Anal Cancer

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

Anal cancer is a rare cancer of the digestive system. Anal cancer is typically a squamous cell cancer. It can also be a rarer type of anal adenocarcinoma or anal melanoma. This cancer usually begins in the anal canal or the perianal area and region.[1]

Anal cancer stages I, II, and III are not metastatic and are typically treated with chemotherapy and radiation (chemoradiation). Radiation therapy is not recommended specifically for metastatic anal cancer. Chemotherapy is usually the treatment of choice for metastatic disease. Perianal cancers stage I and IIA may be treated with local excision only if it has not invaded the nearby lymph nodes. The margin of at least 1 cm must be disease-free. If margins contain cancer cells or less than 1 cm margin is excised, further treatment is required. Definitive/Adjuvant radiation therapy and palliation radiation therapy are indicated for anal cancer. [2]

Techniques for the treatment of anal cancer have developed in parallel with technologic advances in radiation therapy (RT). Combined chemotherapy and RT have replaced radical surgical resection as the cornerstone of treatment for anal malignancies. 5-fluorouracil (5-FU) and mitomycin-C (MMC) combined with pelvic RT yielded improved local control rates with sphincter preservation. Randomized trials have since shown that combined modality therapy with RT, 5-FU, and MMC improves long-term, disease-free survival and sphincter preservation rates in patients with anal cancer compared with RT alone, neoadjuvant cisplatin-based chemotherapy alone, or RT combined with 5-FU alone. Mitigating these gains is the high rate of treatment-related morbidity associated with chemoradiation. For example, 87% of patients in the phase III Radiation Therapy Oncology Group (RTOG) 98-11 trial (which did not use intensity-modulated radiation therapy [IMRT] techniques) experienced grade 3 to 4 acute toxicity. RT interruptions, whether through intent or treatment-related toxicity, may compromise therapeutic efficacy.[2]

Intensity modulated radiation therapy (IMRT), image guided radiation therapy (IGRT) and three dimensional conformal radiation therapy (3D-CRT) are typically utilized in patients undergoing definitive therapy. More advanced disease of the anal margin is treated similarly to anal canal cancers. Treatment for perianal cancers is the same as for anal canal cancer.

DEFINITIONS

- **Adjuvant radiation therapy -** Additional radiation therapy given after the primary treatment to lower the risk of cancer recurrence.
- **Boost –** After radiation therapy, further treatment may be required (called a boost). This boost increases the amount of radiation given to the area at highest risk for recurrence. The boost radiation session is similar to a regular session.
- **Definitive radiation therapy -** Radiation therapy used with curative intent.

- **External beam radiation therapy (EBRT) -** External radiation (or external beam radiation) is the most common type of radiation therapy used for cancer treatment. A machine aims high-energy rays (or beams) from outside the body into the tumor.
- **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.
- **High dose-rate (HDR) -** High dose-rate (HDR) is an advanced cancer treatment that delivers a highly concentrated dose of radiation near or in the tumor, while sparing the surrounding health tissue.
- **Hypofractionated radiation therapy -** A form of radiation treatment in which the total dose of radiation is divided into small doses and treatments are given more than once a day.
- **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 radiation therapy (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) -** Used to treat cancer in its early stages, this radiation technology delivers very high doses of focused radiation to a small area. By using very sophisticated technology, the radiation oncologist can increase the intensity of the radiation while compressing the amount of radiation into only three to five sessions. With higher dose-rates, SBRT is much more convenient for patients and offers improved success rates.
- **Three dimensional conformal radiation therapy (3D-CRT) -** A procedure that uses a computer to create a three dimensional picture of the tumor. This allows doctors to give the highest possible dose of radiation to the tumor, while sparing the normal tissue as much as possible.

POLICY

The following table outlines the criteria that must be met for the number of fractions and dosing relative to anal cancer radiation treatments. This 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.

Anal Cancer			
	Number of Fractions	**Total Dose**	**Technique**
Definitive /Adjuvant	25-33	45-59.4 Gy	3D, IMRT, IGRT
Palliation	1-15	8-37.5 Gy	3D

REFERENCES

1. What is anal cancer? American Cancer Society. https://www.cancer.org/cancer/anal-cancer/about/what-is-anal-cancer.html. Accessed May 5, 2022.
2. Pepek JM, Willett CG, Czito BG. Radiation Therapy Advances for Treatment of Anal Cancer. *Journal of the National Comprehensive Cancer Network*. 2010;8(1):123-129. doi:10.6004/jnccn.2010.0008
3. Radiation therapy for anal cancer. American Cancer Society. https://www.cancer.org/cancer/anal-cancer/treating/radiation-therapy.html. Accessed May 5, 2022.
4. Wegner RE, Abel S, Hasan S, et al. Trends in Radiation Dose and Technique For Anal Canal Squamous Cell Carcinoma. *American journal of clinical oncology*. 42(6), 519–526.
5. Kachnic LA, Winter K, Myerson RJ, et al. RTOG 0529: A Phase 2 Evaluation of Dose-Painted Intensity Modulated Radiation Therapy in Combination With 5-Fluorouracil and Mitomycin-C for the Reduction of Acute Morbidity in Carcinoma of the Anal Canal. *International Journal of Radiation Oncology Biology Physics*. 2013;86(1):27-33.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Anal Carcinoma. (Version 1.2022). Available at https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf. ©National Comprehensive Cancer Network, 2022.

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

CODING [ICD 10 AND 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**
DDY8CZZ	Intraoperative RT (IDRT) of anus
C21.1	Malignant neoplasm of anal canal
C44.500	Unspecified malignant neoplasm of anal skin
C4A.51	Merkel cell carcinoma of anal skin
C43.51	Malignant melanoma of anal skin
C21.0	Malignant neoplasm of anus, unspecified
Z85.048	Personal history of other malignant neoplasm of rectum, rectosigmoid junction, and anus
Z51.0	Encounter for antineoplastic radiation therapy
Z51.5	Encounter for palliative care
Z92.3	Personal history of radiation

Code	Description
G6003	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: up to 5 MeV
G6004	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: 6-10 MeV
G6005	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: 11-19 MeV
G6006	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: up to 5 MeV
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

REVISION AND REVIEW HISTORY

No.	Description	Metadata
1	Original Effective Date:	5/2022
2	Policy Review Dates:	4/26/2022, 4/27/2022, 5/4/2022, 5/5/2022, 5/26/2022, 5/27/2022, 7/20/2022
3	Policy Revision Dates:	4/26/2022, 4/27/2022, 5/4/2022, 5/5/2022, 5/26/2022, 5/27/2022, 7/20/2022
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	4/27/2022, 5/5/2022, 5/27/2022
6	Revision Changes:	