



Associazione  
Italiana  
Radioterapia  
Oncologica

## **Volumi clinici nell'irradiazione delle neoplasie ginecologiche**

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**XXII CONGRESSO  
NAZIONALE AIRO**  
Roma, 17-20 novembre 2012

# Endometrial carcinoma

## Postop - RT:

## Meta-analysis

# Adjuvant radiotherapy for stage I endometrial cancer: systematic review and meta-analysis

Study	Methods	Participants	Interventions	Outcomes	Notes	Allocation concealment
Aalders 1980	Methods of randomisation not specified. Attrition rate and application of intention-to-treat analysis were not mentioned	Patients with stage I endometrial cancer following TAH and BSO. Also included patients with stage Ib and grade 1 tumour	All had intravaginal radium. Intervention group received further pelvic RT but not the control group. Follow-up was 3–10 years	Pelvic RT reduced vaginal and pelvic recurrences (1.9% versus 6.9%, $P < 0.001$ ) but not overall survival rate	Only patients with grade 3 and stage 1c tumour might have benefited from pelvic RT	B
GOG study	A balanced block randomisation scheme was used. Fifty-six women were excluded from the intention-to-treat analysis on the basis that they were ineligible either because of inadequate staging or because of histology or FIGO stage	Patients with stage Ib and 1c, also IIa (occult) and IIb (occult) and had TAH and BSO and selective bilateral pelvic, and paraaortic lymphadenectomy with removal of any enlarged or suspicious nodes	Patients were randomised to either whole pelvic RT or no additional therapy. Median follow-up was 56 months with 9% followed for <2 years	Pelvic RT reduced pelvic and vaginal recurrences but not the overall survival as pelvic recurrences were often effectively treated with second-line therapy		A
PORTEC	Multicentre RCT. Centre-blocked randomisation by telephone was done at the trial office with variable block sizes and was stratified by radiation oncology centre and depth of myometrial invasion. Intention-to-treat analysis was used	Patients with stage I endometrial carcinoma (grade 1 with deep myometrial invasion, grade 2 with any invasion or grade 3 with superficial invasion). All had TAH and BSO without lymphadenectomy	Patients were randomised to pelvic RT or no further treatment. Intravaginal brachytherapy was not given. Follow-up was 5–7 years	Pelvic RT reduced locoregional recurrence (4% versus 14%, $P < 0.001$ ) but not overall survival or endometrial cancer-related death. Treatment-related complications occurred in 25% of RT patients and in 6% of the control group		A
Soderini 2003	Only an abstract. Methods of randomisation not specified. Attrition rate and application of intention-to-treat analysis were not mentioned	Patients with intermediate risk (Ib grades 2–3 to 1c) endometrioid endometrium carcinoma. All patients had TAH-BSO, pelvic–paraortic lymphadenectomy and peritoneal washings	Patients were randomised to pelvic RT 50 Gy or no RT	Recurrence rate was lower in RT arm although not statistically significant	Only an abstract is available	B

# Adjuvant radiotherapy for stage I endometrial cancer: systematic review and meta-analysis

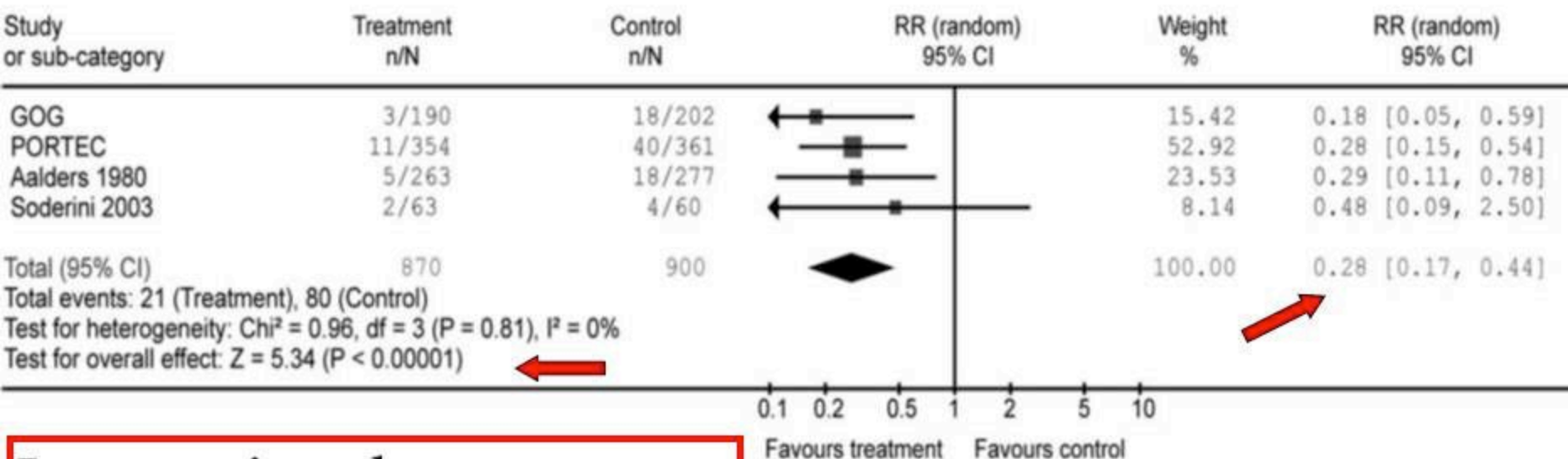
reduced

RR of 0.28

local regional recurrence

B

Review: Adjuvant radiotherapy for stage I endometrial cancer  
Comparison: 01 Figure 1: All Stage I patients: External beam radiotherapy vs. No external beam radiotherapy  
Outcome: 02 Figure 1b: Locoregional recurrence



Locoregional recurrence.

Absolute risk reduction: 6%



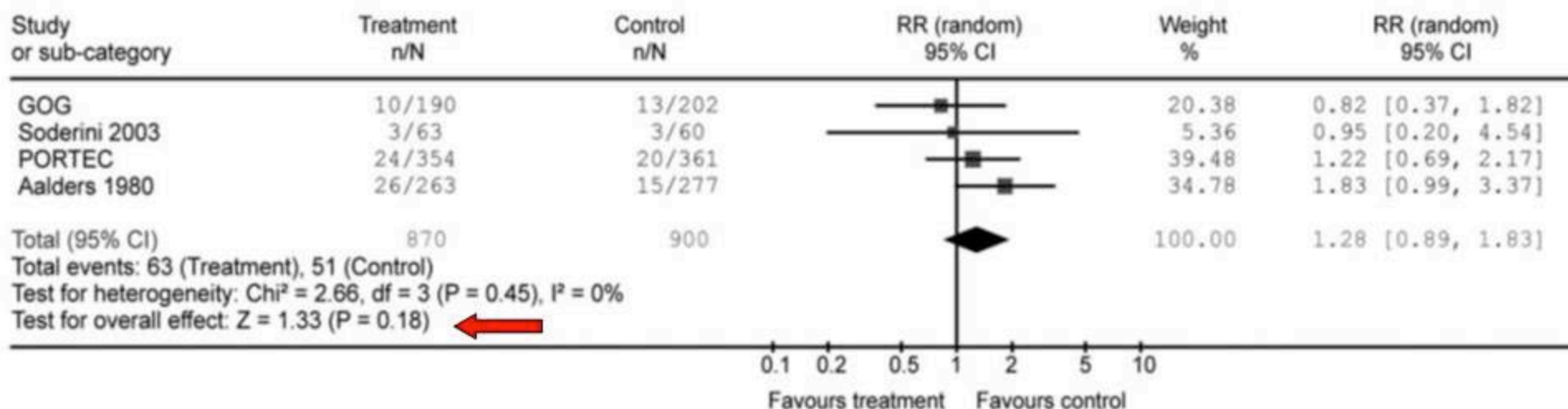
# Adjuvant radiotherapy for stage I endometrial cancer: systematic review and meta-analysis

RR of 1.28 for the treatment

$P = 0.18$

C

Review: Adjuvant radiotherapy for stage I endometrial cancer  
Comparison: 01 Figure 1: All Stage I patients: External beam radiotherapy vs. No external beam radiotherapy  
Outcome: 03 Figure 1c: Distant recurrence



Distant recurrence.

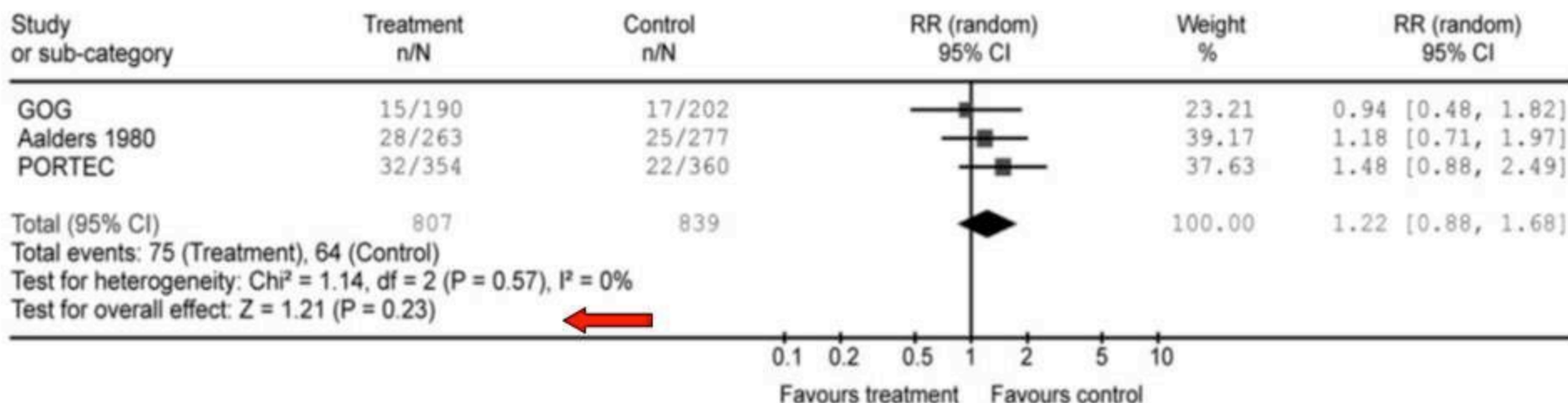
# Adjuvant radiotherapy for stage I endometrial cancer: systematic review and meta-analysis

RR of 1.22

$P = 0.57$

D

Review: Adjuvant radiotherapy for stage I endometrial cancer  
Comparison: 01 Figure 1: All Stage I patients: External beam radiotherapy vs. No external beam radiotherapy  
Outcome: 04 Figure 1d: Endometrial carcinoma-related death



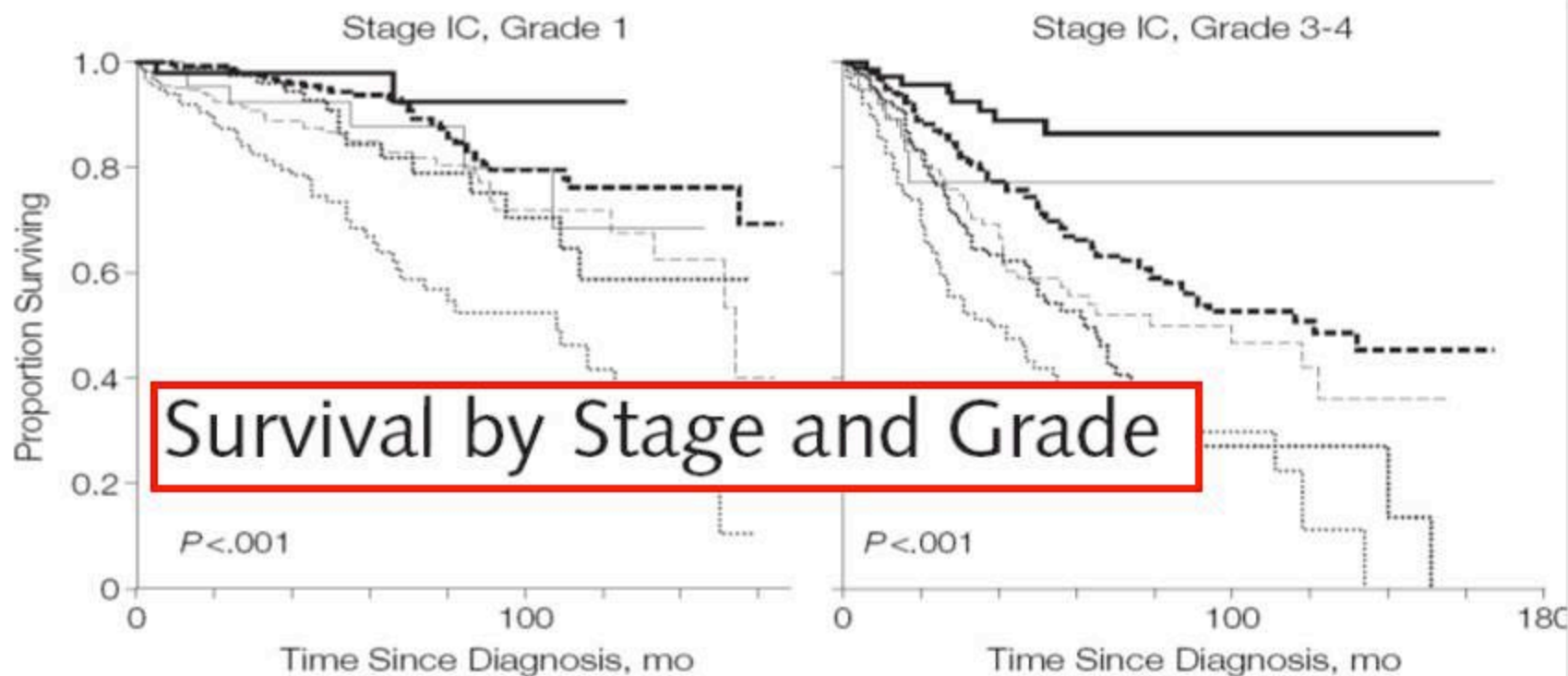
Endometrial carcinoma-related death.

## **Adjuvant radiotherapy for stage I endometrial cancer: systematic review and meta-analysis**

In conclusion, the data showed that external beam pelvic radiotherapy should be considered in patients with multiple high-risk factors including stage 1c and grade 3 since it reduced locoregional recurrence with a trend towards reduction in deaths from all causes and endometrial cancer. However, it carries an inherent risk of damage and toxicity and should be avoided in stage 1 endometrial cancer patients with no high-risk factors.

# Frequency and Effect of Adjuvant Radiation Therapy Among Women With Stage I Endometrial Adenocarcinoma

SEER



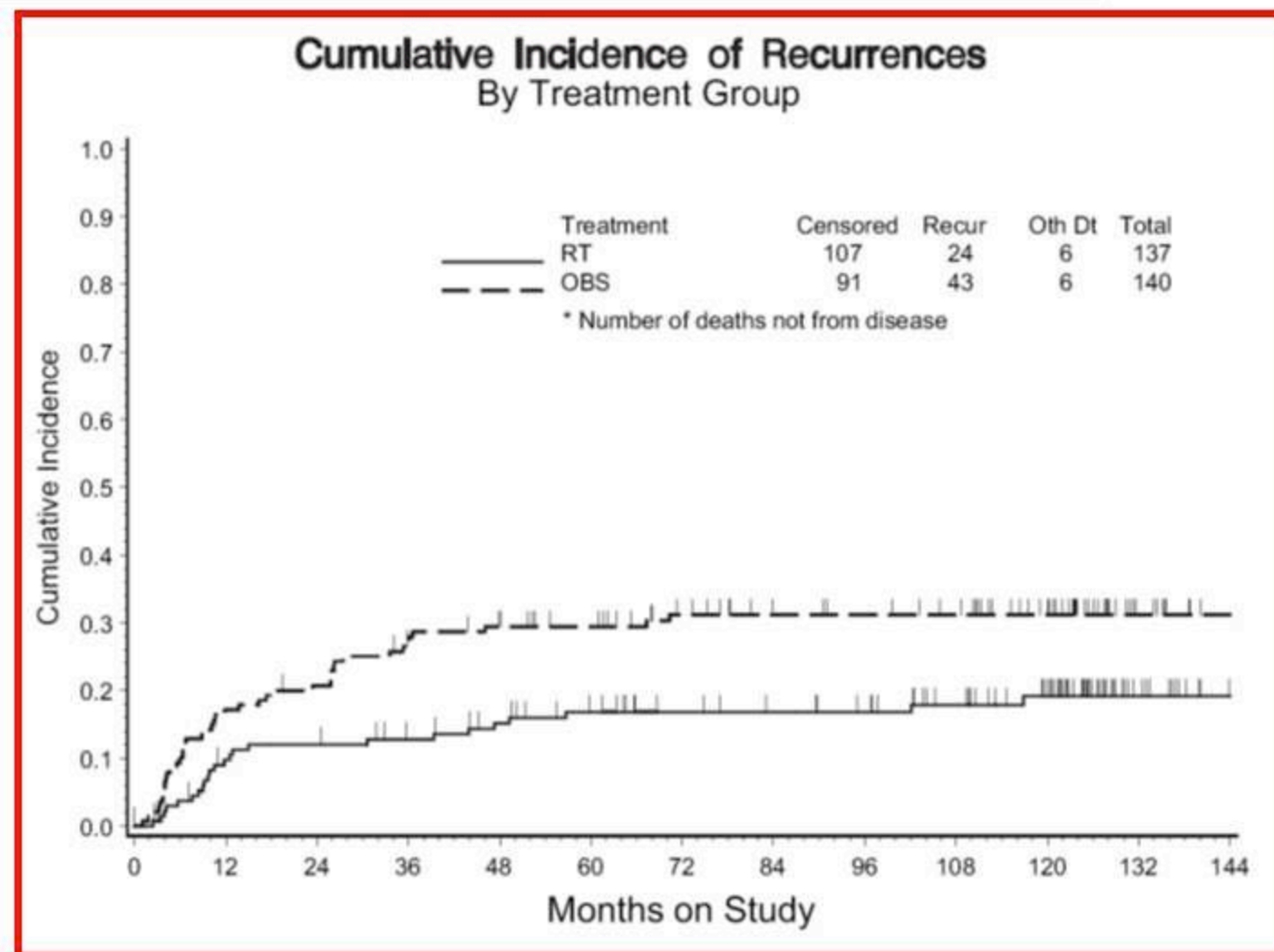
No. at Risk													
Radiation	435	312	199	96	45	16	555	316	154	77	30	10	
No Radiation	459	270	153	76	31	9	325	142	69	26	11	4	

— Radiation  
— No Radiation

Cancer of the Cervix:  
postoperative pelvic  
irradiation



# A PHASE III RANDOMIZED TRIAL OF POSTOPERATIVE PELVIC IRRADIATION IN STAGE IB CERVICAL CARCINOMA WITH POOR PROGNOSTIC FEATURES: FOLLOW-UP OF A GYNECOLOGIC ONCOLOGY GROUP STUDY



**A PHASE III RANDOMIZED TRIAL OF POSTOPERATIVE PELVIC  
IRRADIATION IN STAGE IB CERVICAL CARCINOMA WITH POOR  
PROGNOSTIC FEATURES: FOLLOW-UP OF A GYNECOLOGIC  
ONCOLOGY GROUP STUDY**

Table 2. Site of first recurrence and treatment regimen

Site	Radiation therapy ( <i>n</i> = 137)		Observation ( <i>n</i> = 140)	
	No.	%	No.	%
No evidence of disease	113	82.5	97	69.3
Recurrences	24	17.5	43	30.7
Local	19	→ 13.9	29	→ 20.7
Vagina	2		8	
Pelvis	16		19	
Vagina and pelvis	1		2	
Distal	4	2.9	12	8.6
Unknown	1	0.7	2	1.4

Cervical carcinoma:  
patterns of regional  
recurrences

**Table 66.19****CARCINOMA OF THE UTERINE CERVIX: INCIDENCE OF CENTRAL/PELVIC RECURRENCES CORRELATED WITH METHOD OF THERAPY**

Author (Reference)	Stage	Incidence of Pelvic Failures		<i>p</i> Value
		External-Beam Only	External-Beam and Intracavitary	
Hanks et al. (228)	III	33/38 (86%)	55/109 (50%)	0.0002
Montana et al. (417)	III	14/35 (40%)	12/37 (32%)	0.6725
Coia et al. (90)	I,II,III	(53%)	(22%)	<0.0100
Longsdon & Eifel <sup>a</sup> (382)	IIIB	641 (45%)	266 (24%)	<0.0001

<sup>a</sup>Five-year disease-free survival.

Modified from Stehman FR, Perez CA, Kurman RJ, et al. Uterine cervix. In: Hoskins WJ, Perez CA, Young RC, eds. *Principles and practice of gynecologic oncology*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2000:841–918.

## **PATTERNS OF REGIONAL RECURRENCE AFTER DEFINITIVE RADIOTHERAPY FOR CERVICAL CANCER**

1



Morris M, Eifel PJ, Lu J, *et al.* Pelvic radiation with concurrent chemotherapy compared with pelvic and para-aortic radiation for high-risk cervical cancer. *N Engl J Med* 1999;340:1137–1143.

2



Peters WA 3rd, Liu PY, Barrett RJ 2nd, *et al.* Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. *J Clin Oncol* 2000;18:1606–1613.

3



Rose PG, Bundy BN, Watkins EB, *et al.* Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 1999;340:1144–1153.

4



Whitney CW, Sause W, Bundy BN, *et al.* Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: A Gynecologic Oncology Group and Southwest Oncology Group study. *J Clin Oncol* 1999;17:1339–1348.

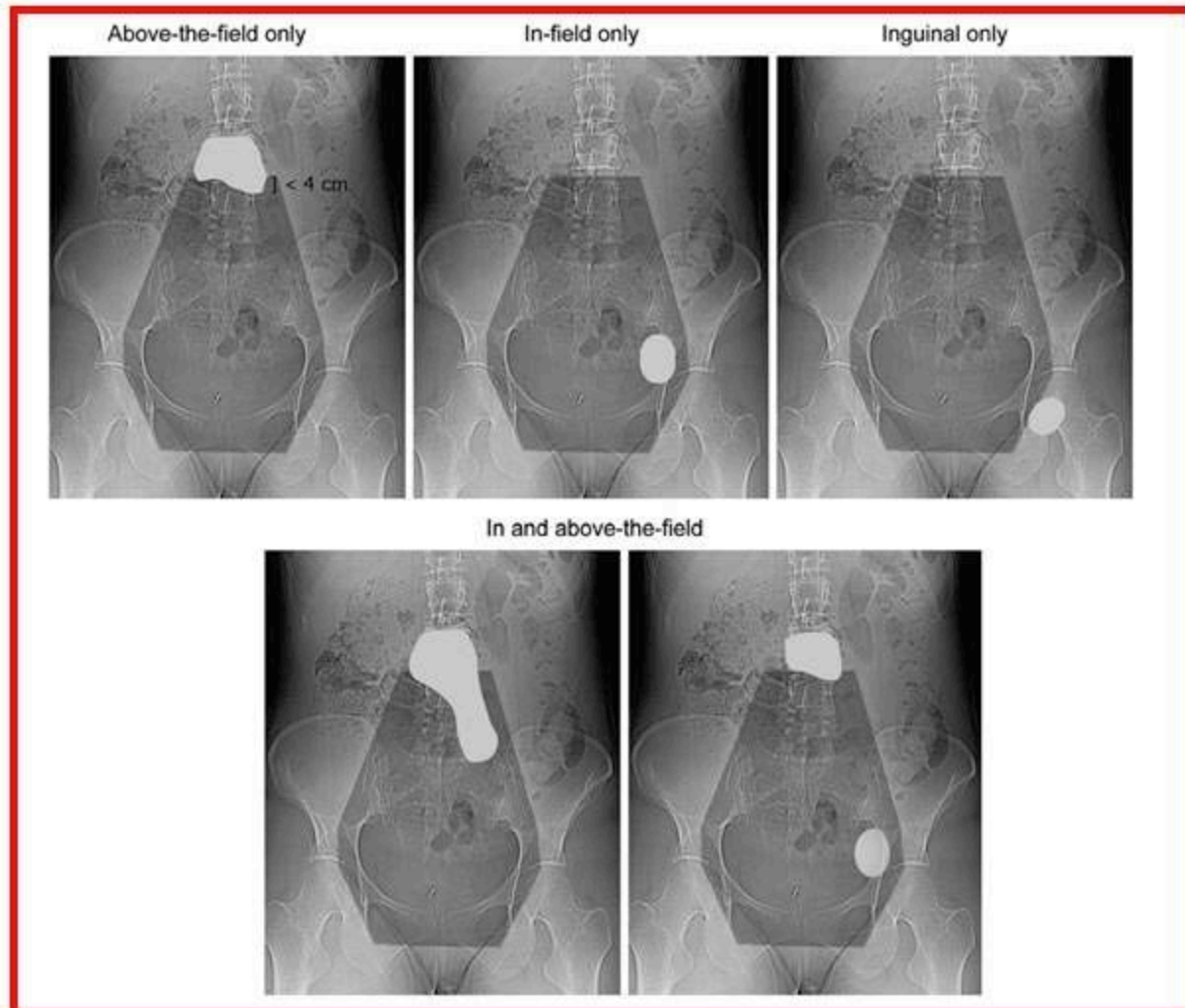
5



Wong LC, Ngan HY, Cheung AN, *et al.* Chemoradiation and adjuvant chemotherapy in cervical cancer. *J Clin Oncol* 1999;17:2055–2060.

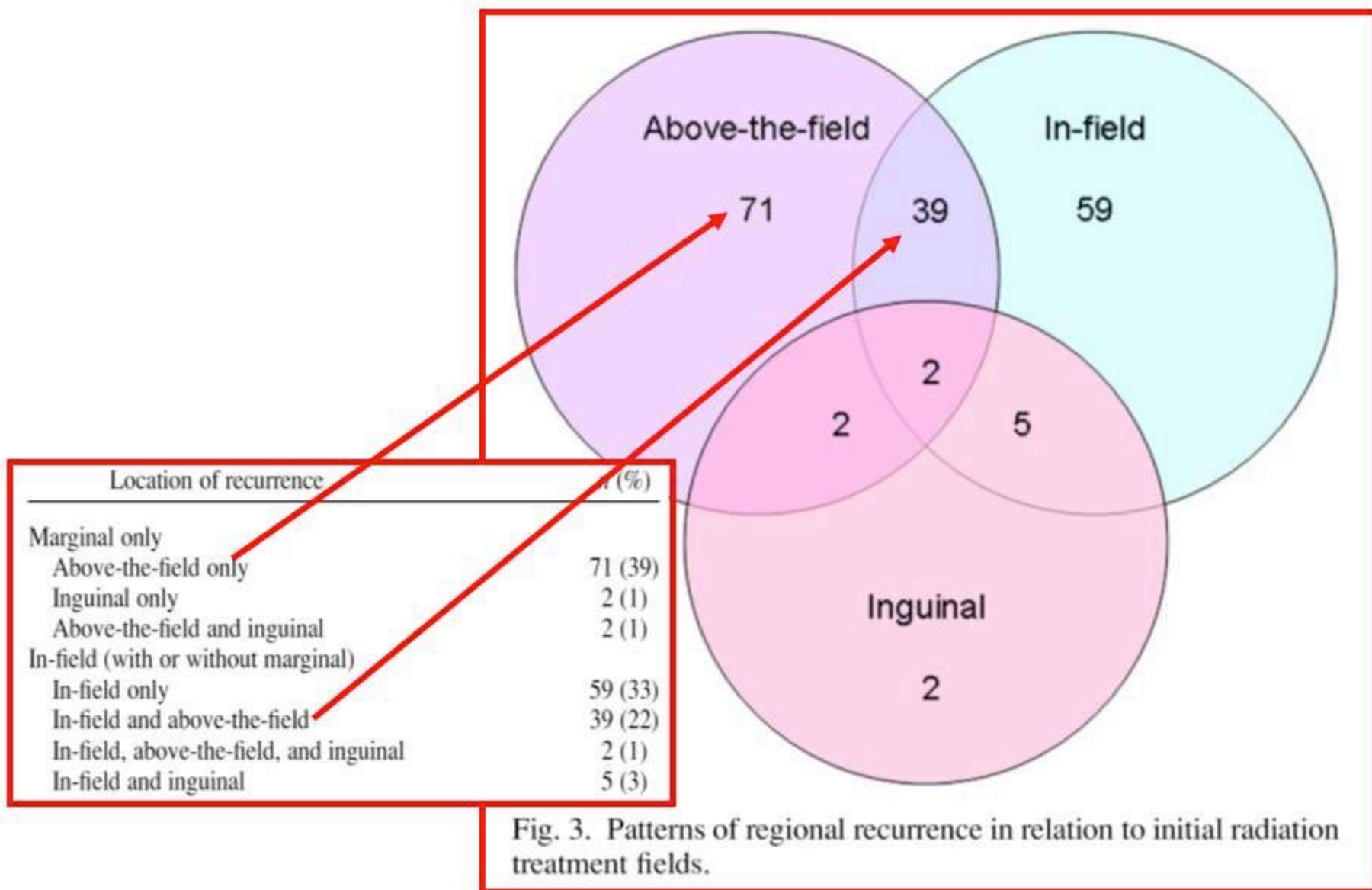


## PATTERNS OF REGIONAL RECURRENCE AFTER DEFINITIVE RADIOTHERAPY FOR CERVICAL CANCER

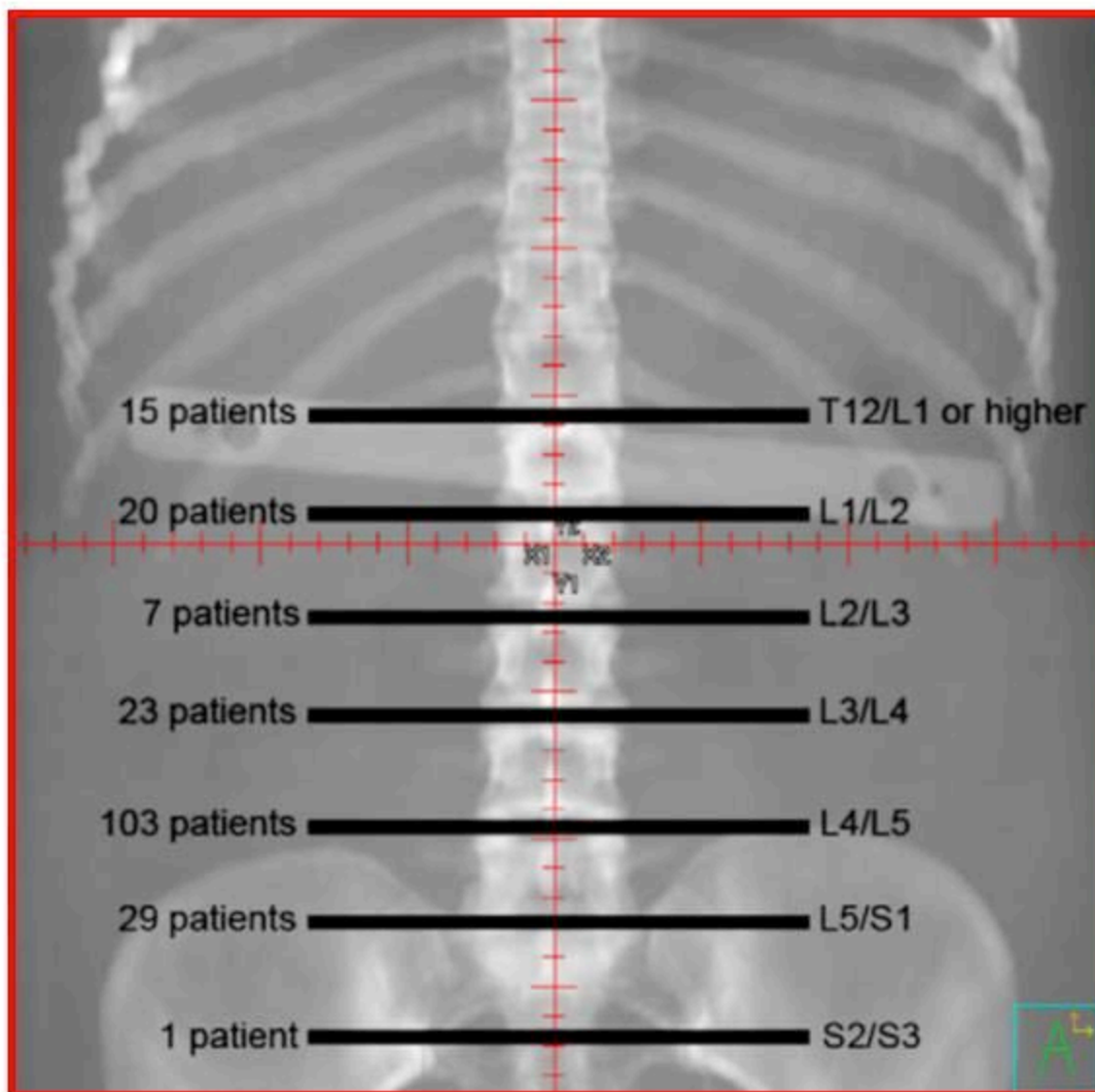


1894 pts; definitive RT; 180 regional failures  
119/180 marginal failures

## PATTERNS OF REGIONAL RECURRENCE AFTER DEFINITIVE RADIOTHERAPY FOR CERVICAL CANCER



## PATTERNS OF REGIONAL RECURRENCE AFTER DEFINITIVE RADIOTHERAPY FOR CERVICAL CANCER



# PATTERNS OF REGIONAL RECURRENCE AFTER DEFINITIVE RADIOTHERAPY FOR CERVICAL CANCER

Table 2. Correspondence between location of regional recurrences and findings on regional imaging at initial diagnosis of cervical cancer

Location of recurrence	Results of initial regional imaging, <i>n</i> (%)			Total
	Negative	Positive	Equivocal	
Above-the-field only	43 (63)	22 (32)	3 (4)	68
In-field and above-the-field	15 (39)	20 (53)	3 (8)	38
In-field only	22 (34)	37 (58)	5 (8)	64
Inguinal only	2 (100)	0 (0)	0 (0)	2
Total	82 (48)	79 (46)	11 (6)	172

$p = 0.03$ .

## PATTERNS OF REGIONAL RECURRENCE AFTER DEFINITIVE RADIOTHERAPY FOR CERVICAL CANCER

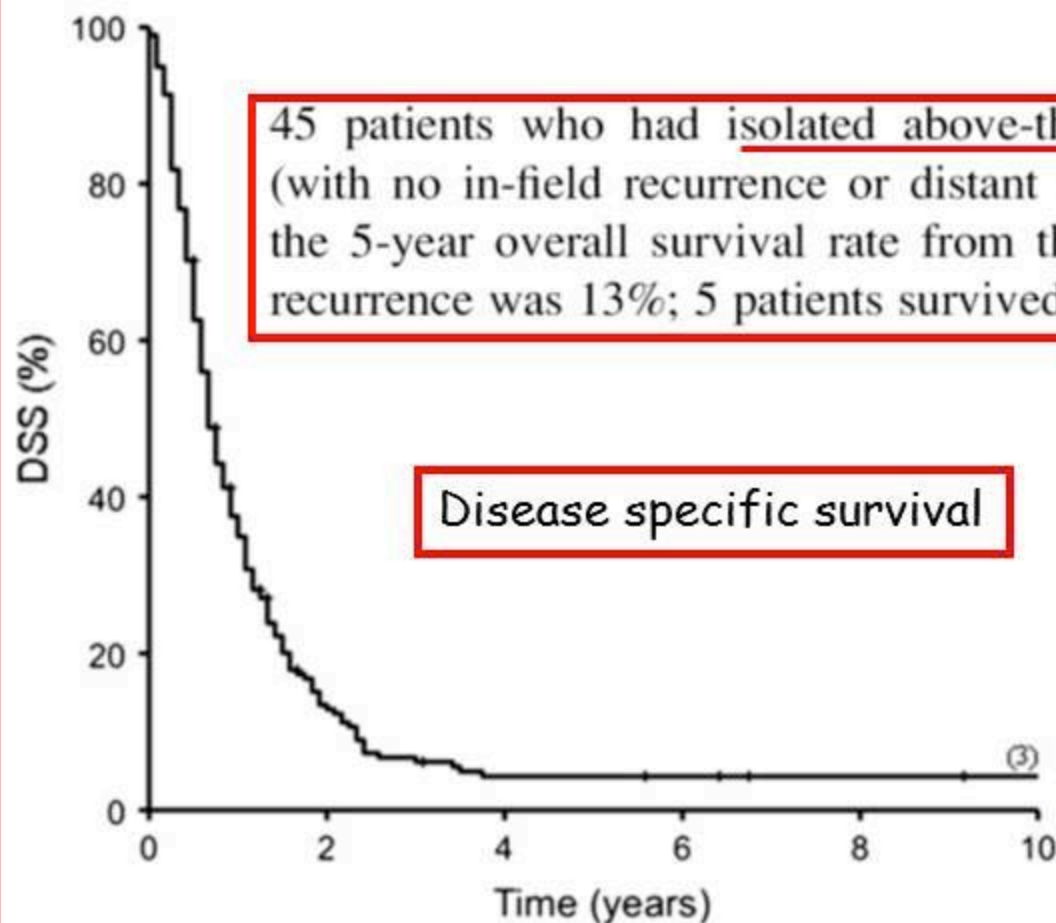


Fig. 4. Kaplan-Meier survival curve for disease-specific survival (DSS) after the diagnosis of a regional recurrence.



1 - Most regional recurrences include a component of marginal failure usually immediately above the radiation field and suggest a deficiency in target volume;

3 - Recurrences in-field suggest:

- a - deficiency in dose
- b - pretreatment staging
- c - field delineation
- d - dose escalation
- e - posttreatment surveillance

Contouring and  
nodal diffusion:  
endometrial vs.  
cervical carcinomas

**A Phase II Study of Intensity Modulated Radiation  
Therapy to the Pelvis for Postoperative Patients With  
Endometrial Carcinoma: Radiation Therapy Oncology  
Group Trial 0418**

unacceptable vaginal and nodal contouring

paravaginal tissues

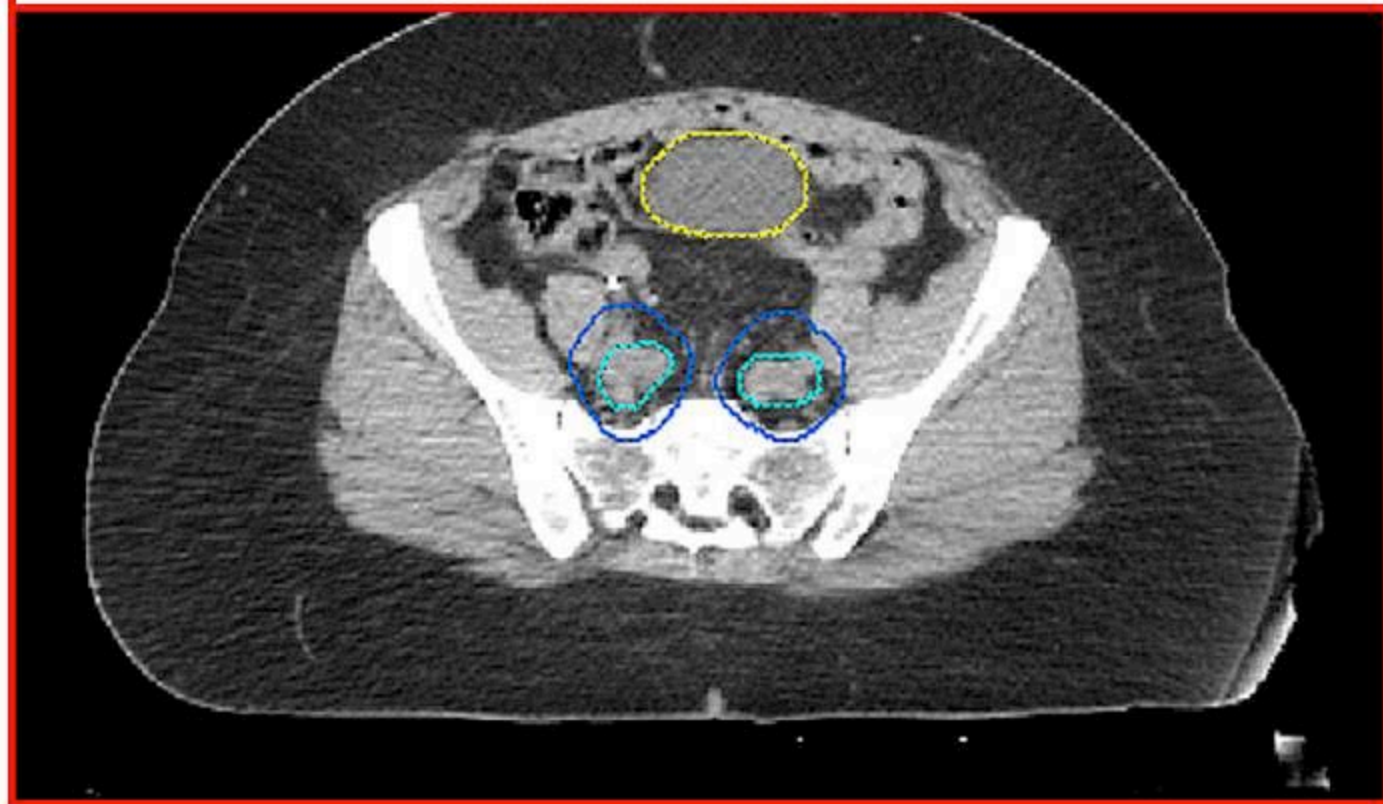
?

vaginal applicator in the vagina

**A Phase II Study of Intensity Modulated Radiation  
Therapy to the Pelvis for Postoperative Patients Wit  
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unacceptable vaginal and nodal contouring

covers only the vessels, not the entire nodal bed

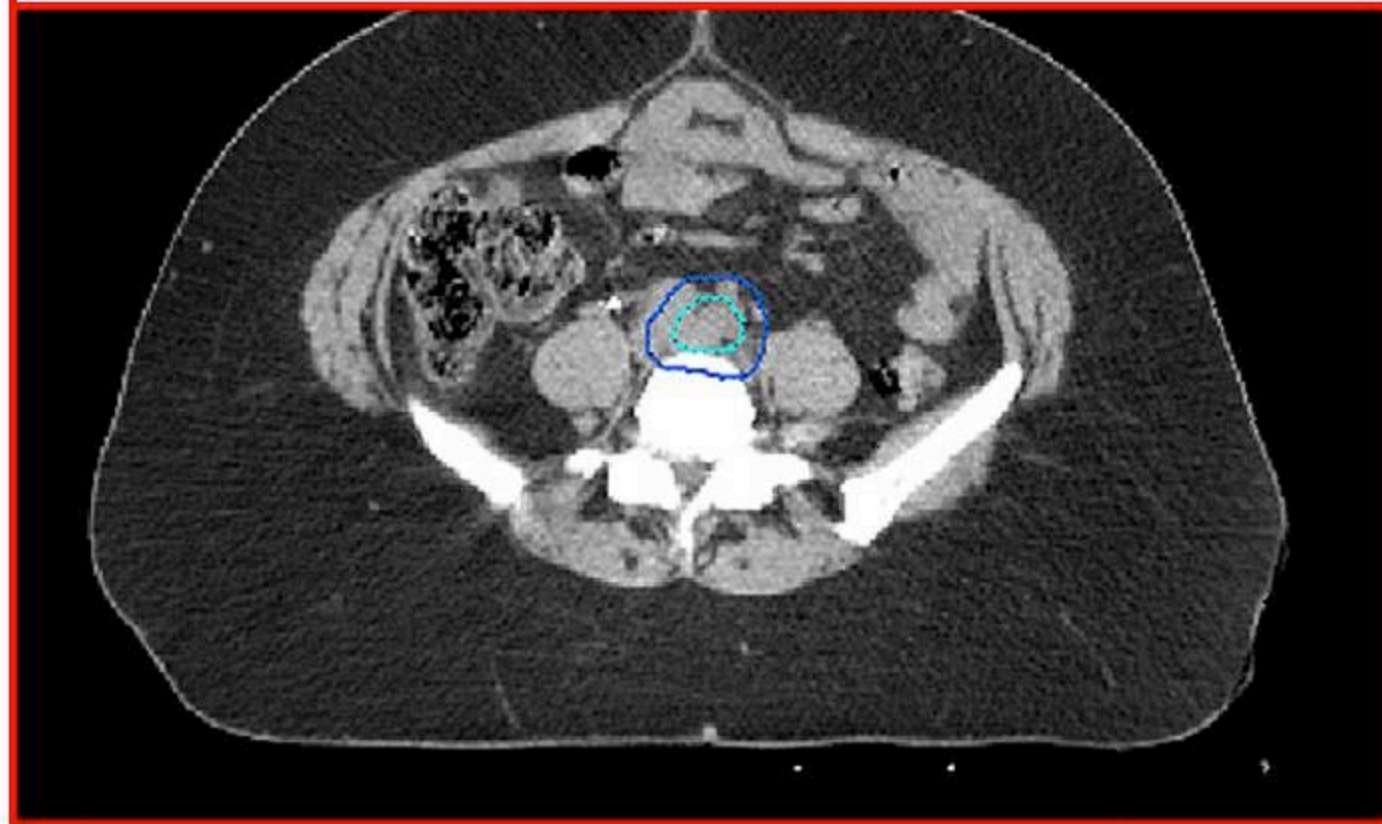




**A Phase II Study of Intensity Modulated Radiation  
Therapy to the Pelvis for Postoperative Patients With  
Endometrial Carcinoma: Radiation Therapy Oncology  
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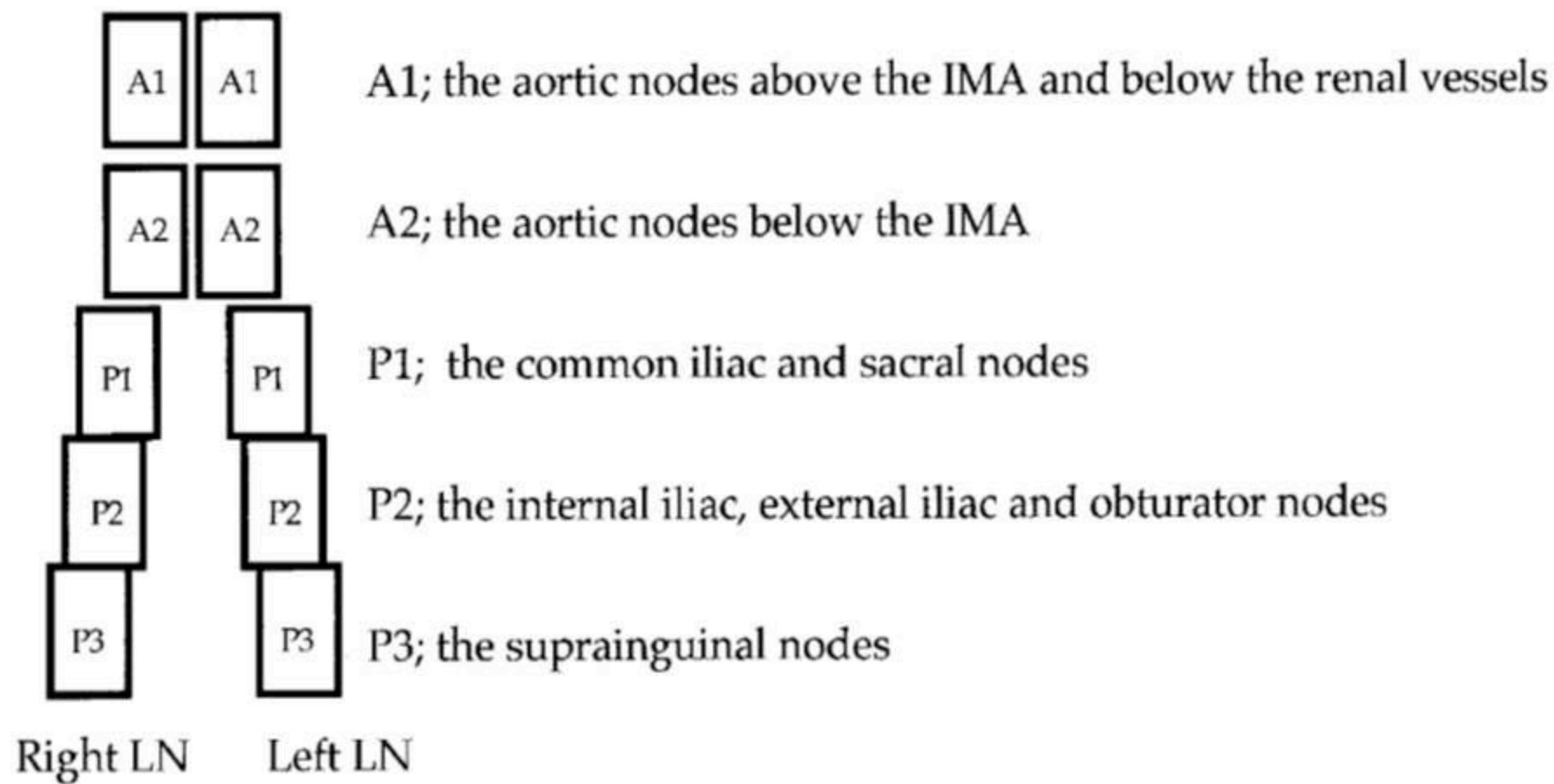
unacceptable vaginal and nodal contouring

covers only the vessels, not the entire nodal bed





## Distinct lymphatic spread of endometrial carcinoma in comparison with cervical and ovarian carcinomas



Distinct lymphatic spread of endometrial carcinoma in comparison  
with cervical and ovarian carcinomas

Average number and range of removed RPLNs

	Total	ALN <sup>a</sup>	PLN <sup>b</sup>
Cervical carcinoma	54.9 (32–89)	19.1 (6–40)	35.8 (23–51)
Endometrial carcinoma	67.3 (38–90)	30.5 (12–48)	36.8 (25–56)
Ovarian carcinoma	65.9 (28–98)	28.6 (8–53)	37.3 (17–57)

Distinct lymphatic spread of endometrial carcinoma in comparison with cervical and ovarian carcinomas

Incidence of PLN and ALN metastasis

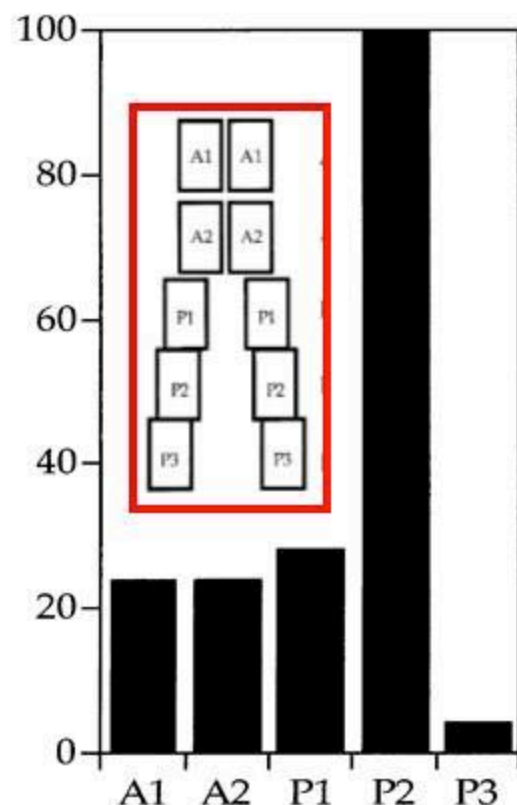
	$PA/(PA + P)^d$	$PA/(PA + A)^e$
Cervical carcinoma	9/25 (36%)	9/9 (100%)
Endometrial carcinoma	18/25 (72%)	18/20 (90%)
Ovarian carcinoma	36/46 (78%)	36/48 (75%)

<sup>d</sup> Incidence of ALN metastasis in patients with PLN metastasis.

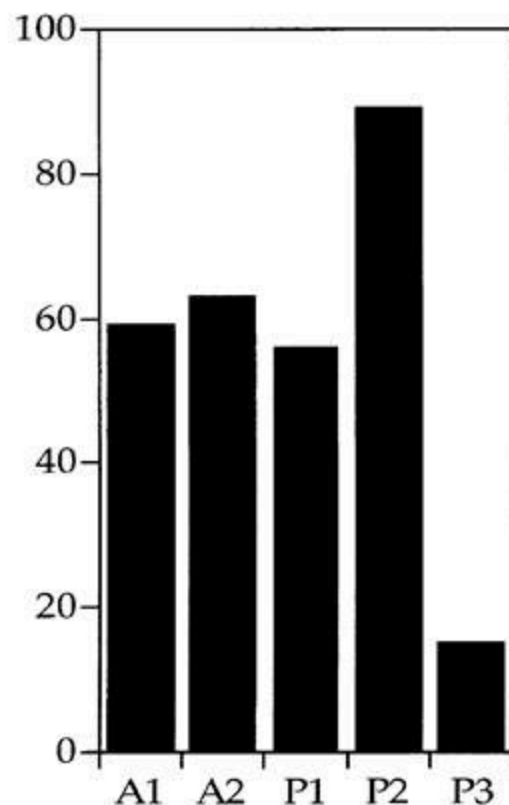
<sup>e</sup> Incidence of PLN metastasis in patients with ALN metastasis.

## Distinct lymphatic spread of endometrial carcinoma in comparison with cervical and ovarian carcinomas

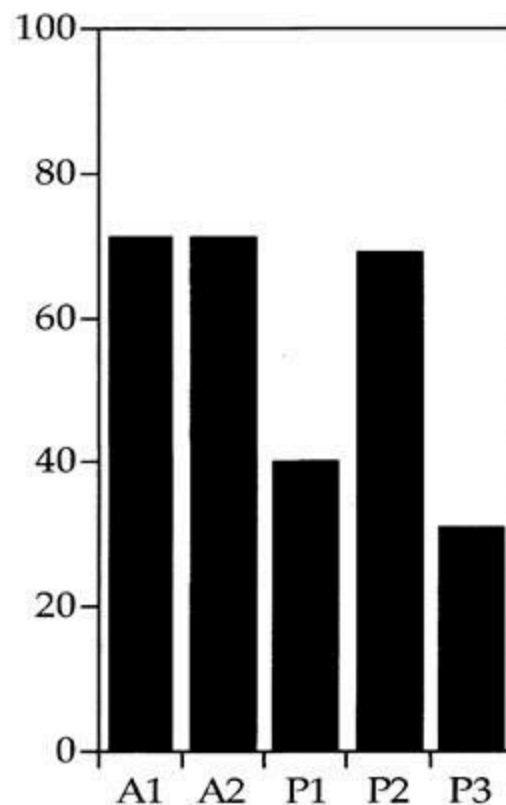
Incidence of metastasis in five LN subgroups.



Cervical  
Carcinoma  
(n = 25)



Endometrial  
Carcinoma  
(n = 27)



Ovarian  
Carcinoma  
(n = 58)

# Lymph Node Metastases and pathologic features in cervical carcinoma



## Incidence and Distribution Pattern of Pelvic and Paraaortic Lymph Node Metastasis in Patients with Stages IB, IIA, and IIB Cervical Carcinoma Treated with Radical Hysterectomy

### Incidence of Pelvic Lymph Node Metastasis in Cervical Carcinoma in Relation to Depth of Cervical Stromal Invasion and Lymph-Vascular Space Invasion

Cervical stromal invasion	Lymph-vascular space invasion	
	Negative	Positive
Not deep <sup>a</sup>	2 of 74 (2.7)	2 of 27 (7.4)
Deep <sup>b</sup>	2 of 20 (10.0)	47 of 87 (54.0)*

<sup>a</sup> Invasion not to the area between compact cervical stroma and extracervical loose connective tissue (parametrial initial zone; PIZ).

<sup>b</sup> Invasion to the depth of PIZ.

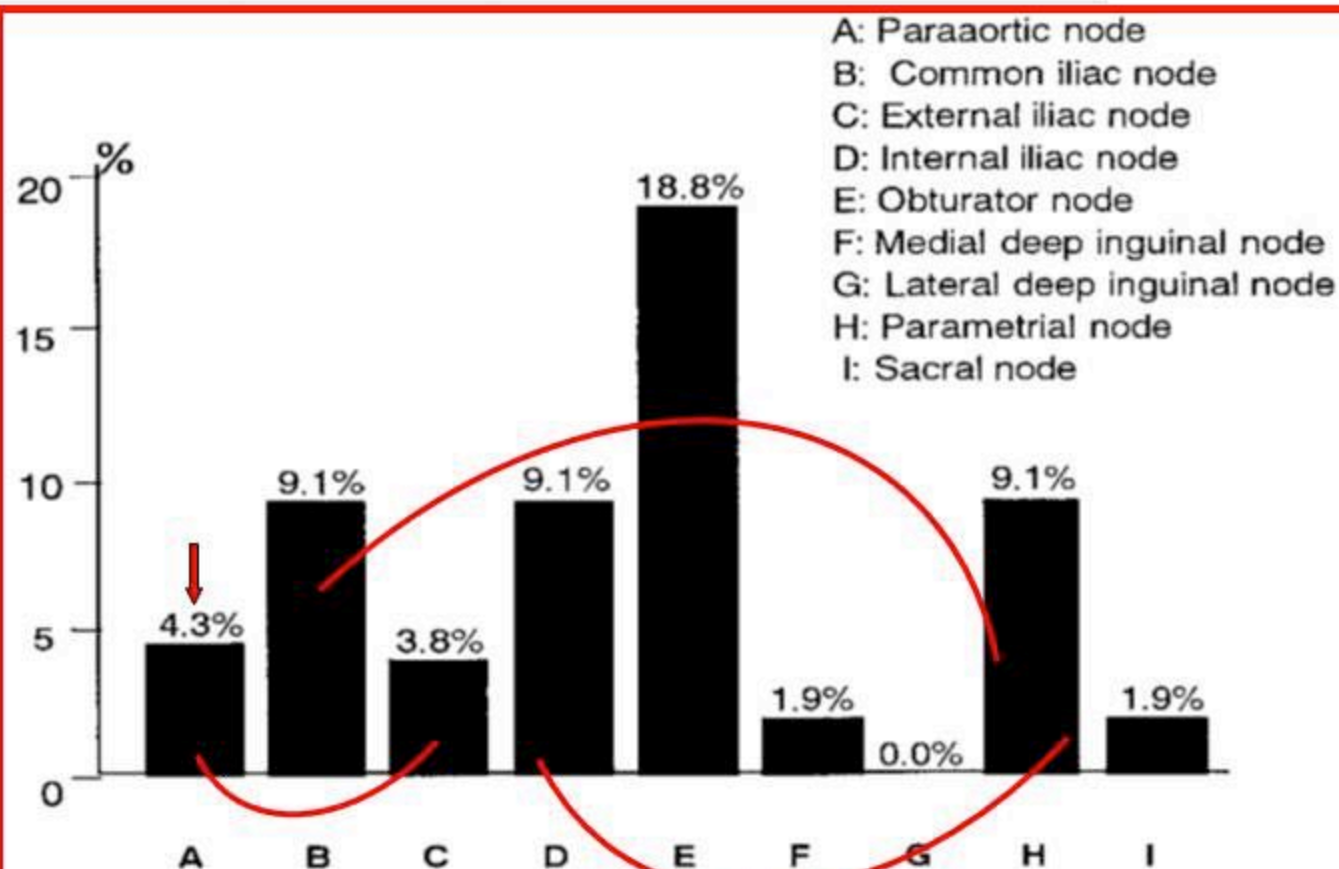
\*  $P < 0.0005$ .

# Incidence and Distribution Pattern of Pelvic and Paraaortic Lymph Node Metastasis in Patients with Stages IB, IIA, and IIB Cervical Carcinoma Treated with Radical Hysterectomy

## Univariate Analysis on Correlation between Clinicopathologic Variables and Paraaortic Lymph Node Metastasis

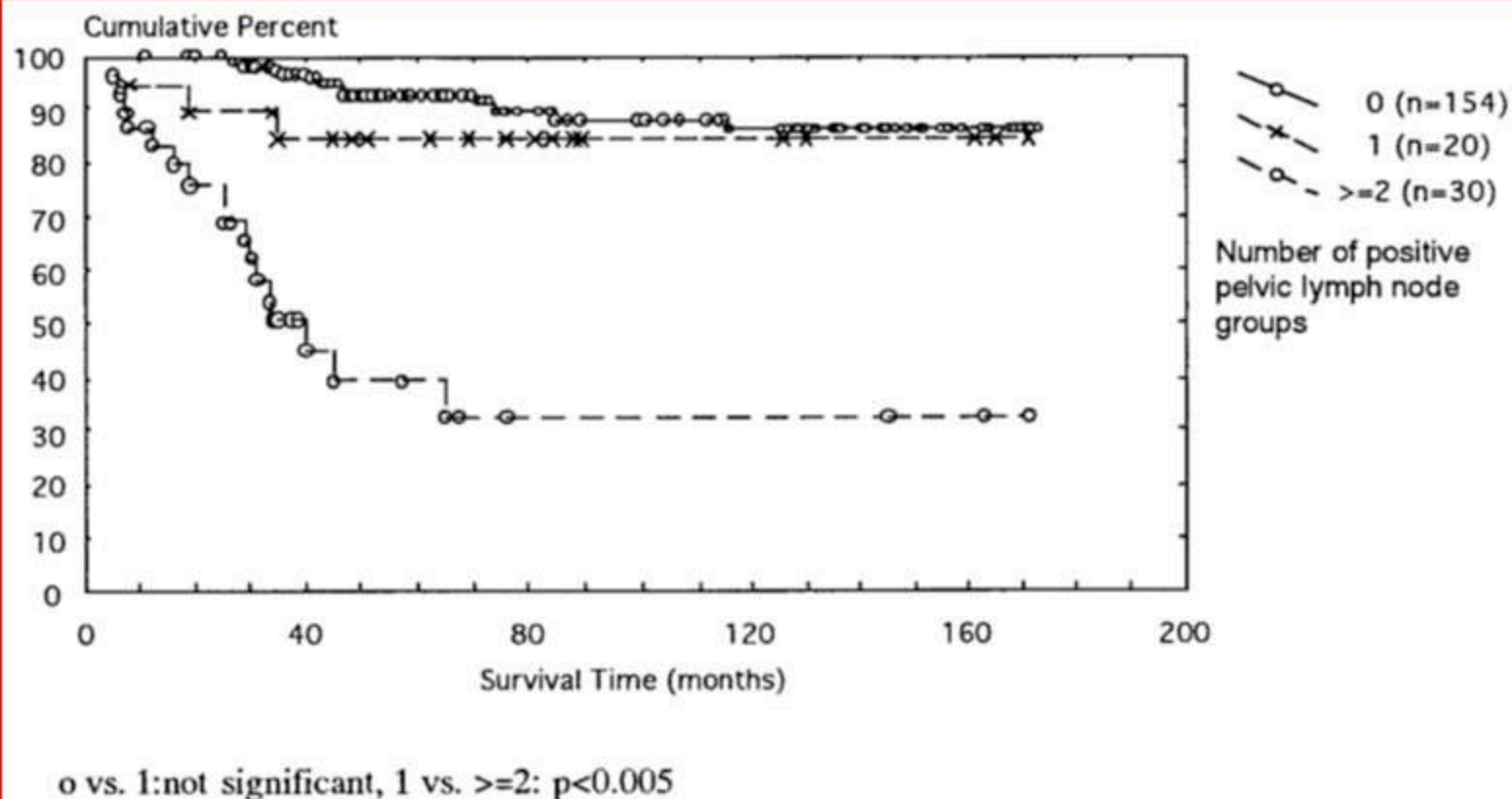
Variable	PAN metastasis (%)	<i>P</i> value
Clinical stage		
Ib, Ila	2 of 111 (1.8)	NS (0.056)
Ilb	7 of 97 (7.2)	
Parametrial invasion		
-	2 of 165 (1.2)	<0.0001
+	7 of 43 (16.3)	
Multiple PLN metastasis (excluding common iliac lymph node)		
-	1 of 179 (0.6) <sup>a</sup>	<0.00001
+	8 of 29 (27.6)	
Bilateral PLN metastasis (excluding common iliac lymph node)		
-	1 of 183 (0.5)	<0.00001
+	8 of 25 (32.0)	
Common iliac lymph node metastasis		
-	2 of 189 (1.1)	<0.00001
+	7 of 19 (36.8)	

## Incidence and Distribution Pattern of Pelvic and Paraaortic Lymph Node Metastasis in Patients with Stages IB, IIA, and IIB Cervical Carcinoma Treated with Radical Hysterectomy



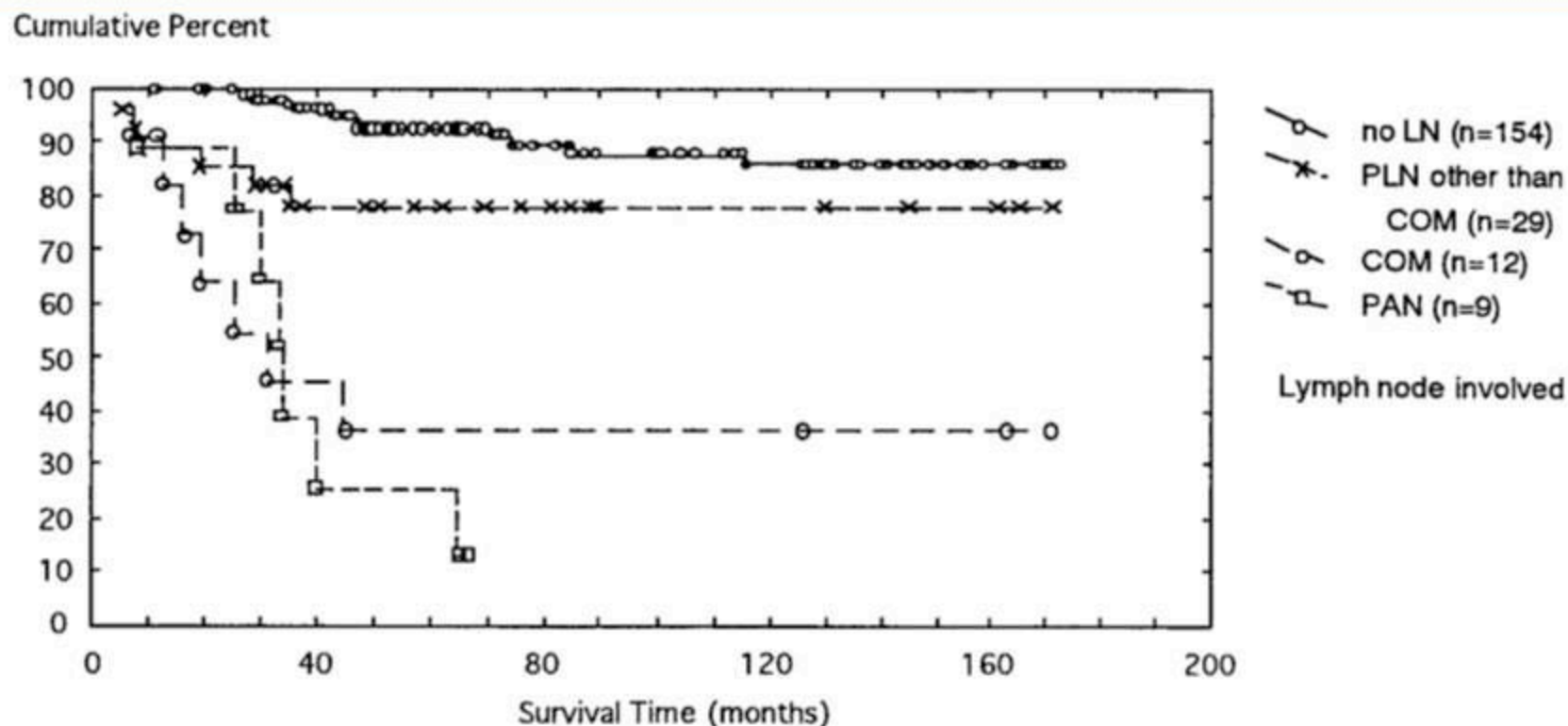
**FIGURE 1.** Positive rate for metastasis to each lymph node group in 208 cases of cervical carcinoma.

# Incidence and Distribution Pattern of Pelvic and Paraaortic Lymph Node Metastasis in Patients with Stages IB, IIA, and IIB Cervical Carcinoma Treated with Radical Hysterectomy



**FIGURE 2.** Survival of patients with cervical carcinoma by the number of pelvic lymph nodes involved.

# Incidence and Distribution Pattern of Pelvic and Paraaortic Lymph Node Metastasis in Patients with Stages IB, IIA, and IIB Cervical Carcinoma Treated with Radical Hysterectomy



LN: lymph node, PLN: pelvic lymph node, COM: common iliac node, PAN: paraaortic node




**FIGURE 3.** Survival of patients with cervical carcinoma by the site of lymph nodes involved.



# Surgical Versus Radiographic Determination of Para-aortic Lymph Node Metastases Before Chemoradiation for Locally Advanced Cervical Carcinoma

*A Gynecologic Oncology Group Study*

## Site of Recurrence for Recurrent Patients by the Method of Staging

Site of recurrence	% Surgical group, n = 219	% Radiographic group, n = 47	P
Out of pelvis			.127
Yes	51.6	63.8	
No	48.4	36.2	
PALN			 .006
Yes	 15.1	 31.9	
No	84.9	68.1	

PALN indicates para-aortic lymph nodes.

## Distinct lymphatic spread of endometrial carcinoma in comparison with cervical and ovarian carcinomas

In summary, the analysis of LN metastasis suggested that CC metastasizes initially to PLN, and then to ALN via common iliac LN metastasis, whereas OC metastasizes almost equally to both PLN and ALN. As for EC, it seems that direct metastases to both PLN and ALN take place with PLN metastasis being dominant, the pattern somewhere between CC and OC. These findings may be of great help in the design of sound therapeutic strategies for these malignancies.

# Mapping Pelvic Lymph nodes

# Pathways of Nodal Metastasis from Pelvic Tumors: CT Demonstration<sup>1</sup>

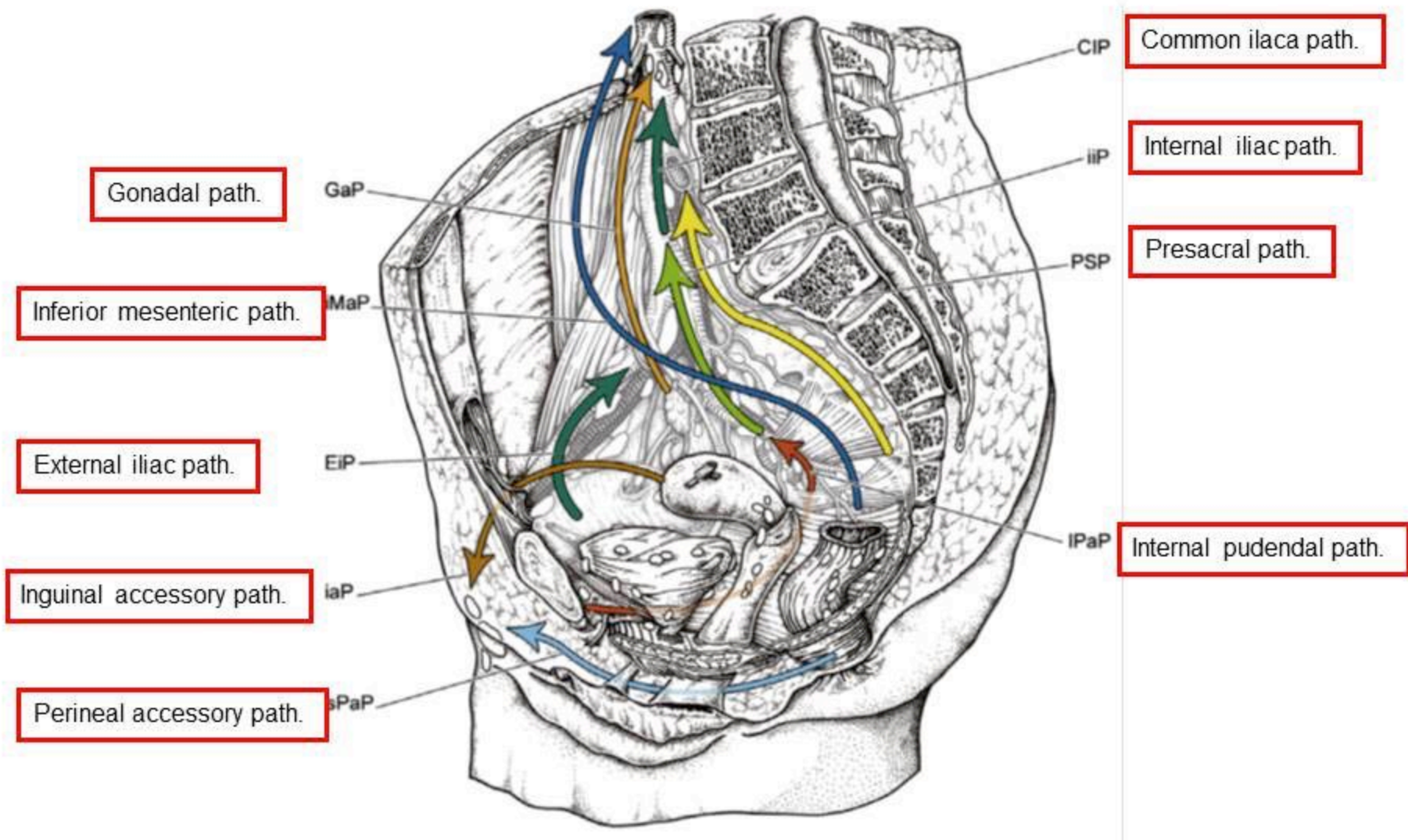
## Common Pathways of Nodal Metastasis from Pelvic Tumors

Pathway	Location of the Primary Tumors
Superficial inguinal pathway	Vulva, penis, lower vagina, lower rectum, anus
Pelvic pathway	
Anterior route	Anterior wall of the bladder
Lateral route	Bladder, prostate, upper vagina, cervix, uterus, ovary, rectum
Hypogastric route	Most pelvic organs
Presacral route	Prostate, cervix, rectum
Paraaortic pathway	Ovary, testis



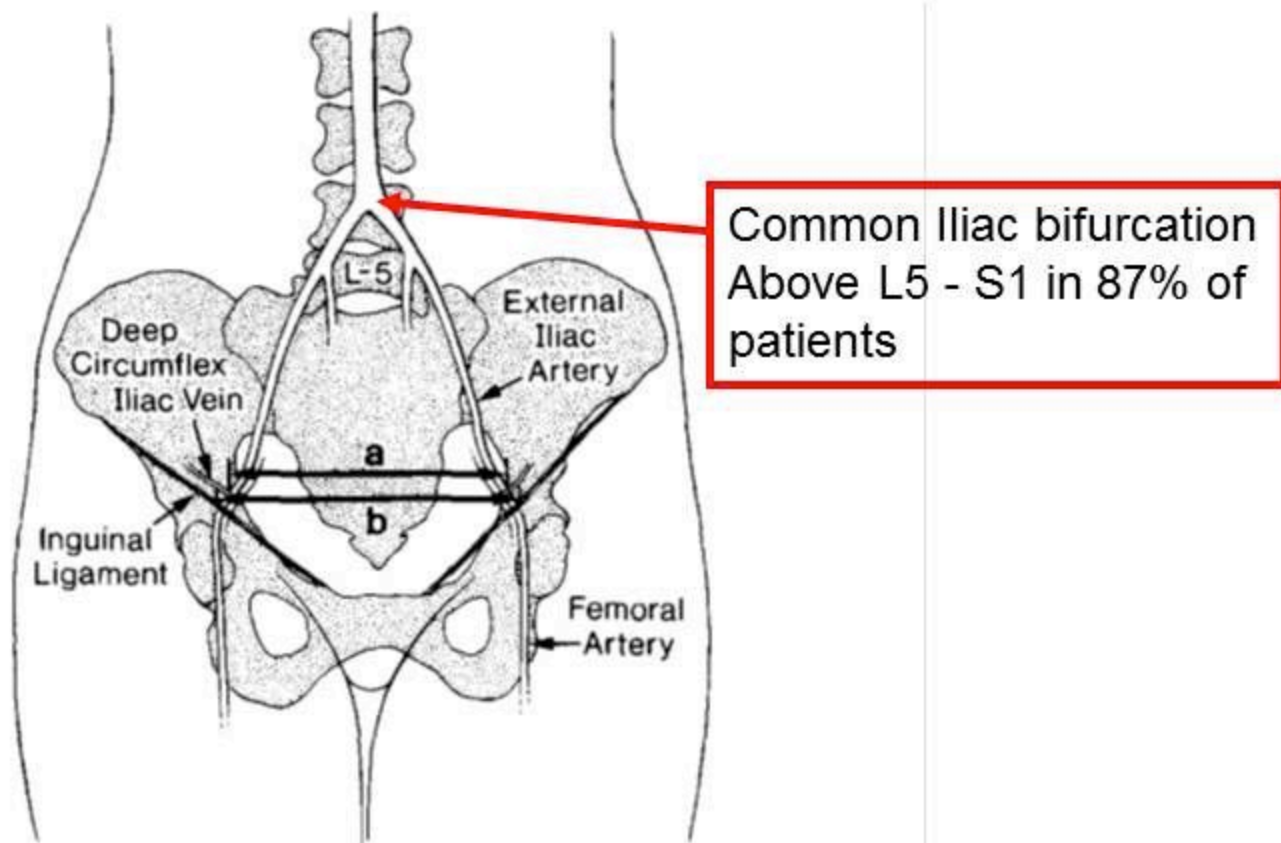
# Anatomical bases for the radiological delineation of lymph node areas.

## Part III: Pelvis and lower limbs



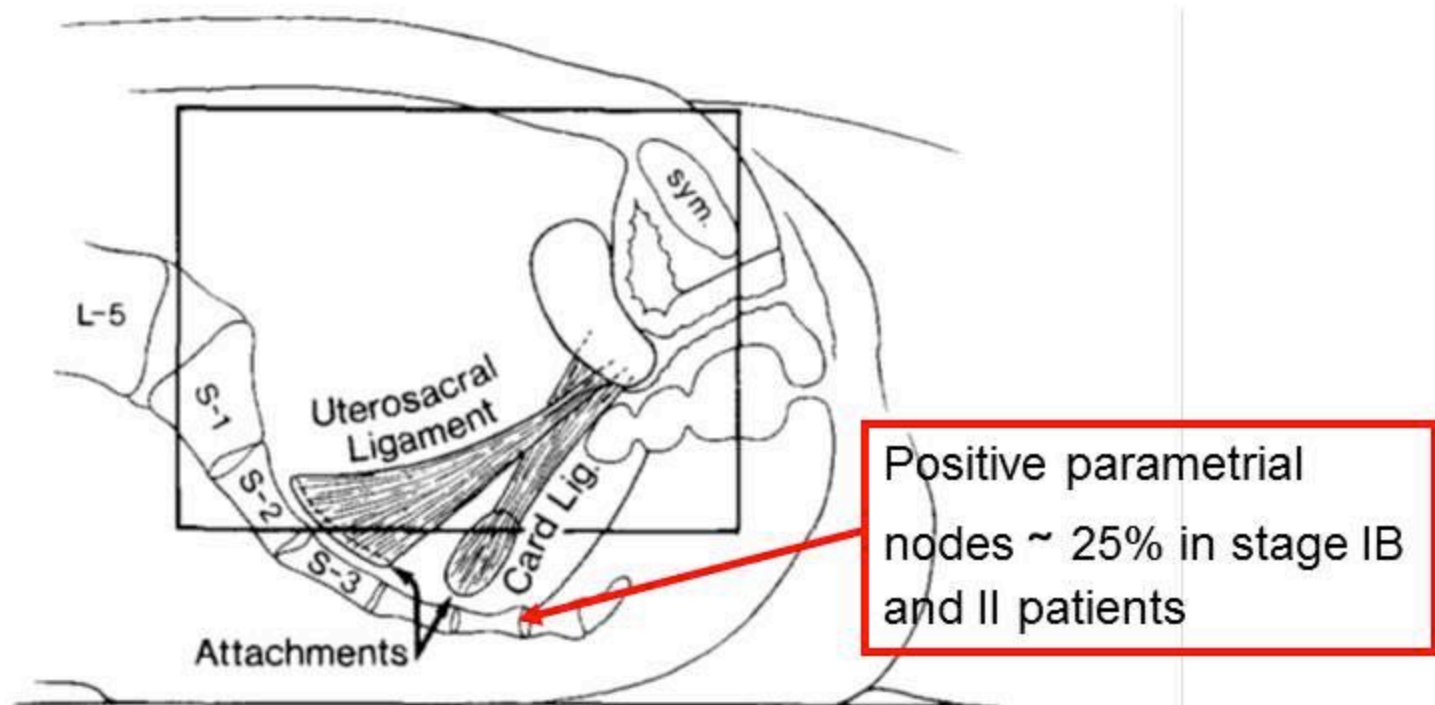


# Gynecologic Radiotherapy Fields Defined by Intraoperative Measurements



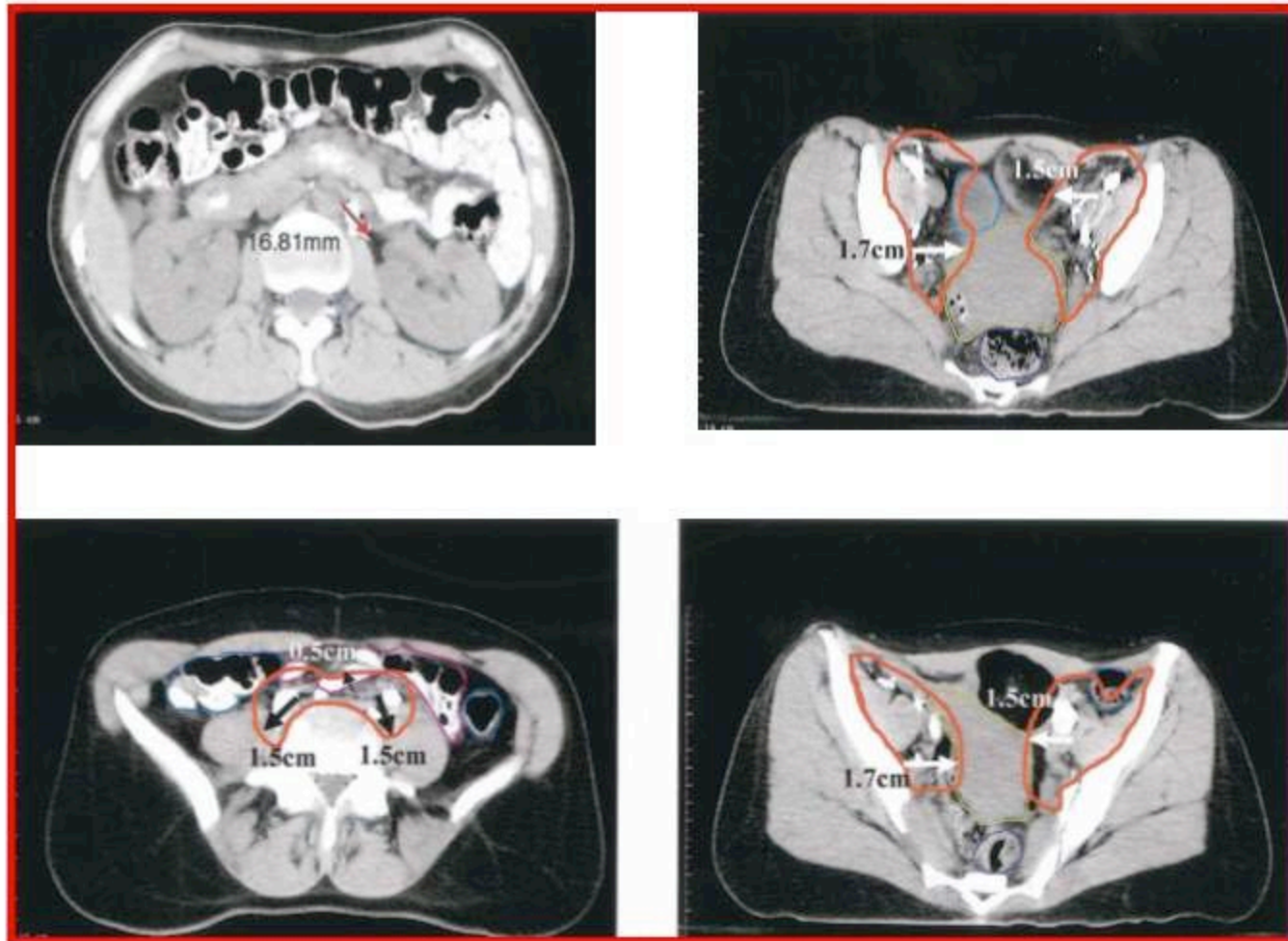
**FIG. 2.** (a) The maximal separation of the external iliac arteries at the deep circumflex veins. (b) The consistently wider separation of the femoral arteries at the level of the inguinal ligaments.

# Gynecologic Radiotherapy Fields Defined by Intraoperative Measurements



**FIG. 3.** Illustration of the posterior extension of the uterosacral and cardinal ligaments to the level of the sacral hollow. The rectangle indicates current conventional lateral pelvic radiotherapy fields with a superior border of L5–S1 and a posterior border at the S2–S3 interspace, which provides inadequate coverage of volume at risk.

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



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

Location of lymphangiogram-avid lymph nodes relative to adjacent anatomic structures	Average distance (mm)
Para-aortic nodes left to aorta	22.1
Para-aortic nodes right to inferior vena cava	9.1
Para-aortic nodes ventral to aorta	1.8
Common iliac nodes, right	11.9
Common iliac nodes, left	15.6
Common iliac nodes, ventral	0.3
External iliac nodes relative to pelvic side wall, right	16.2
External iliac nodes relative to pelvic side wall, left	13.8
Inguinal nodes relative to femoral artery, right	16.8
Inguinal nodes relative to femoral artery, left	15.3



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

## Volume of normal tissue encompassed

Pt. No.	Small bowel (cm <sup>3</sup> )		
	CTV	CTV + 1 cm	CTV + 2 cm
1	58.0	222.5	413.3
2	29.5	162.8	308.6
3	43.0	210.0	395.5
4	70.0	283.7	512.9
5	82.1	252.8	302.4
6	77.5	310.0	499.5
7	89.4	328.8	629.4
8	61.0	284.7	565.2
9	51.1	209.6	356.9
10	19.3	97.5	211.7
Average	58.1	236.2	419.5
SD	22.8	70.8	130.9



# Anatomical bases for the radiological delineation of lymph node areas.

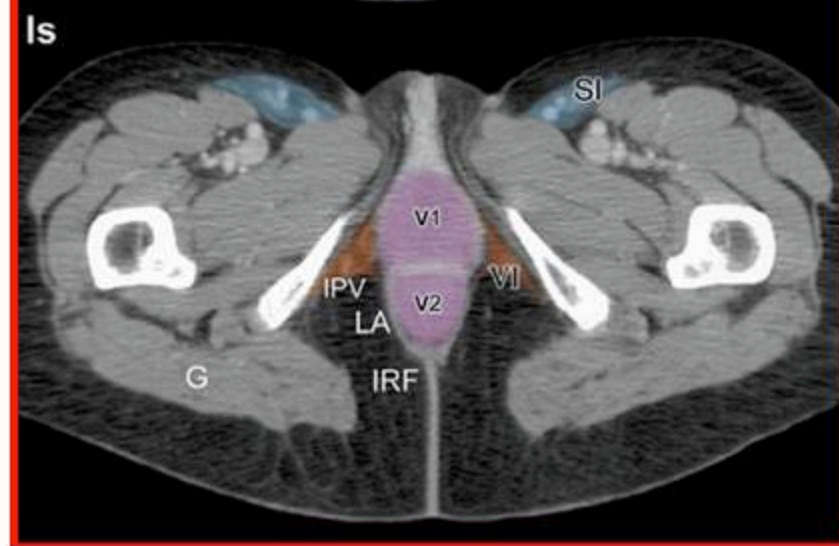
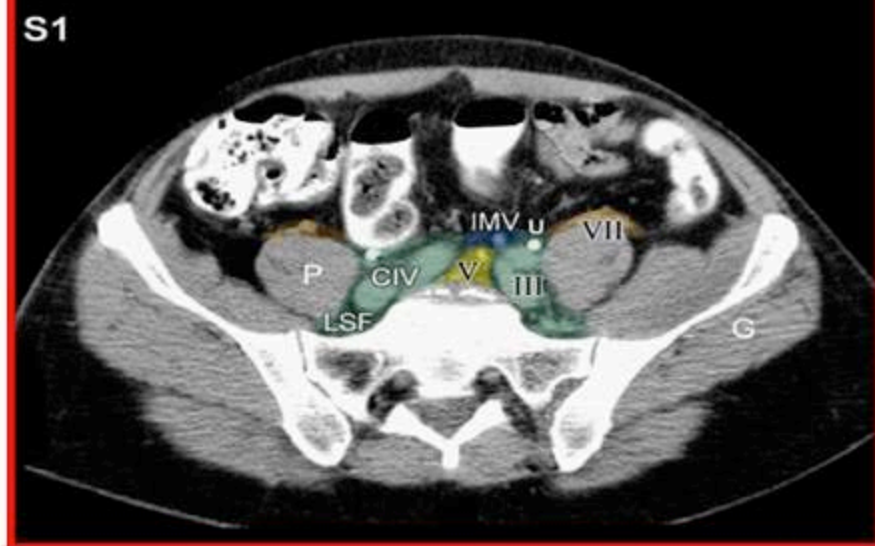
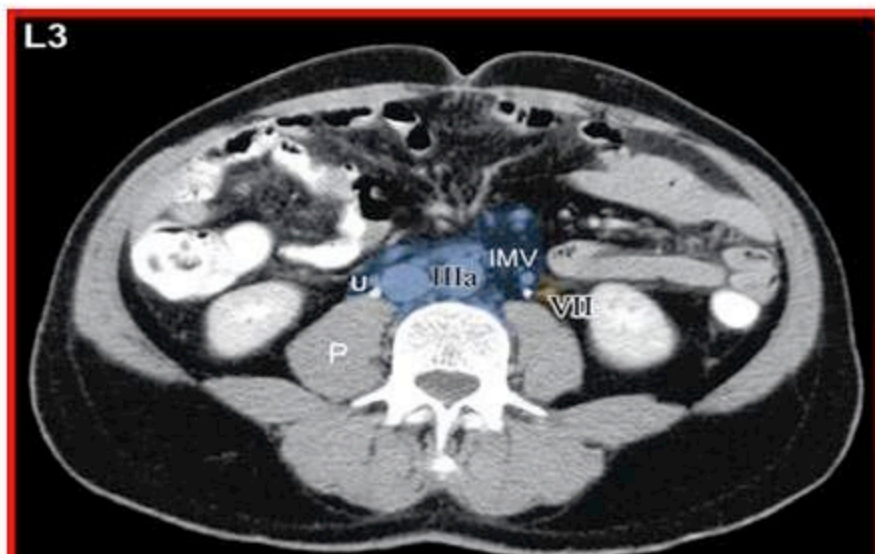
## Part III: Pelvis and lower limbs

Pelvic lymph node levels and corresponding target areas for conformal radiotherapy, with their respective standardized anatomical landmarks.

Levels	Lymph nodes and vessels	Vascular landmarks	Bone landmarks	Muscle landmarks	Anterior boundary	Posterior boundary
Level I	External iliac lymph nodes	Around external iliac vessels	Medial side of iliopubic branch and obturator foramen	Medial edge of psoas, levator ani	Femoral septum	Pelvic ureter
Level II	Internal iliac lymph nodes	Around internal iliac vessels and their branches	Medial side of ischium and greater sciatic aperture	Piriformis, levator ani, obturat. int.	Pelvic ureter	Lat. sacral edge, sacro-iliac joint
Level III	Common iliac lymph nodes	Around common iliac vessels	Lateral side of L5 vertebral body	Medial edge of psoas	Sacro-iliac joint	Sacral wing
Level IV	Presacral lymph nodes	Along median sacral vessels	Anterior aspect of sacrum	None	Fascia recti	Sacral bone concavity
Level V	Subaortic lymph nodes	Below aortic bifurcation	Anterior aspect of L5 vertebral	None	Posterior peritoneal lining	L5 vertebra
Level VI	Internal pudendal lymph vessels	Along internal pudendal vessels	Medial side of ischiopubic branch and obturator foramen	Obturator internus, ischiorectal fossa	Pubic symphysis	Ischial spine
Level VII	Gonadic lymph vessels	Along gonadic vessels	From iliac wing to upper plate of L3 vertebra	Anterior aspect of psoas	Posterior peritoneal lining	Psoas, lateral to lumbar ureter

# Anatomical bases for the radiological delineation of lymph node areas.

## Part III: Pelvis and lower limbs



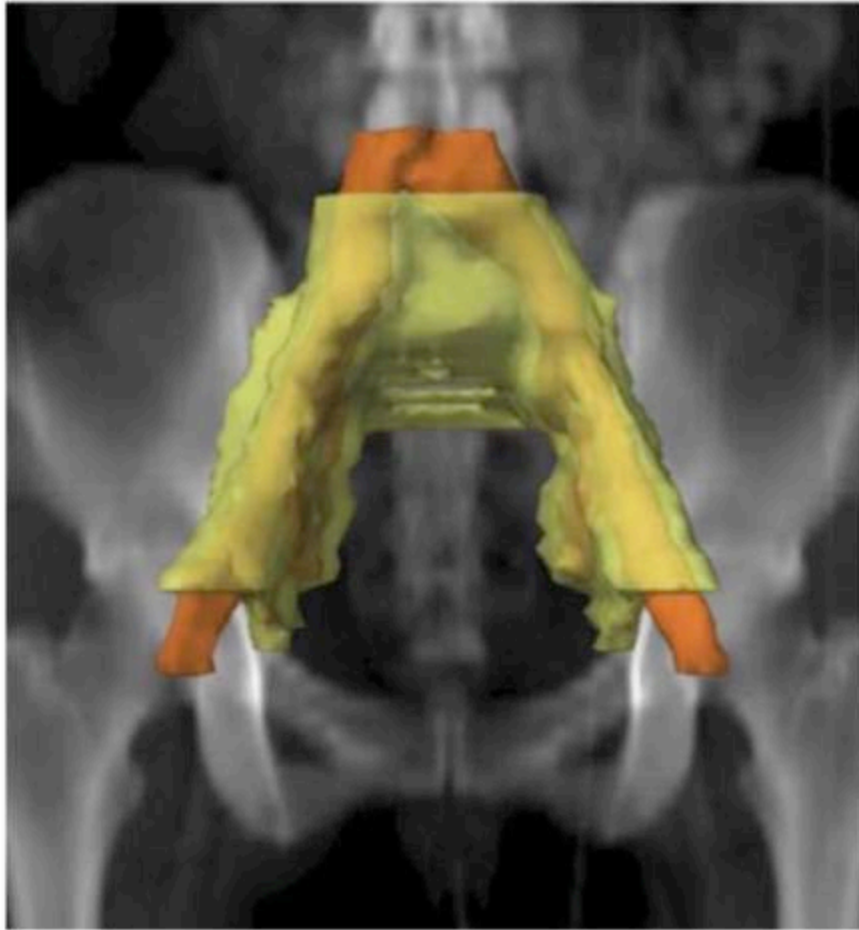
# A Consensus-based Guideline Defining the Clinical Target Volume for Pelvic Lymph Nodes in External Beam Radiotherapy for Uterine Cervical Cancer

**Table 1.** Clinical target volume definition on pelvic nodes related to anatomic landmarks for cervical cancer

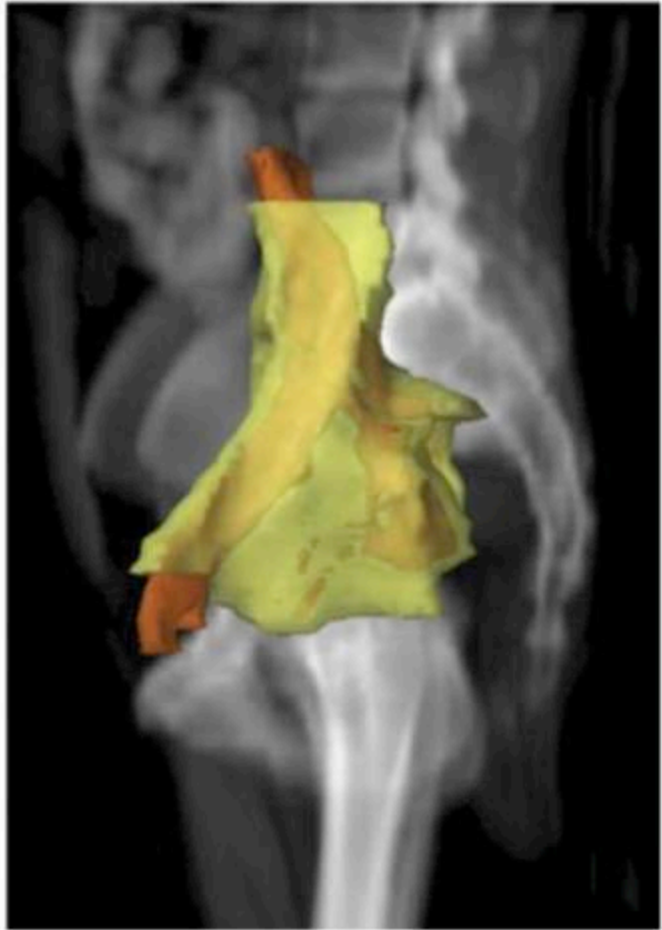
Node chains	Cranial margin	Caudal margin	Anterior margin	Posterior margin	Lateral margin	Medial margin
Common iliac	Aortic bifurcation or L4-5 space	Common iliac a bifurcation	7 mm anterior to a/v	L5—sacrum (adequately involve adipose connective tissue between lateral surface of vertebral body and psoas m <sup>a</sup> )	7 mm lateral to a/v (expanding to psoas major m)	—
External iliac	Common iliac a bifurcation	Superior aspect of femoral head	7 mm anterior to a/v (connecting to obturator region)	7 mm posterior to a/v (connecting to obturator region)	7 mm lateral to a/v (expanding to psoas major m or iliacus m)	7 mm medial to a/v uterus, ovary, bowel, ureter or bladder
Internal iliac	Common iliac a bifurcation	Cranial section of coccygeus m, spine of ischium or uterine a/v (connecting to parametrial region)		Cranial level: wing of sacrum  Middle-caudal level: anterior edge of piriformis m or inferior gluteal a/v	Cranial level: psoas m, iliacs m or lateral edge of sacroiliac joint  Middle level: Iliac bone, psoas m or medial edge of Iliacus m  Caudal level: obturator internus m or piriformis m	7 mm medial to a/v bowel, uterus or ovary
Obturator	Caudal section of sacroiliac joint (connecting to internal iliac region)	Superior part of obturator foramen	Cranial-middle level: connecting to external iliac region  Caudal level: posterior edge of pubic bone	Cranial-middle level: connecting to internal iliac region  Caudal level: posterior edge of obturator internus m	Obturator internus m, iliacus m, psoas m or iliac bone	Bladder, uterus or bowel
Presacral	Common iliac a bifurcation	Lower level of S2 or cranial section of piriformis m	10 mm anterior to sacrum	L5—sacrum	Piriformis m (connecting to external or internal iliac region)	—

## A Consensus-based Guideline Defining the Clinical Target Volume for Pelvic Lymph Nodes in External Beam Radiotherapy for Uterine Cervical Cancer

A



B

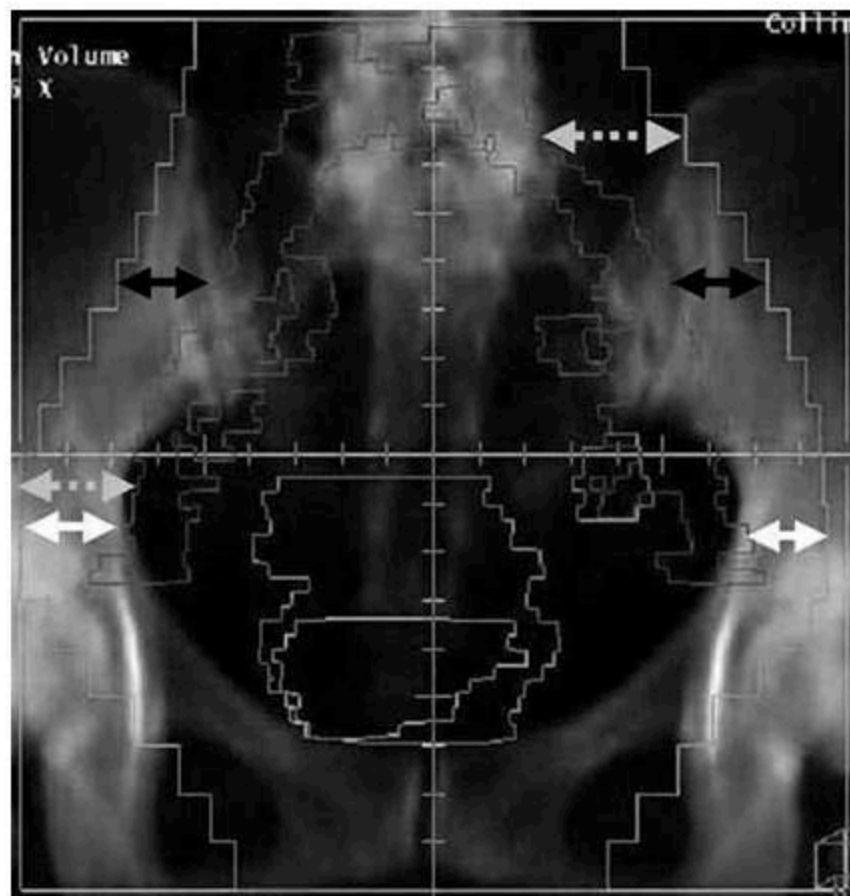


Digitally reconstructed radiographs showing CTV for pelvic lymph nodes (yellow) and vessels (orange)

*Jpn J Clin Oncol* 2010;40(5)456–463



# Vessel-contouring-based Pelvic Radiotherapy in Patients with Uterine Cervical Cancer

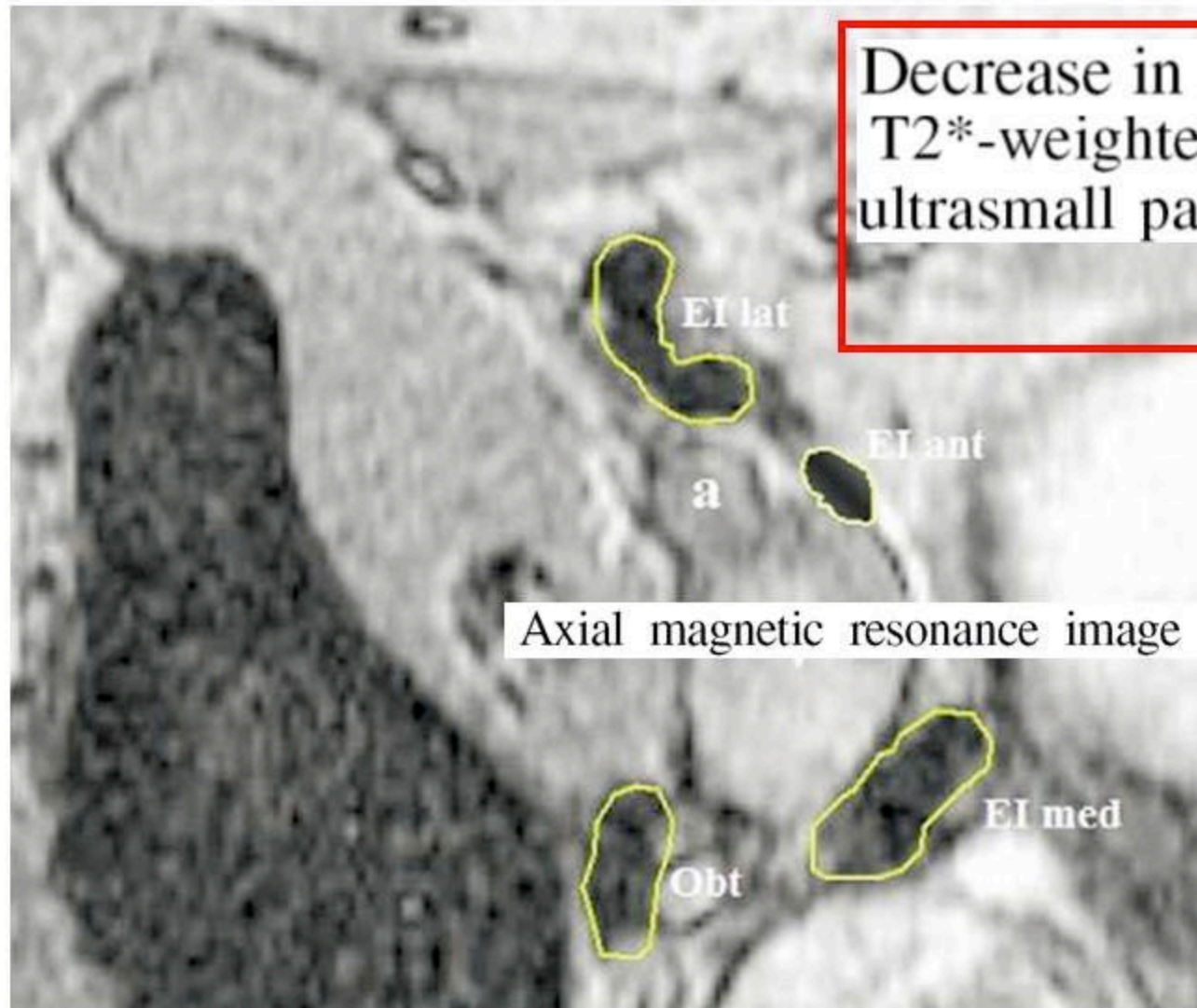


**Table 2.** Distance between major vessels and multi-leaf collimator edges (V–M distance)

	Left (mm)	Right (mm)
Maximum		
Mean (SD)	33 (4.4)	30 (4.6)
Median (range)	32 (24–45)	30 (24–41)
Minimum		
Mean (SD)	16 (2.4)	15 (2.7)
Median (range)	15 (9–27)	15 (7–28)
Midpoint of sacroiliac joint		
Mean (SD)	25 (4.3)	26 (4.9)
Median (range)	25 (18–36)	24 (17–36)



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



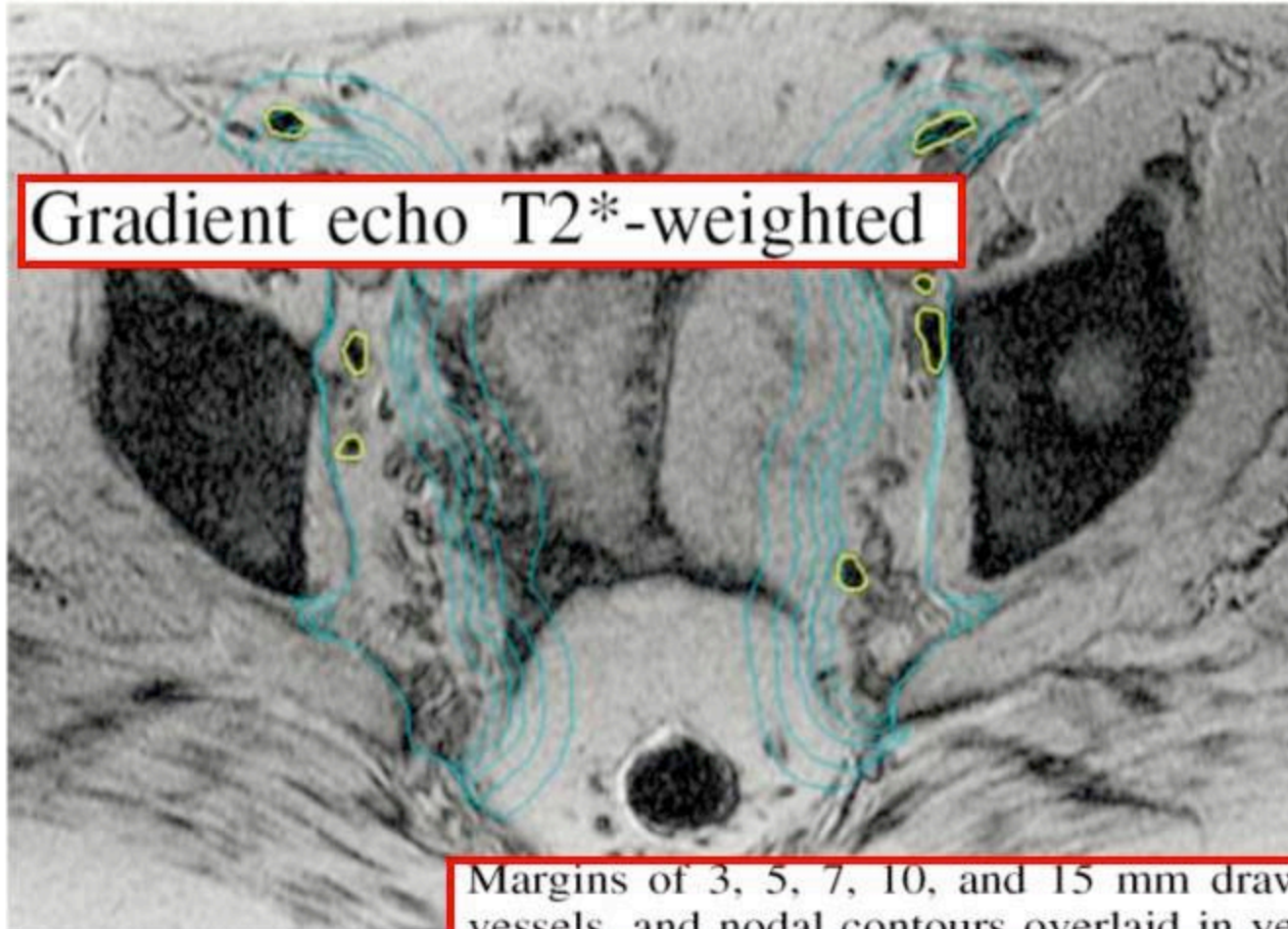
Decrease in signal intensity on T2\*-weighted images after ultrasmall particles of iron oxide (USPIO)

Axial magnetic resonance image of external iliac region

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

Ultrasmall particles of iron oxide (USPIO)

Gradient echo T2\*-weighted



Margins of 3, 5, 7, 10, and 15 mm drawn around pelvic blood vessels, and nodal contours overlaid in yellow.



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

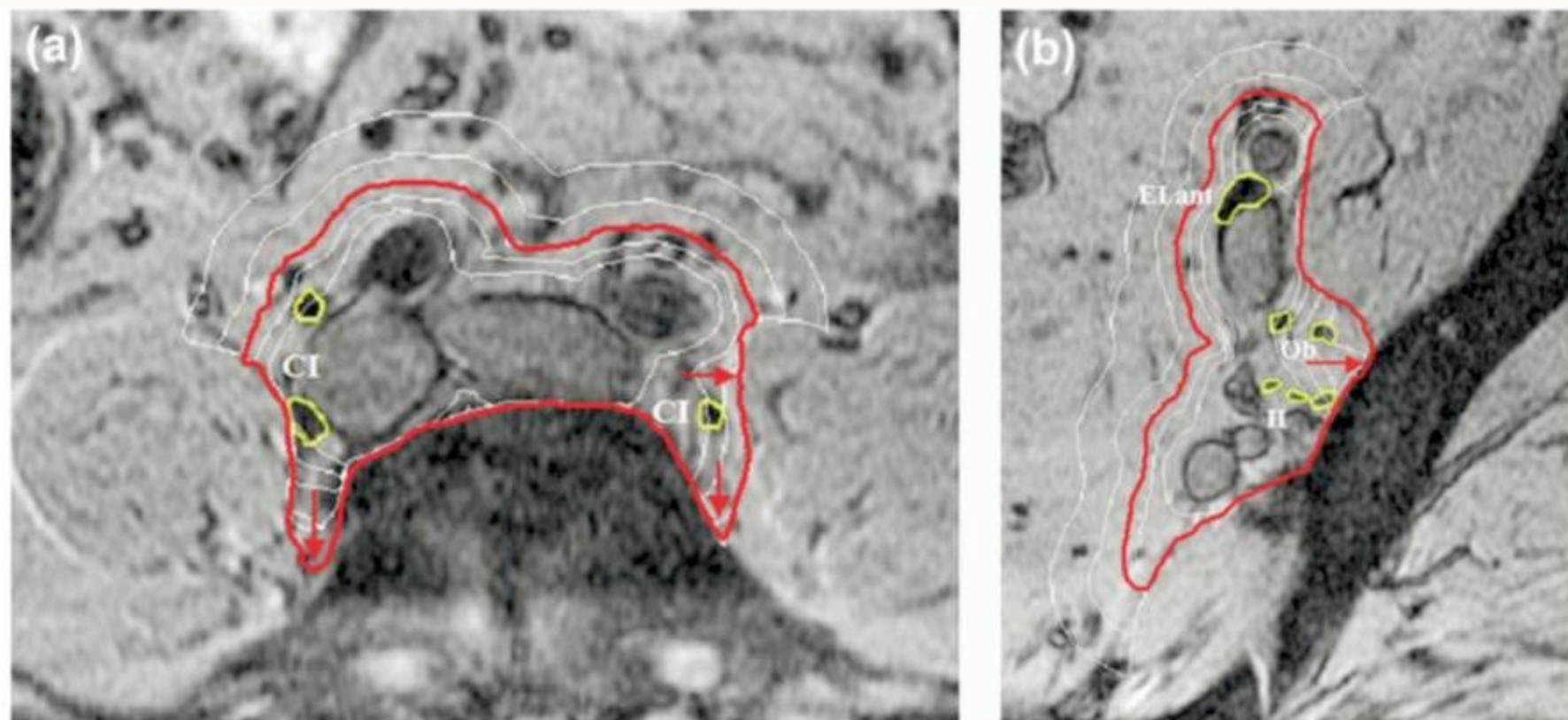


Fig. 4. Modified 7-mm contour to ensure coverage of lymph node groups (red outline). (a) Common iliac nodes can lie in lateral and posterior spaces. (b) Contour must extend fully to pelvic sidewall. (c) To cover distal lateral external iliac nodes, extend anterior border along iliopsoas muscle (i-p) by additional 10 mm. (d) Obturator region covered by extending medial contour around external iliac vessels posteriorly, parallel to pelvic sidewall, to join internal iliac contour. This strip should be 18 mm wide. CI = common iliac; II = internal iliac; EI lat = lateral external iliac; EI ant = anterior external iliac; EI med = medial external iliac; Obt = obturator.

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

## Lymph node contours covered by margin around blood vessels

Lymph node group	3 mm (%)	5 mm (%)	7 mm (%)	10 mm (%)	15 mm (%)
Common iliac ( <i>n</i> = 135)	41 (30.3)	90 (66.7)	123 (91.1)	135 (100)	135 (100)
Medial external iliac ( <i>n</i> = 196)	122 (62.2)	167 (85.2)	193 (98.4)	196 (100)	196 (100)
Anterior external iliac ( <i>n</i> = 241)	124 (51.4)	190 (78.8)	227 (94.2)	241 (100)	241 (100)
Lateral external iliac ( <i>n</i> = 190)	16 (8.4)	41 (21.6)	76 (40)	123 (64.7)	178 (93.7)
Obturator ( <i>n</i> = 303)	275 (90.1)	295 (97.3)	302 (99.7)	303 (100)	303 (100)
Internal iliac ( <i>n</i> = 144)	105 (72.9)	135 (93.8)	142 (98.6)	144 (100)	144 (100)
Presacral ( <i>n</i> = 7)	0 (0)	0 (0)	3 (42.9)	3 (42.9)	3 (42.9)
Total ( <i>n</i> = 1216)	683 (56.2)	918 (75.7)	1066 (87.7)	1145 (94.2)	1200 (98.7)

	5 mm (%)	7 mm (%)	10 mm (%)	15 mm (%)
90 (66.7)	123 (91.1)	135 (100)	135 (100)	
167 (85.2)	193 (98.4)	196 (100)	196 (100)	
190 (78.8)	227 (94.2)	241 (100)	241 (100)	
41 (21.6)	76 (40)	123 (64.7)	178 (93.7)	
295 (97.3)	302 (99.7)	303 (100)	303 (100)	
135 (93.8)	142 (98.6)	144 (100)	144 (100)	
0 (0)	3 (42.9)	3 (42.9)	3 (42.9)	
918 (75.7)	1066 (87.7)	1145 (94.2)	1200 (98.7)	



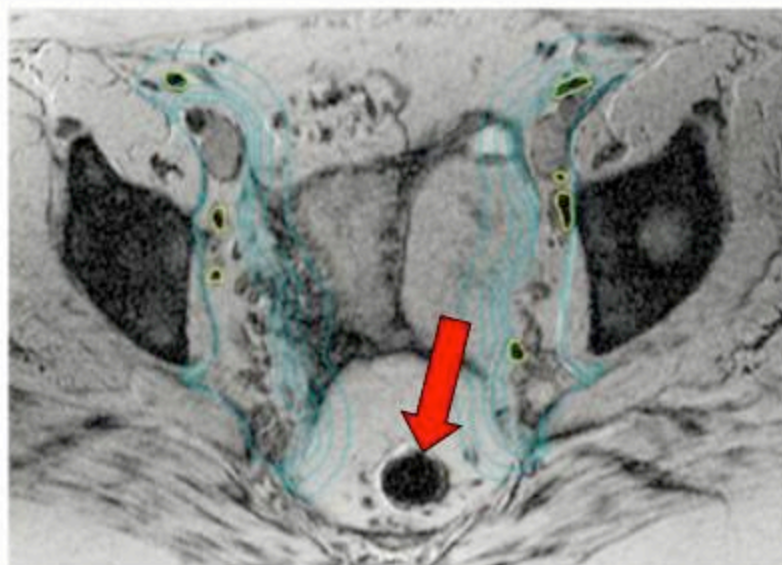
# MAPPING PELVIC LYMPH NODES: GUIDELINES FOR DELINEATION IN INTENSITY-MODULATED RADIOTHERAPY

A. Mean volume of normal structure within CTV (cm<sup>3</sup>)

	Total volume	3 mm	(%)	5 mm	(%)	7 mm	(%)	10 mm	(%)	15 mm	(%)
Bowel	643.7	5.9	(0.9)	16.8	(2.6)	32.4	(5.1)	63.2	(10.2)	123.3	(19.9)
Bladder	131.0	0.7	(0.3)	2.1	(1.0)	3.9	(1.9)	7.4	(3.8)	14.3	(7.7)
Rectum	44.4	0.2	(0.2)	0.5	(0.7)	0.9	(1.4)	2.2	(3.6)	5.4	(9.7)

B. Mean volume of normal structure within PTV (cm<sup>3</sup>)

	Total volume	3 mm	(%)	5 mm	(%)	7 mm	(%)	10 mm	(%)	15 mm	(%)
Bowel	643.7	95.6	(15.4)	120.7	(19.4)	146.9	(23.7)	190.3	(30.8)	265.9	(42.9)
Bladder	131.0	13.1	(7.5)	16.7	(9.8)	21.2	(12.8)	28	(17.5)	40.6	(26.5)
Rectum	44.4	3.9	(6.8)	5.5	(19.9)	7.2	(13.3)	10.4	(19.9)	17.1	(34.1)



15 mm around the vessels

50 Gy to the pelvis

34% of the rectum receiving 50 Gy

10 mm around the vessels

50 Gy to the pelvis

20% of the rectum receiving 50 Gy

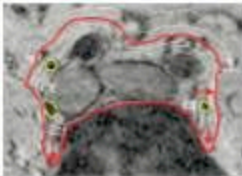
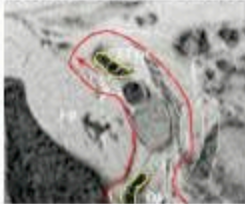
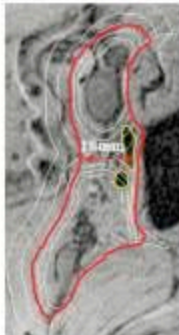
QUANTEC for Rectum

V50<50%, V60<35%, V65<25%. V70<20%



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

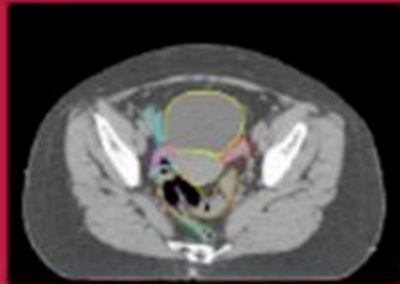
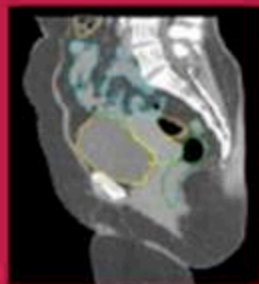
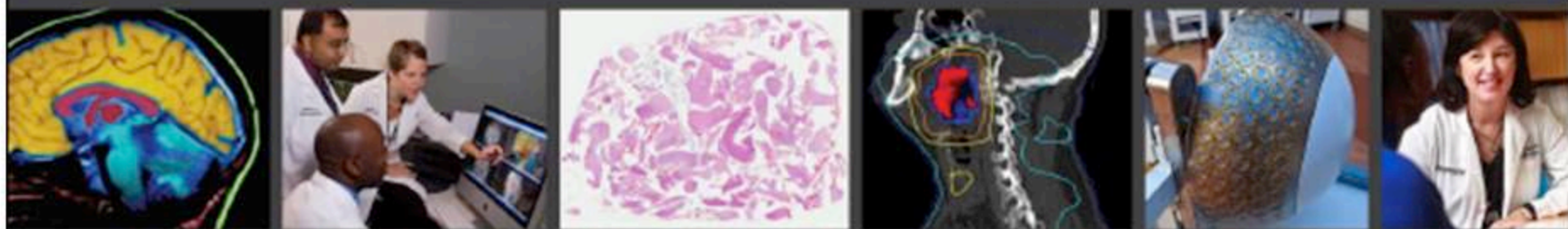
Recommend modifications to margins

Lymph node group		Recommended margins*
Common iliac		7-mm margin around vessels; extend posterior and lateral borders to psoas and vertebral body
External iliac		7-mm margin around vessels; extend anterior border by additional 10-mm anterolaterally along iliopsoas muscle to include lateral external iliac nodes
Obturator		Join external and internal iliac regions with 18-mm-wide strip along pelvic sidewall
Internal iliac		7-mm margin around vessels; extend lateral borders to pelvic sidewall
Presacral		10-mm strip over anterior sacrum

\* Also include any visible nodes.

<http://www.rtog.org/>

CoreLab/ContouringAtlases/  
FemaleRTOGNormalPelvisAtl  
as.aspx



# **FEMALE PELVIS Normal Tissue RTOG Consensus Contouring Guidelines**

Hiram A. Gay, M.D., H. Joseph Bartholdi, M.D., Elizabeth O'Meara, C.M.D., Walter R. Bosch, Ph.D.,  
Issam El Naqa, Ph.D., Rawan Al-Lozi, Seth A. Rosenthal, M.D., Colleen Lawton, M.D., F.A.C.R.,  
W. Robert Lee, M.D., Howard Sandler, M.D., Anthony Zietman, M.D., Robert Myerson, M.D., Ph.D.,  
Laura A. Dawson, M.D., Christopher Willett, M.D., Lisa A. Kachnic, M.D., Anuja Jhingran, M.D.,  
Lorraine Portelance, M.D., Janice Ryu, M.D., William Smail, Jr., M.D., David Gaffney, M.D., Ph.D.,  
Akila N. Viswanathan, M.D., M.P.H., and Jeff M. Michalski, M.D.

Supported by grants from the National Cancer Institute: CA21861, CA32115, and CA37422



# GYN

Organ	Standardized TPS Name	Tumor Category	Consensus Definition
anus + rectum	AnoRectum	GYN	Inferiorly from the anal verge as marked with a radiopaque marker at the time of simulation. Contouring ends superiorly before the rectum loses its round shape in the axial plane and connects anteriorly with the sigmoid. The AnoRectum is used with the Sigmoid and BowelBag.
sigmoid	Sigmoid	GYN	Bowel continuing where the AnoRectum contour ended. Stops prior to connecting to the ascending colon laterally. Contoured when a brachytherapy applicator rests in the uterus. Any sigmoid adjacent or above the uterus or a brachytherapy applicator should be contoured.
bowel bag	BowelBag	GYN	<p>* Inferiorly from the most inferior small or large bowel loop, or above the Rectum (GU) or AnoRectum (GYN), whichever is most inferior. If when following the bowel loop rule the Rectum or AnoRectum is present in that axial slice, it should be included as part of the bag; otherwise it should be excluded.</p> <p>Tips: Contour the abdominal contents excluding muscle and bones. Contour every other slice when the contour is not changing rapidly, and interpolate and edit as necessary. Finally, subtract any overlapping non-GI normal structures. If the TPS does not allow subtraction leave as is.</p>

\*Stop contouring the BowelBag, SmallBowel, and Colon 1 cm above PTV for most coplanar beam plans, but the choice will depend on the treatment technique. Stop these PTVs at distances much greater than 1 cm for non-coplanar beam plans depending on the beam angle and path. Tomotherapy plans will require stopping from 1 to 5 cm above the PTV, depending on the selected field size, which is often 2.5 cm.

Abbreviations: TPS = treatment planning software

### GYN:

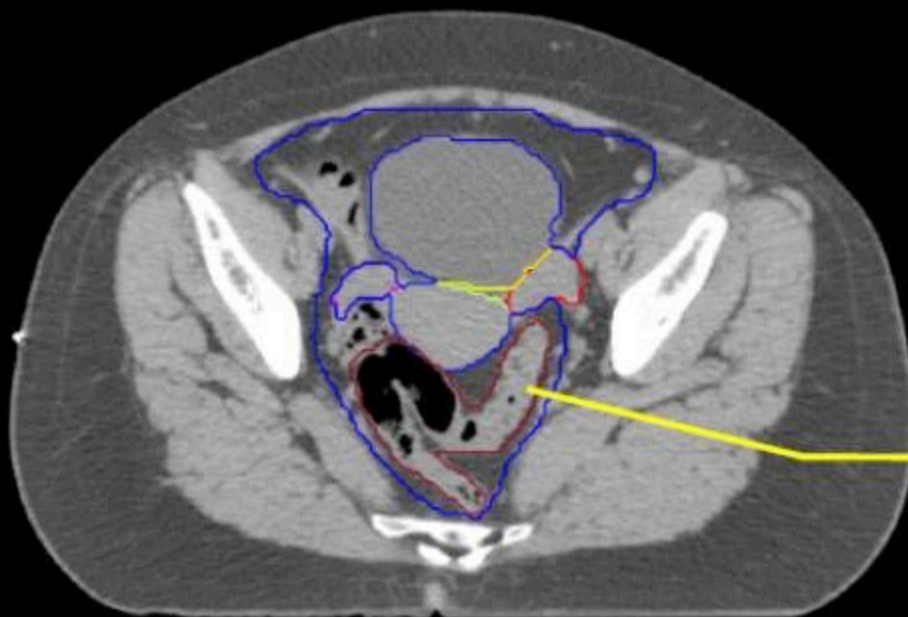
- Sigmoid
- AnoRectum
- BowelBag

### GYN/GI:

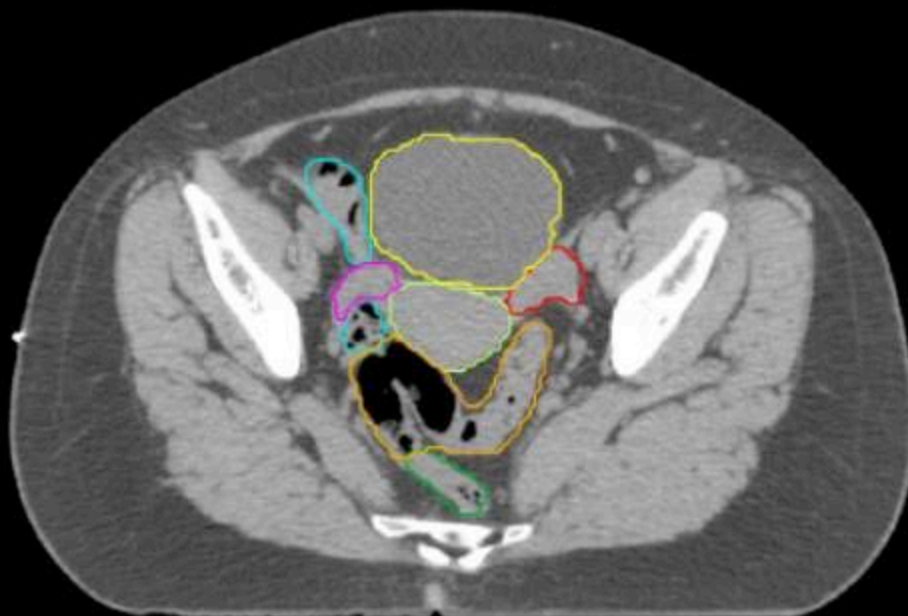
- UteroCervix
- Femur\_L
- Femur\_R
- Adnexa\_R
- Adnexa\_L
- Bladder

### GI:

- Small Bowel
- AnoRectumSig
- Colon



Any Sigmoid adjacent or above the uterus or a brachytherapy applicator should be contoured





GYN:

- Sigmoid
- AnoRectum
- BowelBag

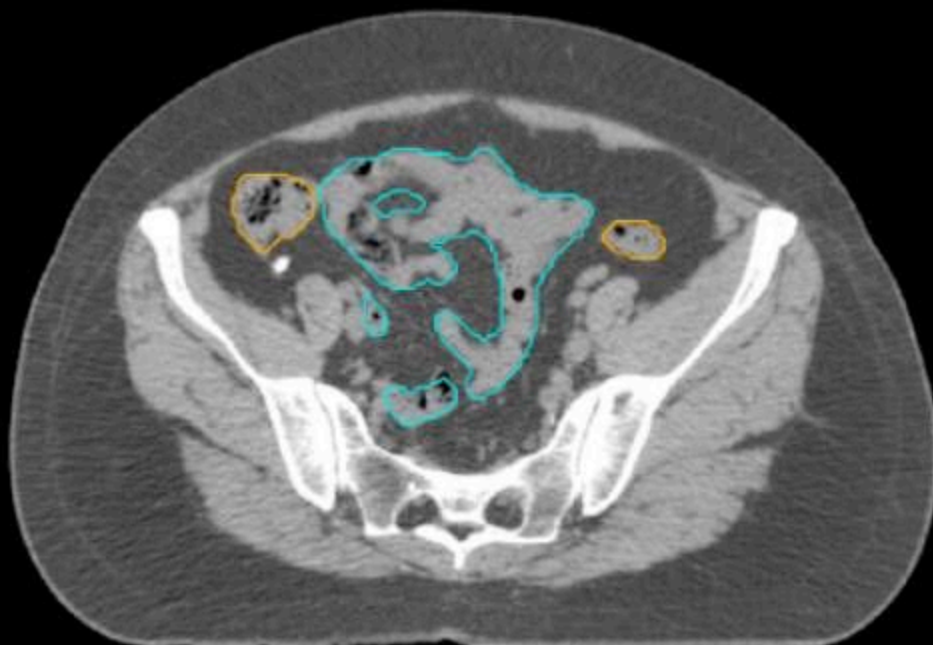
GYN/GI:

- UteroCervix
- Femur\_L
- Femur\_R
- Adnexa\_R
- Adnexa\_L
- Bladder

GI:

- Small Bowel
- AnoRectumSig
- Colon

The BowelBag is bounded by the muscles and bone.



# **Consensus Guidelines for the Deliniation of the CTV in the Postoperative Pelvic Radiotherapy of Endometrial and Cervical Cancer**

**William Small Jr., M.D., Radiation Oncology \***  
**Arno J. Mundt, MD, Radiation Oncology†**

\* Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

† University of California San Diego

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



Fig. 1. Upper common iliac clinical target volume.

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

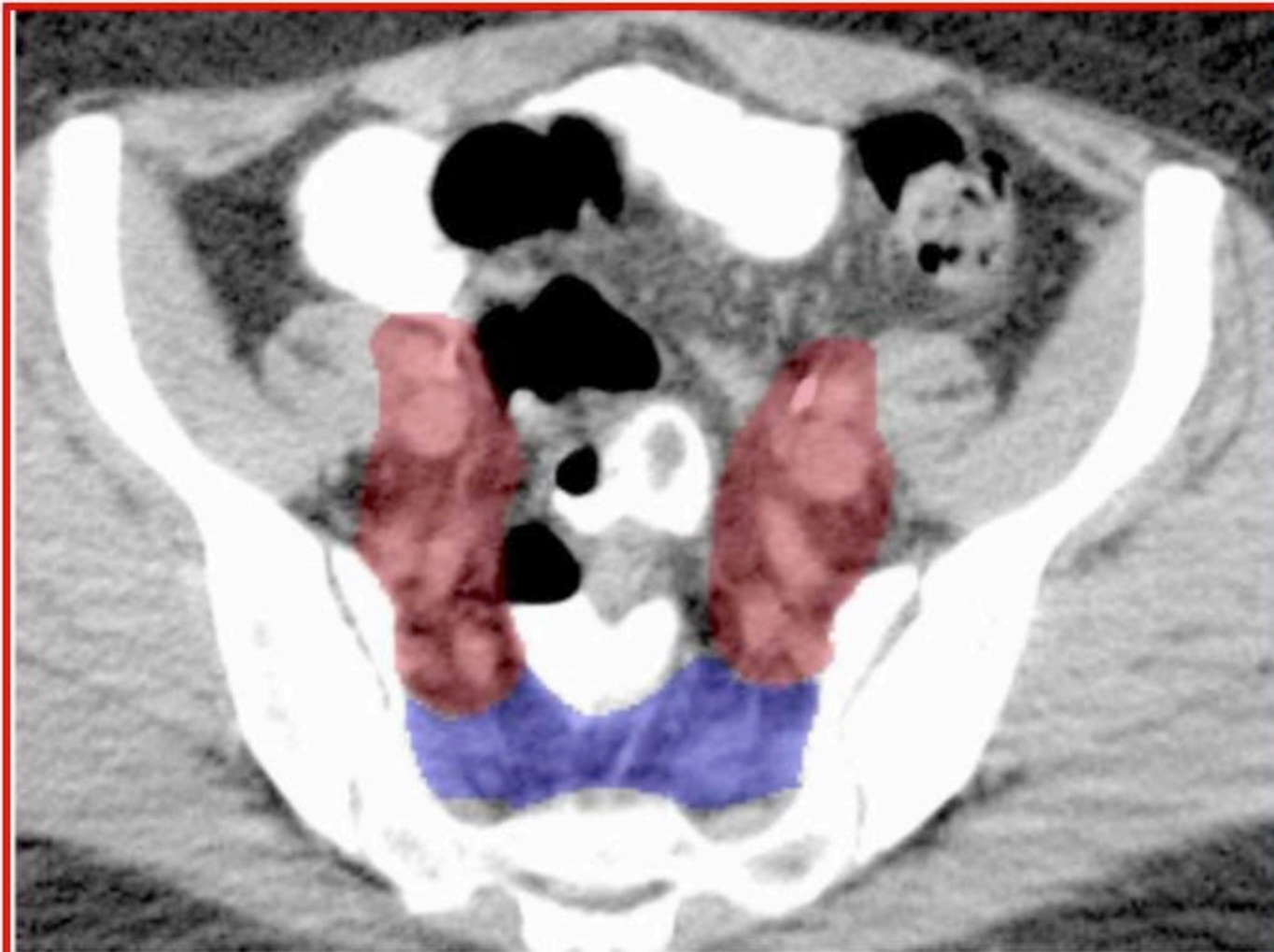


Fig. 4. Upper external and internal iliac (red) and presacral clinical



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

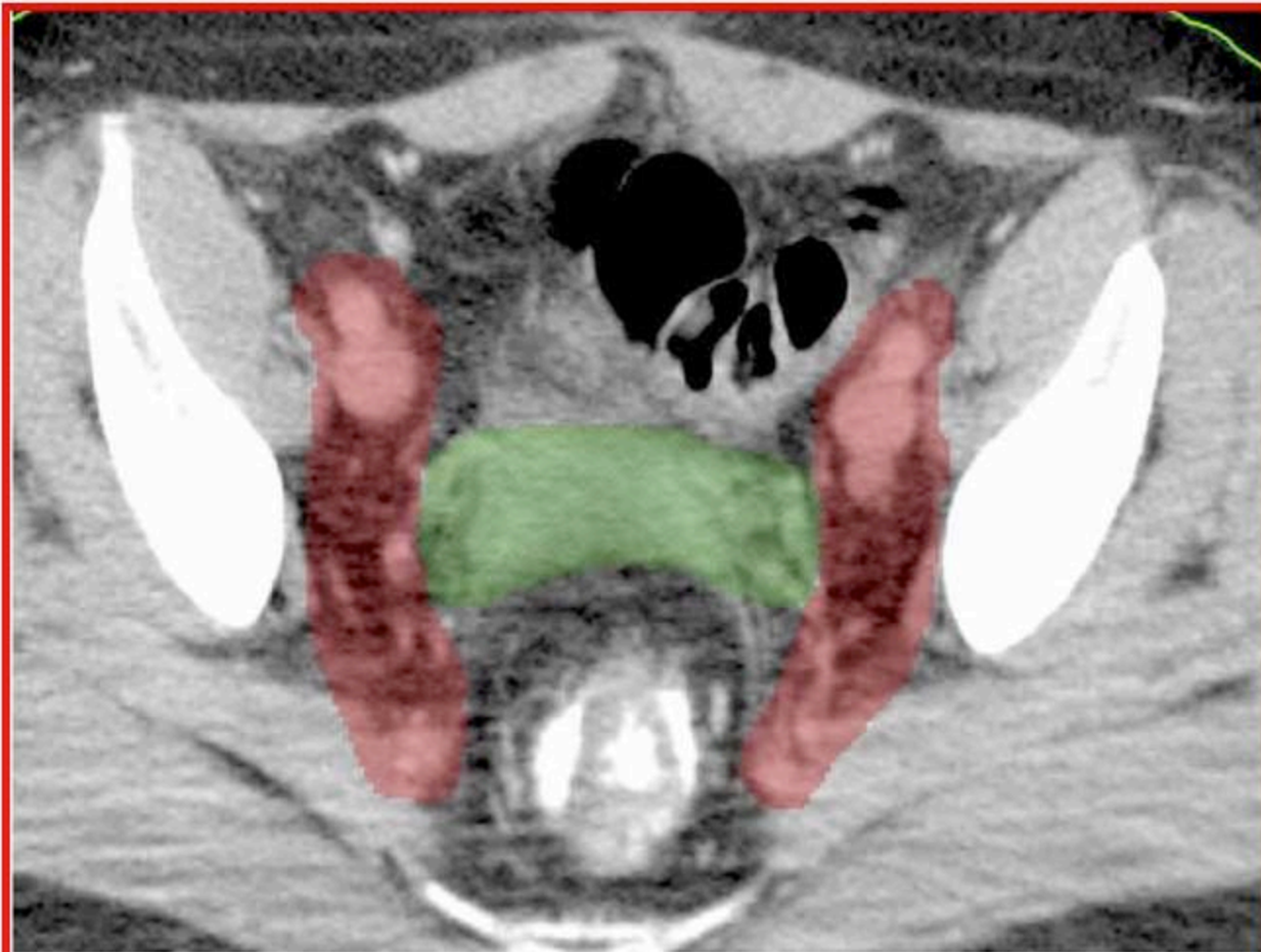


Fig. 6. External and internal iliac (red) and parametrial/vaginal (green) clinical target volume.



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

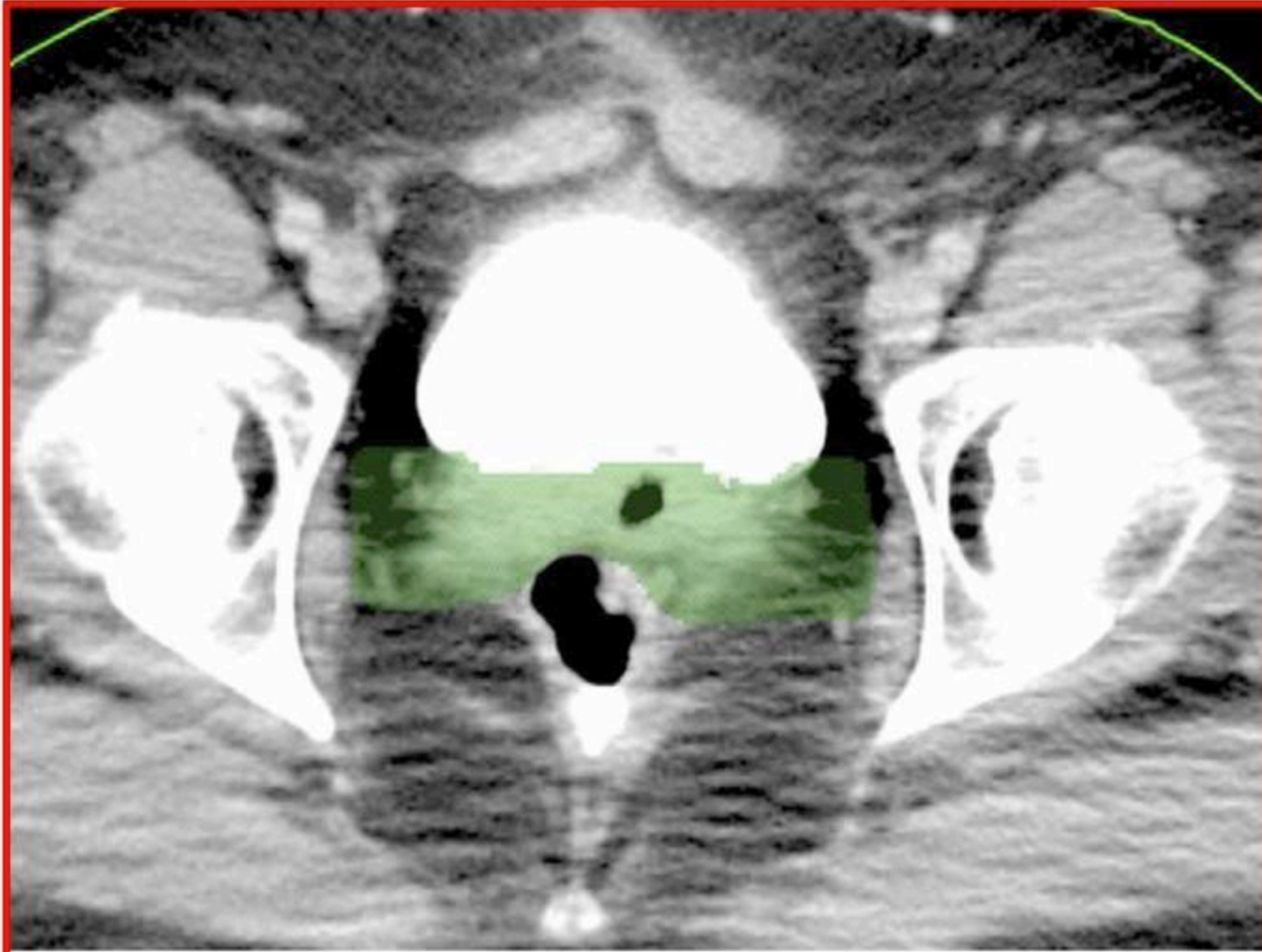
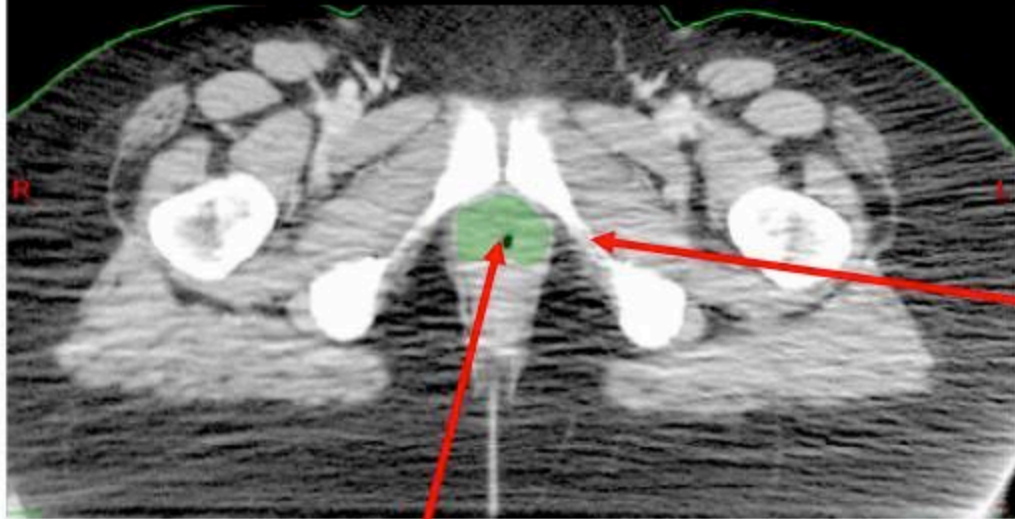


Fig. 7. Parametrial/vaginal clinical target volume.

# Consensus Guidelines for the Delineation of the CTV in the Postoperative Pelvic Radiotherapy of Endometrial and Cervical Cancer



Obturator foramen  
Last "slice"

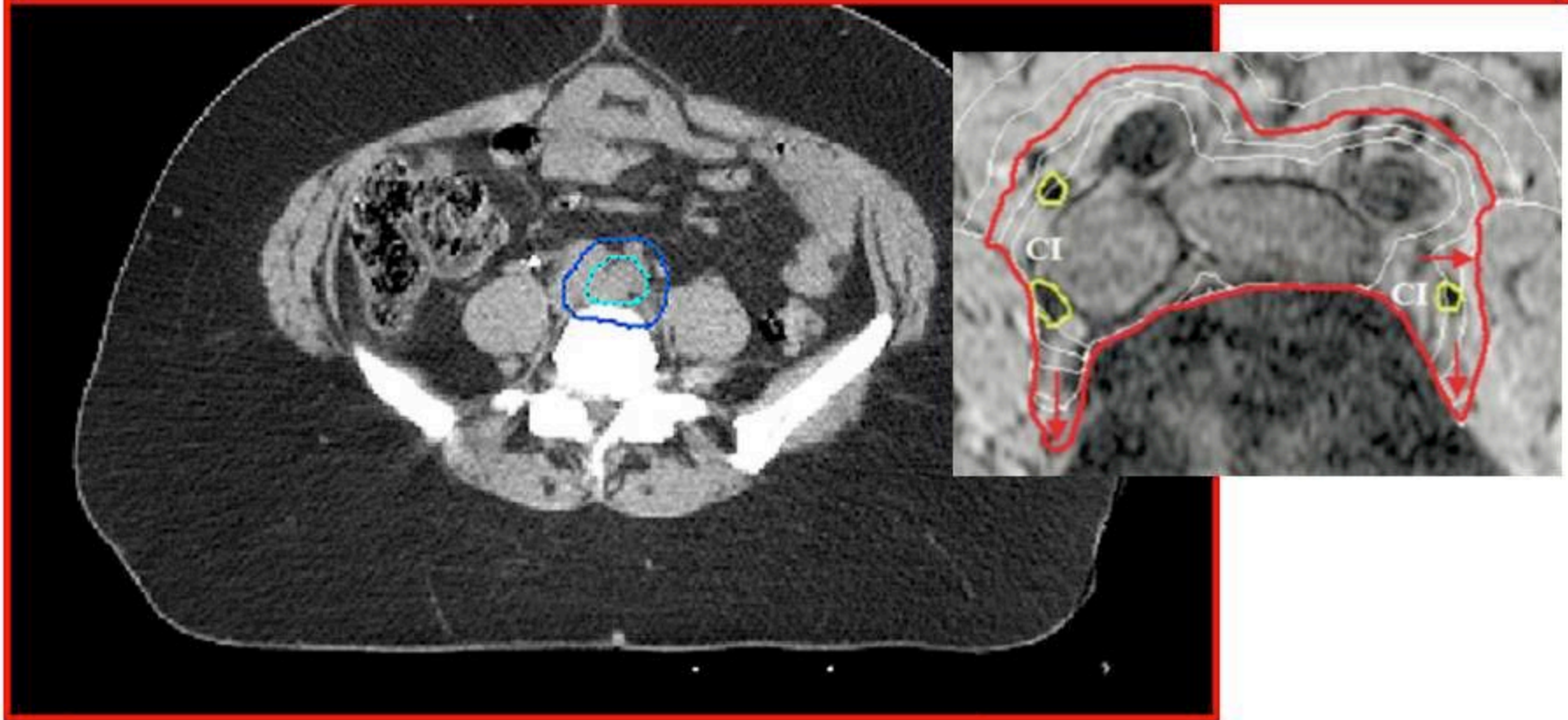
Two thirds of the  
vagina included in the  
CTV



**A Phase II Study of Intensity Modulated Radiation  
Therapy to the Pelvis for Postoperative Patients With  
Endometrial Carcinoma: Radiation Therapy Oncology  
Group Trial 0418**

unacceptable nodal contouring

covers only the vessels, not the entire nodal bed





**A Phase II Study of Intensity Modulated Radiation  
Therapy to the Pelvis for Postoperative Patients With  
Endometrial Carcinoma: Radiation Therapy Oncology  
Group Trial 0418**

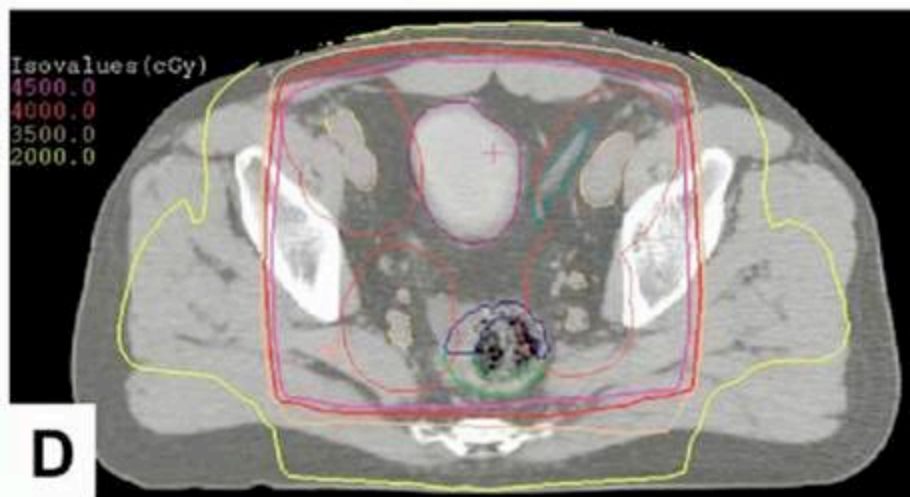
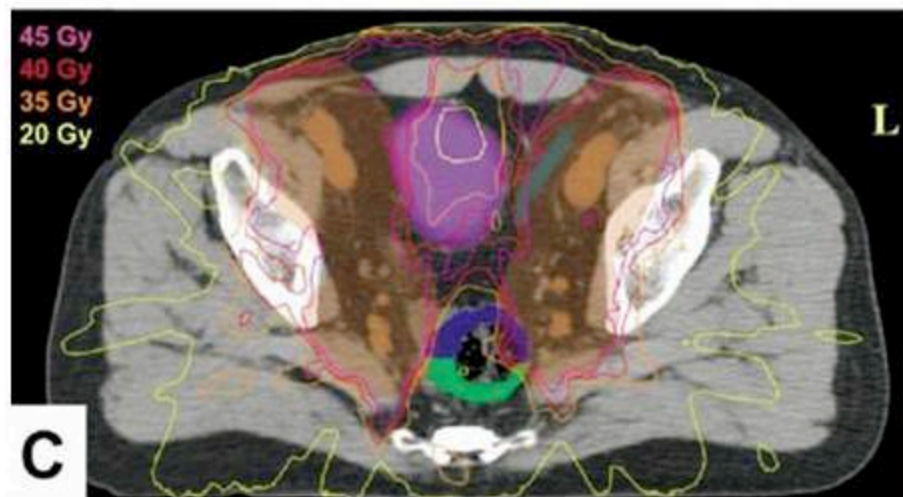
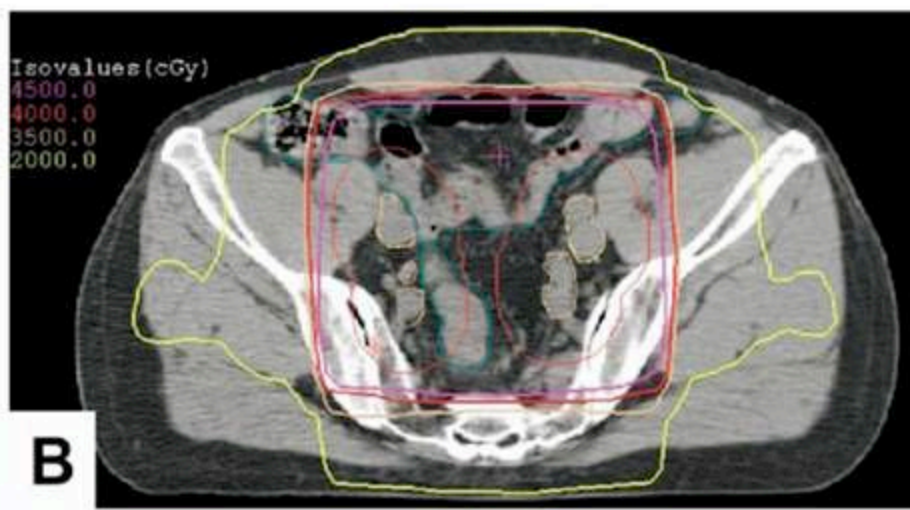
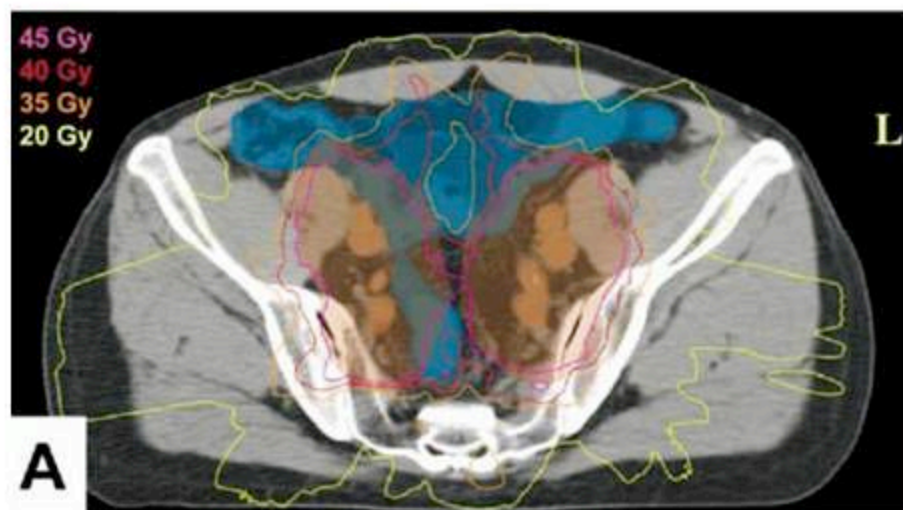
unacceptable nodal contouring

covers only the vessels, not the entire nodal bed





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



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

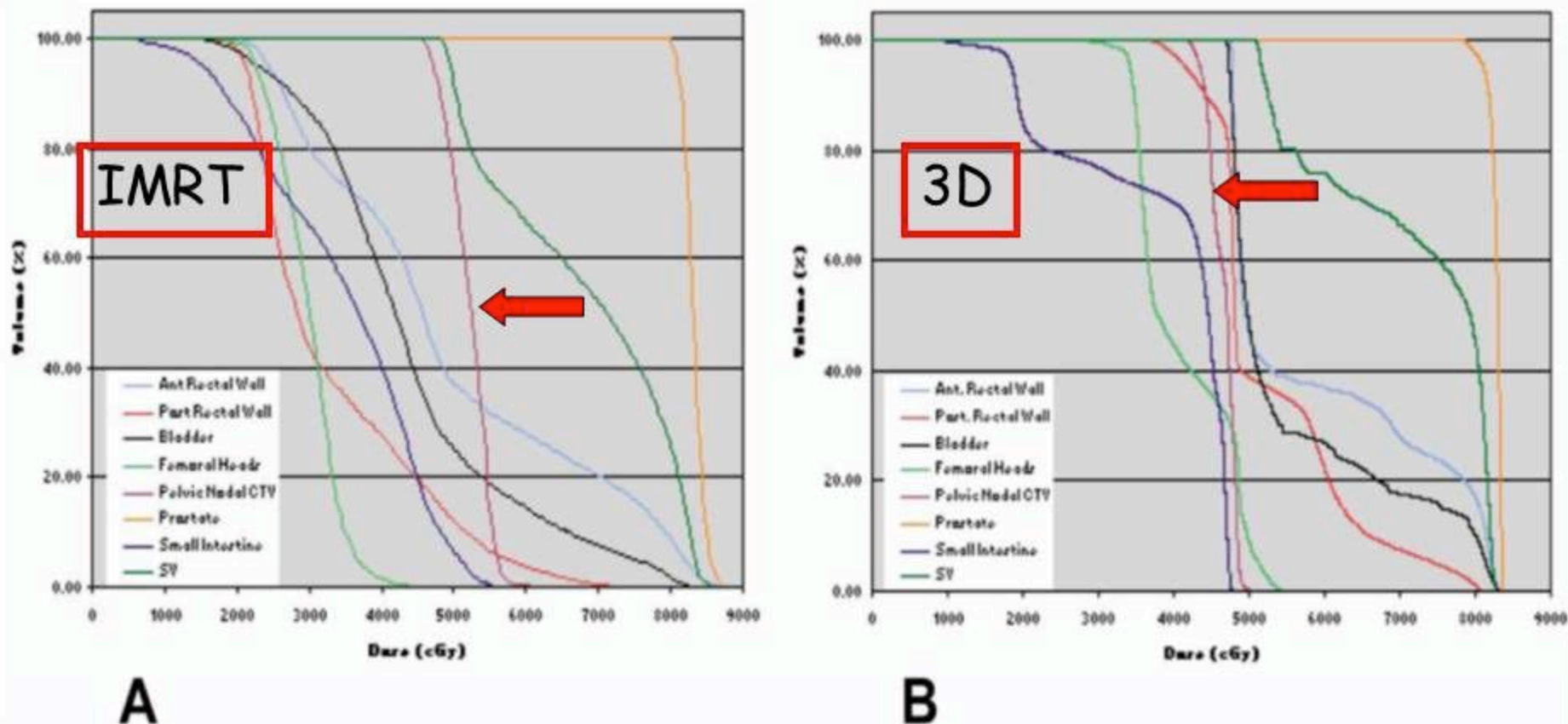


Fig. 6. Dose-volume histograms comparing (A) intensity-modulated radiation therapy and (B) three-dimensional conformal radiotherapy treatment planning methods.

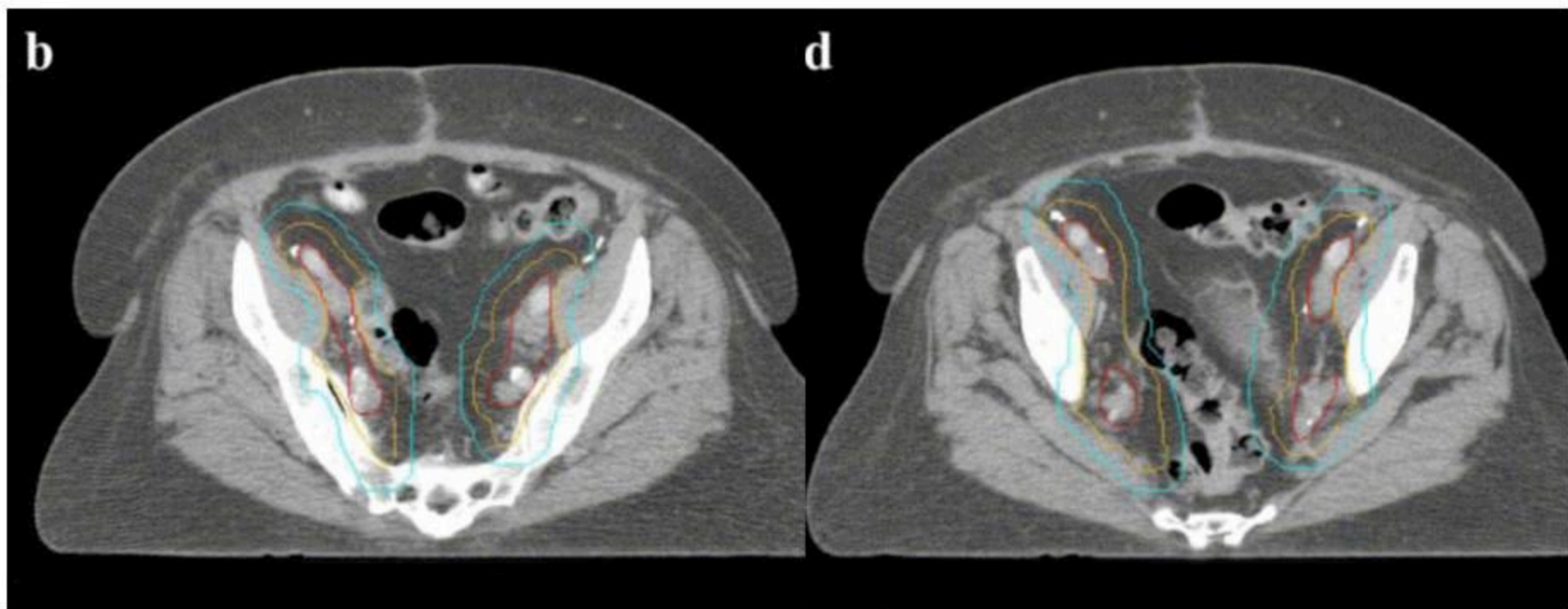


# Assessment of nodal target definition and dosimetry using three different techniques: implications for re-defining the optimal pelvic field in endometrial cancer

**Table 1 Various Guidelines for Pelvic Node CTV Drawing**

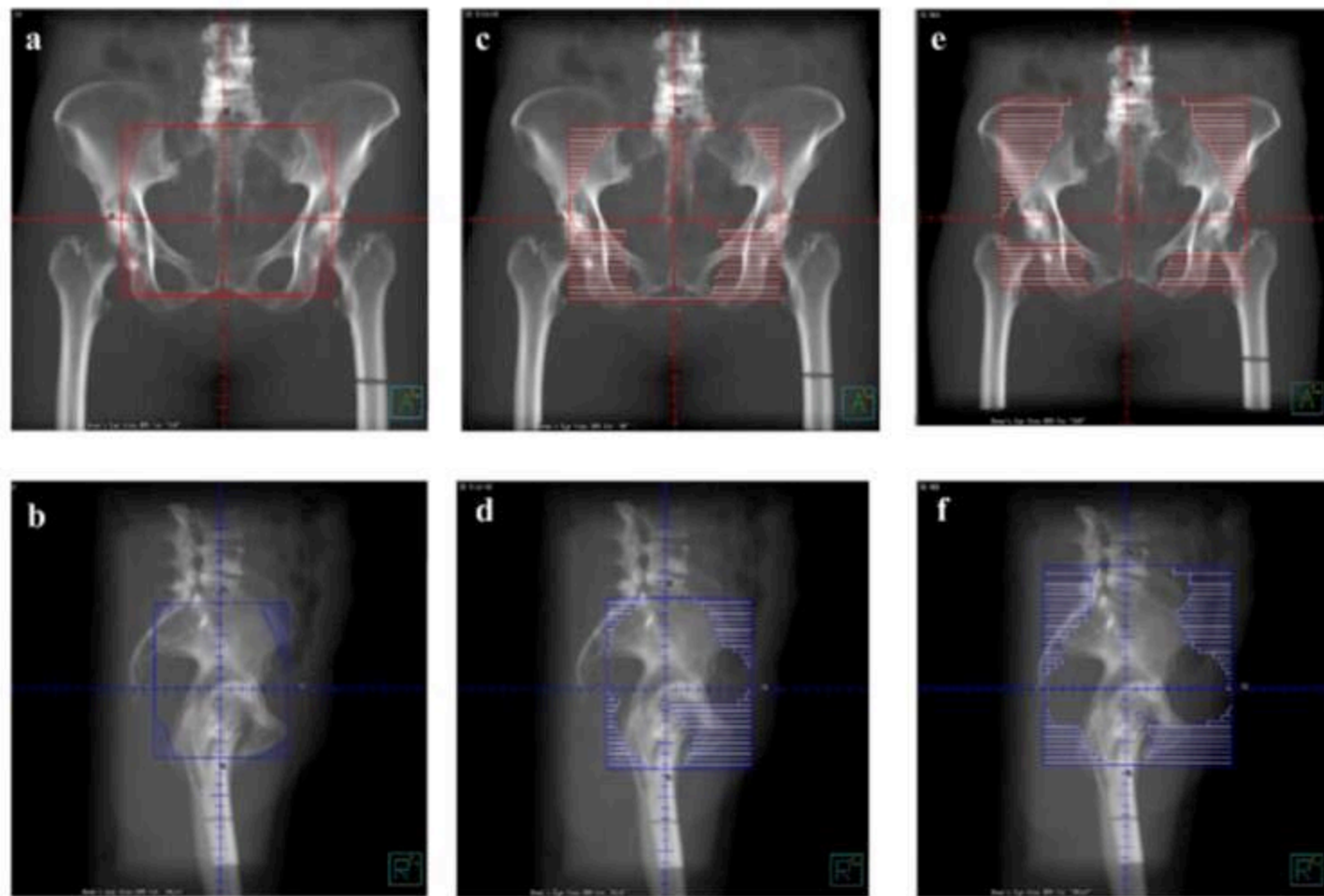
	<b>Common Iliac</b>	<b>External Iliac</b>	<b>Internal Iliac</b>	<b>Obturator</b>
<b>Portaluri*</b>	Cranial: Aortic bifurcation  Caudal: Common iliac bifurcation  Anterior: Mesocolon  Lateral: Psoas muscles Posterior: sacrum	Cranial: Common iliac bifurcation (L5-S1)  Caudal: Femoral ring (disappearance of lateral muscles of abdominal wall, artery becomes lateral)  Anterior: Fat of small bowel, deferent duct or round ligament  Lateral: - Cranial: Psoas, int iliac vein, iliac bone, sacroiliac joint  - Caudal: Piriformis m., internal obturatorius m.  Posterior:  - Cranial: Ext iliac v - Caudal: Pubic bone (superior branch)  Medial: Mesocolon, uterus, bladder	Cranial: Common iliac bifurcation (L5-S1)  Caudal: Cranial sections of coccygeal muscle  Anterior: Bladder, uterus  Lateral: - Cranial: Psoas muscle, int iliac vein, iliac bone, sacroiliac joint  - Caudal: Piriformis m., int obturatorius m.  Posterior:  - Cranial: Sacral wing - Caudal: Piriform muscle  Medial: Mesocolon, uterus, bladder	Cranial: Cranial sections of obturator muscle  Caudal: Superior margin inferior branch of pubic bone  Anterior: External iliac vein  Lateral: - Cranial: Acetabulum  - Caudal: Internal obturator muscle  Posterior: Internal obturator muscle Medial: Bladder
<b>Taylor†</b>	7 mm around common iliac vessels, extending posterior and lateral borders to psoas and vertebral body	7 mm around ext iliac vessels, extending anterior border by additional 10 mm anterolaterally along ilopsoas muscle to include lateral external iliac nodes	7-mm margin around int iliac vessels, extending lateral borders to pelvic sidewall	18-mm wide strip along pelvic sidewall joining external and internal iliac regions
<b>Shih††</b>	2.0 cm expansion around the distal 2.5 cm of common iliac vessels superior to bifurcation	2.0 cm expansion around ext iliac vessels for 9 cm from common iliac bifurcation	2.0 cm expansion around int iliac vessels for 8.5 cm extending from common iliac bifurcation	Not specified
<b>RTOG 0418  </b>	7 mm around common iliac vessels, with superior border at 7 mm below L4-L5 interspace	7 mm around ext iliac vessels, terminating at level of femoral head	7 mm around int iliac vessels	Not specified

Assessment of nodal target definition and dosimetry using three different techniques: implications for re-defining the optimal pelvic field in endometrial cancer





## Assessment of nodal target definition and dosimetry using three different techniques: implications for re-defining the optimal pelvic field in endometrial cancer



**Figure 2** Comparison of 2D, RTOG 0418-3DCRT, and NEW-3DCRT plans for one patient. AP and lateral views of 2D plan (a,b) AP and lateral views of RTOG 0418-3DCRT plan (c,d) AP and lateral views of NEW-3DCRT plan (e,f)

Assessment of nodal target definition and dosimetry using three different techniques: implications for re-defining the optimal pelvic field in endometrial cancer

**Mean V45Gy Coverage of Target and Normal Structures among Different Plans**

	2D	RTOG 0418-3DCRT	NEW-3DCRT	NEW-IMRT
<b>NEW-PTV</b>	50% (p < 0.0009)	69% (p < 0.0009)	98% (p = NS)	97%
<b>Small Bowel</b>	24% (p = 0.019)	20% (p < 0.0009)	32% (p < 0.0009)	14%
<b>Rectum</b>	26% (p = NS)	35% (p = 0.002)	52% (p = 0.016)	26%
<b>Bladder</b>	83% (p = NS)	51% (p = NS)	73% (p < 0.0009)	30%

## INTENSITY-MODULATED WHOLE PELVIC RADIOTHERAPY IN WOMEN WITH GYNECOLOGIC MALIGNANCIES

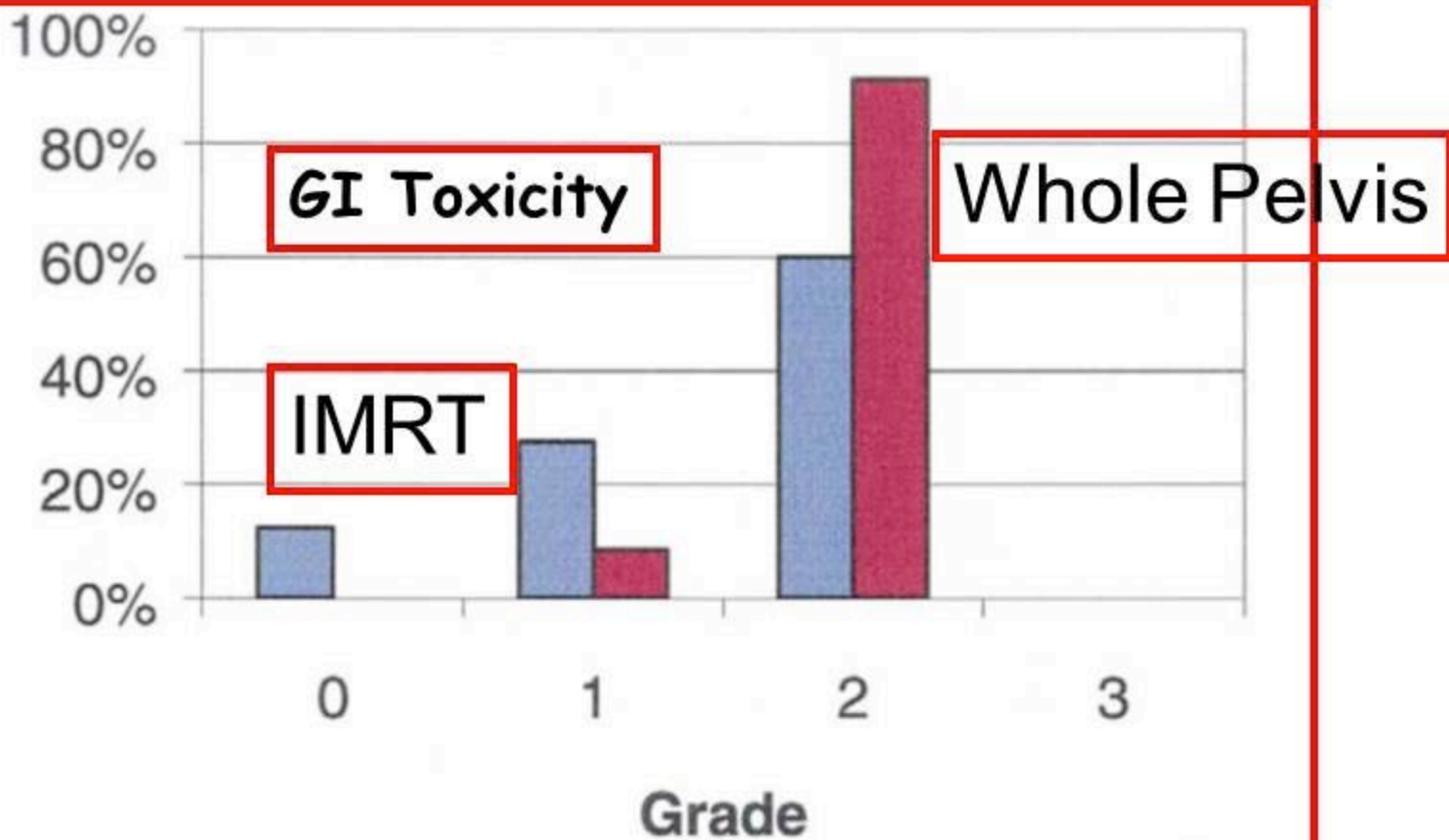


Fig. 4. Incidence of acute GI toxicity in the IM-WPRT (blue bars) and WPRT (red bars) groups.

## INTENSITY-MODULATED WHOLE PELVIC RADIOTHERAPY IN WOMEN WITH GYNECOLOGIC MALIGNANCIES

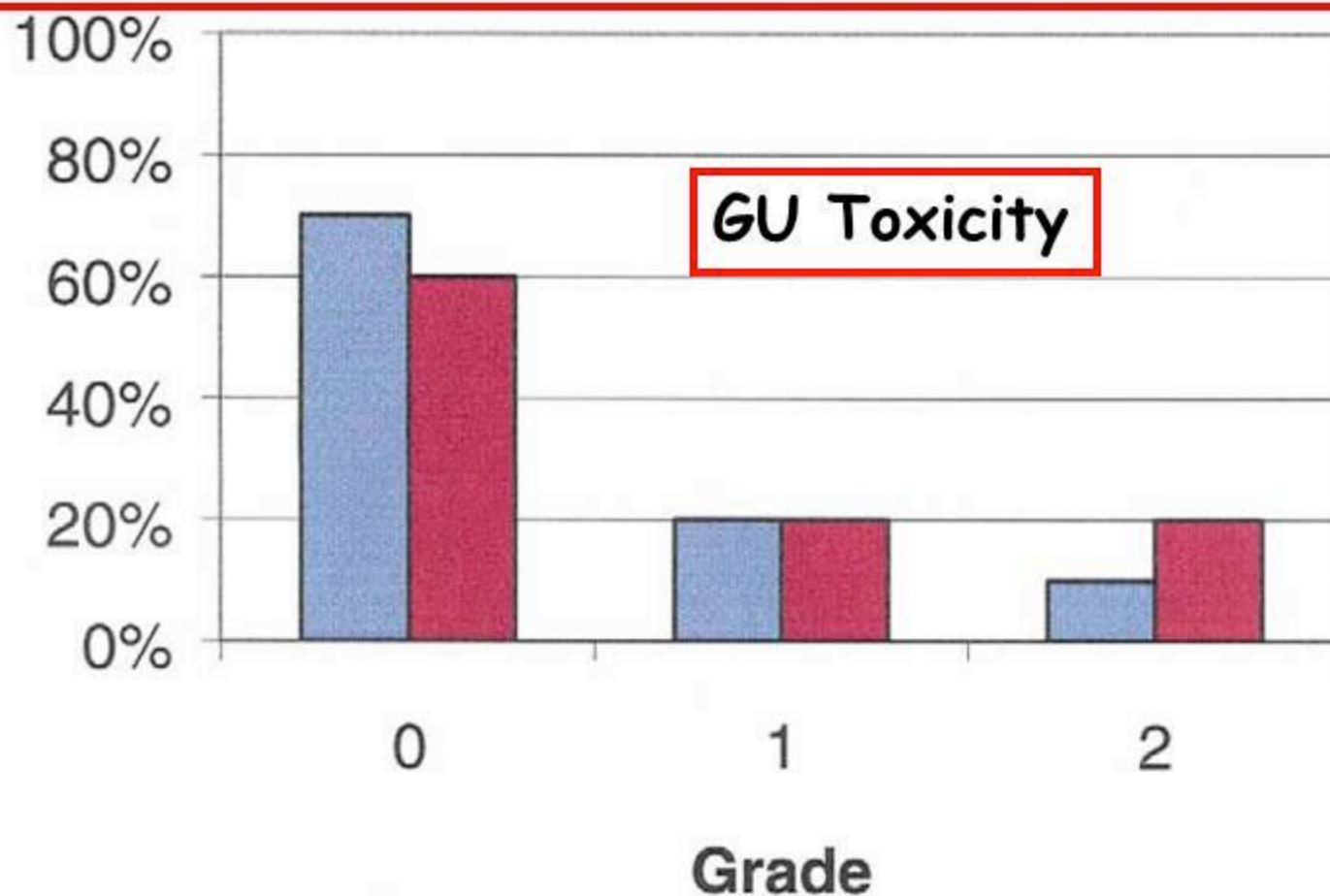
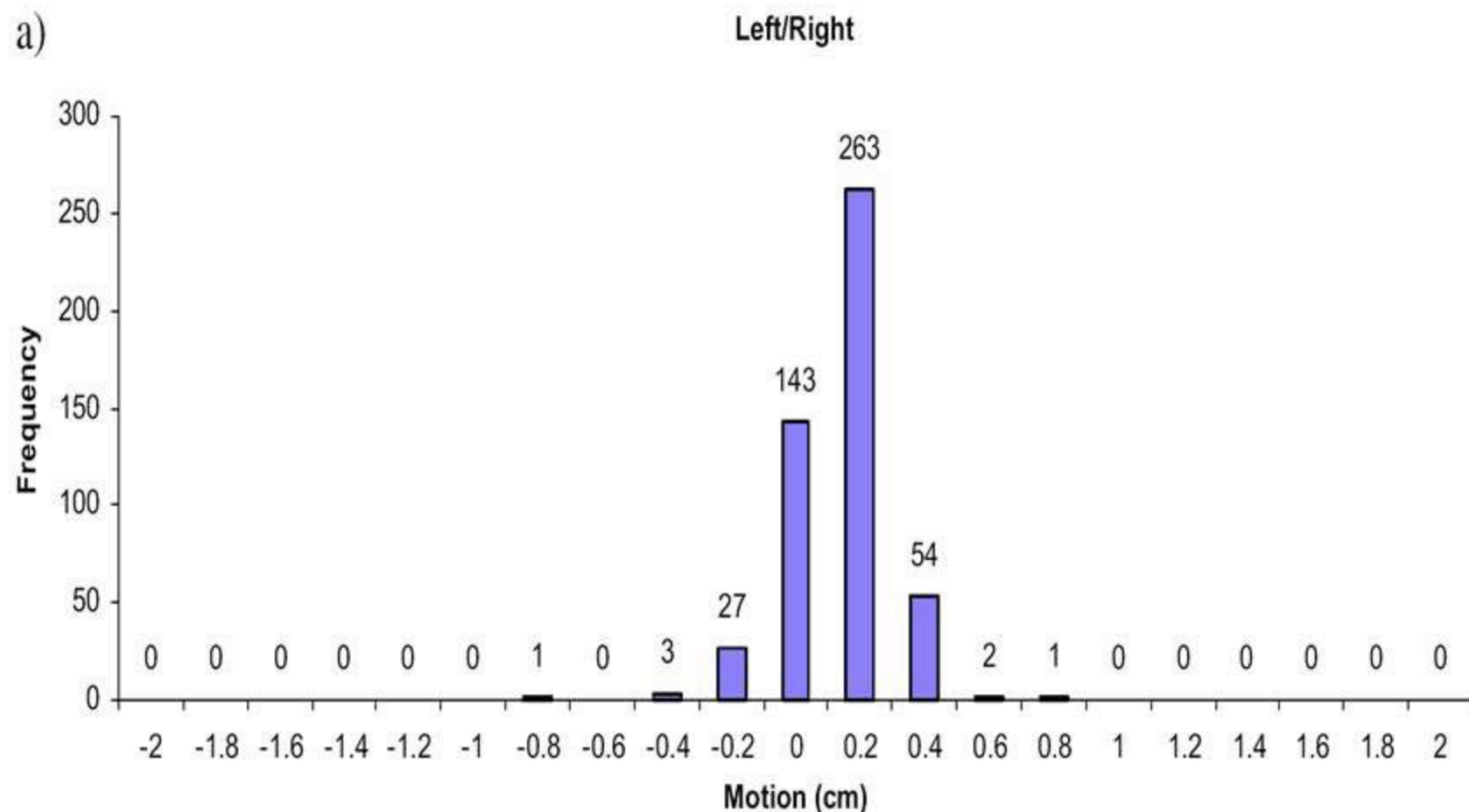


Fig. 5. Incidence of acute GU toxicity in the IM-WPRT (blue bars) and WPRT (red bars) groups.



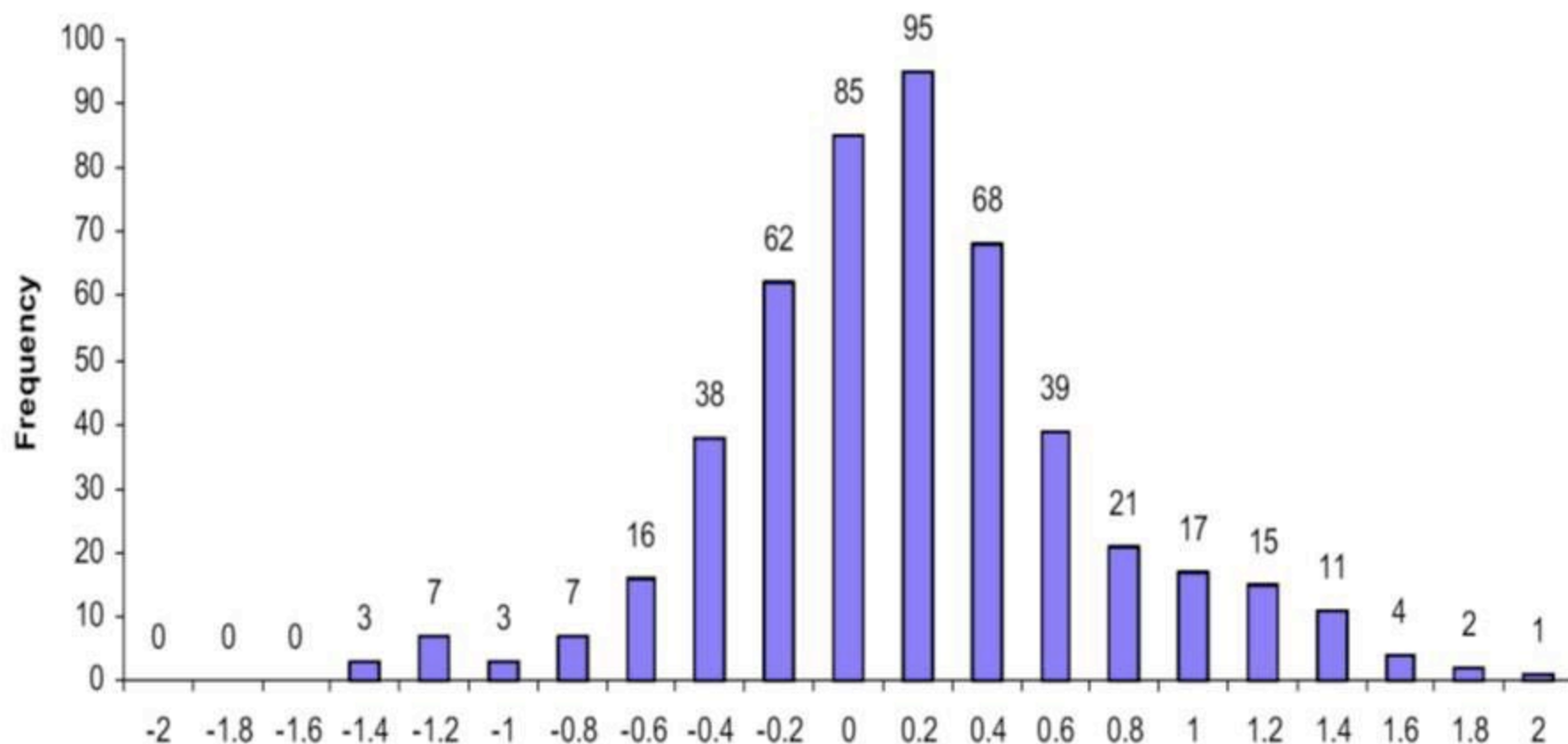
# IMRT and Organ Motion

# ASSESSMENT OF ORGAN MOTION IN POSTOPERATIVE ENDOMETRIAL AND CERVICAL CANCER PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY



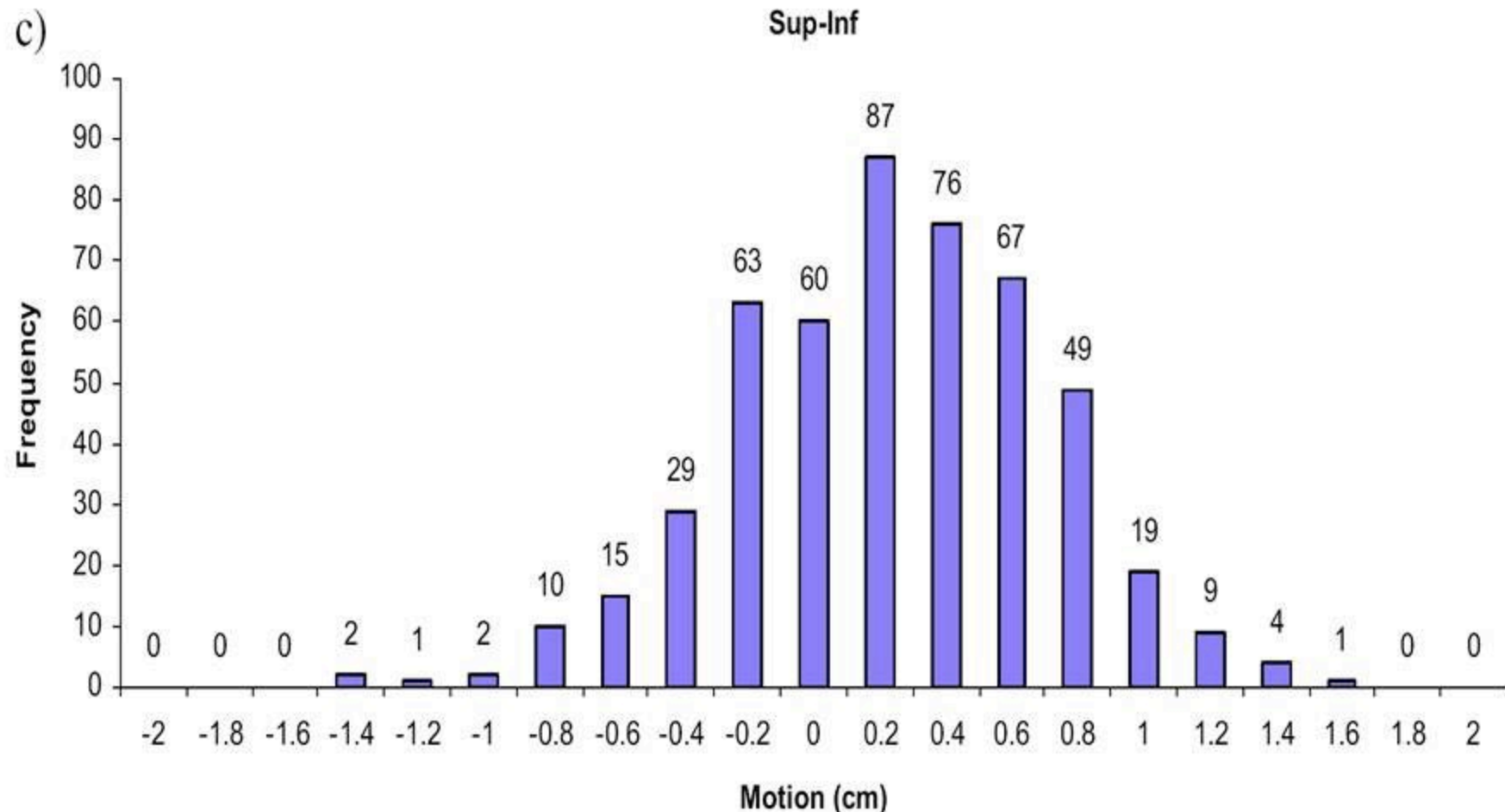
## ASSESSMENT OF ORGAN MOTION IN POSTOPERATIVE ENDOMETRIAL AND CERVICAL CANCER PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY

b) Ant-Post



**Conclusions:** These data suggest a planning target volume margin of 16 mm will account for maximal organ motion in the majority of gynecologic patients undergoing postoperative pelvic IMRT, and it may be possible to incorporate directional motion into the planning target volume margin. © 2011 Elsevier Inc.

## ASSESSMENT OF ORGAN MOTION IN POSTOPERATIVE ENDOMETRIAL AND CERVICAL CANCER PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY

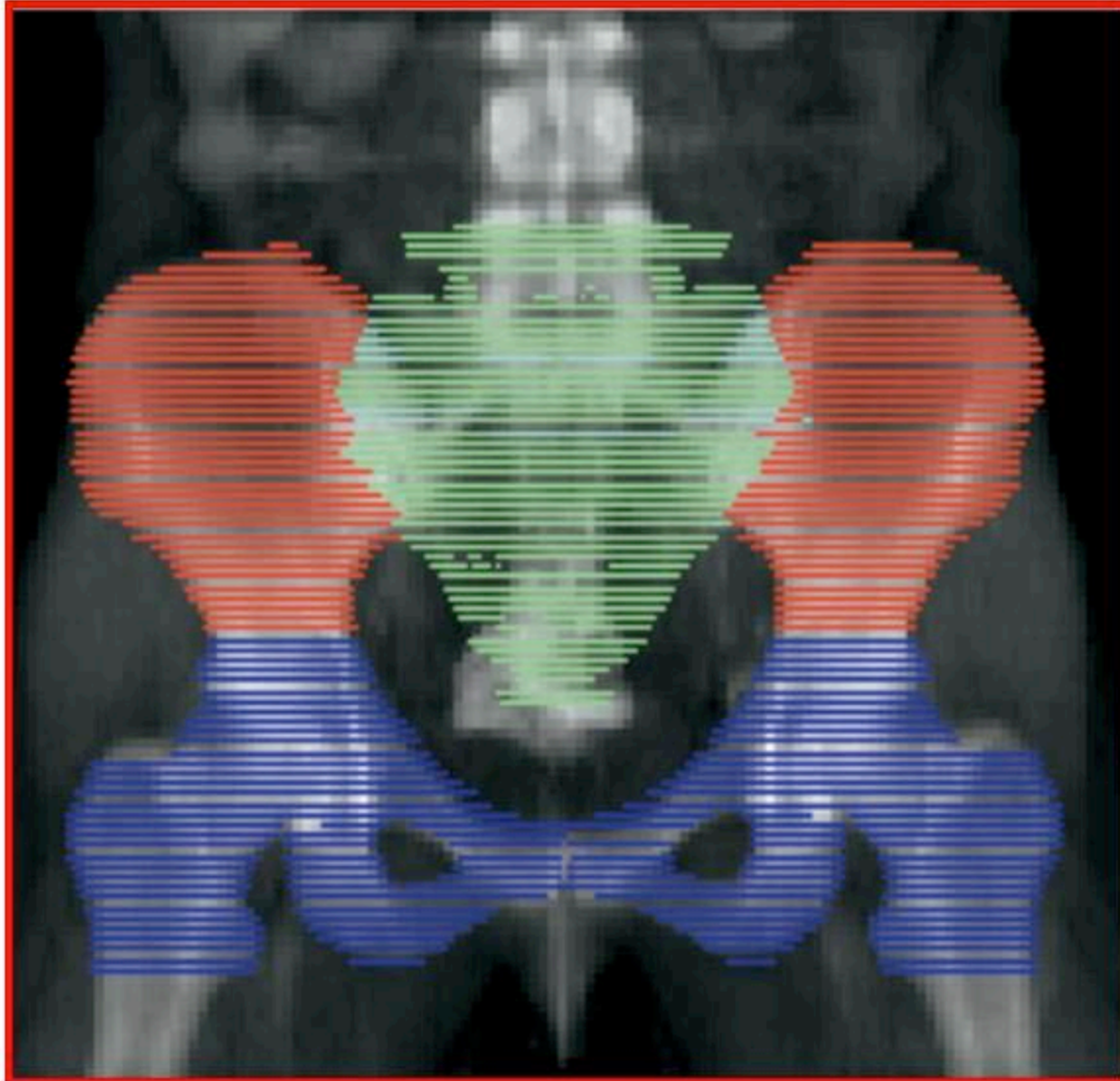


**Conclusions:** These data suggest a planning target volume margin of 16 mm will account for maximal organ motion in the majority of gynecologic patients undergoing postoperative pelvic IMRT, and it may be possible to incorporate directional motion into the planning target volume margin. © 2011 Elsevier Inc.



IMRT and  
hematologic  
toxicity

**DOSIMETRIC PREDICTORS OF ACUTE HEMATOLOGIC TOXICITY IN  
CERVICAL CANCER PATIENTS TREATED WITH CONCURRENT CISPLATIN  
AND INTENSITY-MODULATED PELVIC RADIOTHERAPY**



# DOSIMETRIC PREDICTORS OF ACUTE HEMATOLOGIC TOXICITY IN CERVICAL CANCER PATIENTS TREATED WITH CONCURRENT CISPLATIN AND INTENSITY-MODULATED PELVIC RADIOTHERAPY

	RTOG grade 2+ leukopenia			RTOG grade 2+ neutropenia		
	Odds ratio*	95% CI	<i>p</i>	Odds ratio*	95% CI	<i>p</i>
Pelvic BM						
V <sub>10</sub>	2.09	1.24–3.53	0.006 <sup>†</sup>	1.41	1.02–1.94	0.037 <sup>†</sup>
V <sub>20</sub>	1.40	1.06–1.85	0.017 <sup>†</sup>	1.13	0.96–1.33	0.16
Ilium						
V <sub>10</sub>	1.04	0.88–1.22	0.66	0.99	0.84–1.16	0.87
V <sub>20</sub>	1.06	0.96–1.16	0.27	0.99	0.90–1.09	0.82
LSS						
V <sub>10</sub>	1.66	0.96–2.88	0.070	1.53	0.88–2.68	0.13
V <sub>20</sub>	1.25	1.01–1.57	0.048 <sup>†</sup>	1.11	0.93–1.33	0.24
Lower pelvis						
V <sub>10</sub>				1.15	0.98–1.35	0.078
V <sub>20</sub>				1.10	0.98–1.23	0.11

**BM-V<sub>10</sub> ≥ 90%**

*Abbreviations:* CI = confidence interval; BM = bone marrow; LSS = lumbosacral spine; other abbreviations as in Tables 1 and 3.

\* Odds ratios correspond to 1% increase in V<sub>10</sub> or V<sub>20</sub> (e.g., 1% increase in pelvic BM-V<sub>10</sub> approximately doubled relative odds of Grade 2+ leukopenia).

<sup>†</sup> Statistically significant.

# DOSIMETRIC PREDICTORS OF ACUTE HEMATOLOGIC TOXICITY IN CERVICAL CANCER PATIENTS TREATED WITH CONCURRENT CISPLATIN AND INTENSITY-MODULATED PELVIC RADIOTHERAPY

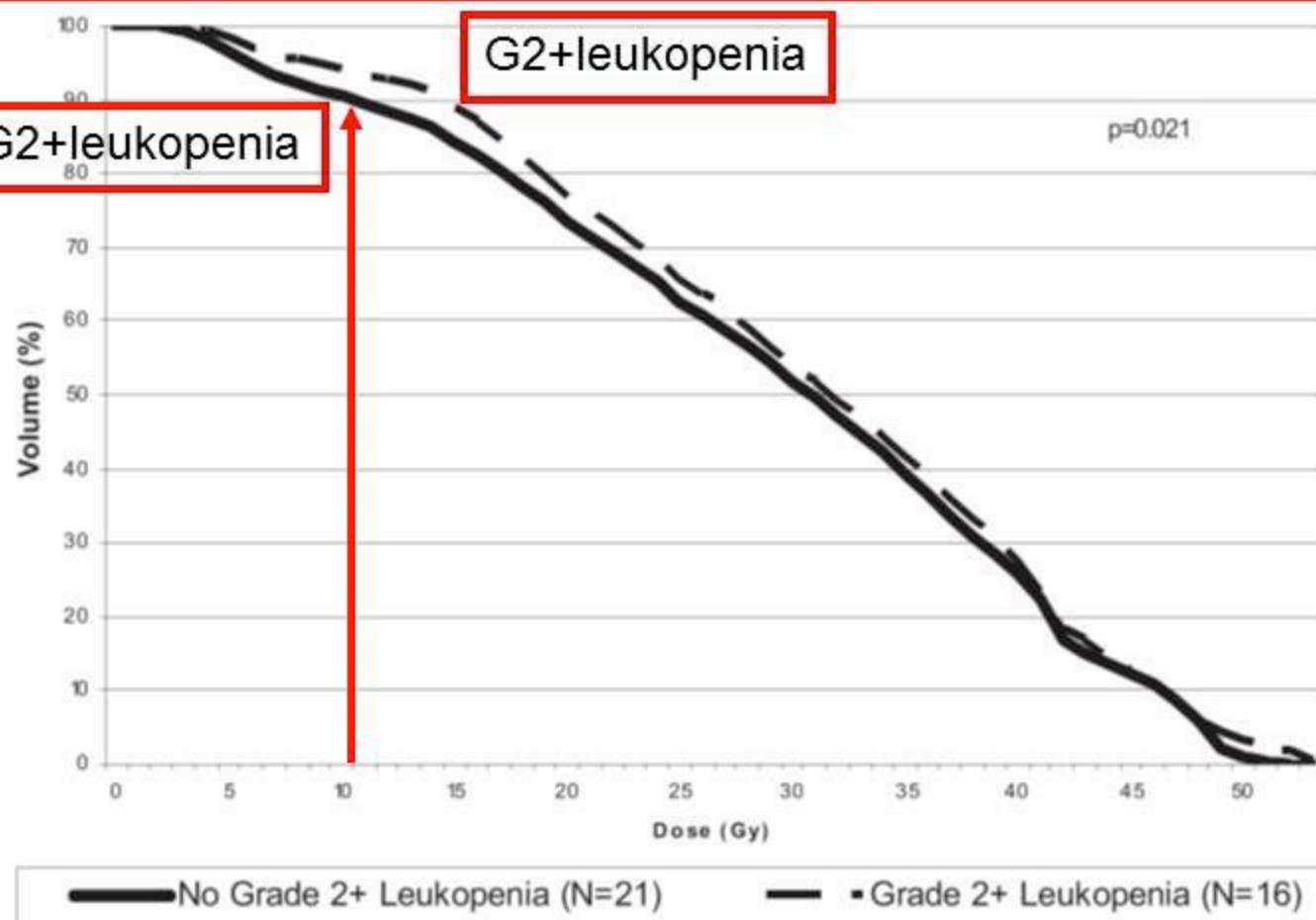
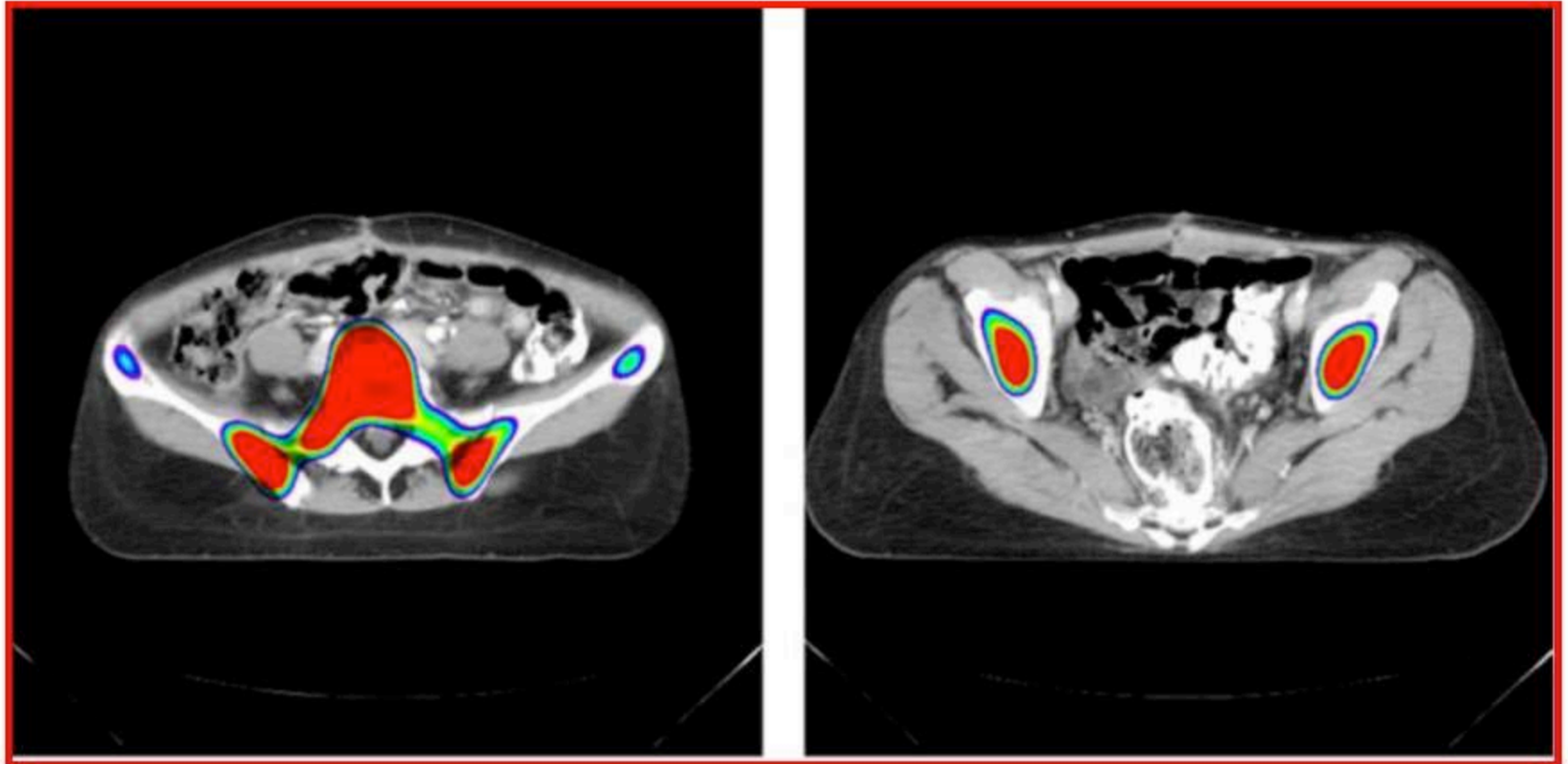


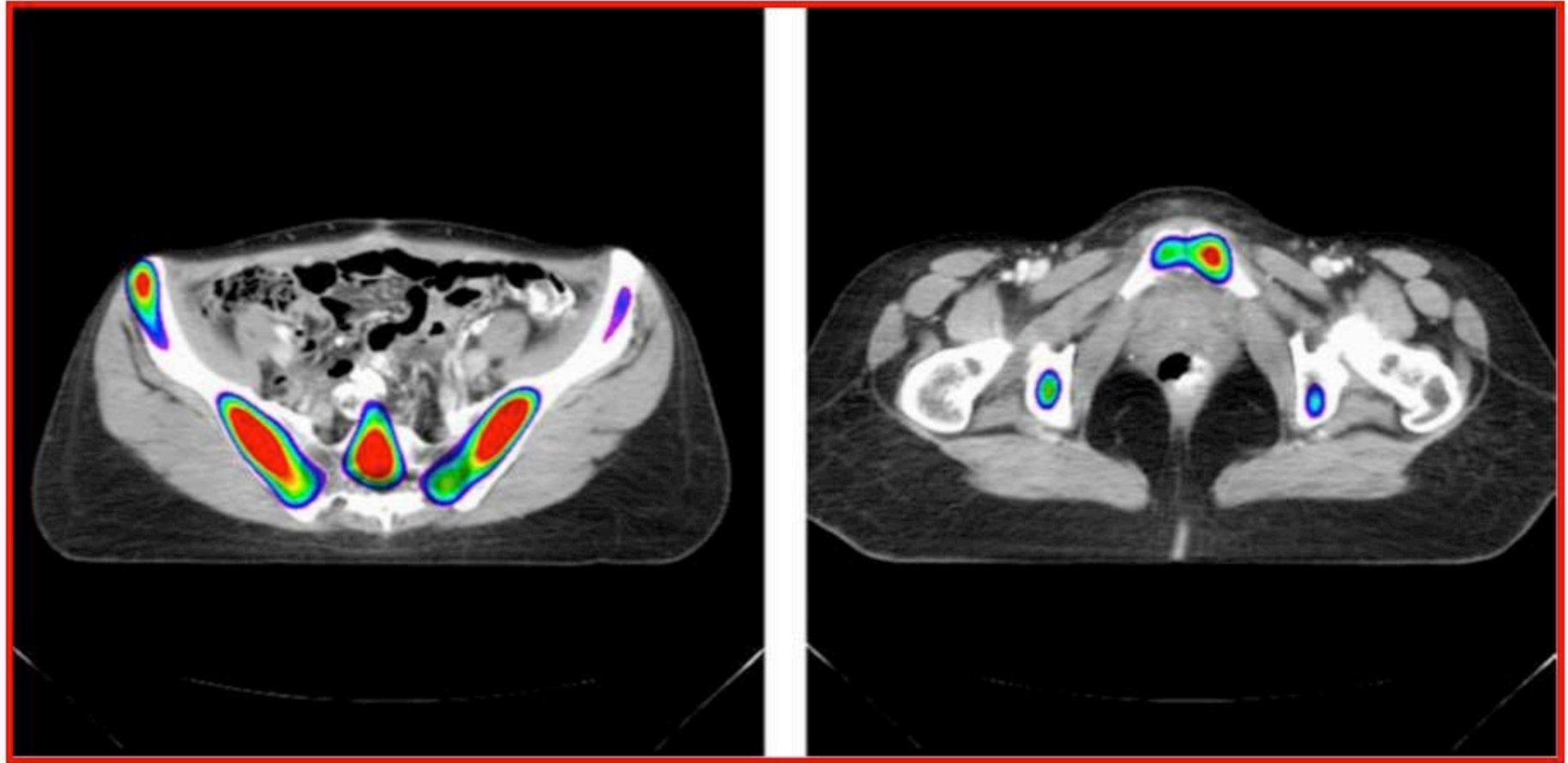
Fig. 4. Comparison of average pelvic bone marrow dose–volume histograms for patients with and without Grade 2 or worse leukopenia ( $p = 0.021$ , Mann-Whitney  $U$  test).



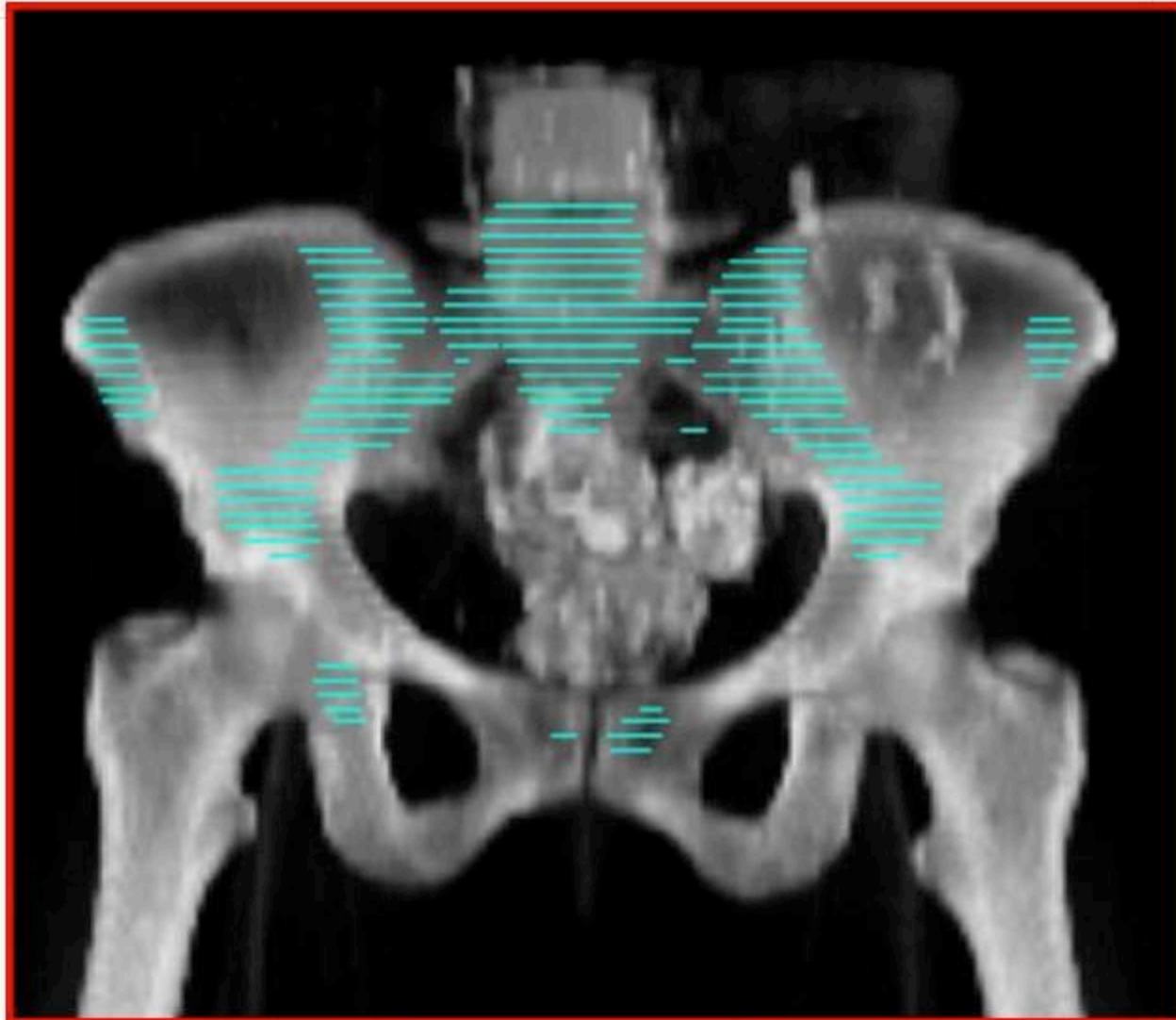
Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies



Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies

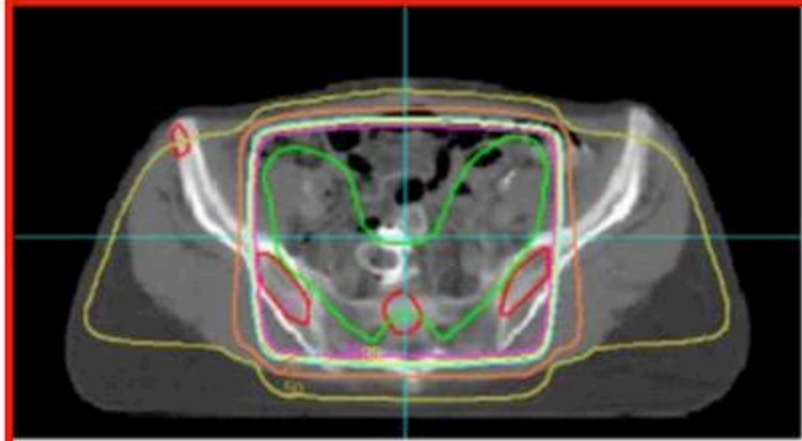


Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies

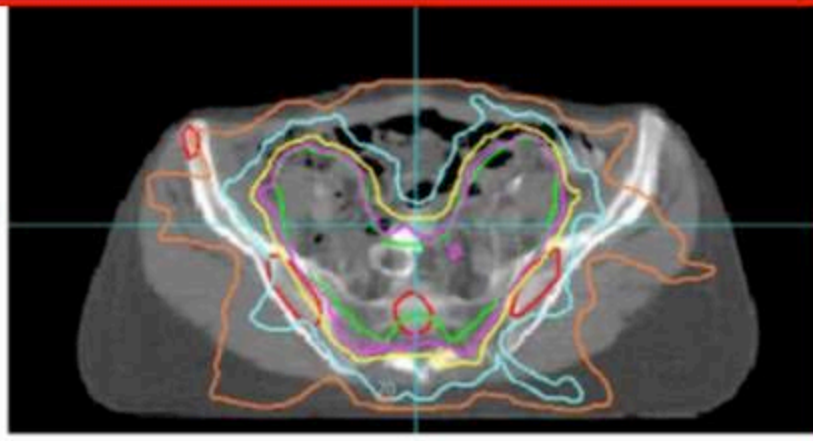


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Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies

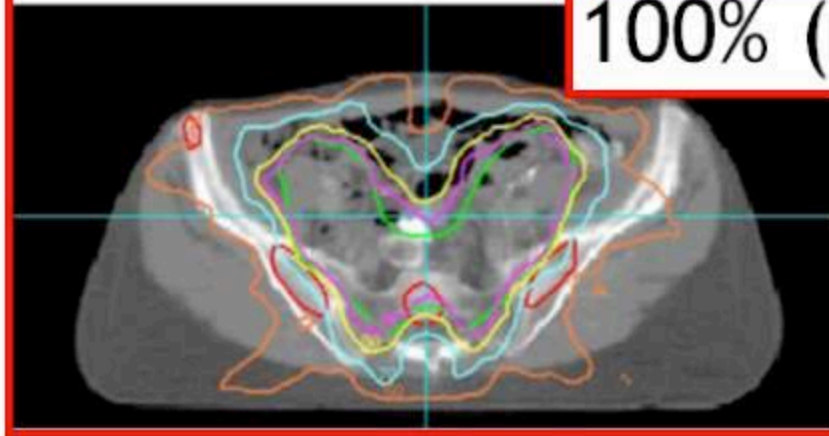


4-field (conventional) plan;

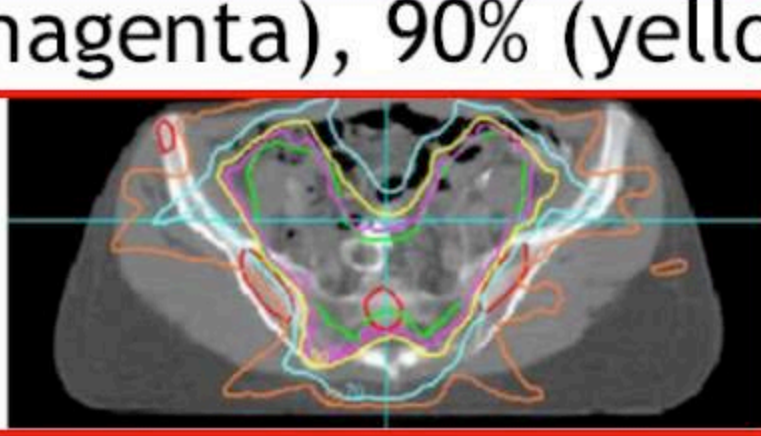


IM-WPRT-no-BM plan;

100% (magenta), 90% (yellow)



IM-WPRT-CT-BM plan



IM-WPRT-SPECT-BM plan.



## Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies

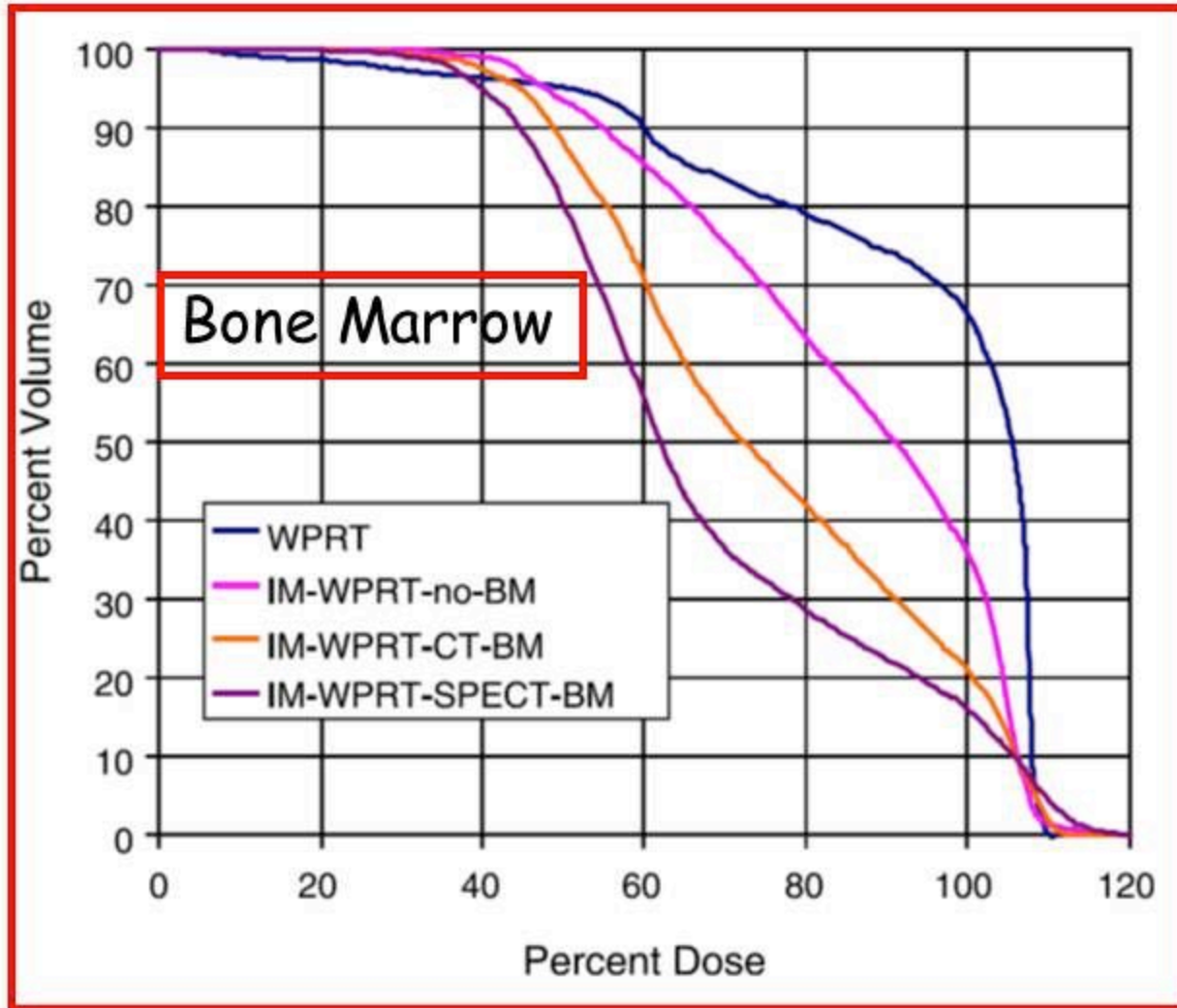
Table 1

Percent volume of bone marrow irradiated

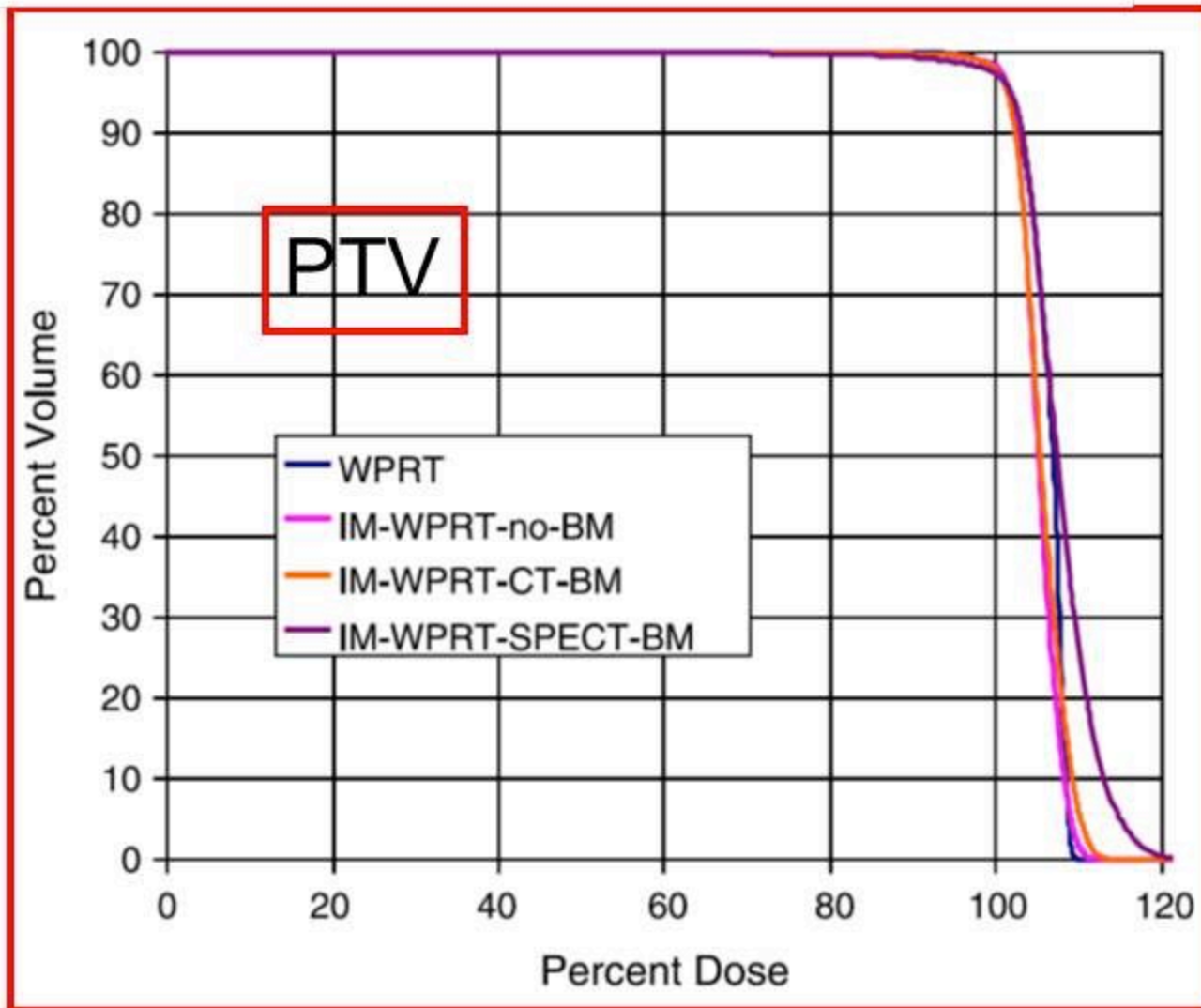
Dose (Gy)	WPRT (%)	IM-WPRT no-BM (%)	IM-WPRT CT-BM (%)	IM-WPRT SPECT-BM (%)
5	99	100	100	100
10	99	100	100	100
15	97	100	99	97
20	96	96	95	88
25	94	88	79	66
30	85	76	57	40
35	80	64	44	30
40	75	49	32	23
45	67	33	21	16

WPRT, whole pelvic radiation therapy; IM-WPRT, intensity modulated whole pelvic radiation therapy; CT, computed tomography; SPECT, single photon computed emission tomography; BM, bone marrow.

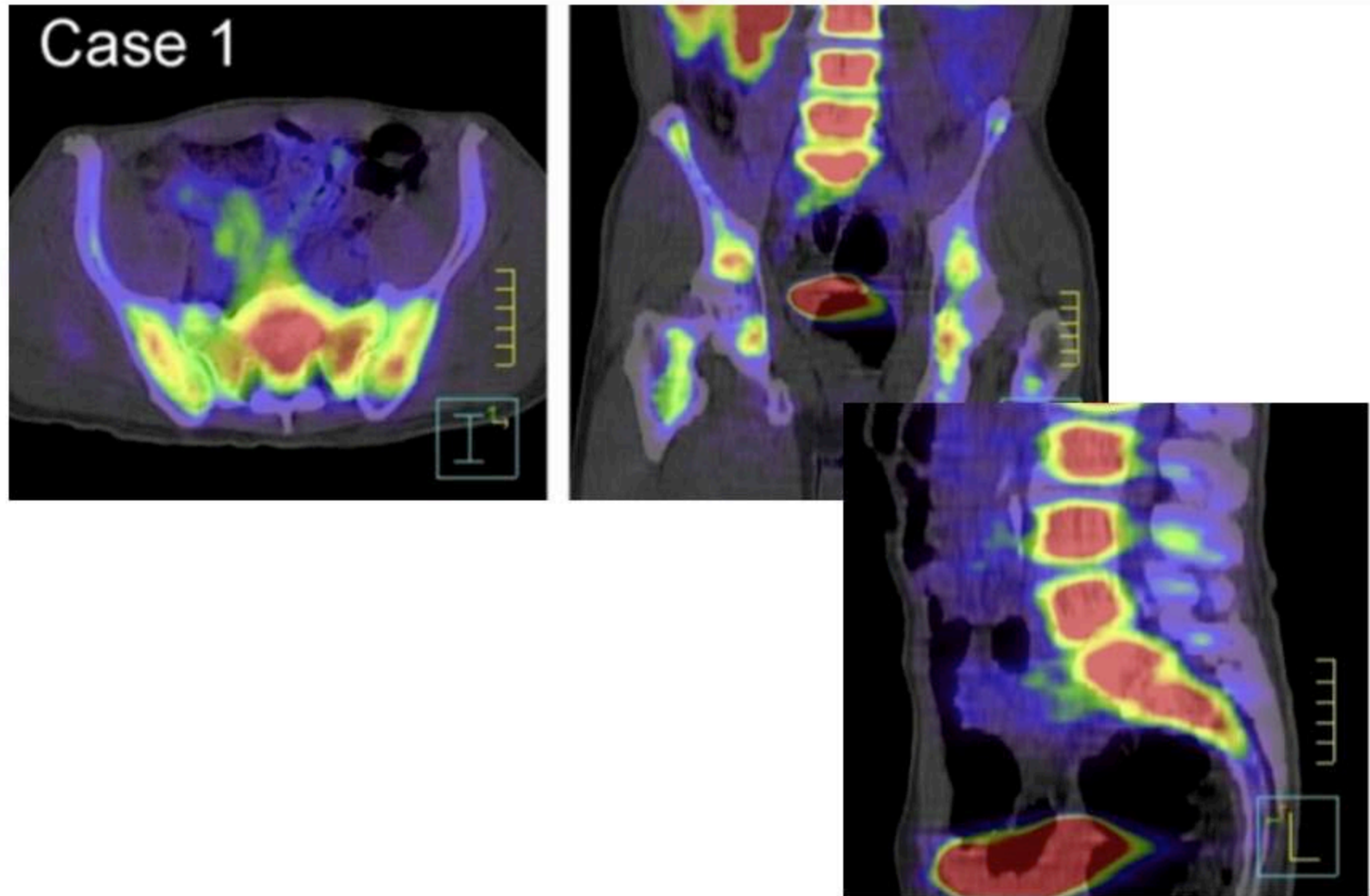
# Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies



# Incorporation of SPECT bone marrow imaging into intensity modulated whole-pelvic radiation therapy treatment planning for gynecologic malignancies

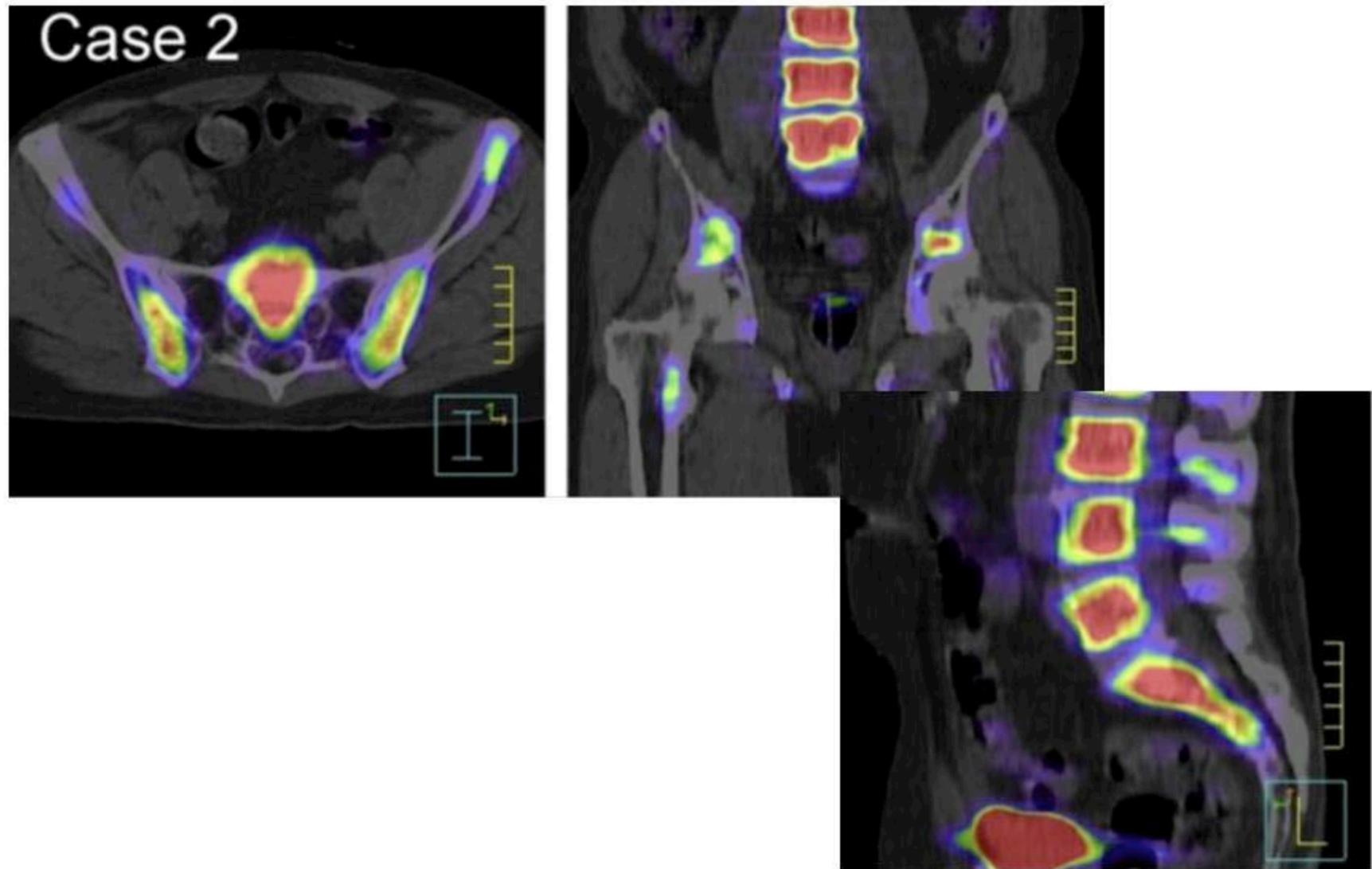


# A methodology for incorporating functional bone marrow sparing in IMRT planning for pelvic radiation therapy

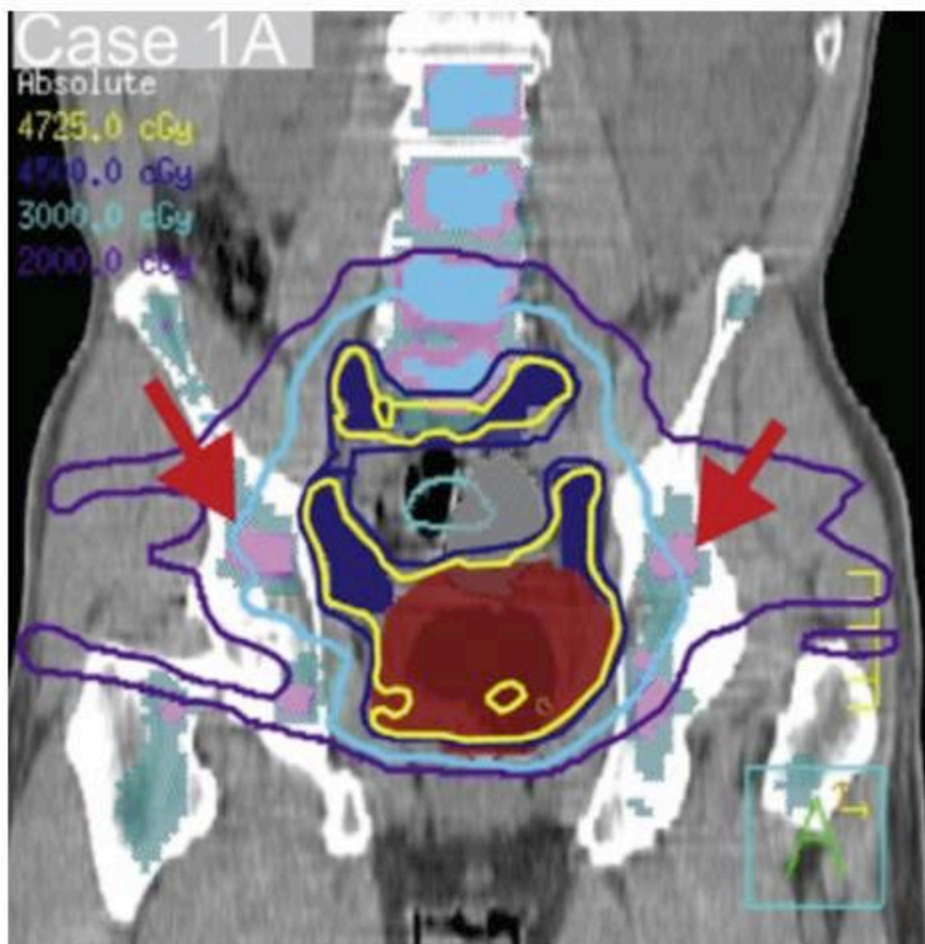




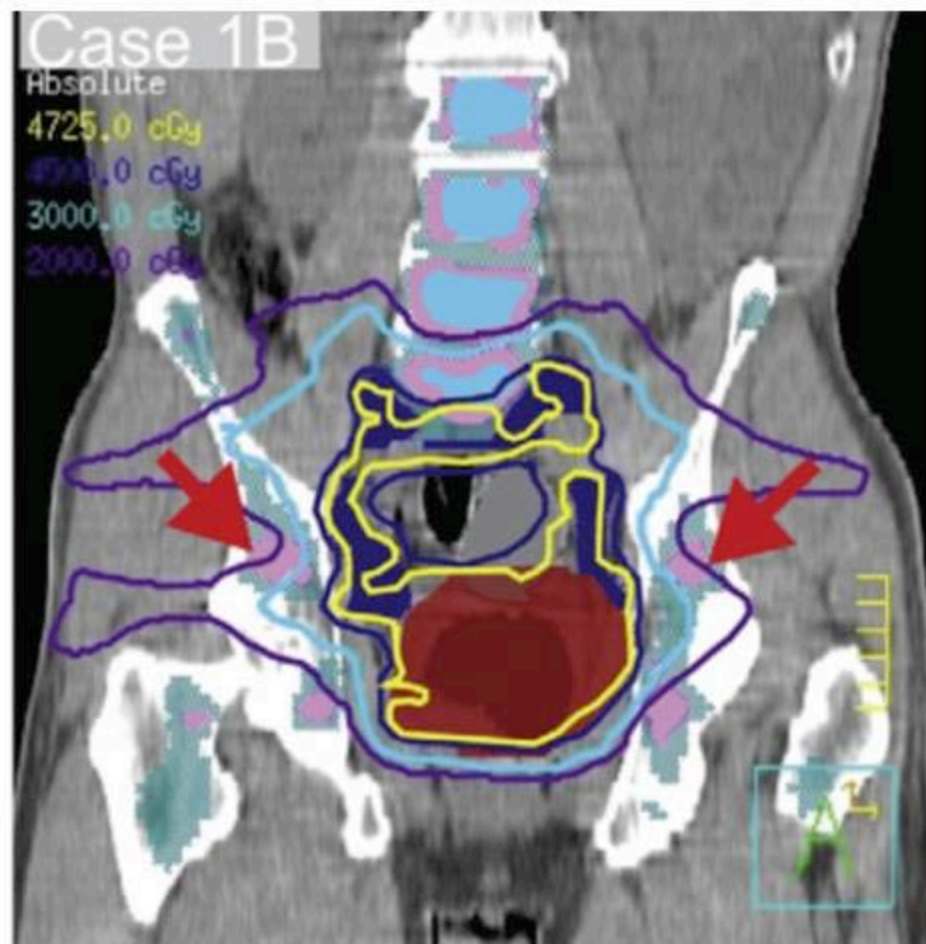
# A methodology for incorporating functional bone marrow sparing in IMRT planning for pelvic radiation therapy



# A methodology for incorporating functional bone marrow sparing in IMRT planning for pelvic radiation therapy

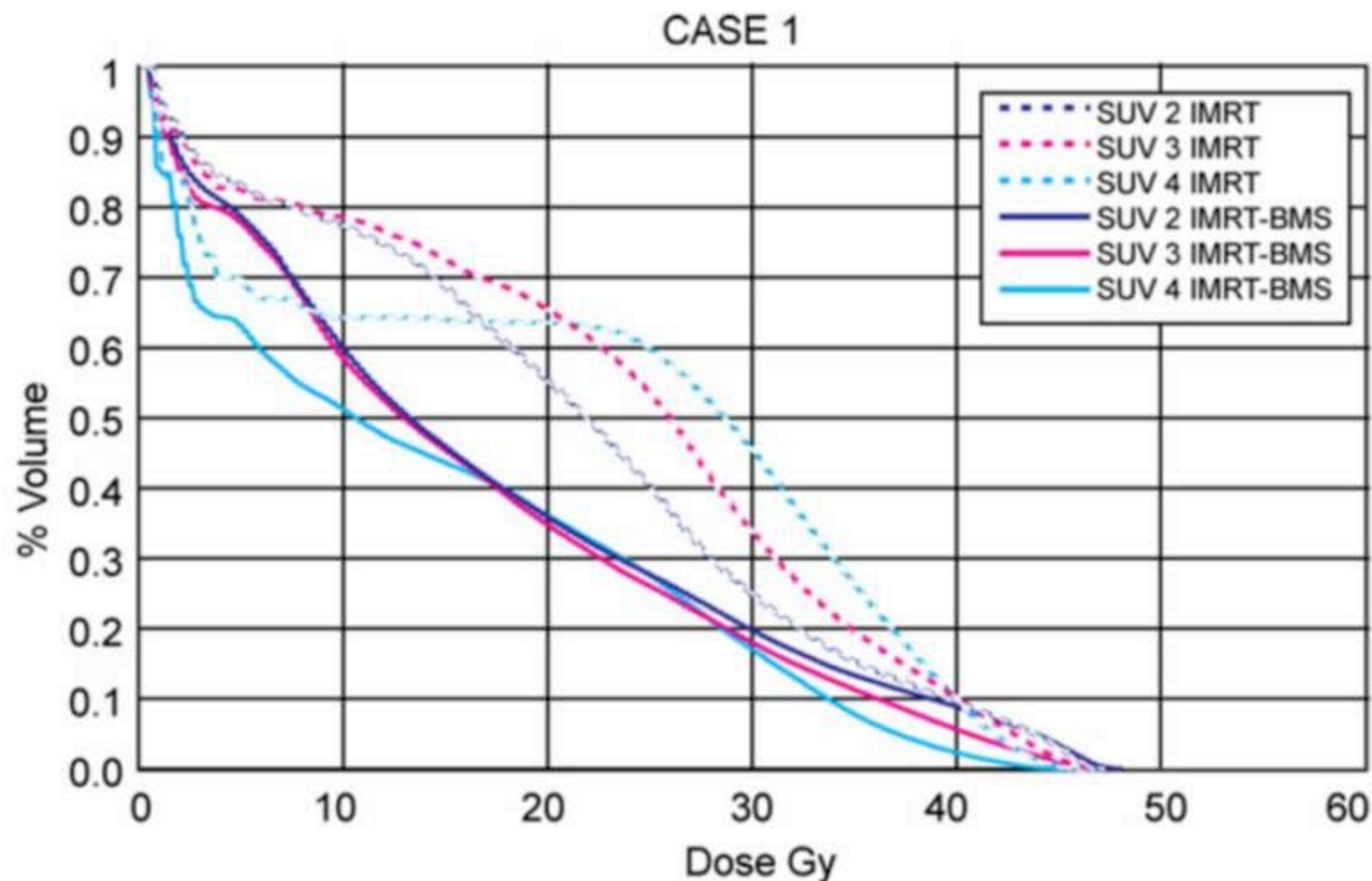


IMRT plan



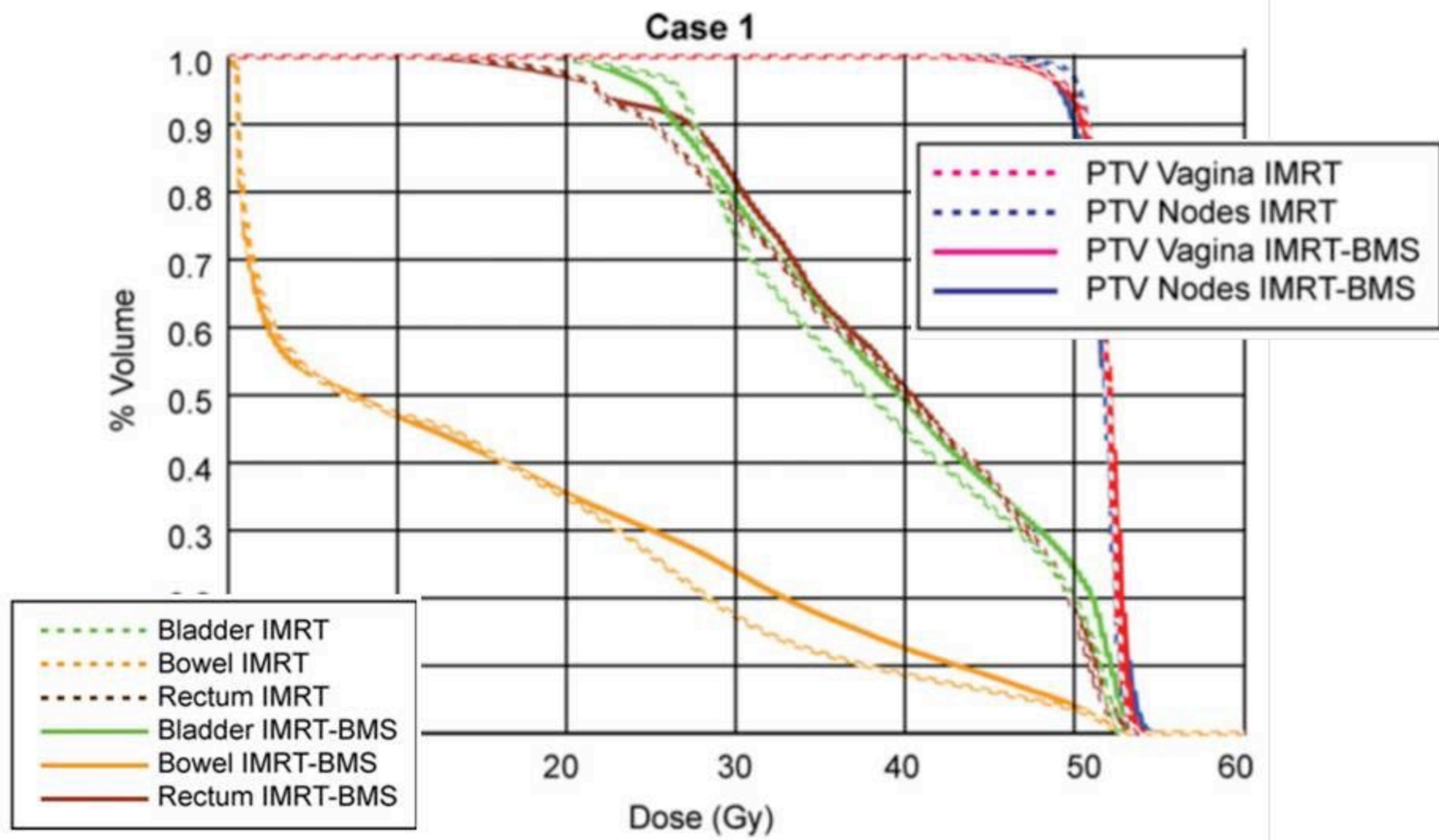
IMRT-BMS

## A methodology for incorporating functional bone marrow sparing in IMRT planning for pelvic radiation therapy





## A methodology for incorporating functional bone marrow sparing in IMRT planning for pelvic radiation therapy





## A methodology for incorporating functional bone marrow sparing in IMRT planning for pelvic radiation therapy

The relative percent change in bone marrow SUV  $V_{10}$  and  $V_{20}$  and PTV  $V_{45}$  between the IMRT and IMRT-BMS plans.

	IMRT plan		IMRT-BMS plan		Relative % difference	
	$V_{10}$ (%)	$V_{20}$ (%)	$V_{10}$ (%)	$V_{20}$ (%)	$V_{10}$ (%)	$V_{20}$ (%)
<i>Case 1</i>						
SUV 2	78.1	58.5	66.9	39.4	−14.3	−32.6
SUV 3	78.0	66.7	64.1	38.1	−17.9	−42.9
SUV 4	64.1	63.5	51.2	36.8	−20.1	−42.1
	$V_{45}$ (%)		$V_{45}$ (%)		$V_{45}$ (%)	
PTV vagina	97.0		97.4		0.4	
PTV nodes	98.9		97.6		−1.4	
<i>Case 2</i>						
SUV 2	70.3	53.8	56.5	38.3	−19.7	−28.8
SUV 3	66.6	52.9	50.0	34.4	−24.9	−35.0
SUV 4	53.7	43.0	37.8	25.5	−29.5	−40.7
	$V_{45}$ (%)		$V_{45}$ (%)		$V_{45}$ (%)	
PTV vagina	99.7		98.3		−1.4	
PTV nodes	98.9		97.2		−1.7	

Adjuvant Chemotherapy and  
Involved Field (IF)

Irradiation: Advanced Endometrial  
Carcinoma

# Adjuvant carboplatin and paclitaxel chemotherapy interposed with involved field radiation for advanced endometrial cancer<sup>☆</sup>

**Table 3**

Frequency of chronic radiation toxicities.

Toxicity		Standard 4-field ( <i>n</i> = 25)		IMAT ( <i>n</i> = 18)	
		Grade 3	Grade 4	Grade 3	Grade 4
Genitourinary	Cystitis <sup>*</sup>	0	0	2	0
Gastrointestinal	Proctitis	1	0	2	0
	SBO	1	0	1	0

\* Subacute — occurred after last cycle of chemotherapy. SBO = small bowel obstruction.

## Adjuvant carboplatin and paclitaxel chemotherapy interposed with involved field radiation for advanced endometrial cancer<sup>☆</sup>

**Table 4**

Site and frequency of initial relapse.

Site of relapse	N (% of total)
Distant	18 (42%)
Peritoneal carcinomatosis <sup>a</sup>	6
Lung <sup>b</sup>	4
Bone <sup>b</sup>	2
Supraclavicular node	1
Liver	1
Rectum <sup>c</sup>	1
Perihepatic	1
Multiple sites <sup>d</sup>	2
Local	2 (5%)
Pelvis	1
Vulva/vagina <sup>b</sup>	1
Local and distant	1 (2%)
Pelvis and carcinomatosis	1

*Conclusion.* Adjuvant carboplatin and paclitaxel chemotherapy interposed with involved field radiation is associated with a low rate of local recurrence and favorable survival for advanced endometrial cancer.



Whole abdominopelvic irradiation  
in high-risk endometrial cancer

## Whole abdominopelvic irradiation in high-risk endometrial cancer

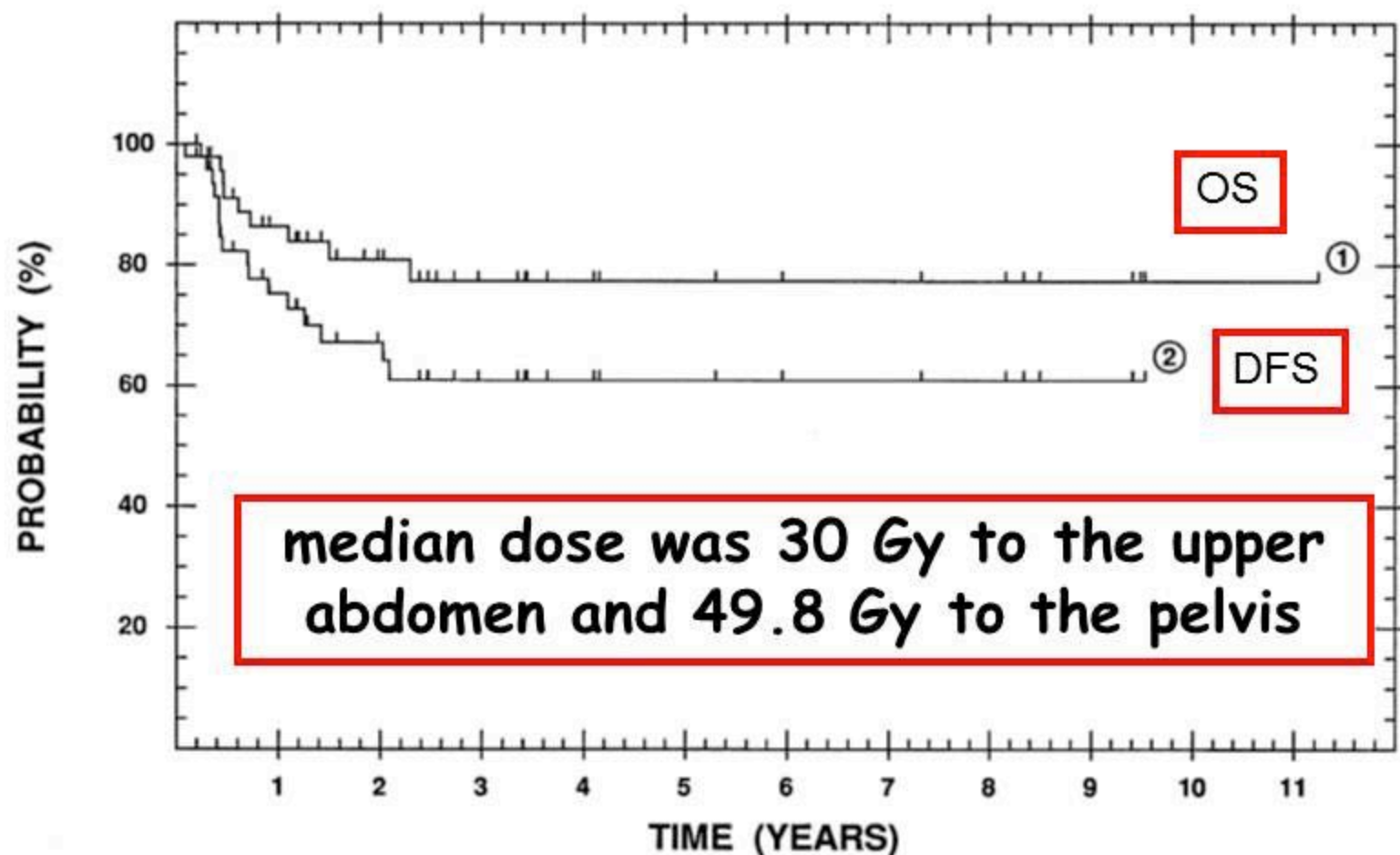


Fig. 1. Probability of survival for patients with uterine ACA or UPSC/CCC following WAPI ( $n = 48$ ). Curve 1 = OS, curve 2 = DFS.

## Whole abdominopelvic irradiation in high-risk endometrial cancer

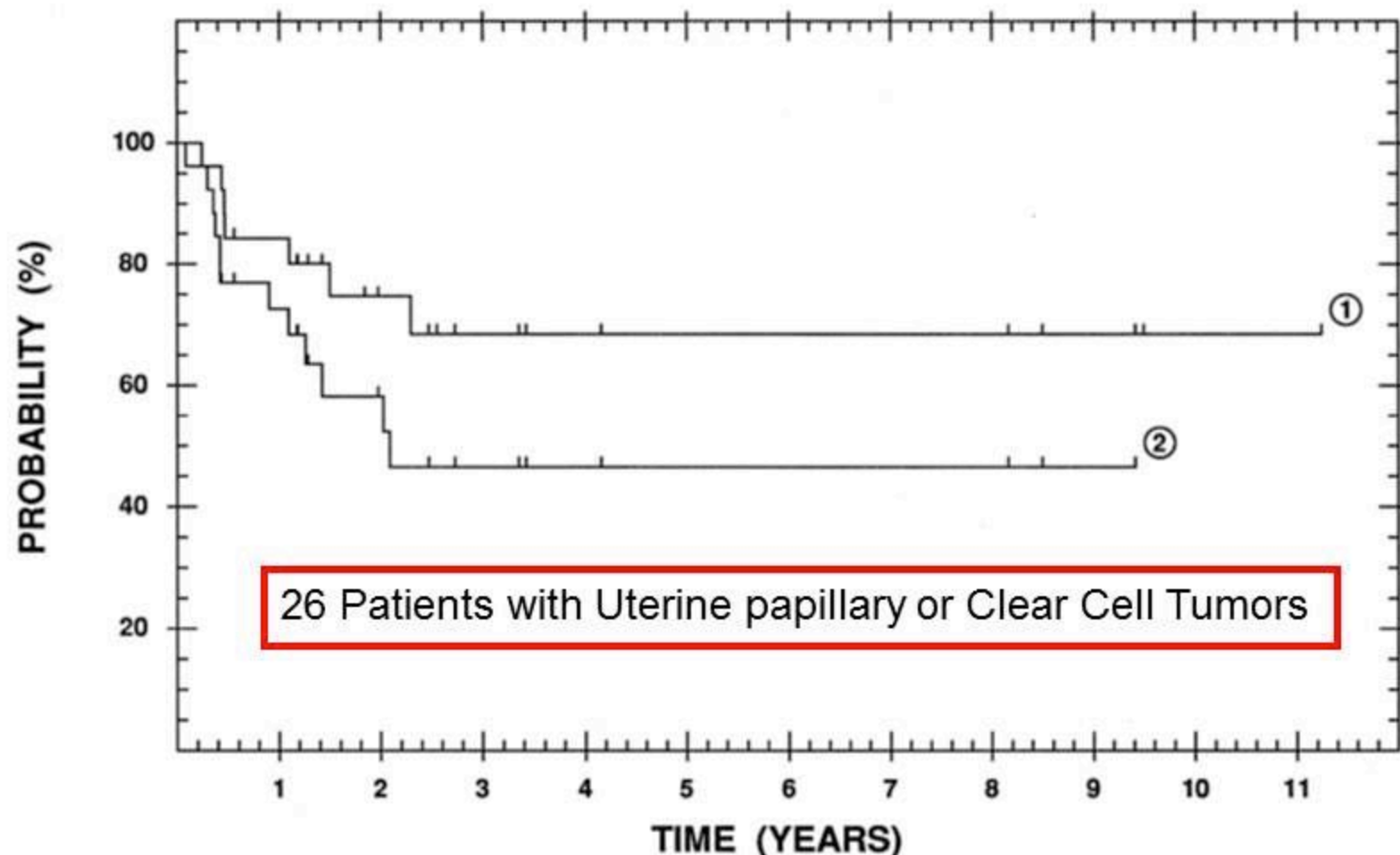


Fig. 3. Probability of survival for patients with Stage I-IV UPSC/CCC following WAPI ( $n = 26$ ). Curve 1 = OS, curve 2 = DFS.

# Whole abdominopelvic irradiation in high-risk endometrial cancer

Table 3. Whole abdominopelvic radiotherapy in high-risk endometrial cancer

Authors (year)	Stage	No. patients	Outcome
Greer and Hamberger [25] (1983)	III and IV	27 17 Stage III 10 Stage IV	5-yr SR: 63% 5-yr DSS: 86% 5-yr DSS: 70%
Loeffler <i>et al.</i> [65] (1988)	I-III	16	17 mo DFS: 50% 17 mo. OS: 50%
Potish [16] (1989)	I-III	41	5-yr DFS: 73% 5-yr OS: 63%
Frank <i>et al.</i> [18] (1991)	I-III	9 (UPSC)	25 mo DFS: 33%
Miller <i>et al.</i> [35] (1995*)	III and IV	58 Stage III 13 Stage IV	8-yr DFS: 63% 8-yr DFS: 33%
Grice <i>et al.</i> [39] (1998)	I-IV	9 (UPSC)	6/9 NED
Current series (2000)	I-IV	26 (UPSC/CCC)	3-yr DFS: 47% 3-yr OS: 68%
	III and IV	22 (other ACA)	3-yr DFS: 79% 3-yr OS: 89%



# Randomized Phase III Trial of Whole-Abdominal Irradiation Versus Doxorubicin and Cisplatin

## A Gynecologic Oncology Group Study

### Treatment completed

WAI 84%

PA\* Cht 63%

\* Doxorubicin + Cisplatin

### Treatment discontinued

WAI 3%

PA Cht 17%

**Table 3.** Patients\* Experiencing Adverse Events

Adverse Event	% of Patients							
	WAI Regimen (n = 190)				AP Regimen (n = 191)			
	Grade				Grade			
	1	2	3	4	1	2	3	4
Leukopenia	4	17	4	< 1	11	23	44	18
Neutropenia	4	4	< 1	0	4	4	18	67
Thrombocytopenia	11	3	2	< 1	34	15	11	10
Other hematologic	18	15	7	< 1	28	31	17	3
Maximum hematologic	17	29	13	2	4	5	20	69
GI	32	36	11	2	20	38	13	7
Hepatic	3	3	2	1	< 1	2	1	0
Genitourinary	13	4	< 1	0	9	9	2	1
Cardiac	0	0	0	0	5	12	11	4
Vascular	1	0	0	0	2	2	< 1	1
Pulmonary	2	2	0	0	4	4	1	< 1
Neurologic	4	1	< 1	0	25	10	6	1
Pain	1	0	< 1	0	8	5	< 1	0
Weakness	2	2	2	0	6	3	3	0
Fatigue	12	5	1	0	14	11	5	< 1
Metabolic	9	6	0	0	6	8	4	< 1
Infection	0	< 1	< 1	0	1	2	4	3
Fever	< 1	2	0	0	6	12	4	2
Allergy	< 1	0	0	0	0	0	0	0
Dermatologic	12	5	< 1	0	10	4	1	< 1
Alopecia†	< 1	0	NA†	NA†	6	69	NA†	NA†

# Randomized Phase III Trial of Whole-Abdominal Irradiation Versus Doxorubicin and Cisplatin

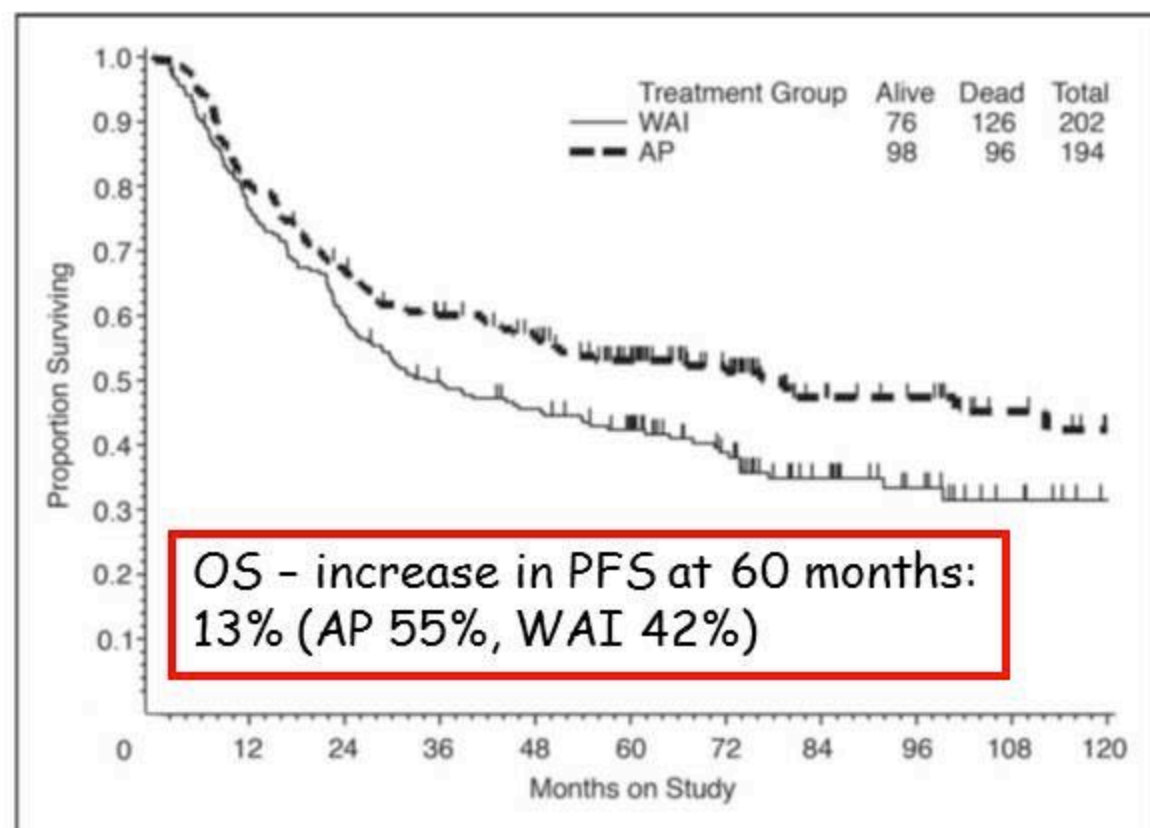
## A Gynecologic Oncology Group Study

**Table 4.** Reason for Treatment Discontinuation

Reason	WAI Regimen (n = 202)		AP Regimen (n = 194)	
	No.	%	No.	%
Completed treatment	170	84.2	123	63.4
Progression	9	4.5	18	9.3
Patient refusal	8	4.0	14	7.2
Toxicity	6	3.0	33	17.0
Death	1	0.5	4	2.1
Other	8	4.0	2	1.0

# Randomized Phase III Trial of Whole-Abdominal Irradiation Versus Doxorubicin and Cisplatin

## A Gynecologic Oncology Group Study



**Fig 2.** Survival by randomized treatment group. AP, doxorubicin and cisplatin; WAI, whole-abdominal irradiation.

HR  
PA vs. WAI 0.68  
( $p = 0.004$ )




Randomized Phase III Trial of Whole-Abdominal  
Irradiation Versus Doxorubicin and Cisplatin  
A Gynecologic Oncology Group Study

In summary, patients with surgical stage III or IV endometrial carcinoma treated with AP experienced a statistically significant improvement in survival when compared with patients who received WAI, but they also experienced more frequent and more severe acute toxicity. Clearly, greater efficacy and less toxicity are needed. Avenues for further progress remain to be explored.



Uterine papillary serous  
and clear cell carcinoma

Table 2. 5-year survival outcomes by stage and histology

Stage and histology	5-year overall survival		
	No RT (%)	RT (%)	<i>p</i> value
Stage IA	74.1	78.5	0.224
Stage IB	66.4	76.3	 0.006
Stage IC	33.9	60.7	0.001
Stage IIA–B	44.5	61.4	0.122
Overall	66	71.1	 0.006
Clear cell histology	72.3	76.8	0.281
UPSC histology	62.3	68.1	 0.005

*Abbreviations:* UPSC = uterine papillary serous carcinoma; RT = radiation.

## Uterine papillary serous and clear cell carcinoma

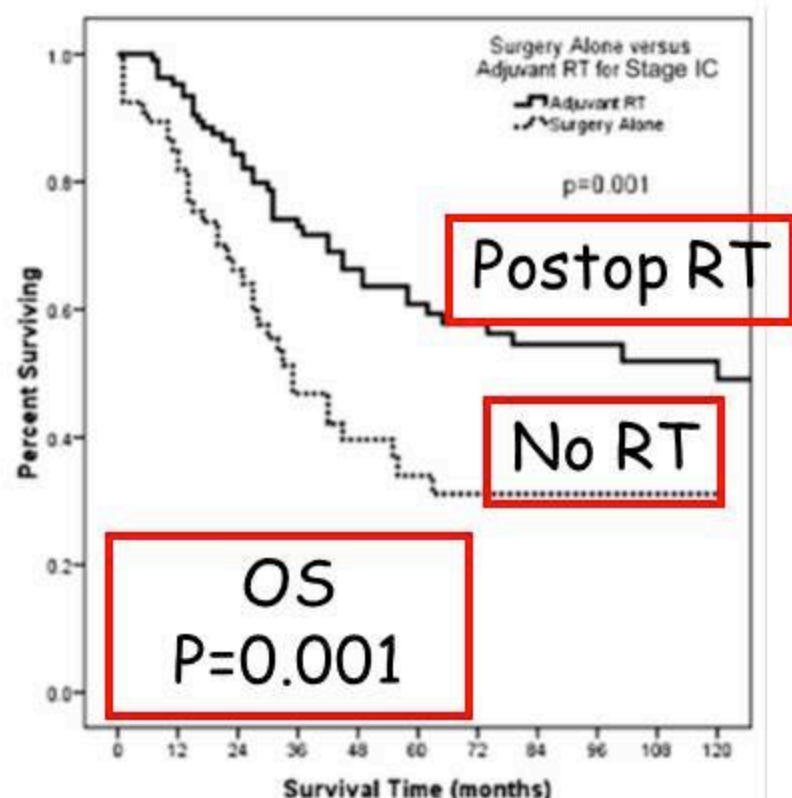


Fig. 3. Kaplan-Meier curves showing improvement in overall survival with the use of adjuvant radiation (RT) for FIGO Stage IC clear cell or uterine papillary serous carcinoma. The median overall survival improved from 35 months with surgery alone to 120 months with adjuvant radiation therapy ( $p = 0.001$ ). The corresponding 5-year overall survival rates were 33.9% and 60.7%.

Table 4. Multivariate analysis for overall survival

Multivariate analysis	Risk ratio	95% confidence interval	$p$ value
Age at diagnosis (continuous variable)	1.061	1.050–1.072	0.000
Nodes examined (continuous variable)	0.989	0.980–0.998	0.014
Radiation therapy (neg vs. pos)	0.808	0.651–1.002	0.052
Histology (UPSC vs. clear cell)	1.167	0.952–1.432	0.138
Stage			
IA	1		
IB	1.106	0.877–1.396	0.394
IC	1.901	1.404–2.574	<0.001
IIA	1.387	0.842–2.285	0.199
IIB	2.893	1.962–4.265	<0.001

Abbreviations: Neg = negative; Pos = positive; UPSC = uterine papillary serous carcinoma; FIGO = International Federation of Gynecology and Obstetrics.

## Uterine papillary serous and clear cell carcinoma

## WART and Abdominal failure

Table 3. Abdominal failure in pathologic Stage I–II papillary serous patients with and without whole abdominal radiation therapy:  
Literature review

Author	n	Abdominal failure	Abdominal failure	
			+WART	–WART
Lim <i>et al.</i> (12)	78*	10	5/58	5/20
Bristow <i>et al.</i> (29)	18	0	–	0/18
Grice <i>et al.</i> (30)	14	0	0/3	0/11
Gehrig <i>et al.</i> (31)	6	0	–	0/6
Piura <i>et al.</i> (3)	14	2	–	2/14
Nguyen <i>et al.</i> (32)	12	0	0/3	0/9
Turner <i>et al.</i> (28)	15	0	0/2	0/13
Carcangiu and Chambers (1)	13	2	1/2	1/11
Mehta (present series)	23	2	–	2/23
	193	16 (8%)	6/68 (9%)	10/125 (8%)

WART: no advantage on abdominal failures



## Uterine papillary serous and clear cell carcinoma

Table 4. Pelvic failure in pathologic Stage I–II papillary serous patients with and without adjuvant radiation therapy: Literature review

Author	n	Pelvic failure	Pelvic failure	
			+RT*	–RT
Lim <i>et al.</i> (12)	78 <sup>†</sup>	13	9/63	4/15
Bristow <i>et al.</i> (29)	18	3	1/6	2/12
Grice <i>et al.</i> (30)	14	1	1/8	0/6
Gehrig <i>et al.</i> (31)	6	2	–	2/6
Piura <i>et al.</i> (3)	14	2	0/9	2/5
Nguyen <i>et al.</i> (32)	12	0	0/10	0/2
Turner <i>et al.</i> (28)	15	0	0/15	–
Tay and Ward <i>et al.</i> (33)	23	8	5/15	3/8
Carcangiu and Chambers (1)	13	0	0/13	–
Mehta (present series)	23	5	0/10	5/13
	216	35 (16%)	16/149 (11%)	18/67 (27%)

Clear advantage on pelvic failures

Uterine sarcomas

A gynecologic oncology group randomized phase III trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide and mesna (CIM) as post-surgical therapy in stage I–IV carcinosarcoma (CS) of the uterus ☆

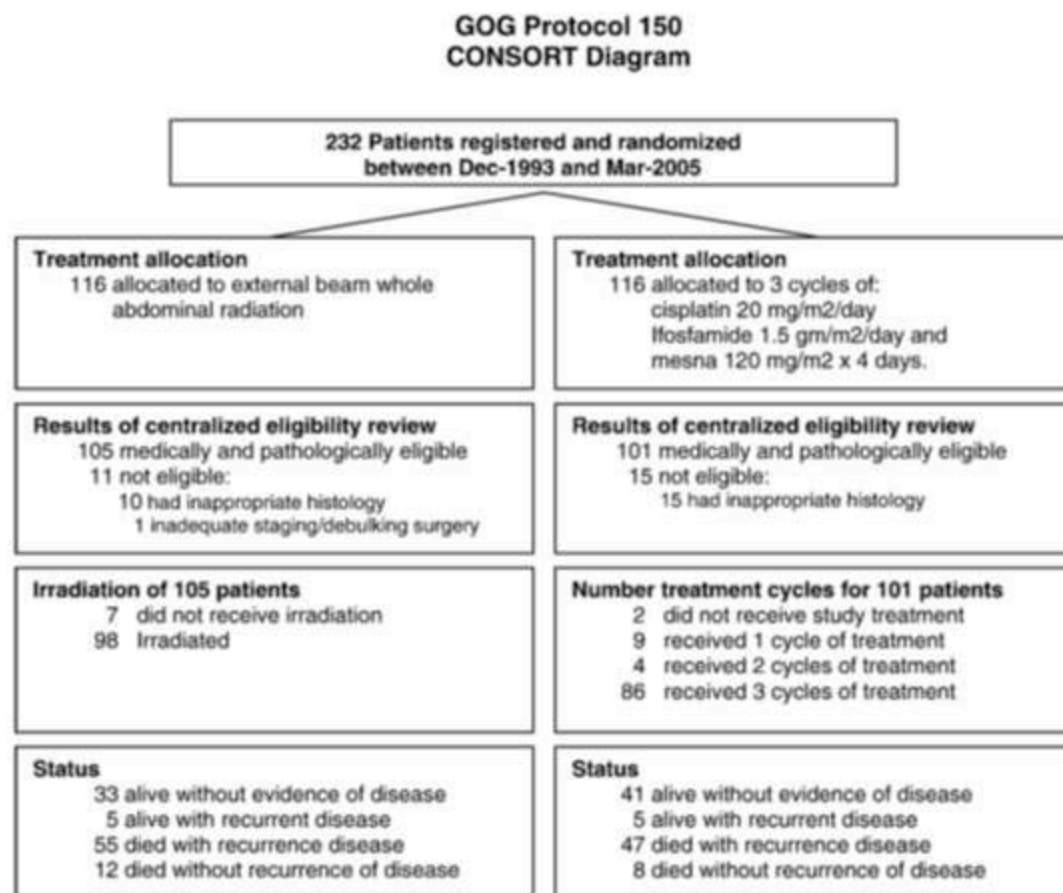


Fig. 1. Consort diagram.

A gynecologic oncology group randomized phase III trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide and mesna (CIM) as post-surgical therapy in stage I–IV carcinosarcoma (CS) of the uterus ☆

Patients experiencing acute adverse events

Adverse event	WAI regimen					CIM regimen				
	(n=98)†					(n=99)†				
	Grade					Grade				
	0	1	2	3	4	0	1	2	3	4
Anemia	88	5	4	1	0	41	12	35	10	1
Gastrointestinal	33	33	21	8	3	37	33	19	8	2
Genitourinary	82	13	3	0	0	77	12	10	0	0
Renal	98	0	0	0	0	97	1	1	0	0
Hepatic	94	2	0	1	1	94	4	1	0	0
Fever	97	1	0	0	0	87	3	9	0	0
Infection	97	0	0	1	0	98	0	0	0	1*
Fatigue	92	5	0	1	0	77	13	6	2	1
Alopecia	98	0	0	0	0	54	12	33	0	0
Peripheral neuropathy	97	1	0	0	0	87	6	4	2	0
Central neuropathy	96	2	0	0	0	79	9	4	7	0
Allergy	98	0	0	0	0	95	2	2	0	0
Cutaneous	89	4	5	0	0	96	3	0	0	0
Cardiovascular	97	0	0	0	1	92	2	1	2	2
Pulmonary	97	0	1	0	0	93	3	3	0	0
Pain	94	2	2	0	0	86	9	3	1	0
Metabolic	97	1	0	0	0	90	2	2	3	2

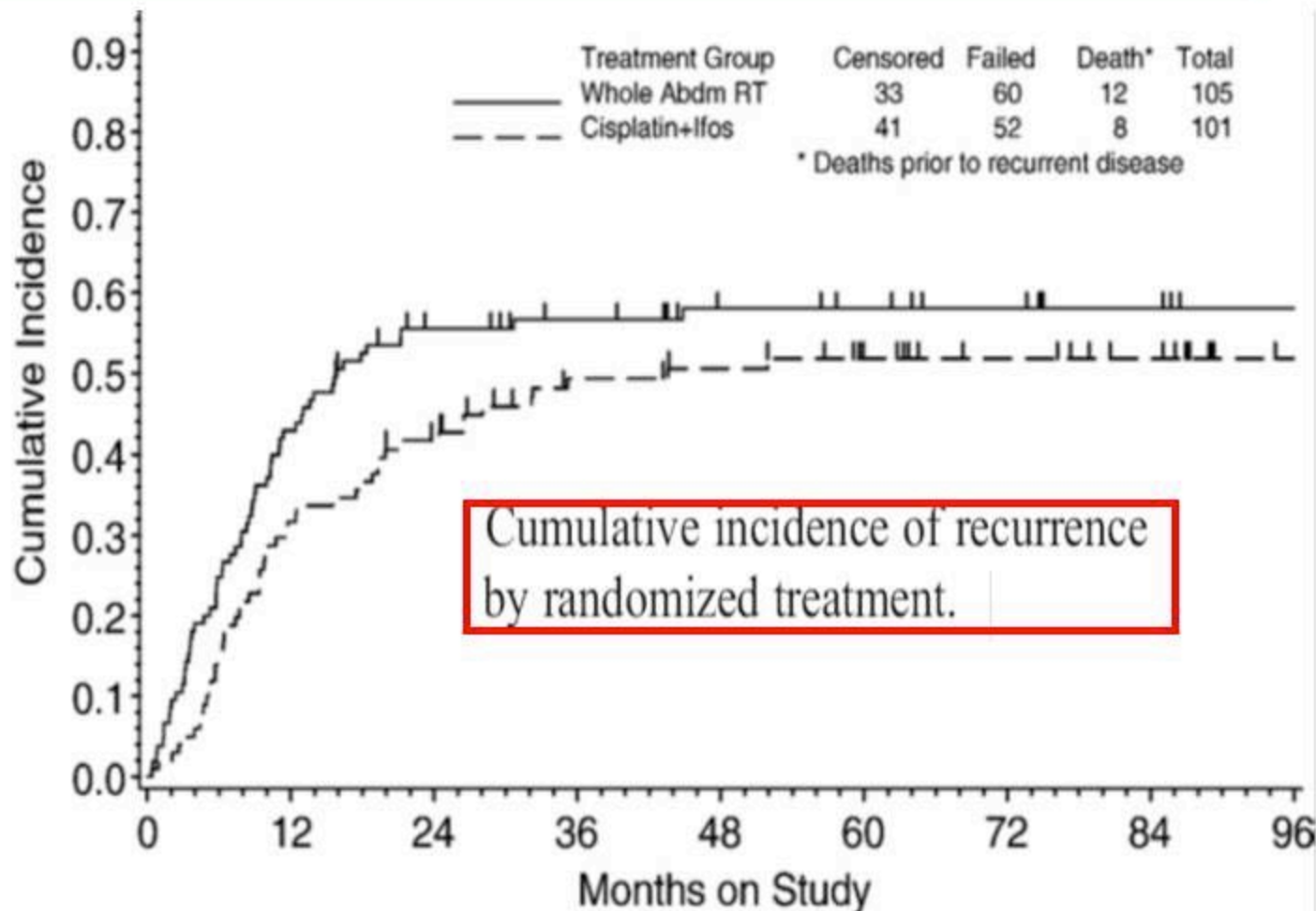
Abbreviations: WAI, whole abdominal irradiation; CIM, cisplatin, ifosfamide with mesna chemotherapy.

†Adverse events summarized for those who initiated study treatment.

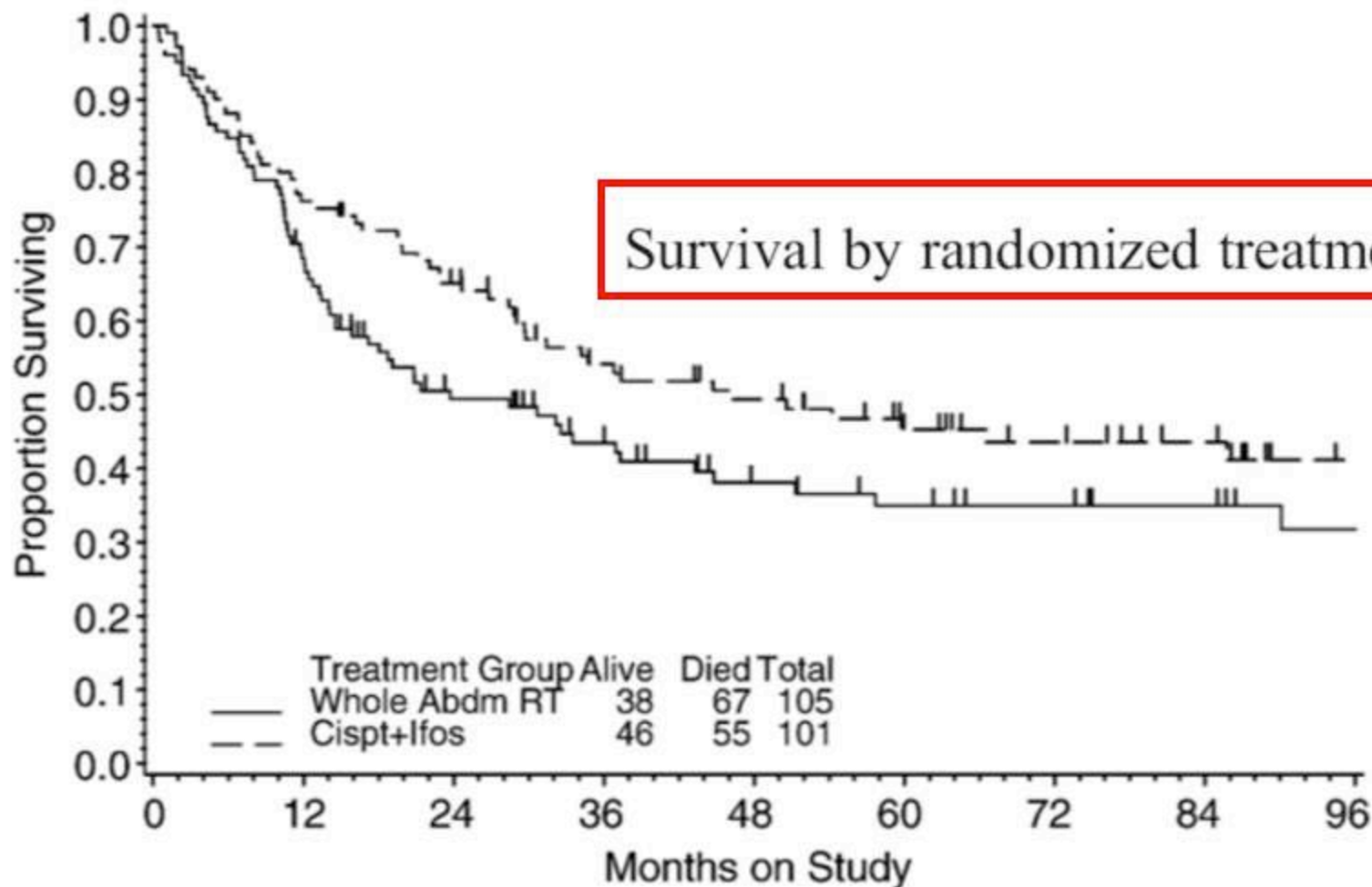
\*One patient died of a systemic infection complicated by neutropenia which was attributed to CIM treatment.



A gynecologic oncology group randomized phase III trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide and mesna (CIM) as post-surgical therapy in stage I–IV carcinosarcoma (CS) of the uterus ☆



A gynecologic oncology group randomized phase III trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide and mesna (CIM) as post-surgical therapy in stage I–IV carcinosarcoma (CS) of the uterus ☆





A gynecologic oncology group randomized phase III trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide and mesna (CIM) as post-surgical therapy in stage I–IV carcinosarcoma (CS) of the uterus ☆

There have been several retrospective reviews of patients with US that have included uterine CS evaluating the effect of adjuvant therapy [17–27]. Those that have involved postoperative pelvic EBRT have shown a consistent decrease in pelvic failures but no significant impact on overall patient survival [17,19–24]. However, two retrospective studies did claim an OS benefit with the addition of adjuvant pelvic irradiation for patients with surgical stages I and II disease [25,26].

**Phase III randomised study to evaluate the role of adjuvant pelvic radiotherapy in the treatment of uterine sarcomas stages I and II: An European Organisation for Research and Treatment of Cancer Gynaecological Cancer Group Study (protocol 55874)**


**Table 5 – The following table displays the different possible sequences of events up to last follow-up and the corresponding frequencies per treatment arm**

	Radiotherapy	Observation	Total
	110	109	219
<i>Sequence of events</i>			
No recurrence – alive	55 (50.0)	49 (45.0)	104 (47.5)
No recurrence – dead	3 (2.7)	5 (4.6)	8 (3.7)
Loco-regional recurrence only	 3 (2.7)	 20 (18.3)	23 (10.5)
Distant metastases only	28 (25.5)	11 (10.1)	39 (17.8)
Loco-regional recurrence followed by distant metastases	1 (0.9)	7 (6.4)	8 (3.7)
Distant metastases followed by loco-regional recurrence	4 (3.6)	3 (2.8)	7 (3.2)
Loco-regional recurrence and distant met. at same time	16 (14.5)	14 (12.8)	30 (13.7)
Local relapse at any time	24 (21)	44 (40)	68 (31)



**Phase III randomised study to evaluate the role of adjuvant pelvic radiotherapy in the treatment of uterine sarcomas stages I and II: An European Organisation for Research and Treatment of Cancer Gynaecological Cancer Group Study (protocol 55874)**

**Table 6 – Sites of recurrence**

	Sites of recurrence			
	CS, n = 91		LMS, n = 99	
	Radiotherapy (n = 46)	Observation (n = 45)	Radiotherapy (n = 50)	Observation (n = 49)
No local recurrence	28 (61%)	21 (47%)	22 (44%)	26 (53%)
Local recurrence only	2 (4%)	11 (24%)	1 (2%)	7 (14%)
Distant metastases	7 (15%)	3 (7%)	18 (36%)	7 (14%)
Local followed by distant	1 (2%)	3 (7%)	0 (0%)	2 (4%)
Distant followed by local	2 (4%)	0 (0%)	2 (4%)	3 (6%)
Simultaneous local and distant	6 (13%)	7 (16%)	7 (14%)	4 (8%)
Any local recurrence	11 (24%)	21 (47%) 	10 (20%)	12 (24%)
Any distant metastases	16 (35%)	13 (29%)	27 (54%)	16 (33%)

## Possible conclusions: CERVICAL CANCER

- 1 - Exclusive RT? YES with CHT and IMRT BM sparing
- 2 - Postoperative pelvic irradiation: YES, no concomitant CHT
- 3 - LA irradiation: not as elective RT but in selected patients
- 4 - Marginal failure (in-field recurrences) above or below the radiation field as a deficiency:
  - in target volume
  - deficiency in dose
  - pretreatment staging
  - field delineation
  - dose escalation
  - posttreatment surveillance
- 5 - Acute and late toxicity: accurate evaluation of the patient before RT (Chronic disease, small bowel distribution, diverticula)
- 6 - IMRT as a solution? Probably YES to reduce acute toxicity. But the late ones?
- 7 - Role of Brachithery? Next AIRO meeting!

## Possible conclusions: ENDOMETRIAL CANCER

	G1	G2	G3	
St. IA	50%			
St. IB				
St. IC				
St. IIA				
St. IIB	25%			
St. III				

# Adjuvant Chemotherapy for Endometrial Cancer

## *Unproven*

*Carien L. Creutzberg, MD, PhD*

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*(Int J Gynecol Cancer 2010;20: S60–S63)*

**Abstract:** High-risk endometrial cancer (EC), only 15% of all EC cases, mainly affects elderly women, often with significant comorbid diseases. Because patients with high-risk EC are at increased risk of distant metastases and EC death, the use of adjuvant chemotherapy has been investigated in several trials. Trials comparing radiotherapy and chemotherapy have not shown survival difference. A first trial comparing combinations of chemotherapy and radiotherapy with radiotherapy alone suggested a progression-free survival benefit. Toxicity and quality-of-life data are lacking. The role of adjuvant chemotherapy for endometrial carcinoma remains unproven. High-risk EC remains the challenge for further research.



# Evidence-based review of the utility of radiation therapy in the treatment of endometrial cancer

*SB Dewdney <sup>†1</sup> & DG Mutch <sup>1</sup> 2010*

***Should women with advanced-stage disease receive adjuvant radiation therapy?***

- The high rate of recurrence and poor survival in this population has been well documented. Management with surgery alone for these patients is associated with poor survival. No prospective randomized trial has ever shown that adjuvant radiation in this patient population improves survival, although it has been shown to reduce the risk of local recurrence.