Taipei Veterans General Hospital Practices Guidelines Oncology

Cervical Cancer

Version 2010.1

VGH Survival Data as of YYYY/MM/DD

Proofing on 2010/MM/DD

Principles of Radiation Therapy

See Practice Guidelines of Radiation Therapy for general standard operating procedures, tolerance dose of critical normal structures, quality assurance, DVH criteria for plan approval, and etc.

- **Radiation therapy for newly diagnosed cervical cancer**
- **Radiation Therapy for recurrent or metastatic disease**

General Radiation Information

General Radiation Information

– Treatment recommendations should be made after joint consultation and/or discussion by a multidisciplinary team including gynecologist, radiation, medical oncologists, radiologists, and pathologists.

– initial Hb, SCC levels, PV&PR Exam, pathology, CT and/or MR scans, Whole body bone scan reports, when available, should be reviewed by the multidisciplinary team. This will allow an informed determination of treatment volume and field borders prior to simulation.

Simulation

– Immobilization device is strongly recommended for reproducibility of daily set-up

To minimize setup variability, a customized immobilization device for both knee and foot was applied to each patient in the supine position.

– CT simulation and 3D treatment planning is necessary.

A treatment planning computed tomography scan is performed using 5-mm slices. The CT scans were obtained from at least the L4 vertebral body to 5 cm below the ischial tuberosities. All patients has a full bladder and empty rectum during scanning and simulation. During daily treatment they are instructed to have a full bladder.

Principle of Target volume delineation

Definitions of target volumes and critical structures

- Following the International Commission on Radiation Units and Measurements ICRU 62 recommendations (), a clinical target volume (CTV) was delineated on individual axial computed tomography slices in all patients by our radiation oncologist and reviewed by another.

Gross Target Volume (GTV) delineation

- Target volume delineation based on CT simulation images. Diagnostic CT/MR reports, and PET/CT scans should be reviewed, when available, for precise delineation of GTV

Clinical Target Volume (CTV) delineation

- The clinical target volume should include GTV and the areas at risk for microscopic disease

For definitive radiotherapy:

- CTV_H: GTV of primary tumor and lymphadenopathy
- CTV_L:
  a. GTV + upper vagina + pelvic LNs + prescaral LNs for pelvic radiotherapy
  b. GTV + upper vagina + pelvic LNs + prescaral LNs + paraaortic LNs for extended field radiotherapy

Fort postoperative radiotherapy:

- CTV:
  a. Tumor bed + upper vagina + pelvic LNs + prescaral LNs for pelvic radiotherapy
  b. Tumor bed + upper vagina + pelvic LNs + prescaral LNs + paraaortic LNs for extended field radiotherapy

- The final target volume should consider the relative risk of nodal metastases at specific nodal location is dependant on the site of the origin of primary tumor.

Principle of Target volume delineation

Planning Target Volume (PTV) delineation

- The margins of PTV should consider *respiratory motion* and *setup errors*
- For single-phase CT simulation, the recommended margins to compensate organ motions are as follows:

  PTV_L = CTV_L + Superior-inferior: 10 mm, Right-left: 10 mm, anterior: 7 mm, posterior: 5 mm

  PTV_H = CTV_H + Superior-inferior: 10 mm, Right-left: 10 mm, anterior: 5 mm, posterior: 4 mm

Field margins for box 4-fields technique

- The anterior field margins: possible extensions of the tumor into the body of the uterus.
- The posterior field margins: tumor extension into the uterosacral ligament and presacral lymph nodes.
- Lateral field margins: include the pelvic lymph nodes.
- For lesions in the lower one third of the vagina, the inguinal lymph nodes need to be treated.
- Extended-field radiation to treat occult or macroscopic para-aortic lymph node disease needs to be carefully planned to ensure adequate dose (45 Gy for microscopic disease) without exceeding bowel, spinal cord, or renal tolerances.

Radiation dose

- Definitive radiotherapy: 50.4 – 70.4 Gy + Brachytherapy (up to 81 – 85 Gy total dose)
- Postoperative radiotherapy: 45 – 50.4 Gy + Brachytherapy

***Radiation technique*:**

- 3D-CRT or IMRT
- Adaptive RT

Brachytherapy

- Intracavitary or interstitial brachytherapy techniques have proven to be a vital component in treatment of invasive cervical tumors. This is particularly true for more advanced stages of disease.
- Initial radiation treatment of 45-50.4 Gy/25-28 Fx to the whole pelvis is often necessary to obtain tumor shrinkage to permit optimal intracavitary placements.
- With intracavitary systems, total doses from brachytherapy and external-beam radiation to point A of at least 80 Gy are currently recommended for small tumors, with doses of at least 85 Gy recommended for larger tumors.
- For postoperative radiotherapy, further vaginal brachytherapy with 15-20 Gy/3-4 Fx to 0.5 cm submucosa, 3.0-4.0 cm active length is recommended for high risk but negative margin patient. Higher dose is also recommended for positive margin patient.

Radiotherapy for recurrent/palliative disease

Local/Regional Therapy

- *Patients with a localized recurrence of cervical cancer after surgery should be evaluated for radiotherapy for relapse.* Salvage rates of approximately 40% have been reported in such situations.
- For patients who experience local/regional recurrences with no prior RT or who experience recurrences outside of the previously treated field, therapy for relapse includes tumor-directed RT and platinum-based chemotherapy with (or without) brachytherapy; surgical resection can be considered if feasible.
- *Patients with central pelvic recurrent disease after RT should be evaluated for pelvic exenteration, with (or without) intraoperative RT (IORT).* In carefully selected patients with small lesions (less than 2 cm), options include radical hysterectomy or brachytherapy. Surgical mortality is generally 5% or lower, with survival rates between 20% and 60%. Women with recurrence after pelvic exenteration should be treated with platinum-based chemotherapy, best supportive care, or be enrolled in a clinical trial.
- Those with noncentral disease should be treated with pelvic exenteration or resection with IORT for close or positive margins, tumor-directed RT with (or without) chemotherapy, platinum-based chemotherapy, best supportive care, or participation in a clinical trial.

Systemic Therapy and Palliation

- Patients with distant metastases who have recurrence(s) at multiple sites or with unresectable recurrence(s) should be treated with chemotherapy or best supportive care.
- For patients with resectable recurrence(s), options include

  1) consider surgical resection with (or without) IORT,

  2) RT with concurrent chemotherapy, or

  3) chemotherapy.
- Occasionally, patients may benefit from radiotherapy to a localized recurrence(s). Generally, these areas would be supraclavicular, bone metastases, or painful para-aortic nodal recurrences.

Cancer of Cervix

Cancer of Cervix

- The NCCN algorithm provides RT dosage recommendations. These RT dosages should not be interpreted as stand-alone recommendations, because RT techniques and clinical judgment are an essential part of developing an appropriate treatment regimen.
- The external-beam doses represent the range of doses employing conventionally fractionated regimens of treatment (45-50 Gy to CTV). The brachytherapy doses used are for low-dose-rate applications (40 to 70 cGy/h), with doses to point A added to the external-beam doses to permit treatments to be compared. These doses may be modified for individual patients to provide adequate tumor coverage and to take into account normal tissue tolerances.
- External-beam RT and brachytherapy techniques have improved, as well as a better understanding of the influence of overall treatment time on outcome. Optimum staging of patients to precisely delineate the primary tumor volume and draining lymph nodes, including abdominopelvic radiologic studies (CT, MRI, or PET scans), is recommended in patients with bulky or advanced-stage tumors.

Planning Treatment Fields

- The use of 3-dimensional treatment planning for both the external-beam RT fields and the brachytherapy placements may assist in customized shaping of dose distributions to ensure adequate tumor coverage in all dimensions and to minimize normal tissue exposure.
- Field margins

  - The anterior field margins should include, where indicated, possible extensions of the tumor into the body of the uterus.

  - The posterior field margins should include tumor extension into the uterosacral ligament and presacral lymph nodes.

  - Lateral field margins need to adequately include the pelvic lymph nodes.
- For lesions in the lower one third of the vagina, the inguinal lymph nodes need to be treated. The use of extended-field radiation to treat occult or macroscopic para-aortic lymph node disease needs to be carefully planned to ensure adequate dose (45 Gy for microscopic disease) without exceeding bowel, spinal cord, or renal tolerances.
- Intracavitary or interstitial brachytherapy techniques have proven to be a vital component in treatment of invasive cervical tumors. This is particularly true for more advanced stages of disease.
- Initial radiation treatment of 40 Gy to the whole pelvis is often necessary to obtain tumor shrinkage to permit optimal intracavitary placements. With low-dose-rate intracavitary systems, total doses from brachytherapy and external-beam radiation to point A of at least 80 Gy are currently recommended for small tumors, with doses of at least 85 Gy recommended for larger tumors.

Minimizing Tissue Damage

- Adjustments must be made to minimize radiation doses to normal surrounding tissues (eg, bladder, rectum, and sigmoid colon).
- Coned-down shaped boost fields should be used with involved pelvic lymph nodes and areas of parametrial extension. These regions should be treated with total doses of 60 to 65 Gy.
- Individualized central blocking techniques should be used to shield from the intracavitary placements those portions of the small bowel, rectum, and bladder that had been included in the high-dose regions. Similar recommendations apply to high-dose-rate intracavitary systems, for which a wide range of treatment regimens have been used (generally using between 3 and 6 fractions, with doses usually between 5 and 10 Gy per fraction).
- Dose modifications may be needed for patients who will undergo hysterectomy or for postoperative treatment.
- Several, but not all, retrospective analyses have suggested an adverse effect of prolonged treatment duration on outcome.
- Extending the overall treatment beyond 6 to 8 weeks can result in approximately a 0.5% to 1% decrease in pelvic control and cause-specific survival for each extra day of overall treatment time. Thus, the entire RT course should be completed in a timely fashion (eg, less than 8 weeks); delays or splits in the radiation treatment should be avoided whenever possible, although no prospective randomized trials have been done.

Acronym

- RT: Radiation Therapy
- 3D-CRT: 3D Conformal Radiation Therapy
- IMRT: Intensity Modulated Radiation Therapy
- CCRT: Concurrent chemoradiotherapy
- GTV: Gross Tumor Volume
- CTV: Clinical Target Volume
- PTV: Planning Target Volume
- MRI: Magnetic Resonance Image
- PET: Positron Emission Tomography
- HDR: High dose rate
- LDR: Low dose rate