RADIOTHERAPY PLANNING IN CARCINOMAURINARY BLADDER

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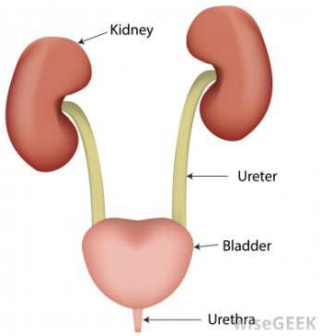
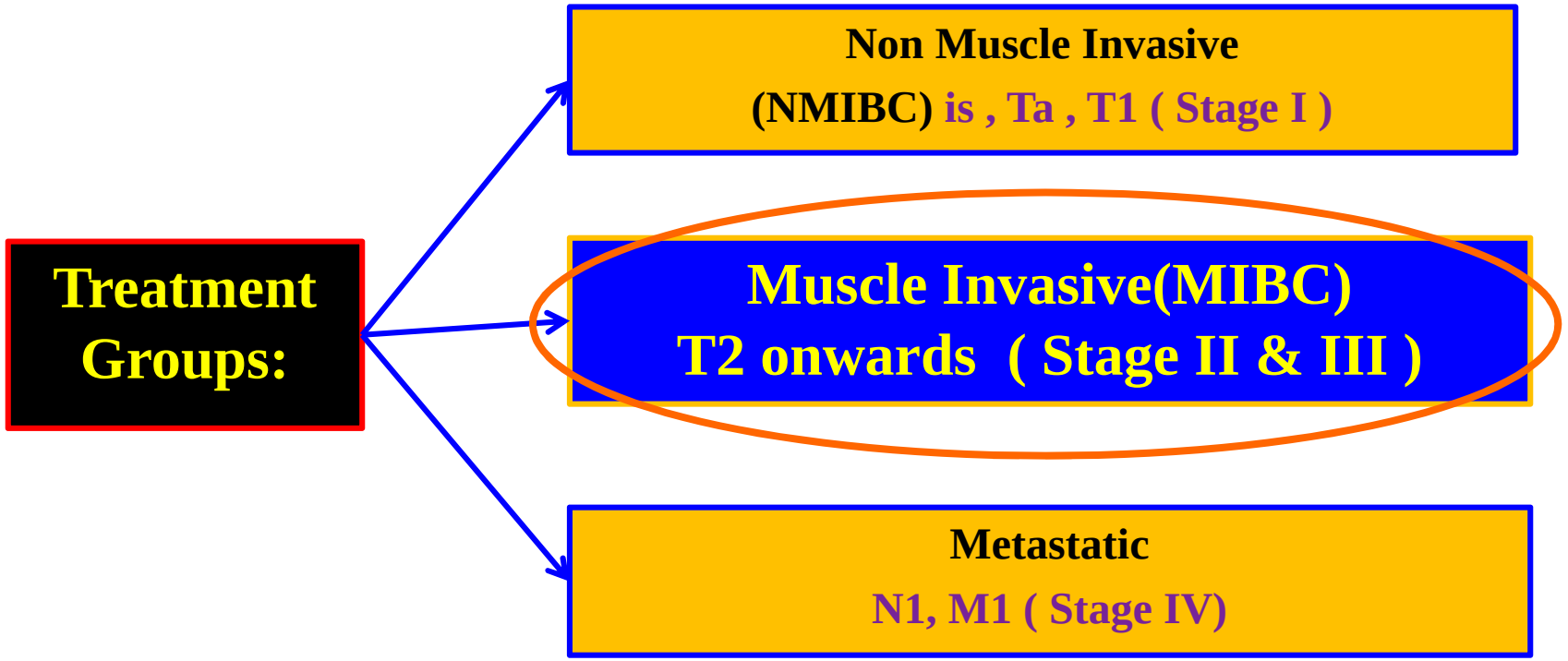
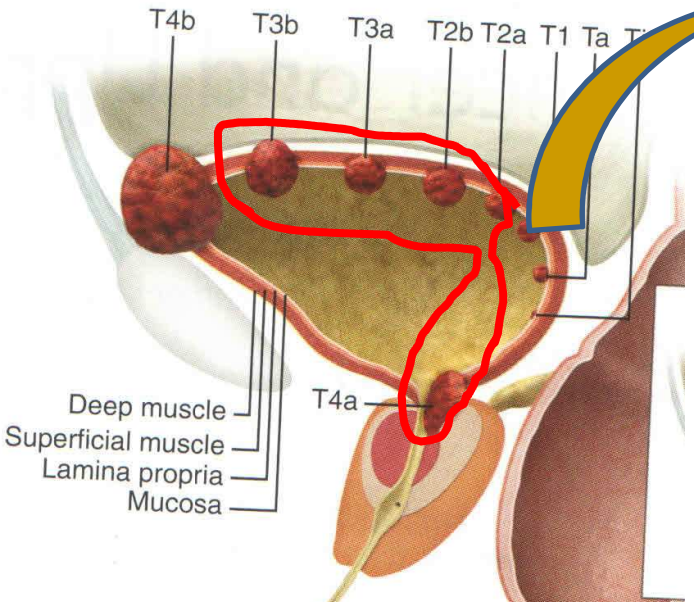



Treatment Groups:
Non Muscle Invasive
(NMIBC) is , Ta , T1 (Stage I)
Muscle Invasive(MIBC)
T2 onwards (Stage II & III)
Metastatic
N1, M1 (Stage IV)

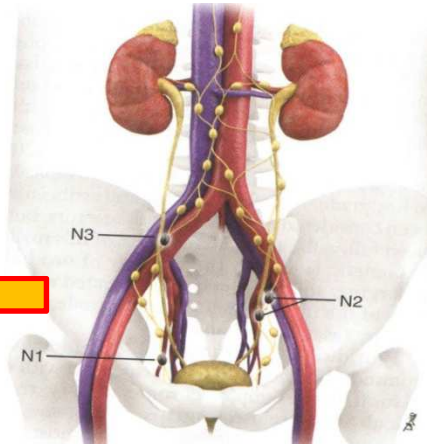


Stage II & III

Role of Radical Radiation

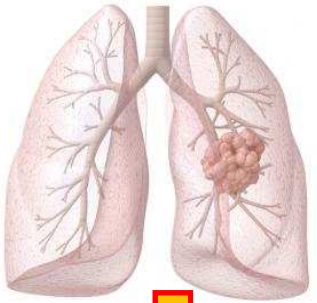
Stage IV

Regional lymph Nodes (N)



Neoadjuvant chemotherapy followed by Radical cystectomy +/- Radiotherapy

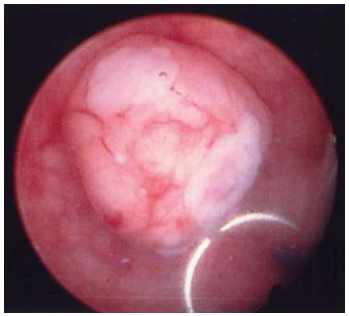
M1: Distant metastasis

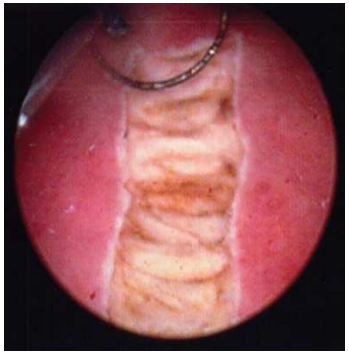


Palliative Radiotherapy and chemotherapy

TURBT : Clinical & Histopathology

NMIBC ⟷ MIBC





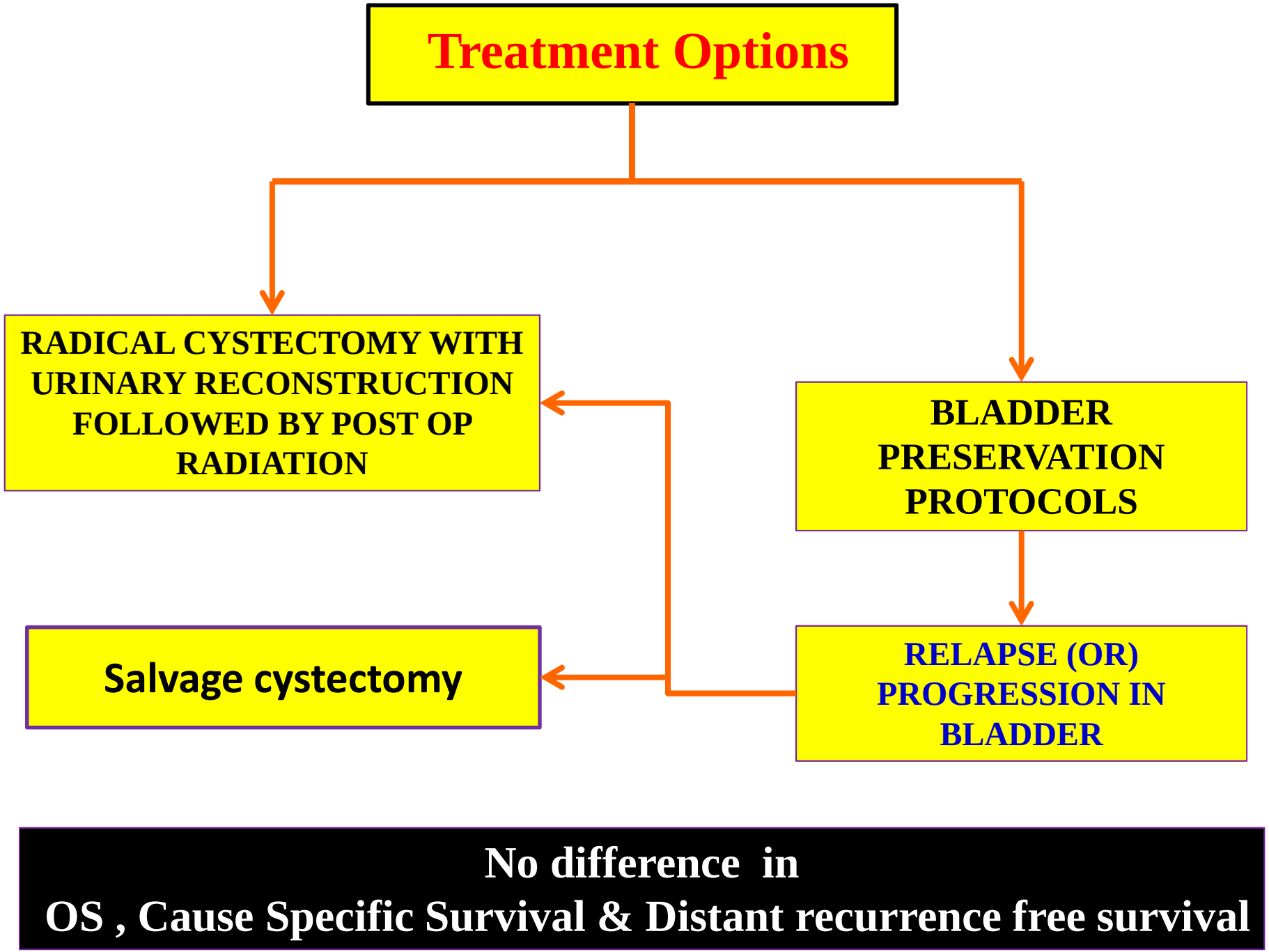
Pathologist should comment on:

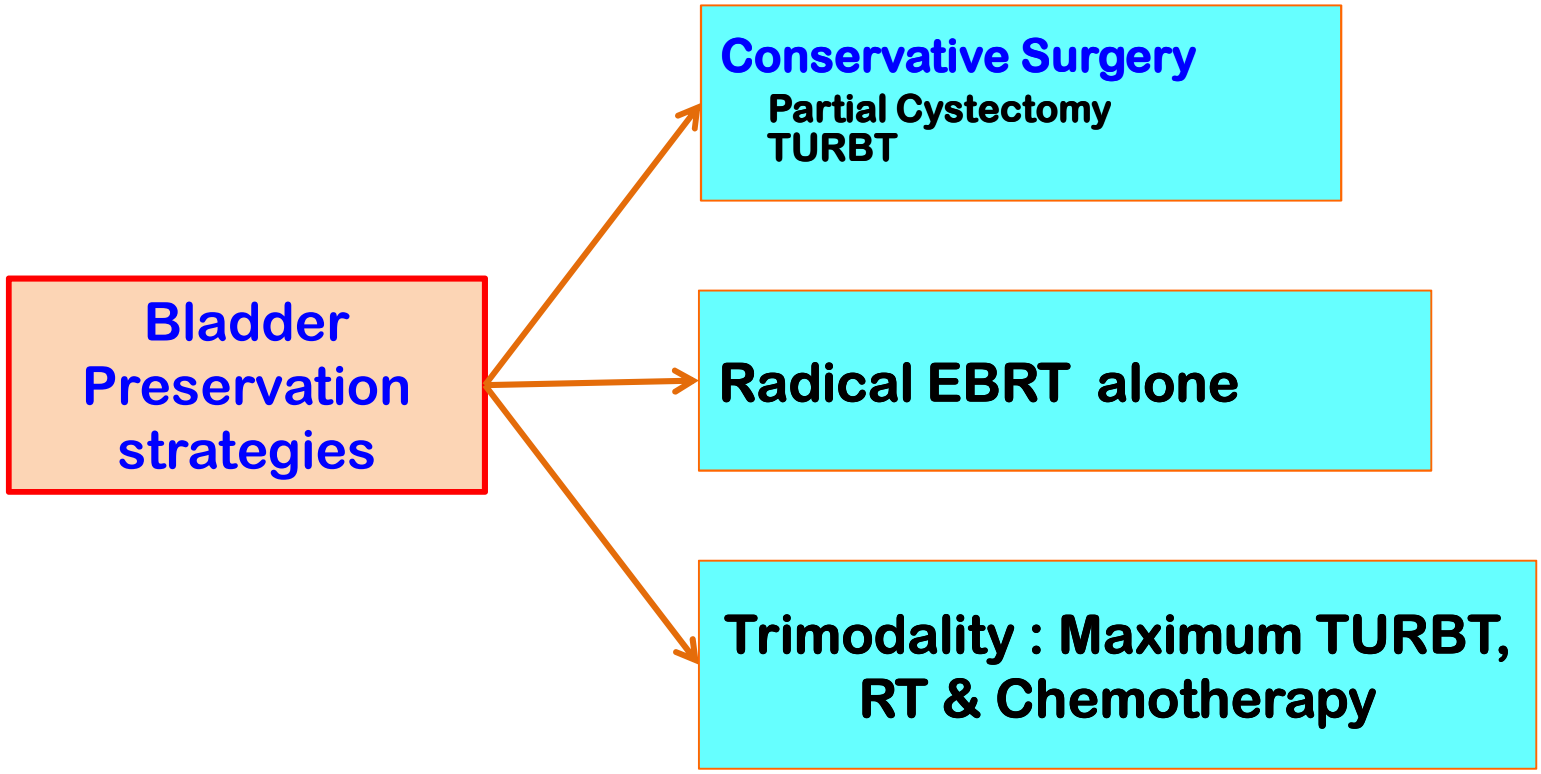
- **Size**
- **Tumor grade**
- **Depth of tumor invasion,**
- **Presence of CIS**
- **Detrusor muscle involvement in the specimen.**
- **Presence of LVI or unusual (variant) histology**

If there is uncertainty over the pathology, a further early re-resection (2-6 wk.) is indicated.

Muscle Invasive Bladder Cancer (MIBC)
(20% of cases)

If left untreated 85% of patients will die by 2yrs


Treatment Options
RADICAL CYSTECTOMY WITH URINARY RECONSTRUCTION FOLLOWED BY POST OP RADIATION
BLADDER PRESERVATION PROTOCOLS
Salvage cystectomy
RELAPSE (OR) PROGRESSION IN BLADDER
No difference in
OS , Cause Specific Survival & Distant recurrence free survival


Bladder Preservation strategies
Conservative Surgery
Partial Cystectomy
TURBT
Radical EBRT alone
Trimodality : Maximum TURBT, RT & Chemotherapy

Survival after radical treatment for transitional cell carcinoma of the bladder

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Table 3. Five- and 10-year overall and disease-specific survival rates (%) after cystectomy or high-dose radiotherapy for carcinoma of the bladder with primary stages Ta–T1 and T2–T3

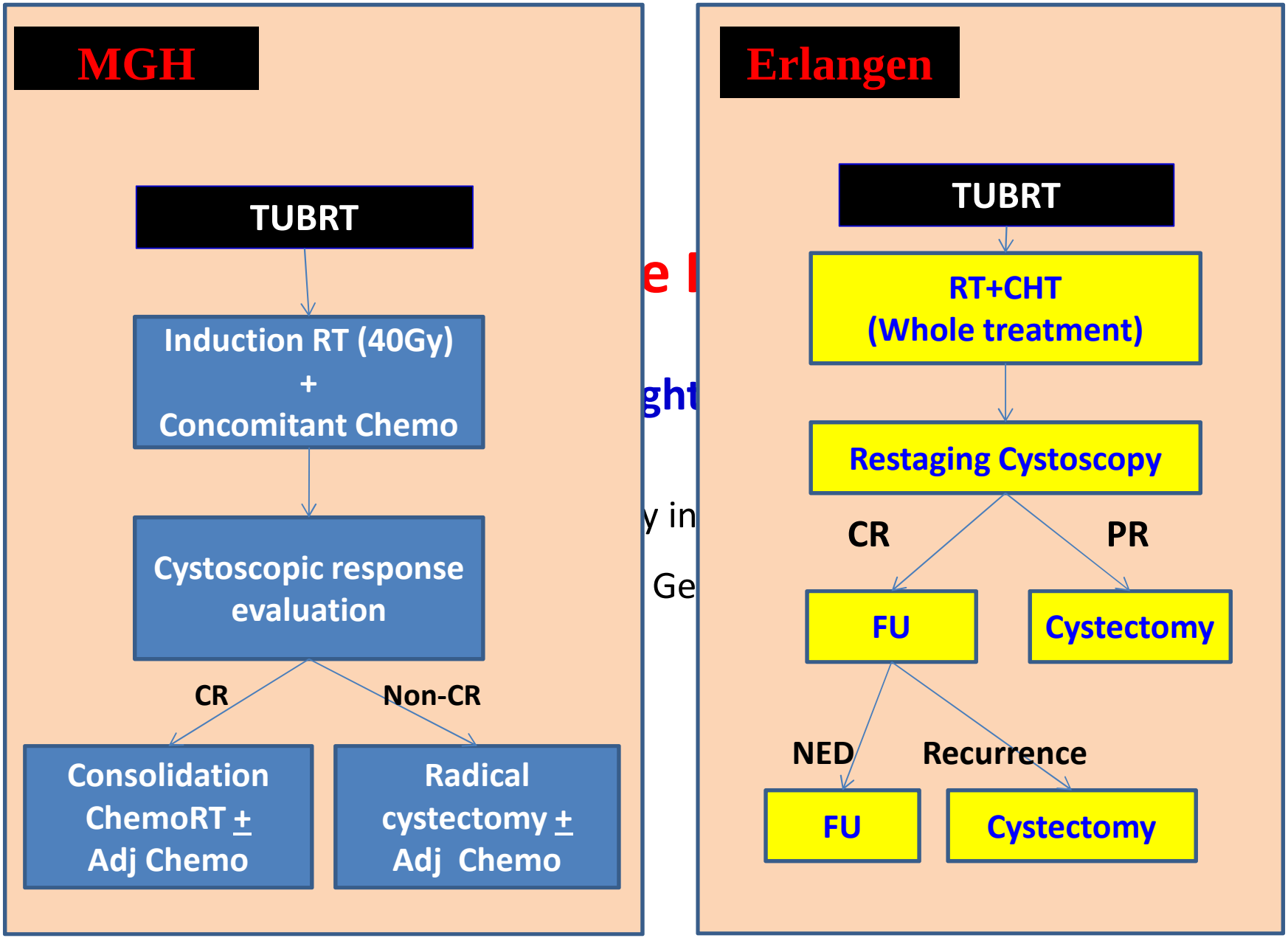
	Cystectomy			Radiotherapy		
Stage	*n*	5 years	10 years	*n*	5 years	10 years
Overall						
All stages	43	72 (7)	49 (8)	66	29 (6)	14 (4)
Ta–T1	24	88 (7)	67 (10)	27	48 (10)	26 (8)
T2–T3	19	53 (11)	26 (10)	39	15 (6)	5 (4)
Disease-specific						
All stages	43	74 (7)	61 (8)	66	45 (6)	29 (7)
Ta–T1	24	88 (7)	79 (8)	27	58 (10)	38 (10)
T2–T3	19	56 (12)	38 (12)	39	35 (9)	21 (9)

Ideal Candidate for Bladder Preservation :

- **Primary T2 to T3a tumors that are unifocal**
- **Tumor size less than 5 cm in maximum diameter**
- **Tumor not associated with extensive CIS**
- **No Ureteral obstruction or tumor-associated Hydronephrosis**
- **Good capacity of the bladder**
- **Visibly complete TURBT**
- **Adequate KFT to allow cisplatin to be given concurrently with irradiation**

Contraindications of pelvic Radiotherapy

- Patients with active inflammatory bowel disease
- Previous Pelvic irradiation
- Extensive prior pelvic surgery
- Chronic Pelvic infections
- High risk of serious late bowel complications.
- Extensive bladder CIS: high risk for tumor recurrence after RT therefore should be considered for **cystectomy**


MGH
TUBRT
Induction RT (40Gy)
+
Concomitant Chemo
Cystoscopic response evaluation
CR
Non-CR
Consolidation ChemoRT ±
Adj Chemo
Radical cystectomy ±
Adj Chemo
Erlangen
TUBRT
RT+CHT
(Whole treatment)
Restaging Cystoscopy
CR
PR
FU
Cystectomy
NED
Recurrence
FU
Cystectomy

RTOG Protocols & Results of Multimodality Treatment for MIBC

Series	Year	Multimodality Therapy Used	No. Patients	5-yr OS	Survival with Intact Bladder
RTOG 8512[236]	1993	TURBT, EBRT + cisplatin	42	52%	42%
RTOG 8802[237]	1996	TURBT, MCV, EBRT + cisplatin	91	51%	44%; (4-yr)
RTOG 8903[209]	1998	TURBT ± MCV, EBRT + cisplatin	123	49%	38%
RTOG 9906[240]	2009	TURBT, twice-daily EBRT + paclitaxel	80	56%	47%
University of Paris[153]	1997	TURBT, 5-FU, EBRT + cisplatin	120	63%	NA
Erlangen[234]	2002	TURBT, EBRT, cisplatin	415	51%	42%

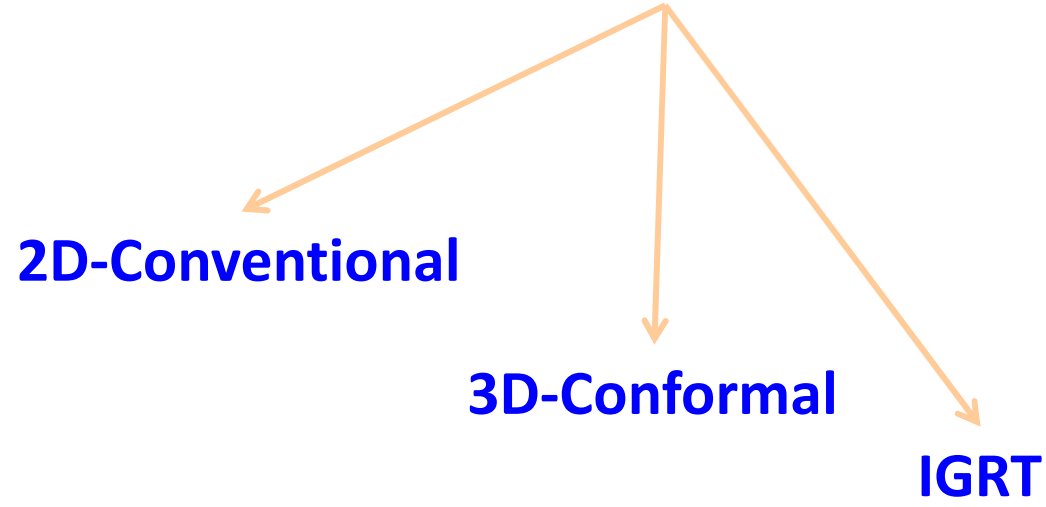
Conclusions :

- **Combined modality provided better bladder preservation.**
- **Cisplatin: Best Radio sensitizer, Safe and easily administered**
- **Accelerated fractionation has given better control rates in Phase II trial**

Cystectomy Vs Trimodality Treatment:

Series	Year	Category	No. Patients	Overall Survival	
				5-yr	10-yr
Cystectomy					
USC[136]	2001	pT2-pT4a	633	48%	32%
MSKCC[137]	2001	pT2-pT4a	181	36%	27%
SWOG/ECOG/CALGB*†[216]	2002	cT2-cT4a	317	49%	34%
Selective Bladder Preservation					
University of Erlangen*[123,234]	2002	cT2-cT4a	326	45%	29%
MGH*[233]	2009	cT2-cT4a	348	52%	35%
RTOG*[209]	1998	cT2-cT4a	123	49%	—

Definitive Radiation Planning

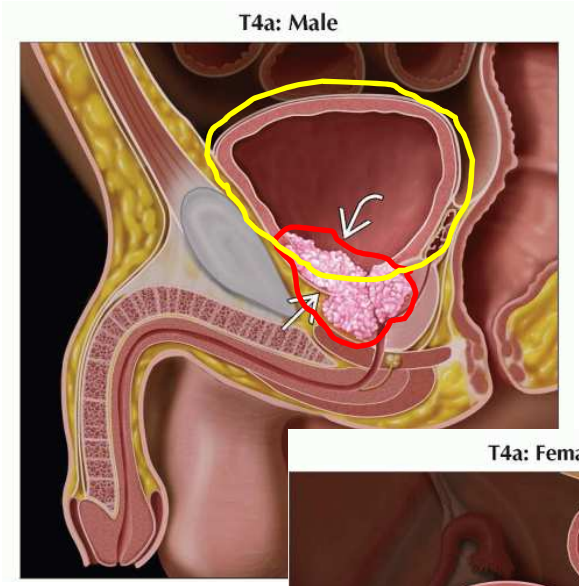


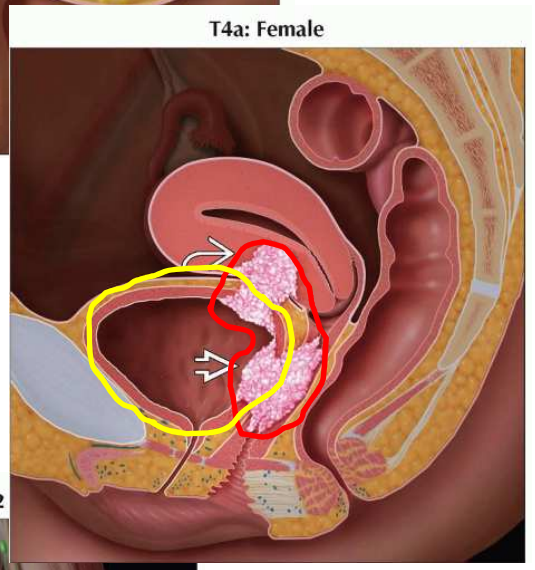
RT-Planning

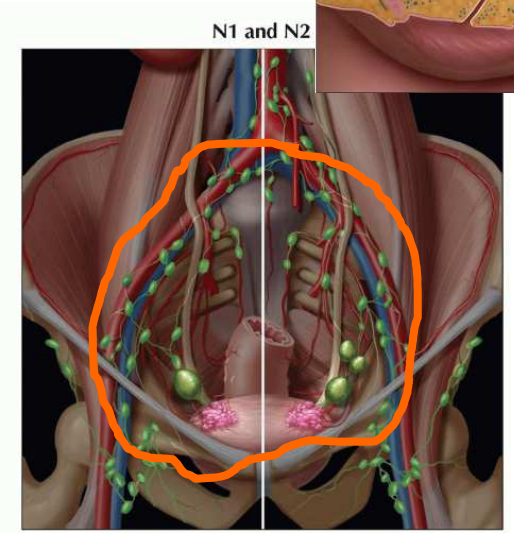
- Explain patient about the procedure
- Positioning
- Immobilization
- Simulation
- Prescription of dose
- Treatment
- Patient care during RT.

Target volume:

- Primary tumor & its local extension,
- Whole bladder ,
- Proximal urethra
- Prostate with prostatic urethra.
- In female proximal 2 Cm of urethra
- Regional LNs: External iliac, Internal iliac, Hypogastric & Obturator LNs.







Patient position

Supine

- Easier for set up,
- More comfortable to pt.
- More reproducible for daily set up.

Patient immobilization

- Knee rest – relaxes lower back muscles on rigid treatment couch,
- Foot rest
- Vac lock
  - Reproducibility of patient set up
  - Limits pts. Movement during treatment
- Advanced localization techniques:
  - Implanted markers

Conventional planning

- Give oral contrast 1 hr before
- Ask patient to voiding urine
- Foley's catheter inserted immediately after voiding urine and measure the residual volume of urine.
- 7CC Hypaque solution to inflate balloon and pull down at base of bladder

- This volume is replaced by an equal volume of hypaque solution plus an additional 25 ml and 10-15 ml of air then clamp the cathetor.
- Hypaque solution- Urographin :NS = 1: 3
- Air will rise to the top & define the anterior extension of bladder.

- **Pt then transferred to simulator couch & positioned.**
- **Pt is adjusted so that pelvis is straight, relative to the axes of treatment couch.**
- **Following simulation & radiographic exposure of anterior fields, rectal contrast may be given & lateral simulation is exposed.**

Bladder : Empty or Full ???

Empty bladder :

- **More reproducible**
- **More comfortable to patient**
- **Overall irradiated volume is smaller.**

Full bladder:

- **Displaces small intestine & some part of rectum out of radiation portals**

Significant changes in bladder volume

- Interval between voiding & T/t delivery
- Patient's state of Hydration
- Use of Diuretic Medications
- Ingestion of diuretic beverages (coffee, soft drinks)
- Extrinsic pressure (rectal filling, tumor mass)

Phase I:

- **The whole pelvis, encompassing the pelvic lymph nodes, bladder, and proximal urethra**

- **Elective irradiation of the pelvic lymph nodes ----still not confirmed (BC 2001 trial treated only bladder with margin in radiologically node negative patients)**

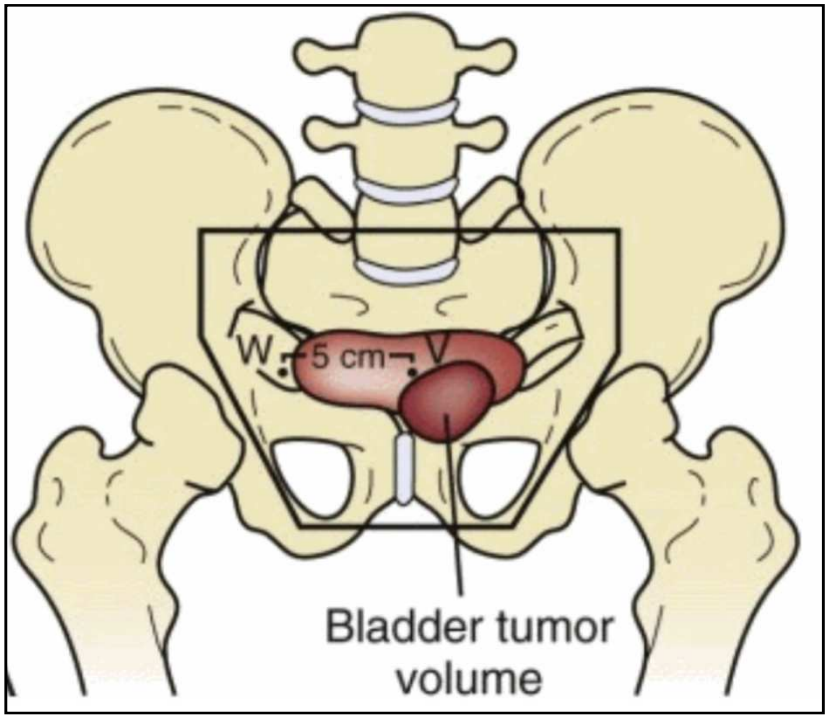
Phase II (Boost)

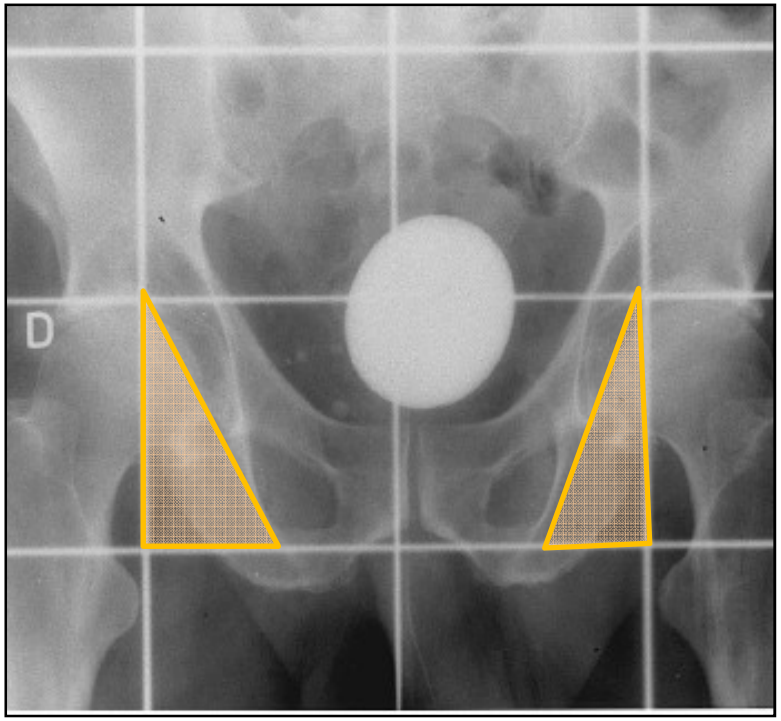
- **Then cone-down to boost the bladder alone / partial bladder (where the primary tumor was present- cystoscopy and radiology)**

Phase I :

AP-PA field

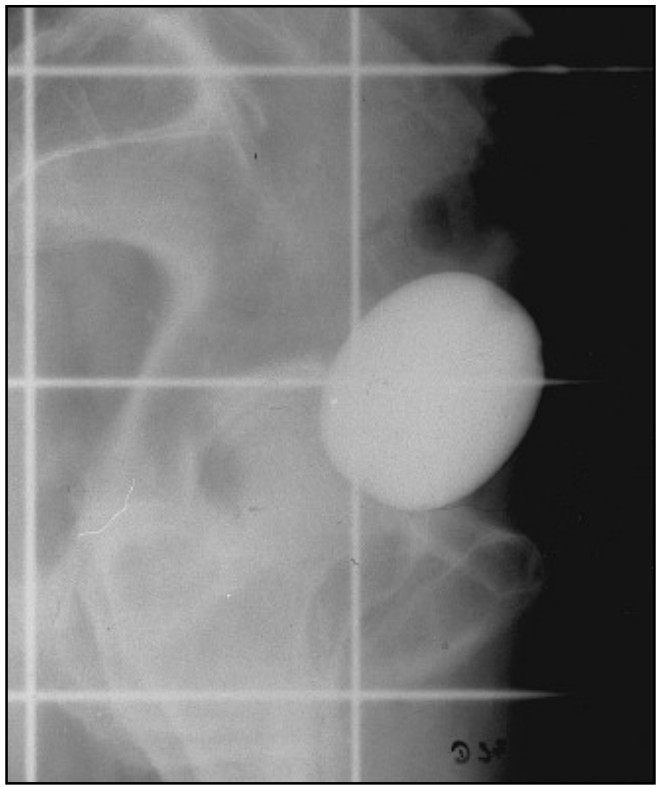
- Superior :at the L5-S1 disc space
- Inferior : below obturator foramen.
- Laterally:1.5-2 cm to the bony pelvis at its widest section

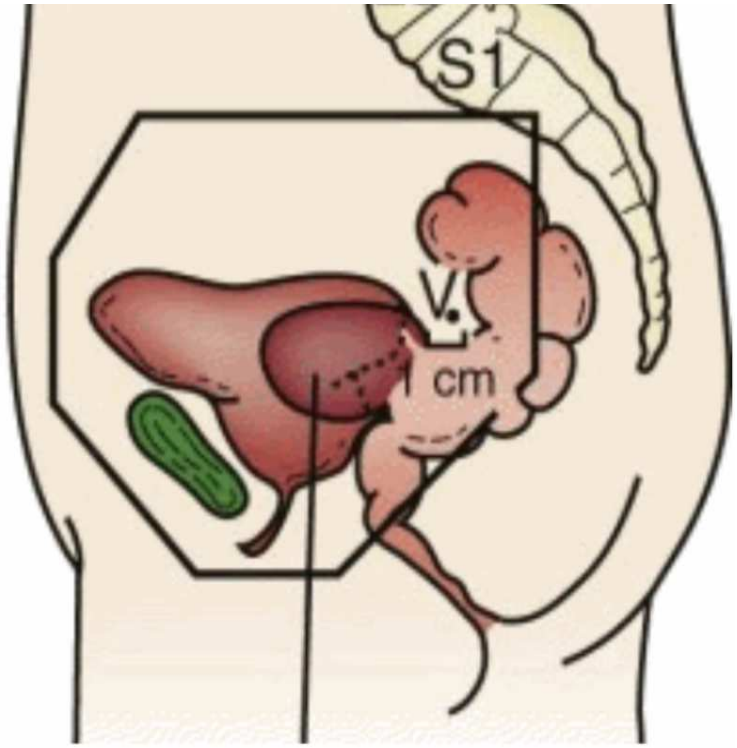




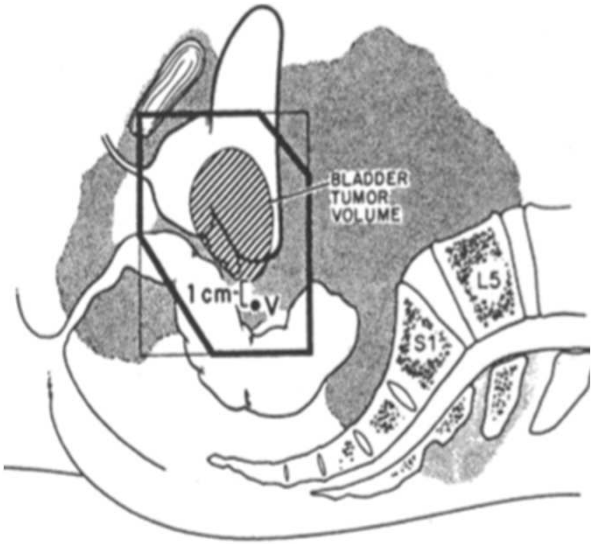
Lateral field

- Superior & Inferior border same as in AP-PA portal
- Anterior : anterior to bladder with a margin with 1.5 – 2cm
- Posterior : 2-3 cm posterior to bladder





Phase II (Boost)



PORTALS :

- Anterior –Bladder with a margin of 1-1.5cm
- Lateral – Bladder with a margin of 1-1.5cm
- Oblique– Selected at an angle which spares the rectum completely and encompasses the bladder with 1.5 cm margin

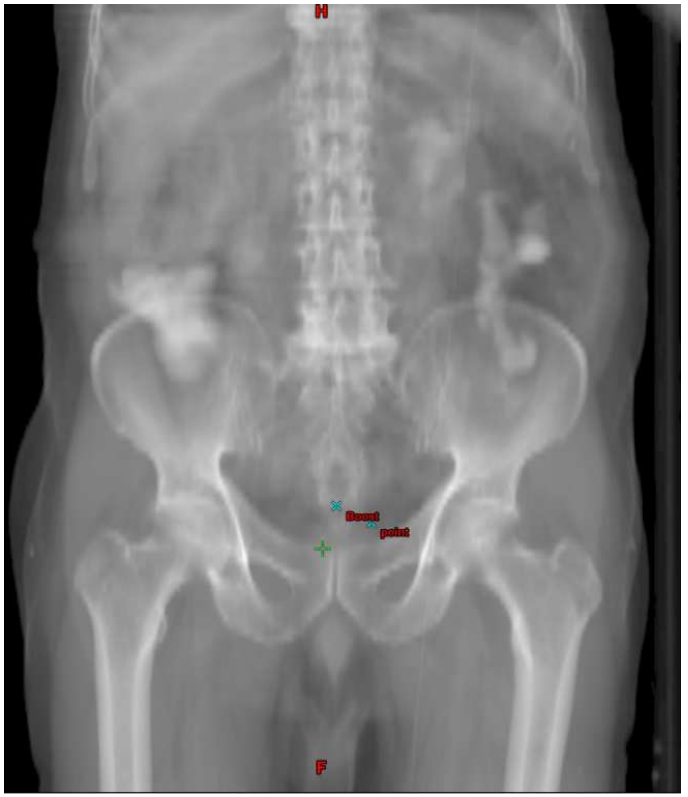
FIELDS : 3 fields

2 laterals and one anterior / 2 obliques and one anterior

Conformal Radiotherapy (3D-CRT) :

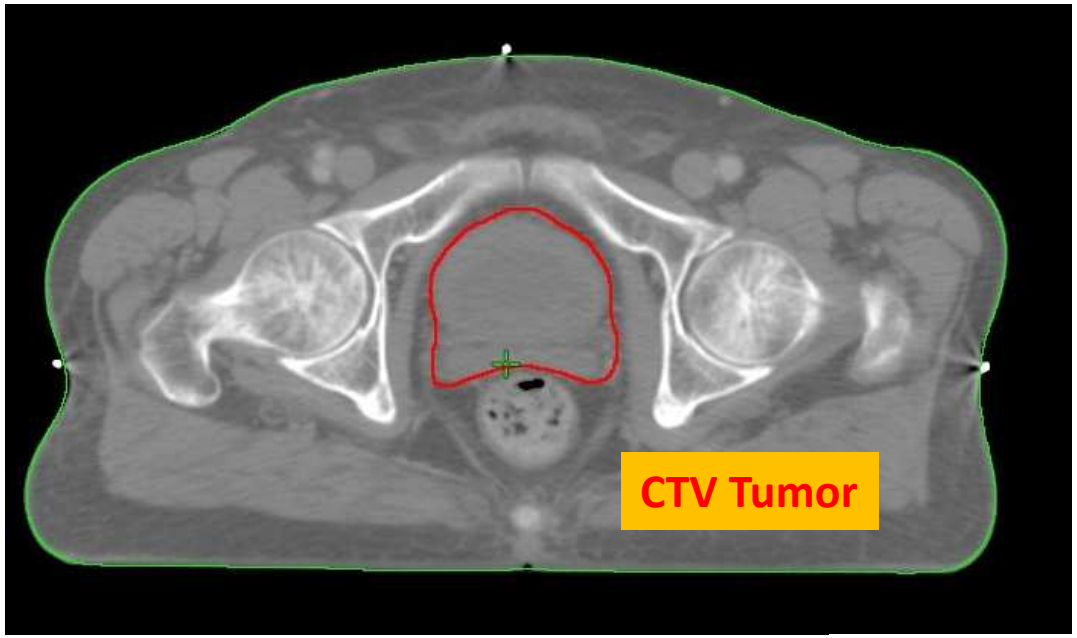
PLANNING CT :

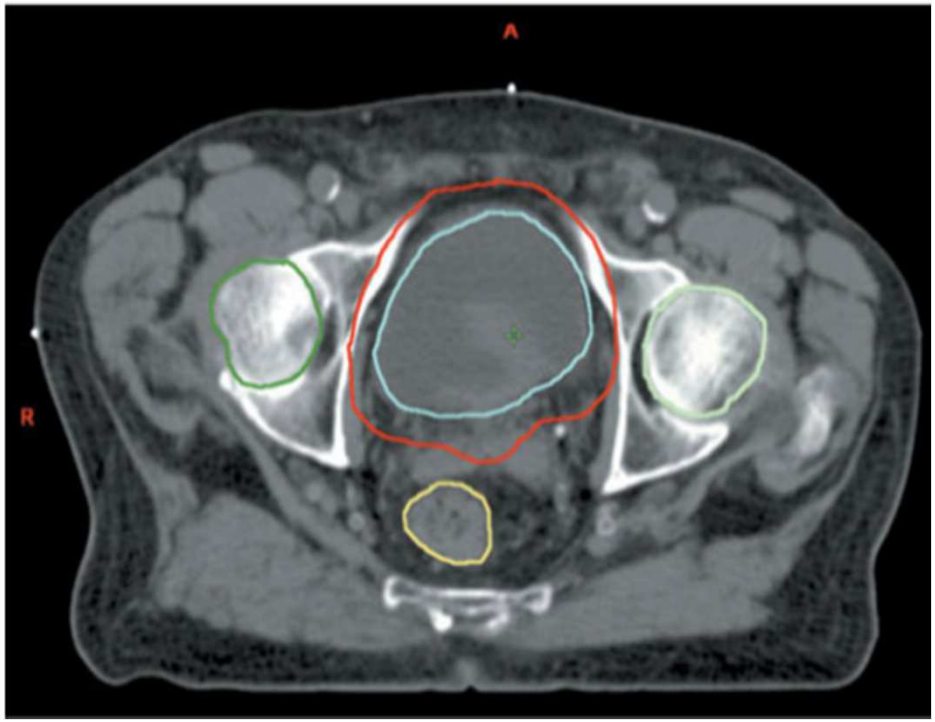
- Supine, arms on chest
- Knee and Ankle immobilization
- Empty Rectum
- Empty Bladder 15 minutes before
- Scan is performed with 2-3 mm slices from the lower border of L5 to the inferior border of the ischial tuberosities.
- All planning and treatment should be carried out with the bladder empty



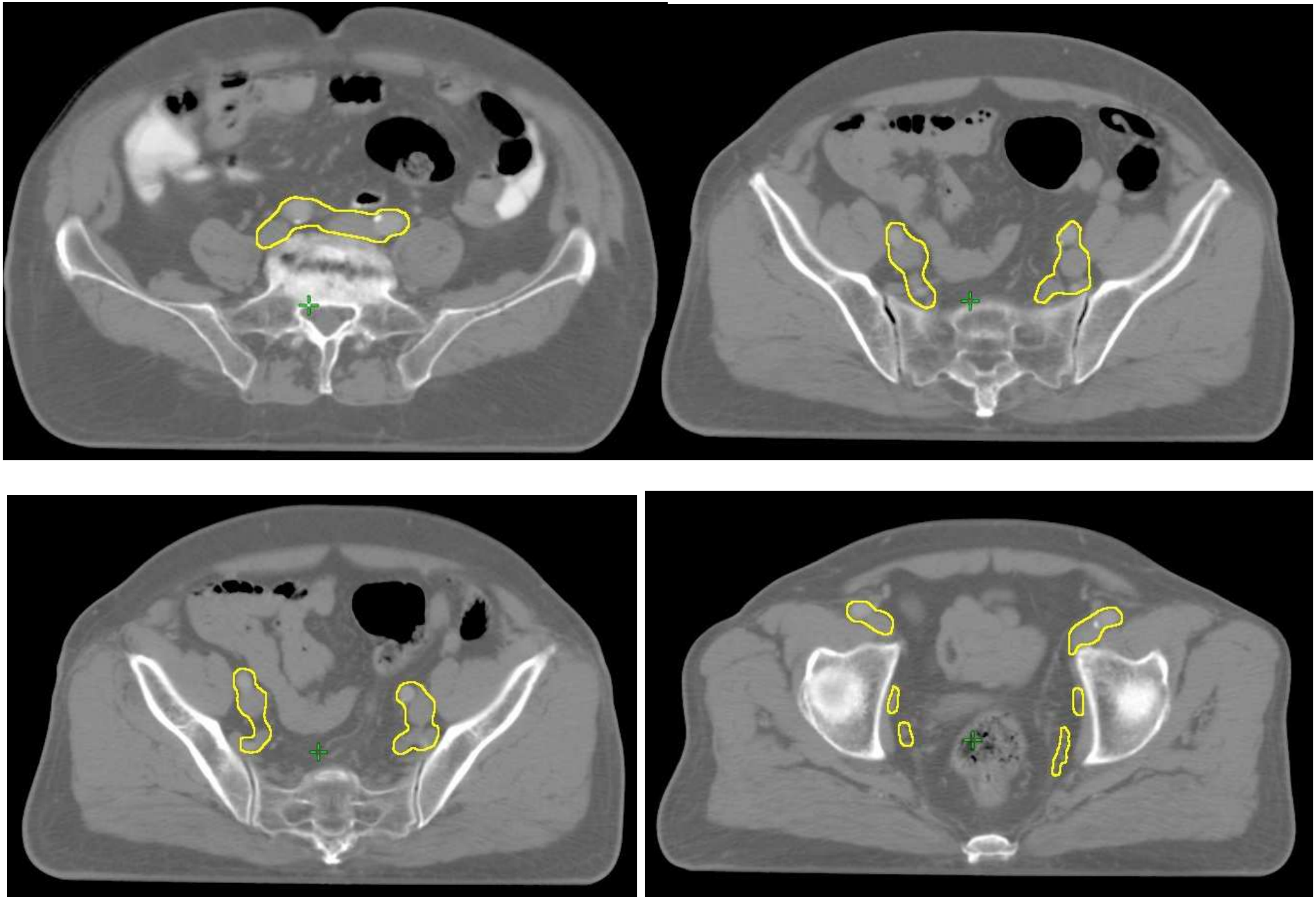
Different Target Volume Contouring :

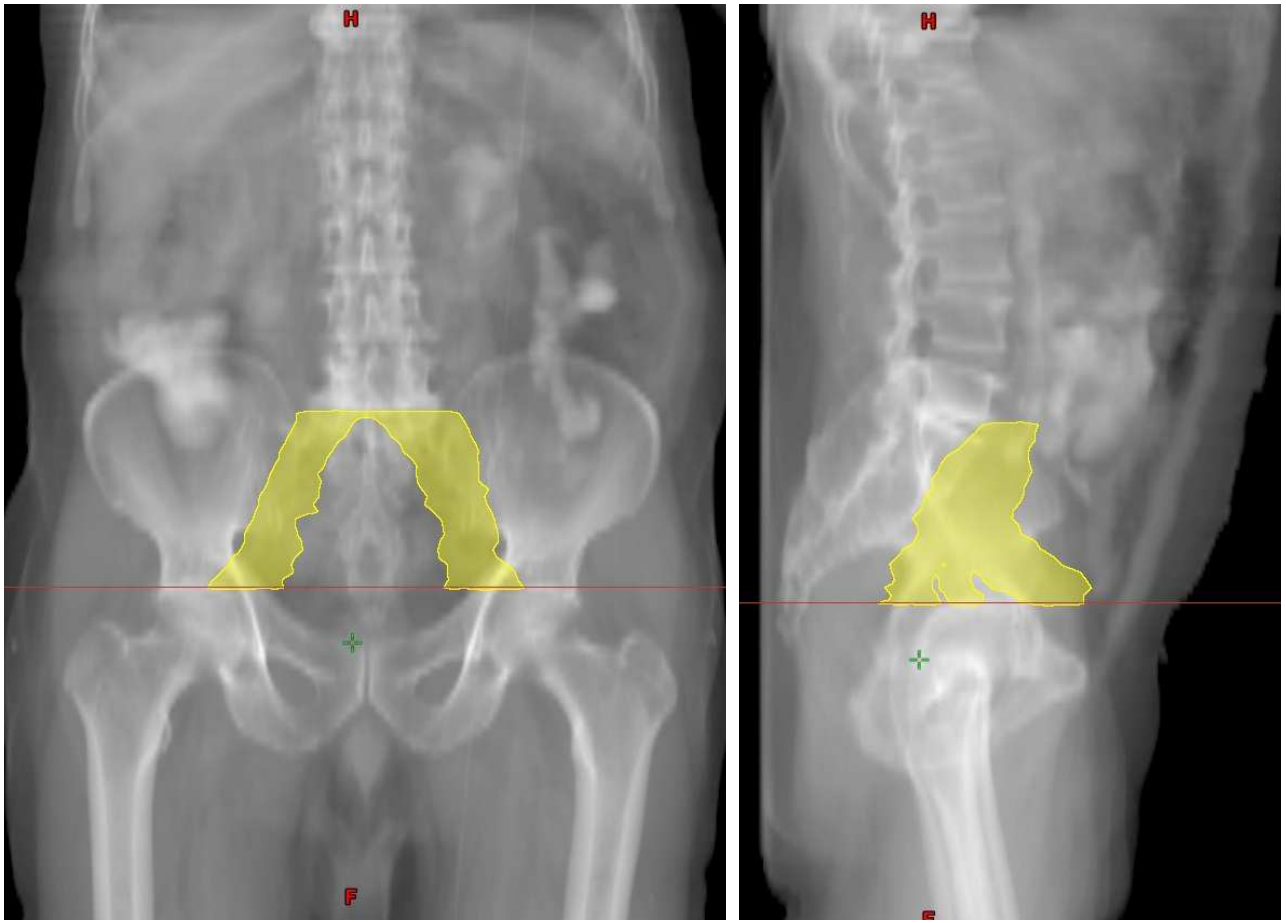
- **GTV = Primary Bladder tumour**
- **CTV Tumour –Whole bladder and any extra-vesical extension**
    - **Men : entire prostate & Seminal Vesicles**
    - **Women : Proximal 2 cm of urethra is also considered as part of the target field**
- **CTV Nodal**
- **CTV Total = CTV Tumour+ CTV Nodal**
- **PTV 1= 1.5-2cm around CTV**
- **PTV Boost= CTV Tumour+ 1cm**


CTV Tumor


A
R

Vessels : From L5 Lower border – femoral Head upper border

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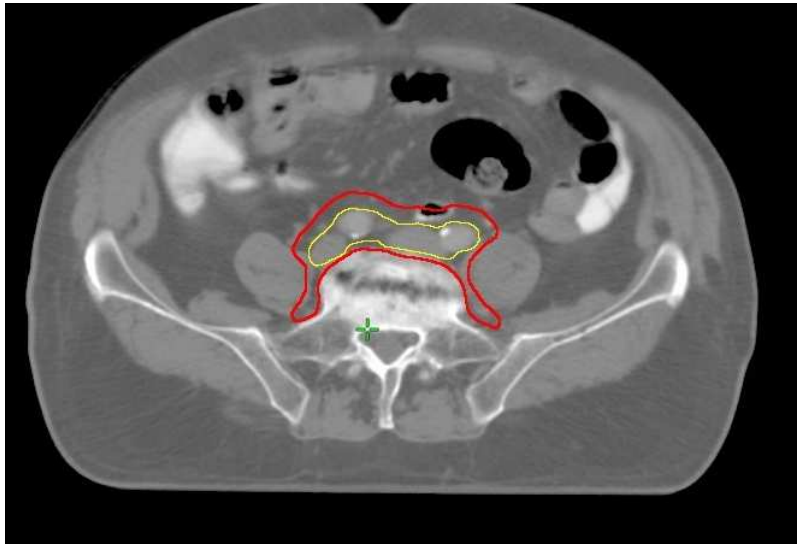
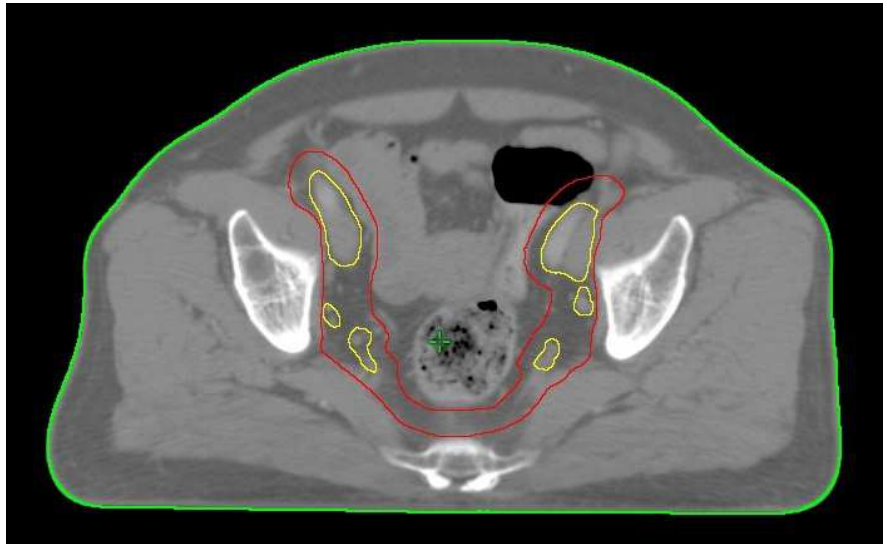
CTV Nodal

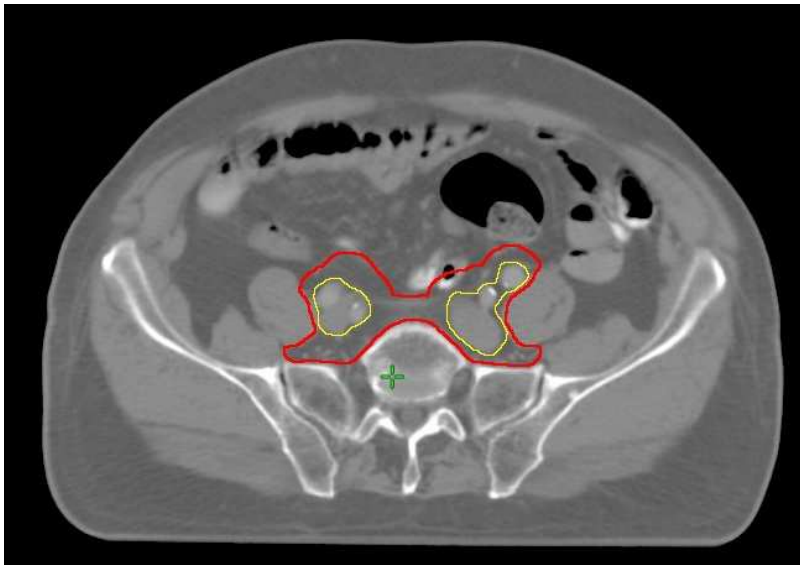
Vessels+ 0.7 cm margin



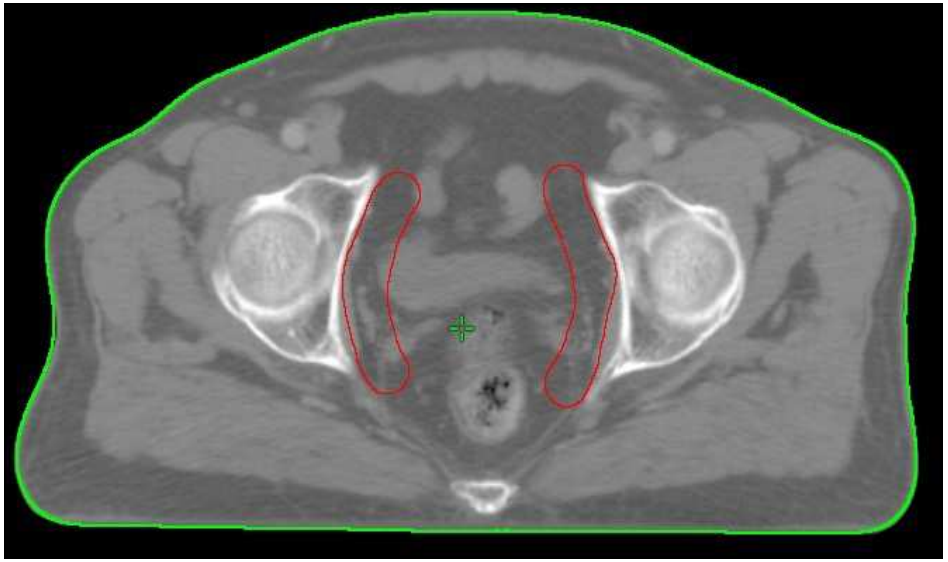
join Ext-int iliac with 1.8 cm brush for Hypogastric LN



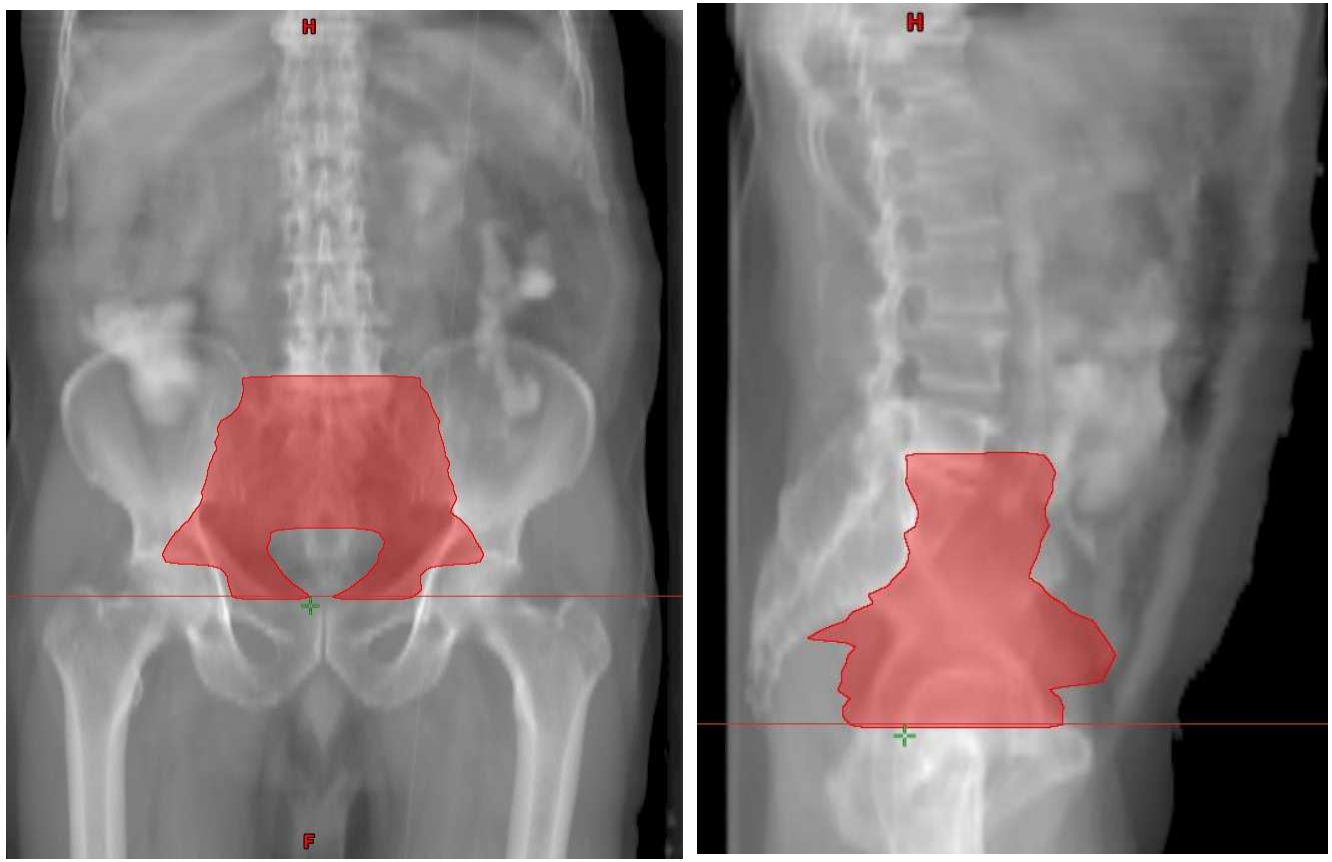
1 cm brush post border of iliopsoas for presacral

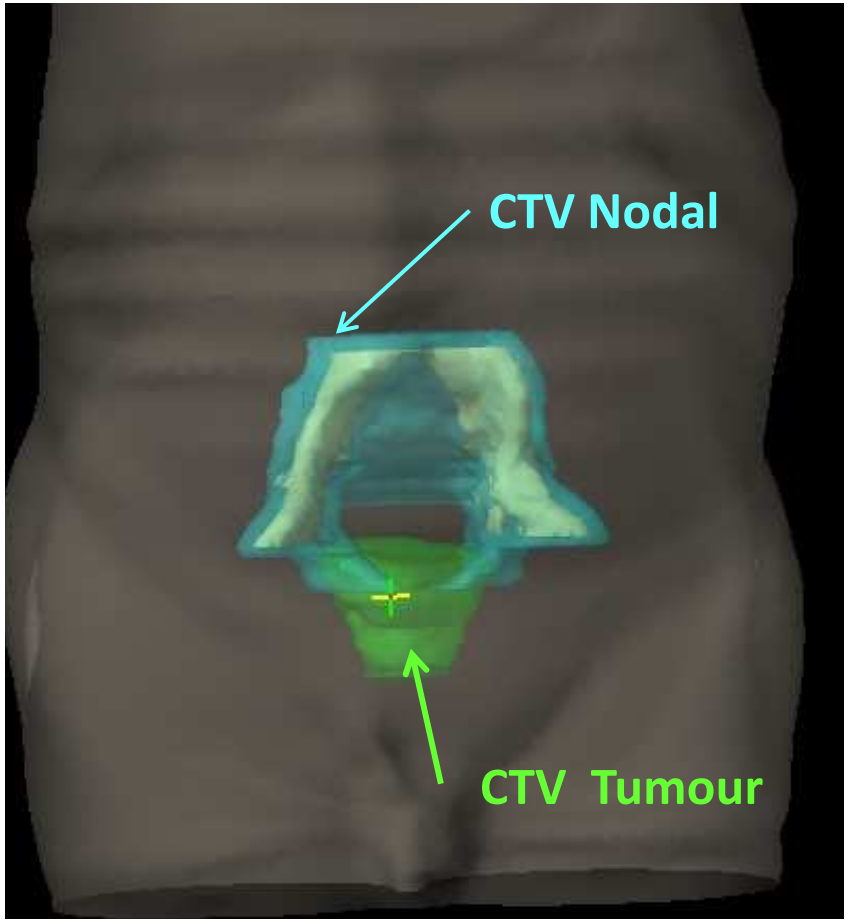


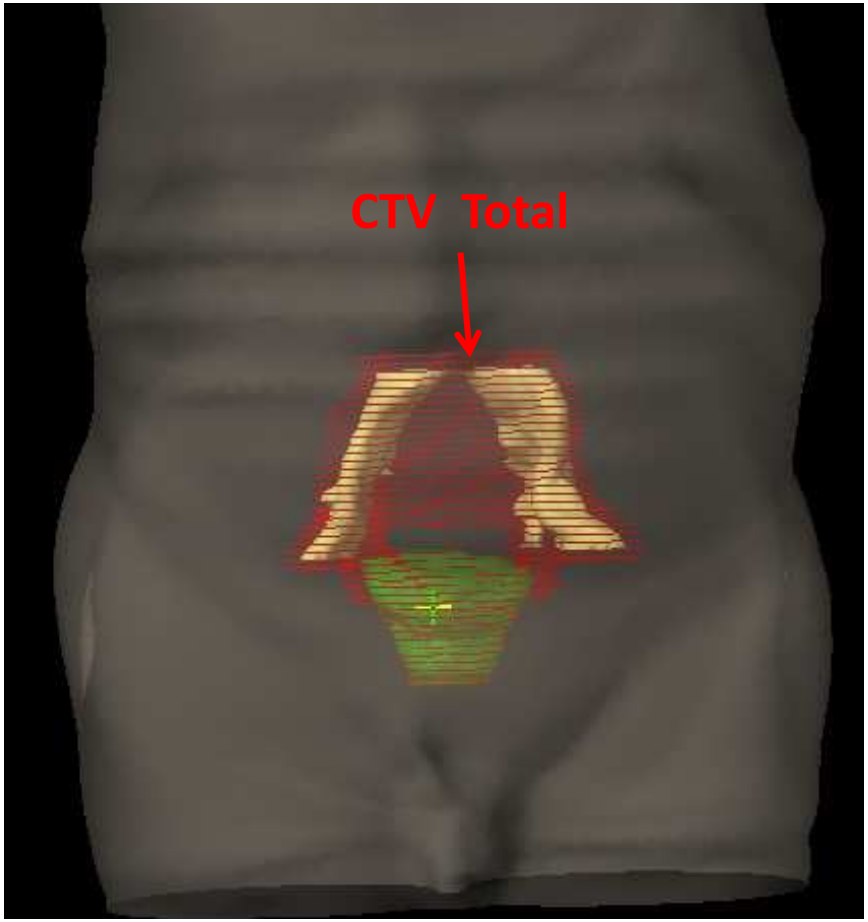
1.8 cm brush obturator strip up to pelvic floor

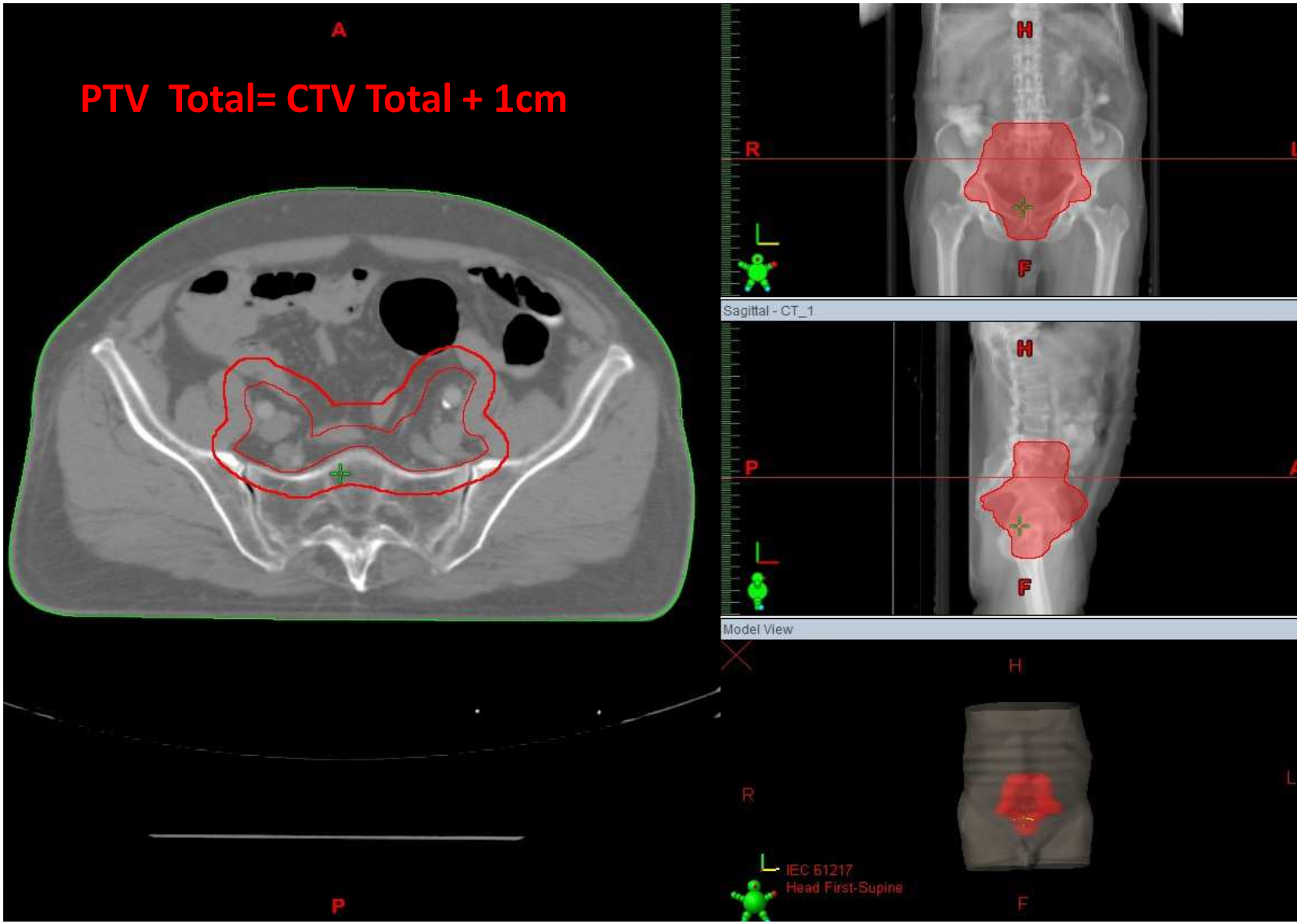


CTV Nodal




CTV Nodal
CTV Tumour


CTV Total


PTV Total= CTV Total + 1cm
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Sagittal - CT_1
H
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Model View
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IEC 61217
Head First-Supine
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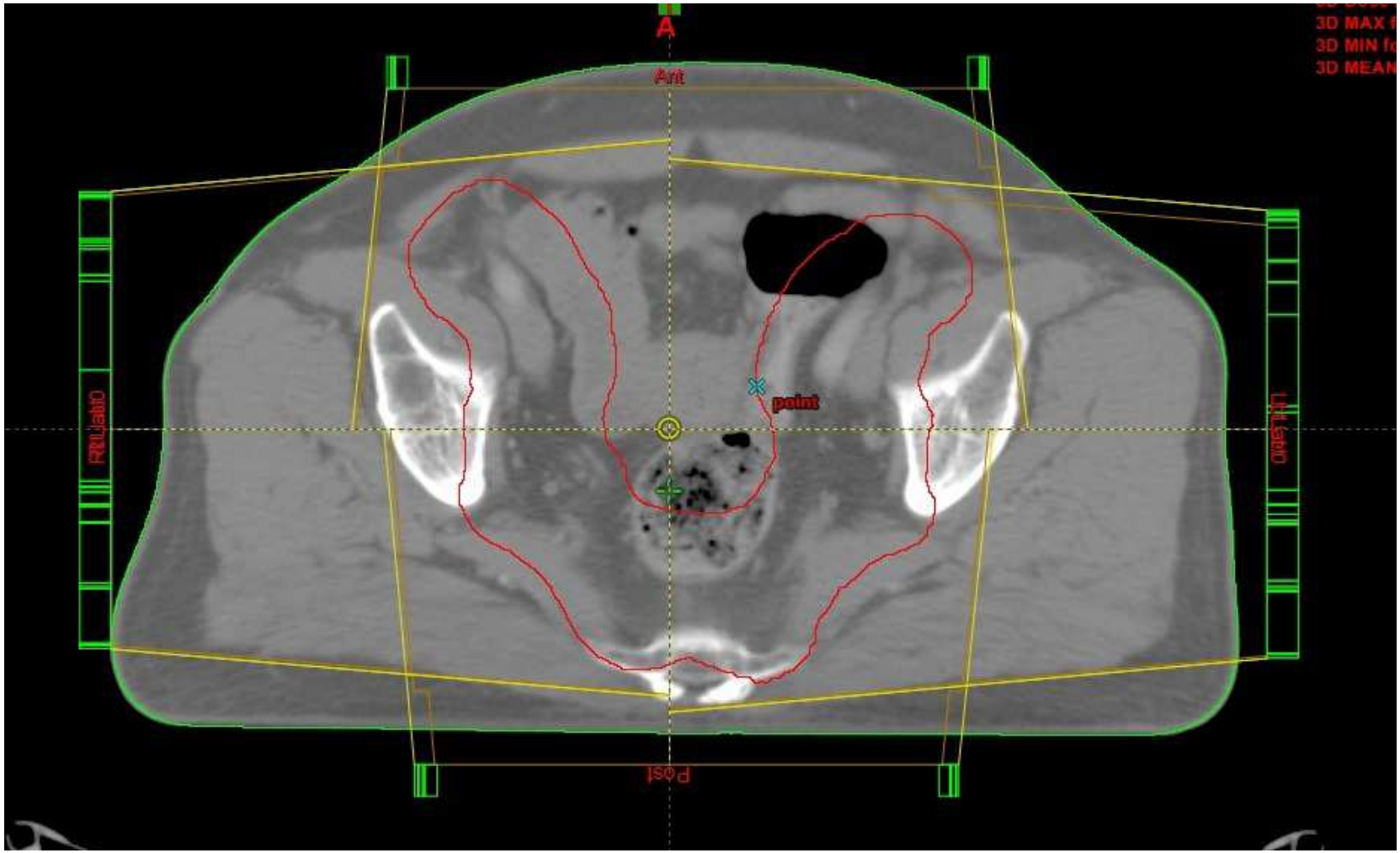
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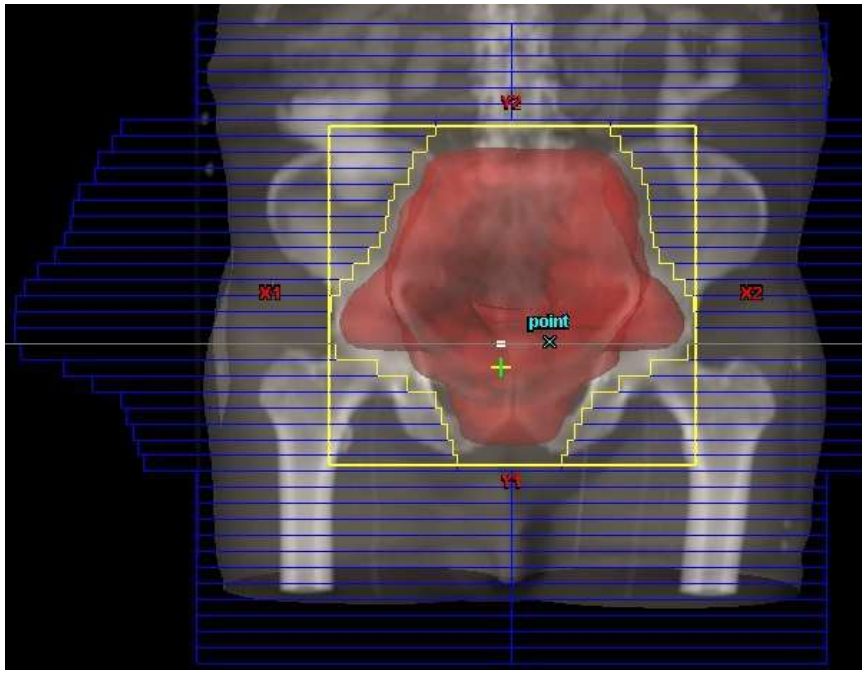
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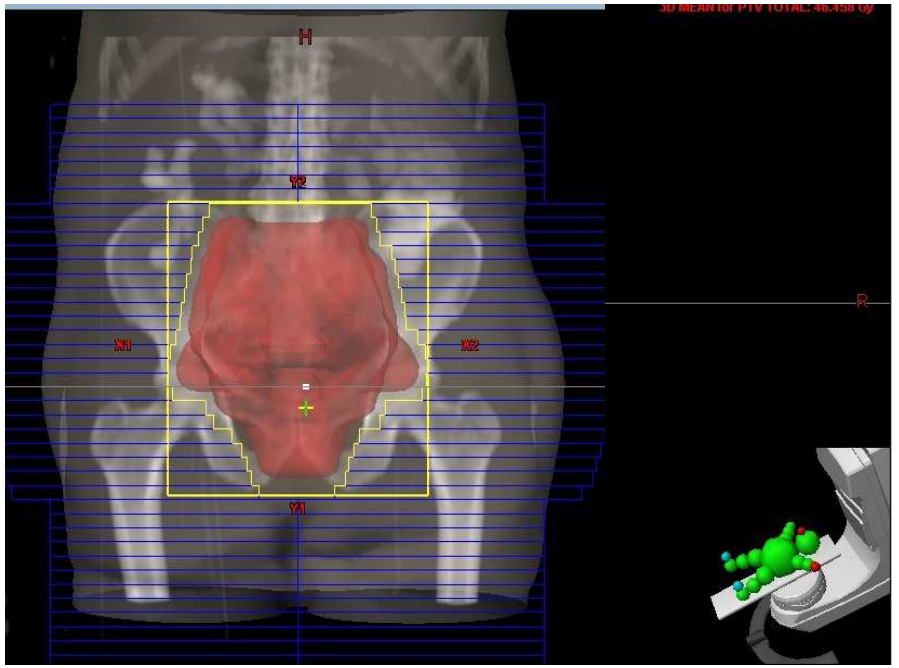
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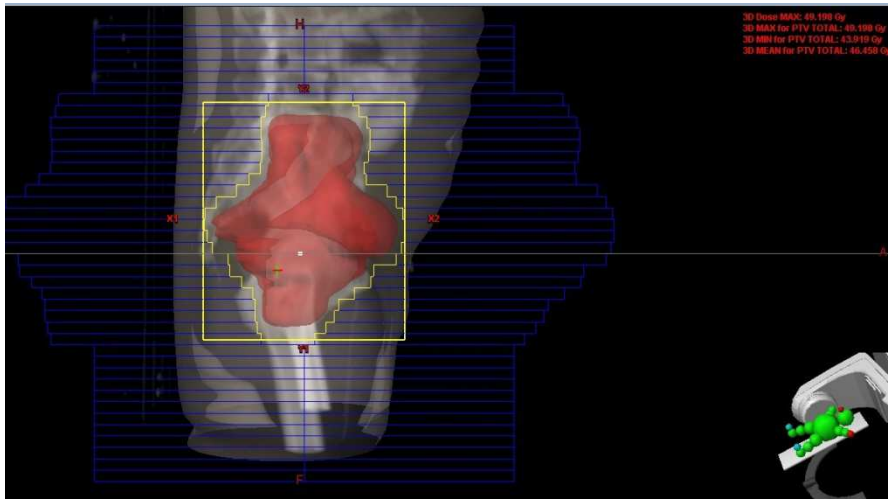
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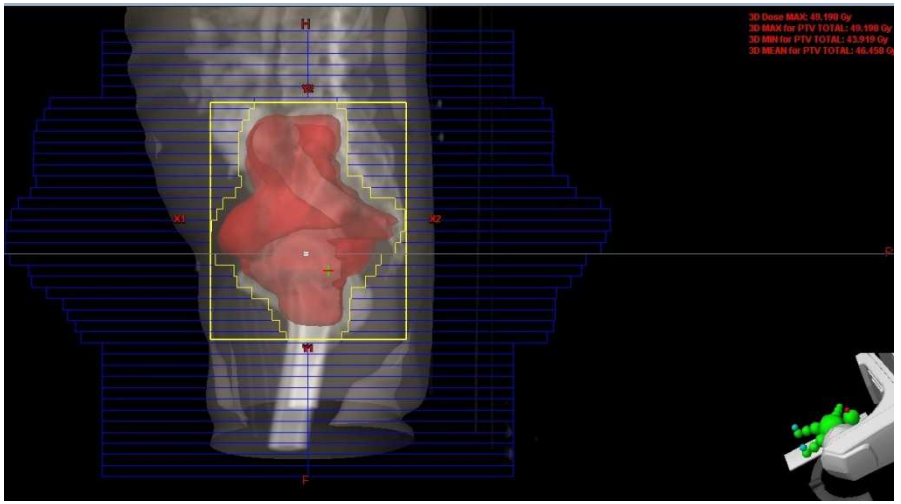
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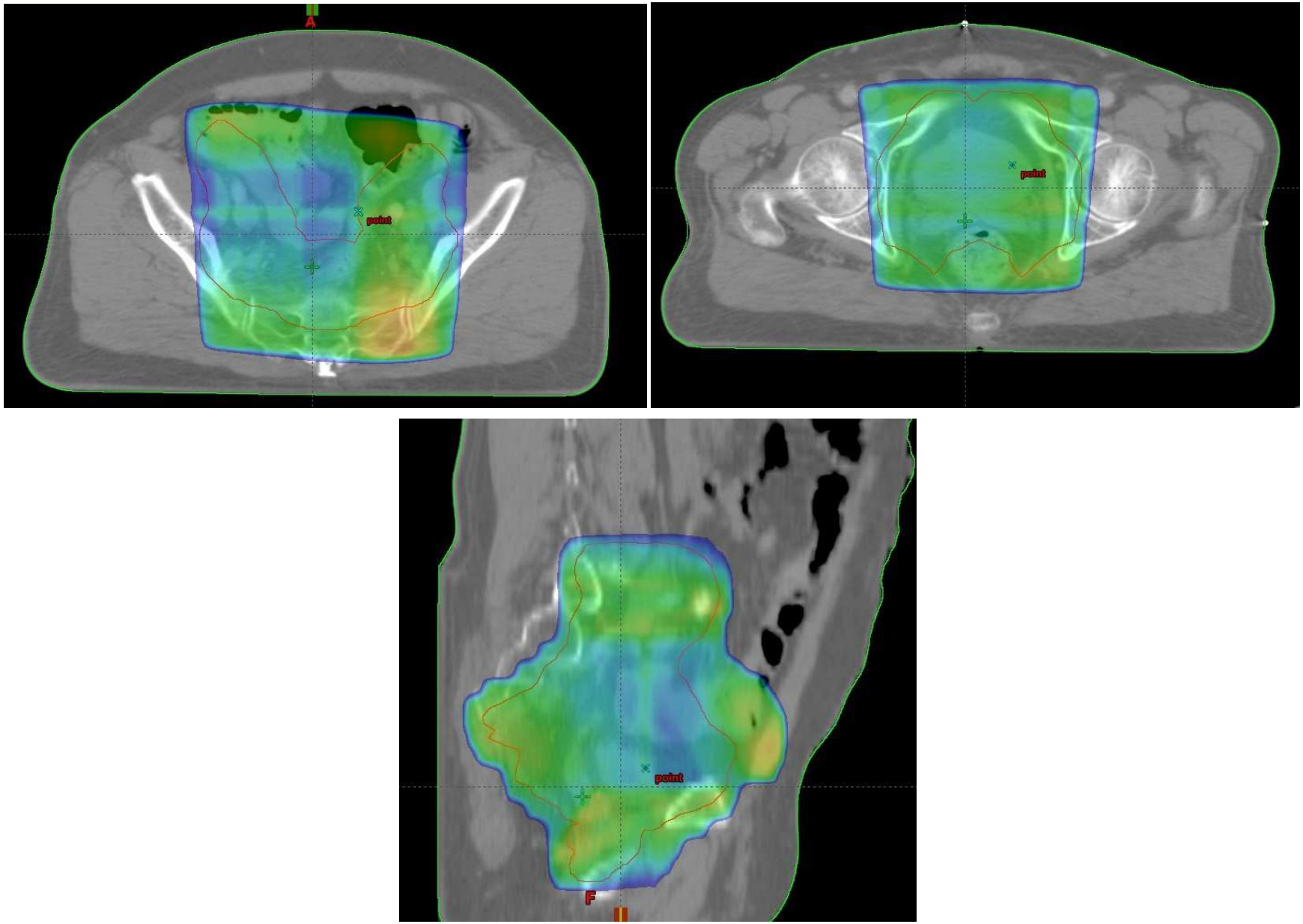
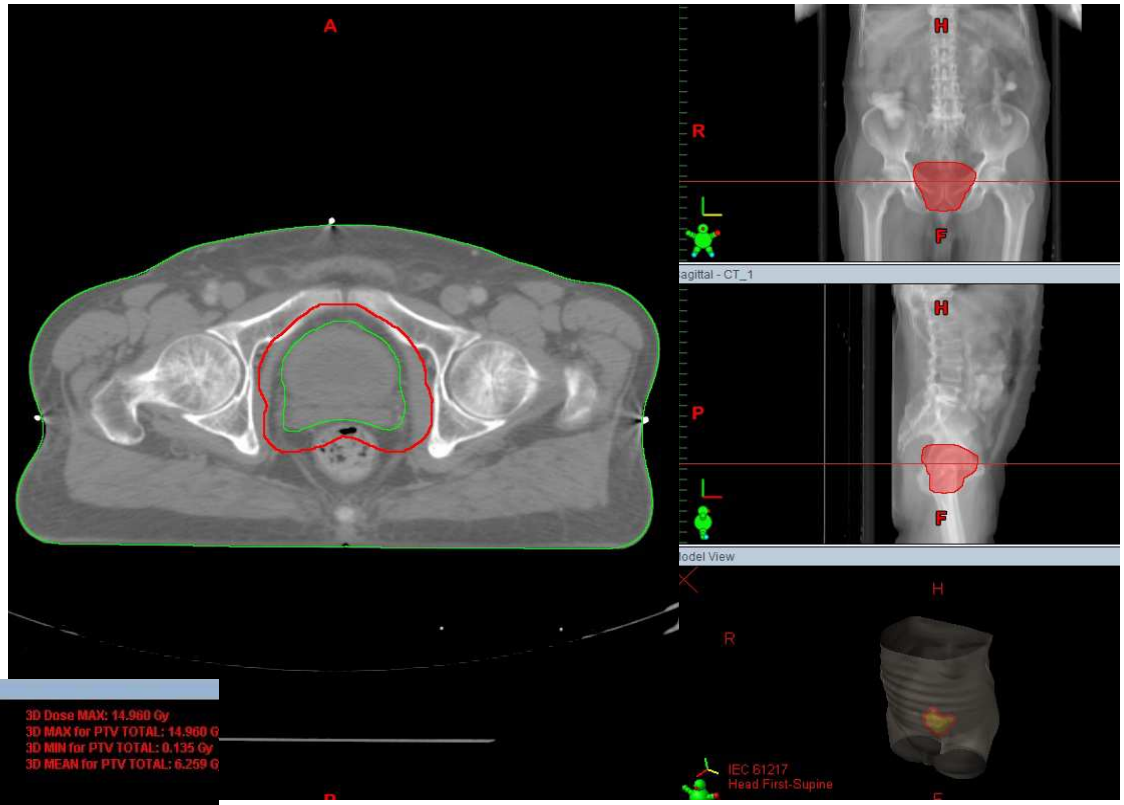
95% Isodose line of prescribed dose



Boost Phase: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agittal - CT_1
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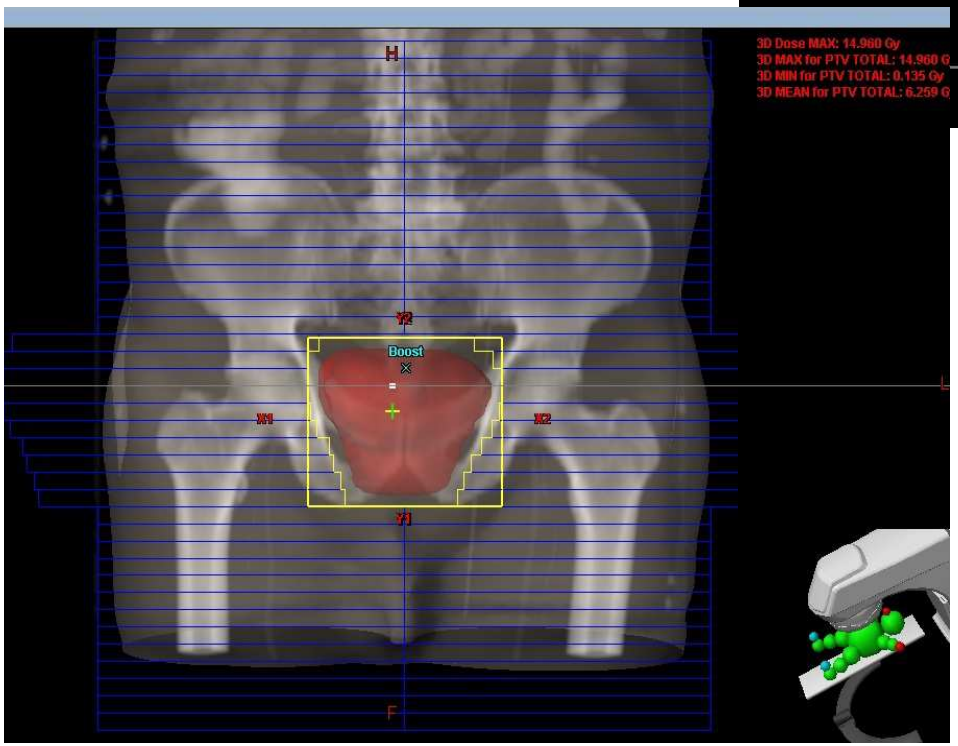
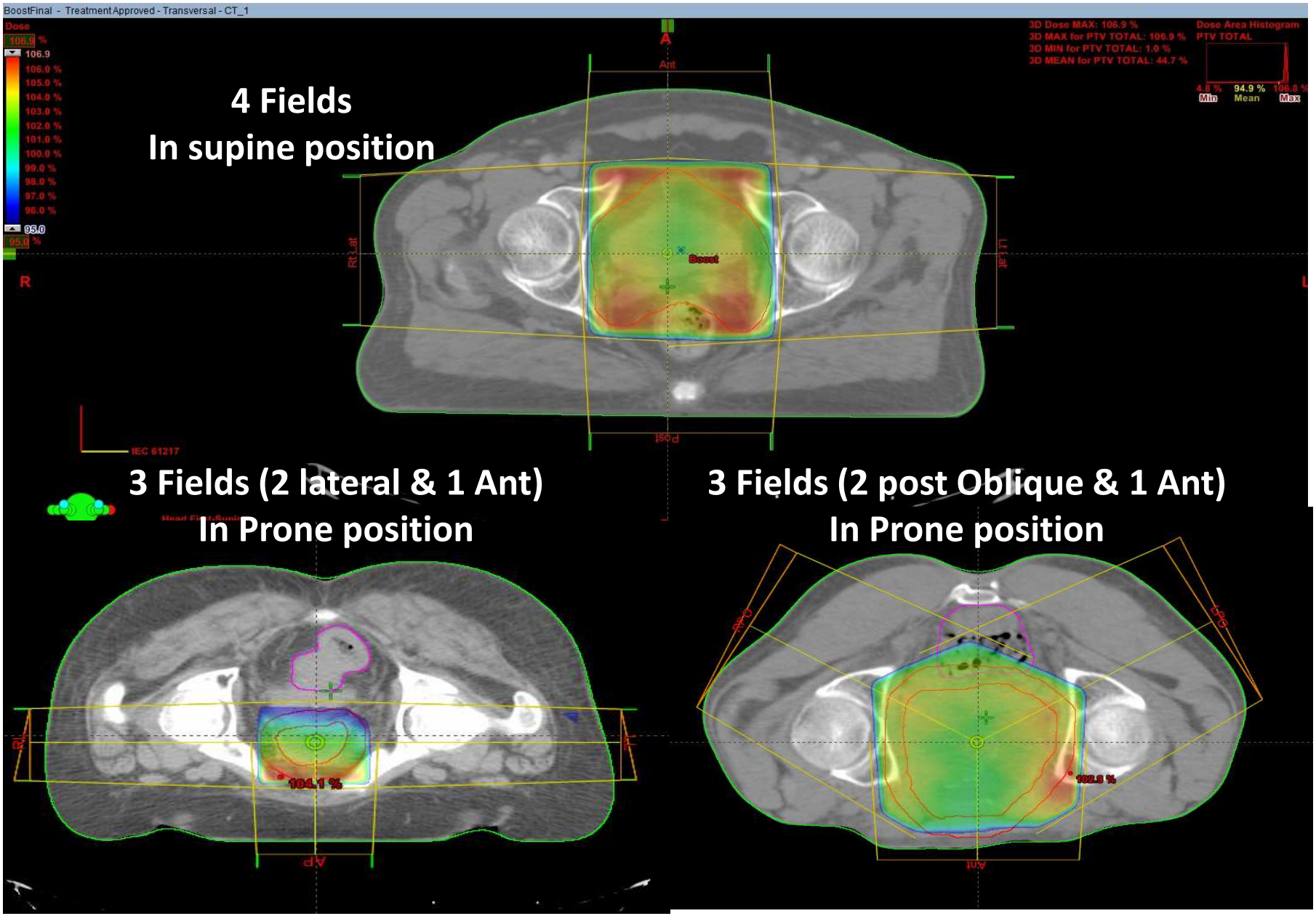
H
R
IEC 61217
Head First-Supine


H
3D Dose MAX: 14.980 Gy
3D MAX for PTV TOTAL: 14.960 G
3D MIN for PTV TOTAL: 0.135 Gy
3D MEAN for PTV TOTAL: 6.259 G
Y2
Boost
X1
X2
Y1
F


BoostFinal - Treatment Approved - Transversal - CT_1
4 Fields
In supine position
3 Fields (2 lateral & 1 Ant)
In Prone position
3 Fields (2 post Oblique & 1 Ant)
In Prone position
Boost
3D Dose MAX: 106.9 %
3D MAX for PTV TOTAL: 106.9 %
3D MIN for PTV TOTAL: 1.0 %
3D MEAN for PTV TOTAL: 44.7 %
Dose Area Histogram
PTV TOTAL
94.9 %
Mean
IEC 61217

Radiation Dose :

Phase I : 40 to 46 Gy at 1.8 – 2Gy per fraction.

Phase II (Boost): 14-20 Gy at 1.8-2 Gy per fraction

Total Dose : 60-66 Gy

Energy : 6-15MV

At PGIMER:

- **Phase I :** 46 Gy @ 2Gy/# in 23fractions.
- **Phase II (Boost):** 18 Gy @ 2Gy/# in 9fractions
- **Total Dose :** 64 Gy in 32 Fractions

Problems in Bladder Radiation:

- Organ motion
- Delineation errors
- Set up errors
- Treatment verification
- Reproducibility of bladder volume

Table 2 CTV to PTV Margin Widths Suggested by Muren et al[12]

Margin	Inferior	Superior	Left	Right	Anterior	Posterior
Set-up margin (SM)	0.6	0.3	0.2	0.3	0.3	0.4
Internal margin (IM)	1.0	2.0	1.1	0.8	2.0	1.4
Total CTV to PTV margin	1.6	2.3	1.3	1.1	2.3	1.8

IGRT

- **Patient-specific direct anatomic or surrogate variations are assessed before treatment delivery and are used to modify the patient setup and treatment plan potentially multiple times during the treatment course.**

- **Goal: Accurate dose delivery to targeted areas and avoidance of normal structures by reducing the margins around the CTV.**

- **Patient-specific variations assessed at treatment console with volumetric 3D imaging modalities fitted to treatment machines, such as kilovoltage CBCT.**

Adaptive Planning – I

Online Adaptive Radiotherapy for MIBC: Results of a pilot study; Farshad Foroudi et all ; IJROBP, Vol. 81, No. 3, pp. 765–771, 2011

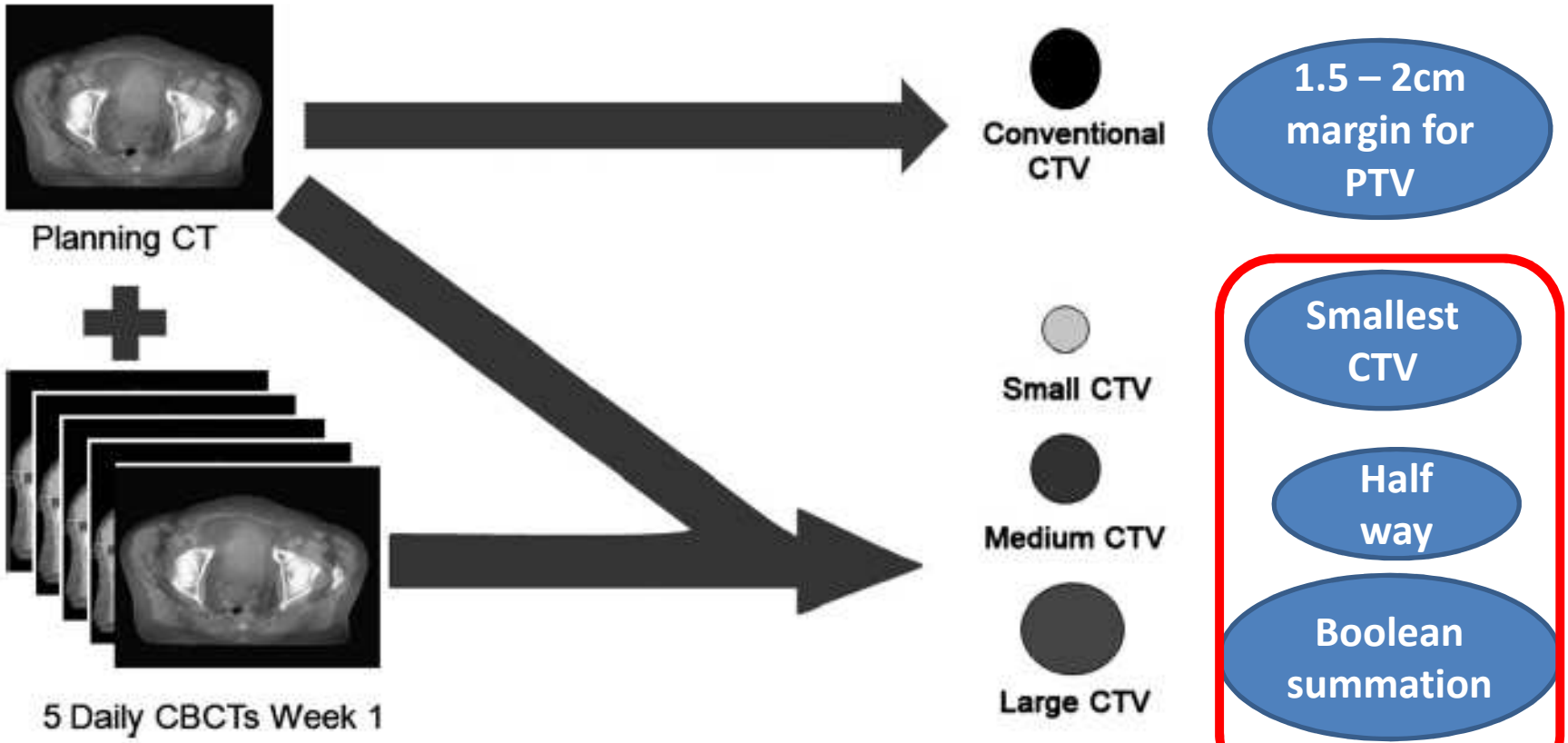


Fig. 1. Technique used for creation of conventional and three adaptive radiotherapy plans. CBCT = cone-beam computed tomography; CTV = clinical target volume.

0.5 cm margin for PTV

Adaptive Planning – II

Adaptive radiotherapy in MIBC – An effective method to reduce the irradiated bowel volume. Laura Tuomikoski et al ; Radiotherapy and Oncology 99 (2011) 61–66

- **Treatment planning was performed in order to determine the changes of volume and shape of the bladder due to filling.**
- **The images were acquired by using four to five repeated planning CTs.**
- **The patients emptied their bladder and drank 2–8 dl of water before the scanning.**
- **The first series of CT images was acquired shortly (with in 3–15 min).**
- **The following 3–4 scans were taken with a time interval of 15–30 min between the successive scans to get a sufficient range of bladder volume changes for treatment planning.**

- **CTVs were then anisotropically expanded with anterior and cranial margins of 10 mm and lateral, posterior and caudal margins of 15 mm to create 3–4 elective PTVs.**

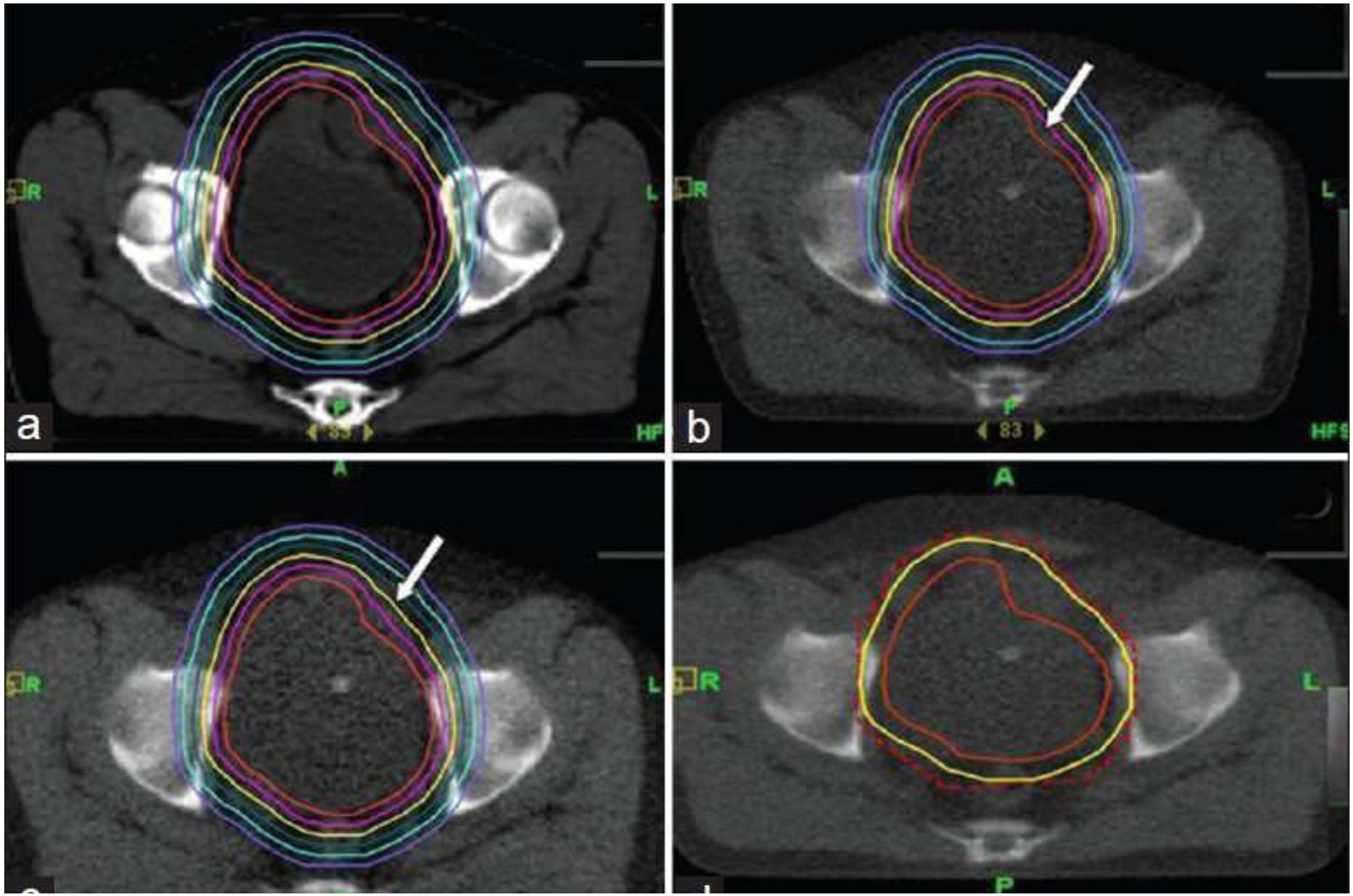
- **Depending on the range of bladder volumes, 3–4 treatment plans for whole bladder PTVs and 2–4 plans for boost PTVs were created.**

- **The bladder volume in every day CBCT images was compared to different PTV contours in the planning CT images by the physicist and the oncologist who had performed contouring.**

- **The plan with the smallest PTV was chosen so that the bladder visible in the CBCT image fitted inside the PTV with margins of at least 3 mm in every direction after optimal matching.**

- **This additional margin was estimated to account for filling of the bladder during the registration and treatment delivery.**

Composite Volume



Dose Constraints

- Small bowel V45 < 195cc
- Femoral head D max < 45GY
- Rectum V40 < 40%

In conclusion: without IGRT, generous margins in the range of 2–3 cm have to be applied in order to account for organ motion, implying large treatment volumes and dose-limiting toxicity.

Disadvantage

- IMRT offers increased conformity and potential dosimetric improvements to organs at risk (Van Rooijen et al. Turgeon et al.)

- IMRT can be used in selected cases to boost defined gross disease.

- Organ motion is the dominant source of error in the planning and delivery of radiotherapy to the bladder

- Disadvantages include prolonged treatment delivery time, increased MU, the close delineation of the radiation field to the tumor might lead to higher risk of geographic miss.

Radiation Toxicity

Acute effects:

- Dysuria
- Urgency
- Frequency
- Diarrhoea

Late effects:

- Chronic irritative cystitis
- Hemorrhagic cystitis
- Bladder contracture
- Rectal stricture
- Small bowel obstruction

79% of patients had normal bladder function at 10 yrs

Take Home Message

- **3DCRT is now standard of care for UB**
- **With advance of RT techniques bladder preservation can easily achievable with dose escalation**
- **Trimodality is "The treatment regimen" for organ preservation in which *Radiation plays principal* role**
- **Newer technology has reduced normal tissue toxicity significantly with improvement in QOL**
- **No significant benefit of Elective nodal irradiation in radiologically node negative patients**
- **IGRT with adoptive technique can deliver higher dose with acceptable toxicity in node negative MIBC**

Acknowledgment

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Thank You