MAYO CLINIC

SG-SFRT: The Use of Surface Imaging for Spatially Fractionated Radiotherapy

Yi Rong, PhD, FAAPM

Professor and Photon Lead Physicist

Mayo Clinic Arizona

Conflict of Interest

- Co-Investigator: Automatic Organ Segmentation Tool for Radiation Treatment Planning of Cancers. Funded by National Cancer Institute. (R44CA254844)
- No other financial COI to disclose

GRID Therapy

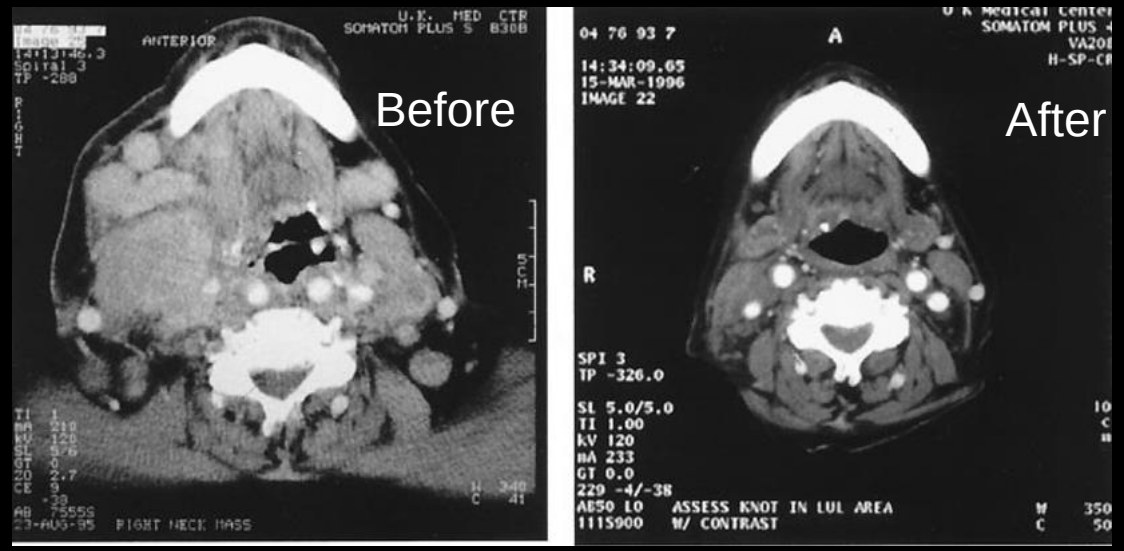
- **GRID** therapy was proposed as early as 1950's, initially for skin cancer treatment to increase tolerance,
- External beam radiation therapy (SFRT, Aka GRID, lattice)
- **GRID** collimator deliberately creates hot and cold spots (dose heterogeneity)
- Large nominal dose used, original only used for one fraction
- Official name is **Spatially fractionated radiation therapy** (SFRT)

CLINICAL INVESTIGATION **Palliative Care**

HIGH-DOSE SPATIALLY-FRACTIONATED RADIATION (GRID): A NEW PARADIGM IN THE MANAGEMENT OF ADVANCED CANCERS

- Early Studies in 1999: In selected patients with bulky tumors (>8cm), SFR radiation can be combined with fractionated external beam irradiation to yield improved local control of disease, both for palliation and selective definitive treatment

IJROBP,Vol.45,No.3,pp.721±727,1999



Neck nodes from primary squamous cell cancer of the oropharynx. 15Gy SFR (grid) and 60Gy external beam radiation.

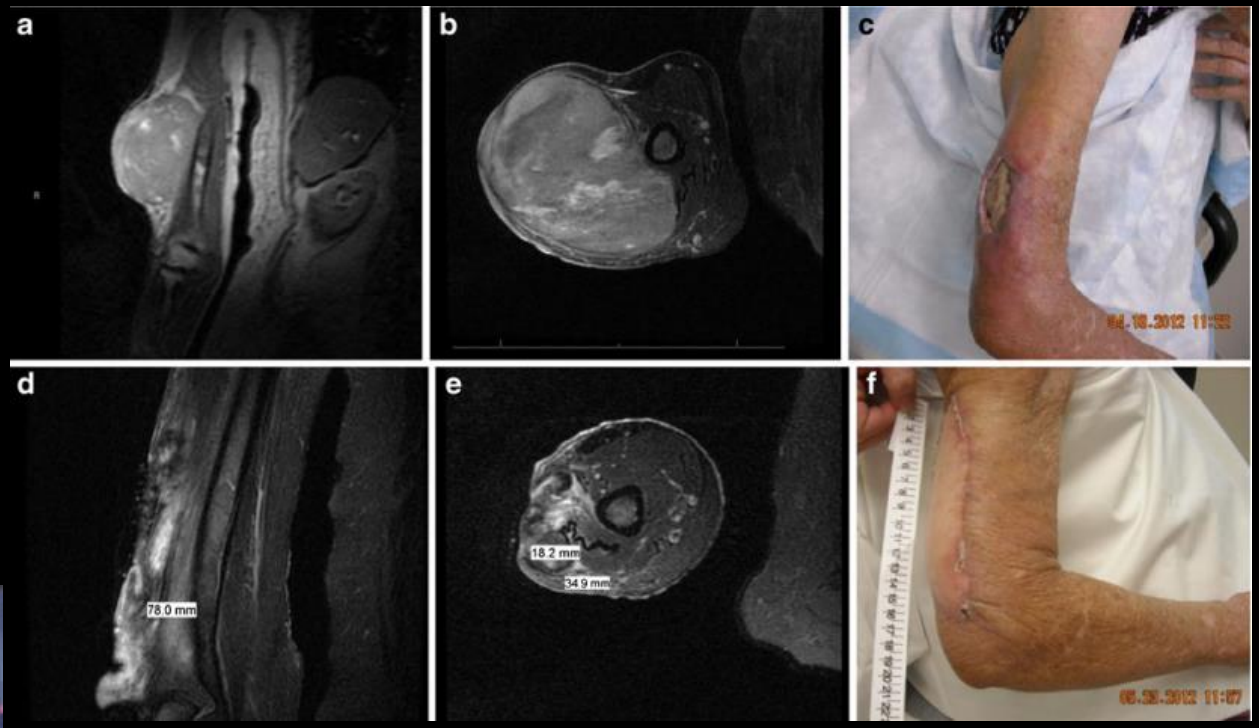
Table 2. Spatially fractionated radiation: Response rate by radiation dose

	No. of pts.	Complete response	Partial response	Total response	No response
SF Grid Dose					
< 1500 cGy	8	1/8 (12%)	4/8 (50%)	5/8 (62%)	3/8 (38%)
≥ 1500 cGy	79	12/72 (17%)	56/72 (68%)	68/72 (94%)	4/72 (6%)
External Beam Dose					
0 cGy	17	0/14 (0%)	12/14 (86%)	12/14 (86%)	2/14 (14%)
< 4000 cGy	25	3/23 (13%)	18/23 (78%)	21/23 (91%)	2/23 (9%)
≥ 4000 cGy	45	10/43 (24%)	30/43 (70%)	40/43 (94%)	3/43 (6%)
		13/80 (16%)	60/80 (75%)	73/80 (91%)	7/80 (9%)

Dramatic response from neoadjuvant, spatially fractionated GRID radiotherapy (SFGRT) for large, high-grade extremity sarcoma

J Radiat Oncol (2013) 2:103–106

- High grade spindle cell sarcoma
- 18 Gy GRID + 50 Gy in 25 fx
- Complete response, 6 weeks

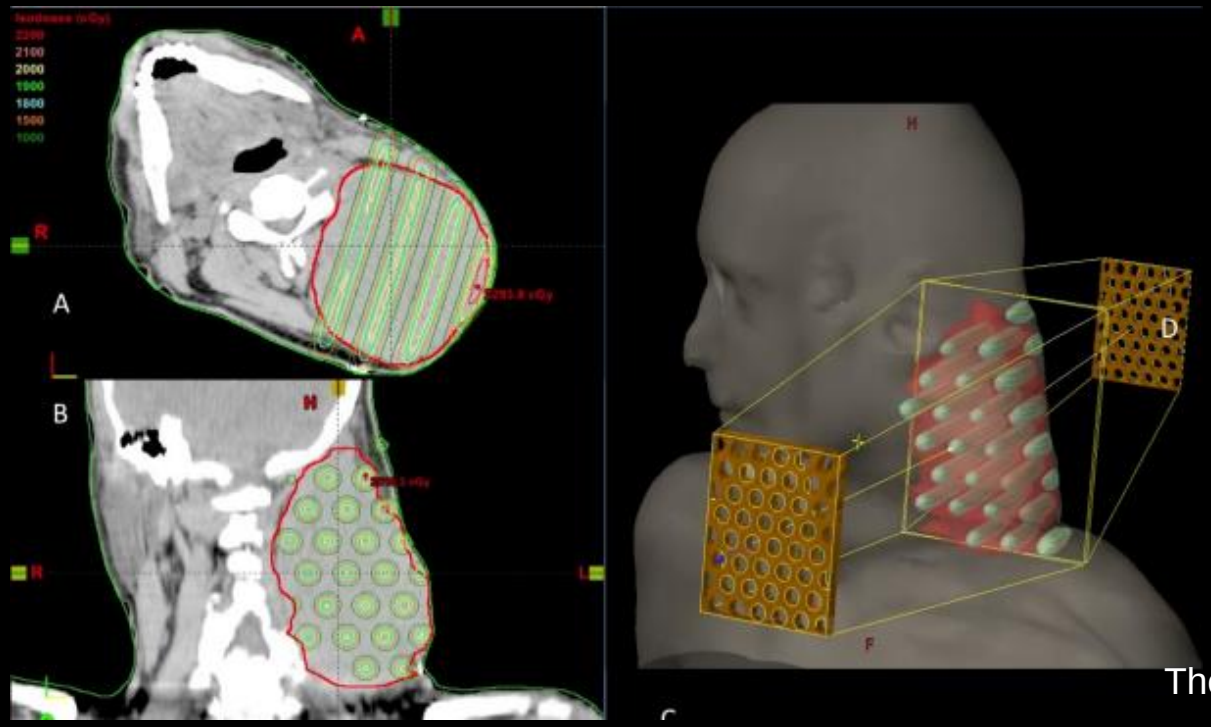


Clinical and radiographic tumor response to neoadjuvant radiation. a Coronal MRI prior to RT. b Axial MRI prior to RT. c Right upper arm before surgery and 6 weeks after completion of radiation. d Coronoal MRI of right upper arm 6 weeks

Right upper arm light field for SF-GRID RT with tumor penetrating through the skin indicated by a blue arrow

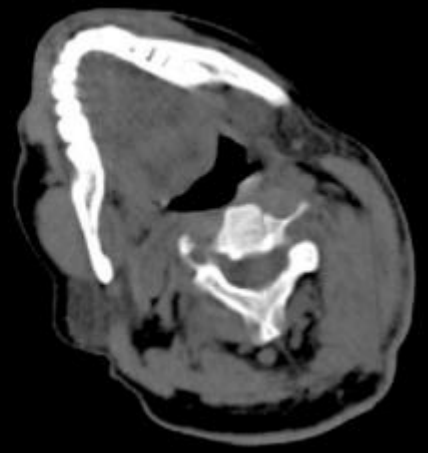
High-Dose Radiation as a Dramatic, Immunological Primer in Locally Advanced Melanoma

- Melanoma, refractory to multiple systemic therapies: 20 Gy GRID + 50 Gy in 25 fx
- Complete response, 5 months



2015 Mohiuddin et al. Cureus 7(12): e417

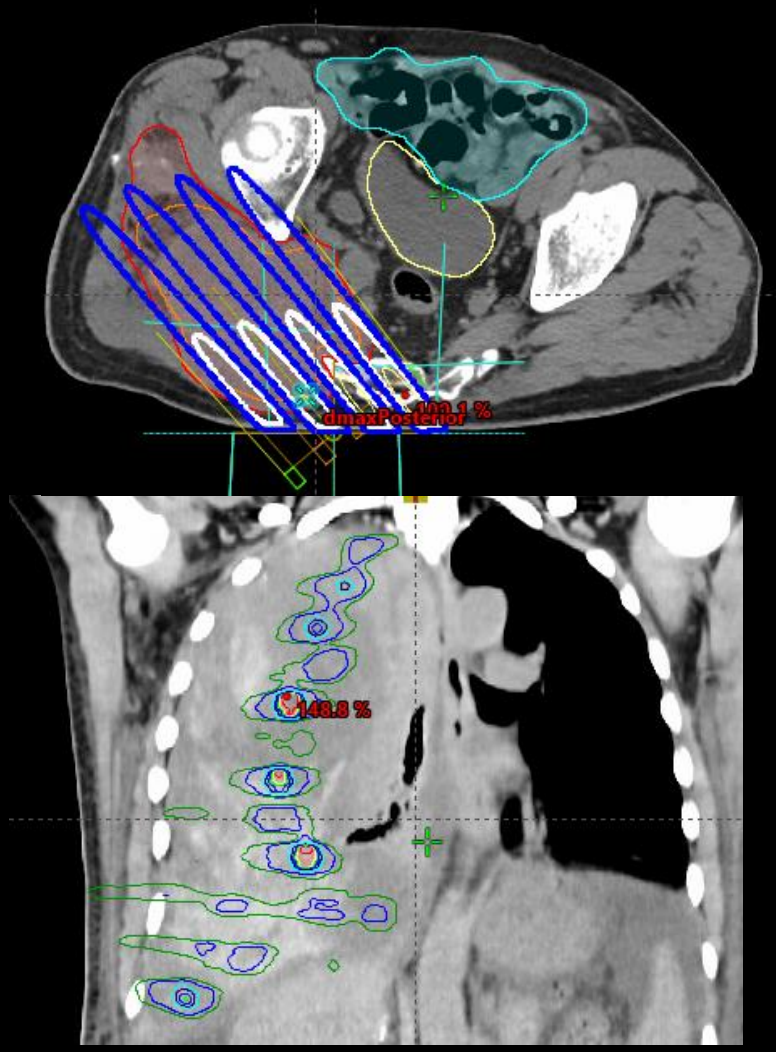
The initial tumor on the left posterior neck of 18 x 15 x 8 cm size, demarcated by wire



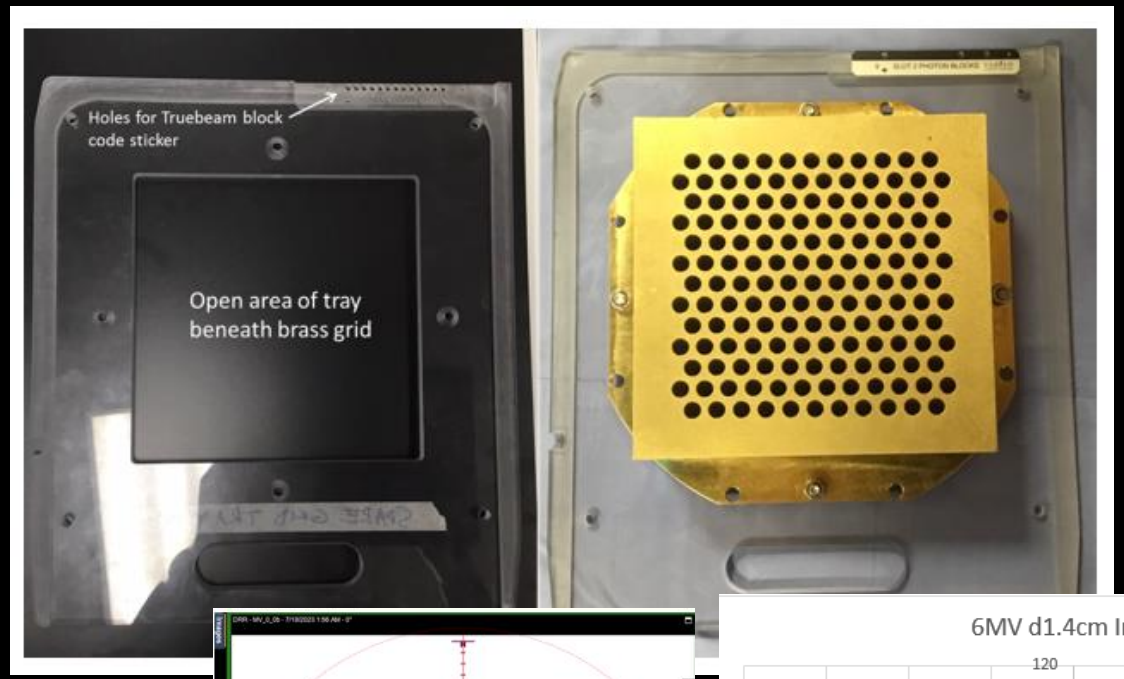
The tumor is completely gone 5 months later clinically and on CT scan

Different Form of Grid Treatment

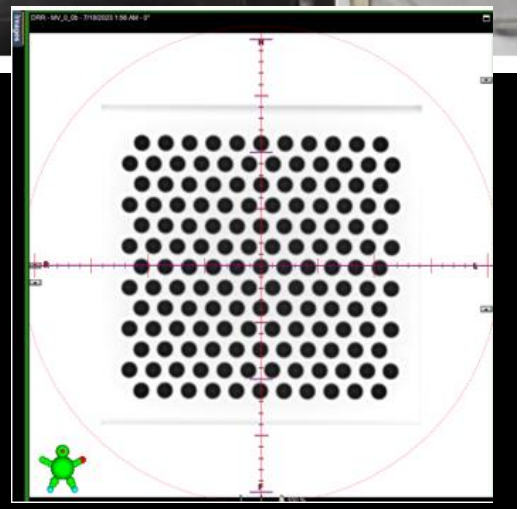
- Photon Brass Grid
  - Well-established modality; Easy to plan; Limited flexibility (max dose at dmax)
  - Dose upstream or downstream of target
  - Prescribe dose at dmax, use couch kicks and gantry positions
- Photon VMAT Lattice
  - Easily accessible; Optimized dose distributions; •Spare normal tissues
  - Longer planning time; No guidelines for location or spacing of high dose regions
- Proton Lattice

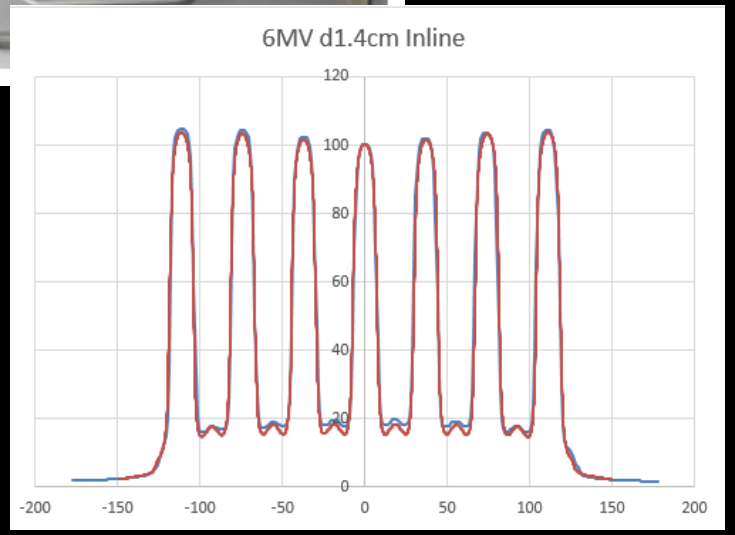


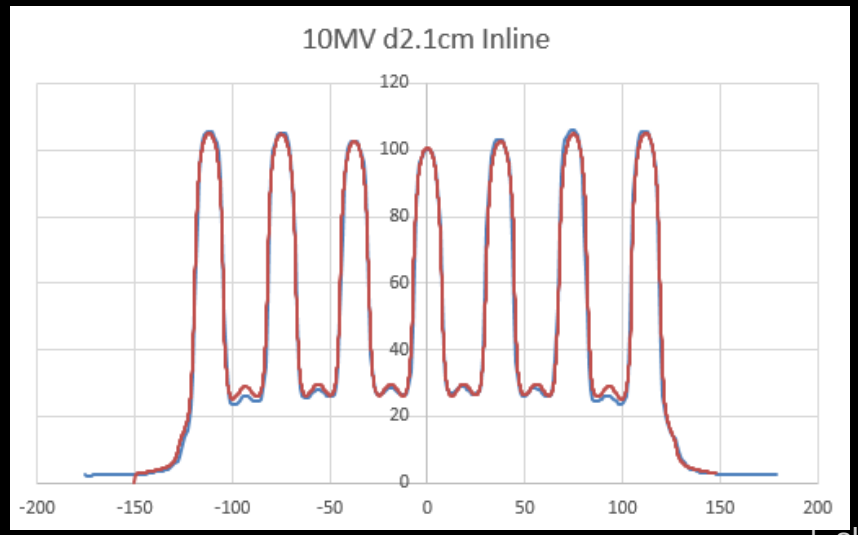
Brass Grid Aperture



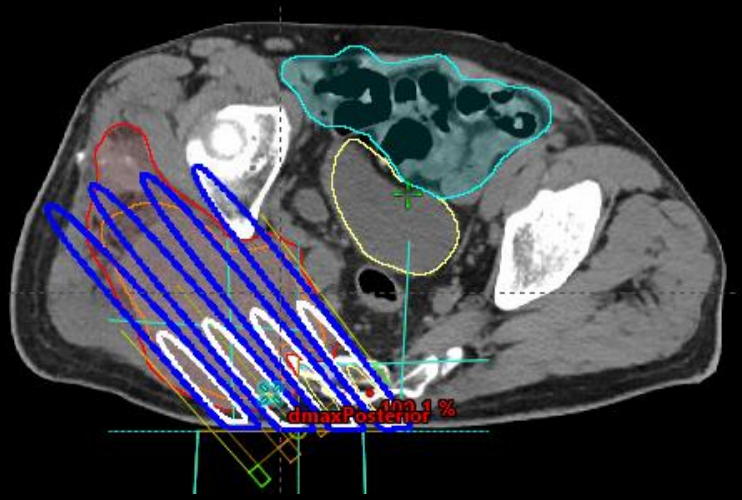
- Brass Grid attachment is about 40 lbs and depending on staff member comfort, placing the attachment can occur at Gantry of 181 or at treatment Gantry position. Treating therapists must perform a dry run of brass grid attachment.

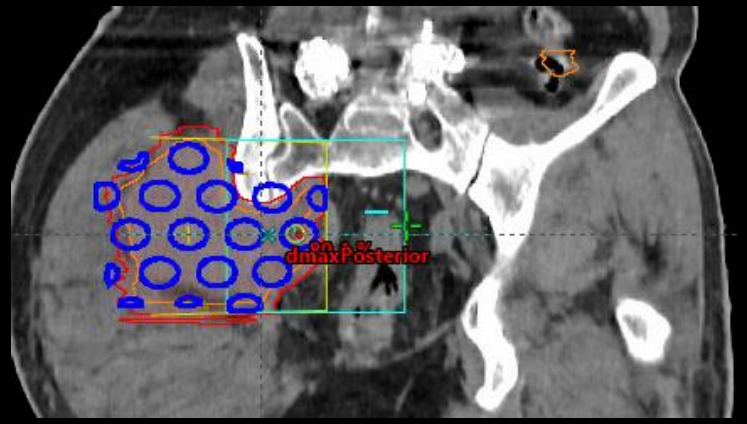


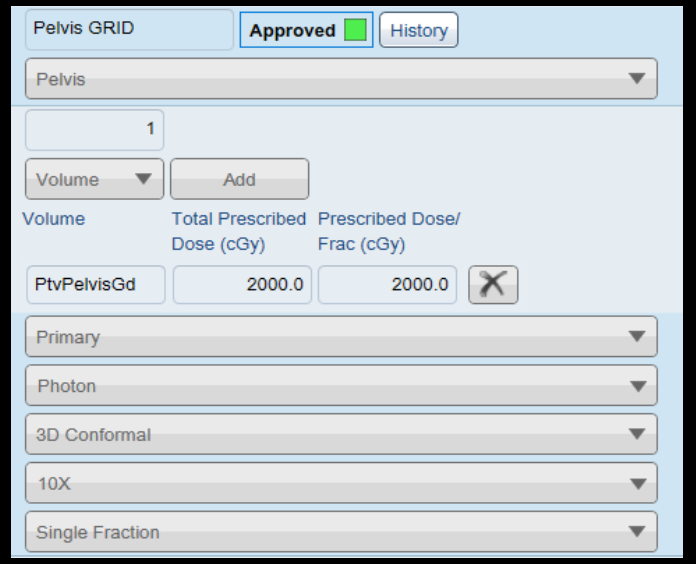




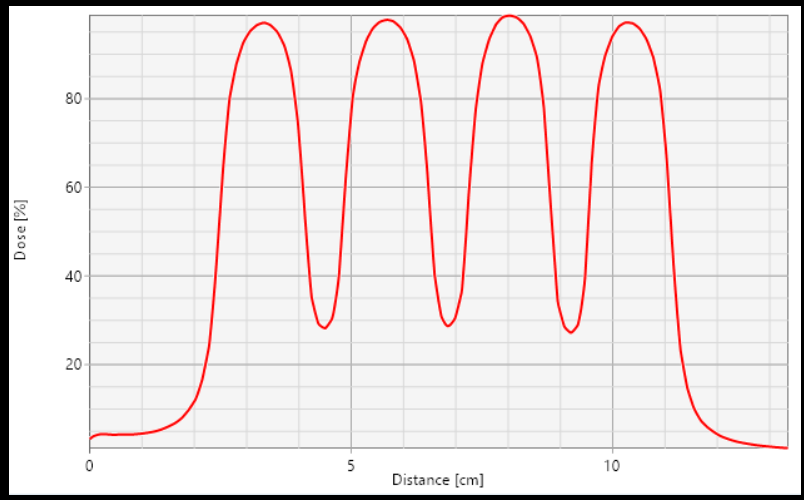
Brass Grid Planning





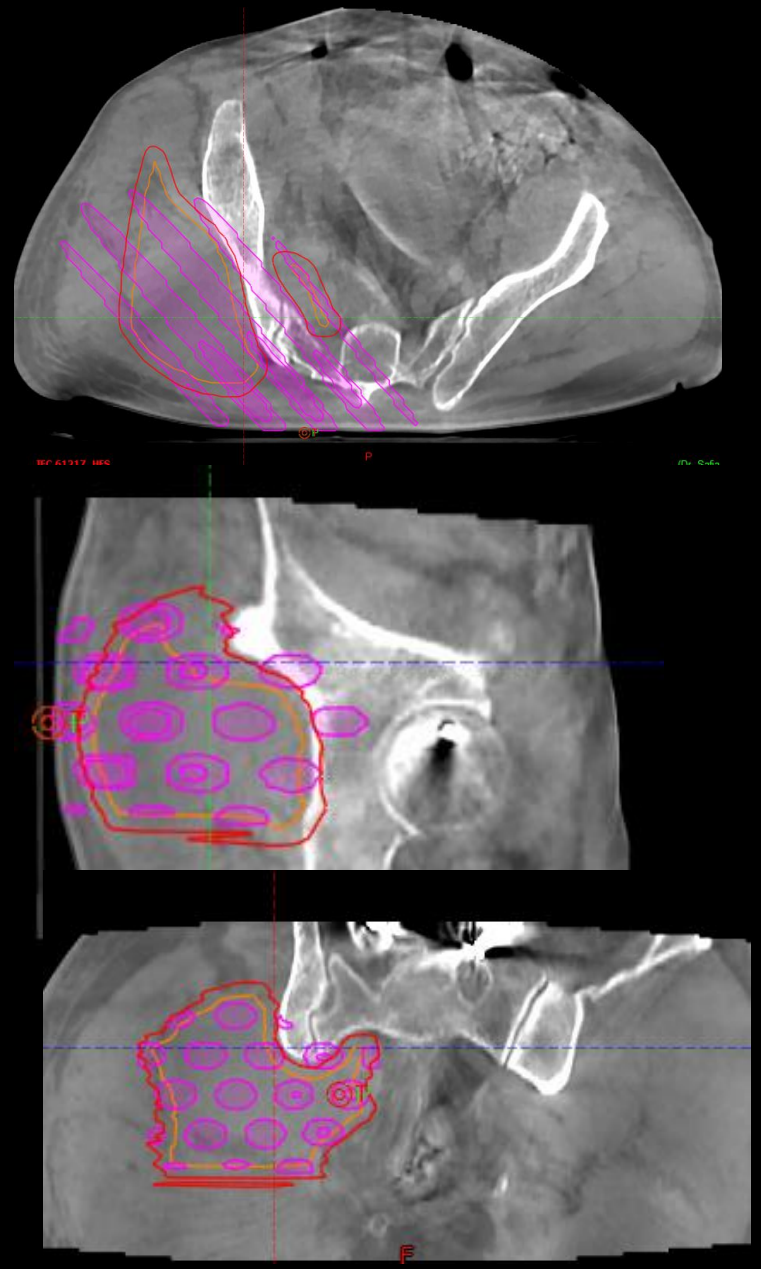


- Select the gantry angle that can cover the most part of the PTV; Clearance check prior to all treatment
- Collimator angle is always 0. Collimate to “z_gtv_sub 5mm” with 0 margin; SSD=100cm
- Normalize the plan 100% to dmax (d=1.4cm for 6X and d=2.1cm for 10X)
- Create 50% and 80% isodose lines into structures for IGRT



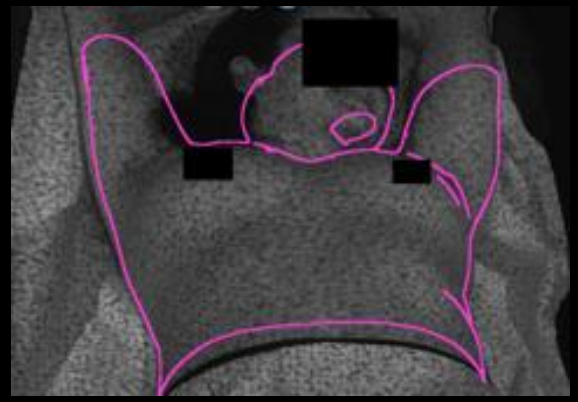
IGRT and Alignment Guideline

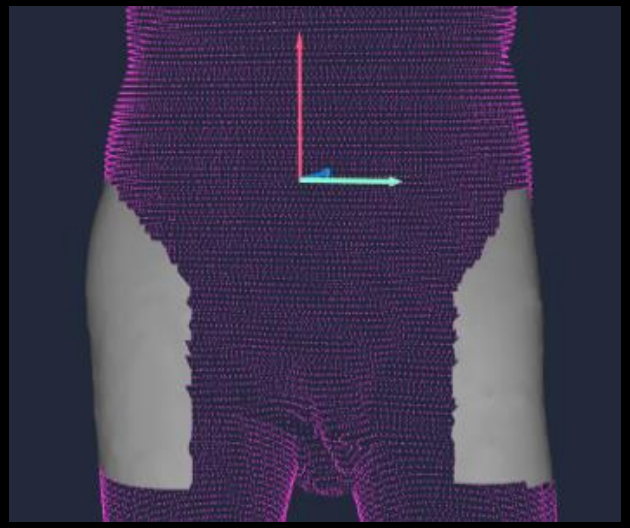
- Journal note: Patient setup SSD=100cm; CBCT (or kV), turn on “z_Gtv_sub_5mm”, Dose 50% and 80%; VisionRT to monitor treatment
- Patient setup
  - Use postural alignment to verify treatment site in position
  - Set 100 cm SSD
  - Take reference capture with VisionRT prior to leaving room.
- IGRT: Perform either CBCT or KV (based on patient pain level/MD order)
  - Treating at 100 SSD, do not adjust table vertical.
  - Pitch and Roll
    - ✓If 3 degrees or less, do not apply these shifts.
    - ✓If over 3 degrees for either, reposition patient to get 3 degrees or under.
    - ✓Send shifts , but do not apply at the treatment console (due to clearance issue)



SGRT Monitoring for Brass Grid

- Perform either CBCT or KV (based on patient pain level/MD preference)
  - For KV, take a new reference capture first.
  - For CBCT, center couch then take a new reference capture first.
  - Monitoring instructions:
    - Treating at 100 SSD, do not adjust table vertical.
    - X, Y, Z: 3mm margin tolerance will be default (MD may make the decision at time of treatment to alter the tolerance.)
    - Rotational tolerance: 2 degree

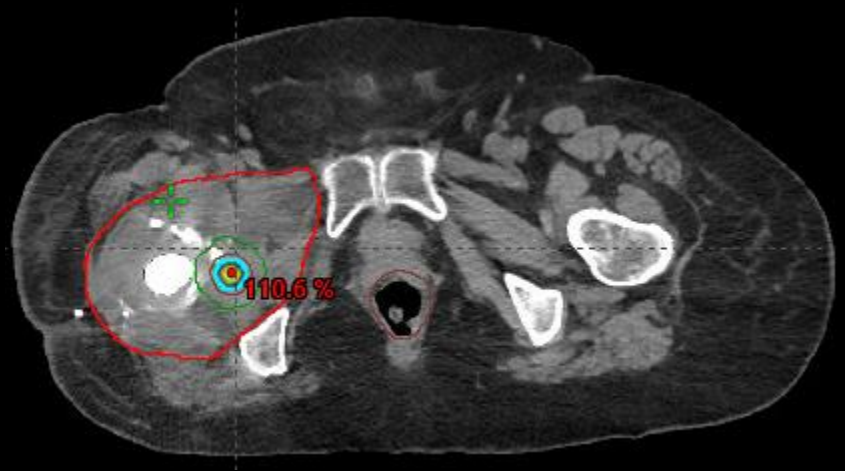


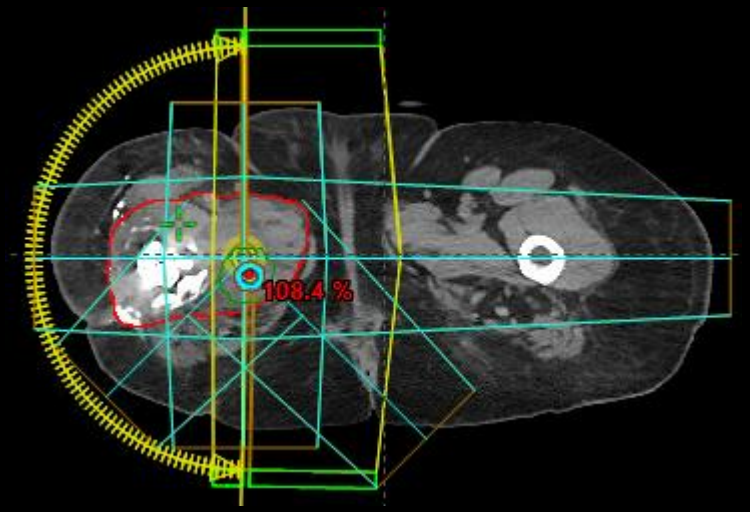


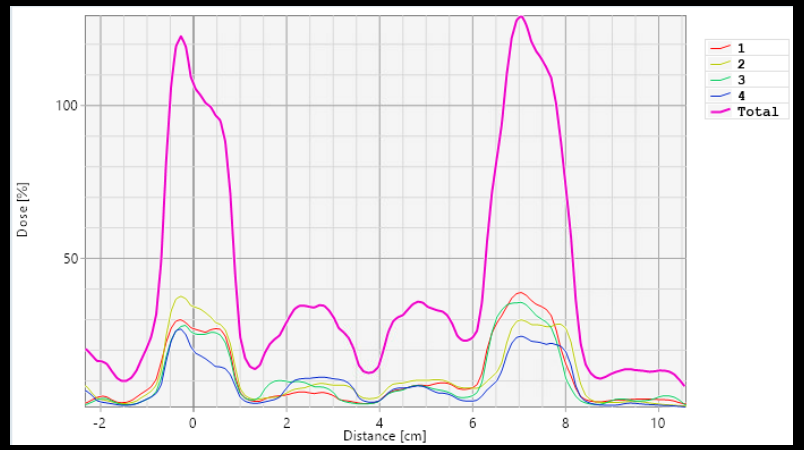
VMAT Grid/Lattice

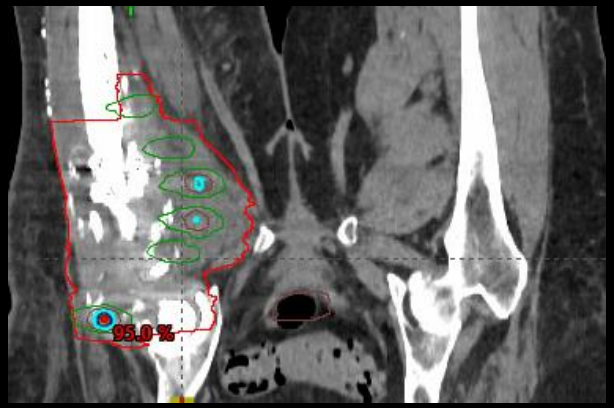
- Mimicking similar dose peak and valley using VMAT technique; Placing spheres for high dose peaks

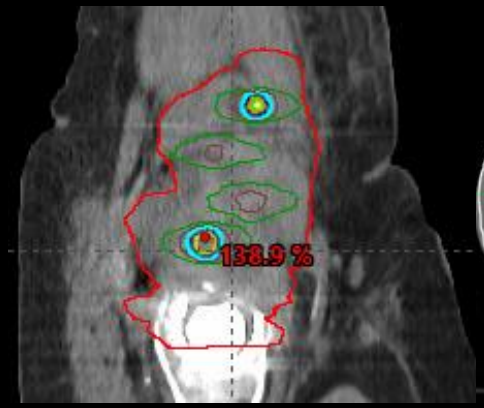
181.0 CW 0.0	2.0
0.0 CCW 181.0	358.0
181.0 CW 0.0	3.0
0.0 CCW 181.0	357.0

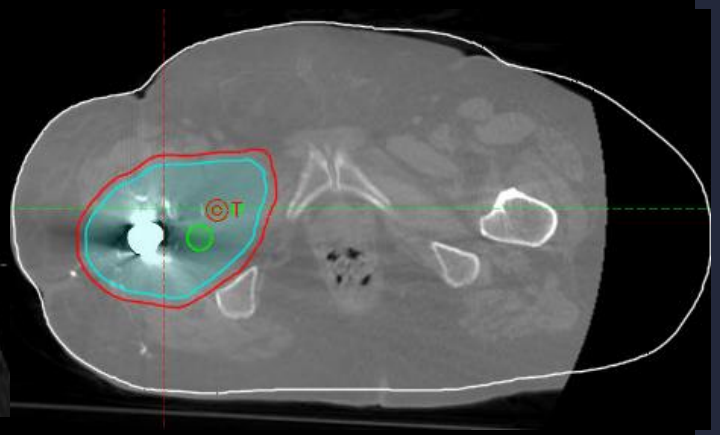


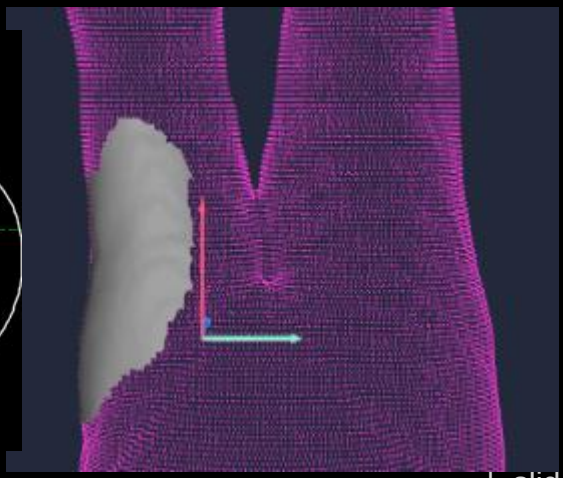






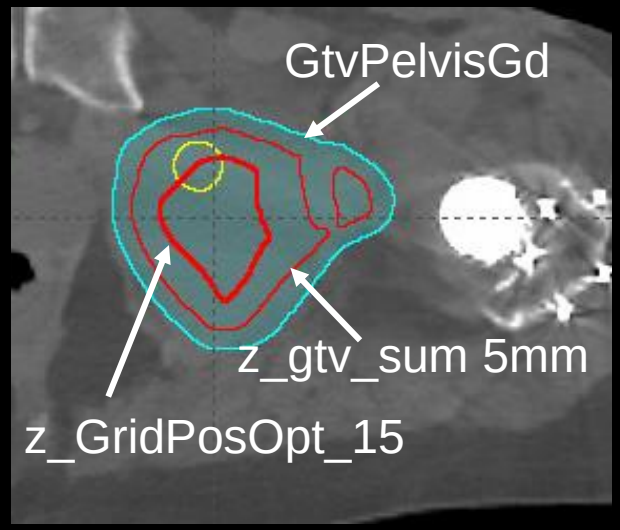


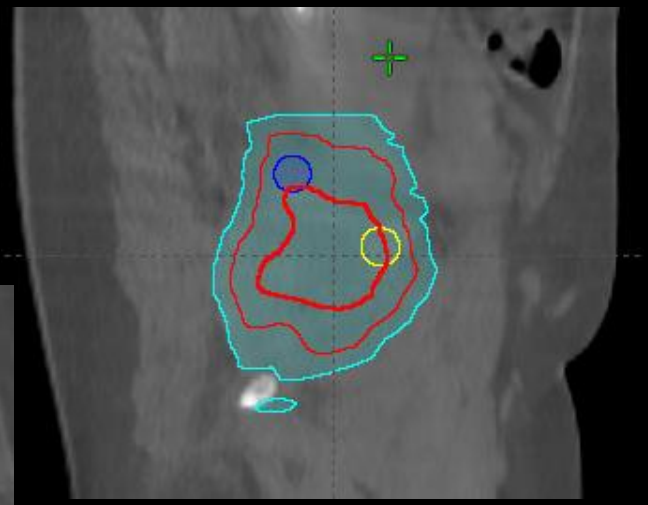


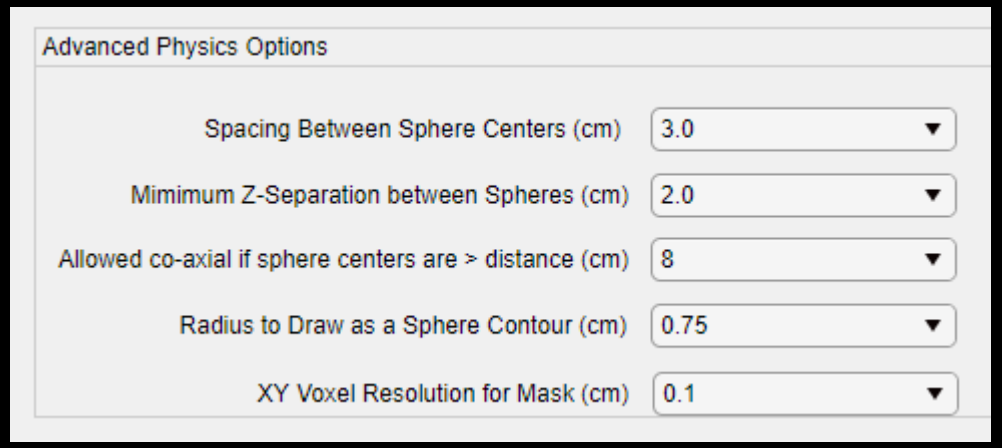


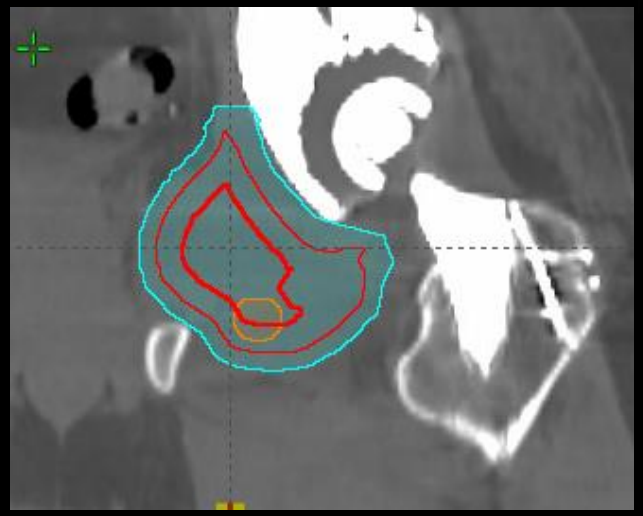
Sphere Placement Rules

- The Monte Carlo algorithm follows these rules
  - All spheres are defaulted to 1.5cm in diameter
  - All sphere centers reside in z_GridPosOpt_15 (for 1.5cm spheres)
  - Default 3cm between sphere center along the longitudinal direction
  - Default 8cm between sphere center along the axis direction

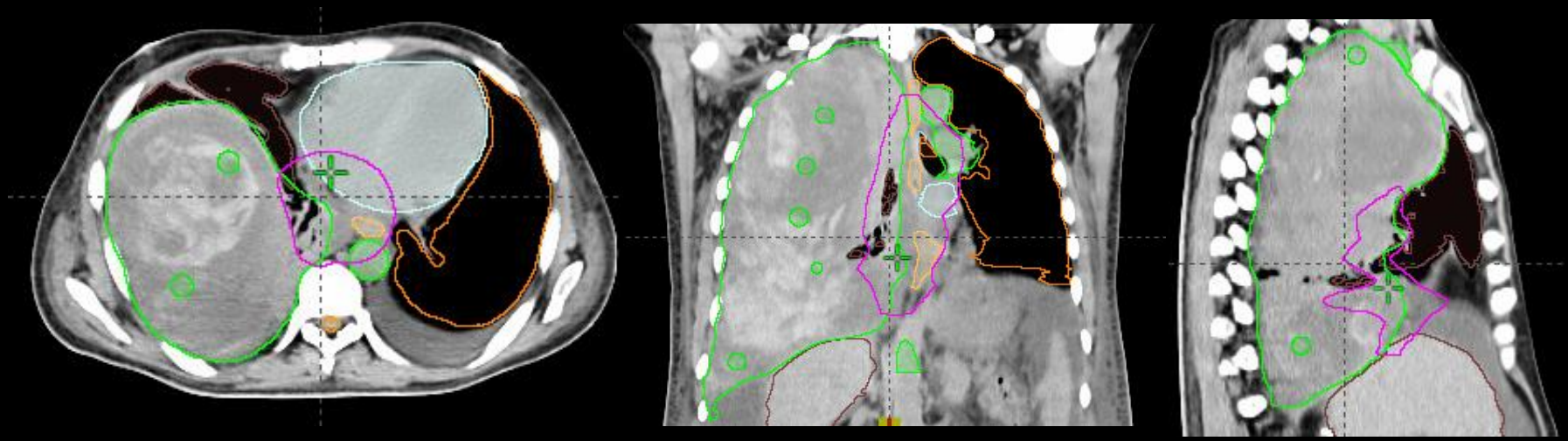


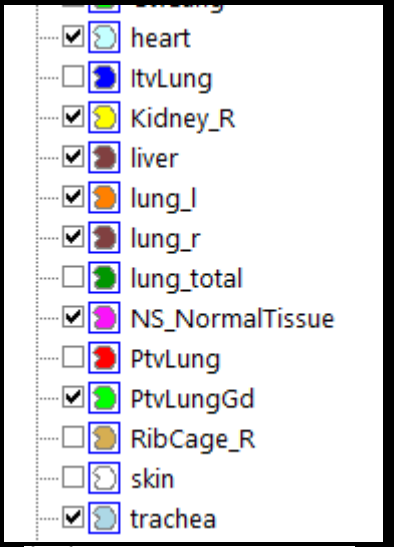


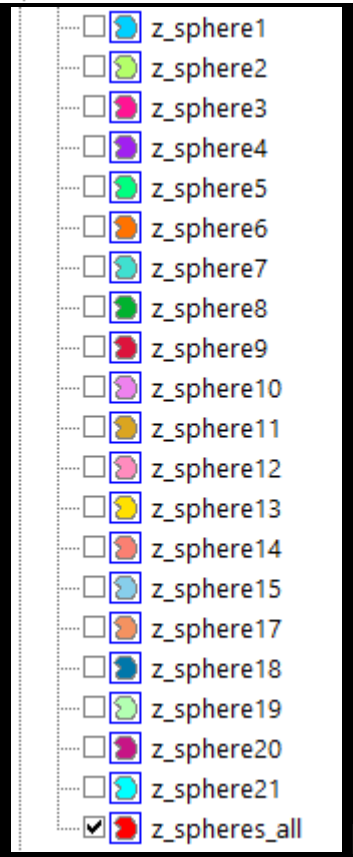




Example





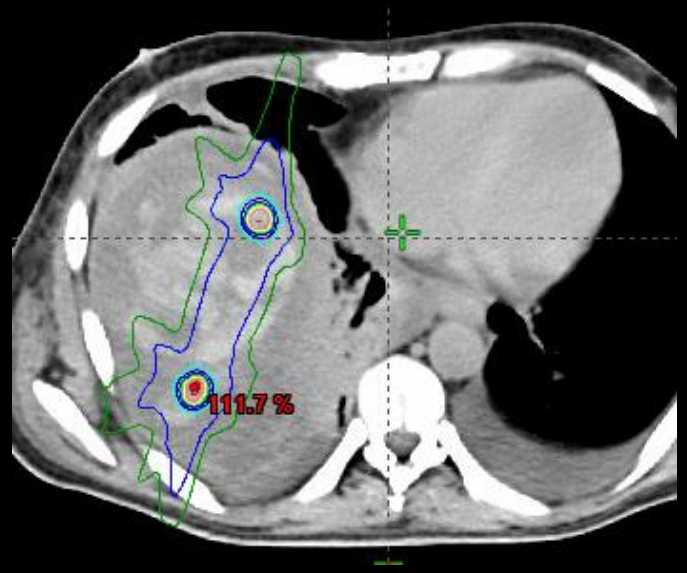


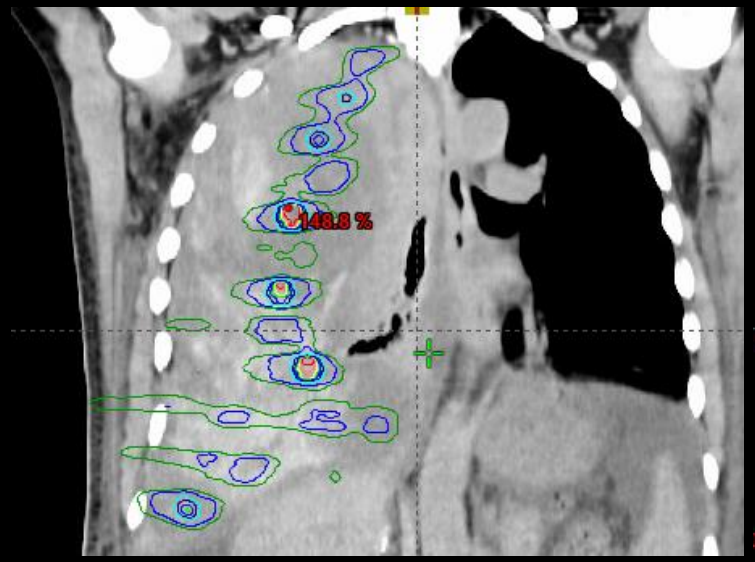
PelvisGd - Sphere Evaluations (GRID Therapy) Constraints

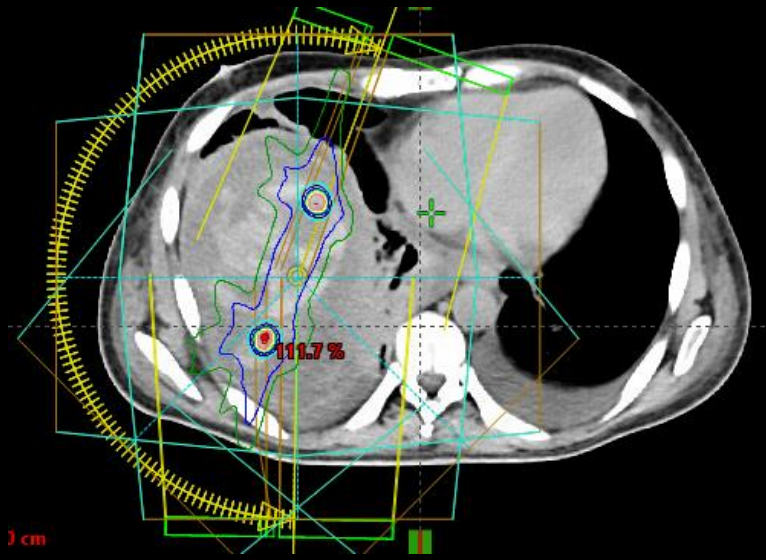
Priority	Structure Template	Structure Plan	Type	Constraint	Goal	PelvisGd	Comment
1	z_sphere1	z_sphere1	Target	D50% ≤	2050cGy	2035.4cGy	
2	z_sphere1	z_sphere1	Target	D50% ≥	1950cGy	2035.4cGy	
3	z_sphere2	z_sphere2	Target	D50% ≤	2050cGy	2045.4cGy	
4	z_sphere2	z_sphere2	Target	D50% ≥	1950cGy	2045.4cGy	
5	z_sphere3	z_sphere3	Target	D50% ≤	2050cGy	2048.9cGy	
6	z_sphere3	z_sphere3	Target	D50% ≥	1950cGy	2048.9cGy	

Dose Peaks and Valleys

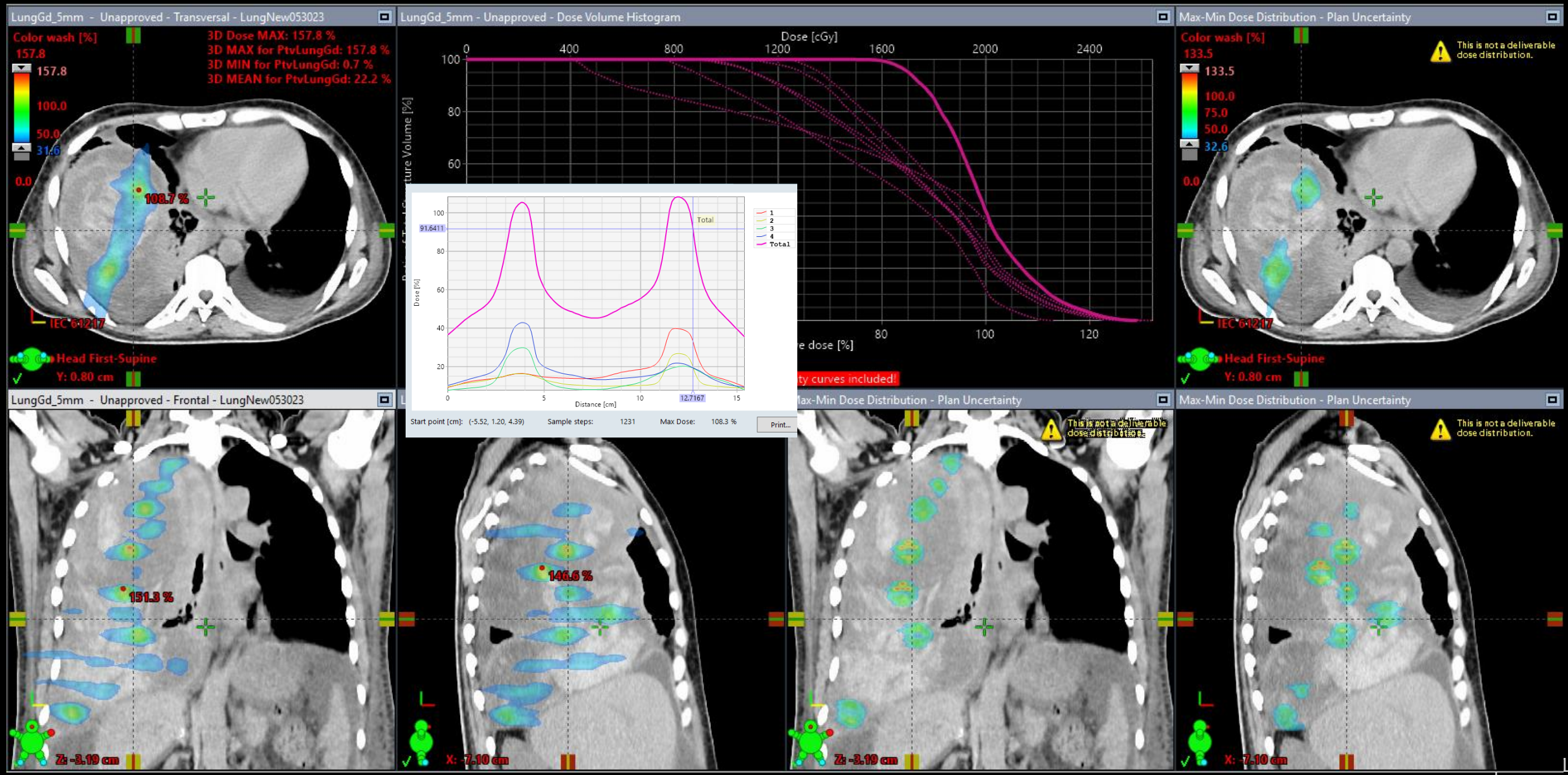
- Single fraction >= 15Gy; for each sphere D50% at Dp +/- 50cGy
- Dose should break up at 30%-40% between spheres
- GTV mean dose typically is around 4-7Gy for a prescription of 20Gy, the control limit should be 3Gy – 11Gy. Any case outside this limit is atypical and requires MD confirmation
- Typical values for Maximum doses for spheres are between 120-140%.



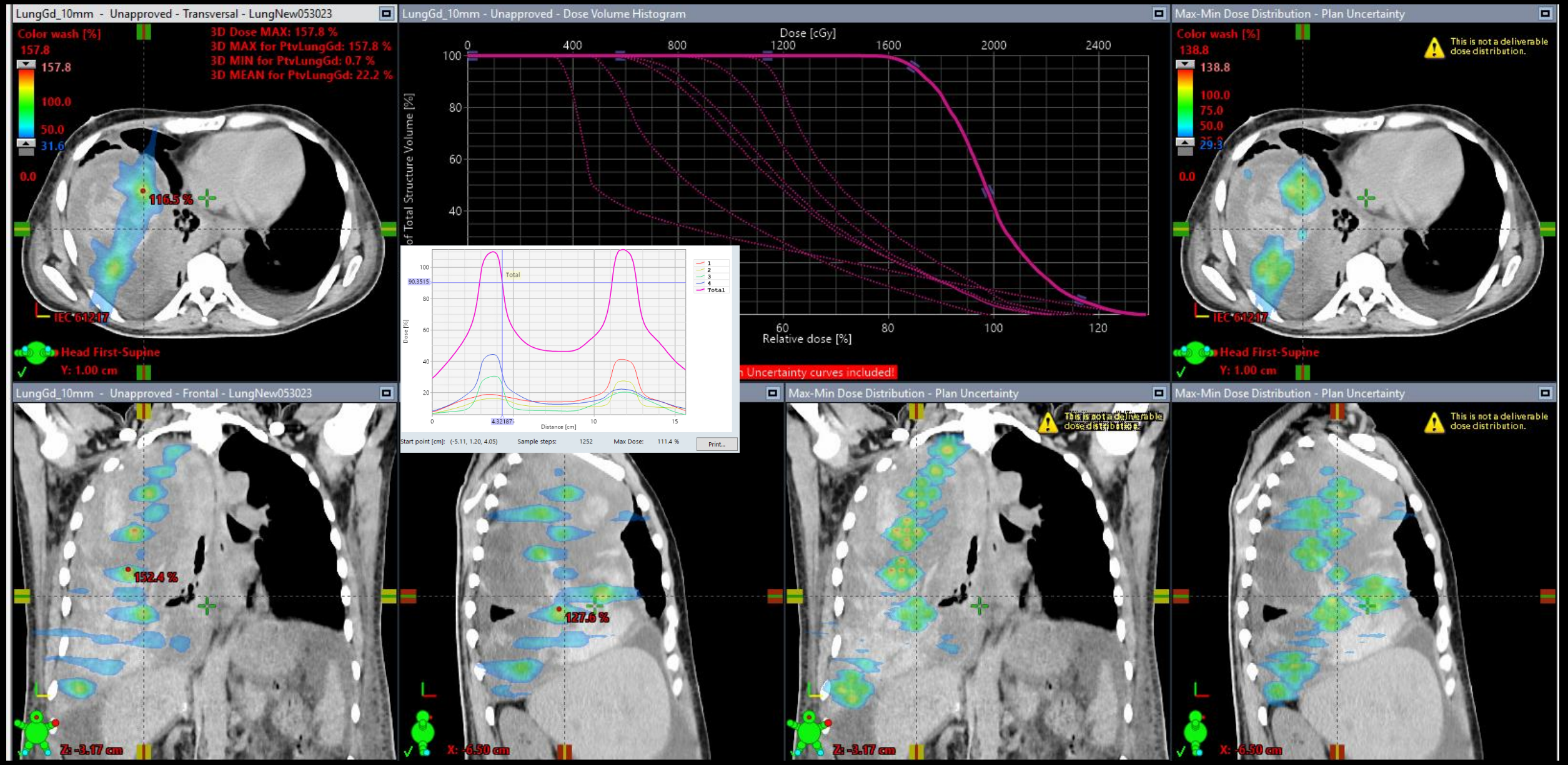




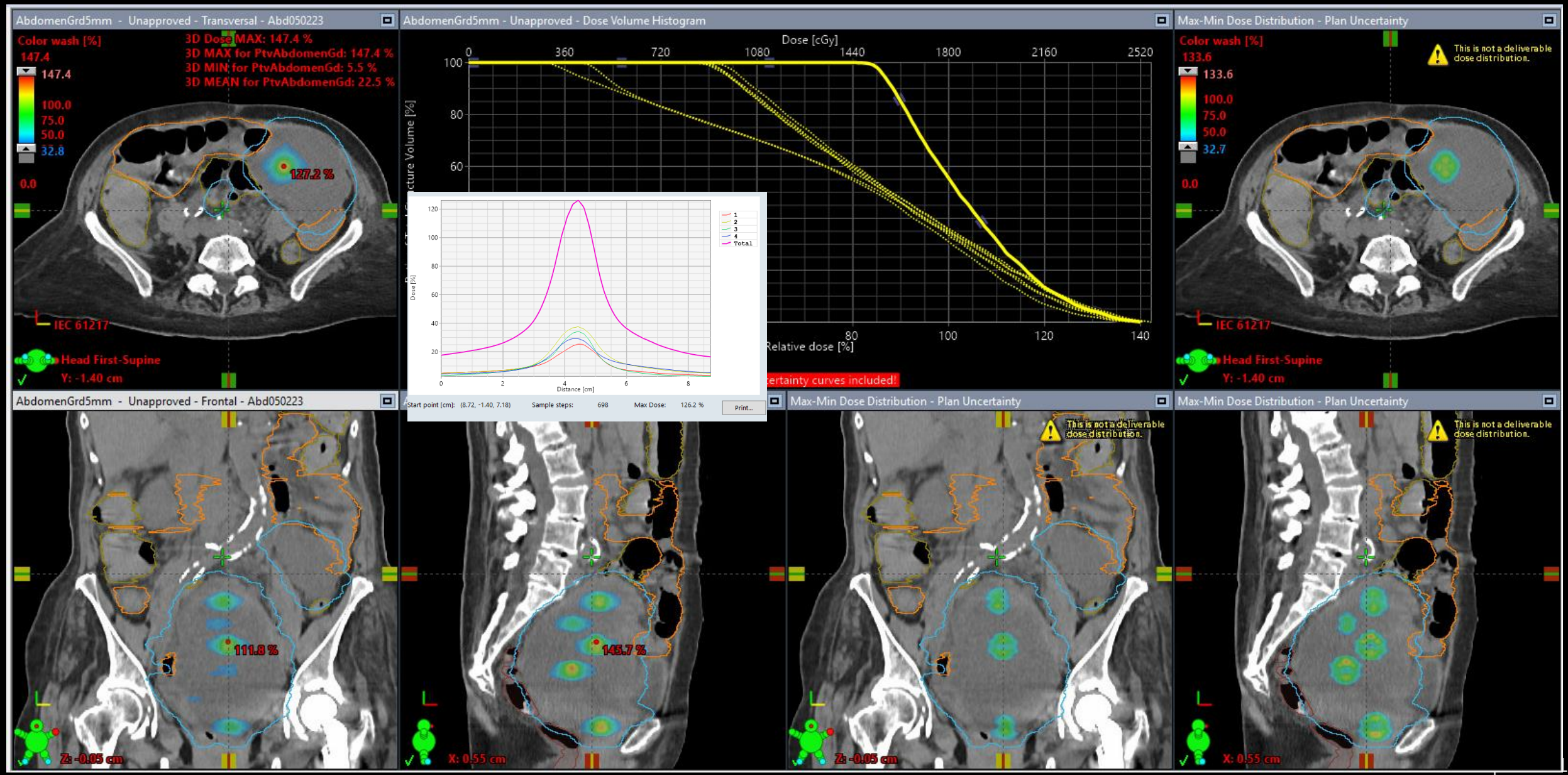
Adding 5mm positional uncertainties



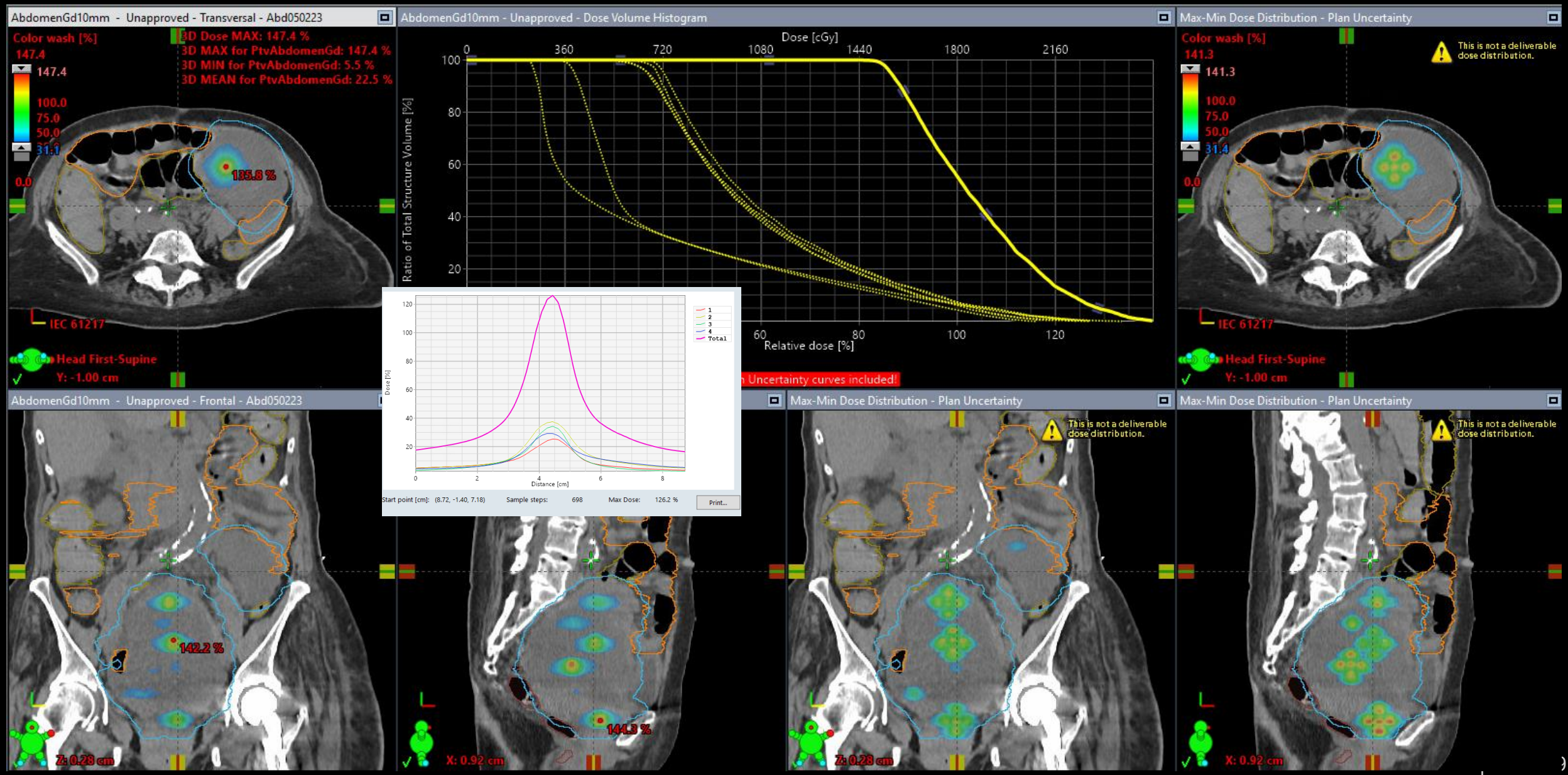
Adding 10mm positional uncertainties



Adding 5mm positional uncertainties

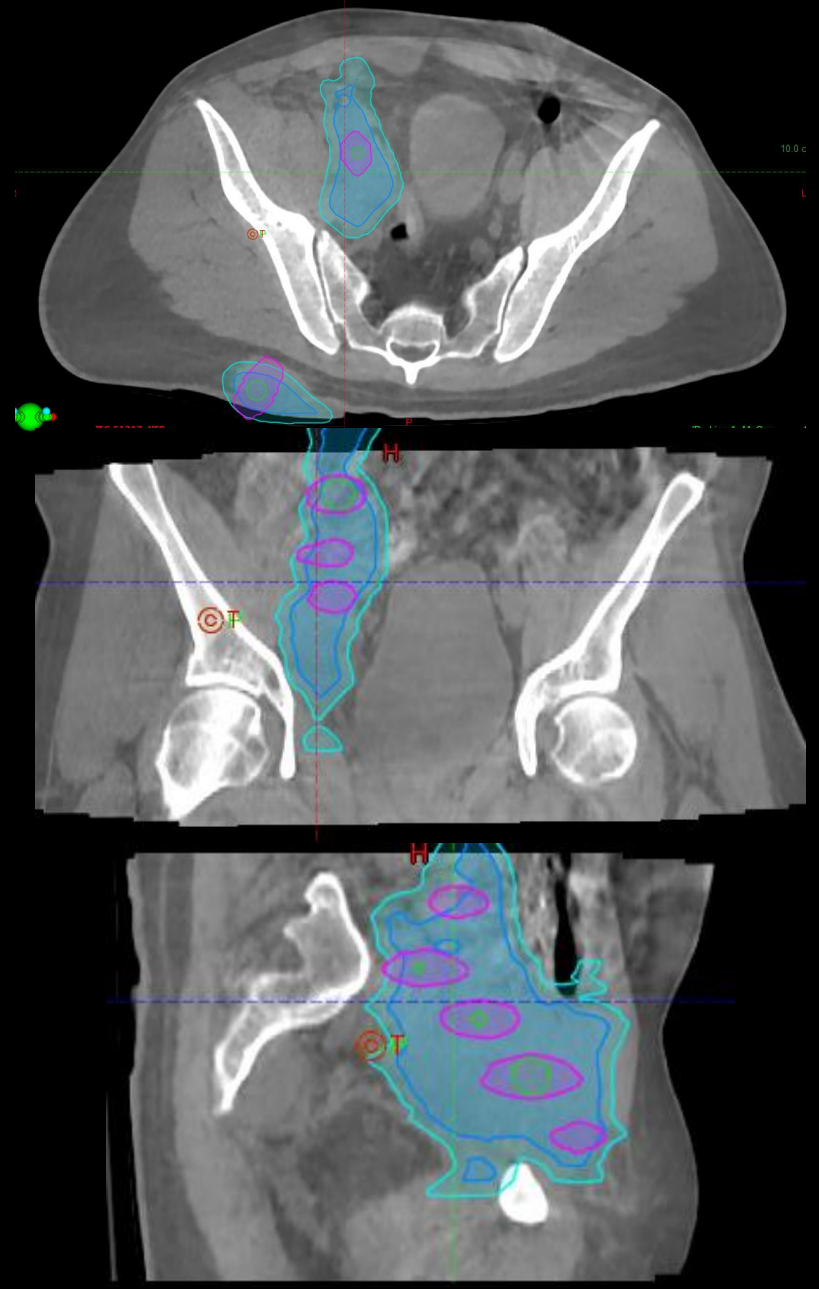


Adding 10mm positional uncertainties



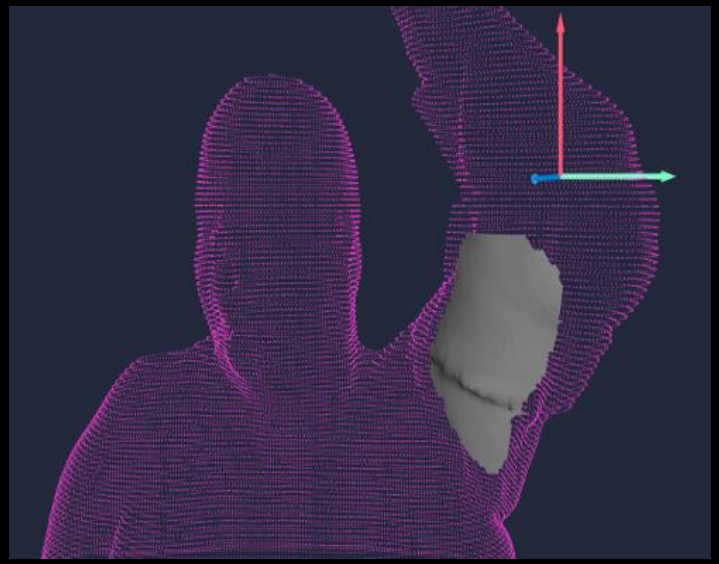
IGRT Guideline

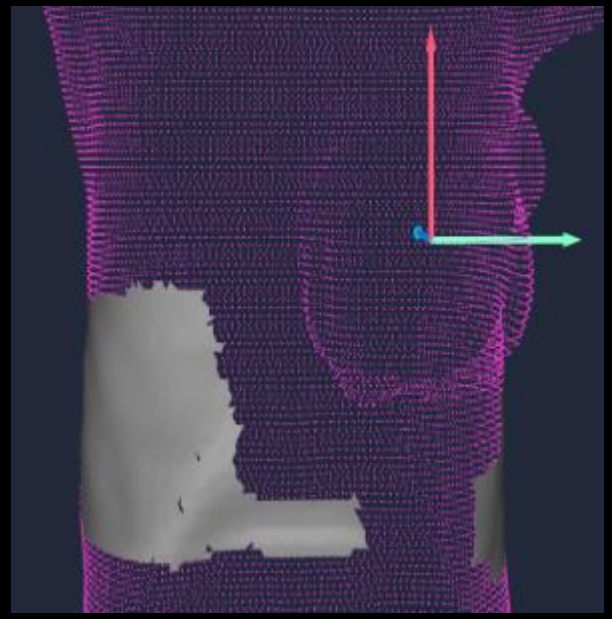
- Journal note: CBCT, turn on z_Gtv_sub_5mm, z_spheres_all, Dose 800cGy; VisionRT to monitor treatment
- IGRT rules:
  1. All spheres need to be included in the CBCT. If the treatment region is longer than 16cm, need to take extended CBCT
  2. MD, physics POD, and RTT need to go through all spheres when reviewing the alignment
  3. Make sure all spheres are within the z_gtv_sub 5mm contour, and no sphere is inside any organs at risk or metal implants
  4. Make sure 800cGy contour is not touching organs at risk (per MD's discretion)

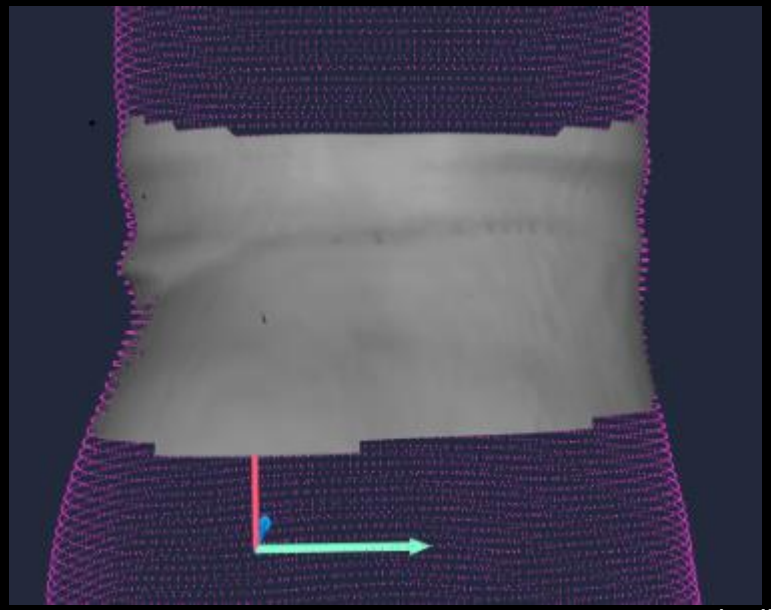


SGRT Monitoring for VMAT Grid

- VisionRT monitoring tolerance: 3mm for x, y, and z; 2 degree rotations
- Treated various sites for sarcoma
  - HN, breast, lung, Abdomen, Pelvis, Extremities
  - Following regular patient simulation, set up, and monitoring SOP







Managing Dose Uncertainty in Patient Positional Shifts: Clinical Decision Points

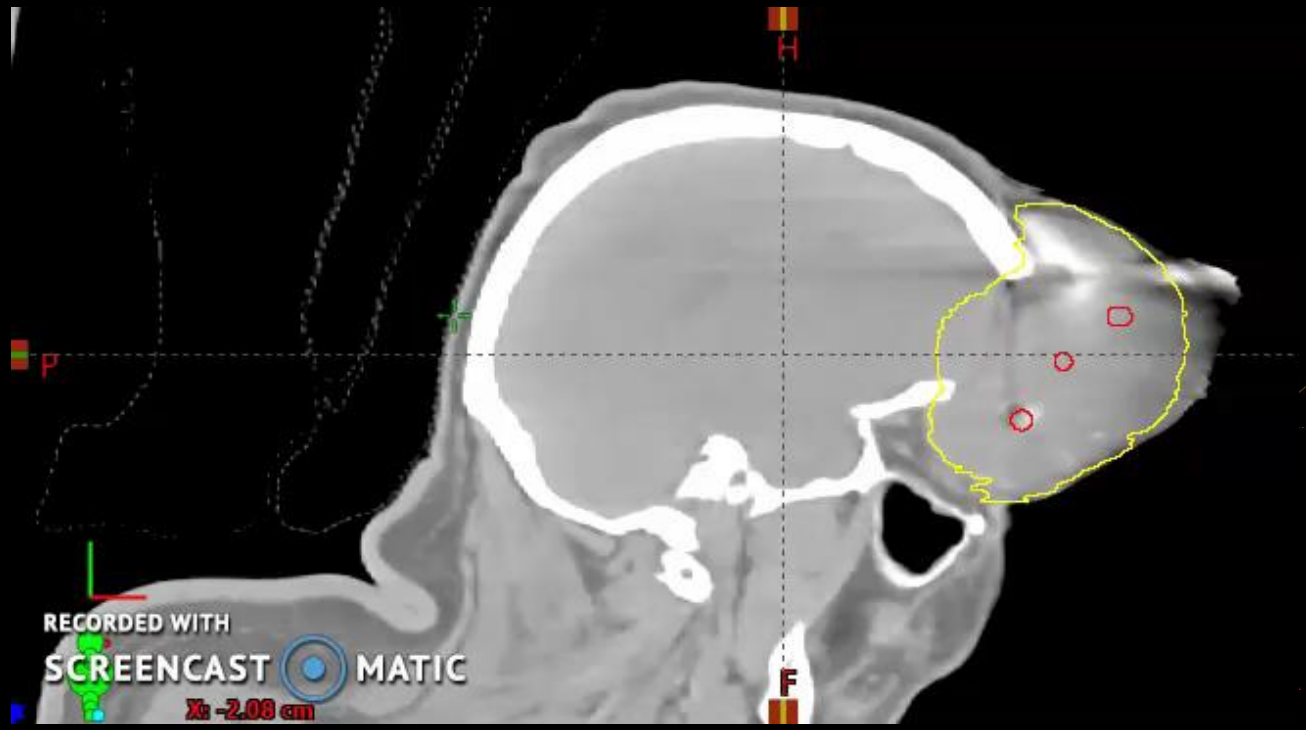
- Based on dose uncertainty evaluation, Peak-Valley dose profiles may be altered/ compromised if patient needs to be shifted. The dose impact depends on the shift magnitude, target size, sphere number/locations, etc.
- The attending physician's decision to continue treatment without the positional shift, or accept the potential compromised dose profiles, or terminate treatment.

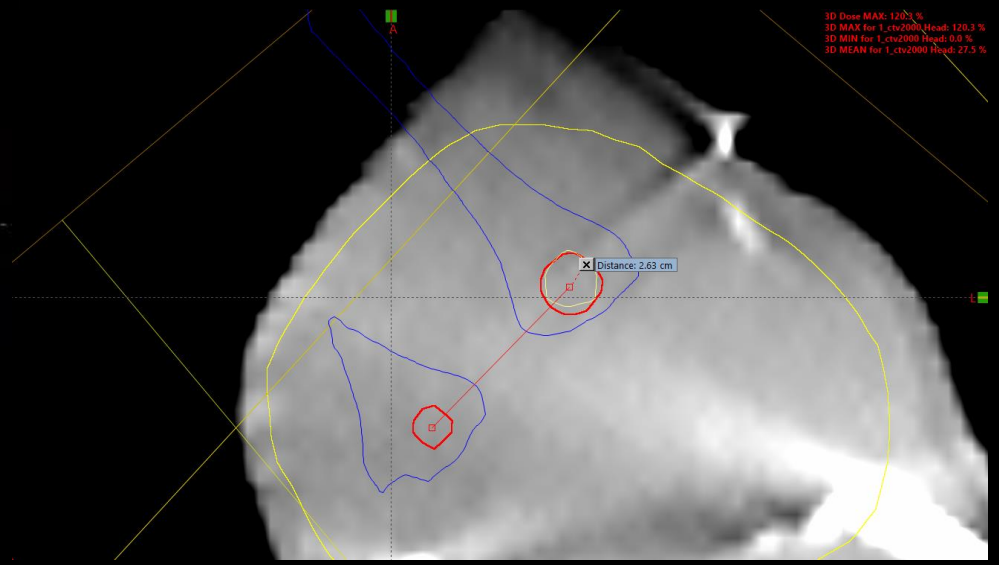
(The Attending physician covers the Grid treatment, or conveys the necessary information to the covering physician)

Use Case for Proton Grid/Lattice

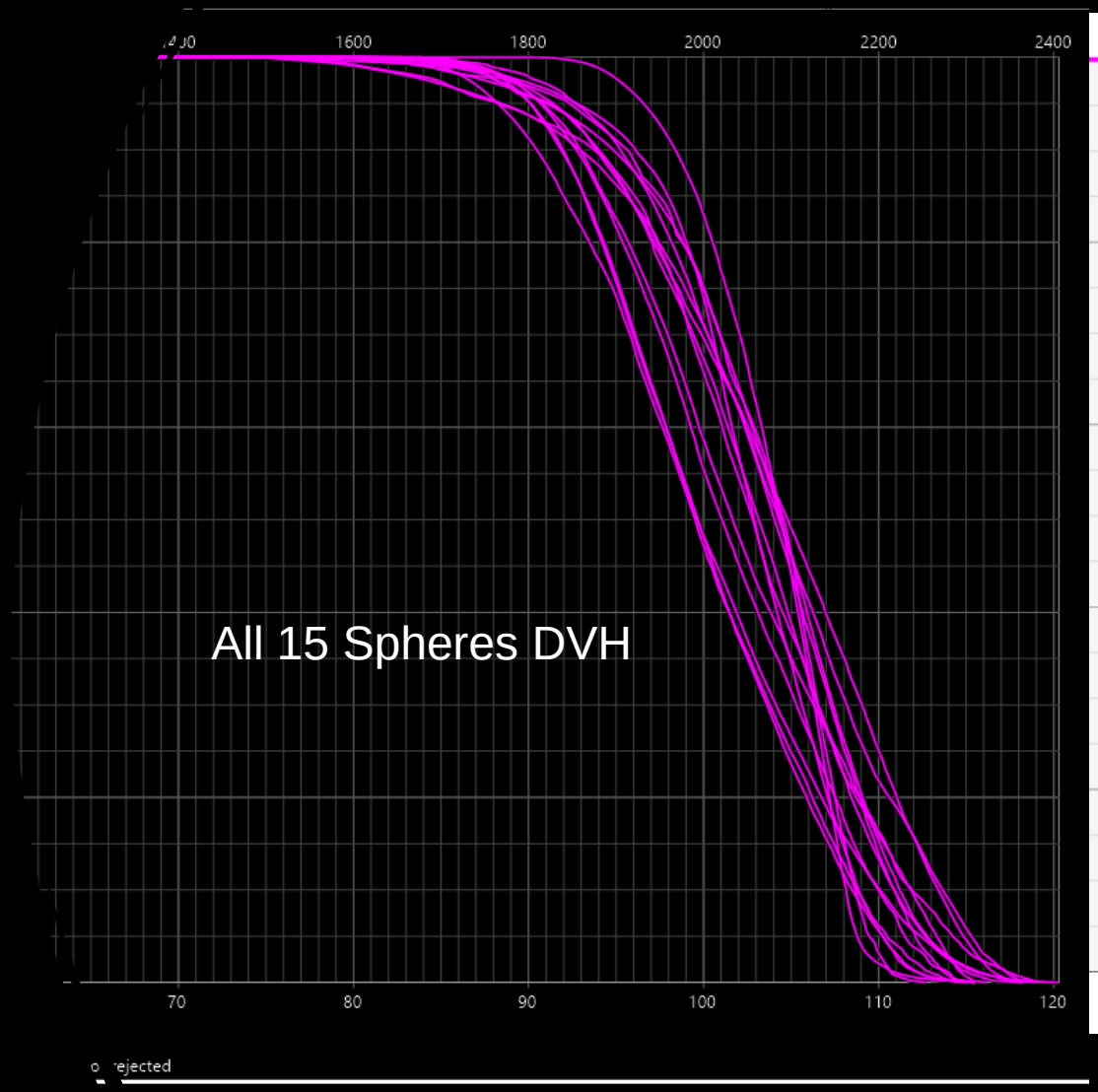
Target Size: 349.6 CC; # of Spheres: 15; with mean separation distance 2cm;
Beam Arrangements: RAO/LAO
Total number of Spots: 20,000; Total Energies: 28
Robustness criteria evaluated: 3 mm setup errors

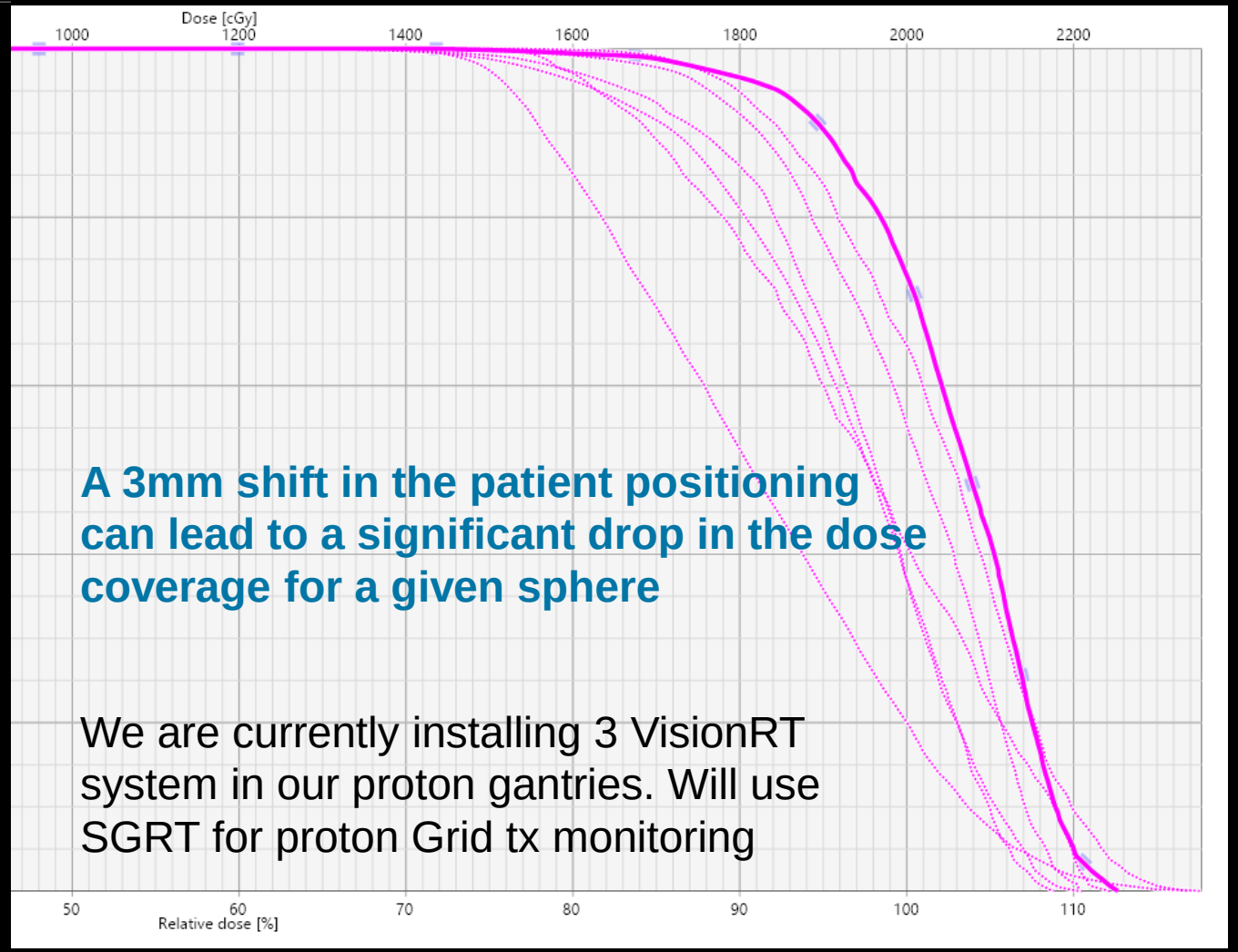
Sphere Placement (W.I.P)





Robustness Evaluation



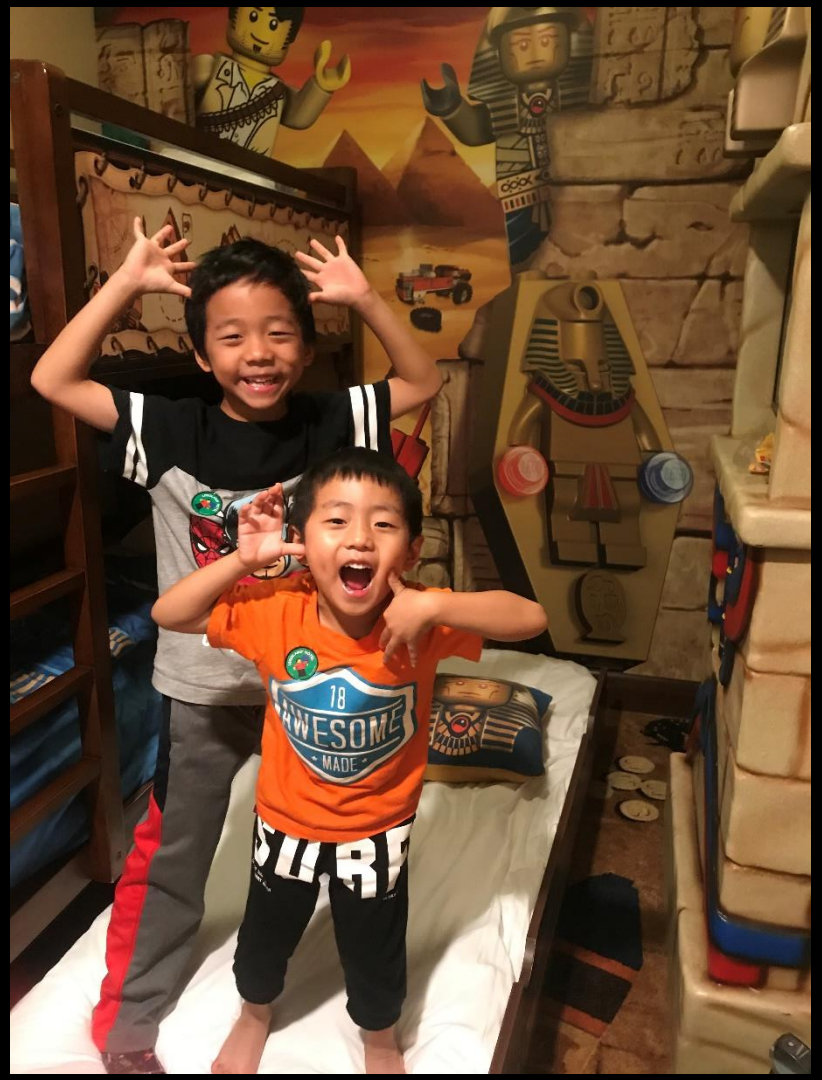


Summary

- SFRT can be delivered in various forms, Brass Grid, VMAT Grid, and proton Grid.
- For VMAT and proton Grid, peak and valley dose delivery requires accurate patient setup and during tx monitoring
- Surface guidance systems play an important role in ensuring accurate dose delivery

Acknowledgement

MAYO CLINIC



Questions?

Biological Mechanism of SFRT

Dose heterogeneity has shown success in reducing tumor size and inducing high rates of symptomatic response with minimal toxicity even if followed by conventional radiation therapy.

Bystander Effects: Biological alterations indicated in un-irradiated cells when induced by signals from nearby irradiated cells. Results in un-irradiated cells exhibiting damaging effects, genomic instability and reduced cell survival.

Abscopal Effects: Phenomenon in which irradiated tissues emit signals to affect un-irradiated tissues outside of an irradiated volume.

Cohort Effects: Under heterogeneous irradiation, high-dose irradiated cells emit signals to affect low-dose irradiated cells and vice versa.