INTRODUCTION:

Uterine cancer accounts for approximately 40,000 new cancer cases diagnosed in the United States and costing 7,500 deaths. The majority of endometrial cancers are adenocarcinomas, with uterine sarcomas accounting for <10%. This clinical guideline will focus primarily on adenocarcinoma of the endometrium.

After a diagnosis of endometrial cancer is made, it is followed by a staging evaluation to determine extent of disease (local, regional, or metastatic), and prognostic findings. For patients in whom cancers of the uterus are suspected, an endometrial biopsy is typically performed. A review of the pathology will determine whether or not the tumors are of epithelial origin (endometrioid, papillary cirrus, clear cell, or carcinosarcoma) or stromal/mesenchymal carcinoma (stromal sarcoma or leiomyosarcoma). The majority of endometrial cancers, however, are adenocarcinomas with tumor typically confined to the uterus. Thus, this disease is often localized with an excellent prognosis. Current workup, including a complete surgical assessment, includes a histological grade, depth of myometrial invasion, and extent of extrauterine involvement. Prognostic factors are based on a pathologic assessment and include the percent of myometrial invasion, myometrial thickness, tumor size and location (upper fundus or lower uterine cervical), cervix involvement, and lymphvascular space involvement. The majority of patients are treated surgically with radiation reserved for patients who are deemed at a high risk of recurrence or for those deemed medically inoperable.

GOAL OF THE GUIDELINE:

This guideline outlines several methods suitable for the employment of radiation therapy. This includes the use of 3-dimensional conformal radiation therapy and/or internal radiation (brachytherapy). IMRT is not indicated as a standard treatment option for uterine cancer. External beam treatments are typically delivered using a high-energy linear accelerator. Brachytherapy is generally delivered using temporary HDR sources such as iridium 192. The purpose of this guideline is to outline the most efficient, comparatively effective, diagnostic and treatment pathway. Treatment is typically broken down into patients in whom disease is limited to the uterus, cervical involvement (either suspected or confirmed), or extrauterine disease.

GENERAL CONSIDERATIONS:

Radiation therapy is typically tailored to surgically define extent of disease. Prognostic factors include age, positive lymphvascular invasion, tumor size, lower uterine involvement,
grade and depth of myometrial invasion. Potential adverse risk factors that may indicate certain radiation therapy options include age, positive lymphvascular invasion and lower uterine involvement. Tumor-directed radiation therapy is defined as radiation therapy to sites of known or suspected disease. Radiation therapy is commonly delivered as external beam and/or brachytherapy. External beam treatment is generally directed to the pelvis with or without para-aortic lymph nodes. Brachytherapy can be delivered to the intact uterus or to the vaginal cuff following a hysterectomy.

**Brachytherapy:**
- Vaginal brachytherapy following hysterectomy should be limited to the upper vagina.
- Vaginal brachytherapy is typically delivered with either low dose rate or high dose rate cylinder. The latter is more commonly used, and dose fractionation when delivered alone includes 7 Gy x3 prescribed with 5mm from cylinder surface, or 6 Gy x5 prescribed to the cylinder surface.

**MEDICALLY NECESSARY INDICATIONS FOR RADIATION THERAPY AND TREATMENT OPTIONS:**

**Post-operative**
- Brachytherapy Only (HDR or LDR, 5 fx maximum)
  - Stage IA – with adverse risk factors
  - Stage IA – without risk factors (Grades G2, 3)
  - Stage IB
  - Stage II – (Grade G1)
- External Beam Radiation Therapy Only (2D, 3D-CRT, 45-50.4 Gy, 28 fx maximum)
  - Stage IA – with adverse risk factors (Grades G2, 3)
  - Stage IB – without adverse risk factors (Grade G3)
  - Stage IB – with risk factors
  - Stage II – (Grade G1)
  - Stage III
  - Stage IV
- External Beam (2D, 3D-CRT, 45-50.4 Gy, 28 fx maximum) and Brachytherapy (HDR or LDR, 5 fx maximum)
  - Stage IA – with adverse risk factors (Grades G2, 3)
  - Stage IB – without risk factors (Grade G3)
  - Stage IB – with risk factors
  - Stage II – (Grades G1, 2, 3)
  - Stage IIIA & IIIB & IIIC (Grades G1, 2, 3)

**Medically Inoperable/ Pre-Operative**
- Brachytherapy Only (HDR or LDR, 7 fx maximum)
  - Stage I & II
- External Beam Radiation Therapy Only (2D, 3D-CRT, 45-50.4 Gy, 28 fx maximum)
  - All Stages
- External Beam (2D, 3D-CRT, 45-50.4 Gy) and Brachytherapy (HDR or LDR, 4 fx maximum)
  o All Stages

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*Unless otherwise indicated standard radiation fractionation consists of 1.8 Gy to 2.0 Gy per day*

**TREATMENT OPTIONS REQUIRING ADDITIONAL CLINICAL REVIEW:**

**Intensity modulated radiation therapy (IMRT)**

IMRT is not indicated as a standard treatment option and should not be used routinely for the delivery of radiation therapy for endometrial cancer. IMRT is strictly defined by the utilization of inverse planning modulation techniques. IMRT may be appropriate for limited circumstances in which radiation therapy is indicated and 3D conformal radiation therapy (3D-CRT) techniques cannot adequately deliver the radiation prescription without exceeding normal tissue radiation tolerance, the delivery is anticipated to contribute to potential late toxicity or tumor volume dose heterogeneity is such that unacceptable hot or cold spots are created.

Clinical rationale and documentation for performing IMRT rather than 2D or 3D-CRT treatment planning and delivery will need to:

- Demonstrate how 3D-CRT isodose planning cannot produce a satisfactory treatment plan (as stated above) via the use of a patient specific dose volume histograms and isodose plans.

- Provide tissue constraints for both the target and affected critical structures.

**Stereotactic Body Radiation Therapy (SBRT)**

Stereotactic Body Radiation Therapy is not a standard treatment option for the treatment of endometrial cancer.

**Proton Beam Radiation Therapy**

Proton beam is not an approved treatment option for endometrial cancer. Proton beam has not been proven superior treatment to conventional radiation therapy.
REFERENCES


