

Chapter 29

Cervical Cancer

R. Scott Bermudez, Kim Huang, and I-Chow Hsu

PEARLS

- Leading cause of cancer mortality in women in developing countries and third most common gynecological cancer in the US.
- Screening with Pap smear decreases mortality by 70%, accounting for the steady decline in incidence in developed nations.
- ACS recommends screening for all women who are sexually active or >20 years old. Following three normal annual exams after age 30, screening may be performed less frequently, at least once every 3 years.
- Fifty percent of newly diagnosed cancers occur in women who have never been screened.
- Risk factors: early first intercourse, multiple partners, history of other STD's, high parity, smoking, immunosuppression, and prenatal DES exposure (clear cell CA).
- Ninety to ninety-five percent of cases are associated with HPV infection.
- HPV types 16 and 18 confer the highest risk of SCC and adenocarcinoma, respectively. HPV 6 and 11 are associated with benign warts.
- In 2006, the FDA approved the quadrivalent HPV recombinant vaccine for prevention of cancers caused by HPV types 6, 11, 16, and 18 for women aged 9–26 years.
- Eighty to ninety percent of invasive tumors are SCC, 10–20% are adenocarcinoma, and 1–2% are clear cell.
- SCC originates in the squamocolumnar junction with invasive disease frequently associated with adjacent CIS.
- Preinvasive disease: atypical squamous cells of uncertain significance (ASCUS), low-grade squamous intraepithelial lesion (LGSIL), and high-grade squamous intraepithelial lesion (HGSIL).
- ASCUS: 2/3 resolve spontaneously. Repeat Pap in 6 months and, if abnormal, perform colposcopy.

- LGSIL=Mild dysplasia/CIN 1. Half resolve spontaneously. Repeat Pap in 6 months and, if abnormal, perform colposcopy.
- HGSIL=Severe dysplasia / CIN 2/3/CIS. One-third resolve spontaneously. All undergo colposcopy with biopsy.
- The mean age of women diagnosed with cervical intraepithelial neoplasia (CIN) is 15–20 years younger than those diagnosed with invasive disease.
- Prognostic factors include LN metastases, tumor size, stage, uterine extension, and Hgb level <10.
- Risk of pelvic LN involvement for stage I, II, and III disease is approximately 15%, 30%, and 45%, respectively.
- Most common site for metastases are pelvic lymph nodes followed by lungs and paraaortic nodes.

WORKUP

- H&P including gynecologic history, abnormal vaginal bleeding or discharge, and pelvic pain. Examine abdomen, nodes (SCV, groins). Perform pelvic EUA, including bimanual palpation, jointly with a Gynecologic Oncologist.
- Pap smear if not bleeding.
- Colposcopy with 15× magnification, cold conization if no gross lesion noted and cannot visualize entire lesion with colposcope. Alternatively, four quadrant punch biopsies or D&C for pathology.
- Cystoscopy, sigmoidoscopy, and/or barium enema for IIB, III, or IVA disease, or for symptoms.
- Laboratories: CBC, LFTs, chemistries, BUN/Cr, urinalysis.
- Imaging: CT/MRI of abdomen and pelvis and CXR. Consider lymphangiogram and IVP (if no CT).
- PET scans are sensitive (~85–90%) and specific (~95–100%).
- If stage IIIB, place renal stent prior to starting chemo.
- Note: FIGO clinical staging does not allow CT, MRI, bone scan, PET, lymphangiography, or laparotomy.

STAGING: CERVICAL CANCER

Editors' note: All TNM stage and stage groups referred to elsewhere in this chapter reflect the 1988 FIGO/2002 AJCC staging nomenclature unless otherwise noted as the new system below was published after this chapter was written.

(AJCC 6TH ED., 2002/FIGO 1988)**FIGO/AJCC Clinical Staging**

TX:	Primary tumor cannot be assessed
T0:	No evidence of primary tumor
0/Tis:	Carcinoma in situ*
I/T1:	Cervical carcinoma confined to uterus (extension to corpus should be disregarded)
IA/T1a**:	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
IA1/T1a1:	Measured stromal invasion 3 mm or less in depth and 7 mm or less in horizontal spread
IA2/T1a2:	Measured stromal invasion more than 3 mm and not more than 5.0 mm with a horizontal spread 7 mm or less
IB/T1b:	Clinically visible lesion confined to the cervix or microscopic lesion greater than IA2 / T1a
IB1/T1b1:	Clinically visible lesion 4.0 cm or less in greatest dimension
IB2/T1b2:	Clinically visible lesion more than 4.0 cm in greatest dimension
II/T2:	Cervical carcinoma invades beyond uterus, but not to pelvic wall or lower third of vagina
IIA/T2a:	Tumor without parametrial invasion
IIB/T2b:	Tumor with parametrial invasion
IIIA/T3a:	Tumor involves lower third of vagina, no extension to pelvic wall
IIIB/T3b:	Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctioning kidney

(AJCC 7TH ED., 2010/FIGO 2008)

Primary tumor (T)	FIGO Stages
TNM Categories	
TX	
T0	
Tis*	
T1	I
T1a**	IA
T1a1	IA1
T1a2	IA2
T1b	IB
T1b1	IB1
T1b2	IB2

Primary tumor cannot be assessed
 No evidence of primary tumor
 Carcinoma in situ (preinvasive carcinoma)
 Cervical carcinoma confined to uterus (extension to corpus should be disregarded)
 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
 Measured stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread
 Measured stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less
 Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2
 Clinically visible lesion 4.0 cm or less in greatest dimension
 Clinically visible lesion more than 4.0 cm in greatest dimension

continued

IVA/T4:	Tumor invades mucosa of bladder, rectum, and/or extends beyond true pelvis (bullous edema is not sufficient to classify a tumor as T4)
NX:	Regional lymph nodes cannot be assessed
N0:	No regional lymph node metastasis
N1:	Regional pelvic lymph node metastasis
MX:	Distant metastasis cannot be assessed
M0:	No distant metastasis
IVB/M1:	Distant metastasis (including paraaortic and inguinal nodal metastases)

*Bethesda or WHO system is used to further classify
 **All macroscopically visible lesions – even with superficial invasion – are T1b/IB

AJCC stage	~LC	~Survival
0:	TisN0M0	IA: 95–100%
I:	T1N0M0	IB1: 85–90%
IA:	T1aN0M0	IB2: 60–80%
IA1:	T1a1N0M0	IIA: 80–85%
IA2:	T1a2N0M0	IIIB: 60–80%
IB:	T1bN0M0	IIIA: 60%
IB1:	T1b1N0M0	IIIB: 25–50%
IB2:	T1b2N0M0	IVA: 15–30%
II:	T2N0M0	IVB: <10%
IIA:	T2aN0M0	
IIIB:	T2bN0M0	
III:	T3N0M0	
IIIA:	T3aN0M0	
IIIB:	T3b any N M0, T1-T3aN1M0	
IVA:	T4 any N M0	
IVB:	Any T any N M1	

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	IIIB	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.

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

continued

Distant metastasis (M)*TNM**FIGO**Categories**stages*

M0

No distant metastasis

M1

Distant metastasis (including peritoneal spread, involvement of supraclavicular, mediastinal, or paraaortic lymph nodes, lung, liver, or bone)

Anatomic stage/prognostic groups (FIGO 2008)

0*: Tis N0 M0

I: T1 N0 M0

IA: T1a N0 M0

IA1: T1a1 N0 M0

IA2: T1a2 N0 M0

IB: T1b N0 M0

IB1: T1b1 N0 M0

IB2: T1b2 N0 M0

II: T2 N0 M0

IIA: T2a N0 M0

IIA1: T2a1 N0 M0

IIA2: T2a2 N0 M0

IIB: T2b N0 M0

III: T3 N0 M0

IIIA: T3a N0 M0

IIIB: T3b Any N M0

I1-3: T1-3 N1 M0

IVA: T4 Any N M0

IVB: Any T Any N M1

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

Used with the permission from the American Joint Committee on Cancer (AJCC), Chicago, IL. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010), published by Springer Science+Business Media.

SUMMARY OF STAGING CHANGES

- Stage IIA is subdivided into stage IIA1 and IIA2 based on size (≤ 4 vs. >4 cm).
- Microinvasive and invasive adenocarcinoma should be staged as squamous cell carcinoma of the cervix.
- The use of diagnostic imaging techniques to assess the size of the primary tumor is encouraged, but not mandatory.
- For those institutions with access to MRI/CT scanning, radiological tumor volume and parametrial invasion should be recorded and sent to the FIGO Annual Report Editorial Office for data entry and inclusion in the Annual Report. Other investigations (i.e., examination under anesthesia, cystoscopy, sigmoidoscopy, and intravenous pyelography) are optional and no longer mandatory.

~LOCAL CONTROL AND SURVIVAL BY STAGE

~LC	~Survival
IA: 95–100%	IA: 95–100%
IB1: 90–95%	IB1: 85–90%
IB2: 60–80%	IB2: 60–70%
IIA: 80–85%	IIA: 75%
IIB: 60–80%	IIB: 60–65%
IIIA: 60%	IIIA: 25–50%
IIIB: 50–60%	IIIB: 25–50%
IVA: 30%	IVA: 15–30%
	IVB: <10%

TREATMENT RECOMMENDATIONS**SURGICAL TECHNIQUES**

- Class I: total abdominal hysterectomy (extrafascial). Removal of cervix, small rim of vaginal cuff, and outside of the pubocervical fascia.
- Class II: modified radical hysterectomy (extended). Unroofing of ureters to resect parametrial and paracervical tissue medial to ureters (cardinal and uterosacral ligaments) and vaginal cuff (1–2 cm).
- Class III: radical abdominal hysterectomy (Wertheim-Meigs). Mobilization of ureters, bladder, and rectum to remove parametrial tissue to pelvic sidewall and vaginal cuff (upper 1/3–1/2), and lymphadenectomy.
- Class IV: extended radical hysterectomy. Removal of superior vesicular artery, part of ureter and bladder, and more vaginal cuff.

INDICATIONS FOR POST-OP RT/CHEMO-RT.

- Post-op pelvic RT: LVSI, >1/3 stromal invasion, or >4 cm tumor.
- Post-op chemo-RT: +margin, +LN, or parametrial or greater extension.

2002 Stage	Recommended treatment
Preinvasive	■ Conization or loop electrosurgical excisional procedure (LEEP) or laser or cryotherapy ablation or simple hysterectomy
IA	<ul style="list-style-type: none"> ■ Total abdominal hysterectomy or trachelectomy or large cone biopsy with negative margins and close follow-up (if fertility preservation desired). Radical hysterectomy preferred for IA2 lesions OR ■ Brachytherapy alone (LDR 65–75 Gy or HDR 7 Gy×5–6 fx). If high-risk pathologic features, treat as IB
IB1	<ul style="list-style-type: none"> ■ Radical hysterectomy with pelvic LN dissection OR ■ Definitive RT: EBRT to WP (45 Gy) and brachytherapy (HDR 6 Gy×5 fx, 7 Gy×4 fx or LDR 15–20 Gy×2 fx)
IB2–IIA	■ Concurrent chemo-RT with cisplatin. WP RT (45 Gy). Brachytherapy=HDR 6 Gy×5 fx, 7 Gy×4 fx or LDR 15–20 Gy×2 fx
IIB	■ Concurrent chemo-RT with cisplatin. WP RT (45–50.4 Gy). Brachytherapy=HDR 6 Gy×5 fx, 7 Gy×4 fx or LDR 15–20 Gy×2 fx
IIIA	■ Concurrent chemo-RT with cisplatin. RT to WP, vagina, and inguinal LN (45 Gy–50.4 Gy). Brachytherapy=HDR 6 Gy×5 fx, 7 Gy×4 fx or LDR 17–20 Gy×2 fx
IIIB–IVA	■ Concurrent chemo-RT with cisplatin. WP RT (50–54 Gy). Brachytherapy=HDR 6 Gy×5, 7 Gy×4 fx or LDR 20 Gy×2. If LN+, add paraaortic LN IMRT (45–60 Gy)
IVB	■ Combination chemotherapy

STUDIES

SURGERY VS. RADIATION

- Landoni et al. (1997): 343 patients with IB–IIA randomized to RT vs. surgery ± RT. Surgery was radical hysterectomy + pelvic LND with optional adjuvant RT to 50.4 Gy for stage > IIA, < 3 mm uninvolved cervix, +margin or LN+. Forty-five Gy given to +PAN. Sixty-three percent of patients in surgery arm received adjuvant RT, including 83% with tumors > 4 cm. RT alone arm was 47 Gy EBRT + LDR 76 Gy point A dose. No significant differences in 5-year OS (83%), DFS (74%), or recurrence (25%). Morbidity worse with surgery ± RT arm vs. RT alone arm (28 vs. 12%).

EXTENDED-FIELD RT (EFRT)

- *RTOG 79-20* (Rotman et al., 1995, 2006): 337 patients with IIB without clinical or radiographically involved PAN randomized to WP 45 Gy or EFRT 45 Gy. EFRT improved 10-year OS (55 vs. 44%), but no difference on LRC (65%) or DM (25–30%). Toxicity increased with EFRT (8 vs. 4%).

CHEMO-RT

- *RTOG 90-01* (Morris et al., 1999; Eifel et al., 2004): 386 patients with surgically staged IIB–IVA, IB–IIA ≥ 5 cm, or LN + randomized to EFRT + brachytherapy (total 85 Gy point A dose) or to WPRT + brachytherapy (total 85 Gy point A dose) + cisplatin/5FU. Chemo-RT improved 8-year OS (67 vs. 41%), DFS (61 vs. 46%), and decreased LRF (18 vs. 35%) and DM (20 vs. 35%). Chemo-RT had a nonsignificant increase in PAN failures (8 vs. 4).
- *GOG 120* (Rose et al., 1999, 2007): 526 patients with IIB–IVA (surgically staged -PAN) randomized to WP + LDR brachytherapy (total 81 Gy point A dose) + 3 different chemo regimens: weekly cisplatin vs. cisplatin/5FU/hydroxyurea vs. hydroxyurea alone. Cisplatin arms decreased stage IIB and III 10-year LR (21–22 vs. 34%) and improved PFS (43–46 vs. 26%), OS (53 vs. 34%). No difference in grade 3–4 late toxicities among three regimens.
- *NCIC* (Pearcey et al., 2002): 353 patients with IA, IIA > 5 cm, or IIB randomized to WP45 Gy + LDR 35 Gy × 1 or HDR 8 Gy × 3 vs. same RT + weekly cisplatin 40 mg/m² × 6. No difference in 5-year OS (62 vs. 58%).
- *GOG 123* (Stehman et al., 2007; Keys et al., 1999): 369 patients with IB2 randomized to WP + LDR RT (total 75 Gy to point A) followed by adjuvant simple hysterectomy vs. same RT + concurrent weekly cisplatin (40 mg/m²) × 6c followed by same surgery. Chemo-RT improved 5-year PFS (71 vs. 60%) and OS (78 vs. 64%), without increasing serious late adverse effects.

- *GOG 165* (Lanciano et al., 2005): 316 patients with IIB, IIIB, and IVA randomized to WP 45 Gy+parametrial boost+IC brachytherapy with standard weekly cisplatin (40 mg/m²) vs. same RT with six cycles protracted venous infusion (PVI) 5-FU. Study closed prematurely when planned interim analysis demonstrated a 35% higher distant failure rate with RT+PVI 5-FU.

ADJUVANT HYSTERECTOMY AFTER RT

- *GOG 71* (Keys, 1997, 2003): 282 patients with >4 cm tumors randomized to EBRT+brachytherapy (80 Gy point A dose) vs. same RT (except 75 Gy point A dose) followed by adjuvant hysterectomy. No difference in OS (61 vs. 64%), but trend for higher LR without surgery (26 vs. 14%, $p=0.08$).

POST-OP RT

- *GOG 92 / RTOG 87-06* (Rotman et al., 2006; Sedlis et al., 1999): 277 patients with bulky IB treated with radical hysterectomy with negative margins and LNs, but with ≥ 2 risk factors (LVSI, >1/3 stromal invasion, or ≥ 4 cm tumors) randomized to observation vs. post-op WP RT (46–50.4 Gy). Post-op RT reduced local and distant recurrences (31→18%), and improved PFS (65→78%).

POST-OP CHEMO-RT

- *GOG 109/SWOG 8797* (Peters et al., 2000): 243 patients s/p radical hysterectomy with IA2, IB, IIA, and +LN or +margin or +parametria randomized to WP RT (49.3 Gy with 45 Gy to PAN if common iliac LN+) vs. WP RT+cisplatin/5FU every 3 weeks $\times 4$ c. Post-op chemo-RT improved 4-year PFS (80 vs. 63%) and OS (81 vs. 71%). Re-analysis demonstrated that chemo-RT decreased LR by 50% and DM by 30%. Approximately 20% OS benefit from chemo for tumors >2 cm and patients with ≥ 2 +LN.

RADIATION TECHNIQUES

EBRT SIMULATION AND FIELD DESIGN

- Place two radiopaque gold seed markers in cervix and at distal margin of any vaginal disease. Use vaginal and anal markers as needed.
- There is no standard pelvic EBRT field. Blocking should be based on 3D imaging when treating with four field or AP/PA technique.
- Simulate patient supine with CT planning. Borders: superior=L4/5; inferior=3 cm below most inferior vaginal involvement as marked by gold seeds (often at inferior obturator

foramen); lateral = 2 cm lateral to pelvic brim; posterior = include entire sacrum; anterior = 1 cm anterior to pubic symphysis.

- Treat inguinal nodes if stage IIIA (lower 1/3 vagina). Inferior border is vaginal introitus or flash.
- If common iliac nodes involved, raise superior border to allow for at least a 4 cm margin (~L3/4 level).
- EFRT for paraaortic nodes: superior border = T12/L1, lateral = encompass tips of transverse processes. Block kidneys as determined by CT planning. Use IMRT to minimize dose to kidneys and small bowel.
- When used, midline block is to avoid excess dose adjacent to the implant and to deliver higher dose to potential tumor bearing regions outside the implant. Midline block reduces dose to bladder and rectum, but may underdose sacrum. Since T&O has 100% dose through point A, which is ~2 cm from midline, a 4 cm midline block would be at the 100% IDL. Superior border of midline block = midsacroiliac joint. If concerned about toxicity, use a wider midline block (6 cm, ~50% IDL), or if concerned about tumor dose, use a narrower block. Midline blocks narrower than 5 cm may include the ureters which are ~2–2.5 cm from midline.
- At some institutions, it is preferred to deliver higher EBRT doses with a midline block for advanced lesions. After 45 Gy to the WP, the superior border may be lowered to the midsacroiliac joint and EBRT continued to 50 Gy. At 50 Gy, the superior border is further lowered to the bottom of the sacroiliac joint and treated to 54 Gy. If parametrial tumor persists after 50–54 Gy, it may boost parametria to 60 Gy.
- If bulky Unresectable LN+, use 3DCRT or IMRT boost to 60 Gy to involved nodes.

BRACHYTHERAPY

- If possible, proceed when tumor <4 cm (so point A dose covers) without prolonging overall treatment time.
- Unless greater shrinkage is needed, first intracavitary insertion is after 10–20 Gy EBRT. Second application is 1–2 weeks later. Smitt sleeve may be left in cervical canal between insertions.
- If small lesion and narrow vagina, treat first with IC RT before EBRT causes vaginal narrowing.
- If large lesion and narrow vagina, use EBRT first to shrink the tumor.
- If superficial vaginal involvement, use a combination of a T&O applicator alternating with a tandem and vaginal cylinder appli-

cator (with packing to spare rectum or bladder). Alternatively, use two tandem and vaginal cylinder insertions.

- For deep or thicker vaginal involvement, use IS brachytherapy.
- Use gauze packing imbedded with radiopaque wire to push bladder and rectum away. Always Use Triple-Sulfate soaked gauze for LDR and K-Y Jelly for HDR.
- LDR is generally Cs-137 at 0.4–0.8 Gy/h. 0.4–0.6 Gy/h may have less complications than 0.8– Gy/h.
- HDR is generally an Ir-192 high activity (~10 Ci) source with dose rate ~12 Gy/h.
- ICRU system: report applicator type, source type, loading, and orthogonal radiographs. Use reference air-kerma strength, volume treated to 60 Gy.
- Prescribe to point A=2 cm superior to external cervical OS (or vaginal fornices) and 2 cm lateral to central canal / tandem. Point A dose is very sensitive to ovoid position relative to the tandem.
- Point B=3 cm lateral to point A, represents parametrial (obturator nodes). Receives ~1/3–1/4 of dose to point A.
- Bladder point=posterior surface of foley balloon on lateral X-ray and center of balloon on AP film. Foley balloon filled with 7 cm³ radiopaque fluid and pulled down against urethra.
- Rectal point=5 mm behind posterior vaginal wall between ovoids at inferior point of last intrauterine tandem source, or midvaginal source.
- Vaginal point=lateral edge of ovoid on AP film and midovoid on lateral film.
- Tandem placement: use a looping suture through the cervix for countertraction. Hegar uterine dilators are used to dilate the os to 6 mm. Tandem length is usually 6–8 cm (4 cm for postmenopausal women). For tandems >8 cm, avoid loading/active source at end to protect small bowel. Tandem should be located centrally between the ovoids on the AP view and bisect the ovoids on the lateral view.
- Typical tandem loading with Cs-137 = 30–40 mgRaEq with three 10–15 mgRaEq sources (e.g., 15-15-10 cephalad to caudad).
- Ovoids: cervix should be marked with 2 gold seeds (usually at 12 and 6 o'clock). Use largest ovoids possible separated by 0.5–1 cm. Standard ovoid loadings = 10–15 mgRaEq for 2 cm (small) ovoids, 15–20 mgRaEq for 2.5 cm (medium) ovoids, or 5–10 mgRaEq for miniovoids.
- Pack anteriorly and posteriorly to spare the bladder and rectum.
- Take plain films in the OR so that system may be repositioned and/or repacked if suboptimal.
- Implant evaluation:

- Anterior film: tandem bisects ovoids and tandem not rotated; phlange close to cervical marker seeds; ovoids high in fornices <1 cm from marker seeds with 0.5–1 cm spacing between them.
- Lateral film: tandem bisects ovoids and is midway between sacrum and bladder, at least 3 cm from sacral promontory; sufficient anterior and posterior packing; foley balloon firmly pulled down.
- With optimally placed system, LDR dose rate at point A is ~45–55 cGy/h.
- Attempt to keep overall treatment time <7 weeks; prolongation of treatment time increases failure rate by 0.6%/d in IB–IIA and by 0.9%/d in IIB.
- Image-guided brachytherapy requires modification of dwell time based on 3D images. Treatment delivery is accomplished by HDR and PDR remote afterloaders. Recommendations regarding 3D MRI/CT image-guided brachytherapy treatment planning have been published by the GEC-ESTRO Working Group (Pötter et al., 2006; Haie-Meder et al., 2005).

DOSE PRESCRIPTIONS

- EBRT: 1.8 Gy/fx. Whole pelvis = 45 Gy. Side wall boost = 50–54 Gy. Persistent or bulky parametrial tumor = 60 Gy. Paraaortic LN (if treated) = 45 Gy. Bulky LN = 60 Gy
- Brachytherapy
 - LDR = 15–20 Gy × 2 fx
 - HDR = 6 Gy × 5 fx or 7 Gy × 4 fx
- Desired cumulative doses
 - Point A: IA = 65–75 Gy, IB1–IIB 75–85 Gy, III–IVA 85–90 Gy
 - Sidewall dose: IB–IIA = 45–50 Gy, IIB = 45–54 Gy, III–IVA = 54–60 Gy

DOSE LIMITATIONS

- HDR: limit bladder and rectal points to <70% of point A dose with HDR.
- LDR: limit rectal point <70 Gy and bladder point <75 Gy.
- Limit upper vaginal mucosa <120 Gy, midvaginal mucosa <80–90 Gy, and lower vaginal mucosa <60–70 Gy. Vaginal doses >50–60 Gy cause significant fibrosis and stenosis.
- Ovarian failure with 5–10 Gy and sterilization with 2–3 Gy.
- Limit uterus <100 Gy, ureters <75 Gy, and femoral heads <50 Gy.

COMPLICATIONS

- Acute: pruritis, dry/moist desquamation, nausea, colitis, cystitis, and vaginitis.
- HDR and LDR morbidity are equivalent: uterine perforation (<3%), vaginal laceration (<1%), DVT (<1%).
- Late: vaginal stenosis, ureteral stricture (1–3%), vesicovaginal or rectovaginal fistula (<2%), intestinal obstruction or perforation (<5%), femoral neck fracture (<5%).
- Recommend vaginal dilation as needed to maintain vaginal vault size and sexual function.
- Standard post-op complications. Surgical mortality 1%.

FOLLOW-UP

- H&P every month for 3 months, then every 3 months for 9 months, then every 4 months for 1 year, then every 6 months for 2 years, then annually.
- Follow-up Pap smears controversial due to post-RT change.
- CXR annually × 5 years.

REFERENCES

- Eifel PJ, Winter K, Morris M, et al. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: an update of radiation therapy oncology group trial (RTOG) 90-01. *J Clin Oncol* 2004;22:872-880.
- Haie-Meder C, Pötter R, Van Limbergen E, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother Oncol* 2005;74(3):235-245.
- Keys HM, Bundy BN, Stehman FB, et al. Adjuvant hysterectomy after radiation therapy reduces detection of local recurrences in “bulky” stage IB cervical without improving survival: results of a prospective randomized GOG trial. *Cancer J Sci Am* 1997;3:117(abstr).
- Keys HM, Bundy BN, Stehman FB, et al. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *N Engl J Med* 1999;340:1154-1161.
- Keys HM, Bundy BN, Stehman FB, et al. Radiation therapy with and without extrafascial hysterectomy for bulky stage IB cervical carcinoma: a randomized trial of the Gynecologic Oncology Group. *Gynecol Oncol* 2003;89:343-353.
- Lanciano R, Calkins A, Bundy BN, et al. Randomized comparison of weekly cisplatin or protracted venous infusion of fluorouracil in combination with pelvic radiation in advanced cervix cancer: a Gynecologic Oncology Group study. *J Clin Oncol* 2005;23:8289-8295.
- Landoni F, Manco A, Colombo A, et al. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. *Lancet* 1997;350:535-540.
- 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.
- Pearcey R, Brundage M, Drouin P, et al. Phase III trial comparing radical radiotherapy with and without cisplatin chemotherapy in patients with advanced squamous cell cancer of the cervix. *J Clin Oncol* 2002;20:966-972.
- Peters WA III, Liu PY, Barrett RJ II, 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.

- Pötter R, Haie-Meder C, Van Limbergen E, et al. 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. *Radiother Oncol* 2006;78(1):67-77.
- Rose PG, Ali S, Watkins E, et al. Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group study. *J Clin Oncol* 2007;25:2804-2810.
- 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.
- Rotman M, Sedlis A, Piedmonte MR, et al. 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. *Int J Radiat Oncol Biol Phys* 2006;65:169-176.
- Rotman M, Pajak TF, Choi K, et al. Prophylactic extended-field irradiation of para-aortic lymph nodes in stages IIB and bulky IB and IIA cervical carcinomas. Ten-year treatment results of RTOG 79-20. *JAMA* 1995;274:387-393.
- Sedlis A, Bundy BN, Rotman MZ, et al. A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study. *Gynecol Oncol* 1999;73:177-183.
- Stehman FB, Ali S, Keys HM, et al. Radiation therapy with or without weekly cisplatin for bulky stage IB cervical carcinoma: follow-up of a Gynecologic Oncology Group trial. *Am J Obstet Gynecol* 2007;197(5):503.e1-6.

FURTHER READING

- Greene FL, American Joint Committee on Cancer, American Cancer Society. *AJCC cancer staging manual*. 6th ed. New York: Springer; 2002.
- Koh W, Moore DH. Cervical Cancer. In: Gunderson LL, Tepper JE, et al., editors. *Clinical radiation oncology*. 2nd ed. Philadelphia: Churchill Livingstone; 2007. pp. 1323-1357.
- National Comprehensive Cancer Network. *Clinical Practice Guidelines in Oncology: Cervical Cancers*. Available at: http://www.nccn.org/professionals/physician_gls/PDF/cervical.pdf. Accessed on May 28 2009.
- Perez CA, Kavanagh BD. Uterine Cervix. In: Halperin CE, Perez CA, Brady LW, et al., editors. *Principles and practice of radiation oncology*. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2008. pp. 1532-1609.
- Swift PS, Hsu IC. Cancer of the Uterine Cervix. In: Leibel SA, Phillips TL, editors. *Textbook of radiation oncology*. 2nd ed. Philadelphia: Saunders; 2004. pp. 1055-1100.