



חידושים בטיפול קרינתי וברכיתרפיה לסרטן צוואר הרחם

ד"ר עמיחי מאירוביץ

מנהל המרכז לקרינה ממוקדת

מכון שרת, הדסה ע"כ

How do we focus the radiation to the target (and not to the surrounding normal tissues)

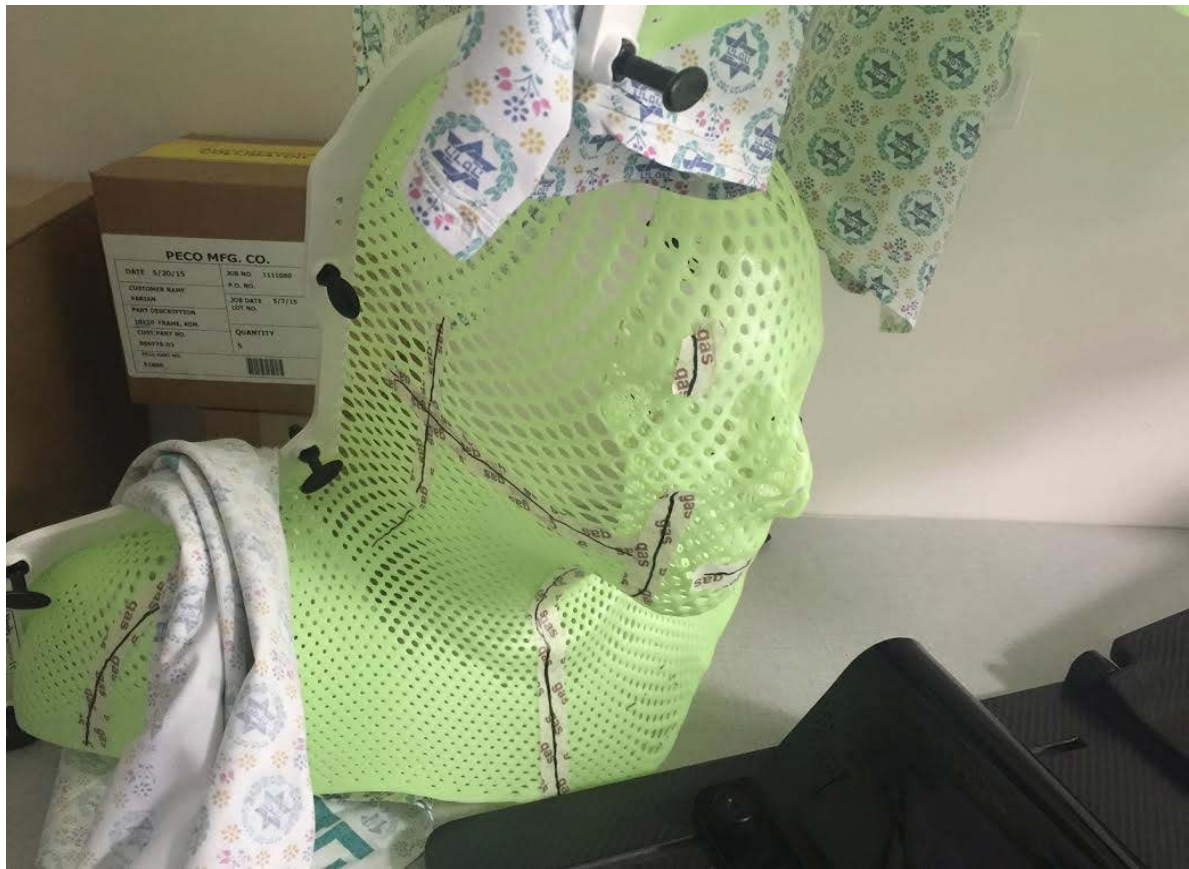
- Fast accurate instance modulated radiotherapy – **IMRT-Rapid-Arc**
- Stereotactic Radiosurgery (brain) - **SRS**
- Stereotactic Body radiotherapy – **SBRT**
 - Liver
 - Lung
- **Brachytherapy** – bringing the source of radiation to the target
- Radiolabeled Targeted therapy
 - Selective internal radiation therapy – **SIRT**
 - Radium **Ra²²³ dichloride** – Xofigo
 - Peptide Receptor Radionuclide Therapy – **PRRT**
 - Lu177- DOTATATE
 - **Lu177 - PSMA**

IMRT-Rapid-Arc











Cervical Cancer

- The 3rd most common GYN cancer in USA, but in many countries 2nd most common cancer, and 2nd cancer cause of death.
- HPV related in majority of the cases
- FIGO clinical staging system is still the most common (But pelvic LN involvement = IIIb).
- Surgically treated in early stage, chemo-radiation in early and later stages.



- Chemotherapy significantly add to treatment outcome when combined with radiation. (both as primary and adjuvant setting).
- Treatment length effect outcome.
- Clear dose response curve with radiation.
- Brachytherapy is integrated part of the primary treatment



Chemo-Radiation

Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis.

Cochrane Database Syst Rev. 2010

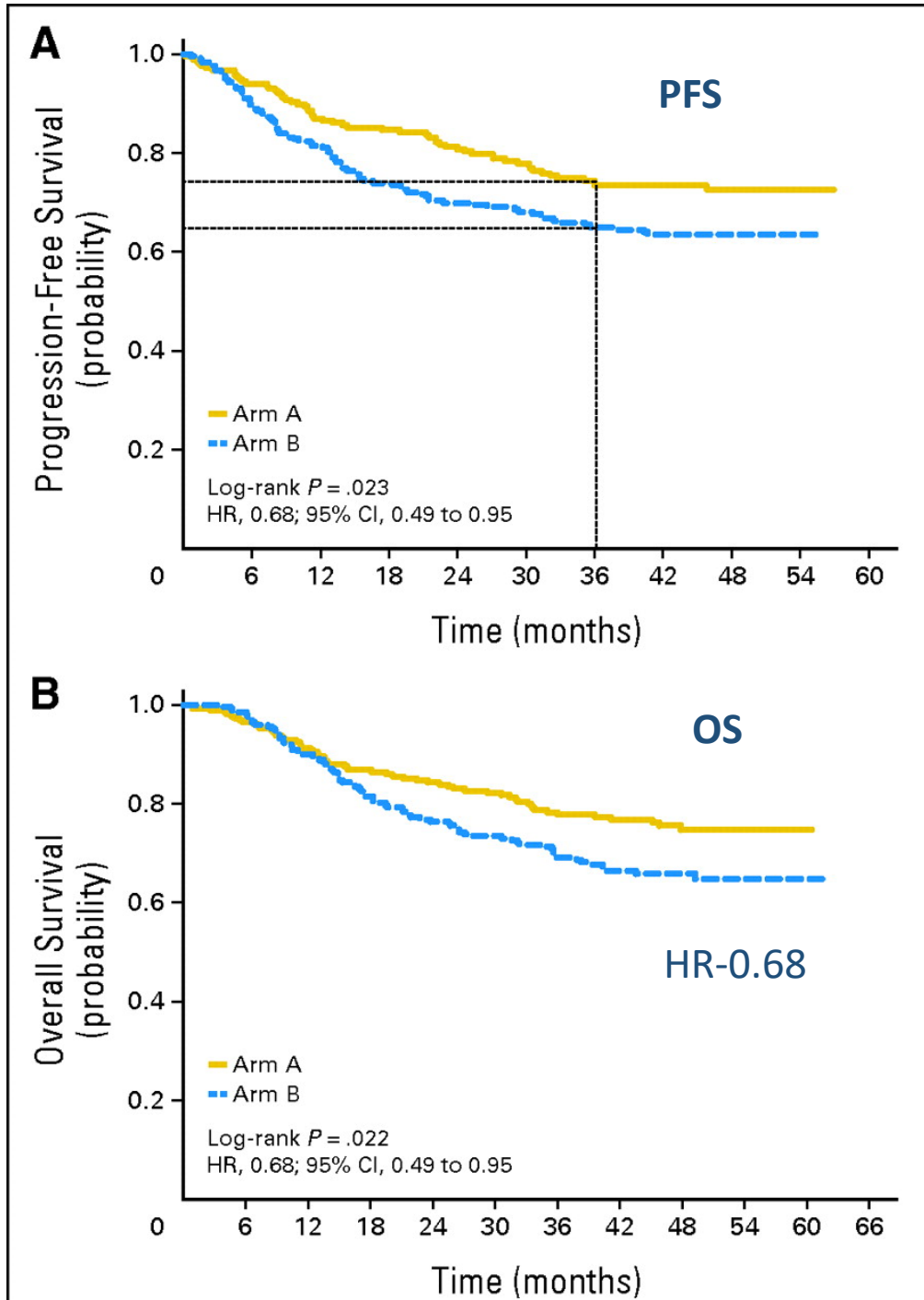
- A reduction in the risk of death (HR 0.69, 95% CI 0.61-0.77), =>10 % absolute improvement in survival.
- The survival benefit decreased with increasing stage.
- For women with stage IB to IIA, IIB, and III to IVA cervical cancer, the 5y survival benefit was 10, 7, and 3%, respectively ($p = 0.017$).
- A reduction in the risk of recurrence (HR 0.66, 95% CI 0.59-0.73), =>13 percent absolute improvement in PFS.
- Higher rates of serious (grade 3/4) adverse events including gastrointestinal toxicity (OR 1.98, 95% CI 1.49-2.63).



Combining Gemcitabine to the treatment.

Phase III, open-label, randomized study comparing concurrent gemcitabine plus cisplatin and XRT followed by adjuvant gemcitabine and cisplatin versus concurrent cisplatin and XRT in patients with stage IIB to IVA ca. of the cervix. Dueñas-González et al, JCO 2011 (Mexico)

- 515 pt. stage IIB to IVA disease and Karnofsky performance score ≥ 70
- XRT-50.4 Gy, followed by brachytherapy 30 to 35 Gy
- **Weekly cisplatin 40 mg/m² and gemcitabine 125 mg/m²**
- Radiation given in 4 field box
- Post chemoRT – consolidation chemo with full dose.
- **Toxicity grade 3/4 - 86.5% v 46.3%, ; $P < .001$), including 2 deaths**



PFS at 3 years is shown by the dotted black lines and was 74.4% for arm A and 65.0% for arm B ($P = .029$).

**OS HR- 0.68
(95% CI, 0.49 to 0.95; log-rank $P = .0224$)**



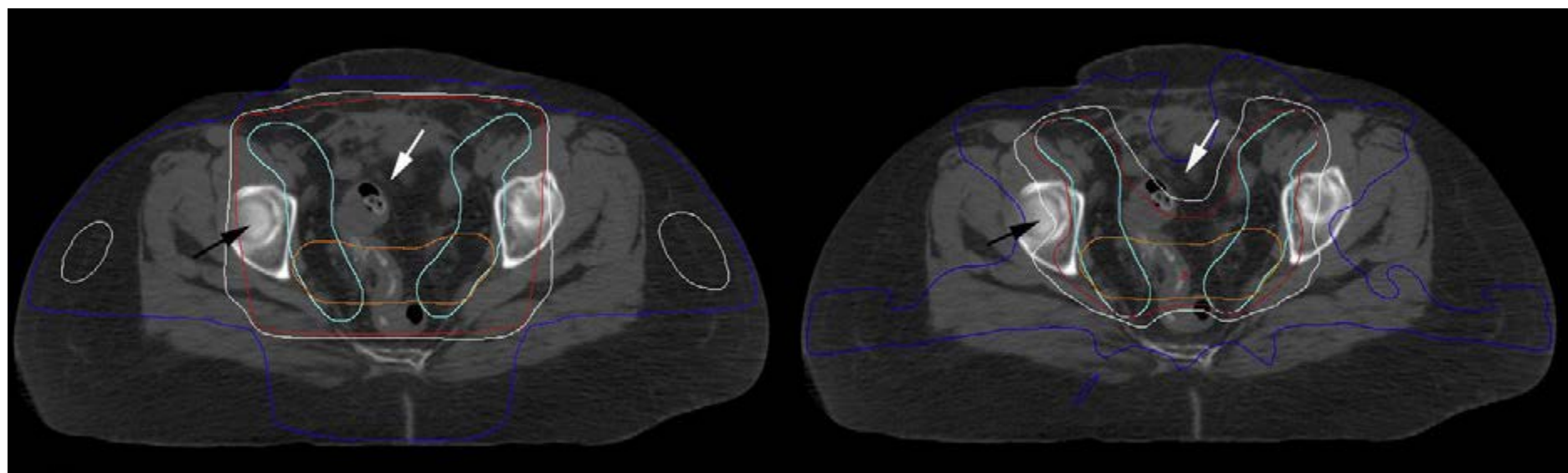
IMRT in cervical cancer

- Dosimetric advantage in bowel, rectal and bone marrow dose.
- The need meticulous delineation and set-up as rapid fall of the high dose may miss the target.



IMRT reduce toxicity

- **Preliminary analysis of chronic gastrointestinal toxicity in gynecology patients treated with intensity-modulated whole pelvic radiation therapy.** Mundt et al, IJROBP 2003
- reduction in grade 2 toxicities from 16.7% to 2.8%, and grade 3 toxicity from 3.3% to 0% ($p = 0.001$).





IMRT and dose escalation

Duodenal and Other GI Toxicity in Cervical and Endometrial Cancer Treated With Extended Field IMRT to Paraaortic Lymph Nodes.

Poorvu et al, IJROBP 5,2013

46 patient with extended ParaAortic field IMRT treatment were evaluated to toxicity.

Only 3/46 patients (6.5%) experienced acute grade 3 GI toxicity and 3/46 patients (6.5%) experienced late grade 3 GI toxicity.

- Treatment of the paraaortic nodes with IMRT is associated with a low rate of acute and late gastrointestinal toxicities.
- This technique may allow sufficient dose sparing of the bowel to enable safe dose escalation to at least 65 Gy. (?!AM)



The effect of treatment time in locally advanced cervical cancer in the era of concurrent chemoradiotherapy song et al , Cancer 2013

113 patients Ib2-IIIb, retrospective review from 1997

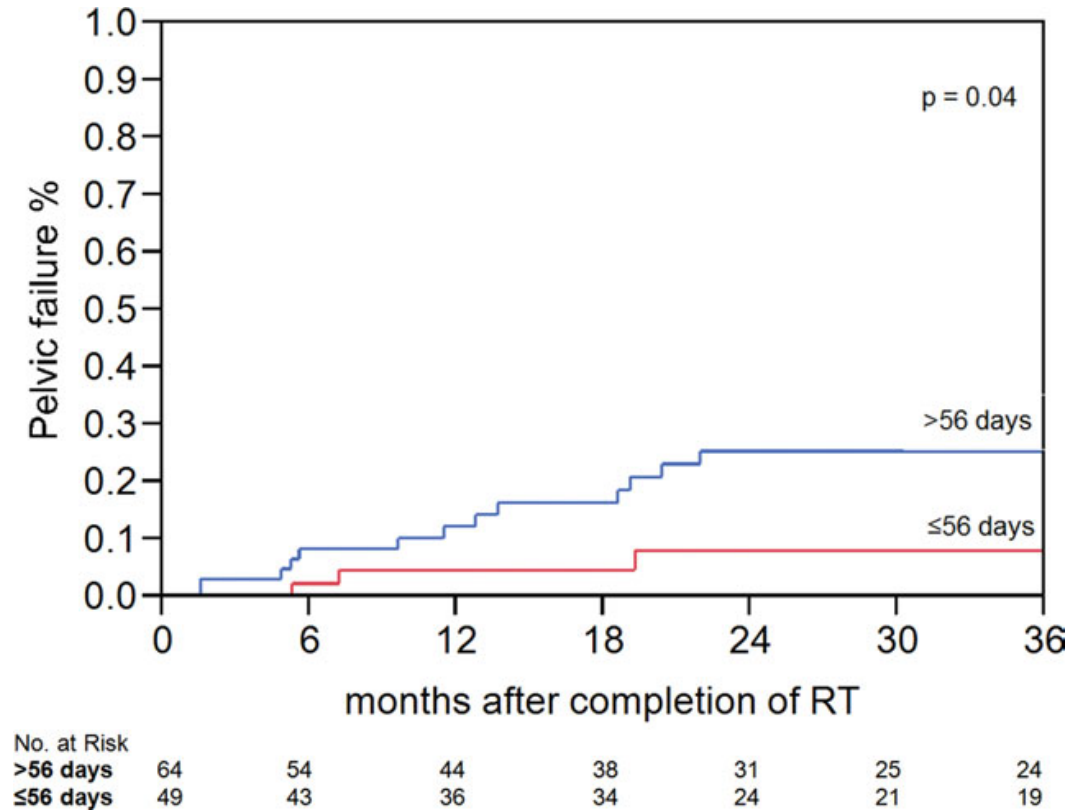
Treated with chemo-XRT +brachytherapy

45Gy pelvis, brachy 30Gy in 5# (when use HDR) and parametrial boost.

Time to complete BT –calculated from fist day of external radiation.

On multivariate analysis, time to completion of BT >56

**days was associated with increased Pelvic Failure (HR- 3.8; 95%
CI, 1.2-16; P = 0.02).**



Conclusion: To maximize pelvic control,
we recommend completing BT in 8 weeks or less.

Song et al, Cancer 2013



HDR dosimetry schemes

5-8 Gy/ fx x 3-6 fractions

GOG 6 Gy x 5

RTOG 5.3-7.4 Gy x 4-7

NCIC 8 Gy x 3

Deliver 1-2 fractions/week

If fractions >7.5 Gy, rectal dose should be limited to 60% Pear shaped distribution



Brachytherapy

- **Image-guided brachytherapy (IGBT) combined with whole pelvic intensity-modulated radiotherapy (WP-IMRT) for locally advanced cervical cancer: a prospective study from Chiang Mai University Hospital, Thailand.** Tharavichitkul et al, J Contemp Brachytherapy, 2013
- Toxicity profiles of 15pt. using image-guided brachytherapy (IGBT) combined with whole pelvic IMRT for locally advanced cervical cancer
- **45Gy to the pelvis + 7 Gy × 4 HDR brachy**
- **The combination of IGBT and WP-IMRT helped to improve significantly the target coverage, while it maintained high curative doses for HR-CTV and avoiding overdose in OARs.**



- Long and short terms toxicity are major problem in the treatment application – limiting the ability to intensify treatment.
- Emerging new techniques and new chemotherapy strategies enable safer treatment.
- Although the technology adapted by many, the treatment intensification did not.

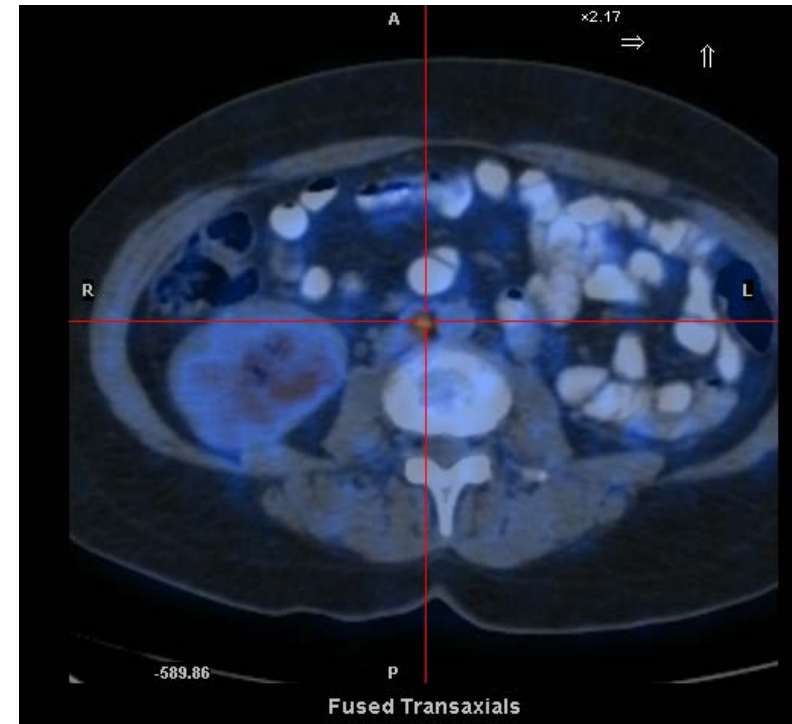
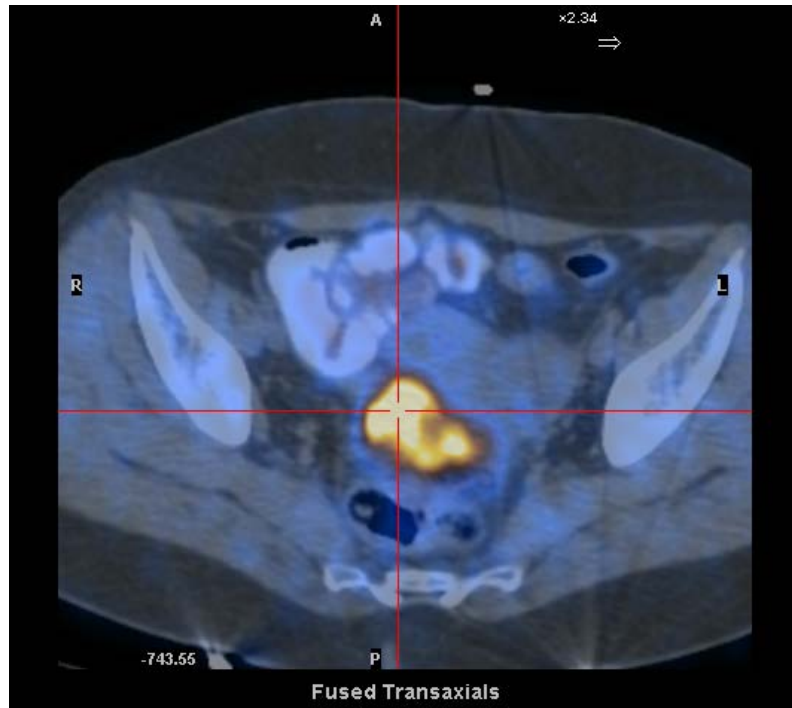


What are we doing ?

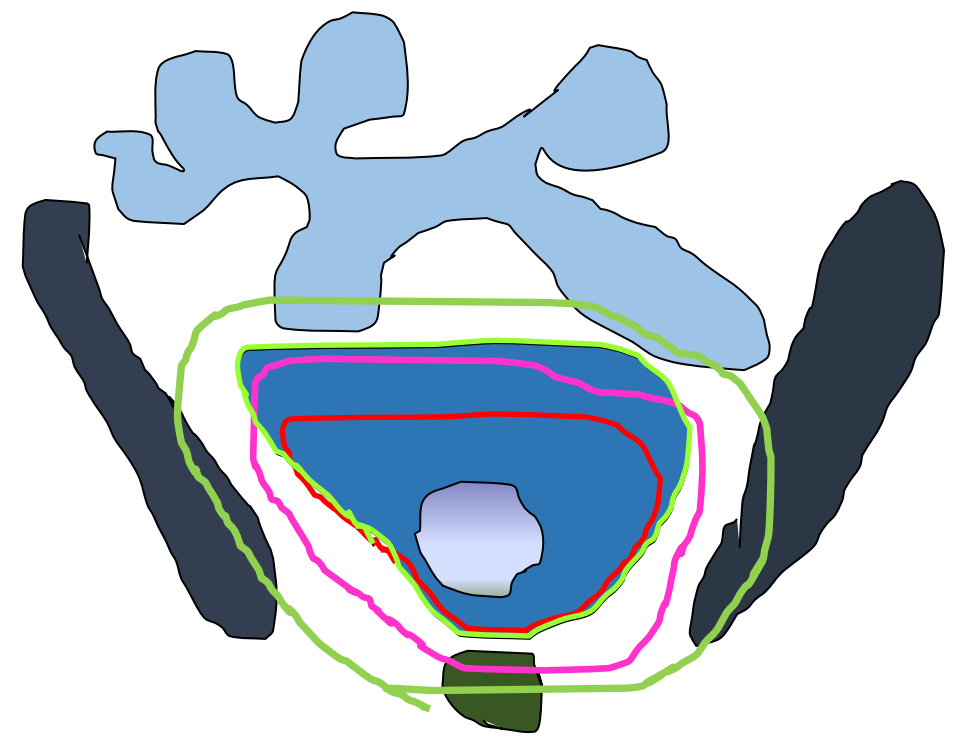
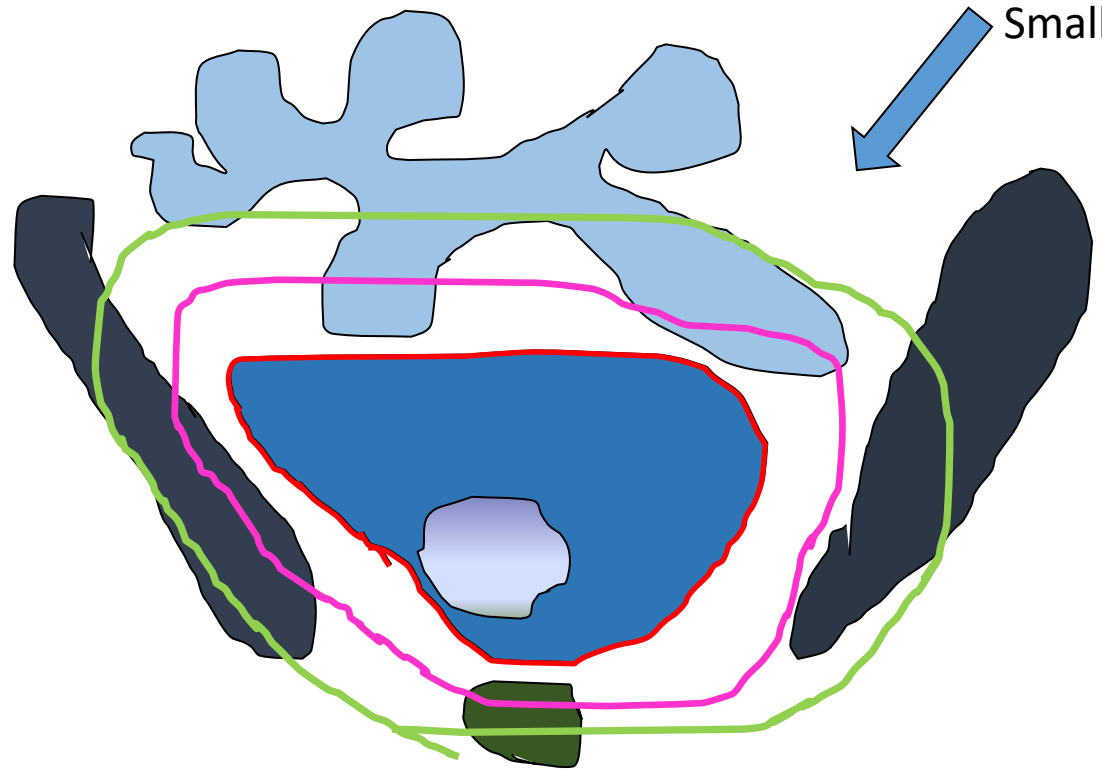
- For stage IIIb – using cisplatin 40mg/m² + Gemcitabine 100mg/m² – no consolidation!
- IMRT with dose painting
- Integrated boost (60.2 in 2.15Gy to high risk regions 50.4 to the rest.
- PET/MRI based brachytherapy early in the treatment. (6Gy x 5).
- Interstitial brachytherapy to selected cases

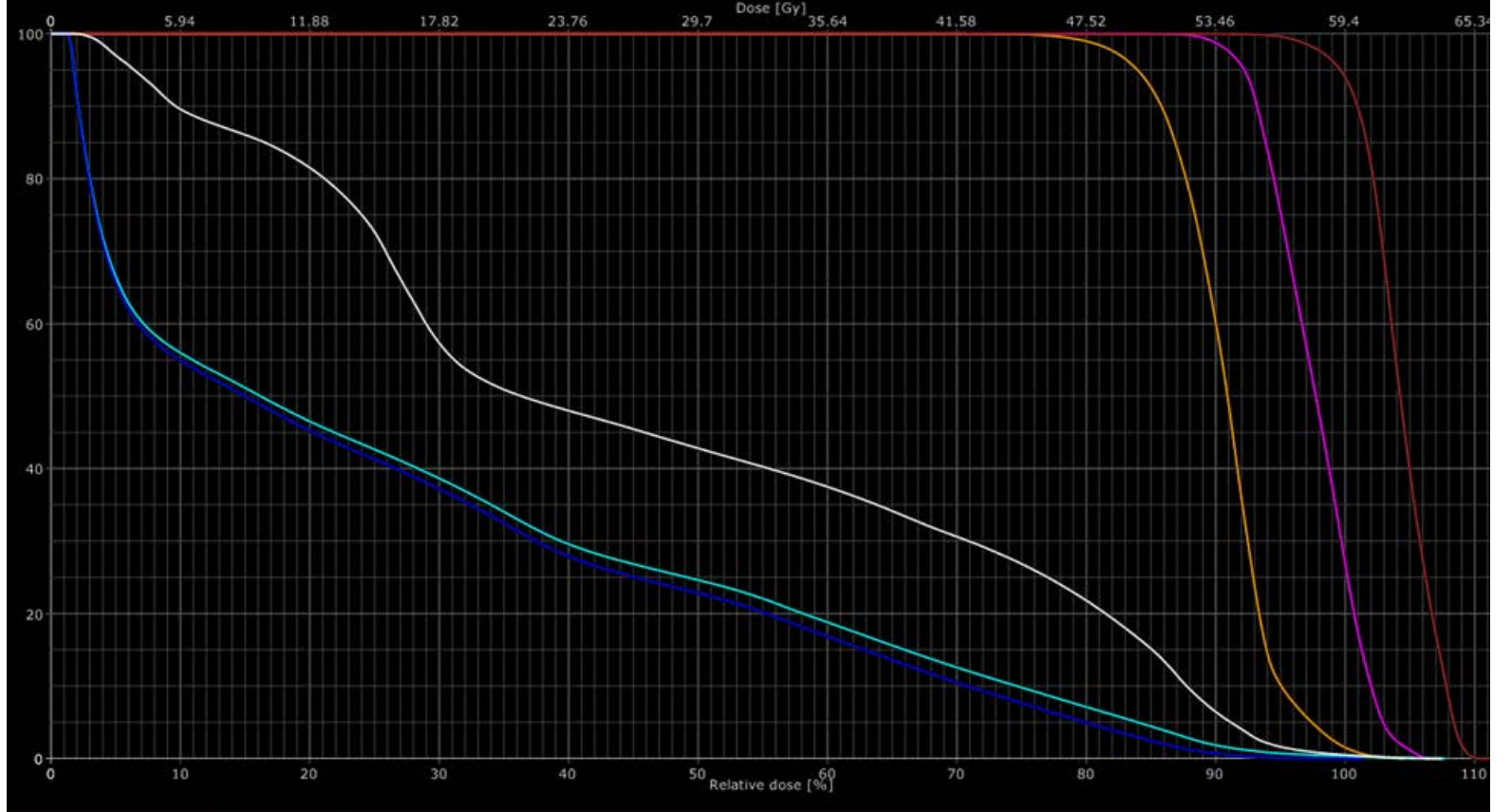
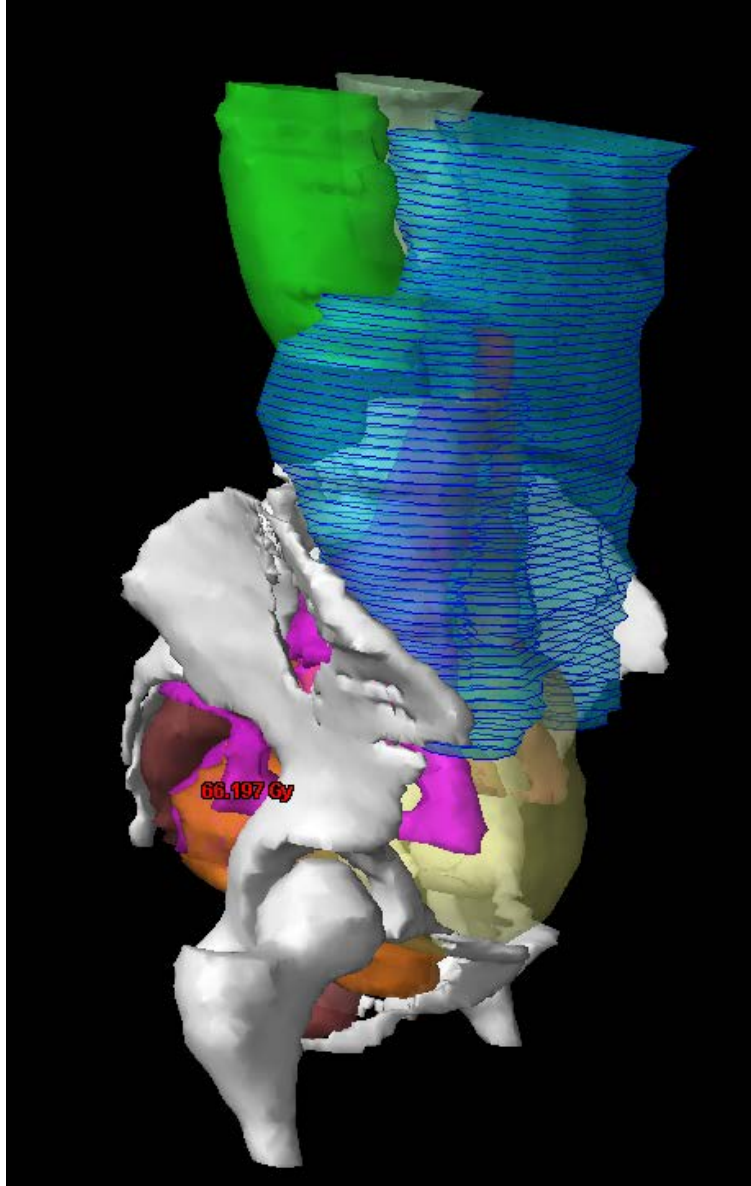


IMRT with dose painting



Small bowel



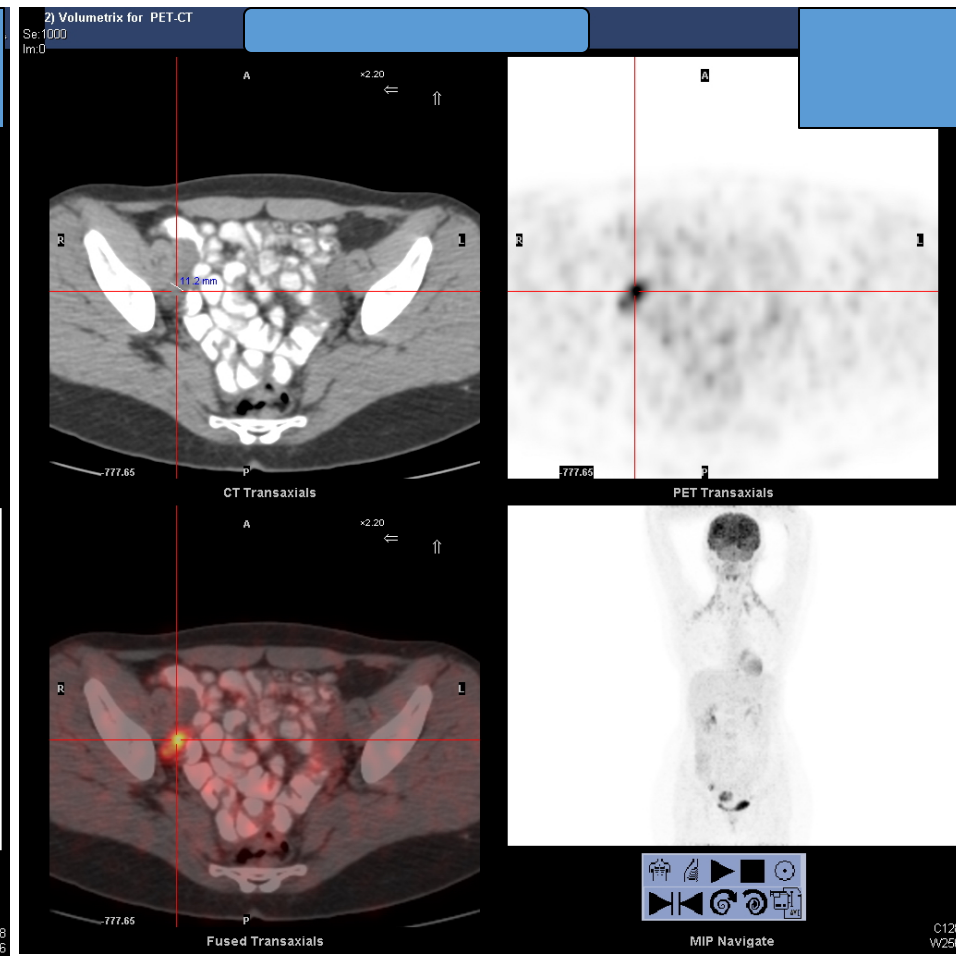
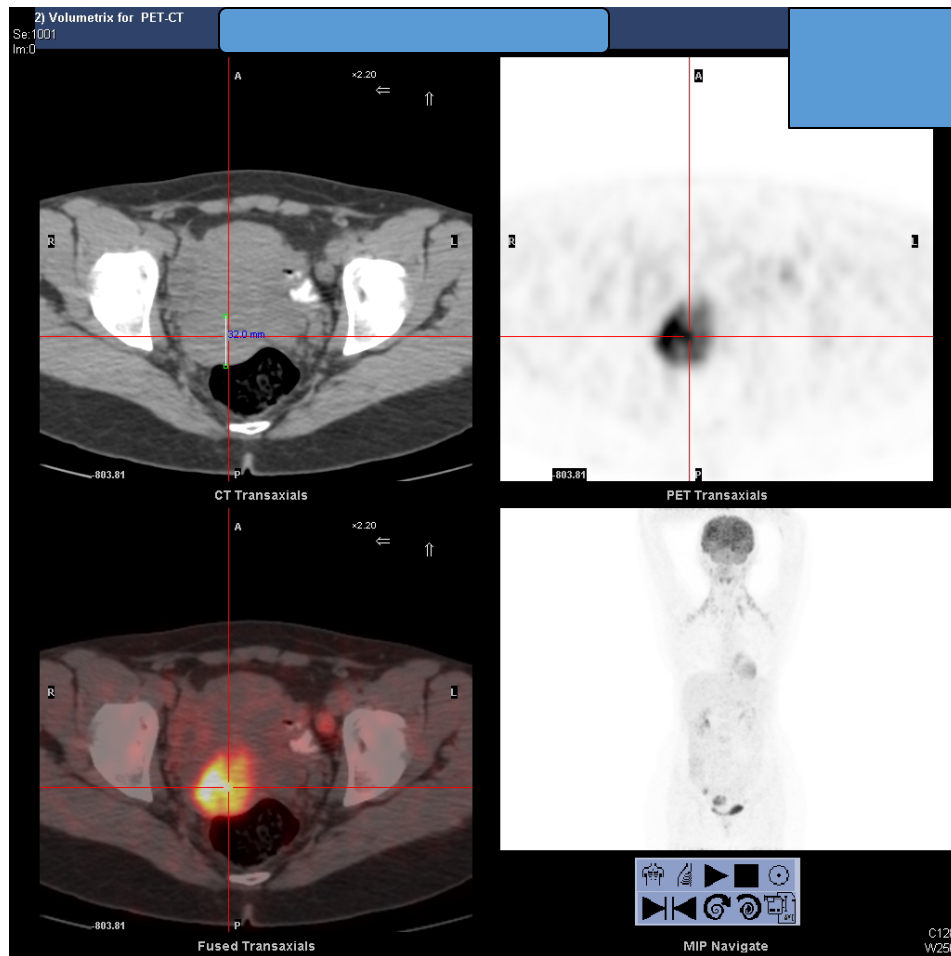


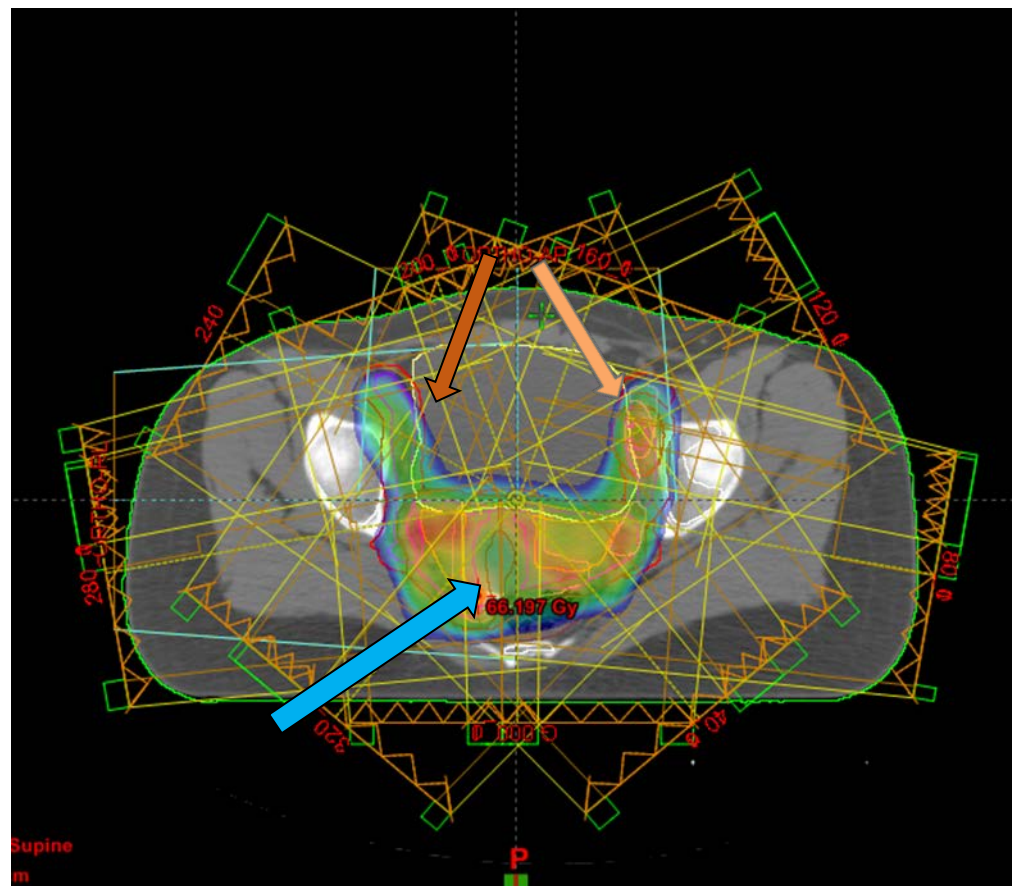
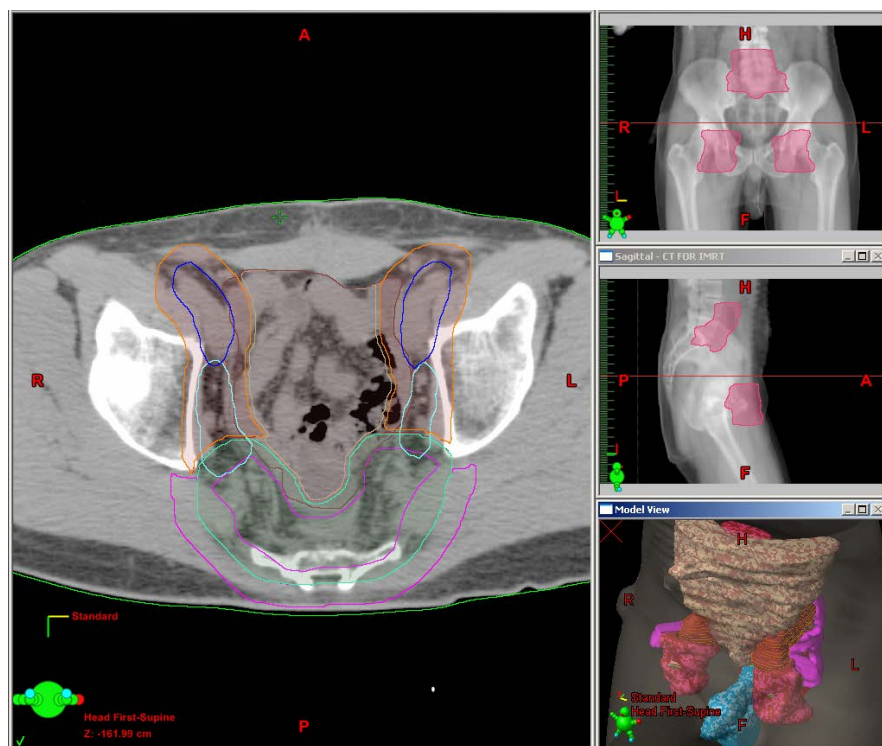
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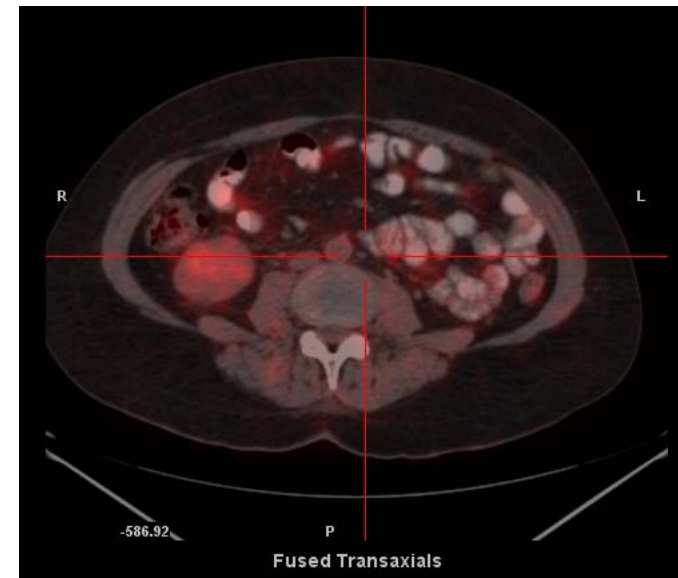
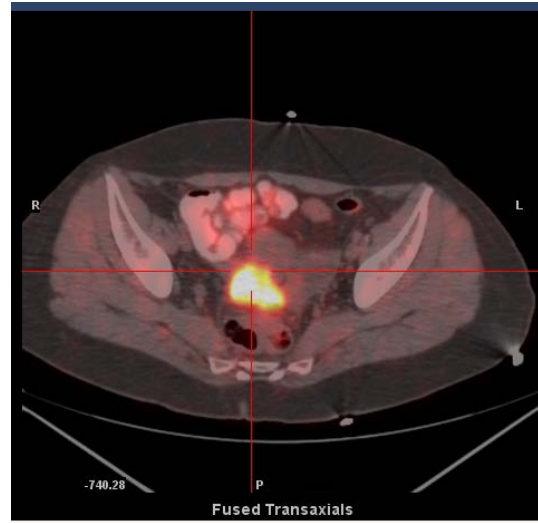
ds Dose Prescription Field Alignments Plan Objectives Optimization Objectives Dose Statistics Calculation Models Plan Sum

DVH Line	Structure	Approval Status	Plan	Course	Volume [cm ³]	Dose Cover. [%]	Sampling Cover...	Min Dose [%]	Max Dose [%]	Mean Dose [%]
max	max	Approved	IMRT CERVI #	1						
BM	BM	Approved	IMRT CERVI #	1	470.3	100.0	100.0	1.8	107.5	46.8
PTV1	PTV1	Approved	IMRT CERVI #	1	581.7	100.0	100.0	82.3	111.4	104.2
PTV2	PTV2	Approved	IMRT CERVI #	1	168.5	100.0	100.1	82.5	106.5	97.6
PTV3	PTV3	Approved	IMRT CERVI #	1	357.1	100.0	100.0	64.0	104.6	90.6
SB-PTV	SB-PTV	Approved	IMRT CERVI #	1	1594.1	100.0	100.0	1.2	101.5	26.5
Small Bowel	Small Bowel	Approved	IMRT CERVI #	1	1632.2	100.0	100.0	1.2	107.8	28.0

User: meirovitz Group: Oncologist Site: Main NUM





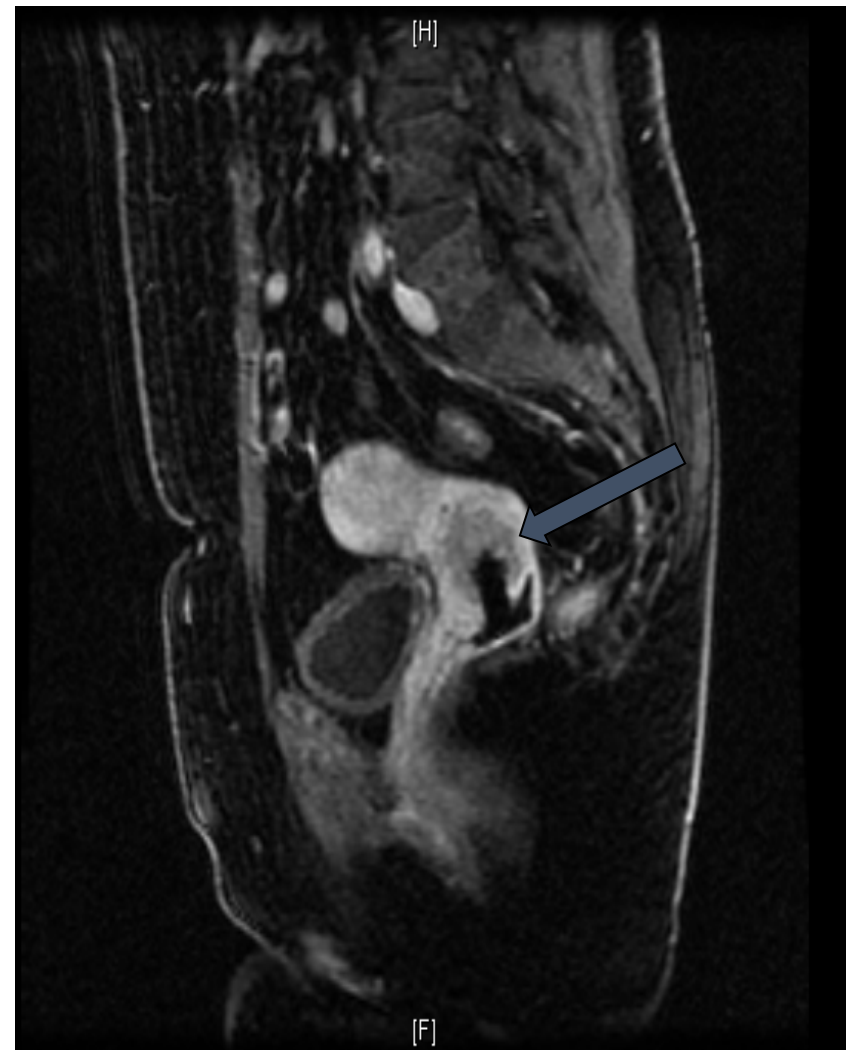
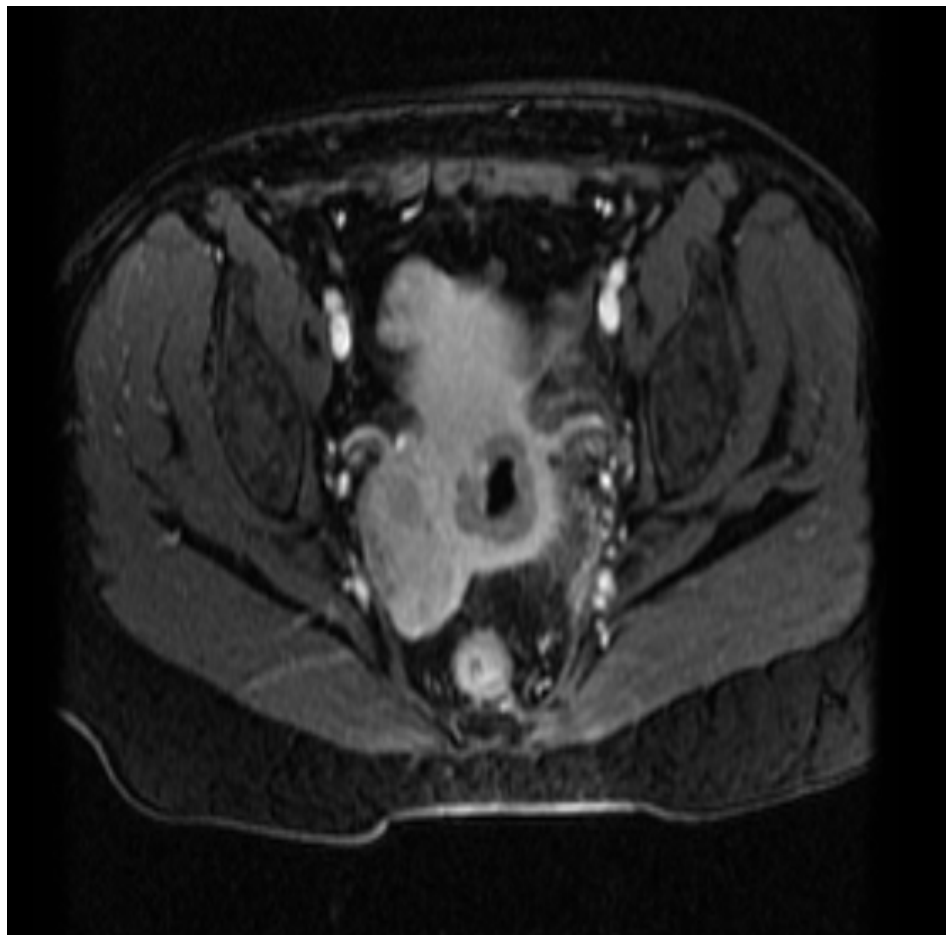


Starting on week 2-3 of external beam

Weekly 6Gy to CT based planning

Point A – goes down from 105% on average to 70% on last application.

Integrating interstitial brachytherapy when indicated.





Volumeix for PET-CT

ADAR MESHUMAD CHAVIA PET-CT SCAN

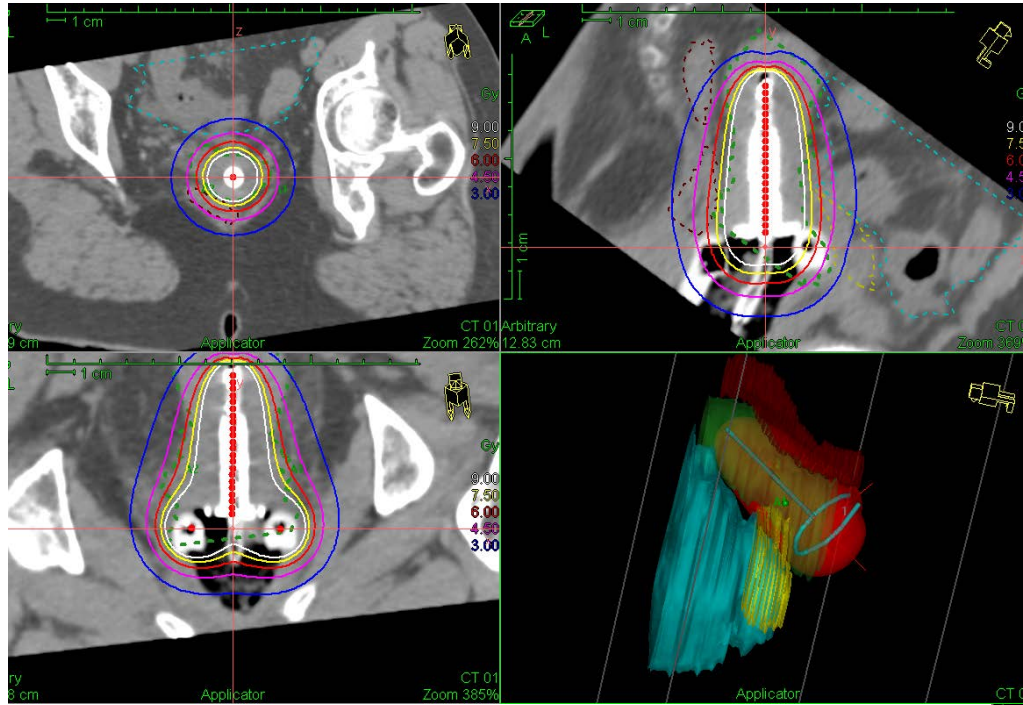
ScreenCap0355

CT Transaxiale

PET Transaxiale

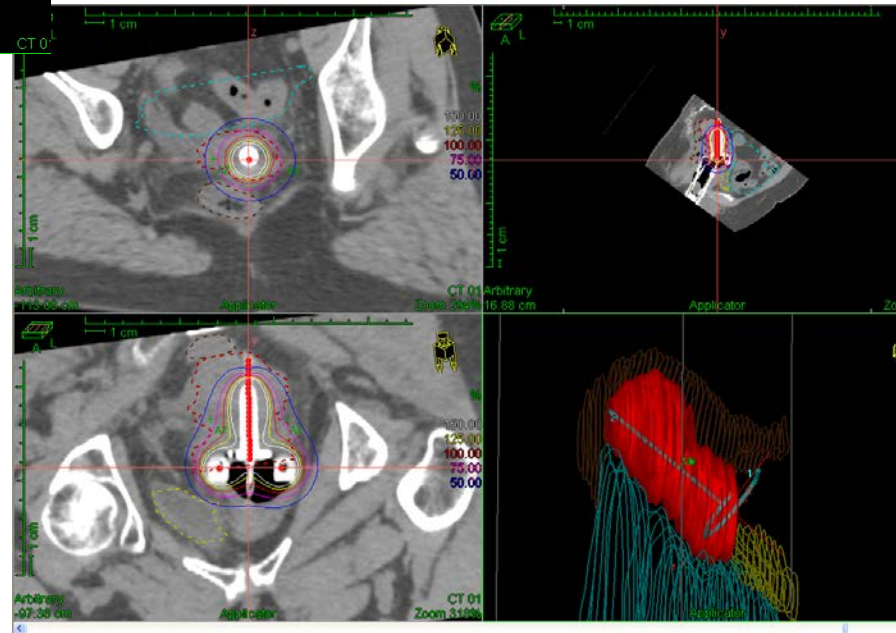
Fused Transaxiale

MIP Navigation



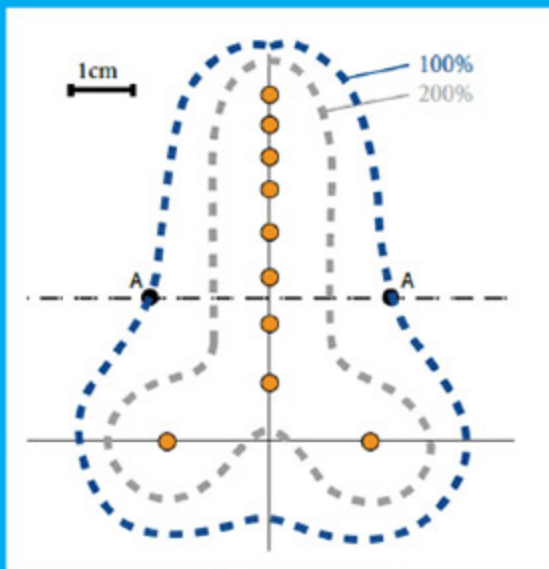
First application
Point A- 110%

Last (5th) application:
Point A- 65%

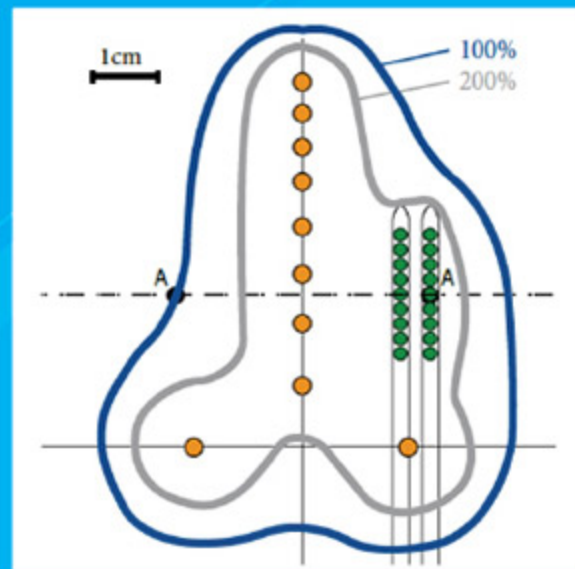




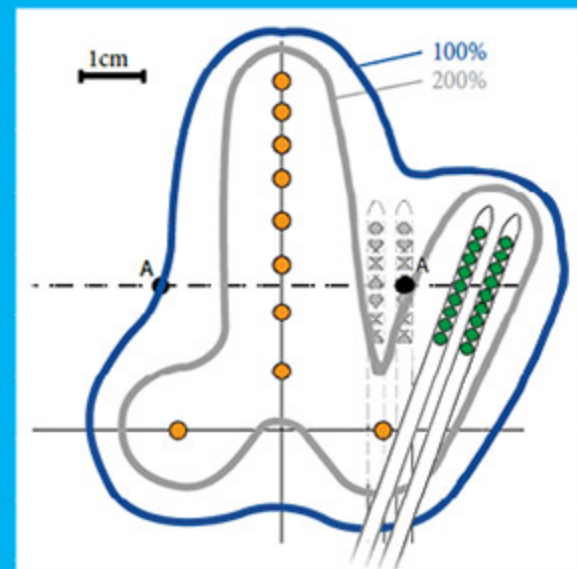
Venezia: optimizing dose distribution with interstitial needles



Intracavitary brachytherapy



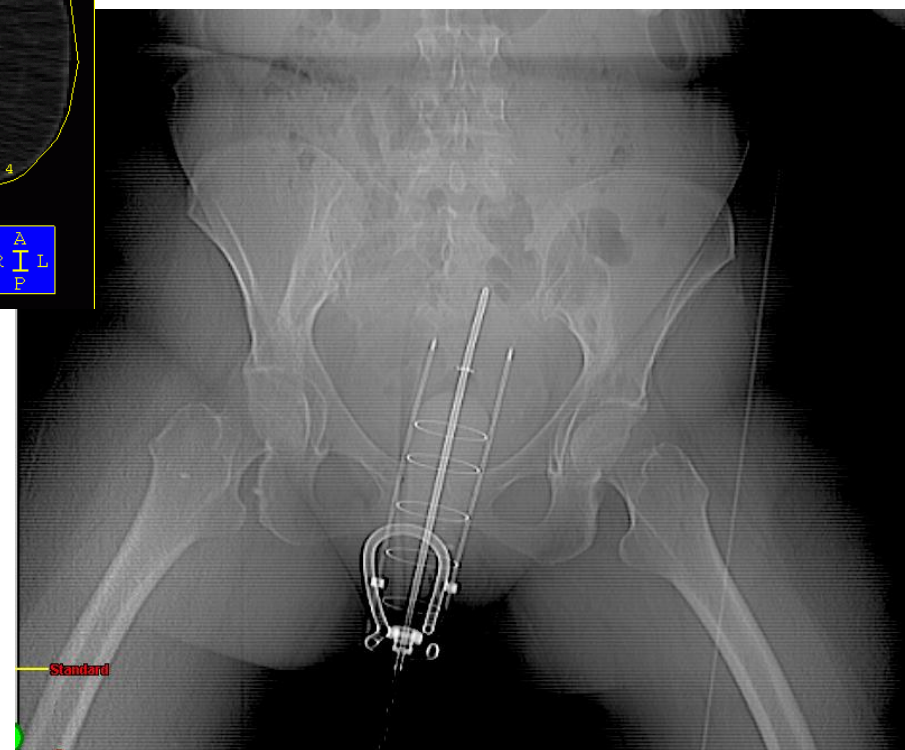
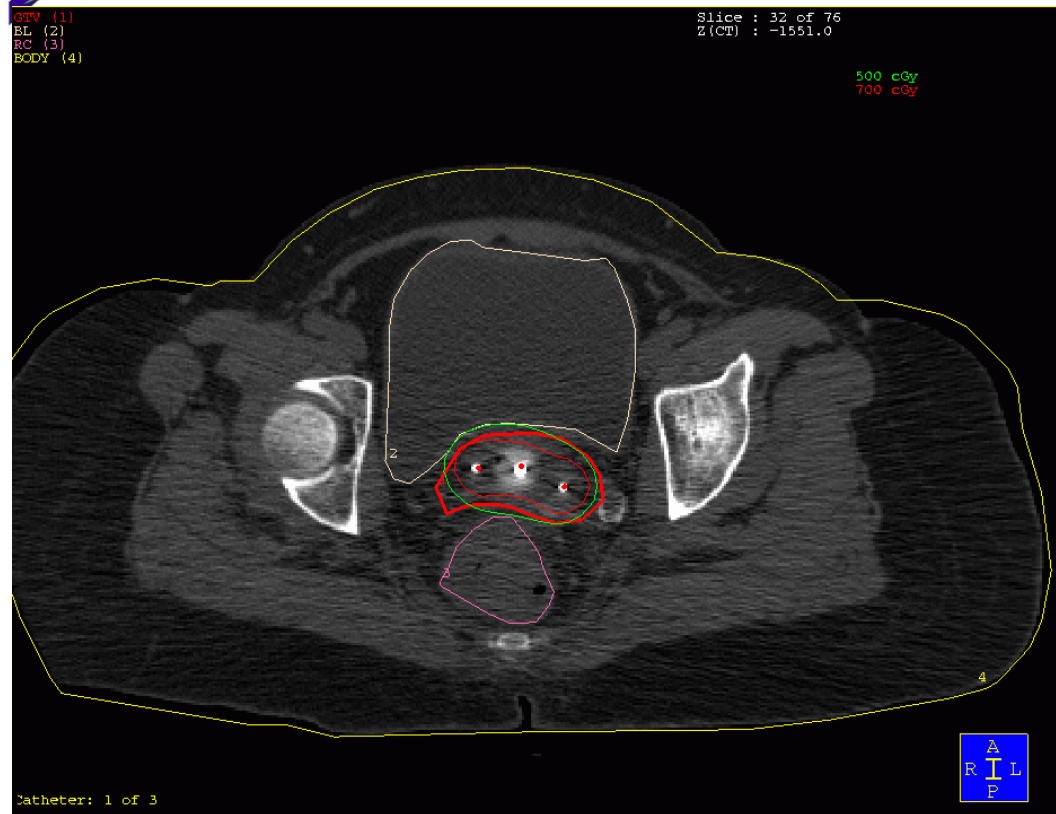
With parallel needles

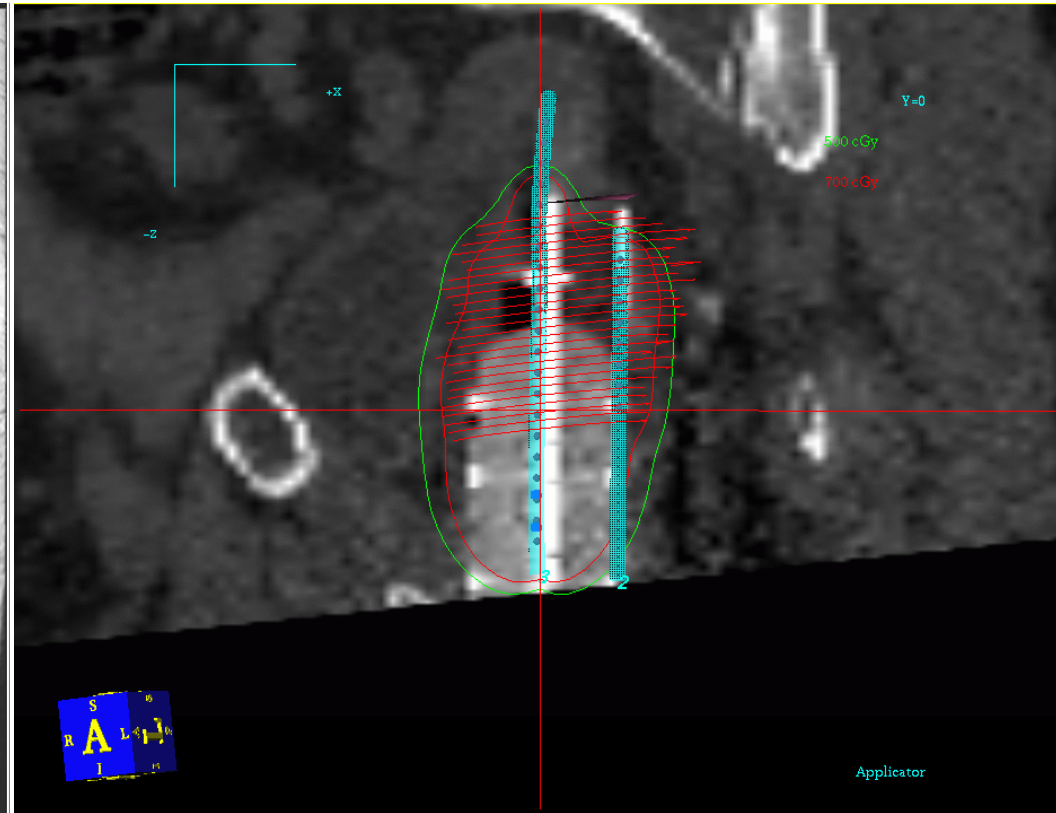


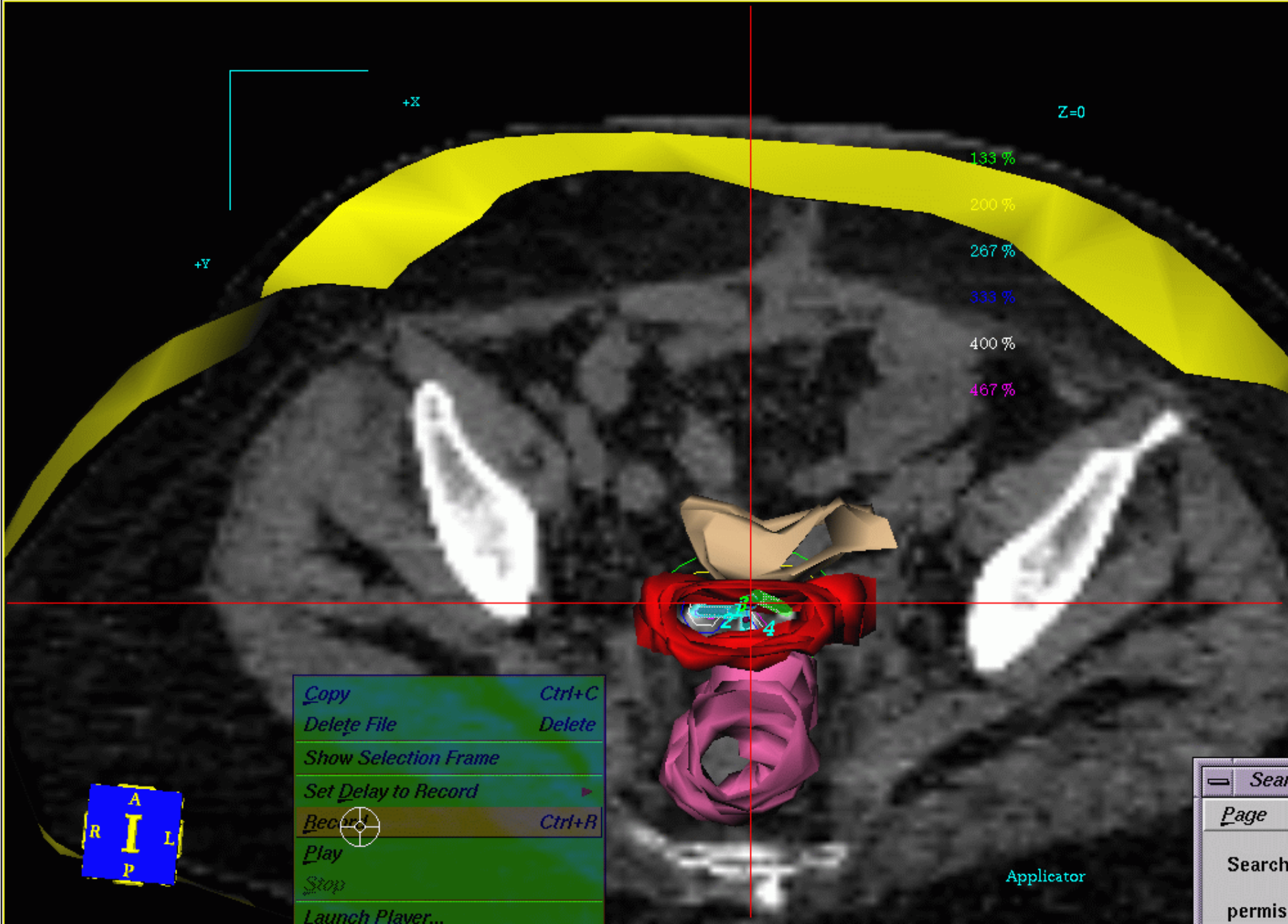
With parallel and oblique needles

(The parallel needles are not on the same plane)

Adapted from Kirisits C et al¹²





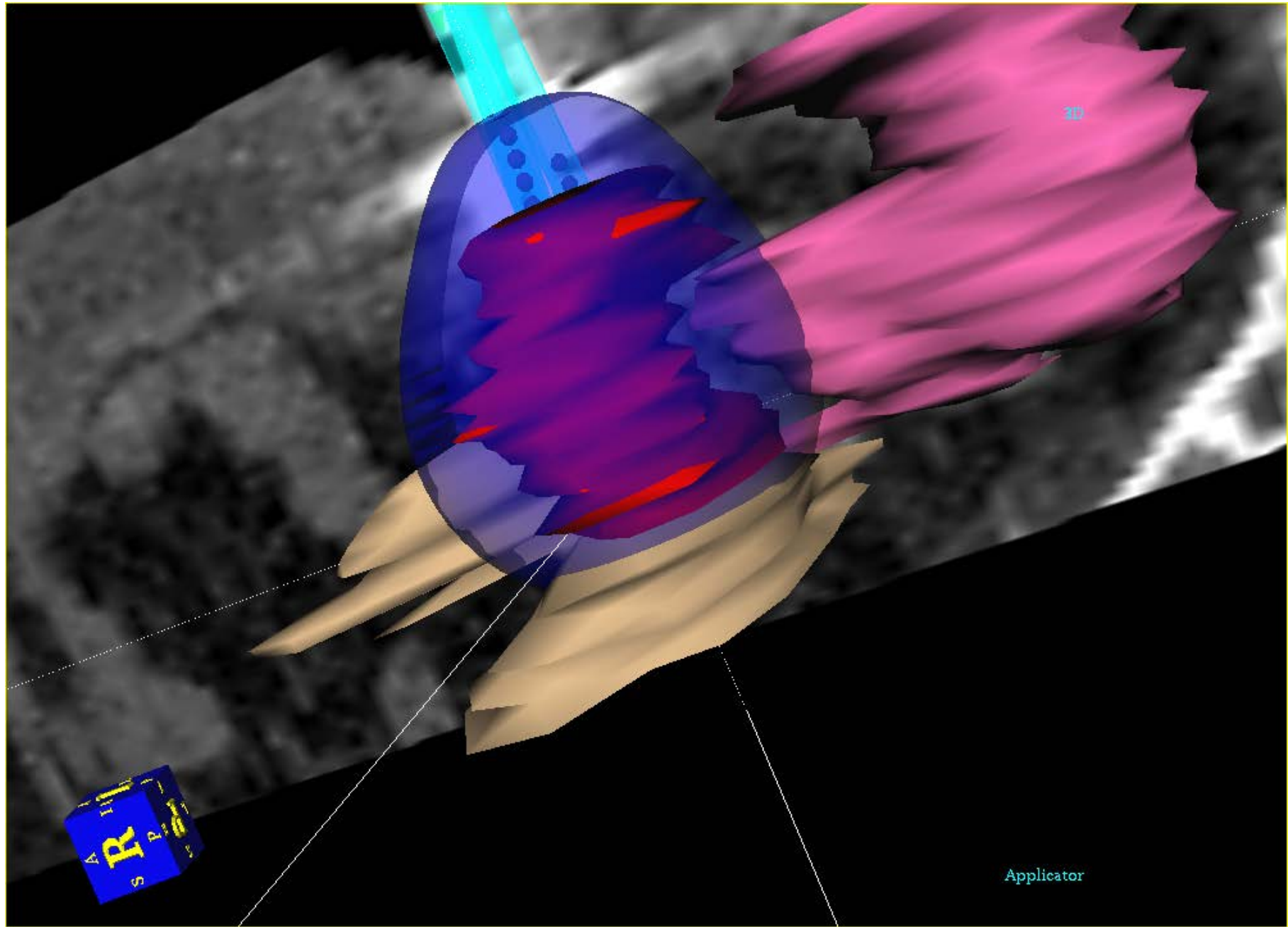


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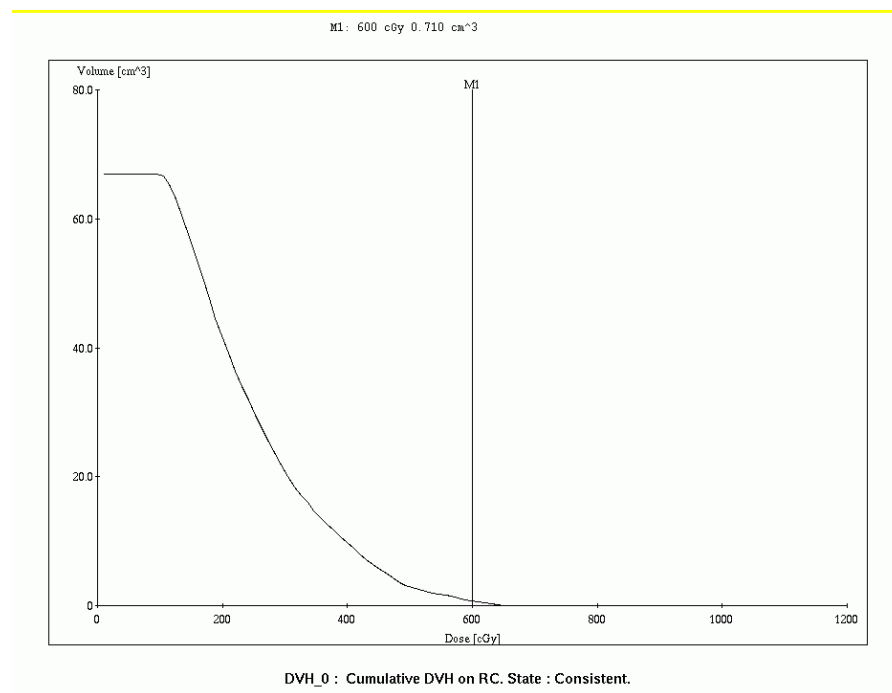
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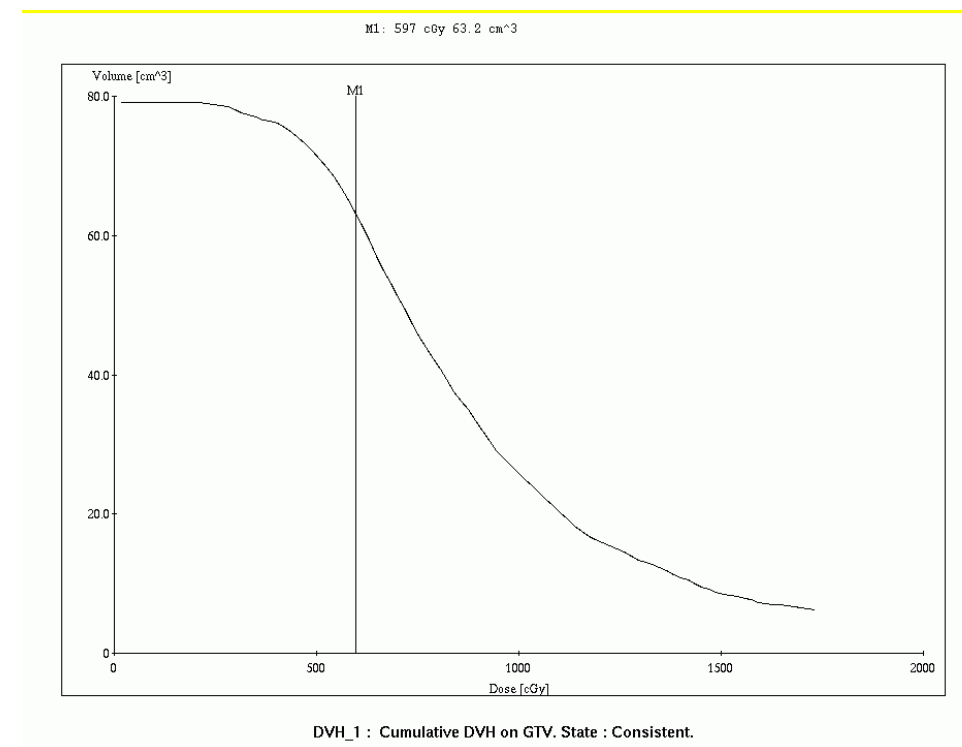
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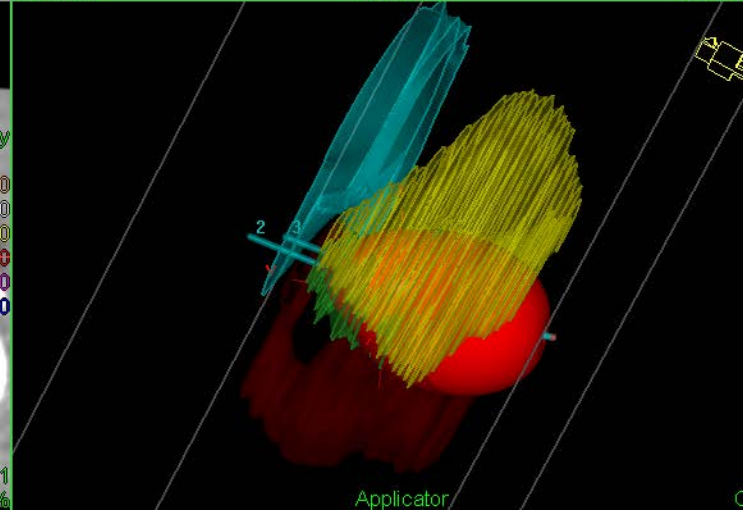
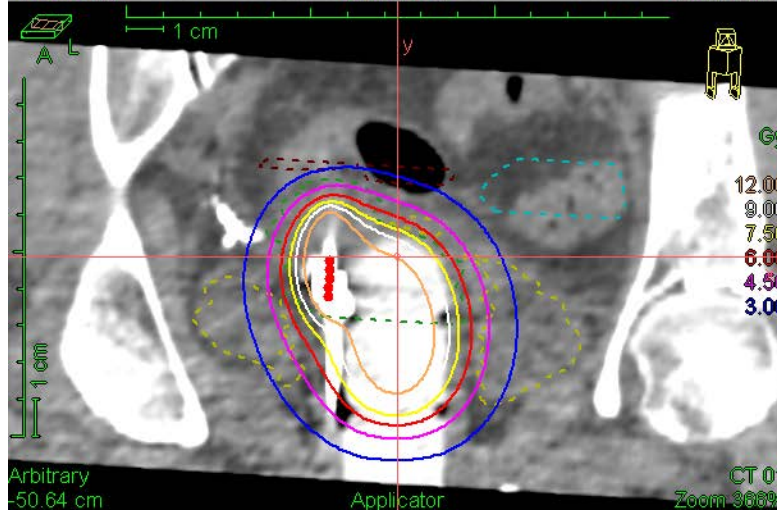
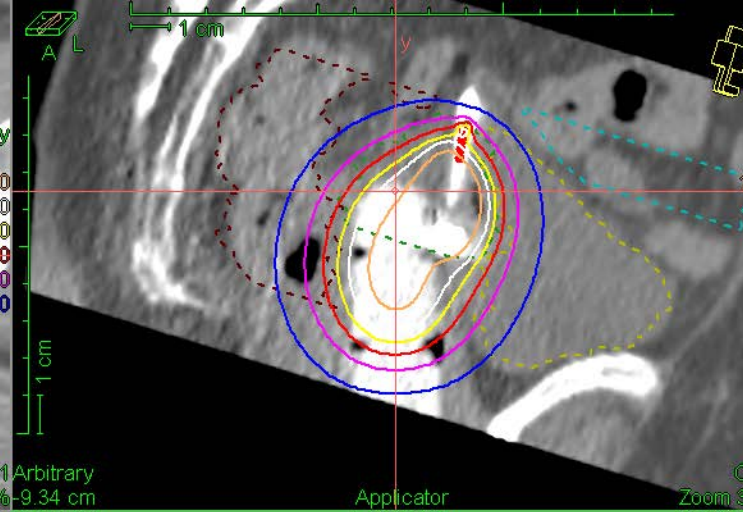
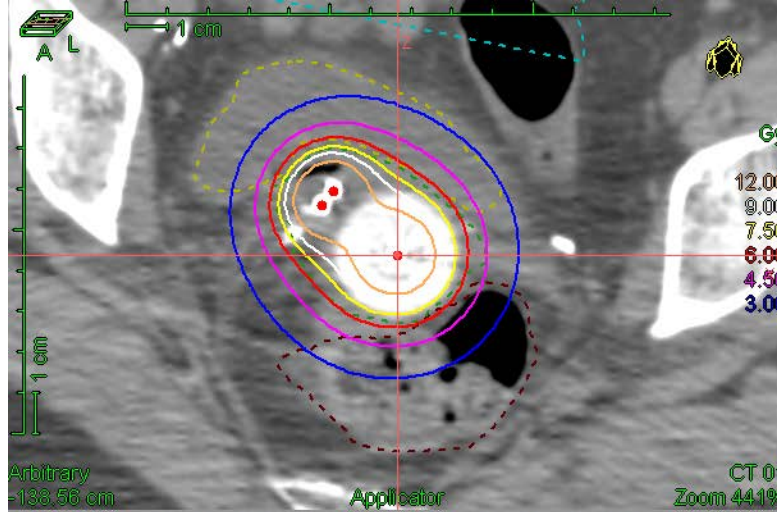


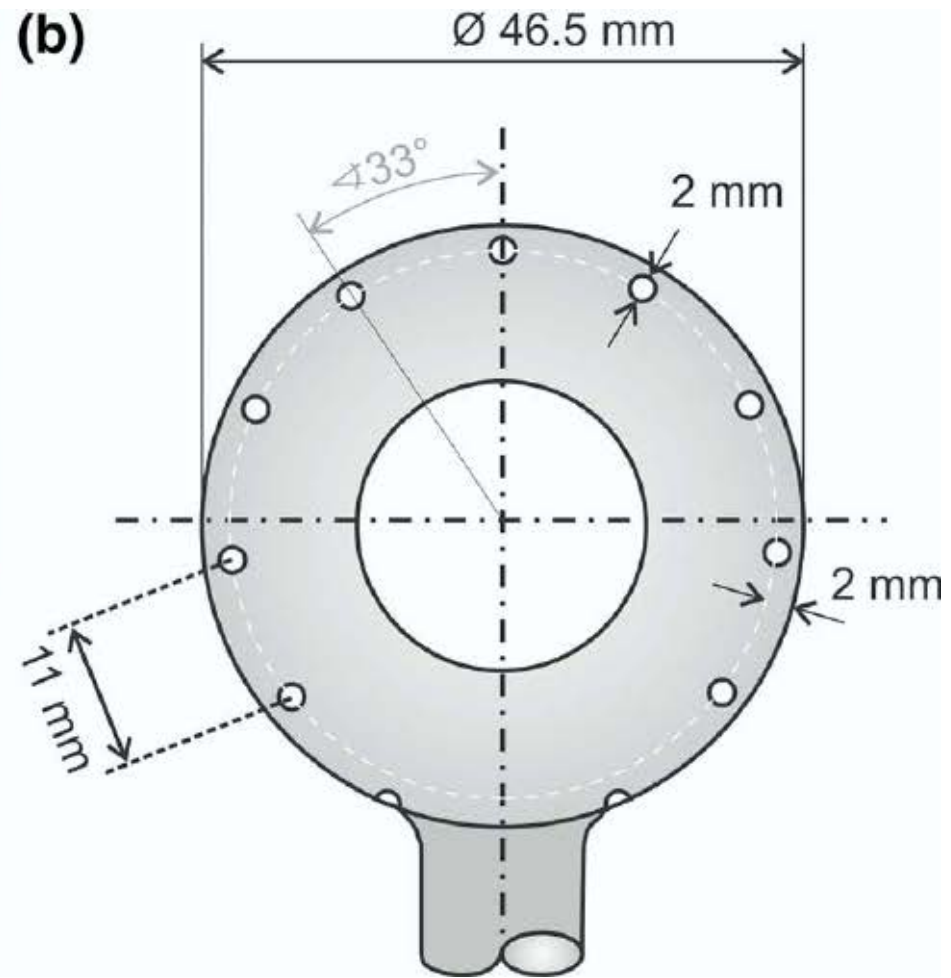
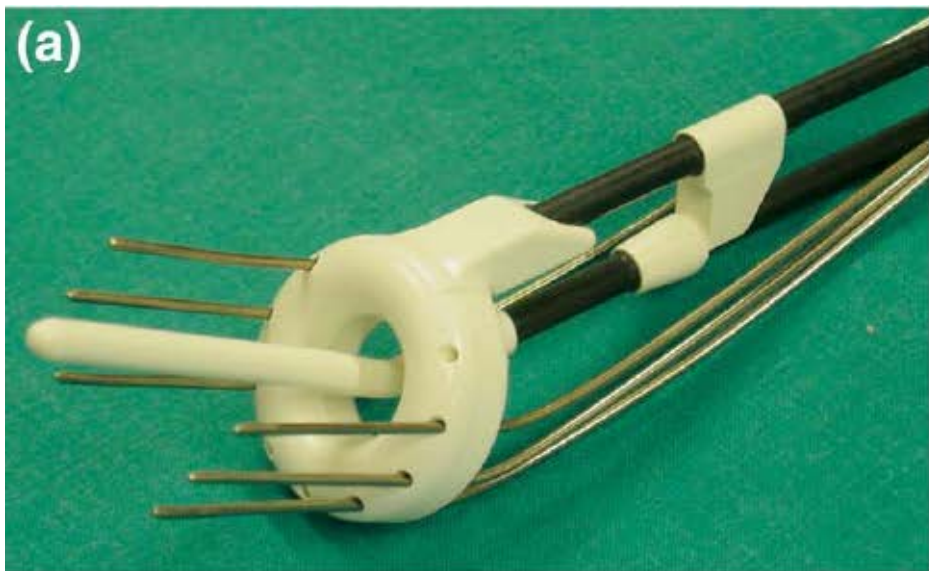
RECTUM

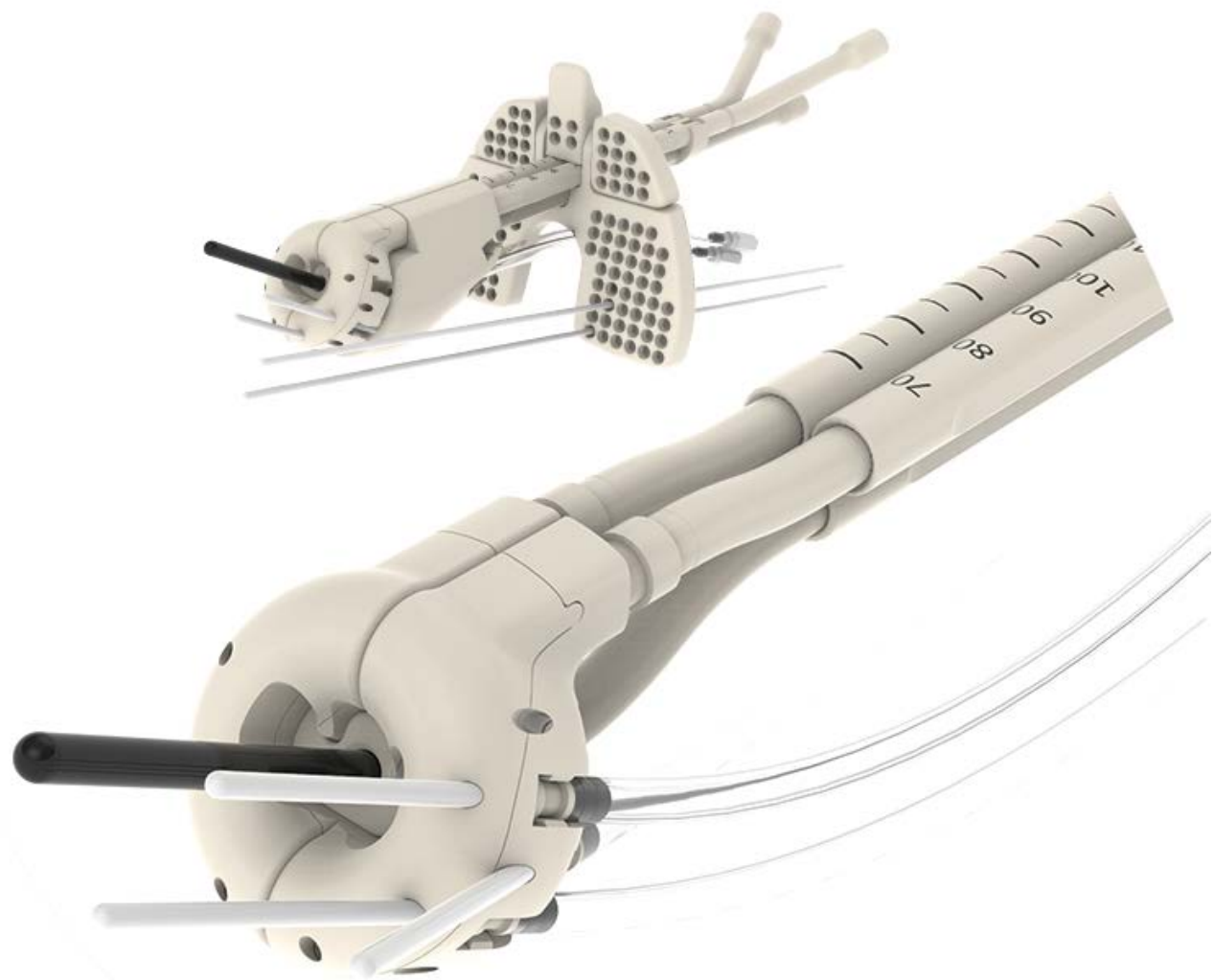


GTV



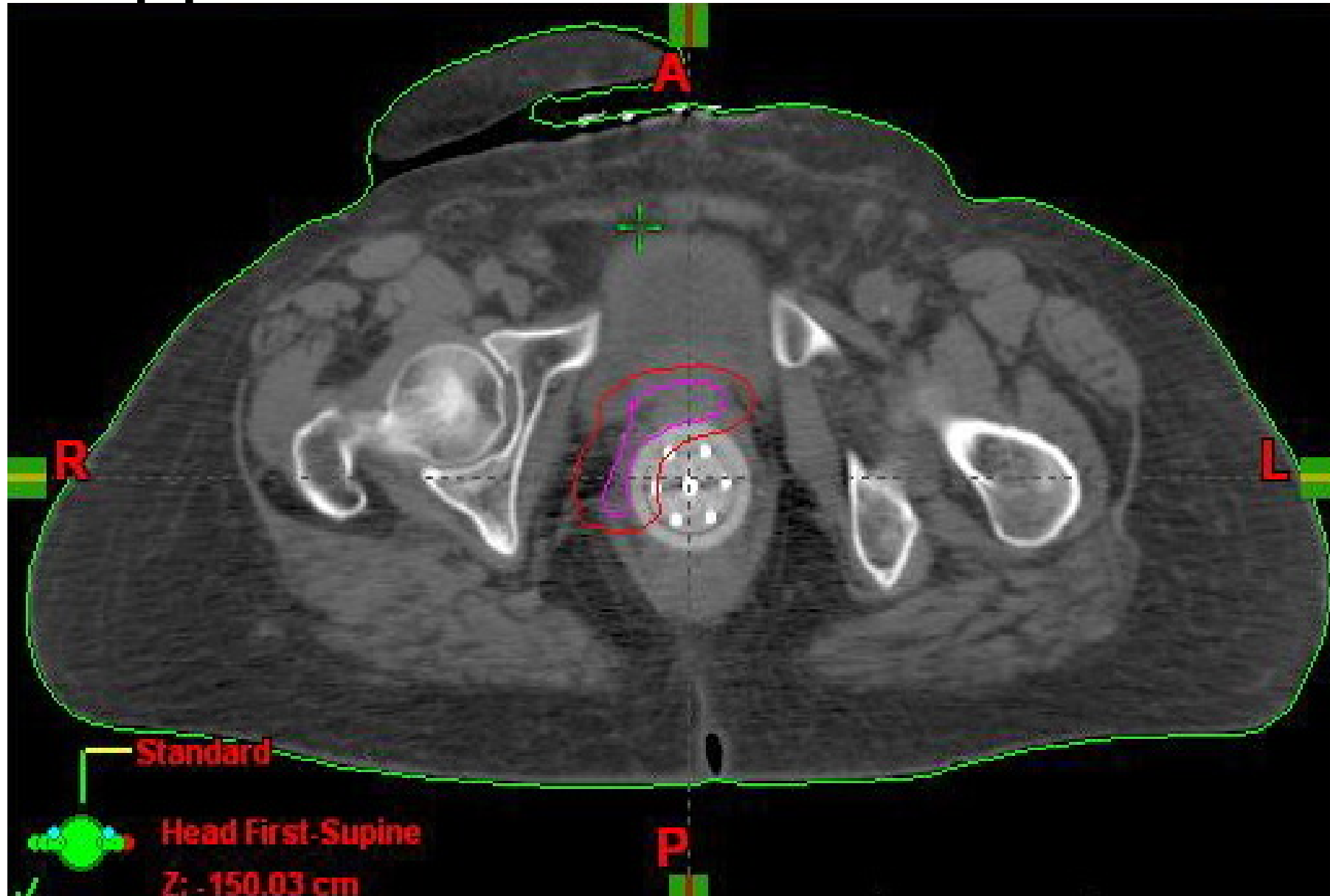


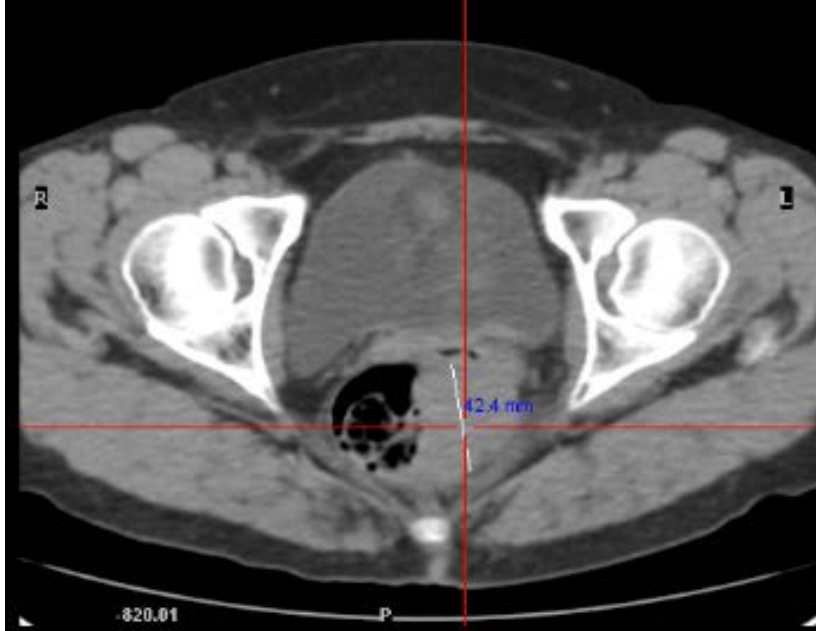






Miami Applicator





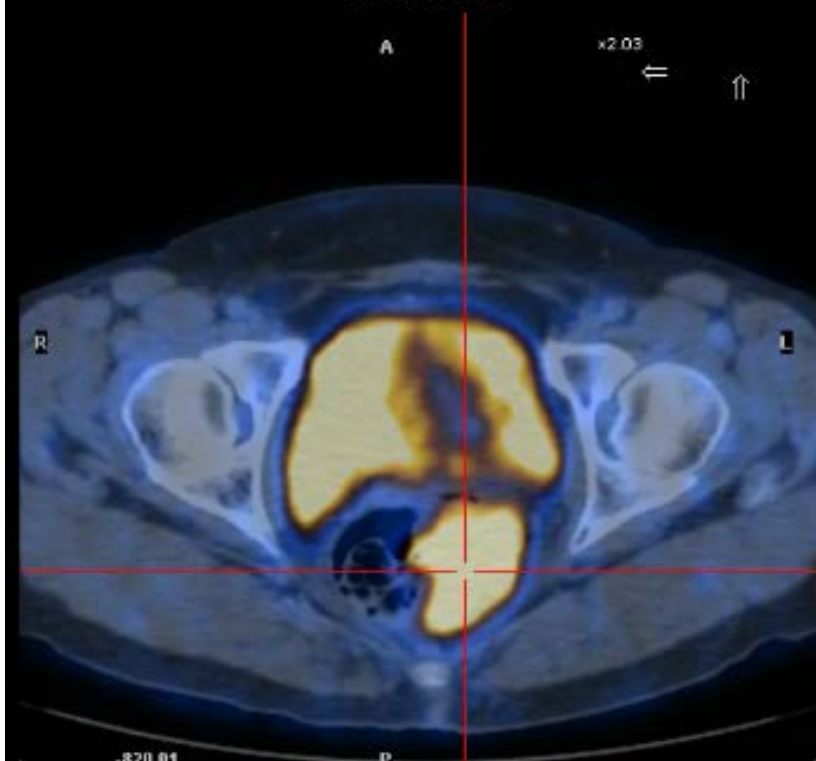
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CT Transaxials

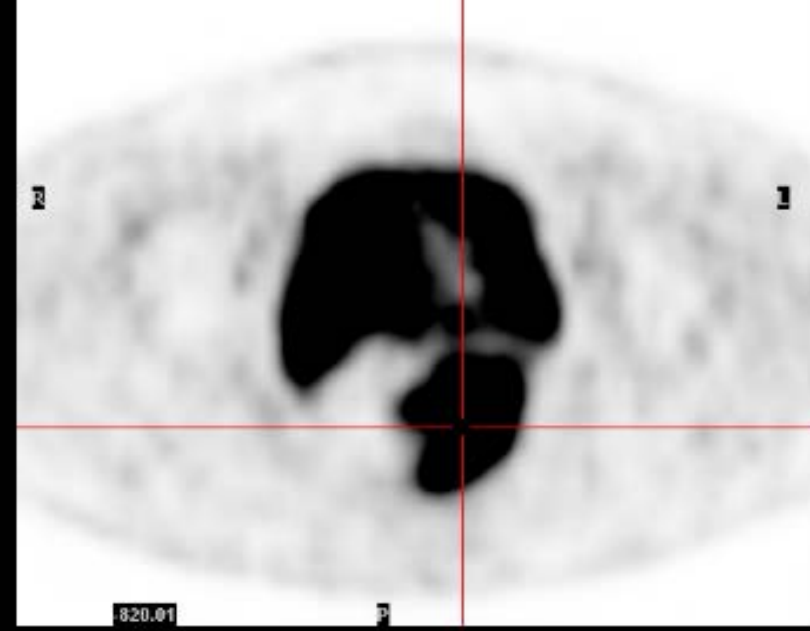
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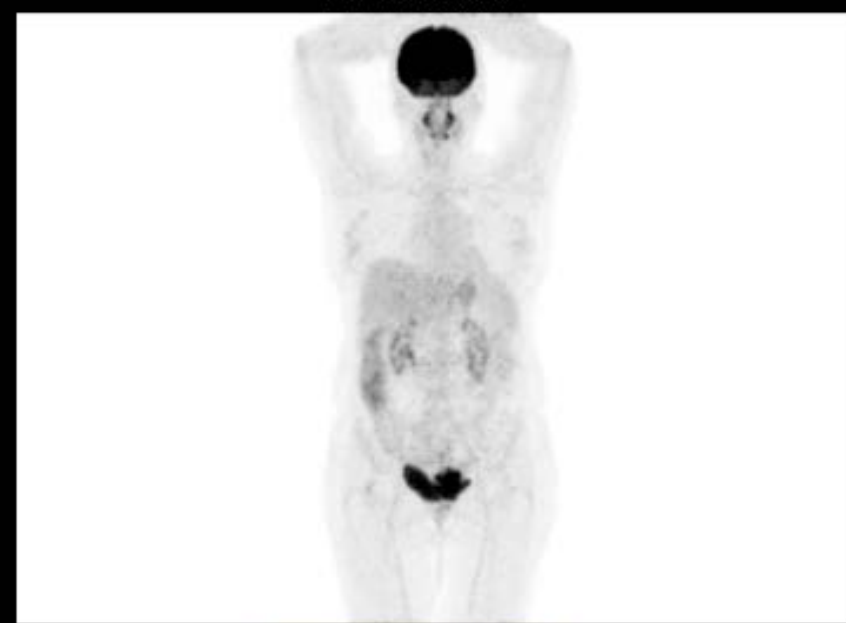
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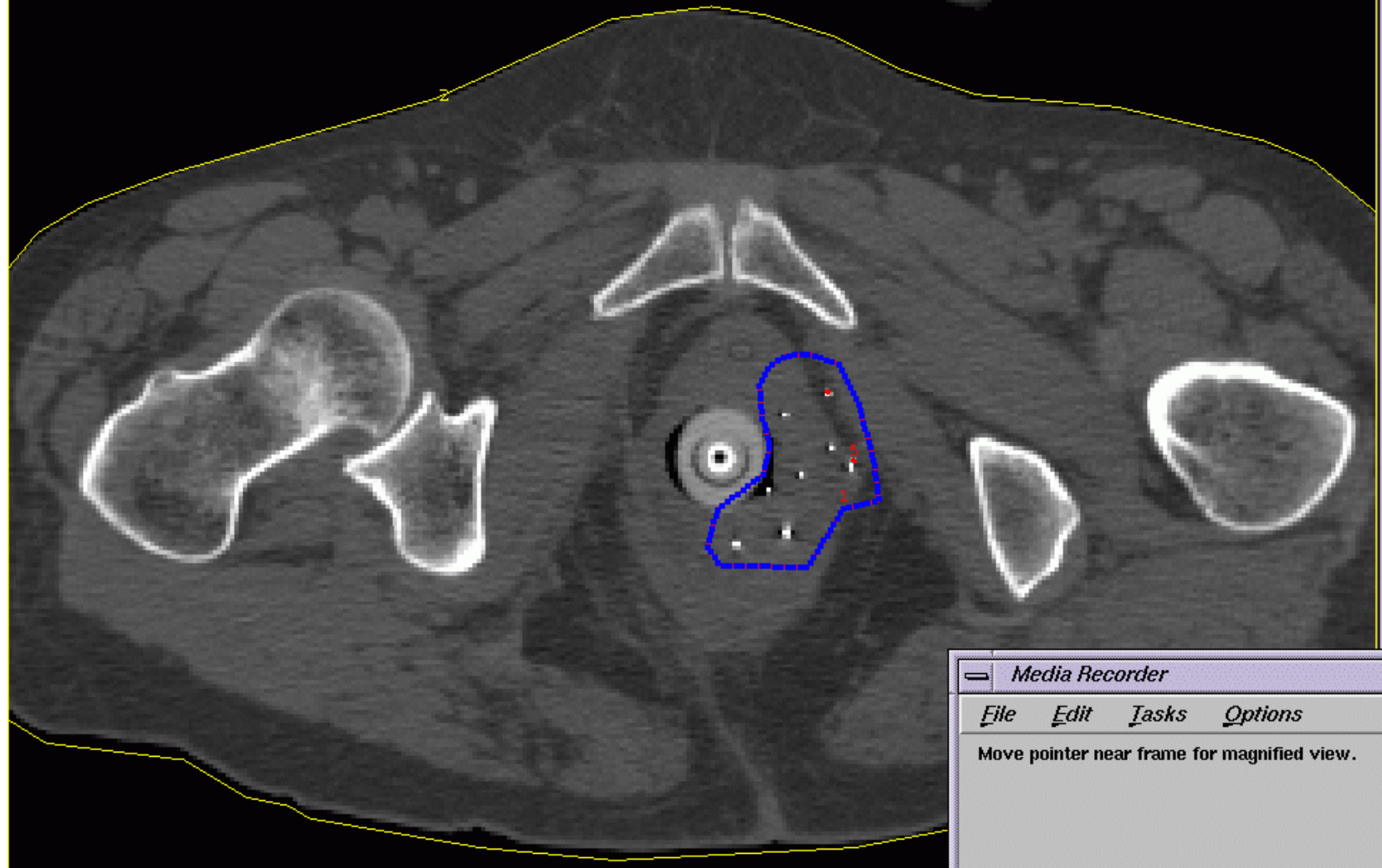
PET Transaxials





GTV (1)
body (2)

Slice : 55 of 130
Z (CT) : -1835.3



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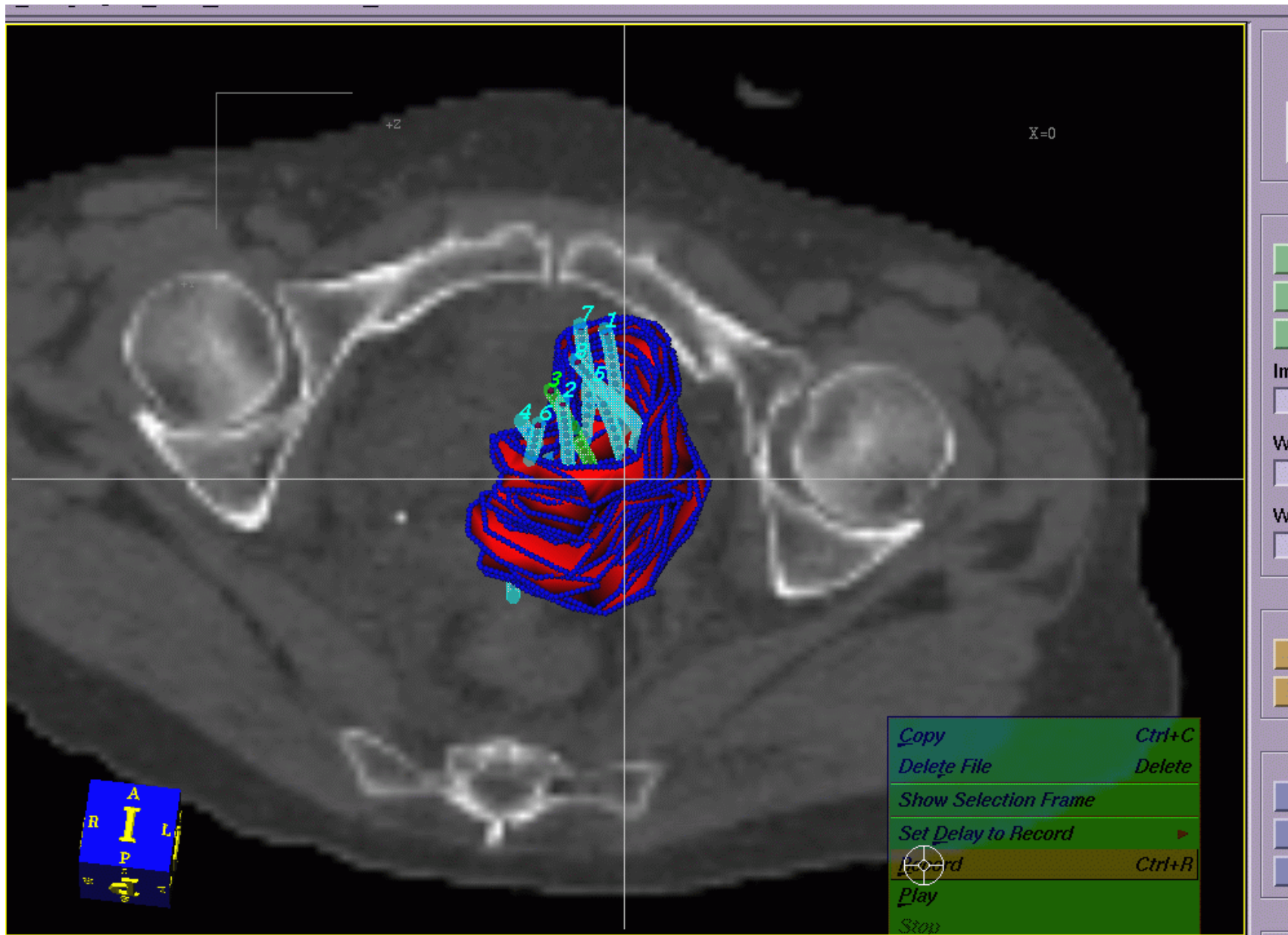
Catheter: 1 of 8

Media Recorder

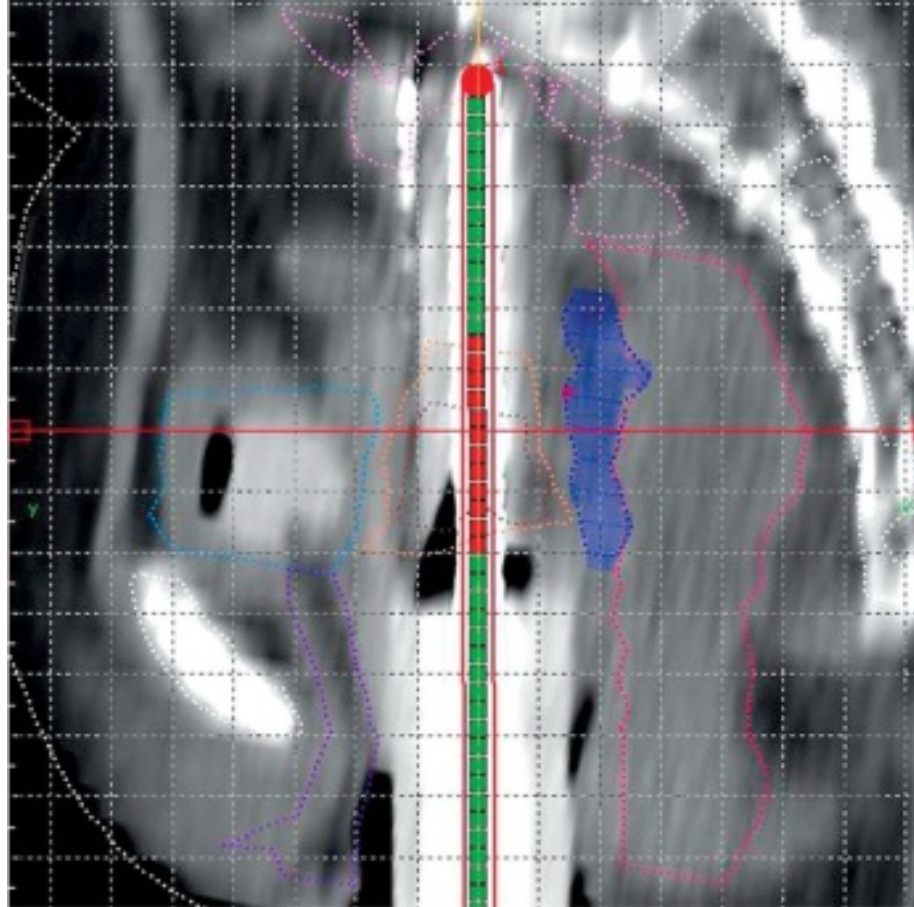
File Edit Tasks Options

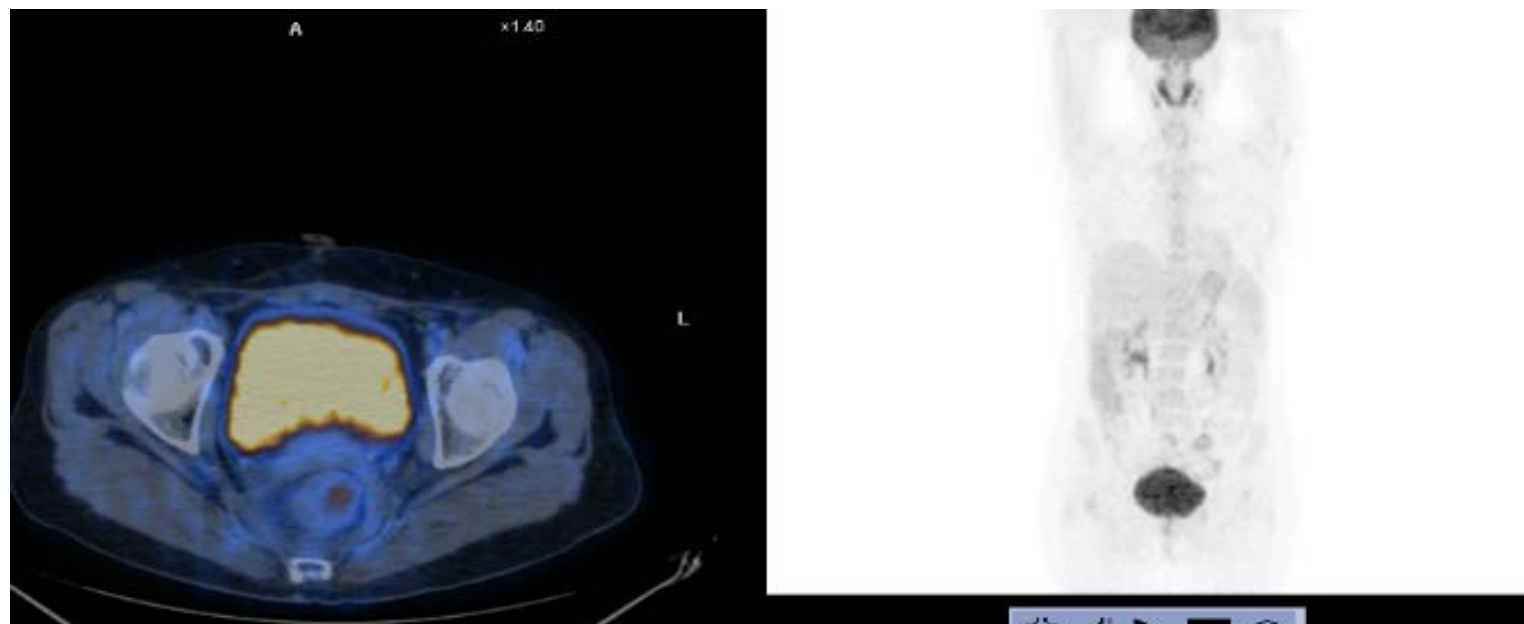
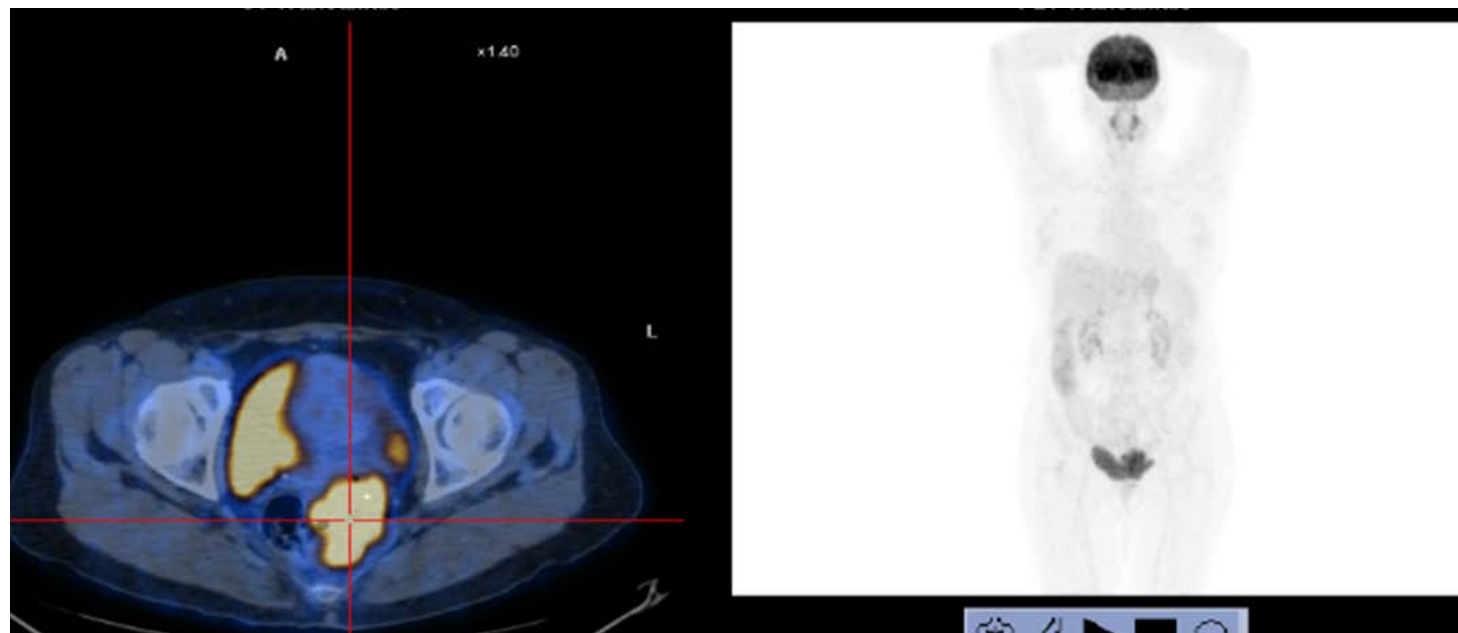
Move pointer near frame for magnified view.





Rectal separation using hydroxypropyl methylcellulose in intracavitary brachytherapy of cervical cancer: an innovative approach

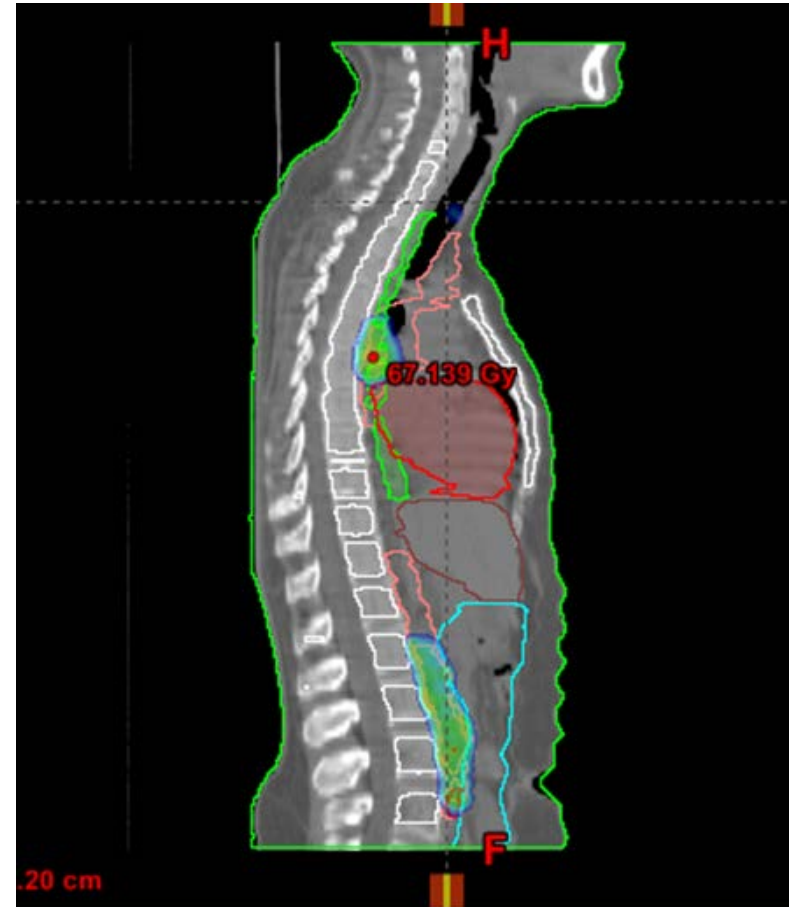
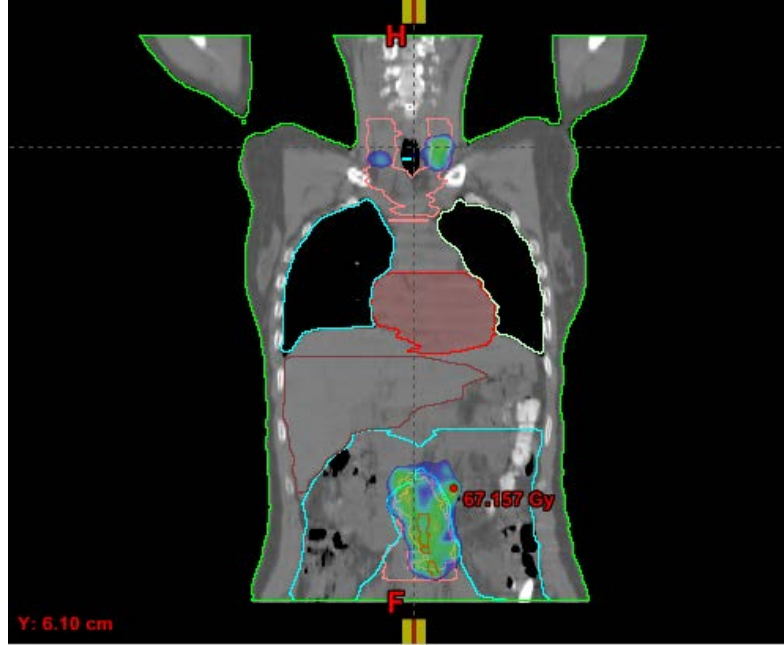




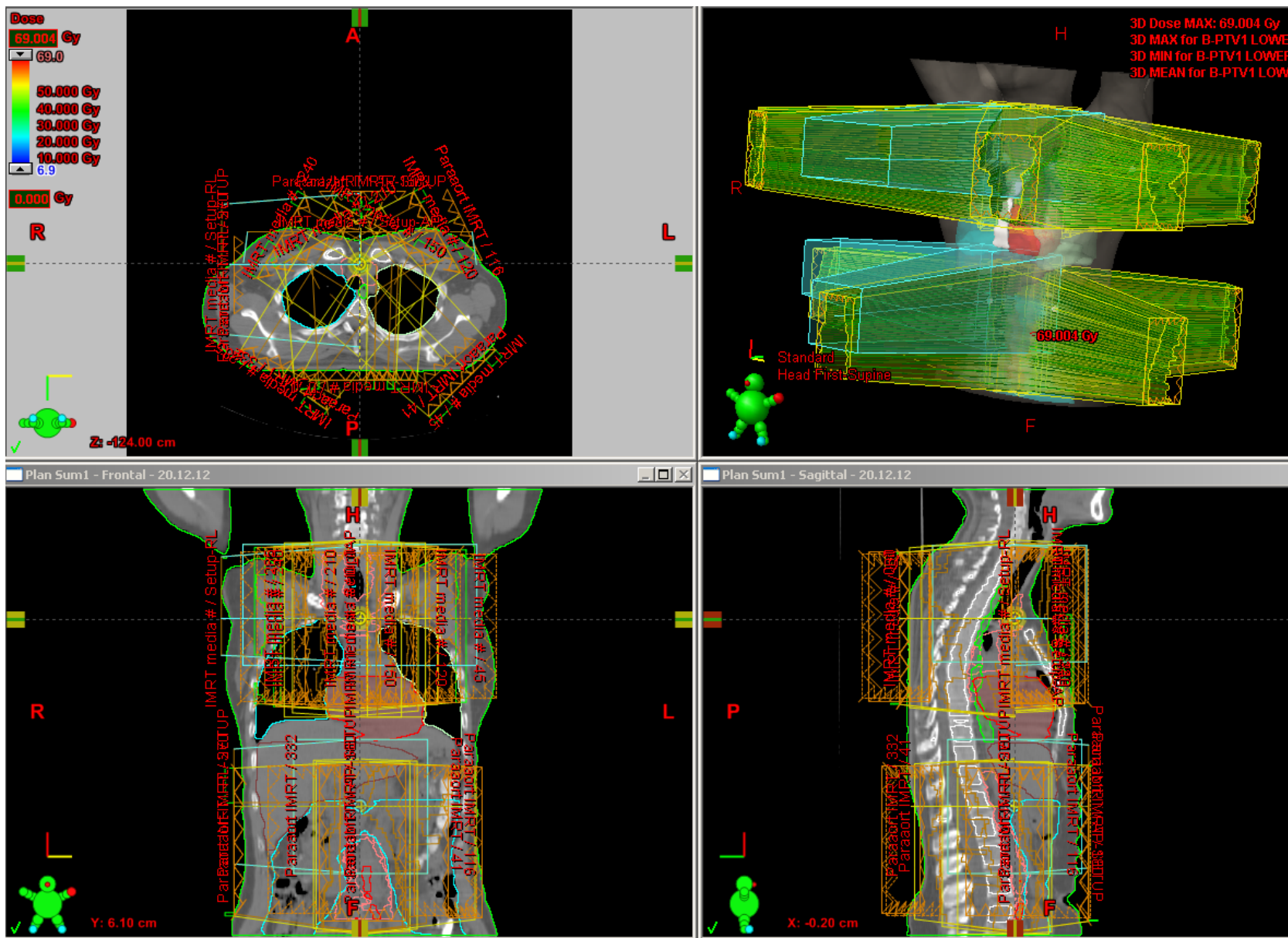


Salvage therapy



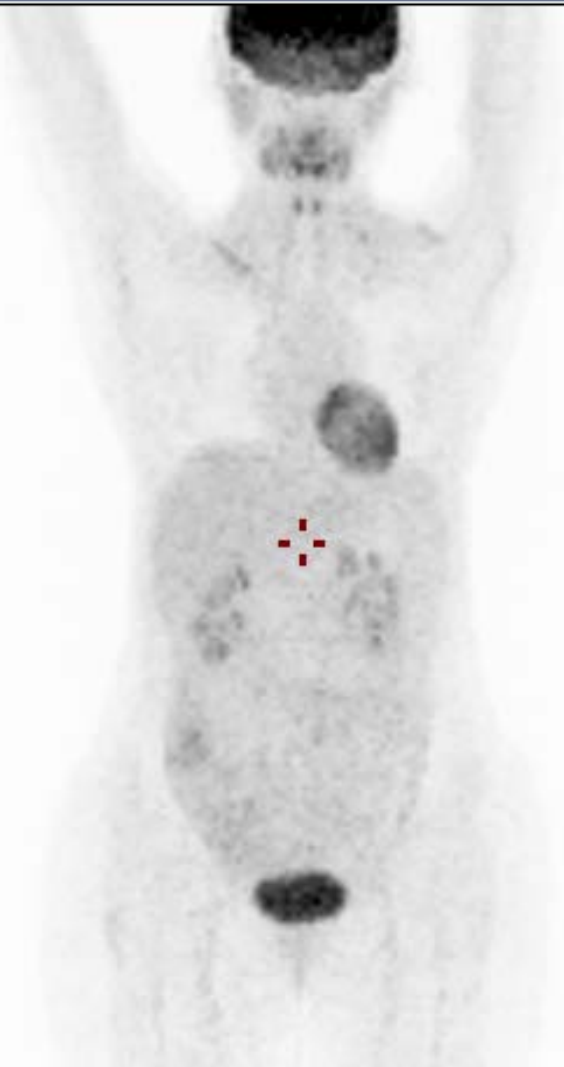


60 Gy in 2Gy#



6/13

ADJ DATE: 22/05/21
Acq Time: 13:12:
Order Date: 22/05/21
MF



10/12



dstbay86

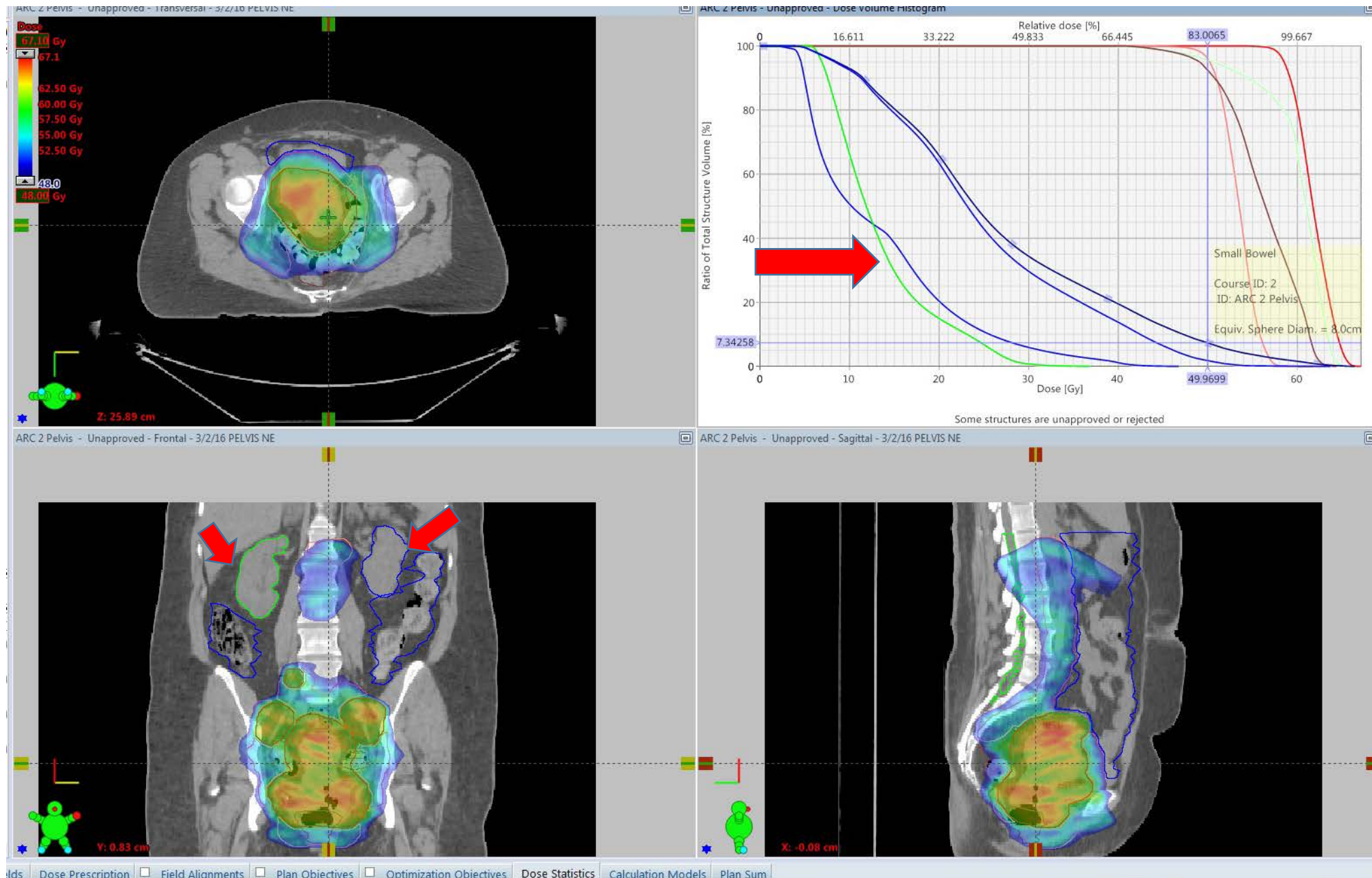
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PET Transaxials

7/12



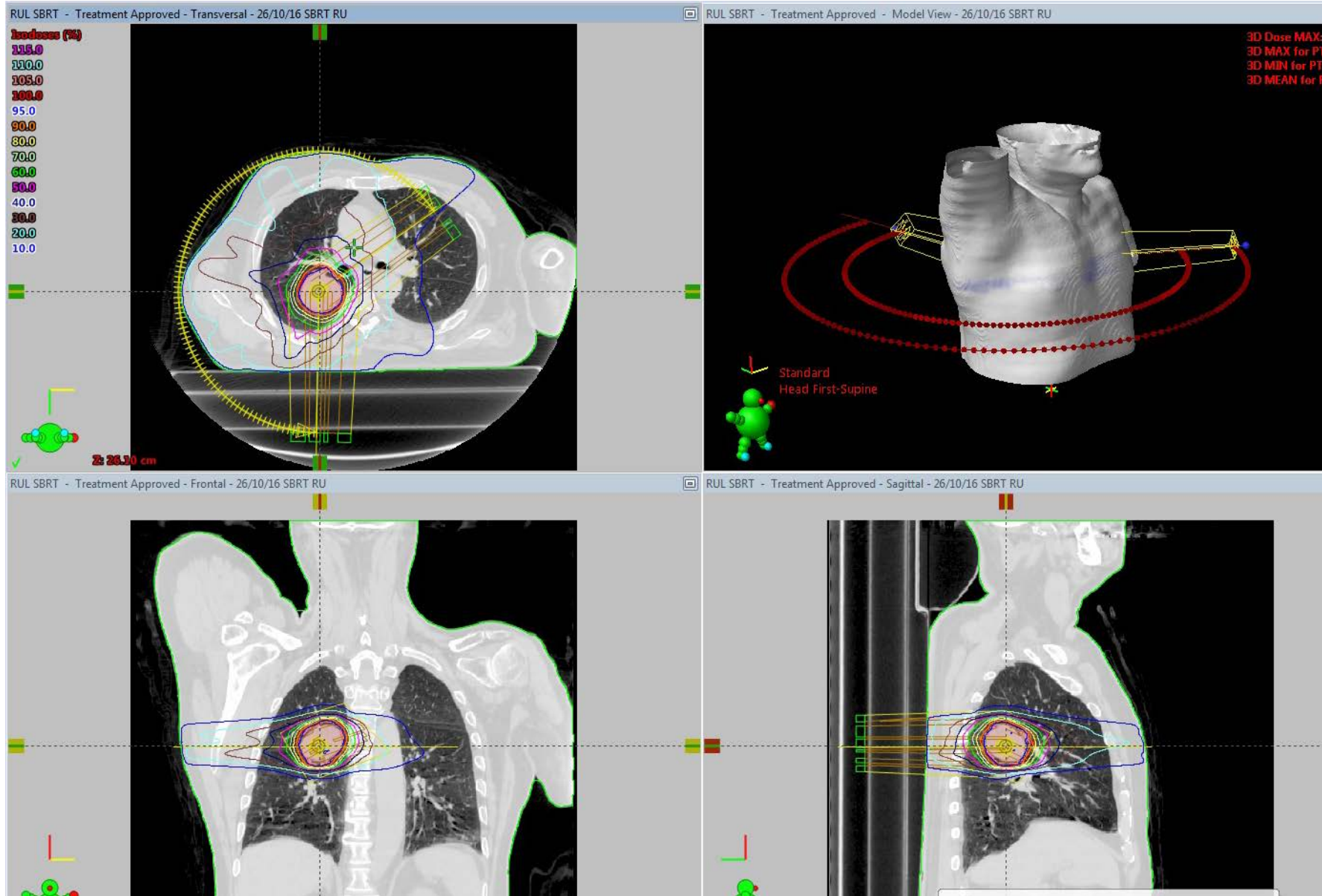
Pelvic Rapid Arc Treatment



Rehabilitation

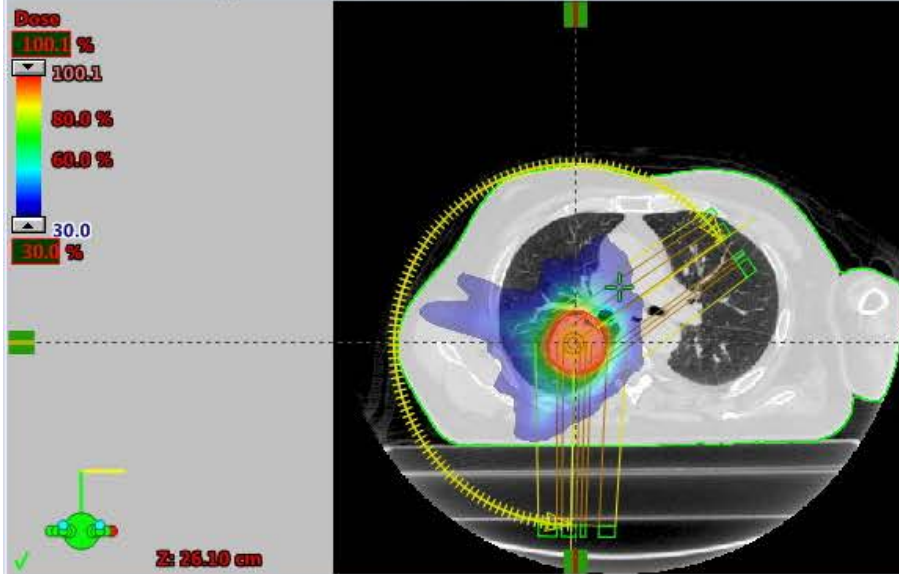


Lung SBRT

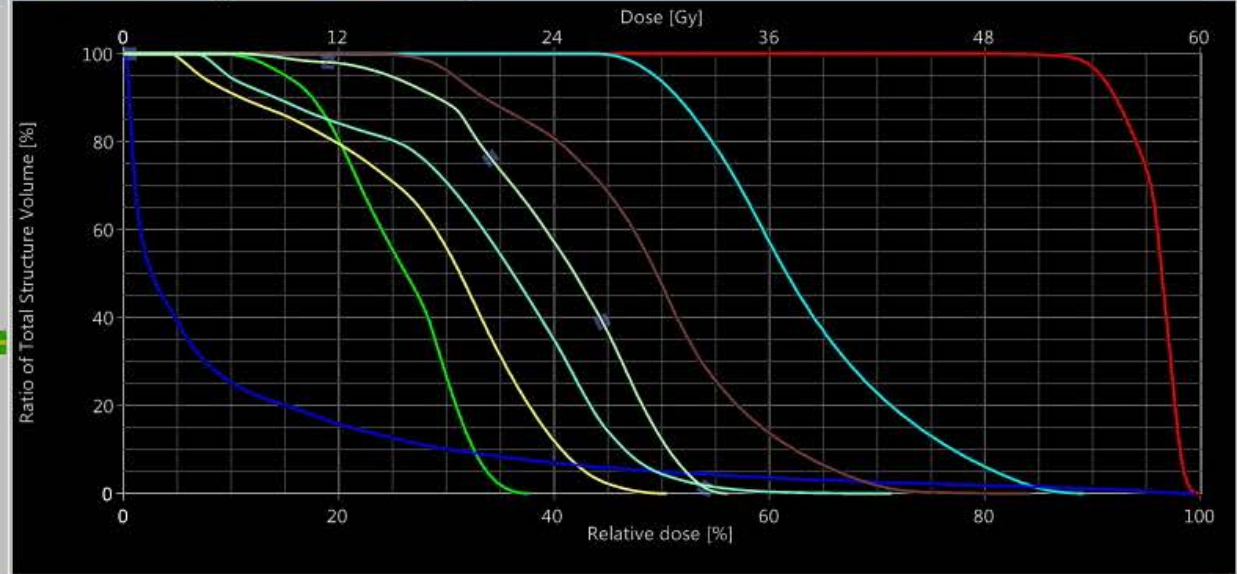


Lung SBRT

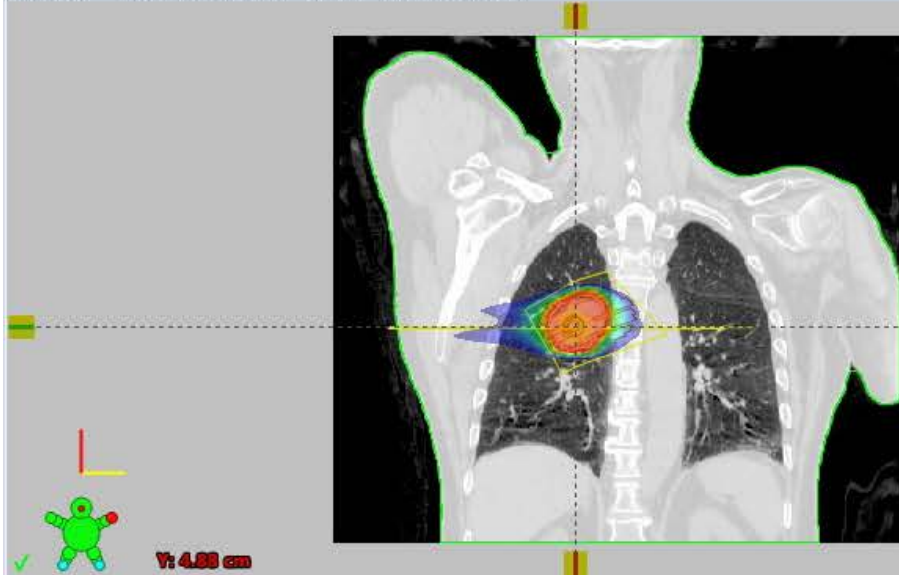
RUL SBRT - Treatment Approved - Transversal - 26/10/16 SBRT RU



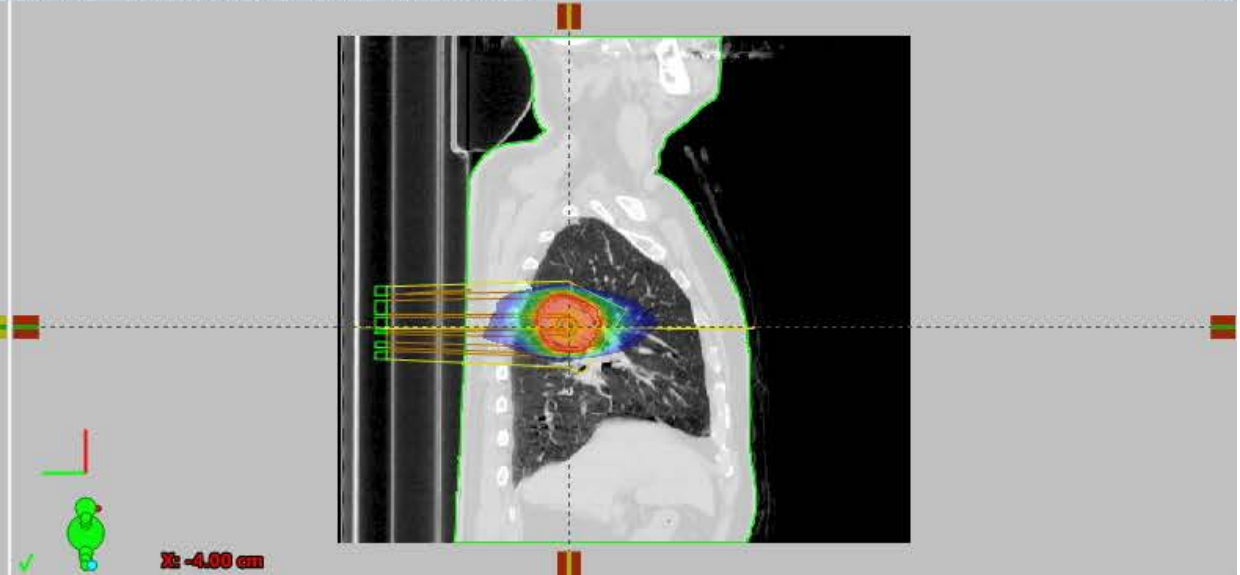
RUL SBRT - Treatment Approved - Dose Volume Histogram



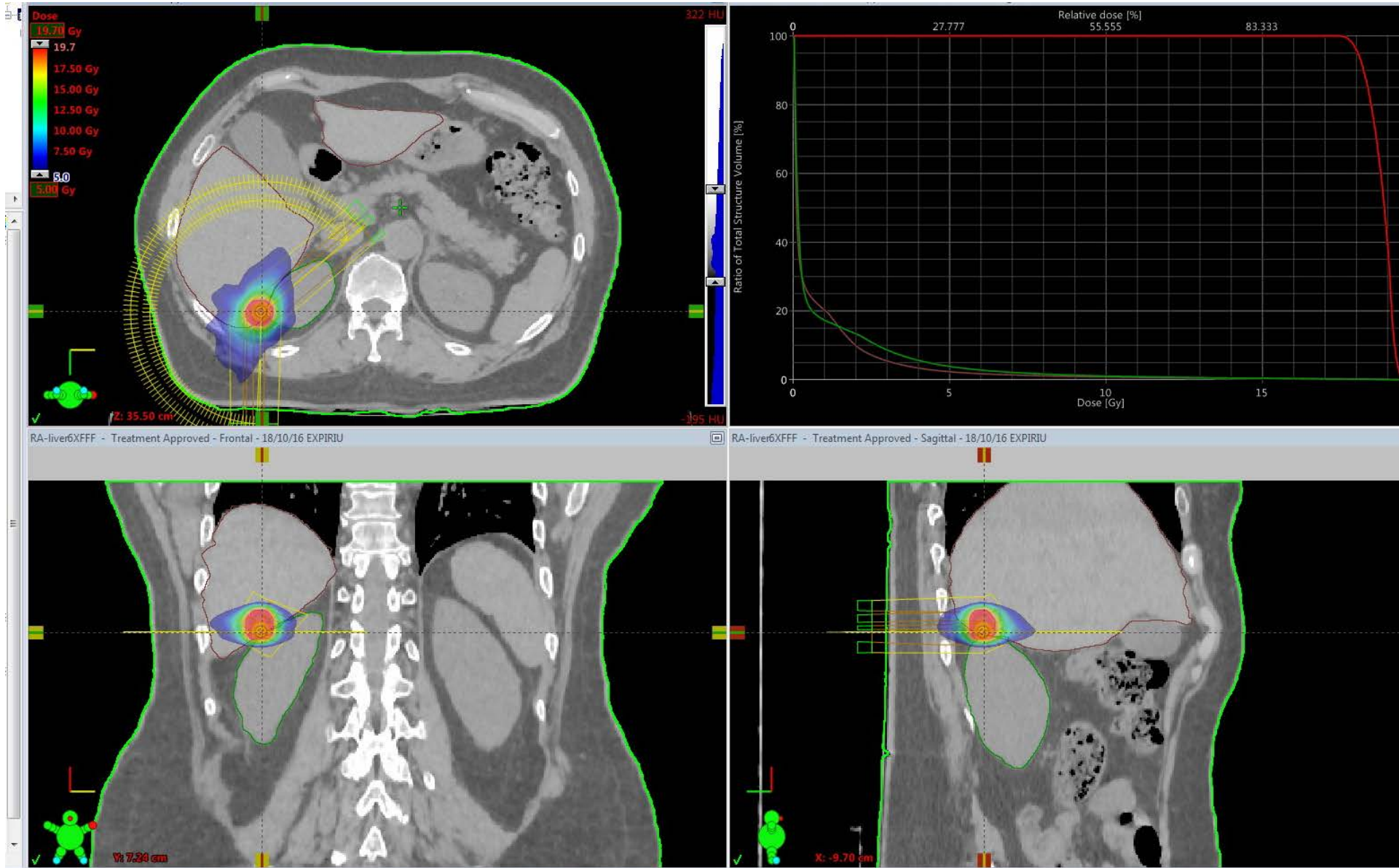
RUL SBRT - Treatment Approved - Frontal - 26/10/16 SBRT RU



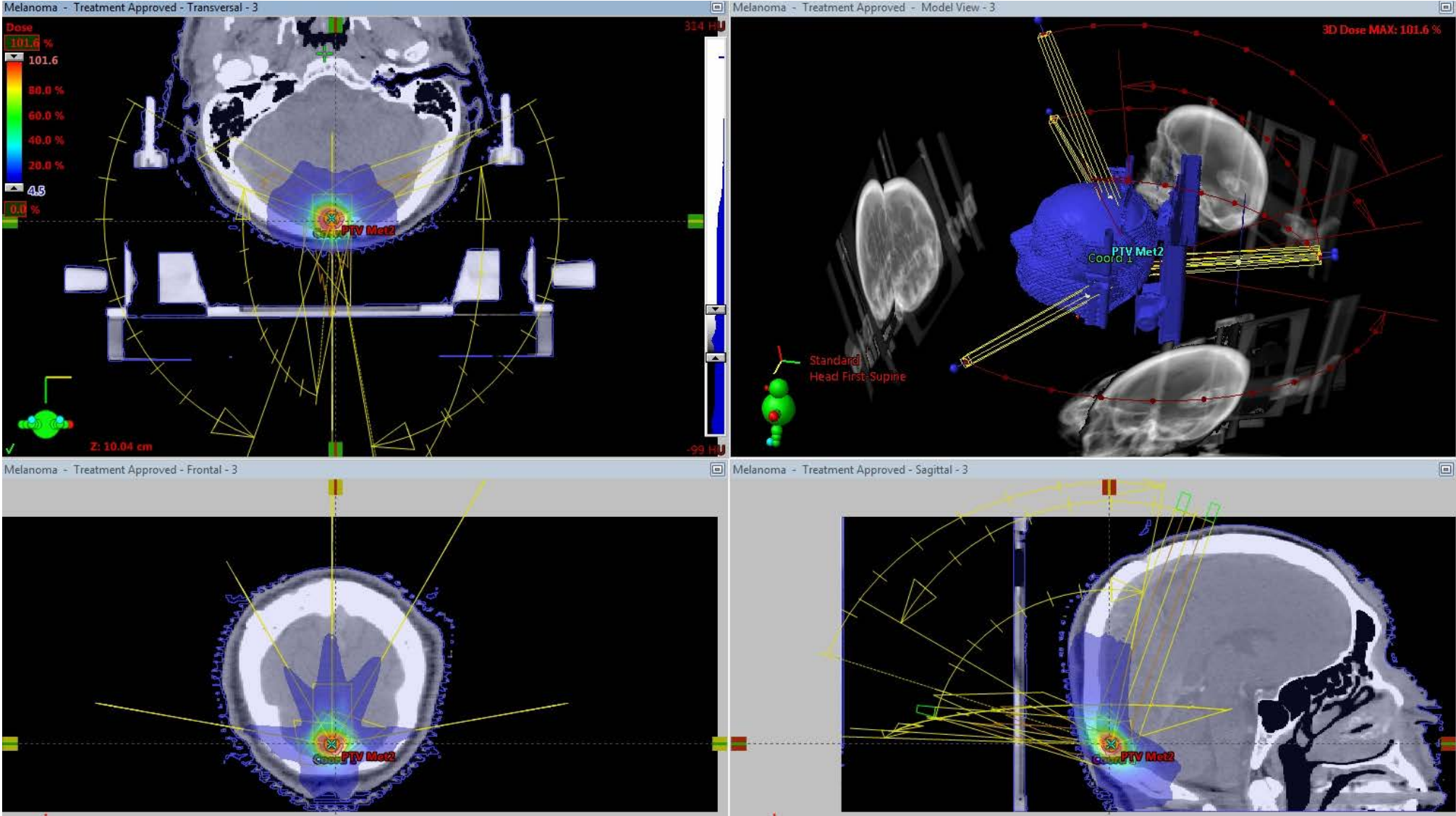
RUL SBRT - Treatment Approved - Sagittal - 26/10/16 SBRT RU



Liver SBRT

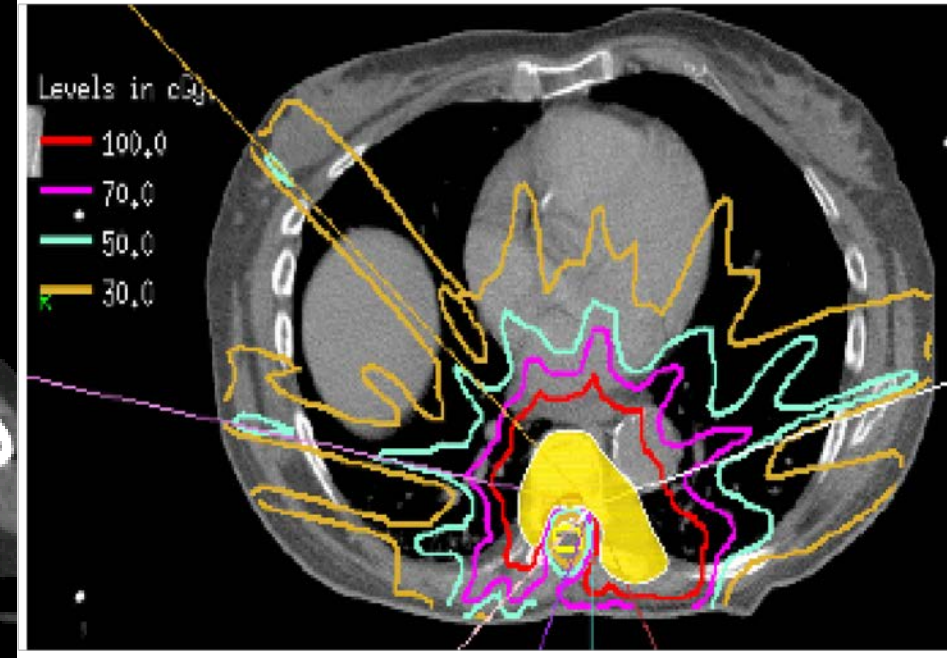
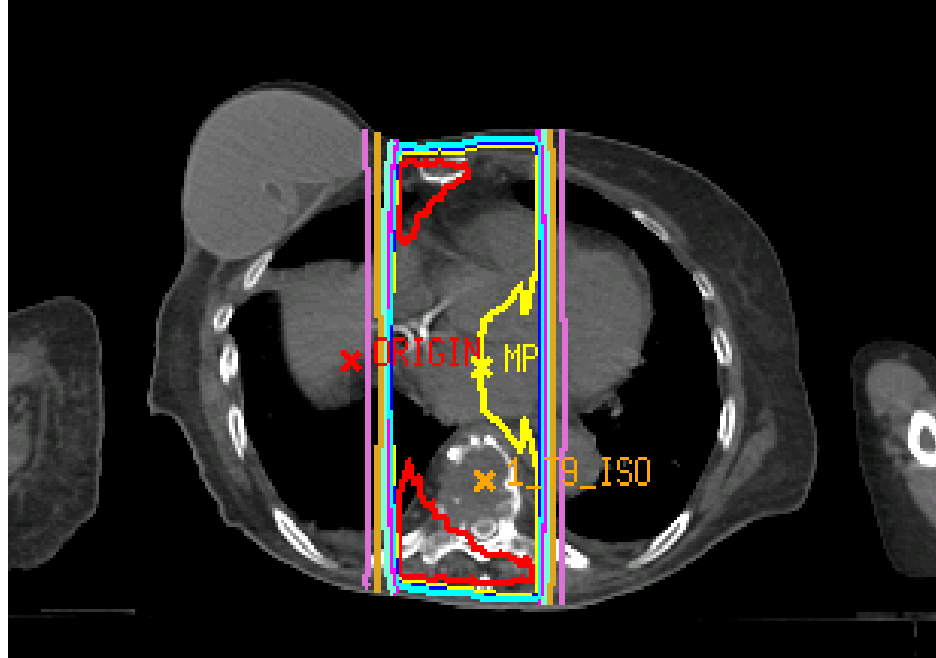


Brain SRS



Spinal metastasis

- **Bone metastasis the most common reason for palliative XRT**
- **30-58% of patients with bone metastasis will experience spinal column metastasis**
- **20,000 cases of cord/cauda equina compression annually in the US**
- **Breast, lung, prostate cancers account for 50% of cord compression**
- **85% of lesions are located anterior to the spinal cord**

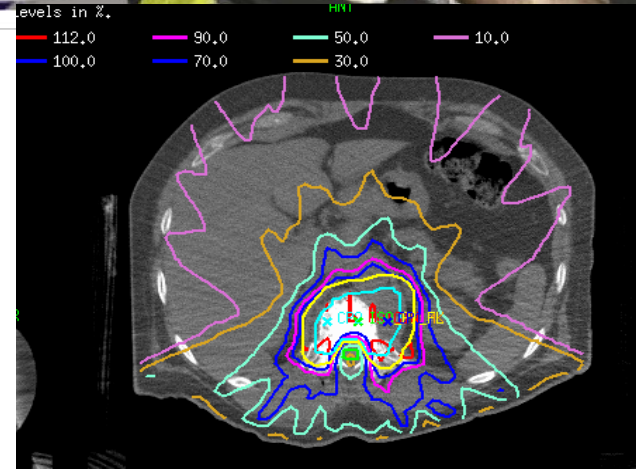
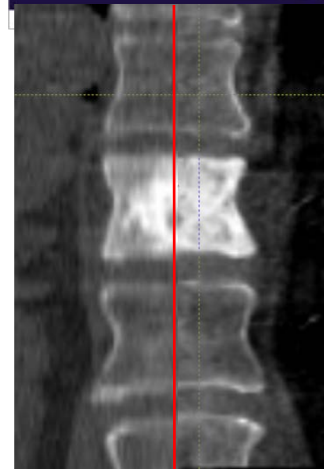
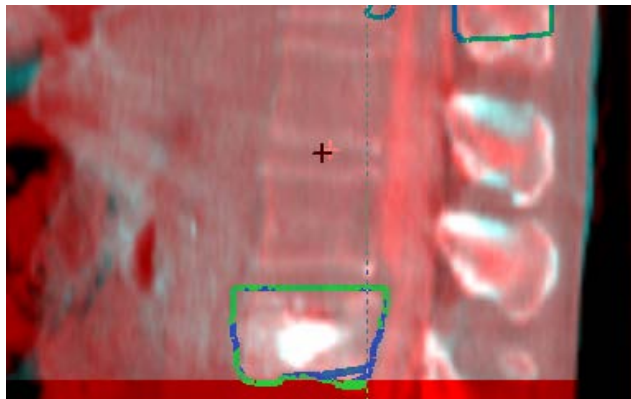
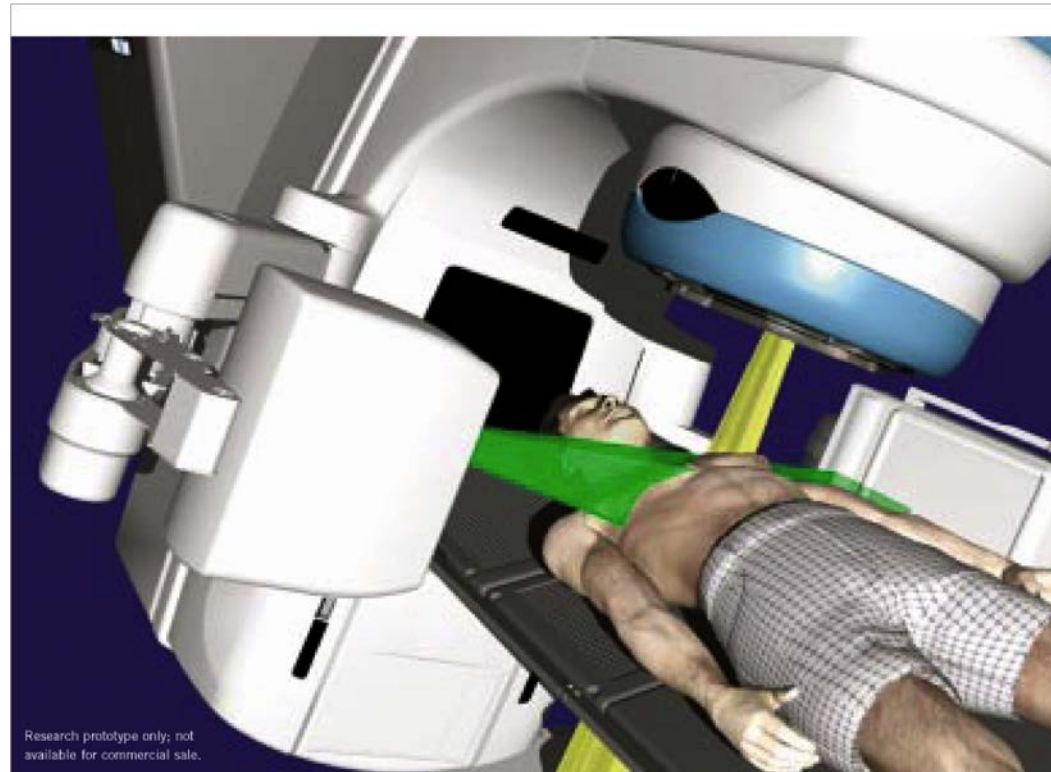


- **Conventional XRT**
- Lower doses per fraction
- More fractions
 - Less complex
 - Fast
 - Larger volumes
 - Cheaper
 - Hot spots near surface
- **Conformal XRT**
- High doses per fraction

- Less normal tissue dose
 - Smaller margins
 - Important for surgical complication risks!
- Higher dose to tumor
- More technical/labor intensive
- More expensive

Image Guided Radiotherapy

- Near real time 3D imaging for position verification
- Positional corrections in X, Y,Z planes
- Accuracy within +/- 1mm





Thank You!!!

