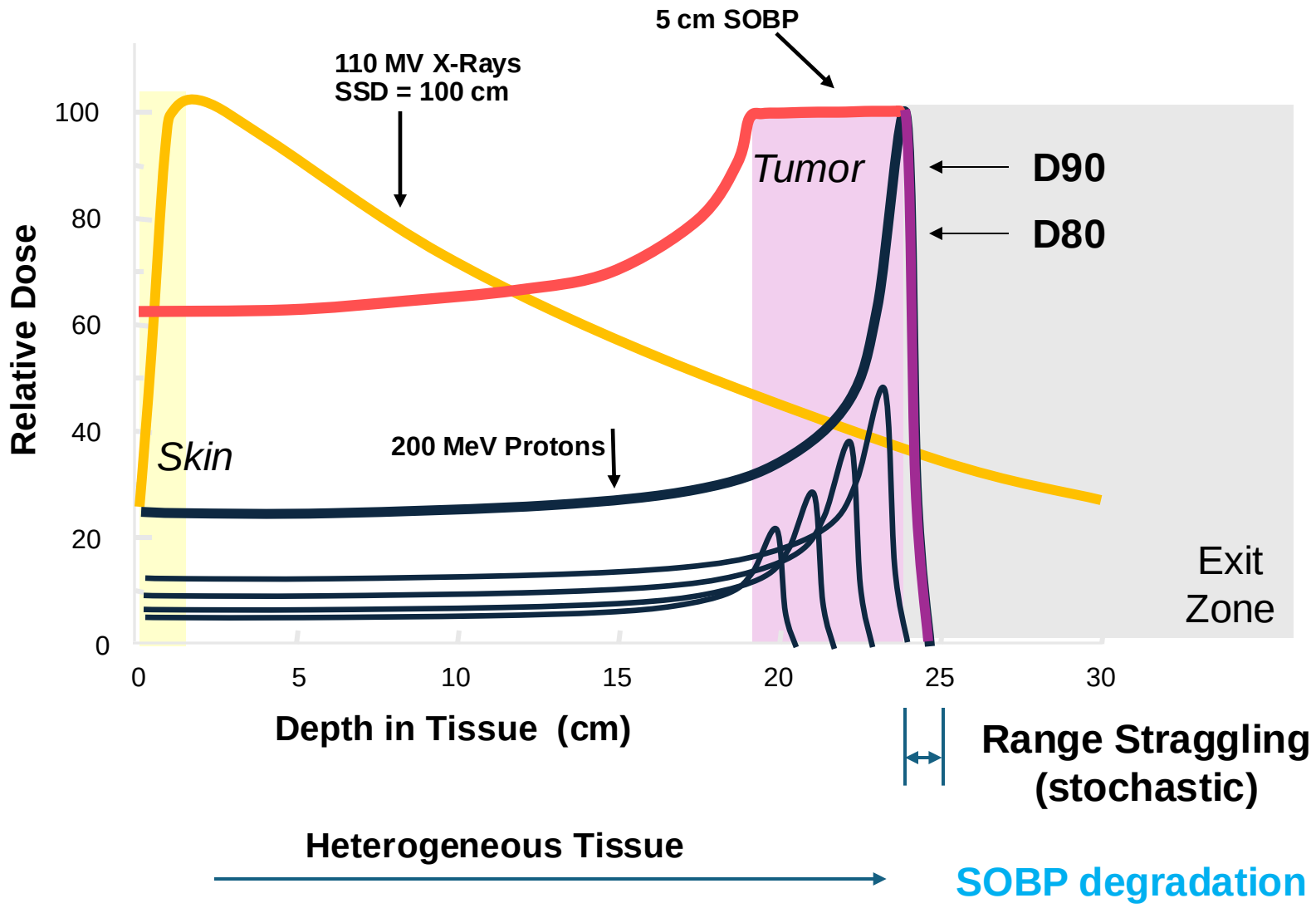




Spot Scanning Proton Beamline

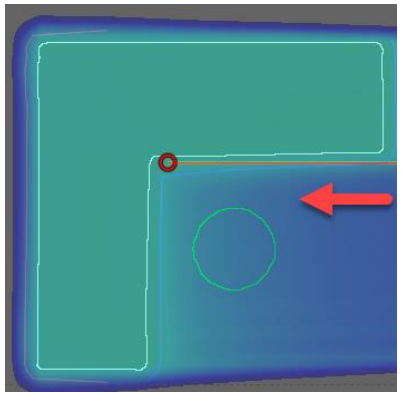


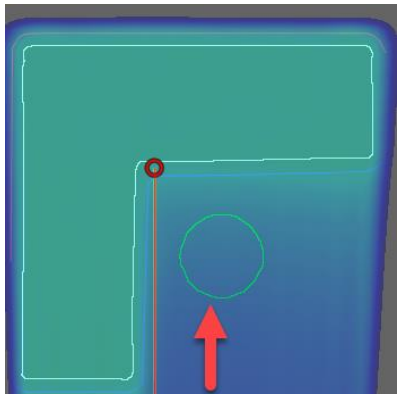
Beam characteristics: distal fall off

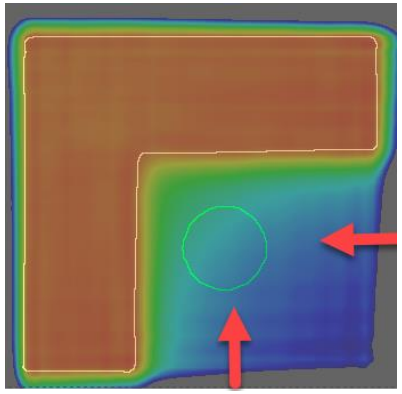


Achieving therapeutic conformity

Single Field Uniform Dose (SFUD)



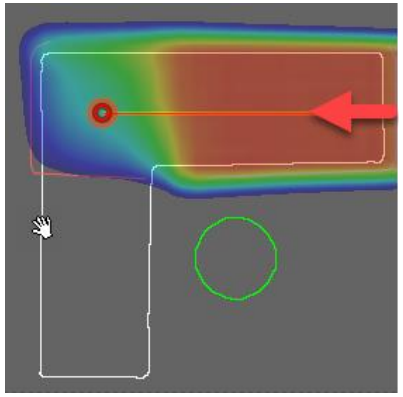


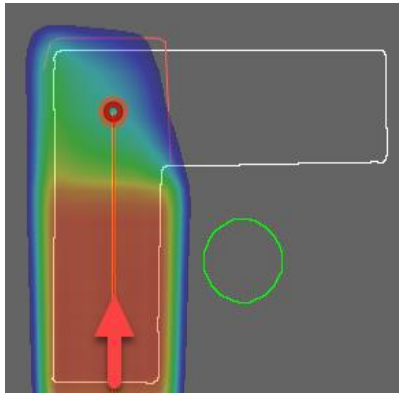


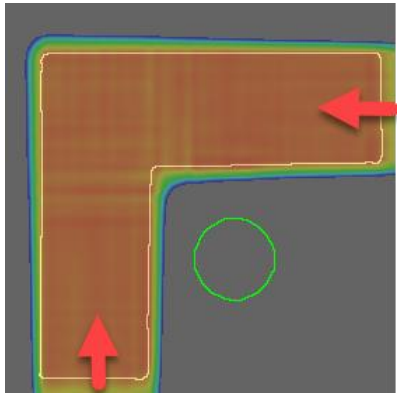
Double Scatter

Spot Scanning

Intensity Modulated Proton Therapy (IMPT)

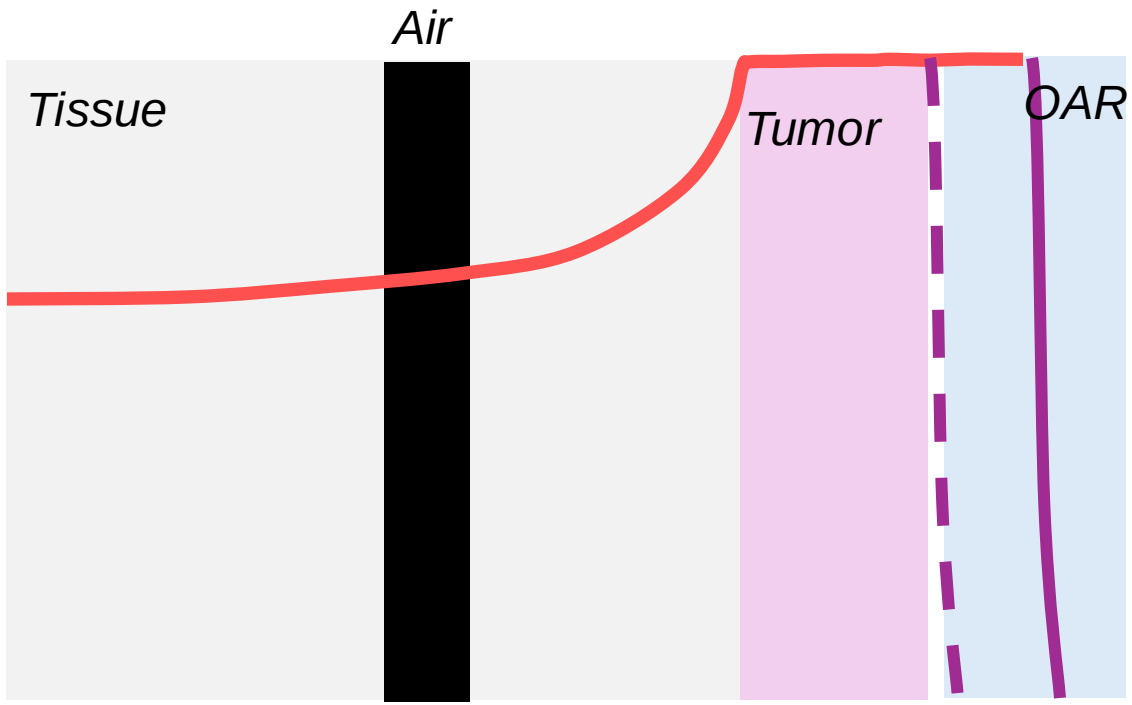




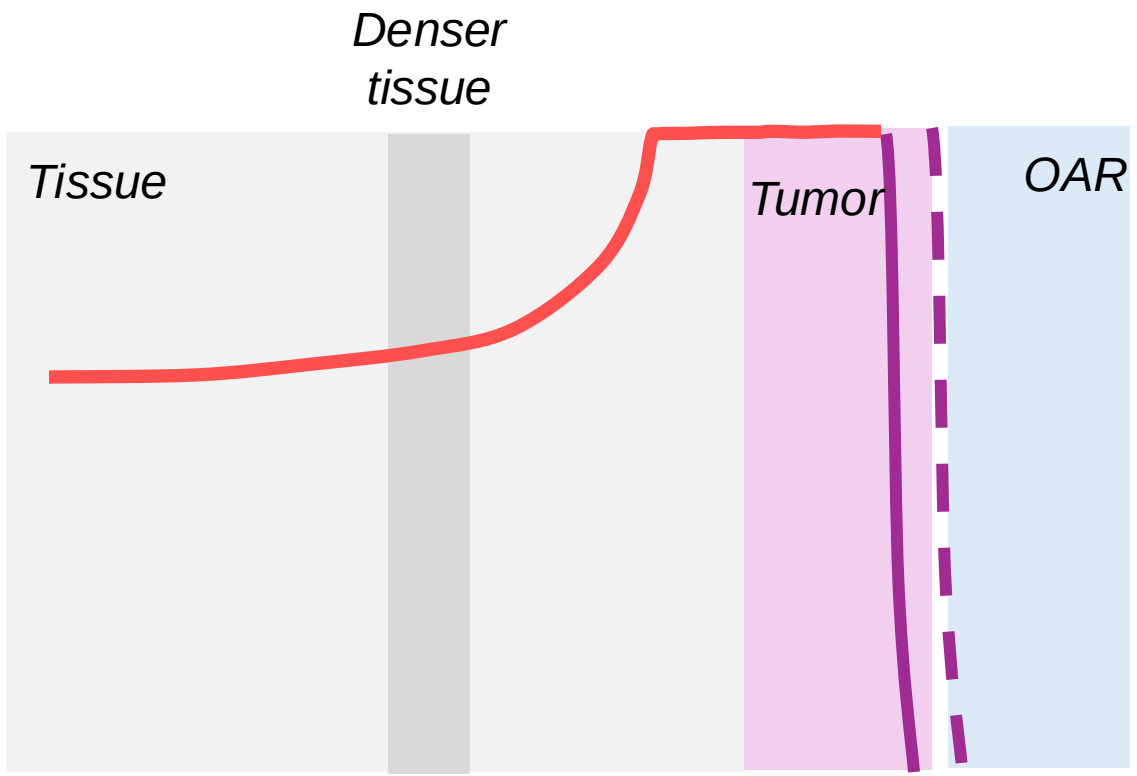


Spot Scanning

Practical consideration: range errors

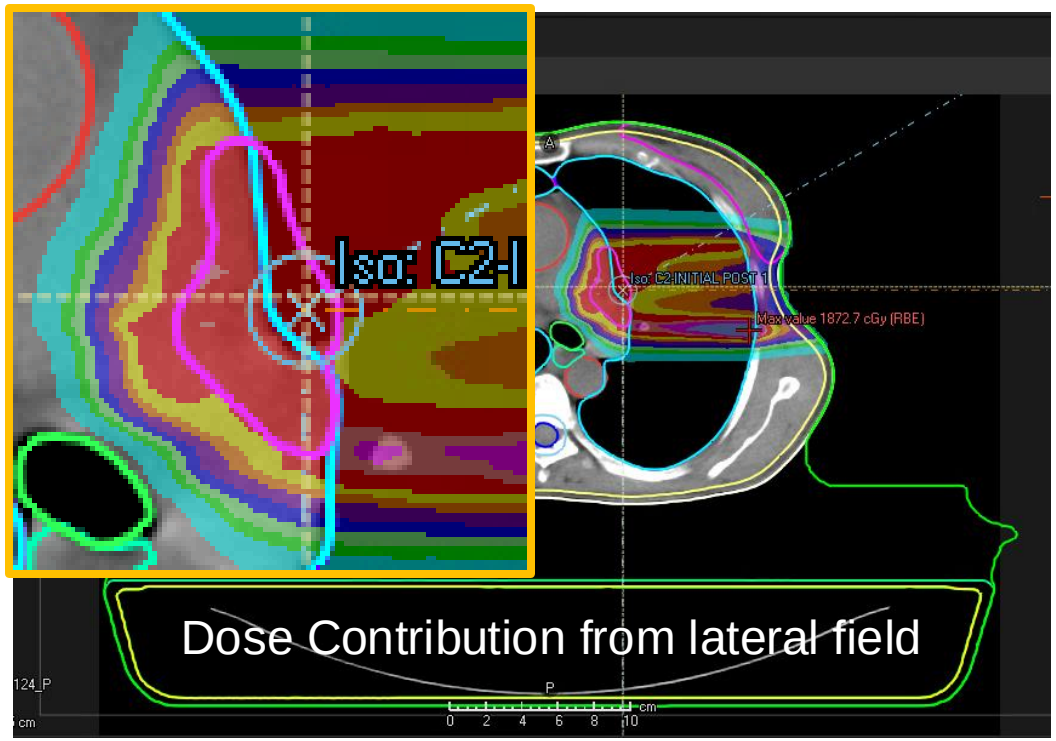


Practical consideration: range errors

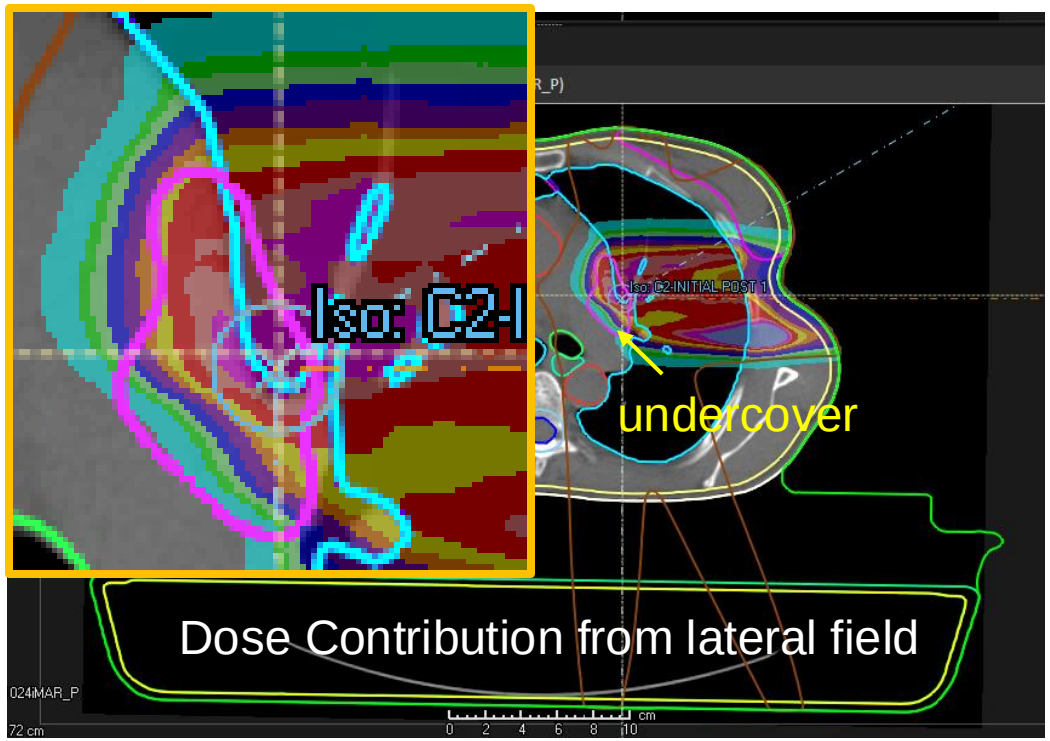


Risks of single field

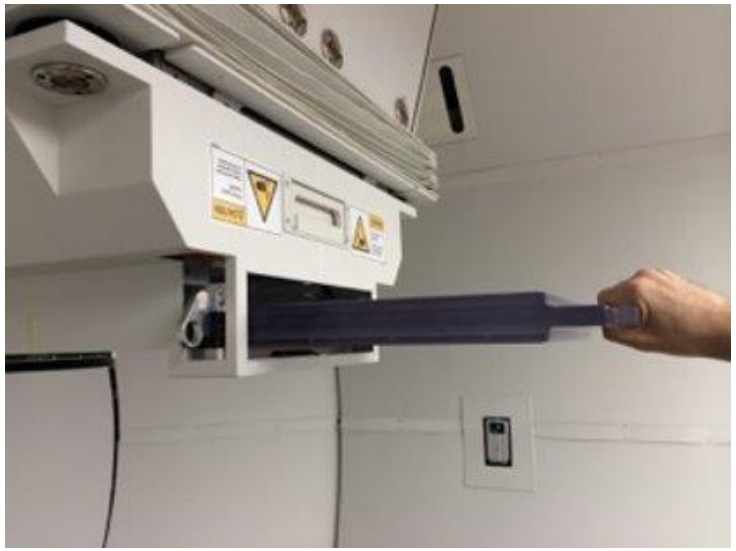
Original Plan

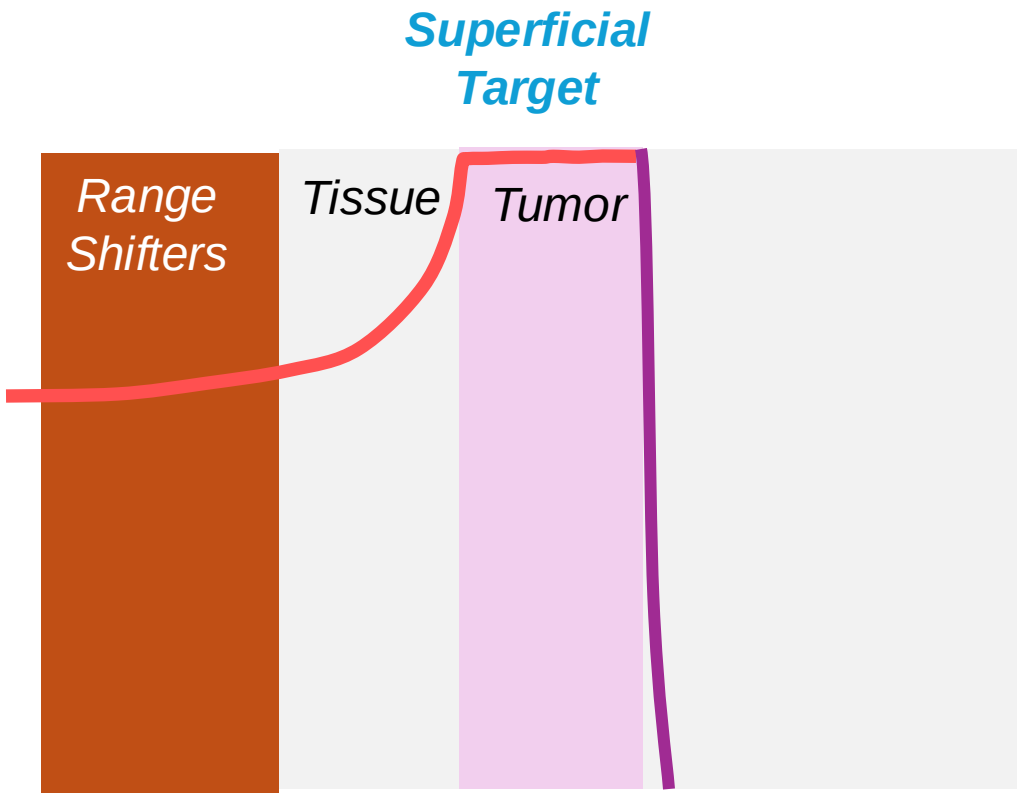


Verification Scan (VScan)



Range Shifters (RS)

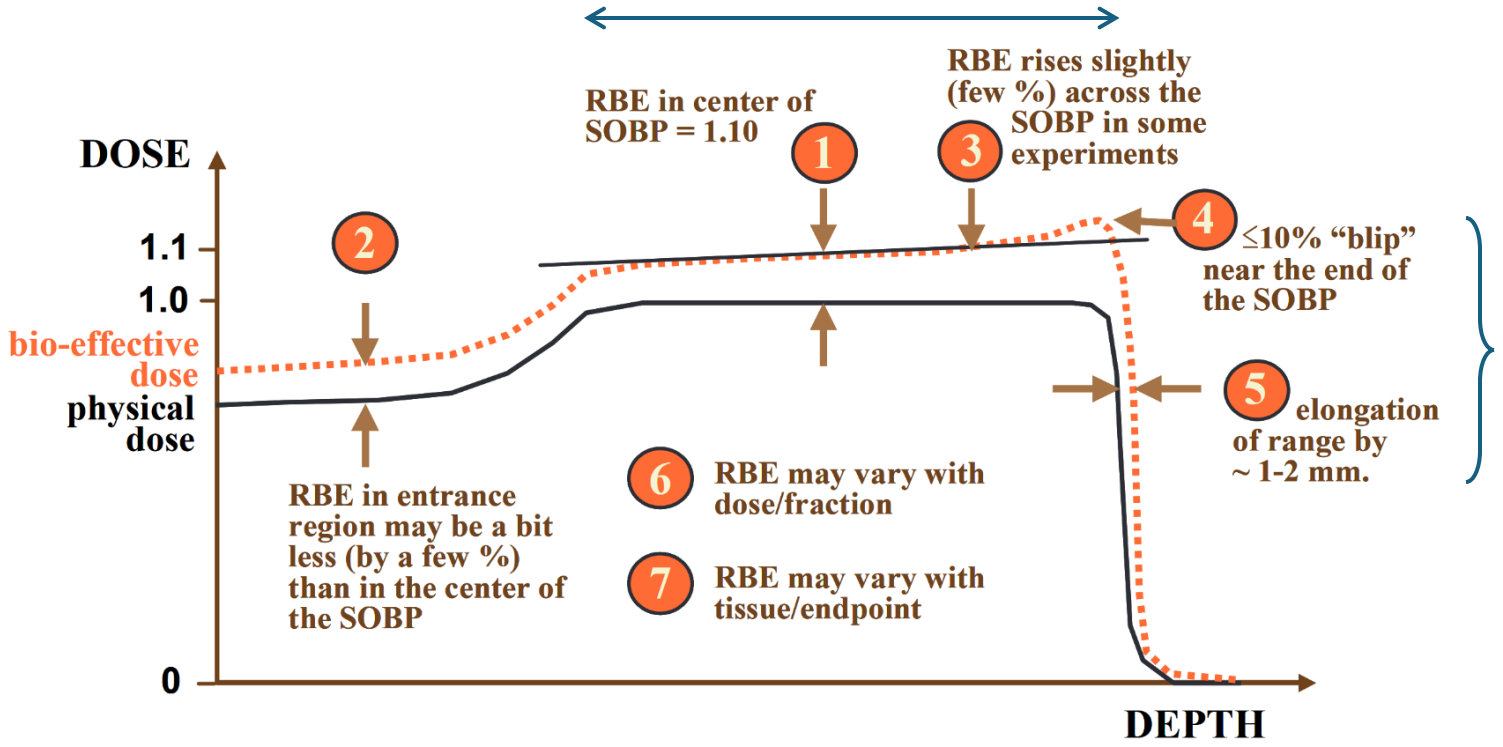




Consideration of biological effect

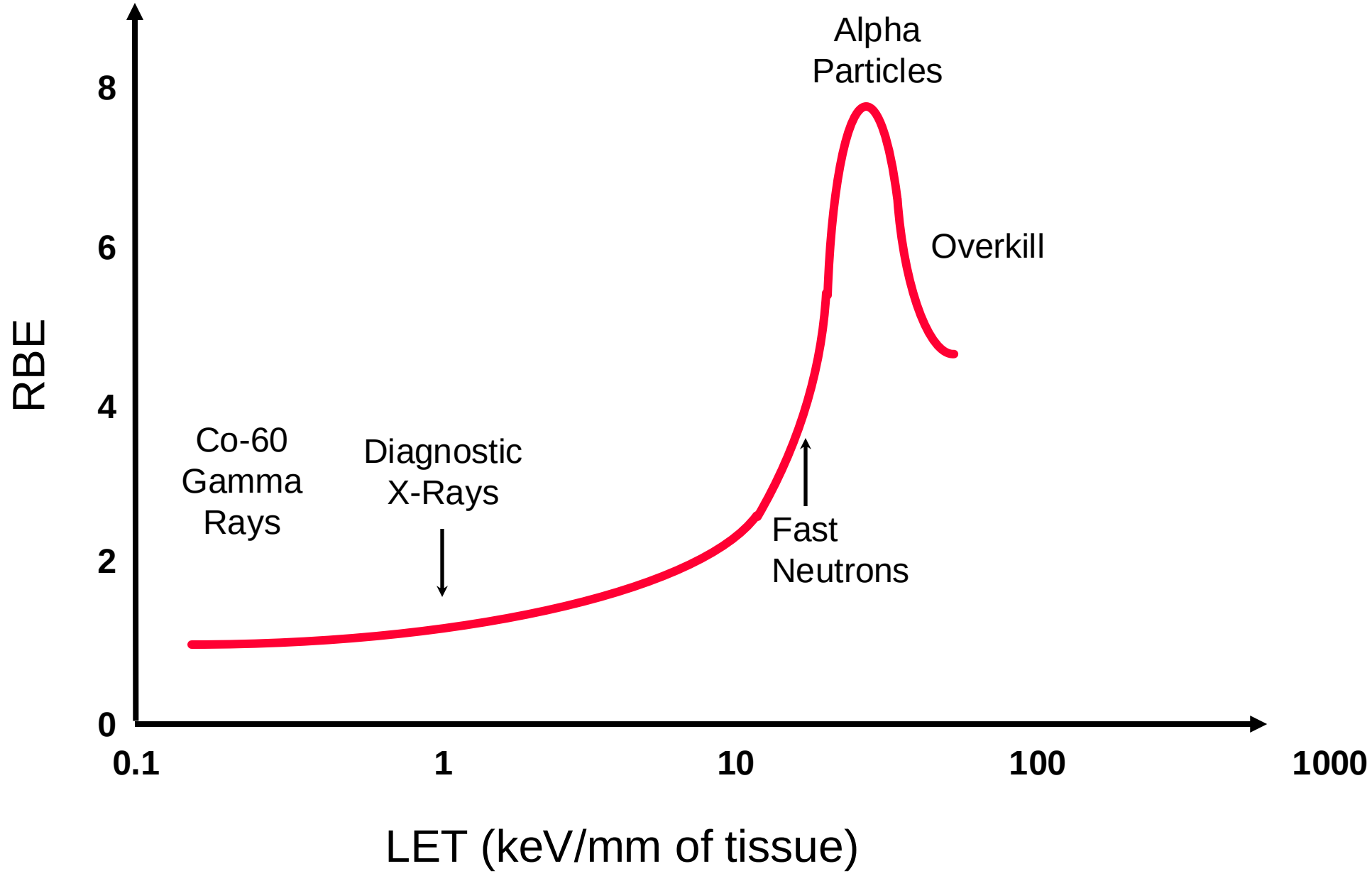
ICRU 78 recommend

RBE value of 1.1

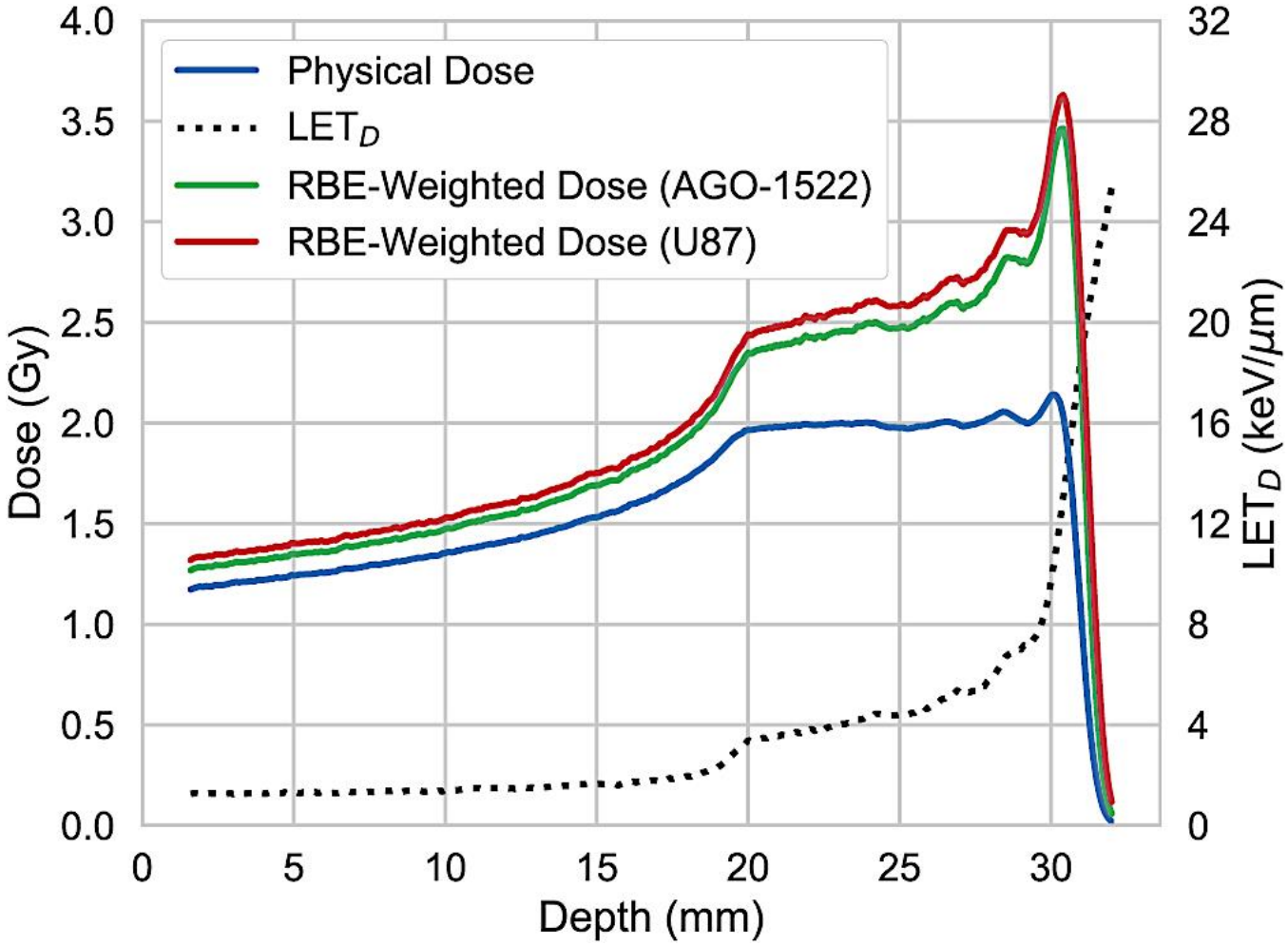


M Goiten, "Radiation Oncology: A physicist's Eye View" @ Springer 2007

Consideration of LET (Qualitative)



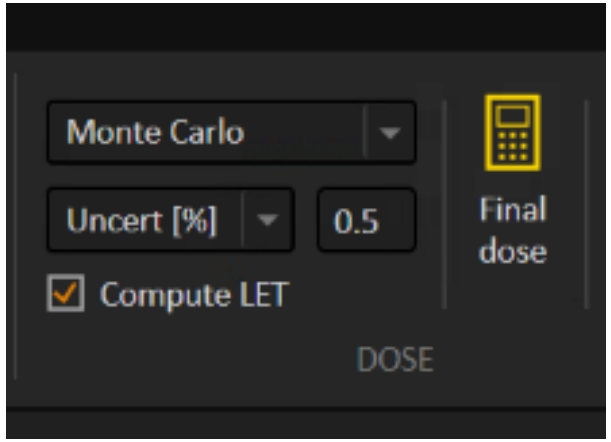
Consideration of Proton LET



Stephen J McMahon et al 2018 Phys. Med. Biol. 63 225009

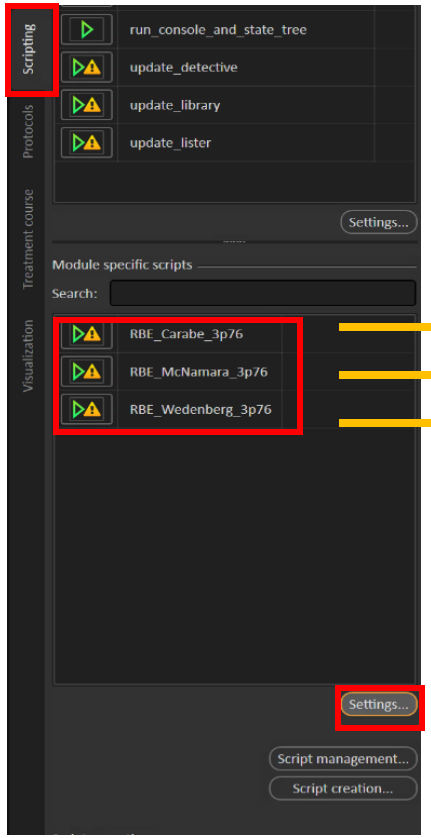
Consideration of LET (Raystation)

LET Calculation



Input

RBE Dose



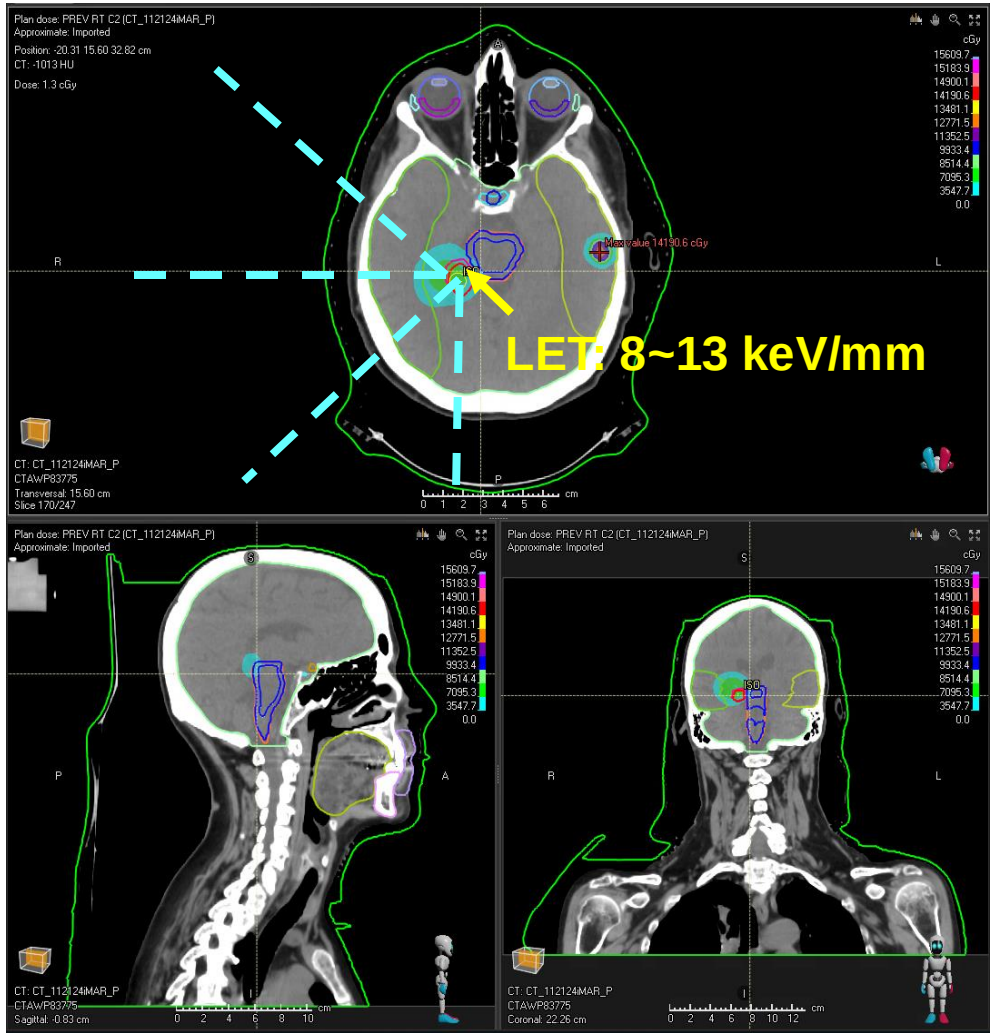
$$\mathrm{RBE}\left[D_P, \left(\frac{\alpha}{\beta_x}\right), \mathrm{LET}_d\right]$$

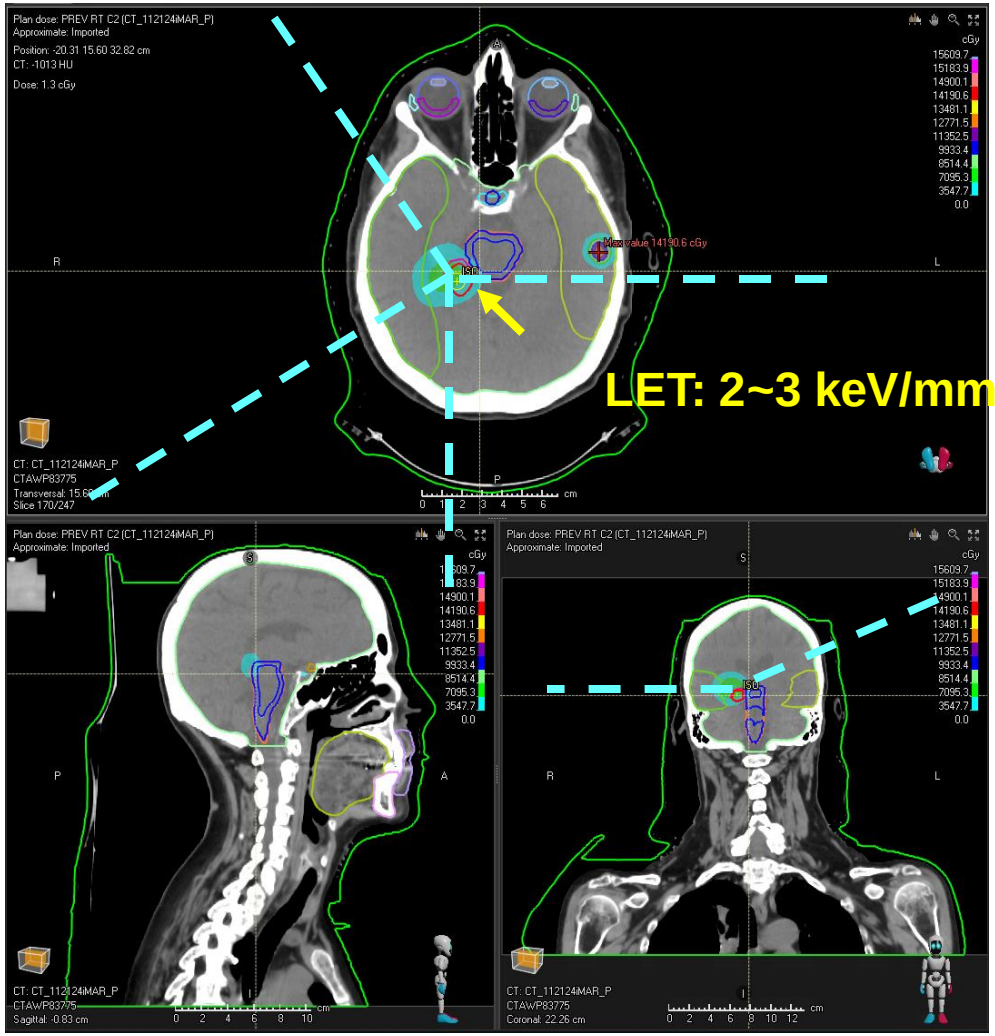
$$= \frac{1}{2D_p}\left(\sqrt{\left(\frac{\alpha}{\beta}\right)_x^2 + 4D_p\left(\frac{\alpha}{\beta}\right)_x\left(0.999064 + \frac{0.35605}{(\alpha/\beta)_x}LET_d\right) + 4D_p^2} \right.$$
$$\left. \sqrt{\left(1.1012 - 0.0038703\sqrt{(\alpha/\beta)_x}\,LET_d\right)^2 - \left(\frac{\alpha}{\beta}\right)_x}\right)$$

- Carabe et al. (2012)
- McNamara et al. (2015)
- Wedenberg et al. (2013)

α/β ratio =3.76

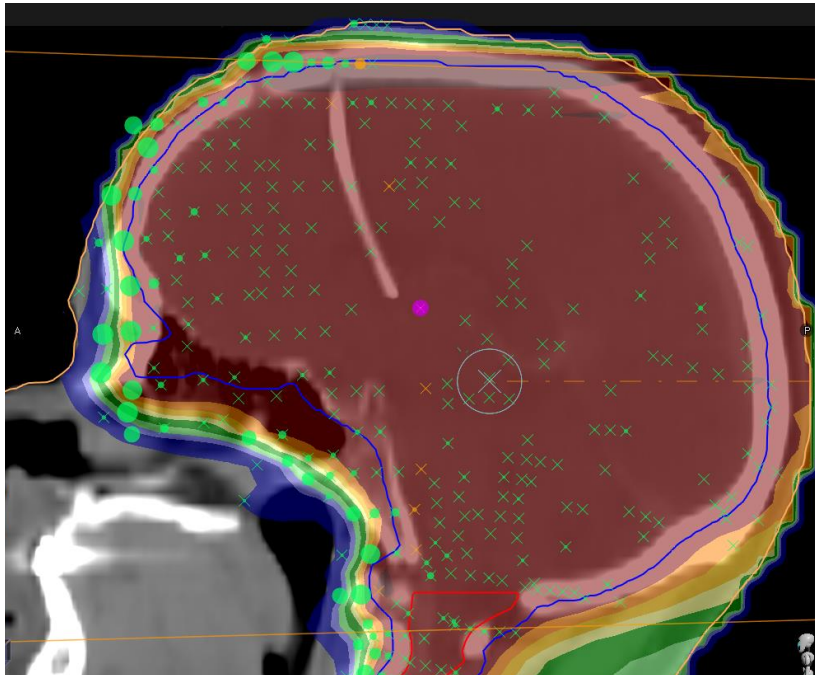
Consideration of LET in treatment planning



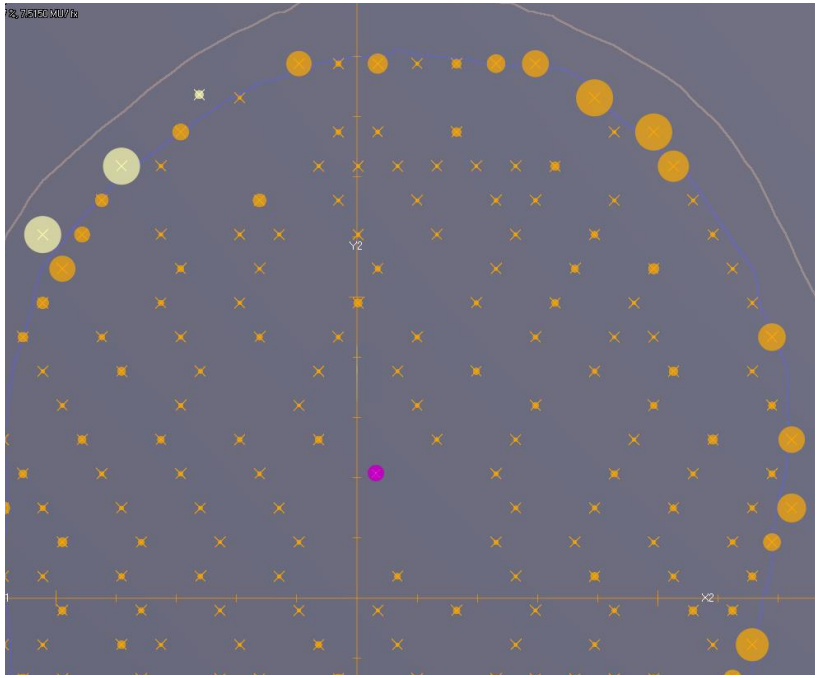


Consideration of Bragg Peak location

Bragg Peak in 2D CT slices

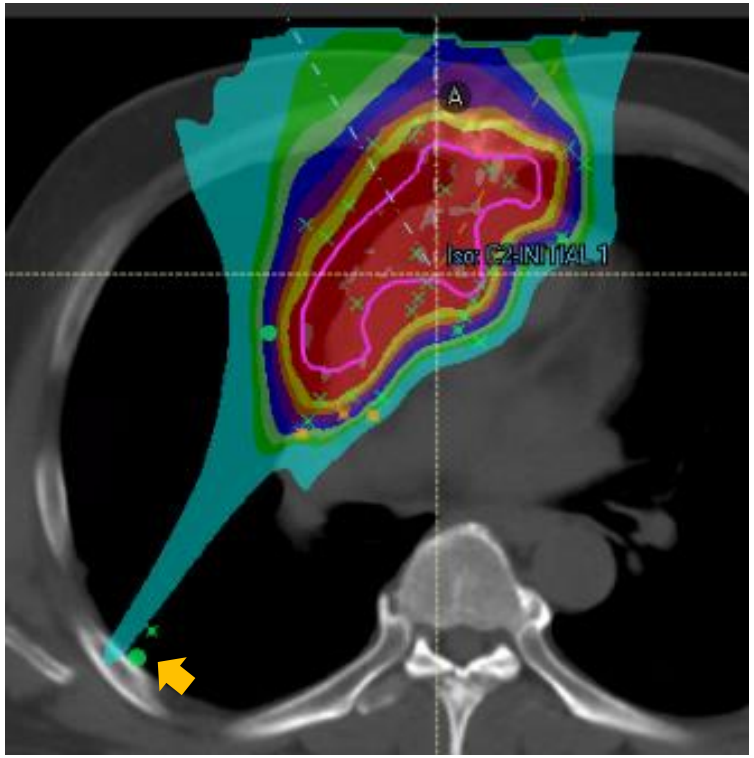


Spots in BEV

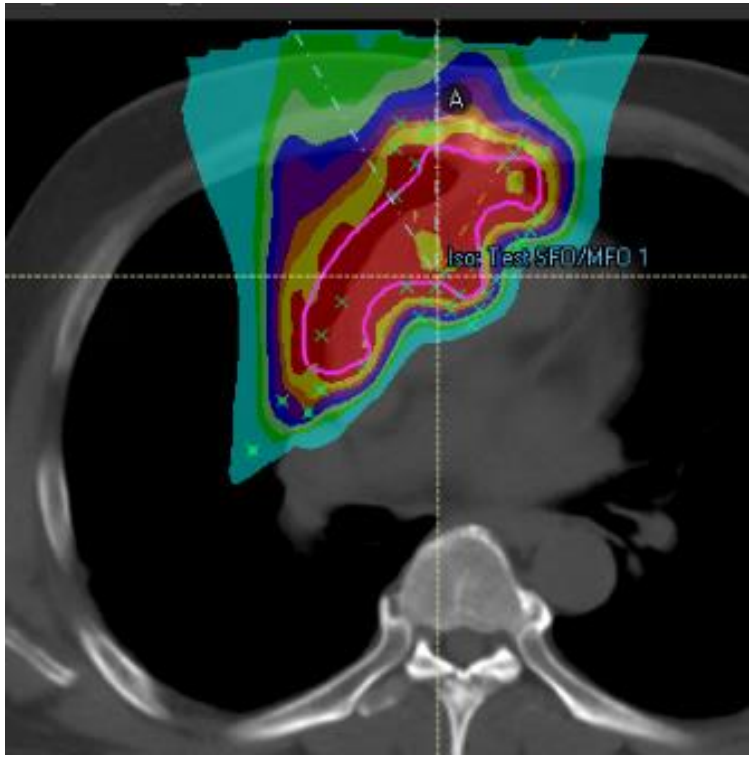


Consideration of Bragg Peak location

SFUD Robust Planning



IMPT Robust Planning



Beam characteristics: lateral penumbra

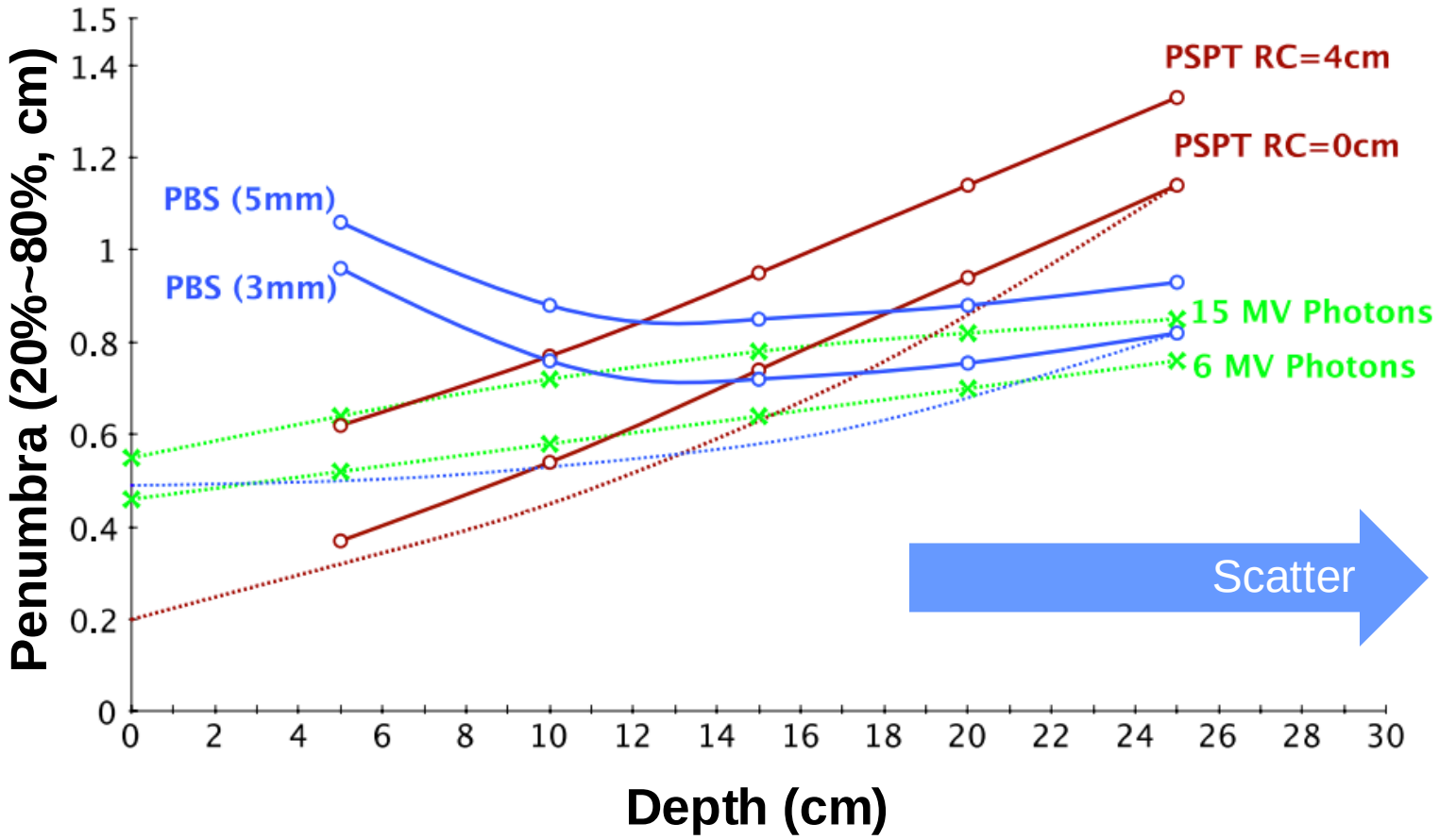
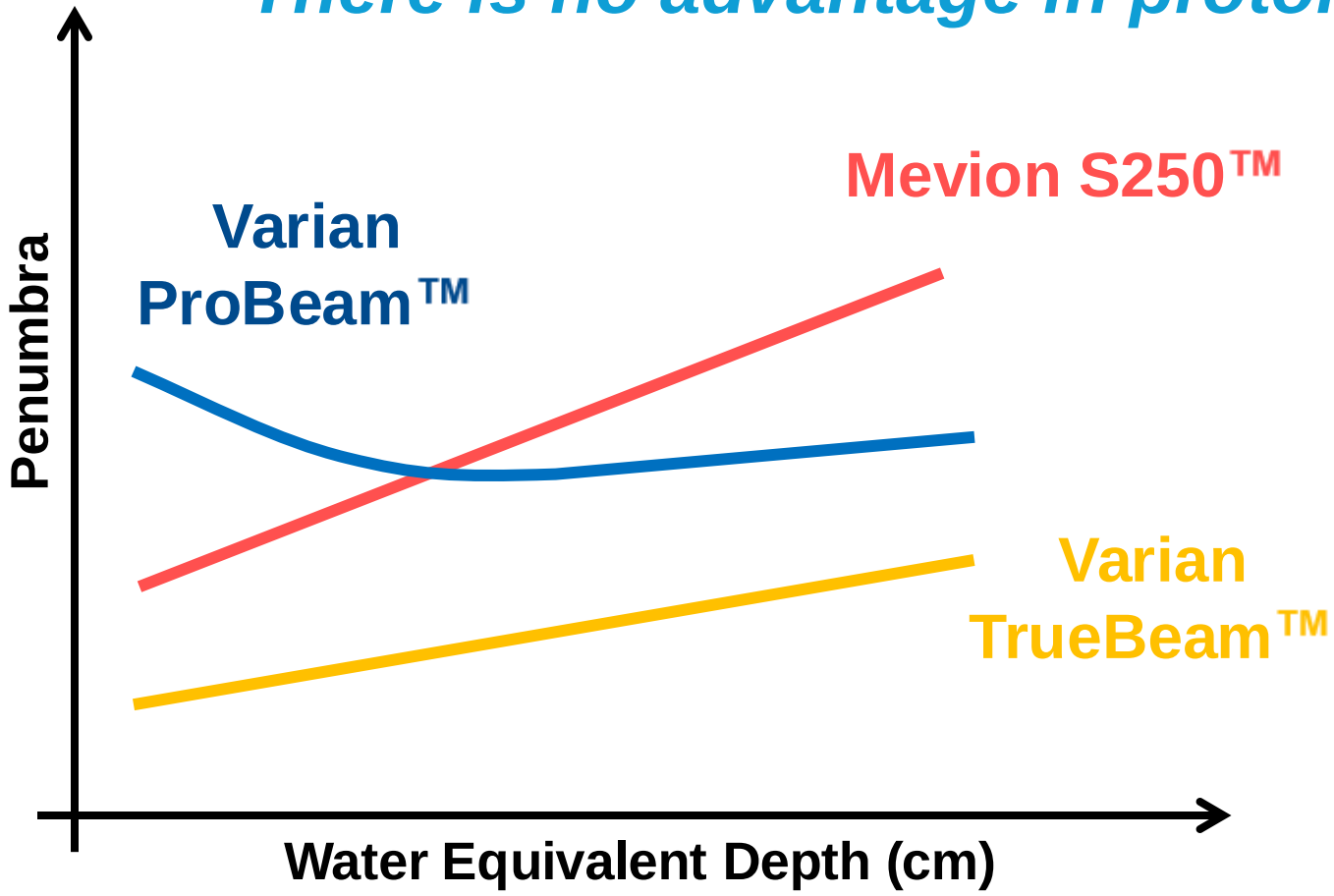


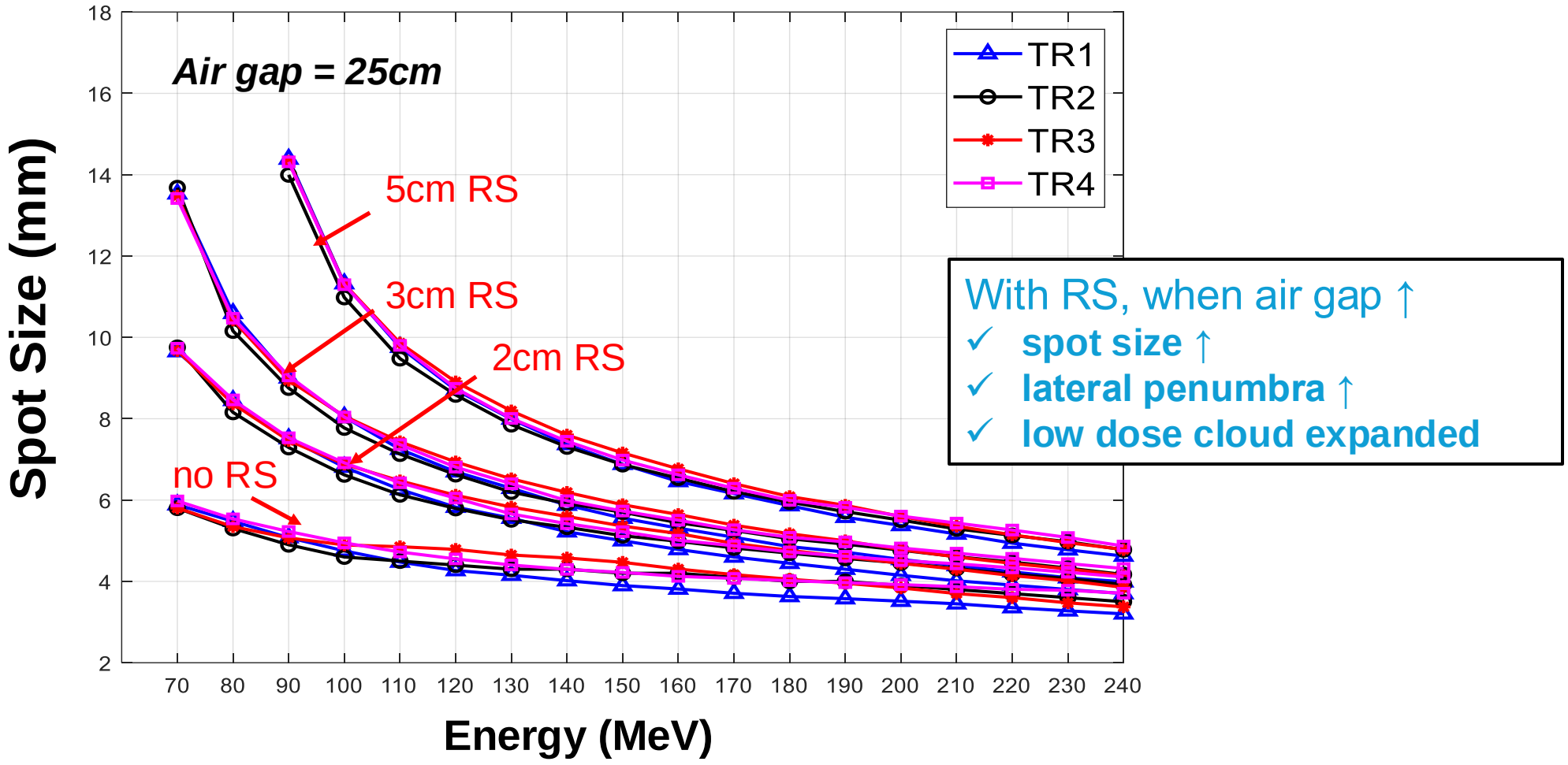
Figure cropped from Engelsman 2013, RO

A simplified view of lateral penumbra

There is no advantage in proton therapy!



Pencil-beam: spot size vs energy, RS, air gap



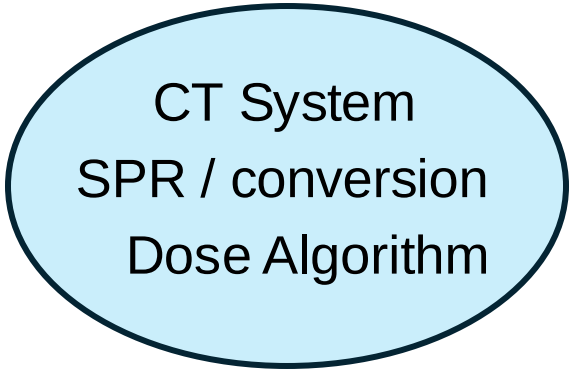
With RS, when air gap ↑

- ✓ **spot size ↑**
- ✓ **lateral penumbra ↑**
- ✓ **low dose cloud expanded**

Commissioning Data from Varian ProBeam @NYPC

Uncertainty in proton therapy

Modeling



Uncertainty in proton therapy

Modeling

CT System
SPR / conversion
Dose Algorithm

Static

Reproducibility
Setup Error
Metal Position

Longitidudinal

Tumor Change
Anatomical Variation
Separation Change

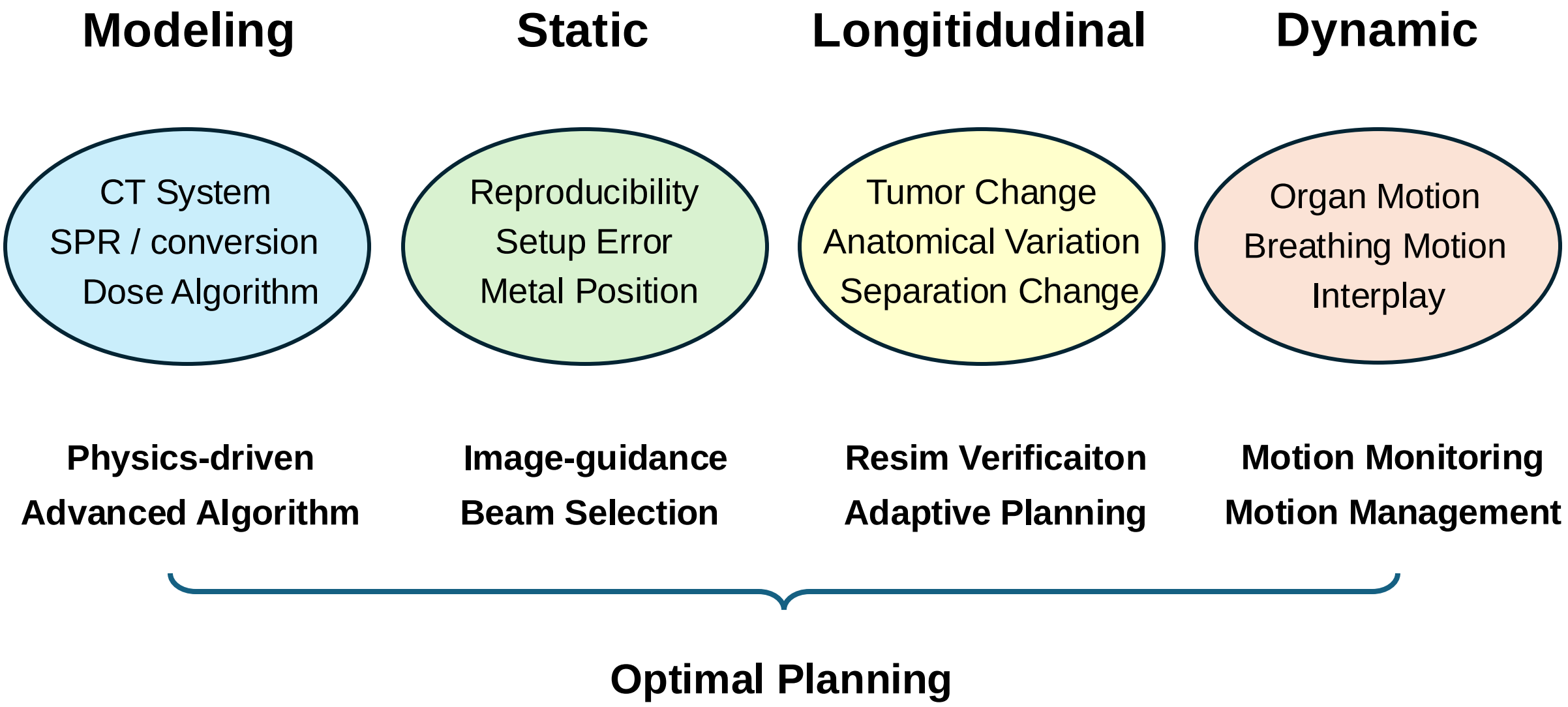
Dynamic

Organ Motion
Breathing Motion
Interplay

Machine

Proton Energy Beam Delivery

Uncertainty in proton therapy



Uncertainty in proton therapy

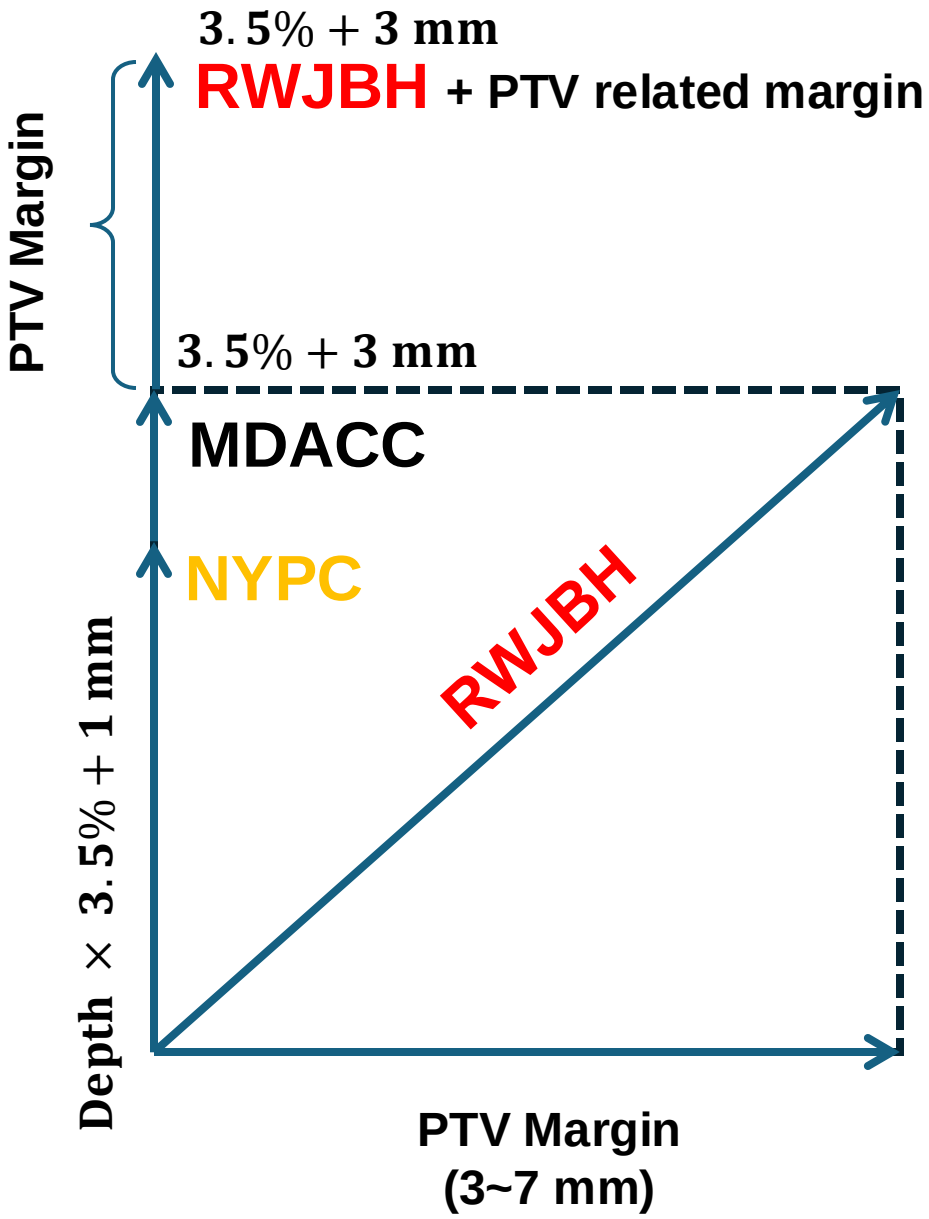
Modeling	Static	Longitidudinal	Dynamic
CT System SPR / conversion Dose Algorithm	Reproducibility Setup Error Metal Position	Tumor Change Anatomical Variation Separation Change	Organ Motion Breathing Motion Interplay
Physics-driven **Advanced Algorithm**	**Image-guidance** **Beam Selection**	**Resim Verificaiton** **Adaptive Planning**	**Motion Monitoring** **Motion Management**

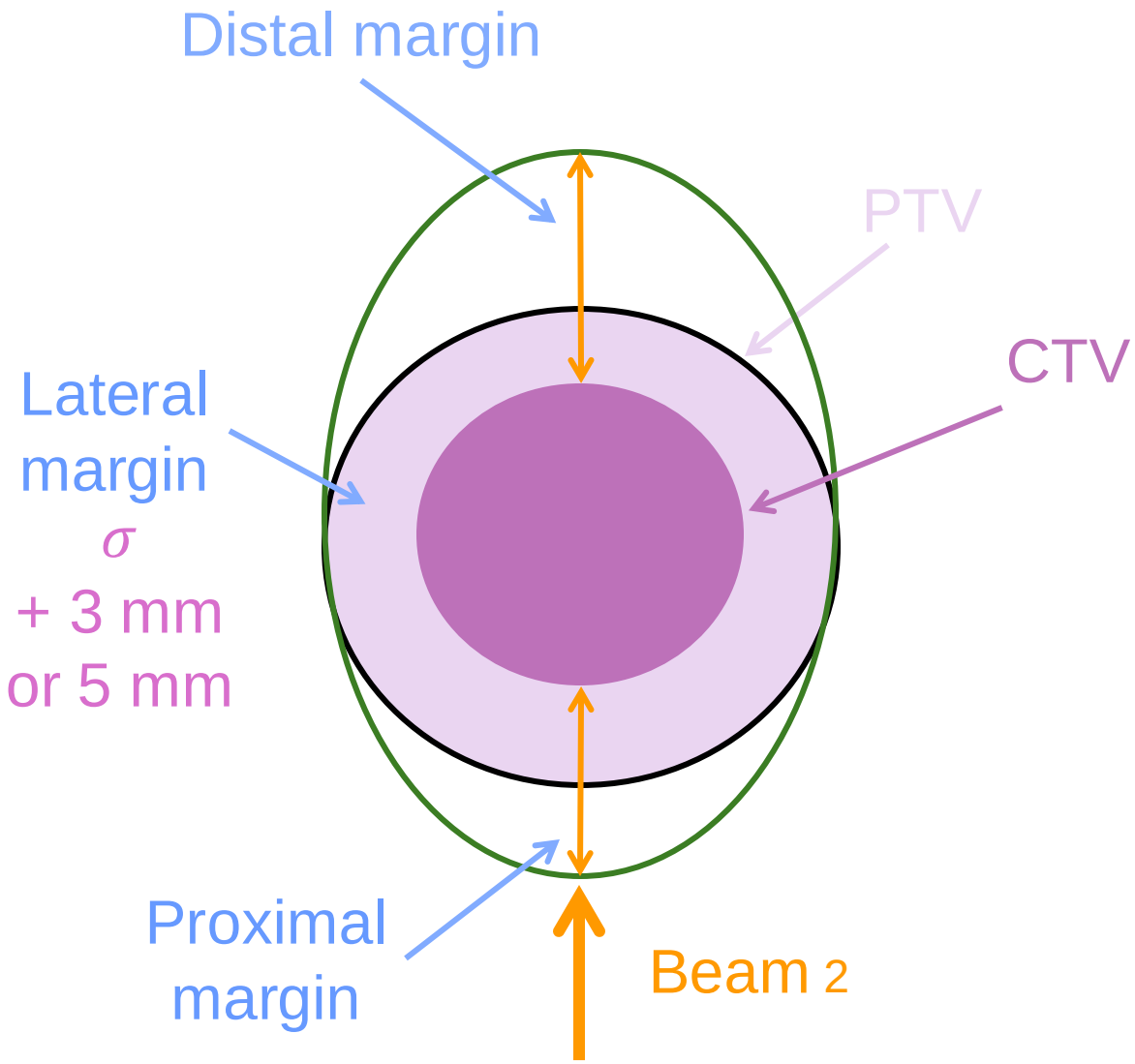
Optimal Planning

Range Uncertainty

Uncertainty Sources		Rel. Uncertainties in SPR (1σ)		
		Lung	Soft Tissues	Bone Tissues
Residual Error (human tissue composition variations considered)		0.18%	1.2%	1.6%
CT Related	Modeling uncertainties in predicted CT HU number	3.8%	0.75%	0.53%
	CT imaging uncertainties	3.3%	0.56%	1.5%
SPR Related	Uncertainties in mean excitation energy	0.17%	0.23%	0.65%
	Variations with proton energy	0.17%	0.17%	0.41%
Consensus Uncertainty			3.5%	

Beam-specific "PTV"



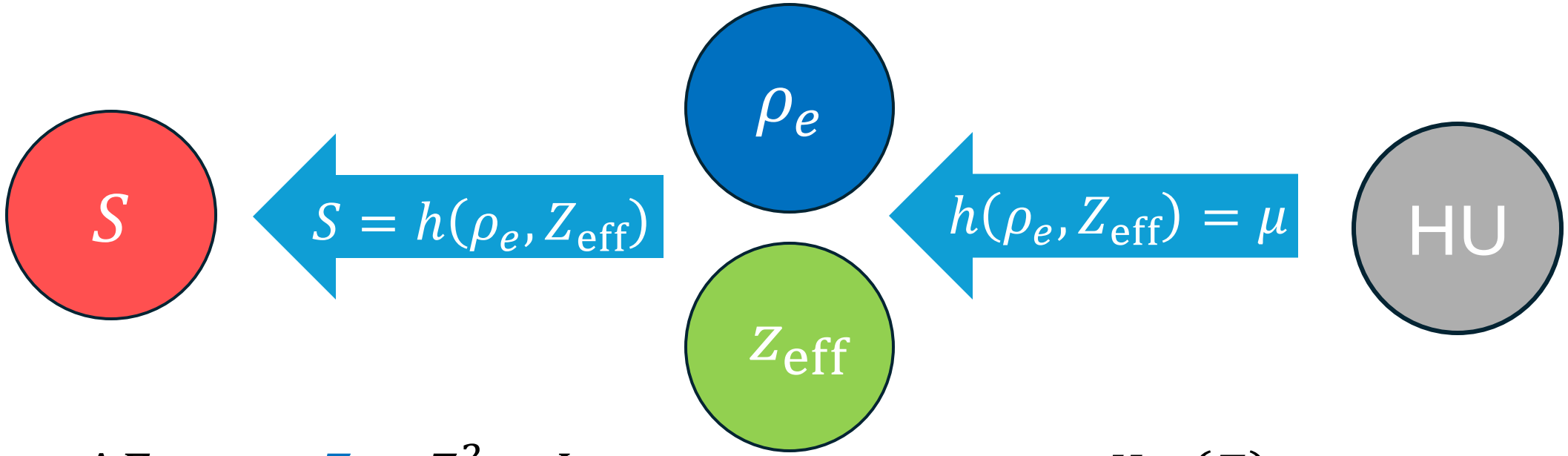


Tradeoff in treatment planning

Dose Spillage

Robustness

Uncertainty from SPR conversion



$$S = \frac{\Delta E}{\Delta x} = \left[N_A \frac{Z}{A} \rho\right] \frac{Z_1^2}{\beta^2} \ln \frac{I_{\max}}{I_{\min}}$$

$$S = \frac{\Delta E}{\Delta x} = \rho_e \frac{Z_1^2}{\beta^2} \ln \frac{I_{\max}}{I(Z_{\text{eff}})}$$

$$\rho_e(\vec{x}) \begin{bmatrix} K_{\text{CS}}(E) \\ +Z_{\text{eff}}(\vec{x})^n K_{\text{PE}}(E) \end{bmatrix} = \mu(\vec{x}, E)$$

Material Decomposition

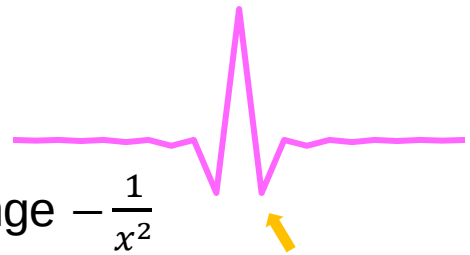
$$\mu_a(\vec{x}) f_a(\vec{x}) + \mu_b(\vec{x}) f_b(\vec{x})$$

Metal artifact on CT images

Inconsistent data → **Ramp filtering** → **CT number Inaccuracy**

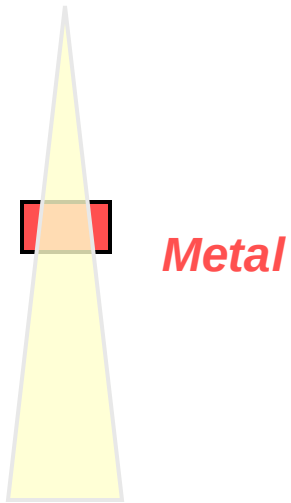
Blooming
Shading
Streaking

⊛ Digitized Ramp



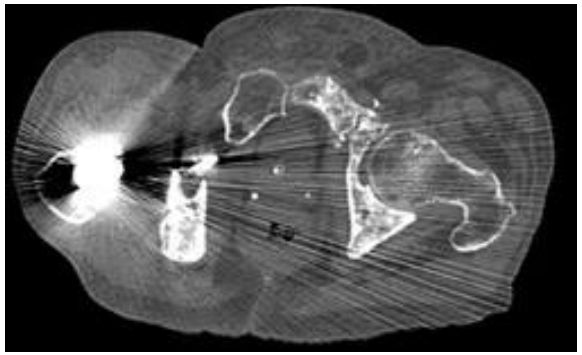
Long Range $-\frac{1}{x^2}$

Undershoot



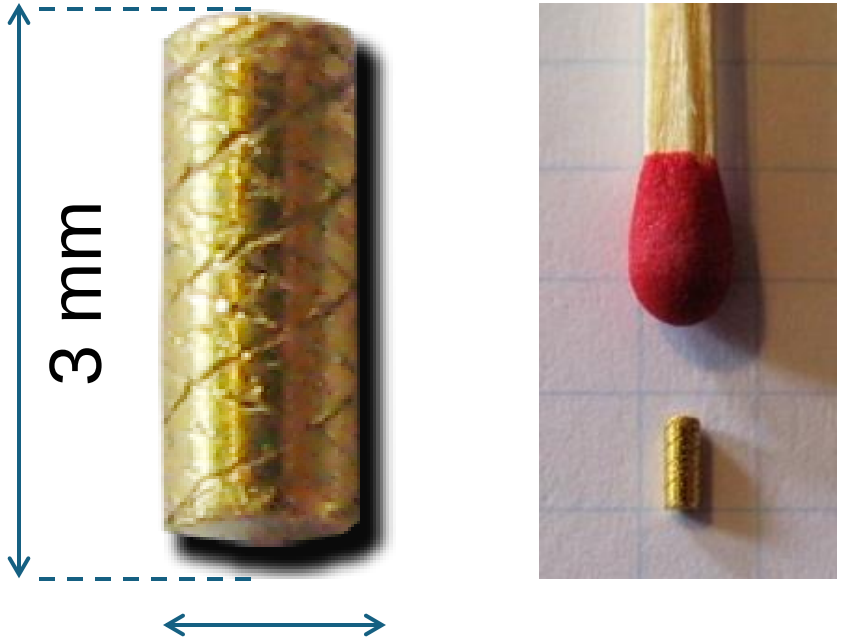
Metal

Beam Hardening
Photon Starvation

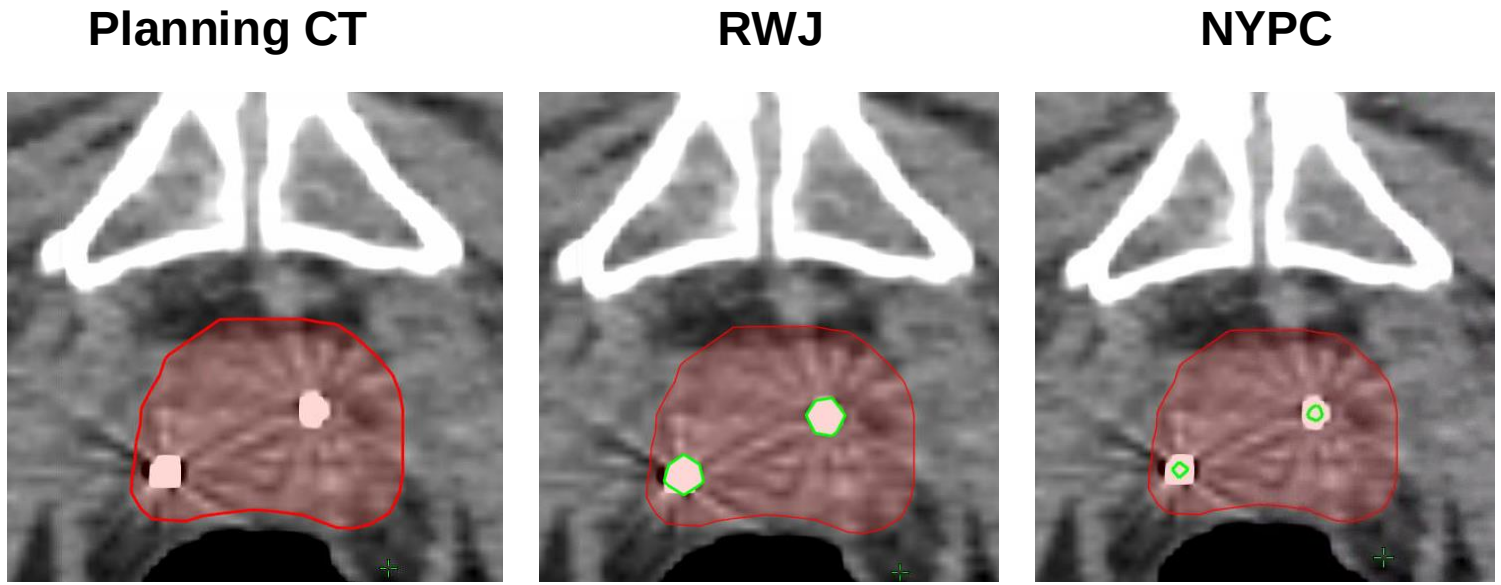


Uncertainty from metal implants

Civco® gold fiducial

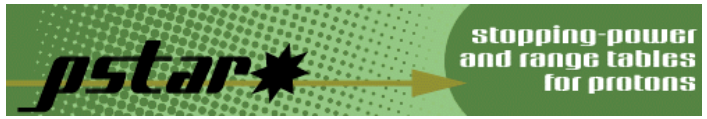


"Volume Average" Effect



Blueprint Volume	Low Res Contour	High Res Contour
~0.001 cc	0.1 cc	<0.1 cc

Small-volume metal override



mean energy
125 MeV

Compound

$$\left(\frac{dE}{\rho dx}\right)_{\text{contour}} = w_1\left(\frac{dE}{\rho dx}\right)_{\text{metal}} + w_2\left(\frac{dE}{\rho dx}\right)_{\text{water}}$$

Weight average Mass Stopping Power
- Attix Page 178

$$\left(\frac{dE}{dx}\right)_{\text{contour}} = f_1\left(\frac{dE}{dx}\right)_{\text{metal}} + f_2\left(\frac{dE}{dx}\right)_{\text{water}}$$

Volume average Stopping Power
(Derived)

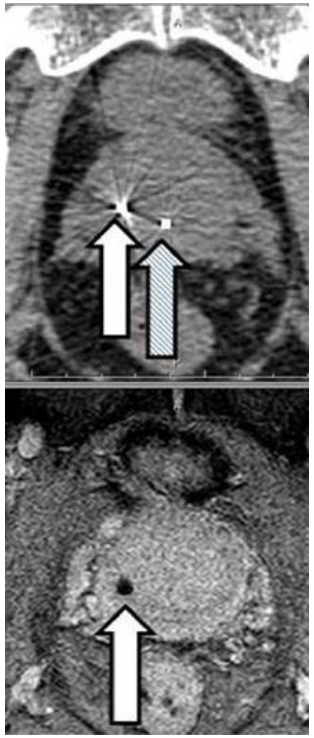
$$\hat{S}_{\text{contour}} = f_1\hat{S}_{\text{metal}} + f_2$$ **relative**

A variety of fiducial markers

RWJ?

Gold Anchor™	• Spherical • linear		• 0.28 mm x 10-20 mm • 0.40 mm x 10-20 mm
Visicoil™	• Coil		• 0.35 mm x 10-30 mm • 0.5 mm x 5-30 mm • 0.75 mm x 5-30 mm • 1.1 mm x 5-30 mm
X-MARK™	• Guide wire and band		• 0.85 mm x 5-30 mm • 1.15 mm x 5-30 mm
CIVCO	• "Standard" (knurled)		• 0.8-0.9 mm x 3 mm • 1.2 mm x 3 mm • 1.6 mm x 3 mm
	• "CyberMark"		• 1.0 mm x 5 mm
	• "Align"		• 0.8 mm x 10 mm • 1.2 mm x 10 mm
	• "FlexiCoil" • "FlexiMarc"		• 0.9 mm x 10-30 mm • 1.2 mm x 10-30 mm
Goldlock®	• Cylinders (star shaped)		• 0.8-1.0 mm x 3 mm • 1.2 mm x 3 mm
Best®	• Cylinders (smooth)		• 0.8 mm x 1.5-7 mm • 1.0 mm x 1.5-7 mm • 1.2 mm x 3-5 mm
Qfix	• Cylinders (smooth)		• 1.0 mm x 3-5 mm • 1.2 mm x 3 mm
JRT Associates	• Cylinders (smooth)		• 1.2 mm x 3-5 mm

NYPC's default choice



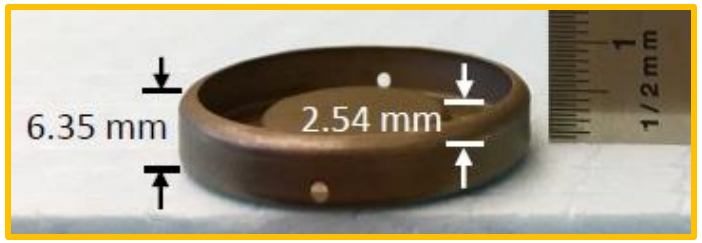
CT

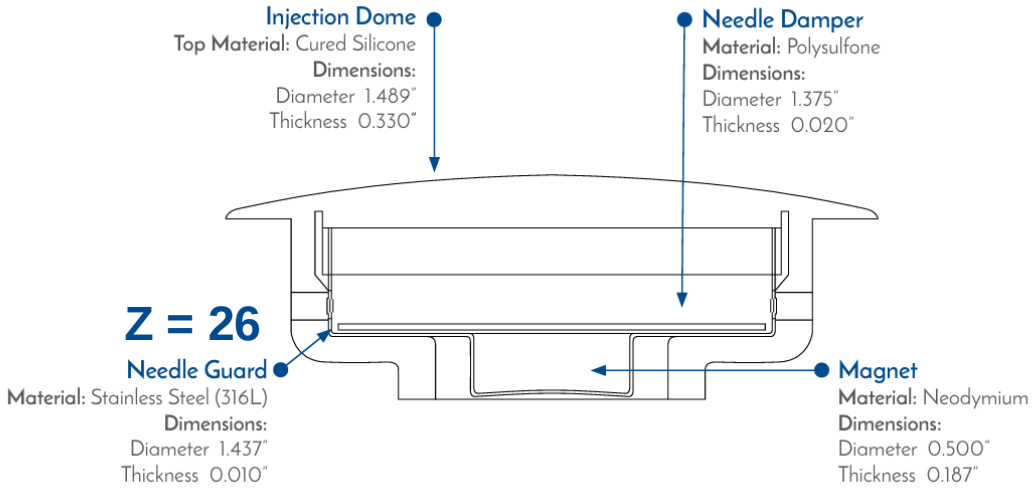
MRI

0.28 mm
Gold Anchor

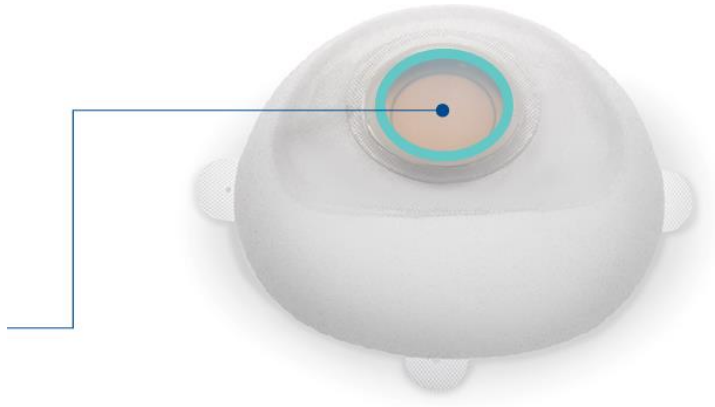
0.35 mm
VISICOIL

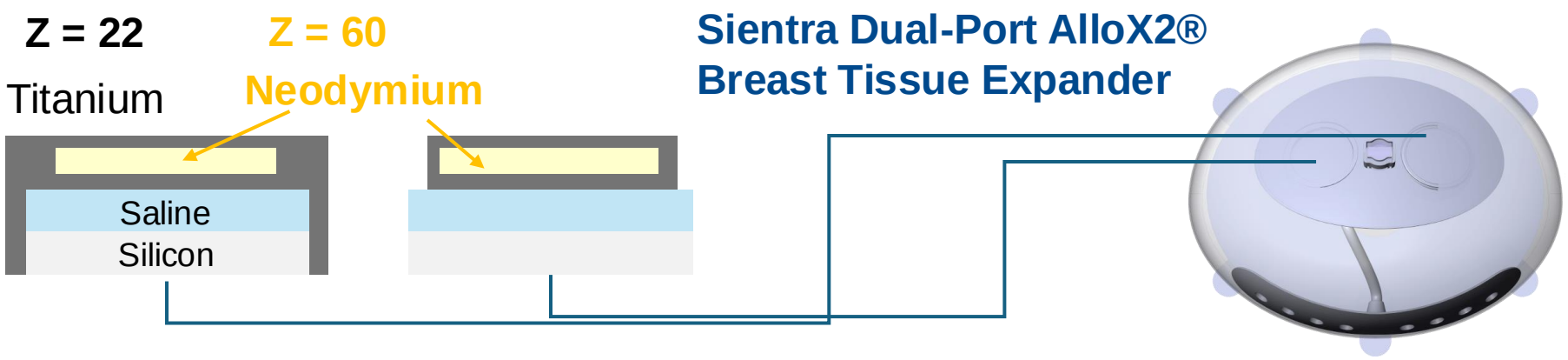
Uncertainty from metal implants





CPXTM 4 SILTEX™
Breast Tissue Expander

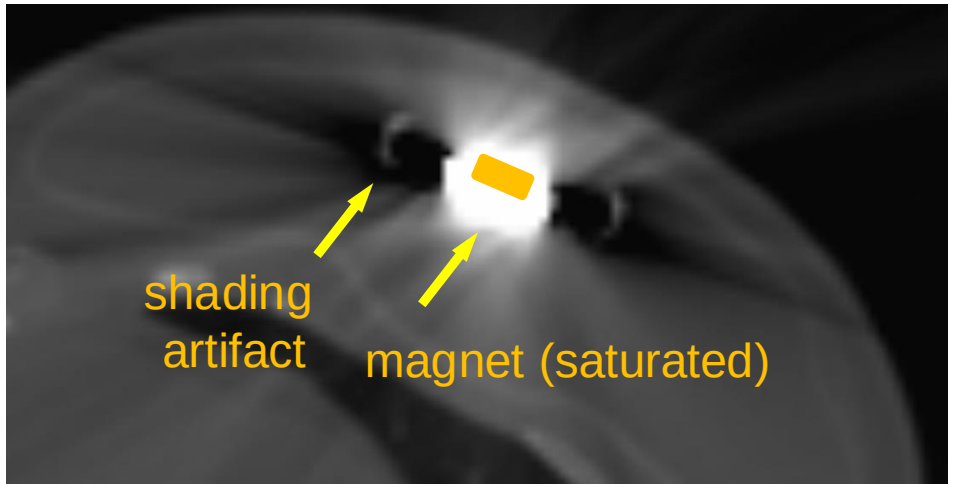




Sientra Dual-Port AlloX2®
Breast Tissue Expander

Breast tissue expander

Magnet (High Z)

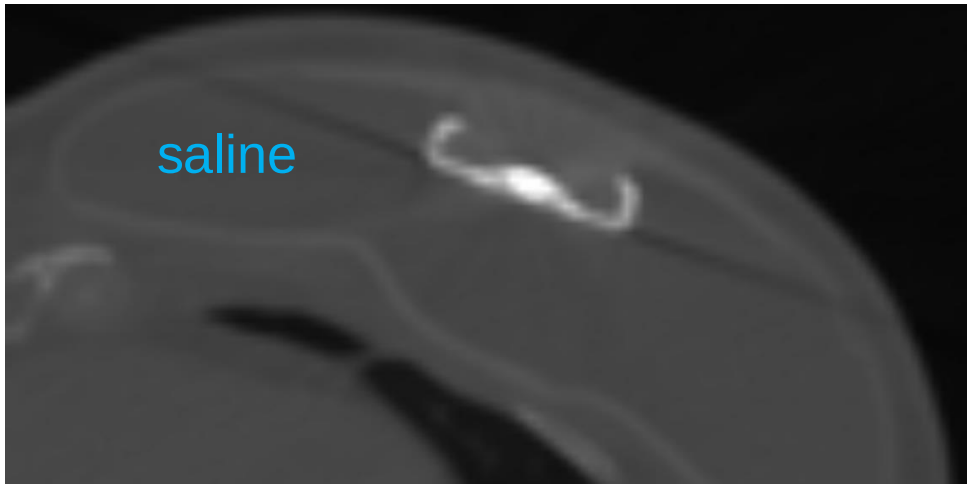


-1000
HU

3024
HU

(saturated)

Titanium/SS Case



Considerations for metallic implants

Pre-Planning

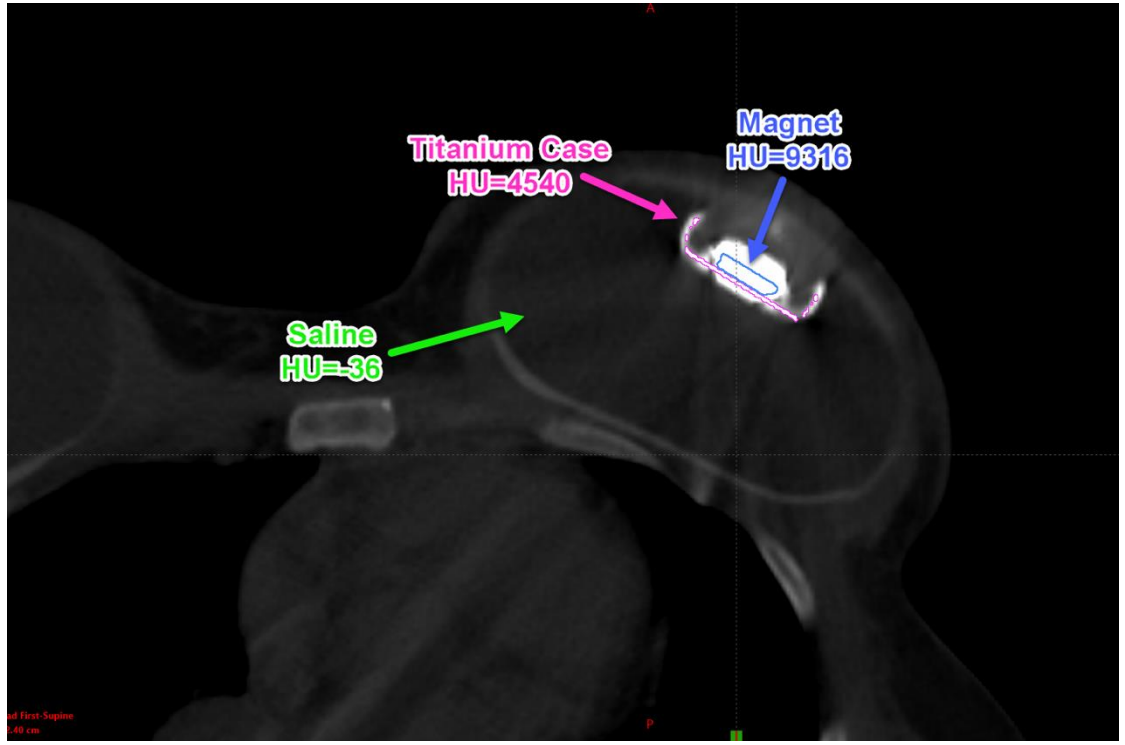
- Density override
- Unsure material and dimension
- Avoid shoot through > 2 mm

Physicist support

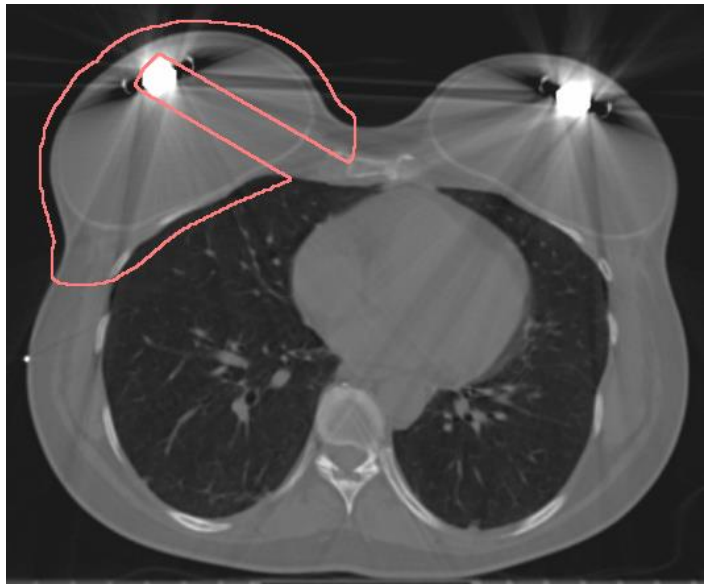
- Acquire information
- Monte-Carlo simulation
- Contour, density override
- Template overlay

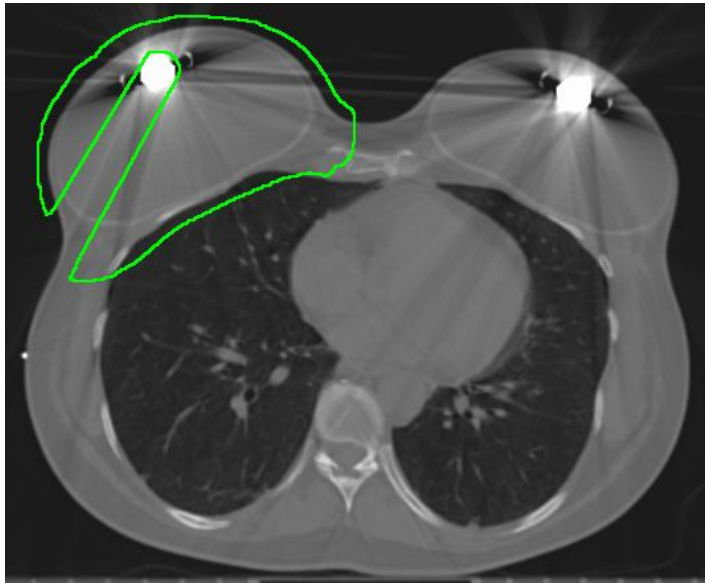
Density override for breast tissue expander

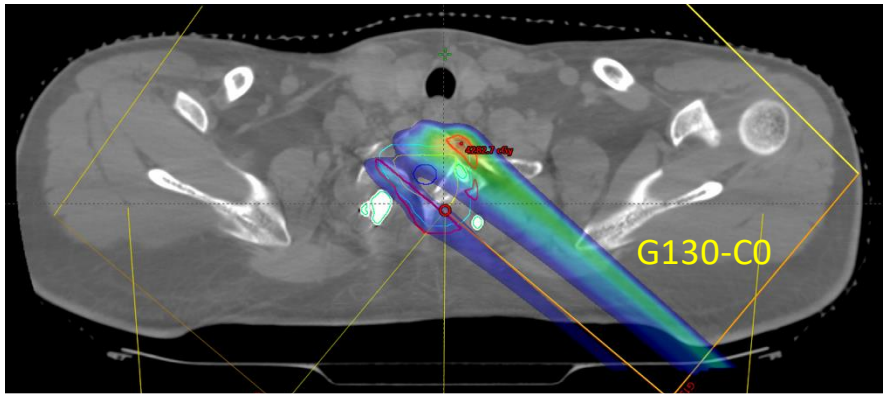
Template Override

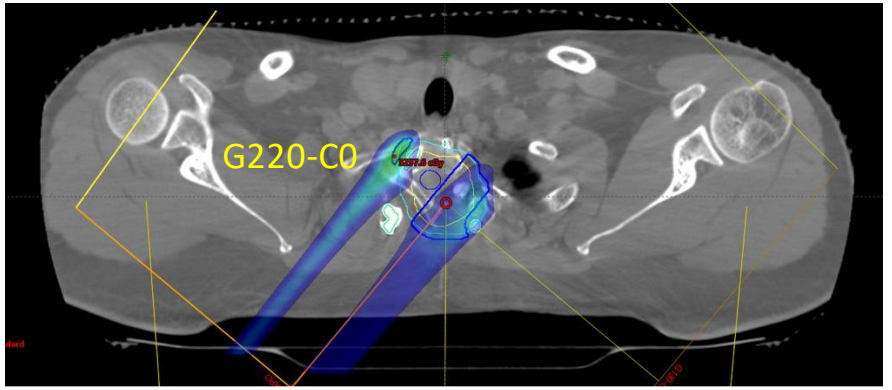


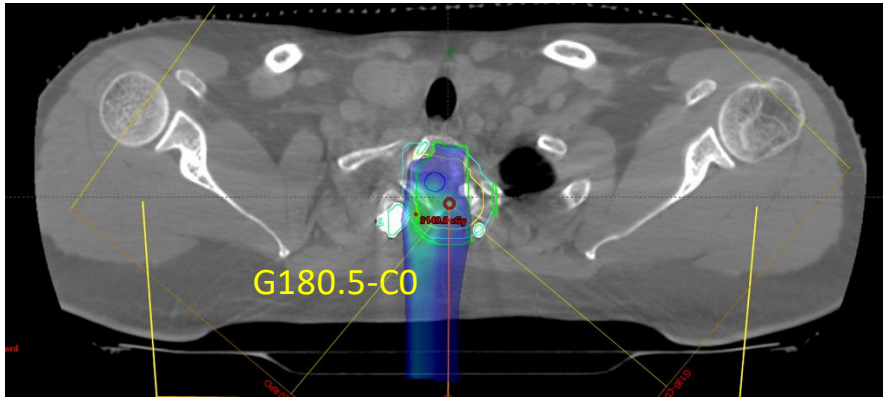
“non-fly zone”





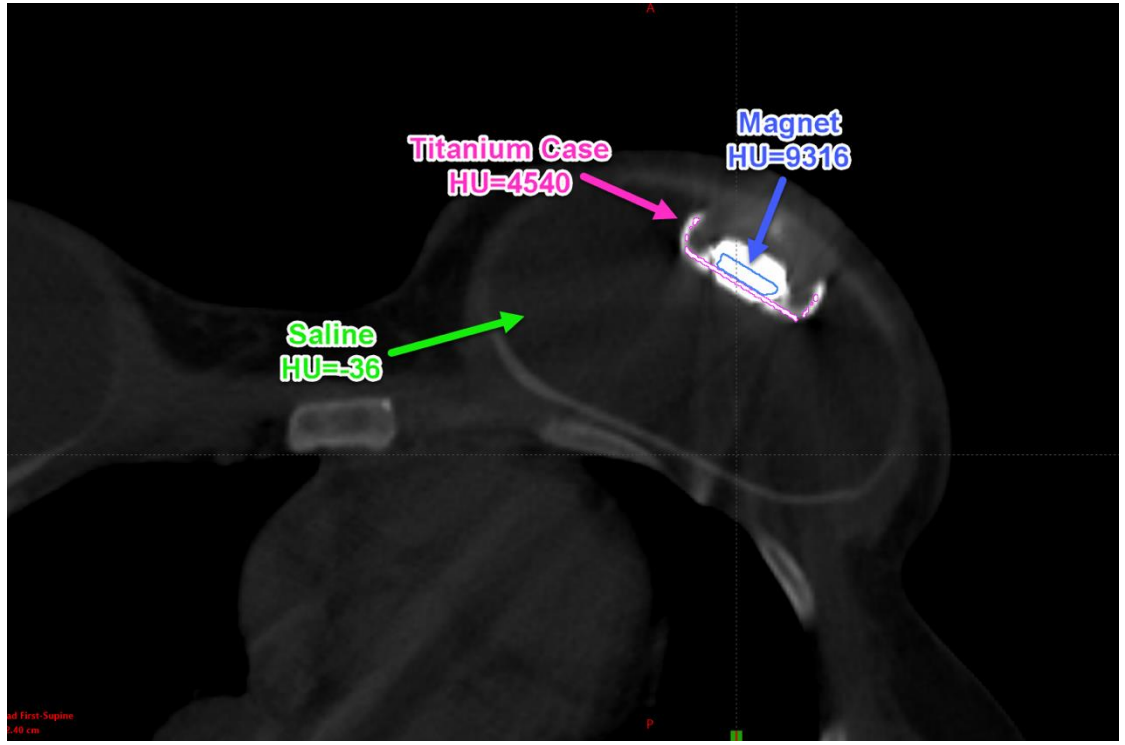




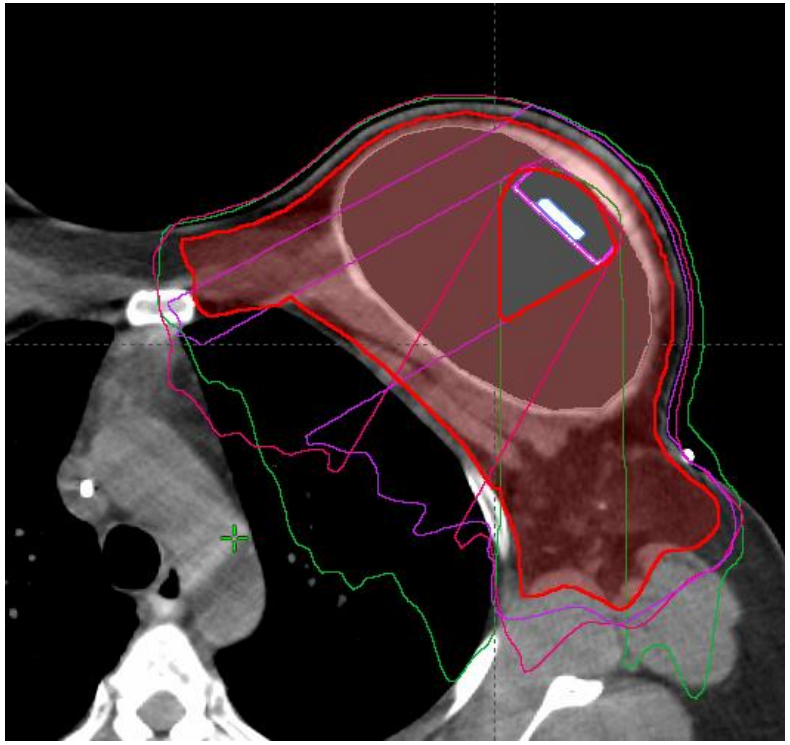


Density override for breast tissue expander

Template Override

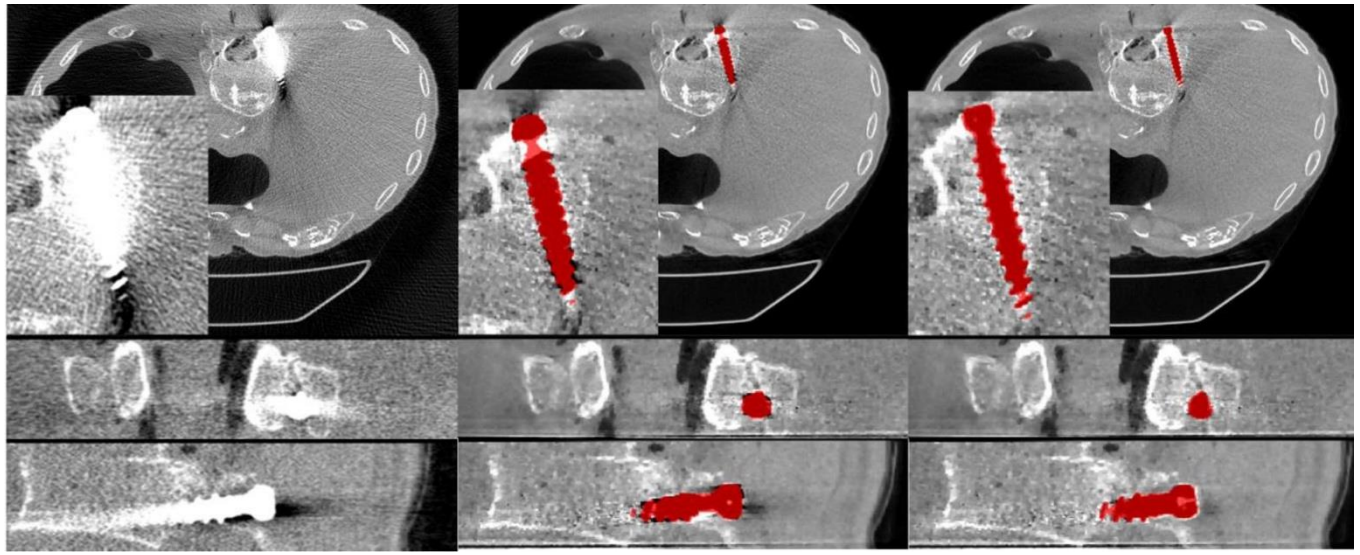


MFO Plan



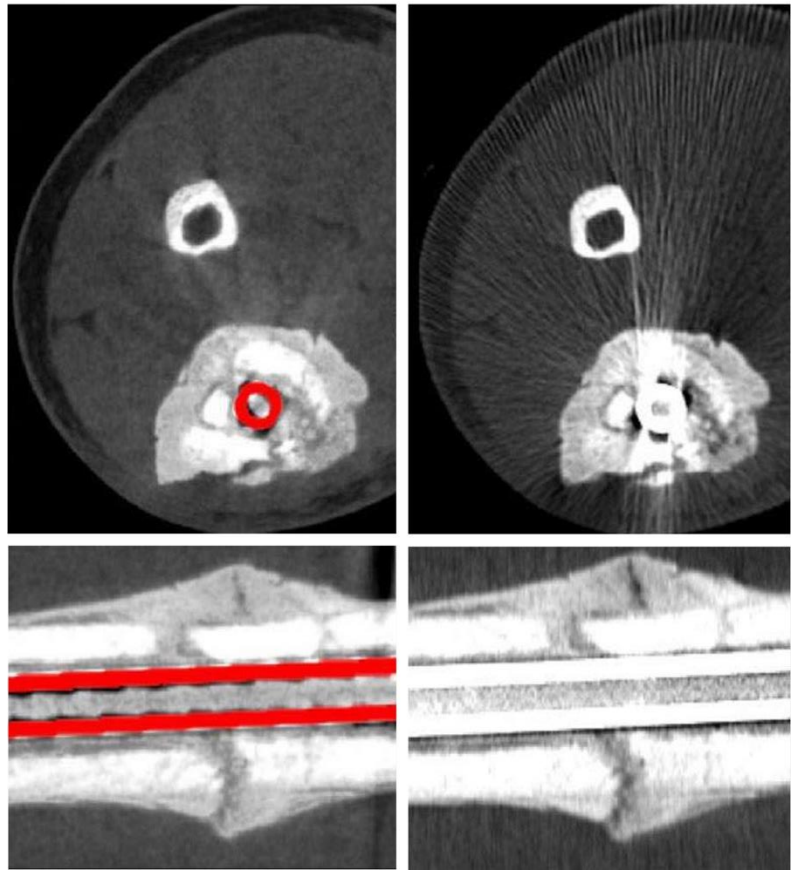
Known/Unknown Component Reconstruction

FBP | Unknonw Component | Known Component



C Zhang, JMI, 2017

Unknonw Component | FBP

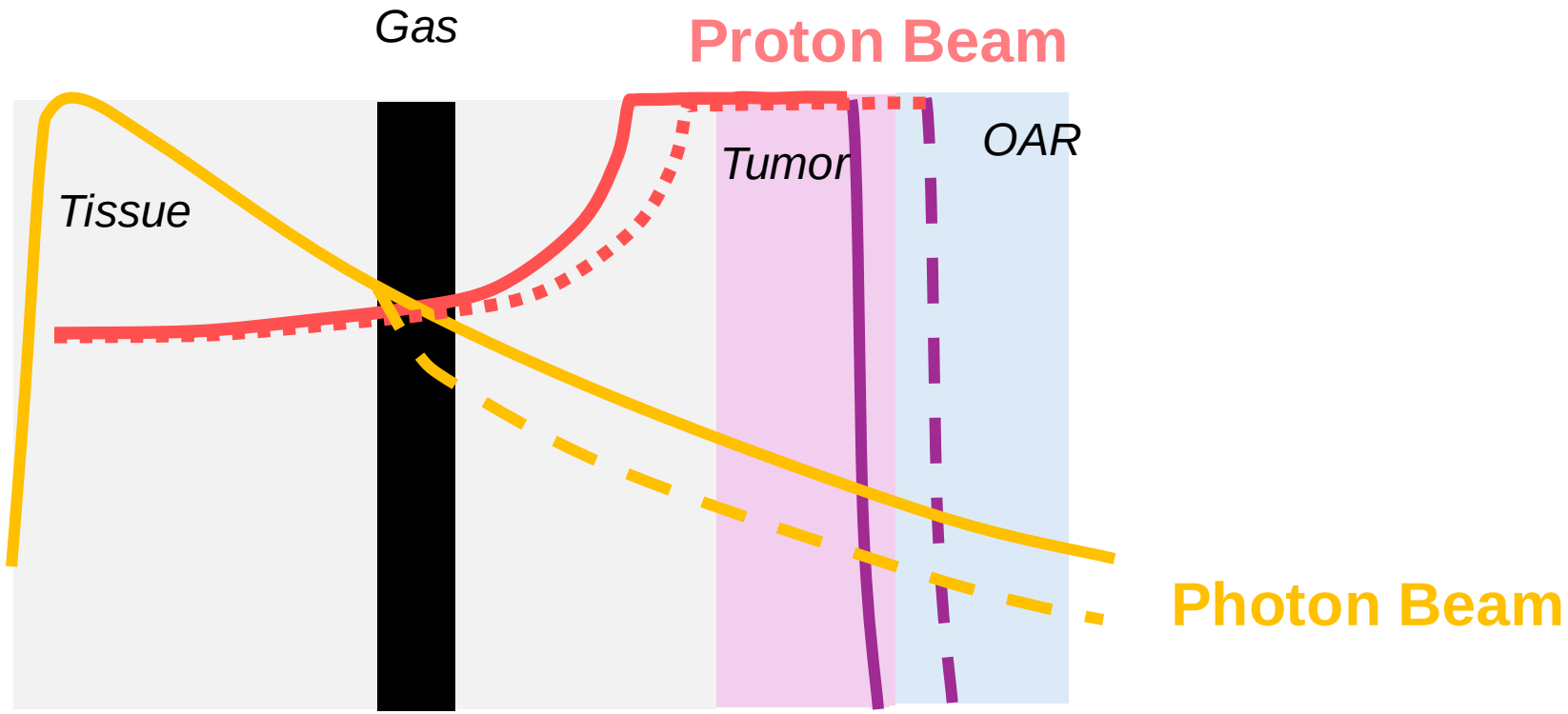


Uncertainty in proton therapy

Modeling	Static	Longitidudinal	Dynamic
CT System SPR / conversion Dose Algorithm	Reproducibility Setup Error Metal Position	Tumor Change Anatomical Variation Separation Change	Organ Motion Breathing Motion Interplay
Physics-driven **Advanced Algorithm**	**Image-guidance** **Beam Selection**	**Resim Verificaiton** **Adaptive Planning**	**Motion Monitoring** **Motion Management**

Optimal Planning

Why so serious?



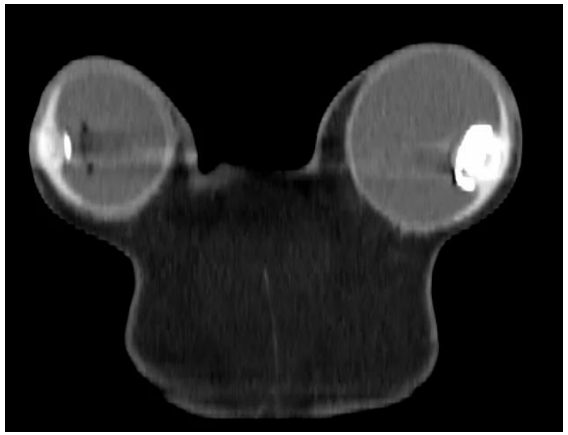
Beam angle selection

- ❑ Shortest beam path
- ❑ En-face beam
- ❑ Homogenous
- ❑ Less WET variation

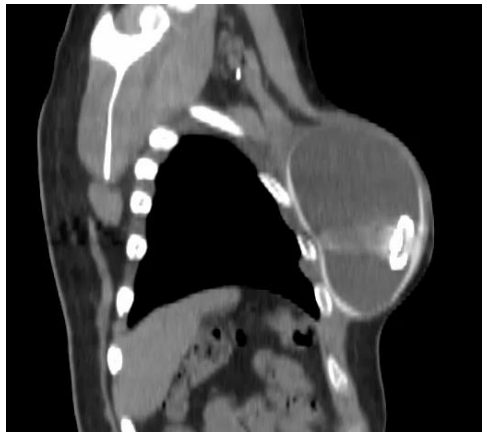
- ❑ Avoid range out at OARs (<1/3)
- ❑ Avoid variable anatomy
- ❑ Avoid non-reproducible region
- ❑ Avoid large motion
- ❑ Avoid cardiac device,chemo port

Unclear metal position

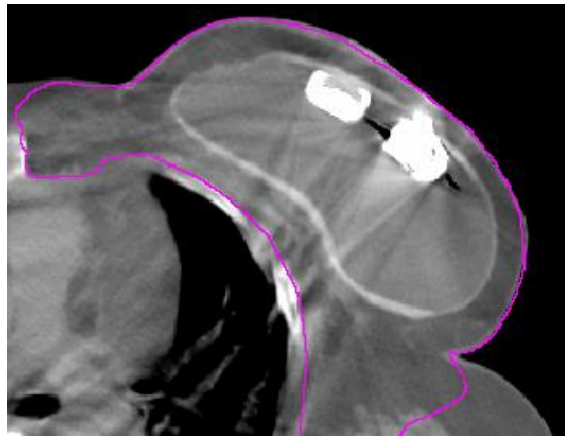
Axial



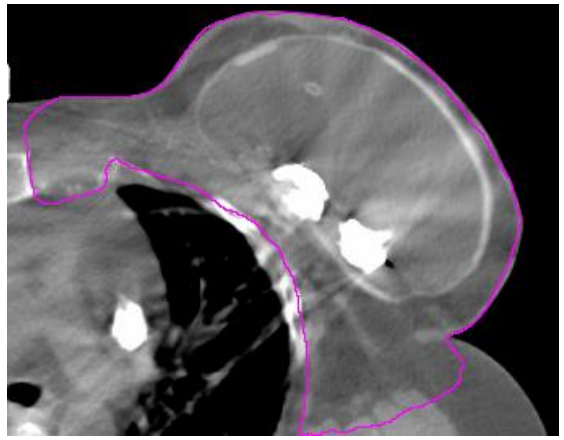
Saggital



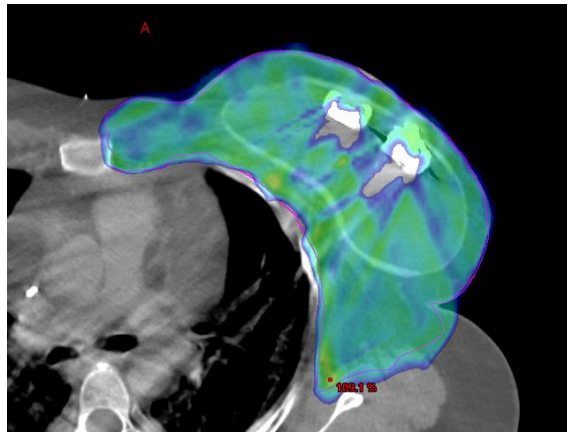
Original

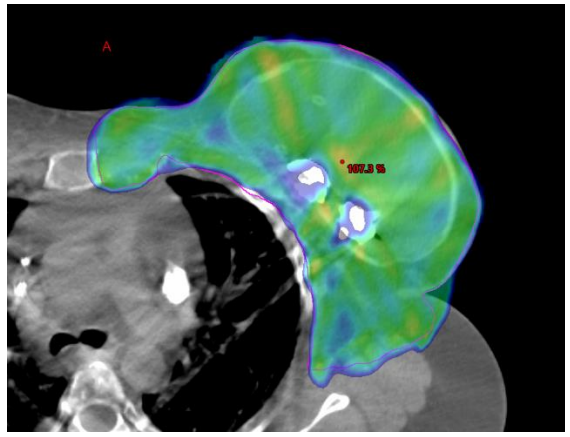


Flipped



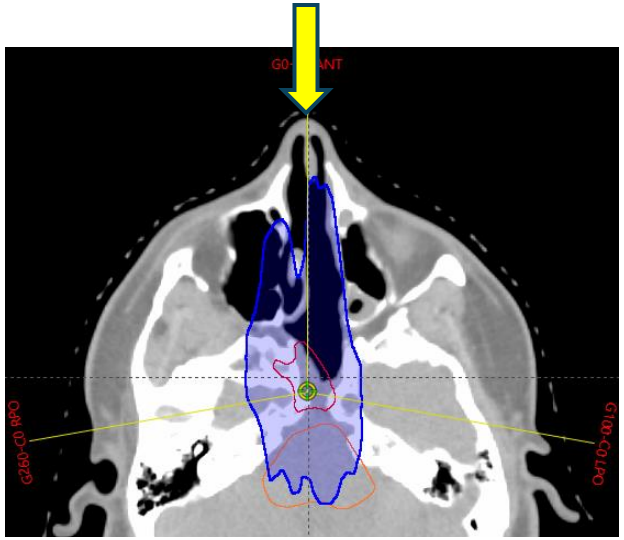
Natrelle®
Magna-Finder

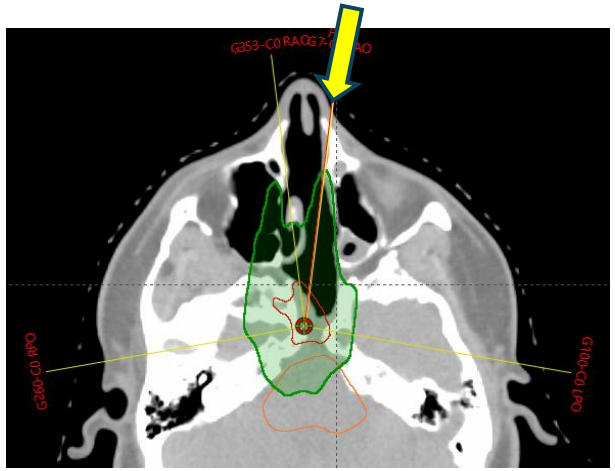


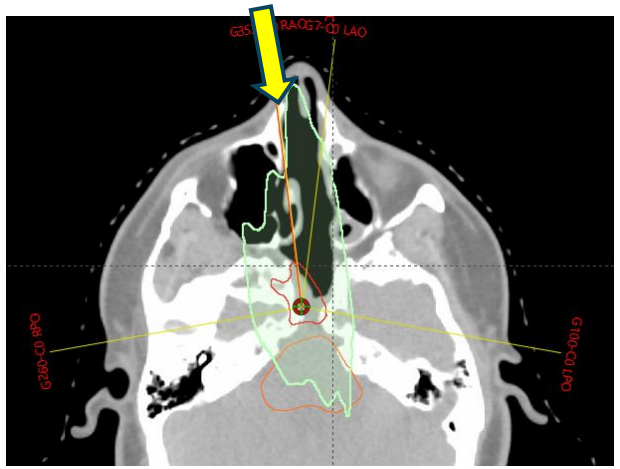


Tissue-air interface

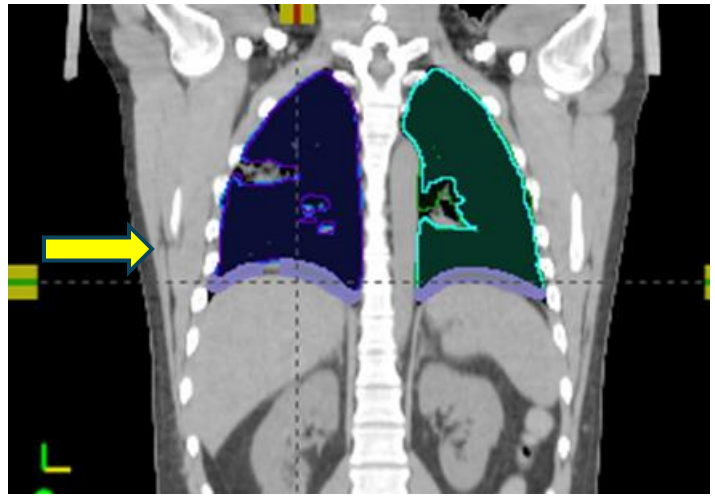
Nasal Area





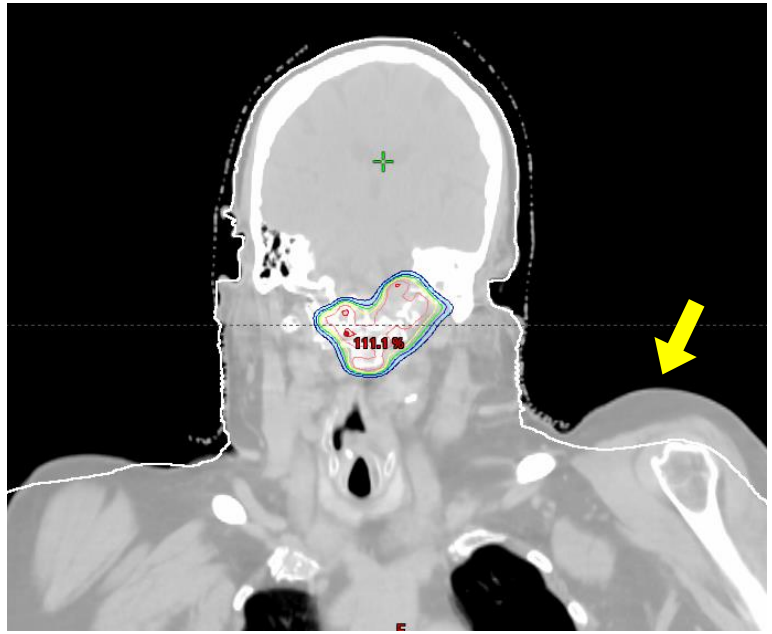


Diaphramic Region

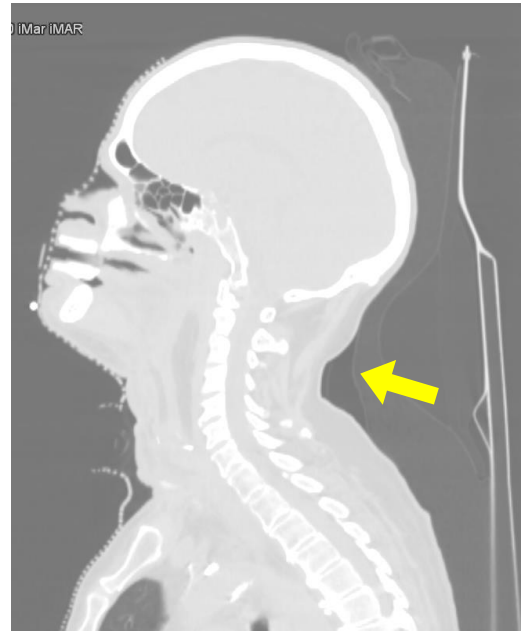


Non-reproducible setups (1)

Chin down



Shoulder up

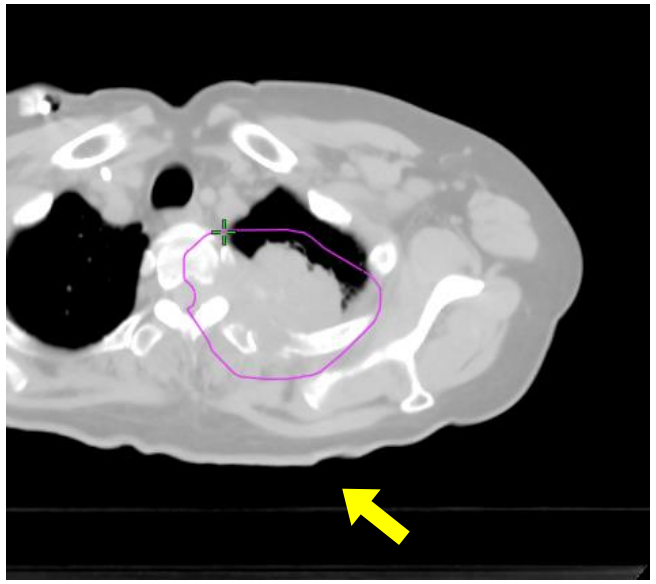


Air gap

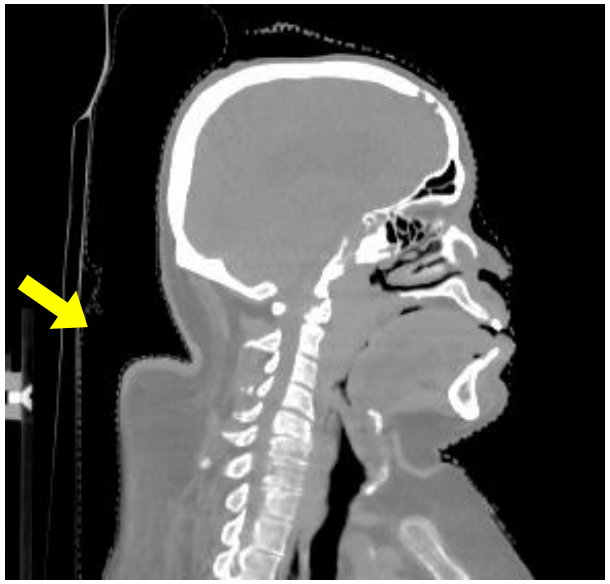
Hand Pegs for Shoulder Positioning

Five-point Mask (may be loose)

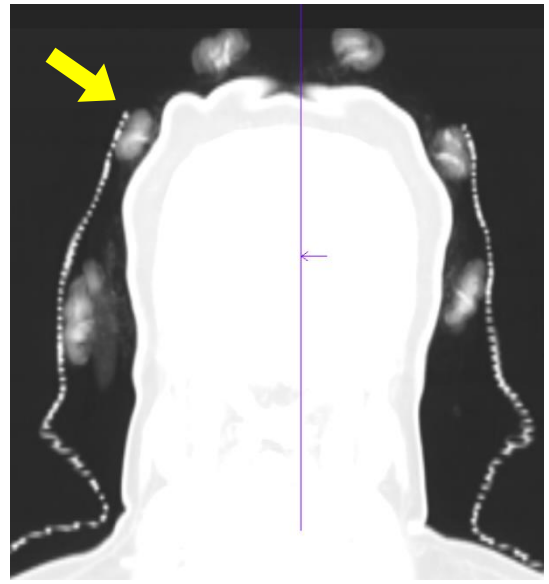
Non-reproducible setups (2)



Ripples

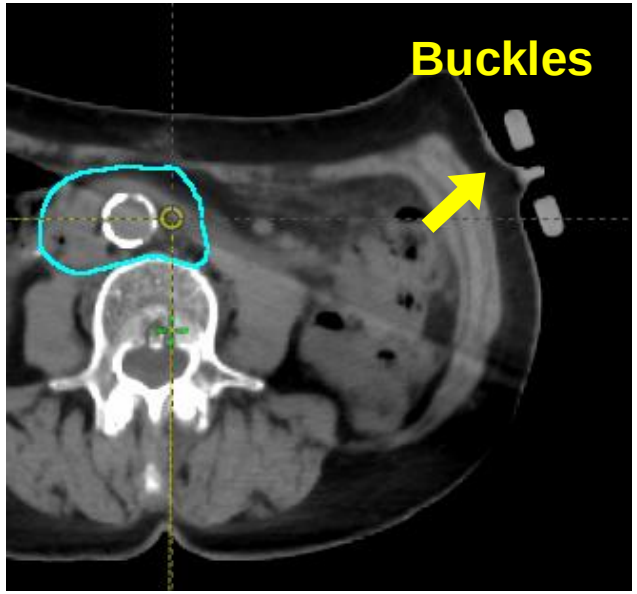


Skin Folds

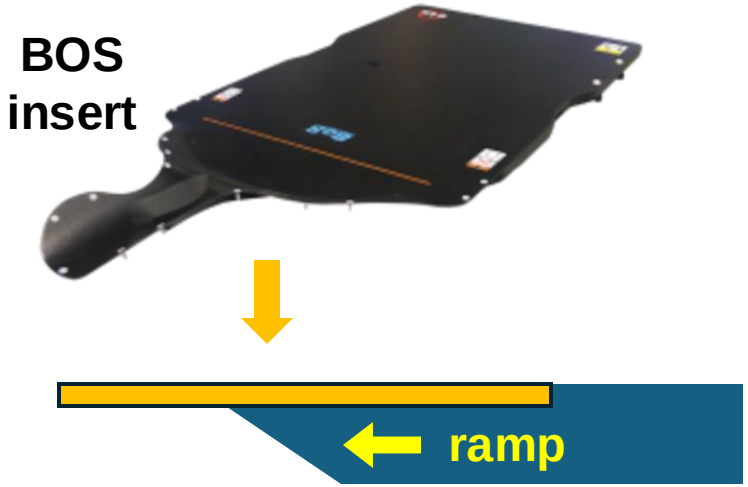


Hair Clusters

Non-reproducible setups (3)



Belt Buckle



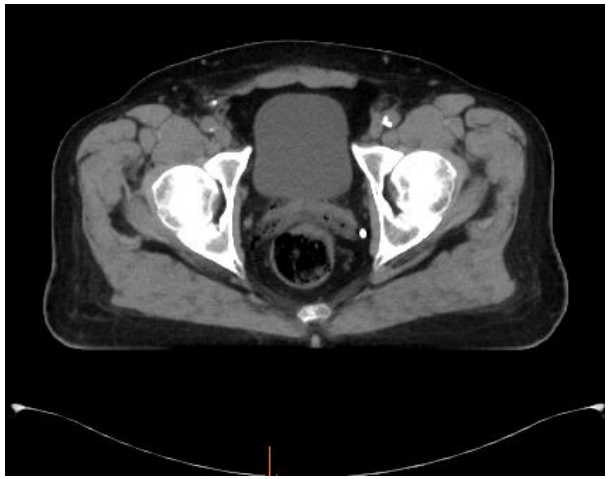
Couch Ramp

Uncertainty in proton therapy

Modeling	Static	Longitidudinal	Dynamic
CT System SPR / conversion Dose Algorithm	Reproducibility Setup Error Metal Position	Tumor Change Anatomical Variation Separation Change	Organ Motion Breathing Motion Interplay
Physics-driven **Advanced Algorithm**	**Image-guidance** **Therapist Training**	**Resim Verificaiton** **Adaptive Planning**	**Motion Monitoring** **Motion Management**

Optimal Planning

Intrafractional anatomical variation/movement



- Bladder Filling
- Rectal Gas
- Coughing
- Swallow
- Stomach Filling
- Tongue movement
- (In)voluntary Movement

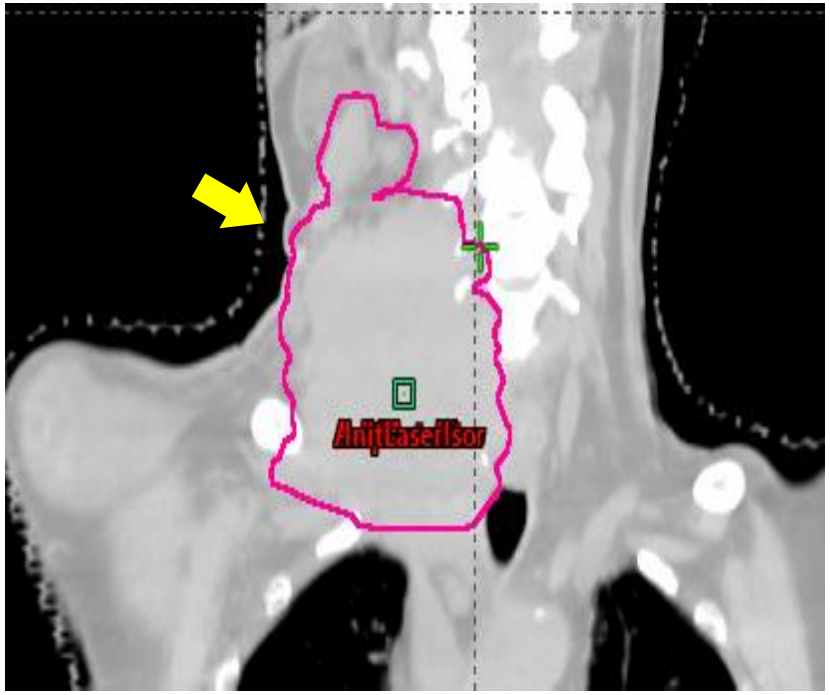
Aquaplast Mask

Tongue Depressor

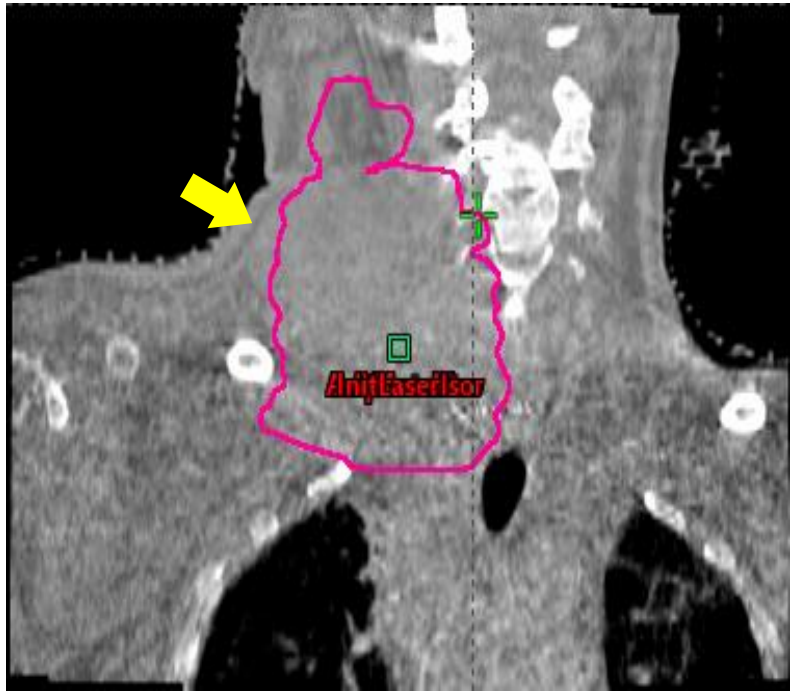
Pediatric Patients Require Anesthesia

Interfractional: Tumor Change

Original

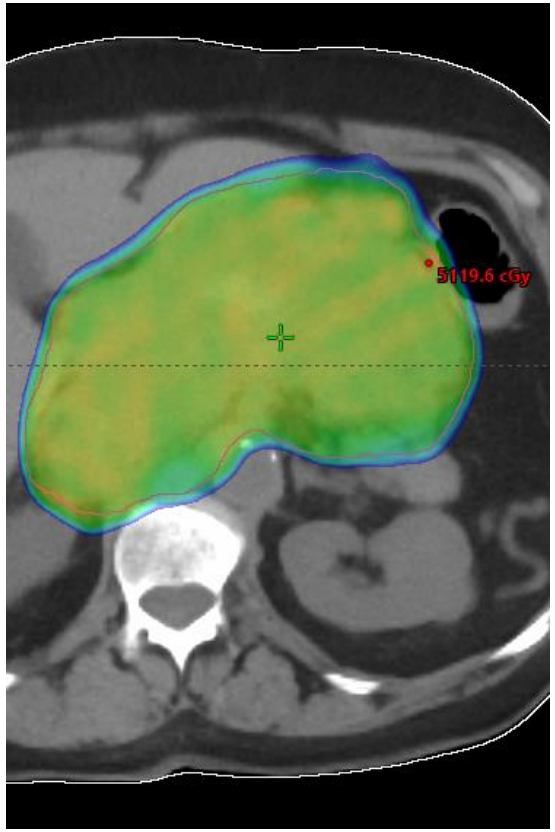


VScan

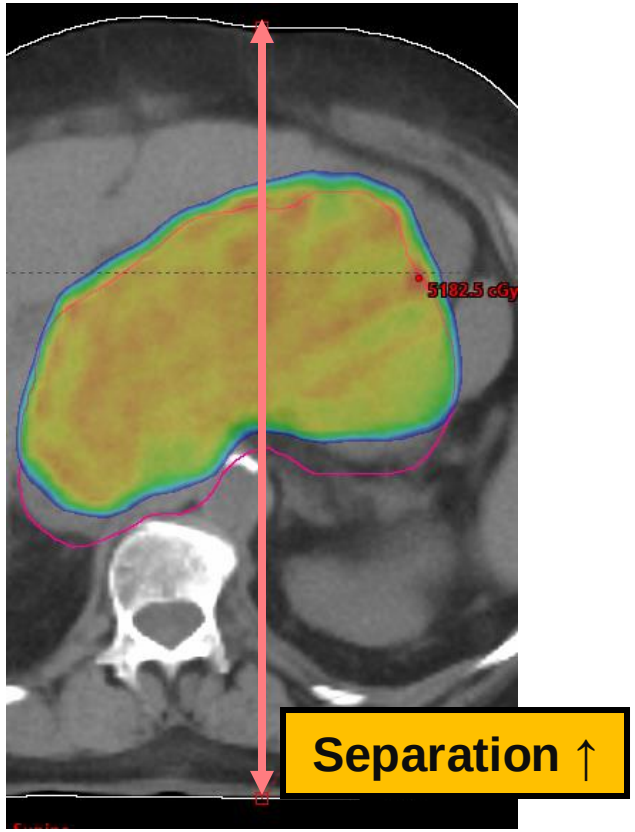


Interfractional: Separation Change

Original

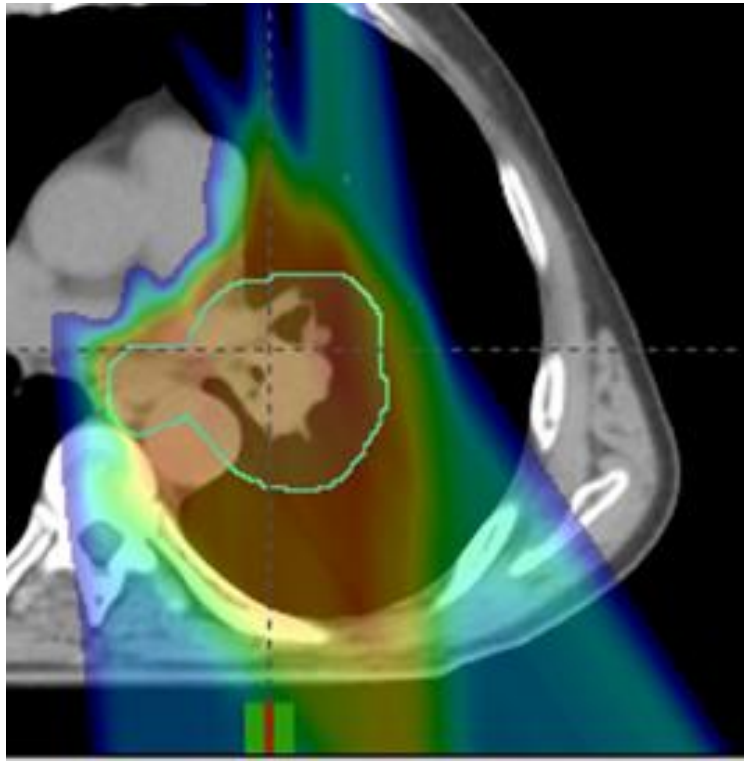


VScan

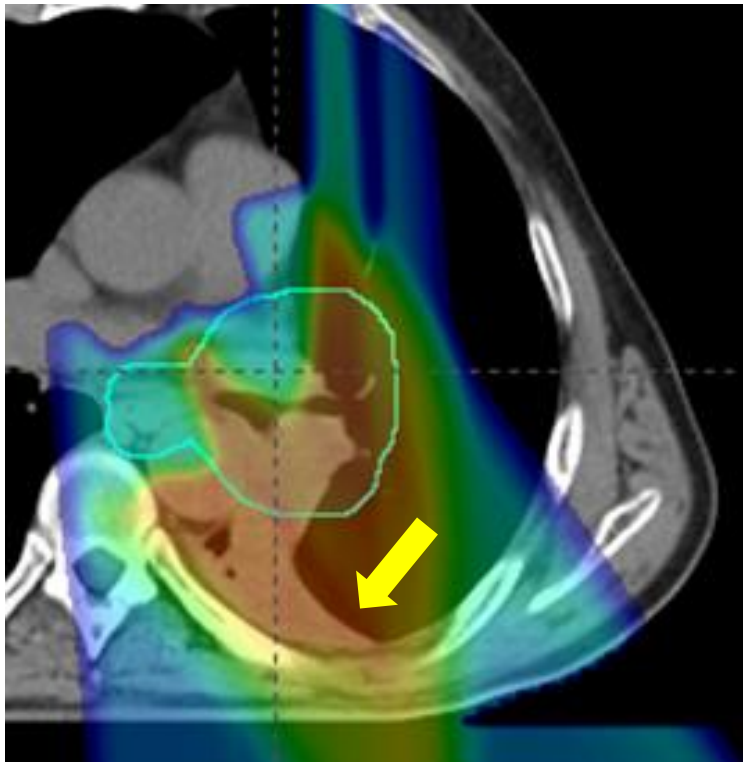


Interfractional: Pleural Effusion

Original

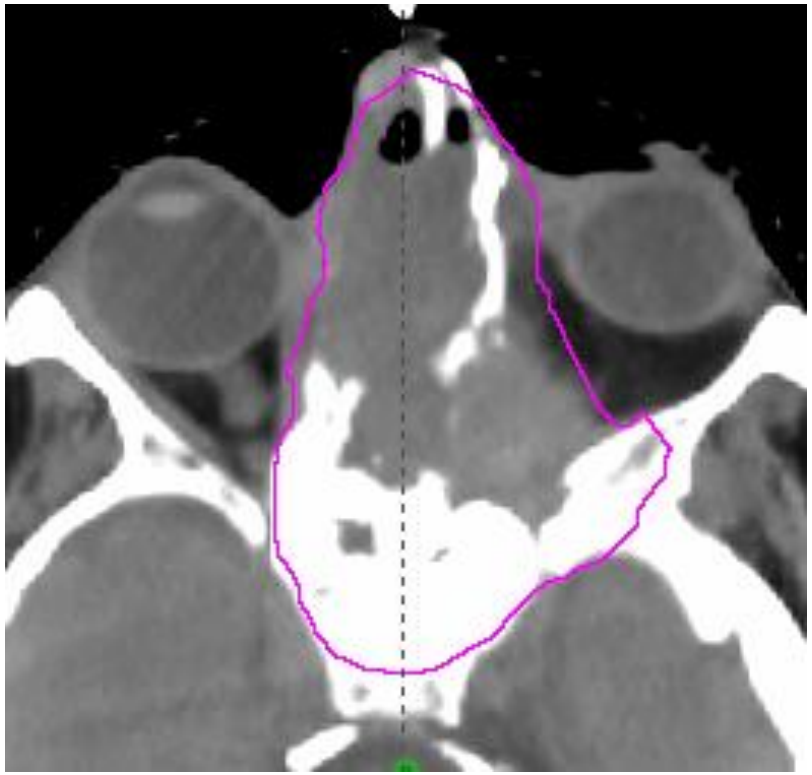


VScan

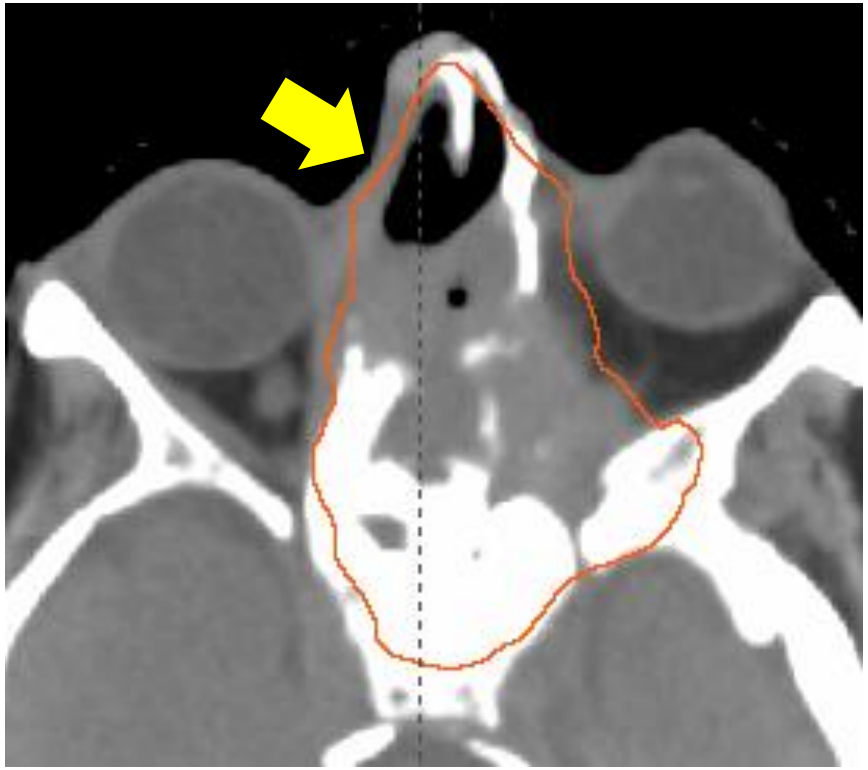


Interfractional: Nasal Filling

Original



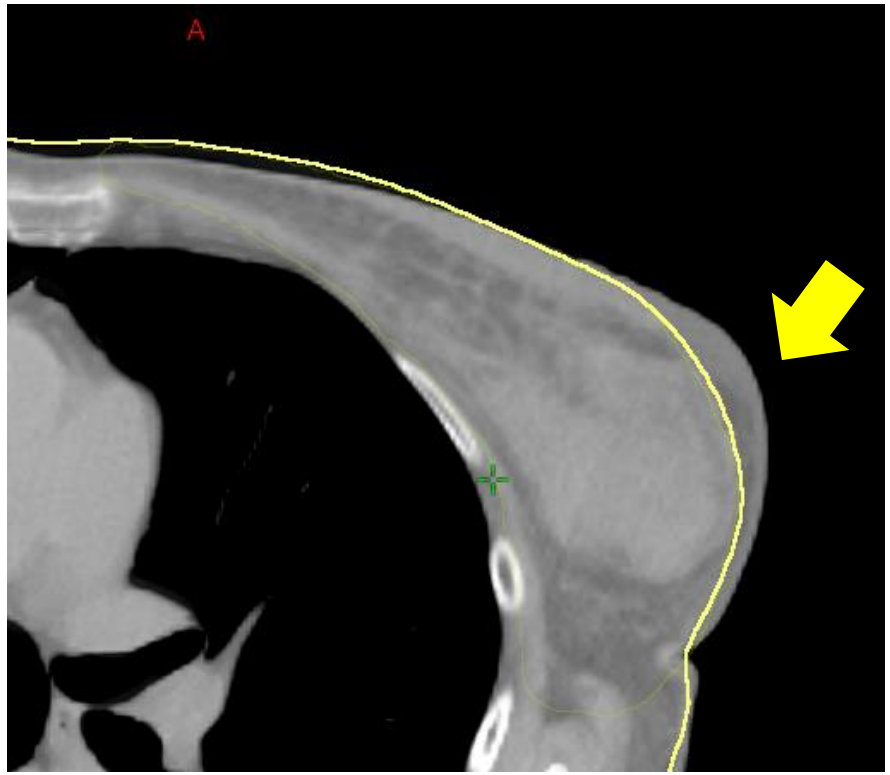
VScan



Interfractional: Breast Swelling

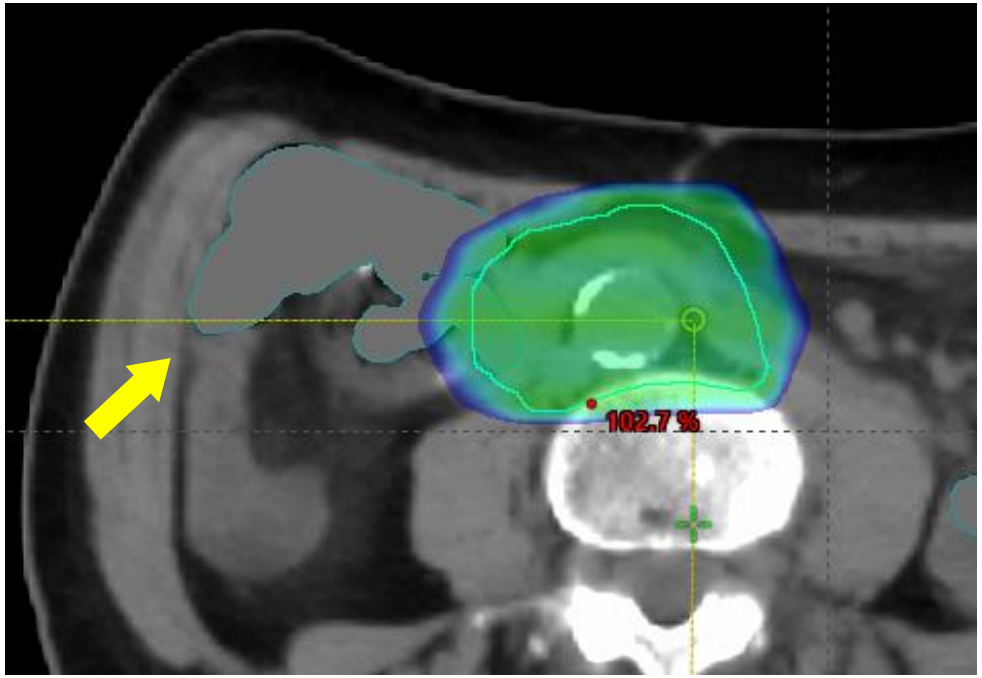
Original

VScan

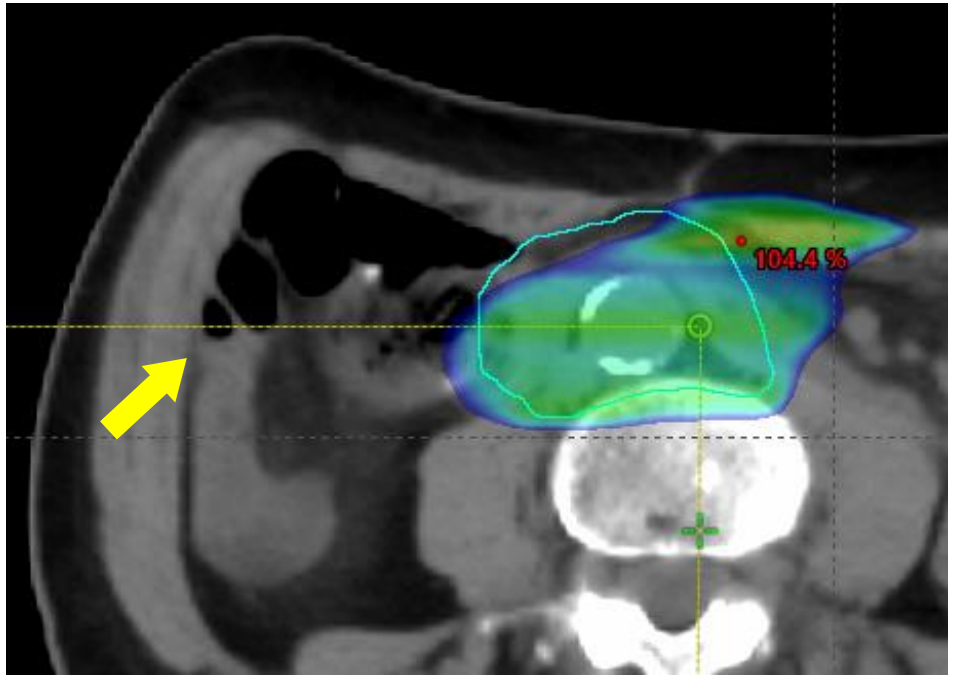


Interfractional: Bowel Gas

Original

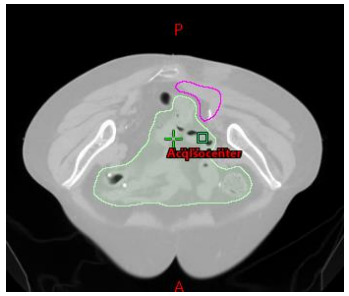


VScan

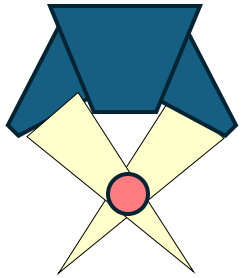


Adaptive planning trigger machnism

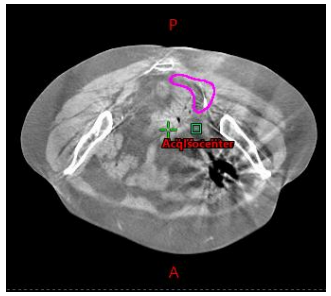
Planning CT



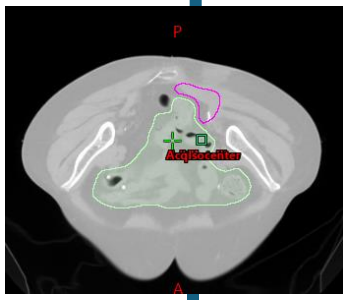
kV



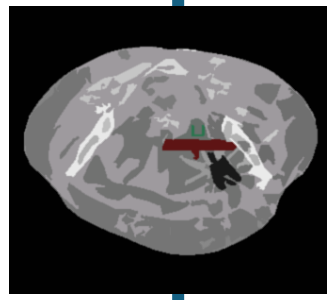
CBCT



Verficiation CT

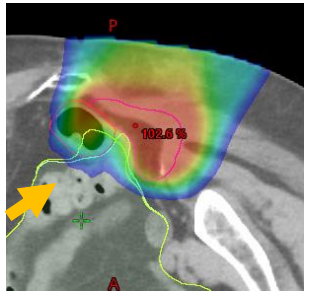


Synthetic CT

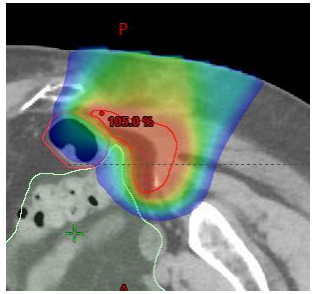


EVAL

Target -5%
OAR hot



Adaptive



Uncertainty in proton therapy

Modeling	Static	Longitidudinal	Dynamic
CT System SPR / conversion Dose Algorithm	Reproducibility Setup Error Metal Position	Tumor Change Weight Change Separation Change	Organ Motion Breathing Motion Interplay
Physics-driven Advanced Algorithm	Image-guidance Therapist Training	Resim Verificaiton Adaptive Planning	**Motion Monitoring** **Motion Management**

Optimal Planning

Motion Management

Respiratory Motion

bowel movement

Swallow motion

Cardiac motion

Organ Motion

Management of Motion

Simulation

Immobilization
Breath Hold
4DCT + ITV

Planning

SFUD
More Fields
RS+Air Gap
Repainting
Fractionation

Robustness

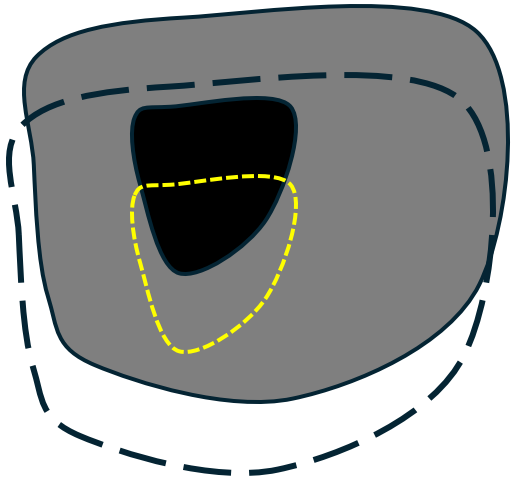
Robustness Evaluation

&

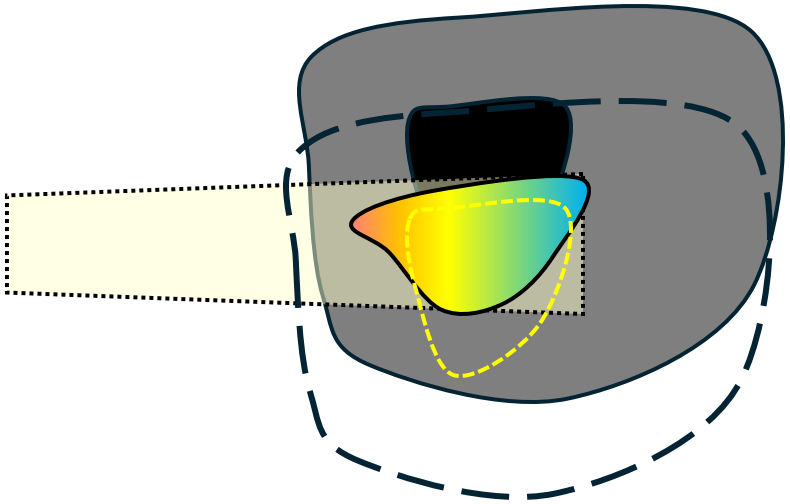
Optimization

Motion Evaluation

Translational Evaluation

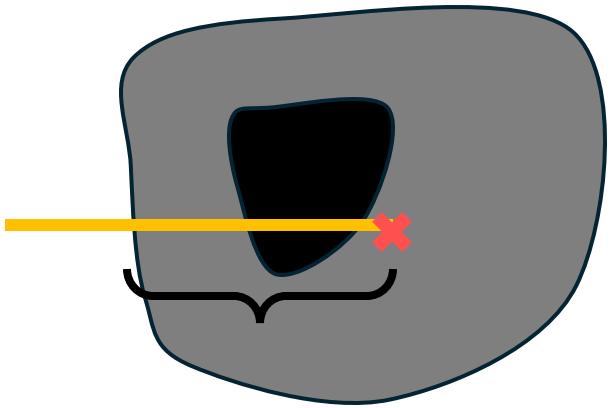


Dosimetric Evaluation

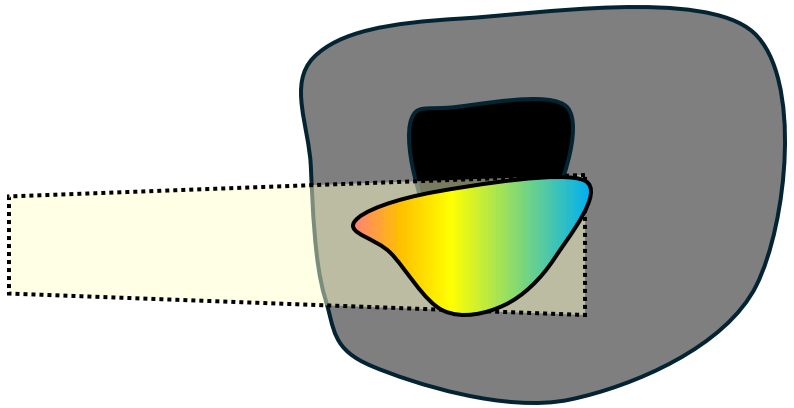


Motion Evaluation

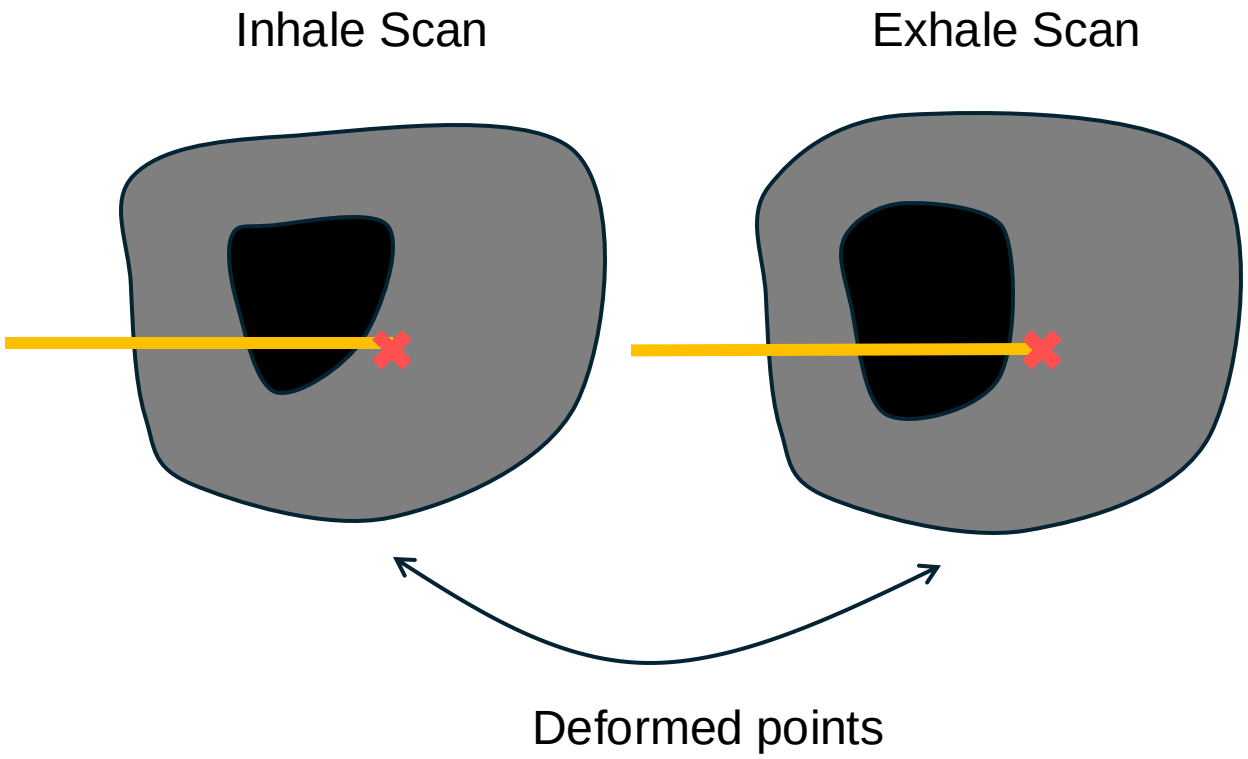
WET Evaluation

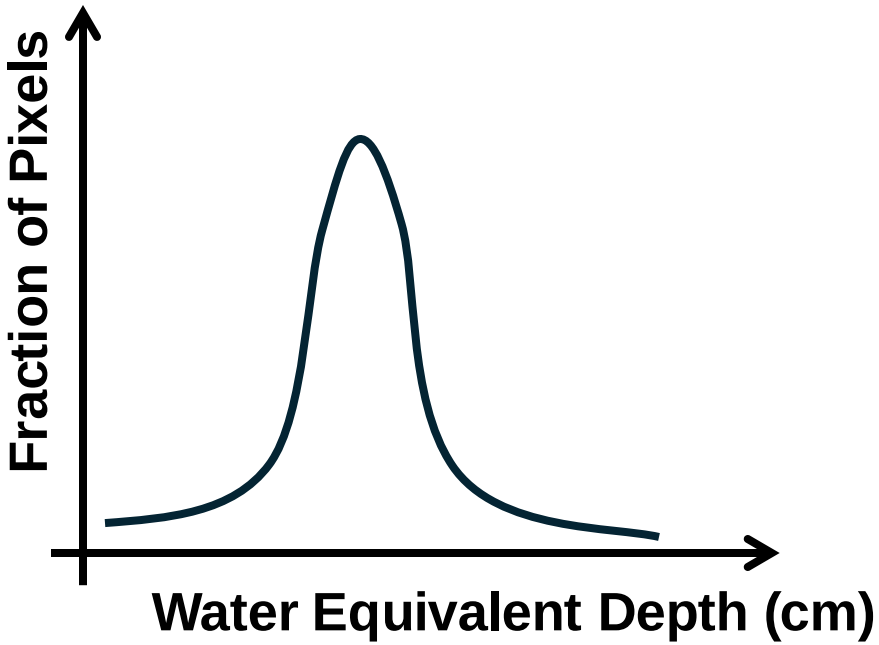


Dosimetric Evaluation

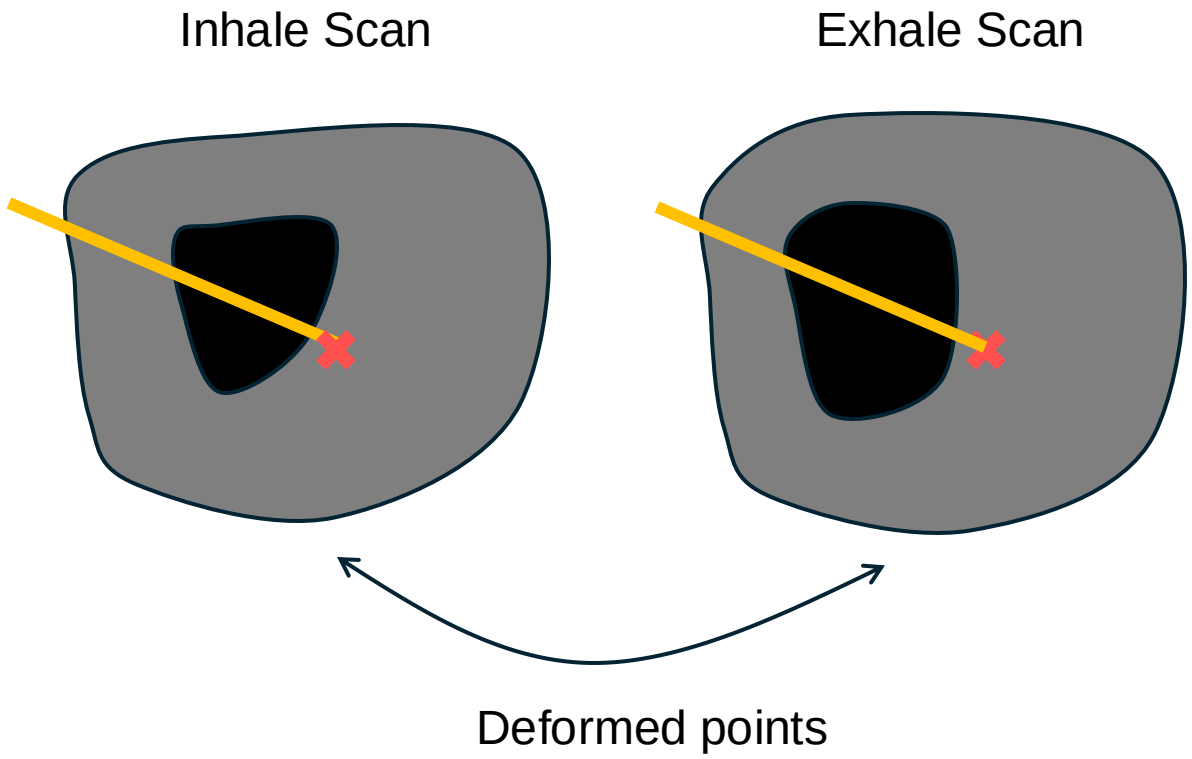


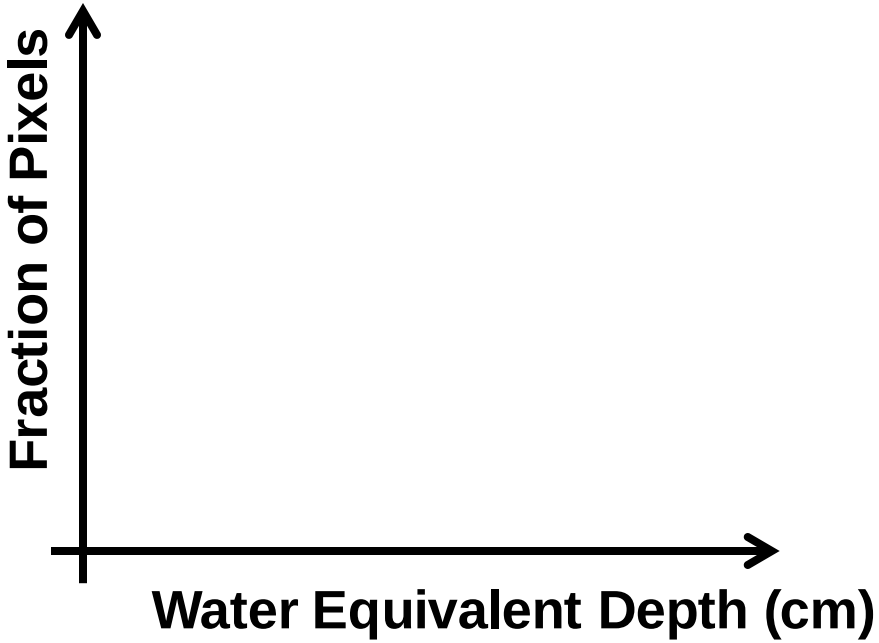
Motion Evaluation





Motion Evaluation





Motion Evaluation

Motion analysis

Target volume increase (itv) : 11%

Target center motion [mm] : 0.9 (left-right), 3.5 (ant-post), 6.4 (sup-inf), 7.4 (3D)

Average motion [mm] : 1.1 (left-right), 3.6 (ant-post), 6.8 (sup-inf), 8.1 (3D)

Maximum motion [mm] : 6 (left-right), 8.3 (ant-post), 13.5 (sup-inf), 14.1 (3D)

80-percentile motion [mm] : 1.9 (left-right), 4.4 (ant-post), 10.4 (sup-inf), 11.1 (3D)

90-percentile motion [mm] : 2.7 (left-right), 4.8 (ant-post), 11.6 (sup-inf), 12.1 (3D)

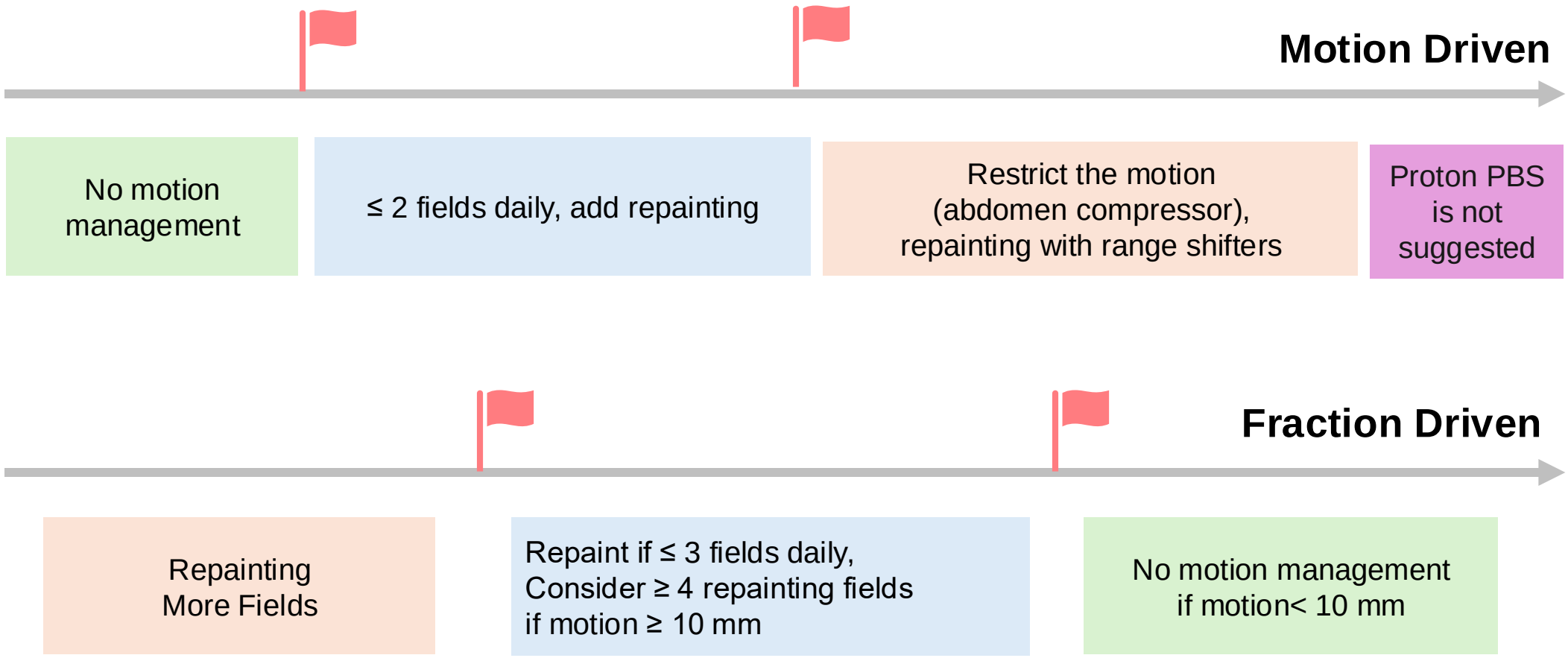
Average WET variation [mm] : 3.1 (0°), 6.9 (180°), 4.4 (240°), 3.3 (270°), 2.7 (300°), 2.7 (330°)

Maximum WET variation [mm] : 48.8 (0°), 38 (180°), 65.2 (240°), 64.5 (270°), 51.9 (300°), 45.4 (330°)

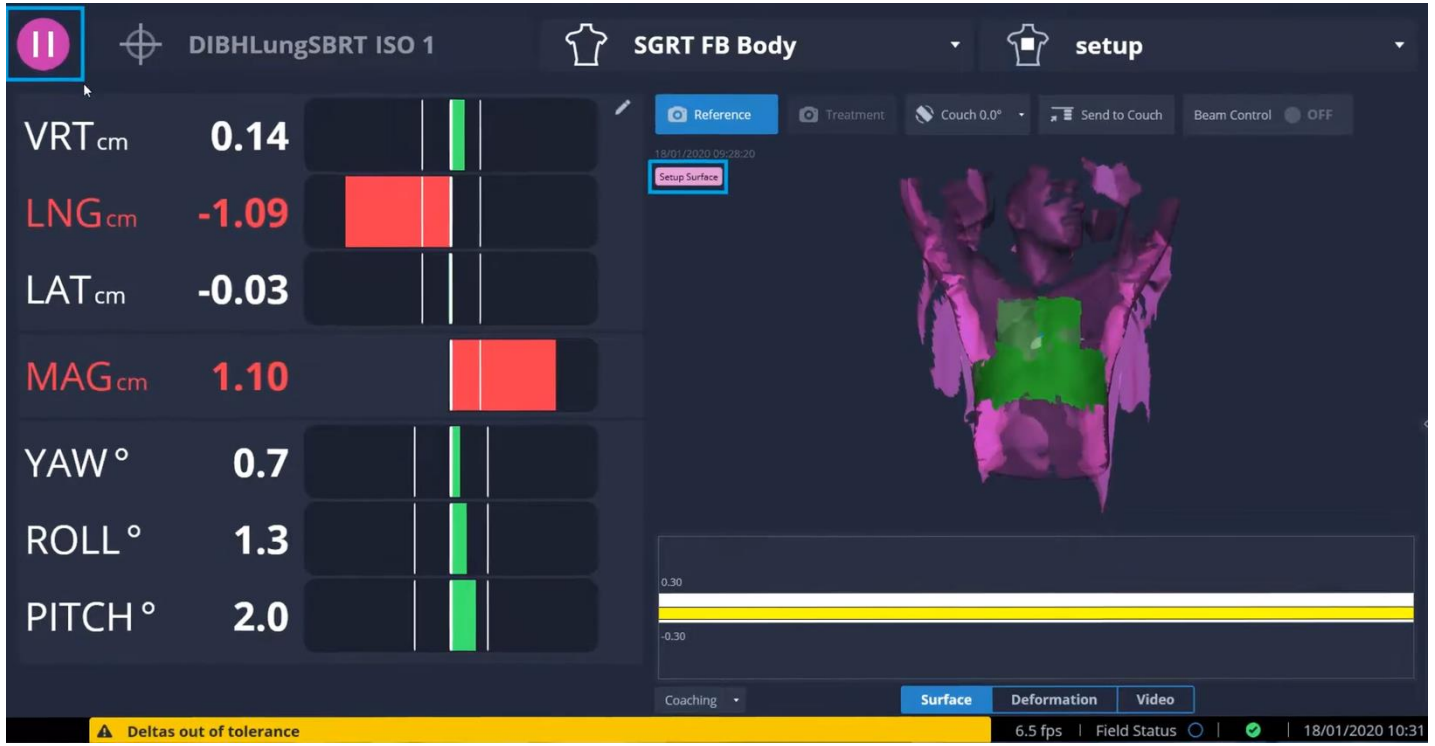
80-percentile WET variation [mm] : 3.8 (0°), 11.6 (180°), 7.7 (240°), 4.3 (270°), 2.3 (300°), 2.7 (330°)

90-percentile WET variation [mm] : 5 (0°), 14.3 (180°), 12.3 (240°), 9.4 (270°), 5.8 (300°), 4.2 (330°)

Patient triage with motion management



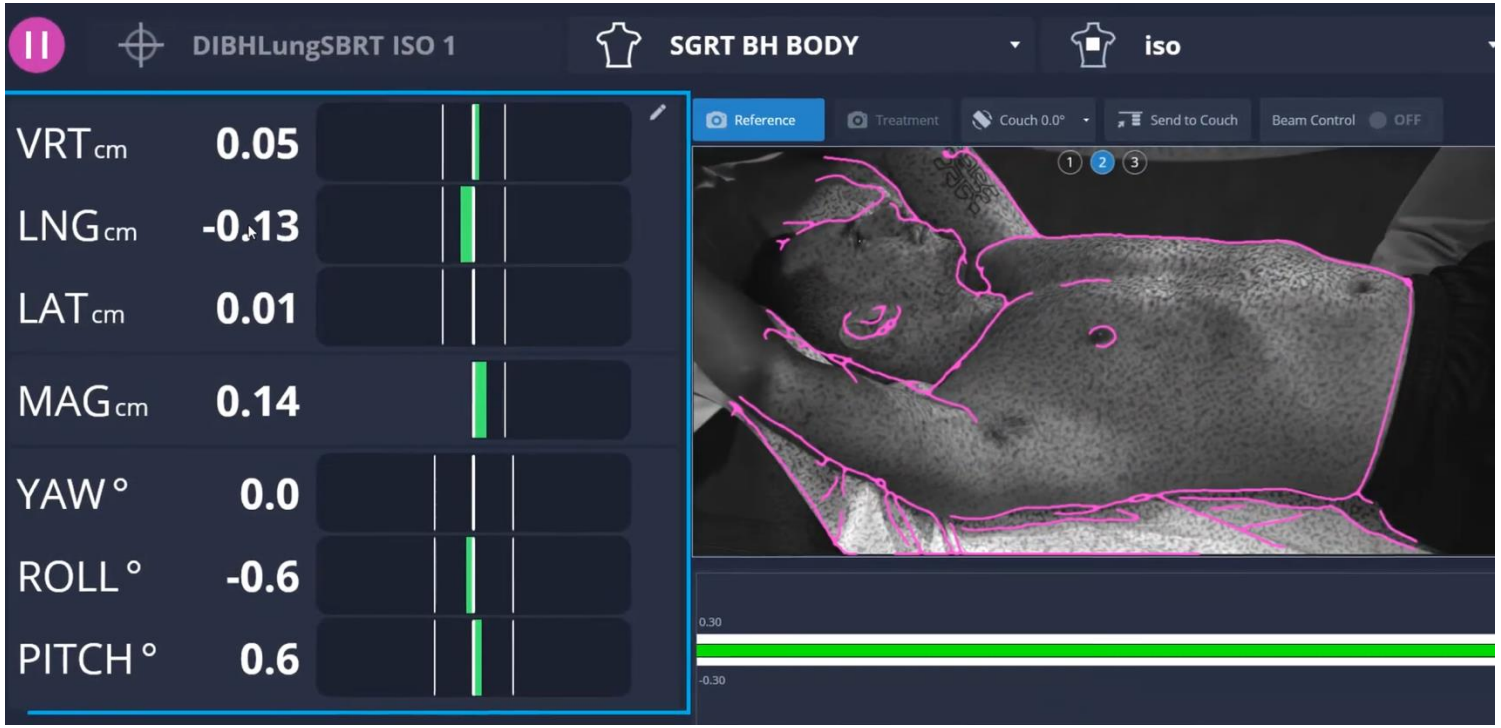
Management of respiratory motion (RWJ)



Free Breathing Setup

Only available in TR2 @NYPC

Management of respiratory motion (RWJ)



Posture Video for DIBH

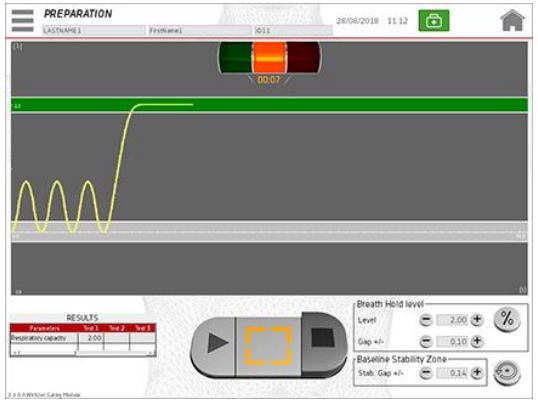
Only available in TR2 @NYPC

Management of respiratory motion (NYPC)

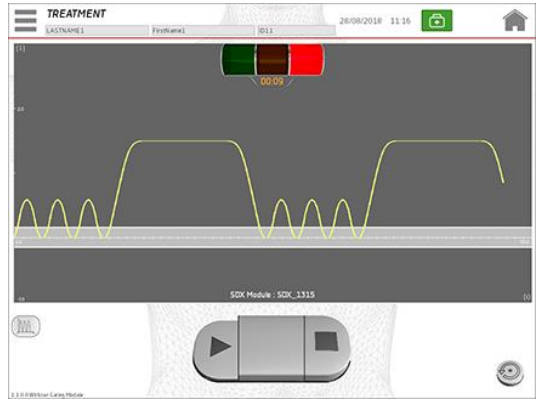
SDX® Breath Hold

Site: Lung, Liver

Training/Imaging

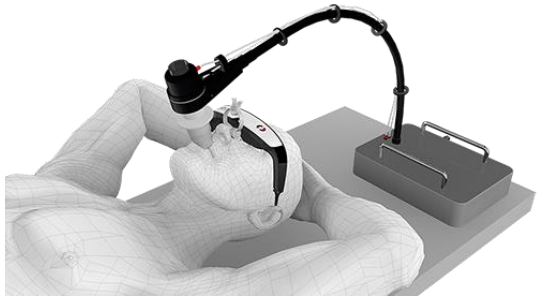


Treatment



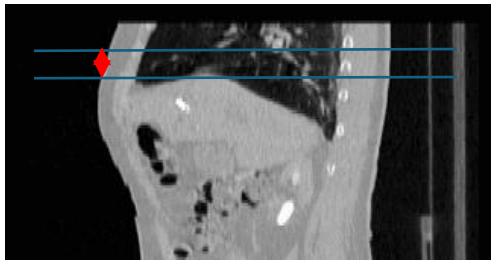
Management of respiratory motion

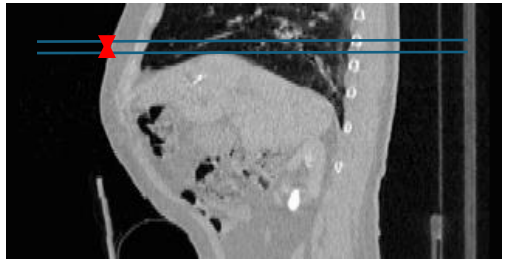
VisionRT/SDX®
Breath Hold



Patient cannot perform breath hold / hold to the level during treatment

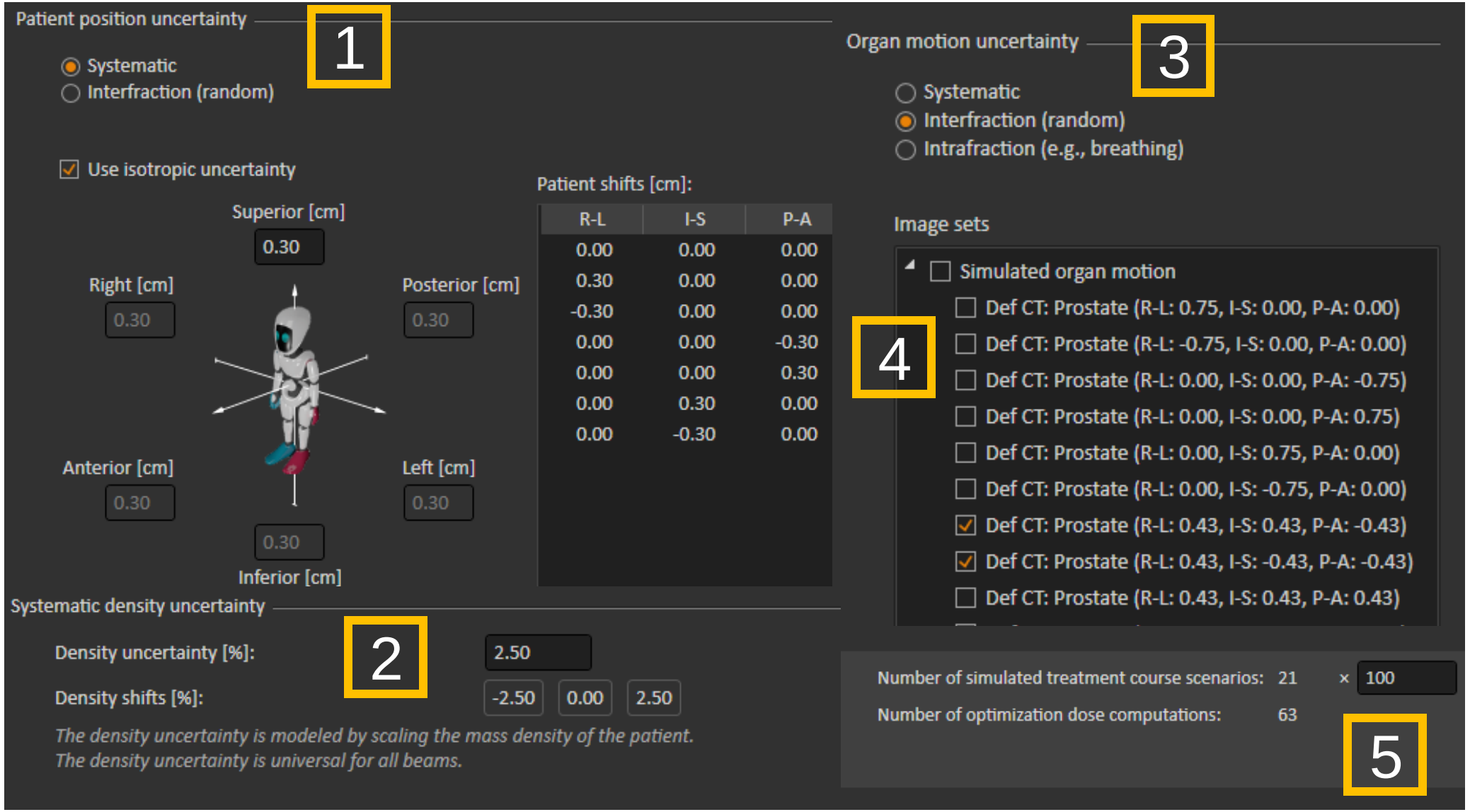
Compression Belt





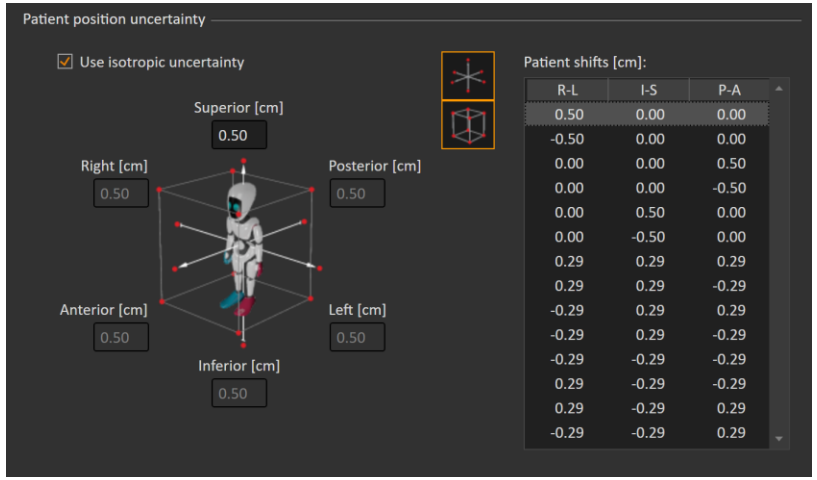
Irregular breath → 4DCT artifact

Comprehensive Robust Planning (Raystation only)

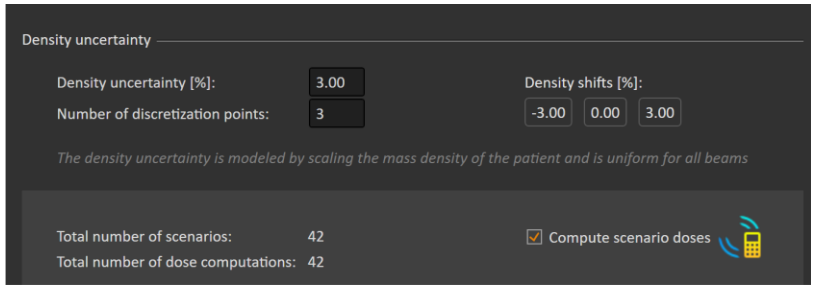


Robustness Evaluation (Raystation Version)

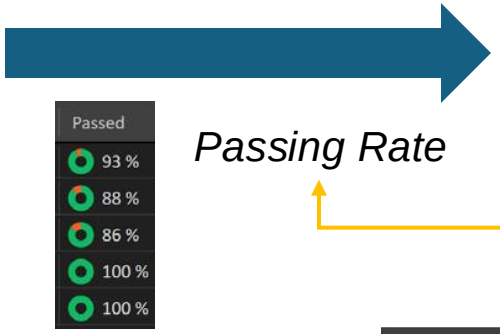
Setup Uncertainty



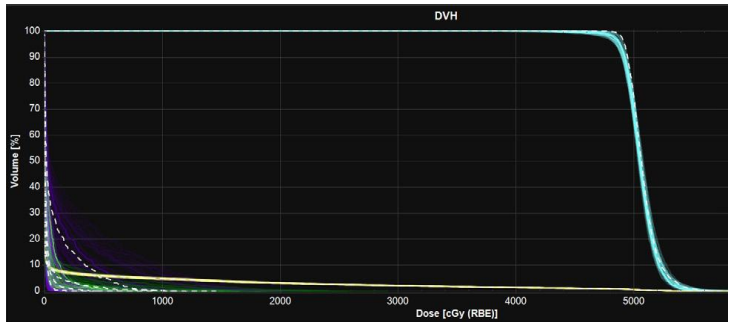
Range Uncertainty



Robust Optimization

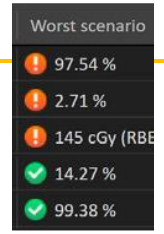


Passing Rate

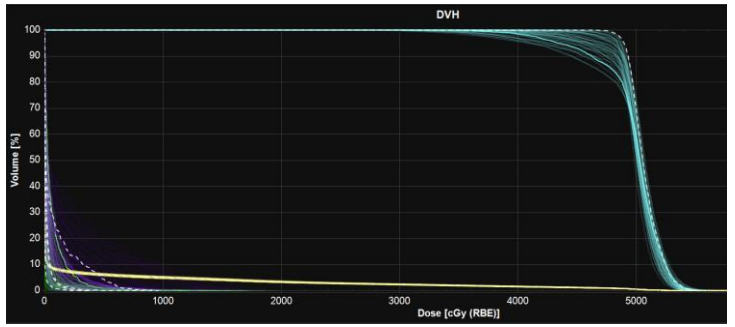


Priority	ROI/POI	Clinical goal	Passed	Current scenario	Worst scenario	Nominal result
1	CTV	At least 98.00 % volume at 4750 cGy (RBE) dose	93 %	98.79 %	97.54 %	99.96 %
2	CTV	At most 2.00 % volume at 5420 cGy (RBE) dose	88 %	0.64 %	2.71 %	1.77 %
3	esophagus	At most 100 cGy (RBE) dose at 10.00 % volume	86 %	131 cGy (RBE)	145 cGy (RBE)	43 cGy (RBE)
3	Right Lung	At most 15.00 % volume at 2500 cGy (RBE) dose	100 %	11.89 %	14.27 %	13.03 %
4	CTV	At least 98.00 % volume at 4400 cGy (RBE) dose	100 %	99.84 %	99.38 %	100.00 %

Worst Scenario



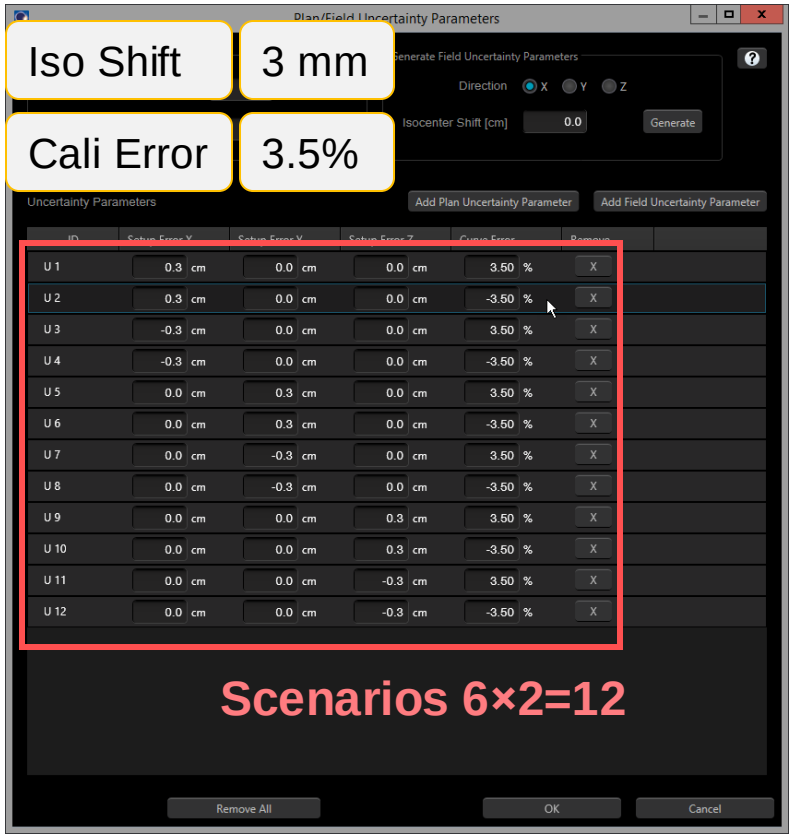
Non-robust Optimization



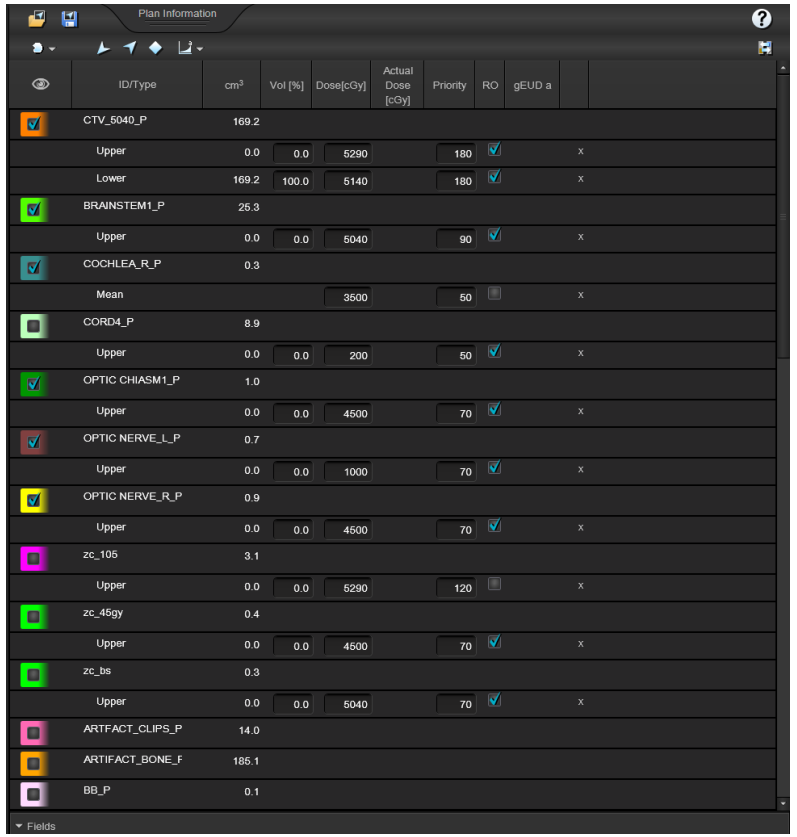
Priority	ROI/POI	Clinical goal	Passed	Current scenario	Worst scenario	Nominal result
1	CTV	At least 98.00 % volume at 4750 cGy (RBE) dose	14 %	86.61 %	82.39 %	99.72 %
2	CTV	At most 2.00 % volume at 5420 cGy (RBE) dose	100 %	0.67 %	1.94 %	0.89 %
3	esophagus	At most 100 cGy (RBE) dose at 10.00 % volume	76 %	179 cGy (RBE)	228 cGy (RBE)	47 cGy (RBE)
3	Right Lung	At most 15.00 % volume at 2500 cGy (RBE) dose	71 %	12.99 %	16.65 %	14.57 %
4	CTV	At least 98.00 % volume at 4400 cGy (RBE) dose	43 %	94.43 %	90.61 %	100.00 %

Robust Planning (ECLIPSE version)

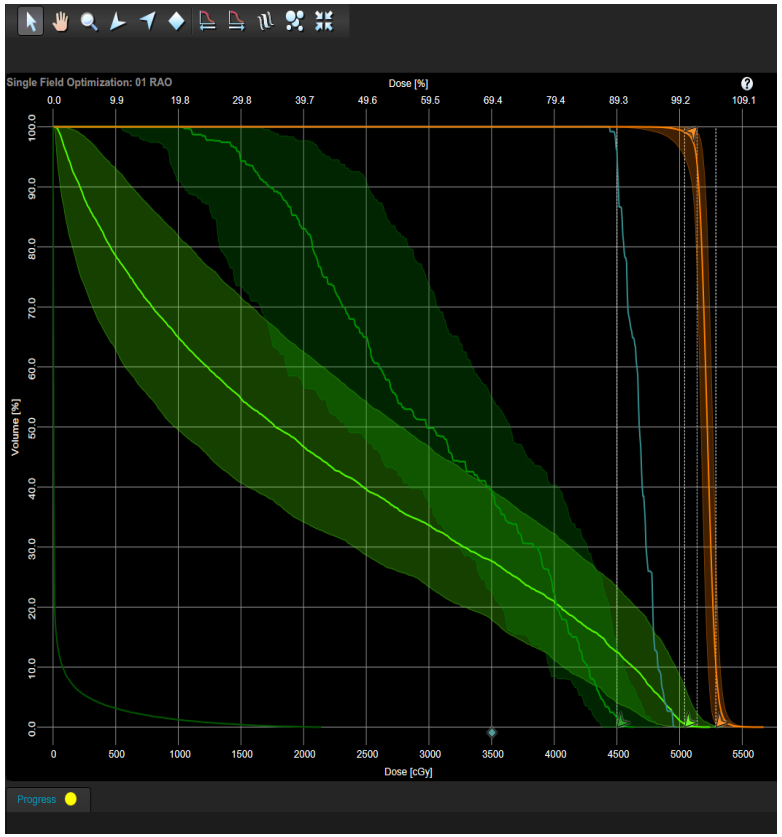
Setup Uncertainty



Optional RO



DVH band Visualization



Robustness Evaluation (ECLIPSE version)

Setup Uncertainty

Generate Plan Uncertainty Parameters

Isocenter shift: 0.30 [cm]

Calibration curve error: 3.50 [%]

Generate

Plan Uncertainty Parameters

Isocenter shift coordinates are expressed in the planning coordinate system selected in RT Administration.

ID	Patient Setup Error			Curve Error [%]	Calculation Status	Remove
	X [cm]	Y [cm]	Z [cm]			
U1	+0.30	0.00	0.00	+3.50	Calculated	Remove
U2	+0.30	0.00	0.00	-3.50	Calculated	Remove
U3	-0.30	0.00	0.00	+3.50	Calculated	Remove
U4	-0.30	0.00	0.00	-3.50	Calculated	Remove
U5	0.00	+0.30	0.00	+3.50	Calculated	Remove
U6	0.00	+0.30	0.00	-3.50	Calculated	Remove
U7	0.00	-0.30	0.00	+3.50	Calculated	Remove
U8	0.00	-0.30	0.00	-3.50	Calculated	Remove
U9	0.00	0.00	+0.30	+3.50	Calculated	Remove
U10	0.00	0.00	+0.30	-3.50	Calculated	Remove
U11	0.00	0.00	-0.30	+3.50	Calculated	Remove
U12	0.00	0.00	-0.30	-3.50	Calculated	Remove

Add New | Remove All

Plan Uncertainty Dose Calculation

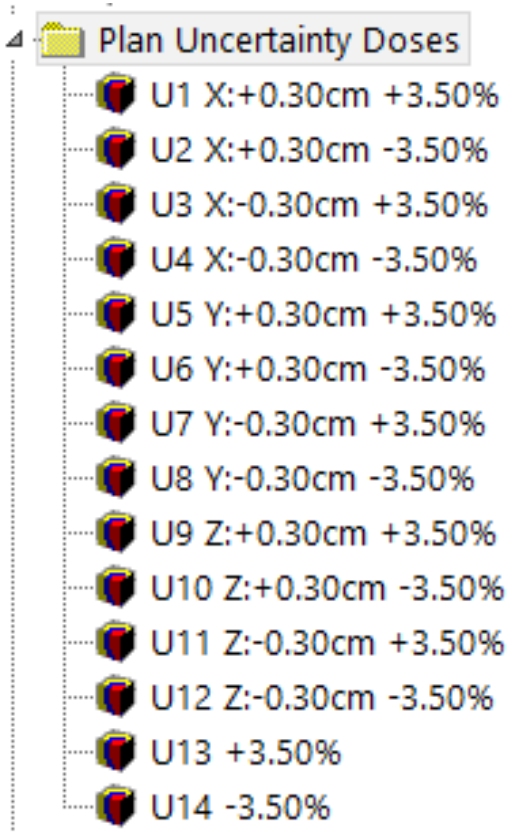
☐ Calculate automatically after nominal dose calculation

☐ Calculate after clicking OK

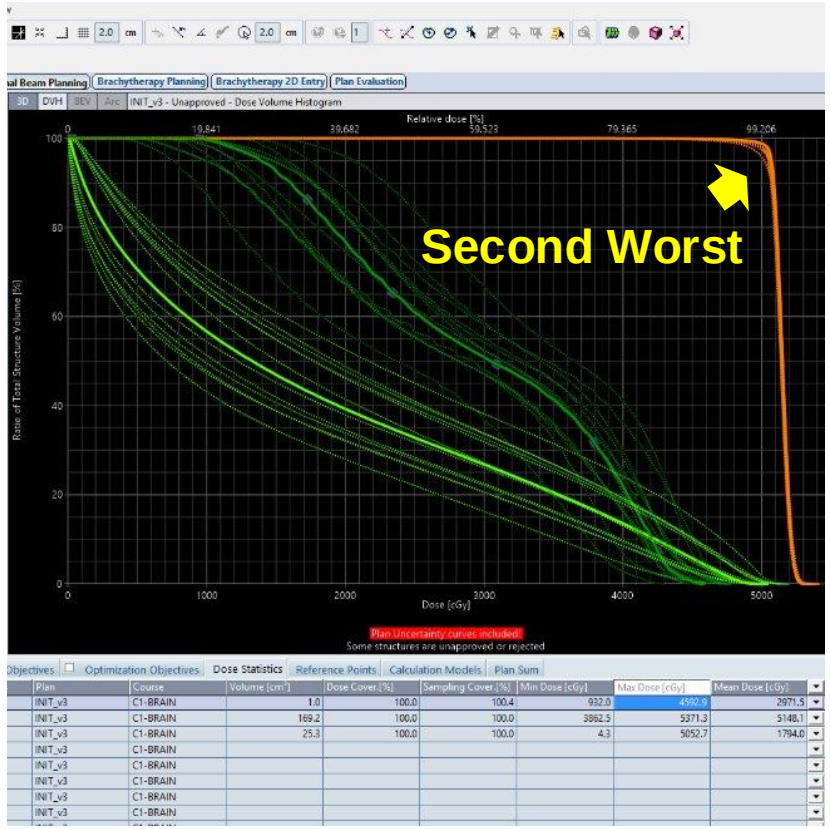
Plan uncertainty doses are calculated for each parameter set. Memory consumption may affect the performance of your computer.

OK | Cancel

Calculated Scenarios

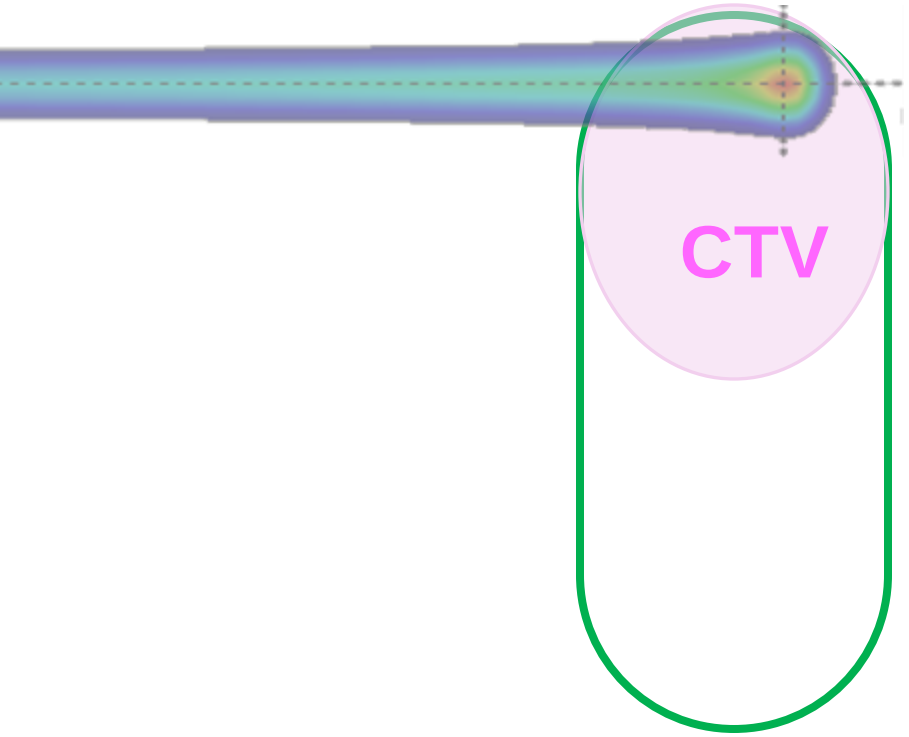


DVH Evaluation

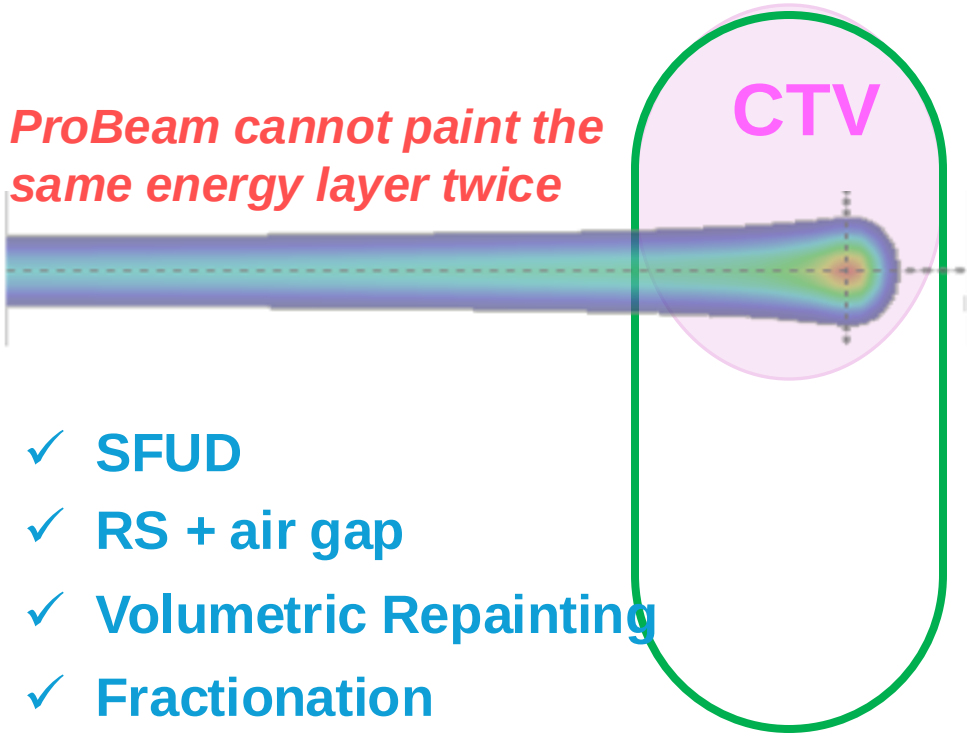


Interplay Effect

Interplay



ProBeam cannot paint the same energy layer twice

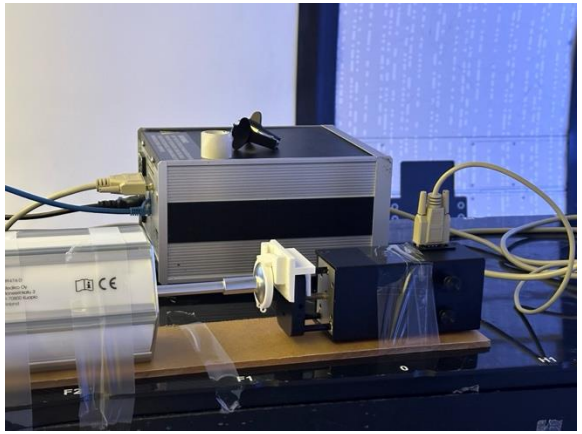


- ✓ SFUD
- ✓ RS + air gap
- ✓ Volumetric Repainting
- ✓ Fractionation

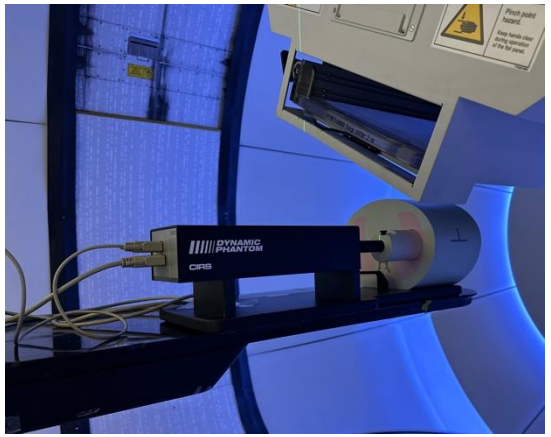
Evaluation of Interplay Effect (Phantom)

SDX 3L

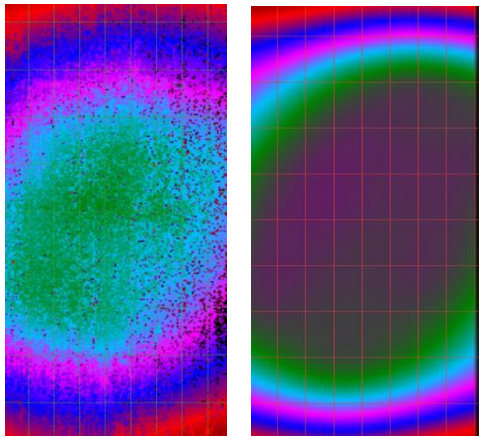
Motion Simulator



Lung Phantom

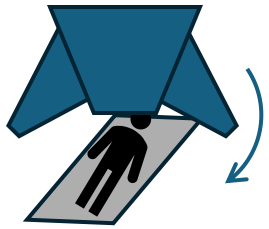


Film Measurement



Evaluation of Interplay Effect (Patient Evaluation)

Treatment Delivery



Varian Log File

Time Points
Energy, spot size, MU
No transition information

Temporal Simulation

Gating File

Offline Simulation

Summary

- Proton therapy benefits from distal fall-off with proper management of range uncertainty.
- Careful consideration of reproducibility and close onboard monitoring of anatomical variation is crucial ensure the integrity of the plan.

Acknowledgement

RWJBarnabas HEALTH

Dr Ke Nie

Rihan Davis

Dr Xiao Wang

NEW YORK PROTON CENTER

Dr Haibo Lin

Dr Alex Shouyi Wei

Lee Xu

Peter Park

Contact: cz453@cinj.rutgers.edu