Gynecologic (GYN) Cancers

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

DISCUSSION

Gynecological (GYN) cancers involve the cervix, ovaries, fallopian tubes, uterus, and vulva. According to the American Cancer Society, 115,130 women in 2022 will be diagnosed with some form of gynecologic cancer and more than 33,000 will die from the disease.[1,2,3,4] Cancers of the uterus, cervix, and ovary make up the majority of the 102,460 new cases each year. Radiation therapy is often an integral component of multi-modality management within the definitive (primary), adjuvant, and palliative settings.

Cervical Cancer Overview

Incidence

An estimated 14,100 women in the U.S. will be diagnosed with invasive cervical cancer this year and nearly 4,280 women are expected to die from the disease.[1] The estimated five-year survival rate is 92% for early-stage disease and 56% for locally advanced disease. According to the NCCN guidelines, cervical cancer is highly treatable if detected early—80% of women with early stage (stages I-II) are cured and 60% of women with stage III.[5]

Radiation Treatment

Radiation is an integral part of cervical cancer treatment, either following surgery for patients at risk of recurrence or as a primary definitive treatment. The regimen involves pelvic external beam radiation therapy (EBRT), often combined with chemotherapy and a brachytherapy boost. Radiation used in the primary or definitive setting includes locally advanced disease or poor surgical candidates. Radiation is used in the adjuvant setting following radical hysterectomy for those who have one or more risk factors (for example, positive lymph nodes, parametrial infiltration, positive surgical margins, large tumor size, deep stromal invasion, LVSI). Medically inoperable Stage IB2-IVA or Stage IB1-IIA1 and advanced disease are treated with concurrent platinum-based chemotherapy (chemoradiation) followed by brachytherapy. In the postoperative setting following radical hysterectomy, radiation with concurrent platinum-based chemotherapy (chemoradiation) is recommended for patients with high risk factors such as positive margins. Postoperative radiation therapy is recommended for patients with intermediate risk factors such as larger tumors. [5]

Ovarian (and Fallopian Tubes) Cancer Overview

Incidence

In 2022, an estimated 19,880 women in the US will be diagnosed this year and 12,810 will die from the disease. The 5-year survival is about 48% but can be longer in select patients with certain rarer subtypes. Epithelial ovarian cancer comprises many malignant ovarian neoplasms (about 90%) and other less common include malignant germ cell and sex cord-stromal cell tumors.[3]

Radiation Treatment

Standard of care in the initial treatment of primary epithelial ovarian cancer involves surgical resection or debulking and or systemic chemotherapy. Radiation therapy (EBRT) is used to treat malignant sex cord-stromal tumors in limited

and palliative settings. It is also recommended in the palliative setting for epithelial ovarian cancer/fallopian tube cancer, primary peritoneal cancer, and germ cell tumor types.[6]

Uterine or Endometrial Cancer Overview

Incidence

It is estimated that 65,950 new uterine cancer cases will occur in 2022, with 12,550 deaths resulting from the disease.[2] Major types include epithelial or uterine sarcomas and uncommon types (3%) are made up by stromal or mesenchymal sarcomas; treatment is dependent on the type of cancer, extent (stage and grade), location, and medical condition risk factors, and includes some type of combination of surgery, chemotherapy, immunotherapy, and radiation therapy.

The FIGO system is most used for staging uterine cancer. Particularly useful in stage I and II endometrial cancers, and critical to the staging process is the use of sentinel node mapping which helps to determine lymph node involvement. The NCCN Guidelines divide pure endometrioid cancer into three categories for delineating treatment: 1) disease limited to the uterus; 2) suspected or gross cervical involvement; and 3) suspected extrauterine disease.[7]

Clinical Considerations[7]

- Radiation should be initiated when healing has occurred, preferably within 6-8 weeks.
- Bolus should be placed over vulva for treatment to ensure adequate dosing to the superficial target volume at the primary site and when the lymph nodes are just below skin surface.
- Doses to the primary site should be verified using dosimeters at first treatment.

Principles of Radiation Therapy for Uterine Neoplasms

General Principles

RT is directed at sites of known or suspected tumor involvement and may include EBRT and/or brachytherapy, imaging is required to assess locoregional extent and to rule out distant metastases before administration of RT. In general, 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.[7]

General Treatment Information

Target Volumes

- Pelvic radiotherapy should target the gross disease (if present), the lower common iliacs, external iliacs, internal iliacs, obturators, parametria, upper vagina/para-vaginal tissue, and presacral lymph nodes (in patients with cervical involvement). [7]
- Extended-field radiotherapy should include the pelvic volume and 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 be at least 1-2 cm above the level of the renal vessels. [7]
- Pelvic tissues at risk, especially in the post-hysterectomy setting, can be highly variable depending on bowel and bladder filling. In this situation, the integrated target volume (ITV), which encompasses the range of organ movement and deformation, is considered the clinical target volume (CTV), and should be fully covered in the treatment volume. [7]

Vulvar Cancer Overview

Incidence

In 2022, an estimated 6,330 women in the US will be diagnosed with vulvar cancer and 1,560 will die from the disease.[4] Most cancers of the vulva are squamous cell carcinomas. This type of cancer starts in squamous cells, the main type of skin cells. There are several subtypes of squamous cell carcinoma. The keratinizing type is the most common. Basaloid, warty types and verrucous carcinoma are less common. Adenocarcinomas and melanomas are other types of vulvar cancer. [4]

Principles of Radiation Therapy-Vulvar Cancer

General Principles

RT is often used in the management of patients with vulvar cancer as adjuvant therapy following initial surgery, as part of primary therapy in locally advanced disease, or for secondary therapy/palliation in recurrent/metastatic disease.[8]

Radiation technique and doses are important to maximize tumor control while limiting adjacent normal tissue toxicity. Tumor directed RT refers to RT at sites of known or suspected tumor involvement. In general, tumor-directed ERBT is directed to the vulva and/or inguinofemoral, external, and internal iliac nodal regions. Brachytherapy can sometimes be used as a boost to anatomically amenable primary tumors. Careful attention should be taken to ensure adequate tumor coverage by combining clinical examination, imaging findings, and appropriate nodal volumes at risk to define the target volume. For example, invasion into the anus above the pectinate line would necessitate coverage of the perirectal nodes. [8]

Ensure coverage of gross tumor burden with margin. In highly selected cases where only a superficial vulvar target is to be treated, an enface electron beam may be used. [8]

Utilization of imaging studies are an important part of the treatment planning process. The use of CT-based treatment planning and conformal blocking is considered the standard of care for EBRT. [8]

Acute effects during RT (for example, diarrhea, bladder irritation, fatigue, mucocutaneous reaction) are expected to some degree in most patients and can be further accentuated by concurrent chemotherapy. These toxicities should be aggressively managed (for example, local skin care, symptomatic medications), and treatment breaks should be avoided or minimized. Many patients may develop an overgrowth of Candida albicans; treatment with oral and local antifungal agent will markedly reduce skin reaction. If bacterial infection develops, prompt recognition and appropriate treatment is essential. These acute effects generally resolve several weeks after completion of radiation.

Postoperative adjuvant treatment should be initiated as soon as adequate healing is achieved, preferably in 6-8 weeks.[8]

Treatment Information – 3-D Conformal/Anterior-Posterior (AP/PA) Fields

Target Volume

The target is best defined by both physical examination and CT-based treatment planning; contouring of the target structure is recommended. When an AP/PA technique is primarily used, often wide AP and narrower PA fields are used with electrons supplementing the dose to the inguinal region if the depth of the inguinal nodes allows electron coverage. More conformal techniques such as three-or four-field approaches may allow greater sparing of bowel and/or bladder, depending on tumor extent and patient anatomy. CT or MRI planning, with possible image fusion technology, should be utilized to assure there is adequate dosing and coverage with contouring of the primary, and the inguinofemoral and iliac nodes. Radio-opaque markers should be placed on key landmarks at the time of simulation to assist in definition of primary target. [8]

The superior field border should be no lower than the bottom of the sacroiliac joints or higher than the L4/L5 junction unless pelvic nodes are involved. If pelvic nodes are involved, the upper order can be raised to at least 2 cm above the most cephalad-positive node. The superior border should extend as a horizontal line to cover the inguinofemoral nodes at the level of the anterior superior iliac spine. The lateral border will be a vertical line drawn from the anterior-inferior iliac spine. To adequately cover the inguinal nodes, the inferior-lateral inguinal nodal border should be parallel to the inguinal crease and inferior enough to encompass the inguinofemoral nodal bed to the intertrochanteric line of the femur or 1.5 cm to 2 cm distal to the saphenofemoral junction. The inferior vulvar border will be lower and should be at least 2 cm below the most distal part of the vulva. Care should be taken to spare the femoral heads and necks.[8]

In both the locally advanced and postoperative settings, especially when there is greater than or equal to 1 LN clinically suspicious or pathologically positive, the bilateral inguinal and pelvic lymphatic regions are typical included in the radiotherapy clinic target volume (CVT). Selective coverage of the primary may be appropriate. While classic indications for treating the primary site include close/positive margin, lymphovascular space invasion (LVSI), and >5 mm depth of invasion, groin involvement may also be considered a relative indication to include primary site. While it may be tempting to add a midline block in the postoperative setting to avoid radiation toxicity to sensitive central structures, use of a midline block in stage III-IV vulvar cancer has been associated with a high rate of central reoccurrence; thus, such practice is usually discouraged. Conversely, there may be clinical situations in which it is desirable to cover the primary site only and avoid the nodes.[8]

Treatment Information – Intensity-Modulated Radiation Therapy (IMRT)

The vulvar and nodal target should be contoured on the planning CT. Any gross vulvar disease should be contoured as a gross tumor volume (GTV) and include any visible and/or palpable extension. The vulvar CTV target is defined as the GTV or tumor bed plus the adjacent skin, mucosa, and subcutaneous tissue of the vulva excluding bony tissue. A wire placed clinically to define the vulvar skin borders and the GTV during CT simulation is essential. In addition, a marker on the anus, urethra, clitoris, and the wiring of any scars will aid in planning.

To ensure adequate distal margin the vulvar target volume, a “false structure” or bolus should be placed over the vulva for treatment planning purposes. Doses to target areas should be confirmed using a thermoluminescent dosimeter (TLD) at first treatment.

Symmetrical geometric expansions on the vessels should NOT be used for the inguinofemoral nodes. The inguinofemoral nodal CTV will extend laterally from the inguinofemoral vessels to the medial border of the sartorius and rectus femoris muscles, posteriorly to the anterior vastus medialis muscle, and medially to the pectineus muscle or 2.5 cm to 3 cm medially from the vessels. Anteriorly, the volume should extend to the anterior border of the sartorius muscle (the most anterior muscle on the lateral inguinofemoral border). The caudal extent of the inguinofemoral nodal basin is the top of the lesser trochanter of the femur.

The pelvic nodal CTV is the vasculature of the bilateral external iliac, obturator and internal iliac nodal regions with a minimum of 7 mm of symmetrical expansion excluding bone and muscle. The groin CTV volume will not extend outside the skin and should be trimmed by 3 mm in the absence of skin involvement (with skin involvement the CTV should extend to the skin with bolus material applied during treatment). Planning target volume (PTV) expansion is then 7 mm to 10 mm. Image-guided IMRT is an essential component of treatment (to account for vulva edema or marked tumor regression). Plan with care to respect normal tissue tolerances such as rectum, bladder, small bowel, and femoral head and neck.[8]

Radiation Treatment

The following radiation therapeutic regimens for vulvar/vagina cancer are considered medically necessary for ANY of the following settings:

- Brachytherapy and intensity-modulated radiation therapy (IMRT) are appropriate for treatment of vulvar/vaginal cancer.
- Stereotactic body radiation therapy (SBRT) is appropriate for vulvar/vaginal cancer only to treat a previously irradiated field.

Clinical Considerations[8]

- Minimize breaks.
- Initiate radiation when healing has occurred, preferably within 6 to 8 weeks.
- Bolus should be placed over vulva for treatment to ensure adequate dosing to the superficial target volume at the primary site and when the lymph nodes are just below the skin surface.
- Verify doses to the primary site using dosimeters at first treatment.

DEFINITIONS

- **Brachytherapy (BT) -** Brachytherapy is a procedure that involves placing radioactive material inside your body. Brachytherapy is sometimes called internal radiation.
- **External beam radiation treatment (EBRT) -** External beam radiation therapy (EBRT) is radiation delivered from outside the body and is most often used to treat bone cancer.
- **Fractions -** A way of dividing a total dose of radiation into separate doses to be administered over a period of time.
- **Gray (Gy) -** One of the two units used to measure the amount of radiation absorbed by an object or person, known as the absorbed dose. One gray (Gy) is the international system of units (SI) equivalent of 100 rads, which is equal to an absorbed dose of 1 Joule/kilogram.
- **Image-guided radiation therapy (IGRT) -** Image-guided radiation therapy (IGRT) is the use of imaging during radiation therapy to improve the precision and accuracy of treatment delivery. IGRT is used to treat tumors in areas of the body that move, such as the lungs. Radiation therapy machines are equipped with imaging technology to allow your doctor to image the tumor before and during treatment. By comparing these images to the reference images taken during simulation, the patient's position and/or the radiation beams may be adjusted to more precisely target the radiation dose to the tumor. To help align and target the radiation equipment, some IGRT procedures may use fiducial markers, ultrasound, MRI, X-ray images of bone structure, CT scan, 3D body surface mapping, electromagnetic transponders, or colored ink tattoos on the skin.
- **Intensity-modulated radiotherapy (IMRT) -** Intensity-modulated radiation therapy (IMRT) is an advanced mode of high-precision radiotherapy that uses computer-controlled linear accelerators to deliver precise radiation doses to a malignant tumor or specific areas within the tumor. IMRT allows the radiation dose to conform more precisely to the three-dimensional shape of the tumor by controlling the intensity of the radiation beam in multiple small volumes. IMRT also allows higher radiation doses to be focused to regions within the tumor while minimizing the dose to surrounding normal critical structures.
- **National Comprehensive Cancer Network® (NCCN) -** An alliance of 32 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Palliative radiation therapy -** Treatment given to help relieve the symptoms and reduce the suffering caused by cancer or other life-threatening diseases. Palliative therapy may help a person feel more comfortable, but it does not treat or cure the disease. Palliative therapy may be given with other treatments from the time of diagnosis until the end of life.
- **Stereotactic body radiation therapy (SBRT) -** Treatment outside the brain is called stereotactic body radiation therapy (SBRT). SBRT may be used for certain lung, spine, and liver tumors.

POLICY

The following table outlines the criteria that needs to be met for the number of fractions and dosing relative to gynecological cancer radiation treatments. The following dosing table represents evidence-based doses and fractions for the designated type of cancer treatment. Variations outside of the ranges may indicate a deviation from standard treatment.

Cervical Cancer			
	Number of Fractions	**Total Dose**	**Technique**
Definitive EBRT with HDR Brachytherapy	20-28 5	40-50.4 Gy EBRT 30 Gy Brachy	3D, IMRT, IGRT, Brachytherapy
Definitive EBRT with LDR Brachytherapy	20-28 1-2	40-50.4 Gy EBRT 30-45 Gy Brachy	3D, IMRT, IGRT, Brachytherapy
Adjuvant EBRT	20-28	40-50.4 Gy	3D, IMRT, IGRT,
Adjuvant EBRT with HDR Brachytherapy	20-28 2-3	40-50.4 Gy EBRT 11-18 Gy Brachy	3D, IMRT, IGRT, Brachytherapy
Adjuvant EBRT with LDR Brachytherapy	20-28 1-2	40-50.4 Gy EBRT 20-25 Gy Brachy	3D, IMRT, IGRT, Brachytherapy

Endometrial Cancer			
	Number of Fractions	**Total Dose**	**Technique**
Definitive EBRT with Optional HDR brachytherapy boost or EBRT Boost	23-28 2-3 5-11	45-50.4 Gy EBRT 8 -18 Gy Brachy 10-20 Gy EBRT	3D, IMRT, IGRT, Brachytherapy 3D, IMRT, IGRT
Definitive EBRT	23-28	45-50.4 Gy EBRT	3D, IMRT, IGRT
Adjuvant	23-28	45-50.4 Gy	3D, IMRT, IGRT
Adjuvant EBRT with Optional HDR Brachytherapy Boost or EBRT Boost	23-28 2-3 5-11	45-50.4 Gy EBRT 11-18 Gy Brachy 10-20 Gy EBRT	3D, IMRT, IGRT, Brachytherapy 3D, IMRT, IGRT
Adjuvant HDR Brachytherapy	2-6	21-37.5 Gy	Brachytherapy

Uterine Cancer			
	Number of Fractions	**Total Dose**	**Technique**
Uterine Sarcoma - Adjuvant with Boost	23-28 5-11	45-50.4 Gy 10-20 Gy	3D, IMRT, IGRT

Vulvar / Vaginal Cancer			
Definitive or Adjuvant EBRT	**Number of Fractions**	**Total Dose**	**Technique**

	25-39	45 -70.2 Gy	3D, IMRT, IGRT
Palliative	1-15	8-37.5 Gy	3D

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Please see all related radiation therapy treatment policies for additional information on the treatment modalities. (3D-CRT, BT, EBRT, IGRT and IMRT)

CODING [ICD-10, HCPCS]*

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C51.0 – C51.9	Malignant neoplasm vulva
C52	Malignant neoplasm vagina
C53.0 – C53.9	Malignant neoplasm cervix
C54.0 – C55	Malignant neoplasm uterus
C57.7 – C57.9	Malignant neoplasm other and unspecified female genital organs
D07.0	Carcinoma in situ of endometrium
D07.1	Carcinoma in situ of vulva
D07.2	Carcinoma in situ of vagina
D07.39	Carcinoma in situ of other female genital organs [uterus]
G0339	Image-guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session or first session of fractionated treatment

Code	Description
G0340	Image-guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum 5 sessions per course of treatment
G6015	Intensity-modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
G6016	Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator convergent beam modulated fields, per treatment session
Z92.3	Personal history of irradiation

REVISION AND REVIEW HISTORY

No.	Description	Metadata
1	Original Effective Date:	5/2022
2	Policy Review Dates:	5/20/2022, 5/23/2022, 7/20/2022, 9/1/2022
3	Policy Revision Dates:	5/20/2022, 5/23/2022, 7/20/2022, 9/1/2022, 10/4/2022, 10/24/2022
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	5/20/2022, 5/23/2022, 9/1/2022, 10/4/2022, 10/24/2022
6	Revision Changes:	9/1/2022-Change EBRT with HDR Brachytherapy minimum from 12Gy to 11Gy. Added American Brachytherapy Society. 10/4/2022- Changed Definitive HDR Brachy minimum from 11Gy to 8 Gy. Removed neoadjuvant RT from vulvar/vaginal and minimum dose changed from 50.4 to 45 Gy. Changed vulvar cancer Definitive or Adjuvant EBRT minimum to 25 vs 28. 10/24/2022- Added to Definitive EBRT with Optional HDR Brachytherapy Boost or EBRT Boost with dosing 5-11 fractions and 10-20 Gy EBRT. Added to Adjuvant EBRT with Optional HDR Brachytherapy Boost or EBRT Boost with dosing 5-11 fractions and 10-20 Gy EBRT.