# Provincial Cervical Cancer Treatment Guidelines

Approved at the Provincial Gyne-Oncology Guideline Meeting
January 11, 2013

Clinical practice guidelines have been developed after multi-disciplinary consensus based on best available literature. As the name suggests, these are to be used as a guide only. These guidelines do not replace physician judgment which is based on multiple factors including, but not limited to, the clinical and social scenario, comorbidities, performance status, age, available resources and funding considerations. The Saskatchewan Cancer Agency disclaims all liability for the use of guidelines except as expressly permitted by the Agency. No portion of these guidelines may be copied, displayed for redistribution to third parties for commercial purposes or any non-permitted use without the prior written permission from the Agency.

Recommendations for drug treatment presented in the Cancer Agency guidelines for a cancer site may not reflect provincial cancer drug funding. Please refer to the current Saskatchewan Cancer Agency drug formulary at www.saskcancer.ca for information on cancer drug listing and funding.

Benefits and risk of the proposed should be discussed with patient.

Participating in clinical trials is encouraged when available. Involvement of a multidisciplinary team is strongly recommended.

**Screening.**
Screening can prevent cervical cancer by finding abnormal cell changes that can be treated at an early stage before cancer develops and is strongly advised. Please refer to Prevention Program for Cervical Cancer at www.saskcancer.ca.

**Referral:**
All patients with a positive diagnosis should be referred to a gyne-oncologist, with all physical pertinent information provided, for discussion at multi-disciplinary tumour board rounds who will triage patient for further management.

**Diagnosis and Work-up:**
- History and clinical examination, including pelvic examination
- Cervical biopsy; pathology review should be performed by a pathologist with experience in gynecologic pathology. Cone biopsy as indicated
- Blood work (CBC, LFT, renal function studies)
- Examination under anesthesia (EUA), cystoscopy/proctoscopy if necessary
  Imaging (optional for ≤ stage IB1) can include: MRI pelvis, CT abdomen; chest x-ray; CT/PET optional
- PET scan is suggested for patients with FIGO IIB-IVA and/or pelvic /paraortic lymphadenopathy suspicious for metastases.

**Staging:**
The Féderation Internationale de Gynécologie et d'Obstétrique (FIGO)

| **Stage** | |
|---|---|
| I (T1) | The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded). |
| IA (T1a) | Invasive carcinoma, which can be diagnosed only by microscopy with deepest invasion ≤5 mm and largest extension ≥7 mm. |
| IA1 (T1a1) | Measured stromal invasion of ≤3.0 mm in depth and extension of ≤7.0 mm. |
| IA2 (T1a2) | Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm. |
| IB (T1b) | Clinically visible lesions limited to the cervix uteri or preclinical cancers greater than stage IA.[b] |
| IB1 (T1b1) | Clinically visible lesion ≤4.0 cm in greatest dimension. |
| IB2 (T1b2) | Clinically visible lesion >4.0 cm in greatest dimension. |
| II (T2) | Cervical carcinoma invades beyond the uterus but not to the pelvic wall or to the lower third of the vagina. |
| IIA (T2a) | Without parametrial invasion. |
| IIA1 (T2a1) | Clinically visible lesion ≤4.0 cm in greatest dimension. |
| IIA2 (T2a2) | Clinically visible lesion >4.0 cm in greatest dimension. |
| IIB (T2b) | With obvious parametrial invasion. |
| III (T3) | The tumour extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydronephrosis or nonfunctioning kidney.[c] |
| IIIA (T3a) | Tumour involves lower third of the vagina with no extension to the pelvic wall. |
| IIIB (T3b) | Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney. |
| IV (T4) | The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV. |
| IVA (T4) | Spread of the growth to adjacent organs. |
| IVB (M1) | Spread to distant organs. |

**Management of Invasive Carcinoma of Cervix:**

## FIGO IA1

- Conization with free margins for cancer without LVI
- Trachelectomy
- Simple hysterectomy
- Modified radical hysterectomy

### FIGO IA2

- Conizationwithpelvic lymphadenectomy - Simple or modified radical hysterectomy with pelvic lymphadenectomy +/- PALND
- Radical trachelectomy for fertility preservation with pelvic lymphadenectomy +/- PALND

*Lymphovascular space involvement, consider pelvic lymphadenectomy.*
*Radiation should be reserved for women who are not surgical candidates*

### FIGO IB1

- Radical hysterectomy + pelvic lymphadenectomy +/- PALND;
  *Adjuvant post-operative radiotherapy is considered only when adverse pathological findings are found*
- Radical trachelectomy + pelvic lymphadenectomy +/- PALND could be considered for patients wishing fertility preservation
- Pelvic RT + HDR brachytherapy. To be considered for woman who are not candidates for surgery. Concurrent chemo- radiation may be considered.

### FIGO IB2

- Preferred Approach: Pelvic RT + concurrent chemotherapy (cisplatin × 5 - 6 cycles) ; HDR brachytherapy
- Radical hysterectomy + pelvic lymphadenectomy +/- PALND for women who are not candidates for pelvic radiation.
  *Adjuvant post-operative radiotherapy is considered only when adverse pathological findings are found*

### FIGO IIA1

- Radical hysterectomy + pelvic lymphadenectomy +/- PALND
  *Adjuvant post-operative radiotherapy is considered only when adverse pathological findings are found*

*or*

- Pelvic RT + concurrent chemotherapy (cisplatin × 5 - 6 cycles) ; HDR Brachytherapy for women who are not candidates for surgery.

### FIGO IIA2

- Pelvic RT + concurrent chemotherapy (cisplatin × 5 - 6 cycles) ; HDR brachytherapy
  *Hysterectomy is not recommended because of excessive morbidity and no overall survival benefit.*

### FIGO IIB/IIIA/IVA

- Pelvic RT+ concurrent chemotherapy (cisplatin × 5-6 cycles); HDR brachytherapy.
- Parametrial boost may be considered.
- Paraaortic radiation for CT/MRI/PET or biopsy positive paraaortic lymphadenopathy.

- Hysterectomy for women who had a poor response to chemoradiation or have evidence of persistent disease following chemoradiation. Routine hysterectomy after chemoradiation is not recommended.

*At this stage, there is no evidence for adjuvant chemotherapy but the results as per clinical trials are awaited.*

**FIGO IVB**
- Clinical trial
- Palliative chemotherapy cisplatin based
- Palliative Radiation therapy

**Post-operative Adjuvant Therapy Indications:**

When deciding on adjuvant treatment options:

Intermediate Risk Adverse features:

Tumour size
Depth of stromal invasion
Lymphovascular space invasion (LVSI)

**Pelvic Radiation ± HDR Brachytherapy Indications:**

- LVSI plus deep one-third cervical stromal invasion and tumour of any size
- LVSI plus middle one-third stromal invasion and tumour size ≥2 cm
- LVSI plus superficial one-third stromal invasion and tumour size ≥5 cm
- No LVSI but deep or middle one-third stromal invasion and tumour size ≥4 cm

High Risk Adverse features:

Nodal status positive
Parametrial involvement
Positive surgical margins

**Concurrent Pelvic/para-aortic radiation and Cis-Platinum Chemotherapy ± HDR indications**:

- One feature or more

**Radiation Therapy:**
- Pelvic RT: 45 – 50.4 Gy in 25 – 28 fractions (1.8 to 2.0 Gy per fraction) over 5-5.5 weeks
  Boost to the parametria 3-5 fractions may be given as clinically indicated.
- Para-aortic radiation may be considered for CT or PET positive lymphadenopathy or biopsy positive paraaortic lymph nodes
- Brachytherapy- HDR :
  Intracavitary brachytherapy 3000cGy in 5 fractions. CT or MRI volume based.
  Vaginal HDR Brachytherapy 1200-1500cGy/3 fractions
  Vaginal brachytherapy as single modality 2100cGy/3 fractions
  Interstitial HDR Brachytherapy may be considered in selected cases.
- 3D conformal or IMRT boost may be considered for women who are not intracavitary HDR or surgical candidates.

An attempt should be made for *Radiation therapy to be completed within 8 weeks from the start of chemo-RT.*

*It is recommended to maintain adequate hemoglobin during radiotherapy > 100 g/l however use of Erythropoeitin is not recommended as it is shown to decrease the survival*

**Concurrent Chemotherapy:**
Cisplatin 40 mg/m2 (max = 80) IV weekly for 5 - 6 cycles during EBRT

**Follow up:**
- Recommendation to use vaginal dilator after pelvic radiation
- Physical examination and review of symptoms every 3 - 4 months for the first three Years by a GyneOncologist or Radiation Oncologist. After 3 years, all patients will be followed by the Family Physician every 6 months for 2 years and then annually thereafter.
- Pap test/vaginal vault cytology annually. - MRI, CT and/or PET if recurrence suspected
- Laboratory assessment as indicated

**Management of Local Recurrence/Metastases**
- History and clinical examination
- Blood work (CBC, LFT, renal function,)
- Chest x-ray;CT; MRI of pelvis; CT-PET

Treatment options:
- Recurrence in the pelvis following radical surgery may be considered for radiation in combination with chemotherapy.
- Central recurrence after radical radiotherapy may be considered for radical surgery, e.g., pelvic exenteration.
- Incurable pelvic recurrence/distant metastases:
    - Clinical trial
    - Palliative chemotherapy with platinum dublet is the preferred option. Platinum refractory patients can be treated with other agents.

*First Line*
- Paclitaxel 175 mg/m2 IV Day 1 plus Carboplatin AUC = 6 (if no prior RT) or AUC = 5 (if prior RT) IV Day 1 every 3 weeks
- Cisplatin 50 mg/m2 IV Day 1 plus Topotecan 0.75 mg/m2 IV Days 1,2,3 every 3 weeks (Dr. Al-Hayki has used this regimen, but I don't think this was discussed at the guideline meeting, and it does not seem to be listed in the latest UpToDate summary)

*Second Line*
- Vinorelbine 25-30 mg/m2 IV Day 1 and 8 every 3 weeks
- Topotecan 1.5 mg/m2 IV Days 1,2,3,4,5 every 3 weeks

- Palliative radiation therapy

**Pregnancy:**
During pregnancy, no therapy is warranted for pre-invasive lesions of the cervix, including carcinoma *in situ*, though expert colposcopy is recommended to exclude

invasive cancer. Treatment of invasive cervical cancer during pregnancy depends on the stage of the cancer and gestational age at diagnosis. The traditional approach is to recommend immediate therapy appropriate for the disease stage when the cancer is diagnosed before fetal maturity and to delay therapy only if the cancer is detected in the final trimester.[13,14] However, other reports suggest that deliberate delay of treatment to allow improved fetal outcome may be a reasonable option for patients with stage IA and early IB cervical cancer. The decision on management lies with the patient in careful consultation with the oncologist. The factors to consider are the natural history of the cancer process, the gestational age and the wishes of the parents.

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