

# Gynecologic Cancers: E-Contouring

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# Gynecologic IMRT

Growing in popularity

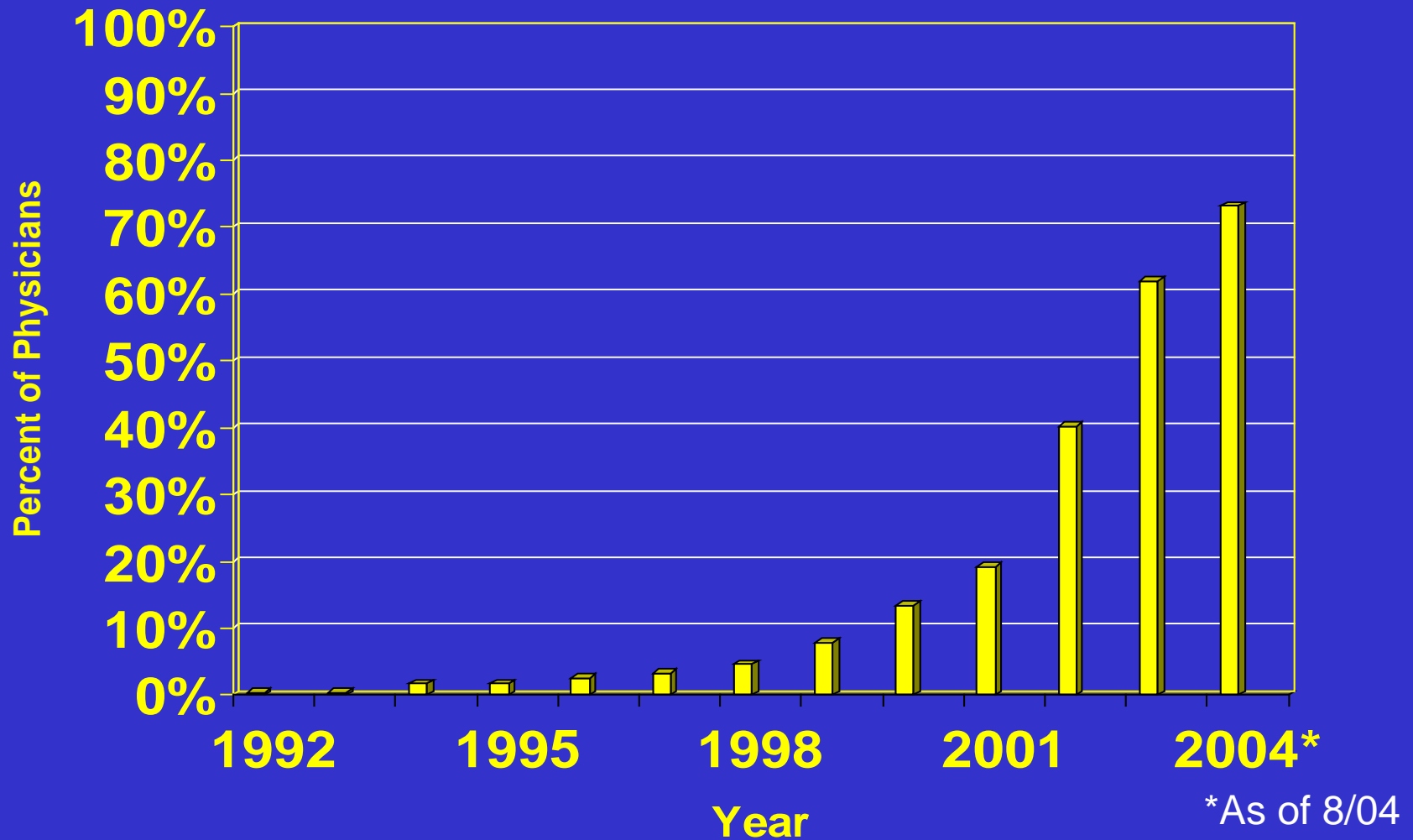
2002 IMRT Survey- 15% respondents using IMRT  
in gynecology patients

2004 IMRT Survey- 35% using IMRT in  
gynecology patients

Mell LK, Roeske JC, Mundt AJ. Survey of IMRT Use in the United States.  
*Cancer* 2003;98:204-211

Mell LK, Mundt AJ. Survey of IMRT Use in the USA- 2004  
*Cancer* 2005;104:1296

# Cumulative IMRT Adoption (USA)



Mell LK, Mundt AJ. Survey of IMRT Use in the USA  
Cancer 2005;104;1296

# IMRT Practice Survey (2004)

Site	%
Prostate	85%
Head and Neck	80%
CNS Tumors	64%
→ Gynecology	35%
Breast	28%
GI	26%
Sarcoma	20%
Lung	22%
Pediatrics	16%
Lymphoma	12%

Mell LK, Mundt AJ. Survey of IMRT Use in the USA- 2004  
*Cancer* 2005;104:1296

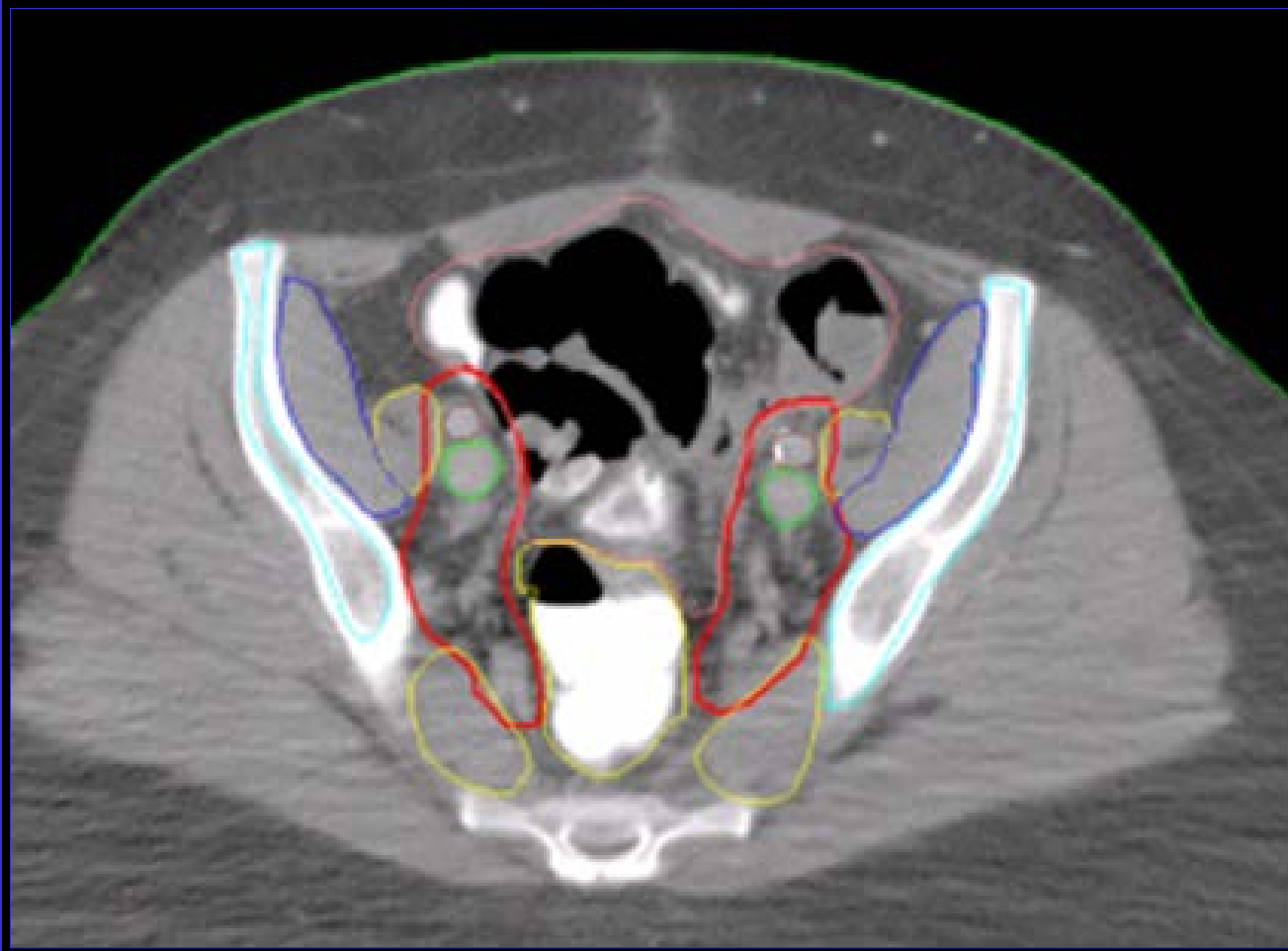


# Gynecologic IMRT

## Rationale

- Improved delivery of conventional doses
  - ↓Dose to normal tissues
  - Small bowel, bladder, rectum, marrow
- Dose escalation in high risk patients
  - Node positive
  - Gross residual disease
- Replacement for Brachytherapy

# Contouring



# Contouring

- Target Delineation
- Normal Tissue Delineation

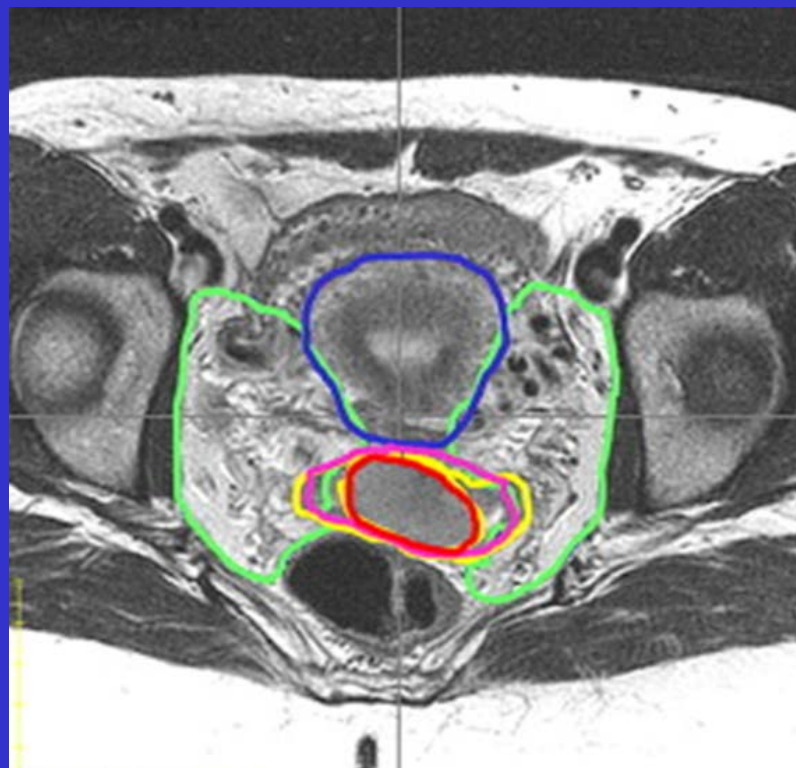
# Target Delineation in Gynecology Patients

- Postoperative Cervix/Endometrial
- Intact Cervix
- EFRT, Pelvic-Inguinal, WART
- Volume-Directed Brachytherapy

# Intact Cervix

The intact setting has **much less of almost everything** compared to the postop setting:

Much less experience  
Much less consensus  
Much less acceptance  
Much less comfort



**ONE THING WE DO HAVE IS  
OUTCOME DATA!**

# Cervical Cancer

	n	FU	Stage	DFS	Pelvic Control
<i>Intact Cervix</i>					
Kochanski	44	23 m	I-IIA	81%	93%
			IIB-IIIB	53%	67%
Beriwal	36	18 m	IB-IVA	51%	80%
Kidd	135	22 m	IA2-IVB	70%	86.7%
Hasselle	89	27 m	I-IIA	69.8%	94.7%
			IIB-IVA	51.4%	70.8%
<i>Postoperative Cervix</i>					
Kochanski	18	21 m	I-II (node+)	79%	94%
Chen	35	35 m	I-II (node+)	NS	93%
Hasselle	22	27 m	I-II (node +/-)	95.2%	100%
Folkert	34	44 m	I-II (node +/-)	91.2%	94%

Kochanski et al. *IJROBP* 2005;63:214

Beriwal et al. *IJROBP* 2007;68:166

Chen et al. *IJROBP* 2001;51:332

Kidd et al. *IJROBP* 2010;77:1080

Hasselle et al. *IJROBP* 2011;80:1436

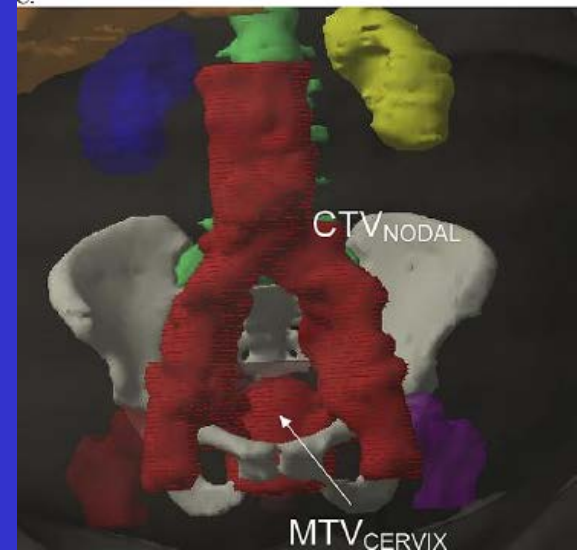
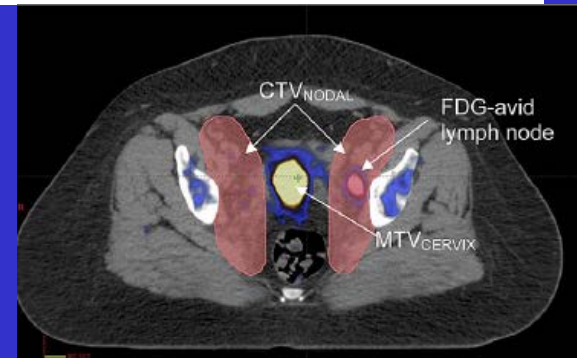
Folkert et al. *Gyne Oncol* 2013;128:288

## CLINICAL INVESTIGATION

### CLINICAL OUTCOMES OF DEFINITIVE INTENSITY-MODULATED RADIATION THERAPY WITH FLUORODEOXYGLUCOSE-POSITRON EMISSION TOMOGRAPHY SIMULATION IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

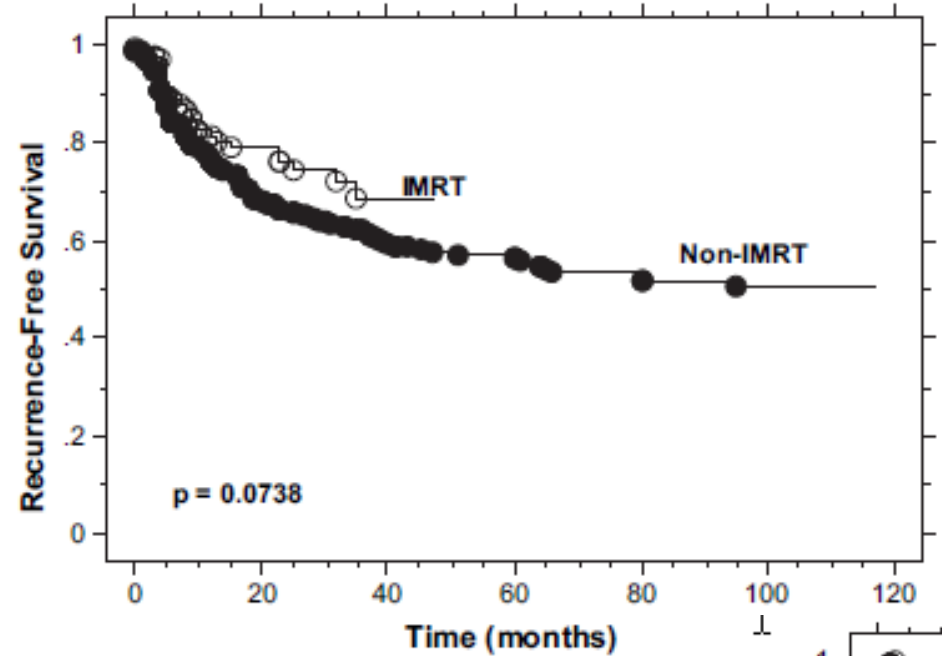
ELIZABETH A. KIDD, M.D.,\* BARRY A. SIEGEL, M.D.,<sup>†‡</sup> FARROKH DEHDASHTI, M.D.,<sup>†‡</sup>  
JANET S. RADER, M.D.,<sup>‡§</sup> SASA MUTIC, M.S.,\* DAVID G. MUTCH, M.D.,<sup>‡§</sup> MATTHEW A. POWELL, M.D.,<sup>‡§</sup>  
AND PERRY W. GRIGSBY, M.D.\*<sup>†‡§</sup>

135 cervical cancer IMRT pts  
All underwent PET/CT simulation  
Comparison group = 317  
conventional RT pts  
Pelvic +/- PA IMRT + Brachy  
Median FU (72 months conventional,  
22 months IMRT)  
Reduction in chronic toxicity  
Improvements in relapse-free  
( $p=0.07$ ) and cause-specific  
survivals ( $p<0.0001$ ).

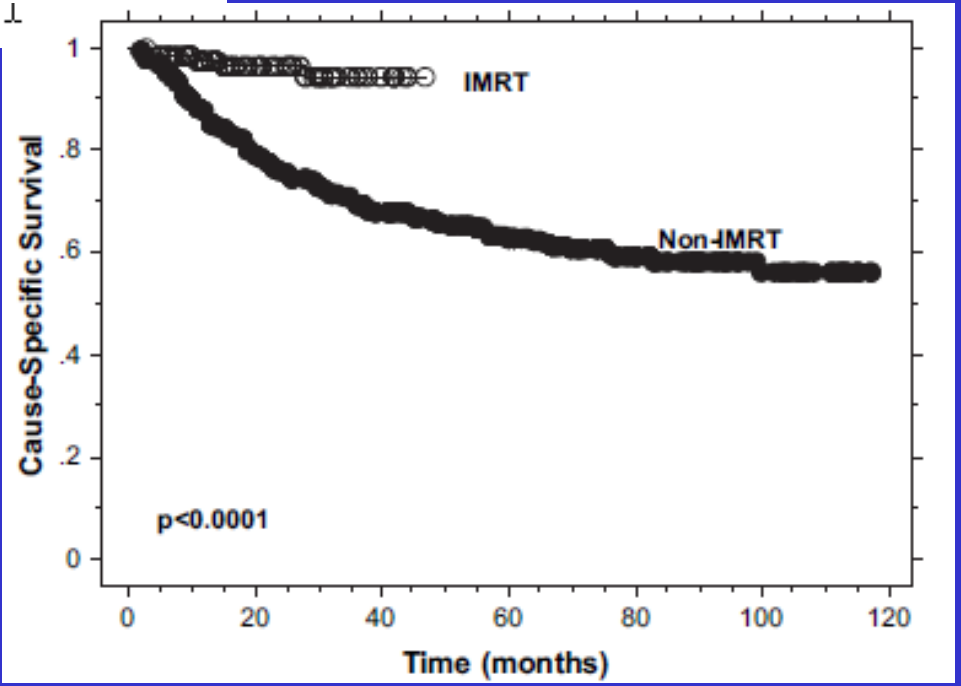




Recurrence-free  
Survival



Cause-Specific  
Survival



**CLINICAL OUTCOMES OF INTENSITY-MODULATED PELVIC RADIATION THERAPY  
FOR CARCINOMA OF THE CERVIX**

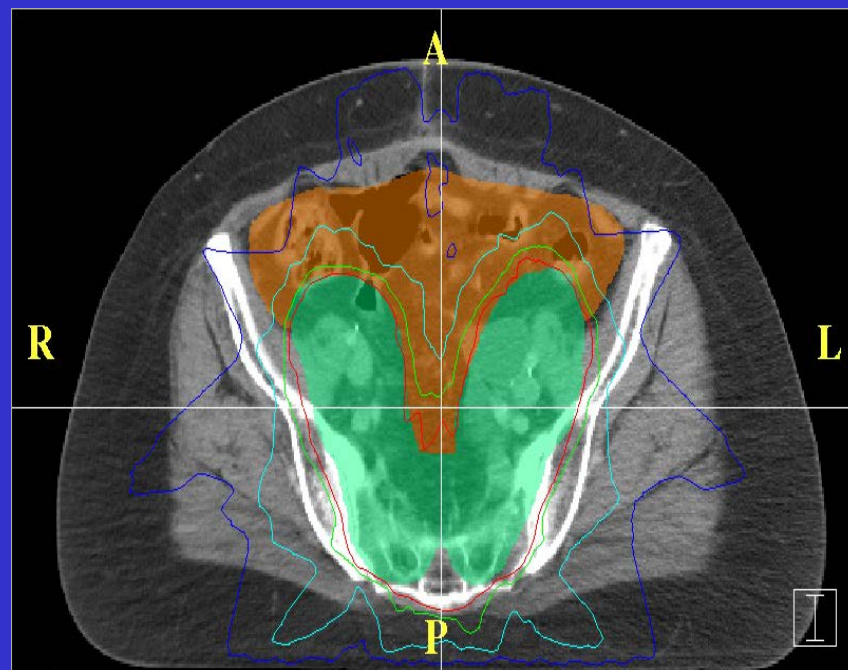
MICHAEL D. HASSELLE, M.D.,\* BRENT S. ROSE, M.D.,† JOEL D. KOCHANSKI, M.D.,\*  
SAMEER K. NATH, M.D.,† ROUNAK BAFANA, B.S.,‡ CATHERYN M. YASHAR, M.D.,† YASMIN HASAN, M.D.,\*  
JOHN C. ROESKE, PH.D.,§ ARNO J. MUNDT, M.D.,† AND LOREN K. MELL, M.D.†

\*Departments of Radiation and Cellular Oncology, University of Chicago, Chicago, IL; †Department of Radiation Oncology, Center for Advanced Radiotherapy Technologies, University of California, San Diego, La Jolla, CA; ‡Wayne State University School of Medicine, Detroit, MI; and §Department of Radiation Oncology, Loyola University, Maywood, IL

111 cervical cancer pts  
89 intact cervix, 22 postop  
Pelvic IMRT +/- Brachy  
Median FU = 27 months  
Excellent pelvic control

- IB-IIA intact = 94.7%
- IIB-IVA intact = 70.8%
- Postop patients = 100%

Grade  $\geq$  3 chronic toxicity = 7%



And we are starting to get at least some  
consensus

**CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUME FOR  
INTENSITY-MODULATED PELVIC RADIOTHERAPY FOR THE DEFINITIVE  
TREATMENT OF CERVIX CANCER**

KAREN LIM, M.B.B.S.,\* WILLIAM SMALL, JR., M.D.,<sup>†</sup> LORRAINE PORTELANCE, M.D.,<sup>‡</sup>  
CARIEN CREUTZBERG, M.D., PH.D.,<sup>§</sup> INA M. JÜRGENLIEMK-SCHULZ, M.D., PH.D.,<sup>||</sup> ARNO MUNDT, M.D.,<sup>¶</sup>  
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BETH ERICKSON, M.D.,<sup>§§</sup> JENNIFER DE LOS SANTOS, M.D.,<sup>|||</sup> DAVID GAFFNEY, M.D., PH.D.,<sup>¶¶</sup>  
CATHERYN YASHAR, M.D.,<sup>¶</sup> SUSHIL BERIWAL, M.D.,\*\*\* AARON WOLFSON, M.D.,<sup>†††</sup>  
ALEXANDRA TAYLOR, F.R.C.R.,<sup>†††</sup> WALTER BOSCH, PH.D.,<sup>§§§</sup> ISSAM EL NAQA, PH.D.,<sup>§§§</sup>  
AND ANTHONY FYLES, M.D. \* FOR THE GYN IMRT CONSORTIUM.

- Consensus guidelines for CTV design for the intact cervical cancer patient
- Preparation for a planned Phase II RTOG Trial
- Meant to supplement the consensus guidelines for postoperative patients

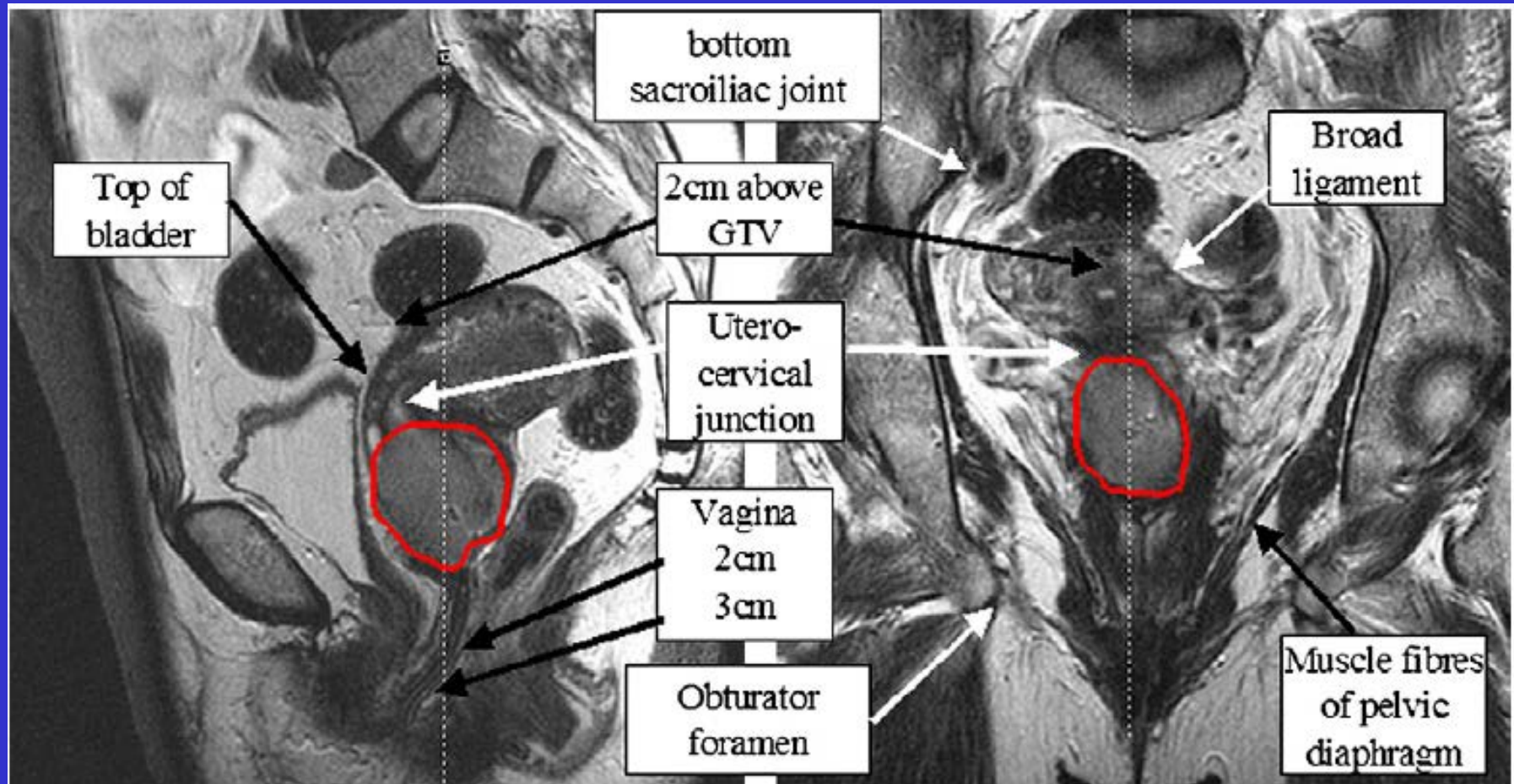
# Intact Cervix CTV

- June 2008 RTOG Meeting
- 16 representatives from the GYN IMRT Consortium: RTOG, NCIC, Japan Clinical Oncology Group, EORTC
- Questionnaire regarding CTV definitions, imaging used, prevalence of IMRT use etc.
- Each contoured using MR (sagittal T2-weighted) and axial CT images
- Statistical software to generate consensus volumes

# Intact Cervix Consensus

- General agreement on which structures to include but less agreement regarding their definition for the purposes of contouring
- CTV structures: GTV, cervix, uterus, parametria, vagina and regional lymph nodes
- Delineation of the **parametrium** was particularly controversial
- All agreed that the lateral boundary should be the pelvic sidewall and the medial boundary should abut the GTV, cervix, uterus, and vagina

# But little consensus about the superior and inferior extents





## Amount of normal tissues to include in the CTV also differed considerably

- 42% of respondents felt it was not always necessary to include the entire fundus
- Length of vagina included in the CTV varied from 1.5 cm to the bottom of the pubic symphysis (~4 cm below tumor)



## Other interesting observations

- 91% used CT for target delineation
  - 55% also used MRI
  - 46% also used PET
- Also large variations in recommended PTV margins
  - Tumor: 1-5 cm
  - Nodes: 0.5-1 cm

# Consensus Recommendations

Table 2. CTV components

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GTV	Entire GTV; intermediate/high signal seen on T <sub>2</sub> -weighted MR images
Cervix	Entire cervix; if not already included within GTV contour
Uterus	Entire uterus
Parametrium	Entire parametrium, including ovaries; include entire mesorectum if uterosacral ligament involved
Vagina	Minimal or no vaginal extension: upper half of the vagina Upper vaginal involvement: upper two-thirds of the vagina Extensive vaginal involvement: entire vagina

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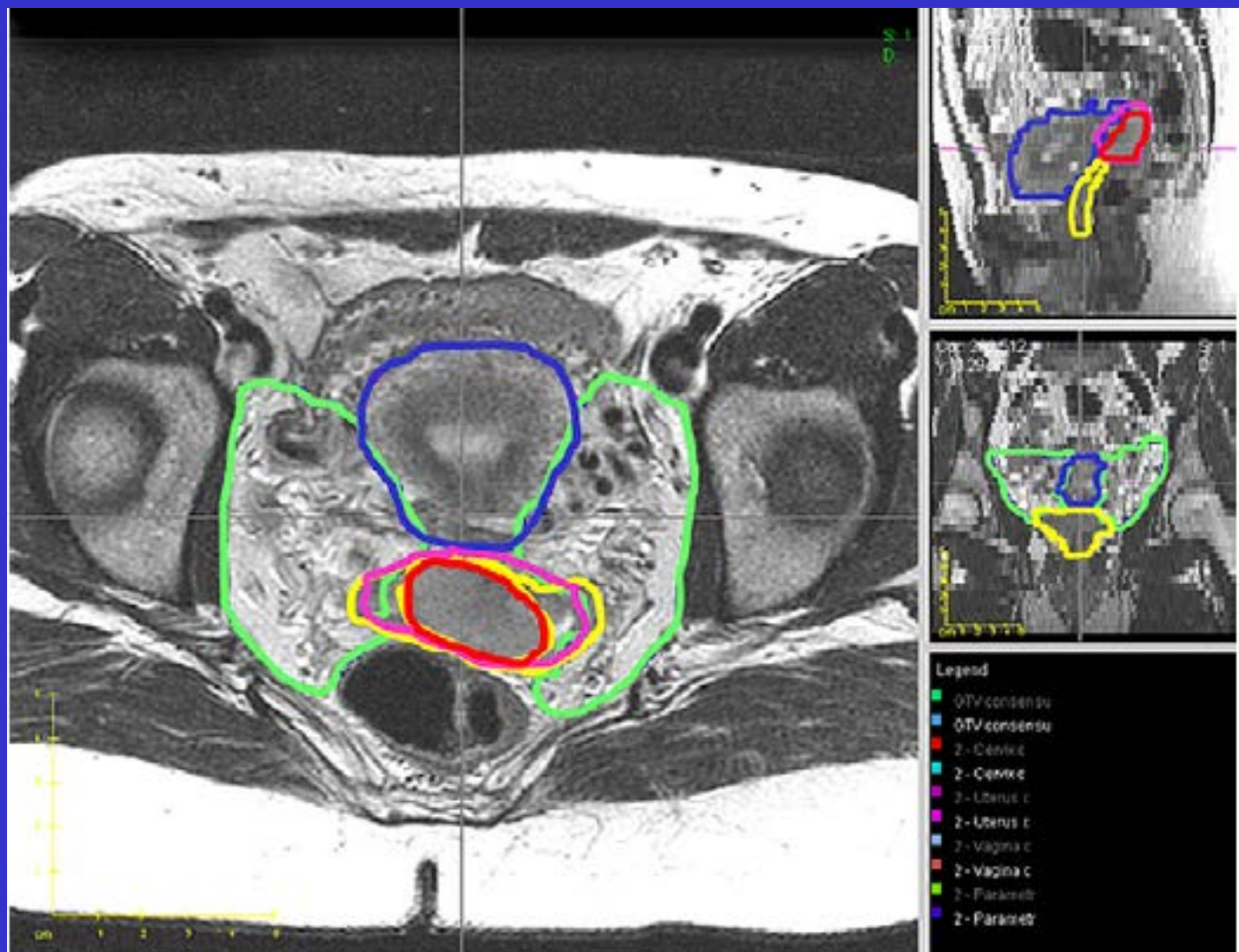


Fig. 2. Axial and reconstructed sagittal and coronal views of T<sub>2</sub>-weighted MR images from a clinical contouring case showing 95% agreement contours for GTV (red), cervix (pink), vagina (yellow), parametria (green), and uterus (blue).

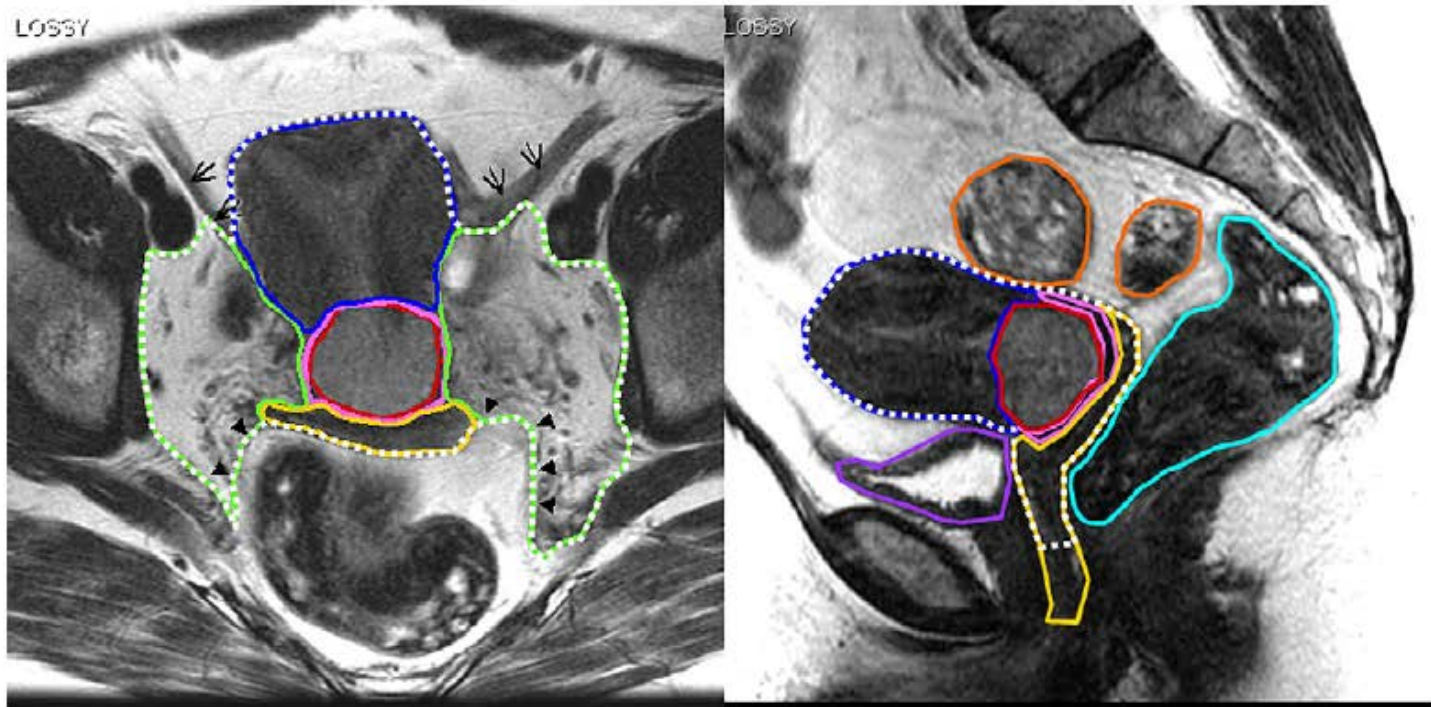


Fig. 3. T<sub>2</sub>-weighted MR axial (left) and sagittal (right) images of one patient demonstrating GTV (red), cervix (pink), uterus (blue), vagina (yellow), parametrium (green), bladder (purple), rectum (light blue), and sigmoid (orange). Arrow heads refer to uterosacral ligaments and mesorectal fascia. Arrows refer to the broad ligament and top of the fallopian tube. Dashed white lines represent the CTV.

# Parametria Delineation

- Parametrial tissue is encompassed by the broad ligament but is often poorly seen on axial imaging

Table 3. Anatomical boundaries of parametria

Location	Anatomic structures
Anteriorly	Posterior wall of bladder or posterior border of external iliac vessel
Posteriorly	Uterosacral ligaments and mesorectal fascia
Laterally	Medial edge of internal obturator muscle/ ischial ramus bilaterally
Superiorly	Top of fallopian tube/ broad ligament. Depending on degree of uterus flexion, this may also form the anterior boundary of parametrial tissue.
Inferiorly	Urogenital diaphragm



# Parametria Delineation

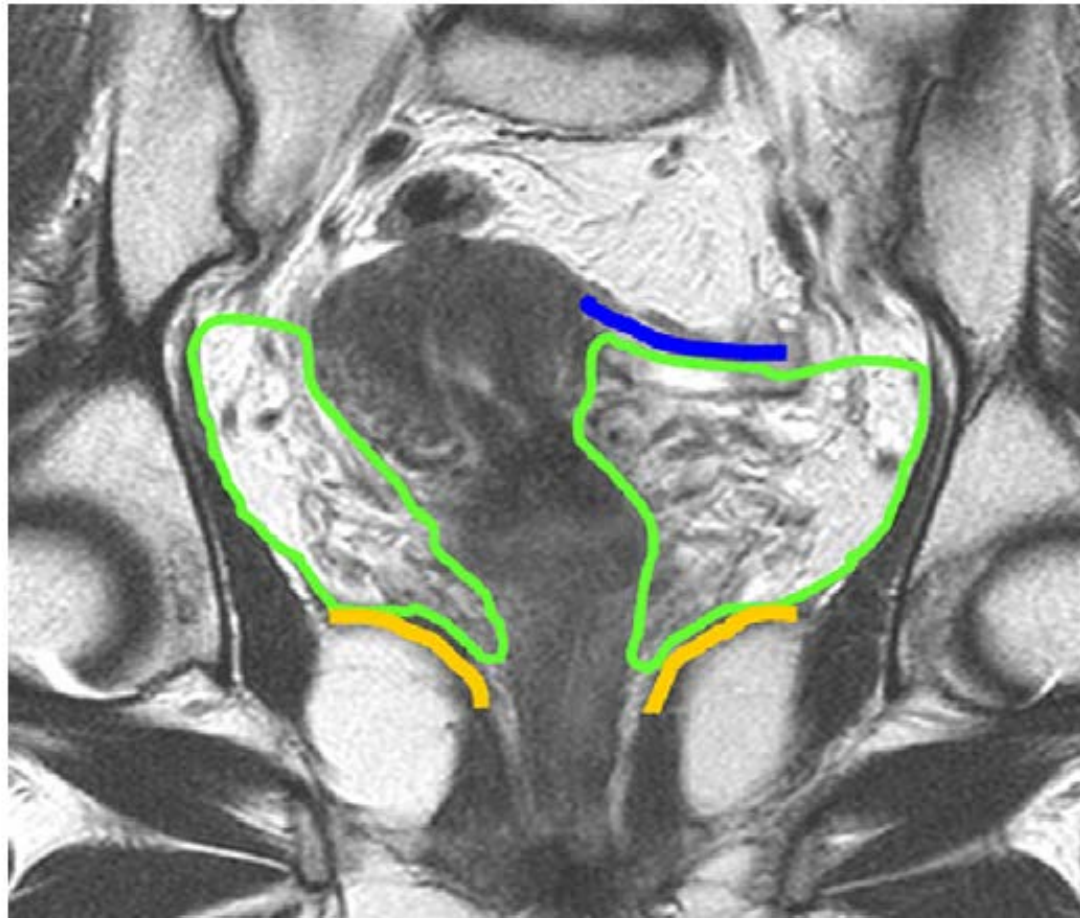


Fig. 4. Coronal T<sub>2</sub>-weighted MR image of a patient with a relatively upright uterus, demonstrating the superior and inferior boundaries of parametria. Top of broad ligament (blue), pelvic diaphragm (yellow), parametria (green).

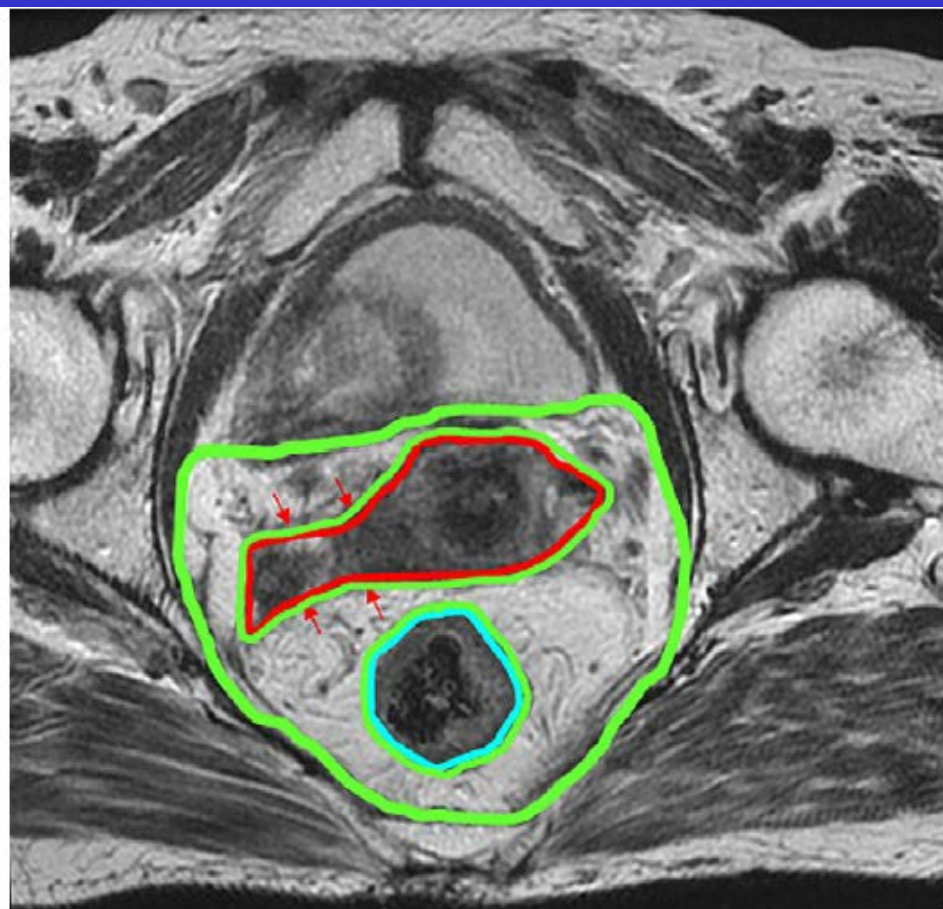


Fig. 5. Axial T<sub>2</sub>-weighted MR image of a patient showing the GTV (red contour), modified parametrium (green), and rectum (light blue); red arrows indicate right proximal uterosacral ligament invasion.

- Posteriorly, the parametrial tissue is bounded by the mesorectal fascia and uterosacral ligaments
- The entire uterosacral ligament should be included in patients with disease involvement
- Patients with IIB disease and/or extensive nodal involvement should also have the entire mesorectum included

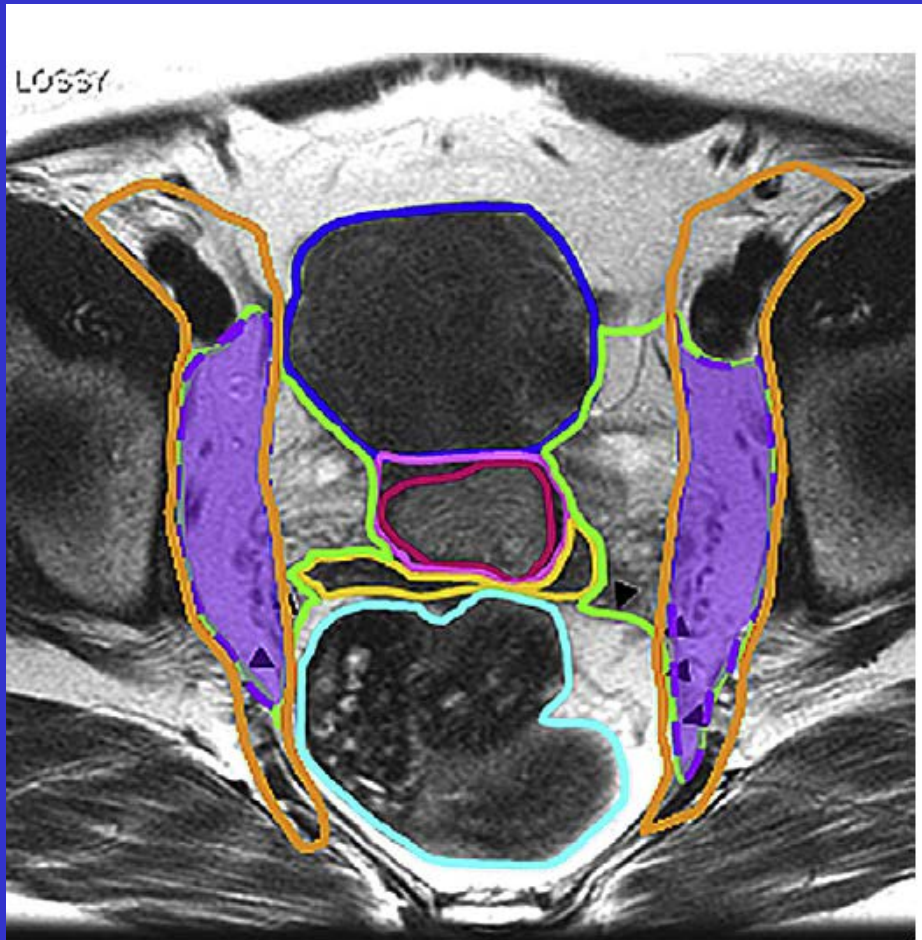


Fig. 6. Axial T<sub>2</sub>-weighted MR image showing overlap (purple-shaded region) between nodal clinical target volume (orange contour) and lateral portion of parametrial volume (green contour).

- Laterally, the parametrial volume should extend to the pelvic sidewall (excluding bone and muscle)
- There should be some overlap of this volume with the nodal CTV, particularly along the obturator strip



# CTV Delineation

## *Vagina*

- Minor/no vaginal involvement: Upper  $\frac{1}{2}$  vagina
- Upper involvement: Upper  $\frac{2}{3}$ rds of the vagina
- Extensive involvement: Entire vagina

## *Nodal CTV*

- Identical to the postop setting

# Cautionary Figure

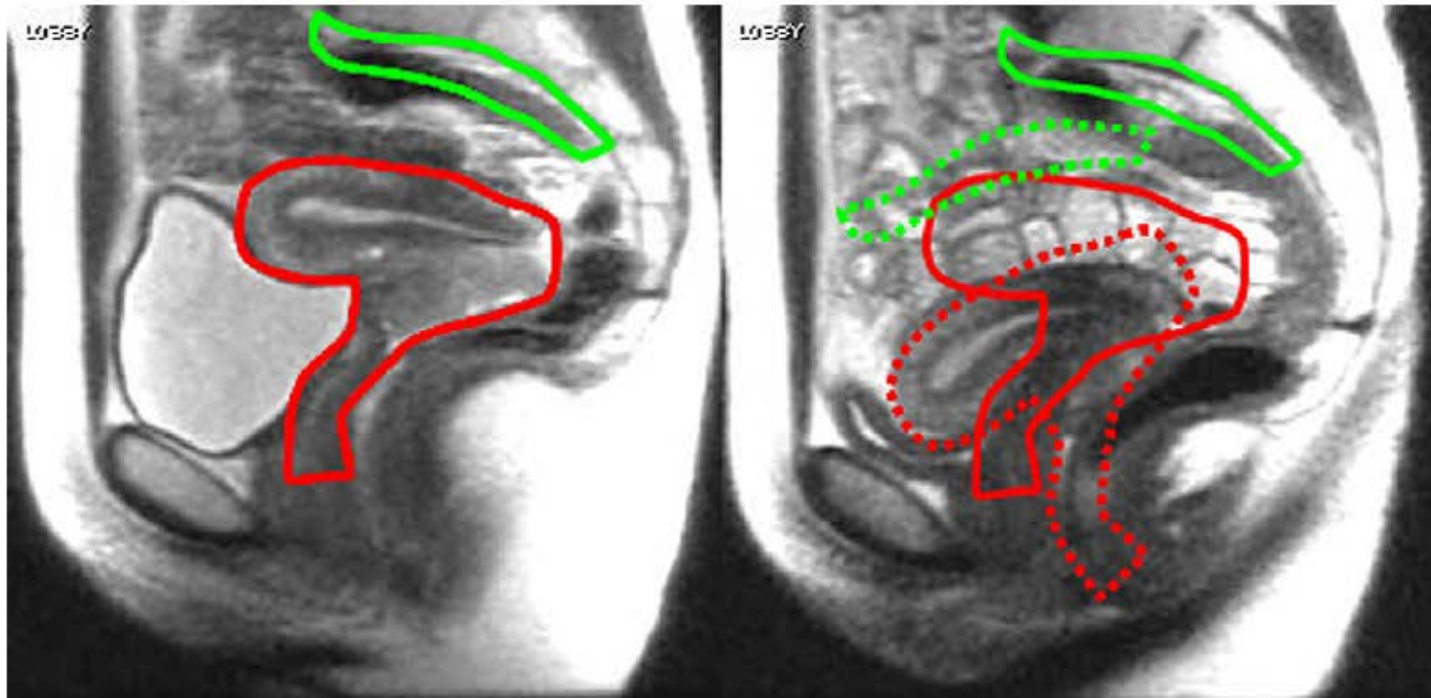


Fig. 7. Sagittal T<sub>2</sub>-weighted MR images obtained 1 week apart from the same patient, demonstrating the marked difference between uterus and cervix positions, with altered bladder filling. Primary tumor CTV (red contour) and nodal CTV (green) contours overlaid. Solid lines represent targets at week 1, dashed lines represent the targets at week 2 if a direct translational shift is made to compensate for the change in the primary tumor CTV position. Nodal CTV and portions of tumor CTV in week 2 are missed.

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## **A Consensus-based Guideline Defining Clinical Target Volume for Primary Disease in External Beam Radiotherapy for Intact Uterine Cervical Cancer**

**Takafumi Toita<sup>1,\*</sup>, Tatsuya Ohno<sup>2</sup>, Yuko Kaneyasu<sup>3</sup>, Tomoyasu Kato<sup>4</sup>, Takashi Uno<sup>5</sup>, Kazuo Hatano<sup>6</sup>, Yoshiki Norihisa<sup>7</sup>, Takahiro Kasamatsu<sup>4</sup>, Takeshi Kodaira<sup>8</sup>, Ryoichi Yoshimura<sup>9,10</sup>, Satoshi Ishikura<sup>11</sup> and Masahiro Hiraoka<sup>7</sup> for the JCOG Radiation Therapy Study Group**

- RT Study Group Japan Clinical Oncology Group
- Nodal CTV atlas (Toita et al. JJCO 2010; 40:456)
- 10 radiation oncologists, 2 gynecologic oncologists
- Contoured on CT/MRI of 2 patients
- Reached consensus by discussion

# CTV Consensus

## *Components*

GTV, cervix, uterus, parametria, vagina and ovaries

## *Definitions*

GTV: Gross disease on a T2-weighted MRI and any palpable lesions

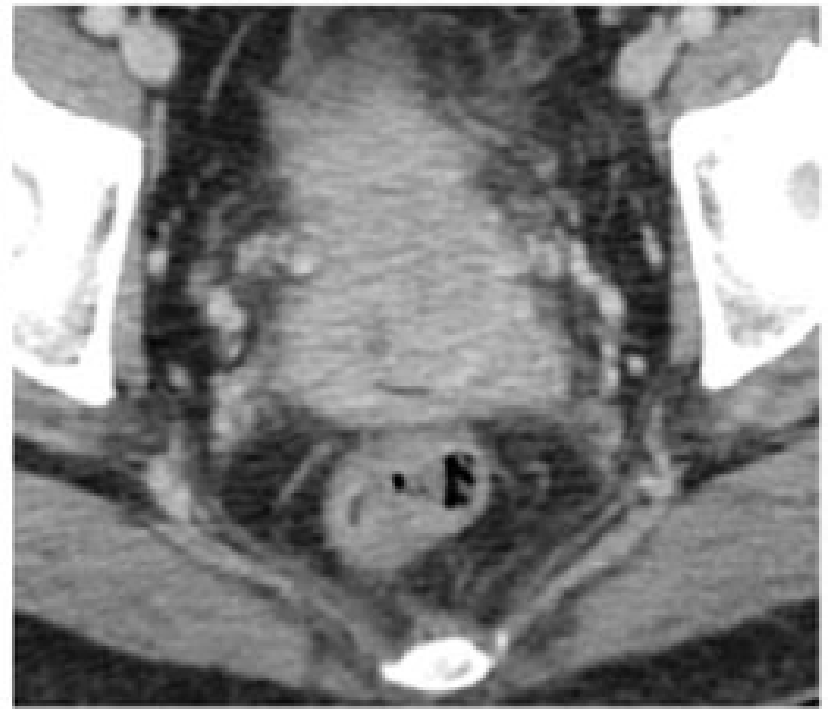
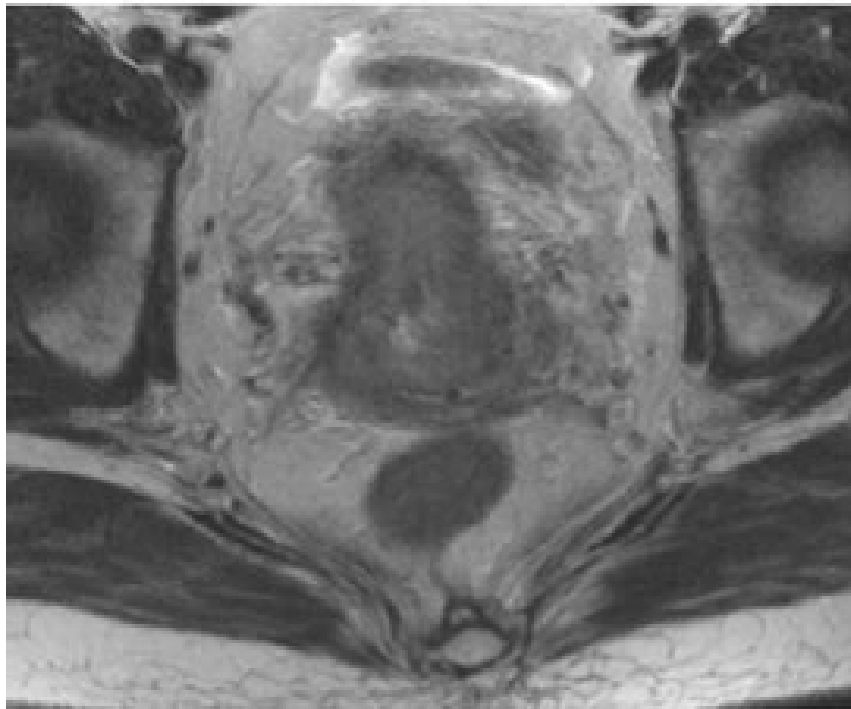
Cervix: Entire cervix (if not already included)

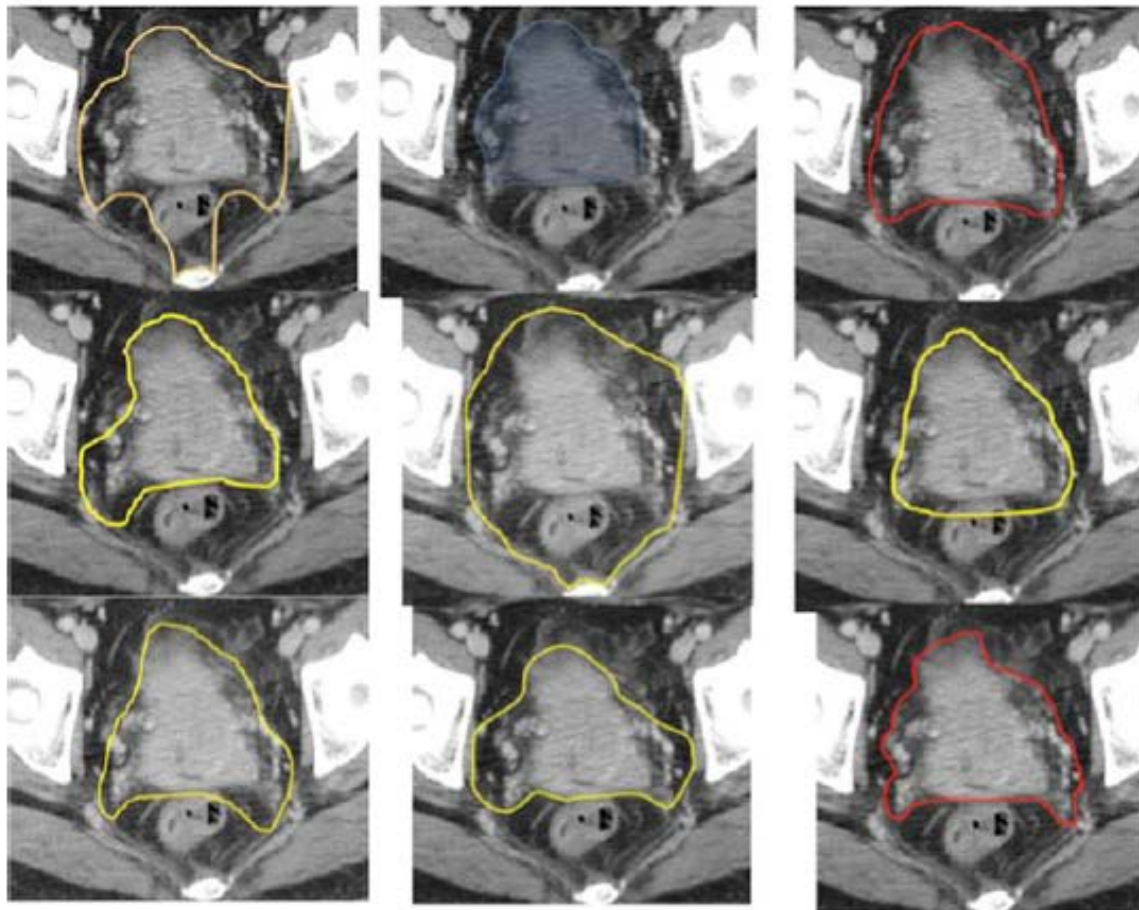
Uterus: Visualized corpus

# Study Case: IIB Cervix

## Bilateral parametrial invasion with right pelvic fixation

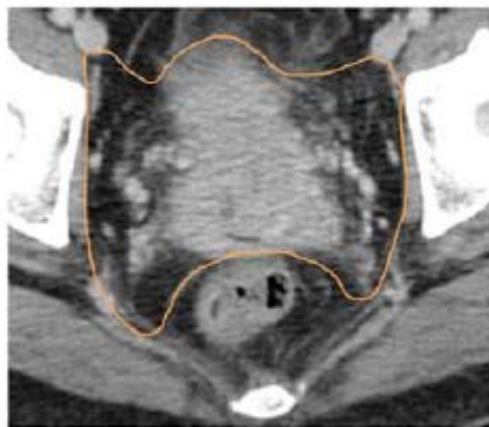
(a)





CTVs by  
Working Group  
Members

(c)

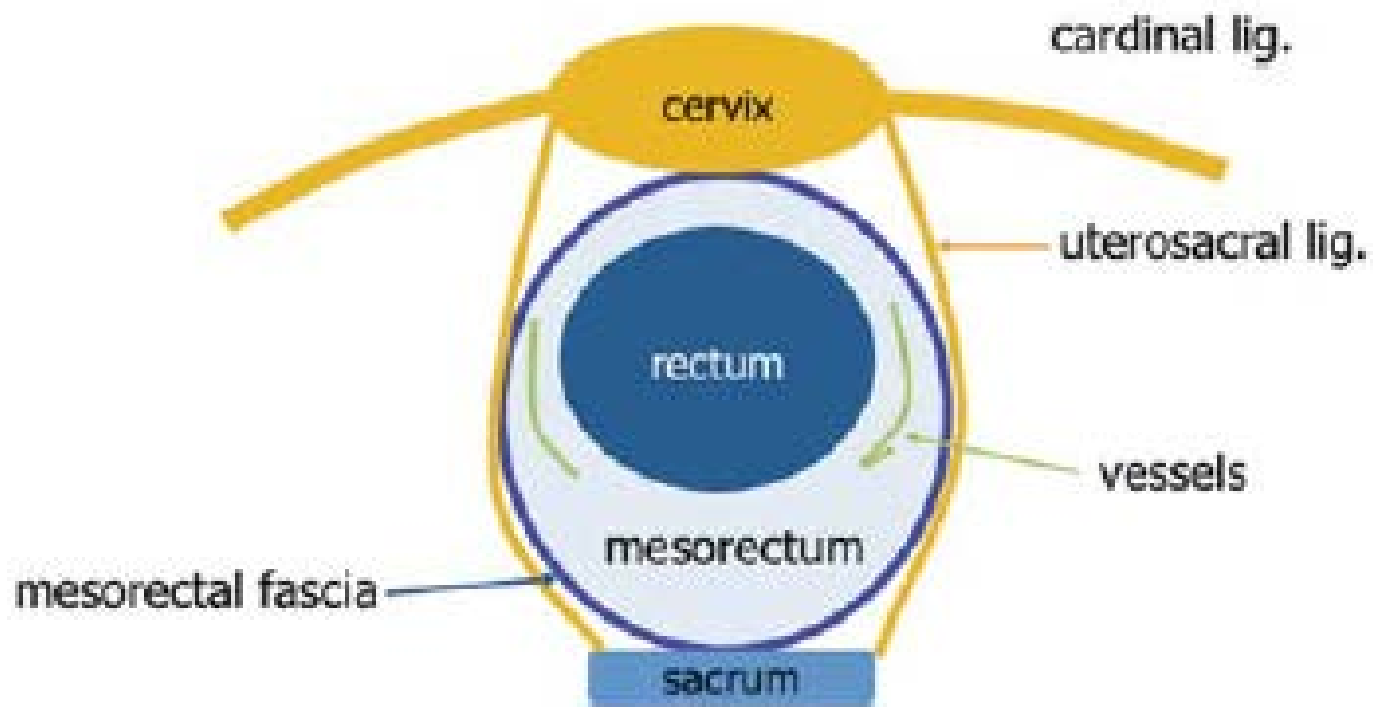


Consensus  
CTV

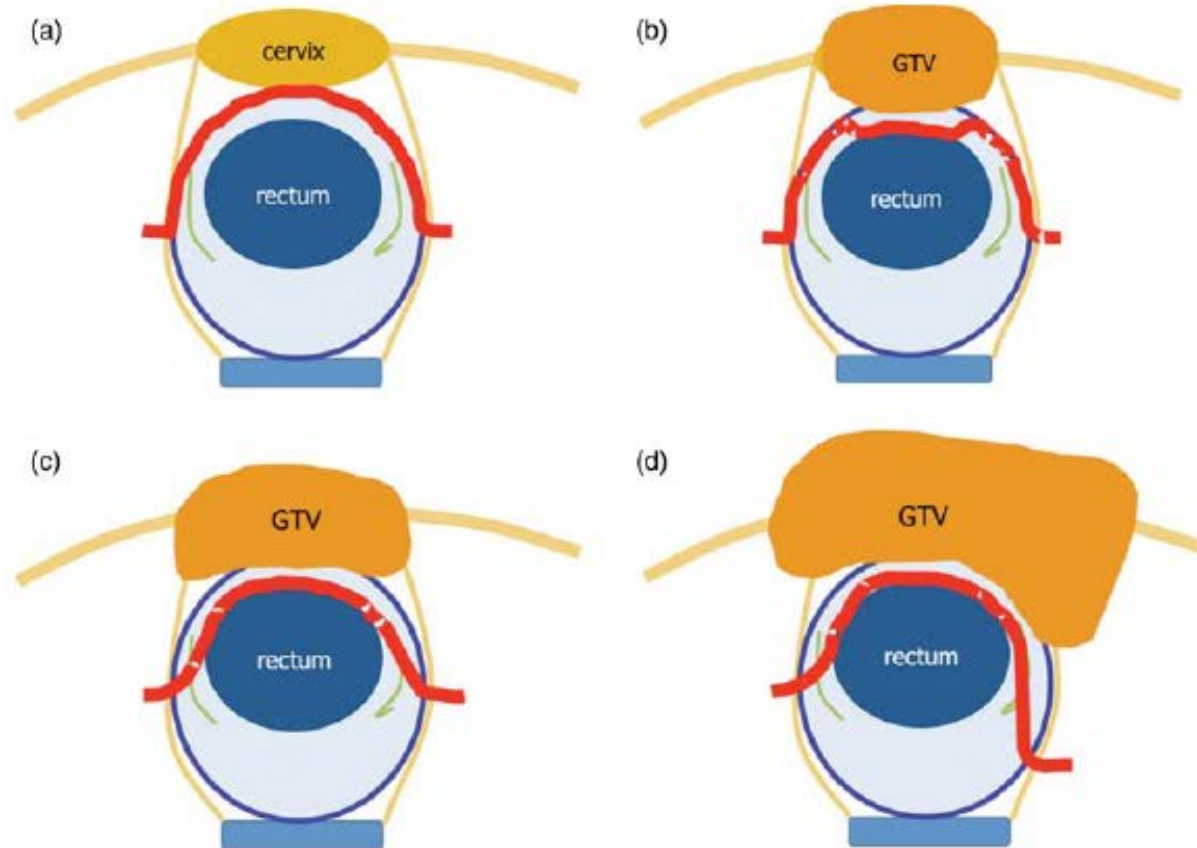
# Parametrial Definition

**Table 1.** Anatomical boundaries of clinical target volume for parametrium

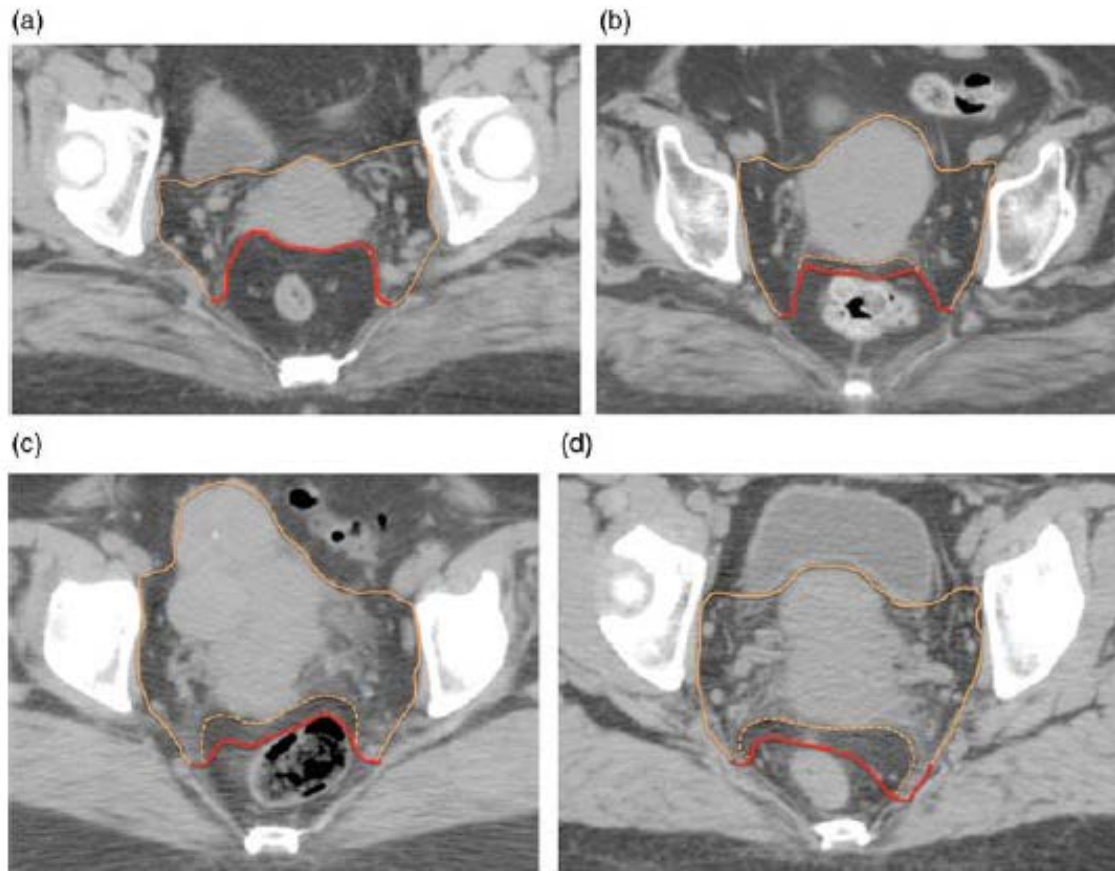
Margin	Structures
Cranial	Isthmus of uterus (=level where uterine artery drains into) *Contouring would stop at the level where bowel loops are seen
Caudal	Medial boarder of levator ani (Fig. 5)
Anterior	Posterior boarder of bladder or posterior boarder of external iliac vessels
Posterior	Anterior part (semicircular) of mesorectal fascia *In case with bulky central tumor or significant parametrial invasion, some modification would be considered (Figs 3 and 4)
Lateral	Medial edge of internal obturator muscle, piriformis muscle, coccygeus muscle and ischial ramus







**Figure 3.** Stage-specific delineation schemes for the posterior border of the parametrium (solid red line). (a) Non-bulky early-stage (IB1 or IIA1) disease. (b) Bulky early-stage (IB2 or IIA2) disease. (c) Stage IIB disease (slight parametrial involvement). (d) Stage IIIB disease (massive parametrial involvement).



**Figure 4.** Actual delineations of the primary CTV (solid orange line) and posterior border of the parametrium (solid red line) according to disease status. Dotted orange lines indicate the anterior border of the perirectum. (a) A case with non-bulky Stage IB1 disease. (b) A case with bulky Stage IB2 disease. (c) A case with Stage IIB disease (bilateral parametrial involvement on pelvic exam). (d) A case with Stage IIIB disease (massive parametrial involvement with fixation to the left pelvic wall on pelvic exam).

Normal Tissues  
Organs at Risk (OAR)

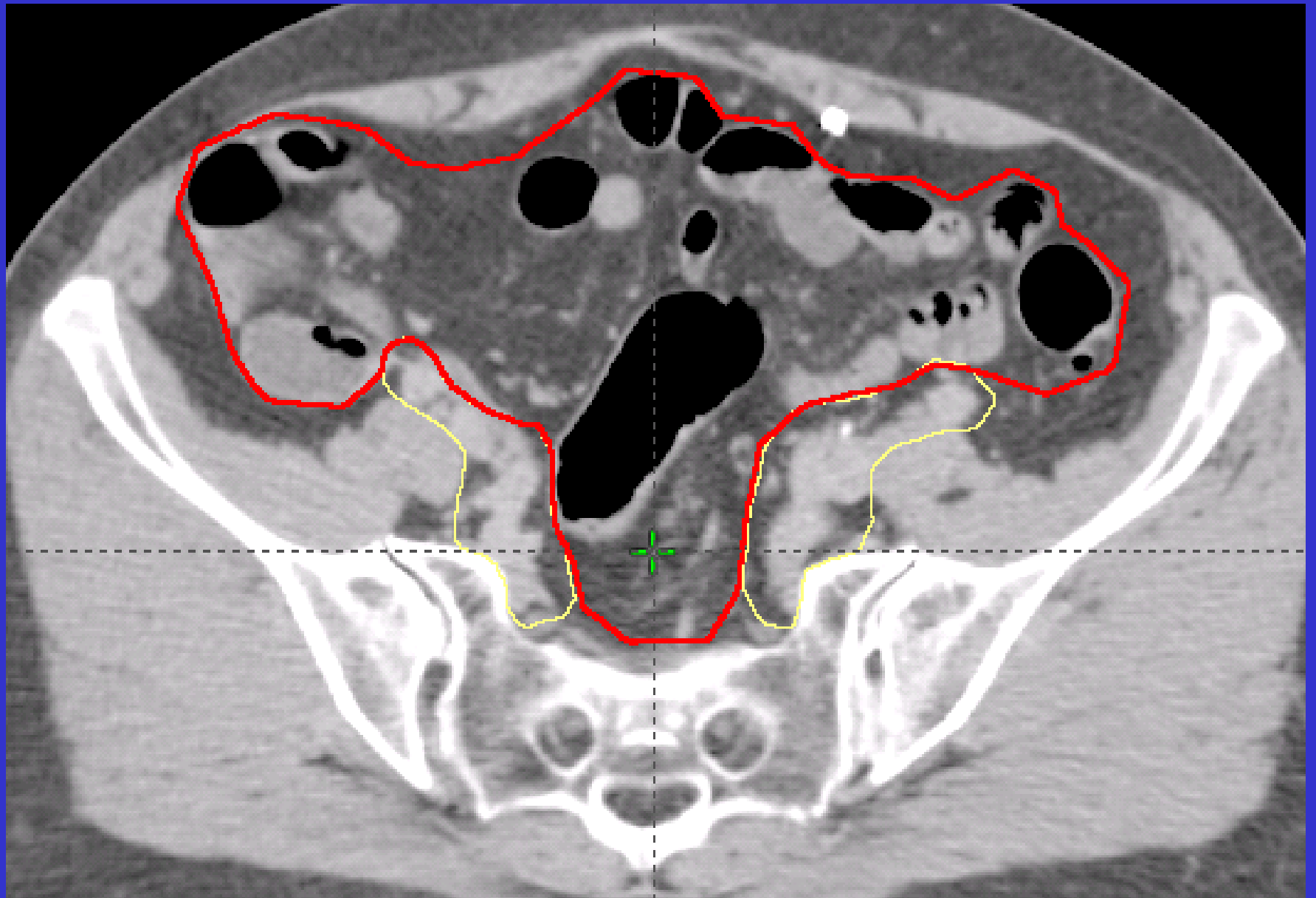
# Normal Tissues

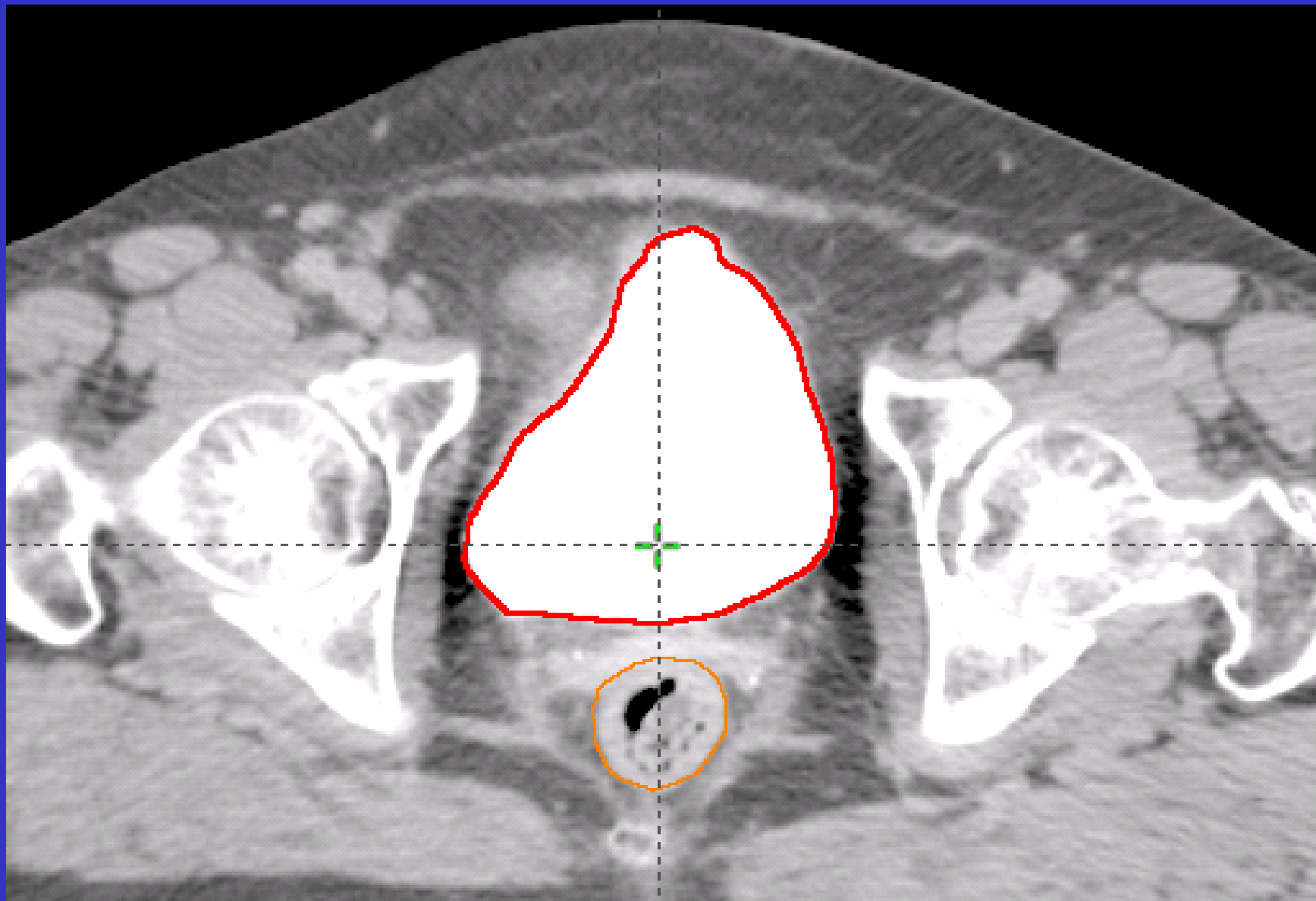
- Normal tissues depend on the clinical case
- In most patients:
  - **Small bowel, rectum, bladder**
- In pts receiving concomitant or sequential chemotherapy, **bone marrow** may be included
- Some centers include the **femoral heads\***
- Kidneys and liver included only if treating more comprehensive fields

\*I only do in pelvic-inguinal RT cases

# Normal Tissues

- Be consistent with contouring
  - Helps with DVH interpretation
- **Rectum**: Outer wall (anus to sigmoid flexure)
- **Small bowel**: Outermost loops from the L4-5 interspace
  - Include the colon above the sigmoid flexure as well in the “small bowel” volume

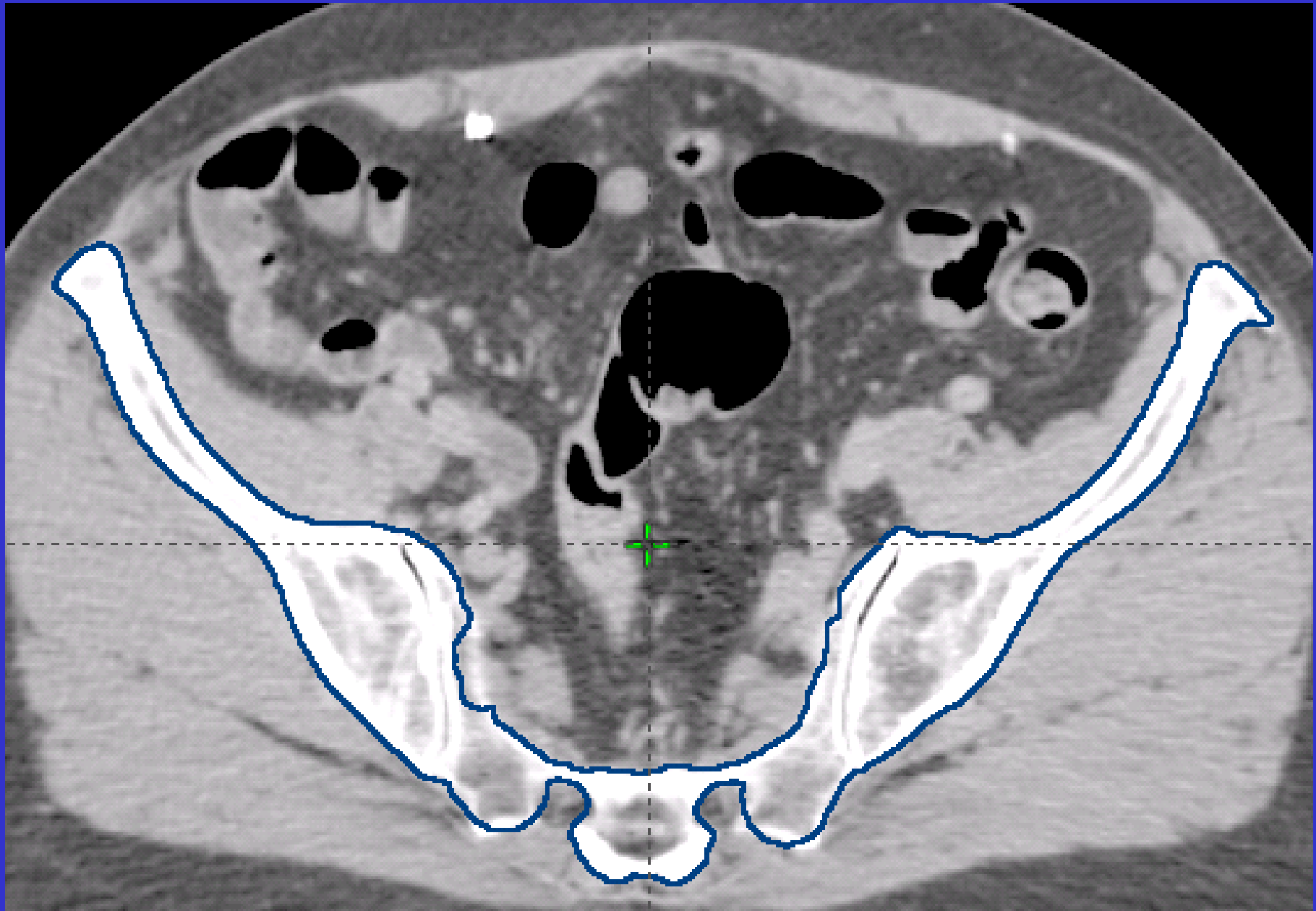






# Bone Marrow Contouring

- Controversial subject
- Initial attention focused on sparing the iliac crests
- More recent data suggests that this might not be optimal



# Intact Cervix

- What is needed is a CT-based atlas\* for target delineation since obtaining a MRI may be difficult
- MRI is also needed at the time of brachytherapy and two MRIs may not be approved

\*under development

# Intact Cervix Target Delineation

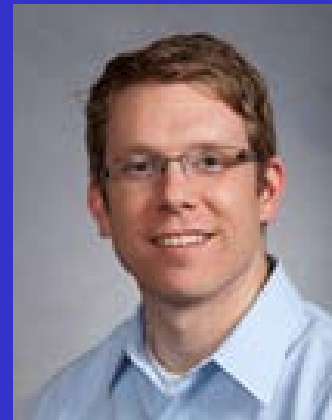
- Remains a work in progress
- Debate whether intact cervix IMRT is ready for primetime

# Intact Cervix Target Delineation

IRTOC

International Radiotherapy  
Technologies and Oncology Consortium

INTERTECC Trial  
International Phase II/III  
Gyne IMRT Study



Loren Mell MD  
Director, Clinical and Translational  
Research  
UC San Diego

# IRTOC

International Radiotherapy  
Technologies and Oncology Consortium

- University of California San Diego
- Tata Memorial Hospital (Mumbai)
- Peking Union Medical College (Beijing)
- Instituto do Cancer do Estado de Sao Paulo
- King Chulalongkorn Univ. (Bangkok)
- Artemis Health Institute (Delhi)
- University of Chicago
- Loyola University (Chicago)
- University of Miami
- University of South Florida (Tampa)
- University of Pittsburgh
- University of Iowa (Iowa City)
- Istanbul Bilim University (Istanbul)
- University Hospital Hradec Keálové
- Far Eastern Memorial Hospital (Taipei)
- Leiden University Medical Center (Leiden)



# INTERNATIONAL EVALUATION OF RADIOTHERAPY TECHNOLOGY EFFECTIVENESS IN CERVICAL CANCER (INTERTECC)

## PHASE II/III CLINICAL TRIAL OF INTENSITY MODULATED RADIATION THERAPY WITH CONCURRENT CISPLATIN FOR STAGE I-IVA CERVICAL CARCINOMA

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Bone Marrow Delineation	<a href="#">View</a>
Target Delineation (Intact)	<a href="#">View</a>
Treatment Planning	<a href="#">View</a>

<http://radonc.ucsd.edu/research/irtoc/Pages/videos.aspx>



# Intact Cervix YouTube Instructional Video



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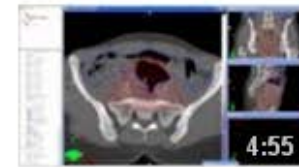
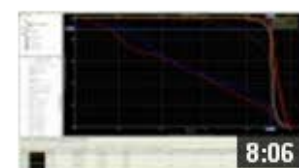
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# Intact Cervical Cancer

- A GTV and 3 CTVs are outlined
  - GTV                      Primary Tumor
  - CTV1                     GTV + Uterus + Uninvolved Cervix
  - CTV2                     Paravaginal/parametrial/parauterine tissues  
Adenexa, proximal vagina
  - CTV3                     Pelvic lymph nodes

**Table 1. Target Volumes Used in Intact Cervical Cancer Patients Undergoing IMRT**

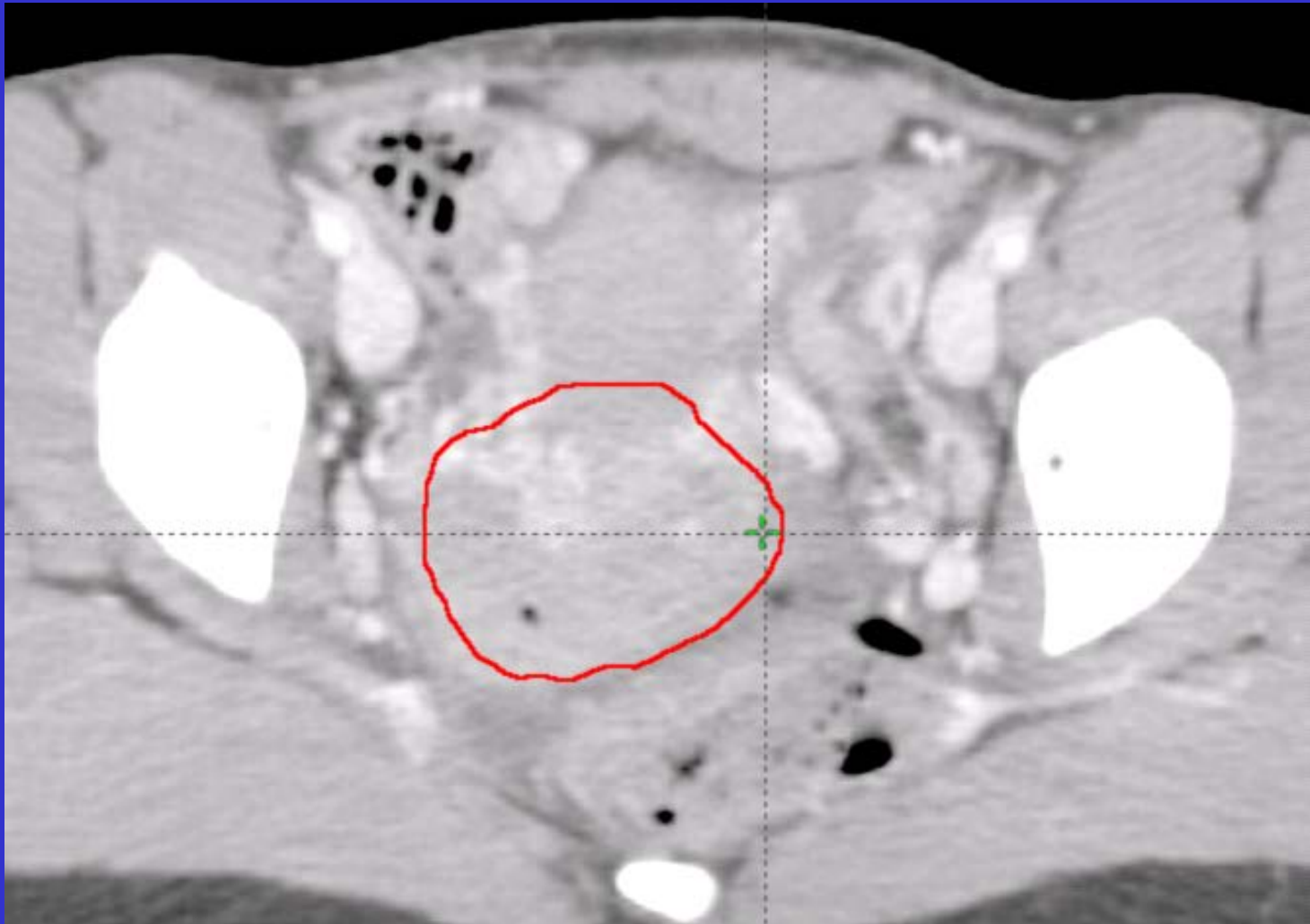
<b>Target Volumes</b>	<b>Definition and description</b>
GTV	Primary tumor defined on PET or PET/CT imaging
CTV <sub>1</sub>	GTV + uterus + cervix (if not already encompassed in the GTV) Entire uterus should be delineated including the uterine fundus
CTV <sub>2</sub>	<u>Parametrial/paravaginal tissues</u> , <u>paratuerine fat</u> , ovaries and proximal vagina If there is only minimal or no vaginal tumor extension, the upper ½ of the vagina is included In patients with involvement of the upper vagina, the proximal two-thirds of the vagina should be treated If there is more extensive vaginal involvement, the entire vagina should be included in the CTV <sub>2</sub>
CTV <sub>3</sub>	Soft tissues to the medial edge of internal <u>obturator muscle/ischial ramus</u> should be included. Includes common iliac*, external and internal iliac nodal regions and pre-sacral regions The common iliac, external and internal iliac regions are defined by including the pelvic vessels plus a 7 mm expansion (excluding bone, muscle and bowel) as well as all suspicious lymph nodes, <u>lymphoceles</u> and pertinent surgical clips). Soft tissues between the internal and external iliac vessels along the pelvic sidewall are included. The pre-sacral area consists of the soft tissues anterior (minimum 1.0 cm) to the S1-S2 vertebrae Upper extent: 7 mm inferior to L4-5 <u>interspace</u> Lower extent: Superior aspect of femoral head (lower extent of external <u>iliacs</u> ) and <u>paravaginal tissues</u> at level of vaginal cuff (lower extent of internal <u>iliacs</u> )
PTV <sub>1</sub>	CTV <sub>1</sub> + 15 mm
PTV <sub>2</sub>	CTV <sub>2</sub> + 10 mm
PTV <sub>3</sub>	CTV <sub>3</sub> + 7 mm

IMRT = Intensity modulated radiation therapy, GTV = gross tumor volume, PET = positron emission tomography, CT = computed tomography, CTV = clinical target volume, PTV = planning target volume

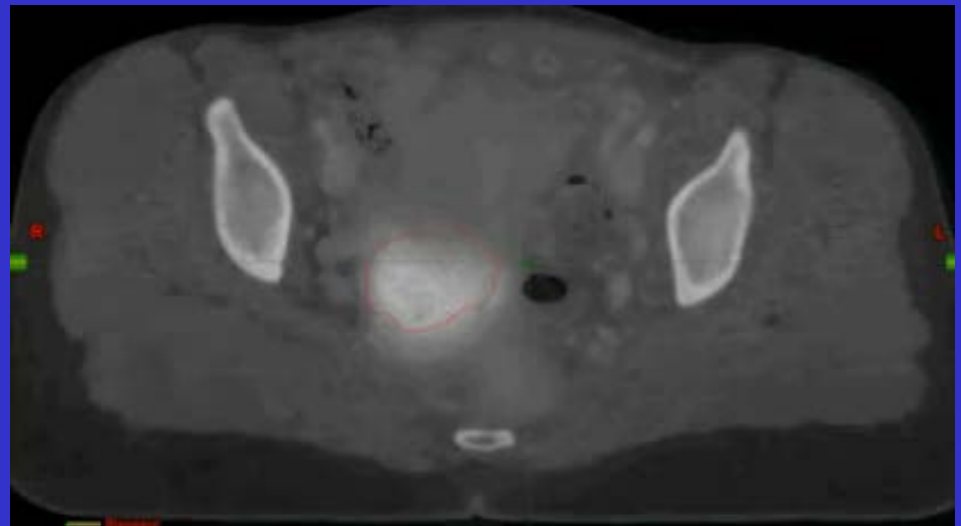
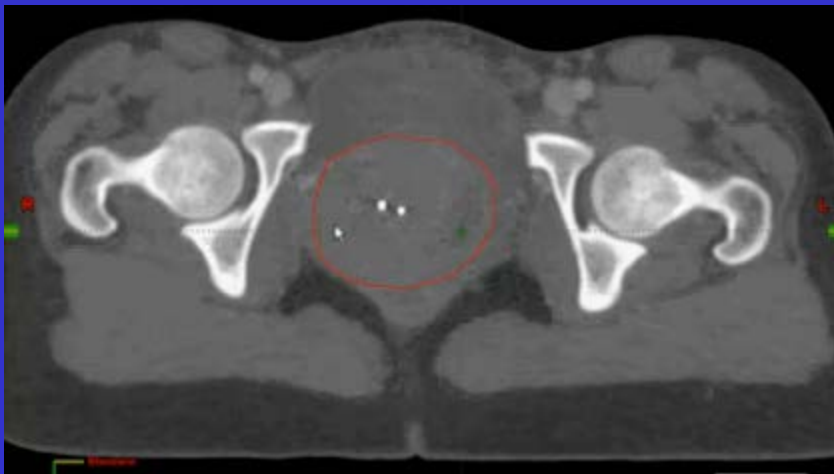
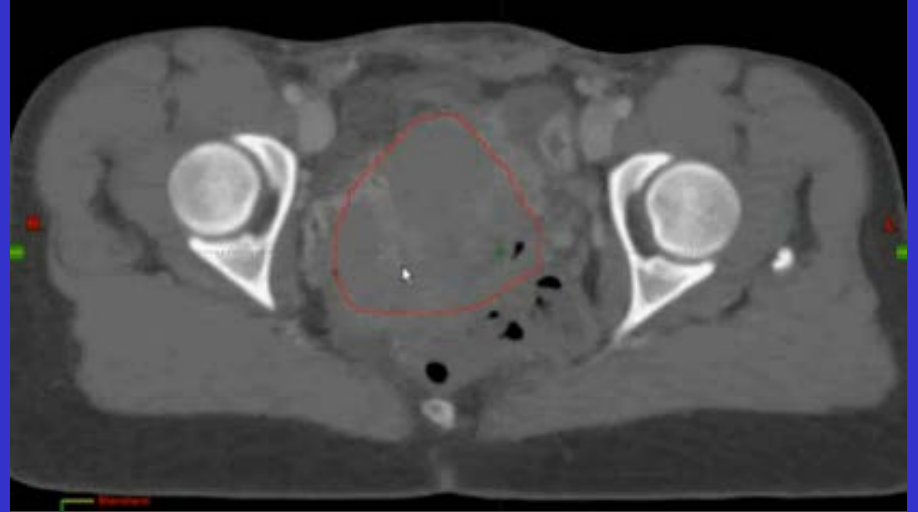
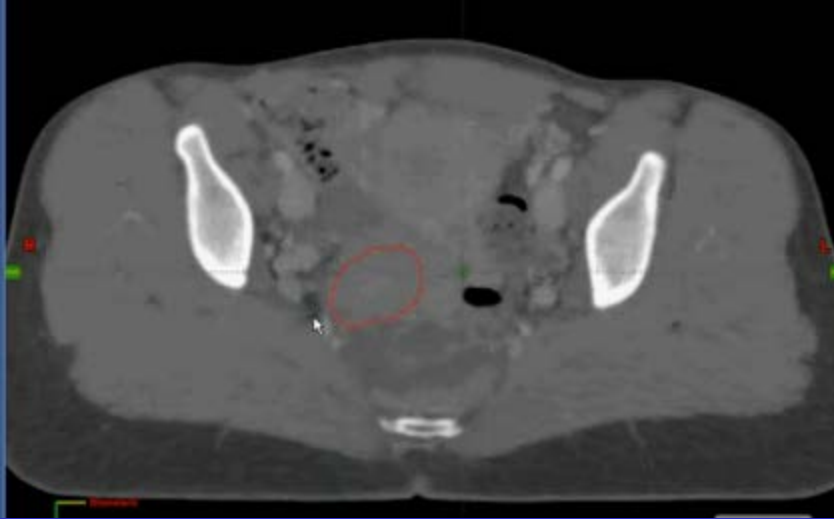
The final PTV is then generated by the union of the PTV<sub>1</sub>, PTV<sub>2</sub> and PTV<sub>3</sub>: PTV = PTV<sub>1</sub> ∪ PTV<sub>2</sub> ∪ PTV<sub>3</sub>

\* to the level of L4-5 which will not include the entire common iliac nodal region in many patients

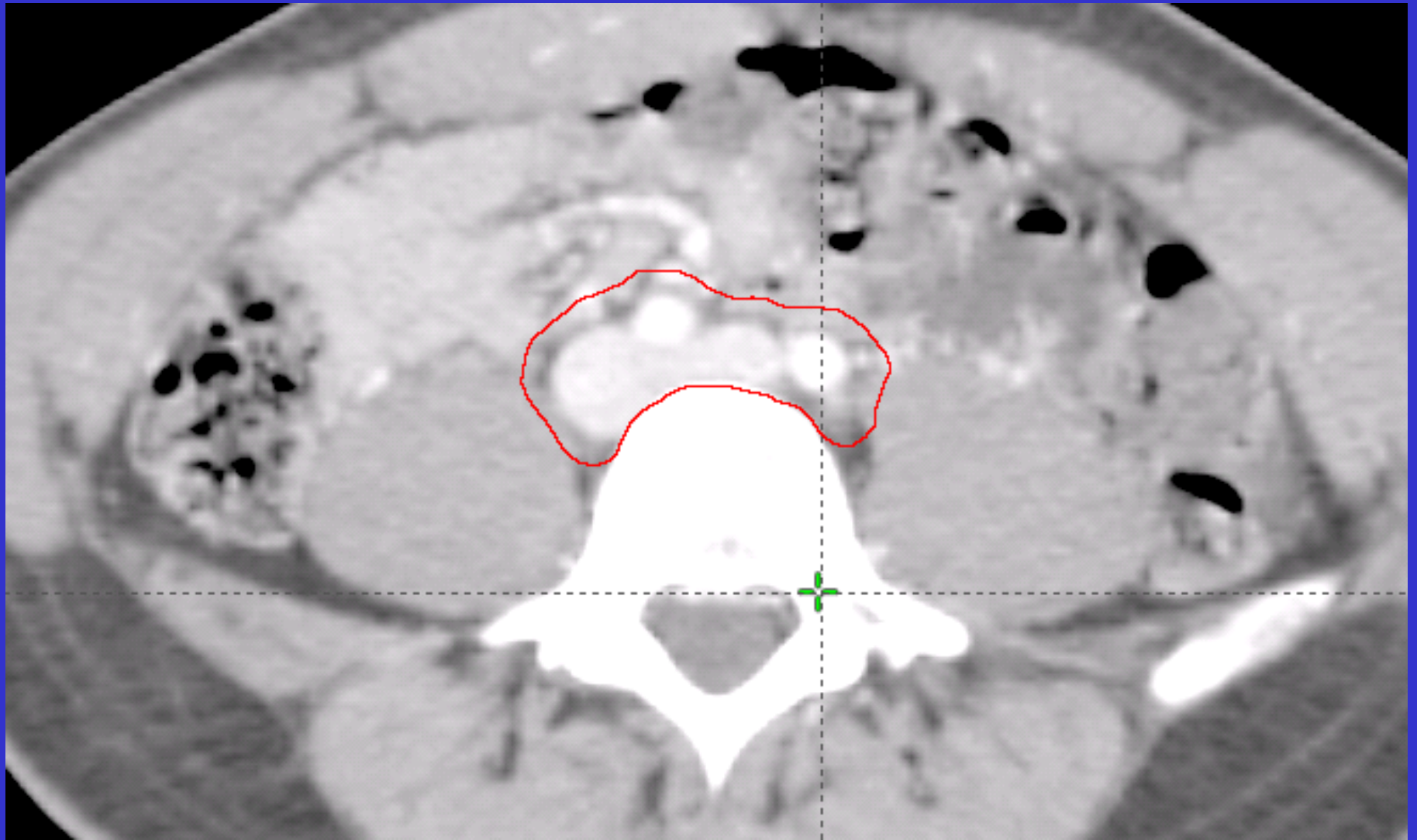
GTV

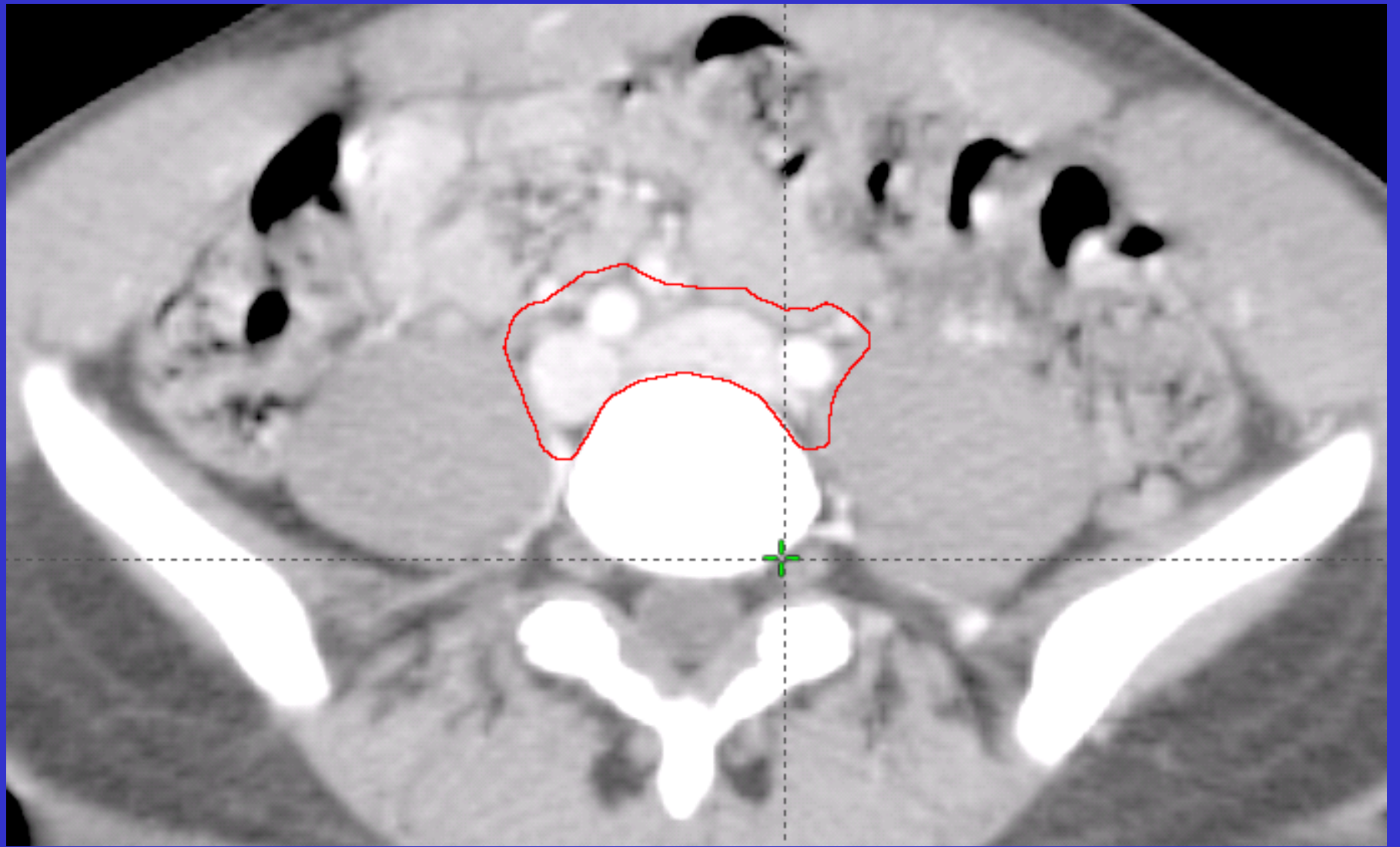


# Stage IIB Cervix Case GTV



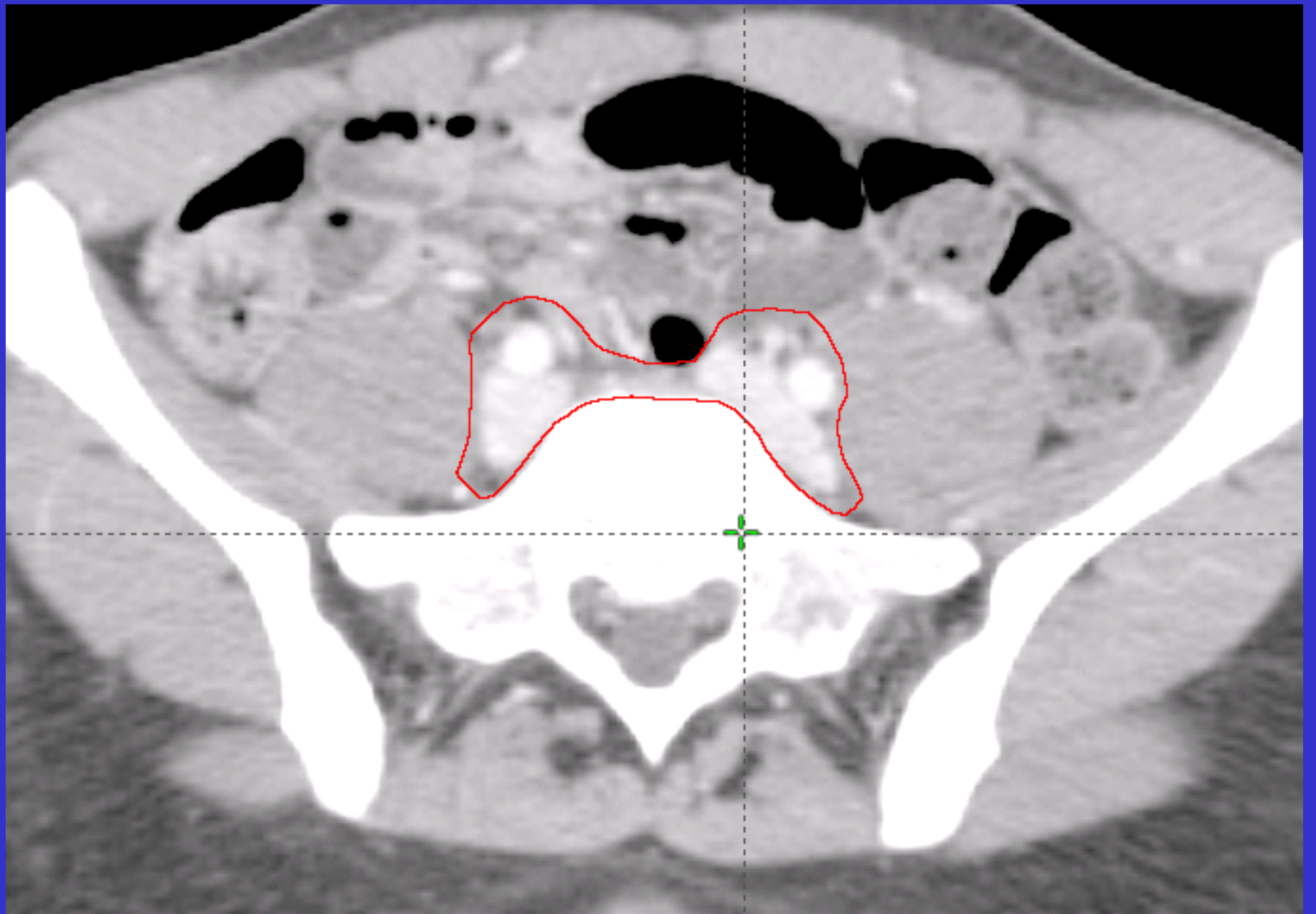




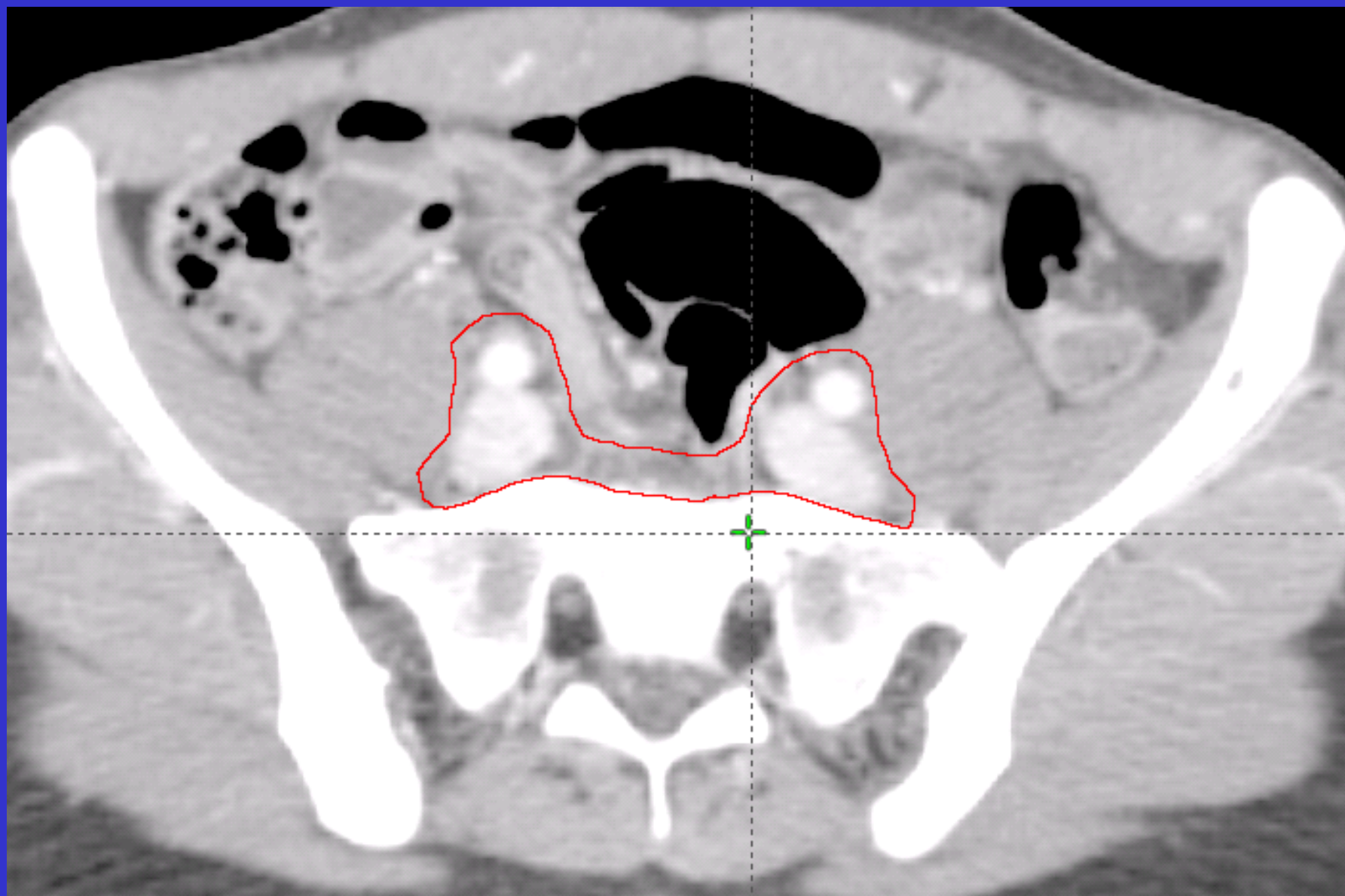


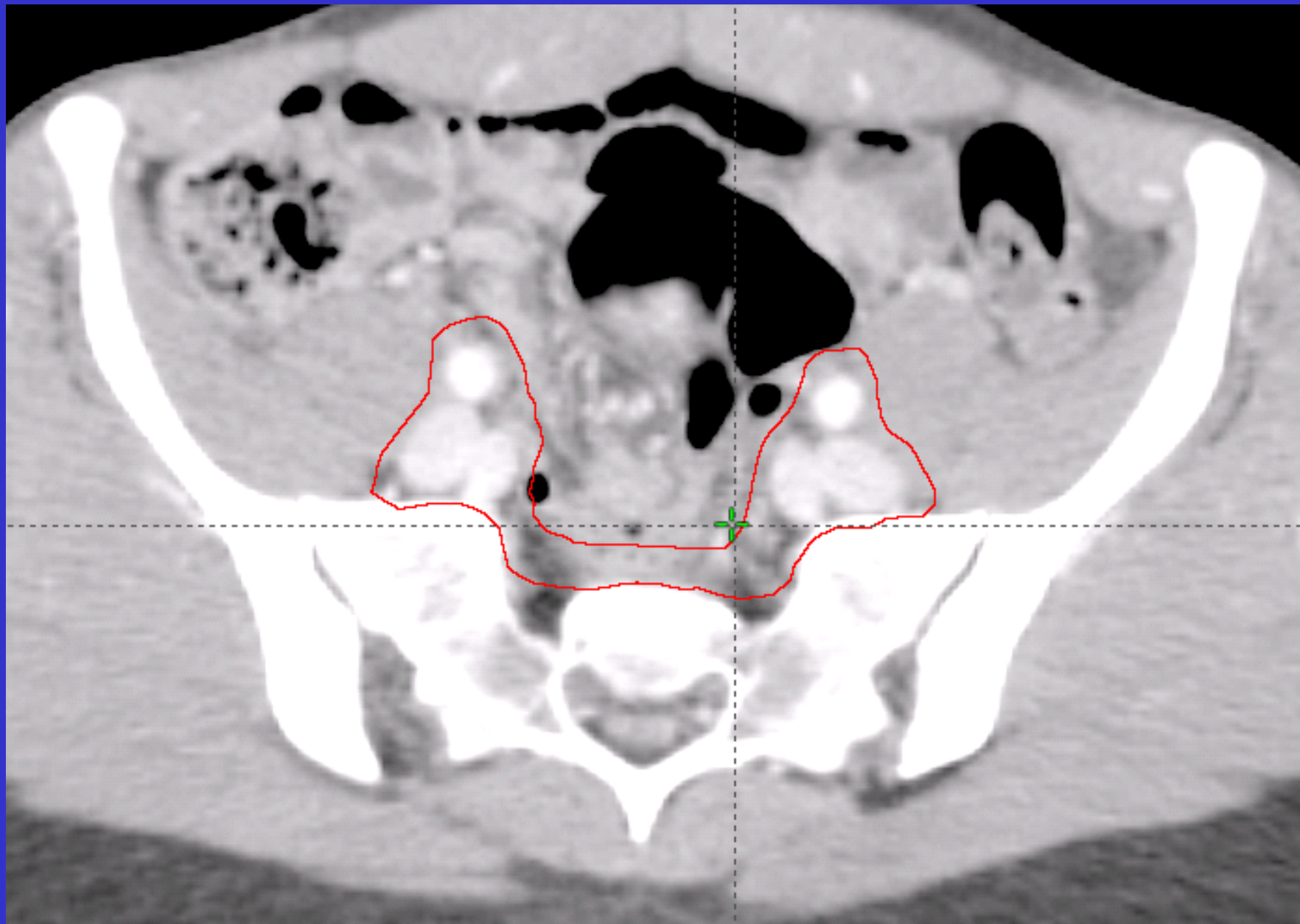




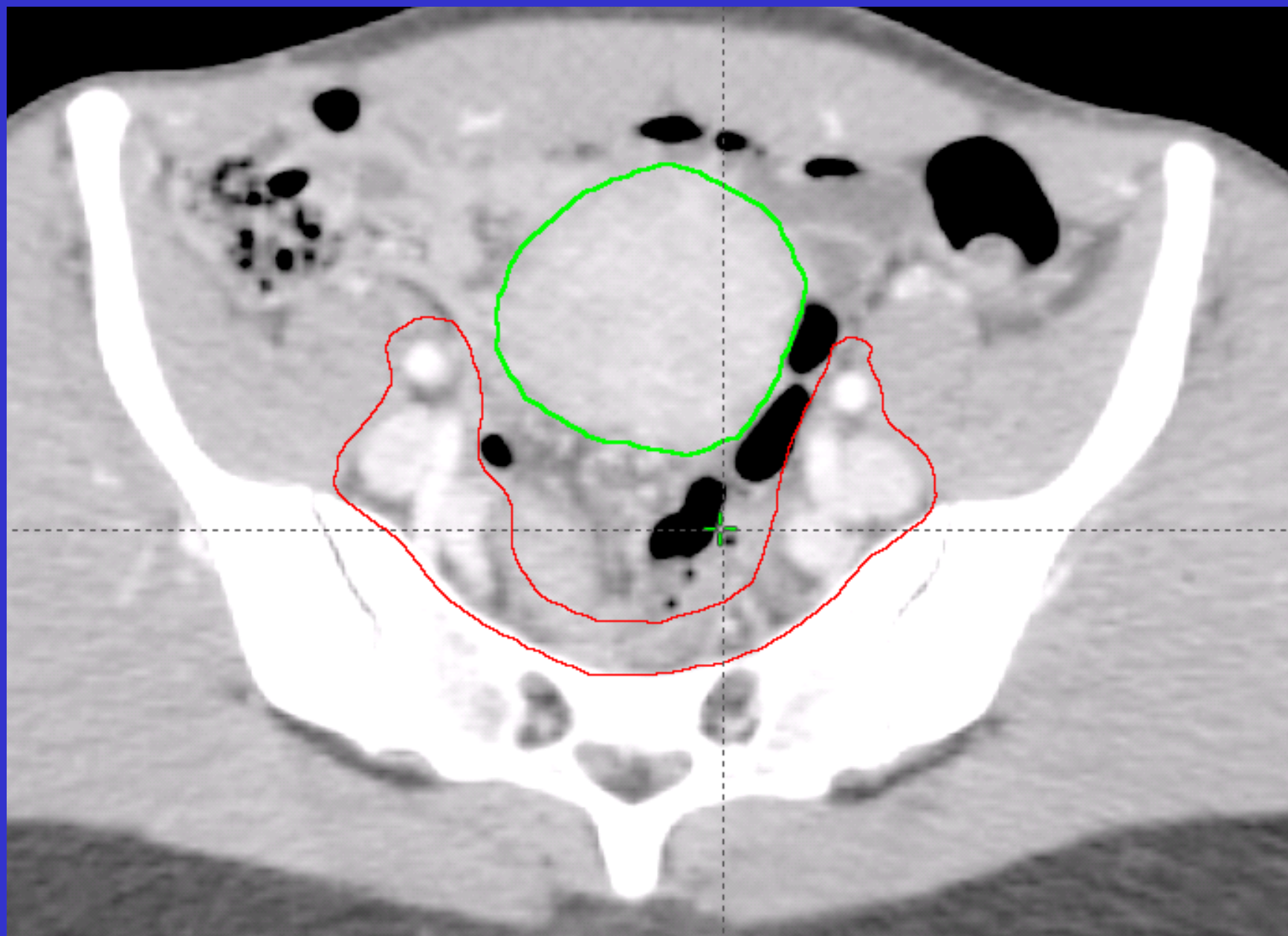


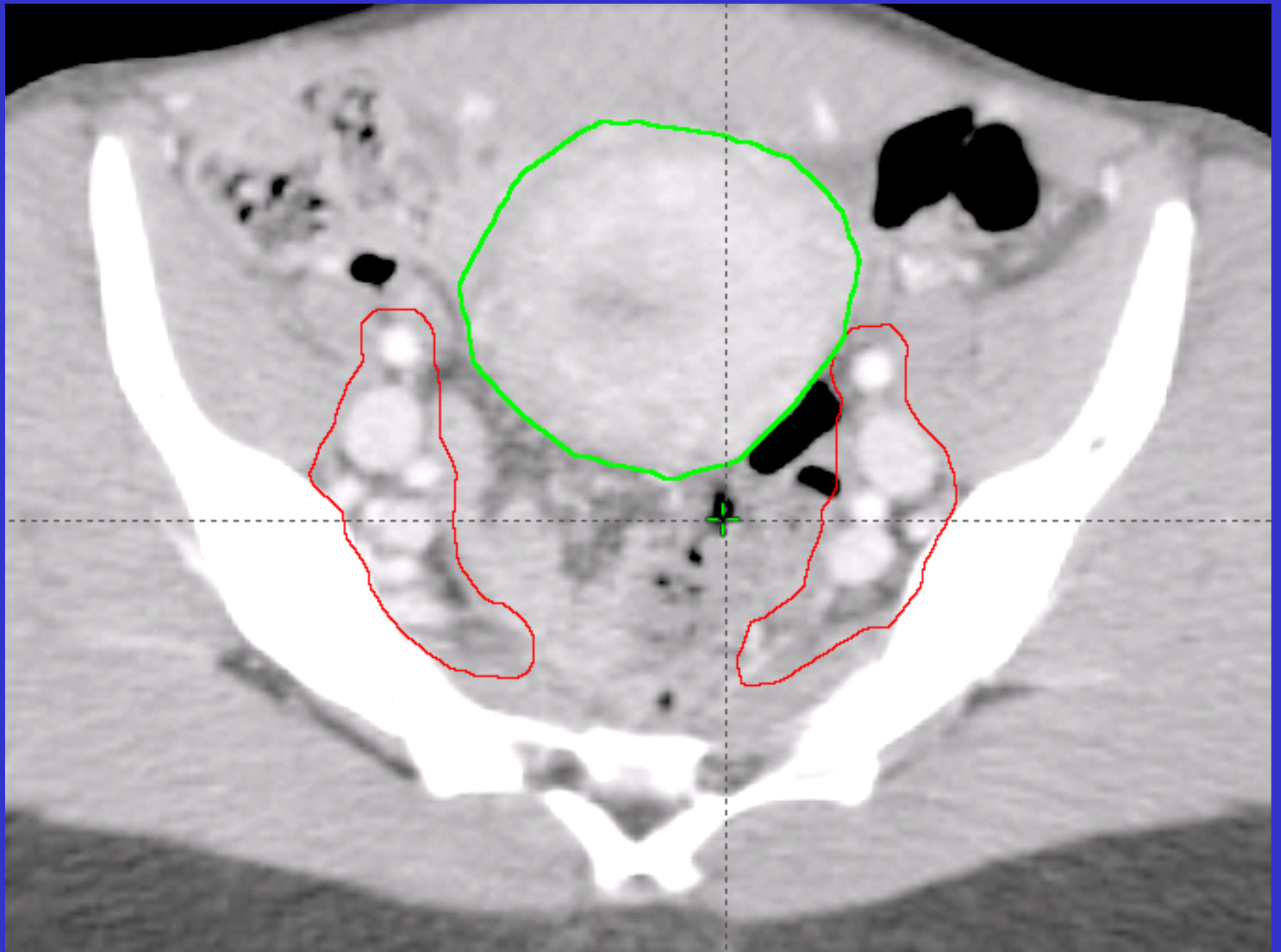




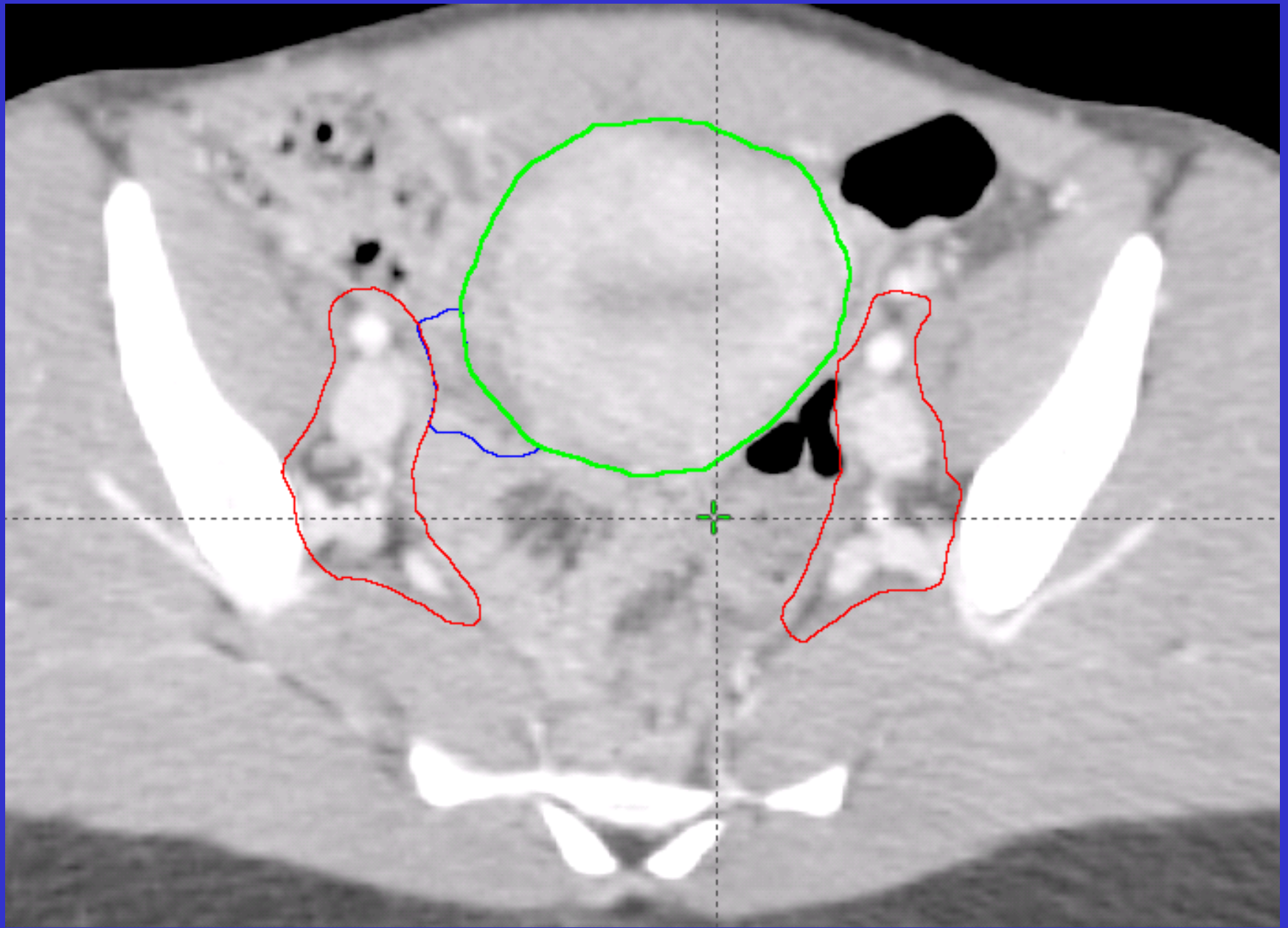




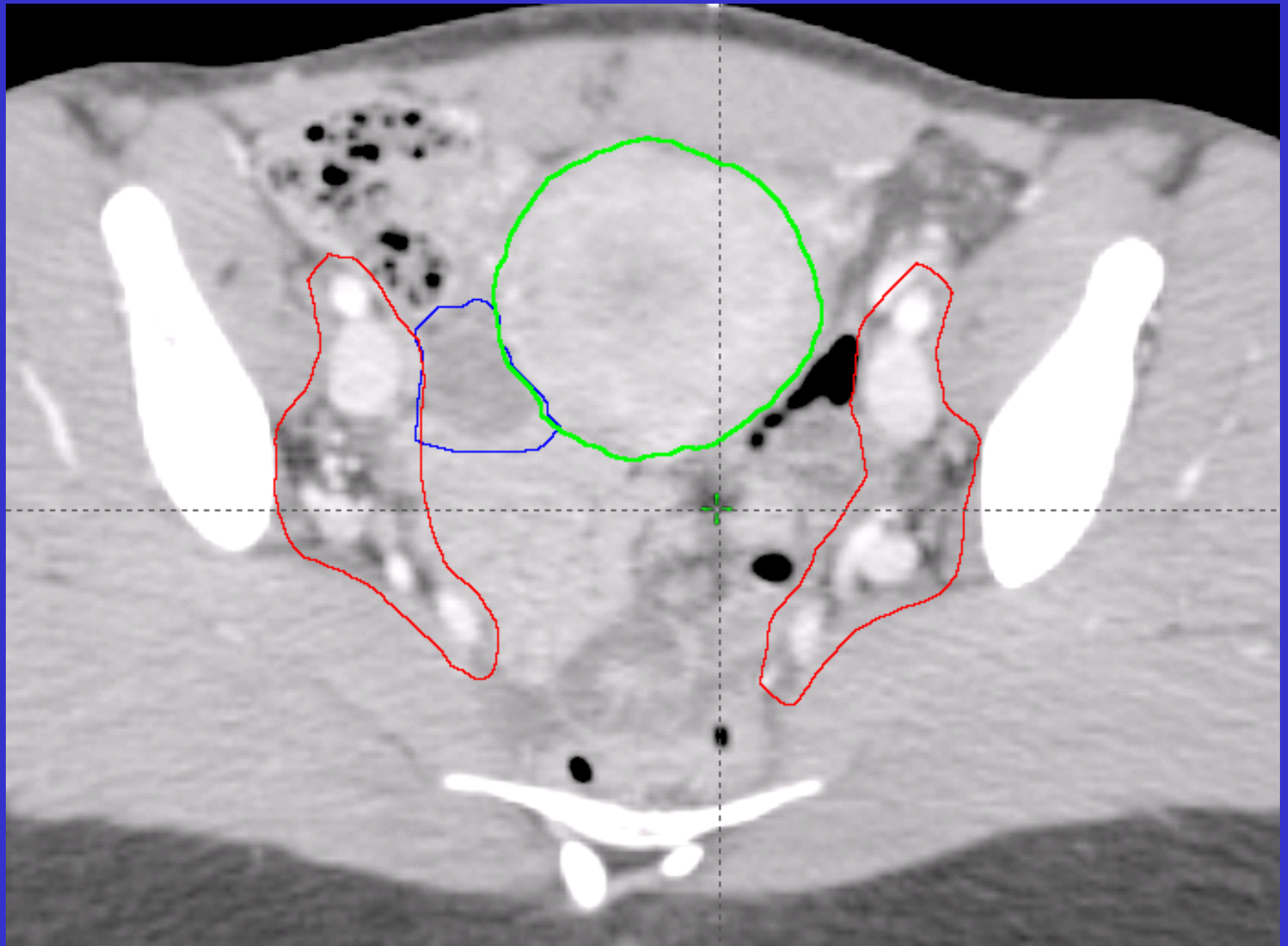


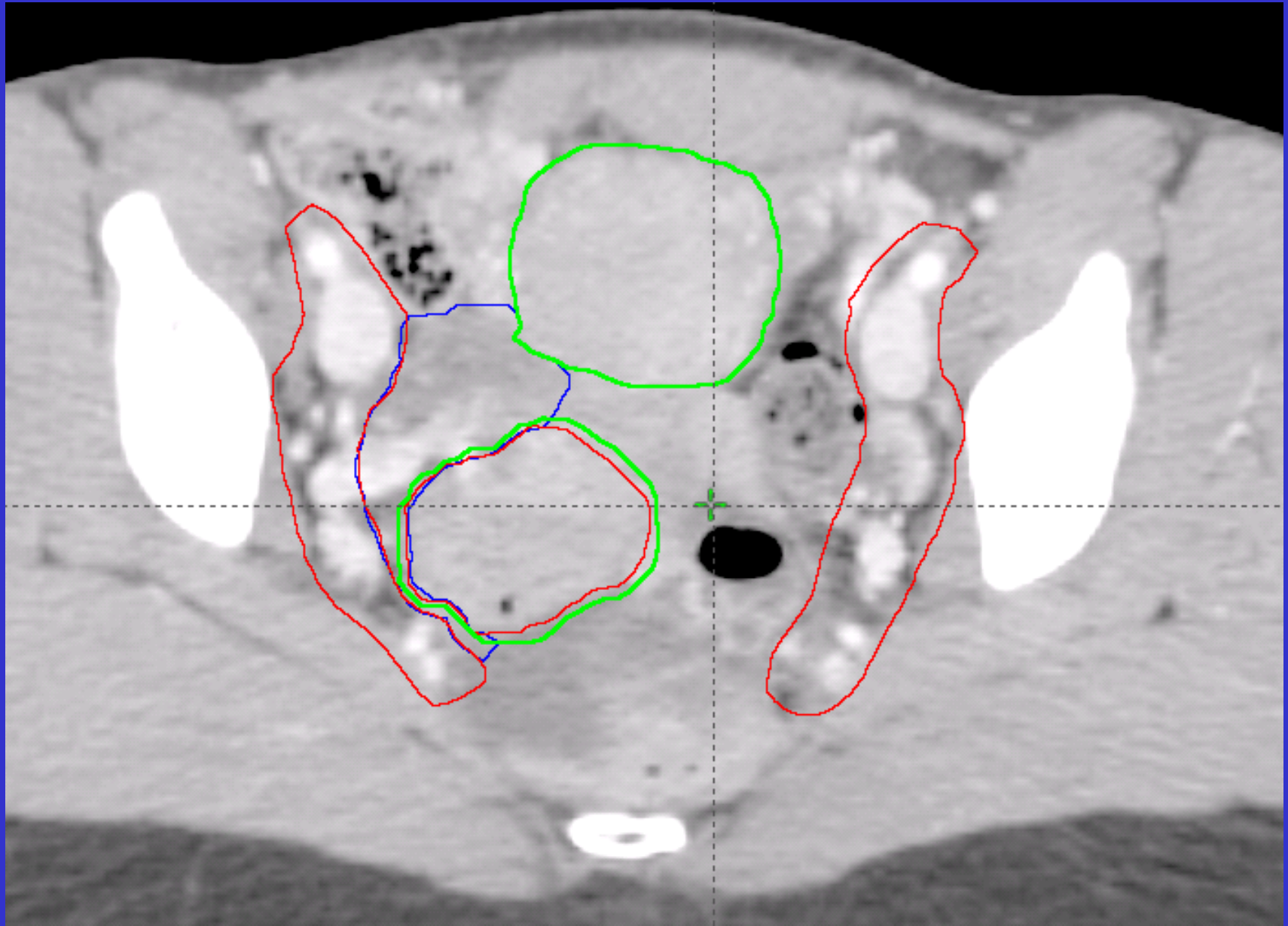




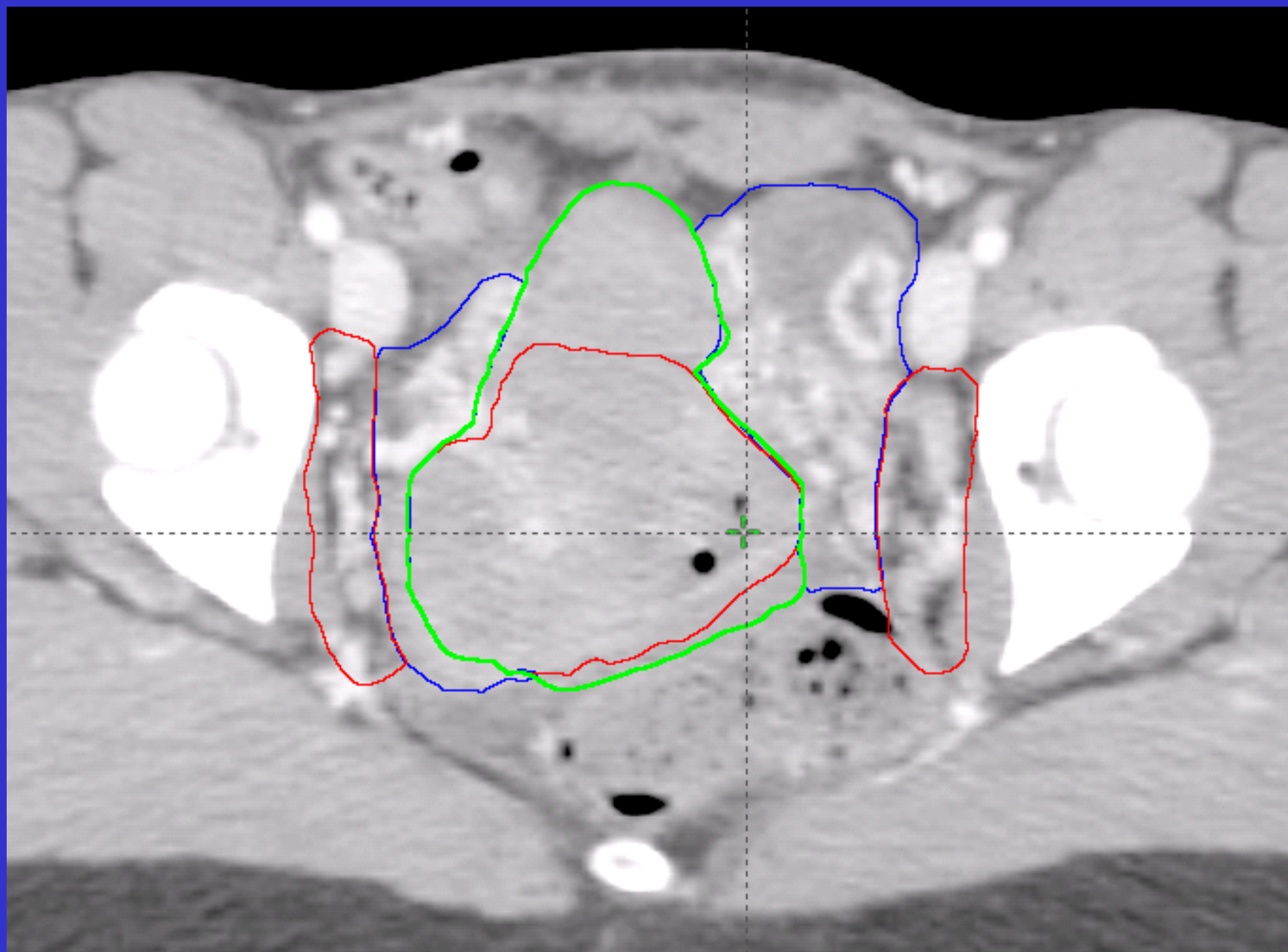


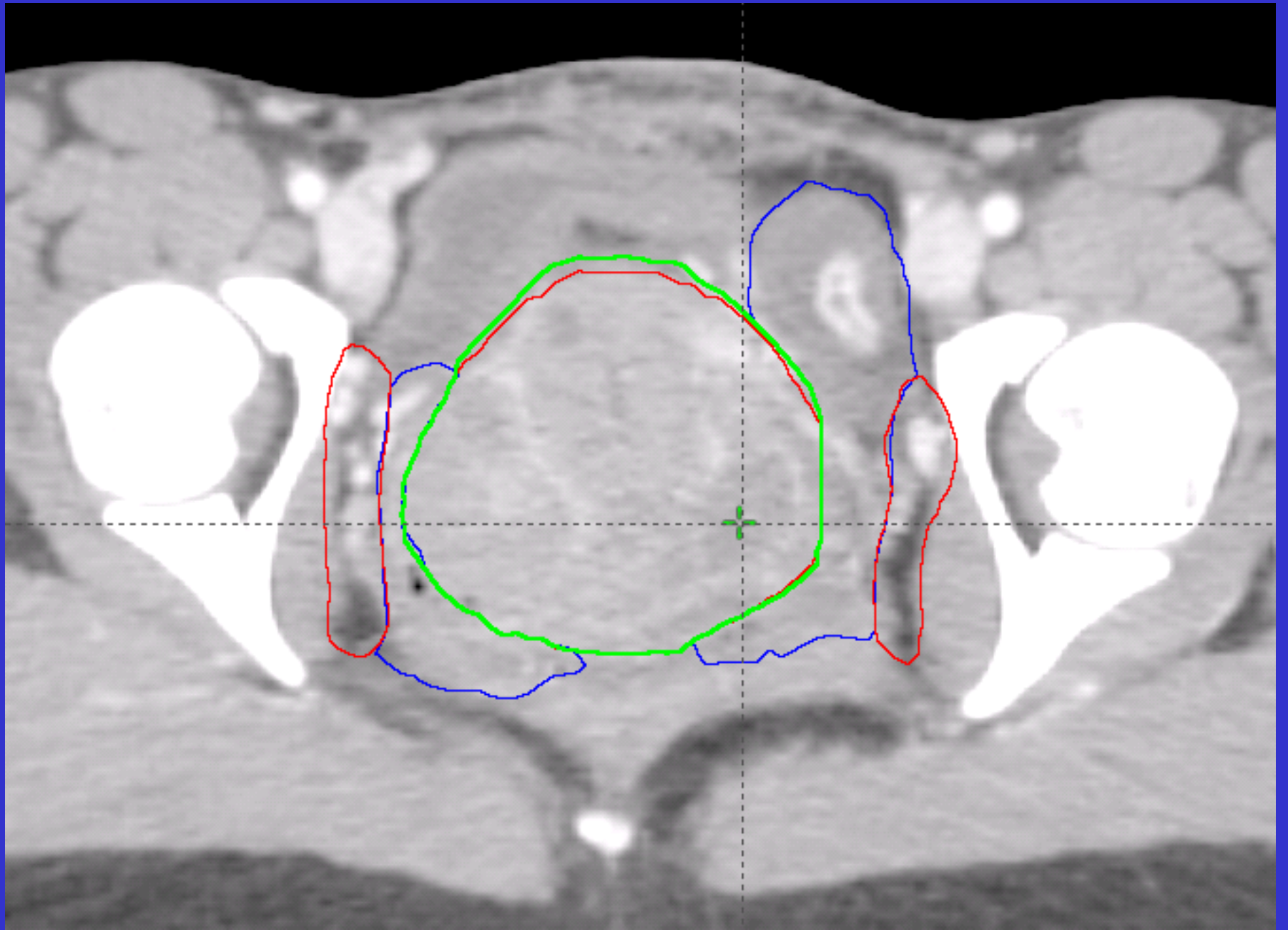




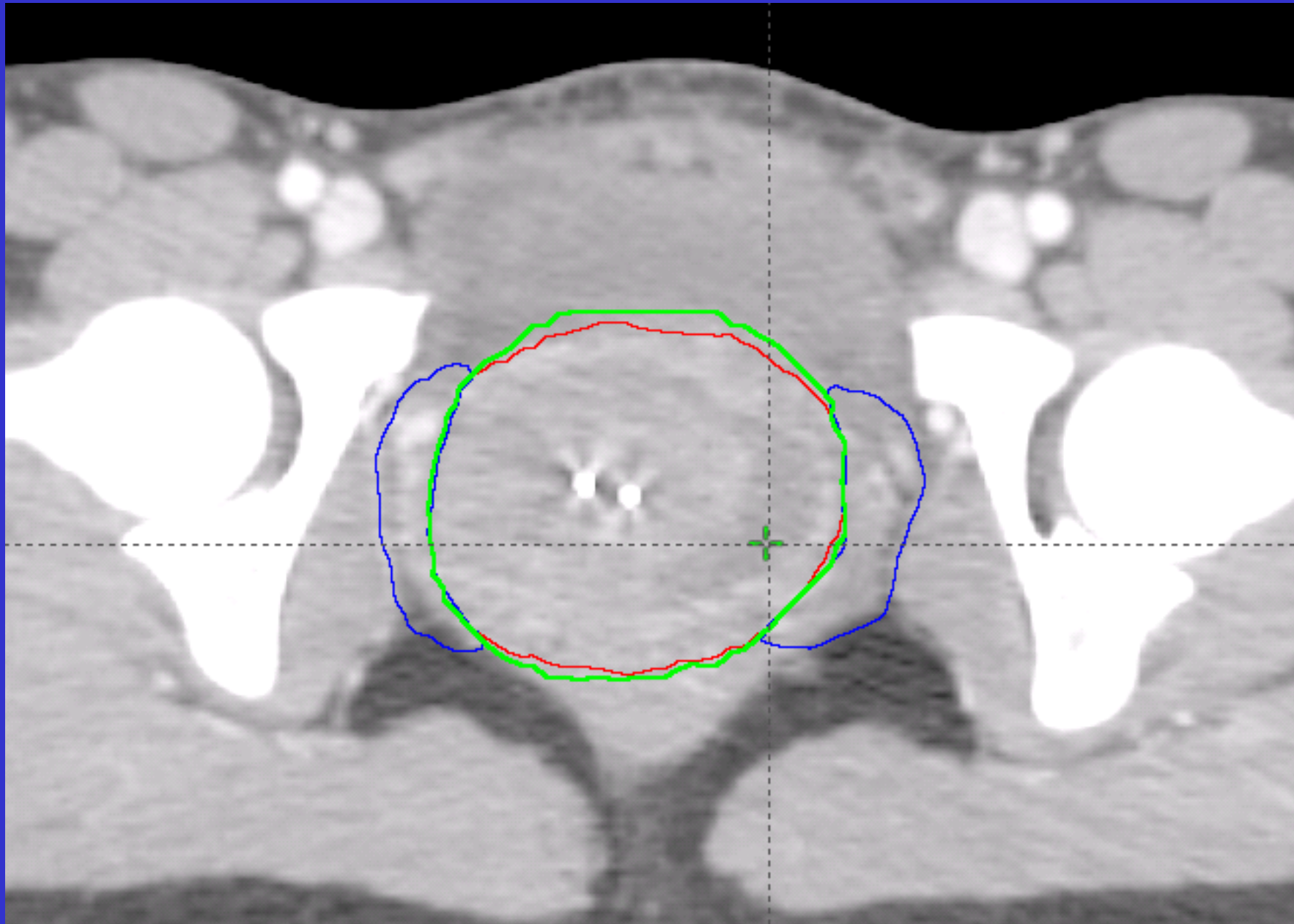


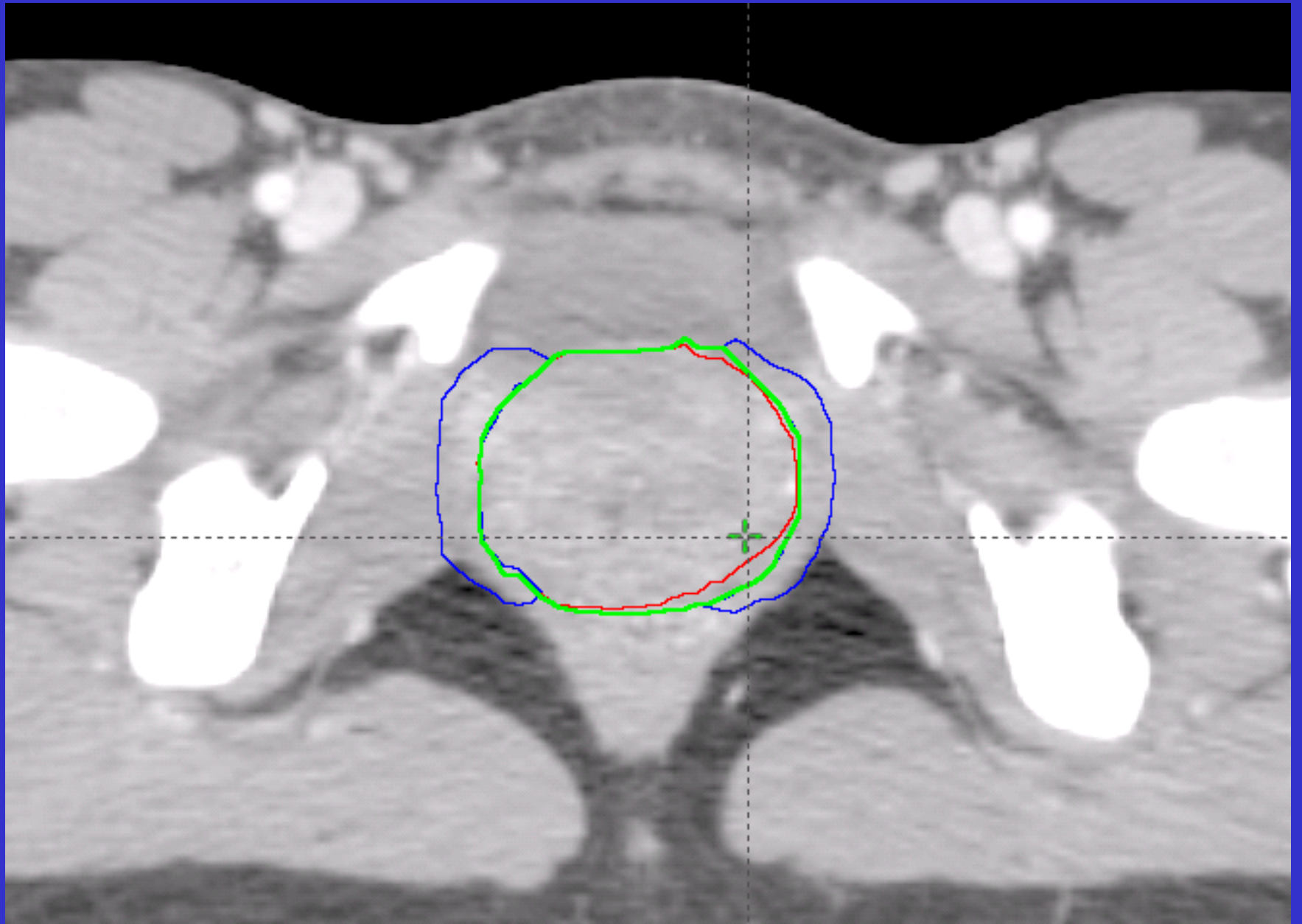




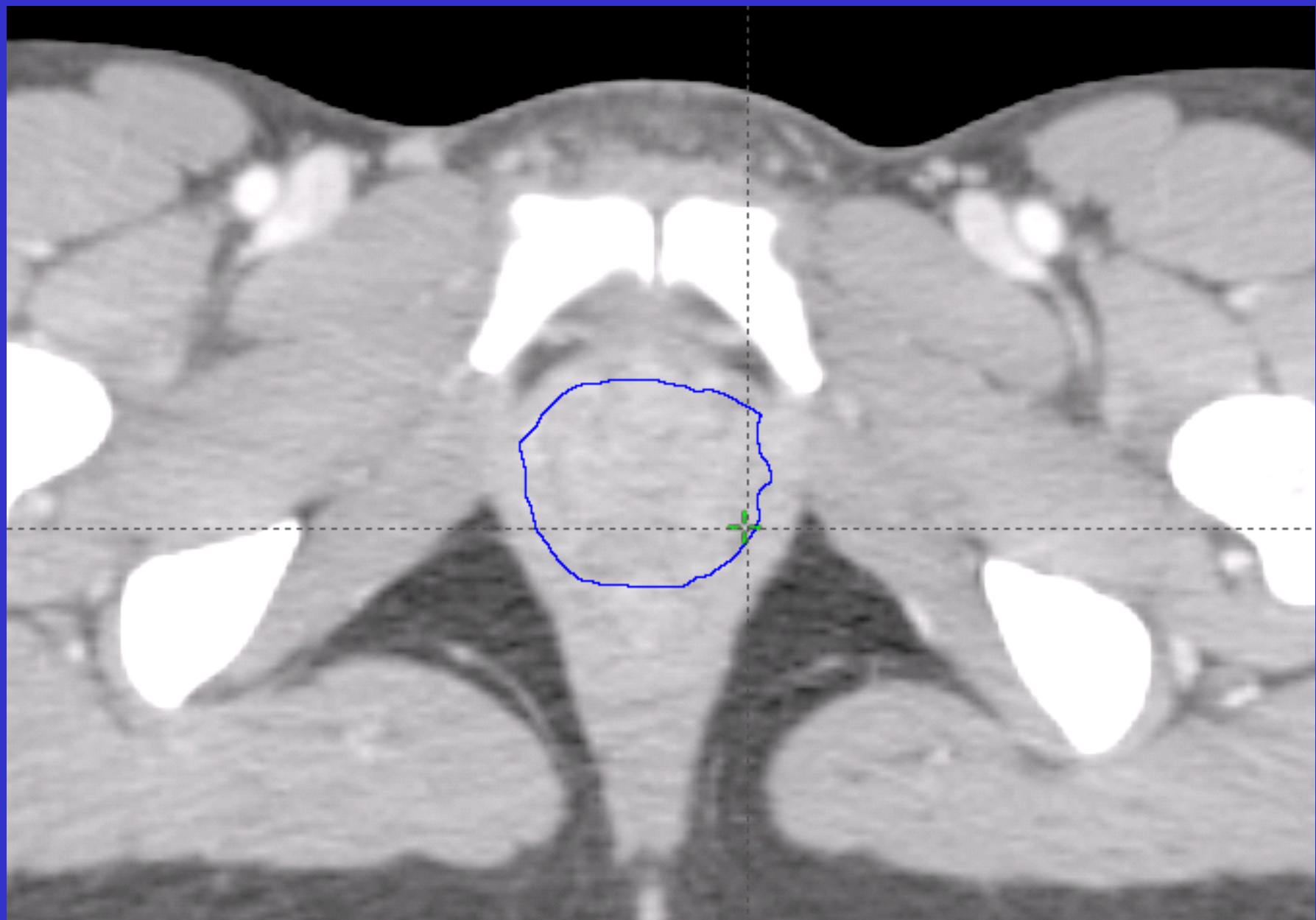










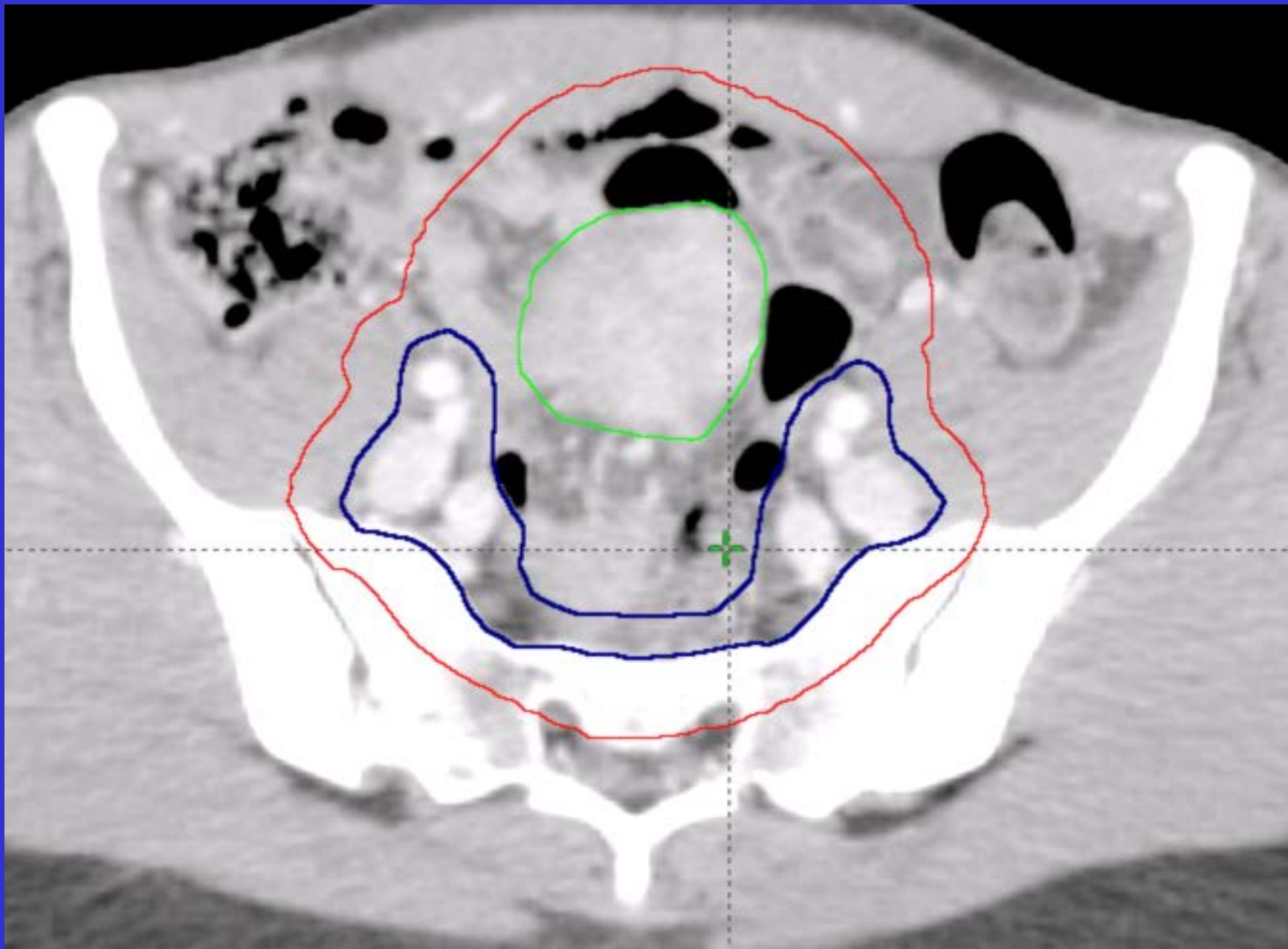


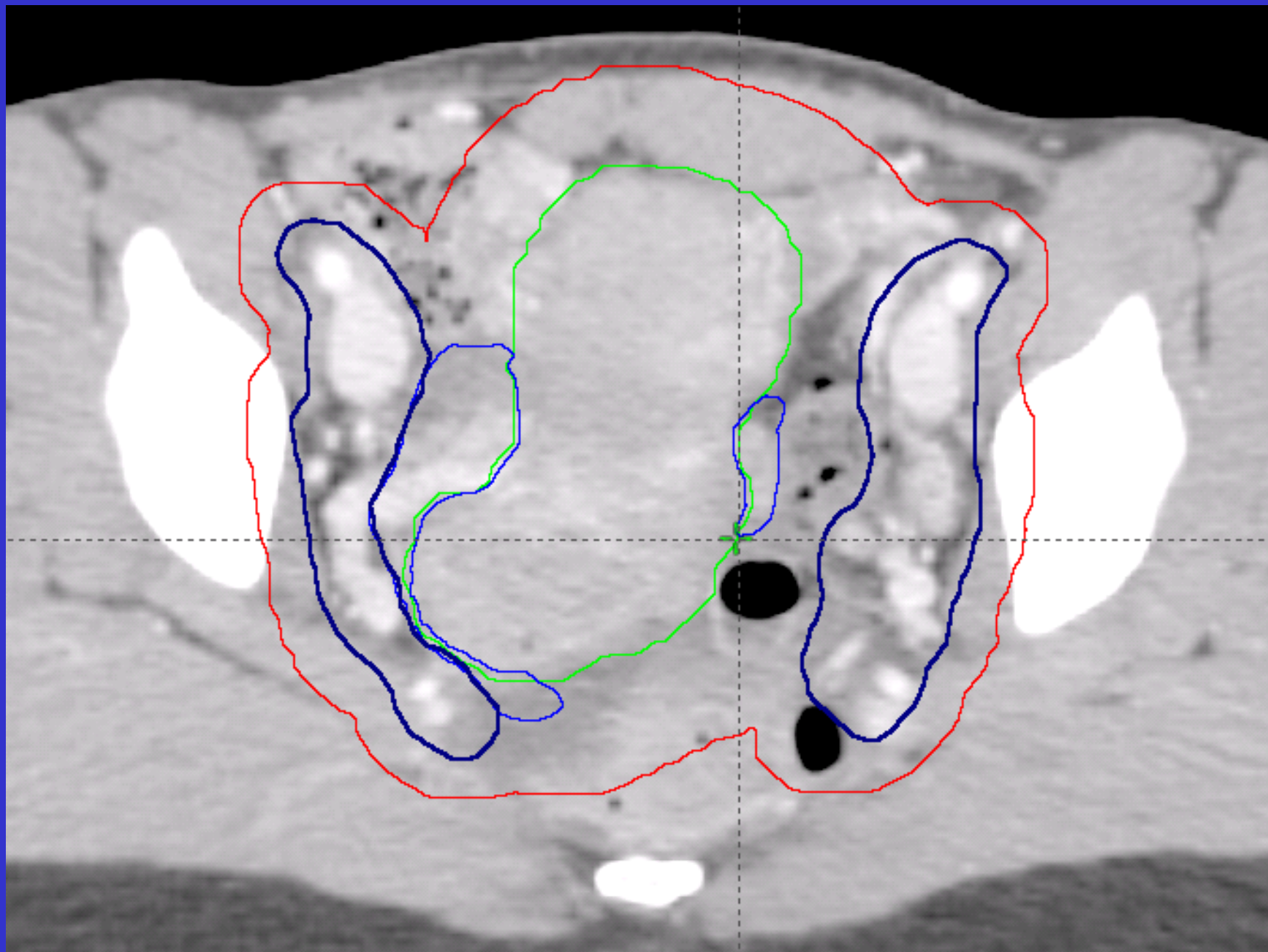
# PTV Design

- Planning target volumes (PTVs) are created for each CTVs
- The final PTV used for treatment planning is generated by combining the individual PTVs
- Different CTV-PTV expansions are used for each CTV based on its degree of internal organ motion and setup uncertainty.

$PTV_1$	$CTV_1 + 15 \text{ mm}$
$PTV_2$	$CTV_2 + 10 \text{ mm}$
$PTV_3$	$CTV_3 + 7 \text{ mm}$







# “Gyn IMRT Insurance Package”

## *Dosimetric Studies*

Mundt AJ et al. Red Journal 2000;48:1613

Heron D et al. Gynecol Oncol 2003;91:39

## *Outcome Studies*

Mundt AJ et al. Red Journal 2002;52:1330

Mundt AJ et al. Red Journal 2003;56:1354

Hasselle M et al. Red Journal 2011;80:1436

Kidd EA et al. Red Journal 2010;77:1085

Thank you for your attention



# Contouring the Female Pelvis

Beth Erickson, MD, FACR, FASTRO  
Medical College of Wisconsin

Arno Mundt, MD, FASTRO  
University of California San Diego

2013



# Disclosures

- Non-paid consultant to Nucletron and Varian
- Varian and Nucletron Travel Grants
- Chart Rounds participant

# Learning Objectives

1. Review pelvic anatomy
2. Define pelvic targets
3. Contour post-op endometrial/cervix cancer cases
4. Discuss volumes and challenges for intact cervix cancer



To Eradicate  
Cancer You Must  
“Hit the Target”

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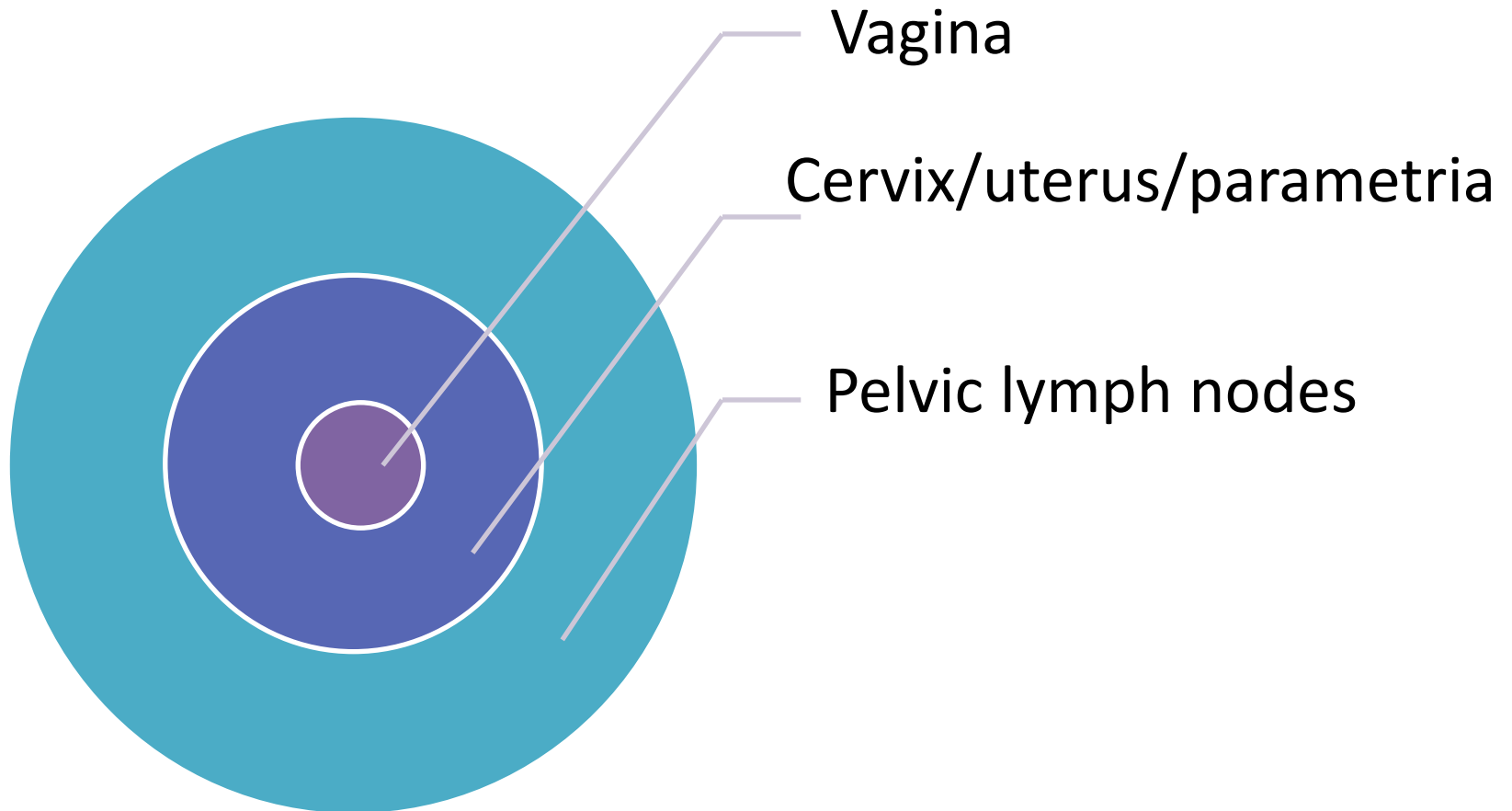


# Target Definition

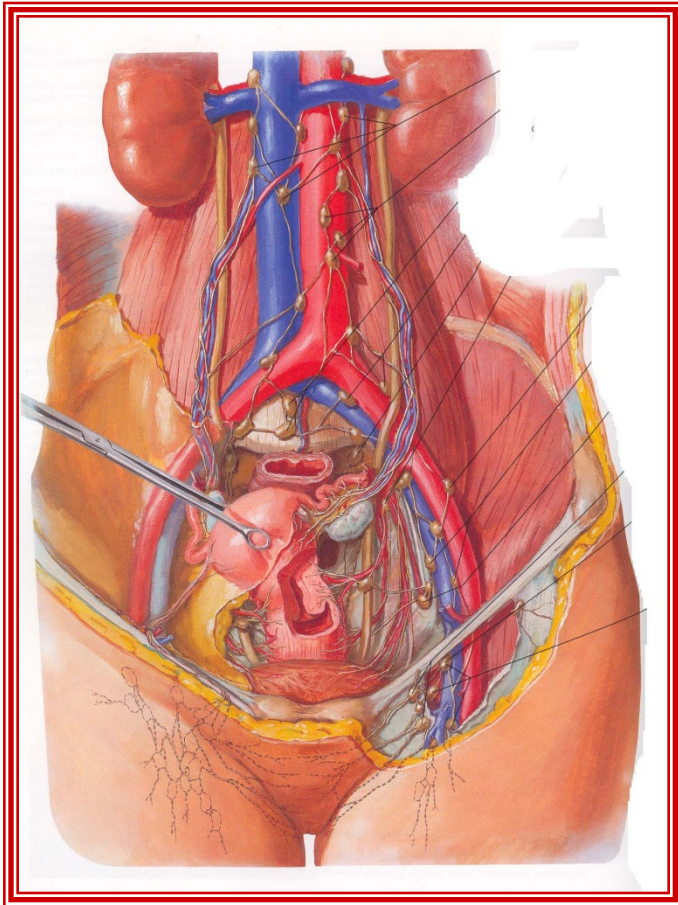
Knowledge of  
the anatomy  
is essential,  
especially in  
the era of  
IMRT

If you don't  
define it, it  
might not get  
treated or  
spared

# What Are the Targets?



# Where Are the Pelvic Nodes?



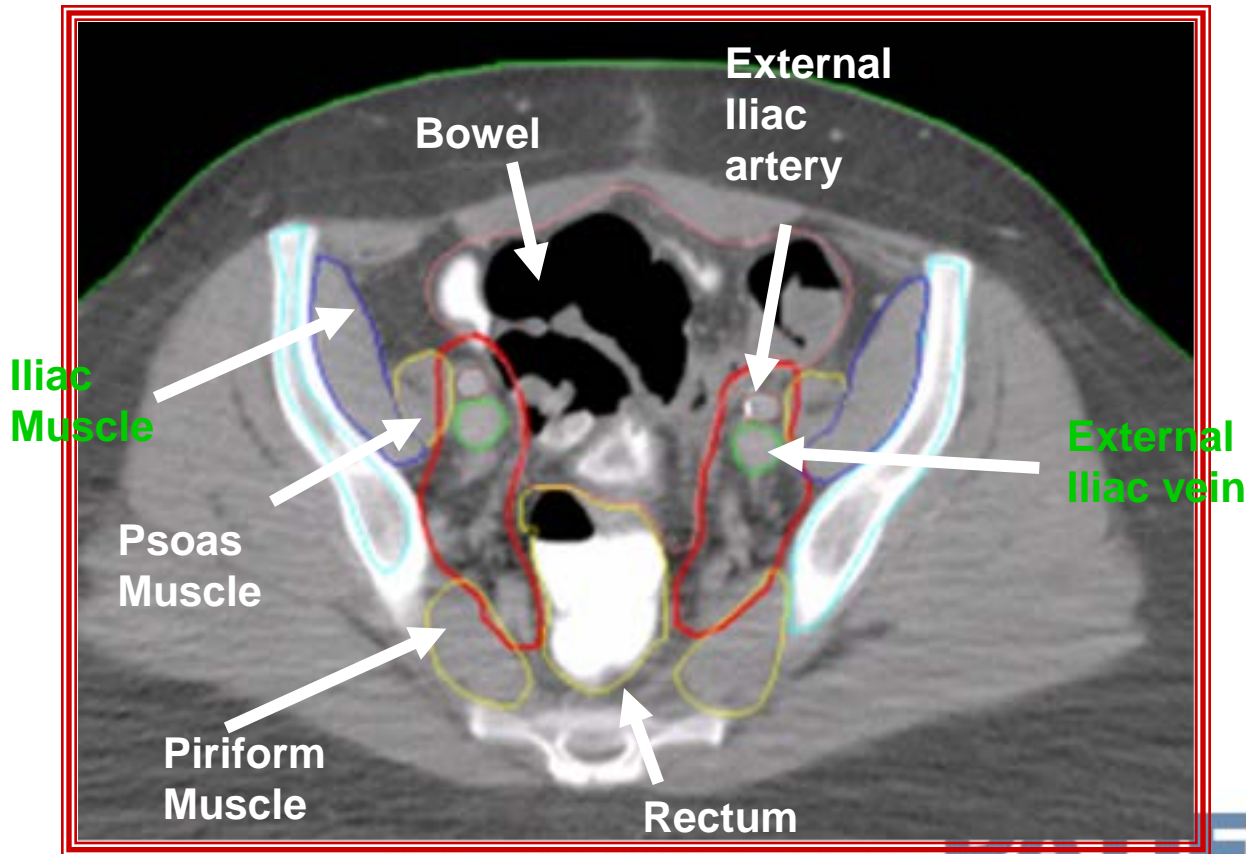
- Most “normal-sized” lymph nodes are too small to be visualized directly with standard imaging
- Anatomic studies demonstrated that pelvic lymph nodes lie adjacent to major blood vessels

Netter F. Atlas of Human Anatomy 4<sup>th</sup> Ed.

# Where Are the Pelvic Nodes?

- Use the blood vessels with a margin as a surrogate target for lymph nodes

Mell et al. Gynecologic Tumors IMRT: A Clinical Perspective BC Decker 2005



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# Contouring Guidelines



Int. J. Radiation Oncology Biol. Phys., Vol. 71, No. 2, pp. 428–434, 2008  
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0360-3016/08/\$-see front matter

doi:10.1016/j.ijrobp.2007.09.042

**CLINICAL INVESTIGATION**

**Uterus**

## CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUME FOR INTENSITY-MODULATED PELVIC RADIOTHERAPY IN POSTOPERATIVE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER

WILLIAM SMALL, JR., M.D.,\* LOREN K. MELL, M.D.,† PENNY ANDERSON, M.D.,‡  
CARIEN CREUTZBERG, M.D.,§ JENNIFER DE LOS SANTOS, M.D.,¶ DAVID GAFFNEY, M.D., PH.D.,||  
ANUJA JHINGRAN, M.D.,# LORRAINE PORTELANCE, M.D.,\*\* TRACEY SCHEFTER, M.D.,††  
REVATHY IYER, M.D.,‡‡ MAHESH VARIA, M.D.,§§ KATHRYN WINTER, M.S.,¶¶ AND ARNO J. MUNDT, M.D.,|||

## RTOG Gynecologic Atlas

<http://www.rtog.org/gynatlas/main.html>

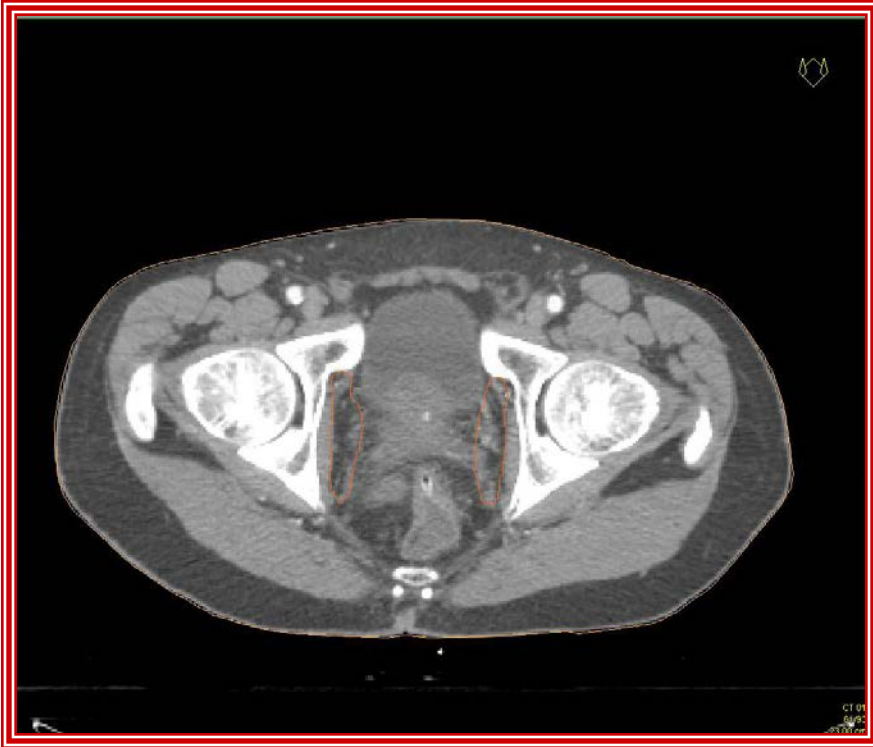
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# RTOG Revised Post Op Gynecologic Atlas

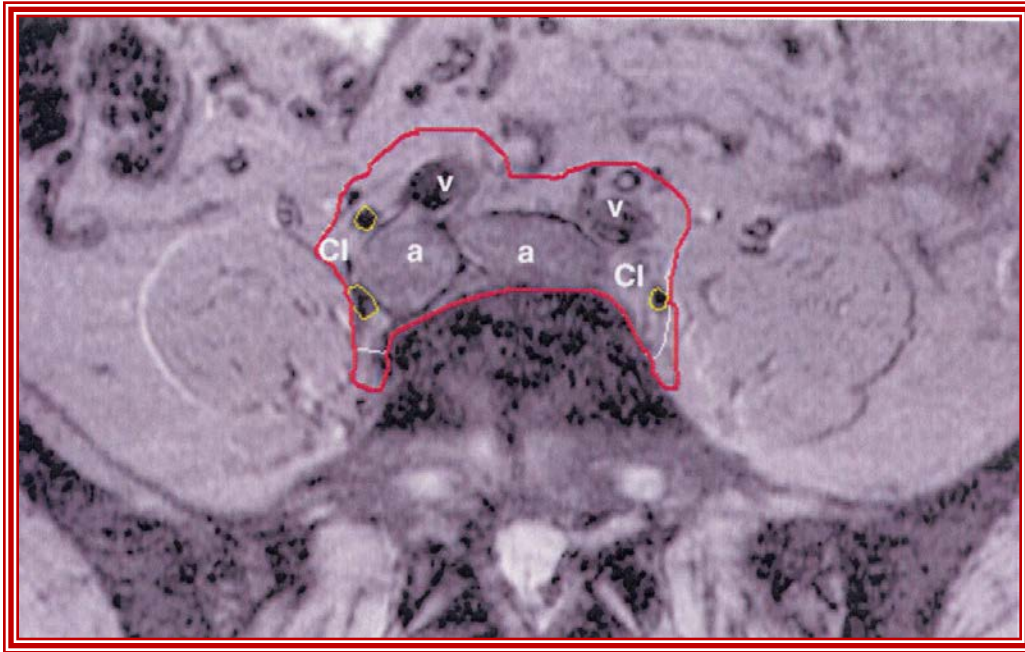
- Under construction
- Better coverage of the obturator LNs
- More reasonable sculpting of the CTV around bowel and rectum
- Use vessels rather than bony landmarks to define the common iliacs and upper field border
- Encourage IV and oral contrast



RTOG Prostate Atlas-obturator nodes



# Common Iliac Lymph Nodes



Taylor et al; IJROBP 63(5):1604-1612, 2005

Small et al; IJROBP 71(2):428-434, 2008

Vi Larino-Varela et al; Radiother Oncol 89:192-196, 2008

- Common iliac nodes lie in lateral and posterior spaces
- Margins (CTV) of 7 mm around vessels except near vertebral body (10 mm)

\*Iron Oxide particles (USPIO) in the lymph nodes - black

# Common Iliac Lymph Nodes

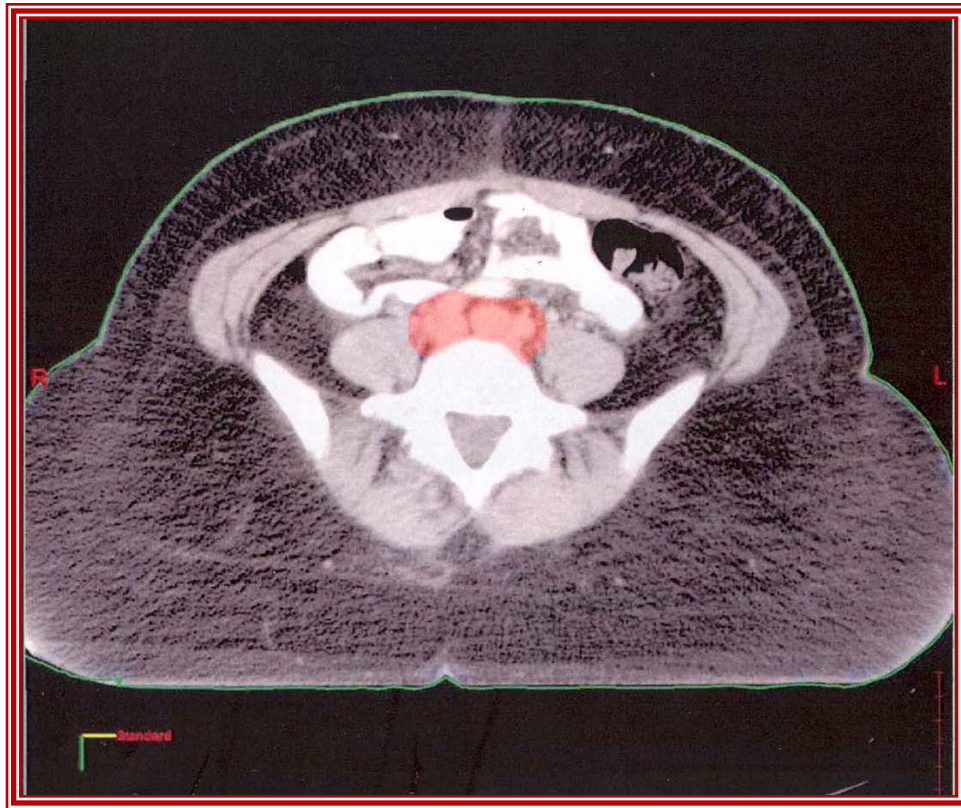
## 3D conformal fields

- Avoid splitting vertebral bodies on lateral fields to avoid underdosing common iliac lymph nodes
- Common iliac nodes can be as high as L3



Park; Radiographics 14:1994

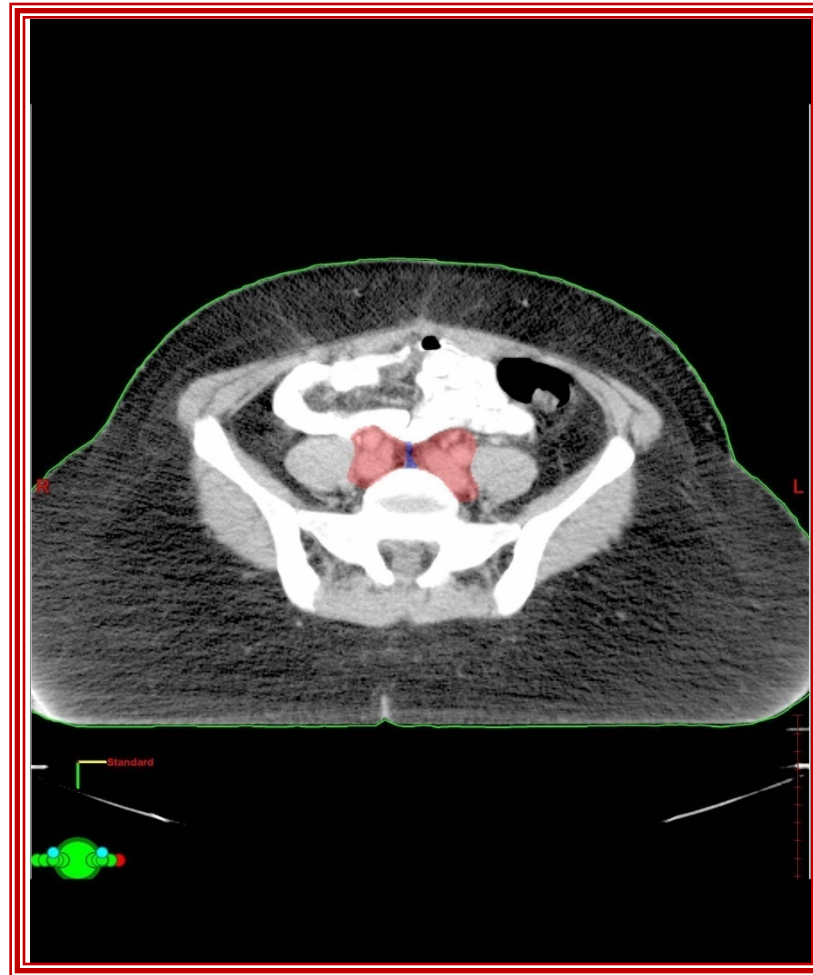
# Common Iliac Lymph Nodes



- Common iliac CTV should include a minimum of 1.5 cm of soft tissue anterior to the vertebral body at the midline
- Should exclude vertebral body, psoas muscle, and bowel

Small et al; IJROBP, 71(2):428-434, 2008

# Mid-Common Iliac Lymph Nodes



Small et al; IJROBP 71(2):428 -434, 2008

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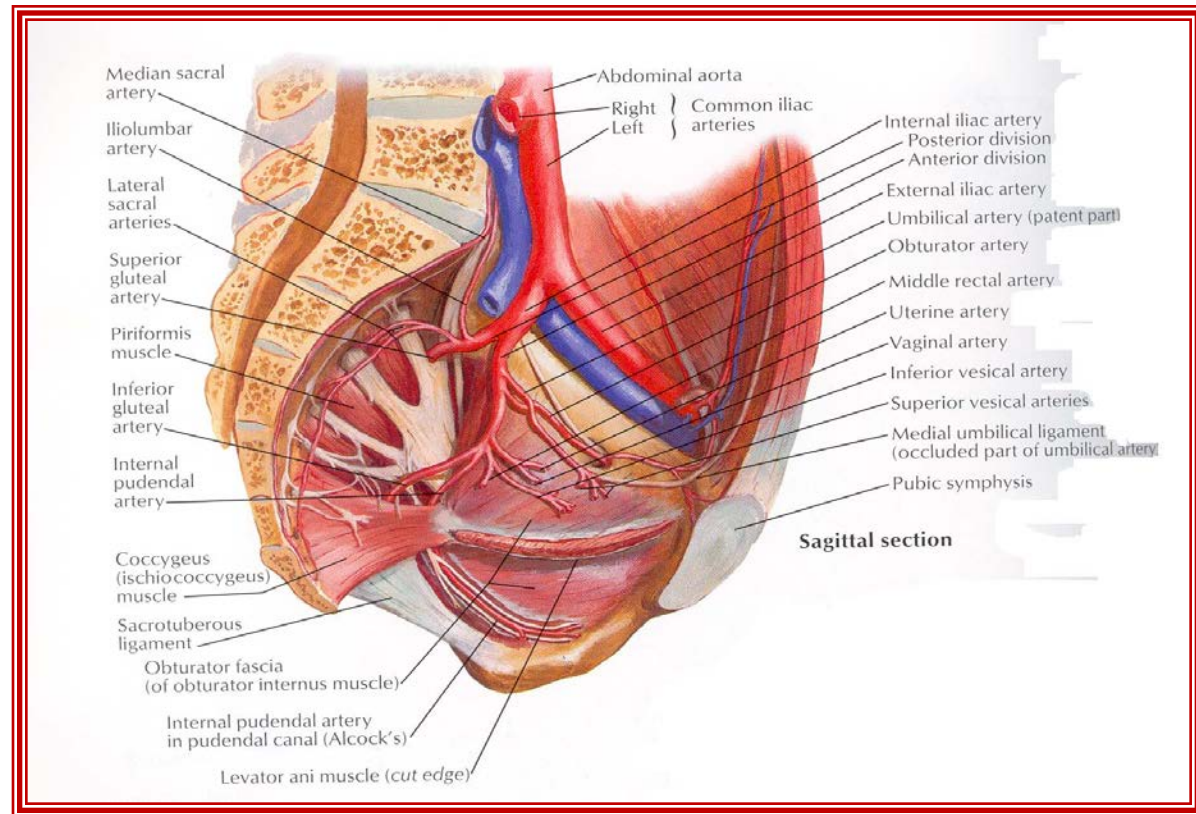


Common Iliac  
Lymph Nodes  
Images 40-58



# Presacral Lymph Nodes

- Anterior to sacrum/coccyx
- Divided into subaortic below the aortic bifurcation over the sacral promontory and the perirectal nodes within the mesorectal fascia in the sacral hollow



Netter F. Atlas of Human Anatomy 4<sup>th</sup> Ed

# Presacral Lymph Nodes

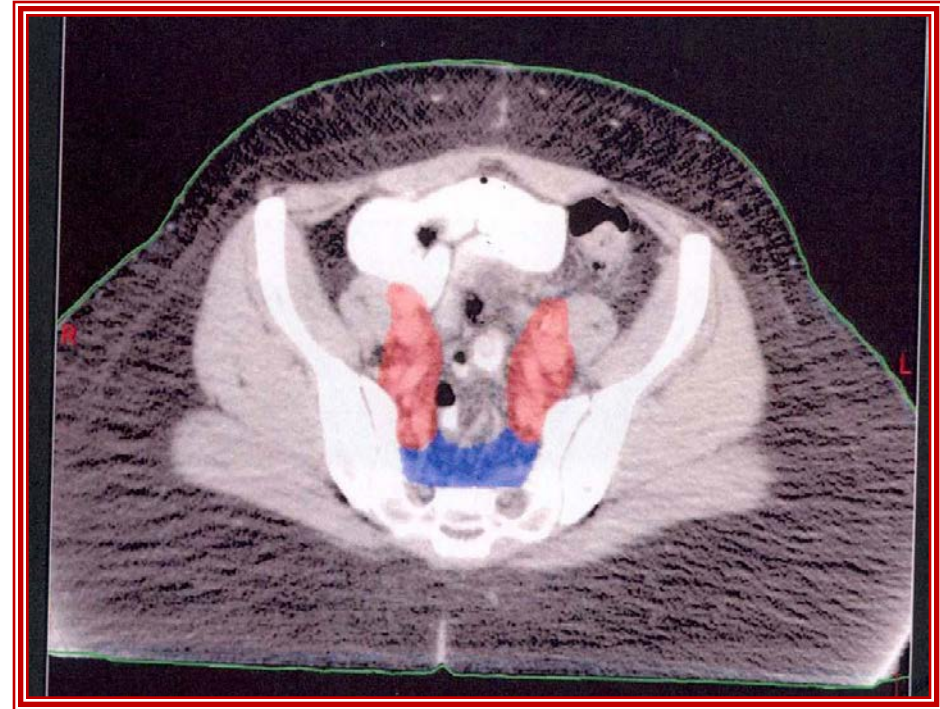
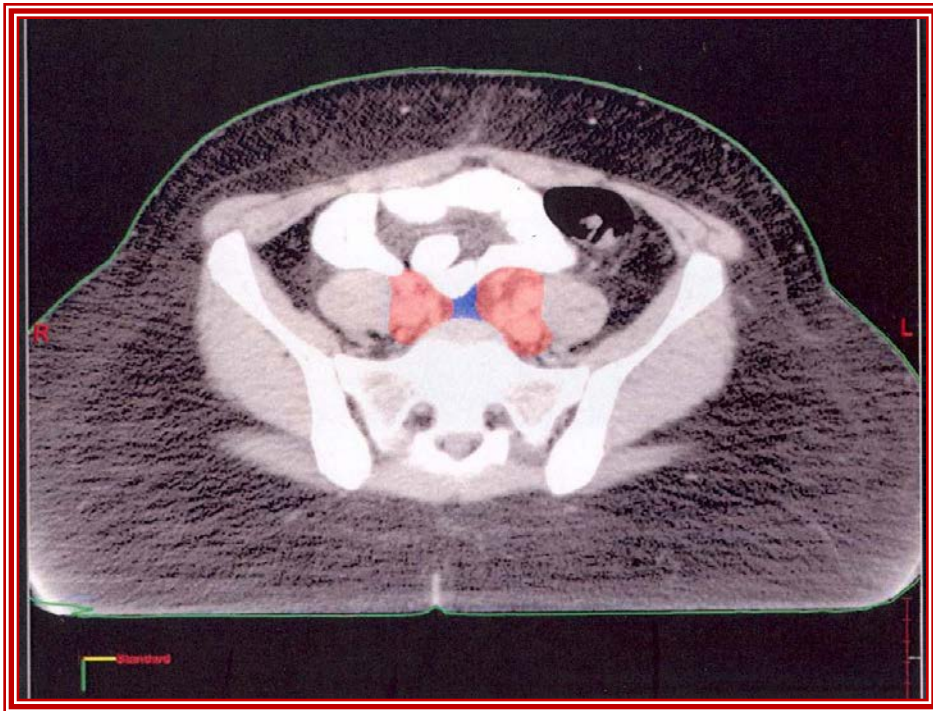
- A 10 mm strip over sacral prominence connecting the common iliac/EI/II contours would include the subaortic presacral nodes



Taylor et al. IJROBP 63(5):1604-1612, 2005



# Presacral Lymph Nodes



Small et al; IJROBP 71(2): 428-434, 2008

# Presacral Lymph Nodes

- Includes 1-2 cm of tissue anterior to S1, S2, S3 between the anterior border of CTV and the vertebral body or sacrum
  - Should not extend into sacral foramina
  - Presacral nodal coverage should discontinue when piriform muscle becomes clearly visible (approximately inferior border S2/S3)
- The lower presacral (perirectal) nodes would be included in the mesorectal/lower pelvic CTV contours as in the RTOG anorectal atlas

# Presacral Lymph Nodes

- Include in patients with cervical cancer or stage II endometrial cancer
- Subaortic (S1-S3) Typically included in Gyn cases
- Perirectal (S4, S5, mesorectal) typically included in anorectal cancers but may also be needed for intact cervix







Pre Sacral Lymph  
Nodes

Slices (40)63-70



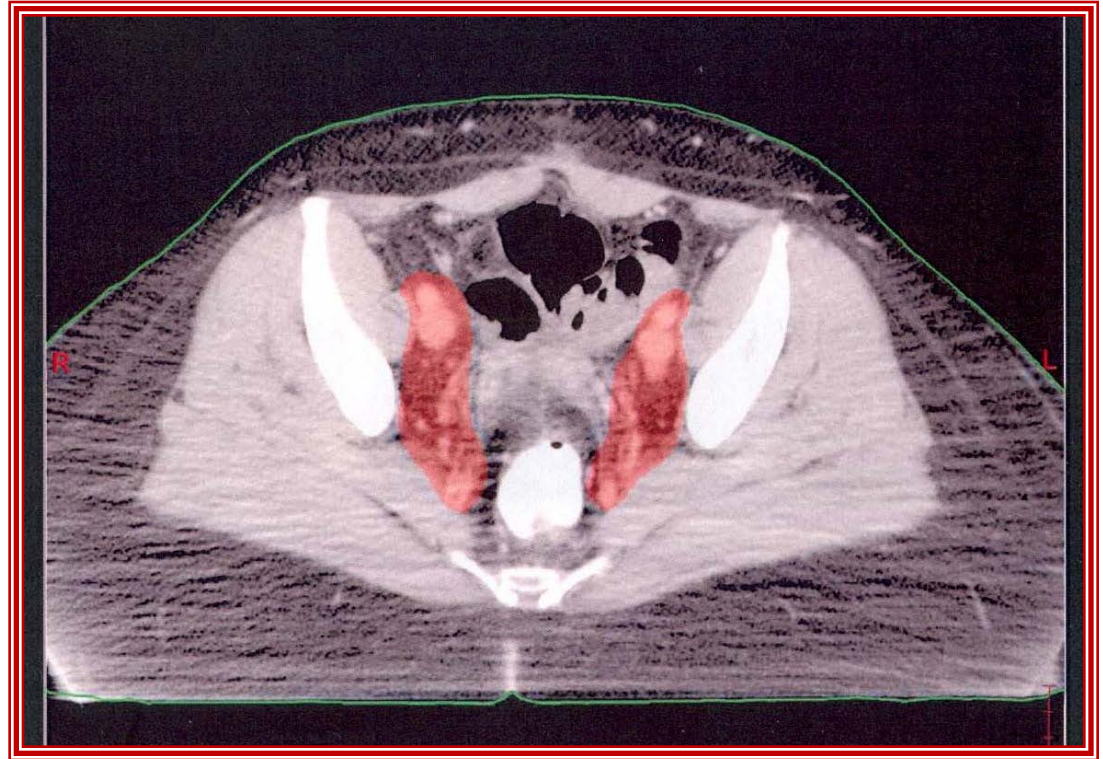
Home work

Pelvic Lymph nodes

Slices 63,69

# Pelvic Node Delineation

- Nodal CTV – vessel, perinodal tissue and any pertinent clips
- ? Lymphoceles
- CTV should be bounded by the piriform muscle even when internal iliac vessels disappear
- Average margin 7 – 10 mm (CTV) around vessels

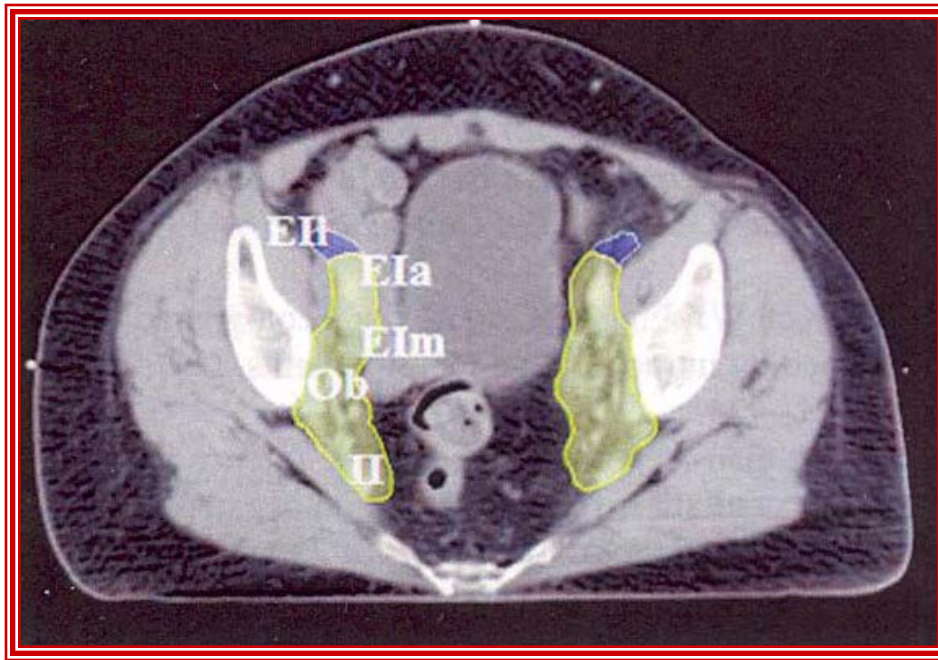


Small et al; IJROBP 71(2):428-434, 2008



# External Iliac Lymph Nodes

- Divided into lateral, medial, and anterior divisions



Taylor et al. IJROBP 63(5):1604-1612, 2005

**EI lat**-lateral to external iliac artery

**EI ant**-anteromedial to external iliac vein

**EI med**-medial and posterior to external Iliac vein

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# Pelvic Node Delineation

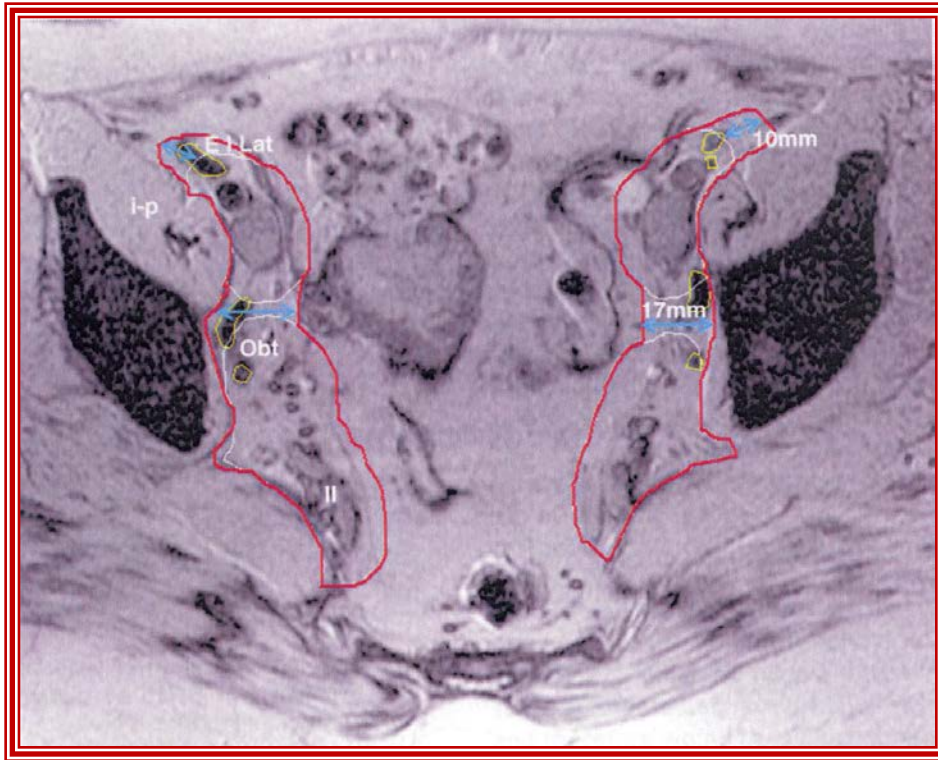


- Extend contours to pelvic wall but exclude bone and muscle (psoas and piriform)

Taylor et al. IJROBP 63(5):1604-1612, 2005



# Pelvic Node Delineation



- Extend contours 10 mm (CTV) around lateral external iliac lymph nodes and 7 mm around the medial and anterior iliac lymph nodes.

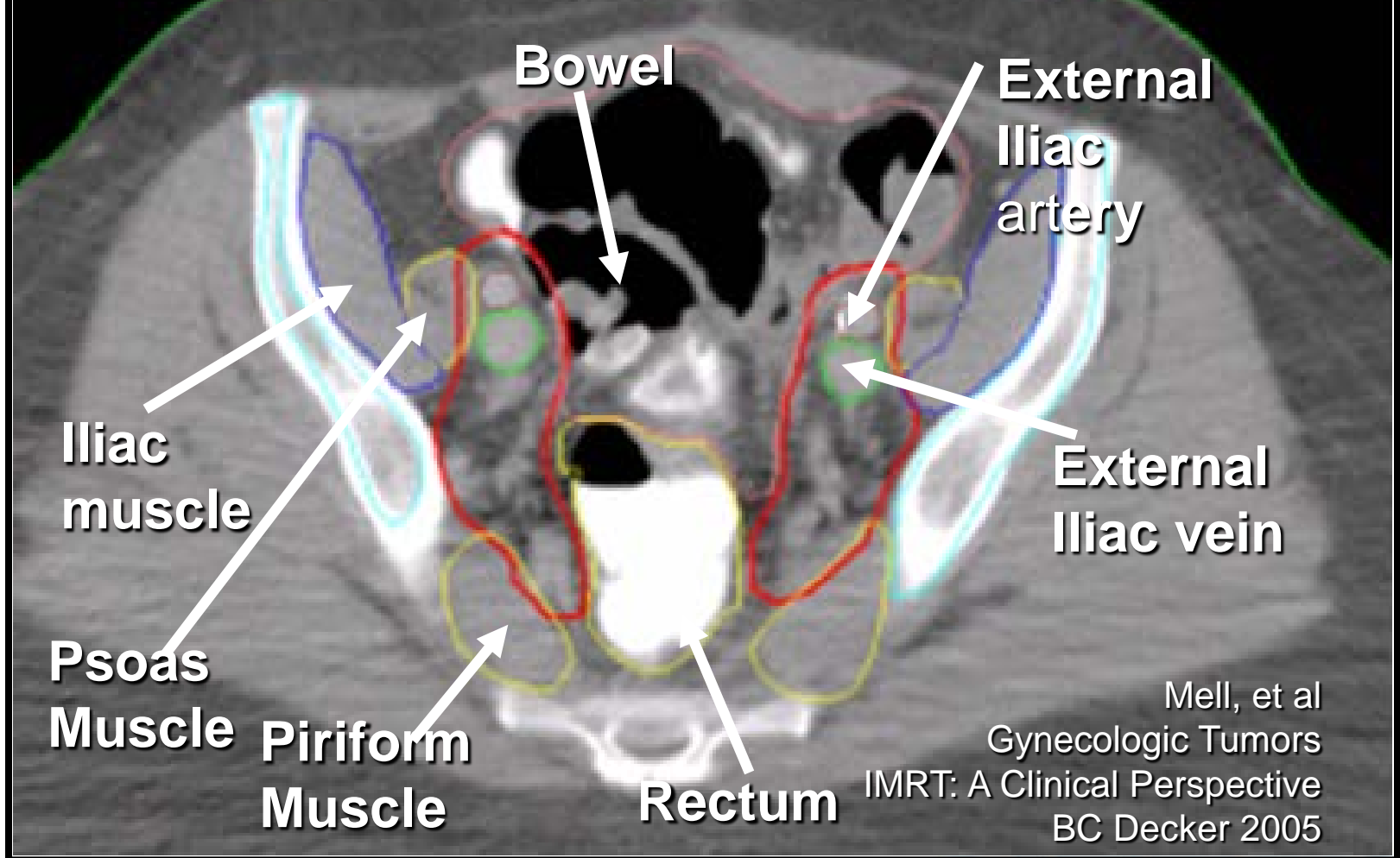
Taylor et al. IJROBP 63(5):1604-1612, 2005

ViLarino-Varela et al; Radiother Oncol 89:109-196, 2008.

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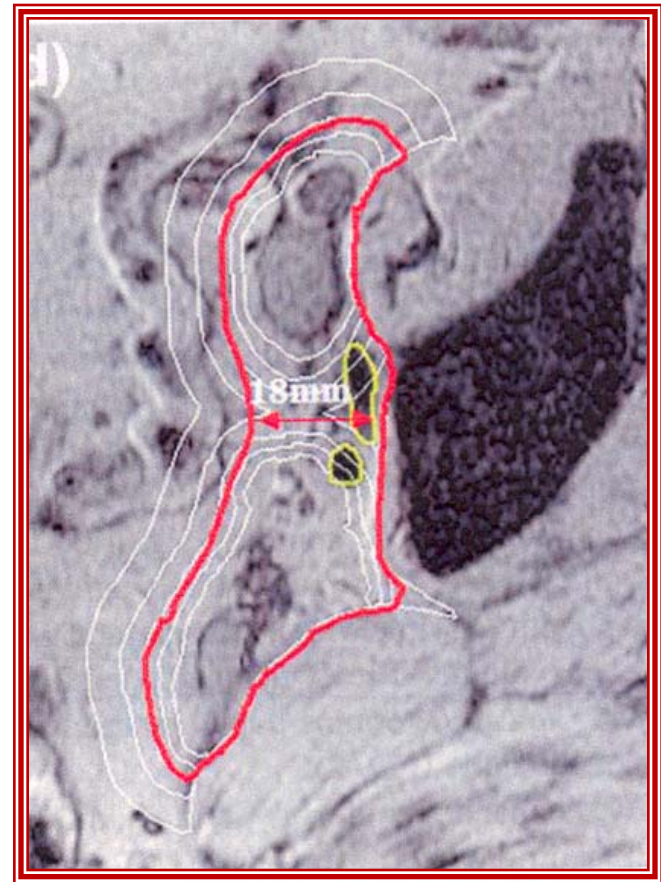
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# Psoas and piriform muscles, pelvic bones, small bowel and rectum help define the CTV



# Obturator Lymph Nodes

- Lie between internal and external iliac vessels
- Next to obturator internus muscle
- End near top of pubic symphysis

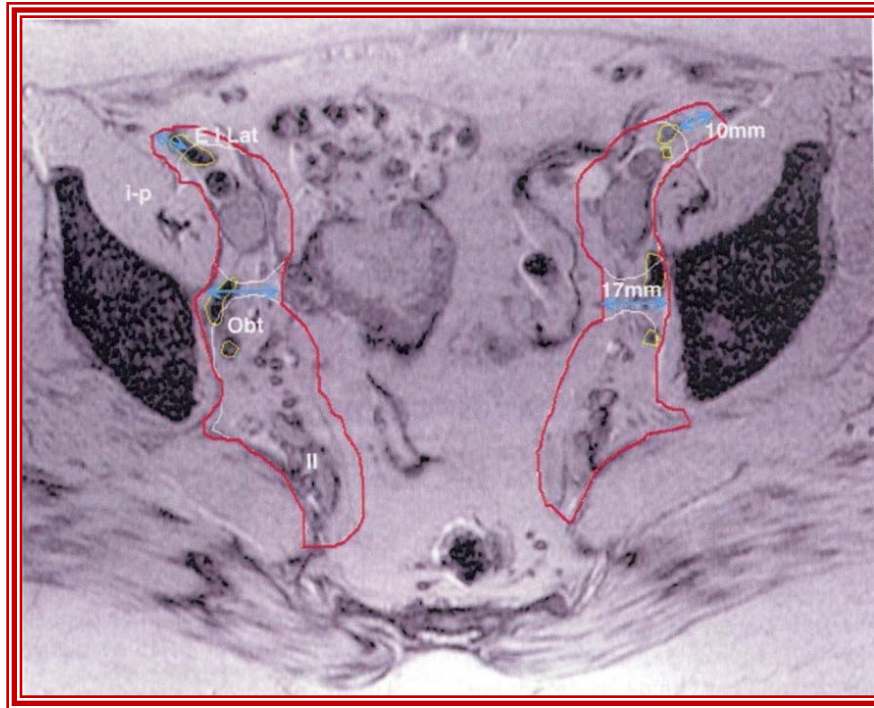


Taylor et al. IJROBP 63(5):1604-1612, 2005



# Obturator Lymph Nodes

- Need a strip of tissue 17 mm wide between internal-external iliacs to cover the obturator nodal region



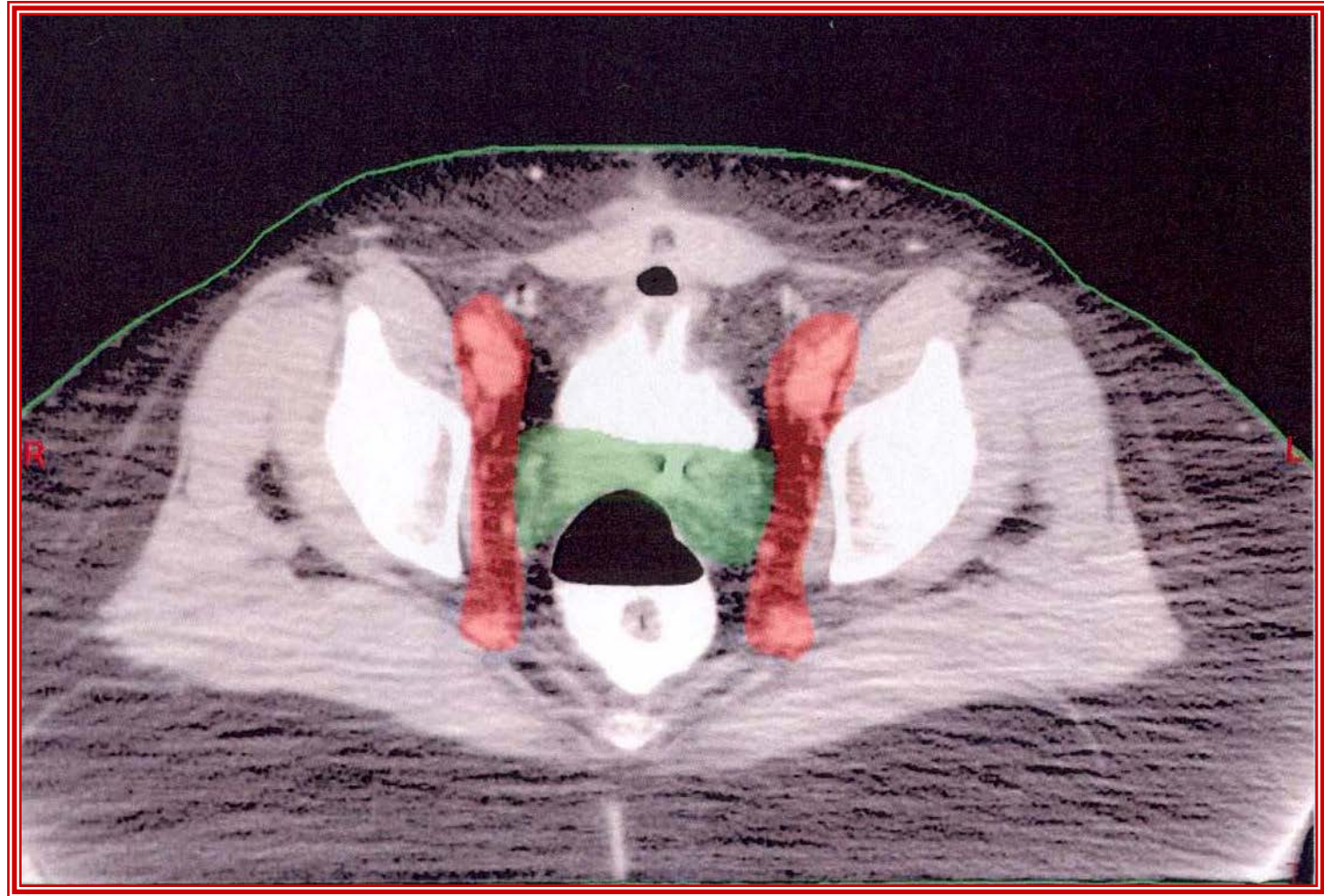
Taylor et al. IJROBP 63(5):1604-1612, 2005

ViLarino-Varela et al; Radiother Oncol 89:109-196, 2008.

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# Obturator Lymph Nodes



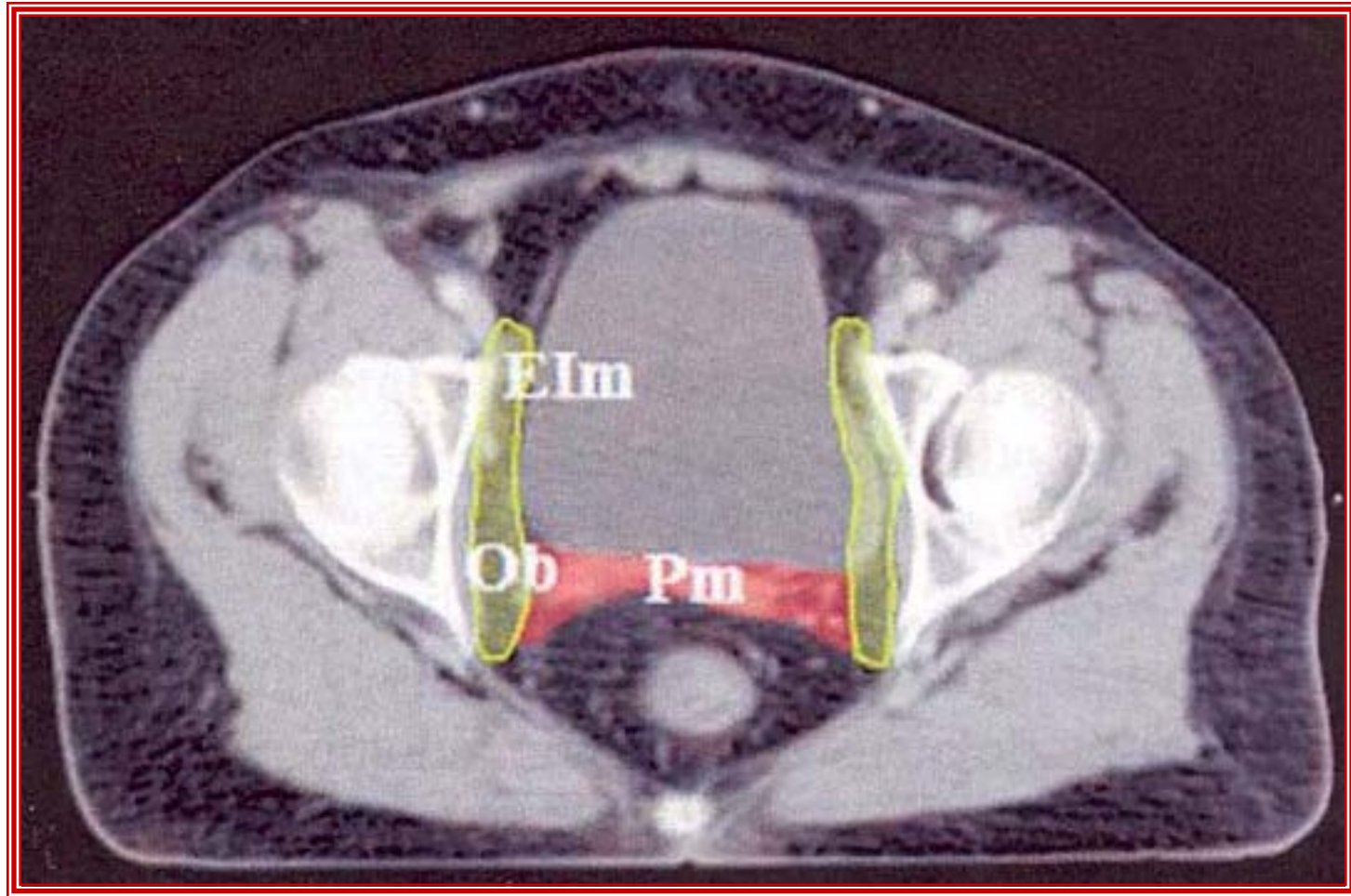
Small et al; IJROBP 71(2): 428-434, 2008

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# Obturator Lymph Nodes



Taylor et al. IJROBP 63(5):1604-1612, 2005

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# Obturator Lymph Nodes

## RTOG Pelvic LN Atlas-prostate



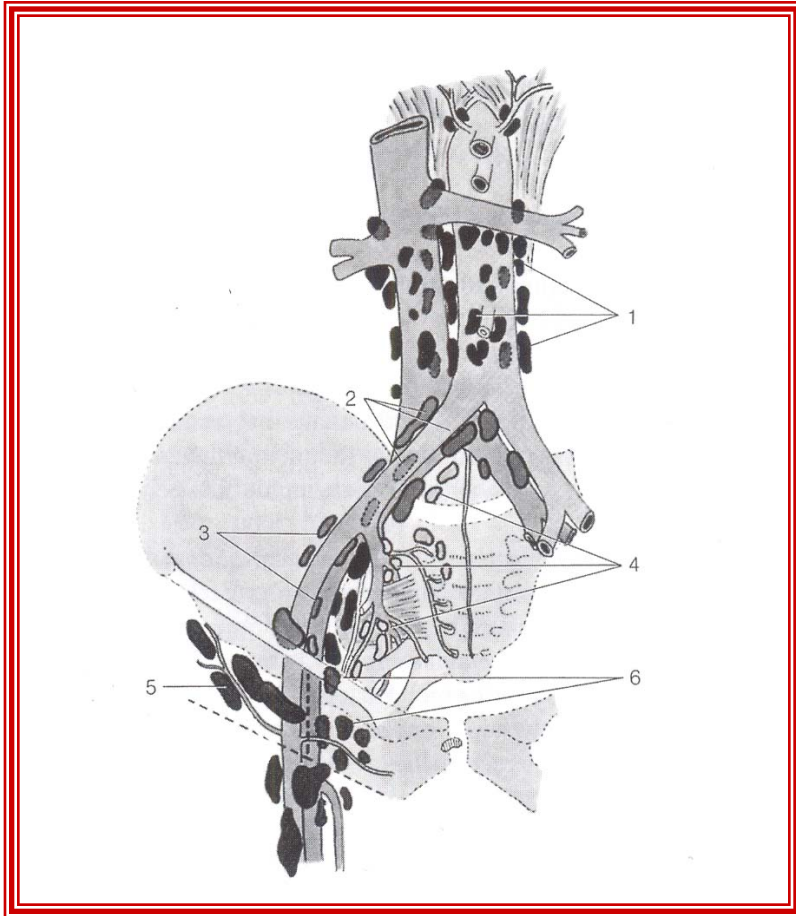
Above the top of pubic symphysis

Lawton et al. IJROBP 74(2)383-387,2009

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# Where Do the External Iliac Nodes End and the Inguinal Nodes Begin?



1. Inguinal ligament

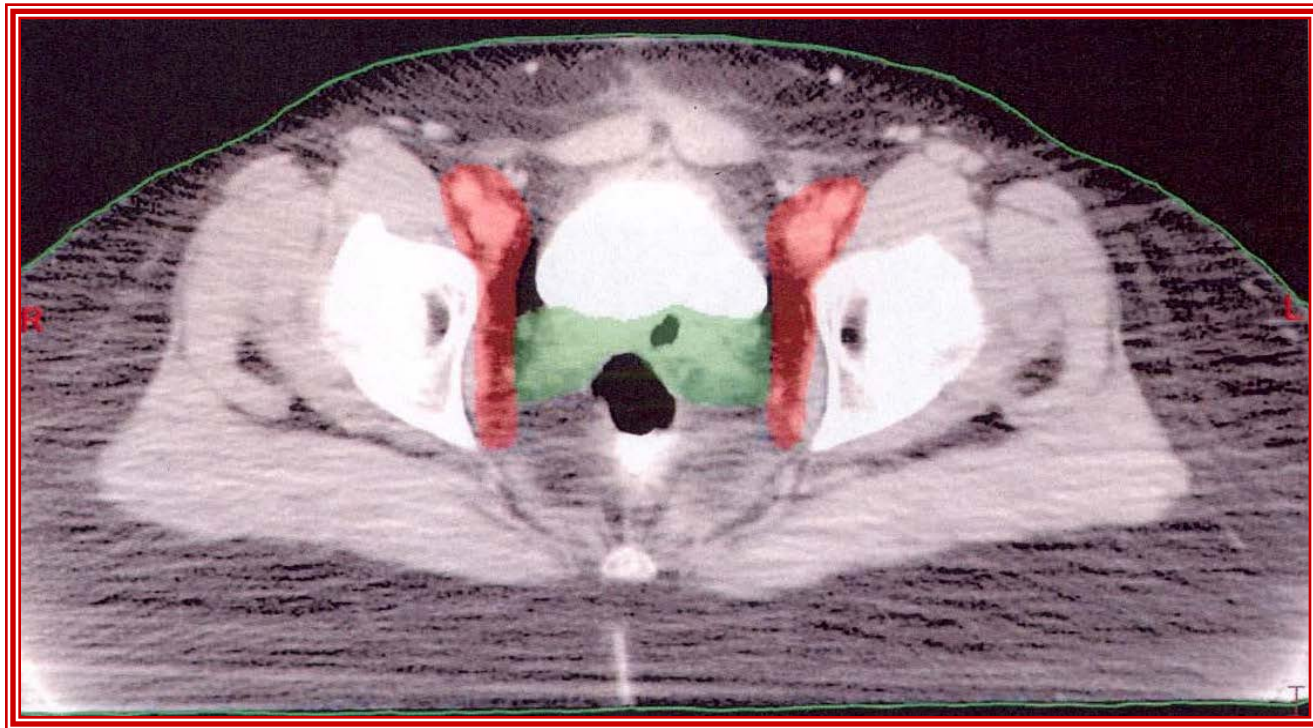
Richter et al, Normal Lymph Node Topography 2<sup>nd</sup> Ed, 2004

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# Where Do the External Iliac Nodes End and the Inguinal Nodes Begin?

## 2. Femoral head or superior pubic ramus



Small et al; IJROBP 71(2): 428-434; 2008

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# Pelvic Lymph Nodes

Slices 71-89





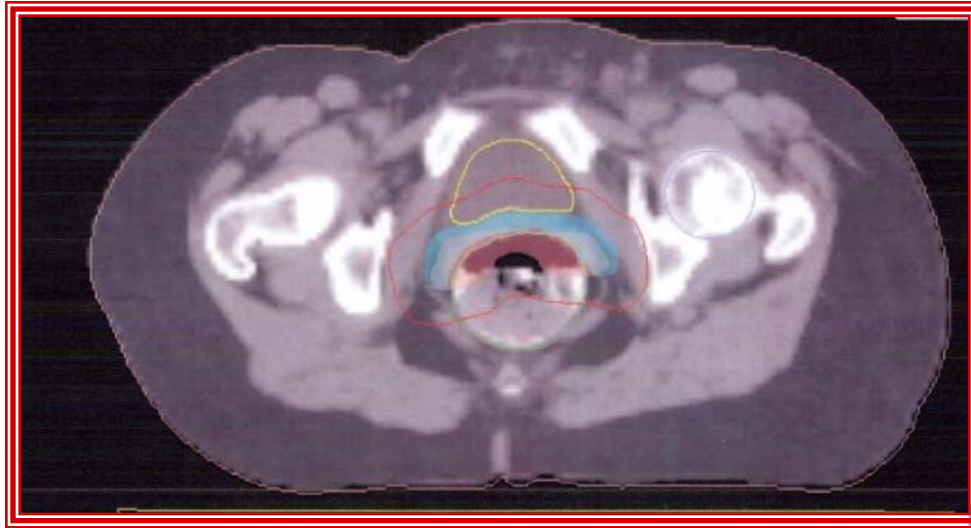
Home Work

Pelvic Lymph  
Nodes

Slice 75,89

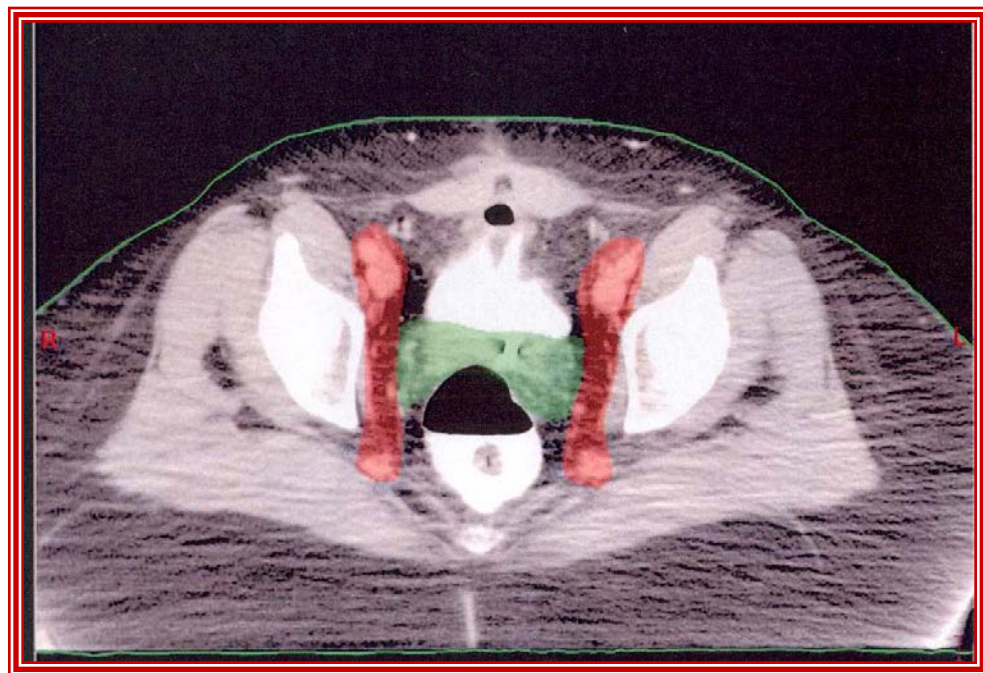
# Vaginal Contouring

- Draw vaginal volume on bladder full CT and empty CT.
- Fuse together and create an ITV
- **ITV** – internal target volume to account for daily variation in location of vaginal cuff related to variation in the daily bladder filling (not rectal)
- Fused vaginal contours are encompassed by a common PTV



# Vaginal Contouring

- Include tissue from the vaginal cuff to the medial edge of the internal obturator muscle/ischial ramus on each side (parametrial and paravaginal tissues)
- Maintain a distance of 15 mm tissue between anterior and posterior borders of CTV

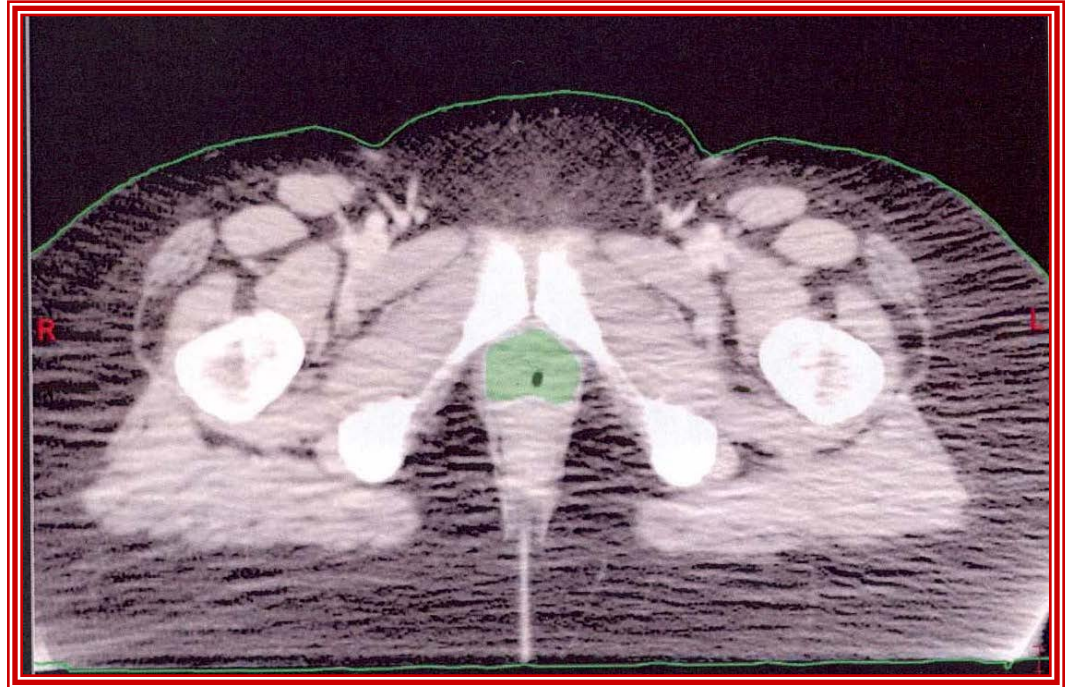


Small et al; IJROBP 71(2): 428-434, 2008

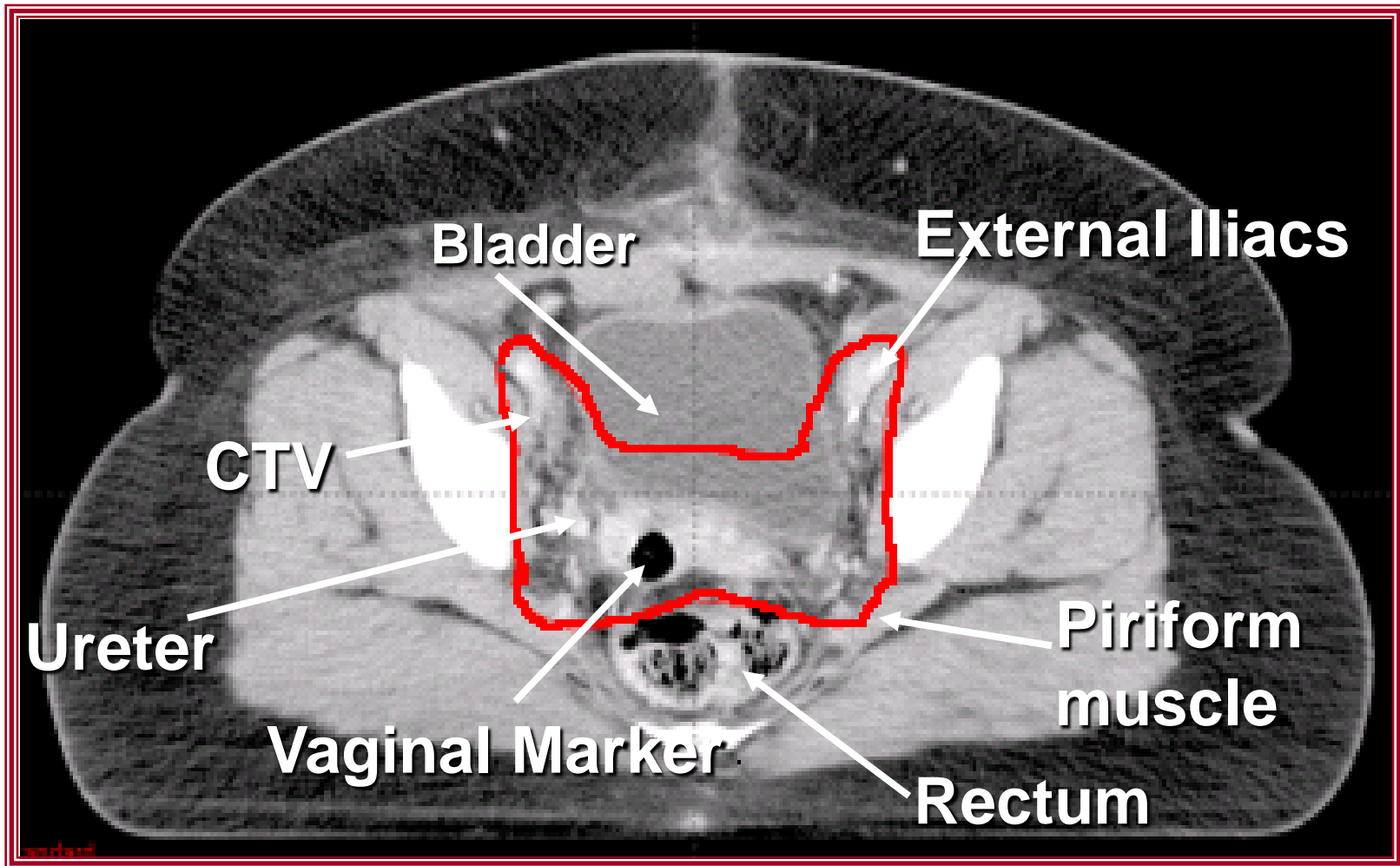


# Vaginal Contouring

- Include at least 3 cm of vagina or at least 1 cm above obturator foramen
- Add 7 mm superiorly, inferiorly, laterally and 5-7 mm posteriorly to create the PTV



Small et al; IJROBP 71(2): 428-434, 2008



Mell et al,  
Gynecologic Tumors  
IMRT: A Clinical Perspective  
BC Decker 2005

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Vaginal contours

Slices 80-101



Home Work

Slice 88, 94-Bladder full

Slice 89, 91-Bladder empty



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# Is IMRT Ready for Prime Time in the Therapy of Cervical and Endometrial Cancer?

For post-operative therapy ?

- Encouraging published data from RTOG 0418-IMRT safe and effective
- Use of an ITV reassuring relative to bladder filling and vaginal motion
- Rectal filling/motion remains a concern

# Is IMRT Ready for Prime Time in the Therapy of Cervical and Endometrial Cancer?

For  
definitive  
therapy in  
cervical  
cancer ??

- CTV and PTV definitions remain controversial
- Consensus guidelines are building
- Organ motion and volume changes during therapy remain a significant issue.
- “unpredictable organ dynamics”



# GYN IMRT International Consortium (RTOG, NCIC, ESTRO, JCOG)

## CTV Definition

### Variability In Delineation Of Clinical Target Volumes For Cervix Cancer Intensity-Modulated Pelvic Radiotherapy

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## CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUME FOR INTENSITY-MODULATED PELVIC RADIOTHERAPY FOR THE DEFINITIVE TREATMENT OF CERVIX CANCER

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Lim IJROBP 79(2): 348-355 2011

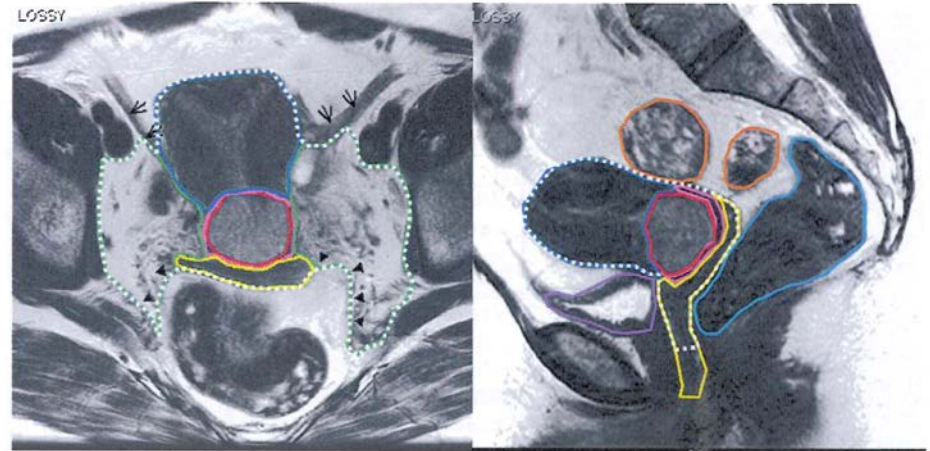
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# Definitive Cervix Contouring

Table 2. CTV components.

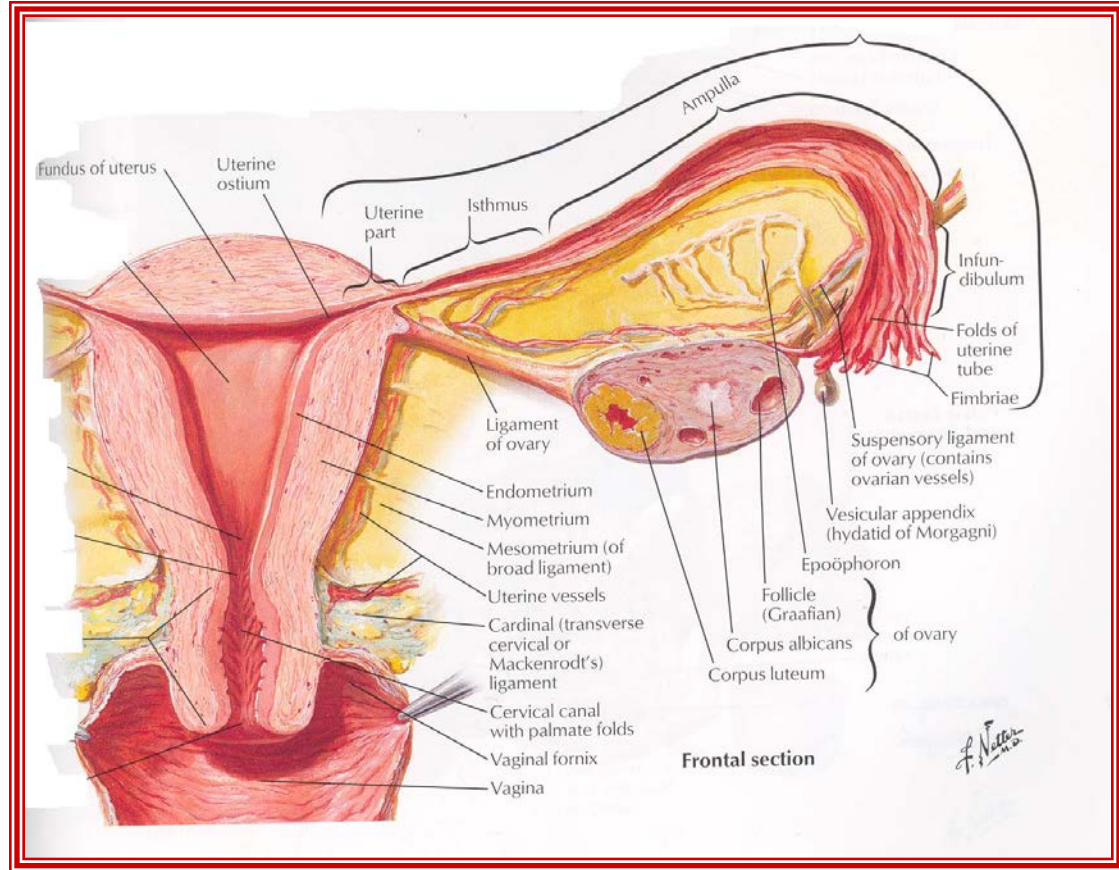
GTV	Entire GTV; intermediate/high signal seen on T <sub>2</sub> -weighted MR images
Cervix	Entire cervix; if not already included within GTV contour
Uterus	Entire uterus
Parametrium	Entire parametrium, including ovaries; include entire mesorectum if uterosacral ligament involved
Vagina	Minimal or no vaginal extension: upper half of the vagina Upper vaginal involvement: upper two-thirds of the vagina Extensive vaginal involvement: entire vagina



Lim et al IJROBP 79(2):  
348-355 2011

# Parametrial/Paracervical Tissue

- Fat and loose connective tissue and smooth muscle around the uterus and cervix
  - Contains blood vessels and lymph nodes

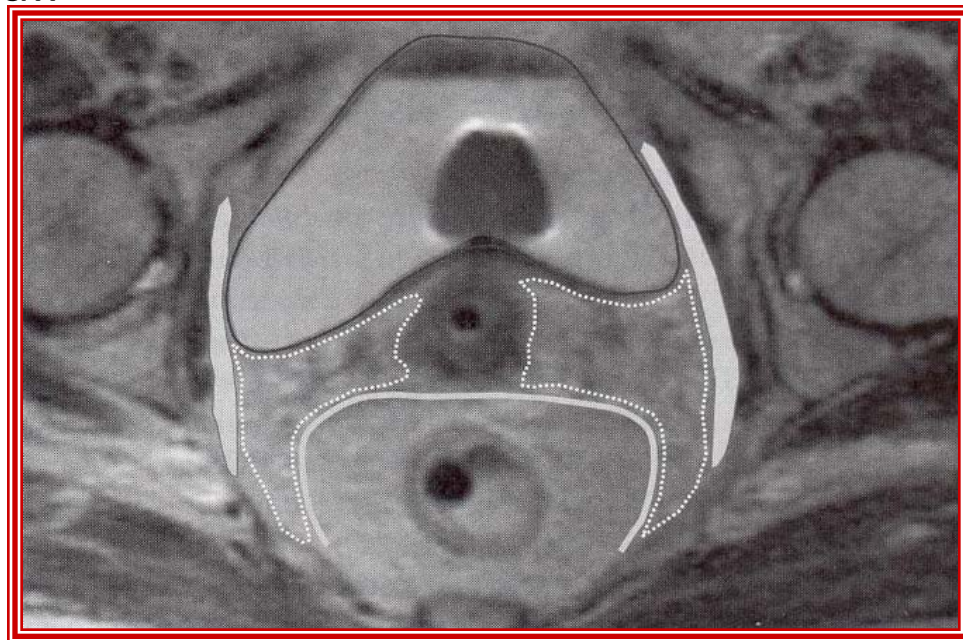


Netter F. Atlas of Human Anatomy 4<sup>th</sup> Ed



# Definition of Parametria

- Borders:
- Anterior – bladder
  - Posterior – perirectal fascia
  - Medial – tumor/cervical rim
  - Lateral – Pelvic wall



Dimopoulos et al IJROBP 64(5):1380-1388, 2006

Table 3. Anatomical boundaries of parametria

Location	Anatomic structures
Anteriorly	Posterior wall of bladder or posterior border of external iliac vessel
Posteriorly	Uterosacral ligaments and mesorectal fascia
Laterally	Medial edge of internal obturator muscle/ ischial ramus bilaterally
Superiorly	Top of fallopian tube/ broad ligament. Depending on degree of uterus flexion, this may also form the anterior boundary of parametrial tissue.
Inferiorly	Urogenital diaphragm

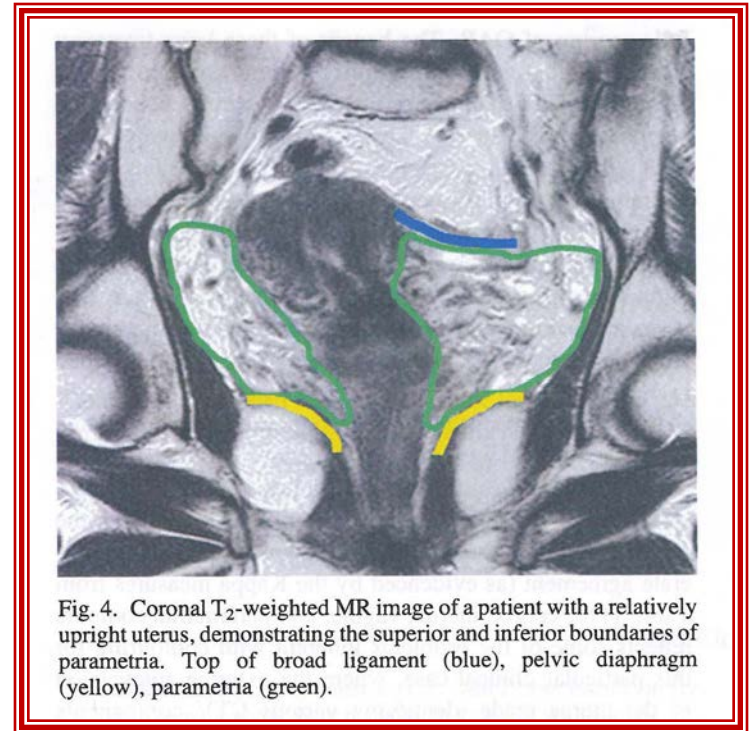
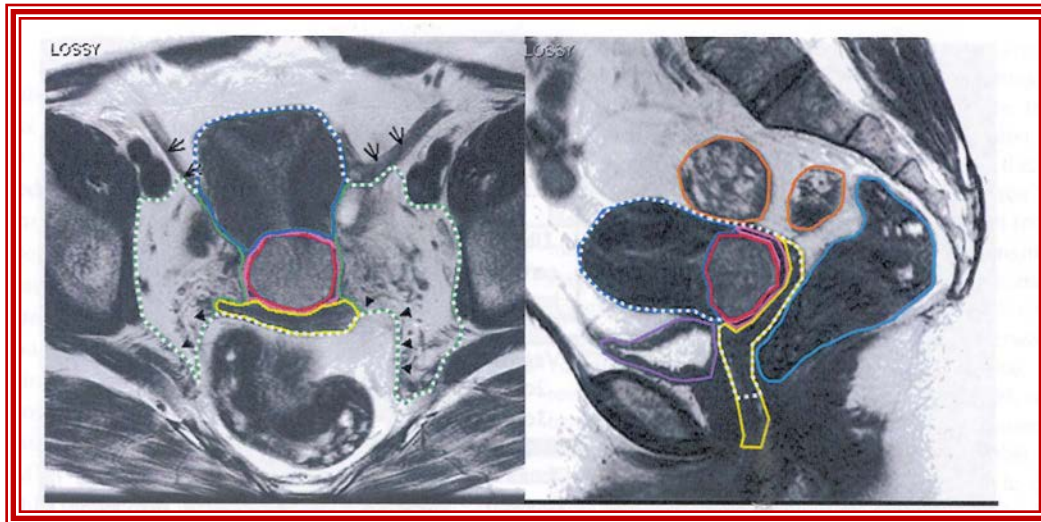


Fig. 4. Coronal T<sub>2</sub>-weighted MR image of a patient with a relatively upright uterus, demonstrating the superior and inferior boundaries of parametria. Top of broad ligament (blue), pelvic diaphragm (yellow), parametria (green).

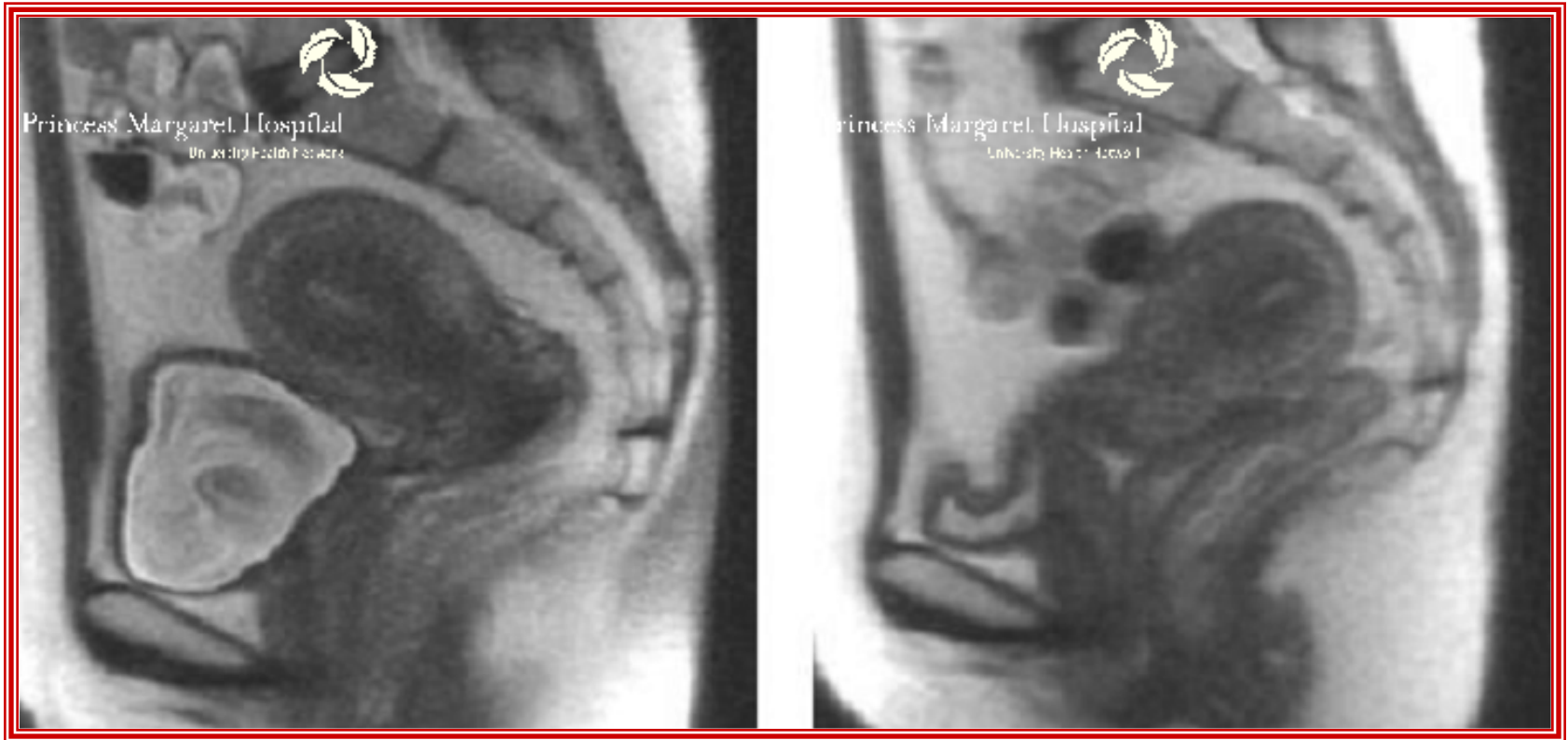
Lim et al IJROBP, 2010



# Uterus Contouring

- Include whole uterus?
  - International consortium-yes
  - Interconnecting lymphatics
  - Hard to know where cervix ends and uterus begins
- Account for motion?-Varies with bladder filling

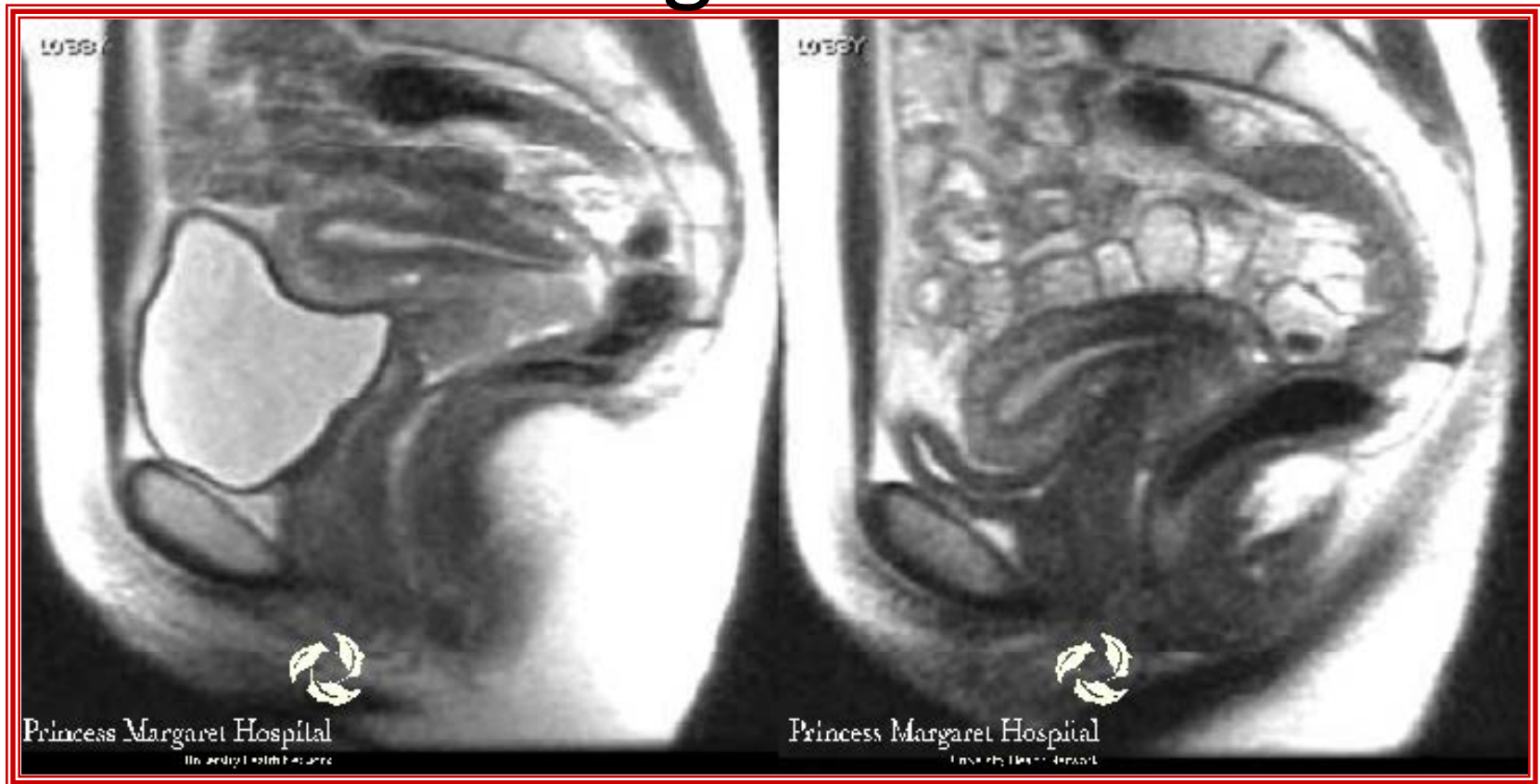
# Challenges for IMRT



## Mobile uterus

Courtesy of Karen Lim, Princess Margaret Hospital

# Challenges for IMRT

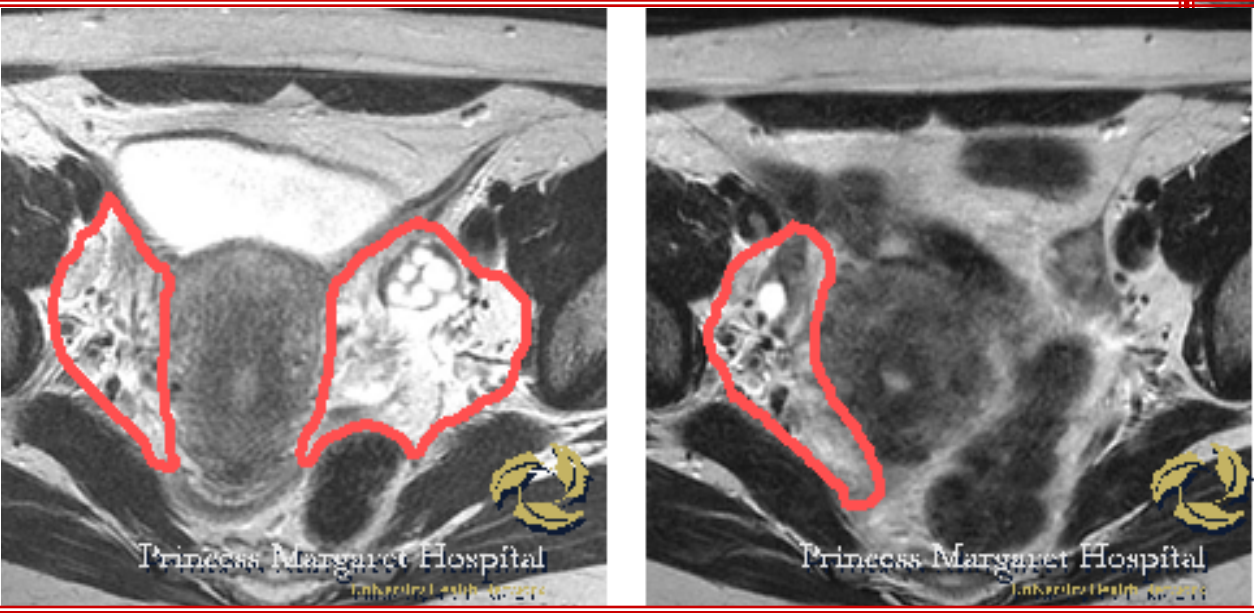
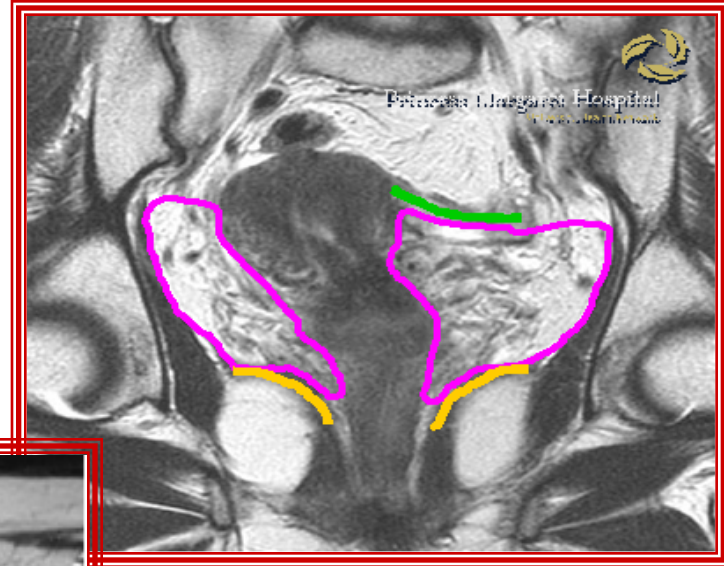


## Another mobile uterus

Courtesy of Karen Lim, Princess Margaret Hospital

# IMRT Challenges

Parametria & change depending on volume of bladder



Courtesy of Karen Lim, Princess Margaret Hospital

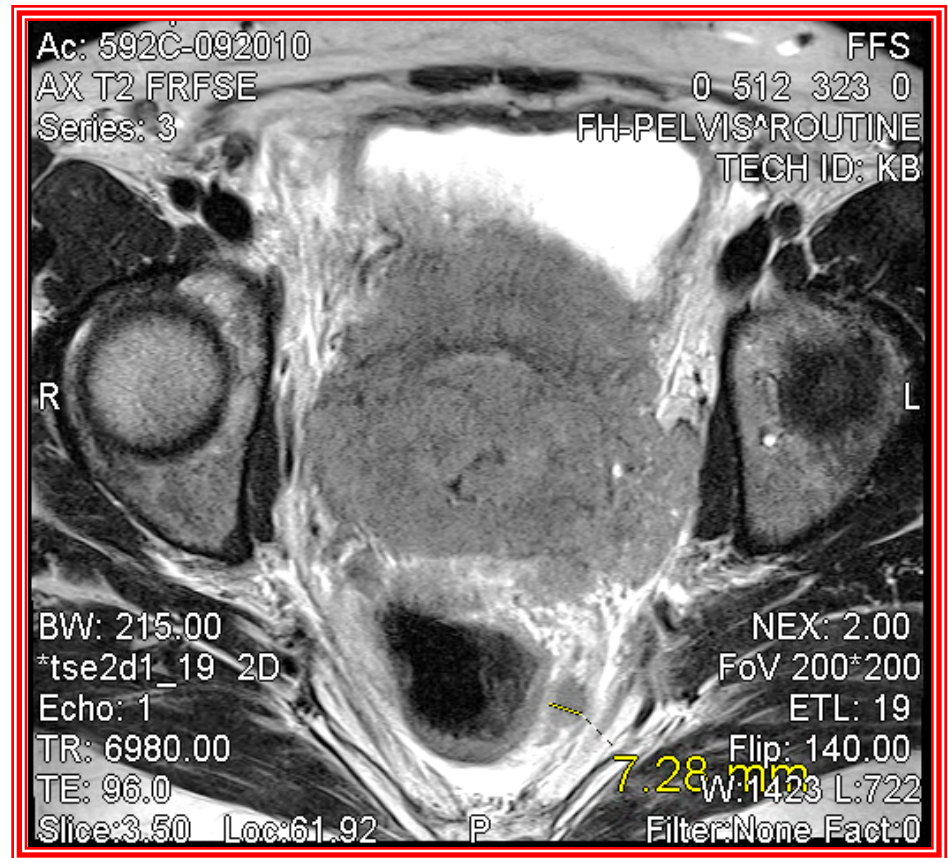
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# Rectal Sparing

- May be dangerous due to need to include presacral nodes (mesorectal), uterosacral ligaments, and internal iliac nodes
- Rectal filling may vary



# Mesorectal Lymph Nodes

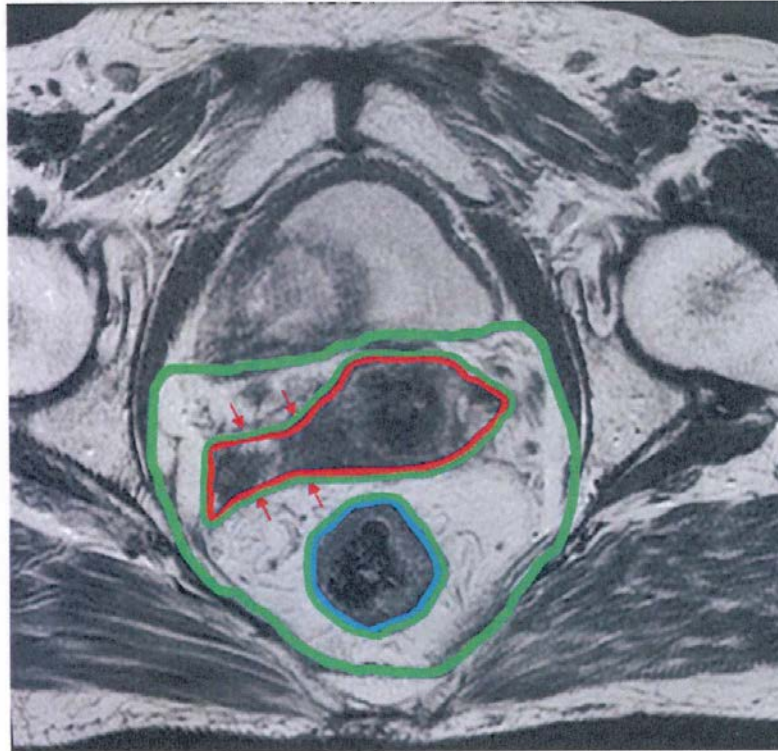
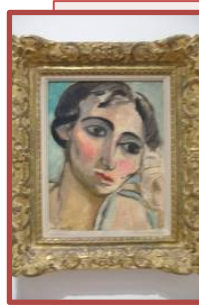


Fig. 5. Axial T<sub>2</sub>-weighted MR image of a patient showing the GTV (red contour), modified parametrium (green), and rectum (light blue); red arrows indicate right proximal uterosacral ligament invasion.

# The Challenge of the PTV



Are we really sparing bowel and other tissues if our PTV is too large?



PTV of 1.0 – 2.0 cm around non-nodal CTV (Uterus/cervix, vagina, parametria) if IGRT



PTV > 2.0 cm if no IGRT???



Nodal PTV of 7-10 mm

- The nodal PTV and non-nodal PTV may move in different directions

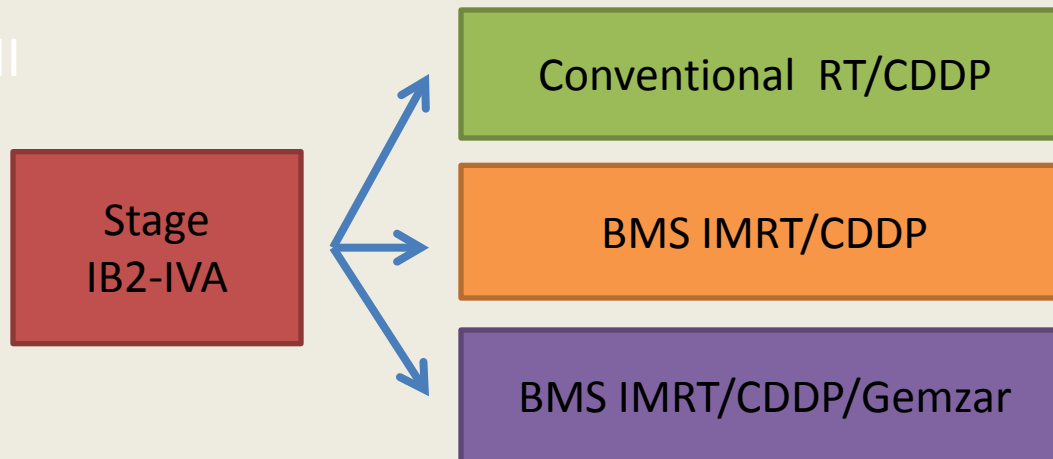
# INTERTECC

## International Evaluation of Radiotherapy Technology Effectiveness in Cervical Cancer Phase II/II trial of IMRT with CDDP

### Phase II

- Eligible – Stage I-IVA Cervical carcinoma
- IMRT (Bone Marrow Sparing-BMS) + Cisplatin
- 35/90 planned patients enrolled
- Primary outcome is grade 2+ GI or grade 3+ Heme toxicity

### Phase III



Courtesy of Catheryn Yashar



# IMRT for Intact Cervix

INTERTECC gives guidelines for PTV and dose constraints in the trial setting

Full protocol available on the UCSD web

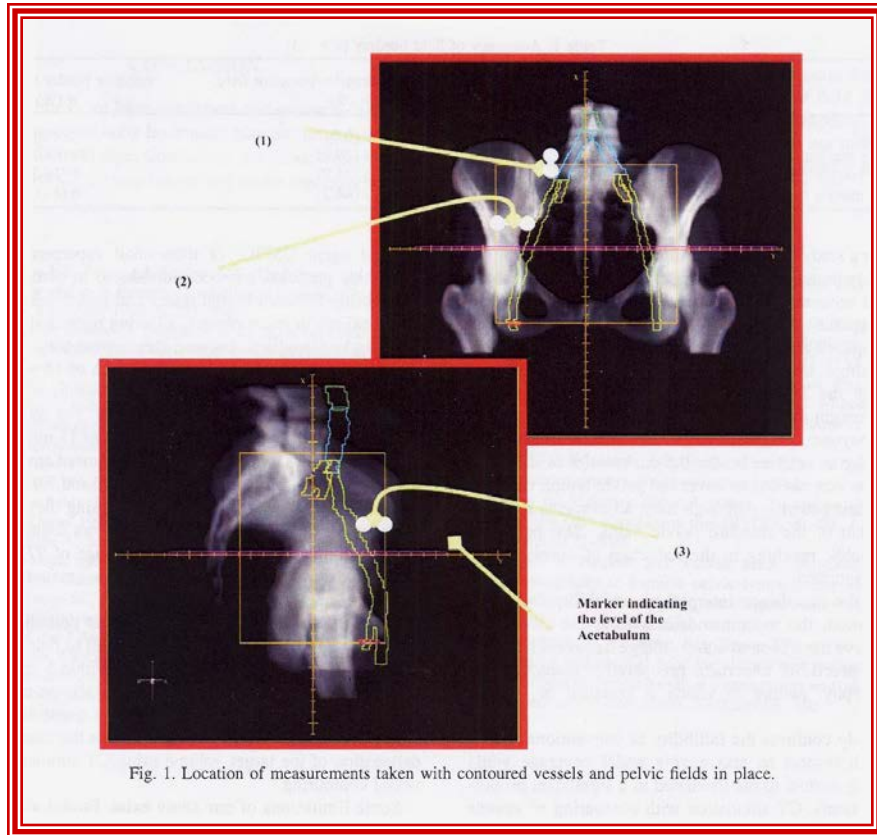


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# Traditional Field Design Boney Anatomy is Not Enough!

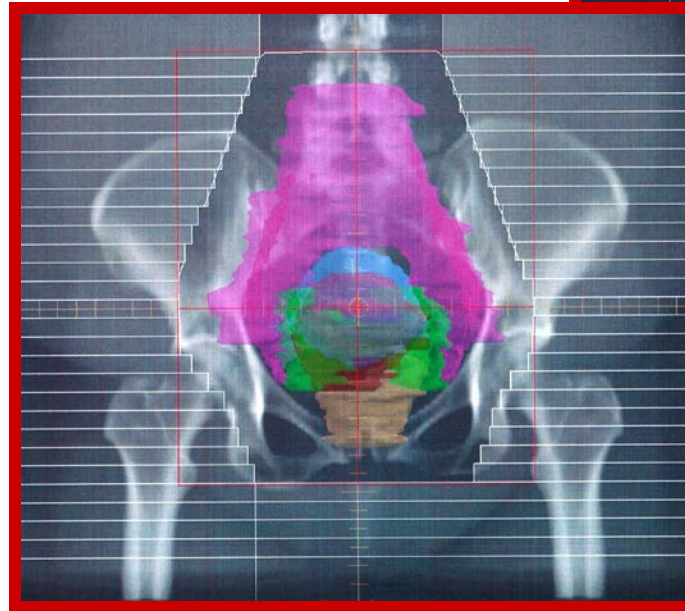
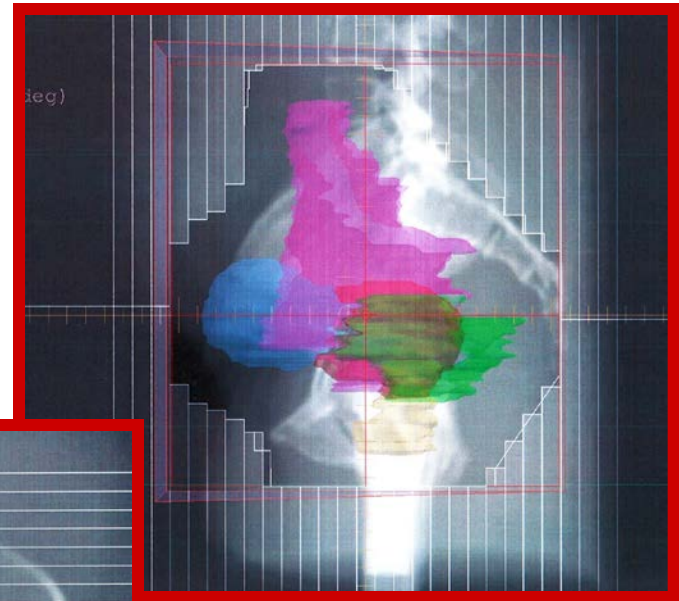


- Most inclusive-  
"Through and Through"
- Irradiated all tissue in the field
- Could miss external iliac LNs anteriorly
- Could miss pre-sacral, perirectal and internal iliac LNs posteriorly

Finlay, et al IJROBP 64(1):205-209, 2006

# Contemporary Field Design

- CT-based field design is intelligent!
- MR-based field design may even be better for cervical and vaginal cancers







**CLINICAL INVESTIGATION**

**Endometrium**

**CLINICAL OUTCOME OF ADJUVANT TREATMENT OF ENDOMETRIAL CANCER  
USING APERTURE-BASED INTENSITY-MODULATED RADIOTHERAPY**

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ANDRÉ FORTIN, M.D., M.Sc.,\* AND ISABELLE GERMAIN, M.D., M.Sc.\*

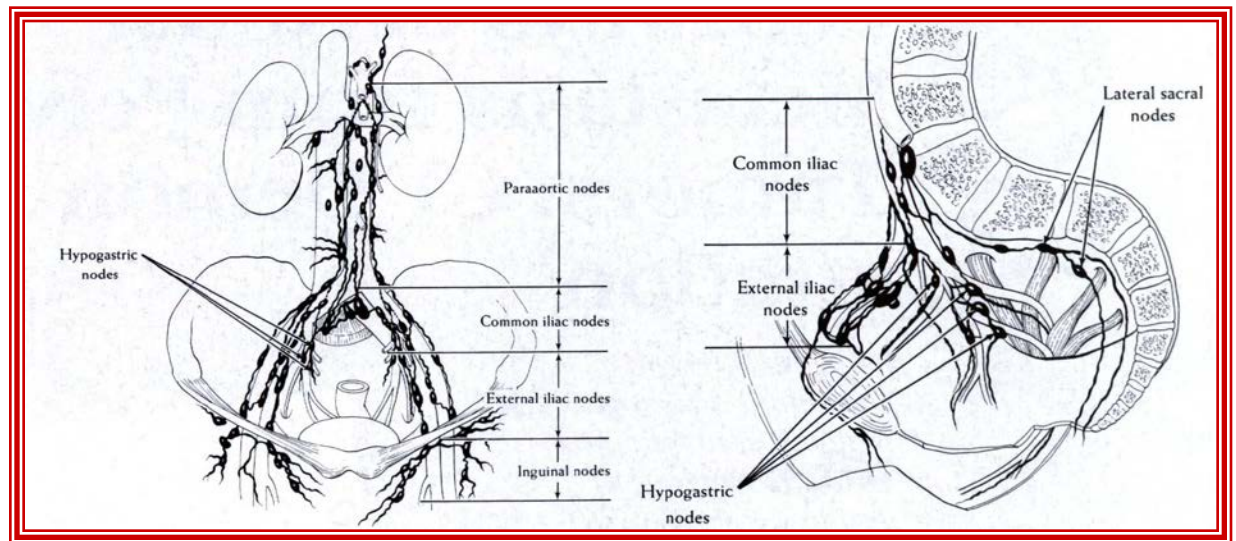
\*Département de Radio-oncologie et Centre de Recherche de L'Hôtel-Dieu de Québec, Centre Hospitalier Universitaire de Québec,  
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IMRT improved target coverage (93% vs 76%) when compared to a conventional 4 field technique in post-op endometrial patients

“We” have not done a good job of identifying and hitting the targets

# Pelvic Lymph Nodes

- Common iliac
- Internal iliac (hypogastric)
- External iliac/obturator
- +/- presacral
- +/- inguinal



Park; Radiographics 14:1994

# RTOG Post-op Gynecologic Atlas



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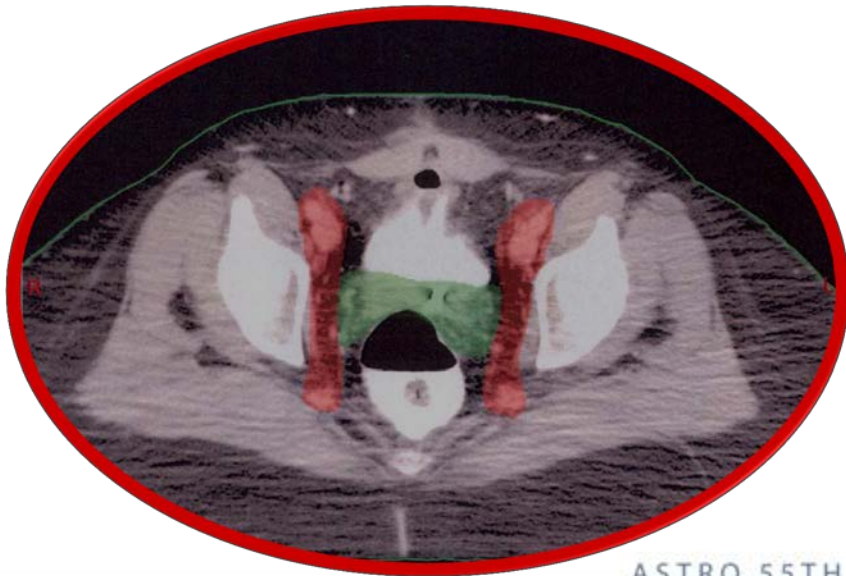
doi:10.1016/j.ijrobp.2007.09.042

## CLINICAL INVESTIGATION

## Uterus

### CONSENSUS GUIDELINES FOR DELINEATION OF CLINICAL TARGET VOLUME FOR INTENSITY-MODULATED PELVIC RADIOTHERAPY IN POSTOPERATIVE TREATMENT OF ENDOMETRIAL AND CERVICAL CANCER

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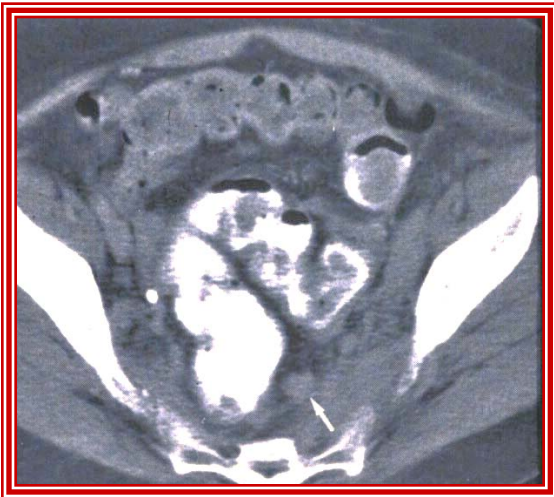
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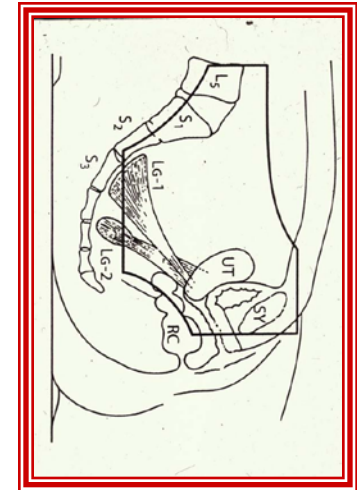
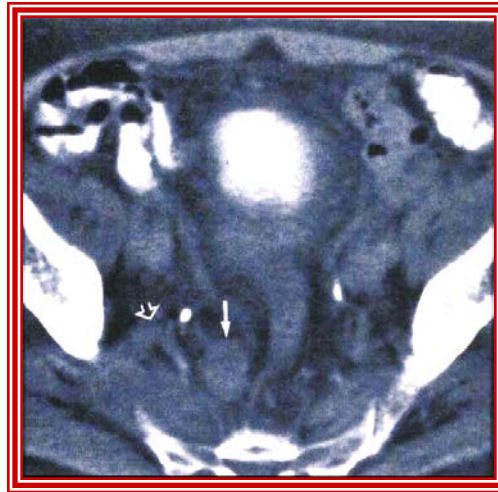
# 3D Conformal External Beam Field Design

- Posterior Border Laterals

- Need to include entire sacrum to cover disease in uterosacral and cardinal ligaments and superior rectal and sacral nodes



Park; Radiographics 14:1994

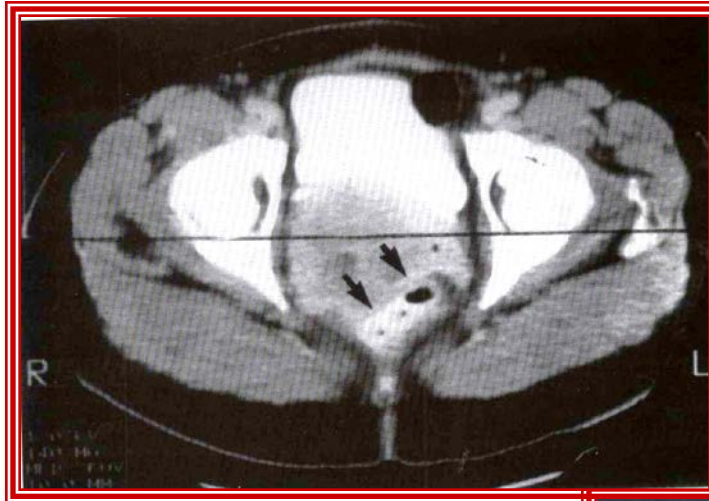


Greer; Gyn Onc 38:1990



# 3D Conformal External Beam Field Design

- Posterior Border  
Laterals
  - Need to include entire rectum to avoid missing perirectal tumor extensions or internal iliac lymph nodes (most rectal complications are on the anterior rectal wall).



Kim; Radiother  
Oncol 30:1994

Park;  
Radiographics  
14:1994

