Target Delineation: Gynecologic IMRT

Arno J. Mundt M.D.
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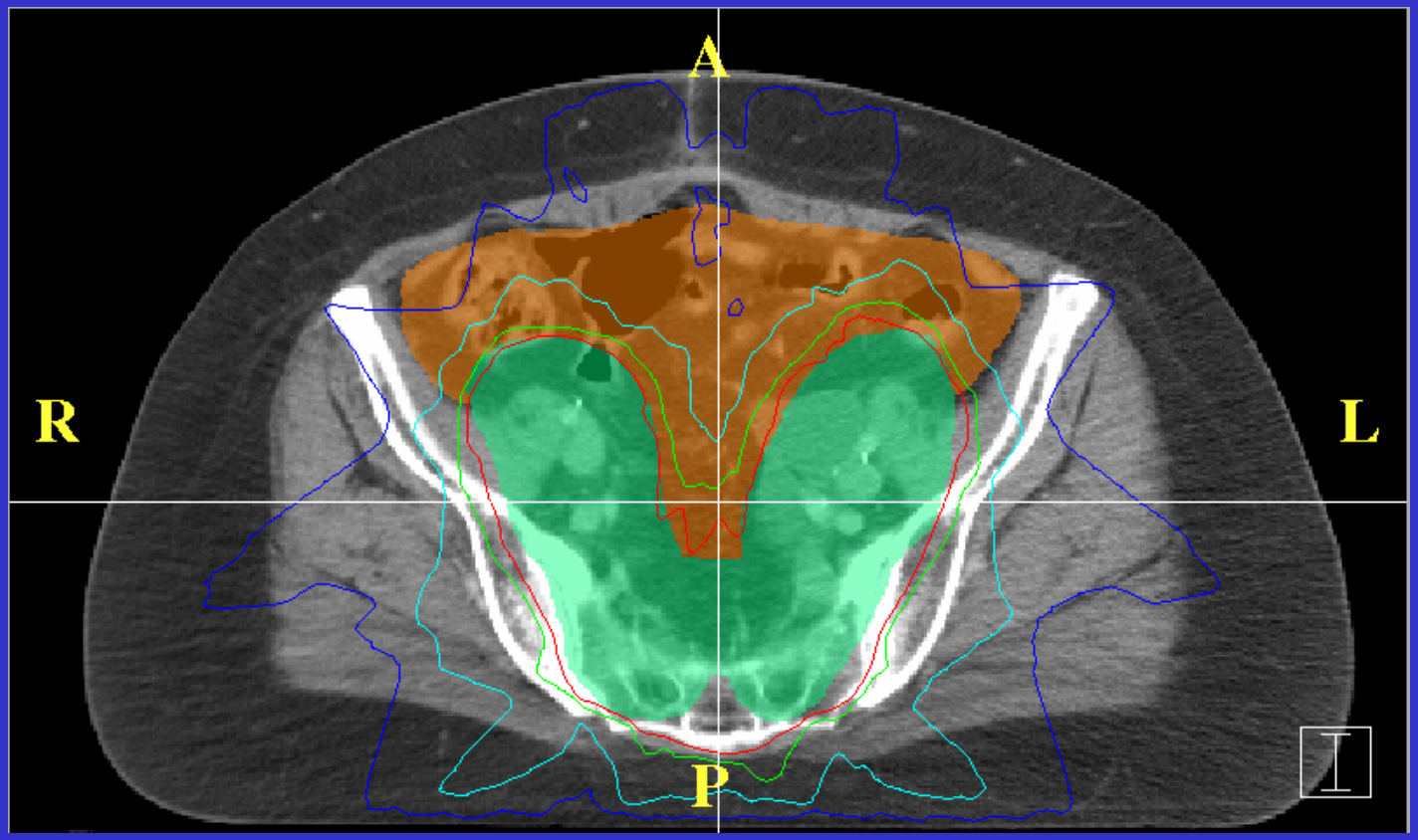

Gynecologic IMRT

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

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

Gynecologic IMRT

- Strong evidence supporting IMRT
- Dosimetric studies have demonstrated its superiority over conventional techniques, particularly in normal tissue sparing
  - Small bowel, bladder, rectum, femoral heads, and bone marrow

PHYSICS CONTRIBUTION

INTENSITY-MODULATED WHOLE PELVIC RADIATION THERAPY IN PATIENTS WITH GYNECOLOGIC MALIGNANCIES

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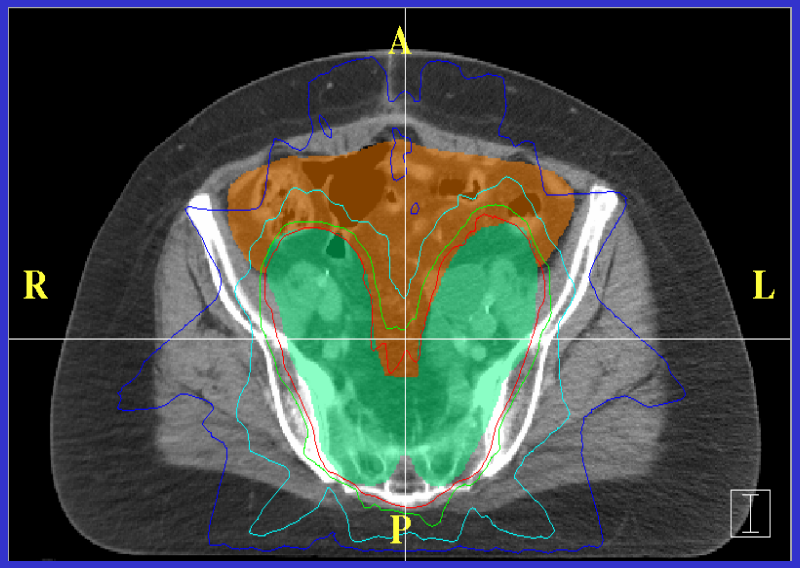
STEVE E. WAGGONER, M.D.,† DIANE YAMADA, M.D.,† AND ARNO J. MUNDT, M.D.*

*Department of Radiation and Cellular Oncology, and †Department of Obstetrics and Gynecology, Section of Gynecologic Oncology, University of Chicago, Chicago, IL

- 1st gynecology IMRT study
- 10 patients
- Compared IMRT vs 3DCRT plans
- Volume of small bowel receiving the prescription dose reduced by a factor of 2
- Volume of bladder and rectum also reduced by 23%



Roeske *et al.*
Red Journal (2000)

Dosimetric Pelvic IMRT Studies

Roeske et al. *IJROBP* 2000;48:1613
Chen et al. *IJROBP* 2001;51:332
Ahamad et al. *IJROBP* 2002;54:42
Heron et al. *Gynecol Oncol* 2003;91:39
Wong et al. *IJROBP* 2005;61:830
Cozzi et al. *Radiother Oncol* 2008;89:180
Mell et al. *IJROBP* 2008;71:1504
Bouchard et al. *IJROBP* 2008;71:1343
Igdem et al. *Eur J Gynecol Oncol* 2009;30:547
Yang et al. *Acta Oncol* 2010;49:230

Intensity Modulated Pelvic RT Planning Studies

	↓Volume Receiving Prescription Dose		
Author	Bowel	Bladder	Rectum
Roeske	↓50%	↓23%	↓23%
Ahamad	↓40-63%*	NS	NS
Chen	↓70%	↓**	↓**
Selvaraj	↓51%***	↓31%***	↓66%***

*dependent on PTV expansion used

**data not shown

***reduction in percent volume receiving 30 Gy or higher

Roeske et al. *Int J Radiat Oncol Biol Phys* 2000;48:1613

Ahamad et al. *Int J Radiat Oncol Biol Phys* 2002;54:42

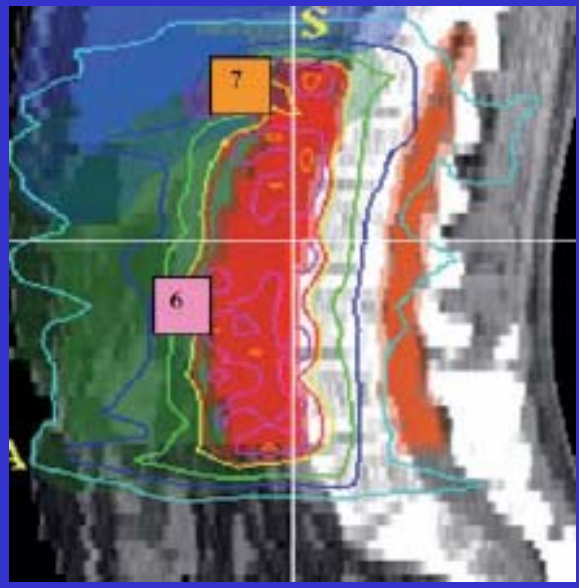
Heron et al. *Gynecol Oncol* 2003;91:39-45

Chen et al. *Int J Radiat Oncol Biol Phys* 2001;51:332

Dosimetric IMRT Studies

Benefits also with more comprehensive fields

- Extended Field RT
  - Portelance et al. IJROBP 2001;51:261
  - Chen et al. IJROBP 2001;51:232
  - Hermesse et al. *Strahlenther Onkol* 2005;181:185
  - Lian et al. IJROBP 2008;70:935
- Pelvic Inguinal RT
  - Beriwal et al. IJROBP 2006;64:1395
  - Garofalo et al. *RSNA* 2002
- Whole Abdominal RT
  - Hong et al. IJROBP 2002;54:278
  - Duthoy et al. IJROBP 2003;57:1019
  - Kim et al. *TCRT* 2009;5:369



Hermesse et al.
Strahlen Onkol (2005)

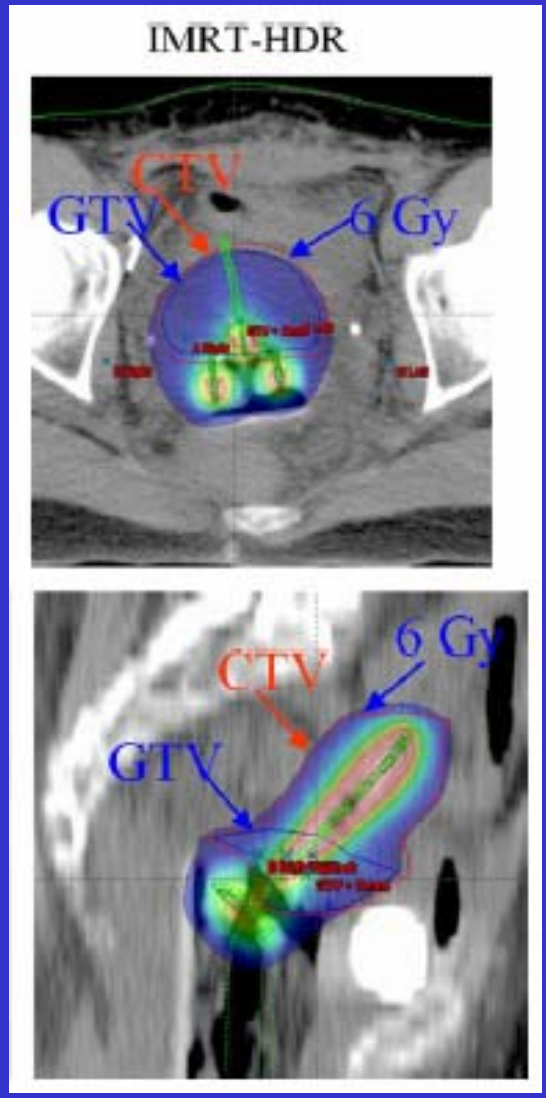
Dosimetric IMRT Studies

Multiple studies suggest IMRT may represent an alternative to brachytherapy

- Roeske et al. *Med Phys* 2000;27:1282
- Low et al. *IJROBP* 2002;52:1400
- Guerrero et al. *IJROBP* 2005;62:933
- Fung et al. *Radiat Oncol* 2006;1:13
- Aydogan et al. *IJROBP* 2006;65:266
- Malhotra et al. *JACMP* 2007;8:2450

Or a beneficial adjunct to brachy

- Assenholt et al. *Acta Oncol* 2008;47:1337
- Duan et al. IJROBP 2008;71:765



Duan et al. IJROBP (2008)

Clinical Outcome Studies

- Increasing number of outcome studies in gynecology patients undergoing IMRT
- Reductions in acute and chronic toxicities, particularly GI toxicity

Acute Toxicity

		GI		GU	
	n	g2	g3	g2	g3
Pelvis					
Mundt (2002)	40	60%	0%	10%	0%
Chen (2007)	33	24%	0%	12%	0%
Beriwal (2006)	47	70%	0%	4%	0%
Tierney (2007)	14	57%	0%	21%	0%
Hsieh (2009)	10	NS	10%	NS	0%
Zhou (2007)	21	NS	0%	NS	0%
Hasselle (2010)	111	45%	2%	16%	0%
Pelvic-Paraortic					
Salama (2006)	13	84%	0%	7%	0%
Beriwal(2006)	36	69%	3%	19%	3%
Gerszten (2006)	22	10%	0%	10%	0%
Pelvic-Inguinal					
Beriwal (2007)	15	20%	6%	13%	0%
Whole Abdominal					
Rochet (2010)	10	NS	10%	0%	0%

Chronic Toxicity

		GI		GU	
	n	g2	g3	g2	g3
Pelvis					
Mundt	35	2.8%	0%	0%	0%
Chen	33	0%	0%	0%	3%
Beriwal	47	0%	0%	0%	0%
Chen	54	NS	0%	NS	1.8%
Hasselle	111	10%	4%	2%	5%
Kidd	135	-------Grade 3-4 GI/GU = 6%-------			
Pelvic-Paraortic					
Beriwal	36	2.7%	5.5%	0%	0%

Mundt et al. Red J 2003;56:1354
Chen et al. Red J 2007;67:1438
Beriwal et al. Gyne Oncol 2006;102:1395
Beriwal et al. Red J 2006;64:1395
Chen et al. Cancer J 2008;14:200
Hasselle et al. Red J (in press)
Kidd et al. Red J (in press)

IMRT Outcome Studies

Evaluated the impact on acute hematologic toxicity

- Several report low rates in patients undergoing concomitant chemoradiotherapy
  - Brixey et al. *IJROBP* 2002;52:1388
  - Mell et al. *IJROBP* 2006;66:1356
  - Lupe et al. *IJROBP* 2007;67:110

- Others studies less favorable
  - Tierney et al. *Radiat Med* 2007;25:439
  - Hsieh et al. *Radiat Oncol* 2009;4:62
  - Zhou et al. *Zhonghua Fu Chan Ke Za Zhi* 2007;42:730

Majority have not intentionally included bone marrow in the inverse planning process

Tumor Control

- Data remain limited
- Increasing number of single institution series published
- Cooperative groups performing clinical trials

Cervical Cancer

	n	FU	Stage	DFS	Pelvic Control
Intact Cervix					
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%
Postoperative Cervix					
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%

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* (in press)

Hasselle et al. *IJROBP* (in press)

CLINICAL INVESTIGATION

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.†

111 cervical cancer pts

89 intact cervix, 22 postop

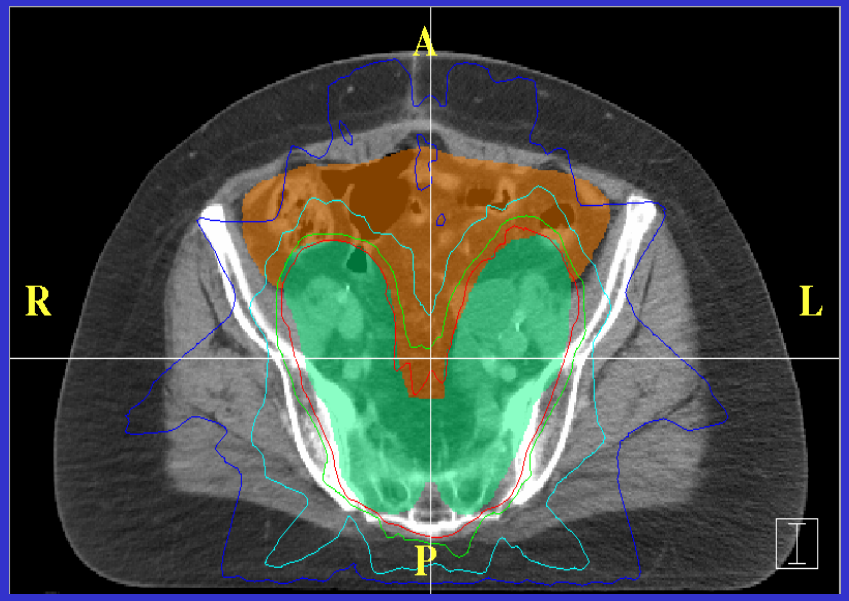
Pelvic IMRT +/- Brachy

Median FU = 27 months

Excellent pelvic control

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

Grade ≥ 3 chronic toxicity = 7%



Hasselle et al. Red J 2010 (in press)

Endometrial Cancer

	n	FU	Stage	DFS	Pelvic Control
Knab	31	24 m	I-III	84%	100%
Beriwal	47	20 m	I-III	84%	100%

Knab et al. *Int J Radiat Oncol Biol Phys* 2004;60:303
Beriwal et al. *Int J Radiat Oncol Biol Phys* 2006;102:195

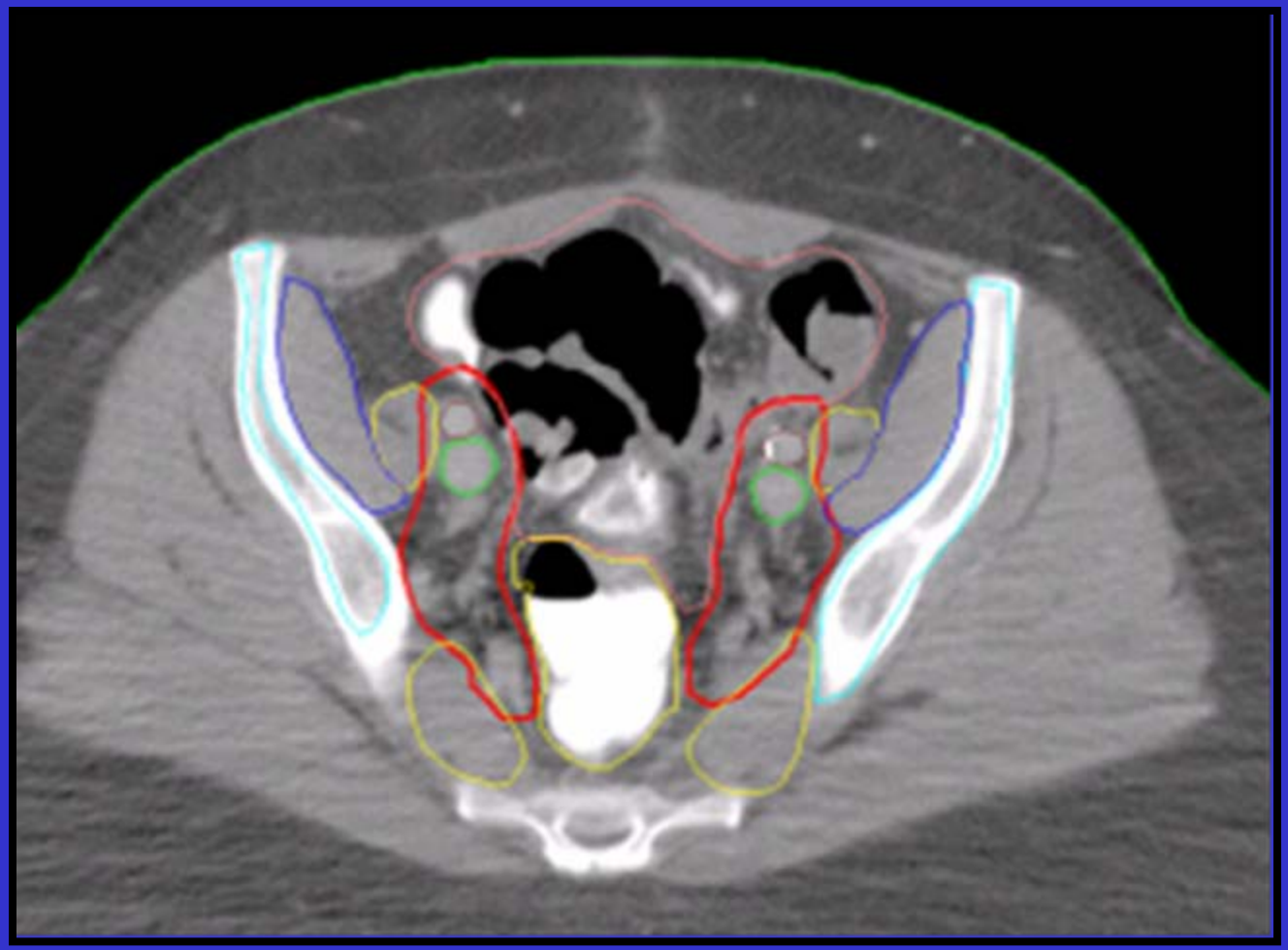
International Cervical Cancer Radiotherapy Consortium

Peking Union Medical College (Beijing)
Tata Memorial Hospital (India)
AC Camargo Hospital (Brazil)
UC San Diego (USA + Mexico)
University of Chicago (USA)
University of Miami (USA)
Artemis Hospital (India)
Loyola University (USA)
University of Pittsburgh (USA)
University of Iowa (USA)
Moffitt Cancer Center (USA)
King Chulalongkorn University (Thailand)
Istanbul Bilim University (Turkey)
University Hospital Hradec Kealove (Czech Republic)
Far Eastern Memorial Hospital (Taiwan)





Target Delineation



Target Delineation

- Step 1 Identify treatment volume
- Depends on the tumor site, disease stage, histology, pathologic features
- Most receive pelvic RT
- More comprehensive volumes in select patients
  - Stage IIIC uterine cancer → EFRT
  - Papillary serous uterine cancer → WART
  - Vulvar cancer → Pelvic-inguinal RT

Target Delineation

- Step 2 Identify individual components of the treatment volume
- More difficult step
- Controversial which components to include
- No consensus even among experts

Target Volume Components
IM-Pelvic RT Patients

Vagina

Upper 1/2

Cervix/uterus (if present)

Parametria tissues

Pelvic Lymph Nodes

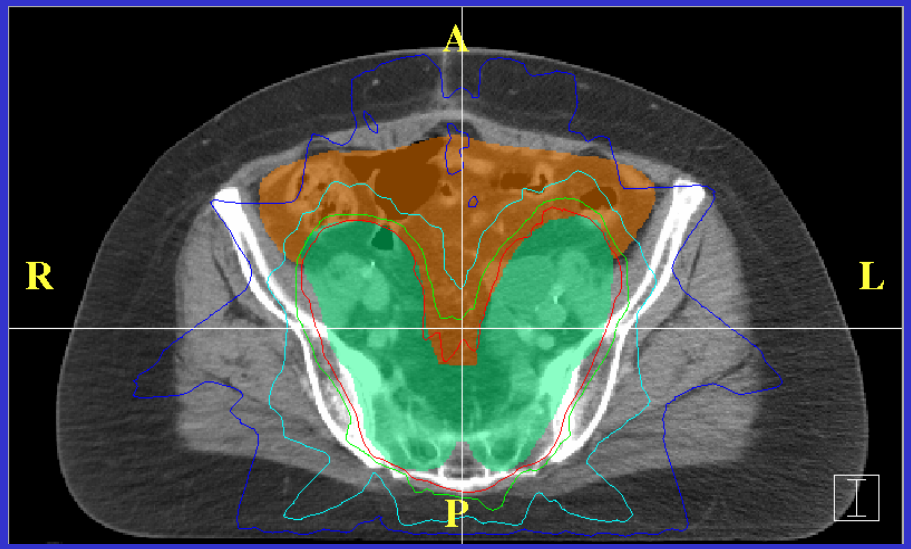
Common, internal and external iliacs

Pre-sacral nodes

In all cervical cancer and uterine cancer with cervical involvement

Target Delineation

- Step 3 Decide *how* to contour the target
- Most difficult step

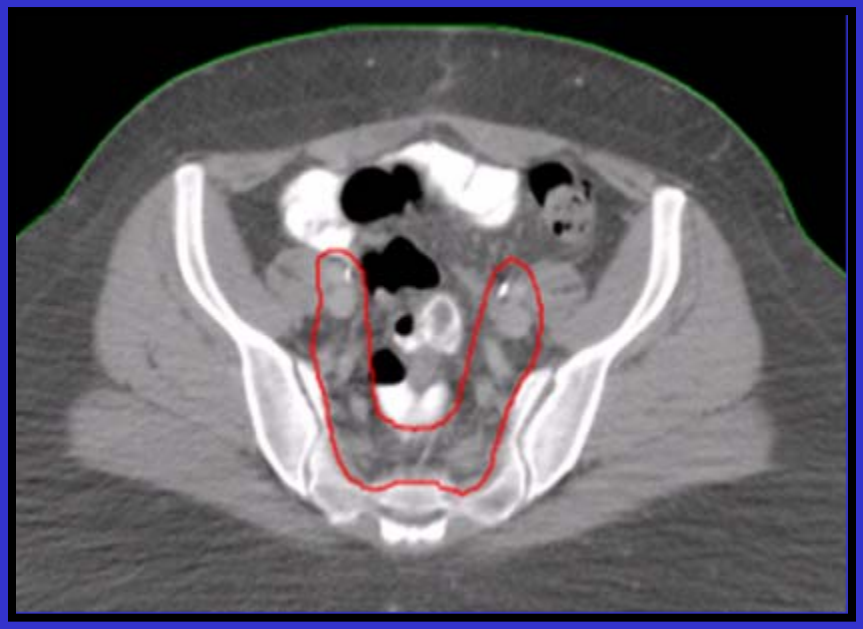


While two physicians may agree on the components of the CTV, they rarely agree on how to contour them

Consensus Guidelines

- Guidelines for target design are being developed

GOG-RTOG-ESTRO-NCIC
Target Consensus Meeting
Philadelphia June 2005
Post-hysterectomy CTV
www.rtog.org
RTOG 0418 (Jhingran)



Guidelines based on participants' opinions and published data

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.‖‖

Red Journal 2008;71:428

http://www.rtog.org/pdf_document/GYN-Atlas.pdf

Fig. 1. Upper common iliac clinical target volume.

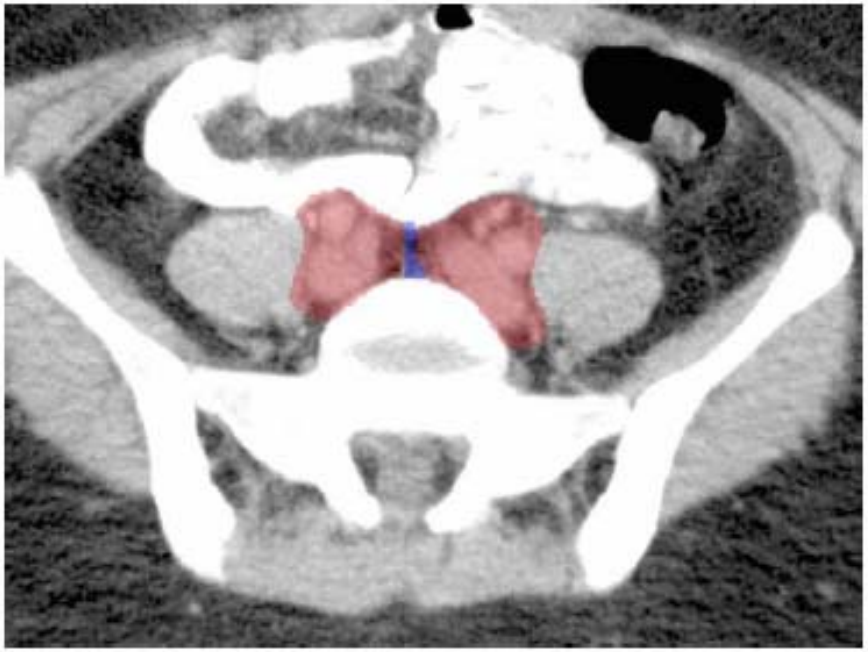


Fig. 2. Mid-common iliac (red) and presacral clinical target volume (blue).

Red Journal 2008;71:428

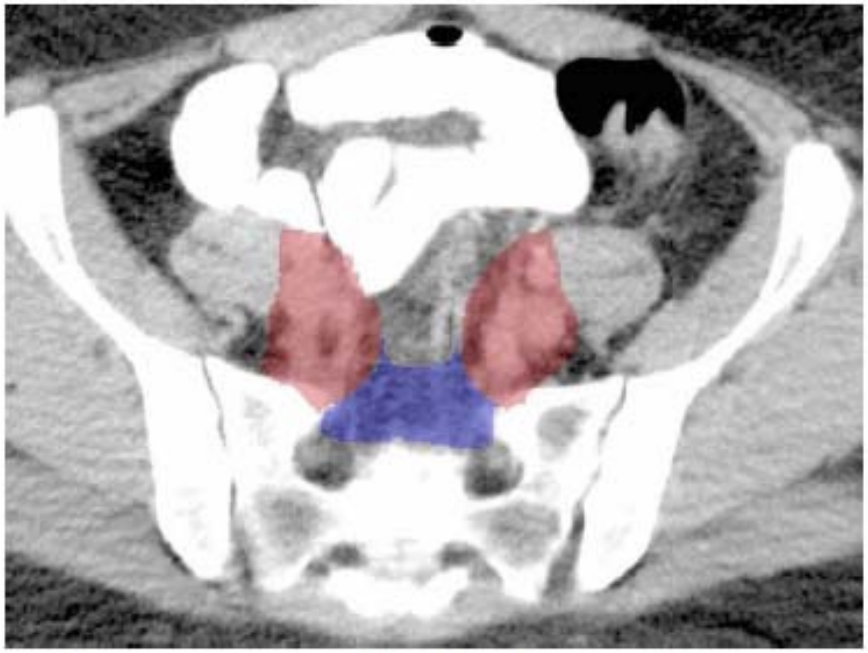


Fig. 3. Lower common iliac (red) and presacral clinical target volume (blue).

Fig. 5. External and internal iliac clinical target volume.

Red Journal 2008;71:428

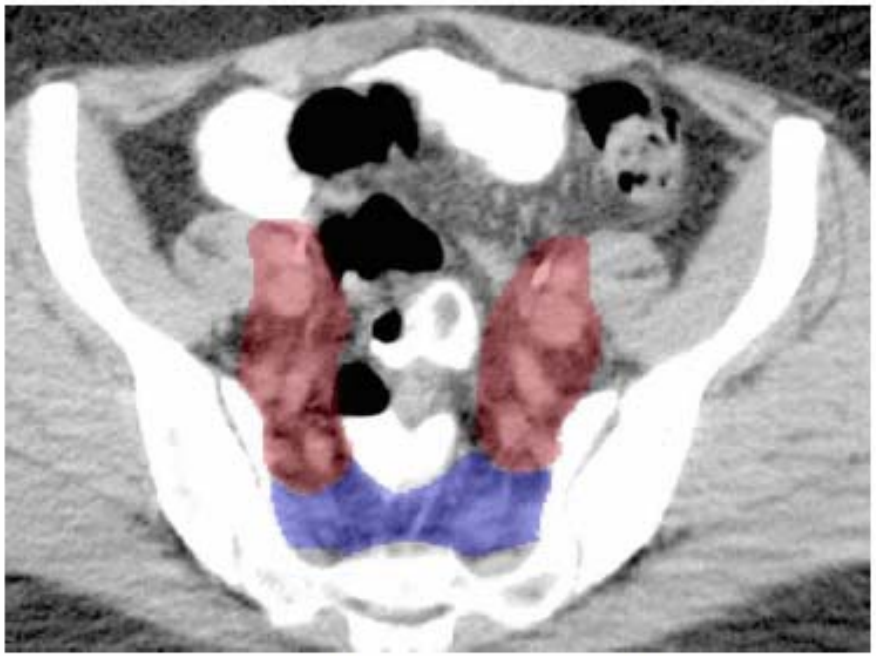


Fig. 4. Upper external and internal iliac (red) and presacral clinical target volume (blue).

Fig. 6. External and internal iliac (red) and parametrial/vaginal (green) clinical target volume.

Red Journal 2008;71:428

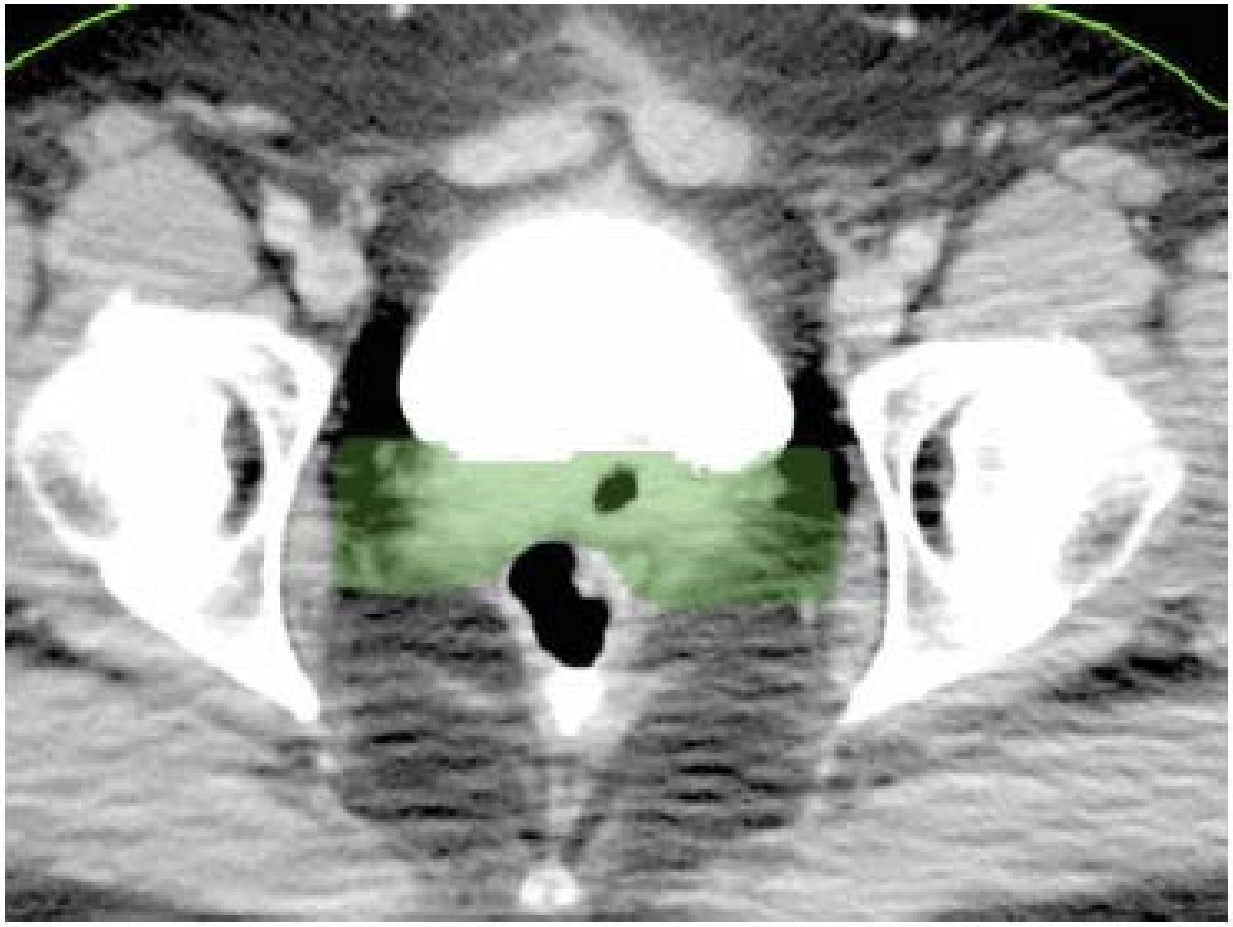


Fig. 7. Parametrial/vaginal clinical target volume.

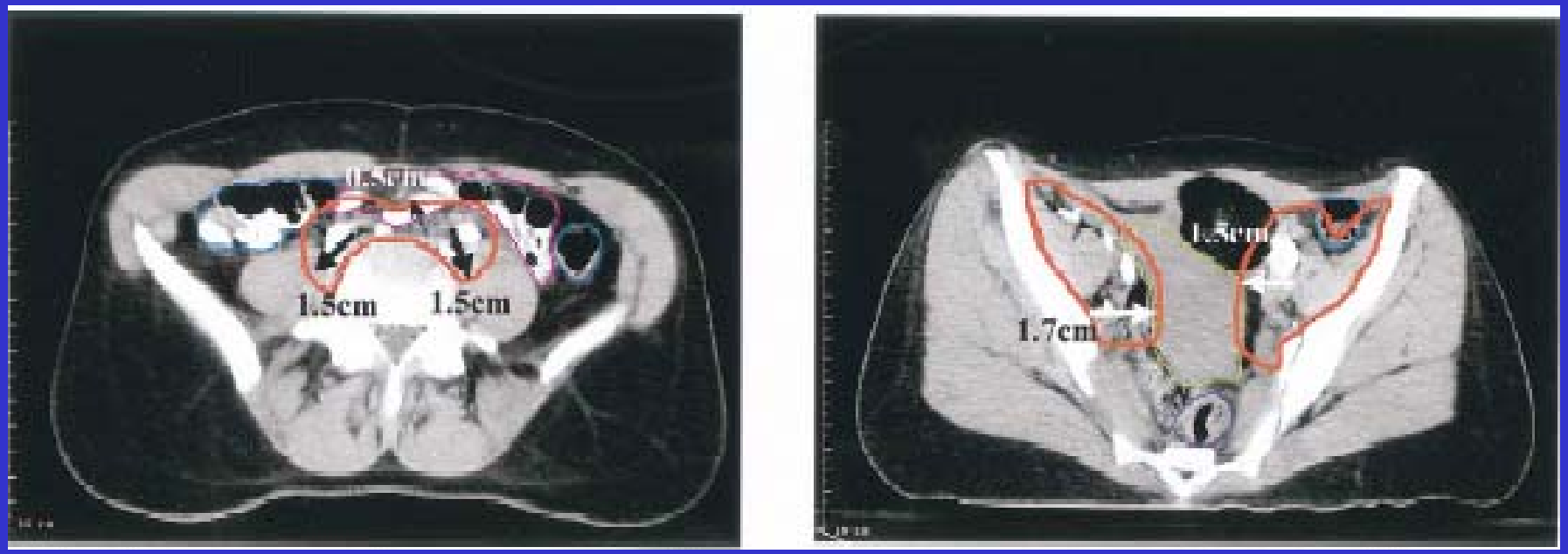
Red Journal 2008;71:428

CLINICAL INVESTIGATION Cervix

LYMPHANGIOGRAM-ASSISTED LYMPH NODE TARGET DELINEATION FOR PATIENTS WITH GYNECOLOGIC MALIGNANCIES

K. S. Clifford Chao, M.D., and Mary Lin, B.S.

Department of Radiation Oncology, Washington University Medical School, St. Louis, MO



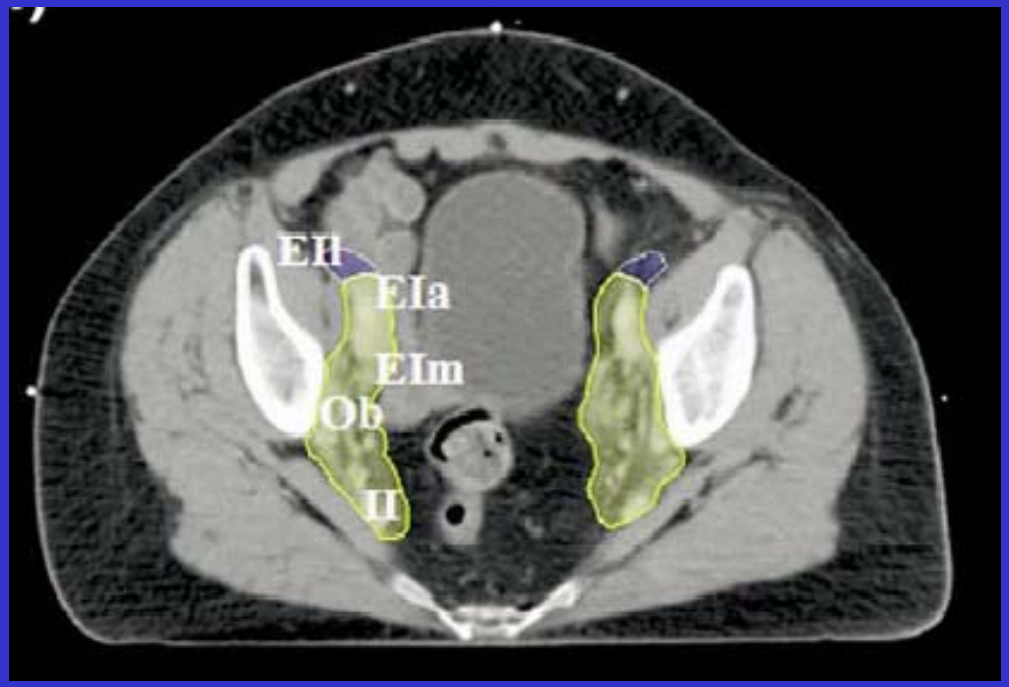
Chao KS et al. *Int J Radiat Oncol Biol Phys* 2002;54:1147-1152

PHYSICS CONTRIBUTION

MAPPING PELVIC LYMPH NODES: GUIDELINES FOR DELINEATION IN INTENSITY-MODULATED RADIOTHERAPY

ALEXANDRA TAYLOR, F.R.C.R.,* ANDREA G. ROCKALL, F.R.C.R.,† RODNEY H. REZNEK, F.R.C.R.,† AND MELANIE E. B. POWELL, M.D., F.R.C.R.*

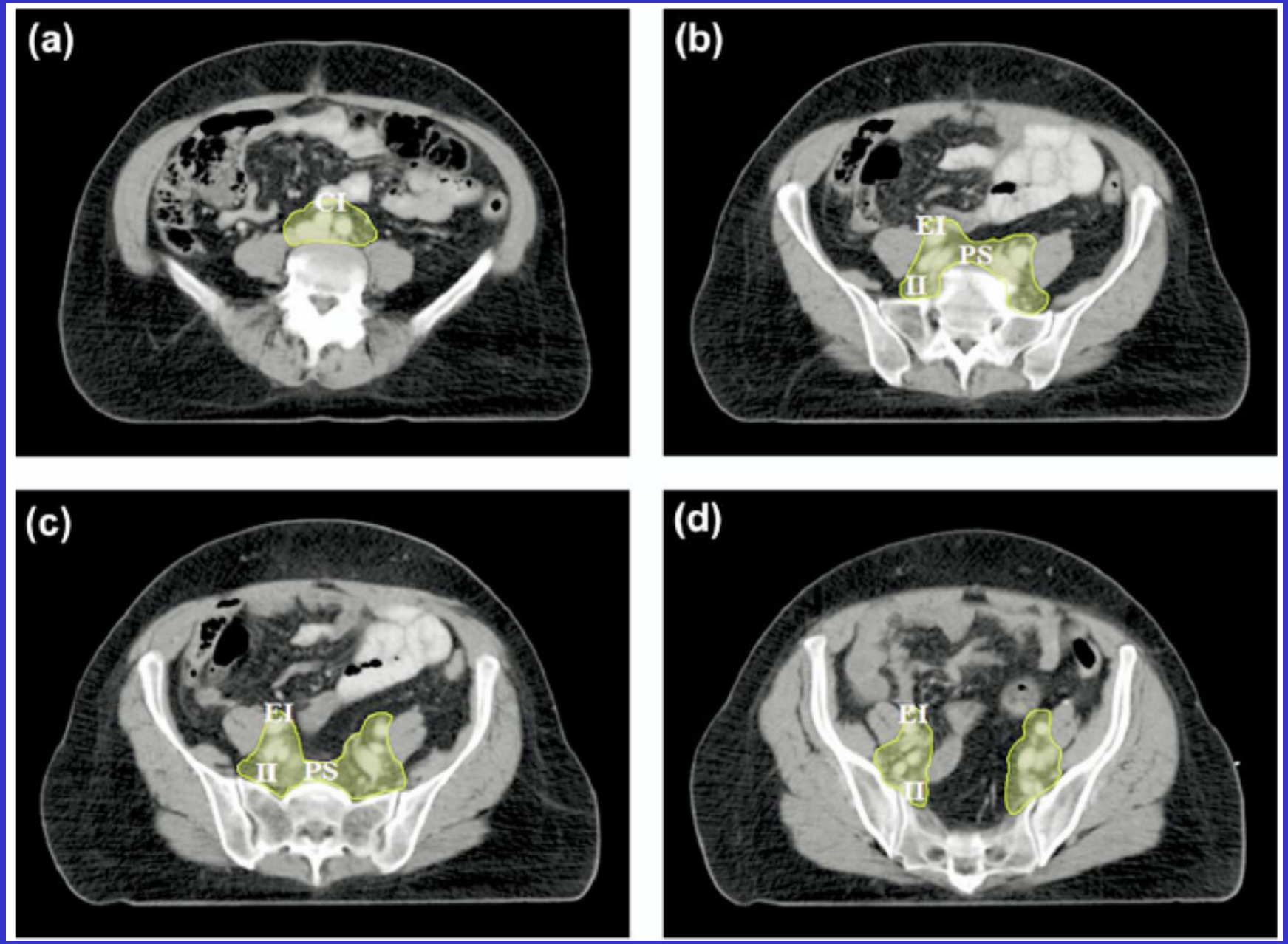
Departments of *Radiotherapy and †Radiology, St. Bartholomew's Hospital, London, United Kingdom



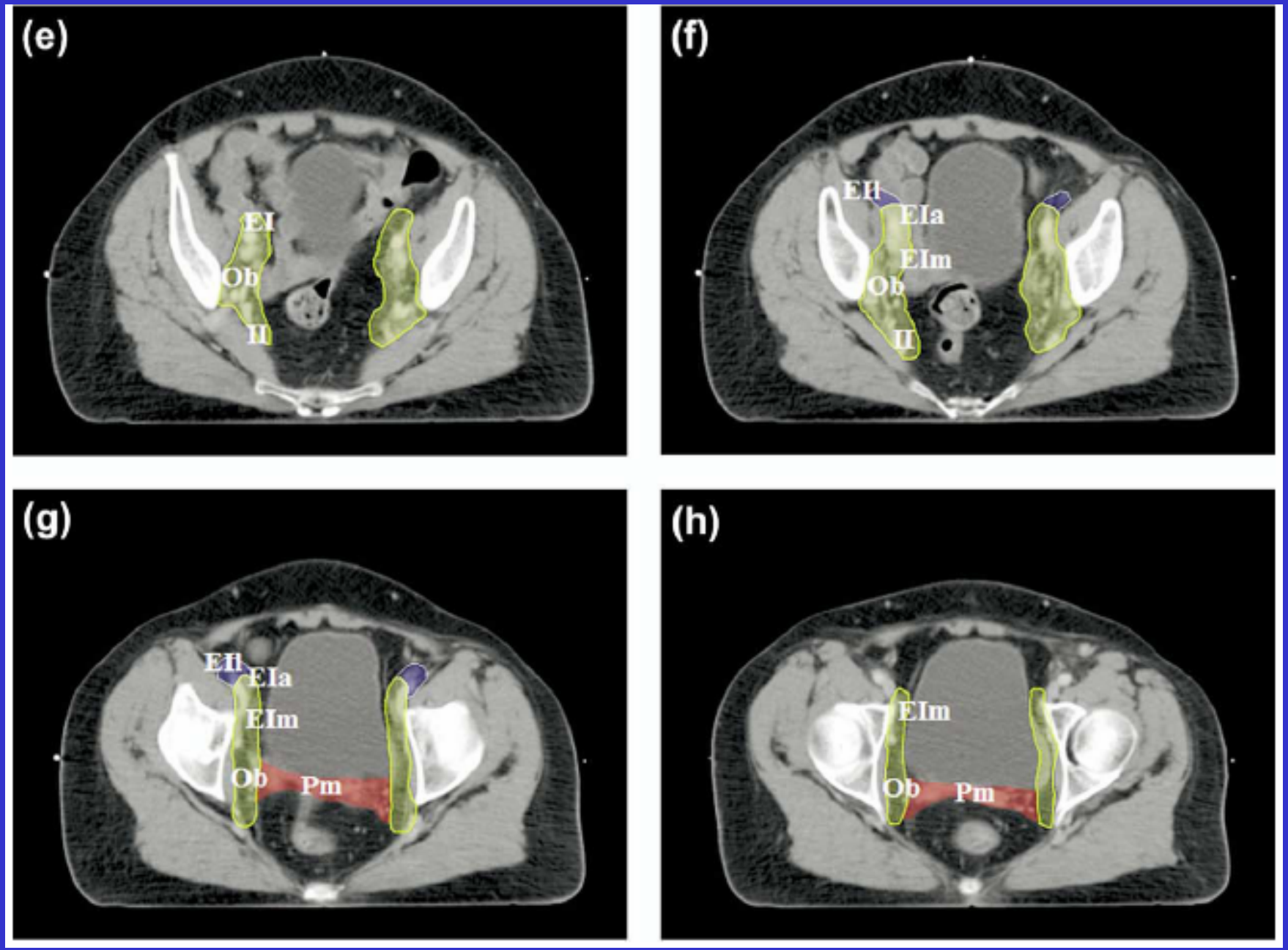
Taylor et al. Red J 2005;63:1604

Fe Oxide nano-particle enhanced MRI

Taken up in benign lymph nodes by macrophages



Taylor et al. Red J (2005)



Taylor et al. Red J (2005)

Target Delineation
Postoperative IMRT

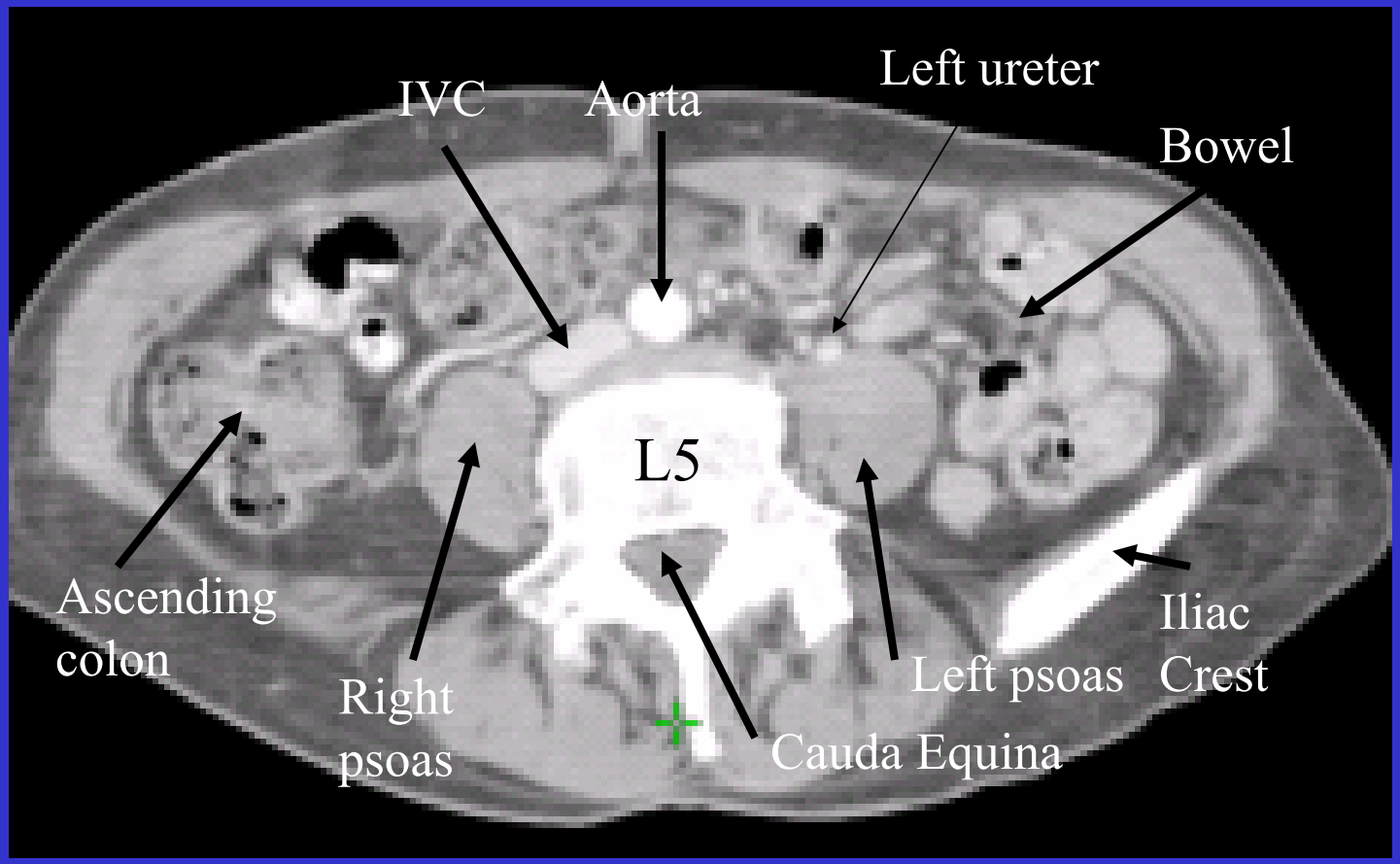
- Only a clinical target volume (CTV) is delineated
- Lymph node regions not delineated with a *symmetric* expansion around vessels
- 0.7 cm margin used to encompass surrounding fat and connective tissues
- 1 cm margin around vaginal cuff
- Normal tissues help define CTV extent

  Psoas/piriform muscles, bowel and bones

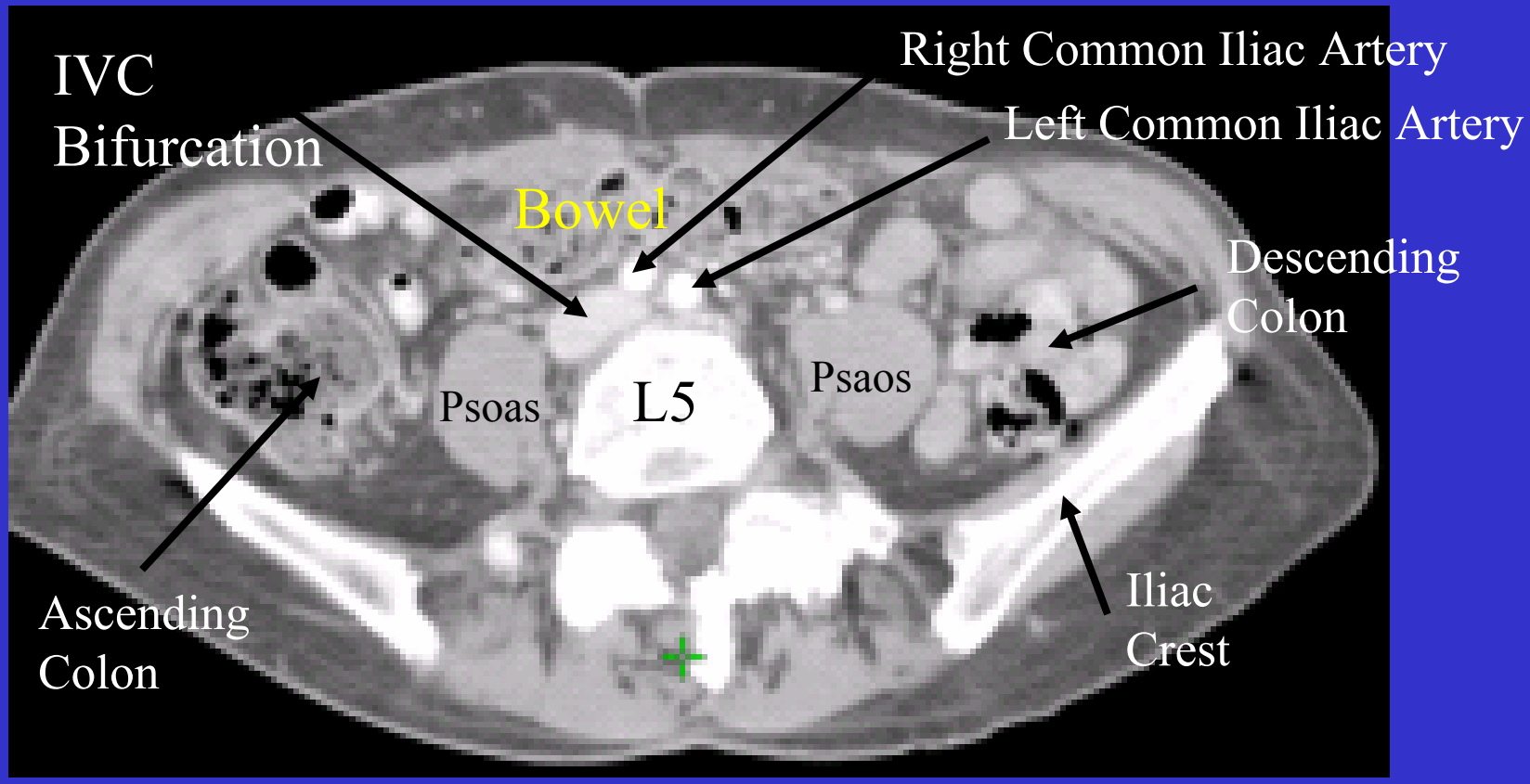
Target Delineation

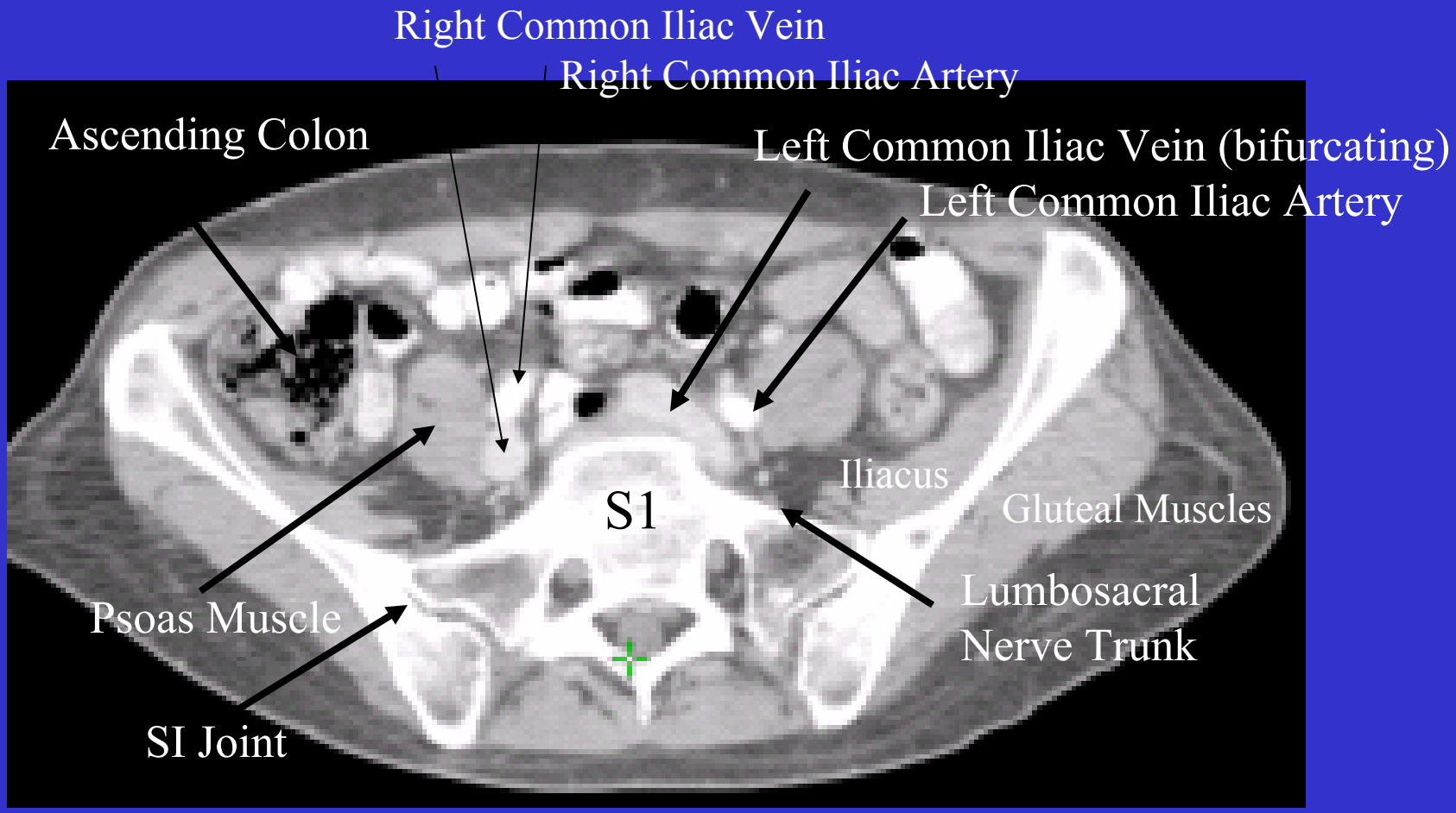
- Knowledge of normal pelvic anatomy very important
- Poor knowledge of normal anatomy results in poor target delineation

Anatomy

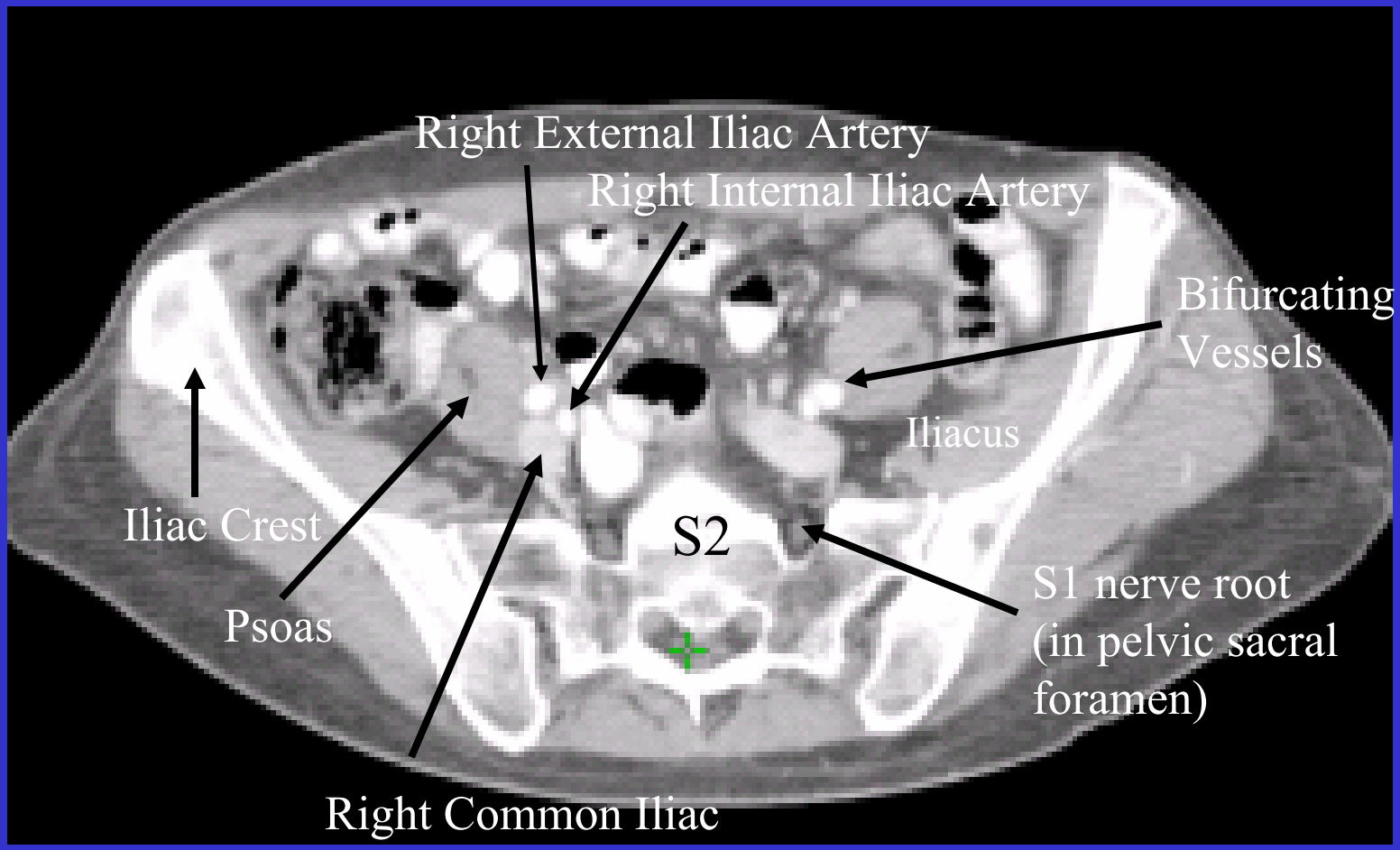

IVC
Aorta
Left ureter
Bowel
L5
Ascending colon
Right psoas
Cauda Equina
Left psoas
Iliac Crest

Anatomy


IVC
Bifurcation
Right Common Iliac Artery
Left Common Iliac Artery
Bowel
Descending
Colon
Psoas
L5
Psaos
Ascending
Colon
Iliac
Crest

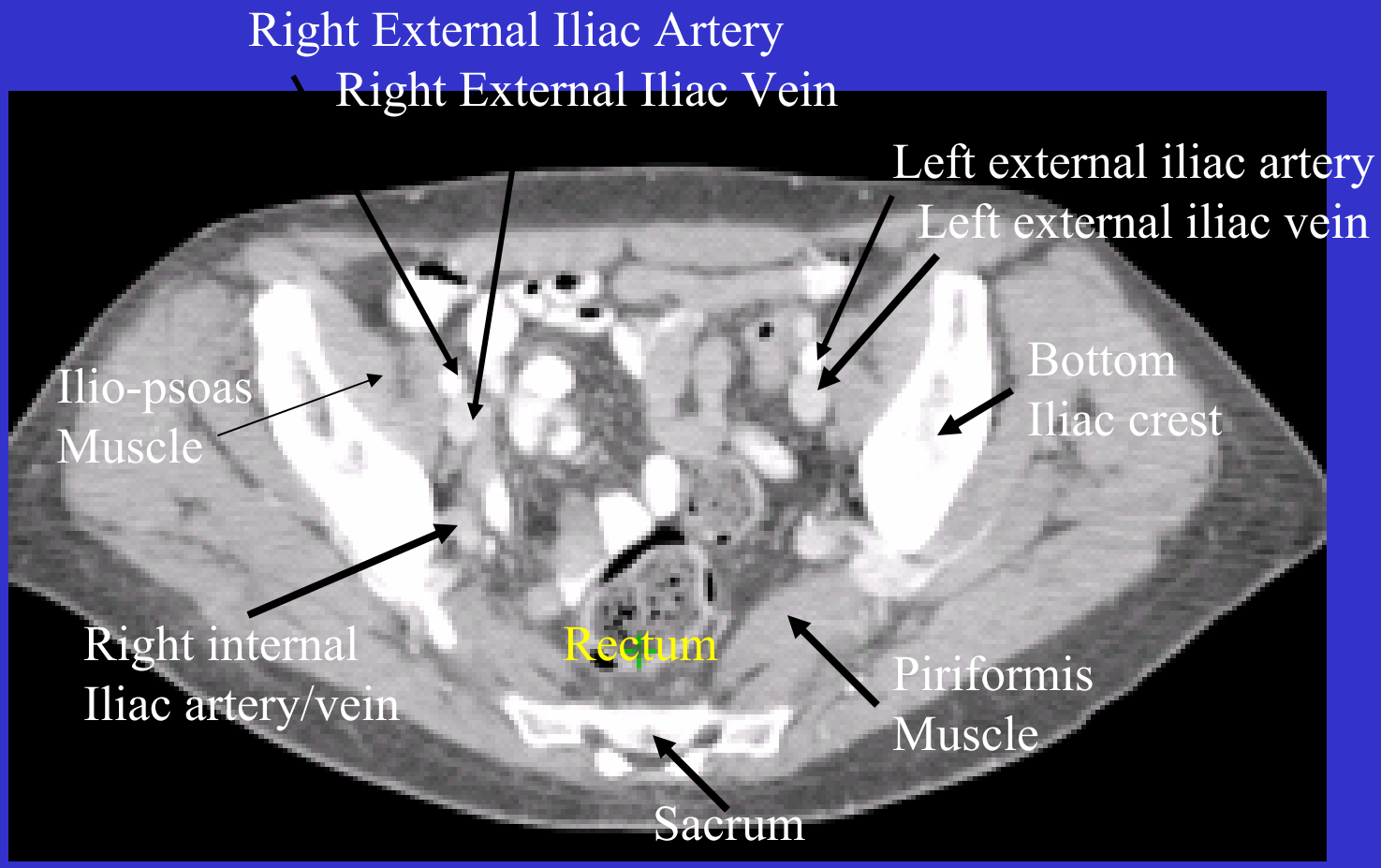

Right Common Iliac Vein
Right Common Iliac Artery
Ascending Colon
Left Common Iliac Vein (bifurcating)
Left Common Iliac Artery
Iliacus
S1
Gluteal Muscles
Psoas Muscle
Lumbosacral
Nerve Trunk
SI Joint

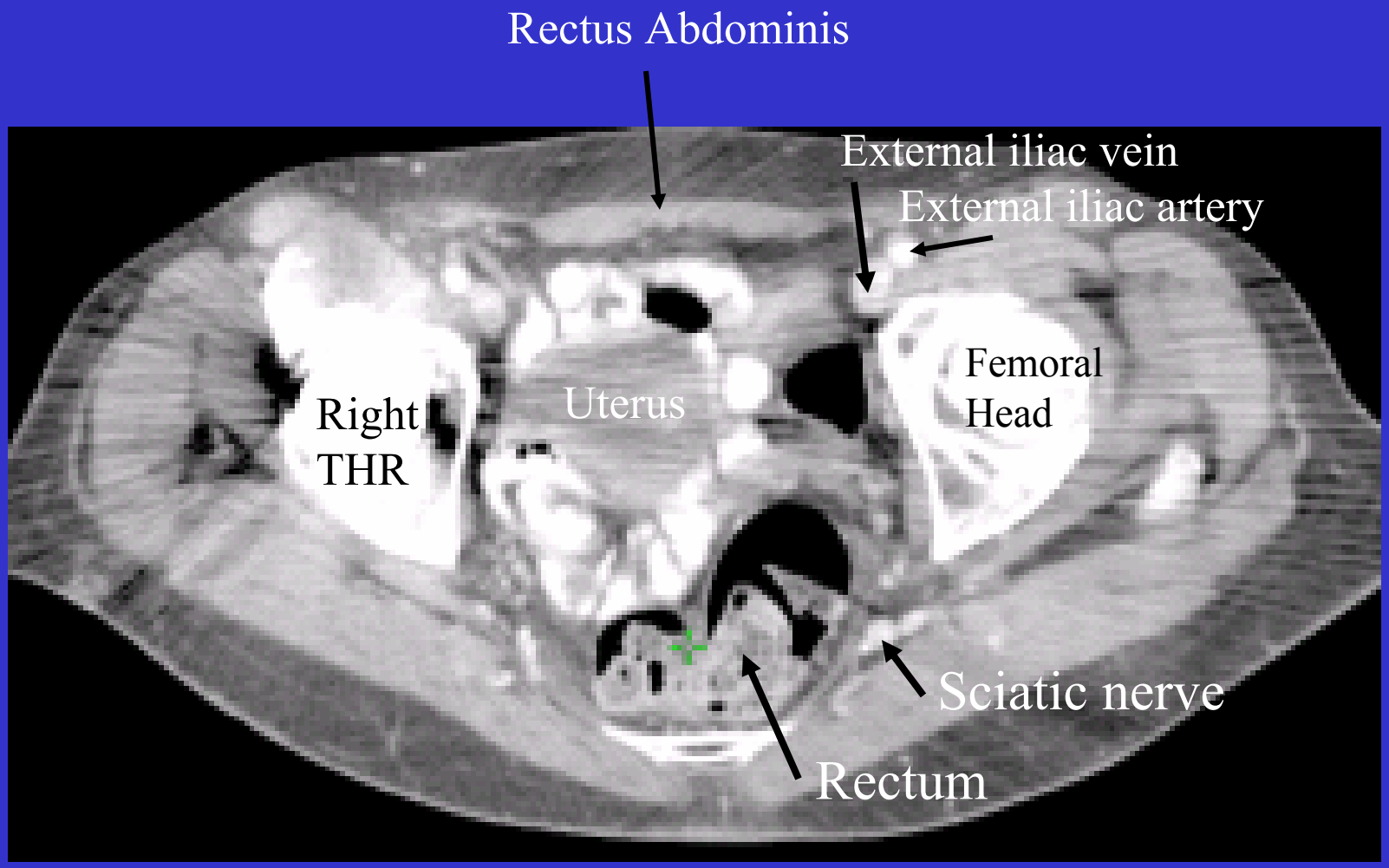
Anatomy

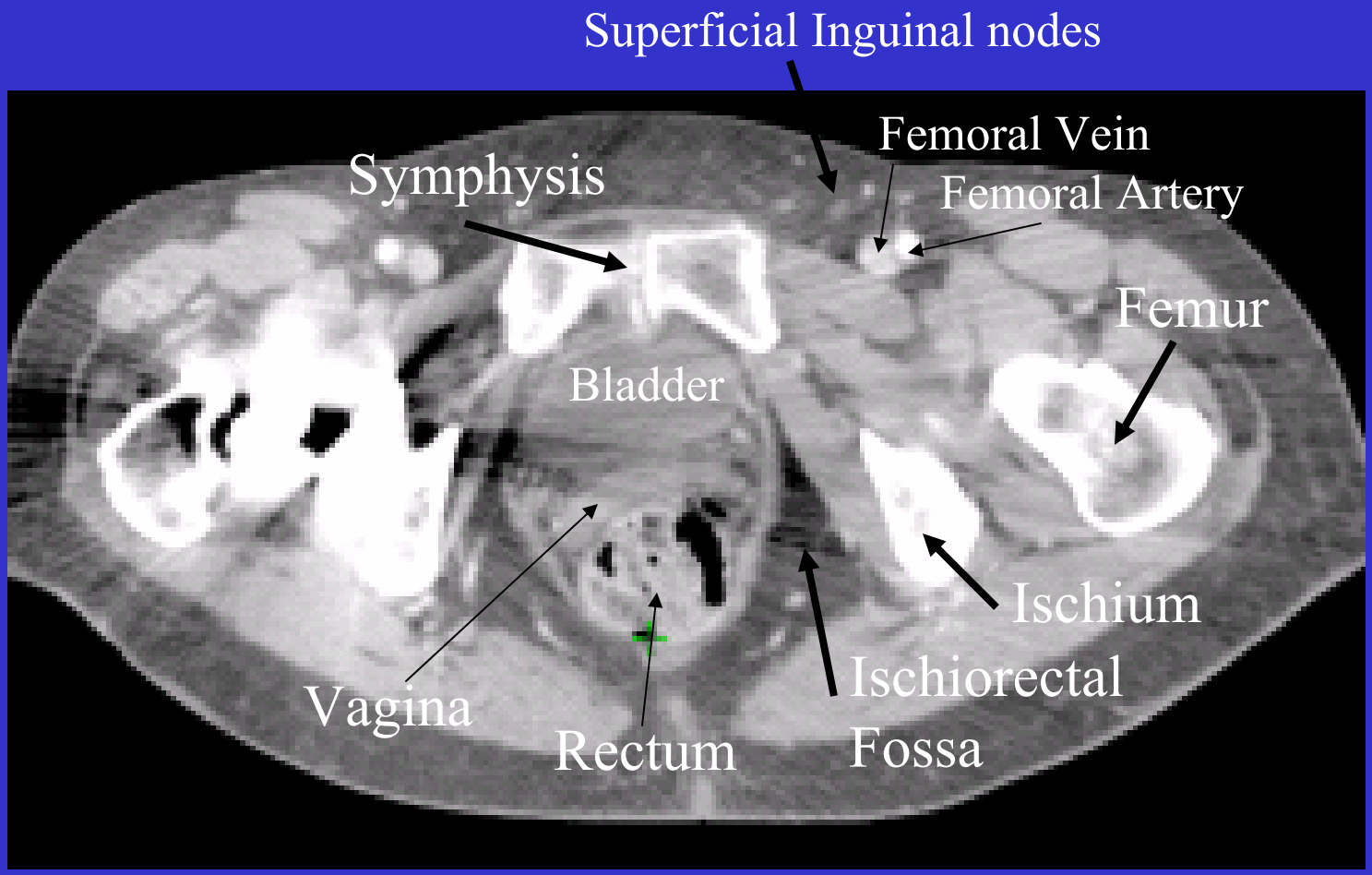

Right External Iliac Artery
Right Internal Iliac Artery
Bifurcating Vessels
Iliacus
Iliac Crest
S2
Psoas
S1 nerve root (in pelvic sacral foramen)
Right Common Iliac Vein

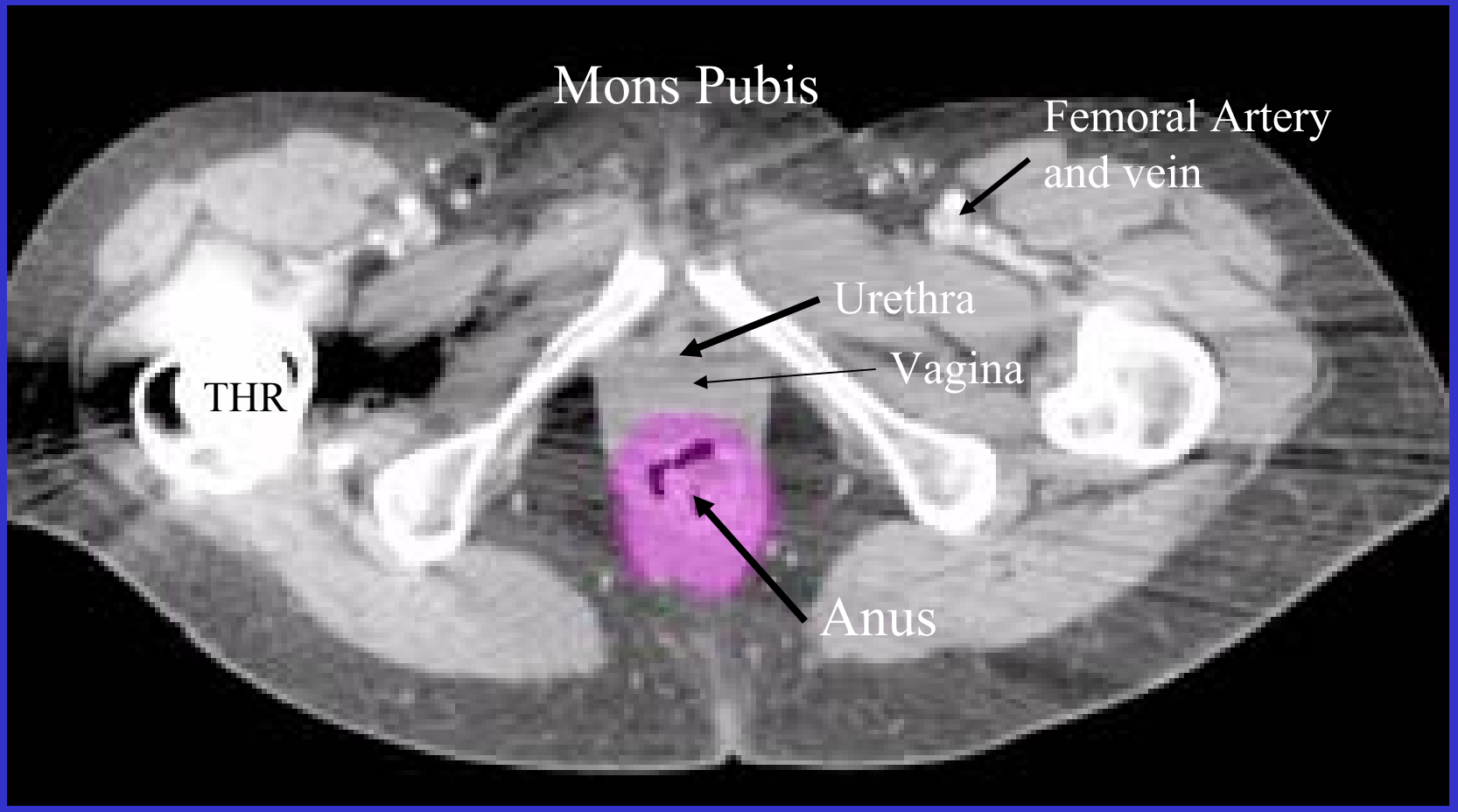
Anatomy


Psoas Muscle
R External Iliac Artery
R External Iliac Vein
R Internal Iliac Artery
R Internal Iliac Vein
Sigmoid
S2

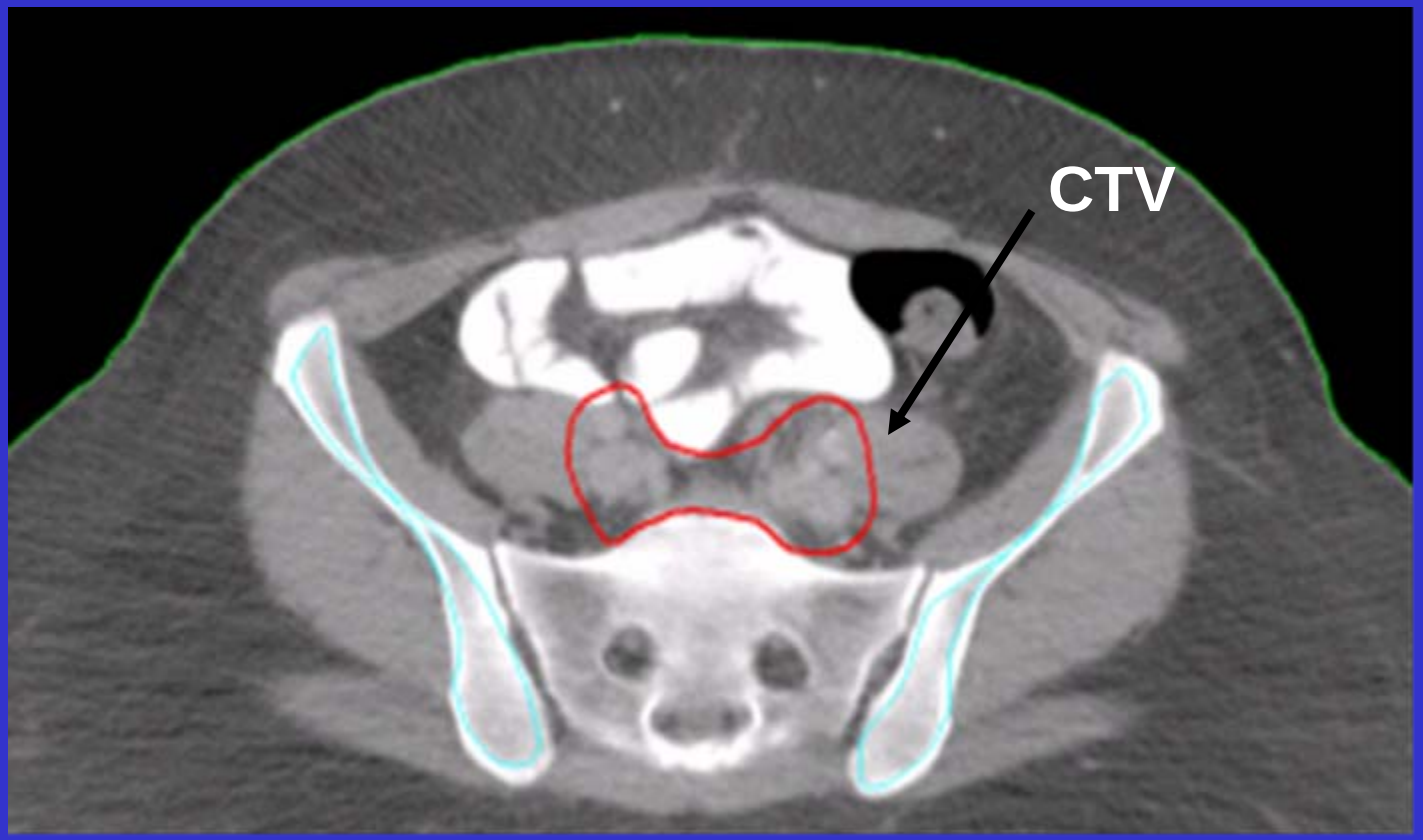

Right External Iliac Artery
Right External Iliac Vein
Left external iliac artery
Left external iliac vein
Ilio-psoas
Muscle
Bottom
Iliac crest
Right internal
Iliac artery/vein
Rectum
Piriformis
Muscle
Sacrum


Rectus Abdominis
External iliac vein
External iliac artery
Femoral Head
Right THR
Uterus
Sciatic nerve
Rectum

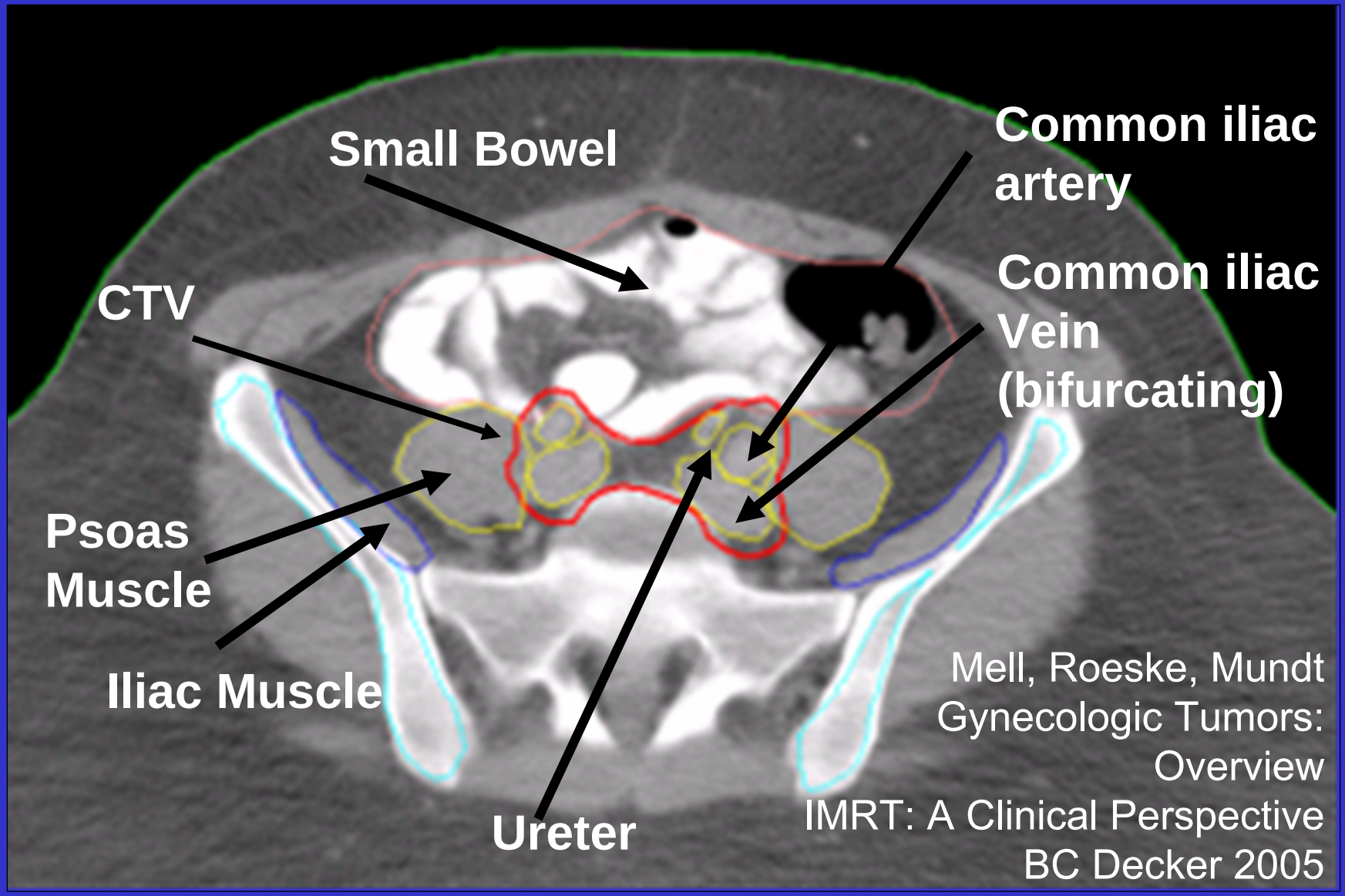

Superficial Inguinal nodes
Femoral Vein
Femoral Artery
Symphysis
Femur
Bladder
Ischium
Vagina
Rectum
Ischiorectal
Fossa


Mons Pubis
Femoral Artery
and vein
Urethra
Vagina
THR
Anus

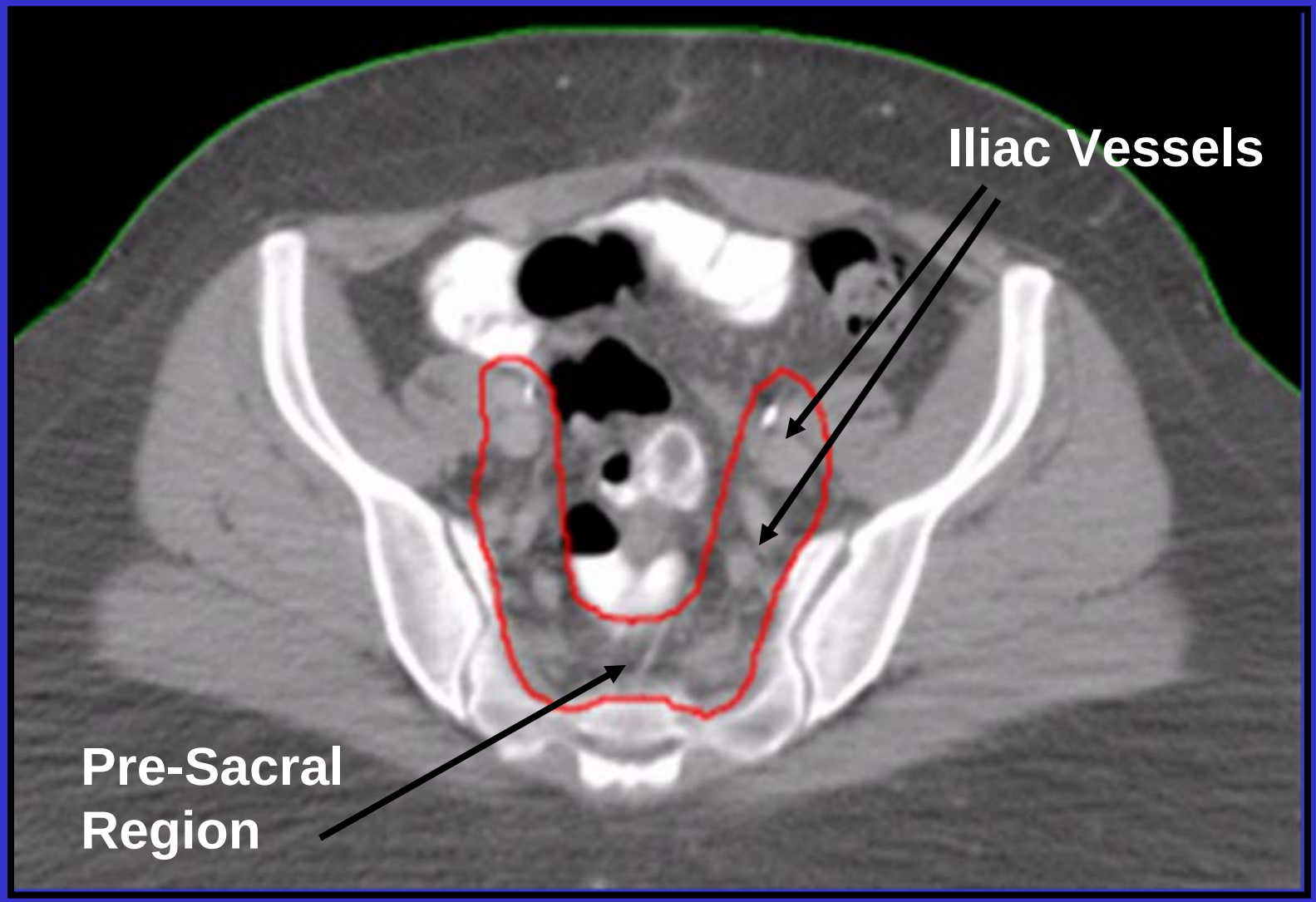
Start CTV contours ~1.5 cm below L4-5 (remember it will be expanded)
CTV is initially small and conical
As vessels bifurcate, it takes on a “bow tie” appearance



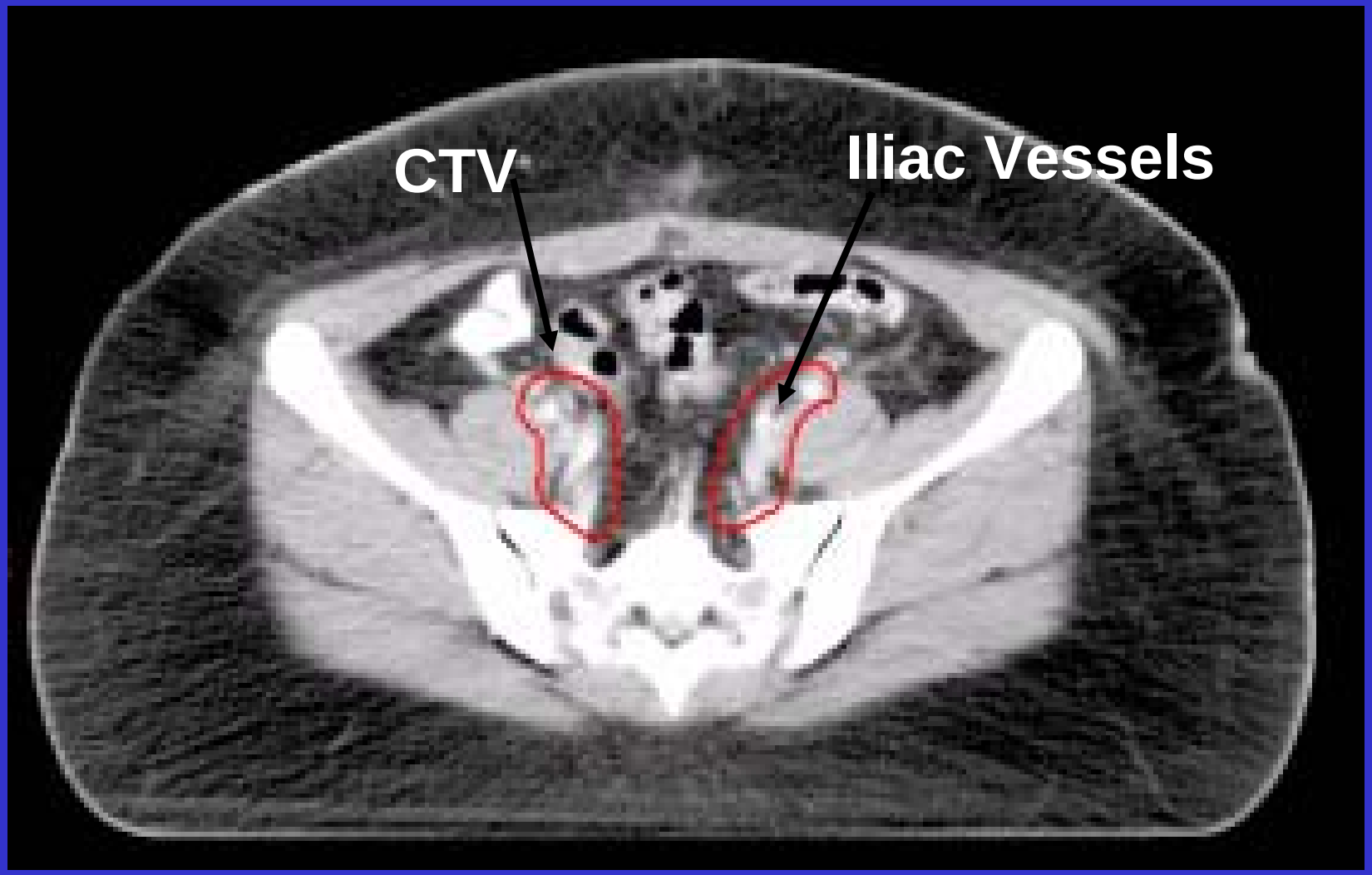
Use psoas muscle, small bowel and lumbosacral spine to help define CTV extent



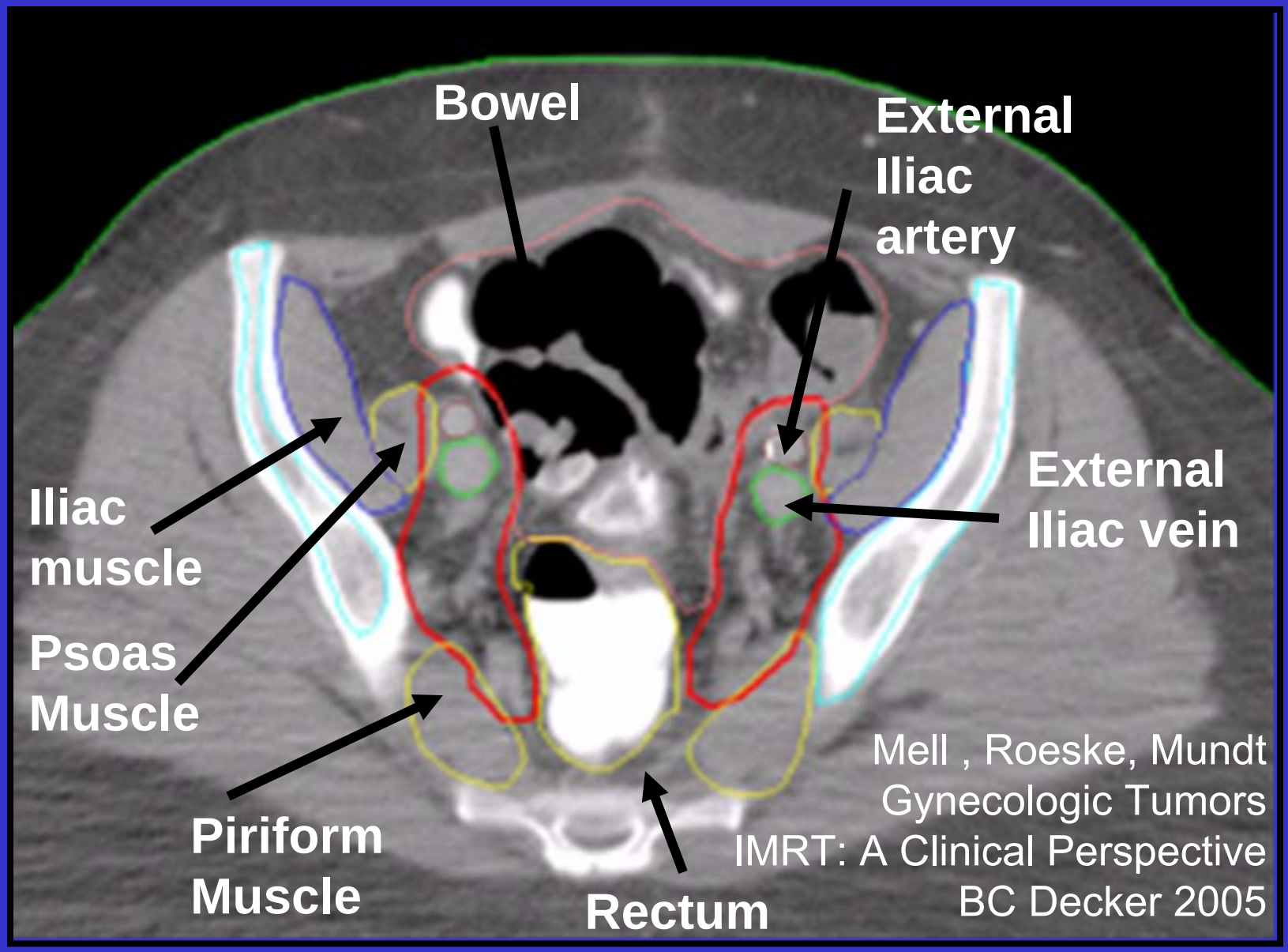
CTV inferiorly becomes U-shaped, encompassing lateral pelvic nodes and posterior presacral region



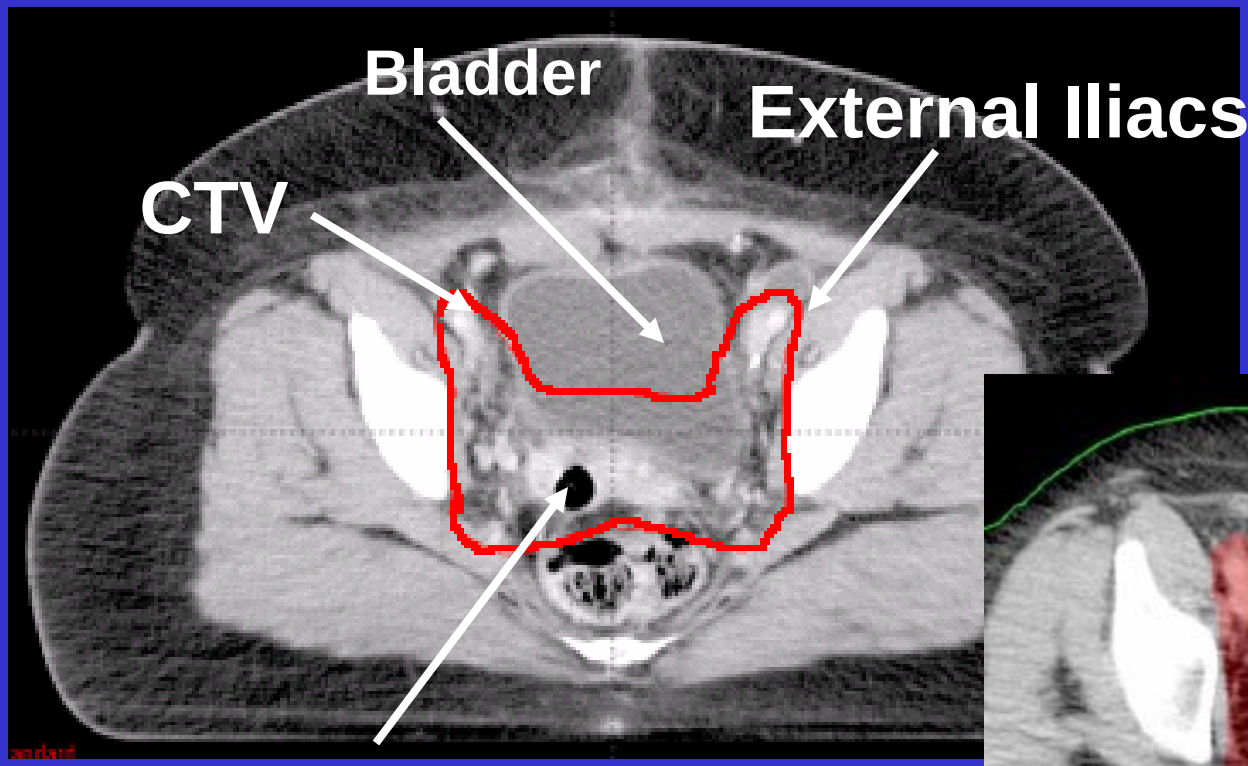
In endometrial cancer pts without cervical extension, *split* the CTV excluding presacral region

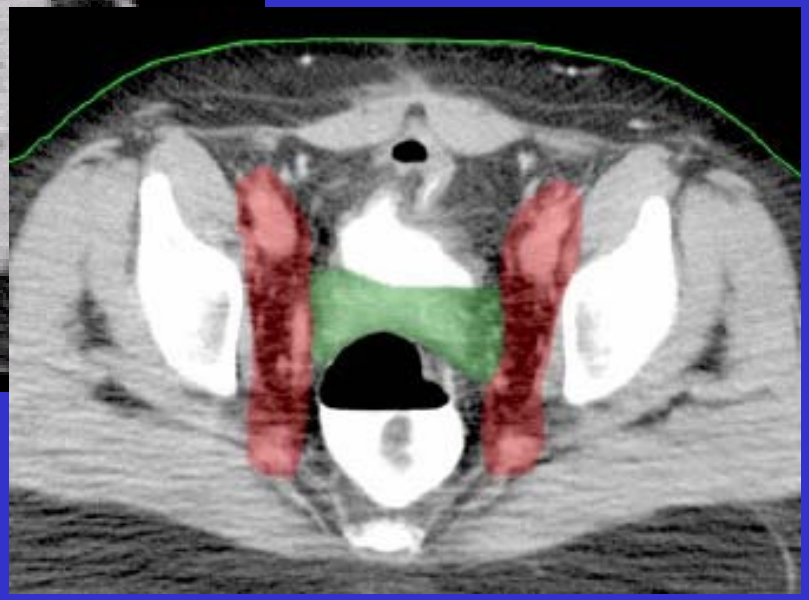


Psoas and piriform muscles are helpful



At the level of the vaginal cuff, The CTV takes on a “bow tie” appearance





RTOG Atlas

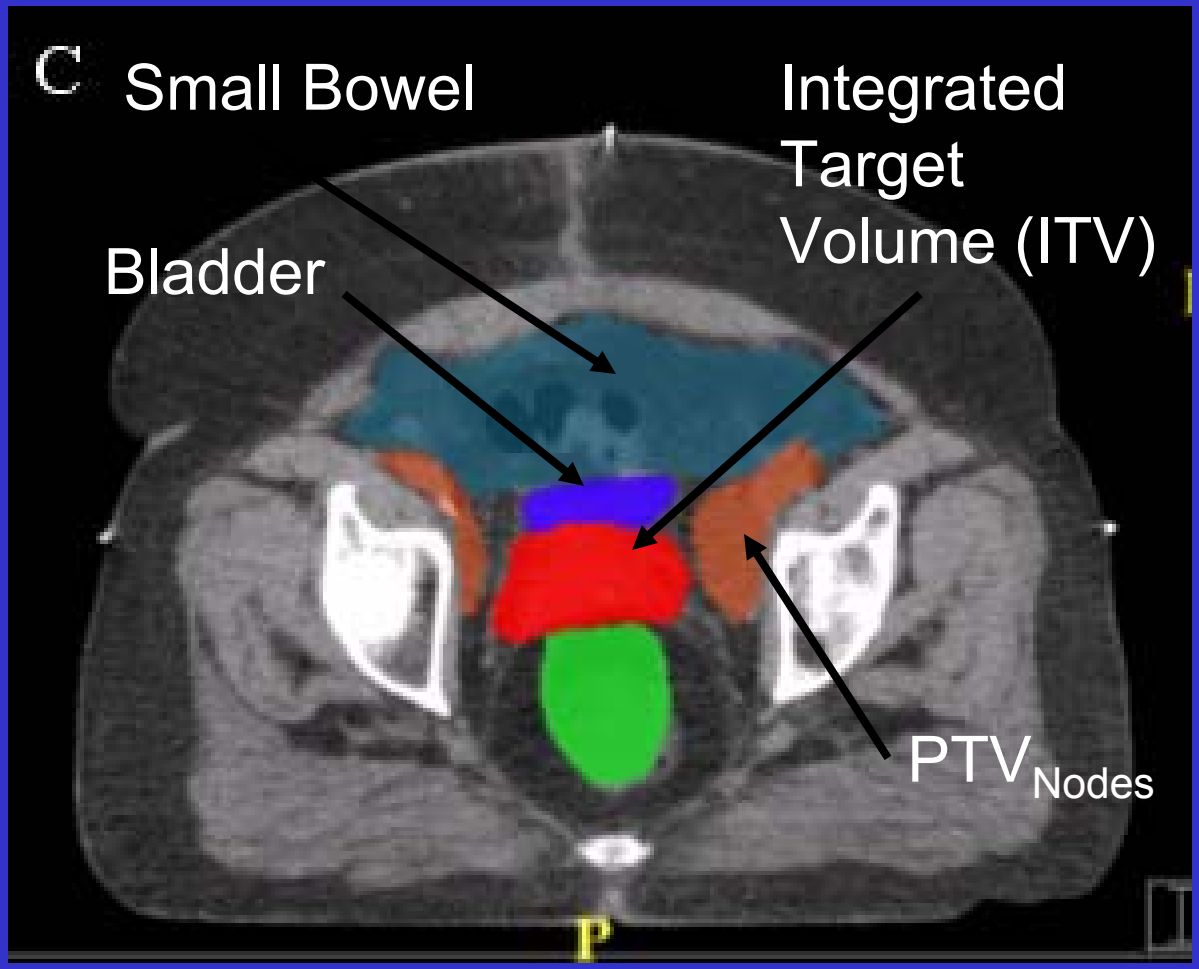
Target Delineation
Myself vs Consensus Conference

- I favor inclusion of 1 cm of bladder and rectum in the CTV
- Yes it goes against the CTV concept!
- Provides a more generous margin around the vaginal cuff due to concerns over organ motion*

**Another* 0.7 cm expansion is then added to form the PTV

"Integrated Target Volume"

- Creative solution to the organ motion problem developed at MDAH
- Two planning scans: one with a full and one with an empty bladder
- Scans are fused
- *Integrated target volume* (ITV) is drawn on the *full* bladder scan (encompassing the cuff and parametria on both scans)
- ITV is expanded by 0.5 cm $\rightarrow$ PTV_{ITV}



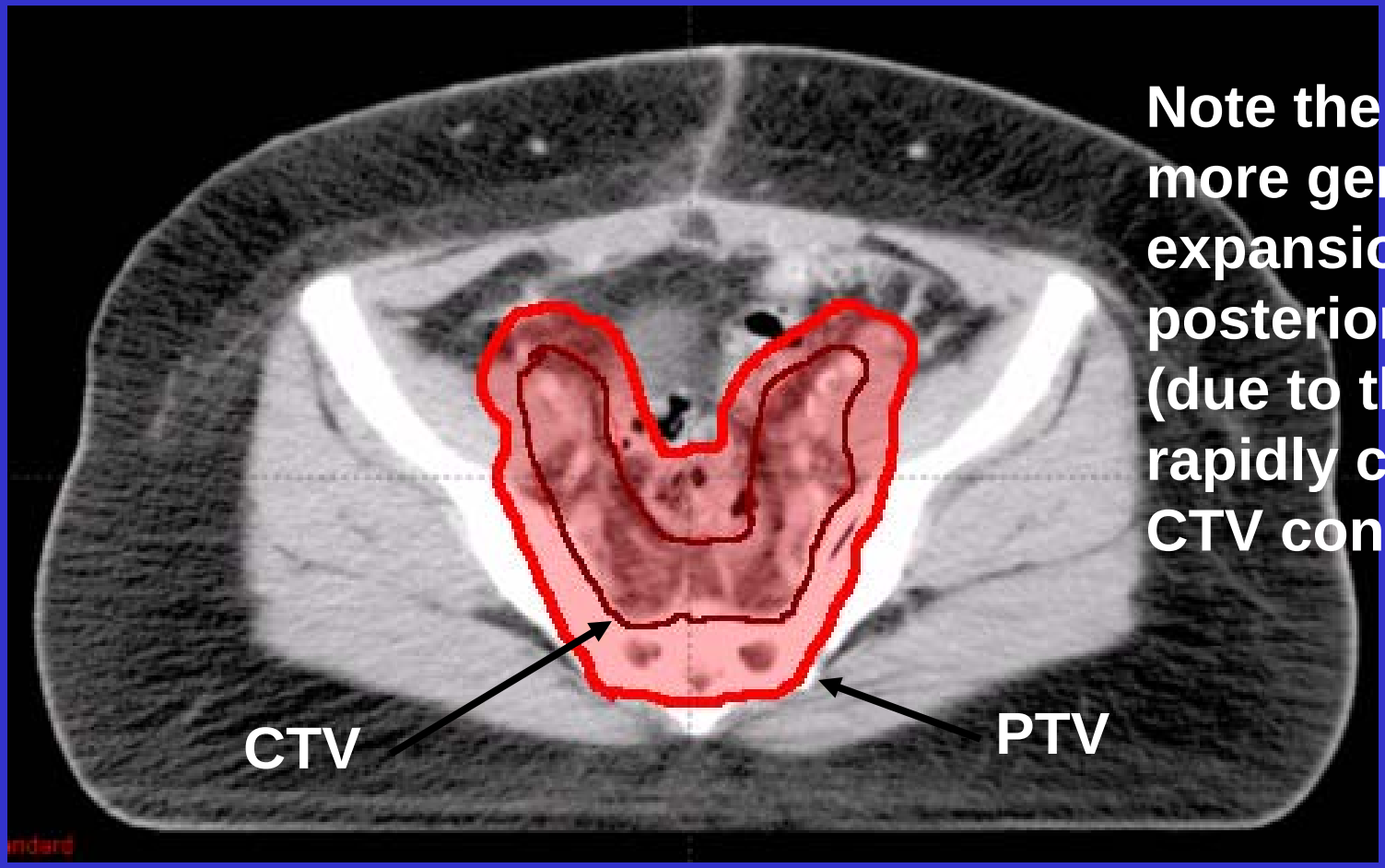
Jhingran A, et al. (MD Anderson)
Endometrial Cancer: Case Study
Chapter 23.2
IMRT: A Clinical Perspective BC Decker 2005

Cautionary Note

Avoid contouring the PTV directly

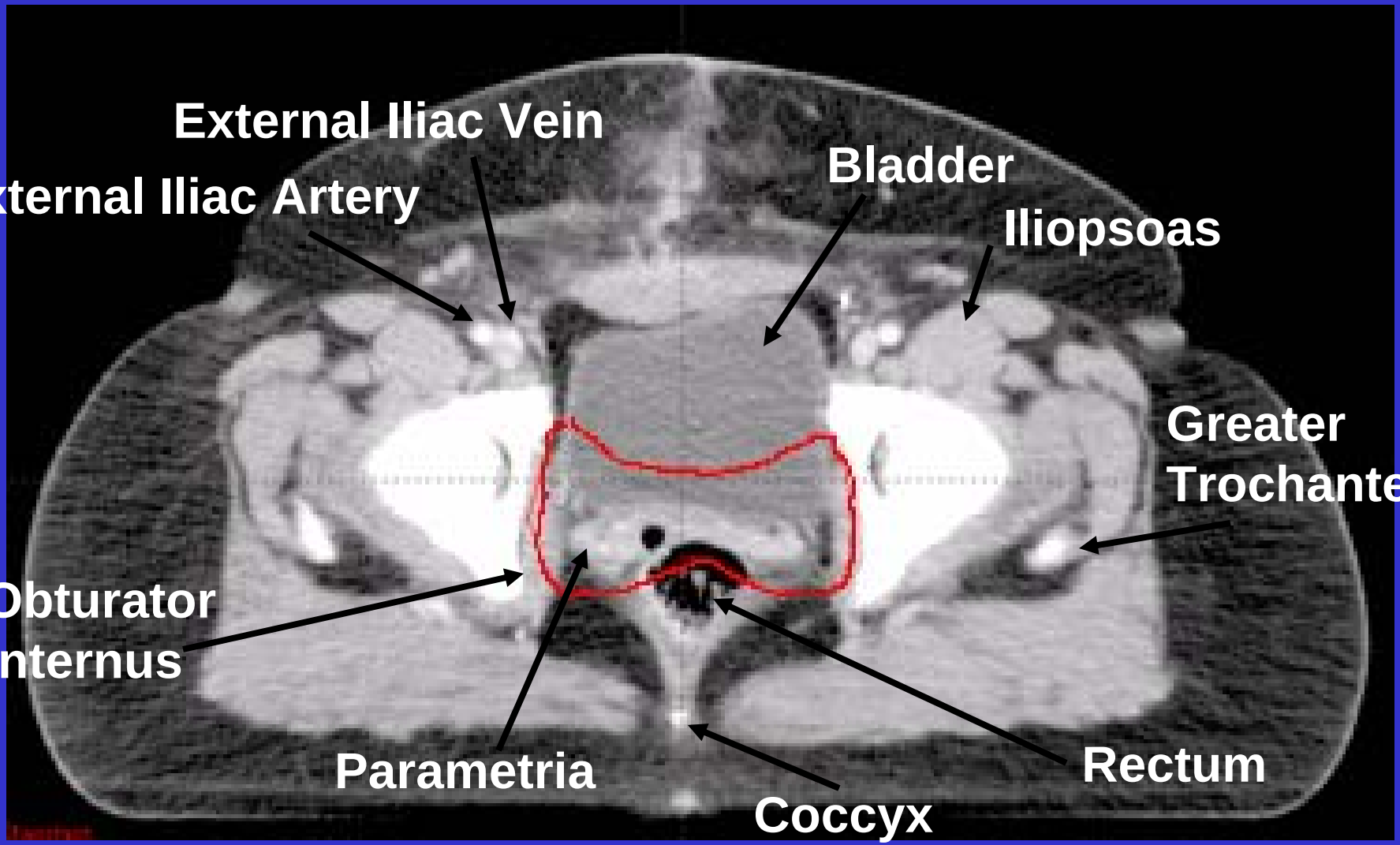
CTV-PTV is a 3-D expansion!!!

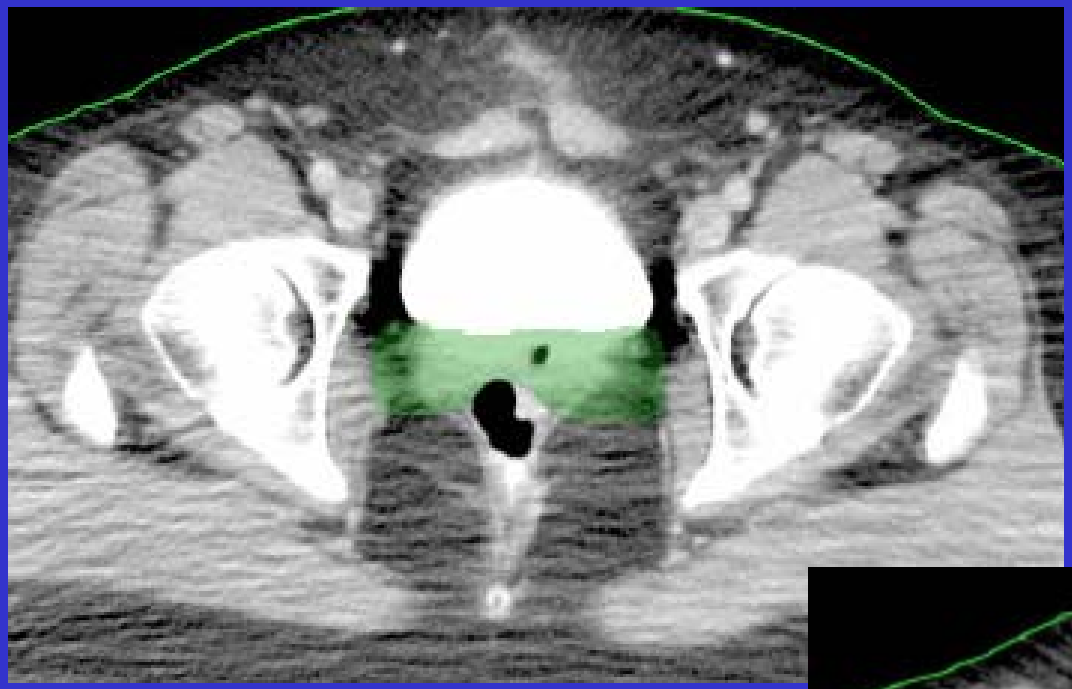
Not always 1 cm on each axial slice



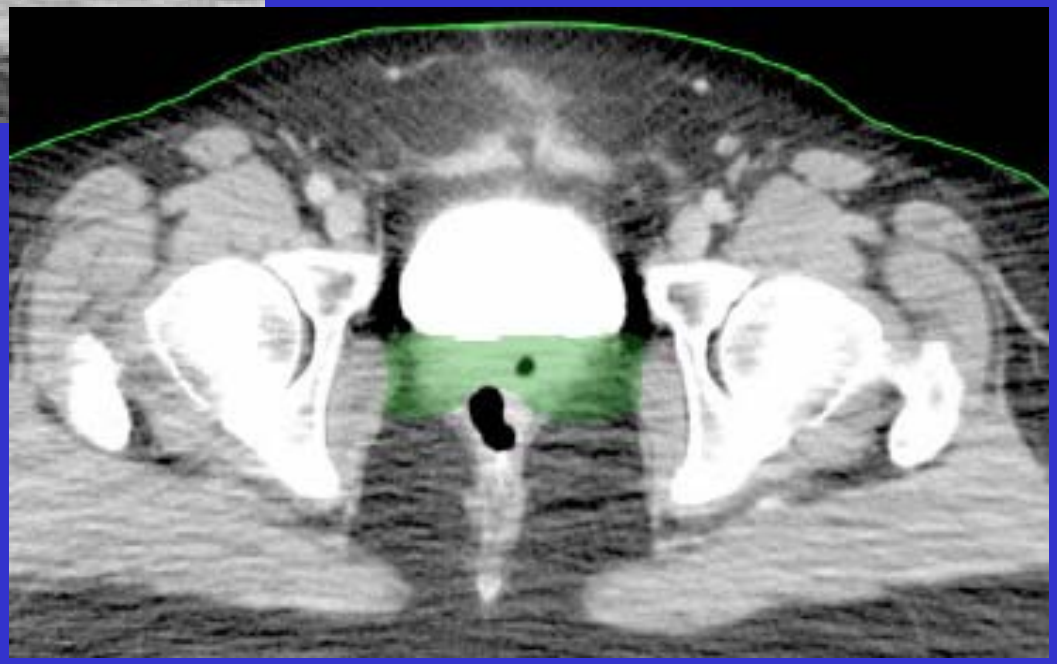
Note the more generous expansion posteriorly (due to the rapidly changing CTV contour)

Inferiorly, the CTV “bow tie” appearance becomes more pronounced

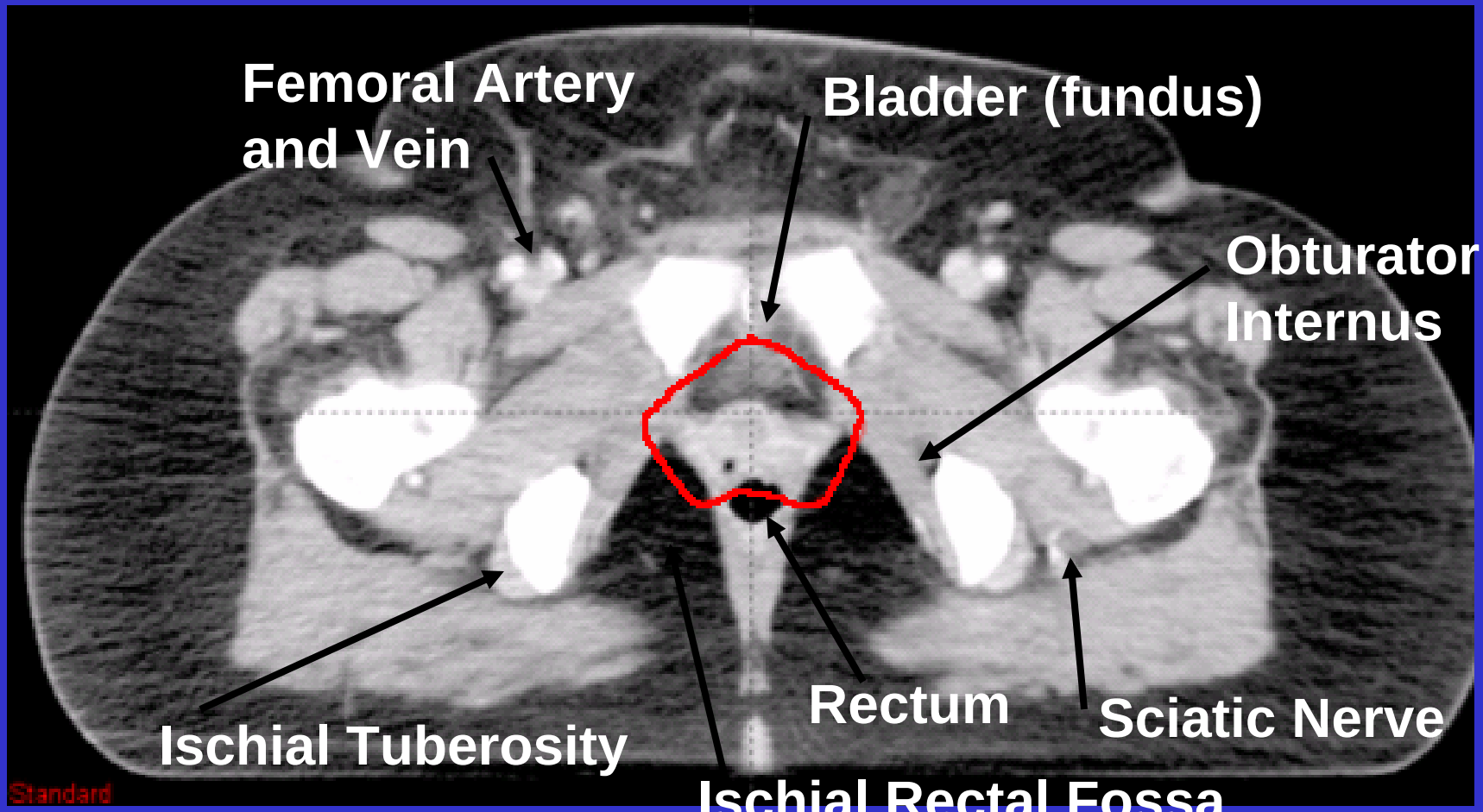




RTOG Atlas
Much tighter



CTV gradually transitions from a “bow tie” to cylindrical shape

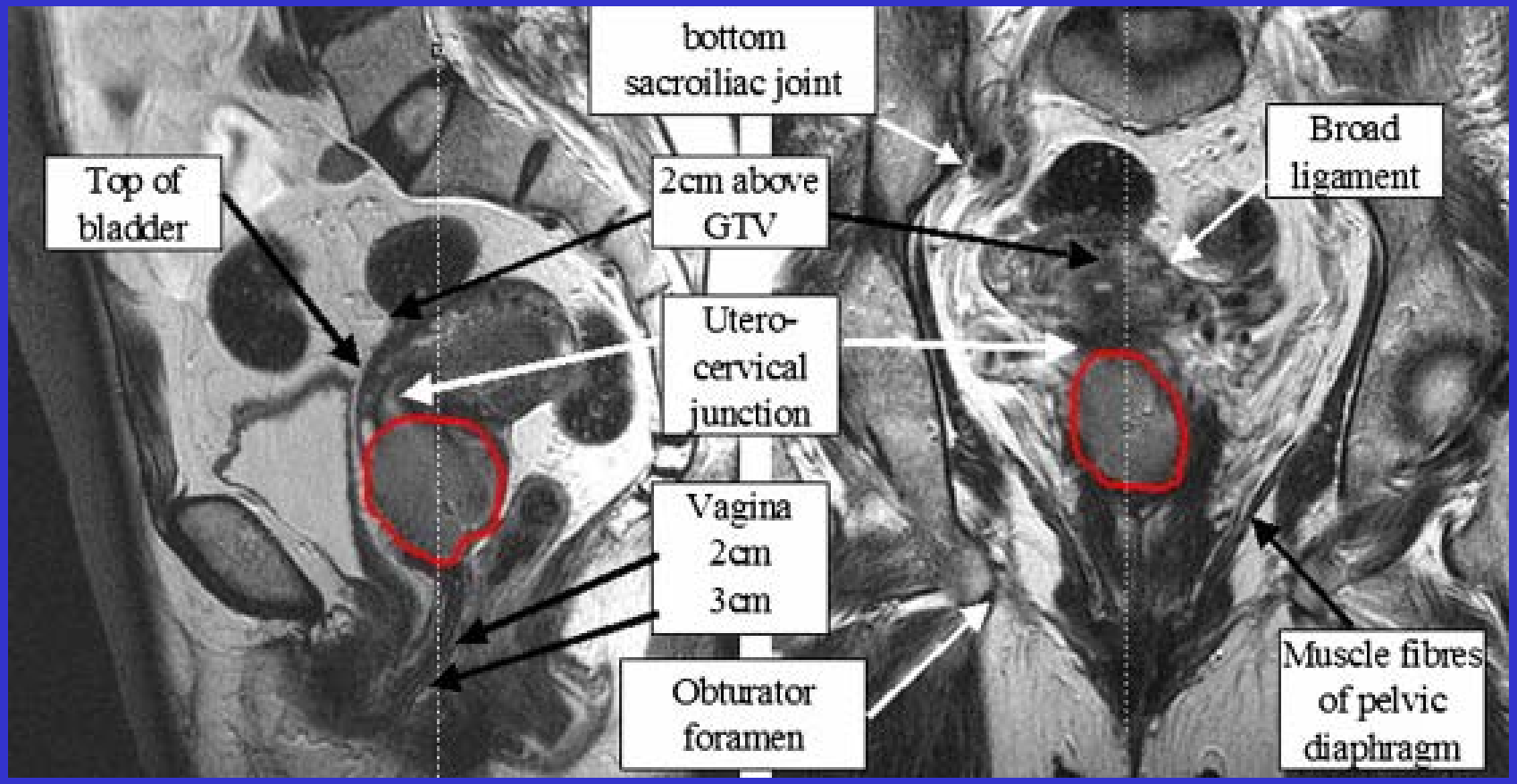


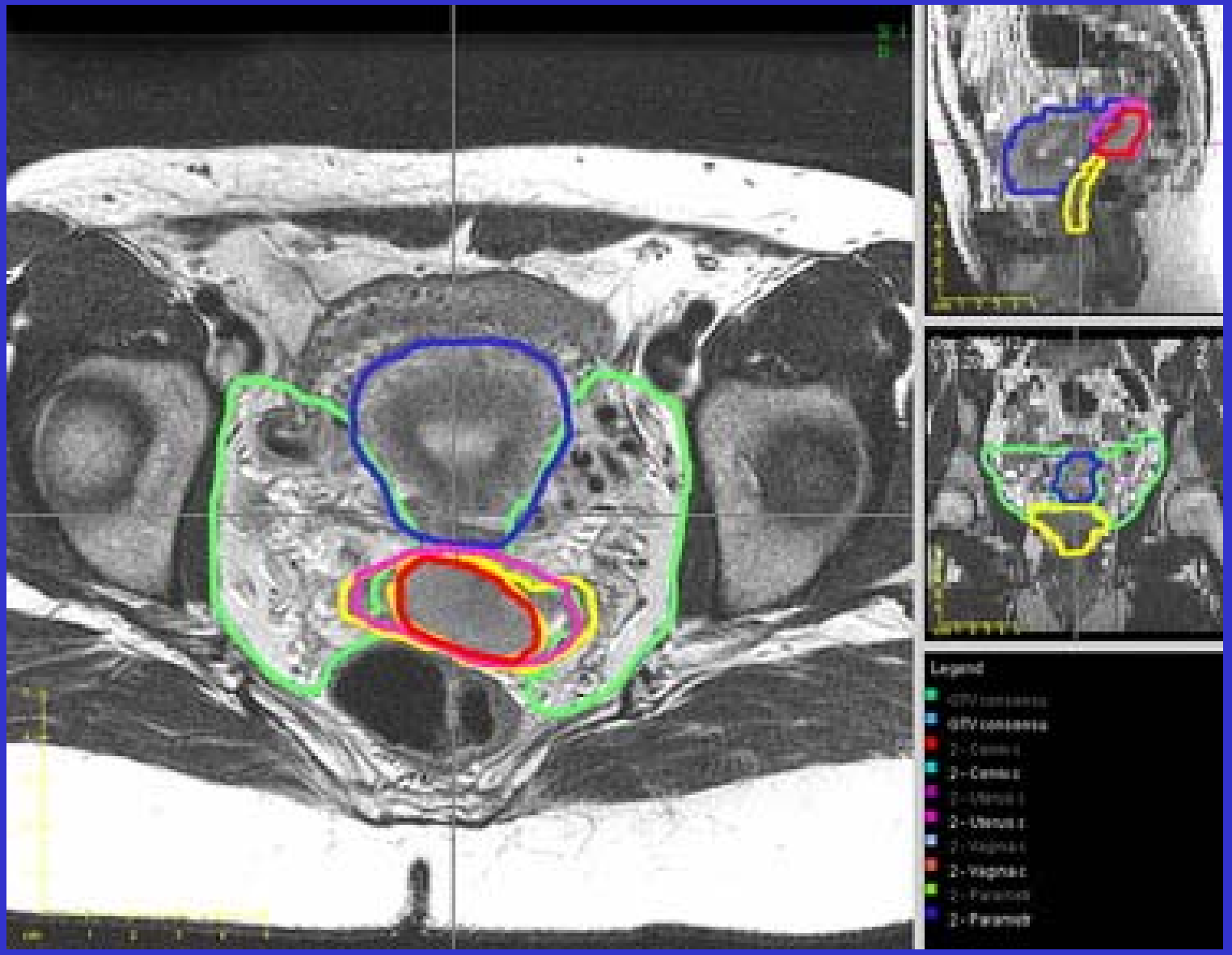
Intact Cervix

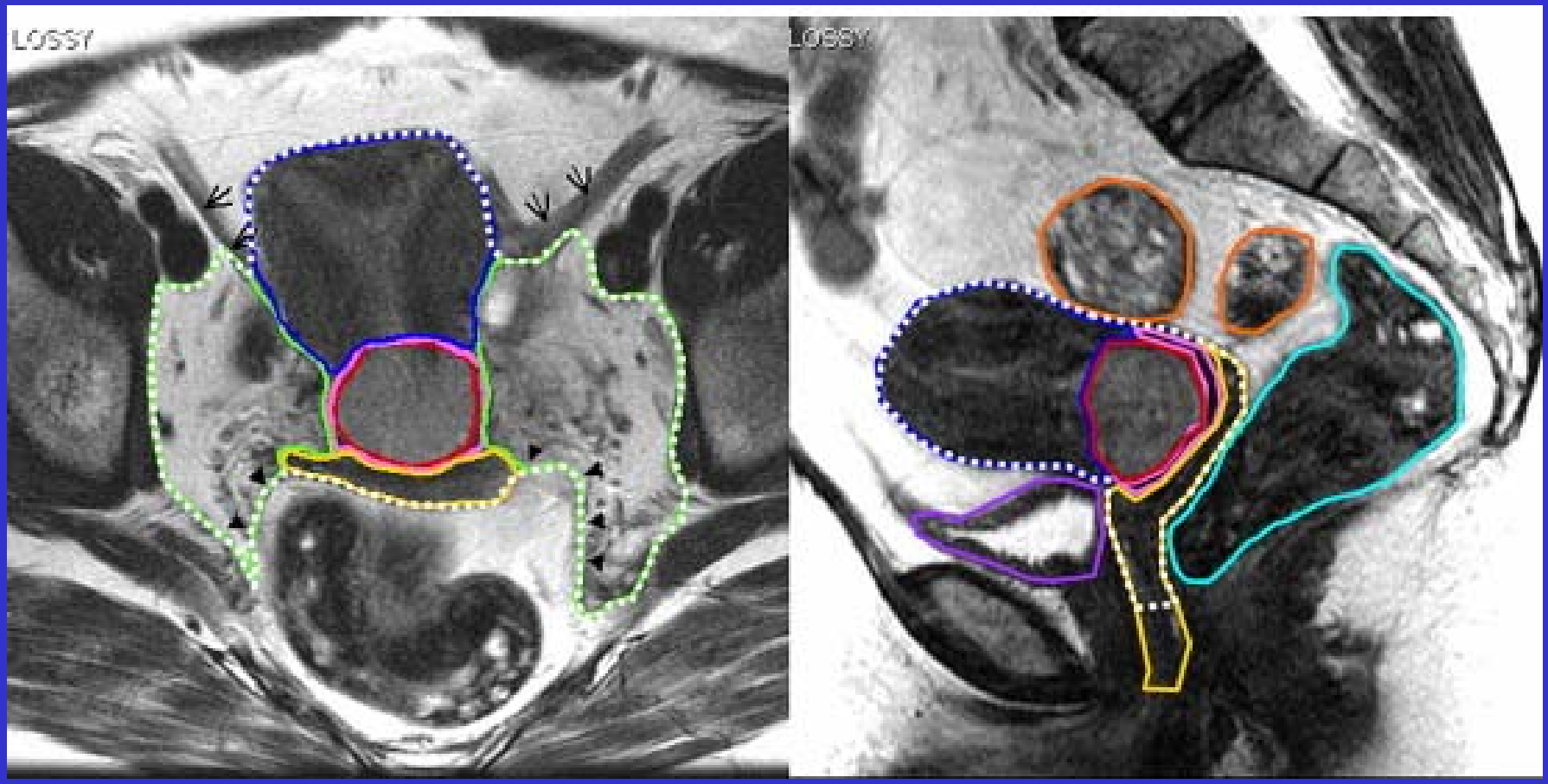
- More challenging process
- Much of the problem is that CT is not the ideal imaging approach for such patients
- Some centers insist on MRI

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.[†], Lorraine Portelance M.D.[‡], Carien Creutzberg M.D., Ph.D.[§], Ina M. Jürgenliemk-Schulz M.D., Ph.D.[||], Arno Mundt M.D.[¶], Loren K. Mell M.D.[¶], Nina Mayr M.D.[**], Akila Viswanathan M.D.[††], Anuja Jhingran M.D.[‡‡], Beth Erickson M.D.[§§], Jennifer De Los Santos M.D.[||||], David Gaffney M.D., Ph.D.[¶¶], Catheryn Yashar M.D.[¶], Sushil Beriwal M.D.[***], Aaron Wolfson M.D.[†††], Alexandra Taylor F.R.C.R.[‡‡‡], Walter Bosch Ph.D.[§§§], Issam El Naqa Ph.D.[§§§], Anthony Fyles M.D.[*], and Gyn IMRT Consortium.




Legend
GTV consensus
2 - Cervix
2 - Uterus
2 - Vagina
2 - Parametr


LOSSY
LOSSY

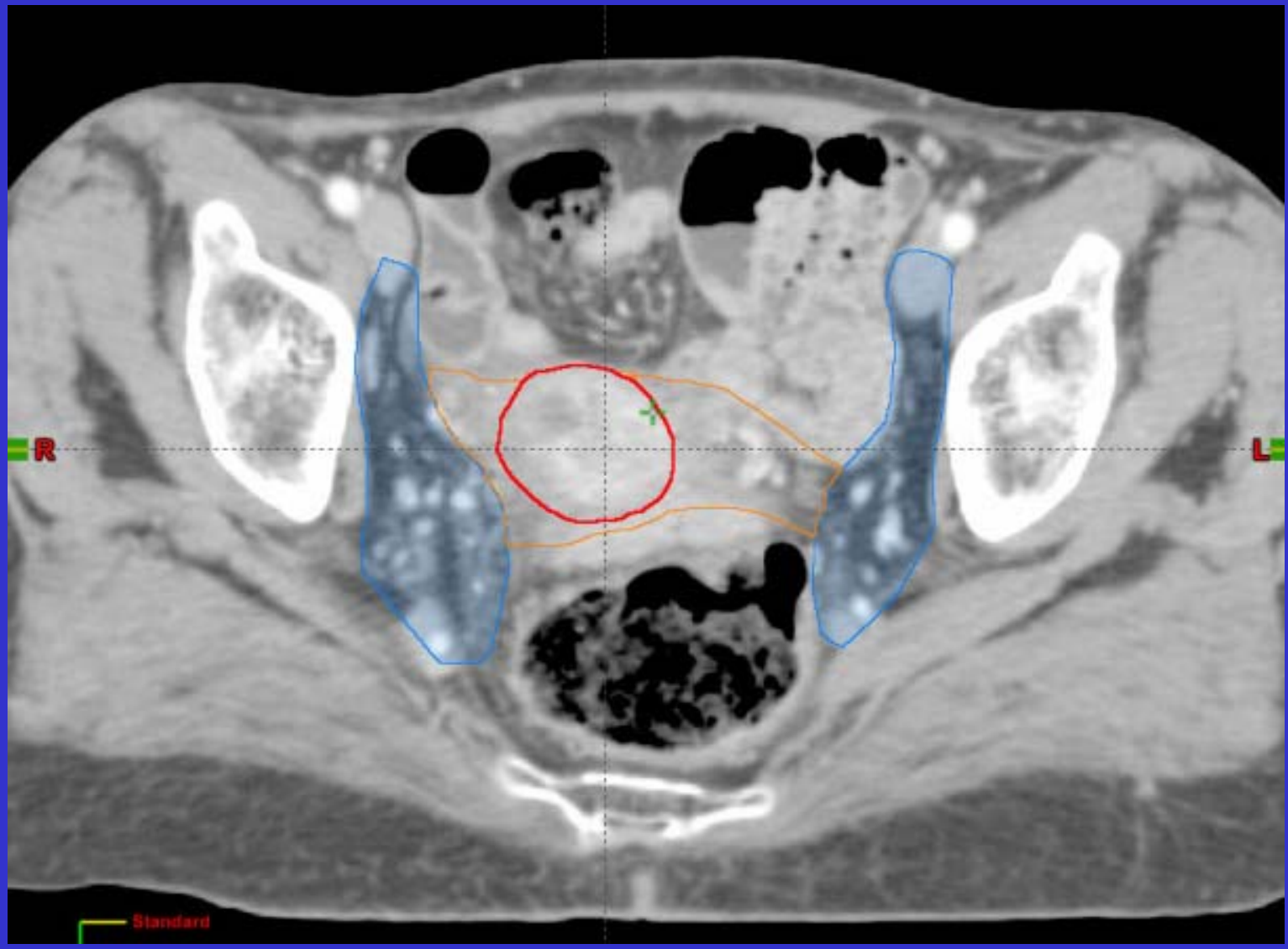
Intact Cervix

- What is needed is a CT-based atlas* for target delineation since obtaining a MRI may be difficult

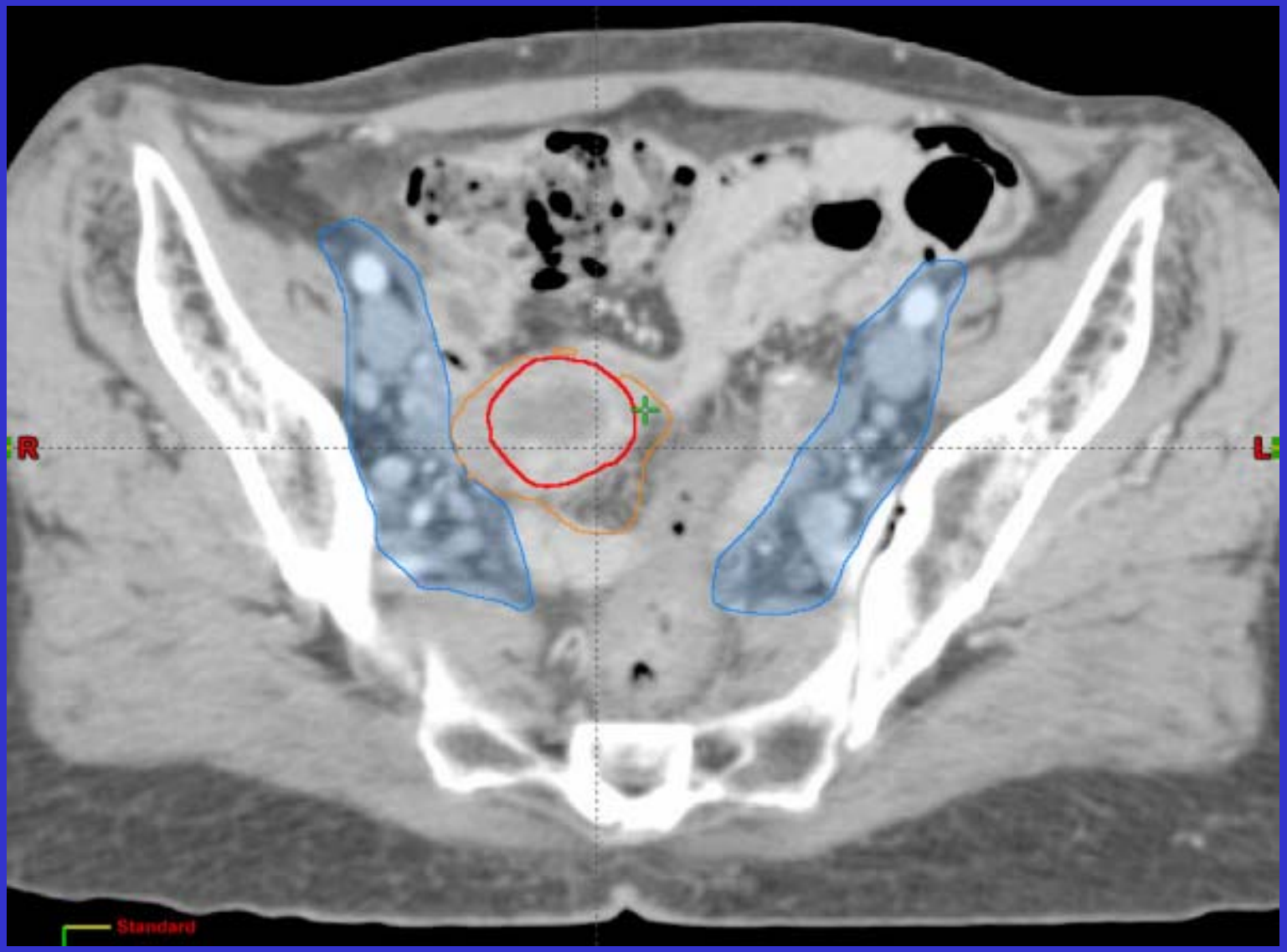
- MRI is also needed at the time of brachytherapy and two MRIs may not be approved

*under development

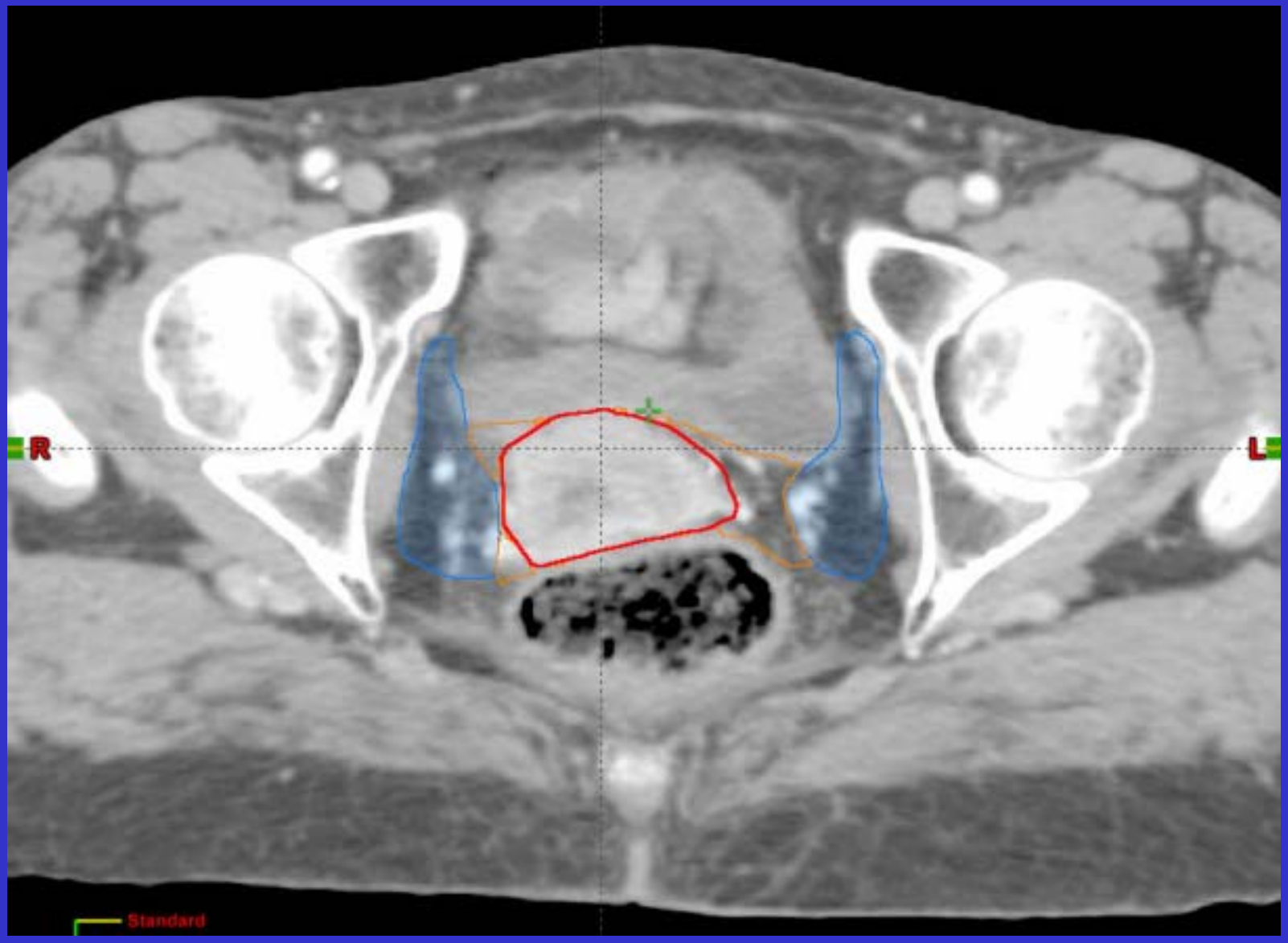
UCSD Approach



UCSD Approach



UCSD Approach



Intact Cervix UCSD Approach

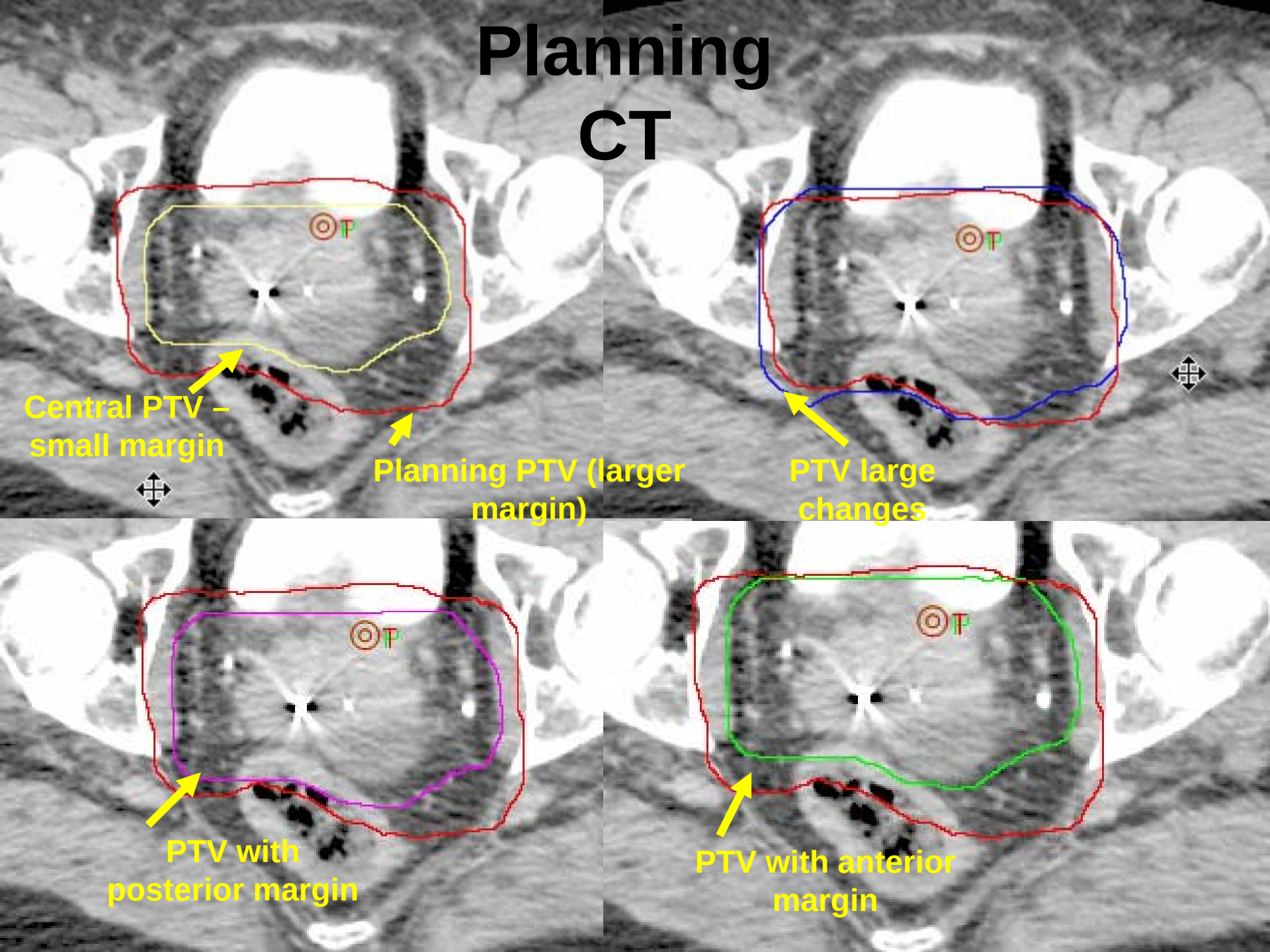
Currently, generating 4 plans for each patient with various asymmetrical margins

- Tight margins (0.5 cm)
- More generous anterior margin (1.2 cm)
- More generous posterior margin (1.2 cm)
- Very generous in all directions (1.5 cm)

At the machine, the best plan is selected for treatment using CBCT

So far, the breakdown is:

- 40% tight margins
- 25% generous anterior
- 25% generous posterior
- 10% very generous in all directions


Planning CT
Central PTV – small margin
Planning PTV (larger margin)
PTV large changes
PTV with posterior margin
PTV with anterior margin

Intact Cervix

- Maybe not ready for prime time
- Focus should be more on the postoperative patient for now

Target Delineation

- Step 4 Identify and contour normal tissues
- Controversial which normal tissues to include
- No consensus even among experts

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: pelvic bones

Conclusions

Target volume definition is a very important and time-consuming aspect of gynecologic IMRT

Knowledge of normal anatomy and patterns of drainage essential in optimal target delineation

UCSD Center for Advanced Radiotherapy Technologies (CART)