CARCINOMA DELL'ENDOMETRIO

- E' la neoplasia ginecologia più frequente
- Rappresenta il 6% di tutte le neoplasie ed il 2% di causa di morte per tumore
- Età media di insorgenza: 68 anni
- La maggioranza dei casi si manifesta dopo la menopausa

Overview

Adenocarcinoma of the endometrium (also known as endometrial cancer, or more broadly as uterine cancer or carcinoma of the uterine corpus) is the most common malignancy of the female genital tract in the United States. It is estimated that 47,100 new uterine cancer cases will occur in 2012, with 8,000 deaths resulting from the disease.[1] Uterine sarcomas are uncommon malignancies accounting for approximately 3% of all uterine cancers.[2]

FATTORI DI RISCHIO

- Obesità
- Diabete
- Dieta ricca di grassi
- Ipertensione
- Anovulazione
- Nulliparità
- Giovane età al menarca, menopausa tardiva
- Terapia Estrogenica Sostitutiva
- Terapia con Tamoxifen

CARCINOMA DELL'ENDOMETRIO

- L'esposizione agli estrogeni contribuisce al rischio di malattia nei sottotipi ormonodipendenti, che originano in endometri ipertrofici
- I sottotipi ormonoindipendenti si manifestano in età anziana ed insorgono su uno sfondo atrofico (prognosi peggiore)

Due tipi di carcinoma endometriale (Bokhman):

1. Carcinoma endometrioide (estrogeno-correlato):

   in donne giovani con obesità, iperlipidemia, segni di iperestrogenismo (endogeno o esogeno).

   fattori di rischio endogeno: obesità, disordini epatici, infertilità.

   fatori di rischio esogeno: terapia ormonale sostitutiva.

2. Carcinomi poco differenziati quali il sieroso papillare (UPSC) e a cellule chiare (non estrogeno-correlato):

   in donne più anziane, magre, assenti fattori di rischio ormonali.

ISTOLOGIA

Histologic Classification	Incidence (%)
Endometrioid	75–80
• Ciliated adenocarcinoma • Secretory adenocarcinoma • Papillary or villoglandular • Adenocarcinoma with squamous differentiation • Adenocanthoma • Adenosquamous	
Clear cell carcinoma	4
Uterine papillary serous	<10
Squamous cell	<1
Mucinous	1
Mixed	10
Undifferentiated	—

In approximately 75% of patients with adenocarcinoma of the endometrium, the invasive neoplasm is confined to the uterus at diagnosis.[13] Many physicians believe that adenocarcinoma of the endometrium is a relatively benign disease, because the early symptoms of irregular vaginal bleeding (in this predominantly postmenopausal patient population) often trigger patients to seek care when the disease is at an early and treatable stage. Thus, endometrial cancer is often localized, yielding a generally high survival rate. However, data show that the mortality rate for uterine cancer has increased more rapidly than the incidence rate.[14] This increased mortality may be related to an increased rate of advanced-stage cancers and high-risk histologies (i.e., serous tumors). In addition, many women did not receive adequate staging.

Tasso di mortalità per carcinoma endometriale è in aumento:

1. Stadio avanzato di malattia
2. Istologie ad alto rischio che include UPSC (uterine papillary serous carcinoma): 10% di tutti i carcinomi endometriali che giustifica il 39% di morti per carcinoma dell'endometrio

UPSC (uterine papillary serous carcinoma)

- sottotipo del carcinoma dell'endometrio
- meno comune dell'EEC (endometrioid carcinoma) e differente morfologicamente e geneticamente
- istologicamente simile al carcinoma sieroso epiteliale ovarico (Lauchlan e Hendrickson).
- aggressivo (ciò giustifica l'aumento di carcinomi dell'endometrio letali)

	EEC	UPSC
Demografia	giovane età obesità	età avanzata magrezza
Fattori di rischio	iperestrogenismo obesità	tumore mammella mutazione BRCA
Pattern di ripresa	locale	a distanza
Lesione precancarosa	iperplasia atipica	displasia endometriale
Grado istologico	basso, intermedio, alto	alto
Alterazioni molecolari	Inattivazione PTEN Difetti di DNA mismatch repair (MSI)	Mutazione p53 Amplificazione gene HER-*2/neu*

	EEC	UPSC
Stadio alla diagnosi (%)	I (73) II (11) III (13) IV (3)	I (54) II (8) III (22) IV (16)
Sopravvivenza in relazione allo stadio (%)	I (85-90) II (70) III (40-50) IV (15-20)	I (50-80) II (50) III (20) IV (5-10)

Creasman (2004): stadio I in donne con EEC vs stadio I in donne con UPSC

Sopravvivenza a 5 aa è di 80-90% con EEC vs 50-80% con UPSC

Women with Lynch syndrome are at higher risk (60%) for endometrial cancer; thus, close monitoring is recommended.[7,11] In relatives with Lynch syndrome but without endometrial cancer, a yearly endometrial biopsy is recommended to assess for cancer.[9] This strategy also enables select women to defer surgery (and surgical menopause) and to preserve their fertility. Prophylactic hysterectomy/bilateral salpingo-oophorectomy can then be done after child bearing is complete or sooner, depending on patient preference.[12] In addition, interventions to decrease the risk from colorectal cancer may also be appropriate (e.g., annual colonoscopy).

Diagnosi

- Sanguinamento vaginale in più del 90% dei casi
- Menometrorragia
- Diagnosi in stadio iniziale:

  Ecografia transvaginale
- Diagnosi istologica

  Pipelle de Cornier (cannula flessibile, di materiale plastico): accuratezza 90%-98%

  Altre procedure: dilatazione e courrettage
  isteroscopia e biopsia endometriale

Diagnosis and Workup

Most patients (90%) with endometrial carcinoma have abnormal vaginal bleeding, most commonly in the postmenopausal period. The workup was previously described (see "Overview" in this Discussion). Diagnosis can usually be made by an office endometrial biopsy.[16,17]

The histologic information from the endometrial biopsy (with or without endocervical curettage) should be sufficient for planning definitive treatment. Office endometrial biopsies have a false-negative rate of about 10%. Thus, a negative endometrial biopsy in a symptomatic patient must be followed by a fractional dilation and curettage (D&C) under anesthesia.[16,18] Hysteroscopy may be helpful in evaluating the endometrium for lesions, such as a polyp, if the patient has persistent or recurrent undiagnosed bleeding.[19]

STADIAZIONE

- Anamnesi
- Esame Clinico
- Prelievo ematico per profilo emato-biochimico
- Rx Torace
- Ecografia transvaginale
- TC addome-pelvi
- RM addome-pelvi

L’utilizzo di TC e RM nella stadiazione delle neoplasie ginecologiche ha reso desueto l’utilizzo di es. RX come urografia e clisma di colon (cistroscopia, rettoscopia)

Sebbene la TC sia più largamente usata, la RM risulta superiore per l’elevata risoluzione di contrasto e la multiplanarità

Staging-Endometrial Carcinoma

Table 1
AJCC Tumor-Node-Metastases (TNM) and International Federation of Gynecology and Obstetrics (FIGO) Surgical Staging Systems for Endometrial Cancer

Primary Tumor (T)

TNM Categories	FIGO* Stages	Surgical-Pathologic Findings
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis**		Carcinoma in situ (preinvasive carcinoma)
T1	I	Tumor confined to the corpus uteri
T1a	IA	Tumor limited to endometrium or invades less than one-half of the myometrium
T1b	IB	Tumor invades one-half or more of the myometrium
T2	II	Tumor invades stromal connective tissue of the cervix but does not extend beyond uterus[#]
T3a	IIIA	Tumor involves serosa and/or adnexa (direct extension or metastasis)[##]
T3b	IIIB	Vaginal involvement (direct extension or metastasis) or parametrial involvement[##]
	IIIC	Metastases to pelvic and/or para-aortic lymph nodes[##]
	IV	Tumor invades bladder and/or bowel mucosa, and/or distant metastases
T4	IVA	Tumor invades bladder mucosa and/or bowel (bullous edema is not sufficient to classify a tumor as T4)

*Either G1, G2, or G3
**Note: FIGO no longer includes Stage 0 (Tis).
[#]Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II.
[##]Positive cytology has to be reported separately without changing the stage.

Regional Lymph Nodes (N)

TNM Categories	FIGO Stages	Surgical-Pathologic Findings
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1	IIIC1	Regional lymph node metastasis to pelvic lymph nodes (positive pelvic nodes)
N2	IIIC2	Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes

Distant Metastasis (M)

TNM Categories	FIGO Stages	Surgical-Pathologic Findings
M0		No distant metastasis
M1	IVB	Distant metastasis (includes metastasis to inguinal lymph nodes intra-peritoneal disease, or lung, liver, or bone. It excludes metastasis to para-aortic lymph nodes, vagina, pelvic serosa, or adnexa)

Continued

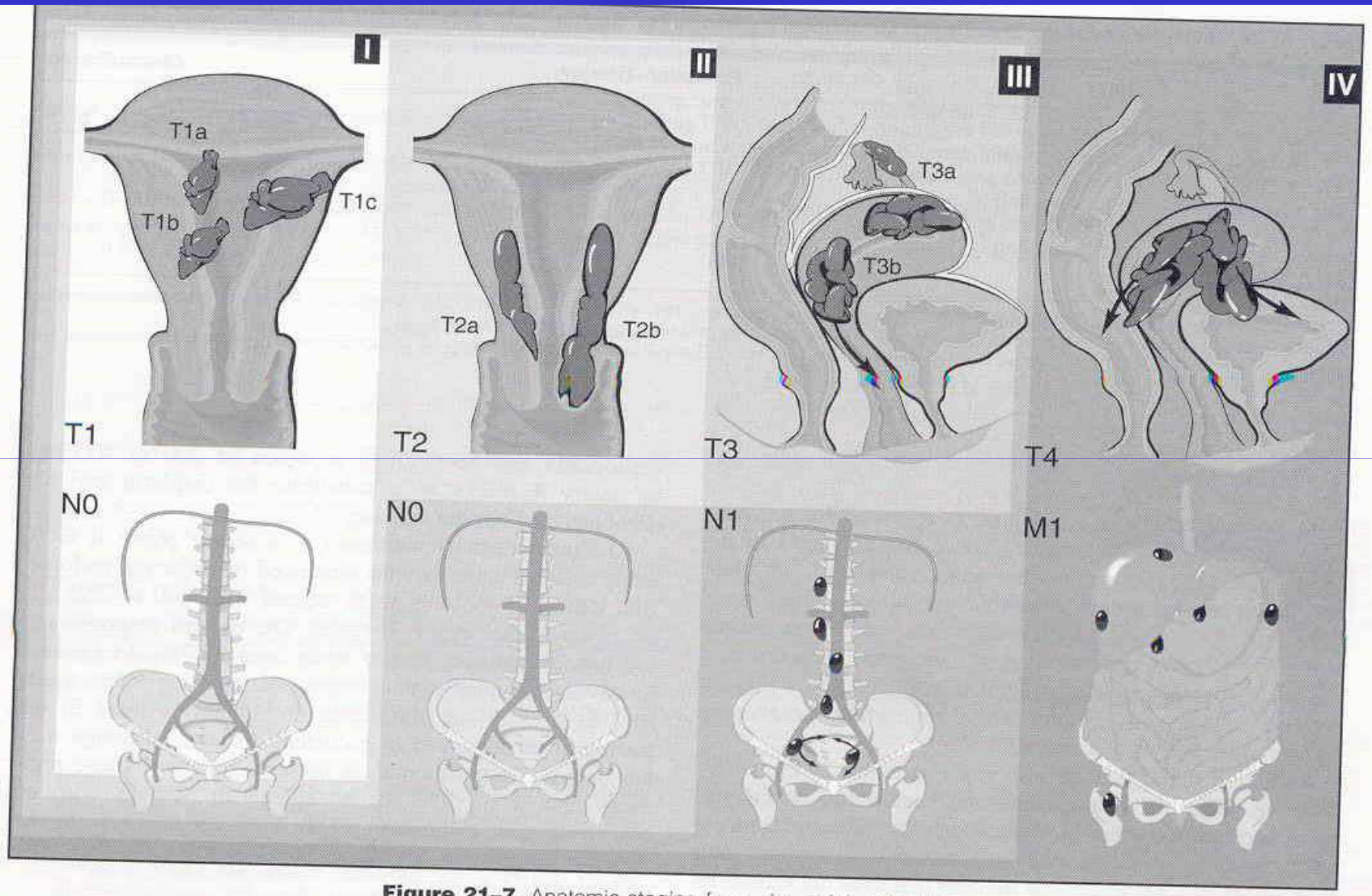


Figure 21–7. Anatomic staging for endometrial carcinoma.

TERAPIA

CHIRURGIA

- Rappresenta il trattamento primario nel 92%-96% dei casi
- Laparoisteroannessectomia + asportazione colletto vaginale ± linfectomia (sampling o linfoadenectomia pelvica ± lomboaortica)

TERAPIA SISTEMICA

RADIOTERAPIA

TERAPIA

Nell'istotipo endometrioide

- il grado di differenziazione della neoplasia
- la profondità di interessamento miometrale
- lo stadio di malattia
- invasione linfovascolare

correlano con la probabilità di recidiva e di interessamento linfonodale (per le pazienti non sottoposte a linfadenectomia)

Lo stadio di malattia è il fattore prognostico più importante

sopravvivenza a 5 anni:

I	86%
II	70%
III	49%
IV	18-19%

Età rappresenta un fattore prognostico

nelle donne giovani le neoplasie sono più differenziate e meno aggressive rispetto alle anziane

National Comprehensive Cancer Network

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Uterine Neoplasms

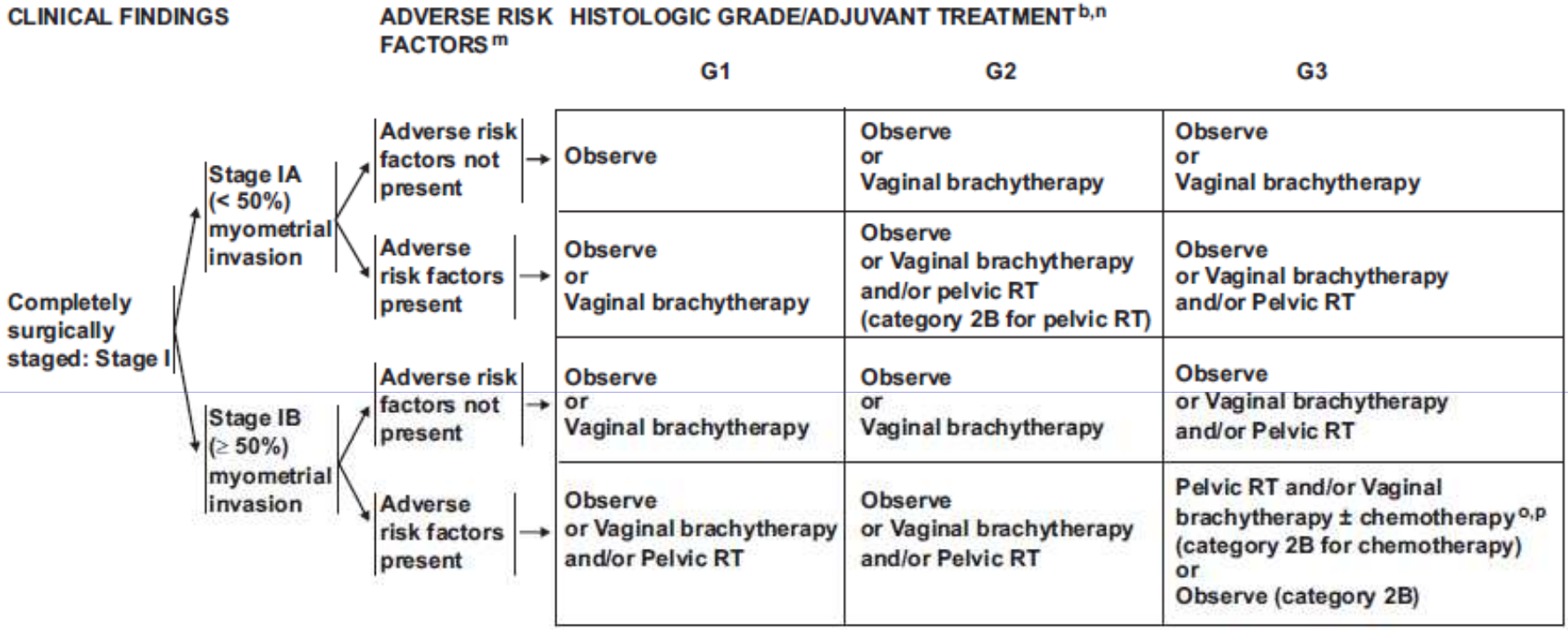
Version 3.2012

NCCN.org

Continue

NCCN Guidelines Version 3.2012
Endometrial Carcinoma

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)



[b] See Principles of Radiation Therapy (UN-A).

[m] Potential adverse risk factors include the following: Age, positive lymphovascular invasion, tumor size, lower uterine (cervical/glandular) involvement.

[n] Adjuvant therapy determinations are made on the basis of pathologic findings.

[o] The role of adjuvant chemotherapy in invasive high-grade uterine confined disease is the subject of current studies. (Creutzberg, CL Clinical Trial: Chemotherapy and Radiation Therapy Compared With Radiation Therapy Alone in Treating Patients With High-Risk Stage I, Stage II, or Stage III Endometrial Cancer; Clinical trial summary from the National Cancer Institute's PDQ® database. Study ID Numbers: CDR0000521447; CKTO-2006-04; ISRCTN14387080; CKTO-PORTEC-3; EU-20664--- http://clinicaltrials.gov/ct/show/NCT00411138;jsessionid=2309E60C1051E921B4E2614F2BE708A4?order=9. Hogberg T, Signorelli M, de Oliveira CF, et al. Sequential adjuvant chemotherapy and radiotherapy in endometrial cancer--results from two randomised studies. Eur J Cancer 2010;46(13):2422-2431.)

[p] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

See Surveillance (ENDO-8)

NCCN Guidelines Version 3.2012
Endometrial Carcinoma

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

CLINICAL FINDINGS	HISTOLOGIC GRADE/ADJUVANT TREATMENT[b,n,p]		
	G1	G2	G3
Completely surgically staged: Stage II[q,r] →	Vaginal brachytherapy and/or pelvic RT	Pelvic RT + vaginal brachytherapy	Pelvic RT + vaginal brachytherapy ± chemotherapy[o,p] (category 2B for chemotherapy)
Completely surgically staged: Stage IIIA →	Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or Pelvic RT ± vaginal brachytherapy	Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or Pelvic RT ± vaginal brachytherapy	Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or Pelvic RT ± vaginal brachytherapy

[b] See Principles of Radiation Therapy (UN-A).

[n] Adjuvant therapy determinations are made on the basis of pathologic findings.

[o] The role of adjuvant chemotherapy in invasive high-grade uterine confined disease is the subject of current studies. (Creutzberg, CL Clinical Trial: Chemotherapy and Radiation Therapy Compared With Radiation Therapy Alone in Treating Patients With High-Risk Stage I, Stage II, or Stage III Endometrial Cancer; Clinical trial summary from the National Cancer Institute's PDQ® database. Study ID Numbers: CDR0000521447; CKTO-2006-04; ISRCTN14387080; CKTO-PORTEC-3; EU-20664-- http://clinicaltrials.gov/ct/show/NCT00411138;jsessionid=2309E60C1051E921B4E2614F2BE708A4?order=9. Hogberg T, Signorelli M, de Oliveira CF, et al. Sequential adjuvant chemotherapy and radiotherapy in endometrial cancer--results from two randomised studies. Eur J Cancer 2010;46(13):2422-2431.)

[p] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

[q] Observation or vaginal brachytherapy is also an option for patients with stage II disease who have had a radical hysterectomy with negative surgical margins and no evidence of extrauterine disease.

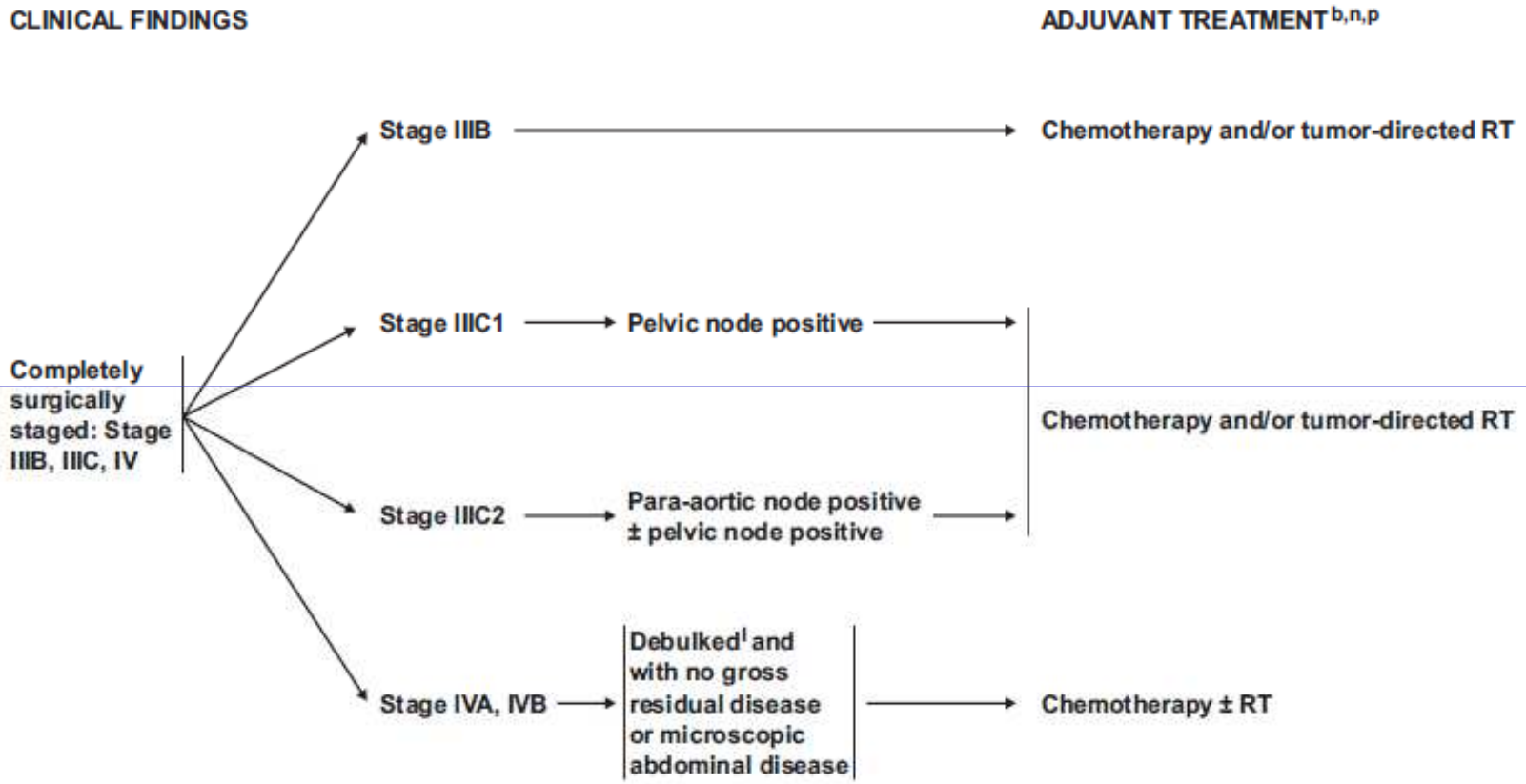
[r] The adverse fundal risk factors influencing therapy decisions for stage I disease (see ENDO-4) may also impact the choice of adjuvant therapy for stage II disease.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

See Surveillance (ENDO-8)

NCCN Guidelines Version 3.2012
Endometrial Carcinoma

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)



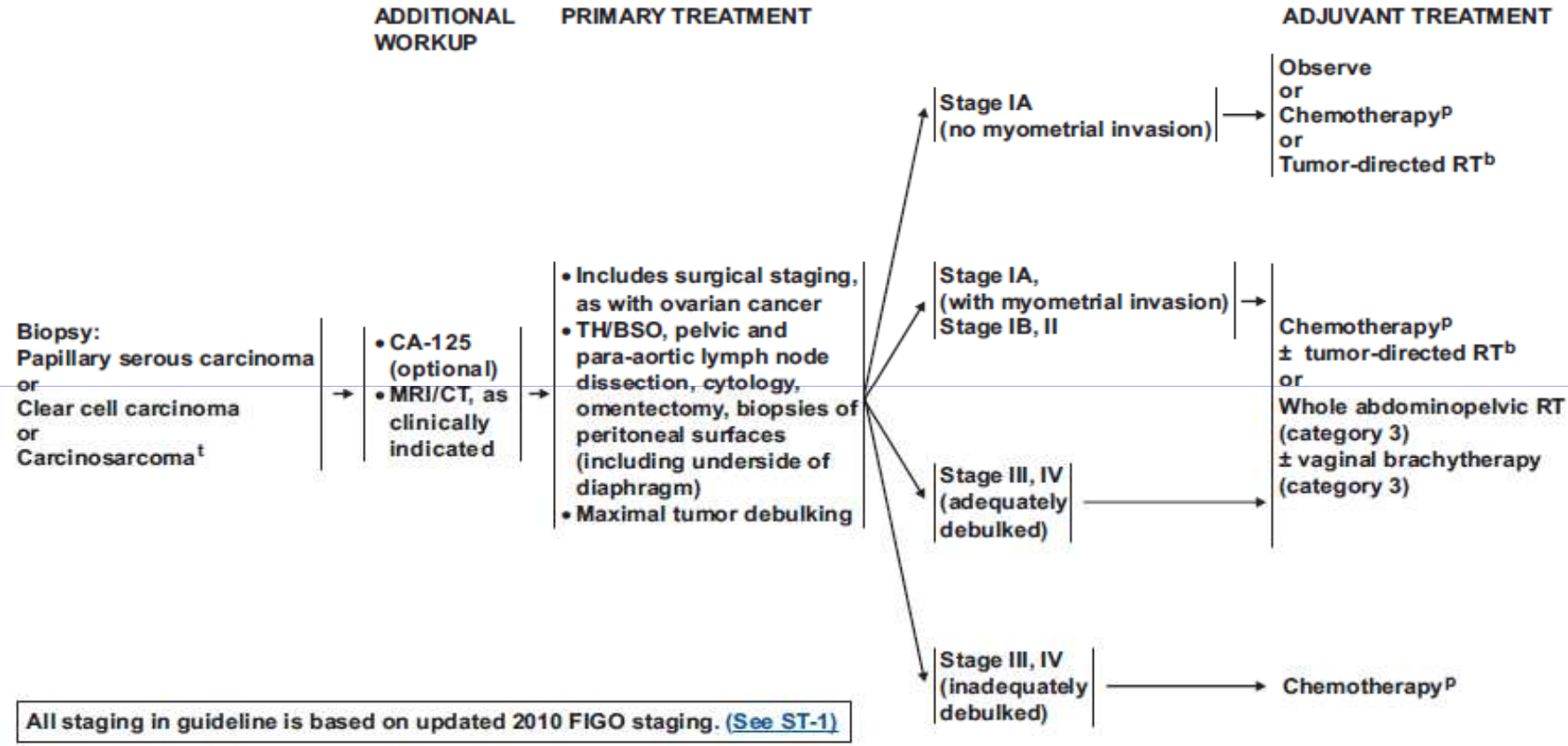
[b] See Principles of Radiation Therapy (UN-A).
[l] The surgical goal is to have no measurable residual disease.
[n] Adjuvant therapy determinations are made on the basis of pathologic findings.
[p] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

See Surveillance (ENDO-8)

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Guidelines Version 3.2012
Endometrial Carcinoma

PAPILLARY SEROUS OR CLEAR CELL CARCINOMA OF THE ENDOMETRIUM OR CARCINOSARCOMA[t]



All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

[b] See Principles of Radiation Therapy (UN-A).

[p] See Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-B).

[t] Also known as malignant mixed mesodermal tumor or malignant mixed Müllerian tumor. Most carcinosarcomas are treated the same as poorly differentiated adenocarcinomas.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

See Surveillance (ENDO-8)

PRINCIPLES OF RADIATION THERAPY

- Tumor-directed RT refers to RT directed at sites of known or suspected tumor involvement, and may include external beam and/or brachytherapy. In general, tumor-directed external-beam RT (EBRT) is directed to the pelvis with or without the para-aortic region. Brachytherapy can be delivered: 1) to an intact uterus, either preoperatively or definitively; or 2) more commonly, to the vagina after hysterectomy. For the purposes of these guidelines, whole abdominal radiotherapy is not considered to be tumor-directed RT.

- Pelvic radiotherapy should target the gross disease (if present), the lower common iliacs, external iliacs, internal iliacs, parametria, upper vagina/para-vaginal tissue, and presacral lymph nodes (in patients with cervical involvement). Extended-field radiotherapy should include the pelvic volume and also target the entire common iliac chain and para-aortic lymph node region. The upper border of the extended field depends on the clinical situation but should at least be to the level of the renal vessels. External-beam doses for microscopic disease should be 45-50 Gy. Multiple conformal fields based on CT-treatment planning should be utilized.

- Brachytherapy doses for definitive therapy are individualized based on the clinical situation. For preoperative therapy in patients with gross stage IIB disease, in general, a total dose of 75-80 Gy low-dose rate equivalent to the tumor volume is recommended. For vaginal brachytherapy, the dose should be prescribed to the vaginal surface or at a depth of 0.5 cm from the vaginal surface; the dose depends on the use of EBRT.
  - The target for vaginal brachytherapy after hysterectomy should be limited to the upper vagina.
  - For high-dose rate brachytherapy, when used as a boost to EBRT, doses of 4-6 Gy X 2-3 fractions prescribed to the vaginal mucosa are commonly used.
  - For high-dose rate vaginal brachytherapy alone, commonly used regimens include 7 Gy X 3 prescribed at a depth of 0.5 cm from the vaginal surface or 6 Gy X 5 fractions prescribed to the vaginal surface.

CARCINOMA DELLA CERVICE UTERINA

- Età media alla diagnosi 52 anni (range 17-90)
- Livelli socio-economici bassi
- Associato con storia di malattie a trasmissione sessuale: HPV tipi 16 e 18 (meno frequentemente 45, 31, 33). Sono stati identificati almeno altri 10 sottotipi più rari
-

Sebbene la persistenza di infezione da HPV sia un fattore necessario nello sviluppo di molti (probabilmente tutti) i carcinomi della cervice uterina,

ORIGINE MULTIFATTORIALE

- **ALTERAZIONI GENETICHE**
- **CONDIZIONI IMMUNOLOGICHE**
- **MALATTIE A TRASMISSIONE SESSUALE**
- **FUMO**
- **FATTORI SCONOSCIUTI**

SCREENING

- Dall'introduzione dell'uso del Pap Test negli anni '40, l'incidenza del cr della portio si è ridotta

- Tuttavia è stata osservata un'aumento costante di incidenza di forme preinvasive

DIAGNOSI

- Perdite vaginali ematiche o siero-ematiche, maleodoranti
- Dolore
- Sintomatologia urinaria: disuria – stranguria - ematuria
- Sintomatologia rettale: tenesmo – proctorragie
- Fistole vescico-vaginali o vescico-rettali

TABLE 21–4. **Histologic Classification of Uterine Cervix Carcinoma**

Type	Incidence (%)
Squamous Carcinoma	
Large cell nonkeratinizing	57
Large cell keratinizing	22
Small cell nonkeratinizing	6
Adenocarcinoma	
Endocervical	10
Endometrioid	2
Clear cell	2
Others	1
Mixed Epithelial Carcinoma	
Adenosquamous	2–5
Glassy cell	1
Neuroendocrine	
Carcinoid	<1
Small cell	1

Modified from Bragg DG, Rubin P, Youker JE (eds): Gynecologic

Diagnosi neoplasie della cervice uterina

- **visita ginecologica in narcosi**
- **TC / RM addome-pelvi**
- **RX torace**
- PET
- *Urografia*
- *RX clisma opaco (stadi IIB-IVA)*
- *cisto e rettoscopia(stadi IIB-IVA)*

NCCN Guidelines Version 2.2013
Cervical Cancer

NCCN Guidelines Index
Cervical Cancer TOC
Discussion

WORKUP

- H&P
- Complete blood count (CBC) (including platelets)
- Cervical biopsy, pathologic review
- Cone biopsy as indicated[a]
- LFT/renal function studies
- Imaging (optional for ≤ stage IB1):
  - Chest x-ray
  - CT or PET-CT scan
  - MRI as indicated

Optional (≥ stage IB2):

- EUA cystoscopy/proctoscopy[b]
- Smoking cessation and counseling intervention

CLINICAL STAGE

Stage IA1	See Primary Treatment (Fertility Sparing) (CERV-2)
	See Primary Treatment (Non-Fertility Sparing) (CERV-3)
Stage IA2 Stage IB1	See Primary Treatment (Fertility Sparing) (CERV-2)
	See Primary Treatment (Non-Fertility Sparing) (CERV-3) and (CERV-4)
Stage IIA1	See Primary Treatment (Non-Fertility Sparing) (CERV-4)
Stage IB2 Stage IIA2	See Primary Treatment (CERV-4) and (CERV-6)
Stage IIB Stage IIIA, IIIB Stage IVA	See Primary Treatment (CERV-6)
Incidental finding of invasive cancer at simple hysterectomy	See Primary Treatment (CERV-9)

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

[a] See Discussion for indications for cone biopsy.
[b] For suspicion of bladder/bowel involvement, cystoscopy/proctoscopy with biopsy is required.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Guidelines Version 2.2013 Staging
Cervical Cancer

NCCN Guidelines Index
Cervical Cancer TOC
Discussion

Table 1 AJCC Tumor-Node-Metastases (TNM) and International Federation of Gynecology and Obstetrics (FIGO) Surgical Staging Systems for Carcinoma of the Uterine Cervix

TNM Categories	FIGO Stages	Surgical-Pathologic Findings
TX		Primary tumor cannot be assessed
T0		No evidence of primary tumor
Tis*		Carcinoma in situ (preinvasive carcinoma)
T1	I	Cervical carcinoma confined to cervix (extension to corpus should be disregarded)
T1a**	IA	Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less. Vascular space involvement, venous or lymphatic, does not affect classification
T1a1	IA1	Measured stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread
T1a2	IA2	Measured stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less
T1b	IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2#
T1b1	IB1	Clinically visible lesion 4.0 cm or less in greatest dimension
T1b2	IB2	Clinically visible lesion more than 4.0 cm in greatest dimension
T2	II	Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina
T2a	IIA	Tumor without parametrial invasion
T2a1	IIA1	Clinically visible lesion 4.0 cm or less in greatest dimension
T2a2	IIA2	Clinically visible lesion more than 4.0 cm in greatest dimension
T2b	IIB	Tumor with parametrial invasion
T3	III	Tumor extends to pelvic wall and/or involves lower third of vagina and/or causes hydronephrosis or nonfunctioning kidney##
T3a	IIIA	Tumor involves lower third of vagina, no extension to pelvic wall
T3b	IIIB	Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney
T4	IVA	Tumor invades mucosa of bladder or rectum, and/or extends beyond true pelvis (bullous edema is not sufficient to classify a tumor as T4)

*Note: FIGO no longer includes Stage 0 (Tis).

**Note: All macroscopically visible lesions–even with superficial invasion–are T1b/IB.

#All macroscopically visible lesions—even with superficial invasion—are allotted to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5.00 mm and a horizontal extension of not >7.00 mm. Depth of invasion should not be >5.00 mm taken from the base of the epithelium of the original tissue—superficial or glandular. The depth of invasion should always be reported in mm, even in those cases with "early (minimal) stromal invasion" (~1 mm). The involvement of vascular/lymphatic spaces should not change the stage allotment.

##On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. All cases with hydronephrosis or non-functioning kidney are included, unless they are known to be due to another cause.

Continued...

Staging-Cervical Cancer

Table 1-Continued AJCC Tumor-Node-Metastases (TNM) and International Federation of Gynecology and Obstetrics (FIGO) Surgical Staging Systems for Carcinoma of the Uterine Cervix

Regional Lymph Nodes (N)

TNM Categories	FIGO Stages	
NX		Regional lymph nodes cannot be assessed
N0		No regional lymph node metastasis
N1		Regional lymph node metastasis

Distant Metastasis (M)

TNM Categories	FIGO Stages	
M0		No distant metastasis
M1	IVB	Distant metastasis (including peritoneal spread, involvement of supraclavicular, mediastinal, or paraaortic lymph nodes, lung, liver, or bone)

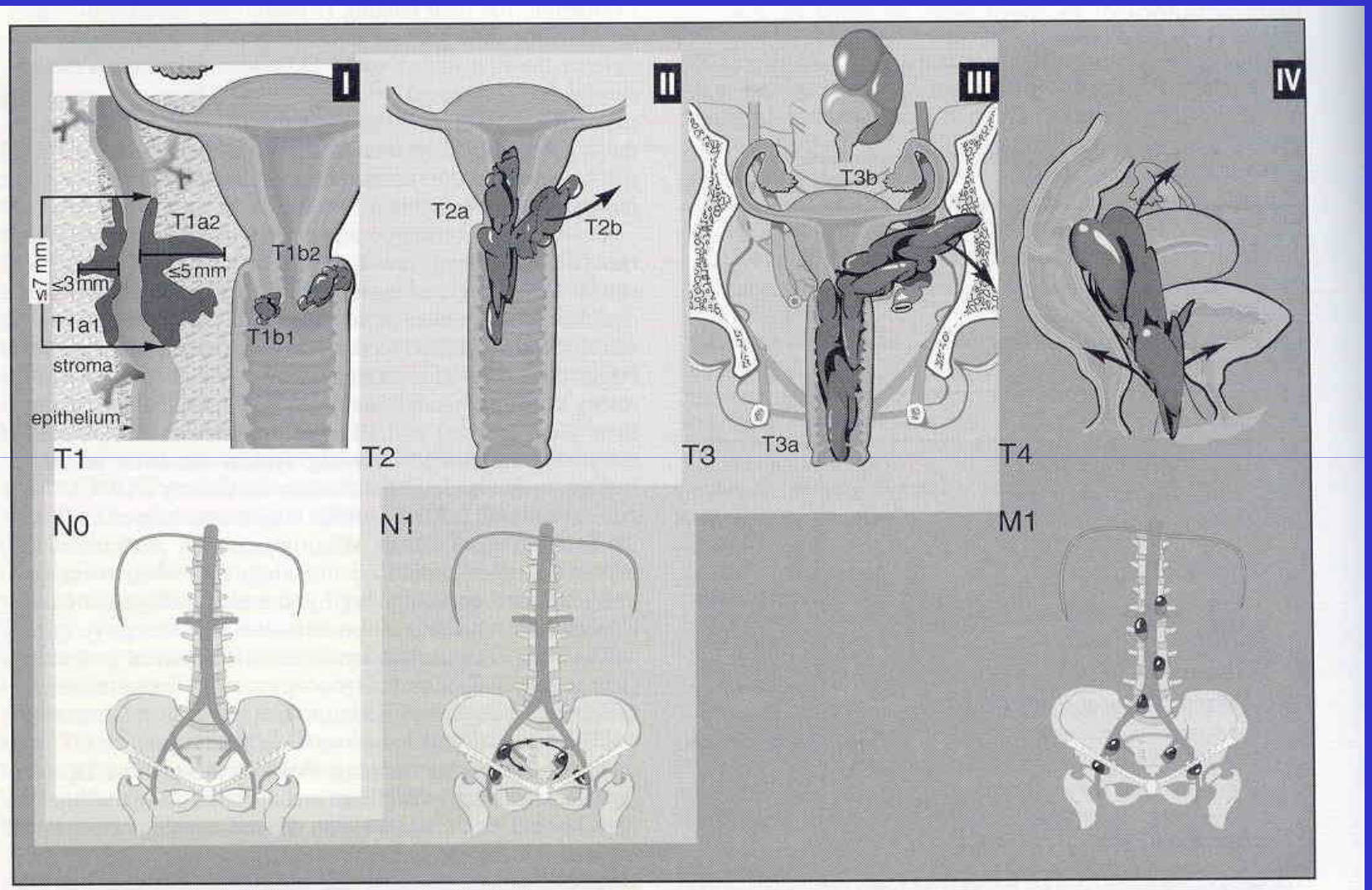


Figure 21–1. Anatomic staging for carcinoma of the uterine cervix.

NCCN Guidelines Version 2.2013
Cervical Cancer

NCCN Guidelines Index
Cervical Cancer TOC
Discussion

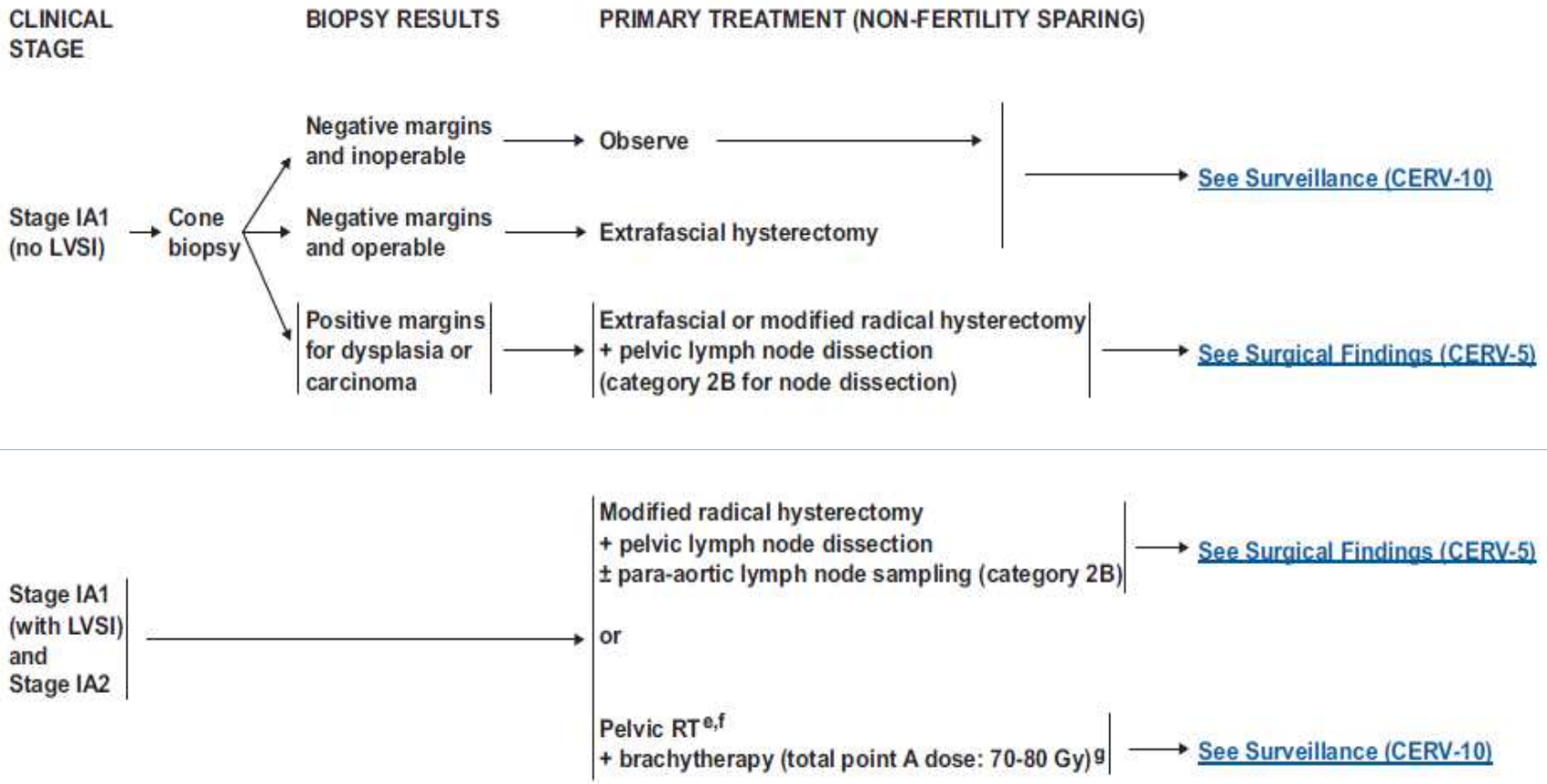
CLINICAL STAGE	PRIMARY TREATMENT (FERTILITY SPARING)[c]	
Stage IA1 (no lymphovascular space invasion [LVSI])	Cone biopsy with negative margins (preferably a non-fragmented specimen with 3-mm negative margins) (If positive margins, repeat cone biopsy or perform trachelectomy)	See Surveillance (CERV-10)
Stage IA1 (with LVSI) and Stage IA2	Cone biopsy with negative margins (preferably a non-fragmented specimen with 3-mm negative margins) + pelvic lymph node dissection or Radical trachelectomy + pelvic lymph node dissection (± para-aortic lymph node sampling [category 2B])	See Surveillance (CERV-10)
Stage IB1[d]	Radical trachelectomy + pelvic lymph node dissection ± para-aortic lymph node sampling	See Surveillance (CERV-10)

[c]No data support a fertility-sparing approach in small cell neuroendocrine tumors or minimal deviation adenocarcinoma (also known as adenoma malignum). Total hysterectomy after completion of childbearing is at the patient's and surgeon's discretion, but is strongly advised in women with continued abnormal pap smears or chronic persistent HPV infection.

[d]Fertility-sparing surgery for stage IB1 has been most validated for tumors ≤2 cm.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN Guidelines Version 2.2013
Cervical Cancer



[e] Radiation can be an option for medically inoperable patients or those who refuse surgery.
[f] See Principles of Radiation Therapy for Cervical Cancer (CERV-A).
[g] These doses are recommended for most patients based on summation of conventional external-beam fractionation and low-dose rate (40-70 cGy/h) brachytherapy equivalents. Modify treatment based on normal tissue tolerance. (See Discussion)

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013
Cervical Cancer

CLINICAL STAGE	PRIMARY TREATMENT (NON-FERTILITY SPARING)	
Stage IB1 and Stage IIA1	Radical hysterectomy + pelvic lymph node dissection ± para-aortic lymph node sampling (category 1)	See Surgical Findings (CERV-5)
	or Pelvic RT[e,f] + brachytherapy (total point A dose: 80-85 Gy)[g] ± concurrent cisplatin-containing chemotherapy[h]	See Surveillance (CERV-10)
Stage IB2 and Stage IIA2 (also see CERV-6 for alternative recommendations for these patients)	Pelvic RT[f] + concurrent cisplatin-containing chemotherapy[h] + brachytherapy (total point A dose ≥85 Gy)[g] (category 1)	See Surveillance (CERV-10)
	or Radical hysterectomy + pelvic lymph node dissection ± para-aortic lymph node sampling (category 2B)	See Surgical Findings (CERV-5)
	or Pelvic RT[f] + concurrent cisplatin-containing chemotherapy[h] + brachytherapy (total point A dose 75-80 Gy)[g] + adjuvant hysterectomy (category 3)	See Surveillance (CERV-10)

[e] Radiation can be an option for medically inoperable patients or those who refuse surgery.

[f] See Principles of Radiation Therapy for Cervical Cancer (CERV-A).

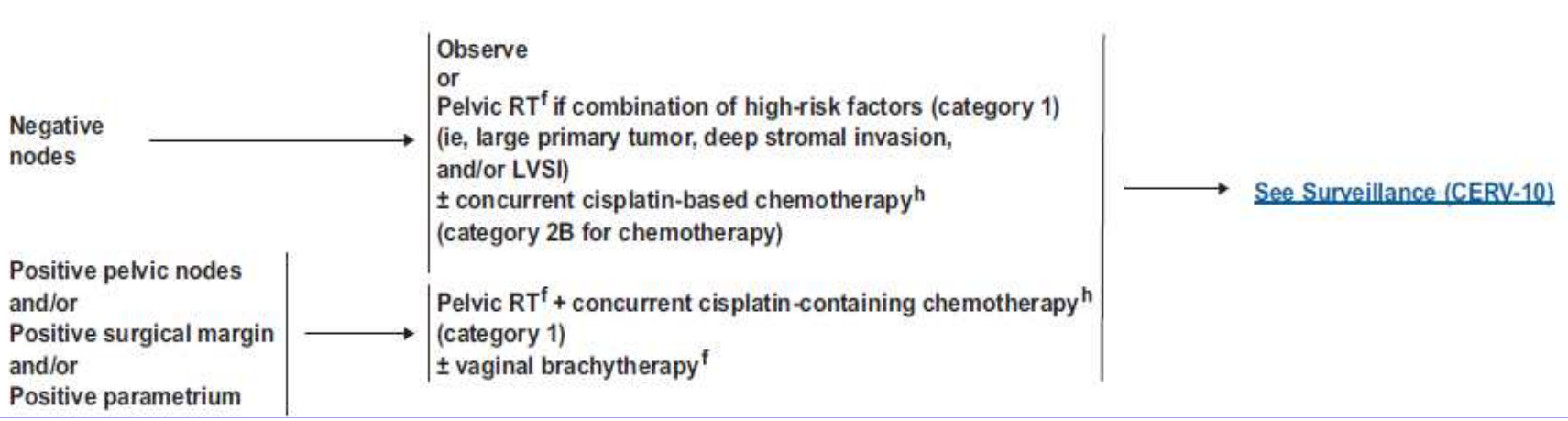
[g] These doses are recommended for most patients based on summation of conventional external-beam fractionation and low-dose rate (40-70 cGy/h) brachytherapy equivalents. Modify treatment based on normal tissue tolerance. (See Discussion)

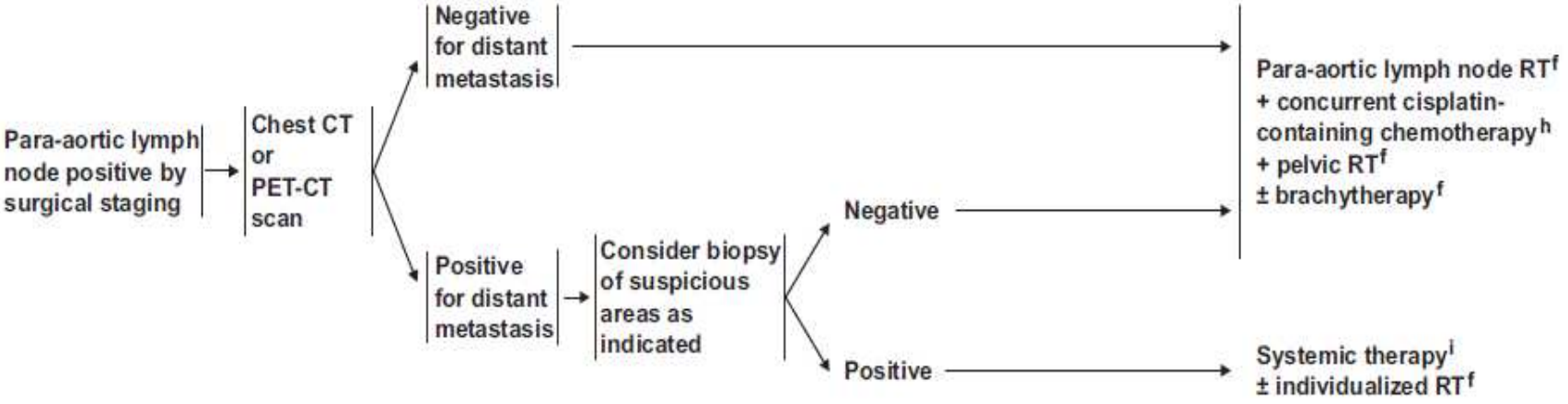
[h] Concurrent cisplatin-based chemotherapy with RT utilizes cisplatin as a single agent or cisplatin plus 5-fluorouracil.

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013
Cervical Cancer

NCCN Guidelines Index
Cervical Cancer TOC
Discussion

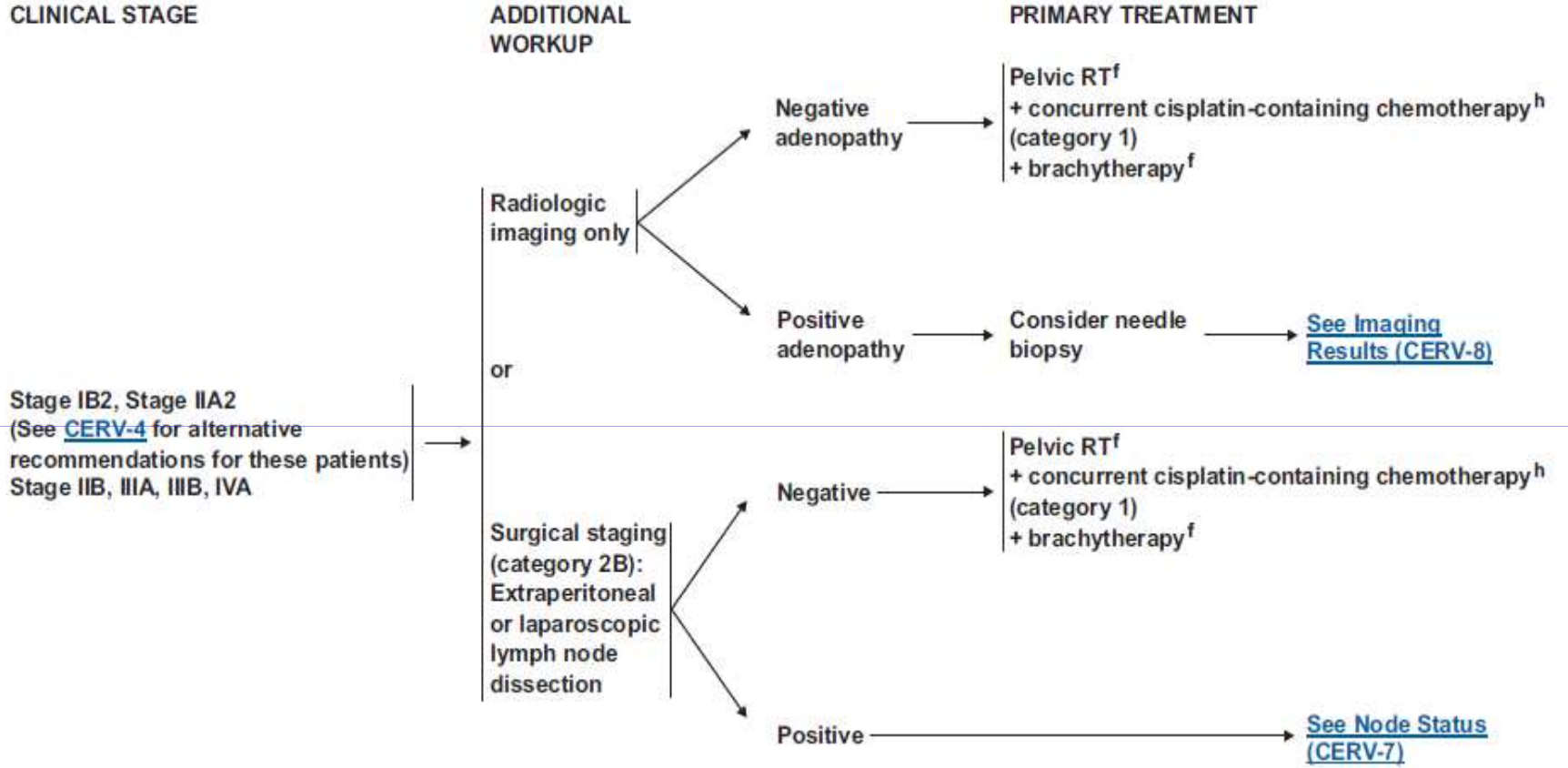




[f] See Principles of Radiation Therapy for Cervical Cancer (CERV-A).
[h] Concurrent cisplatin-based chemotherapy with RT utilizes cisplatin as a single agent or cisplatin plus 5-fluorouracil.
[i] See Chemotherapy Regimens for Recurrent or Metastatic Cervical Cancer (CERV-B).

NCCN Guidelines Version 2.2013
Cervical Cancer

NCCN Guidelines Index
Cervical Cancer TOC
Discussion



[f] See Principles of Radiation Therapy for Cervical Cancer (CERV-A).
[h] Concurrent cisplatin-based chemotherapy with RT utilizes cisplatin as a single agent or cisplatin plus 5-fluorouracil.

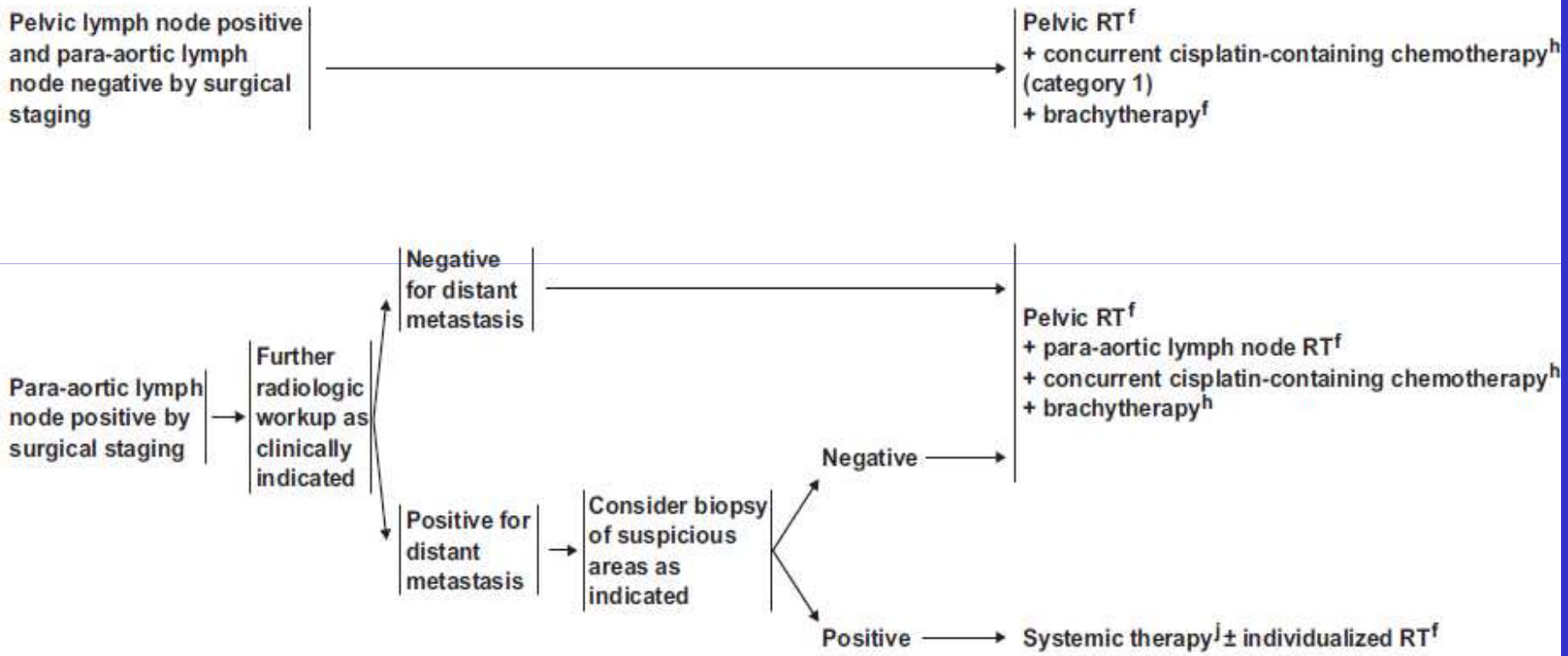
National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013
Cervical Cancer

NCCN Guidelines Index
Cervical Cancer TOC
Discussion

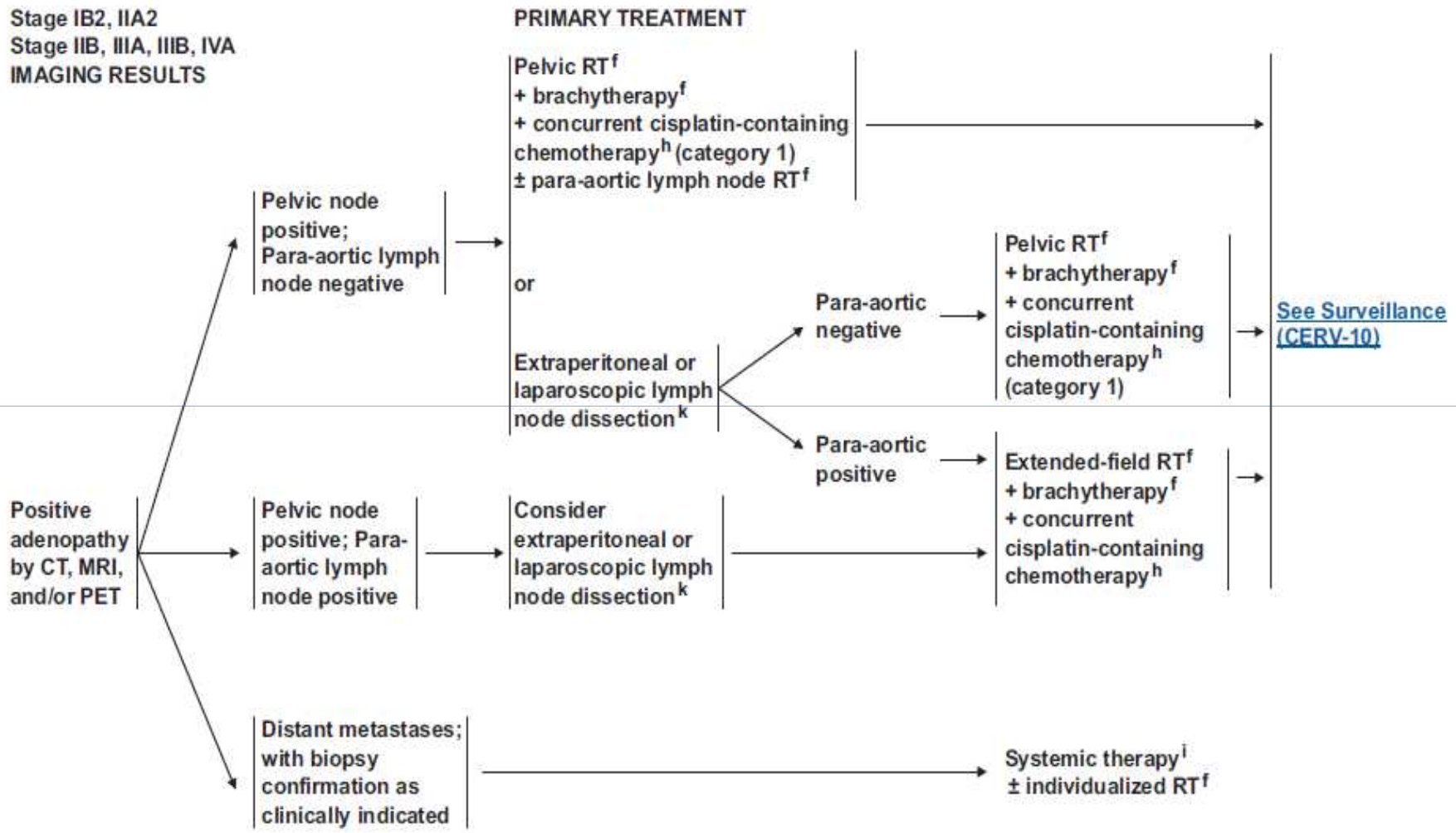
Stage IB2, IIA2; Stage IIB, IIIA, IIIB, IVA
NODE STATUS

PRIMARY TREATMENT



[f] See Principles of Radiation Therapy for Cervical Cancer (CERV-A).
[h] Concurrent cisplatin-based chemotherapy with RT utilizes cisplatin as a single agent or cisplatin plus 5-fluorouracil.
[j] See Chemotherapy Regimens for Recurrent or Metastatic Cervical Cancer (CERV-B).

NCCN Guidelines Version 2.2013
Cervical Cancer



[f] See Principles of Radiation Therapy for Cervical Cancer (CERV-A).
[h] Concurrent cisplatin-based chemotherapy with RT utilizes cisplatin as a single agent or cisplatin plus 5-fluorouracil.
[i] See Chemotherapy Regimens for Recurrent or Metastatic Cervical Cancer (CERV-B).
[k] Consider postoperative imaging to confirm the adequacy of node removal.

NCCN Guidelines Version 2.2013
Cervical Cancer

NCCN Guidelines Index
Cervical Cancer TOC
Discussion

SURVEILLANCE[m]

- Interval H&P
  every 3-6 mo for 2 y,
  every 6-12 mo for 3-5 y,
  then annually based on patient's risk of disease recurrence
- Cervical/vaginal cytology annually[n] as indicated for the detection of lower genital tract neoplasia
- Imaging (chest radiography, CT, PET, PET/CT, MRI) as indicated based on symptoms or examination findings suspicious for recurrence[o]
- Laboratory assessment (CBC, blood urea nitrogen (BUN), creatinine) as indicated based on symptoms or examination findings suspicious for recurrence
- Recommend use of vaginal dilator after RT
- Patient education regarding symptoms

→ Persistent or recurrent disease →

WORKUP

- Additional imaging as clinically indicated
- Surgical exploration in selected cases

→ See Therapy for Relapse (Local/regional recurrence) (CERV-11)

→ See Therapy for Relapse (Distant metastases) (CERV-12)

[m] Salani R, Backes FJ, Fung MF, et al. Posttreatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncologists recommendations. Am J Obstet Gynecol 2011;204:466-478.

[n] Regular cytology can be considered for detection of lower genital tract dysplasia, although its value in detection of recurrent cervical cancer is limited. The likelihood of picking up asymptomatic recurrences by cytology alone is low.

[o] A single PET-CT scan performed at 3-6 months after chemoradiation for locally advanced cervical cancer can be used to identify early or asymptomatic persistence/recurrence. Other imaging studies (such as chest x-ray, CT scan, MRI, and subsequent PET-CT) may also be used to assess or follow recurrence when clinically indicated but are not recommended for routine surveillance. (See Discussion)

PRINCIPLES OF RADIATION THERAPY FOR CERVICAL CANCER

External Beam Radiation Therapy (EBRT)

- The use of CT–based treatment planning and conformal blocking is considered the standard of care for EBRT. MRI is the best imaging modality for determining soft tissue and parametrial involvement in patients with advanced tumors. In patients who are not surgically staged, PET imaging is useful to help define the nodal volume of coverage.
- The volume of EBRT should cover the gross disease (if present), parametria, uterosacral ligaments, sufficient vaginal margin from the gross disease (at least 3 cm), presacral nodes, and other nodal volumes at risk. For patients with negative nodes on surgical or radiologic imaging, the radiation volume should include the entirety of the external iliac, internal iliac, and obturator nodal basins. For patients deemed at higher risk of lymph node involvement (eg, bulkier tumors; suspected or confirmed nodes confined to the low true pelvis), the radiation volume should be increased to cover the common iliacs as well. In patients with documented common iliac and/or para-aortic nodal involvement, extended-field pelvic and para-aortic radiotherapy is recommended, up to the level of the renal vessels (or even more cephalad as directed by involved nodal distribution).
- Coverage of microscopic nodal disease requires an EBRT dose of approximately 45 Gy (in conventional fractionation of 1.8-2.0 Gy daily), and highly conformal boosts of an additional 10-15 Gy may be considered for limited volumes of gross unresected adenopathy. For the majority of patients who receive EBRT for cervical cancer, concurrent cisplatin-based chemotherapy (either cisplatin alone, or cisplatin + 5-fluorouracil) is given during the time of EBRT.
- Intensity-modulated radiation therapy (IMRT) and similar highly conformal methods of dose delivery may be helpful in minimizing the dose to the bowel and other critical structures in the post-hysterectomy setting and in treating the para-aortic nodes when necessary. These techniques can also be useful when high doses are required to treat gross disease in regional lymph nodes. However, conformal external beam therapies (such as IMRT) should not be used as routine alternatives to brachytherapy for treatment of central disease in patients with an intact cervix. Very careful attention to detail and reproducibility (including consideration of target and normal tissue definitions, patient and internal organ motion, soft tissue deformation, and rigorous dosimetric and physics quality assurance) is required for proper delivery of IMRT and related highly conformal technologies.

PRINCIPLES OF RADIATION THERAPY FOR CERVICAL CANCER

Brachytherapy

- Brachytherapy is a critical component of definitive therapy for all patients with primary cervical cancer who are not candidates for surgery. This is usually performed using an intracavitary approach, with an intrauterine tandem and vaginal colpostats. Depending on the patient and tumor anatomy, the vaginal component of brachytherapy in patients with an intact cervix may be delivered using ovoids, ring, or cylinder brachytherapy (combined with the intrauterine tandem). When combined with EBRT, brachytherapy is often initiated towards the latter part of treatment, when sufficient primary tumor regression has been noted to permit satisfactory brachytherapy apparatus geometry. In highly selected very early disease (ie, stage IA2), brachytherapy alone (without external-beam radiation) may be an option.
- In rare cases, patients whose tumor geometry renders intracavitary brachytherapy infeasible may be best treated using an interstitial approach; however, such interstitial brachytherapy should only be performed by individuals and at institutions with appropriate experience and expertise.
- In selected post-hysterectomy patients (especially those with positive vaginal mucosal surgical margins), vaginal cylinder brachytherapy may be used as a boost to EBRT.

PRINCIPLES OF RADIATION THERAPY FOR CERVICAL CANCER

Definitive Radiation Therapy for an Intact Cervix

- In patients with an intact cervix (ie, those who do not have surgery), the primary tumor and regional lymphatics at risk are typically treated with definitive EBRT to a dose of approximately 45 Gy (40-50 Gy). The volume of the EBRT would depend on the nodal status as determined surgically or radiographically (as previously described). The primary cervical tumor is then boosted, using brachytherapy, with an additional 30-40 Gy to point A (in LDR equivalent dose), for a total point A dose (as recommended in the guidelines) of 80 Gy (small volume cervical tumors) to 85 Gy or greater (larger volume cervical tumors). Grossly involved unresected nodes may be evaluated for boosting with an additional 10-15 Gy of highly conformal (and reduced volume) EBRT. With higher doses, especially of EBRT, care must be taken to exclude, or to severely limit, the volume of normal tissue included in the high-dose region(s) (see Discussion).

Posthysterectomy Adjuvant Radiation Therapy

- Following primary hysterectomy, the presence of one or more pathologic risk factors may warrant the use of adjuvant radiotherapy. At a minimum, the following should be covered: upper 3-4 cm of the vaginal cuff, the parametria, and immediately adjacent nodal basins (such as the external and internal iliacs). For documented nodal metastasis, the superior border of the radiation field should be appropriately increased (as previously described). A dose of 45-50 Gy in standard fractionation is generally recommended. Grossly involved unresected nodes may be evaluated for boosting with an additional 10-15 Gy of highly conformal (and reduced volume) EBRT. With higher doses, especially of EBRT, care must be taken to exclude, or to severely limit, the volume of normal tissue included in the high-dose region(s) (see Discussion).

Intraoperative Radiation Therapy (IORT)

- IORT is a specialized technique that delivers a single, highly focused dose of radiation to a tumor bed at risk, or isolated unresectable residual, during an open surgical procedure.[3] It is particularly useful in patients with recurrent disease within a previously radiated volume. During IORT, overlying normal tissue (such as bowel or other viscera) can be manually displaced from the region at risk. IORT is typically delivered with electrons using pre-formed applicators of variable sizes (matched to the surgically defined region at risk), which further constrain the area and depth of radiation exposure to avoid surrounding normal structures.

Carcinoma della cervice uterina
Approccio terapeutico

- **Stadio Ia1** (profondità di infiltrazione < 3 mm): conizzazione se si vuole preservare la fertilità. Ma assenza di invasione linfovascolare e margini liberi

- **Stadi early (Ia,Ib e IIa non bulky)**
  chirurgia ± radioterapia o radioterapia = opzioni terapeutiche equivalenti.

- **Malattia localmente avanzata (IB2-IVA):** radioterapia radicale
  RTE + brachiterapia endocavitaria
  +
  Chemioterapia concomitante

NCI, febbraio 1999
Chemio-radioterapia concomitante per carcinoma della cervice uterina

- 5 studi randomizzati mostrano un aumento di sopravvivenza globale per trattamento combinato RT+CT con CDDP
- Stadi IB2-IVA (non operabili) e I-IIA operati con fattori prognostici sfavorevoli (N+ pelvico, Parametri +, margini +)
- Rischio di morte ridotto del 30-50%
- Forte raccomandazione ad includere CDDP, sebbene non ancora noto miglior regime chemioterapico

Carcinoma della cervice uterina
Terapia adiuvante dopo chirurgia radicale

- La radioterapia postoperatoria da sola è indicata nelle pazienti con almeno 2 fattori di rischio “minori” di ripresa di malattia.

- Un trattamento chemio-radioterapico concomitante è indicato in presenza di fattori di rischio maggiori:

  N+, Margini +, Parametri +

FATTORI PROGNOSTICI

- Stadio

  sopravvivenza a 5 anni

  Ia ~ 100%

  IVb 20%

- Positività linfonodale e numero linfonodi positivi

La Radioterapia ha da sempre un ruolo fondamentale nel trattamento delle neoplasie ginecologiche

- Trattamento esclusivo

  RT esterna + brachiterapia

- Trattamento adiuvante postoperatorio

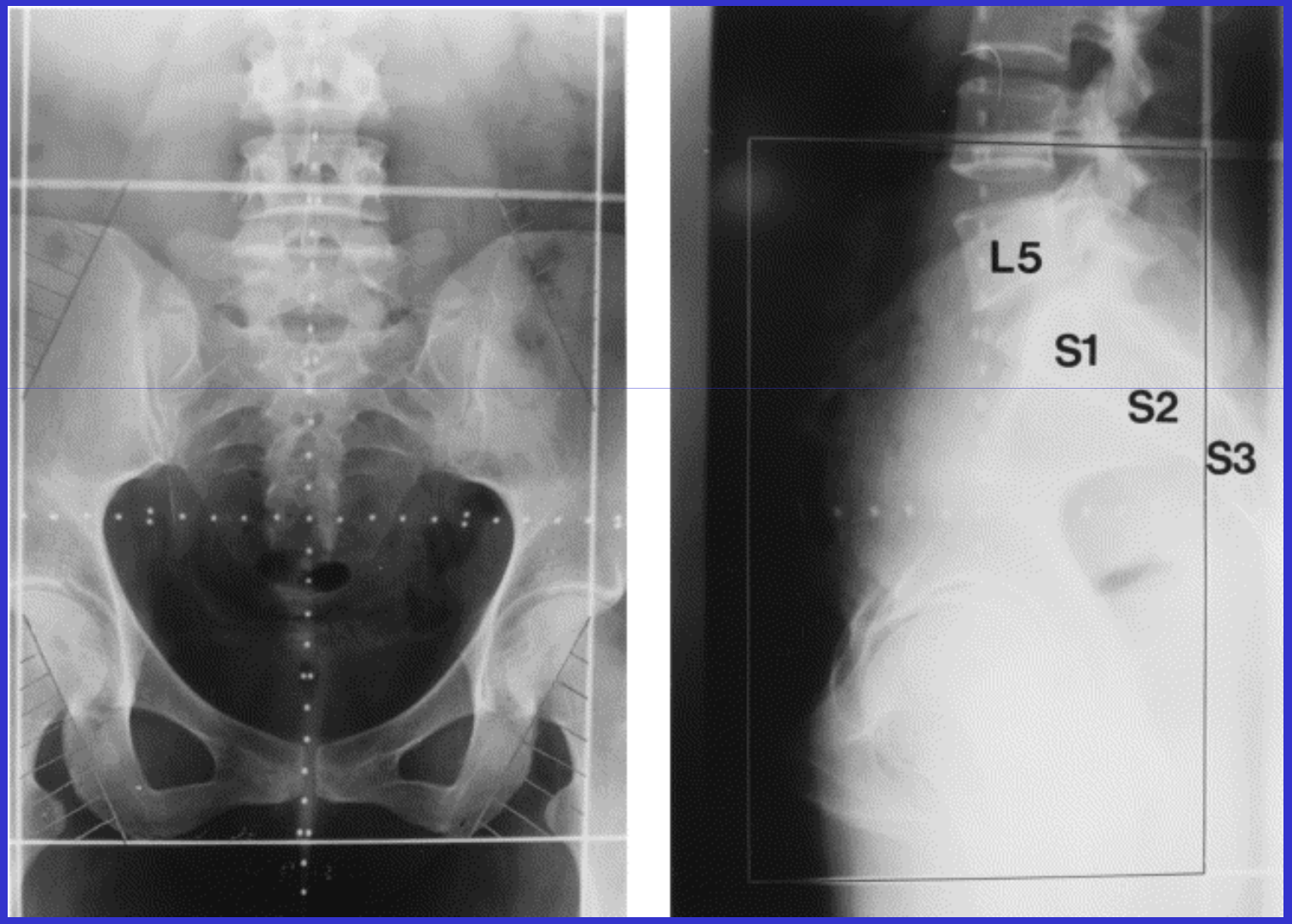
Radioterapia esterna pelvica neoplasie ginecologiche

- L'irradiazione della pelvi viene generalmente effettuata con fotoni di alta energia, con tecnica multiportale (4 campi isocentrici)
- Sistemi di immobilizzazione o dispositivi per ridurre l'irradiazione degli organi di rispetto
- I campi sono opportunamente sagomati
- Dose singola 1.8-2 Gy/die
- Dose totale 45-50 Gy

Vie di drenaggio linfonodale dell'utero

- Linfonodi paracervicali
- Linfonodi iliaci esterni ed otturatori
- Linfonodi ipogastrici
- Linfonodi iliaci comuni
- Linfonodi lomboaortici

Ottimizzazione della RTE



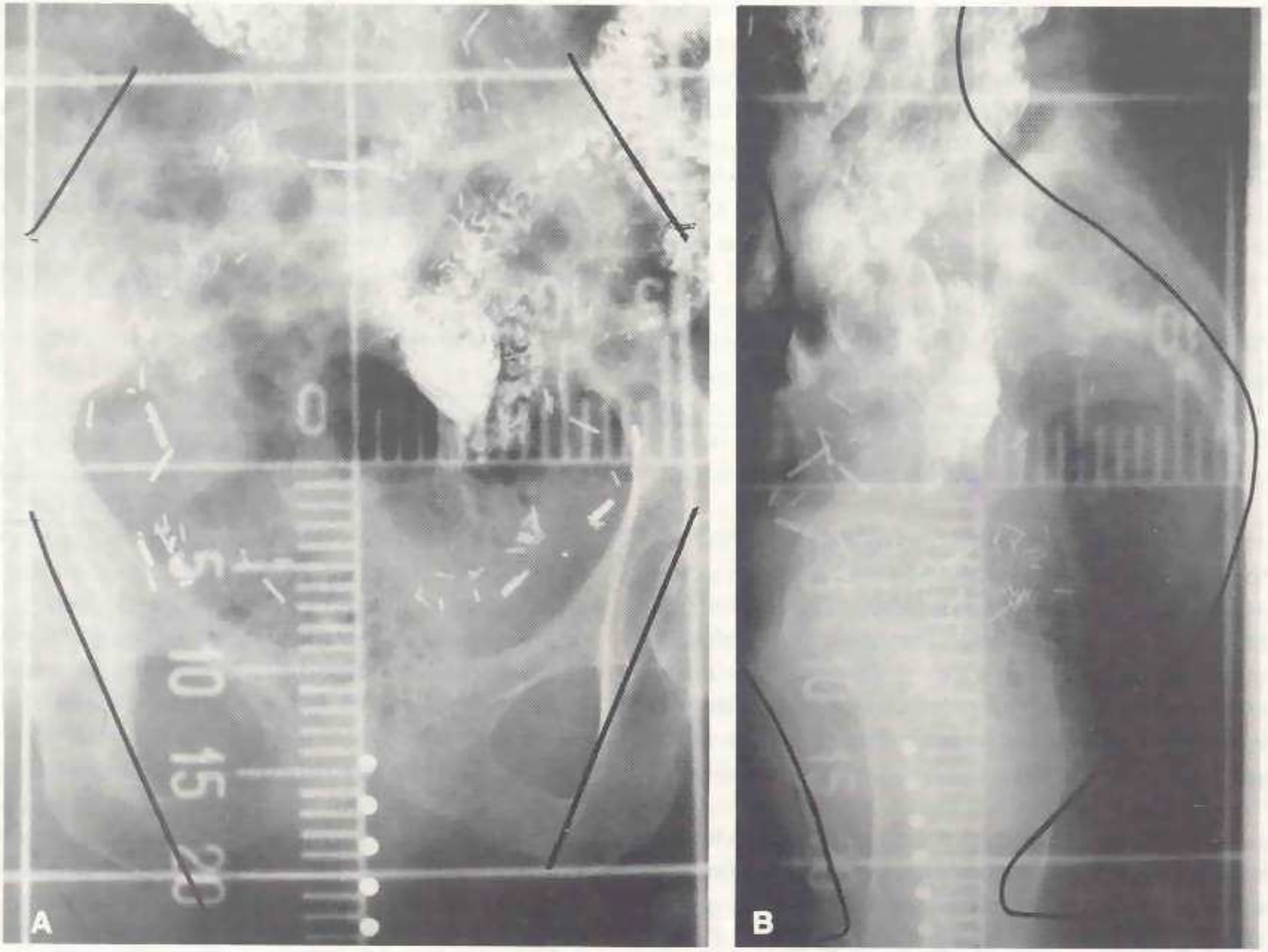


FIGURE 55–1. (**A**) Anterior and (**B**) lateral simulation films for a patient being treated postoperatively for Stage I endometrial carcinoma with areas of shielding outlined and the resulting isodose curve for the same patient on a 6 MV linear accelerator.

Cervicocarcinoma: planning 2D

- 30% omissione geografica (“tecnica box”)

  Kim, IJROBP, 31, 1995

- 32 % sottodosaggio regionale

  Russell IJROBP, 23, 1992

- 49% inadeguata copertura del fondo uterino

  Zunino IJROBP, 23, 1992

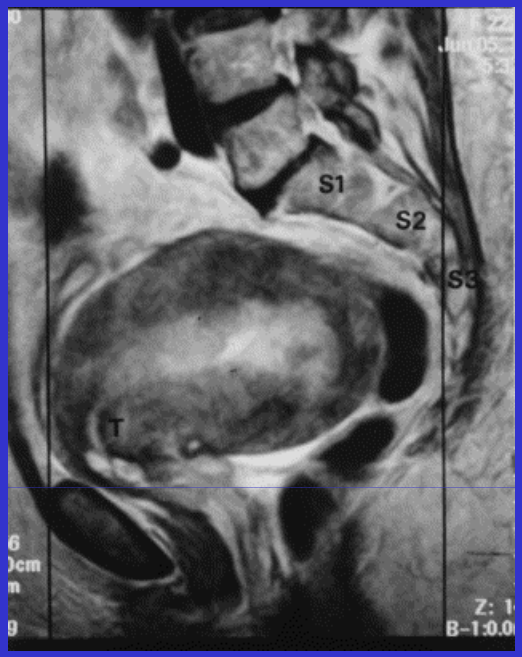
- 45% sottodosaggio LN iliaci esterni

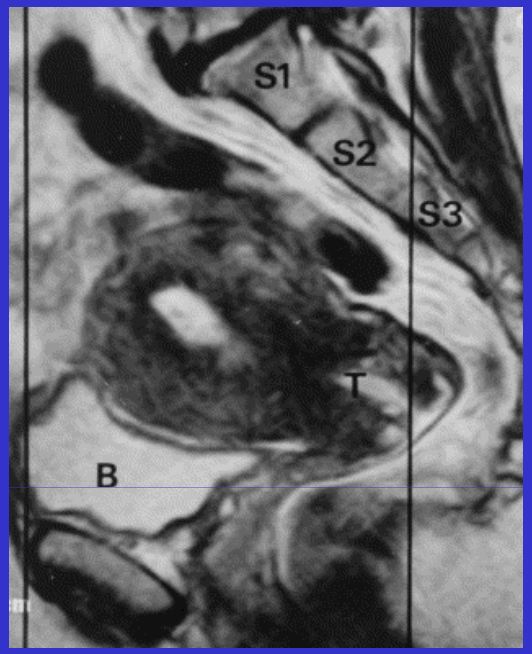
  Bonin IJROBP, 34, 1996

TCP: Inadeguatezza reperi anatomici

- Il limite laterale AP (2.5 cm dal bordo interno delle ossa pelviche) è adeguato nel 90 % dei casi (confronto campi di irradiazione/linfografie - Pendlebury et al)
- Nei campi standard i linfonodi iliaci esterni sono compresi nel 45-62% dei casi (Bonin et al - Pendlebury et al)
- Il limite craniale è adeguato nel 80% dei casi (studio autoptico – Zunino et al)

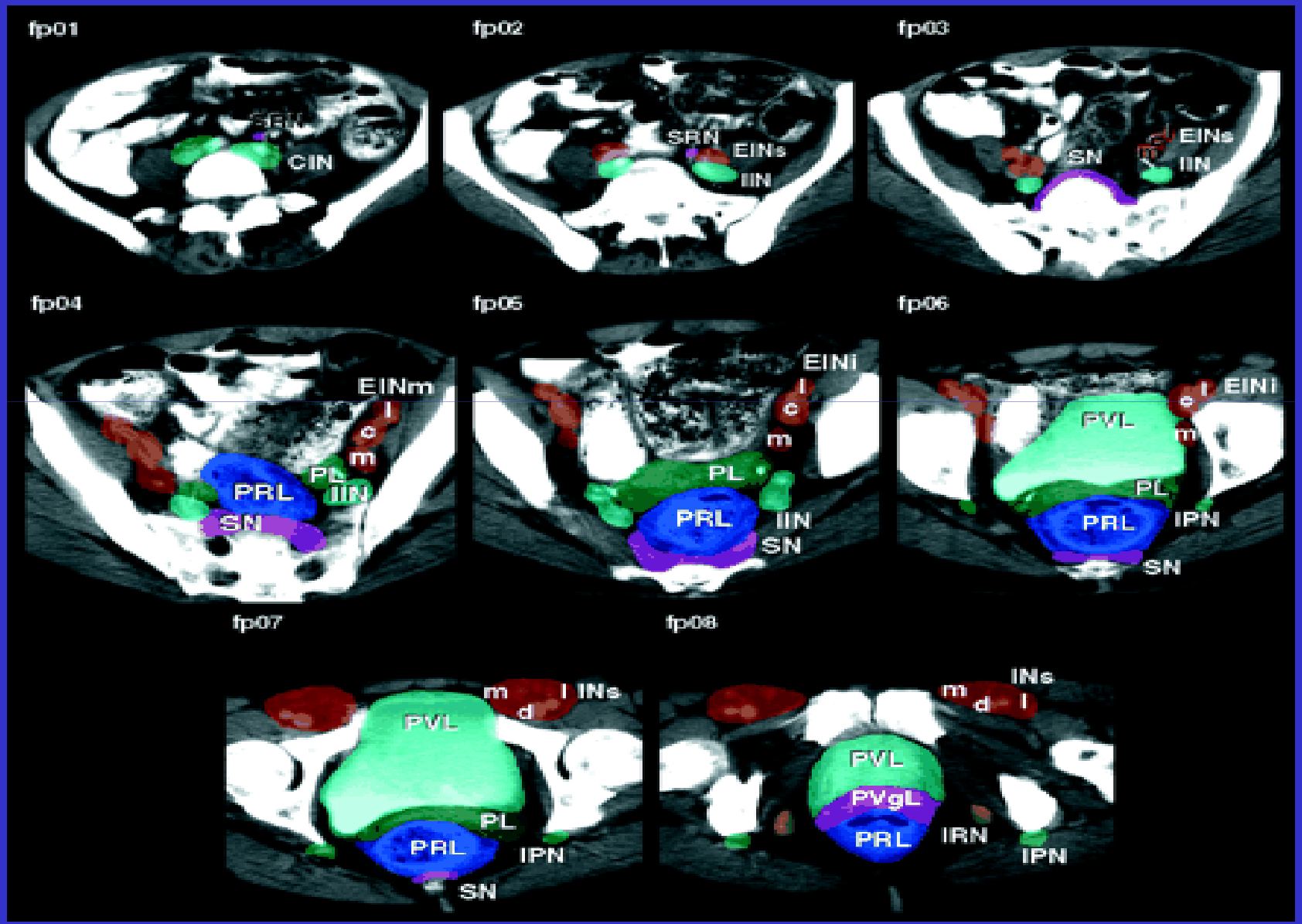
TCP: Inadeguatezza reperi anatomici



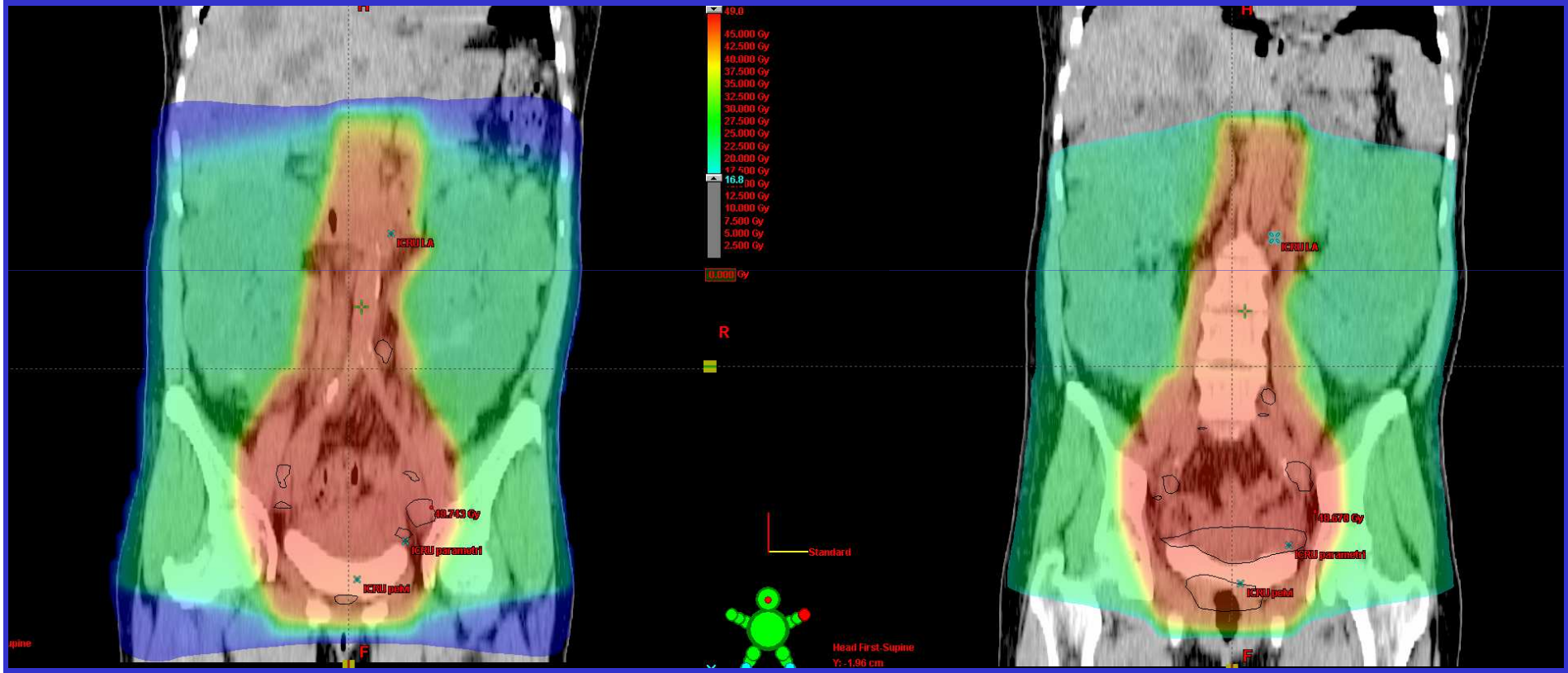


- A margini inadeguati corrisponde un mancato controllo locale: 71% vs il 100% nei IB e 50 % vs 88 % nei IIB (studio retrospettivo a 36 mesi - Kim et alii.)

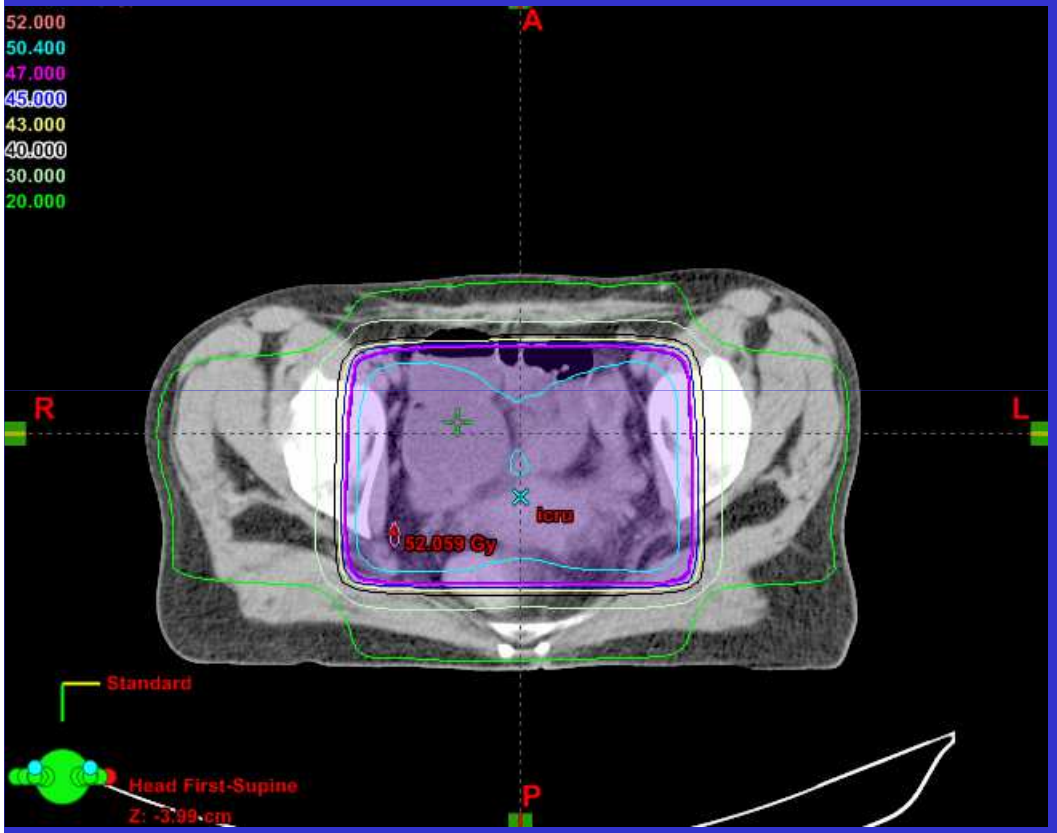
Martinez-Monge et al. *Radiology*, 211:815-828, 1999

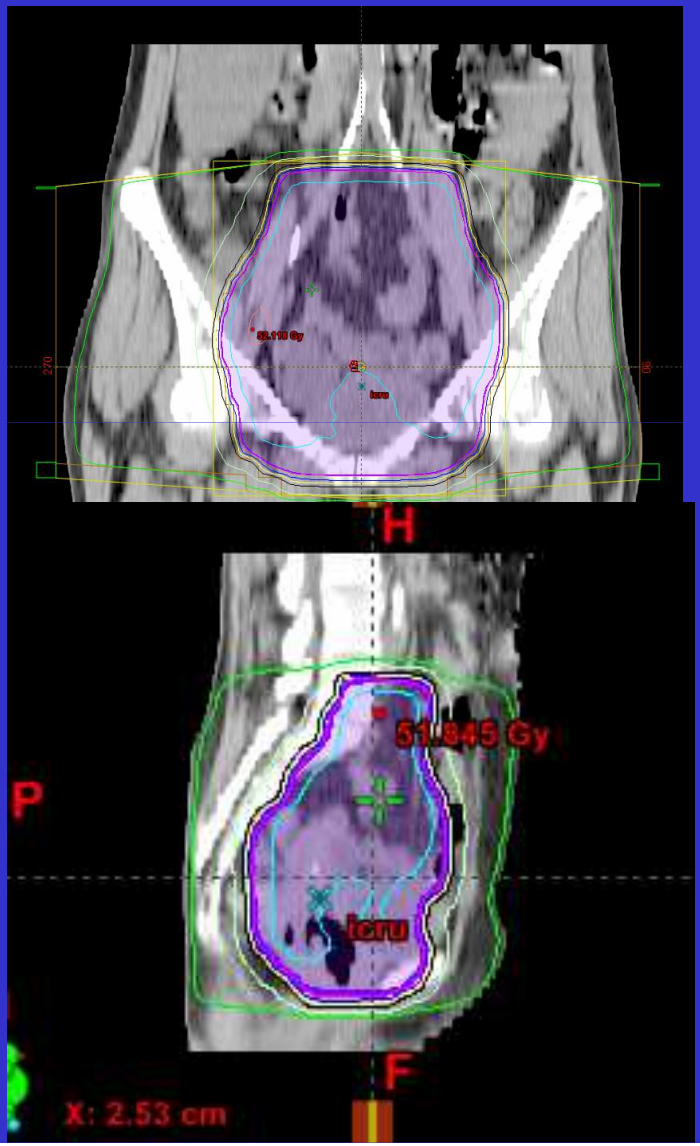


3D

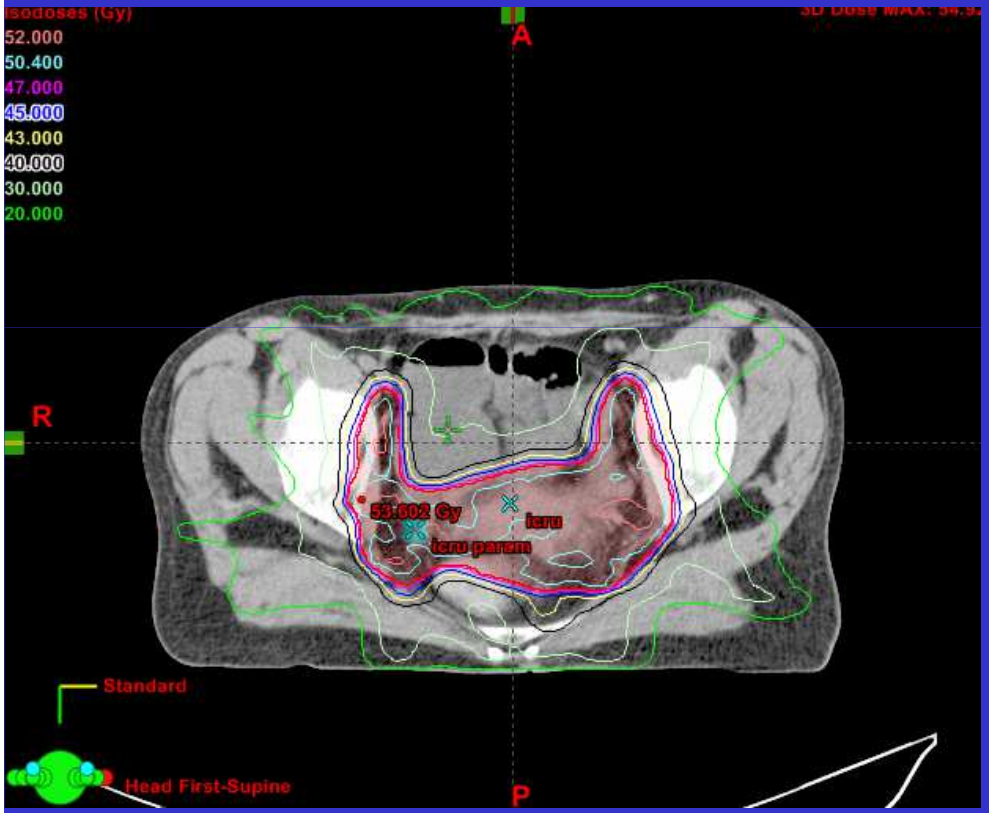

49.0
45.000 Gy
42.500 Gy
40.000 Gy
37.500 Gy
35.000 Gy
32.500 Gy
30.000 Gy
27.500 Gy
25.000 Gy
22.500 Gy
20.000 Gy
17.500 Gy
16.8
12.500 Gy
10.000 Gy
7.500 Gy
5.000 Gy
2.500 Gy
0.000 Gy
R
ICRU LA
ICRU parametri
ICRU pubi
Standard
Head First-Supine
Y: -1,96 cm

Tecnica box: V95



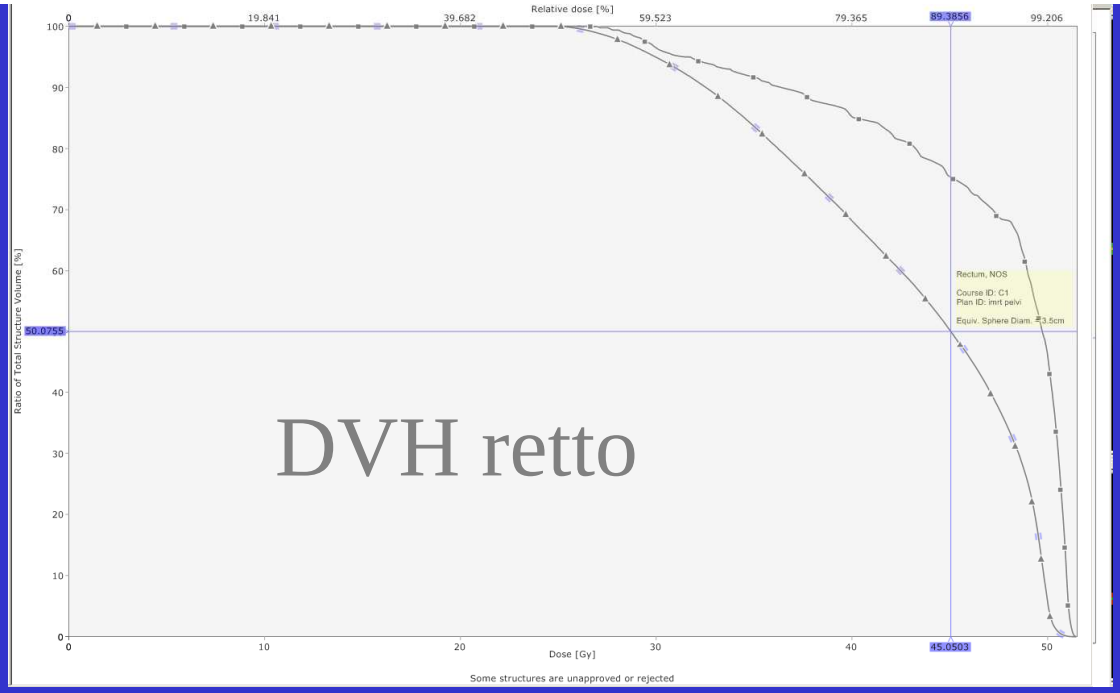


IMRT: V95

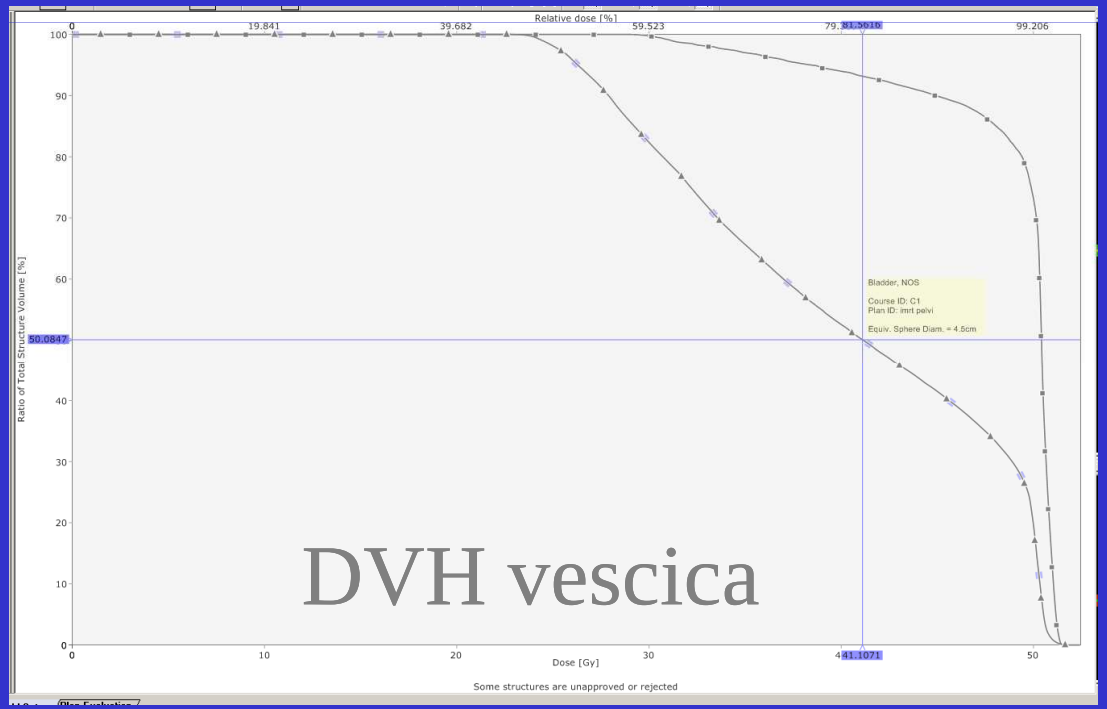

Isodoses (Gy)
52.000
50.400
47.000
45.000
43.000
40.000
30.000
20.000
A
R
P
53.602 Gy
icru
icru param
Standard
Head First-Supine


R
L
F
icru param
52.795 Gy


F
icru param
52.874 Gy

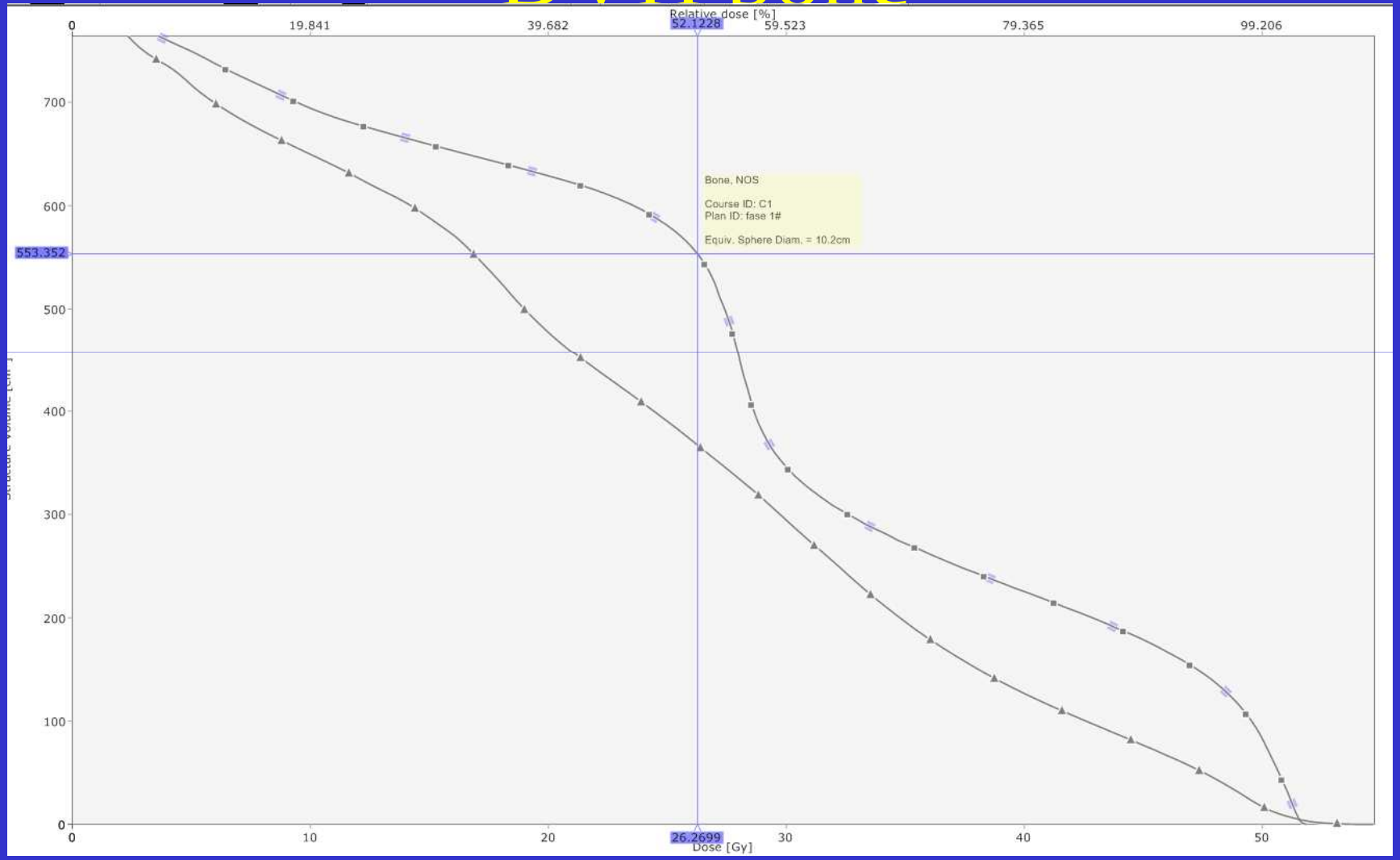


DVH retto



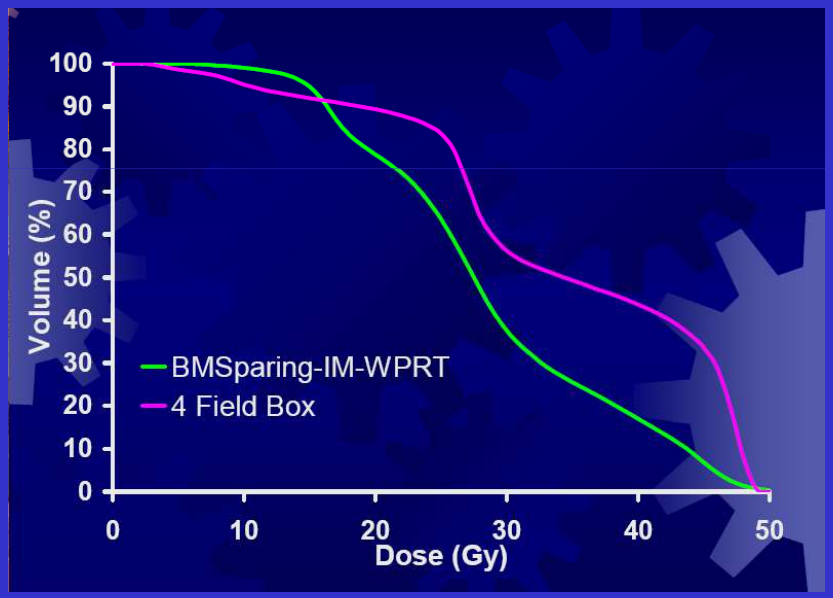
DVH vescica

DVH bone


Relative dose [%]
0
19.841
39.682
52.1228
59.523
79.365
99.206
700
600
553.352
500
400
300
200
100
0
Bone, NOS
Course ID: C1
Plan ID: fase 1#
Equiv. Sphere Diam. = 10.2cm
0
10
20
26.2699
30
40
50
Dose [Gy]

↓ Tossicità midollare

- ↓ midollo osseo irradiato (- 40%)
- ↑ tolleranza ematologica CT concomitante



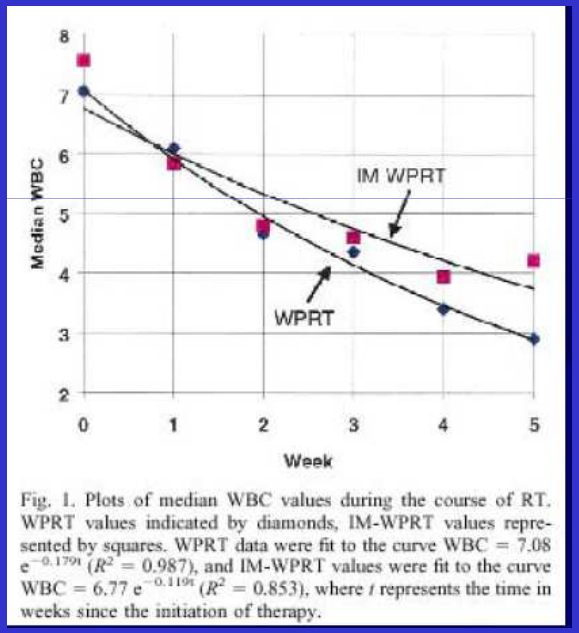


Fig. 1. Plots of median WBC values during the course of RT. WPRT values indicated by diamonds, IM-WPRT values represented by squares. WPRT data were fit to the curve WBC = 7.08 $e^{-0.179t}$ (R^2 = 0.987), and IM-WPRT values were fit to the curve WBC = 6.77 $e^{-0.119t}$ (R^2 = 0.853), where t represents the time in weeks since the initiation of therapy.

Lujan AE et al.: Int J Radiat Oncol Biol Phys 57, 2003

Brixey C, Int J Radiat Oncol Biol Phys 52, 2002

Brachiterapia
neoplasie ginecologiche

Permette di erogare in volumi limitati elevati livelli di dose, con rapido decremento della dose stessa a breve distanza dalla sorgente

posizionando opportune sorgenti radioattive direttamente a contatto o in stretta vicinanza con la neoplasia → aumento indice terapeutico

Brachiterapia endocavitaria

LDR o HDR

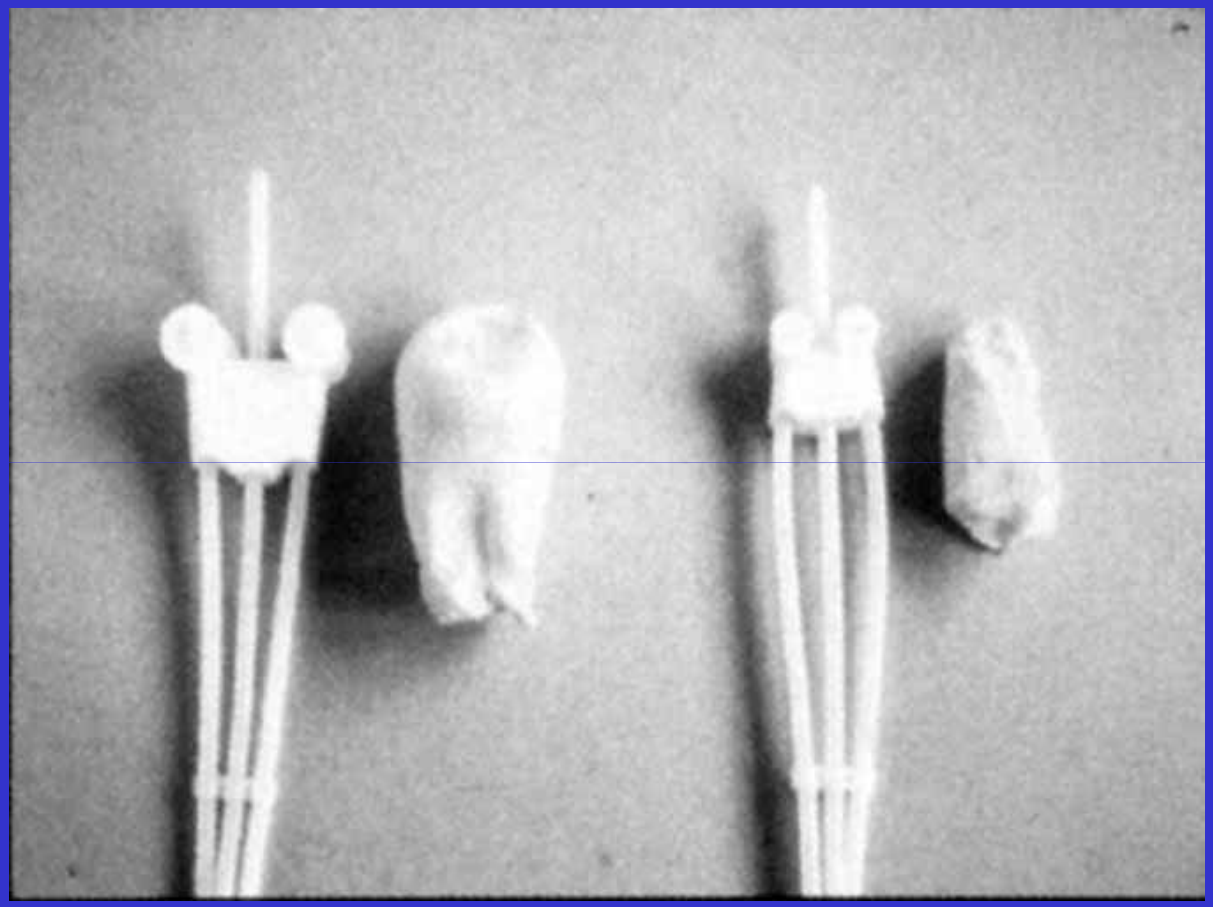
Timing del trattamento radiante

EBRT precede la brachiterapia

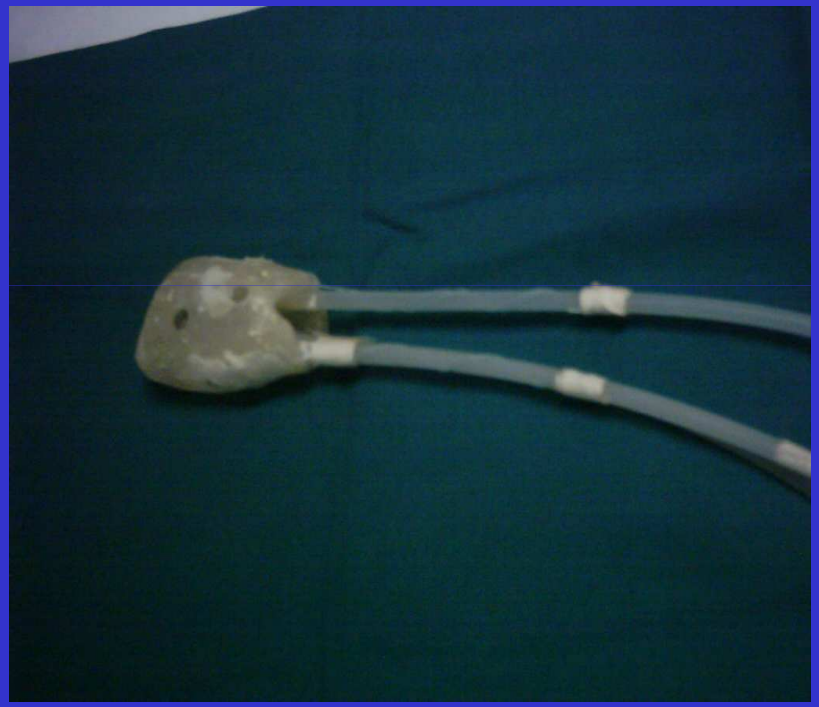
- ridurre massa tumorale
- sterilizzare la malattia paracentrale e linfonodale
- migliorare la geometria tumorale

Brachiterapia

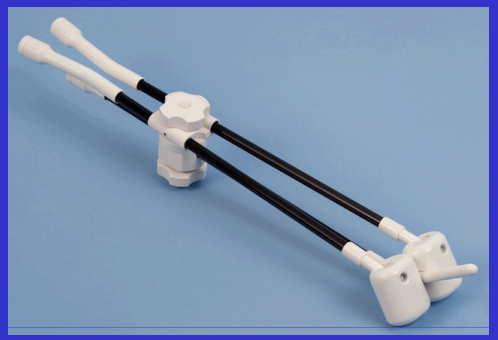
- per aumentare controllo pelvico di malattia
- per aumentare sopravvivenza

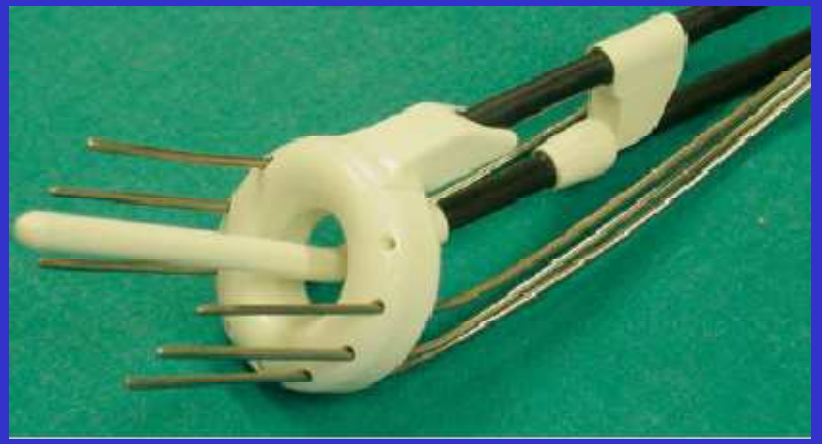


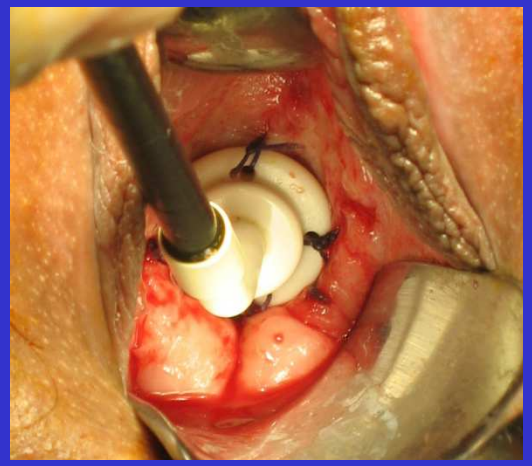
Applicatori detti moulage



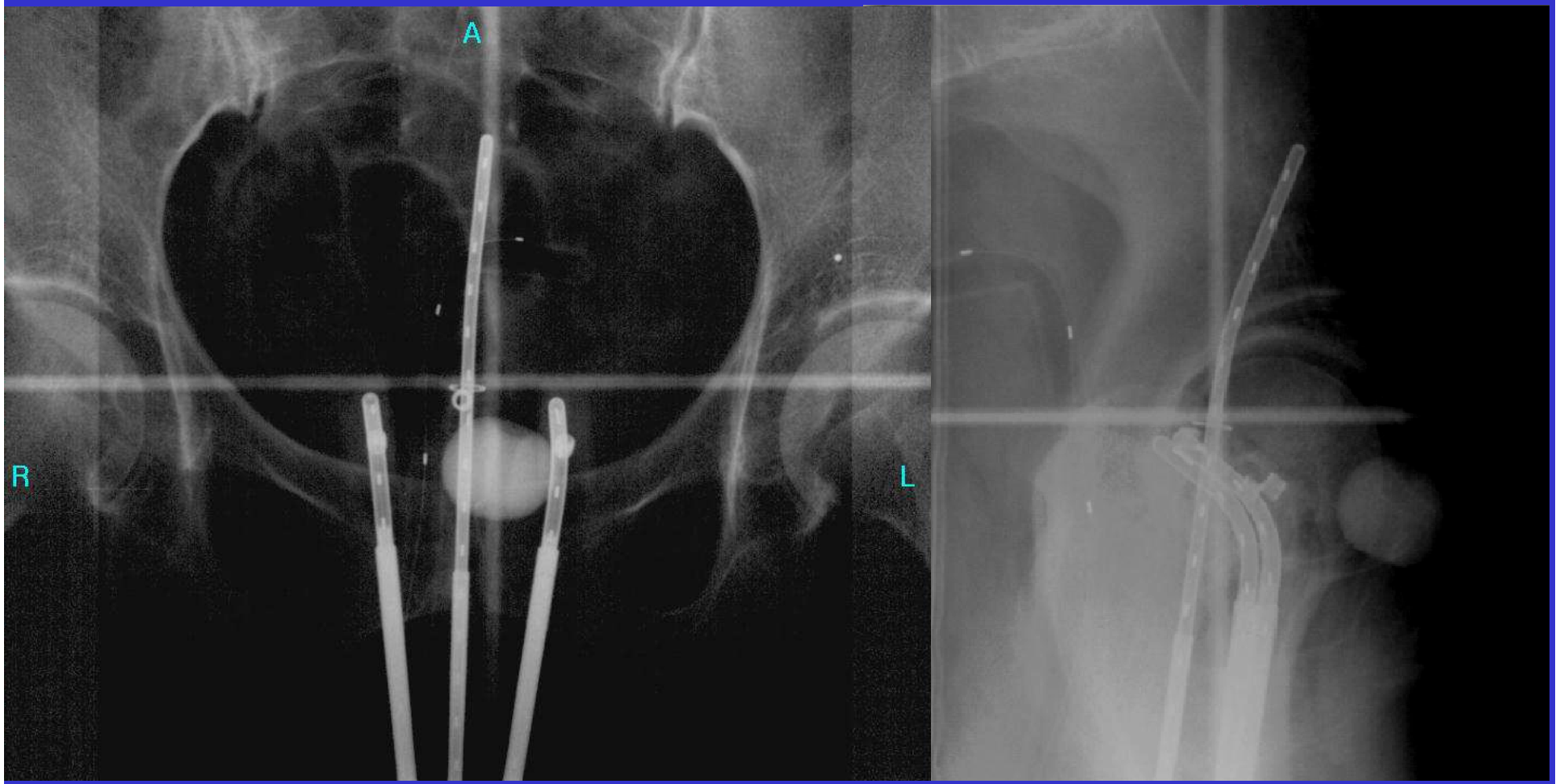
Ottimizzazione della BT





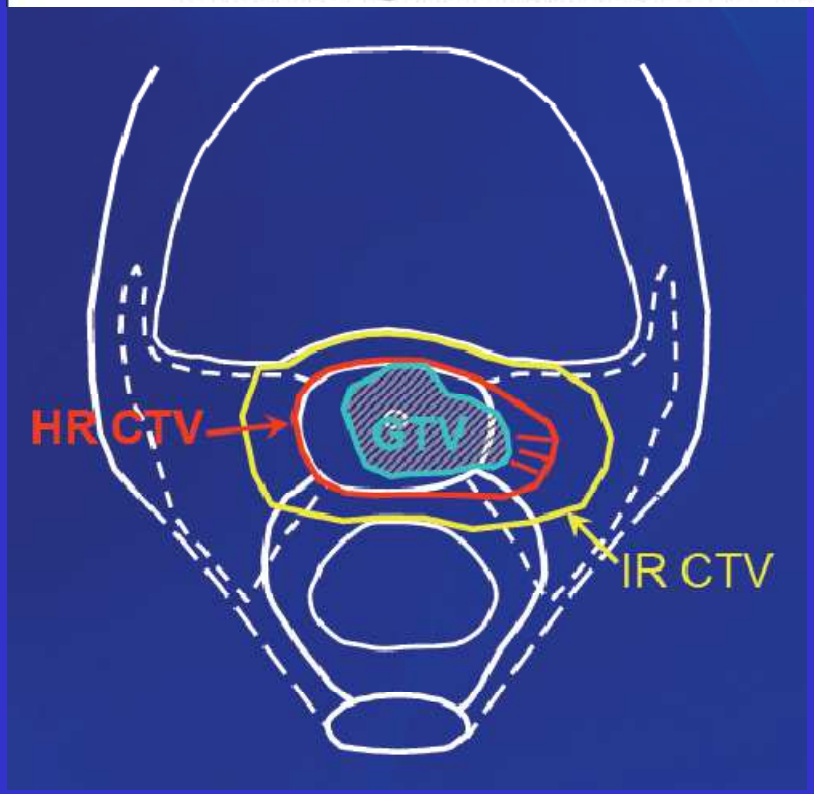


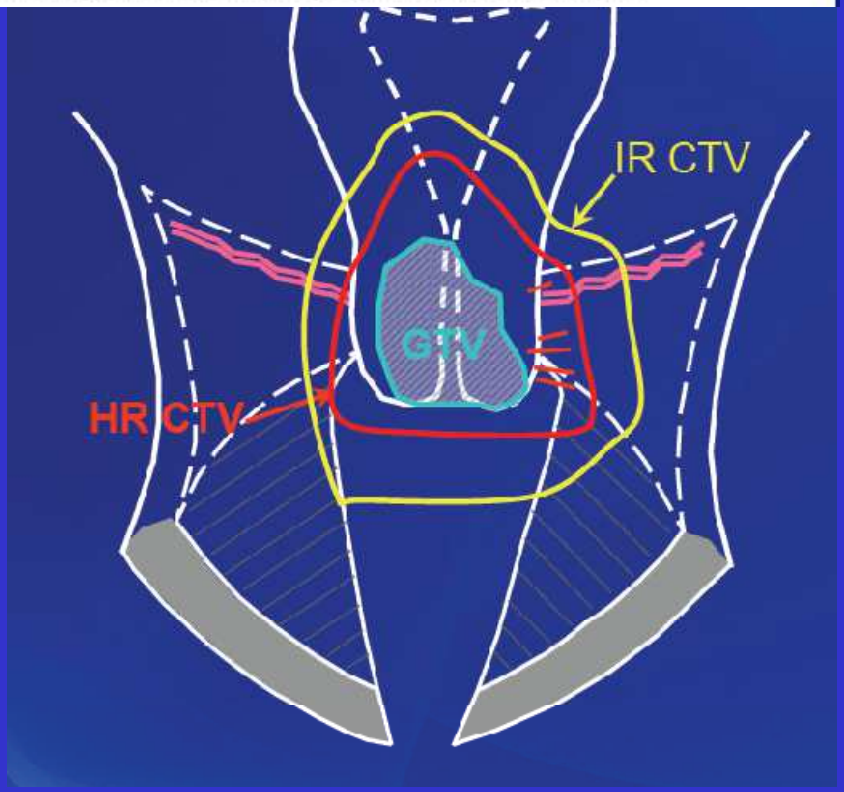
BT 2D



Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

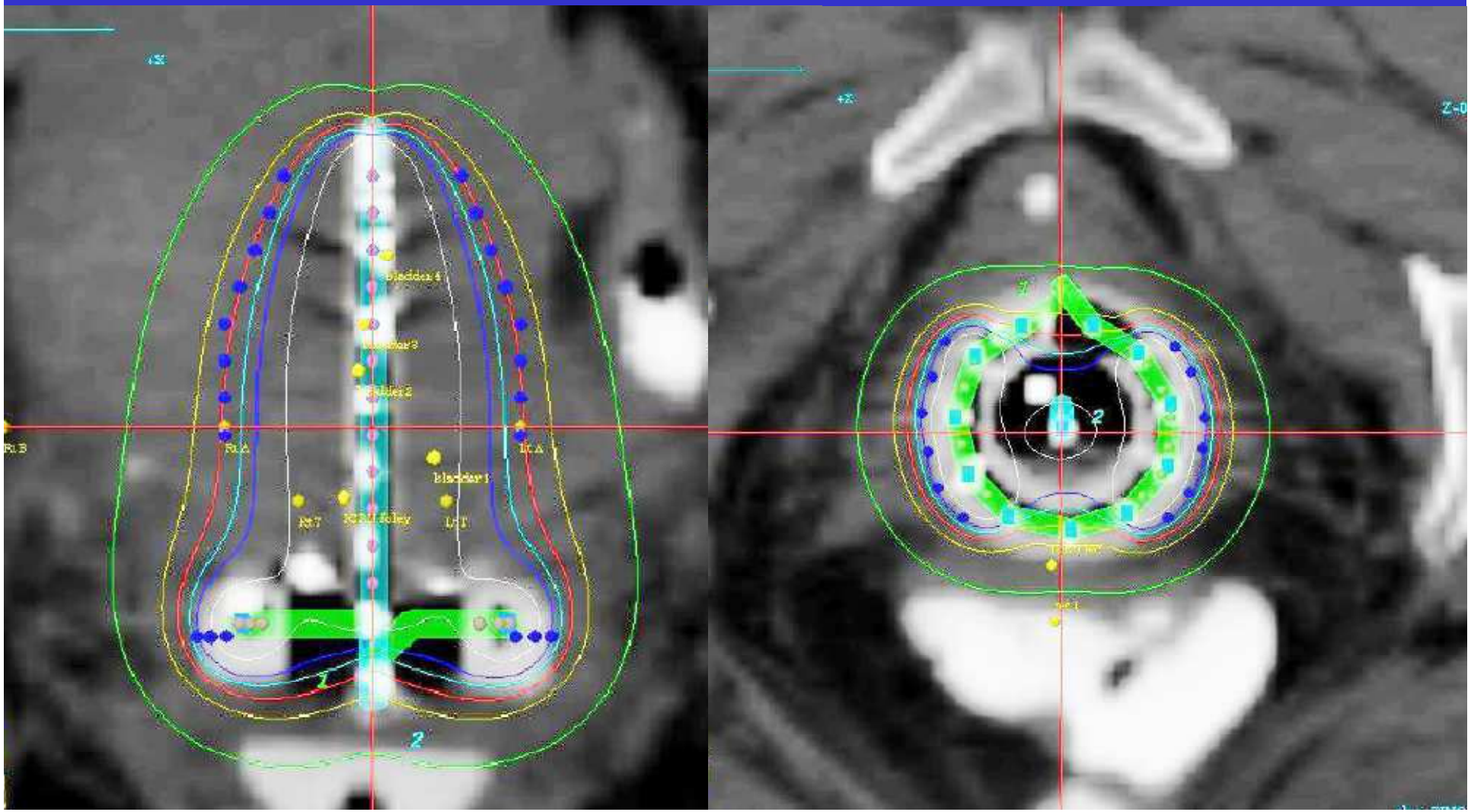
Richard Pötter[a,*], Christine Haie-Meder[b], Erik Van Limbergen[c], Isabelle Barillot[d], Marisol De Brabandere[c], Johannes Dimopoulos[a], Isabelle Dumas[b], Beth Erickson[e], Stefan Lang[a], An Nulens[c], Peter Petrow[f], Jason Rownd[e], Christian Kirisits[a]

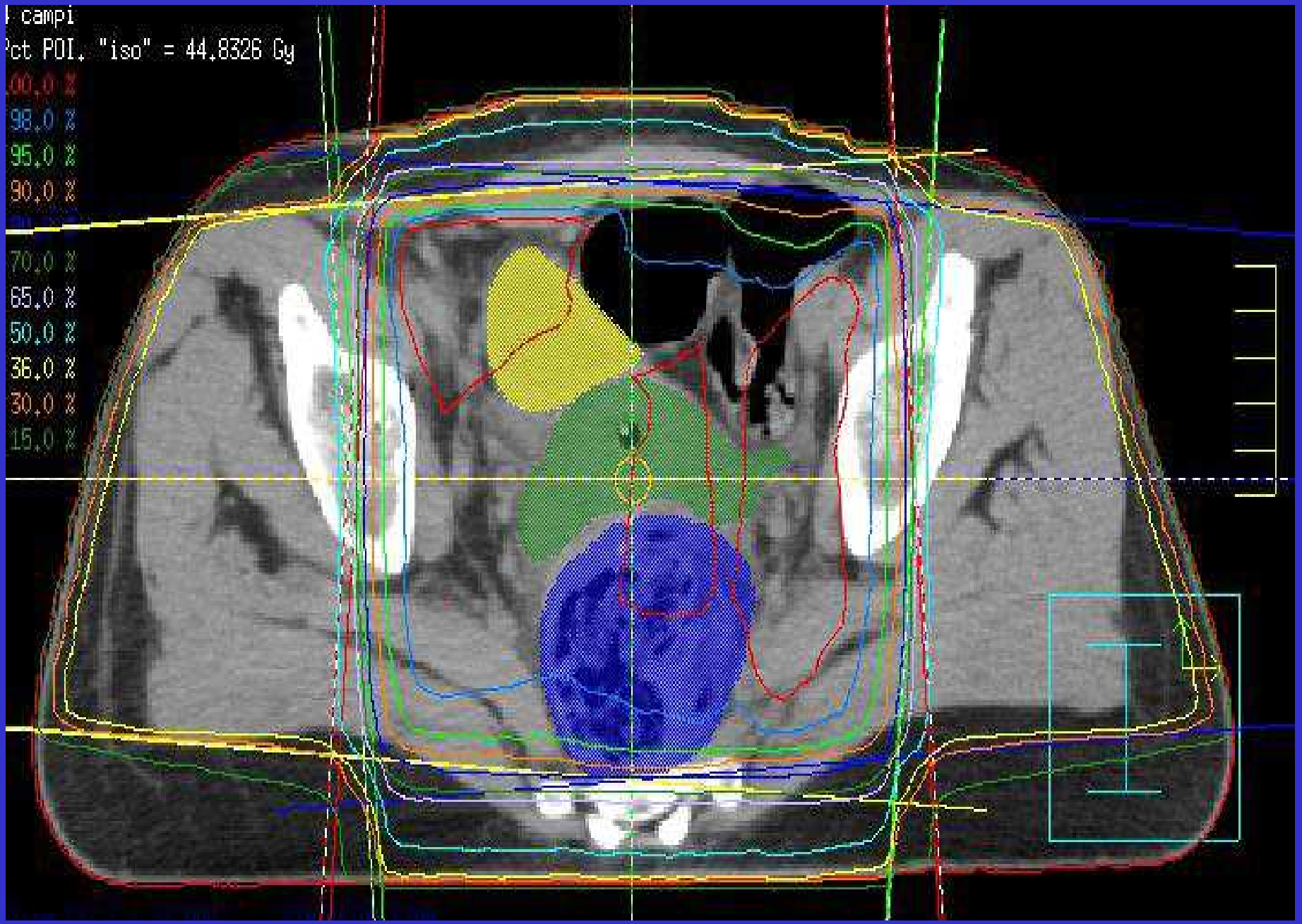




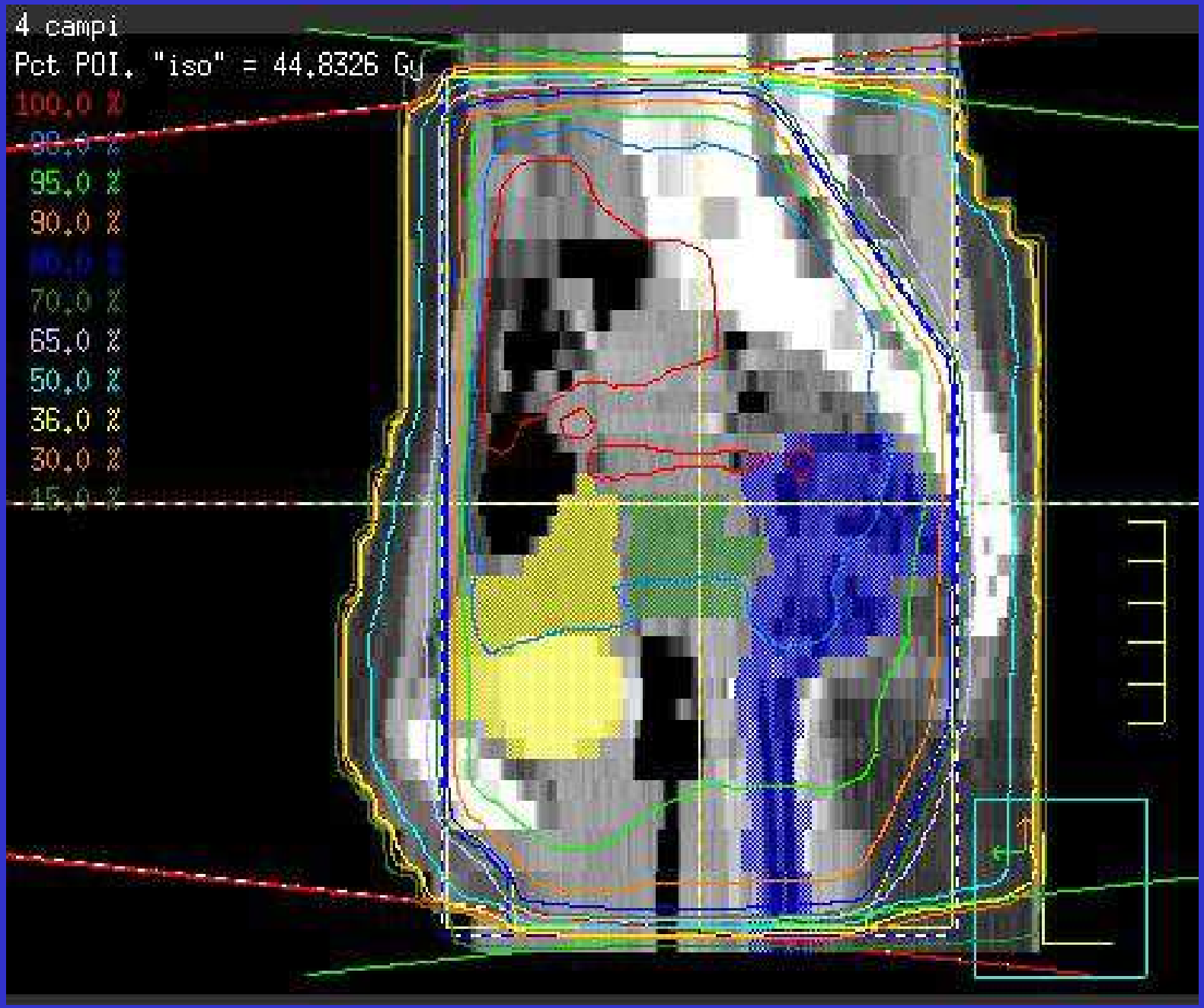
Radiotherapy Oncology 2006:78:67-77

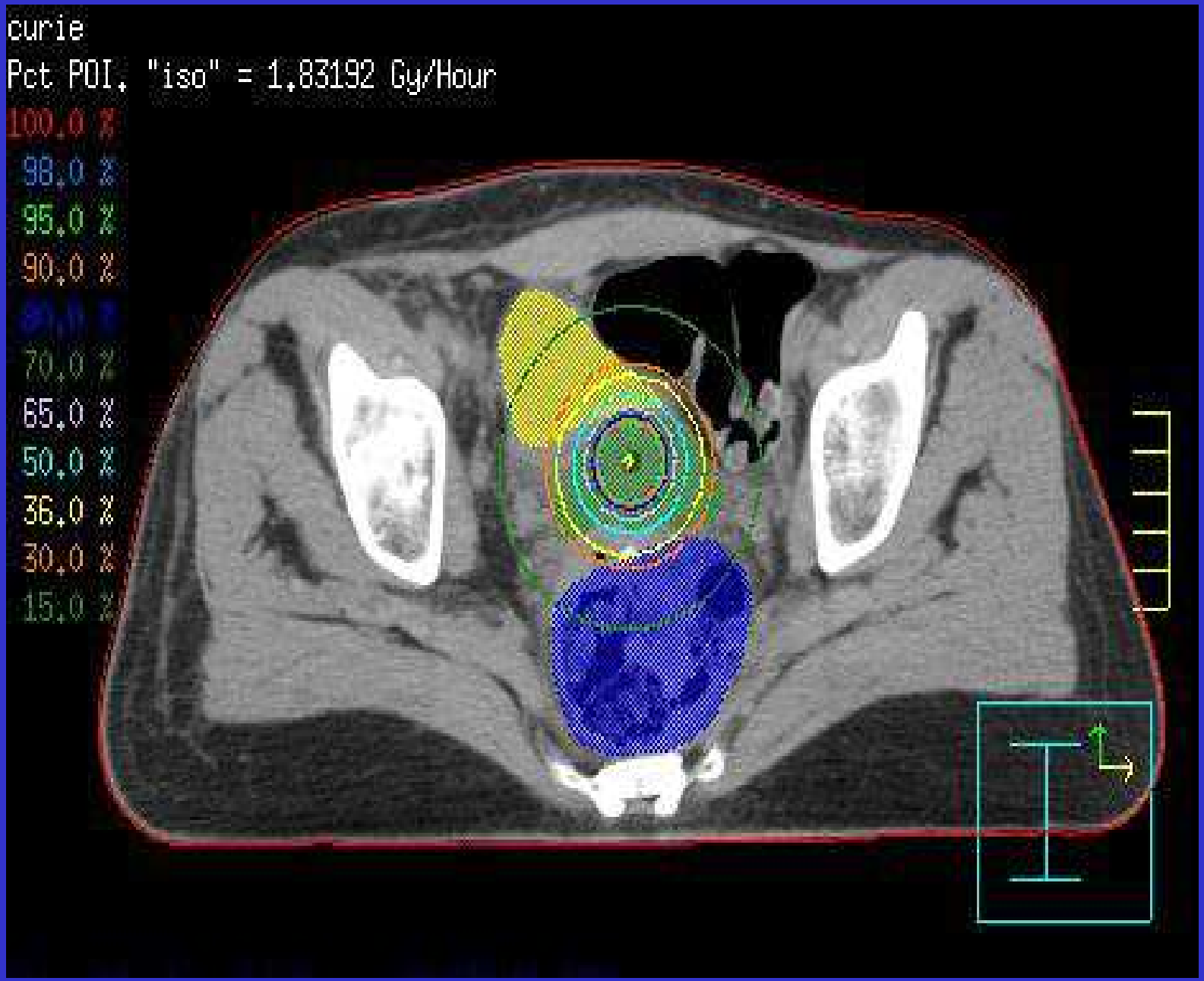
Vari algoritmi di prescrizione e ottimizzazione

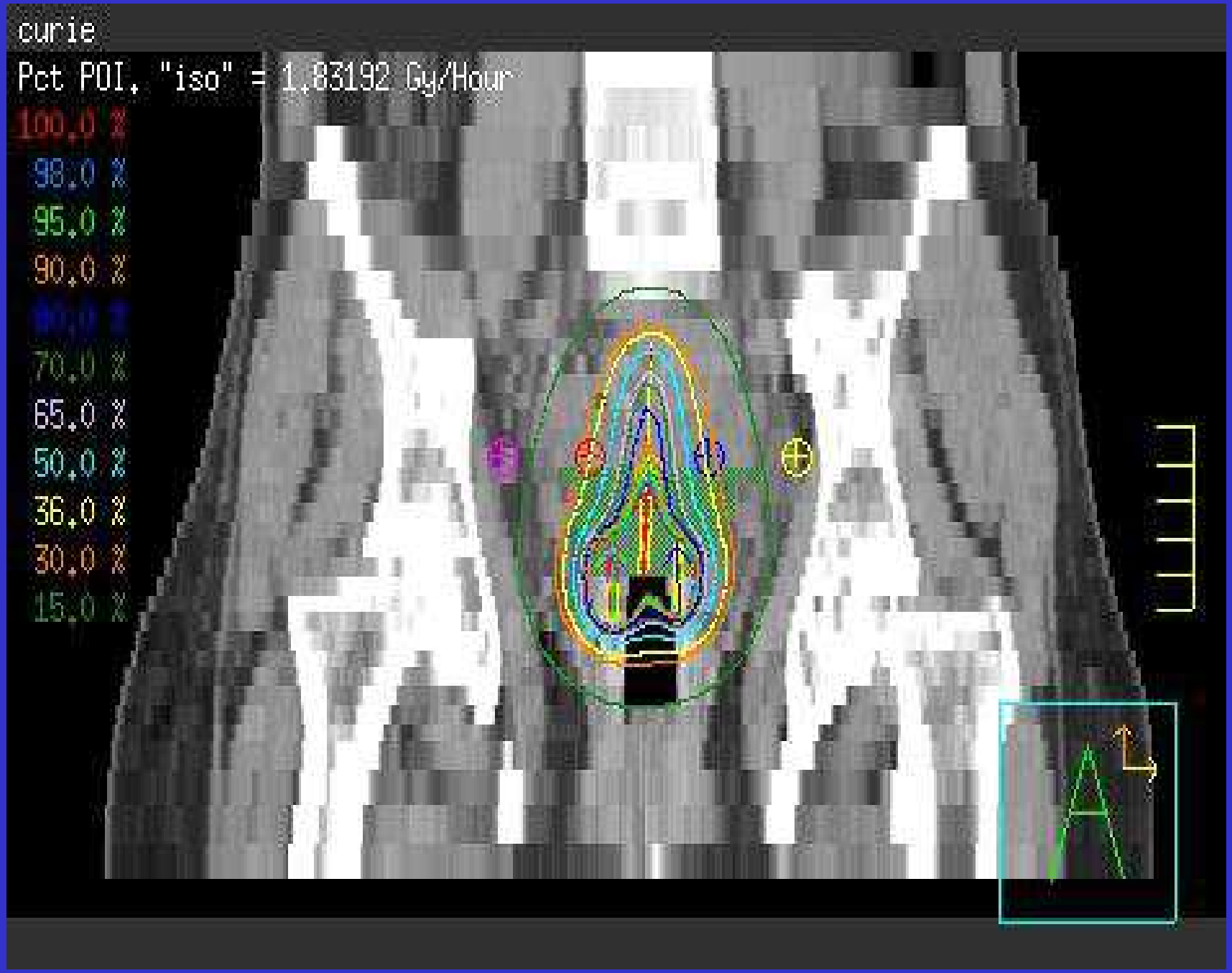


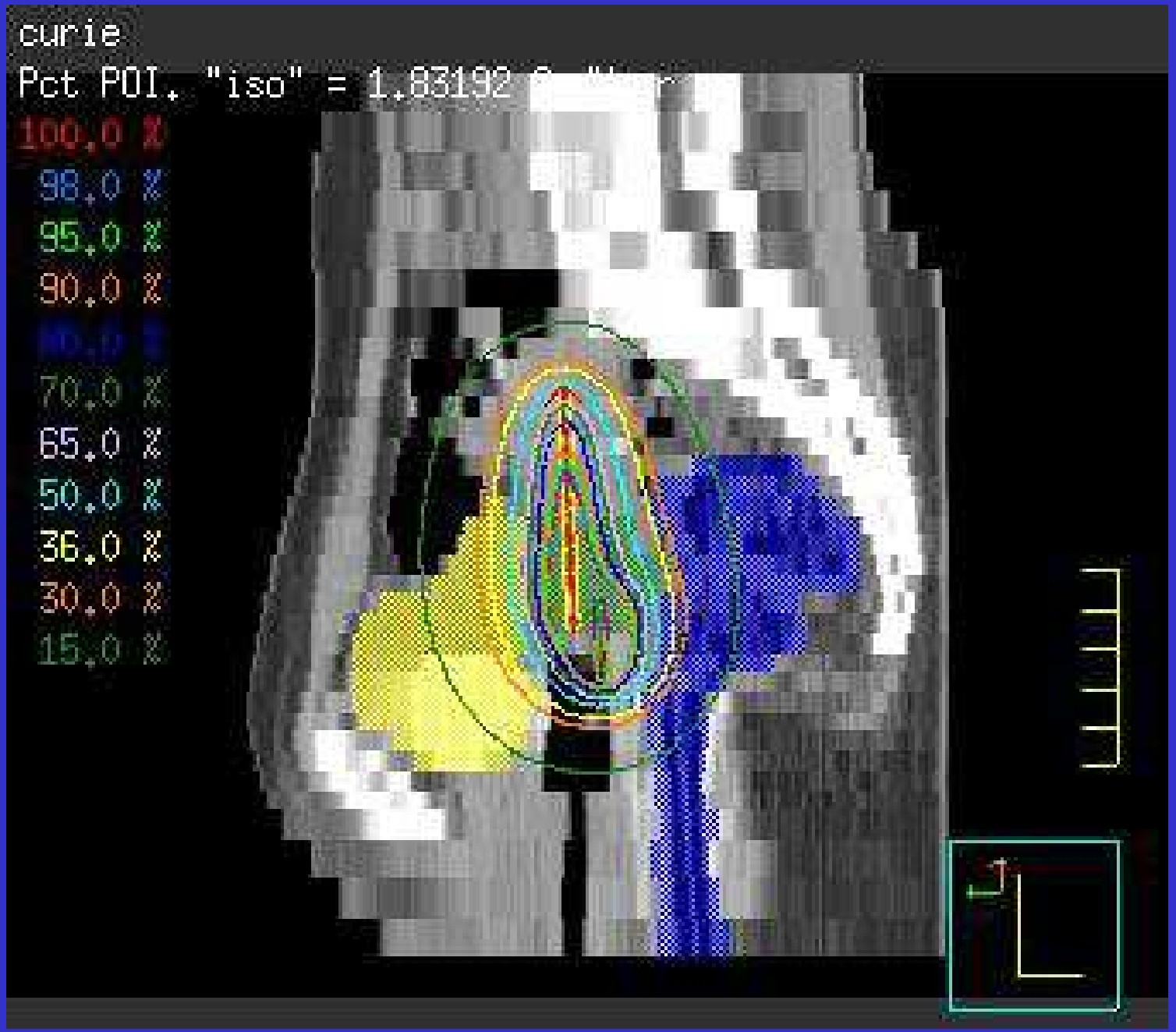

campi
Pct POI, "iso" = 44.8326 Gy
100.0 %
98.0 %
95.0 %
90.0 %
70.0 %
65.0 %
50.0 %
36.0 %
30.0 %
15.0 %

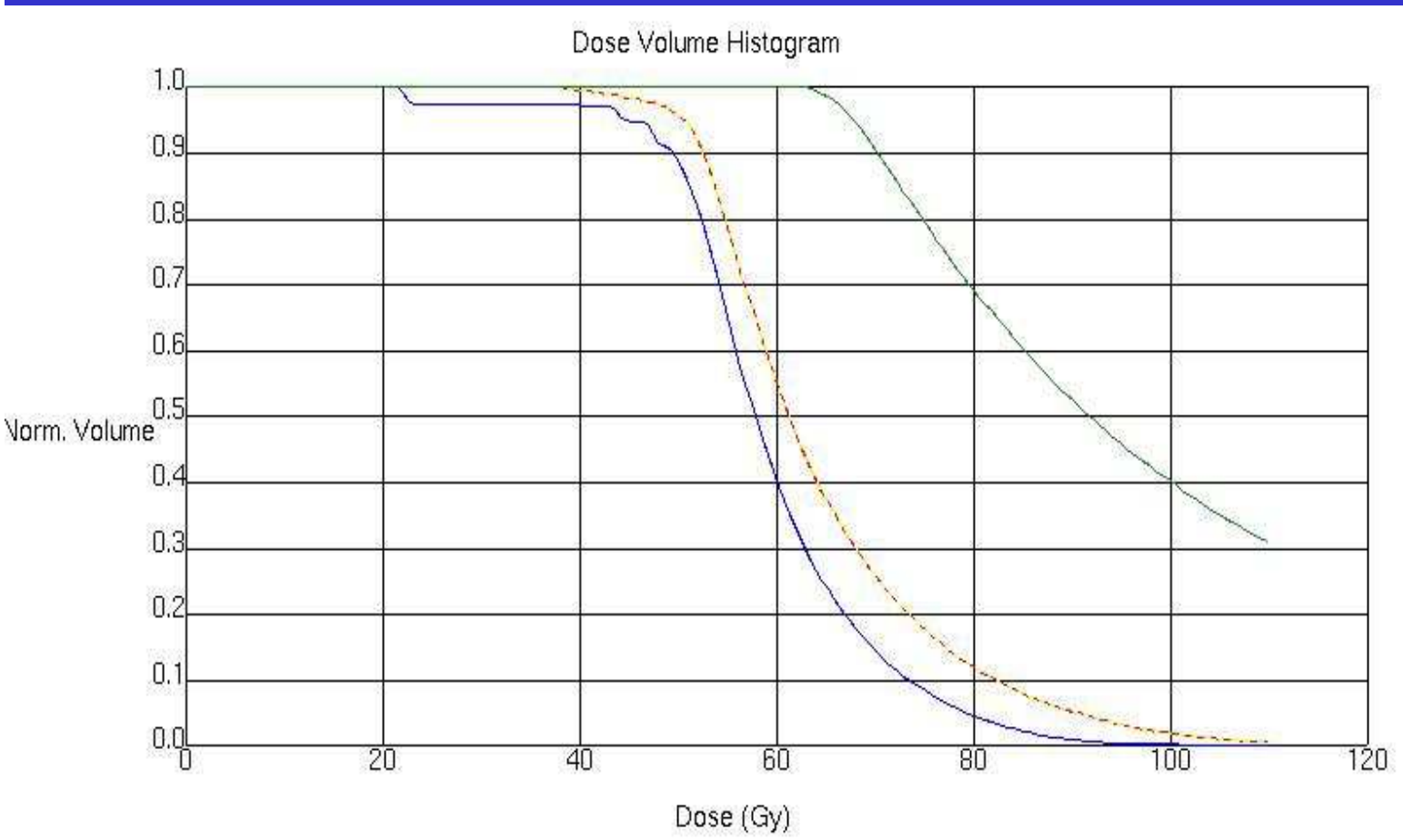

4 campi
Pct POI, "iso" = 44,8326 Gy
100,0 %
95,0 %
90,0 %
70,0 %
65,0 %
50,0 %
36,0 %
30,0 %
15,0 %


4 campi
Pct POI, "iso" = 44,8326 Gy
100,0 %
95,0 %
90,0 %
70,0 %
65,0 %
50,0 %
36,0 %
30,0 %


curie
Pct POI, "iso" = 1.83192 Gy/Hour
100.0 %
98.0 %
95.0 %
90.0 %
70.0 %
65.0 %
50.0 %
36.0 %
30.0 %
15.0 %


curie
Pct POI, "iso" = 1.83192 Gy/Hour
100.0 %
98.0 %
95.0 %
90.0 %
70.0 %
65.0 %
50.0 %
36.0 %
30.0 %
15.0 %


curie
Pct POI, "iso" = 1.83192
100.0 %
98.0 %
95.0 %
90.0 %
70.0 %
65.0 %
50.0 %
36.0 %
30.0 %
15.0 %



DVH Calculation
- Cumulative
- Differential

Dose Axis Display
- Normalized Dose
- Absolute Dose

- Auto-Compute Max
- Specify Max Dose

Max = 110 Gy

Volume Axis Display
- Normalized Volume
- Absolute Volume

Add DVH

Remove Current DVH

Current	Region of Interest	Trial	Beam	Color	Dash Color	% Outside Grid	% > Max	NTCP/TCP
◇	retto	Totale	All Beams/Sources	blue	blue	0.00 %	0.00 %	NTCP = 12%
◇	Vescica	Totale	All Beams/Sources	yellow	red	0.00 %	0.31 %	NTCP = 5%
◆	utero	Totale	All Beams/Sources	forest	No Dash	0.00 %	30.29 %	TCP = 80%

Organi di rispetto nel trattamento radiante della pelvi

- Cute e mucose
- Intestino tenue (dose di tolleranza 40-45 Gy)
- Retto
- Vescica
- Teste femorali

Fattori favorenti la radiotossicità

- Pregressa significativa patologia infiammatoria addominale
- Patologia infiammatoria cronica vescicale e/o intestinale
- Pregressa chirurgia addomino-pelvica maggiore
- Pregressa irradiazione pelvica
- Sclerodermia ed altre collagenopatie in fase attiva
- Obesità
- Diabete
- Vasculopatie

Effetti collaterali acuti da radioterapia pelvica

- Cutanei: eritema, desquamazione secca/umida
- Piccolo e grosso intestino: diarrea, dolori addominali, tenesmo rettale, emorroidi, rettorragia
- Apparato urinario: cistite, cistouretrite
- Apparato genitale: vulvo-vaginite

Effetti collaterali tardivi da radioterapia pelvica

Aumento di probabilità con dosi > 40-50 Gy

- Cutanei: fibrosi, discromie, distrofie e teleangectasie nella zona irradiata, alopecia
- Apparato genitale: menopausa/sterilità, dispareunia, atrofia/secchezza delle mucose, stenosi, fistole vaginali
- Apparato urinario: cistite cronica emorragica
- Piccolo e grosso intestino: malassorbimento, aderenze, ostruzioni, fistole, perforazioni, rettorragia

Correlazione tra effetti collaterali precoci e tardivi da radioterapia

- Pazienti che manifestano tossicità acuta hanno un aumentato rischio di sviluppare tossicità tardiva in particolare a carico dell'apparato genito-urinario e digerente

- Maggiore è il grado di tossicità acuta, maggiore il grado di quella cronica

Fattori che influenzano la tossicità tardiva da radioterapia

- Dose totale (dose di tolleranza dell'organo critico)
- Volume % dell'organo a rischio irradiato (irradiazione totale vs irradiazione parziale)
- Energia utilizzata
- Tecnica di irradiazione
- Combinazione RTE / Brachiterapia
- Ampiezza ed estensione dei campi (stadio avanzato di malattia)
- Precedente chirurgia
- Modelli matematici che permettono di quantificare la probabilità del danno