UNIVERSITY OF KRAGUJEVAC
FACULTY OF MEDICAL SCIENCES

BASIC CLINICAL RADIATION ONCOLOGY

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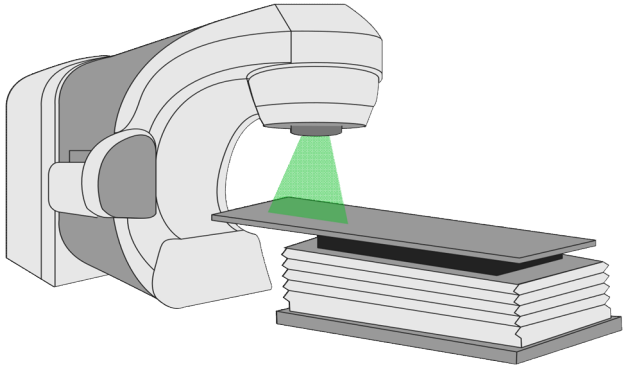
Kragujevac, 2023

Basic steps in the implementation of radiotherapy treatment

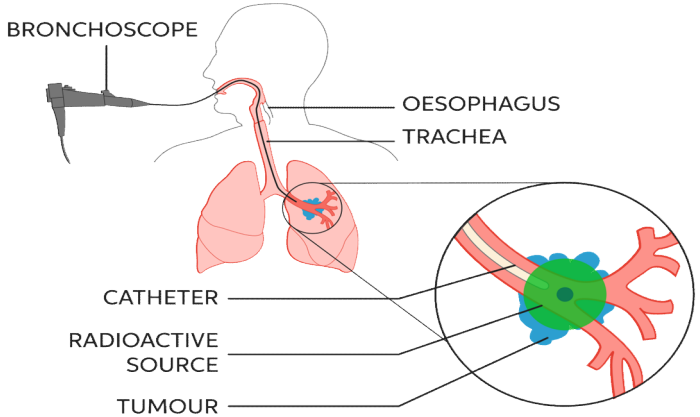
- Multidisciplinary tumor medical board (TMB)decision
- First examination and interview
- Preparation for CT simulation / processing
- CT simulation
- Delineation of organs at risk (OAR) and target volumes
- Radiotherapy planning
- Accuracy check and plan verification
- Positioning
- Treatment implementation
- Quality assurance procedures
- Monitoring of side effects during and after completed radiotherapy treatment

Radiotherapy application

- External beam radiotherapy (EBRT)
- Brachytherapy



External beam radiotherapy

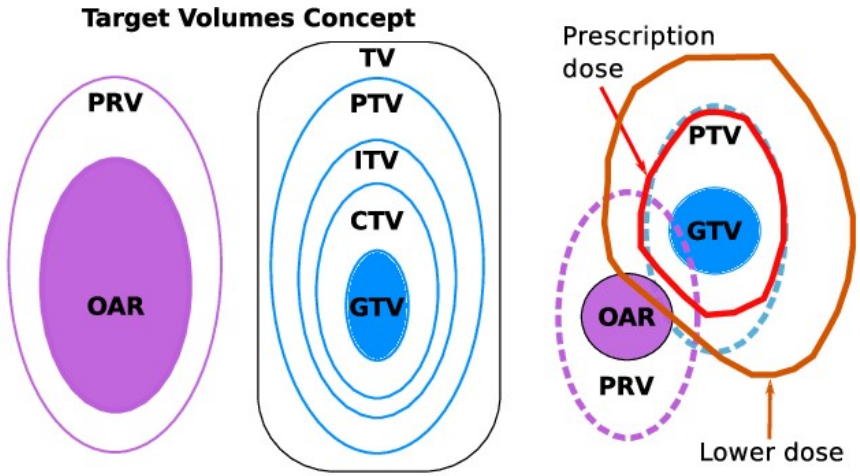


Brachytherapy

Slika dostupna na: https://www.chegg.com/learn/biology/introduction-to-biology/radiation-therapy-in-introduction-to-biology

Radiotherapy techniques

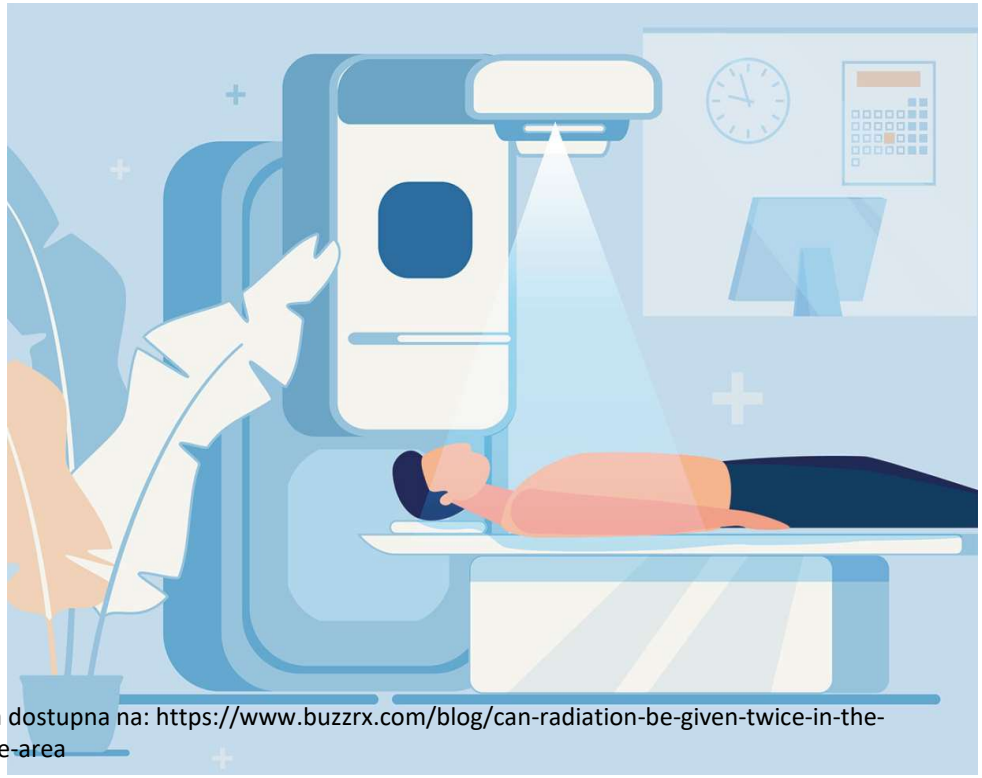
- 1D radiotherapy
- 2D - conventional radiotherapy
- 3D - conformal radiotherapy (3D-CRT)
- Intensity modulated radiotherapy (IMRT)
- Volumetric modulated arc radiotherapy (VMAT)
- Image-guided radiotherapy (IGRT)
- Stereotactic radiotherapy
- Stereotactic radiosurgery
- Intraoperative radiotherapy
- Particle Beam Therapy



Schlachter R, Raidou R, Muren LP, Preim B. State-of-the-Art Report: Visual Computing in Radiation Therapy Planning. Computer Graphics Forum 2019;38: 753-779.

Application of radiotherapy depending on localization

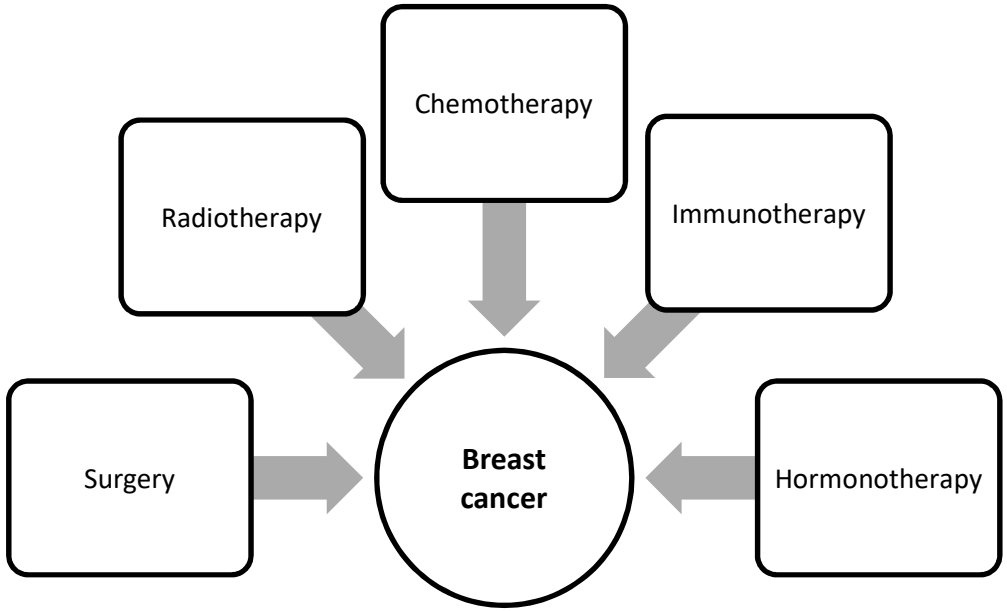
- Breast cancer
- Lung cancer
- Gynecological malignancies
- Urogenital tumors
- Digestive tract tumors
- Lymphomas and leukemias
- CNS tumors
- Skin and soft tissue tumors
- Head and neck tumors
- Tumors in erderly
- Pediatric tumors



Slika dostupna na: https://www.buzzrx.com/blog/can-radiation-be-given-twice-in-the-same-area

Breast cancer radiotherapy

- Locoregional disease control
- Reduces the occurrence of local recurrence by about 70%



Offersen B, Boersma L, Kirkove C et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1. Radiother Oncol.2016;118(1):205–208

Radiotherapy indications

- Radiotherapy after breast conserving therapy (BCT)
- Radiotherapy of hemithorax
- Radiotherapy of regional lymphatics
- Radical radiotherapy of the breast cancer

Offersen B, Boersma L, Kirkove C et al. ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer, version 1.1. Radiother Oncol.2016;118(1):205–208

Fractionation regimes

Conventional fractionation

- Daily dose of 1.8-2 Gy per fraction,
- 5 days a week
- Postoperative radiotherapy – TD 45-50.4 Gy in 23-28 fractions
- Radical radiotherapy – TD 70 Gy in 35 fractions

Hypofractionation

- More than 2.6 Gy per fraction
- 5 days a week
- Total tumor dose of 40-42.5 Gy in 15-16 fractions
- Ultra hypofractionated regimen 26 or 27 Gy in 5 fractions

Gnant M, Harbeck N, Thomssen C. St. Gallen/Vienna 2017: A Brief Summary of the Consensus Discussion about Escalation and De-Escalation of Primary Breast Cancer Treatment. Breast Care (Basel) 201712(2):102-107.
Murray Brunt A, Haviland JS, Wheatley DA, et al; FAST-Forward Trial Management Group. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. Lancet 2020;395(10237):1613-26.

Hypofractionation benefits

- Shortening of treatment from 6-7 to 3-4 weeks
- Cheaper treatment

- Better availability
- Shorter waiting lists

- Equivalent efficiency compared to standard fractionation mode

Gnant M, Harbeck N, Thomssen C. St. Gallen/Vienna 2017: A Brief Summary of the Consensus Discussion about Escalation and De-Escalation of Primary Breast Cancer Treatment. Breast Care (Basel). 2017 May;12(2):102-107.

Postoperative radiotherapy

- Invasion of surgical margins
- Invasion of the pectoral muscle
- Positive more than 4 lymph nodes in the axilla
- Consider radiatiotherapy also in the case of tumors smaller than 5 cm, grade III in younger premenopausal patients, multicentric tumors

Radiotherapy of the axillary region in early breast cancer

- Inadequate axillary dissection
- Rest in the axilla after axillary dissection
- Surgery without axilla dissection
- Positive sentinel lymph node biopsy (SLNB) without further axillary dissection

Radiotherapy of the supraclavicular region

- Positivity of 4 or more lymph nodes (LN) in the axilla
- Positivity of 1-3 lymph nodes with other unfavorable parameters
- Inadequate axillary dissection

Slika dostupna na: https://www.medicalnewstoday.com/articles/supraclavicular-lymph-nodes-swollen

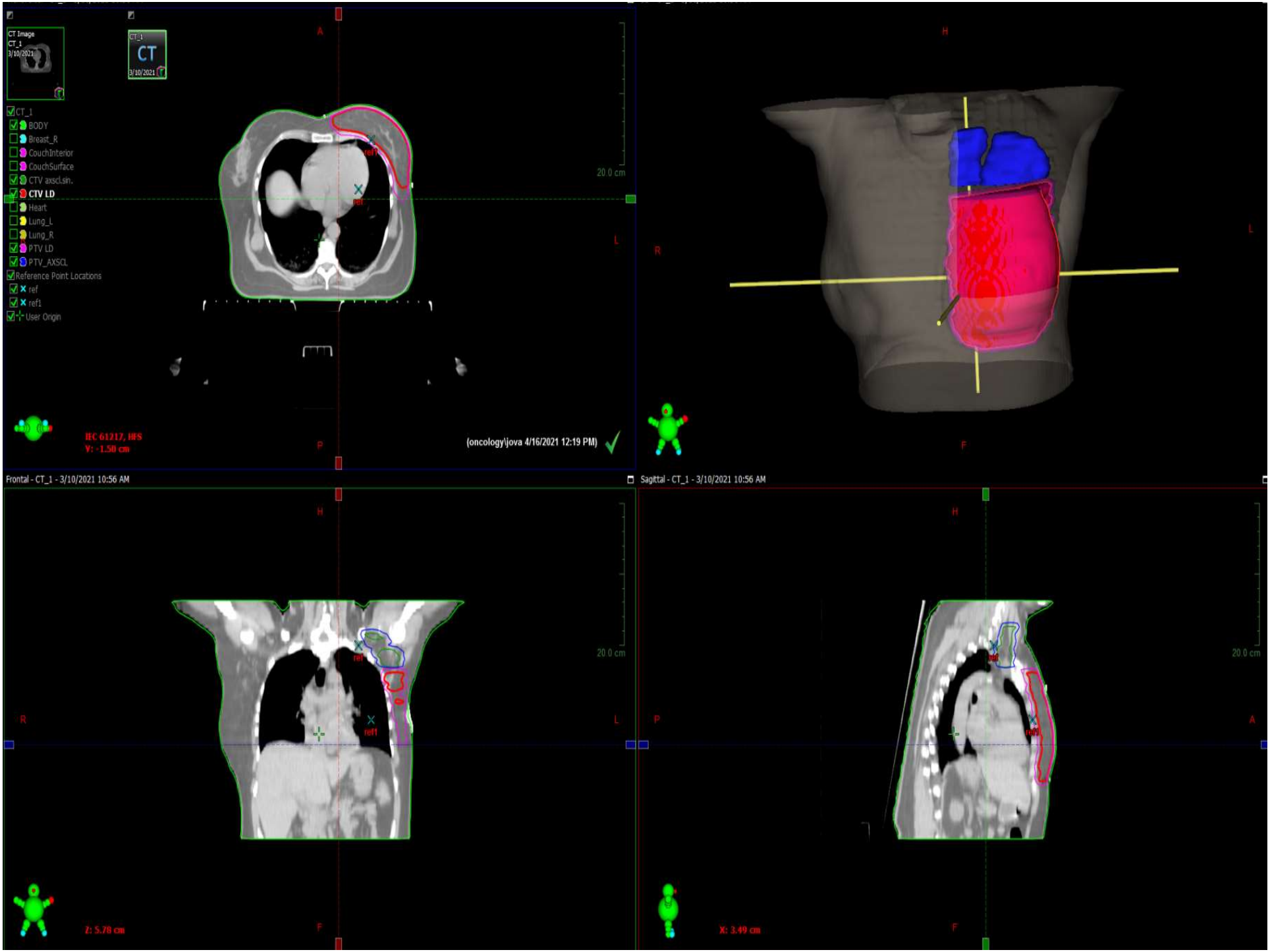
Hemithorax radiotherapy is performed in locally advanced breast cancer

- After neoadjuvant chemotherapy and mastectomy when there is an increased risk for local relapse of the disease
- If the tumor was initially T3 or T4, and/or if more than 4 lymph nodes in the axilla were positive
- High grade tumor
- Extensive extracapsular extension
- Presence of lymphovascular invasion
- Younger age
- Inadequate axillary dissection

Radiotherapy of regional lymphatics in locally advanced breast cancer

- Radiotherapy of the lymphatics around the internal mammary artery if there is clinically or pathohistologically proven involvement
- Radiotherapy of the axillary region when more than 50% of examined LNs are positive or
- When more than 10 LNs are positive regardless of the number of LNs examined

If the tumor is inoperable after neoadjuvant chemotherapy, breast radiotherapy is performed as a radical method.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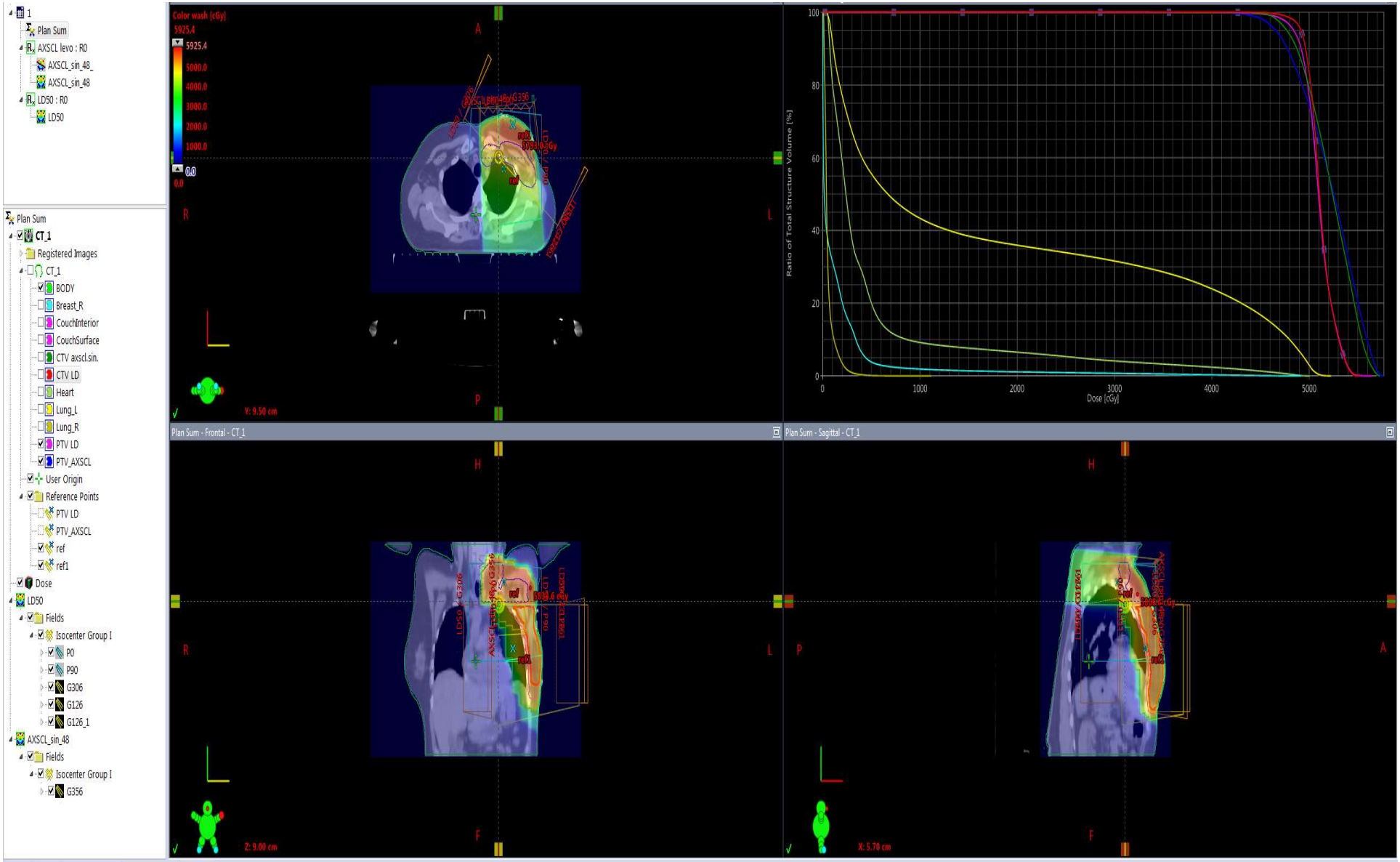
Z: 5.78 cm
Sagittal - CT_1 - 3/10/2021 10:56 AM
X: 3.49 cm



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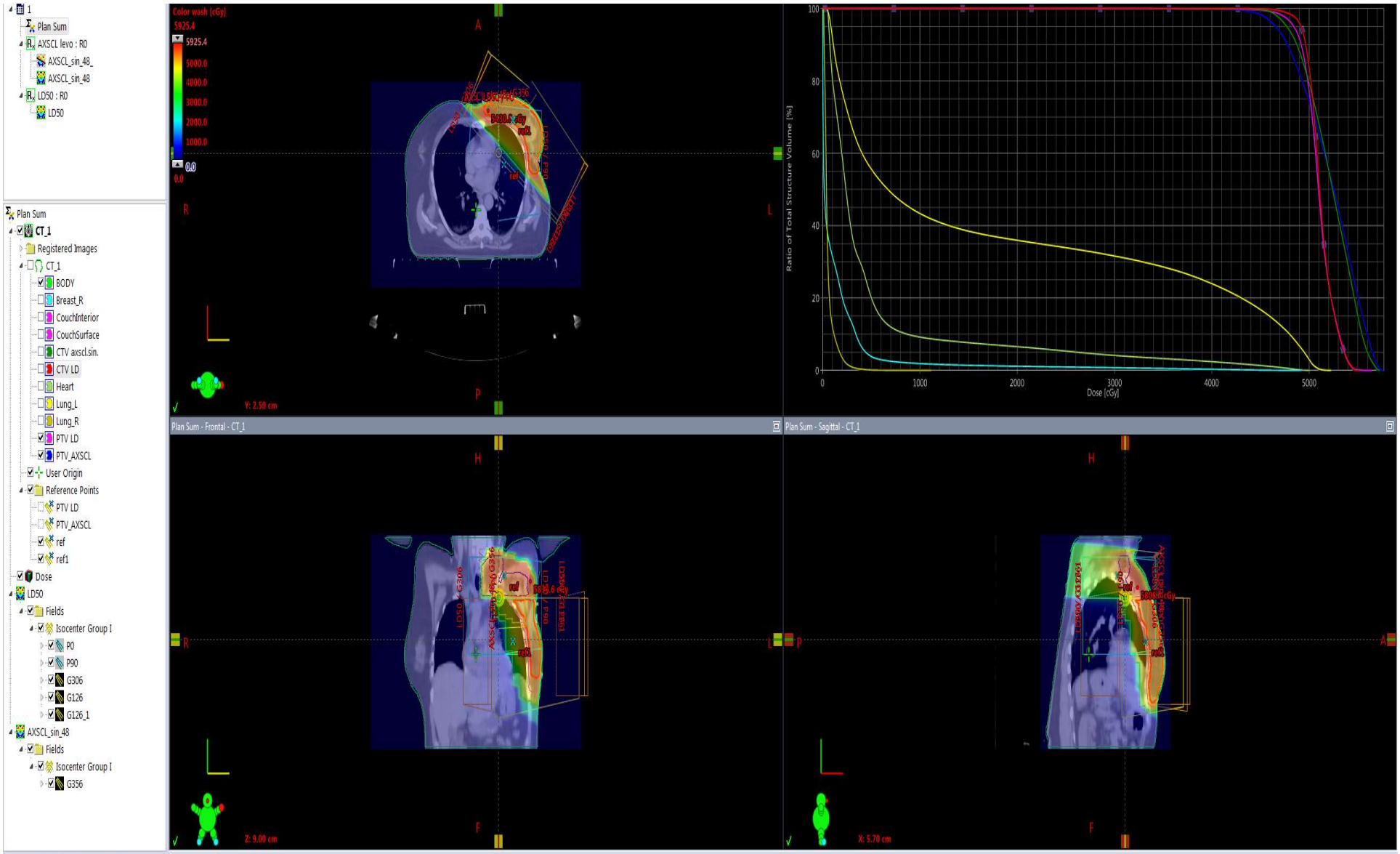
	CTV LD	Approved	Plan Sum	1	881.6	100.0	100.0	2681.4	5516.8	5117.0
	Lung_L	Approved	Plan Sum	1	1172.5	100.0	100.0	20.3	5230.5	1786.4
	Lung_R	Approved	Plan Sum	1	1400.1	100.0	100.0	4.9	1124.1	55.3
	CTV axscl.sin.	Approved	Plan Sum	1	110.7	100.0	100.0	4102.9	5734.3	5222.5
	Breast_R	Approved	Plan Sum	1	913.6	100.0	100.0	0.0	4919.2	140.2
	PTV LD	Approved	Plan Sum	1	1147.7	100.0	100.0	2658.7	5646.1	5097.9
	PTV_AXSCL	Approved	Plan Sum	1	218.4	100.0	100.0	2988.1	5769.2	5211.5



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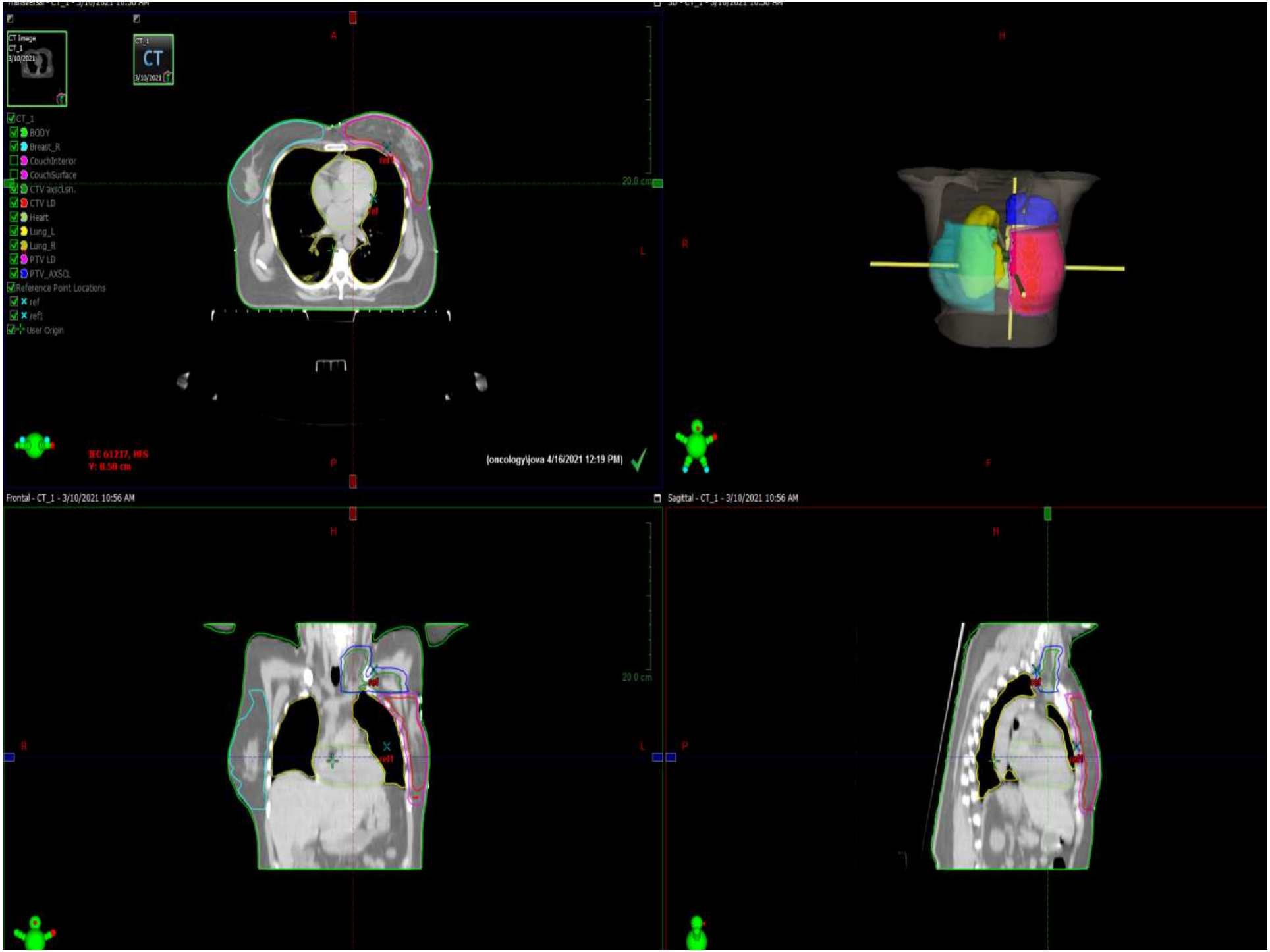
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Y: 0.50 cm
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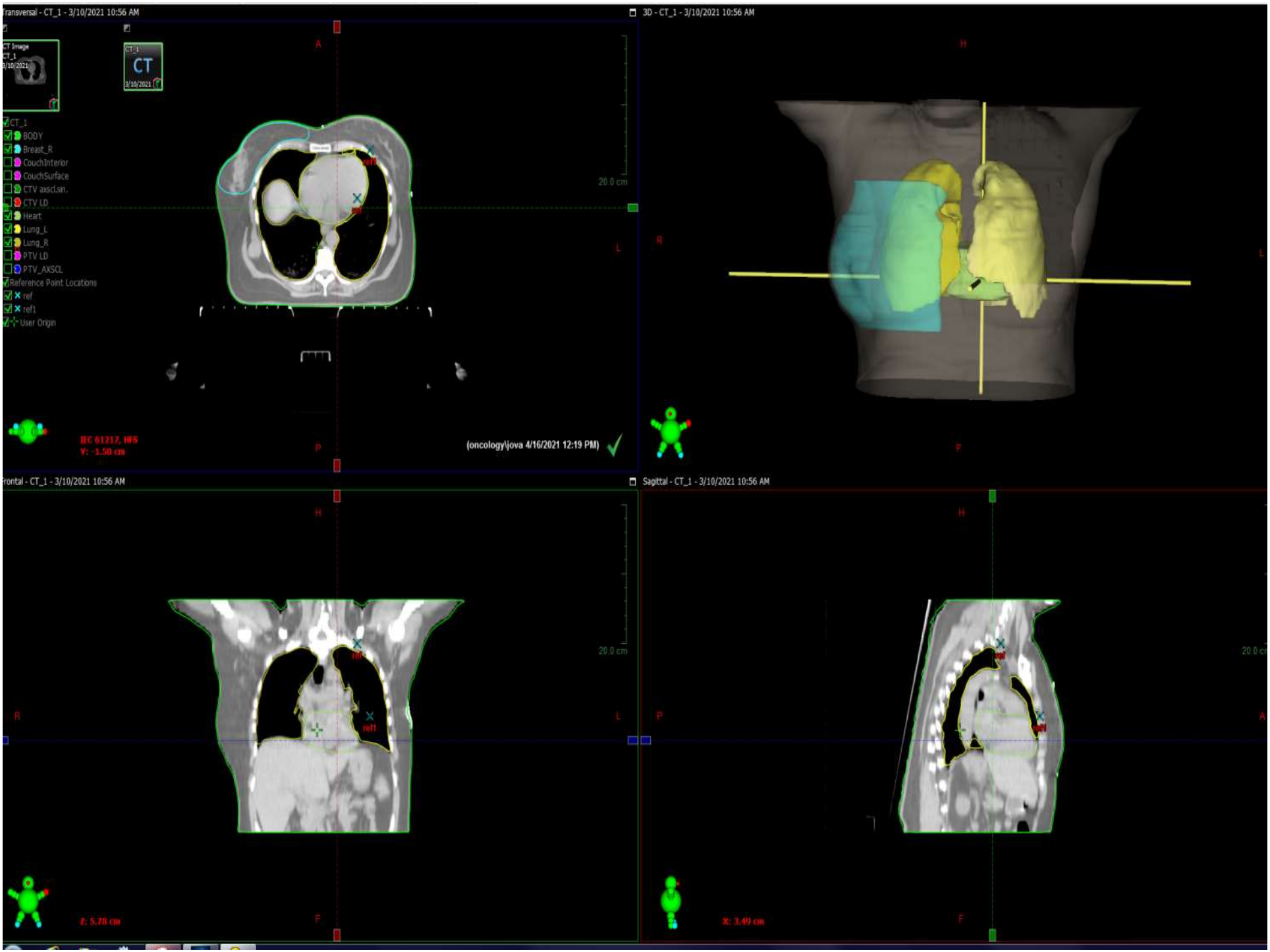
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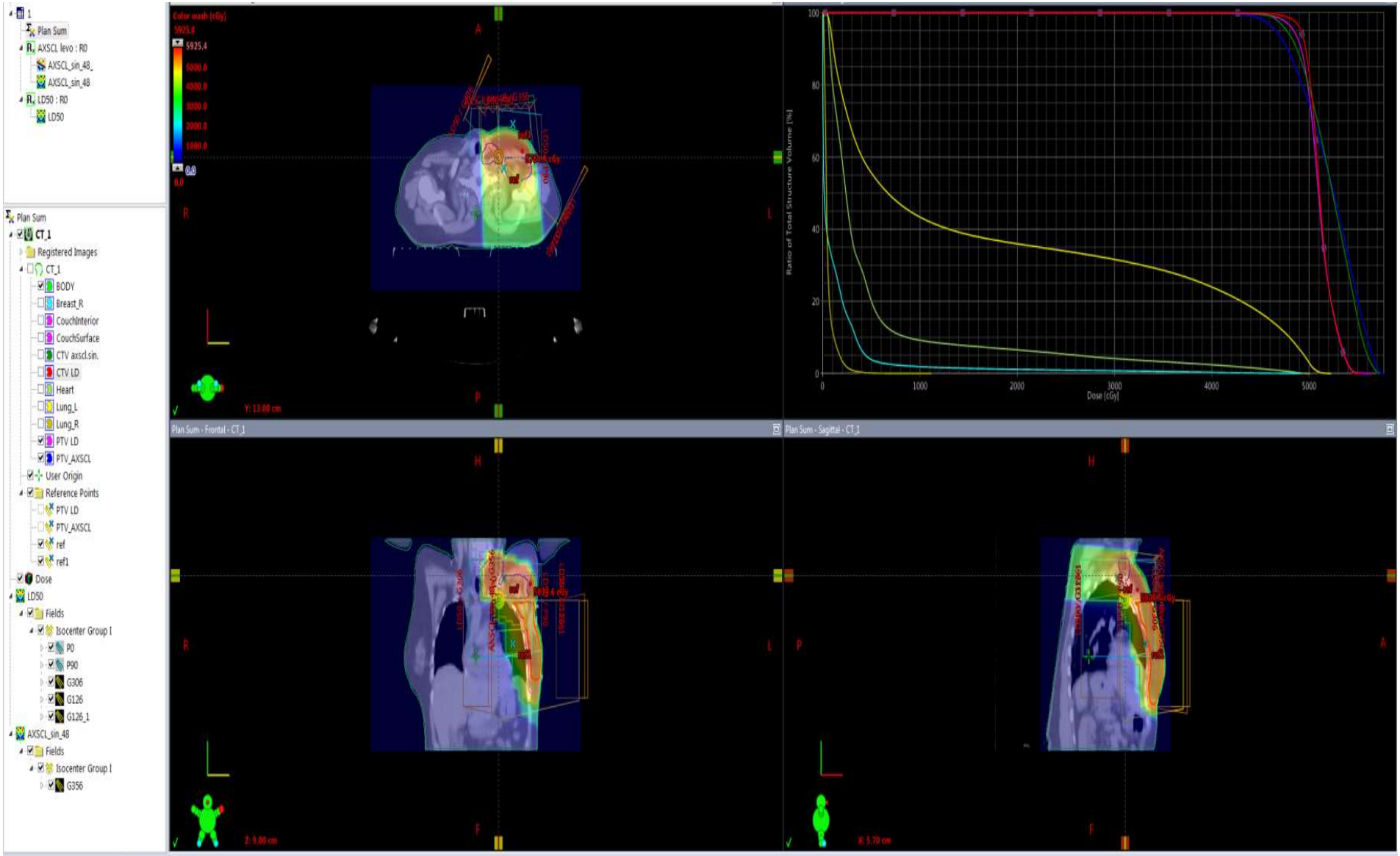

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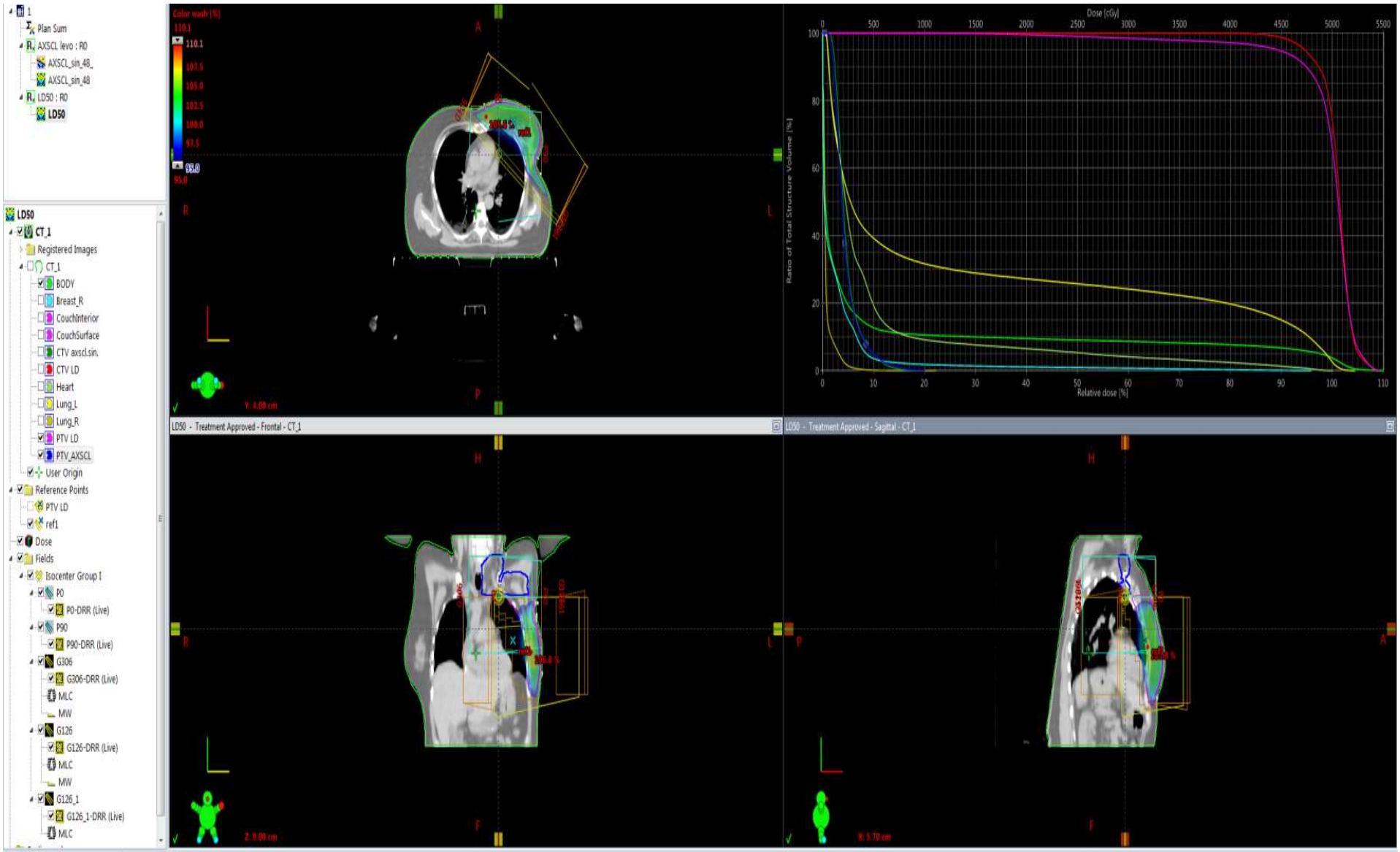

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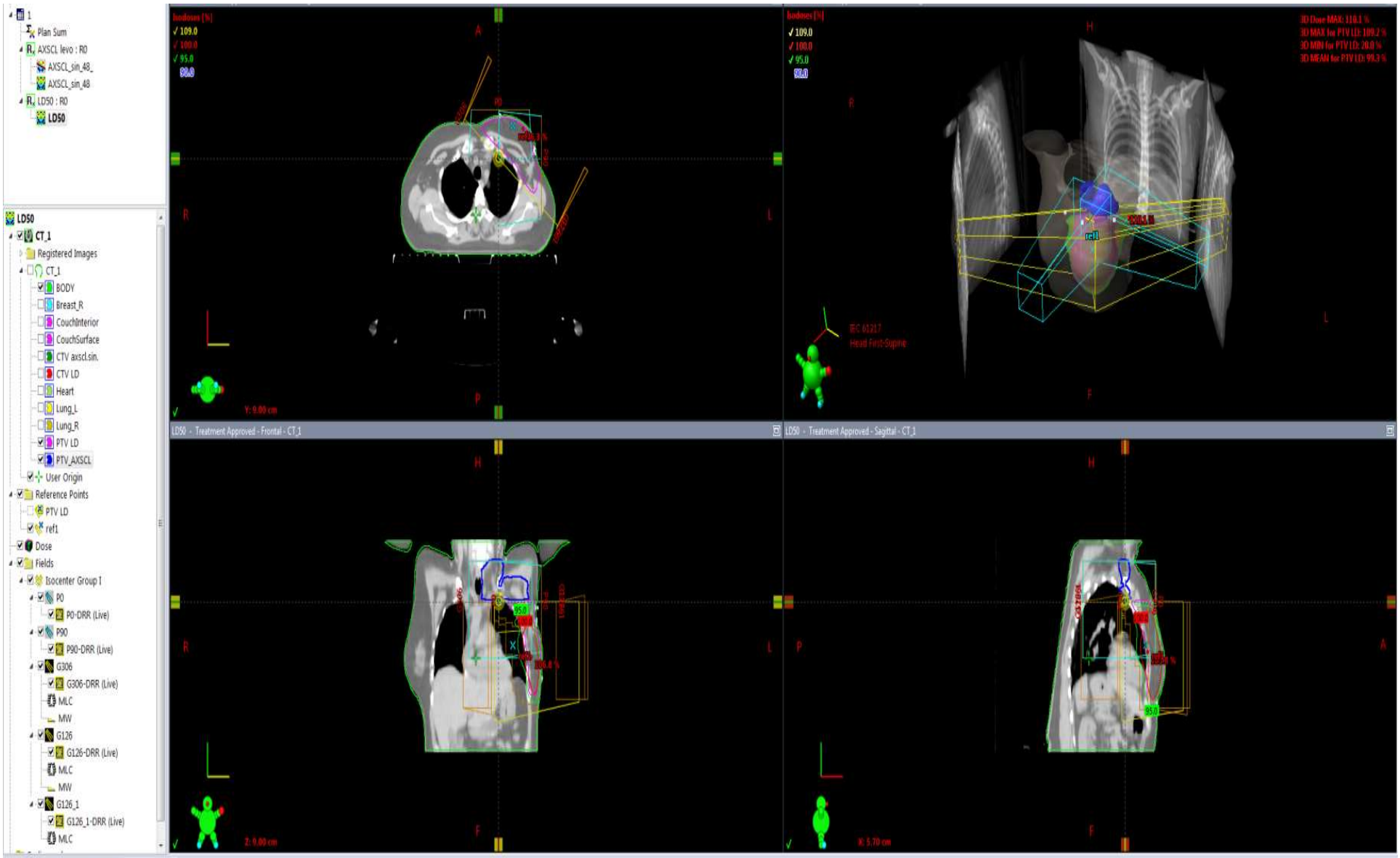
	CTV LD	Approved	LD50	1	881.6	100.0	100.0	53.3	109.2	101.0
	Lung_L	Approved	LD50	1	1172.5	100.0	100.0	0.4	104.5	27.5
	Lung_R	Approved	LD50	1	1400.1	100.0	100.0	0.0	22.4	0.7
	CTV axscl.sin.	Approved	LD50	1	110.7	100.0	100.0	1.4	18.3	4.6
	Breast_R	Approved	LD50	1	913.6	100.0	100.0	0.0	96.0	2.7
	PTV LD	Approved	LD50	1	1147.7	100.0	100.0	20.0	109.2	99.3
	PTV_AXSCL	Approved	LD50	1	218.4	100.0	100.0	1.1	20.1	4.4



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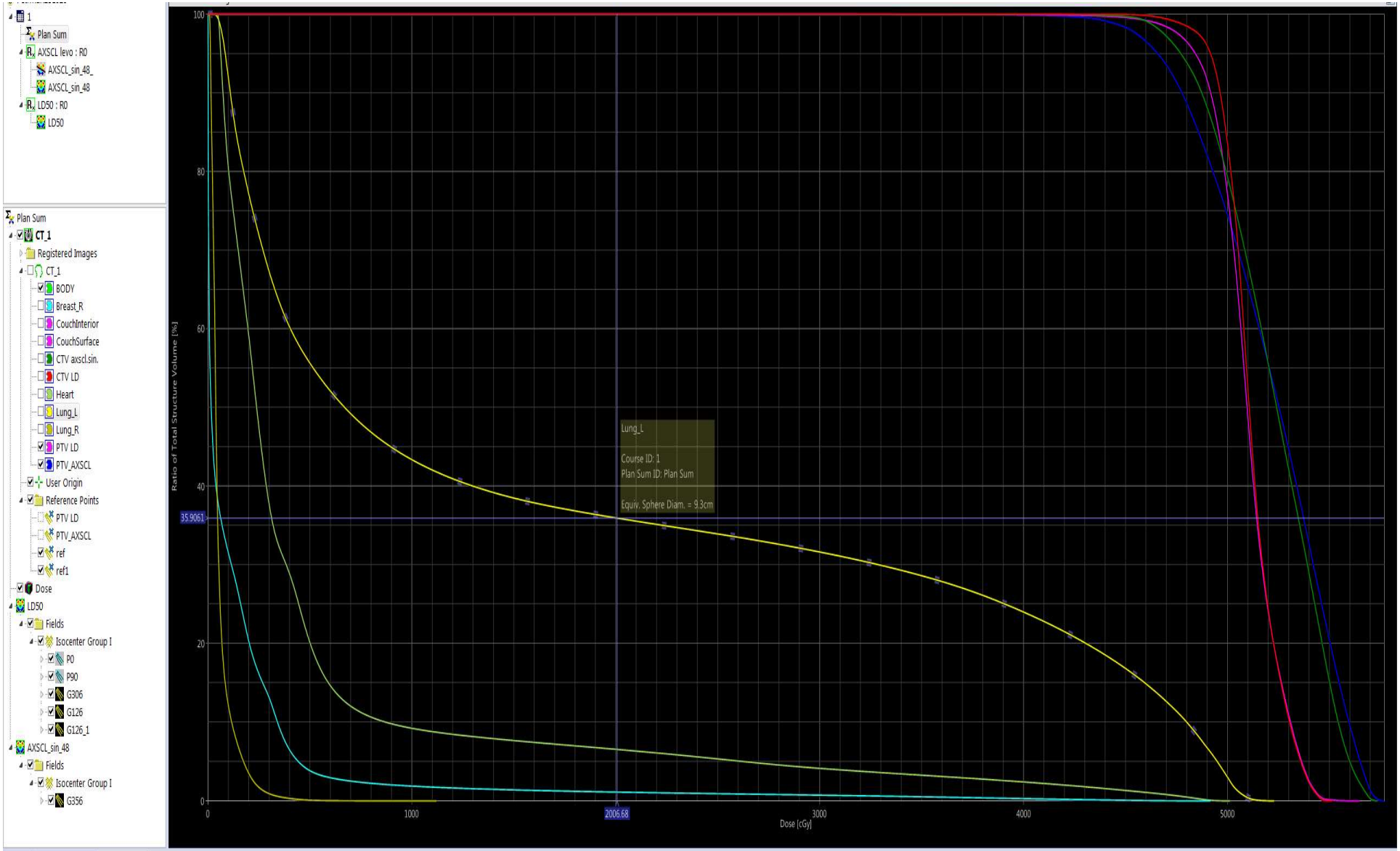
	PTV_AXSCL	Approved	LD50	1	218.4	100.0	100.0	1.1	20.1	4.4



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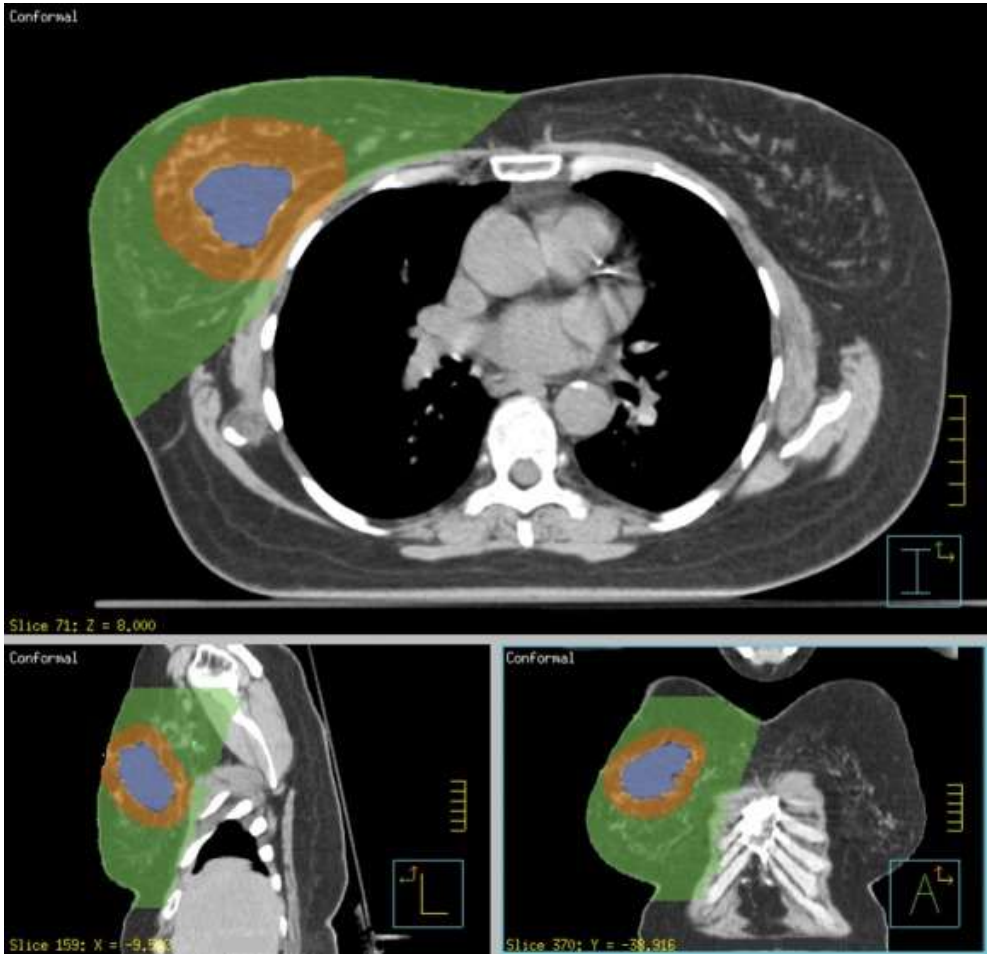
Applying boost dose to the tumor bed

- Patients younger than 50 years old and with grade III tumors
- Older than 50 years with an increased risk of local recurrence



Small K, Kelly C, Beldham-Collins R, Gebski V. Whole breast and excision cavity radiotherapy plan comparison: Conformal radiotherapy with sequential boost versus intensity-modulated radiation therapy with a simultaneously integrated boost. J Med Radiat Sci 2013;60(1):16-24.

Organs at risk (OAR)

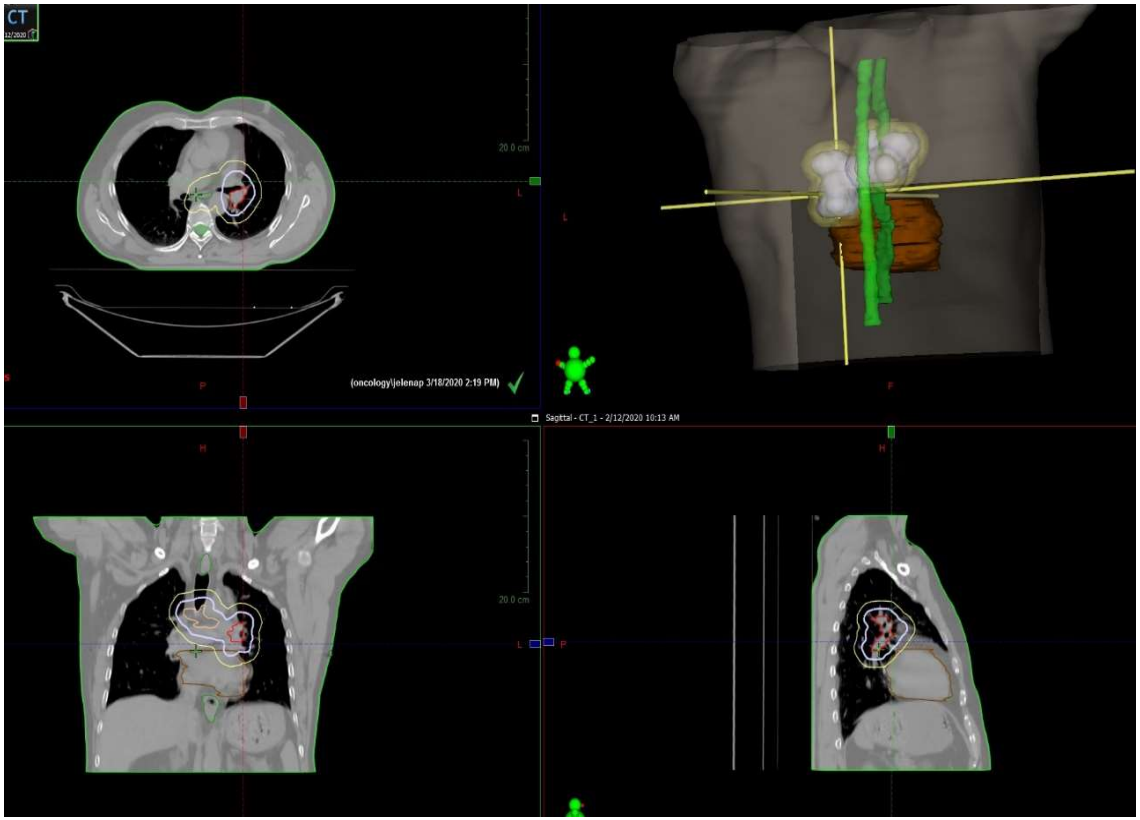
QUANTEC (*Quantitative Analysis of Normal Tissue Efects in the Clinic*) recommendations for tolerance of normal tissues, i.e. dose distribution analysis.

- Skin
- Heart
- Lungs
- Brachial plexus

Moiseenko V, Einck J, Murphy J, Ödén J, Bjöhle J, Uzan J, Gagliardi G. Clinical evaluation of QUANTEC guidelines to predict the risk of cardiac mortality in breast cancer patients. Acta Oncol 2016;55(12):1506-1510.

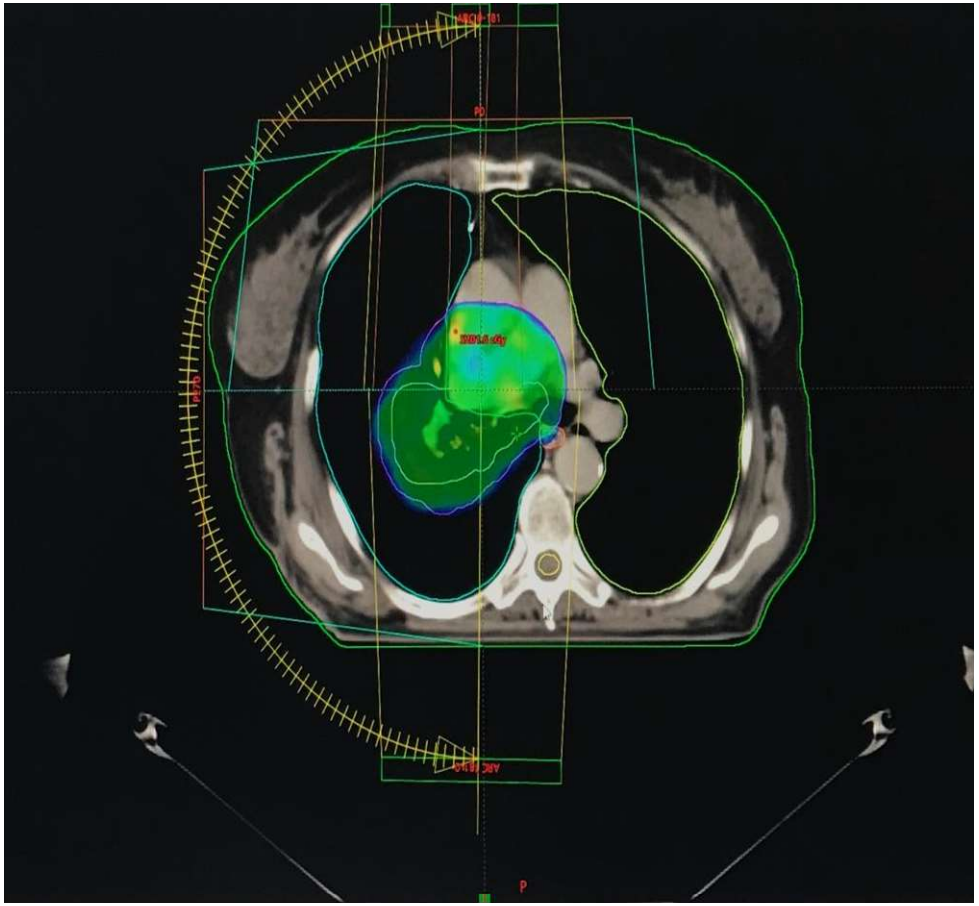
Lung tumors radiotherapy

EBRT alone or in combination with brachytherapy



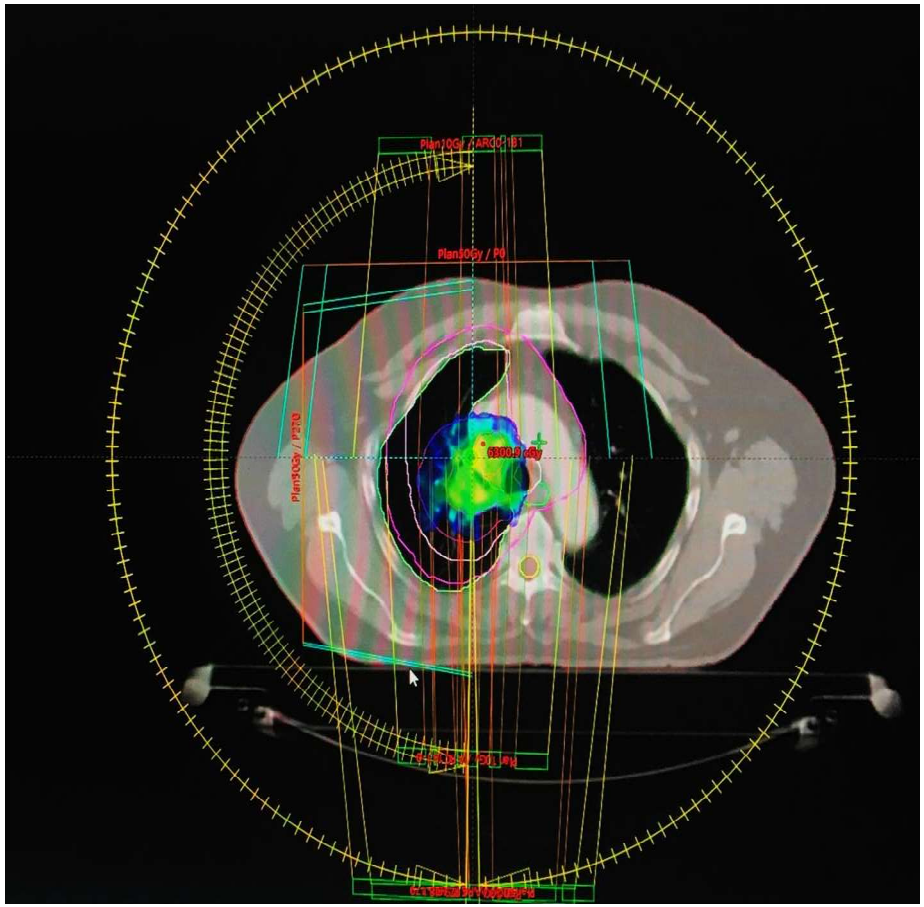
Postoperative radiotherapy of non-small cell lung cancer (NSCLC)

- Improve local control and survival
- Existence of unfavorable prognostic factors
- Inadequate dissection of mediastinal lymph nodes
- Extracapsular spread
- Positivity of multiple hilar lymph nodes
- Positive margins (R1) or close tumor margin
- Unexpectedly verified positivity of mediastinal lymph nodes during surgery



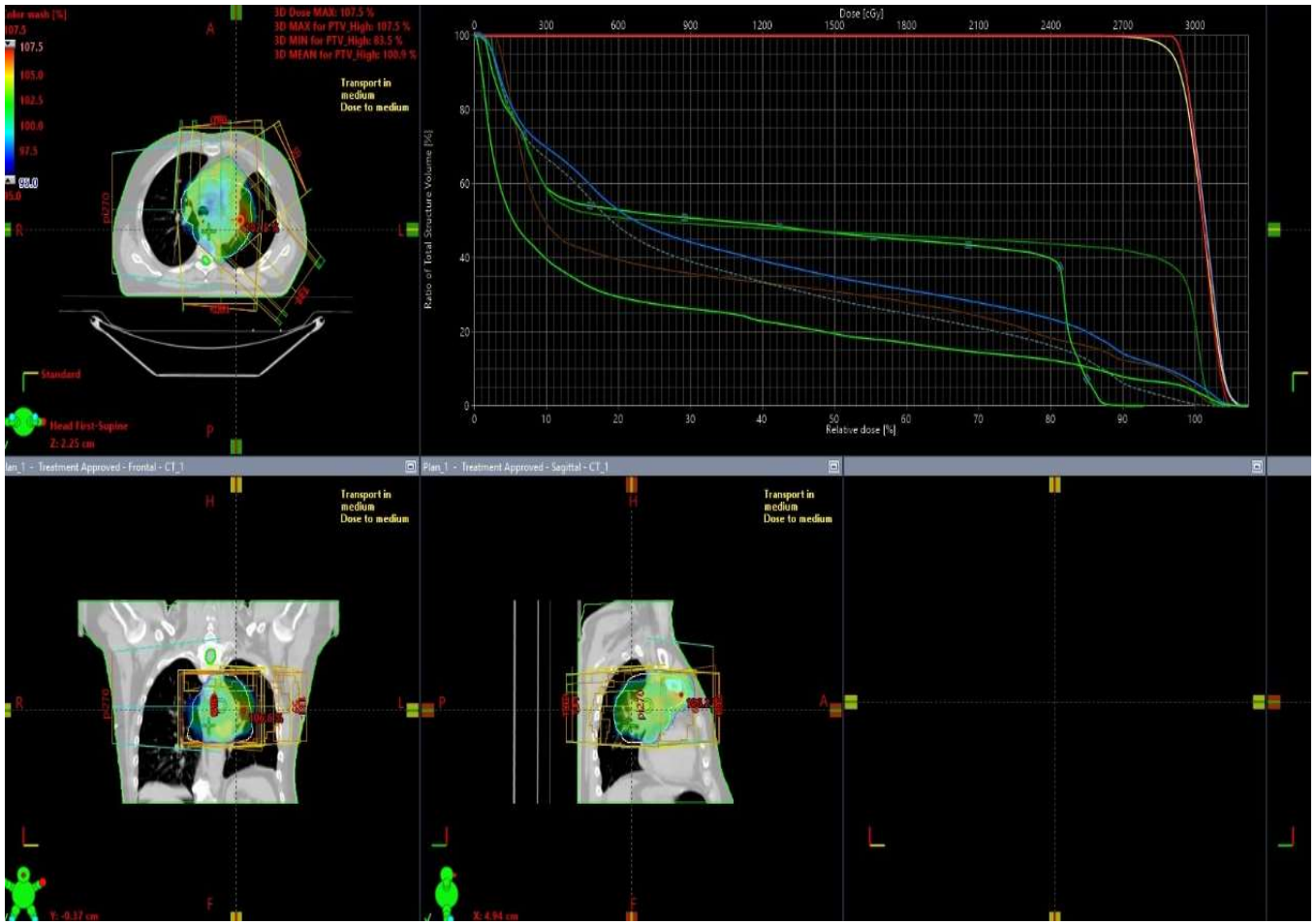
Definitive radiotherapy of locally advanced NSCLC

- Contraindicated surgery
- The patient is refusing surgery
- ECOG performace status (PS) 0 and 1
- High volume disease can be treated with radiatiotherapy
- No weight loss over 10%
- Due to comorbidities, other treatment regimens are contraindicated
- FEV1 at least 1L



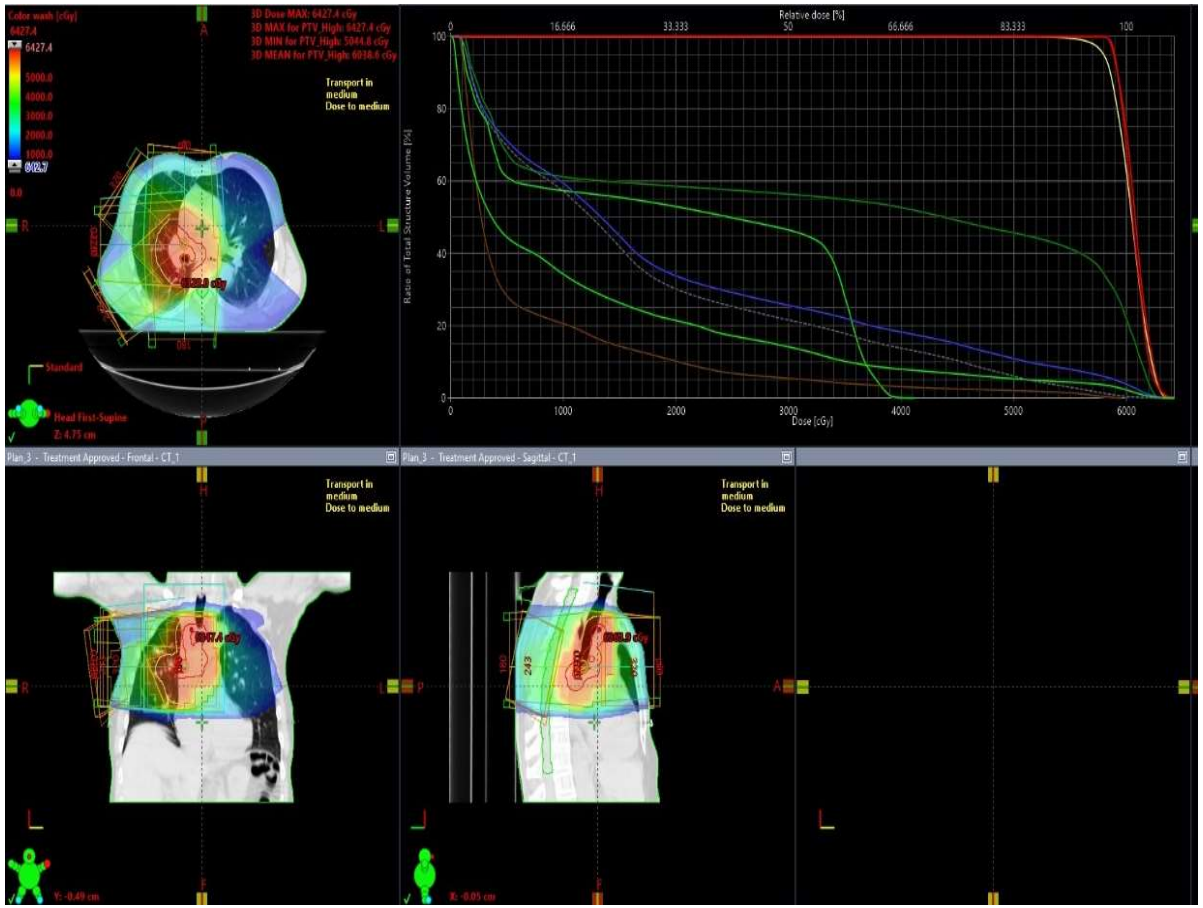
Neoadjuvant chemoradiotherapy

- IIIa stage
- Unresectable sulcus tumors
- Downstaging
- Downsizing



Concurrent chemoradiotherapy

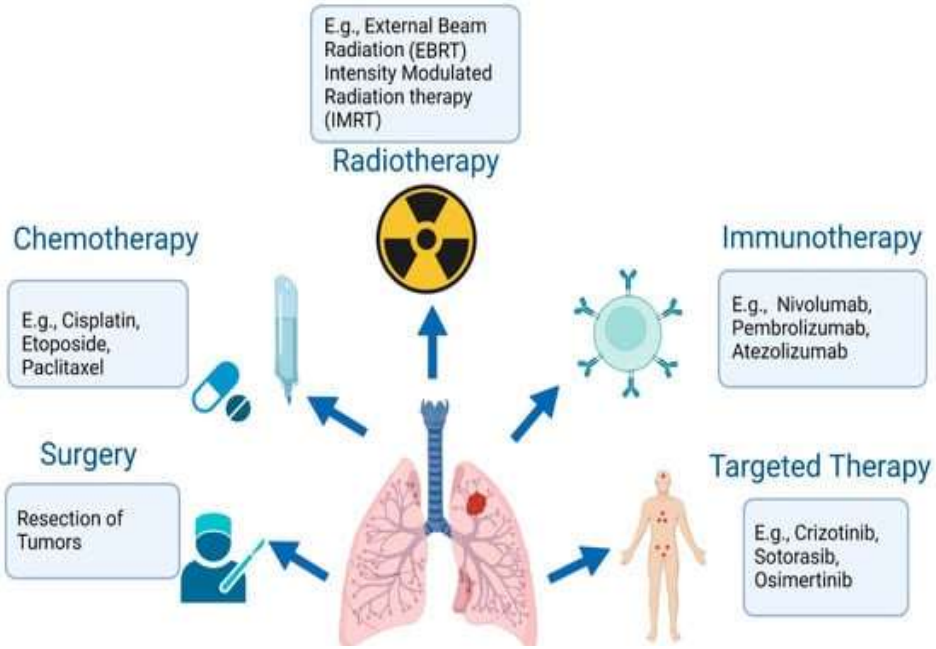
- N2 disease
- Positive resection margins
- IIIb stage
- ECOG PS 1 or 0
- Weight loss below 5%



Immunotherapy and radiotherapy

NSCLC IIIA or IIIB stage

- Definitive concurrent chemoradiotherapy, followed by immunotherapy
- **NSCLC IIIA stage**
- In the adjuvant setting after chemotherapy (CHT)



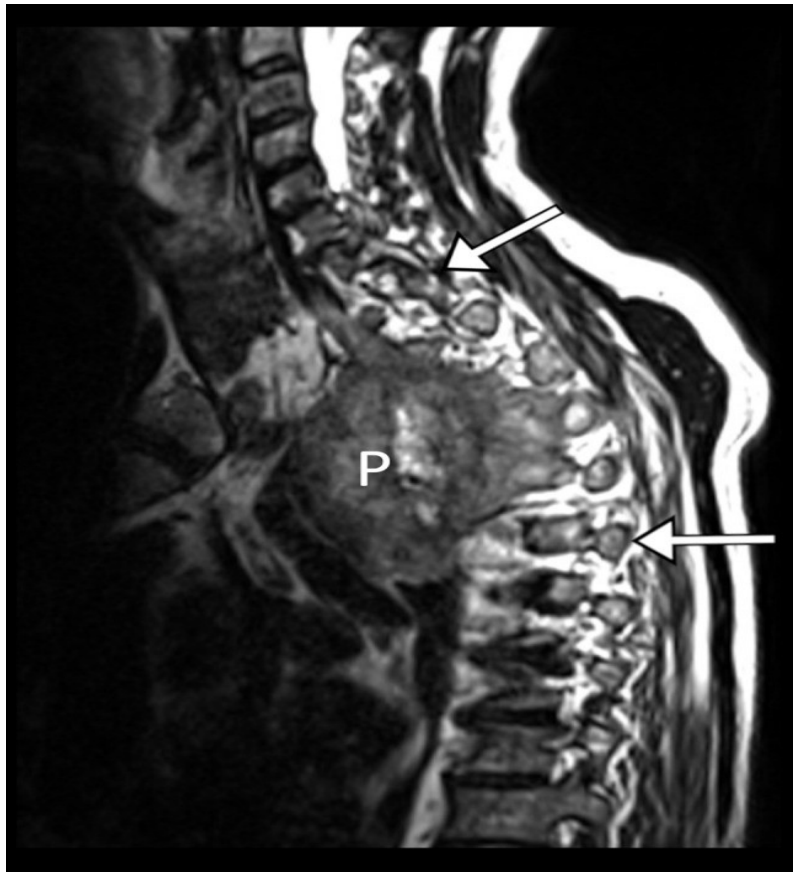
Ashrafi A, Akter Z, Modareszadeh P, Modareszadeh P, Berisha E, Alemi PS, Chacon Castro MDC, Deese AR, Zhang L. Current Landscape of Therapeutic Resistance in Lung Cancer and Promising Strategies to Overcome Resistance. Cancers (Basel). 2022 Sep 20;14(19):4562.

Radiotherapy dose prescription - NSCLC

- Preoperative RT NSCLC 45-54Gy*
- Radical RT NSCLC with CHT 60-70Gy
- Radical RT of NSCLC without HT 66-74Gy
- Definitive SCLC 50-56Gy or 45Gy, 2x1.5Gy per day
- Postoperative RT NSCLC, R0 50Gy/25f
- Postoperative RT NSCLC, R1 60Gy/30f
- Postoperative RT NSCLC, ECE 54Gy/27f
- Postoperative RT NSCLC, R2 66-70Gy/33-35f
- Palliative RT 10Gy/1f; 16Gy/2f; 20Gy/5f; 36Gy/12f
- *except for palliative and SCLC, the standard fractionation regimen was applied (1.8-2Gy per day)

Pancost tumors radiotherapy

- Neoadjuvant CHT-RT (45 Gy) → surgery
- Definitive chemoradiotherapy (same doses as for NSCLC)



Chu EC, Trager RJ, Shum JSF, Lai CR. Pancoast Tumor Presenting as Neck Pain in the Chiropractic Office: A Case Report and Literature Review. Am J Case Rep. 2022 Jul 7;23:e937052.

Radiotherapy of small cell lung cancer (SCLC) in limited disease (LD)

- **Surgical resection** (extremely rare in early stages)
- **Multiagent CHT 4 to 6 cycles** (usually etoposide in combination with carboplatin or cisplatin) **+/- RT**
- Concomitant (age below 75 years, ECOG PS 0-1, absence of significant comorbidities) or sequential
- Early initiation of radiotherapy (at the same time as the 1st or 2nd cycle of chemotherapy) improves survival
- **RT with CHT** in patients with PR or CR with the aim of covering all sites of initial disease
- Extremely chemo- and radiosensitive, but still chemo- and radio-incurable
- A tumor that can be covered by a curative radiotherapy volume

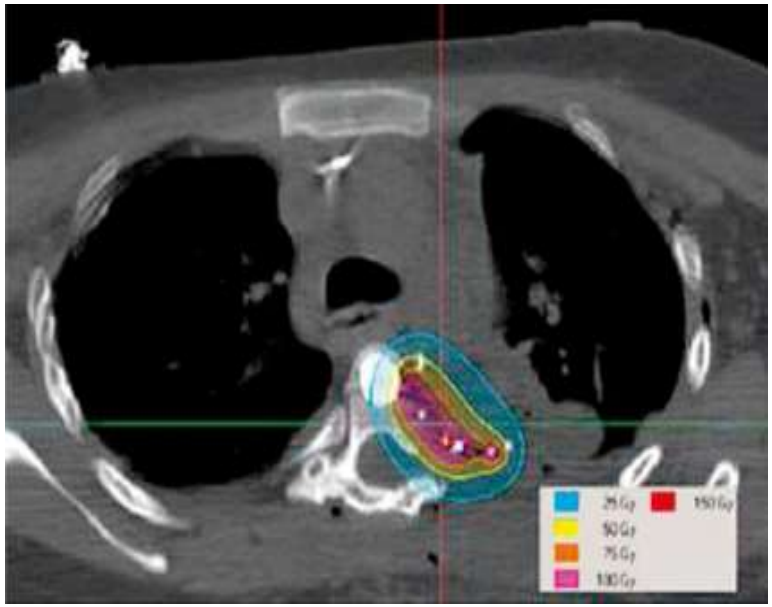
- **RT -** TD 54-56Gy with a standard fractionation or 45Gy hyperfractionated twice a day at 1.5Gy for 3 weeks with an interfraction interval of at least 6h

Radiotherapy SCLC in extended disease (ED)

- The primary treatment is systemic CHT
- Consolidative RT of the chest: strictly selected patients, complete remission of tumors outside the chest, good general condition (reduction of the risk of intrathoracic disease relapse)
- Prophylactic irradiation of the endocranium

Lung cancer brachytherapy

Placement of permanent radioactive sources or high dose rate (HDR) brachytherapy



Skowronek J. Brachytherapy in the treatment of lung cancer - a valuable solution. J Contemp Brachytherapy. 2015 Aug;7(4):297-311.

Prophylactic cranial irradiation (PCI) in patients with SCLC

- Benefits: Reduces the incidence of brain metastases, improves one-year survival from 13% to 27%
- Disadvantages: acute toxicity of PCI and possible long-term effect on cognitive function

- After curative CHT and RT as long as there is a complete or near complete response
- When chest RT follows CHT, the brain and chest should be irradiated simultaneously

- PCI RT - TD 25 Gy in 10 fractions

Radiotolerance of organs at risk (QUANTEC)

Lungs: mean lung dose (MLD): <15 Gy.

V20 (lung volume receiving 20 Gy):

<35% for chemoradiotherapy

<40% for definitive radiotherapy

<10% for postoperative radiotherapy

V30: <25-30%;

V10: <40%;

V5: <60%

Radiotolerance of organs at risk (QUANTEC)

Esophagus: mean esophageal dose (MED): <28 Gy

V20 (volume of esophagus receiving 20 Gy):<45%

V50: <31%

V60:<24%

Dmax<73 Gy.

Heart: mean heart dose (MHD): <26 Gy

V30:<45%

Spinal cord (spinal cord mean dose): <46 Gy

Liver: (liver mean dose): <30Gy

V30:<40%

Kidney:

V20:<32% for both kidneys

V20:<15% for one kidney if the other is dysfunctional

Radiotherapy of gynecological malignancies

- EBRT (2D-conventional, 3D-CRT, IMRT, VMAT)
- 2D or 3D brachytherapy (intracavitary and/or interstitial)

Vulvar cancer radiotherapy

Radical RT +/- CHT potentiation by cisplatin

Contraindications for surgery

Inoperable tumors, T3-T4, N3

Standard:

Regime I (technique I) : 45Gy, 2Gy per fraction + Boost (e-) 10-20Gy, 2Gy per fraction

Regime II (technique II): 55-65Gy, 1.8-2 Gy per fraction (max. dose: vulva up to 65Gy, inguinum up to 55Gy possibility of split course)

Non-standard: TD 45Gy (AP- PA fields + electrons on inguinum) + boost(s) (inguinum+ perineum) 10-20Gy, 1.8-2Gy

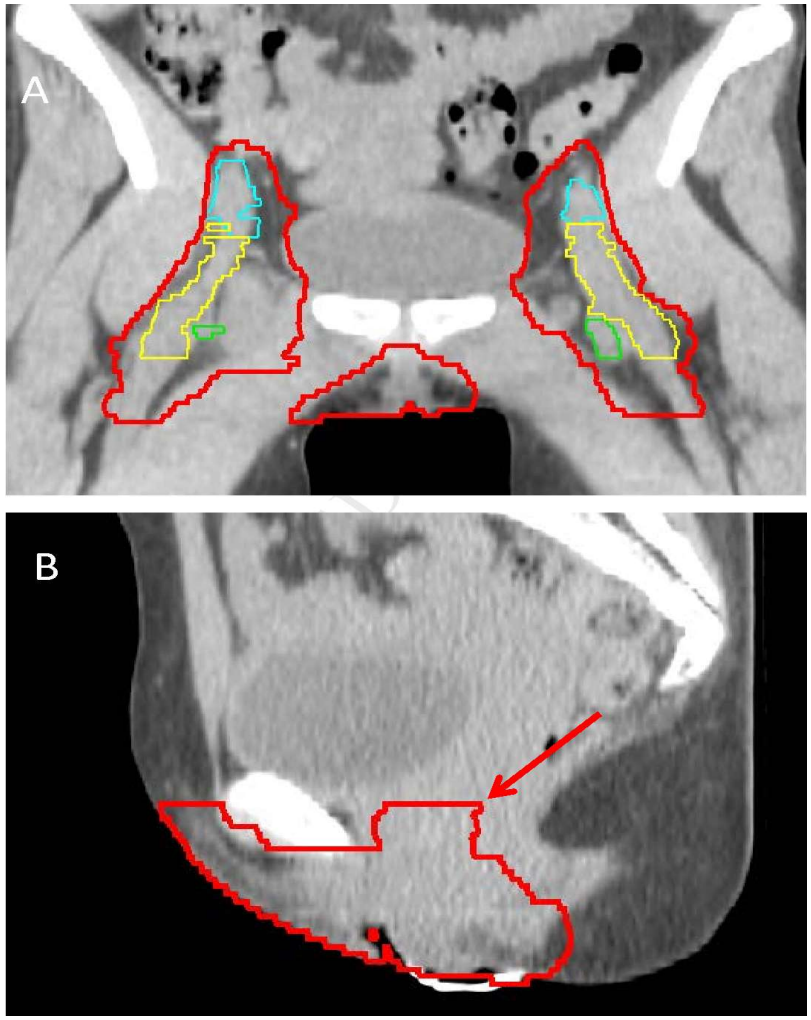
Postoperative RT (start within 6 weeks of surgery)

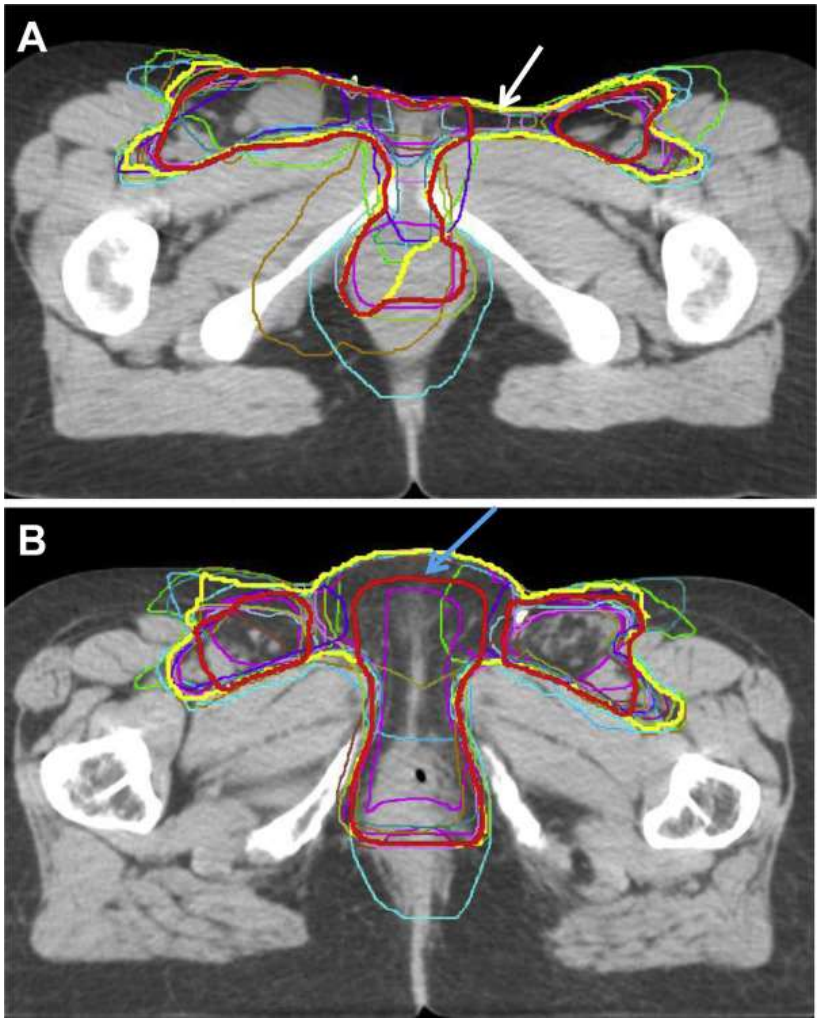
High-risk group, positive resection margins or insufficient margins (optimally 1-2cm), positive inguinal nodes

Regimen I: 45-50Gy,(e) direct fields, 1.8-2 Gy per fraction

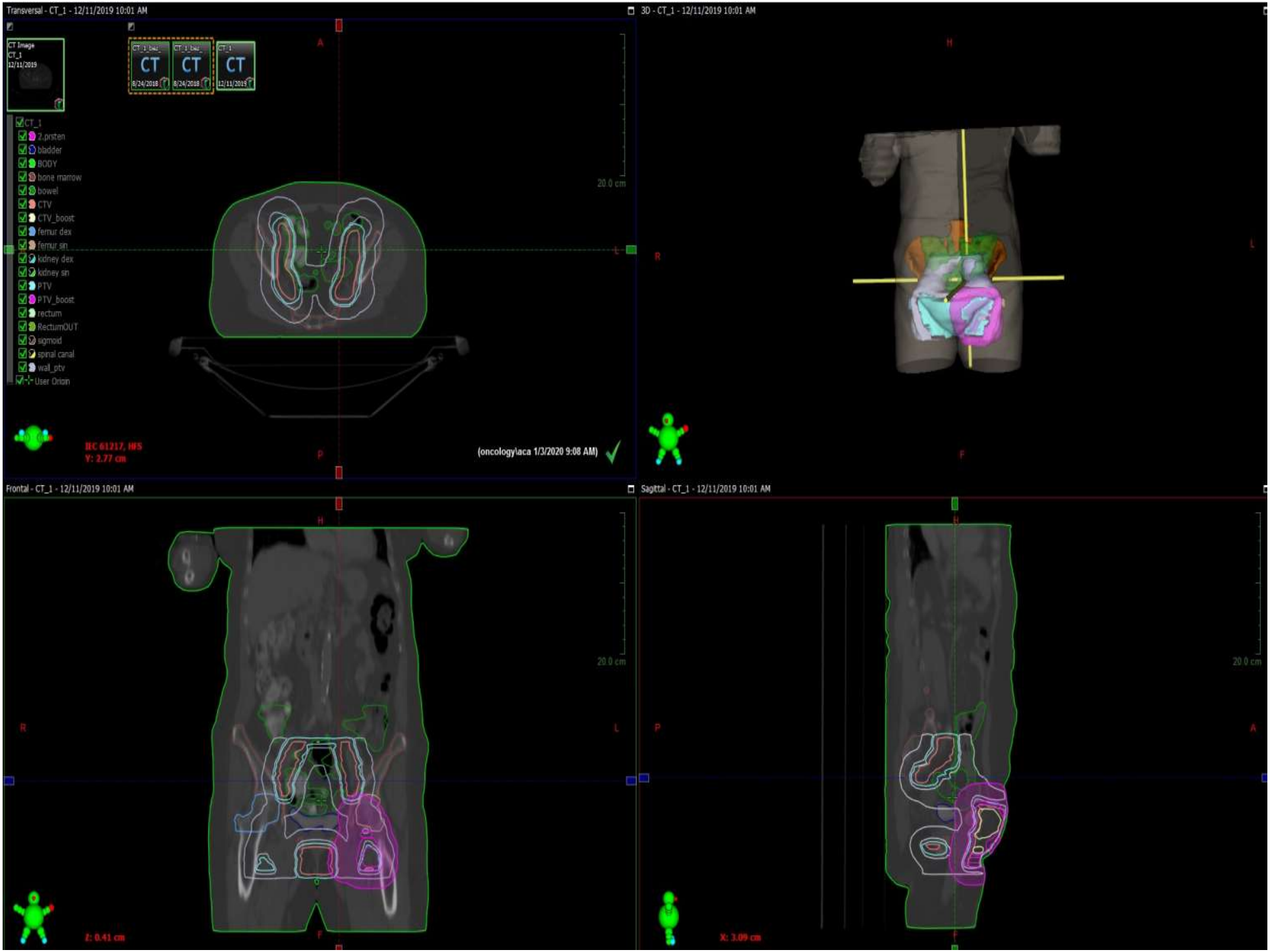
Regime II: 45Gy, (photons), pelvic fields, 2Gy per fraction, all fields + Boost (e) 10-20Gy, 2Gy per fraction

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.





Gaffney DK, et al. Consensus Recommendations for Radiation Therapy Contouring and Treatment of Vulvar Carcinoma. Int J Radiat Oncol Biol Phys 2016;95(4):1191-200.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BODY
bone marrow
bowel
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PTV
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HC 61217, HFS
Y: 2.77 cm
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Frontal - CT_1 - 12/11/2019 10:01 AM
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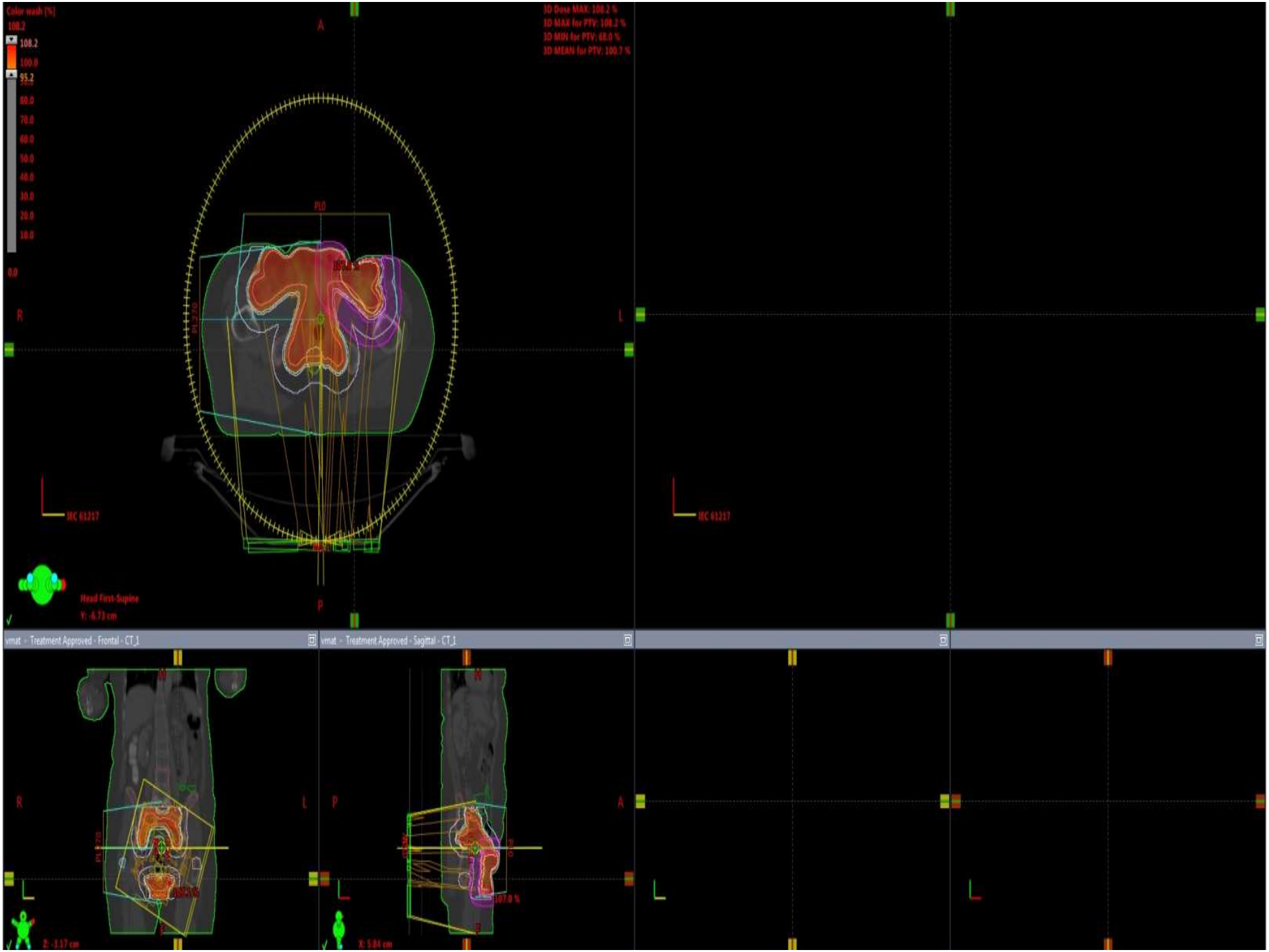
Z: 0.41 cm
Sagittal - CT_1 - 12/11/2019 10:01 AM
20.0 cm
X: 3.09 cm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108.2
100.0
95.2
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70.0
60.0
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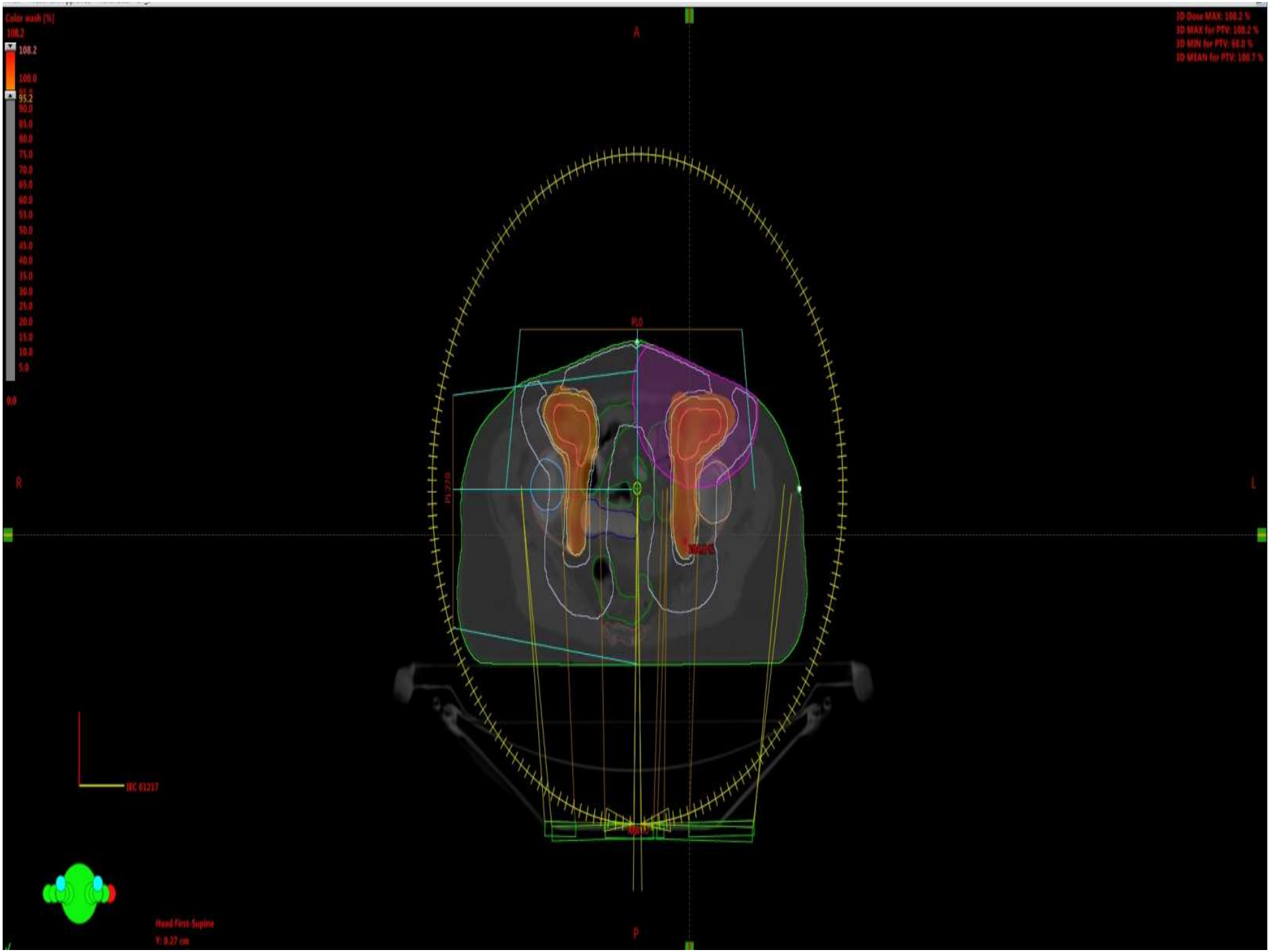
3D Dose MAX: 108.2 %
3D MAX for PTV: 108.2 %
3D MIN for PTV: 68.0 %
3D MEAN for PTV: 100.7 %
A
R
L
P
PL0
IEC 61217
Head First-Supine
Y: -6.73 cm
vmat - Treatment Approved - Frontal - CT_1
vmat - Treatment Approved - Sagittal - CT_1
Z: -1.17 cm
X: 5.84 cm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85.0
80.0
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70.0
65.0
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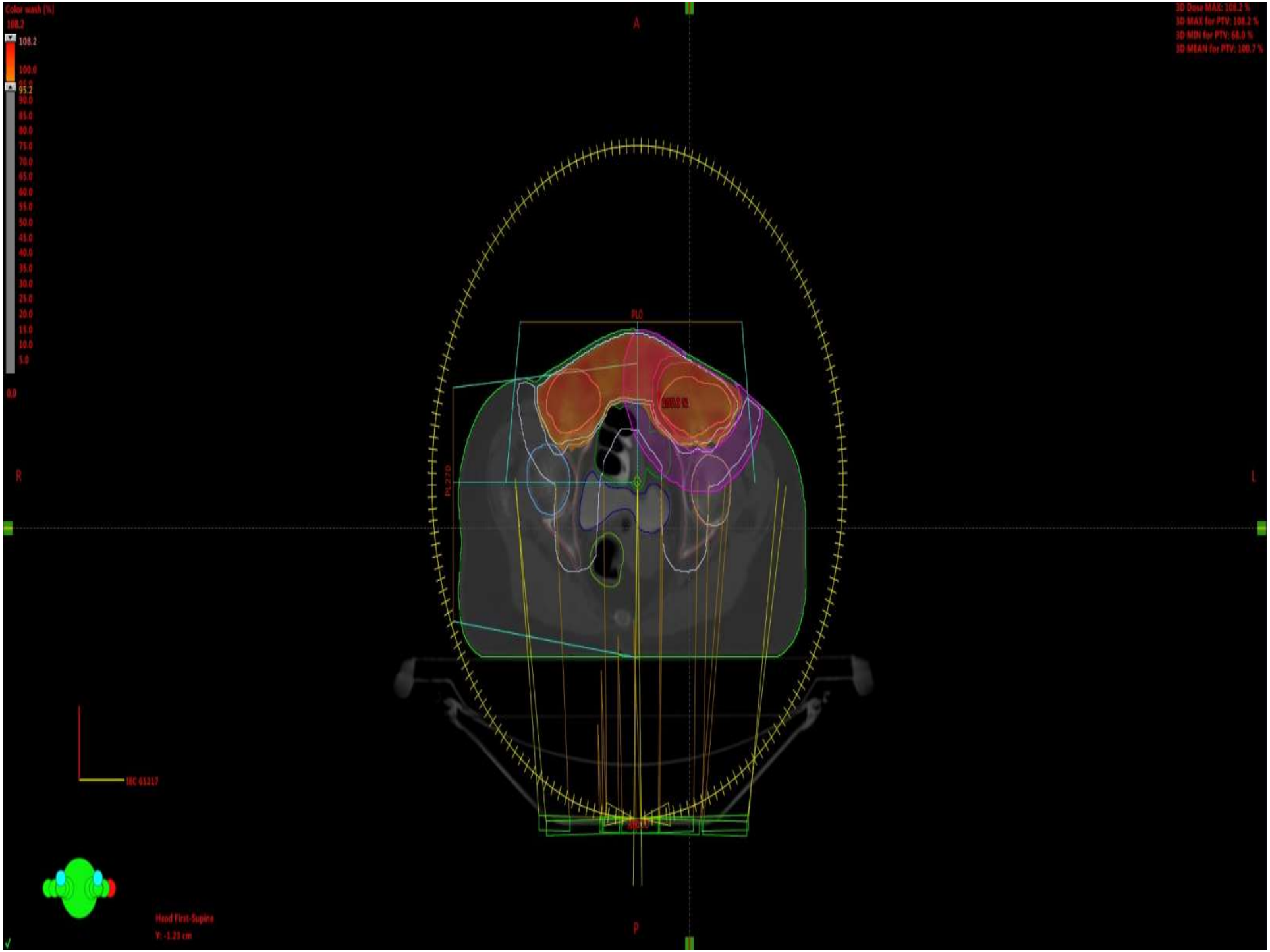
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
3D Dose MAX: 108.2 %
3D MAX for PTV: 108.2 %
3D MIN for PTV: 68.0 %
3D MEAN for PTV: 100.7 %
A
R
L
P
PLO
IEC 61217
Head First-Supine
Y: 0.27 cm


Color wash [%]
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108.2
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3D Dose MAX: 108.2 %
3D MAX for PTV: 108.2 %
3D MIN for PTV: 68.0 %
3D MEAN for PTV: 100.7 %
A
R
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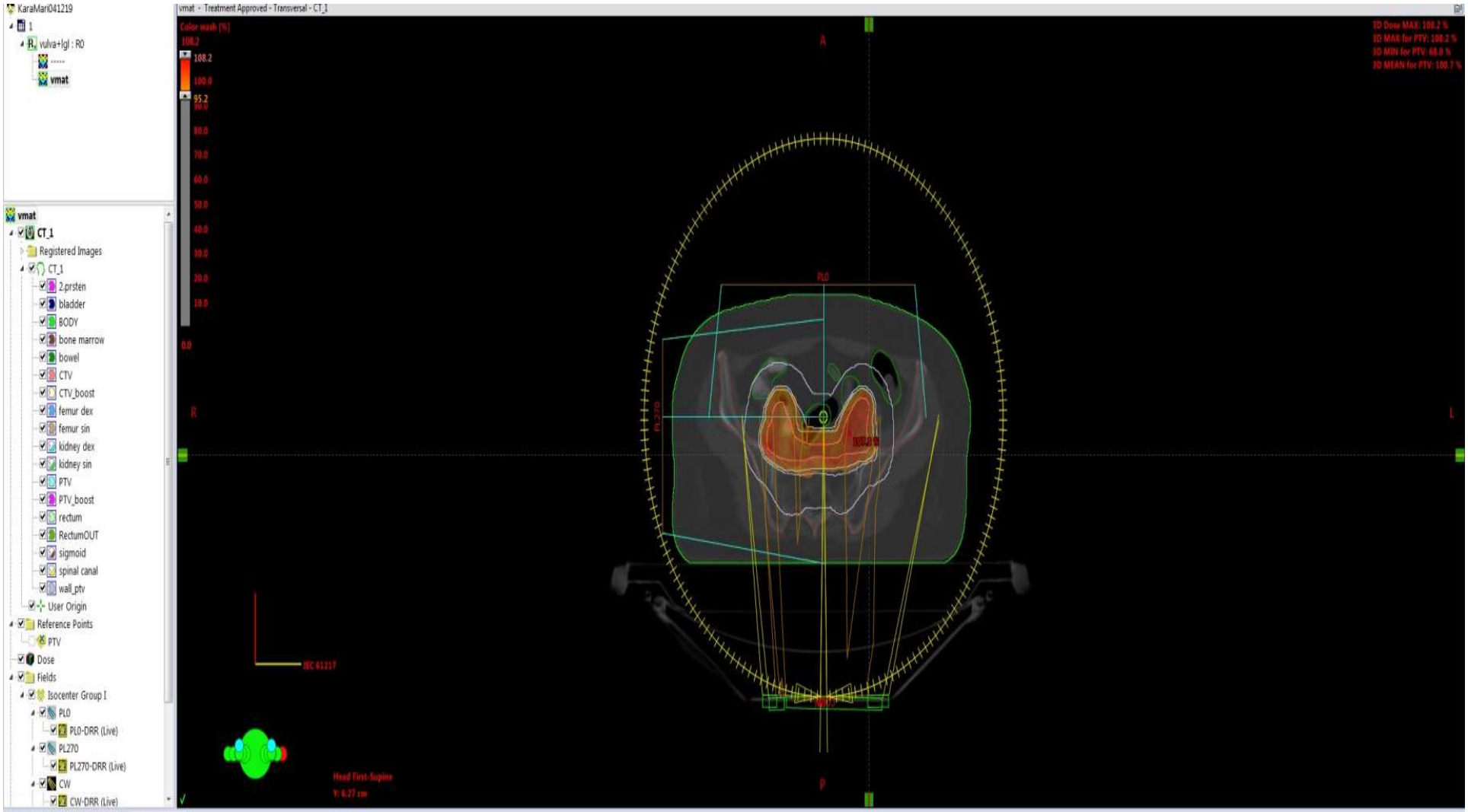
PLO
HU:270
HU:0.93
IEC 61217
Head First-Supine
Y: -1.23 cm



Fields | Dose | Reference Points | Dose Statistics

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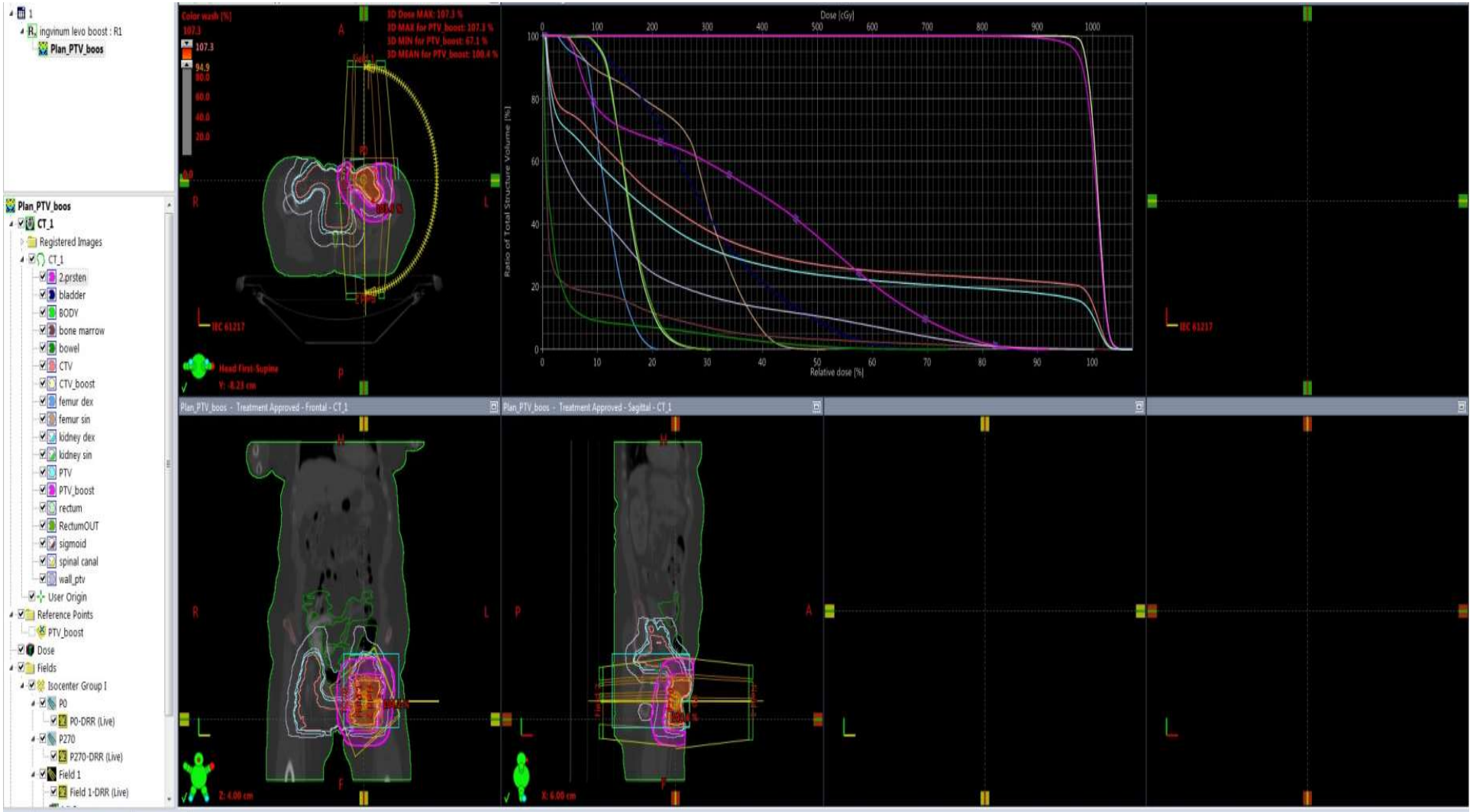
	bladder	Approved	vmat	1	106.9	100.0	100.0	33.9	99.3	56.8	77.0	0.4
	bone marrow	Approved	vmat	1	1314.2	100.0	100.0	1.9	107.3	56.9	65.7	13.1
	bowel	Approved	vmat	1	910.2	100.0	100.0	3.2	101.9	54.5	62.5	12.9
	CTV	Approved	vmat	1	1087.4	100.0	100.0	94.7	108.2	101.3	100.0	100.0
	femur dex	Approved	vmat	1	102.8	100.0	100.0	36.0	98.2	62.0	82.1	0.6
	femur sin	Approved	vmat	1	93.9	100.0	100.0	37.4	101.6	62.1	75.1	1.1
	PTV	Approved	vmat	1	1849.5	100.0	100.0	68.0	108.2	100.7	100.0	99.9
	rectum	Approved	vmat	1	60.7	100.0	100.0	40.0	100.8	61.9	69.4	8.7
	wall_ptv	Approved	vmat	1	2489.8	100.0	100.0	21.1	105.2	75.6	98.5	1.6
	RectumOUT	Approved	vmat	1	51.8	100.0	100.0	40.0	96.0	56.5	64.2	0.1
	2.prsten	Approved	vmat	1	1023.9	100.0	100.0	9.5	107.9	77.2	91.0	24.5
	CTV_boost	Approved	vmat	1	189.6	100.0	100.0	95.2	108.0	101.8	100.0	100.0
	PTV_boost	Approved	vmat	1	304.6	100.0	100.0	73.1	108.2	101.5	100.0	99.3



Fields | Dose | Reference Points | Dose Statistics

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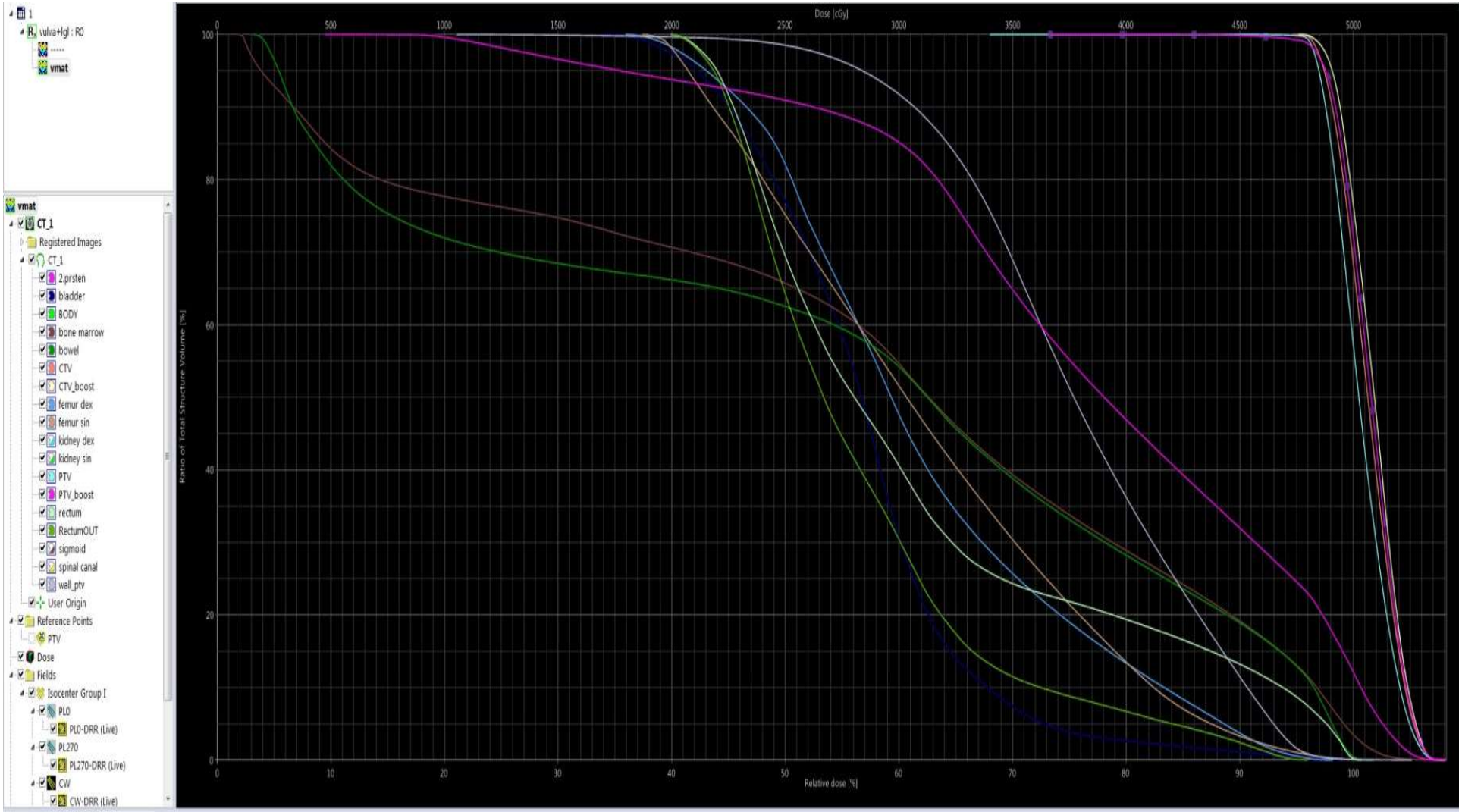
	bladder	Approved	Plan_PTV_boos	1	106.9	100.0	100.0	5.4	69.4	29.5	9.0	0.0
	bone marrow	Approved	Plan_PTV_boos	1	1314.2	100.0	100.0	0.0	104.4	6.6	3.2	0.0
	bowel	Approved	Plan_PTV_boos	1	910.2	100.0	100.0	0.1	73.7	4.3	1.0	0.0
	CTV	Approved	Plan_PTV_boos	1	1087.4	100.0	100.0	0.5	107.3	36.0	27.0	0.0
	femur dex	Approved	Plan_PTV_boos	1	102.8	100.0	100.0	2.6	21.2	11.6	0.0	0.0
	femur sin	Approved	Plan_PTV_boos	1	93.9	100.0	100.0	4.1	51.5	27.3	0.0	0.0
	PTV	Approved	Plan_PTV_boos	1	1849.5	100.0	100.0	0.4	107.3	31.6	23.8	0.0
	rectum	Approved	Plan_PTV_boos	1	60.7	100.0	100.0	3.3	30.7	15.7	0.0	0.0
	wall_ptv	Approved	Plan_PTV_boos	1	2489.8	100.0	100.0	0.4	100.3	15.9	10.6	0.0
	RectumOUT	Approved	Plan_PTV_boos	1	51.8	100.0	100.0	3.3	30.7	15.8	0.0	0.0
	2.prsten	Approved	Plan_PTV_boos	1	1023.9	100.0	100.0	2.2	91.9	37.4	35.9	0.0
	CTV_boost	Approved	Plan_PTV_boos	1	189.6	100.0	100.0	90.6	107.3	100.8	100.0	0.0
	PTV_boost	Approved	Plan_PTV_boos	1	304.6	100.0	100.0	67.1	107.3	100.4	100.0	0.0



Dose | Reference Points | Dose Statistics

Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [%]	Max Dose [%]	Mean Dose [%]	V50.0% [%]	V4750.0cGy [%]
	BODY	Approved	vmat	1	41447.3	100.0	100.2	0.0	108.2	22.4	19.6	5.2
	bladder	Approved	vmat	1	106.9	100.0	100.0	33.9	99.3	56.8	77.0	0.4
	bone marrow	Approved	vmat	1	1314.2	100.0	100.0	1.9	107.3	56.9	65.7	13.1
	bowel	Approved	vmat	1	910.2	100.0	100.0	3.2	101.9	54.5	62.5	12.9
	CTV	Approved	vmat	1	1087.4	100.0	100.0	94.7	108.2	101.3	100.0	100.0
	femur dex	Approved	vmat	1	102.8	100.0	100.0	36.0	98.2	62.0	82.1	0.6
	femur sin	Approved	vmat	1	93.9	100.0	100.0	37.4	101.6	62.1	75.1	1.1
	PTV	Approved	vmat	1	1849.5	100.0	100.0	68.0	108.2	100.7	100.0	99.9
	rectum	Approved	vmat	1	60.7	100.0	100.0	40.0	100.8	61.9	69.4	8.7
	wall_ptv	Approved	vmat	1	2489.8	100.0	100.0	21.1	105.2	75.6	98.5	1.6
	RectumOUT	Approved	vmat	1	51.8	100.0	100.0	40.0	96.0	56.5	64.2	0.1
	2.prsten	Approved	vmat	1	1023.9	100.0	100.0	9.5	107.9	77.2	91.0	24.5
	CTV_boost	Approved	vmat	1	189.6	100.0	100.0	95.2	108.0	101.8	100.0	100.0
	PTV_boost	Approved	vmat	1	304.6	100.0	100.0	73.1	108.2	101.5	100.0	99.3

Vaginal cancer radiotherapy

Radical radiotherapy or postoperative +/- CHT potentiation

- Stage I (infiltration of more than 0.5 cm of mucosa) - IVA
- Adjuvant RT after tumor excision (abnormal)

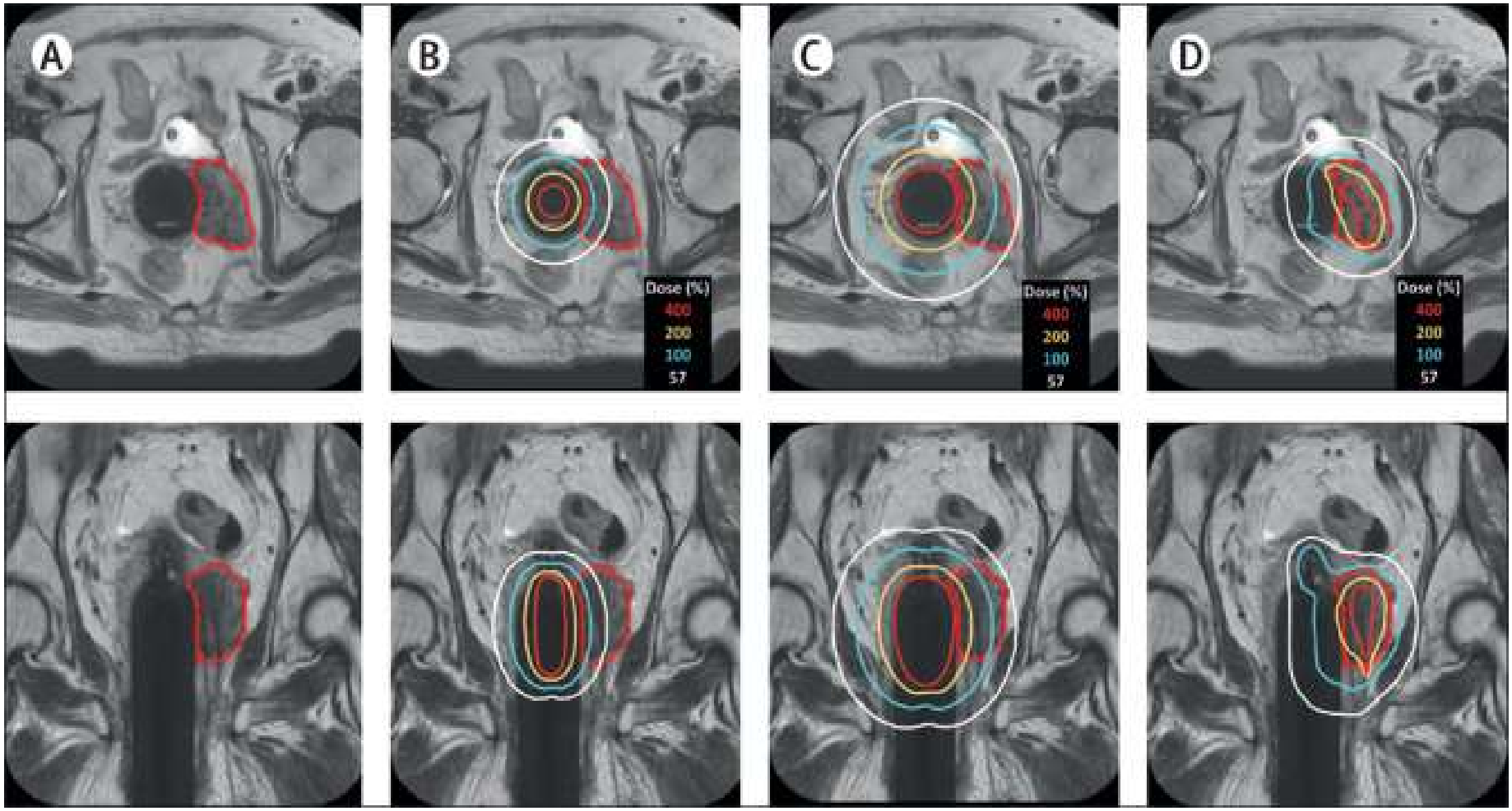
Standard: 46Gy, 1.8-2Gy per day, 5 days/week

- Boost on enlarged inguinal lymphatic(s): up to max 15-20Gy in 7-10 fractions
- Brachytherapy: after 5-10 fractions of EBRT

Non-standard:

- Hemostatic application (before EBRT)
- In advanced tumors with altered topographic relationships after 30Gy EBRT or after completed EBRT

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.



Westerveld H, et al. Definitive radiotherapy with image-guided adaptive brachytherapy for primary vaginal cancer. Lancet Oncol 2020;21(3):e157-67.

Radiotherapy of locally advanced cervical cancer

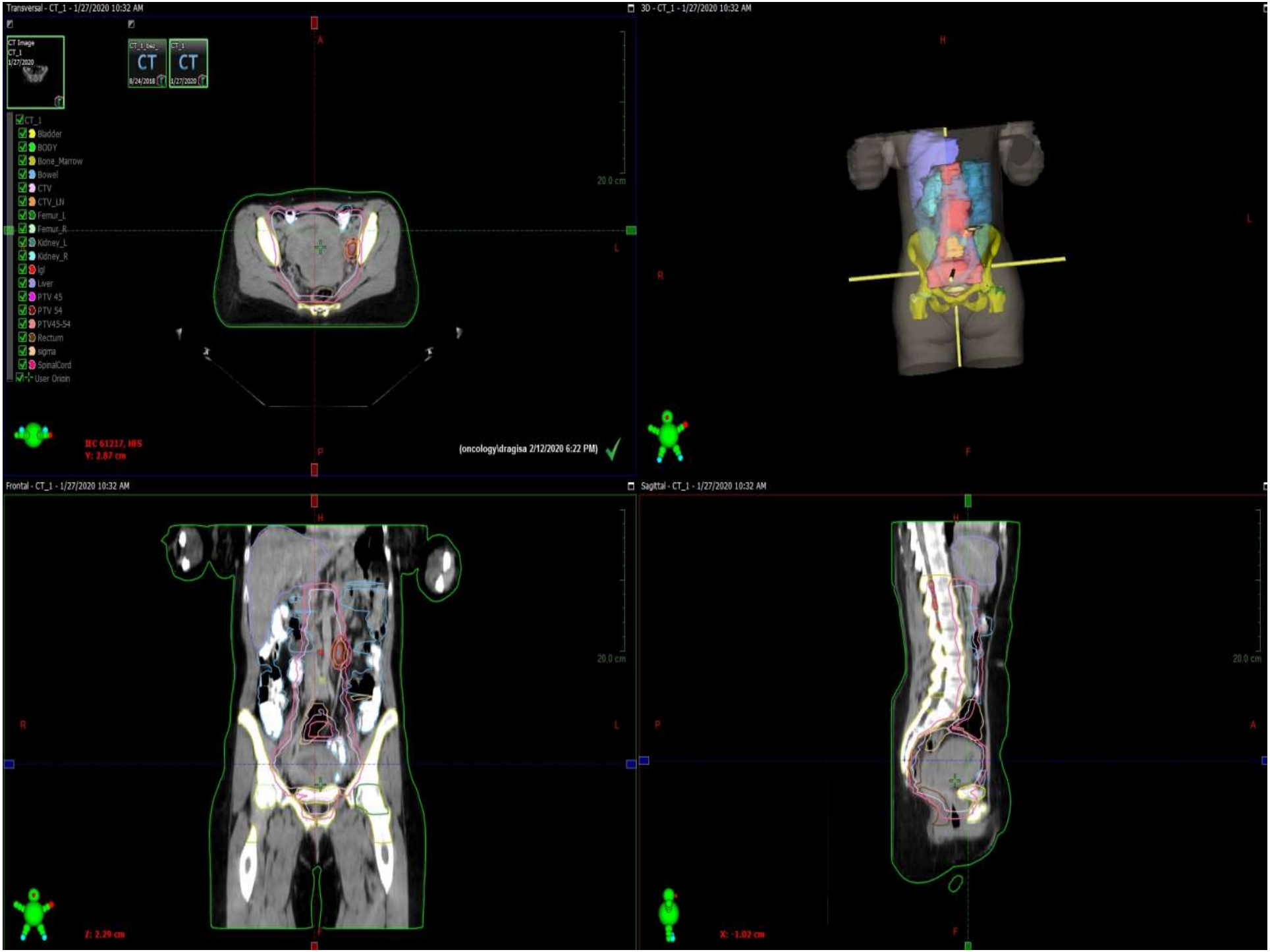
FIGO St. IB bulky, IIA, IIB – IVA

Patient refuses surgery (in the early stages)

- **RT+CHT potentiation (standard) + brachytherapy**
- Standard: 46Gy, 1.8-2Gy per fraction, 5 days/week
- Boost to parameters (tumor rest) 5Gy
- Boost on enlarged inguinal lymphatics: up to max 55Gy
- Prophylactic RT of the para-aortic region up to L3: TD 45 Gy, 1.8 Gy per fraction
- Para-aortic region: 45Gy, 5 days/week, 1.8 Gy per fraction

- Palliative doses: 30 Gy in 10 fractions, 20 Gy in 5 fractions
- Nodal boost:
- 55Gy pelvic lymphatics simultaneous integrated boost (SIB) – within 25 fractions / sequential up to a total dose with a daily dose of 1.8Gy
- 57.5Gy – 60Gy para-aortic lymphatics SIB - within 25 fractions / sequential up to a total dose with a daily dose of 1.8Gy

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.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CT_1
Bladder
BODY
Bone_Marrow
Bowel
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Femur_L
Femur_R
Kidney_L
Kidney_R
lgl
Liver
PTV 45
PTV 54
PTV45-54
Rectum
sigma
SpinalCord
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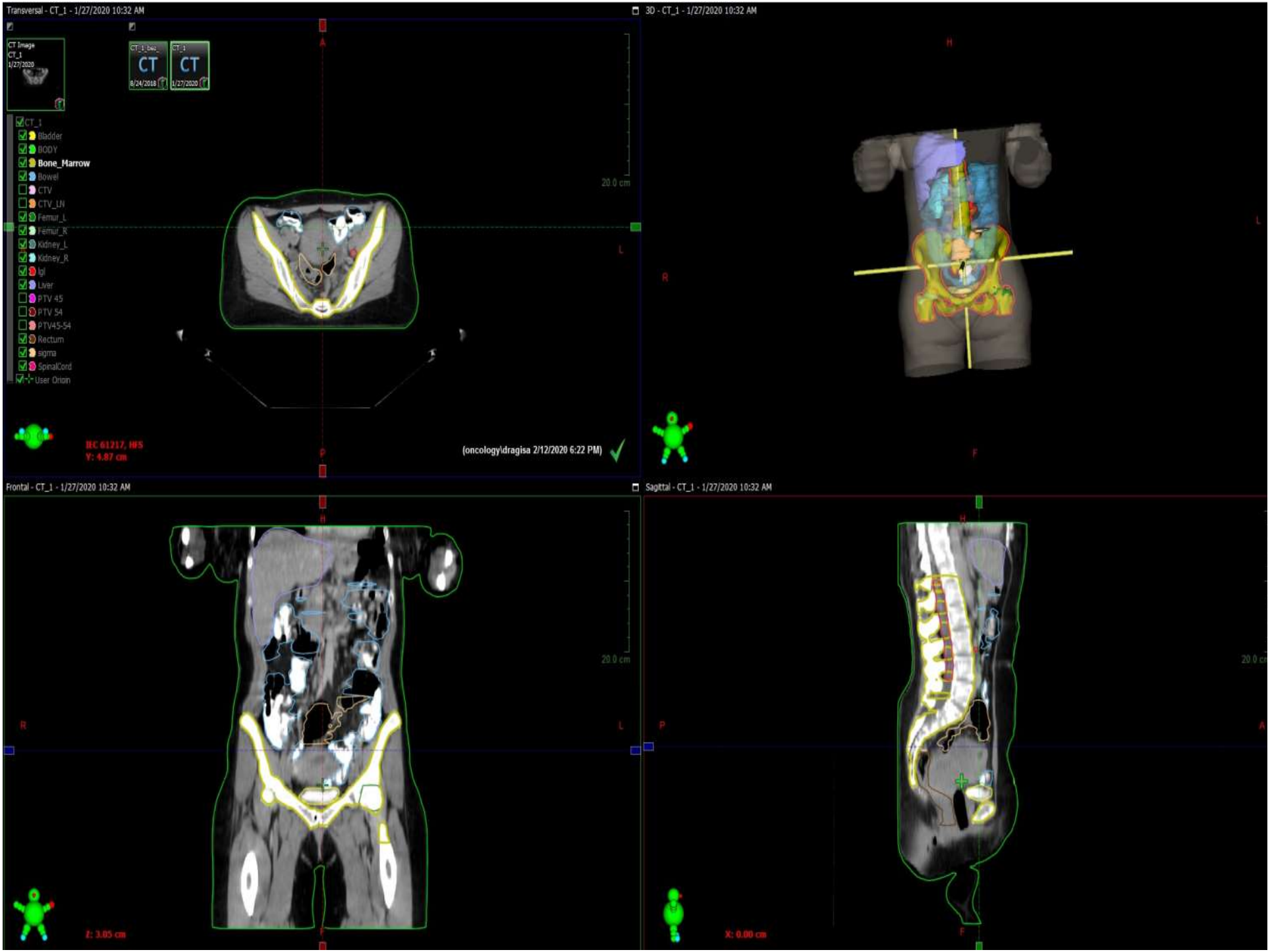
(oncology\dragisa 2/12/2020 6:22 PM)
Z: 2.29 cm
X: -1.02 cm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CT_1
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BODY
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Bowel
CTV
CTV_LN
Femur_L
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Kidney_L
Kidney_R
lgl
Liver
PTV 45
PTV 54
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sigma
SpinalCord
User Origin
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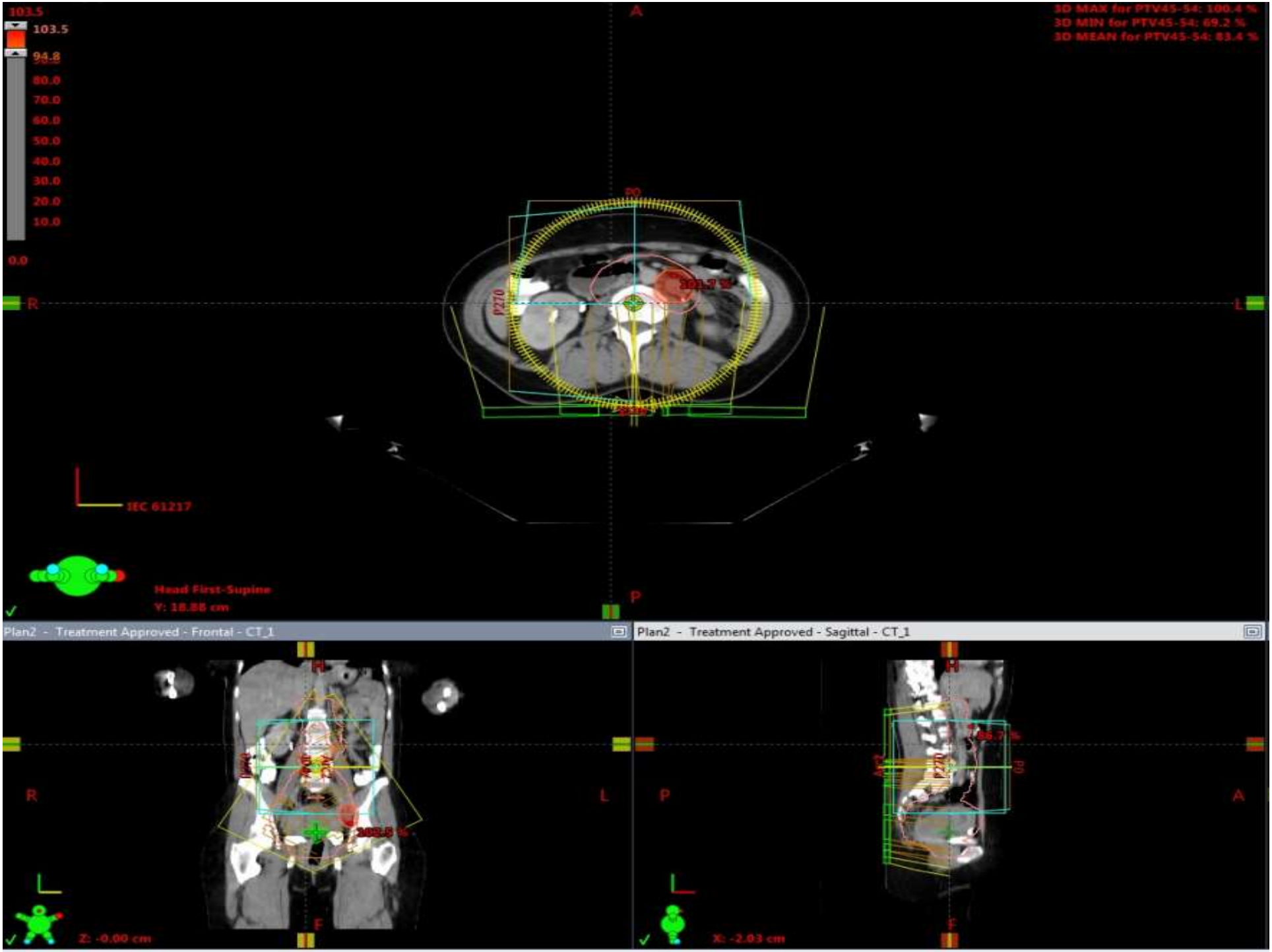
X: 0.00 cm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103.5
94.8
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
A
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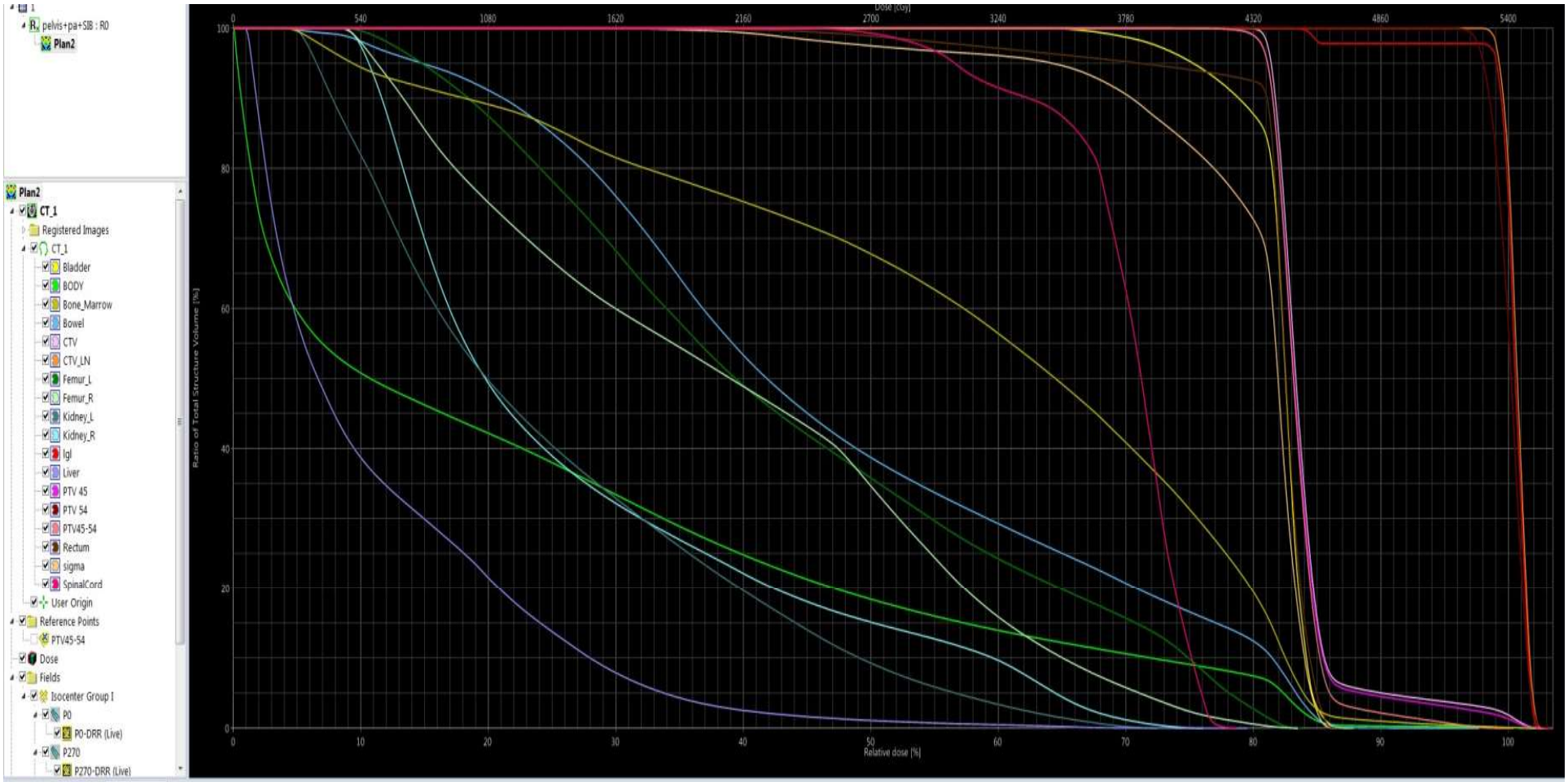
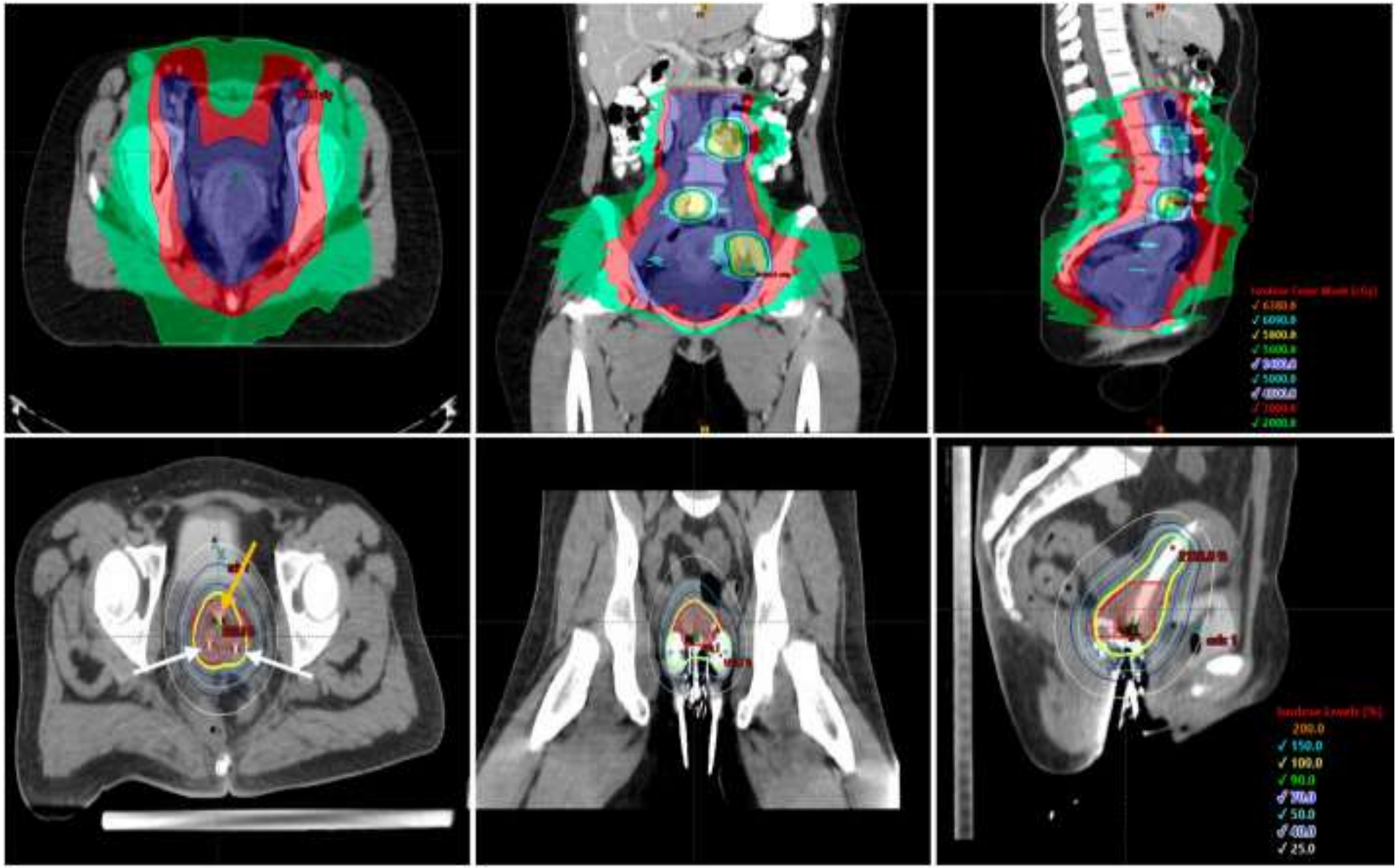
R
L
IEC 61217
Head First-Supine
Y: 18.88 cm
Plan2 - Treatment Approved - Frontal - CT_1
Plan2 - Treatment Approved - Sagittal - CT_1
Z: -0.00 cm
X: -2.03 cm



Dose | Reference Points | Dose Statistics

Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [%]	Max Dose [%]	Mean Dose [%]	V50.0% [%]	V4750.0cGy [%]
☑	BODY	Approved	Plan2	1	39258.6	100.0	99.9	0.0	103.5	23.9	18.4	0.4
☑	Kidney_R	Approved	Plan2	1	199.3	100.0	100.0	8.4	76.1	27.4	15.1	0.0
☑	Kidney_L	Approved	Plan2	1	191.3	100.0	100.0	4.7	72.5	24.8	9.3	0.0
☑	Bladder	Approved	Plan2	1	75.5	100.0	100.0	63.6	87.9	81.9	100.0	0.0
☑	Igl	Approved	Plan2	1	8.9	100.0	100.2	83.0	102.4	100.2	100.0	97.8
☑	Bowel	Approved	Plan2	1	1334.6	100.0	100.0	4.2	97.8	46.8	38.7	0.1
☑	sigma	Approved	Plan2	1	159.2	100.0	100.0	29.7	86.6	79.1	97.5	0.0
☑	Rectum	Approved	Plan2	1	91.2	100.0	100.0	33.7	86.5	81.4	98.9	0.0
☑	Femur_L	Approved	Plan2	1	76.0	100.0	100.0	8.6	83.8	43.2	35.8	0.0
☑	Femur_R	Approved	Plan2	1	81.9	100.0	100.0	8.3	83.5	38.8	34.6	0.0
☑	Liver	Approved	Plan2	1	1519.3	100.0	99.8	0.8	79.5	11.5	1.1	0.0
☑	CTV	Approved	Plan2	1	1587.8	100.0	100.0	78.6	103.5	84.1	100.0	5.7
☑	PTV 45	Approved	Plan2	1	2467.3	100.0	100.0	69.2	103.5	83.8	100.0	5.2
☑	CTV_LN	Approved	Plan2	1	20.2	100.0	100.1	97.9	102.8	100.7	100.0	100.0
☑	PTV 54	Approved	Plan2	1	57.7	100.0	100.1	94.8	103.5	100.1	100.0	100.0
☑	PTV45-54	Approved	Plan2	1	2407.9	100.0	100.0	69.2	100.4	83.4	100.0	2.9
☑	Bone_Marrow	Approved	Plan2	1	1842.3	100.0	100.0	4.0	102.2	57.5	67.8	1.3
☑	SpinalCord	Approved	Plan2	1	26.7	100.0	100.0	44.2	78.8	69.9	99.3	0.0



Williamson CW, et al. Advances in External Beam Radiation Therapy and Brachytherapy for Cervical Cancer. Clin Oncol (R Coll Radiol) 2021;33(9):567-78.


Transversal - CT_1 - 1/13/2020 9:56 AM
CT Image
CT_1
1/13/2020
CT_1
CT
1/13/2020
CT_1
Bladder
BODY
Bowel
CTV_Intermedate
Femur_L
Femur_R
NS_Ring
PTV_Intermedate
rectum
Sygma
User Origin
20.0 cm
BC 61217, HFS
Y: 10.50 cm
(oncology\ivanka 1/15/2020 12:51 PM)
3D - CT_1 - 1/13/2020 9:56 AM
Frontal - CT_1 - 1/13/2020 9:56 AM
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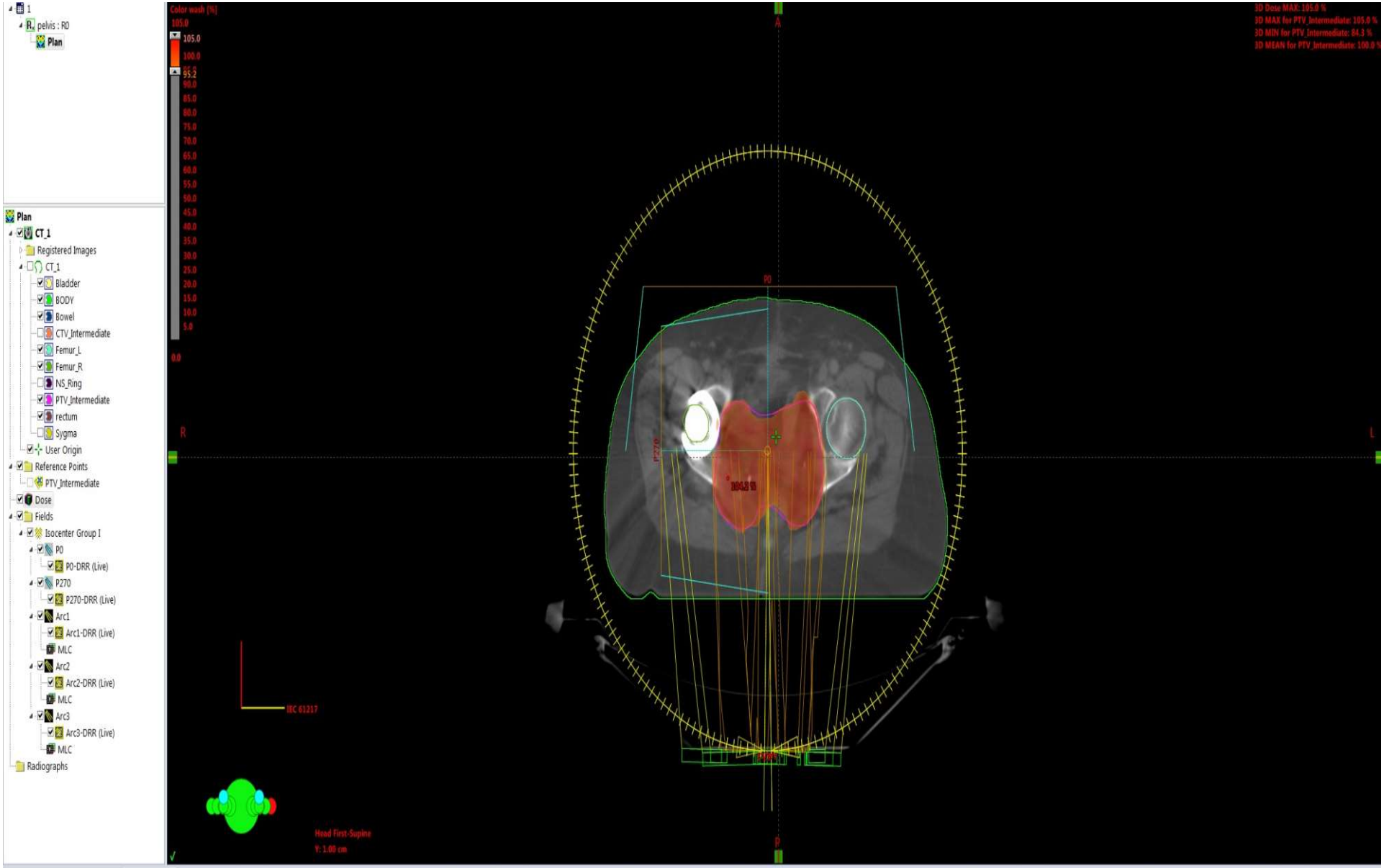
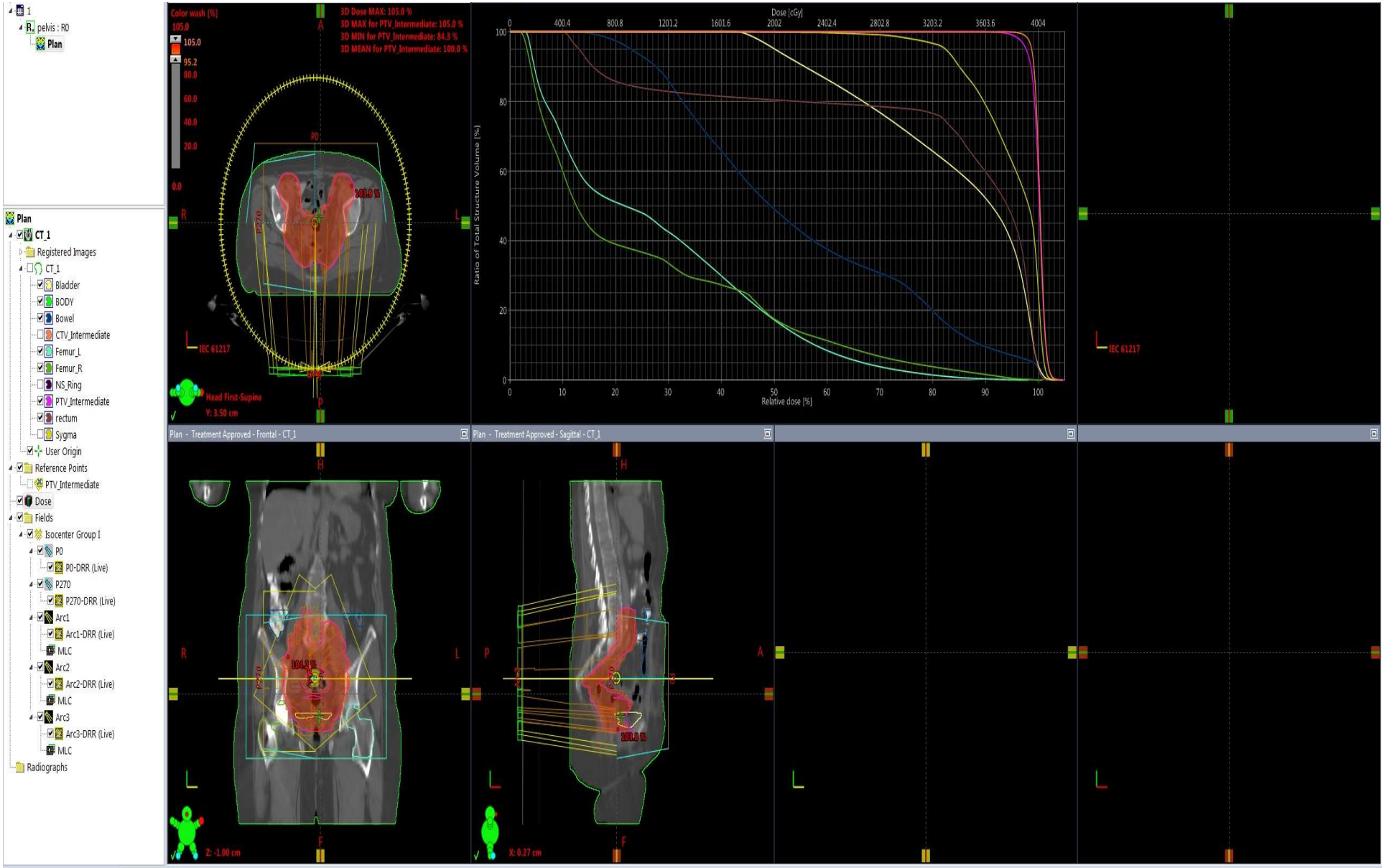
Z: 0.51 cm
Sagittal - CT_1 - 1/13/2020 9:56 AM
20.0 cm
X: 3.11 cm



Fields | Dose | Reference Points | Dose Statistics

Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [%]	Max Dose [%]	Mean Dose [%]	V50.0% [%]	V4750.0cGy [%]
☐	BODY	Approved	Plan	1	39467.7	100.0	100.2	0.0	105.0	21.1	16.9	0.0
☑	Bladder	Approved	Plan	1	65.6	100.0	100.0	42.8	102.9	83.7	95.1	0.0
☑	Femur_L	Approved	Plan	1	138.8	100.0	100.0	2.9	98.1	27.4	17.3	0.0
☑	Femur_R	Approved	Plan	1	109.0	100.0	100.0	1.8	100.8	25.0	17.5	0.0
☑	rectum	Approved	Plan	1	70.3	100.0	100.1	9.9	102.1	78.6	80.4	0.0
☑	Sygma	Approved	Plan	1	260.2	100.0	100.0	42.6	103.5	95.0	99.9	0.0
☑	Bowel	Approved	Plan	1	309.1	100.0	100.0	9.5	103.5	54.8	49.1	0.0
☑	CTV_Intermediate	Approved	Plan	1	903.8	100.0	100.0	91.0	104.6	100.3	100.0	0.0



Fields | Dose | Reference Points | Dose Statistics

Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [%]	Max Dose [%]	Mean Dose [%]	V50.0% [%]	V4750.0cGy [%]
☐	BODY	Approved	Plan	1	39467.7	100.0	100.2	0.0	105.0	21.1	16.9	0.0
☑	Bladder	Approved	Plan	1	65.6	100.0	100.0	42.8	102.9	83.7	95.1	0.0
☑	Femur_L	Approved	Plan	1	138.8	100.0	100.0	2.9	98.1	27.4	17.3	0.0
☑	Femur_R	Approved	Plan	1	109.0	100.0	100.0	1.8	100.8	25.0	17.5	0.0
☑	rectum	Approved	Plan	1	70.3	100.0	100.1	9.9	102.1	78.6	80.4	0.0
☑	Sygma	Approved	Plan	1	260.2	100.0	100.0	42.6	103.5	95.0	99.9	0.0
☑	Bowel	Approved	Plan	1	309.1	100.0	100.0	9.5	103.5	54.8	49.1	0.0
☑	CTV_Intermediate	Approved	Plan	1	903.8	100.0	100.0	91.0	104.6	100.3	100.0	0.0

Postoperative radiotherapy of cervical cancer

4-6 weeks after surgery

- **Medium risk group:** after adequate surgery, parameters are negative, resection margins are negative, lymph nodes are negative

- **High-risk group +/-CHT potentiation**: positive resection margins, positive parameters, positive lymph nodes, inadequate type of surgery

- Pelvis:
- • medium risk group 40-45Gy, 1.8-2 Gy per fraction
- • high-risk group 45-50Gy, 1.8-2 Gy per fraction

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.

Postoperative brachytherapy of cervical cancer

EBRT + Brachytherapy: 2-3 applications with a dose of 6 Gy per application, once a week

Brachytherapy 2-4x6 Gy

- EQD2 dose to the vaginal cuff region is 65-70Gy
- the dose is prescribed at 0.5 cm from the surface of the vaginal ovoids, i.e. the vaginal cylinder
- dose limits for organs at risk are determined in the ICRU reference points B_{max} for the bladder and R_{max} for the rectum according to ICRU-38 recommendations

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.

Radical radiotherapy of endometrial cancer

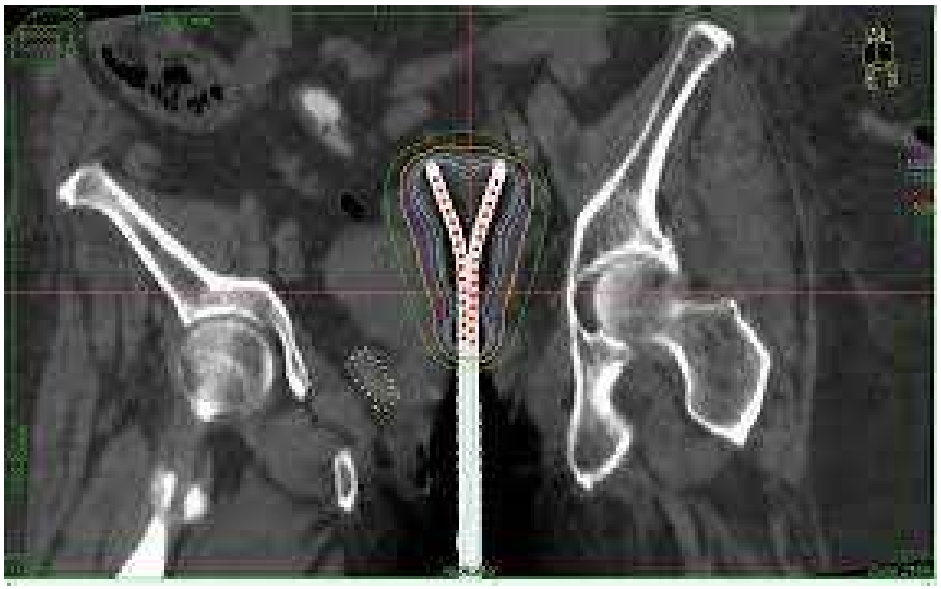
- **Inoperable disease**
- **Contraindications for operative treatment**
- **Patient refuses surgery**

- **EBRT+Brachytherapy+/- CHT**
- Pelvis: 45-50Gy, 5 days/week, 1.8-2 Gy per fraction
- Para-aortic region: 45Gy, 5 days/week, 1.8 Gy per fraction
- Palliative doses: 30 Gy in 10 fractions, 20 Gy in 5 fractions
- Nodal boost:
- 55Gy pelvic lymphatics SIB – within 25 fractions / sequential to total dose
- 57.5 Gy para-aortic lymphatics SIB - within 25 fractions / sequential to total dose

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.

Brachytherapy as part of radical radiotherapy for endometrial cancer

- 2D or 3D brachytherapy
- Intrauterine probe and ovoids
- TD 6-7 Gy in 4-6 fractions once a week
- Dose limits of organs of risk



Schwarz JK, et al. Consensus statement for brachytherapy for the treatment of medically inoperable endometrial cancer. Brachytherapy. 2015;14(5):587-99.

Postoperative radiotherapy of endometrial cancer

- **Low-risk group**: endometrioid histology, G1/2, depth of infiltration ≤ 50%, LVI - **follow-up**
- **Intermediate risk group**: endometrioid histology, G1/2, infiltration depth ≥ 50%, LVI- **adjuvant brachytherapy (optional) or follow-up for patients over 60 years???**
- **Medium-high risk group**: endometrioid histology, G3, depth of infiltration ≥ 50%, regardless of LVI status, endometrioid histology, G1/2, LVI+, regardless of depth of infiltration - adjuvant RT (EBRT + BT) for unknown nodal status
- Adjuvant RT in G1/2 tumors, LVI+, node negative patients (G3??) - ESMO-ESTRO-ESGO recommendation for the whole group is adj BT if nodes are negative (at least 10 lgl, paraaortic??)
- **High-risk group**: endometrioid histology, G3, depth of infiltration ≥ 50%, regardless of LVI status - **adjuvant radiotherapy**

- FIGO stage II, endometrioid histology - adjuvant radiotherapy, adjuvant brachytherapy for G1/2, LVI- tumors, node negative
- FIGO stage III endometrioid histology, tumors of non-endometrioid histology (serous, clear-cell, undifferentiated, carcinosarcoma) - consider starting treatment with **adjuvant HT IV-VI cycles** (mandatory for FIGO IIIC1/2, FIGO III serous and clear-cell histologies, as well as for undifferentiated cancer and carcinosarcoma regardless of stage) **+ sequential adjuvant radiotherapy**

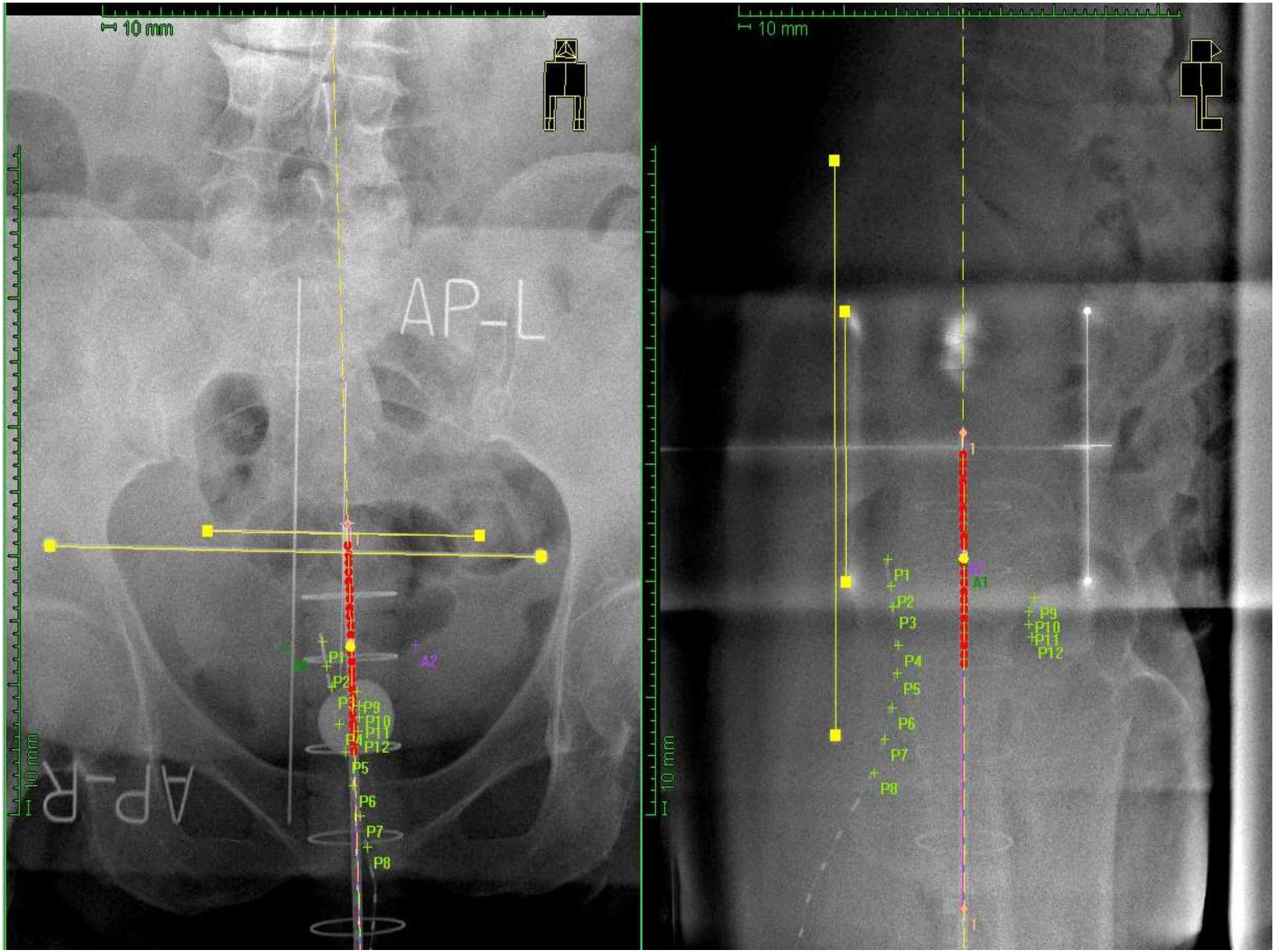
Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.

Postoperative radiotherapy of endometrial cancer

- Pelvis: 40-50 Gy, 5 days/week, 1.8-2 Gy per fraction
- Para-aortic region: 45 Gy, 1.8 Gy per fraction
- Palliative doses: 30 Gy in 10 fractions, 20 Gy in 5 fractions
- Nodal boost:
- 55Gy pelvic lymphatics SIB – within 25 fractions / sequential to total dose
- 57.5Gy para-aortic lymphatics SIB - within 25 fractions / sequential to total dose

- Brachytherapy (2D or 3D)
- Vaginal cylinder
- TD 6-7 Gy in 3-4 fractions

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.


10 mm
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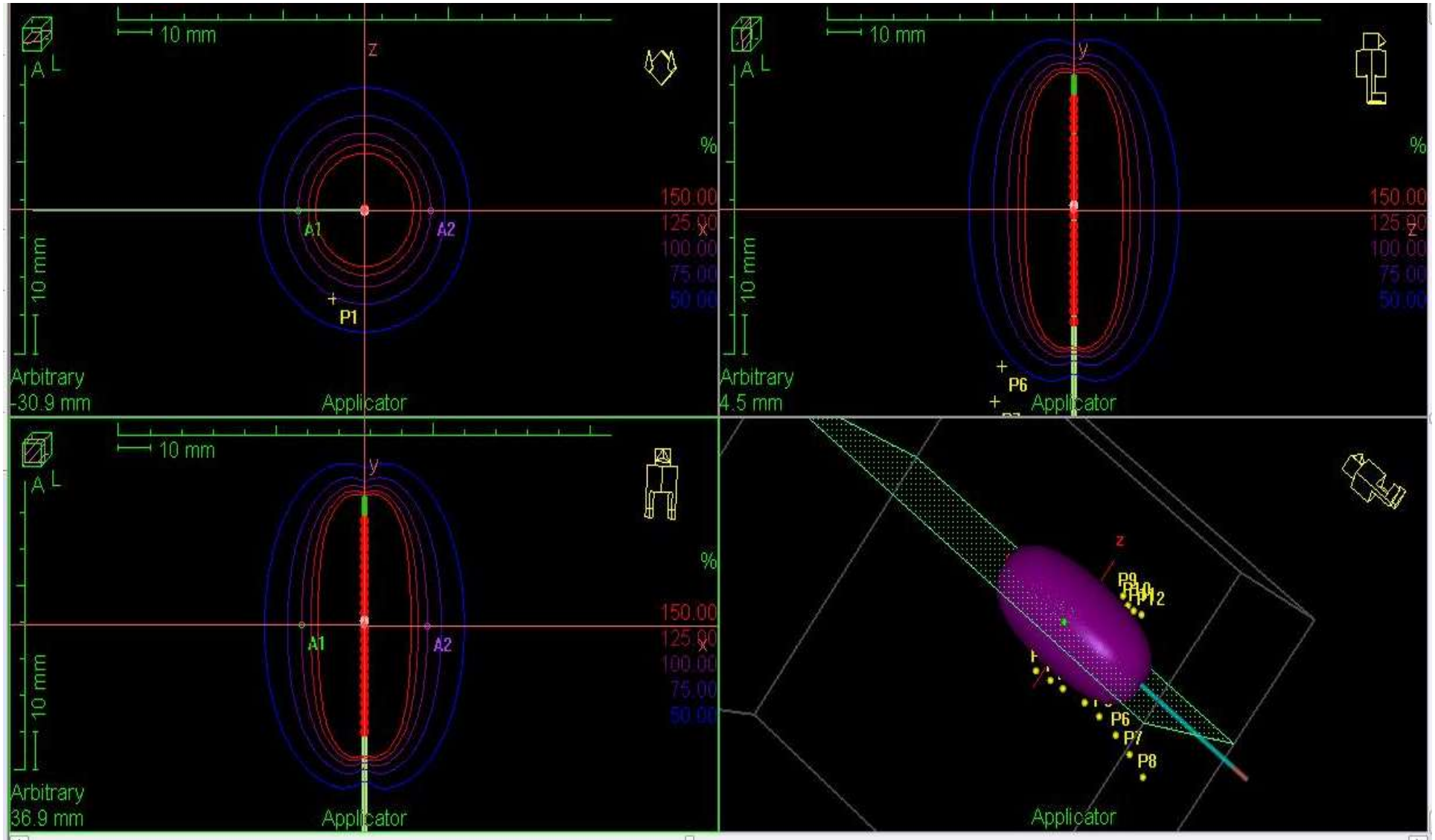


ROI Set
Plans
M2_Plan1_F1
Ap Applicator
Points
rektum
besika
Applicator

Name	X [mm]	Y [mm]	Z [mm]	Coord...	Act. Dos...	Act. Dose [%]	Normalization	Norm. Dose [%]	Optimization	Opt. Rel. Dose [%]	Opt. Weight
A1	-20.0	0.0	0.0	Applic...	701.28	100.18	yes	100.00	no	100.00	100.00
A2	20.0	0.0	0.0	Applic...	698.72	99.82	yes	100.00	no	100.00	100.00

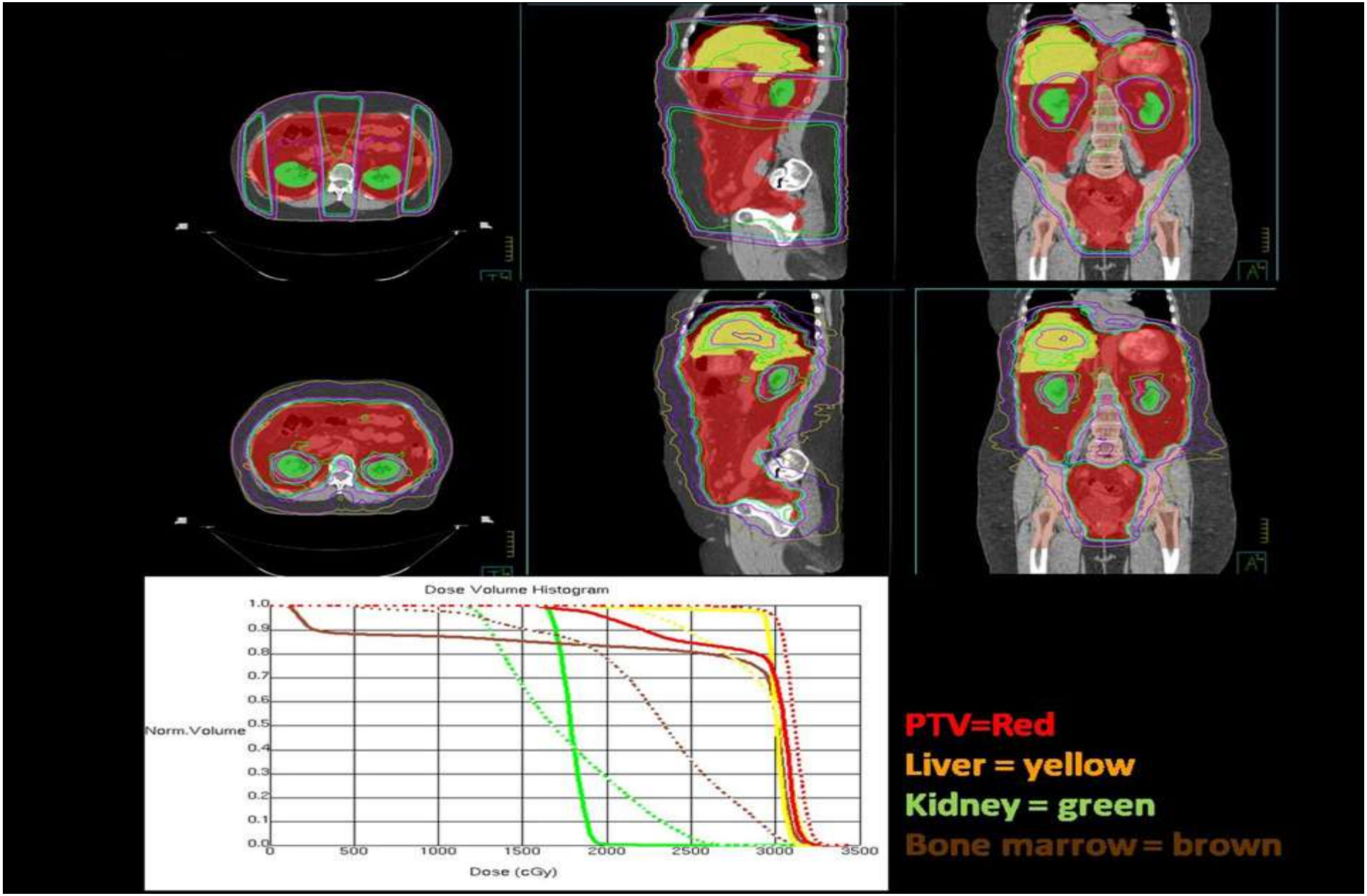
Ovarial cancer radiotherapy

- Not applicable by default
- Indicated in the adjuvant approach in locally advanced tumors (FIGO st. III) and/or the presence of residual disease

It is carried out in two phases:

- I Whole abdomen irradiation - TD 30 Gy/ 20 frakcija
- II Whole pelvis irradiation - total dose TD 45-50,4 Gy

Ministarstvo zdravlja Republike Srbije radne grupe za izradu nacionalnih radioterapijskih protokola za lečenje malignoma. Urednik V. Plešinac Karapandžić. Nacionalni radioterapijski protokoli za lečenje malignoma. Radioterapijski protokol za lečenje karcinoma grlića materice. Beograd, 2022.

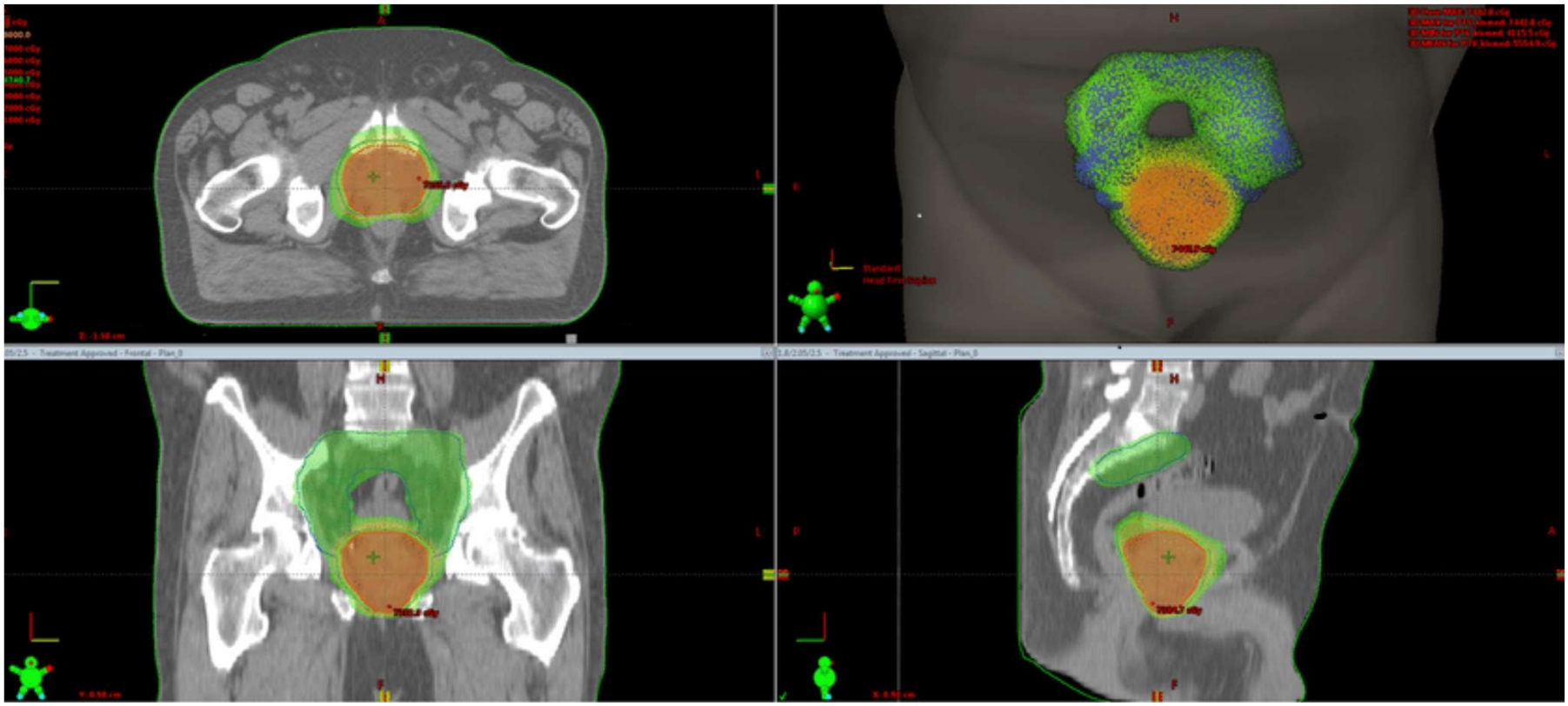


Fields EC, et al. Radiation Treatment in Women with Ovarian Cancer: Past, Present, and Future. Front Oncol 2017;7:177.

Dose limits for organs at risk according to the QUANTEC study

Blader	Dmax < 105% V45Gy < 35% V40Gy < 60% V30Gy < 80%
Rectum	Dmax < 105% V40Gy < 75% V30Gy < 95%
Bowel	Dmax < 105% V40Gy < 30% prihvatljivo V45Gy < 30% ali V40Gy < 70%
Duodenum (para-aortic)	V55Gy < 15ccm
Bone marrow	Dmax < 50Gy V50Gy < 5% V40Gy < 35% V30Gy < 50%
Kidney	Dmean < 15Gy V28Gy < 20% V23Gy < 30% V20Gy < 32% V12Gy < 55%
Spinal cord	Dmax < 45Gy
Femoral head	Dmax < 50Gy V44Gy < 5% V30Gy < 20%
Transposed ovaries (optional)	Dmax < 5-8Gy

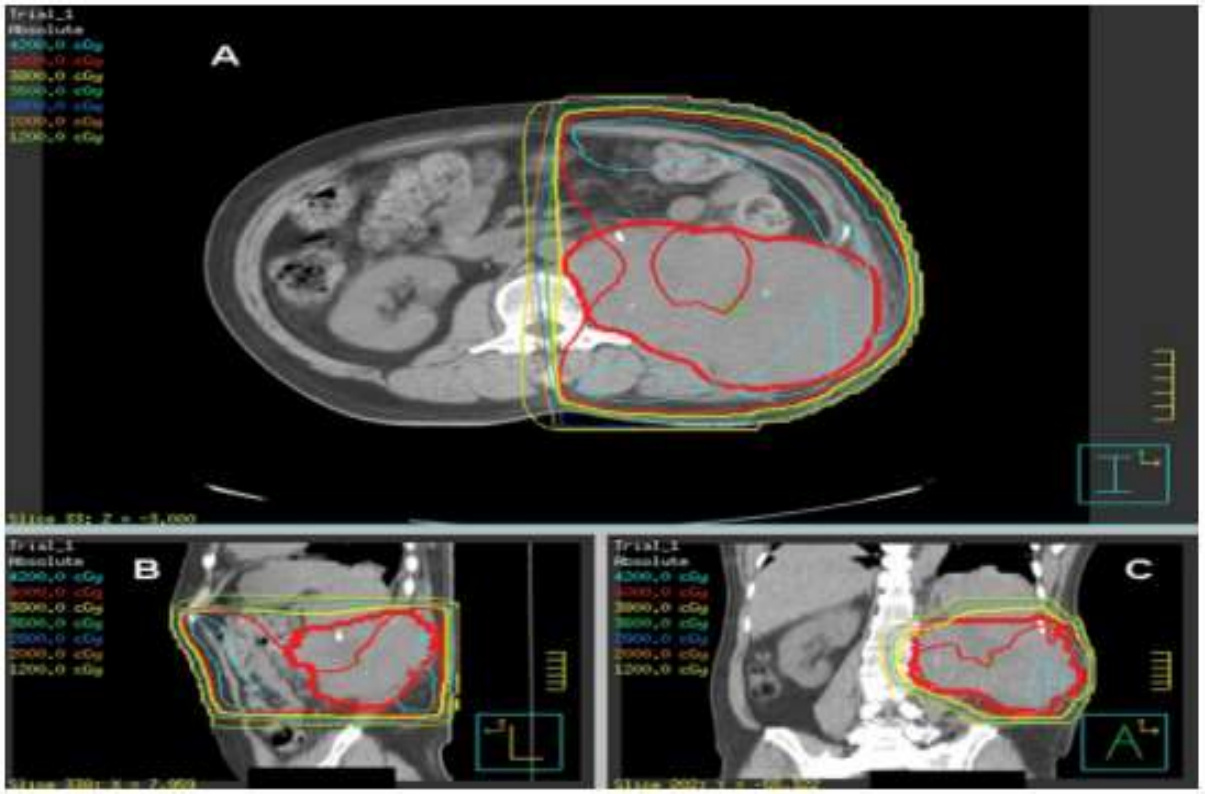
Urogenital tumors radiotherapy



Jorgo K, Polgar C, Major T, et al. Acute and Late Toxicity after Moderate Hypofractionation with Simultaneous Integrated Boost (SIB) Radiation Therapy for Prostate Cancer. A Single Institution, Prospective Study. Pathol Oncol Res 2020;26(2):905-12.

Renal cell cancer (RCC) radiotherapy

- Radioresistant tumor
- Only high RT doses are effective
- Organs at risk: liver, spinal cord, small and large intestine, spleen
- **Preoperative RT** (of unresectable and locally advanced renal carcinoma) TD 46 to 50 Gy
- **Postoperative RT** (reduction of disease recurrence rate, without significant effect on long-term survival) TD 46 to 50 Gy
- **Intraoperative radiotherapy** - monotherapy or in combination with EBRT (locally recurrent and/or locally advanced non-metastatic RCC)



Slika 3. Delineacija ciljnih volumena kod radioterapije karcinoma bubrega (Izvor: *Parashar B, Patro KC, Smith M, Arora S, Nori D, Wernicke AG. Role of radiation therapy for renal tumors. Semin Intervent Radiol 2014;31(1):86-90.*)

Renal cell cancer (RCC) radiotherapy

Stereotactic radiotherapy:

- Tumor smaller than 5 cm
- Without involvement of regional lymph nodes
- Surgical treatment is contraindicated (one functioning kidney, bilateral RCC, medically inoperable tumor or locally recurrent tumor after conservative surgical resection)
- Contraindications: large tumors

Study	Patients (*n*)	Total dose (Gy)	Fractions/fractional dose (Gy)	Outcomes
Beitler et al[20]	9 patients, 2 with bilateral RCC	40	8	4/9 patients alive at median f/u 26.7 mo
Svedman et al[22]	30 patients, 82 lesions	32, 40, 30, 45	8, 10, 15, 15	Stable disease, partial/complete response in 98% of lesions
Teh et al[25]	14 patients, 23 extracranial sites, 2 primary RCC	24–40	3–6	Median f/u 9 mo; 93% symptomatic relief, 87% LC

Renal cell cancer (RCC) radiotherapy

Palliative radiotherapy:

- Pain relief
- Alleviation of neurological symptoms
- Hematuria

- TD 45 to 50 Gy in 1.8/2 Gy per fraction
- TD 30 to 40 Gy in 2/3 Gy per fraction

Hypofractionated regimens are used in locally recurrent and oligometastatic disease.

Bladder cancer radiotherapy

- Superficial or tumors that do not infiltrate the muscle layer (Ta, Tis, T1) - frequent multiple recurrences, R1, HG II/III, (resistance to transureteral resection (TUR) and intravesical chemo/immunotherapy) and if cystectomy is not possible
- **Neoadjuvant RT** before cystectomy for stages >T2 – rare
- **Adjuvant HT/RT** after previously performed TUR or cystectomy
- **"Bladder sparing" approach**: TUR + CHT (neoadjuvant, concomitant or adjuvant) + RT
- **Radical radiotherapy** (invasive and locally/locoregionally advanced tumors (T2 -T4)
- **Palliative radiotherapy** (hematuria, bone metastases, hydronephrosis caused by tumor infiltration of the vesical confluence of the ureter)

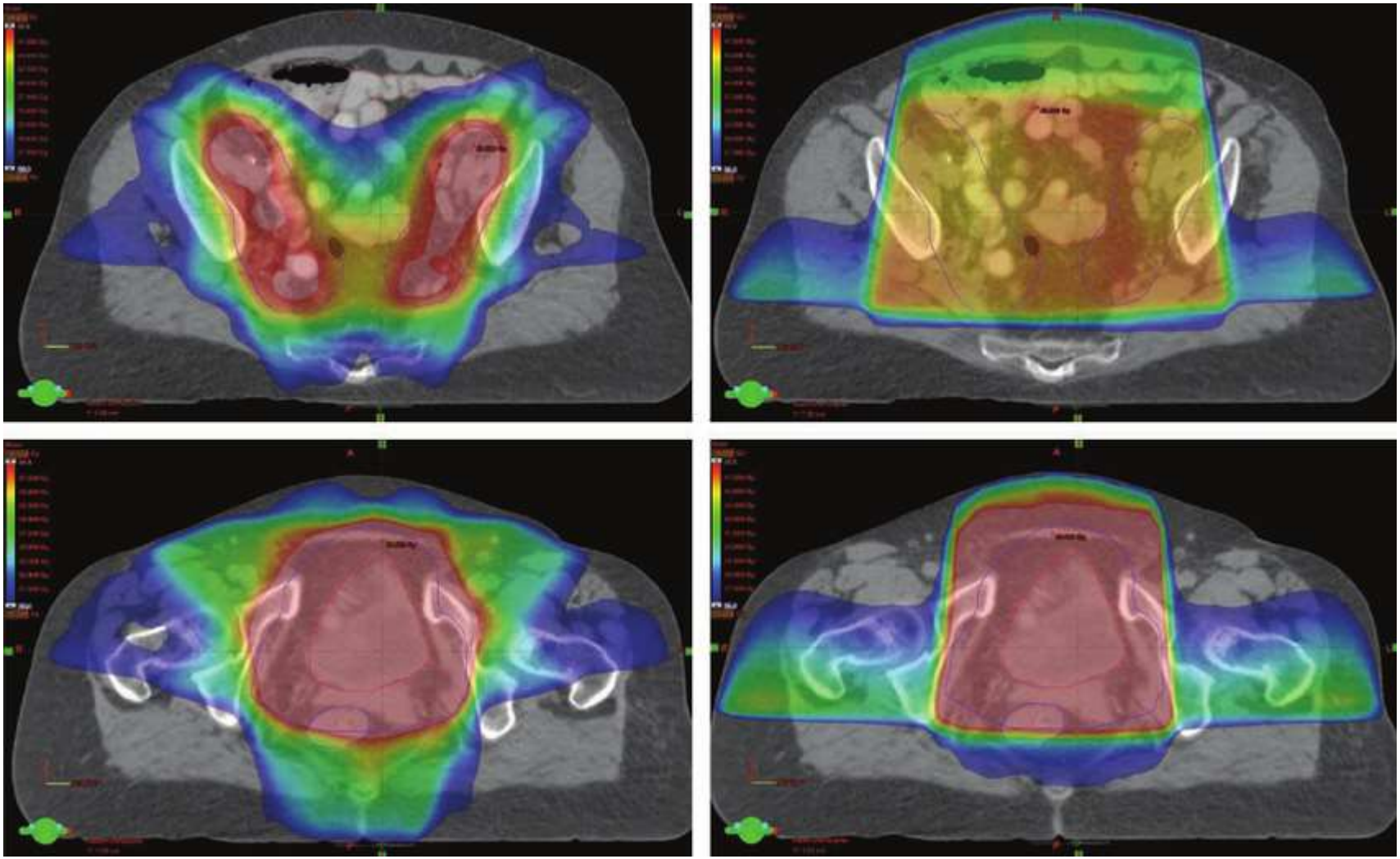
Bladder cancer radiotherapy

Radical RT:

- In one phase with TD 60-66 Gy (1.8-2 Gy per fraction)
- In two phases:
- Phase I TD 45 to 50.4 Gy
- Phase II up to total TD 60-66 Gy

Adjuvant RT:

- Phase I (tumor bed and regional lymph nodes) TD 45-50.4 Gy
- Phase II (target volume, which includes the zone of residual (R1) microscopic disease and the LN+ group with ENE) boost dose to total TD 54-60 Gy



Søndergaard J, et al. The normal tissue sparing obtained with simultaneous treatment of pelvic lymph nodes and bladder using intensity-modulated radiotherapy. Acta Oncol 2009;48(2):238-44.

Radiotherapy of prostate cancer

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INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASE[e]

Risk Group	Clinical/Pathologic Features See Staging (ST-1)			Additional Evaluation[h,i]	Initial Therapy
Very low[f]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core[g] • PSA density <0.15 ng/mL/g			• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-3
Low[f]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL			• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-4
Intermediate[f]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▸ cT2b–cT2c ▸ Grade Group 2 or 3 ▸ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[g]	• Confirmatory testing can be used to assess the appropriateness of active surveillance (See PROS-F 2 of 5)	See PROS-5
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[g]	Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-6
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL			Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5			Bone and soft tissue imaging[j,k] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7

Radiotherapy of prostate cancer

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PRINCIPLES OF RADIATION THERAPY

Table 1: Below are examples of regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.
See PROS-3, PROS-4, PROS-5, PROS-6, PROS-7, PROS-8, PROS-12, and PROS-I for other recommendations, including recommendations for neoadjuvant/concomitant/adjuvant ADT.

Regimen	Preferred Dose/Fractionation	NCCN Risk Group (✓ indicates an appropriate regimen option if RT is given)					
		Very Low and Low	Favorable Intermediate	Unfavorable Intermediate	High and Very High	Regional N1	Low Volume M1[a]
EBRT							
Moderate Hypofractionation (Preferred)	3 Gy x 20 fx 2.7 Gy x 26 fx 2.5 Gy x 28 fx	✓	✓	✓	✓	✓	
	2.75 Gy x 20 fx						✓
Conventional Fractionation	1.8–2 Gy x 37–45 fx	✓	✓	✓	✓	✓	
	2.2 Gy x 35 fx + micro-boost to MRI-dominant lesion to up to 95 Gy (fractions up to 2.7 Gy)		✓	✓	✓		
SBRT Ultra-Hypofractionation	9.5 Gy x 4 fx 7.25–8 Gy x 5 fx 6.1 Gy x 7 fx	✓	✓	✓	✓		
	6 Gy x 6 fx						✓
Brachytherapy Monotherapy							
LDR Iodine 125 Palladium 103 Cesium 131	145 Gy 125 Gy 115 Gy	✓	✓				
HDR Iridium-192	13.5 Gy x 2 implants 9.5 Gy BID x 2 implants	✓	✓				
EBRT and Brachytherapy (combined with 45–50.4 Gy x 25–28 fx or 37.5 Gy x 15 fx)							
LDR Iodine 125 Palladium 103 Cesium 131	110–115 Gy 90–100 Gy 85 Gy			✓	✓		
HDR Iridium-192	15 Gy x 1 fx 10.75 Gy x 2 fx			✓	✓		

[a] High-volume disease is differentiated from low-volume disease by visceral metastases and/or 4 or more bone metastases, with at least one metastasis beyond the pelvis vertebral column. Patients with low-volume disease have less certain benefit from early treatment with docetaxel combined with ADT.

Radiotherapy of prostate cancer

The probability of extracapsular extension (ECE), seminal vesicle invasion (SVI) and lymph node metastases (Lymph Node Metastasis Risk - LNM) is determined based on PSA and Gleason score using Roach's formulas:

ECE(%)= 3/2xPSA + 10 x (*Gleason score* - 6)

SVI(%)= PSA + 10 x (*Gleason score* - 6)

LNM(%)= 2/3PSA + 10x(*Gleason score* - 6)

Radical radiotherapy of prostate cancer

Indications for the locoregional radiotherapy are:

- T3, T4 tumor
- PSA and GS parameters for the high-risk group
- LN invasion (LN+)
- Invasion of seminal vesicles
- LNM risk 15% according to the Roach formula

Indications for local radiotherapy are:

- Early stage (T1-T2)
- PSA and GS parameters for low and medium risk groups
- LNs are not affected
- No seminal vesicle invasion
- LNM risk 15% according to the Roach formula
- High-risk group that is under long-term androgen deprivation therapy (ADT)

Radical radiotherapy of prostate cancer

1. LOCAL RADIOTHERAPY

If the risk for SVI infiltration is < 15% RT is performed in 1 phase:

- 72Gy/36 fractions
- GTV: Not seen by CT imaging
- CTV: Prostate
- PTV: CTV + margin (10mm in all directions except 8mm posteriorly)

If the risk for SVI infiltration is > 15% RT is performed in 2 phases:

Phase 1: 66 Gy/33 fractions

- GTV: Not seen by CT imaging
- CTV1: Prostate + SV
- PTV1: CTV1 + margin (10mm in all directions except 8mm posteriorly)

Phase 2: 6Gy/3 fractions

- CTV2: Prostate only
- PTV2: CTV2 + 5 mm margin in all directions

Radical radiotherapy of prostate cancer

2. LOCOREGIONAL RADIOTHERAPY - STANDARD FRACTIONATION

If the risk for LN infiltration is > 15% RT is performed in 3 stages:

Phase 1: 44 Gy/22 fractions

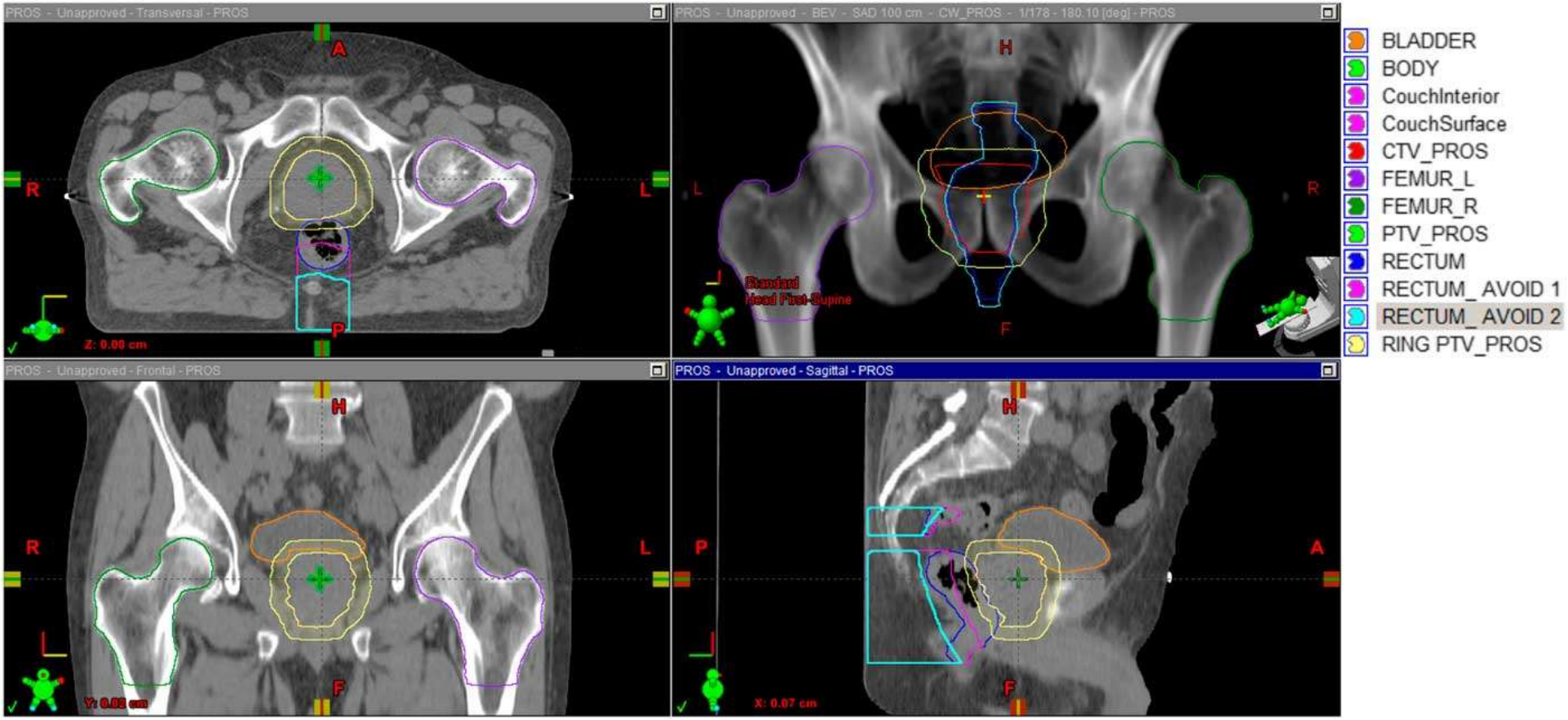
- GTV: Not seen by CT imaging
- CTVln: Regional lymph nodes
- CTV1: Prostate + SV+ CTVln
- PTV1: CTV1 + margin (10mm in all directions except 8mm posteriorly)

Phase 2: 22Gy/11 fractions

- CTV2: Prostate + SV
- PTV2: CTV2 + margin (10mm in all directions except 8mm posteriorly)

Phase 3: 6 Gy/3 fractions

- CTV3: Prostate



Darko J, Osei E, Fleck A, Rachakonda R. Retrospective dosimetric evaluation of VMAT plans for prostate cancer treatment. Journal of Radiotherapy in Practice. Cambridge University Press 2019;18(2):155–64.

Radical radiotherapy of prostate cancer

3. LOCAL RADIOTHERAPY - MODERATELY HYPOFRACTION

- in all stages, except for metastatic disease
- 60 Gy /20 fractions, 70.2 Gy /26 fractions, 70 Gy /28 fractions

4. LOCAL RADIOTHERAPY - ULTRA HYPOFRACTIONATION

- in the absence of positive LN and metastatic disease
- 38 Gy /4 fractions, 40 Gy /5 fractions, 42.7 Gy /7 fractions, 36 Gy /6 fractions

4. RADICAL RADIOTHERAPY IN OLIGOMETASTATIC DISEASE (UP TO 4 BONE METASTASES) WITH ANDROGEN DEPRIVATION THERAPY

- 55 Gy /20 fractions, 36 Gy / 6 fractions

Postoperative/Salvage RT of prostate cancer

- **Postoperative RT** is not routinely administered after surgery if the PSA level is undetectable

Indications:

- **Adjuvant RT** - within 6 months of surgery in high-risk group with positive surgical margins - R1 resection
- **Salvage RT** - if PSA later rises in 3 consecutive measurements (biochemical relapse), i.e. detectable or persistent PSA after RP (PSA after RP of > 0.2 ng/ml) or if local recurrence occurs

Postoperative/Salvage RT of prostate cancer

1. LOCAL REGIONAL RADIOTHERAPY – 2 phases

Phase 1: 44 Gy/22 fractions

- There is no GTV after prostatectomy.
- CTVln: Regional lymph nodes
- CTV1: prostate bed +/- seminal vesicles bed +/CTVln
- PTV1: CTV1 + margin (10mm in all directions except 5mm posteriorly)

Phase 2: 22 Gy/11 fractions

- CTV2: prostate bed +/- seminal vesicles bed
- PTV2: CTV2 + margin (10mm in all directions except 5mm posteriorly)

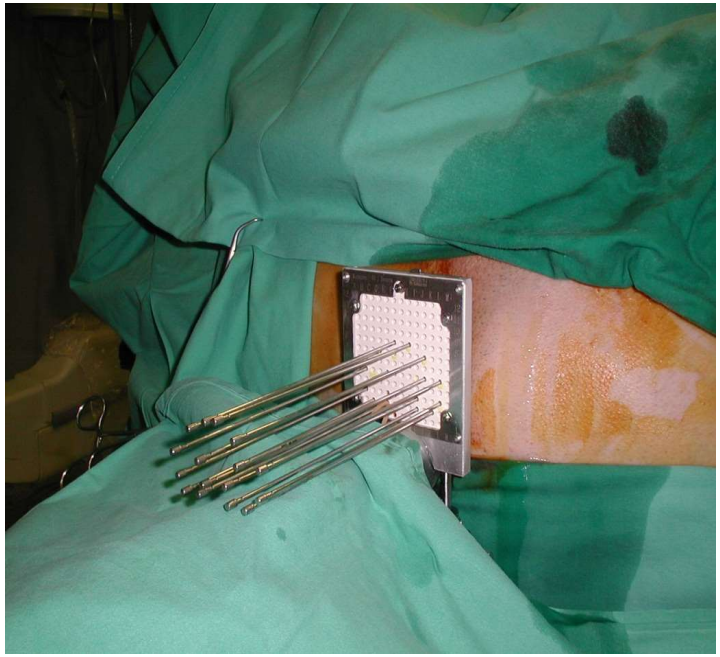
2. LOCAL RADIOTHERAPY – 1 phase

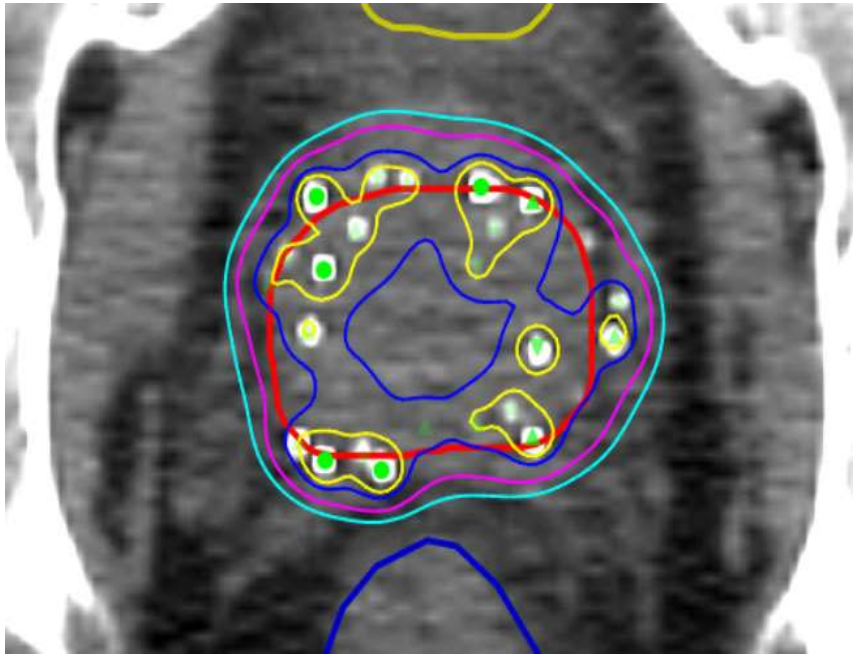
- 66 Gy/33 fractions
- CTV: prostate bed +/- seminal vesicles bed
- PTV: CTV + margin (10mm in all directions except 5mm posterior - additional margin in direction of extracapsular extension (ECE) or positive surgical margin). If the margin passes the rectal wall, do not place an additional margin towards the rectum or 6 mm towards the rectum.

Robin TP, et al. Post-Prostatectomy Radiation Therapy: Patient Selection, Timing, Imaging, and Therapy Intensification. Oncology (Williston Park). 2018;32(7):360-3.

Brachytherapy (interstitial) prostate cancer

- **Monotherapy** (low risk, radical treatment of localized prostate cancer)
- **EBRT and ADT** (medium, and in rare cases also high risk group)





Murthy V, et al. Prostate-Only Versus Whole-Pelvic Radiation Therapy in High-Risk and Very High-Risk Prostate Cancer (POP-RT): Outcomes From Phase III Randomized Controlled Trial. J Clin Oncol 2021 ;39(11):1234-42.

Digestive tract tumors radiotherapy

Slika: https://cdhf.ca/en/digestive-conditions/colon-cancer/

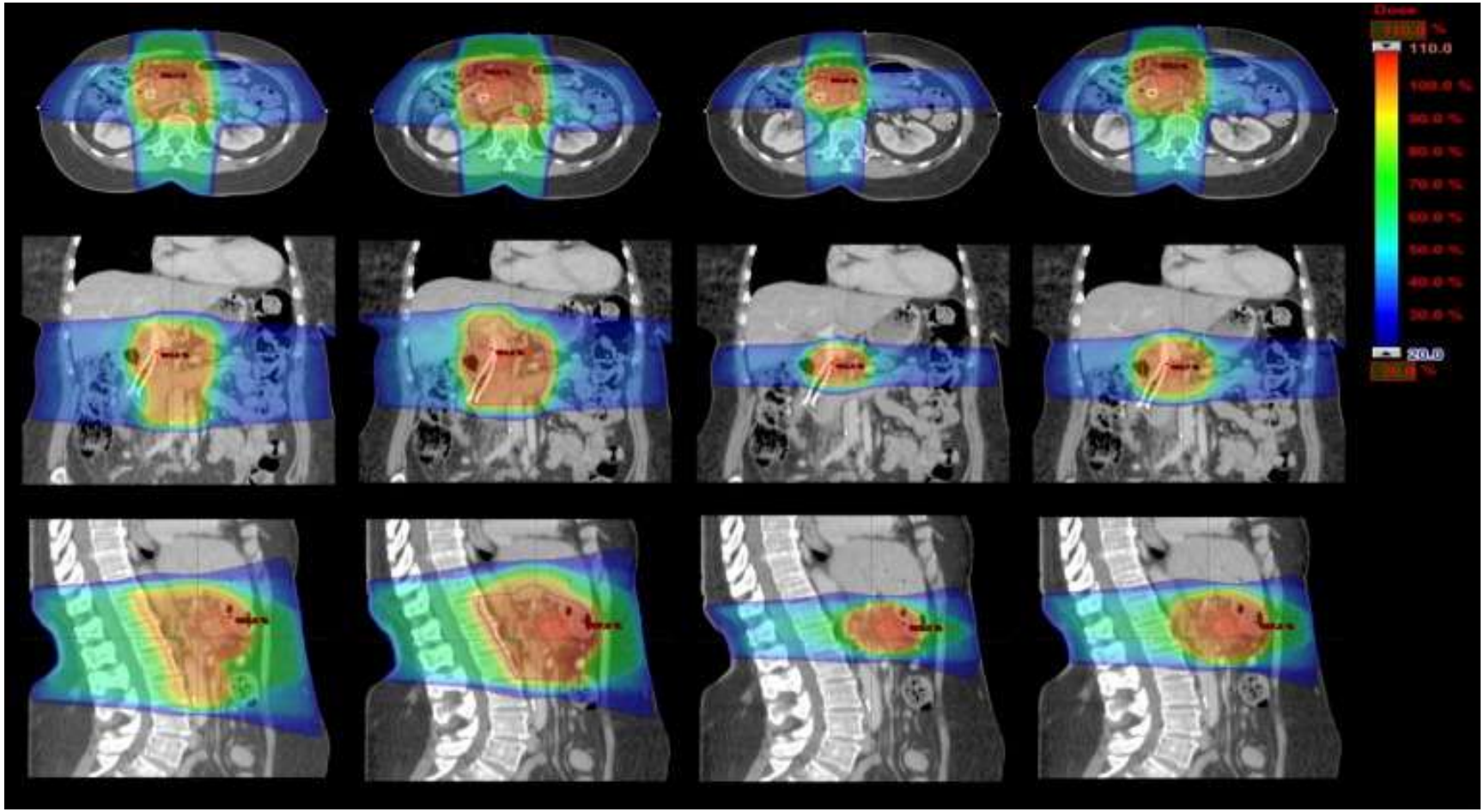
Pancreatic cancer radiotherapy

Preoperative or definitive RT +/- CHT

Adjuvant RT +/- CHT

- local recurrences rate reduction
- highly sophisticated RT techniques 45 Gy (daily dose 1.8 Gy)
- if the surgery is not satisfactory

Using the SBRT radiation technique, it is possible to apply a "boost" dose to the reduced target volume.



Fokas E, et al. A treatment planning comparison of four target volume contouring guidelines for locally advanced pancreatic cancer radiotherapy. Radiother Oncol 2013;107(2):200-6.

Hepatocellular carcinoma (HCC) radiotherapy

- Not applicable by default
- Highly sophisticated techniques
- SBRT shows promising results for the treatment of smaller primary tumor changes
- Precise application of a high therapeutic radiation dose (BED >100 Gy) to a respiratory mobile target volume in the liver

SBRT of liver metastases indications:

- up to 3 (metachronous) metastases
- not larger than 6 cm (best up to 3 cm)
- ECOG status 0-2
- CHT before and after SBRT

Esophageal carcinoma radiotherapy

- **Neoadjuvant CHT-RT** (stages cT1b-T2N+; cT/cT and any cN+)
- Phase I TD of 41.4 Gy applied in 23 fractions
- Phase II TD 9 Gy in 5 fractions (only tumor and PET+ Ln)

- **Definitive CHT-RT** - cT4b stage (potentially curative approach in patients with SCC)

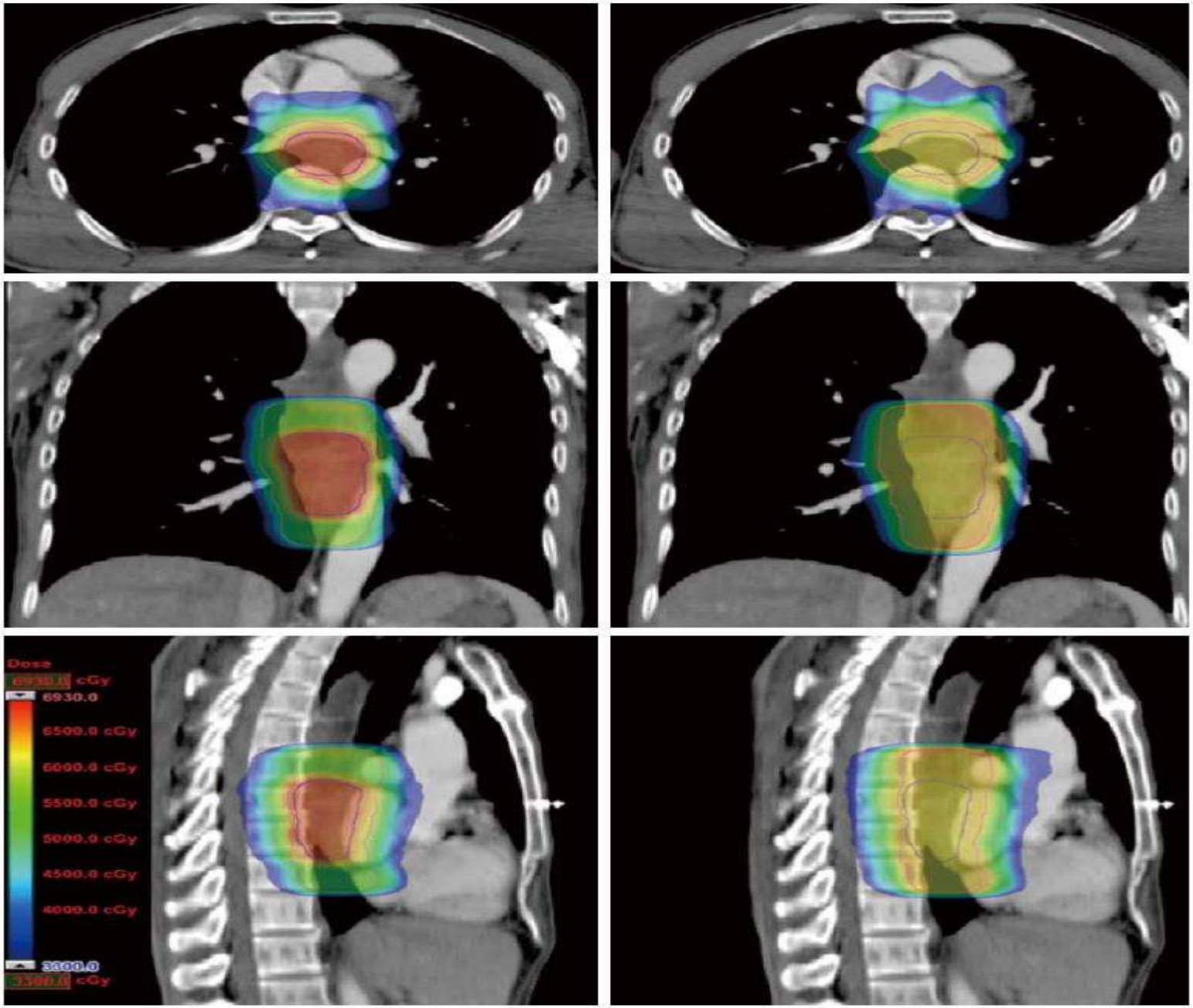
- **Palliative RT**

Recommendations for the treatment of squamous carcinoma (SCC) of the esophagus according to the stage

Stage 0 and Ia (T1a and T1b)	Esophagectomy Endoscopic mucosal resection or submucosal dissection with/without photodynamic therapy or radiofrequency ablation
Stage IB (T2-3N0), II and III (including patients with positive LN) – inoperabins	The general approach for these stages is: preoperative chemotherapy (5-FU + cisplatin) + radiotherapy -» surgery
Stage IV - palliative therapy	Palliative chemotherapy Palliative chemoradiotherapy Palliative radiotherapy Palliative surgery Palliative symptomatic and supportive therapy.

Recommendations for the treatment of adenocarcinoma of the esophagus according to the stage

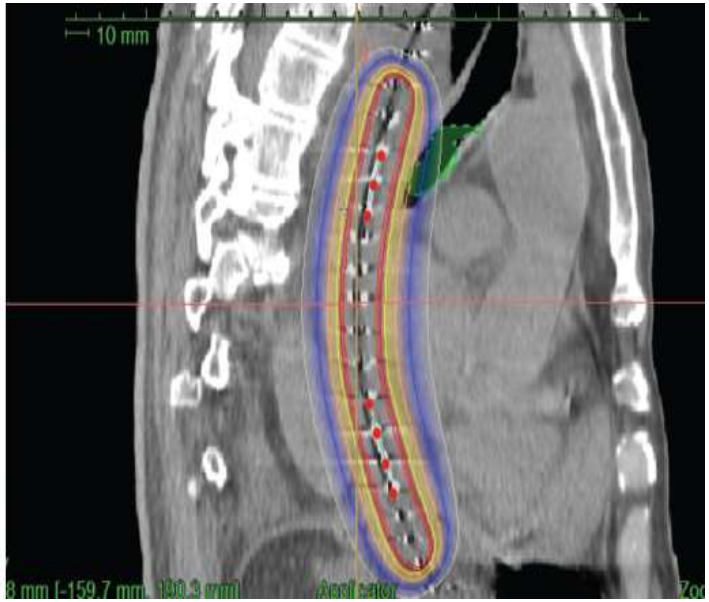
Stage 0 and Ia (T1a and T1b)	Esophagectomy Endoscopic mucosal resection or submucosal dissection with/without photodynamic therapy or radiofrequency ablation
Stage IB (T2-3N0), II and III (including patients with positive LN) – inoperable	Preoperative chemoradiotherapy (5-FU + cisplatin, 50 Gy), followed by diagnostics to assess operability
Stage III and IVA (operable), for patients with ECOG PS 0 or 1	Preoperative chemotherapy (5-FU + cisplatin) + radiotherapy -* surgery
Stage IV - palliative therapy	Cocurrent chemotherapy (5-FU + cisplatin) and radiotherapy Monotherapy such as: radiotherapy, chemotherapy Palliative surgery Palliative symptomatic, supportive and roborant therapy Placement of stents, dilators, endoscopic laser therapy



Zhang WZ, Chen JZ, Li DR, et al. Simultaneous modulated accelerated radiation therapy for esophageal cancer: a feasibility study. World J Gastroenterol. 2014;20(38):13973-80.

Brachytherapy of esophageal cancer

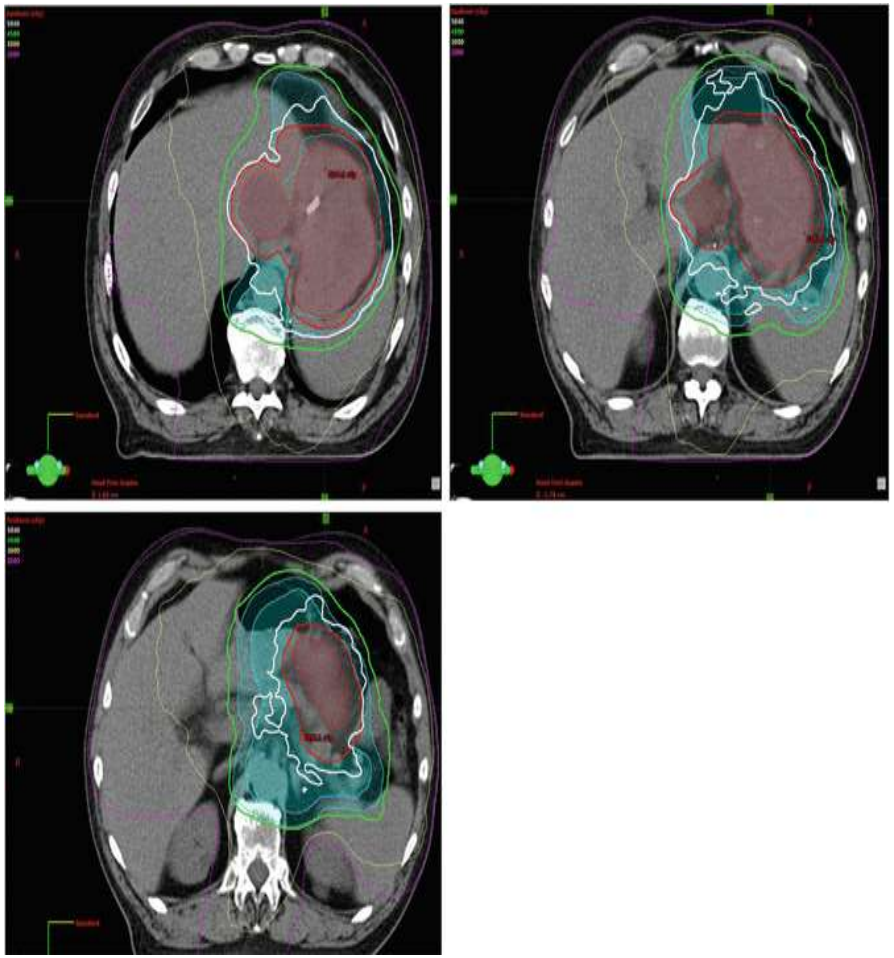
- Intraluminal, alone or in combination with laser ablation or EBRT
- The dose is prescribed at 1 cm lateral to the axis of the catheter
- Simple palliative regimens 1x 15Gy
- Local boost combined with EBRT 1 x 7.5 Gy at the beginning and end of EBRT
- Metastatic esophageal cancer with dysphagic complaints 1-2 x 6-10 Gy



Slika: https://radiologykey.com/gastrointestinal-brachytherapy/

Gastric cancer radiotherapy

- **RT combined with sequential and concomitant CHT** (Cisplatin/5-fluorouracil/leucovorin)
- **Preoperative RT** - 45 Gy in 25 fractions (tumors of the GEJ region, enables R0 resection)
- **Postoperative RT+/- CHT** - TD- 45 Gy in 25 fractions (stages II and III, suboptimal surgery, R1)
- **Metastatic disease** hypofractionated RT: symptomatic locally advanced or recurrent disease, bleeding, obstruction or pain



Hallemeier, C.L., Haddock, M.G. (2017). Gastric Cancer: Radiation Therapy Planning. In: Hong, T., Das, P. (eds) Radiation Therapy for Gastrointestinal Cancers. Springer, Cham. https://doi.org/10.1007/978-3-319-43115-4_6

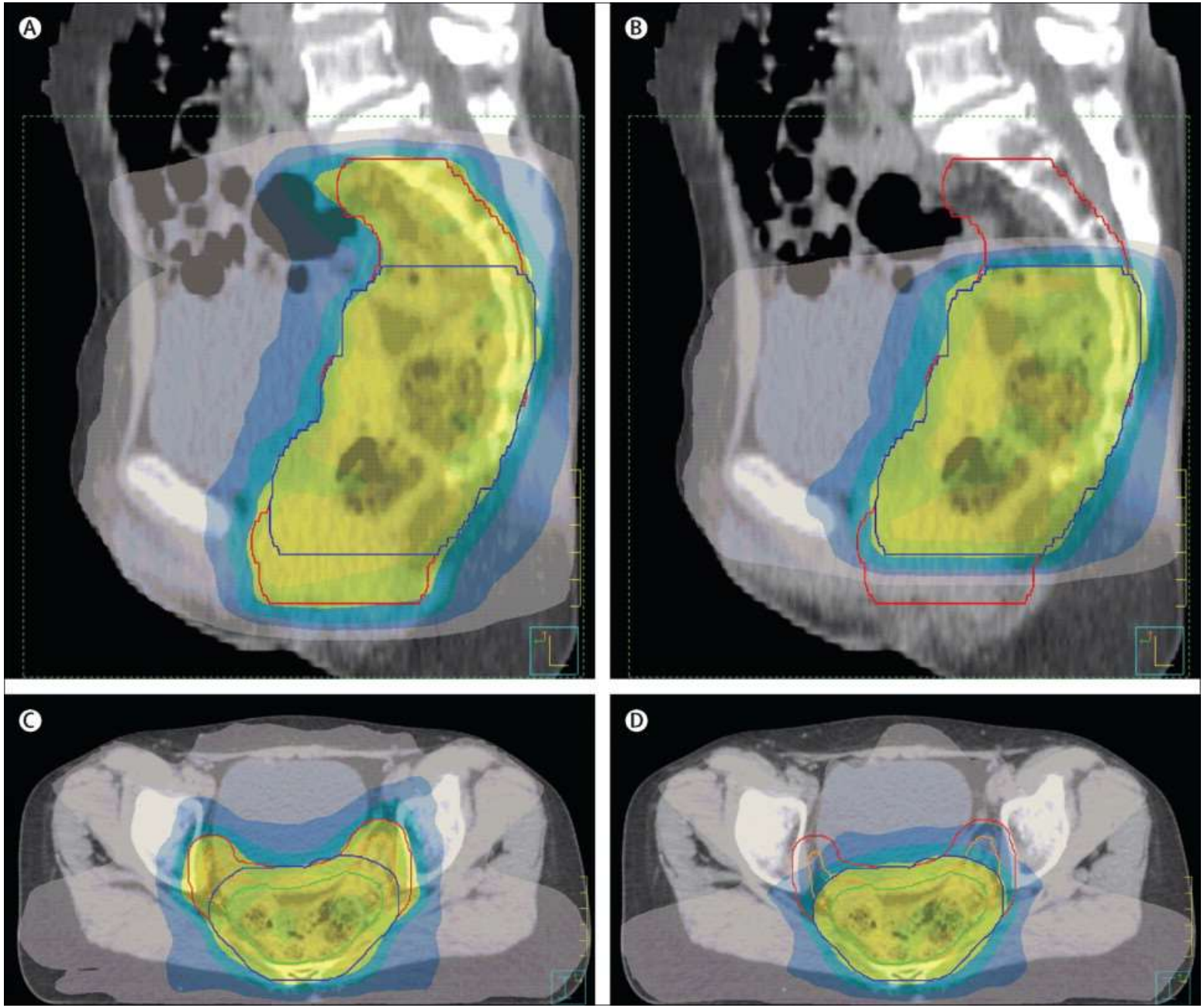
Radiotherapy of colon and rectal cancer

Neoadjuvant RT + CHT (5-Fu +/- oxaliplatin): stage II and III rectal cancer

- Primary aim: downsizing, downstaging, devitalization of tumor cells, increasing the efficiency of surgery, local disease control and long-term survival.
- Surgery follows 10-12 weeks after completion of RT
- In the case of complete responce (CR), with frequent controls, the application of operative treatment can be delayed until a possible relapse of the disease (the so-called "watch and wait" approach)

Preoperative RT as monotherapy in a hypofractionated regimen, and surgery is performed within seven days of RT ("short course")

- Hypofractionated radiation (without chemotherapy), for the same PTV prescribes a dose of 25 Gy in 5 fractions.

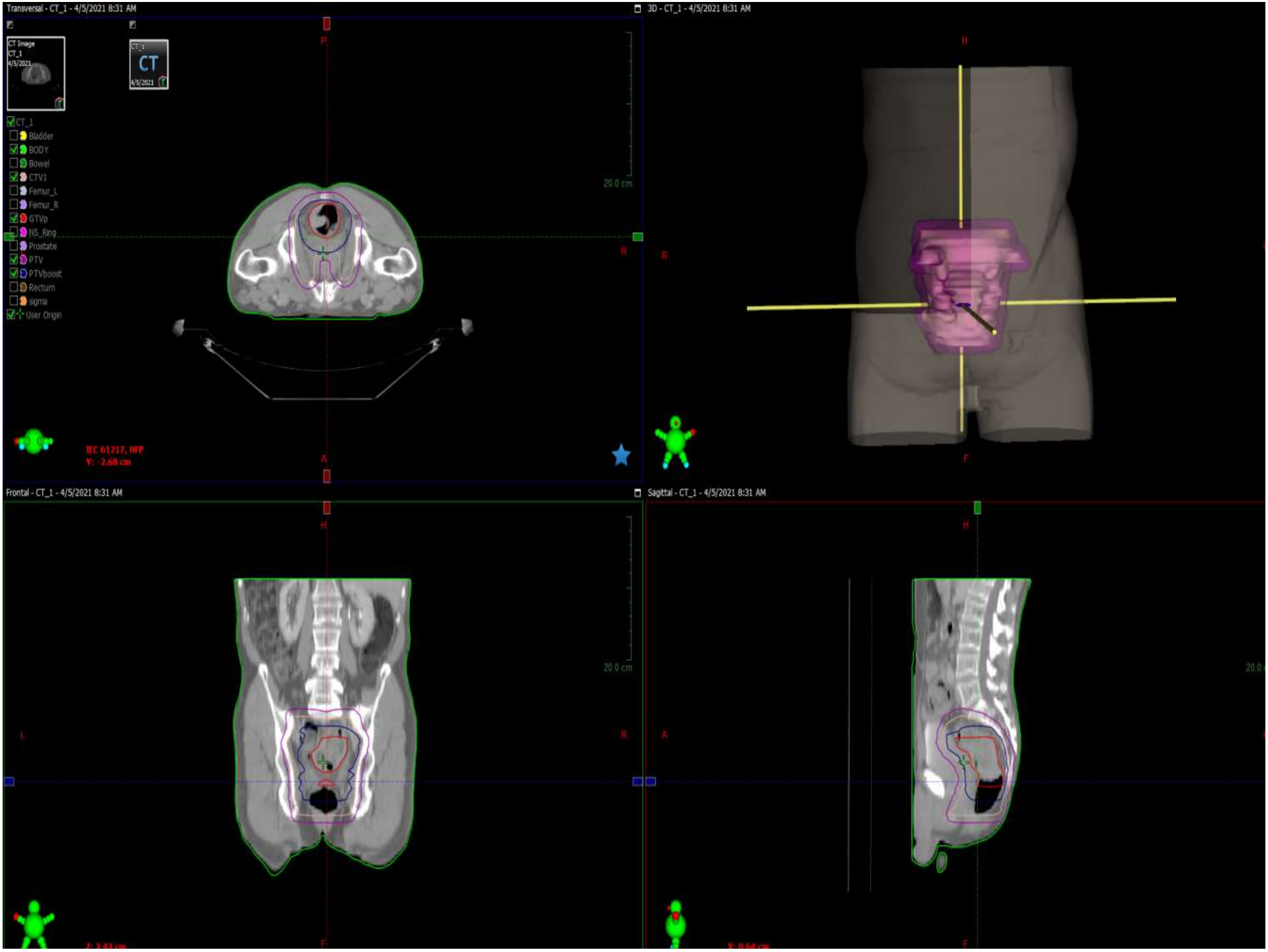


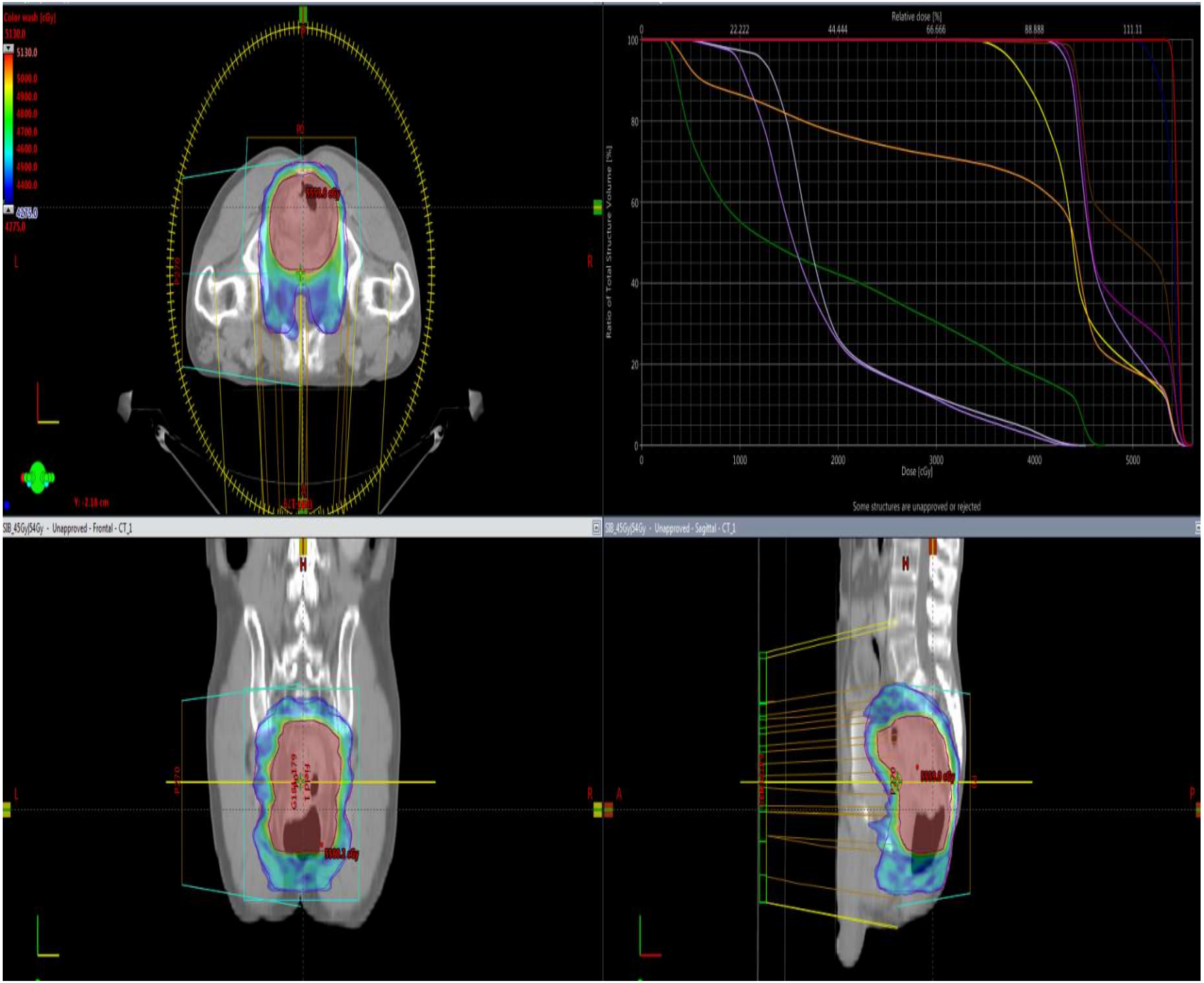
Marijnen CA. Organ preservation in rectal cancer: have all questions been answered? Lancet Oncol. 2015 Jan;16(1):e13-22.

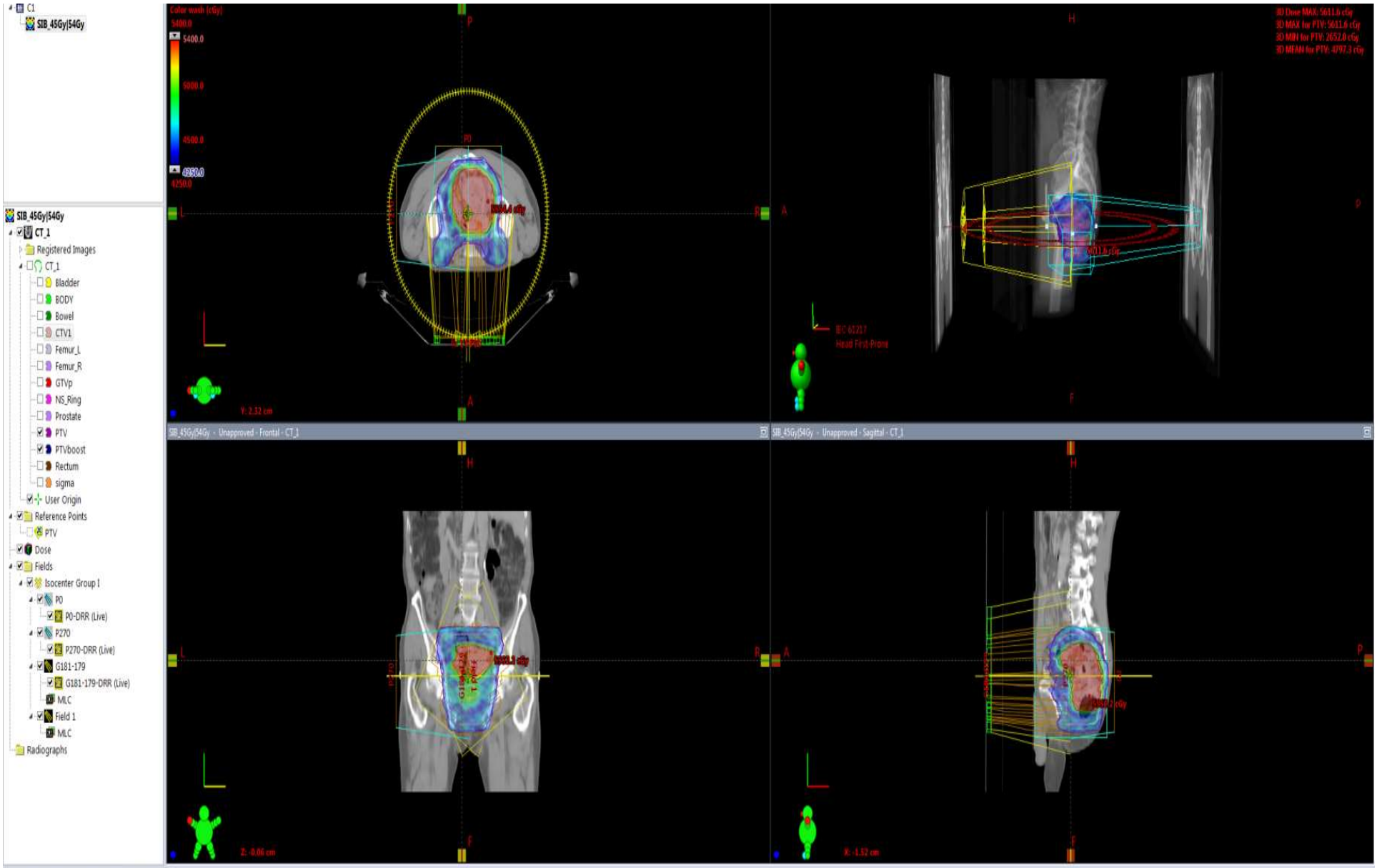
Radiotherapy of colon and rectal cancer

- **Adjuvant (postoperative) RT +/- CHT** (5-Fu) 4-6 weeks after surgery: pT3> pT4, pN+ stage, tumor infiltration of perirectal tissue and surrounding organs, resection margins <3 mm, tumor >3 cm, LVI positive LN or R1/2 resection in pT2N0 stage disease.
- Positive resection margins (R1) after performed preoperative HT-RT and operative treatment - consider postoperative application of a boost dose to the tumor bed of 25 Gy in 5 fractions using the SBRT technique, before performing adjuvant HT


CT Image
CT_1
4/5/2021
CT_1
CT
4/5/2021
CT_1
Bladder
BODY
Bowel
CTV1
Femur_L
Femur_R
GTVp
NS_Ring
Prostate
PTV
PTVboost
Rectum
sigma
User Origin
P
A
R
20.0 cm
IEC 61217, HFP
Y: 2.82 cm
H
F
L
Frontal - CT_1 - 4/5/2021 8:31 AM
Z: 1.53 cm
Sagittal - CT_1 - 4/5/2021 8:31 AM
X: 0.64 cm


Transversal - CT_1 - 4/5/2021 8:31 AM
CT Image
CT_1
4/5/2021
CT_1
CT
4/5/2021
CT_1
Bladder
BODY
Bowel
CTV1
Femur_L
Femur_R
GTVp
N5_Ring
Prostate
PTV
PTVboost
Rectum
sigma
User Origin
P
R
A
20.0 cm
IEC 61217, HFP
Y: -2.68 cm
3D - CT_1 - 4/5/2021 8:31 AM
H
R
F
Frontal - CT_1 - 4/5/2021 8:31 AM
H
L
R
F
20.0 cm
Sagittal - CT_1 - 4/5/2021 8:31 AM
H
A
F


Color wash [cGy]
5130.0
5130.0
5000.0
4900.0
4800.0
4700.0
4600.0
4500.0
4400.0
4275.0
4275.0
Relative dose [%]
0
22.222
44.444
66.666
88.888
111.11
100
80
60
40
20
0
Ratio of Total Structure Volume [%]
0
1000
2000
3000
4000
5000
Dose [cGy]
Some structures are unapproved or rejected
SIB_45Gy|54Gy - Unapproved - Frontal - CT_1
SIB_45Gy|54Gy - Unapproved - Sagittal - CT_1



Fields | Dose | Reference Points | Dose Statistics

Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [cGy]	Max Dose [cGy]	Mean Dose [cGy]
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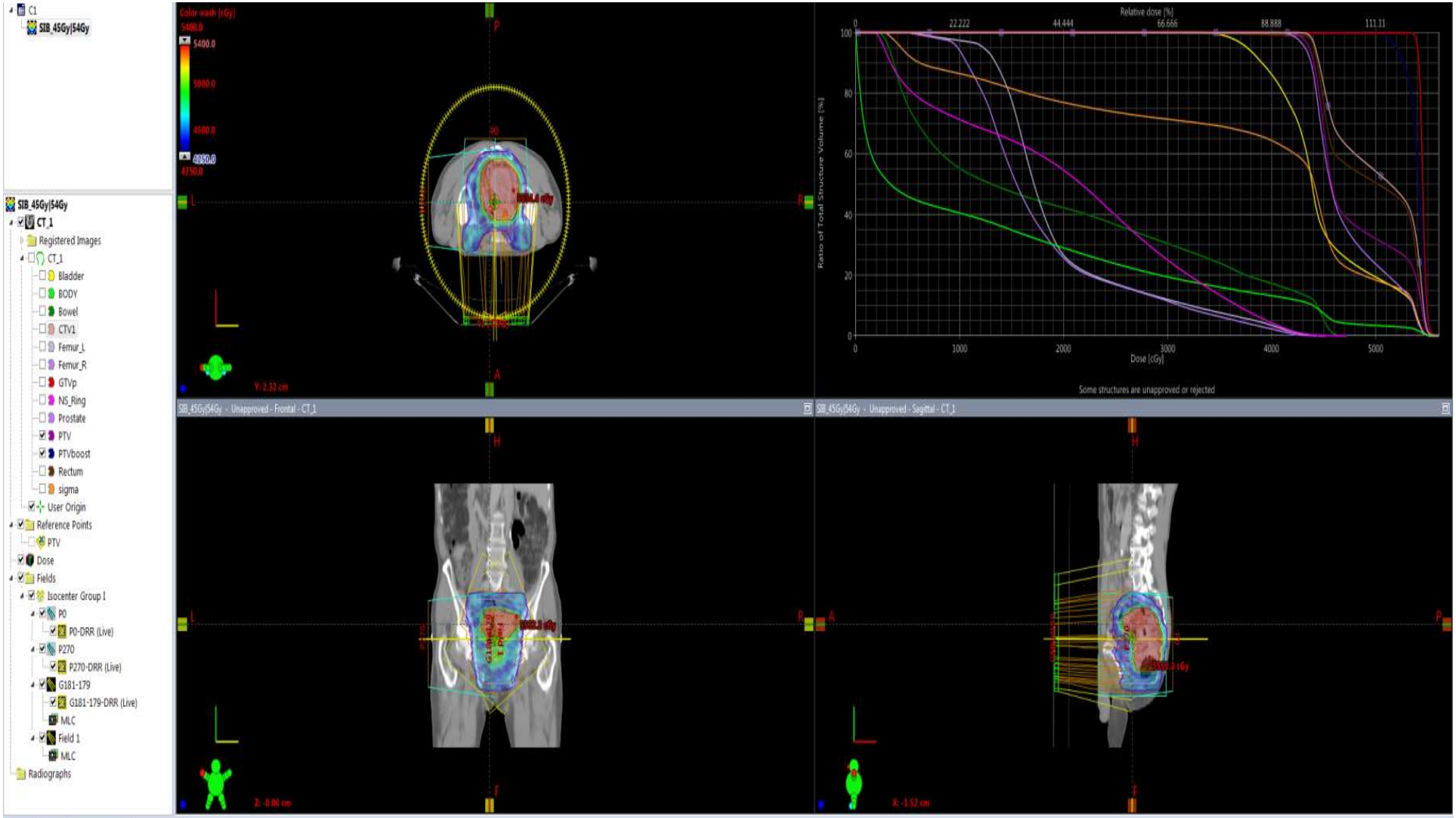
	Bladder	Unapproved	SIB_45Gy/54Gy	C1	244.1	100.0	100.0	3251.9	5530.9	4488.1
	Bowel	Unapproved	SIB_45Gy/54Gy	C1	381.8	100.0	100.0	198.9	4713.9	1942.1
	Femur_L	Unapproved	SIB_45Gy/54Gy	C1	177.5	100.0	100.0	449.9	4521.4	1953.4
	Femur_R	Unapproved	SIB_45Gy/54Gy	C1	178.1	100.0	100.0	434.7	4433.9	1799.6
	Rectum	Unapproved	SIB_45Gy/54Gy	C1	151.4	100.0	100.0	1995.1	5611.6	4949.4
	sigma	Unapproved	SIB_45Gy/54Gy	C1	349.2	100.0	100.0	274.2	5565.1	3642.4
	CTV1	Unapproved	SIB_45Gy/54Gy	C1	1315.4	100.0	100.0	4231.9	5611.6	5007.5



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☑	Bladder	Unapproved	SIB_45Gy|54Gy	C1	244.1	100.0	100.0	3251.9	5530.9	4488.1
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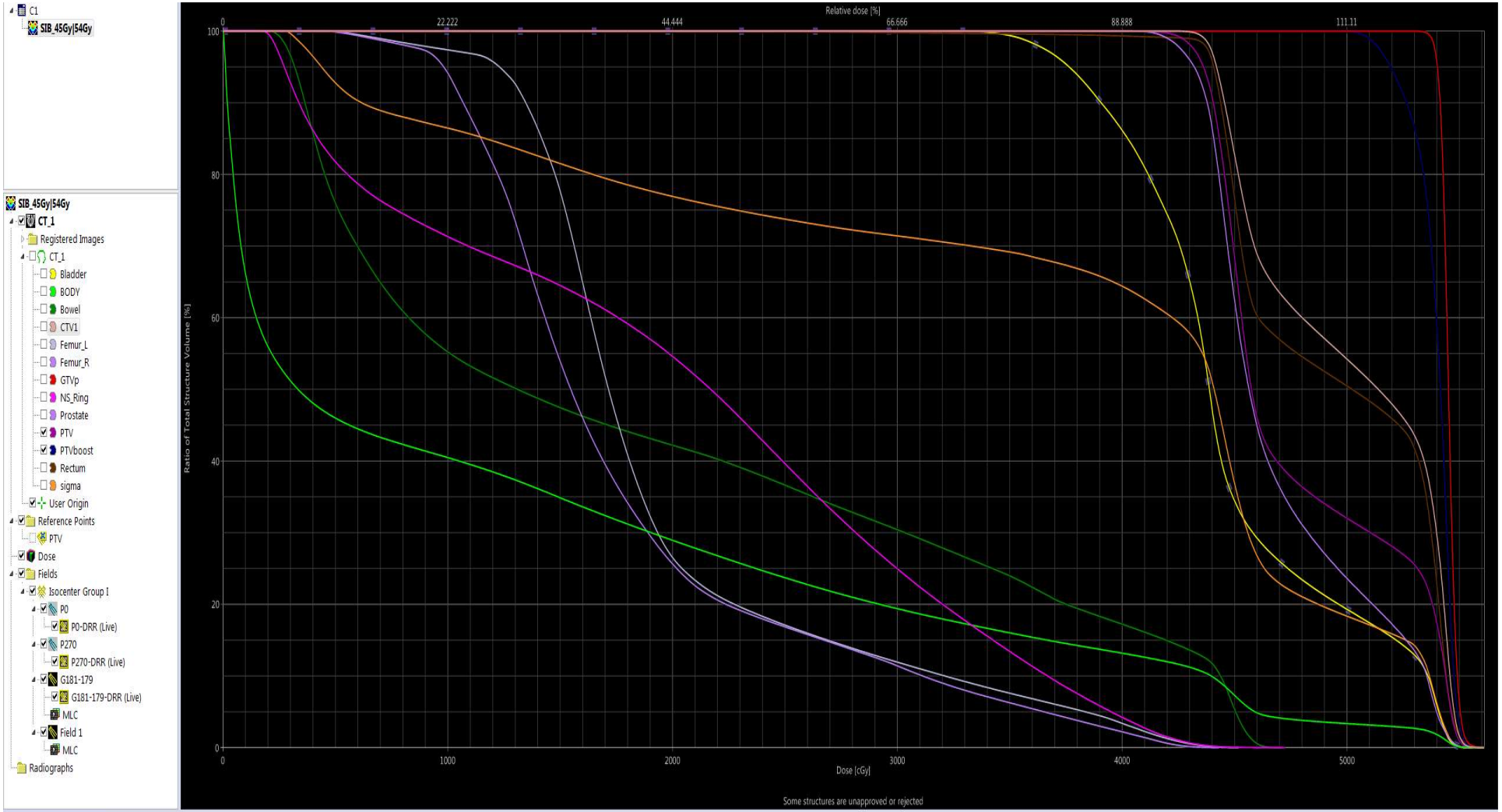
☑	sigma	Unapproved	SIB_45Gy|54Gy	C1	349.2	100.0	100.0	274.2	5565.1	3642.4
☑	CTV1	Unapproved	SIB_45Gy|54Gy	C1	1315.4	100.0	100.0	4231.9	5611.6	5007.5
☑	GTVp	Unapproved	SIB_45Gy|54Gy	C1	162.0	100.0	100.0	5299.6	5603.9	5452.5
☑	PTVboost	Unapproved	SIB_45Gy|54Gy	C1	662.2	100.0	100.0	4823.9	5611.6	5392.2
☑	PTV	Unapproved	SIB_45Gy|54Gy	C1	2245.5	100.0	100.0	2652.0	5611.6	4797.3
☑	Prostate	Unapproved	SIB_45Gy|54Gy	C1	87.4	100.0	100.0	4008.5	5554.1	4713.5
☑	NS_Ring	Unapproved	SIB_45Gy|54Gy	C1	6205.5	100.0	99.7	101.5	4723.4	2030.1



Dose | Reference Points | Dose Statistics

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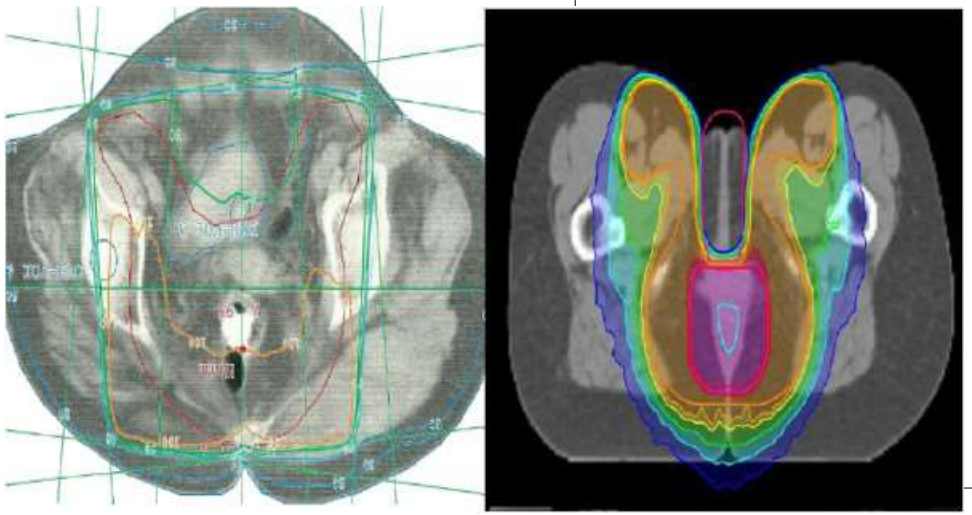
☑	Prostate	Unapproved	SIB_45Gy|54Gy	C1	87.4	100.0	100.0	4008.5	5554.1	4713.5
☑	NS_Ring	Unapproved	SIB_45Gy|54Gy	C1	6205.5	100.0	99.7	101.5	4723.4	2030.1

Anal cancer radiotherapy

- EBRT or brachytherapy
- **Neoadjuvant to competitive EBRT and CHT**
- The original **"Nigro regimen"** of this therapy includes chemotherapy in the first and fifth weeks with continuous radiotherapy.
- D1-D5 for 5 weeks: 5-Fu 1000 mg/m2/day by continuous i.v. infusion D1-D4 and D29-D32 + Mitomycin 10 mg/m2 i.v. Dl and D29.



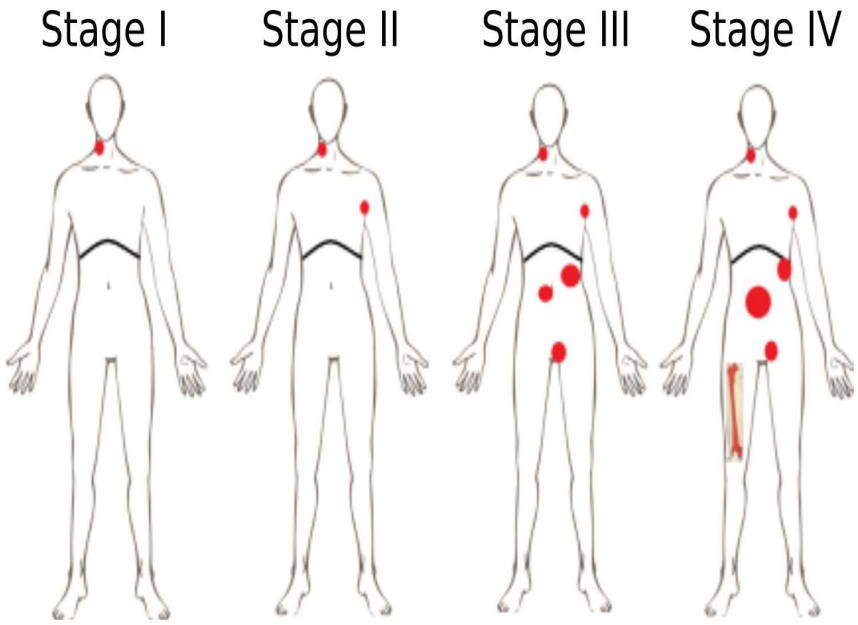
Koerber SA, Slynko A, Haefner MF, Krug D, Schoneweg C, Kessel K, Kopp-Schneider A, Herfarth K, Debus J, Sterzing F. Efficacy and toxicity of chemoradiation in patients with anal cancer--a retrospective analysis. Radiat Oncol 2014;9:113.

Radiotherapy of lymphoma

- Early Hodgkin's disease – Clinical stage (CS) IA or CS IIA
- A modern approach
- "Minimal invasive therapy"
- Short – course CHT + involved field RT

I and II CS - after II-IV cycles of CHT, involved field radiotherapy (IFRT) or involved site radiotherapy (ISRT) (20-30 Gy) is considered

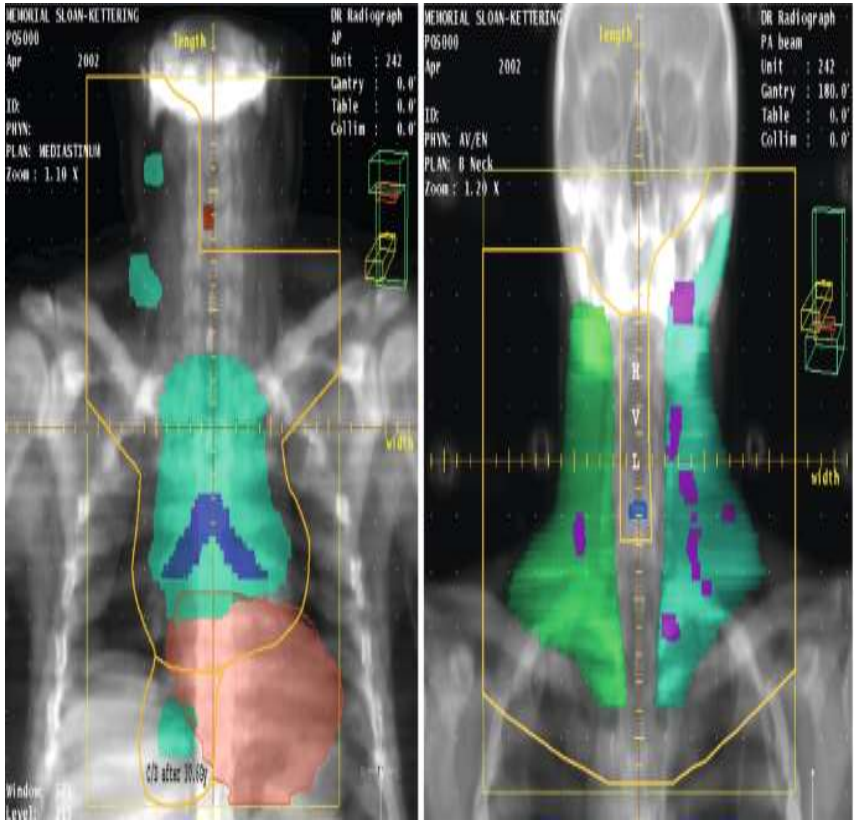
III and IV CS - after CHT effect assessment, ISRT (30 Gy)



Slika: https://filinf.it/en/about-limphomas/prognosis/

Hodgkin's (HL) lymphoma

- 30-36Gy in 20 fractions - macroscopic disease
- 30Gy in 15-20 fractions - prophylactic irradiation regions
- 30-35Gy in 15-20 fractions - postchemotherapy complete remission



Yahalom J, Hoppe BS, Yang JC, Hoppe RT (2020). Principles of Radiation Therapy for Hodgkin Lymphoma. In: Engert A, Younes A. (eds) Hodgkin Lymphoma. Hematologic Malignancies. Springer, Cham.

Involved field - includes the affected, involved, region of the disease with a small margin of surrounding normal tissue

Extended field - includes involved LNs + all other LNs above the diaphragm Mantle or below the diaphragm inverted Y

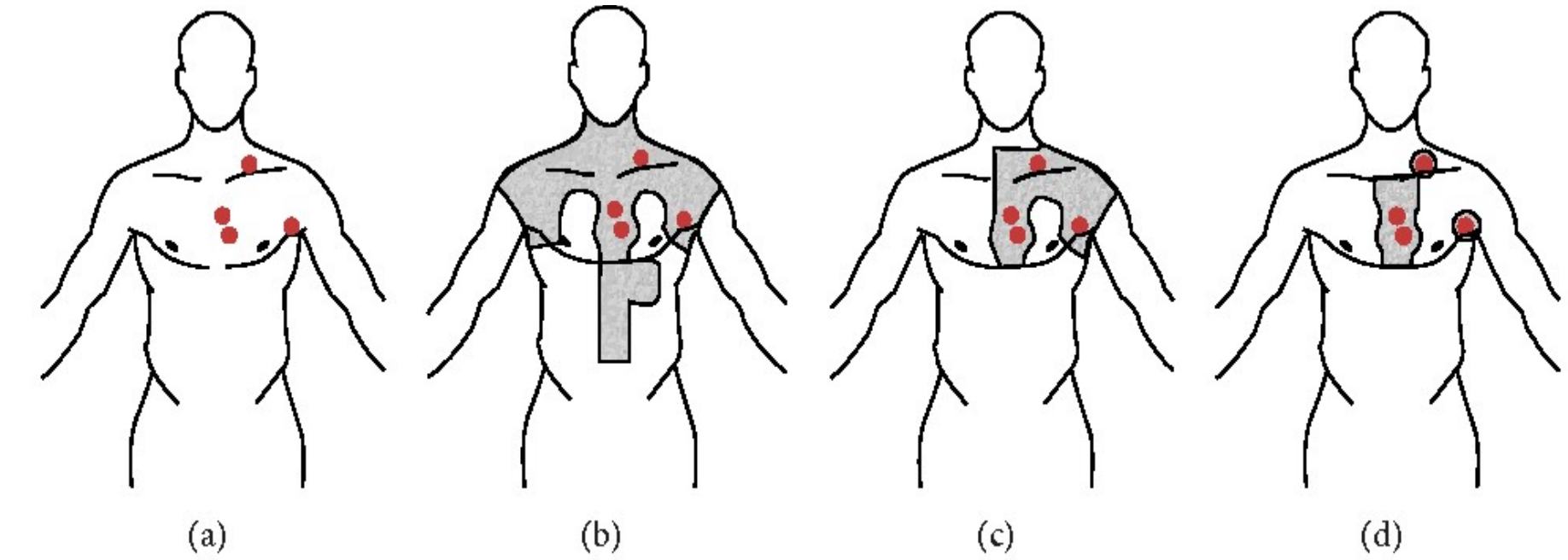
Mantle field: LN neck, axillary, infraclavicular, supraclavicular, paratracheal, hilar, mediastinal LN.

Indications:

- Bulky disease (especially mediastinum)
- Incomplete response to chemotherapy

TD 35Gy in 20 daily fractions

Boost to involved sites 5Gy in 3 daily fractions



(a) Involved lymph nodes, (b) mantle field, (c) IF-RT: involved field radiation therapy, and (d) IN-RT: involved nodal radiation therapy

Witkowska M, Majchrzak A, Smolewski P. The role of radiotherapy in Hodgkin's lymphoma: what has been achieved during the last 50 years? Biomed Res Int. 2015;2015:485071.

- **Inverted Y technique:** para-aortic, pelvic, iliac and femoral LNs.
- **EFRT** defines RT that includes both adjacent first and second lymph node regions
- **Total nodal irradiation** - treatment of all major lymph regions, with a mantle and inverted Y field, with or without a field that includes Waldeyer's ring. It is mainly used in the treatment of HL.
- **Subtotal nodal irradiation** - a special type of field that is often used in supradiaphragmatic HL when only RT is used in treatment. It includes the mantle field, spleen and abdominal para-aortic lymph nodes.

Radiotherapy of Non-Hodgkin's lymphoma

Localized disease - CSI and CSII

- Low-grade (grade 1) - Local radiotherapy
- High-grade (grade 2) - Chemotherapy + radiotherapy of the initial site

Extended disease - CSIII – CSIV

- Low grade - Local radiotherapy + chemotherapy
- High grade - Chemotherapy is more successful than in low grade lymphoma

  Radiotherapy

  Local - residual disease

  Lymphoblastic NHL - CNS RT prophylaxis

30-35Gy in 15-20 fractions, after complete response to chemotherapy

35-40Gy in 20 fractions, after a partial response to chemotherapy

Nodal Non-Hodgkin lymphoma

Localized disease (low grade)

Local radiotherapy – affected region with a wide margin of 5 cm, TD 30Gy in 15 fractions

Techniques Depending on the affected region

- RT lymphatics of the neck
- RT of mediastinal lymph glands
- Mantle technique
- Inverted Y technique
- Modified fields

Localized disease (high grade)

- Target volume and techniques
- Similar to low-grade lymphoma
- Dose 40Gy in 20 fractions

Extranodal Non-Hodgkin lymphoma

Gastric lymphoma:

Postoperative radiotherapy (rare)

In case of residual disease

TD 30-40Gy in 20-25 fractions

Lymphomas of the head and neck, testicles, brain and breast

TD 40Gy in 20 fractions

Bone lymphomas

Whole bone: TD 40Gy in 20 fractions

Tumor volume: TD 15Gy in 10 fractions

Follicular lymphomas are more sensitive to radiation

Palliative radiotherapy

20-30Gy in 5-10 fractions or 35-40Gy in 20 fractions

For palliation, a dose of 4Gy in 2 fractions in 3 days has proven to be effective, providing local control

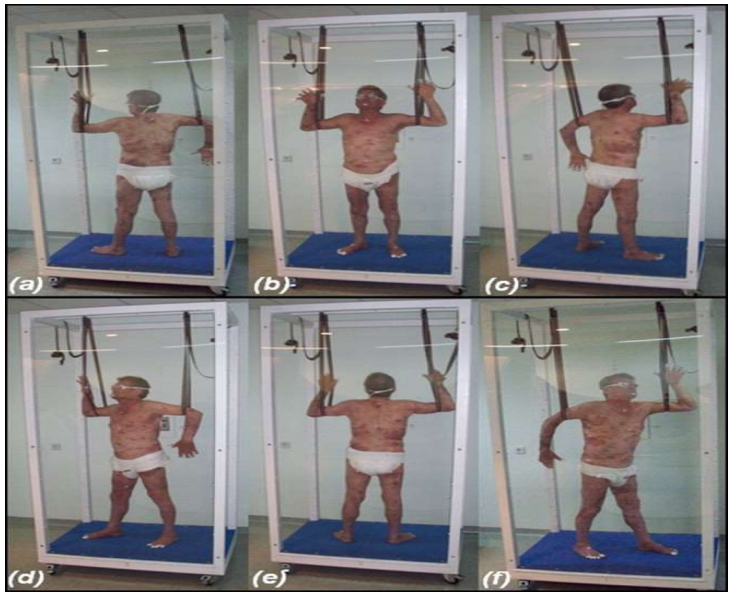
Skin lymphoma

- A standard technique for localized skin lesions with a direct electron field or photons of lower energies
- In case of extended lesions (mycosis fungoides) in specialized centers consider "whole body electron treatment"

Total body electron treatment

- The skin surface of the whole body is treated to a depth of 3-5 mm
- Four to six different patient positions standing and rotating at 60-degree intervals, allowing coverage of the entire body surface
- The treatment is usually carried out in cycles: front and two rear oblique fields day 1 and rear and two front oblique fields day 2
- Protection of eyes, nails, mouth and hands is necessary

- 24Gy in 8 fractions, 3 times a week
- 30Gy in 15 fractions, 4 or 5 times a week



Diamantopoulos S, Platoni K, Kouloulias V, et al. First treatment of mycosis fungoides by total skin electron beam (TSEB) therapy in Greece. Rep Pract Oncol Radiother 2013;19(2):114-9.

Radiotherapy in patients with acute lymphoblastic leukemia (ALL)

Prophylactic cranial irradiation:

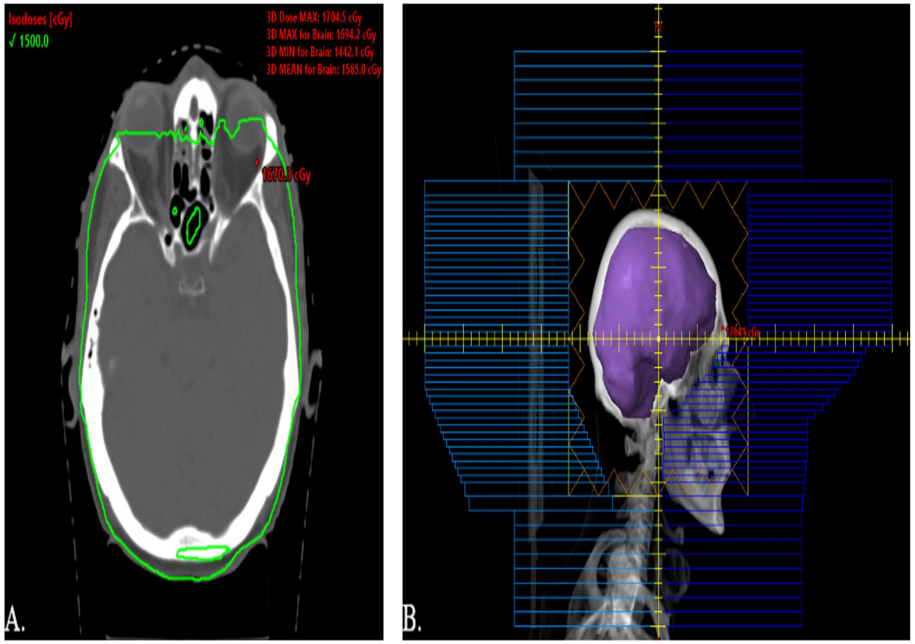
- Dosage prescription:
- TD 12Gy in 8 fractions, 1.5 Gy per day
- TD 24Gy in 15 fractions, 1.6 Gy per day

Testicular irradiation:

- relapse in the testicle region
- CTV- Both testicles, scrotum and inguinal canal superlaterally
- TD 24Gy in 12 fractions

Total body irradiation before transplantation

- CTV – whole body TD 14.4 Gy in 8 fractions with 1.8Gy, twice daily
- Cranial boost: 5.4Gy in 3 daily fractions (reduction of risk for CNS relapse)



Patel N, RIch BJ, Patel S, et al. Emergent Radiotherapy for Leukemia-Induced Cranial Neuropathies Refractory to Intrathecal Therapy. Cureus. 2021;13(5):e15212.

Radiotherapy in patients with acute myeloid leukemia (AML)

- Local techniques (single field or opposing fields) for pain reduction due to changes in the skin, bones and retro-orbital deposits
- TD 5 Gy in one fraction

Payandeh M, Karami A, Karami N, Enayati S, Aeinfar M. Salvage chemotherapy for the treatment of Leukemia cutis in a patient with acute monocytic leukemia. BMRAT [Internet]2019;6(1):2970-3.

Radiotherapy in patients with chronic myeloid (granulocytic) leukemia (CML)

Splenomegaly - not controlled by chemotherapy

Directly anterior or lateral fields (15×10), TD 0.25 Gy per day, increasing from 0.25 Gy per day to 1.5-2 Gy per day up to a dose of 3 Gy

Myeloblastoma - local tumors made of acute myeloblastic leukemic cells, TD 5 or 10Gy in one fraction, one or two opposing fields depending on localization

Prophylactic cranial irradiation - in lymphoblastic transformation

Radiotherapy in patients with chronic lymphocytic leukemia (CLL)

- Inadequate response to CHT
- RT is applied locally to the bulky tumor, TD 20Gy in 4 fractions

Stang K, Alite F, Steber J, Emami B, Surucu M. Leukemia Cutis of the Face, Scalp, and Neck Treated with Non-coplanar Split Field Volumetric Modulated Arc Therapy: A Case Report. Cureus. 2015;7(12):e430.

Radiotherapy of solitary plasmacytoma (SP)

- **The ILORG recommendations** for the use of radiotherapy for the treatment of SP include the use of a standard fractionation (1.8 to 2 Gy per day):
- SP <5 cm: total dose 35 to 40 Gy
- SP ≥5 cm: total dose 40 to 50 Gy
- **Extramedullary SP**: total dose 40 to 50 Gy (in case of small, well-defined lesions or with positive resection margins, a dose of 40 Gy is advised.

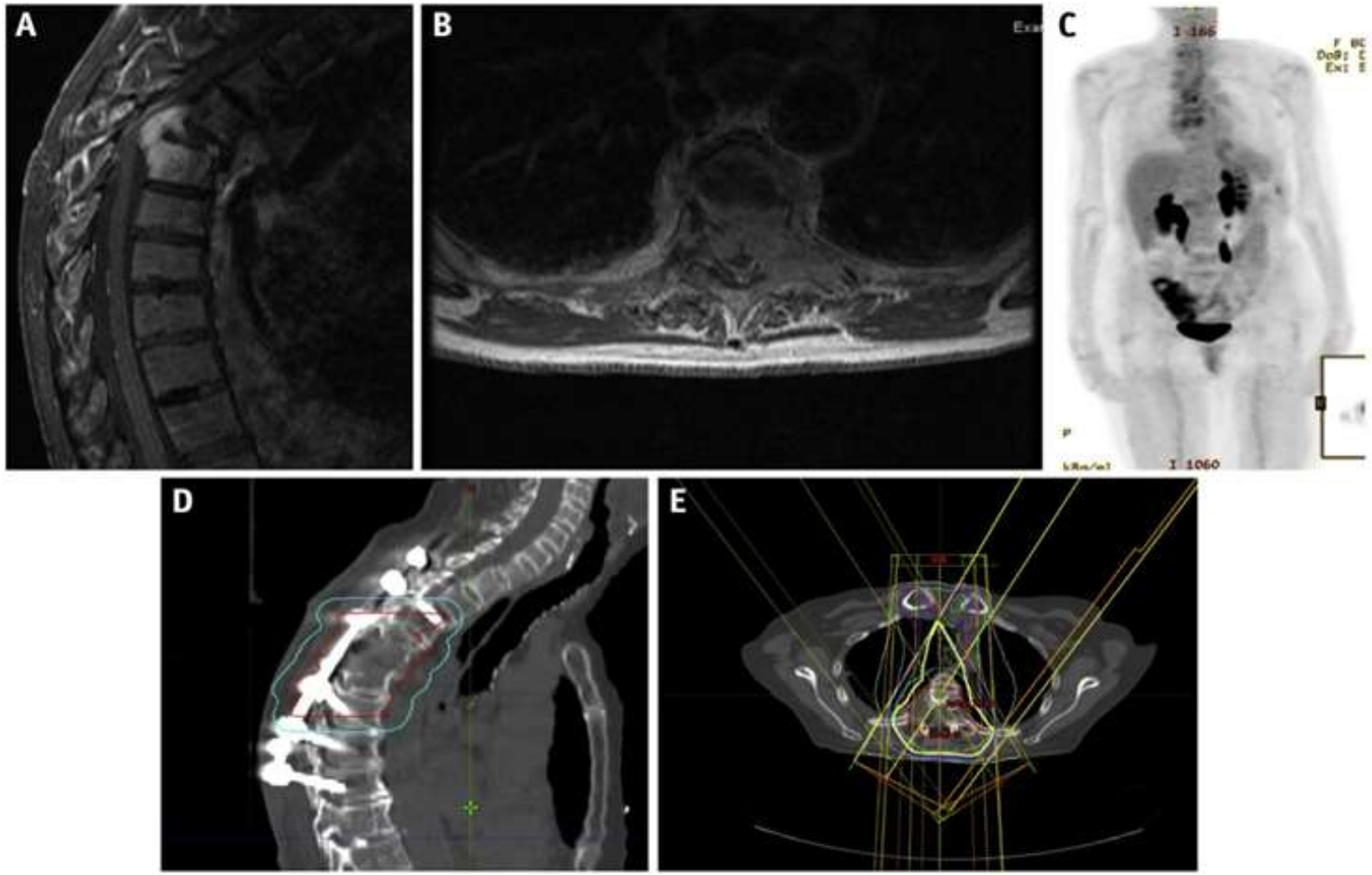
Radiotherapy of multiple myeloma

ILORG recommendations for the use of palliative radiotherapy in MM:

- hypofractionated regimen with a total dose of 8 to 30 Gy (8 Gy in 1 session, 20 Gy in 5 sessions or 30 Gy in 10 sessions) or 8 Gy in 1 session in patients with a poor prognosis.
- retreatment - conventional fractionation regimen: 20 or 30 Gy in 10 or 15 sessions, five sessions per week.
- In the case of epidural spread with spinal cord compression or when there is "bulky" disease, apply a therapeutic dose of 30 Gy in 10 to 15 sessions, five sessions per week.

Radiotherapy of the central nervous system in patients with myeloma:

- Whole brain radiotherapy for limited disease
- Craniospinal radiotherapy (CSI) in people expected to survive longer

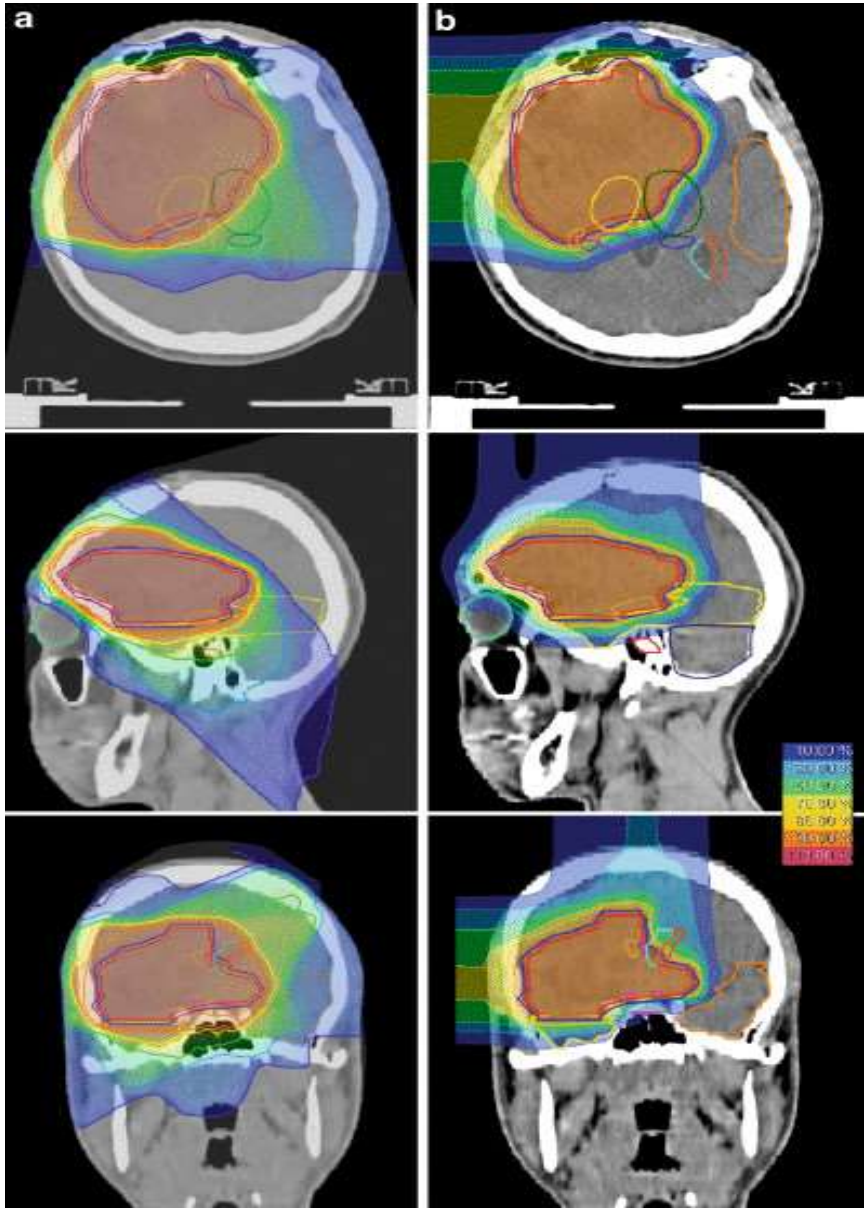


Delineacija ciljnih volumena kod MM u koregistraciji sa PET-CT (Izvor: *Tsang RW, Campbell BA, Goda JS, Kelsey CR, Kirova YM, Parikh RR, et al. Radiation Therapy for Solitary Plasmacytoma and Multiple Myeloma: Guidelines From the International Lymphoma Radiation Oncology Group. Int J Radiat Oncol Biol Phys 2018;101(4):794-808*.)

Radiotherapy of CNS tumors

Low-grade gliomas

- pilocytic astrocytoma WHO grade I,
- subependymal giant cell astrocytoma WHO grade I,
- pleomorphic xanthoastrocytoma WHO grade II,
- diffuse astrocytoma IDH-mutated WHO grade II,
- oligodendroglioma IDH-mutated with 1p/19q codeletion WHO grade II
- **Maximum surgical resection**
- **RT** (residual symptomatic disease or disease progression especially when reoperation is not indicated): TD 50.4-54 Gy, in 28-30 fractions with a daily fraction of 1.8 Gy is standard
- **CHT** (not clearly defined)



Harrabi SB,et al. Dosimetric advantages of proton therapy over conventional radiotherapy with photons in young patients and adults with low-grade glioma. Strahlenther Onkol 2016;192(11):759-69.

Radiotherapy of CNS tumors

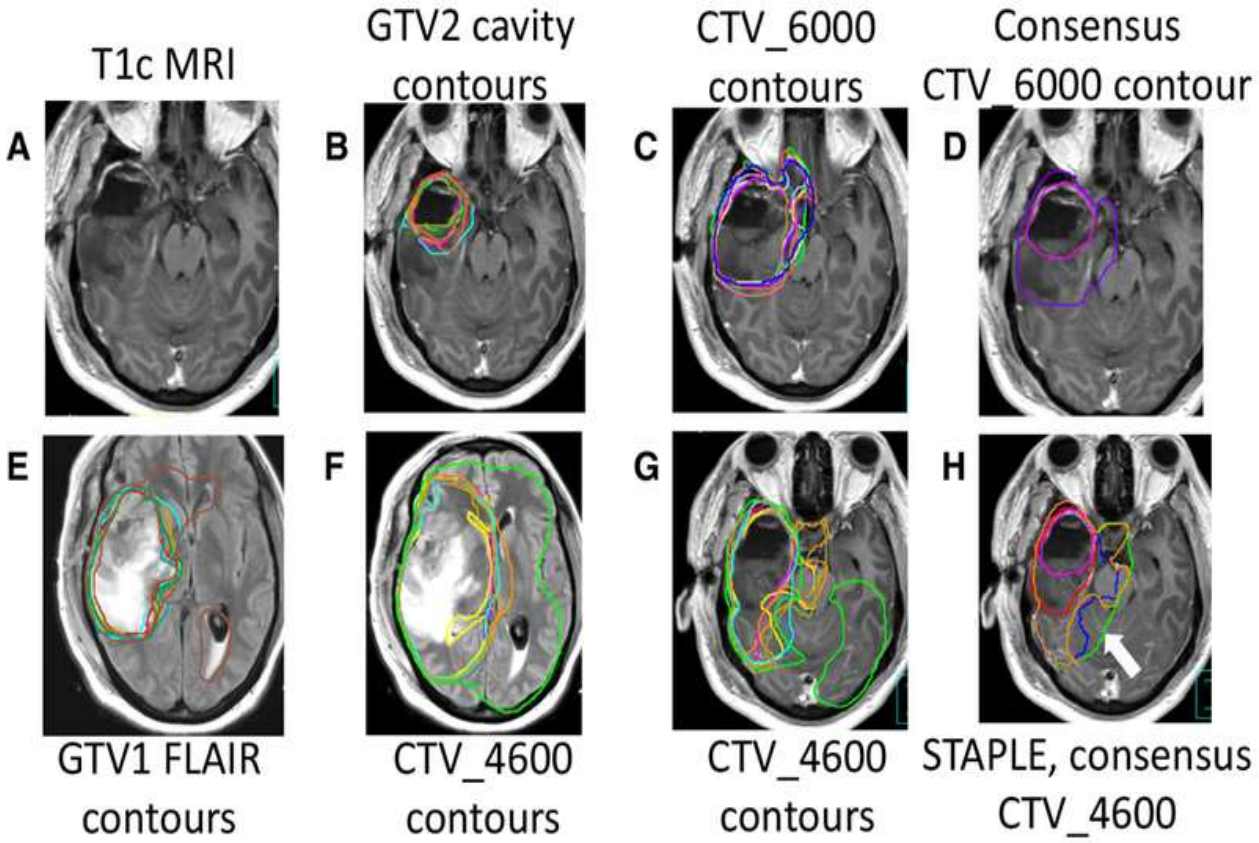
- **<u>High-grade gliomas</u>**
- anaplastic astrocytoma IDH-mutated WHO grade III,
- anaplastic pleomorphic xanthoastrocytoma WHO grade III,
- anaplastic oligodendroglioma IDH-mutated with 1p/19q codeletion WHO grade III,
- glioblastoma IDH-wildtype
- IDH – mutated astrocytoma grade IV

- **Surgery** (maximum tumor resection)
- **CHT** (according to the CCNU or BCNU protocol or concomitantly with temozolomide, which is also continued in the adjuvant approach)
- **RT** (6 weeks from surgery) TD 54-59.4 Gy in 30-33 fractions
- Immunotherapy (VEGF - bevacizumab and VEGF receptor agonist - cediranib)

Radiotherapy of glioblastoma

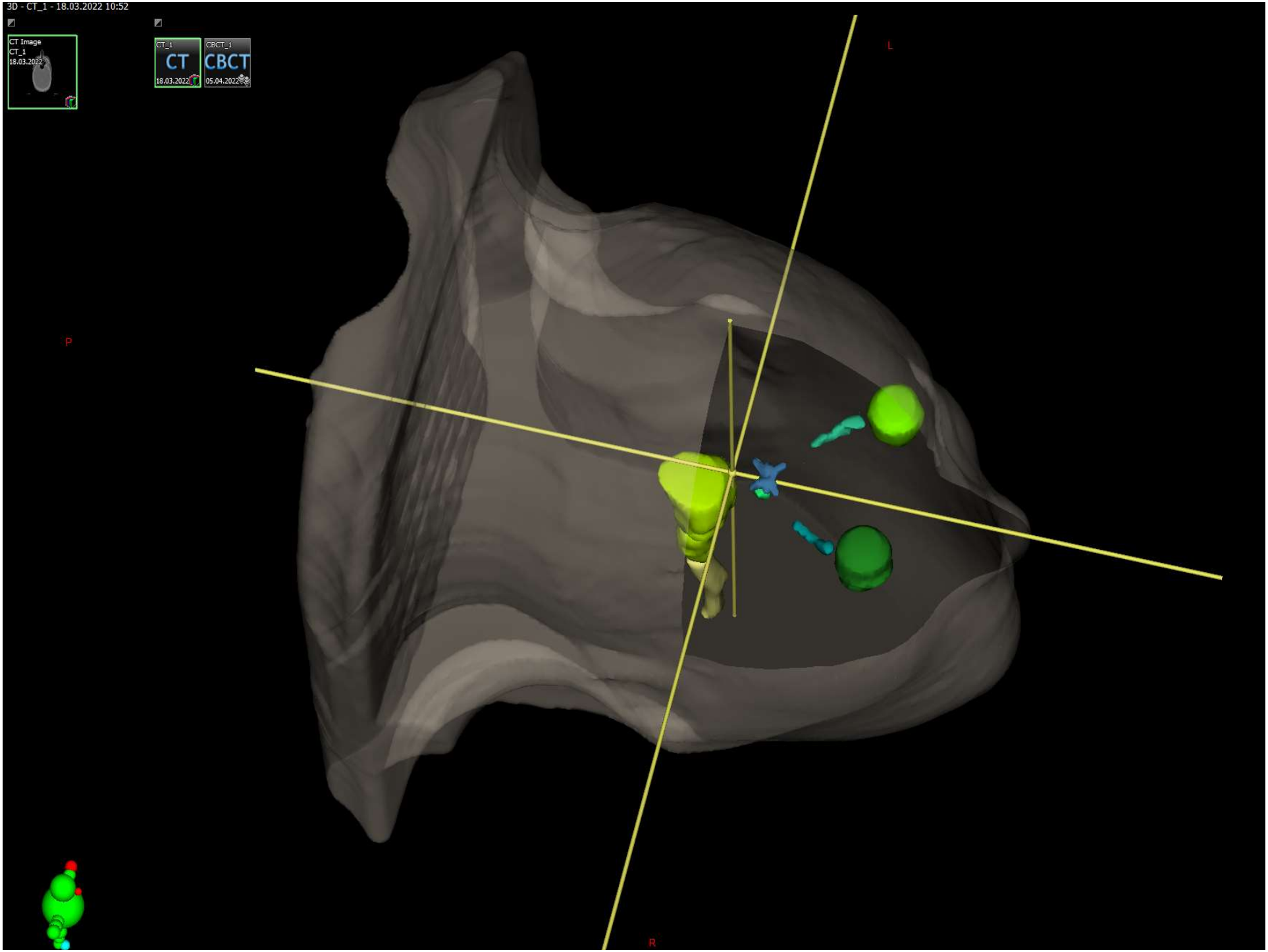
- **Laser Interstitial Thermal Therapy (LITT)** destruction of tumor cells by the effect of localized high temperature with the help of radiofrequency waves, ultrasound, microwaves and magnetic nanoparticles.
- **Tumor Treating Fields (TTF)** is a technology of creating alternative electrical fields of low intensity (1–3 V/cm) and medium frequency (100–300 KHz) that lead to the interruption of cell division.
- **Immunotherapy**
- **Checkpoint inhibitors** (nivolumab, pembrolizumab, durvalumab, atezolizumab, and pidilizumab)
- **T-Cell Therapy** where T-cells are programmed to express chimeric antigen receptors (CARs).
- **Viral therapy** is a part of immunotherapy in which an oncolytic virus exerts an effect on various mechanisms including direct oncolysis, virus-induced antitumor response, and immunoregulation.
- **The vaccine.** Dendritic cell vaccine activates CD8+ and CD4+ T-lymphocytes, which results in tumor destruction (47).

- **Radiotherapy**
- Postoperative RT: TD 60 Gy in 30 fractions concomitant with chemotherapy with temozolomide, an oral alkylating agent that crosses the blood-brain barrier, at a dose of 75 mg/m2.
- After completion, adjuvant chemotherapy is carried out up to a total of VI cycles at a dose of 150-200 mg/m2 temozolomide for 5 days, and cycles of 28 days. Alternative drugs are cisplatin, carboplatin, etoposide, irinotecan.
- Palliative RT: TD 45Gy in 15 fractions or as palliative with TD30 Gy in 6 fractions.



Glioblatom temporalno desno
(A, B) panels show the contrast-enhanced T1 MRI with GTV2 contours (cavity plus enhancement).
(C) CTV_6000 contours demonstrate variability at the interface with the brainstem and optic structures.
(D) the STAPLE GTV2 cavity contour in pink and the consensus CTV_6000 contour.
(E, F) show T2 FLAIR MRI images with submitted GTV1 (FLAIR) contours and CTV_4600 contours.
(G) CTV_4600 contours are demonstrated at level of brainstem and optic nerves with significant variation.
(H) CTV1 expansion (without anatomic trimming) in green and mathematical STAPLE contours in blue. The space between the green and orange consensus CTV_4600 contour reflects anatomic trimming off the cerebellum (white arrow) due to cerebellar falx, while maintaining inclusion of optic and brainstem tissue in direct anatomic contiguity with the right temporal T2 FLAIR signal. (*These principles may also be applied to a simultaneous integrated boost approach of 50 Gy and 60 Gy all given in 30 fractions)

Kruser TJ, Bosch WR, Badiyan SN, Bovi JA, Ghia AJ, Kim MM, Solanki AA, Sachdev S, Tsien C, Wang TJC, Mehta MP, McMullen KP. NRG brain tumor specialists consensus guidelines for glioblastoma


3D - CT_1 - 18.03.2022 10:52
CT Image
CT_1
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CT_1
CT
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CBCT_1
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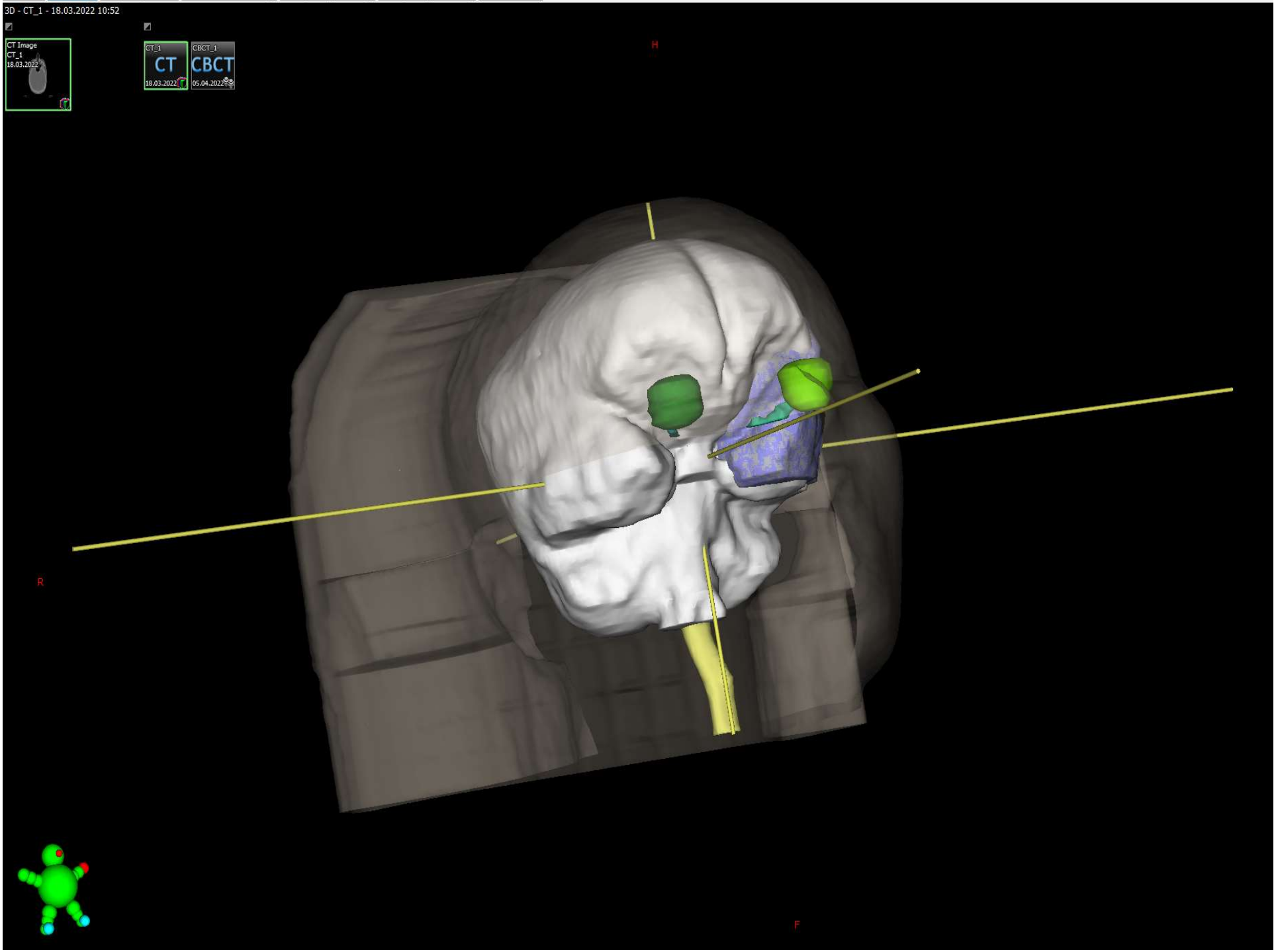
3D - CT_1 - 18.03.2022 10:52
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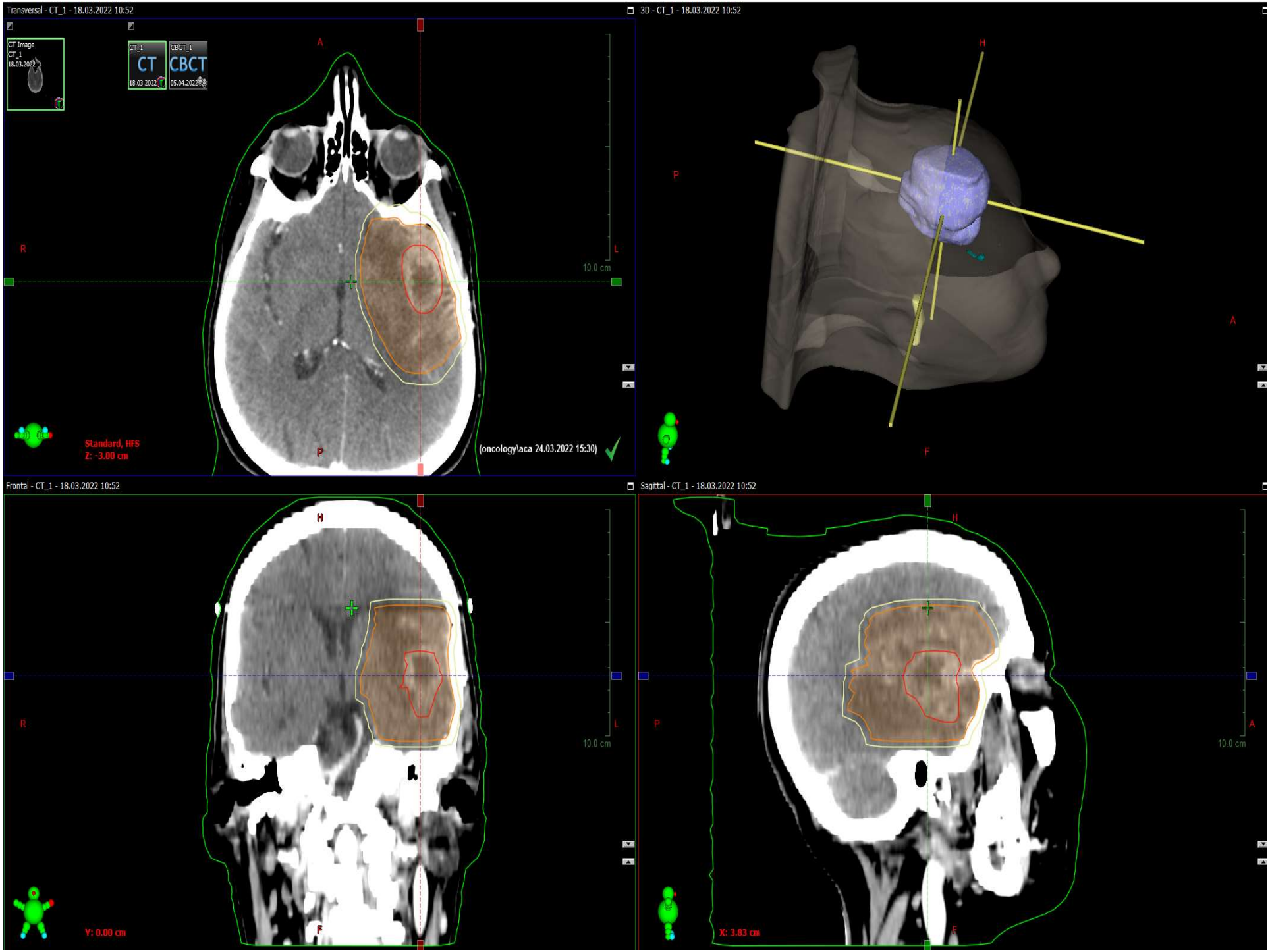
Transversal - CT_1 - 18.03.2022 10:52
3D - CT_1 - 18.03.2022 10:52
Frontal - CT_1 - 18.03.2022 10:52
Sagittal - CT_1 - 18.03.2022 10:52
CT Image
CT_1
18.03.2022
CT_1
CT
18.03.2022
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CBCT
05.04.2022
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10.0 cm
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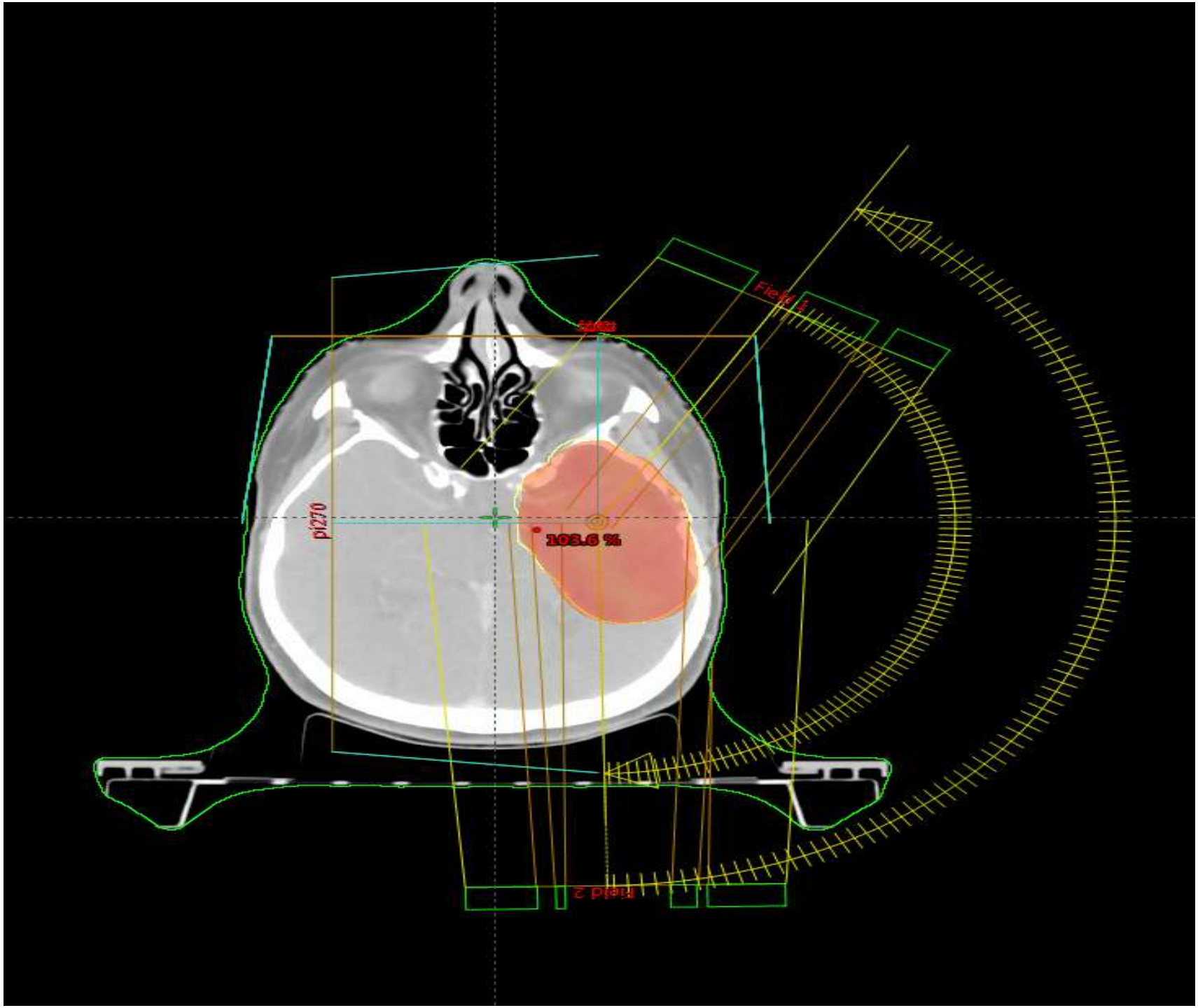
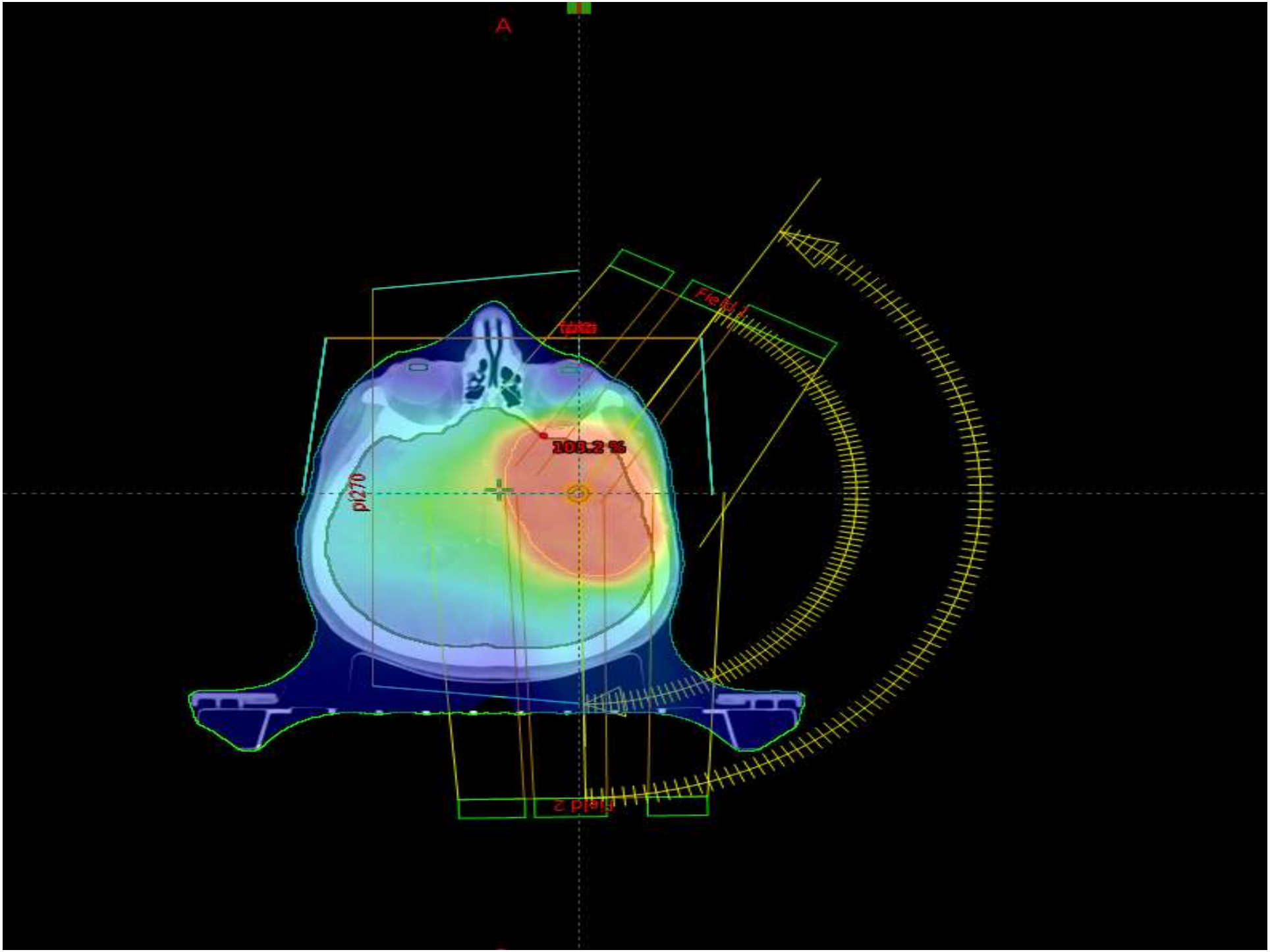
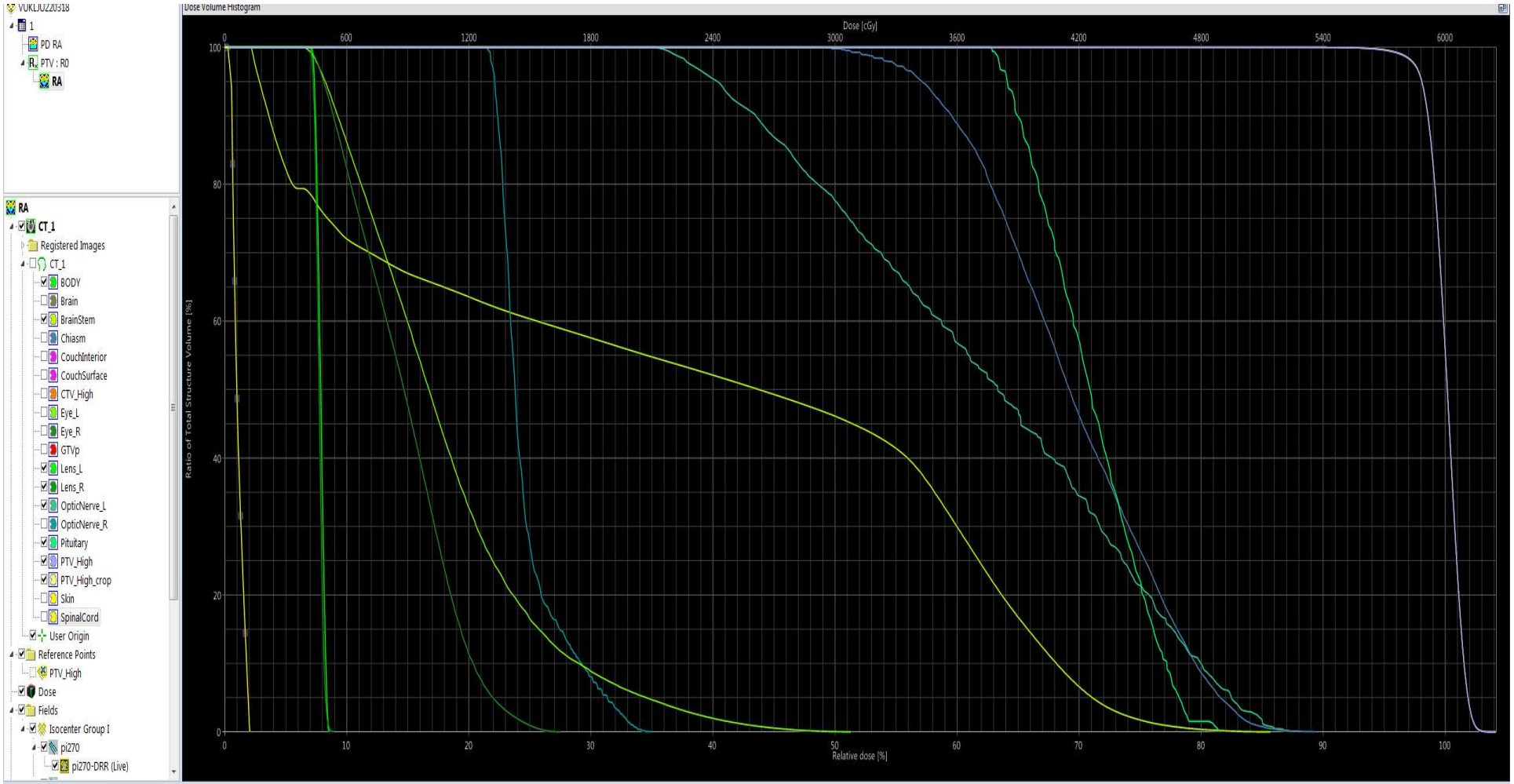
(oncology\aca 24.03.2022 15:30)
Y: 0.00 cm
X: 3.83 cm


Field 1
pi270
103.6 %
Field 2


A
Field 1
103.2 %
pl270
field 2

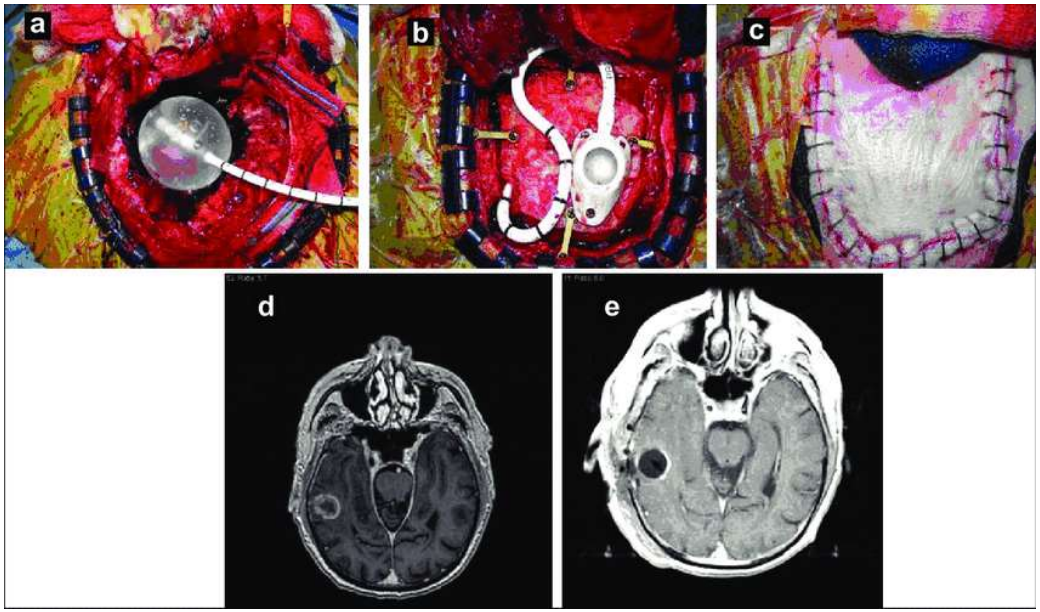


Dose | Reference Points | Dose Statistics

Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [%]	Max Dose [%]	Mean Dose [%]
☐	Brain	Approved	RA	1						
☐	BODY	Approved	RA	1	5547.8	100.0	99.9	0.0	104.2	16.7
☑	BrainStem	Approved	RA	1	15.8	100.0	100.2	2.1	85.7	37.7
☑	SpinalCord	Approved	RA	1	3.4	100.0	100.5	0.2	2.1	1.1
☑	Pituitary	Approved	RA	1	0.2	100.0	99.2	62.8	81.6	71.0
☑	Chiasm	Approved	RA	1	0.2	100.0	99.3	49.2	89.3	69.4
☑	OpticNerve_R	Approved	RA	1	0.1	100.0	98.3	21.5	34.9	24.7
☑	OpticNerve_L	Approved	RA	1	0.3	100.0	100.2	35.4	88.2	62.4
☑	Lens_R	Approved	RA	1	0.1	100.0	99.7	7.0	9.0	7.7
☑	Lens_L	Approved	RA	1	0.1	100.0	100.1	7.1	8.6	7.9
☑	Eye_R	Approved	RA	1	5.3	100.0	100.0	6.8	27.5	14.7
☑	Eye_L	Approved	RA	1	5.1	100.0	100.0	6.4	51.4	18.1
☐	GTVp	Approved	RA	1						
☐	CTV_High	Approved	RA	1						
☑	PTV_High	Approved	RA	1	199.9	100.0	100.0	85.2	104.2	100.1
☐	Skin	Approved	RA	1						
☑	PTV_High_crop	Approved	RA	1	199.8	100.0	100.0	85.2	104.2	100.1

Brachytherapy in high grade glioma

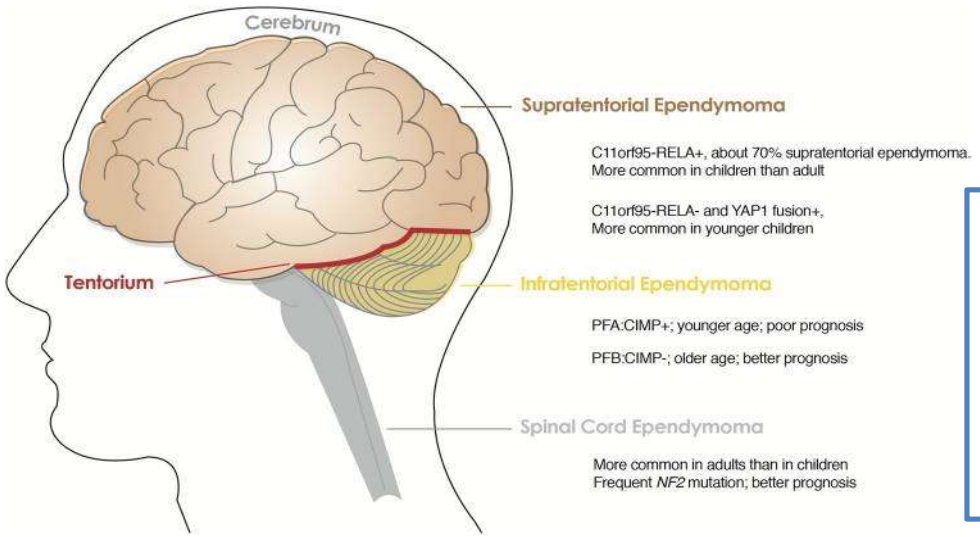
- Boost after EBRT
- Glia Site Radiation Therapy System (Cytyc, Marlborough, MA)
- 1-2 weeks after implantation after the placed catheters are filled with aqueous solution ^{125}I.
- TD of 40 to 60 Gy in 3 to 6 days, after which the device is displaced.



Wernicke AG, et al. Feasibility and safety of GliaSite brachytherapy in treatment of CNS tumors following neurosurgical resection. J Cancer Res Ther 2010;6(1):65-74.

Radiotherapy of ependymoma

Supratentorial ependymomas	*ZFTA, RELA, YAP1, MAML2*
Posterior fossa ependymomas	H3 K27me3, *EZHIP* (methylome)
Spinal ependymomas	*NF2, MYCN*



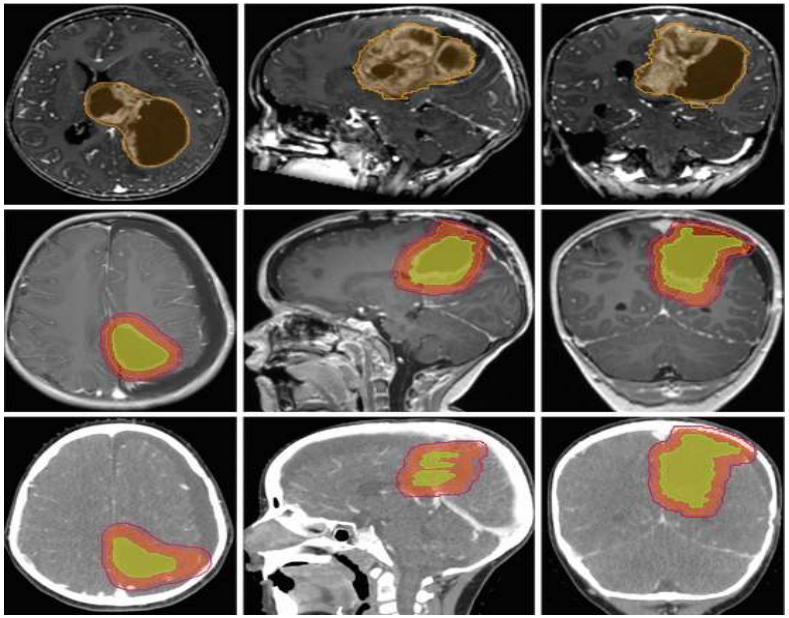
Molecular-biological characteristics of supratentorial, intratentorial and ependymoma of the spinal cord WHO grades II and III.
- Anywhere in the CNS (most commonly within the IV ventricle)
- Low-grade supratentorial → **local RT**
- High-grade supra and infraten → **CSI + boost**
- Low-grade infratentorial - **a controversy?**

Wu J, Armstrong TS, Gilbert MR. Biology and management of ependymomas. Neuro Oncol 2016;18(7):902-13.)

Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, Soffietti R, von Deimling A, Ellison DW. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021 Aug 2;23(8):1231-1251.

Treatment of ependymoma

- **RT**
- craniospinal RT with a TD of 35 to 45 Gy with a boost to areas of primary tumor and active disease up to a total dose of TD of 50.4 to 54 Gy
- **CHT** – limited efficacy, High-grade tumors, resistant to other treatment modalities
- **Surgery** (subtotal resection) + II Cy (HT) + second-look operation



Slika dostuona na:
https://oncohemakey.com/ependymoma-4/

Radiotherapy of meningioma

Meningiomas	*NF2, AKT1, TRAF7, SMO, PIK3CA*; *KLF4, SMARCE1, BAP1* in subtypes; H3K27me3; *TERT* promoter, *CDKN2A/B* in CNS WHO grade 3

- Benign (grade I): few mitosis, slow growth, rare relapse, 10-year progression-free survival is 80%,
- Atypical (grade II): more aggressive than benign, more mitoses, 7-8 times higher risk of relapse than grade I, 10-year progression-free survival is 40-60%,
- Anaplastic (grade III): invasive, poor prognosis; median relapse-free survival is less than 2 years

- Treatment
- **Surgery**
- **Radiotherapy**: unresectable or incompletely resectable tumors due to localization (skull base, cavernous sinus, cerebellopontine angle), the patient does not agree to surgery or it is medically contraindicated. Adjuvant approach in subtotal resection of benign and all atypical and malignant meningiomas
- Dosage prescription:
- Meningioma grade I: 50-54 Gy in 25-30 fractions
- Meningioma grade II and III: 60 Gy in 30-33 fractions
- Meningioma of the optic nerve: 50-54 Gy in 25-30 fractions
- Stereotaxic radiosurgery: 12-20 Gy in one fraction depending on the proximity of critical structures (12 Gy for tumors close to critical structures such as the brainstem, 15-20 Gy if the tumor is not close to extremely critical structures). Doses depend on the size of the tumor: 18 Gy (<1 cm), 16 Gy (1-3 cm), 12-14 Gy (>3 cm)

- **CHT**: in tumor progression after RT and in case of recurrent disease (cyclophosphamide, adriamycin, vincristine, interferon-alpha).

Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, Soffietti R, von Deimling A, Ellison DW. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021 Aug 2;23(8):1231-1251.

Radiotherapy of tumors of the sellar region

Tumors of the sellar region
Adamantinomatous craniopharyngioma
Papillary craniopharyngioma
Pituicytoma, granular cell tumor of the sellar region, and spindle cell oncocytoma
Pituitary adenoma/PitNET
Pituitary blastoma

Craniopharyngioma

Benign tumor of epithelial origin - remnant of Rathke's sac

Surgery

Total resection - curative → postoperative morbidity and mortality

GTR is not always feasible

Recommendation → limited surgical decompression + postoperative RT

Recurrent tumor with a large cystic component

Intracavitary brachytherapy (Beta emitters 32P and 90 Yt and Gamma-Beta emitters 186Ph and 198Au)

Pituitary adenoma

Surgical resection for Tu □ 1 cm – the therapy of choice

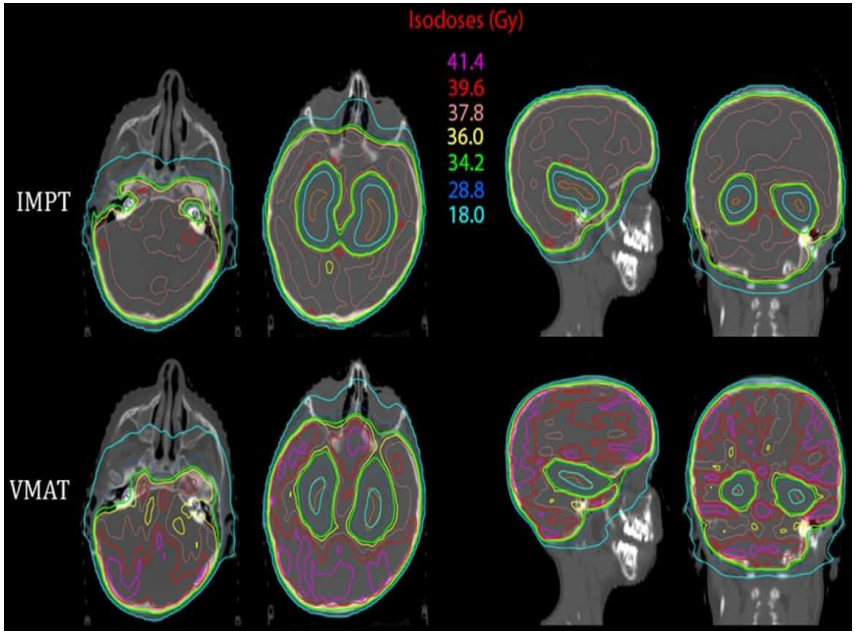
Radiotherapy after partial resection

Most patients - hormone replacement therapy with dopamine agonists (bromocriptine, Cabergoline, quinagolide, Pergolide) - reduction in tumor size and improvement of symptoms

RT: 50-54 Gy in 30 fractions, and dose per fraction 1.67-1.8 Gy

Radiotherapy of intracranial germ cell tumors

- Germinomas
- Embryonic carcinoma
- Choriocarcinoma
- Endodermal sinus tumor
- Teratoma / teratocarcinoma
- Mixed germ cell tumors



Courtesy: J Stoker et al Phys. Imag. Radiat. Oncol.
10.1016/j.phro.2018.11.001

Radiotherapy of central nervous system lymphoma

- **PCNSL in immunocompetent and**
- **PCNSL in immunocompromised patients (occurring in congenital or acquired immunodeficiency)**

- **CHT** - standard in definitive treatment (with or without RT), salvage therapy in disease progression or recurrent disease and as definitive treatment in ocular lymphomas. High doses of methotrexate > 1g/m2.

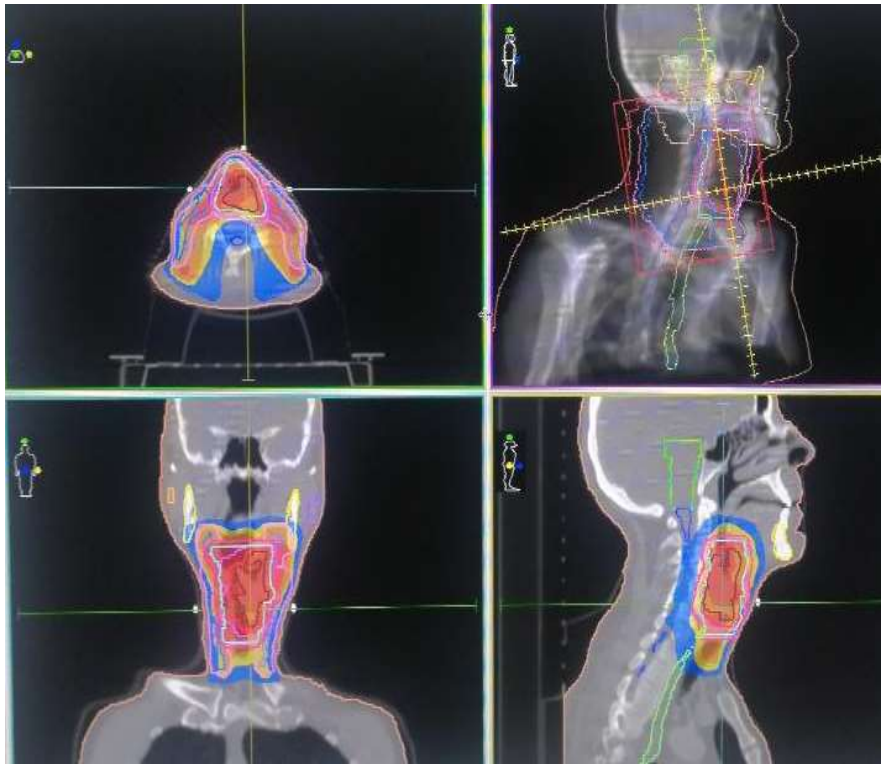
- **RT** after HT or as definitive treatment in patients unfit for chemotherapy (KPS≤40, creatinine clearance <50%) and as definitive treatment for ocular lymphomas.
- irradiation of the entire endocranium with or without administration of a boost dose

- If a CR response is achieved: whole brain RT with 24-36Gy (1.5-2Gy). Consider dose reduction or discontinuation of treatment in patients over 60 years of age due to possible serious neurotoxicity.
- If CR response not achieved: RT to whole brain with 24-36Gy (1.8-2Gy) with boost to residual disease up to 45Gy (1.8-2Gy).

- If it was not possible to apply chemotherapy:
- Whole brain RT up to 45Gy (1.8-2Gy)

Head and neck cancer radiotherapy

- Oral cavity
- Oropharynx
- Epipharynx
- Hypopharynx
- Larynx
- Paranasal sinuses
- Salivary glands
- Regional lymph nodes - neck levels from I-VI +



Head and neck cancer definitive radiotherapy

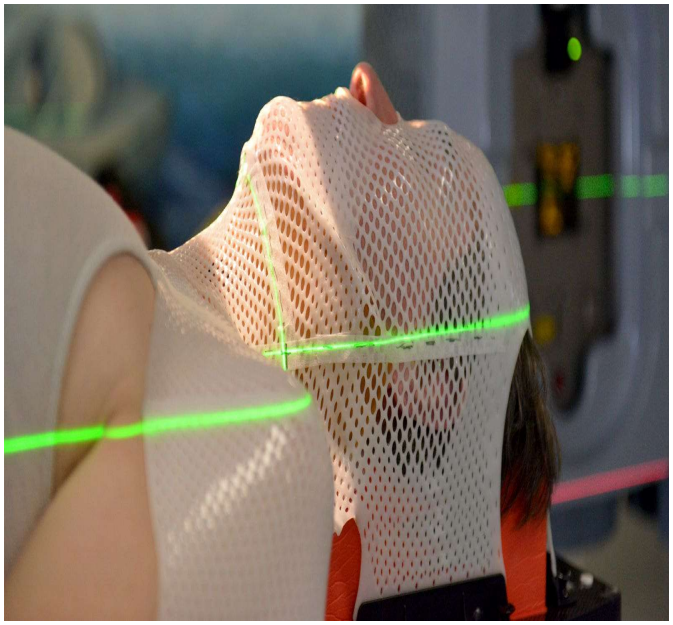
For unresectable head and neck tumors, radical RT ± CHT

- Locally advanced tumors of CS III and IV
- Locally advanced tumors after neoadjuvant

CHT and achieved partial response (PR)

- Resectable tumors with the goal of organ preservation RT + CHT
- (Optional: concomitant Cetuximab biotherapy)

Definitive RT in early stages (results similar to surgery)

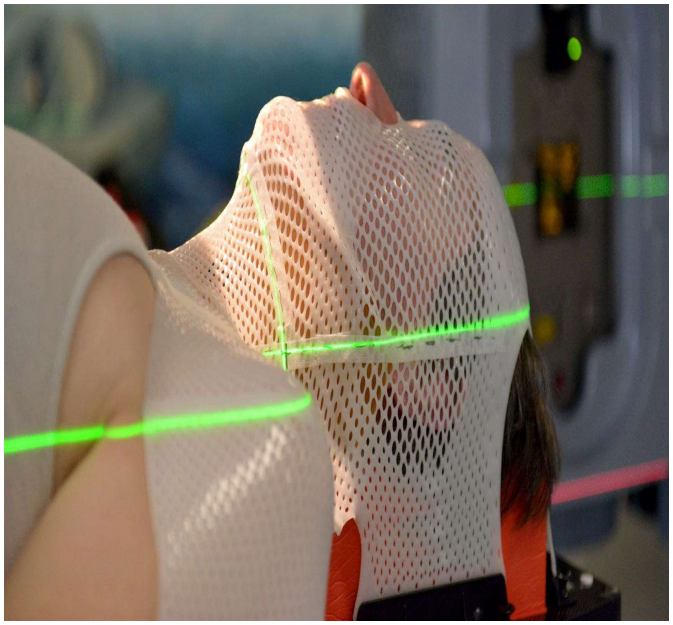


Slika dostupna na: Radiation Speeds Up Biological Aging in Head and Neck Cancer. At: https://www.medpagetoday.com/hematologyoncology/othercancers/92872

Head and neck cancer postoperative radiotherapy

Postoperative RT ± CHT potentiation

- positive resection margins
- lymphnodal metastases
- extracapsular spread in lymphnodal metastases
- close resection margin (<5mm)
- soft tissue and skeletal muscle invasion
- multicentric primary tumor
- perineural invasion
- lymphovascular invasion
- poor histological differentiation of the tumor (G3)
- T3-T4 tumors



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Head and neck cancer radiotherapy

Radical dose: 66-70 Gy in 33-35 fractions

Postoperative dose:
High-risk region: 64-66 Gy in 32-33 fractions
Intermediate risk region: 60 Gy in 30 fractions
Low-risk region: 44-50 Gy in 22-25 fractions

With the simultaneous integrated boost (SiB) technique:
High-risk region: 70 Gy in 33 fractions
Intermediate risk region: 60 Gy in 33 fractions
Low-risk region: 50-54 Gy in 33 fractions

Alternative dose prescription for the SiB technique:
High-risk region: 70 Gy in 35 fractions
Intermediate risk region: 63 Gy in 35 fractions
Low-risk region: 56 Gy in 35 fractions

Radiotolerance of organs at risk according to the QUANTEC study

- **Spinal cord** Dmax ≦ 45 Gy (optional ≦ 50 Gy)
- **Eye lens** Dmax ≦ 8Gy (optional Dmax≦ 10 Gy)
- **Optic nerve/chiasm** Dmax<55 Gy Dmean<50 Gy
- **Mandible** Dmax<70 Gy
- **Cochlea** Dmean ≦ 45 Gy
- **Parotid glands**
- When one parotid gland is spared: Dmean < 20 Gy
- When both parotid glands are spared:
- Dmean < 25 Gy
- **Brain** Dmax<60 Gy
- **Brachial plexus** Dmax<60 Gy
- **Esophagus** V35<50%; Dmax<74 Gy
- **Larynx** Dmean < 44Gy; V50<27%

THANK YOU FOR YOUR ATTENTION!