

Bladder 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

Bladder cancer is the sixth most diagnosed cancer in the United States with the median age of 73 years at diagnosis. The American Cancer Society (ACS) estimated that 81,180 new cases of bladder cancer will be diagnosed in the US in 2022 and 17,100 will die from the disease. Bladder cancer is four times more common in men than in women and two times more common in Caucasian men than African American men.¹

Bladder Cancer Categorization

Bladder cancer is associated with substantial morbidity and mortality. Environmental and occupational exposures to carcinogens are the main risk factors for development of bladder cancer. Most bladder cancers are diagnosed after patients present with blood in the urine. Cases are confirmed after surgical removal of the tumor which also serves as the first stage of treatment.²

Bladder cancer can be categorized into three groups based on the severity level³:

- Non-muscle is the least invasive bladder cancer (NMIBC) (stages Ta, Tis, T1).
- Muscle-invasive bladder carcinoma refers to tumors that have spread into or through the muscle layer of the bladder wall (stages T2-T4).
- Metastatic lesions, which refers to tumors that have spread to distant organs or lymph nodes outside the pelvis.

Types of Bladder Cancer

Non-Muscle Invasive Bladder Cancer

In patients with high-risk non-muscle invasive bladder cancer, radiation therapy has been evaluated as a potential treatment option. However, the use of radiation therapy in this group of patients is not well defined. The NCCN® does not endorse the use of radiation therapy for non-muscle invasive bladder cancer.³ As such, the use of radiation therapy is considered not medically necessary for the treatment of non-muscle invasive bladder cancer.

Muscle-Invasive Bladder Cancer

Definitive radiotherapy alone is considered only for an individual with no evidence of metastatic disease who cannot undergo a cystectomy or concurrent chemoradiation.

Treatment options include a cystectomy or definitive chemoradiation as part of a bladder preserving approach. An ideal candidate for bladder preservation includes one with tumors < 5 cm and a visibly complete transurethral resection of a bladder tumor (TURBT).

Treatment Approach

The goal of radiation therapy is for bladder preservation in non-muscle invasion bladder cancer (NMIBC) whenever possible using a combination of chemotherapy and radiation to preserve the bladder. This organ-preserving approach allows many patients to urinate normally rather than requiring surgical reconstruction for urinary function.

Principles of Radiation Management of Invasive Disease

For patients with stage Ta, T1, or Tis, external beam RT (EBRT) alone is rarely appropriate. For patients with recurrent Ta–T1 disease usually following BCG therapy but without extensive Tis who are not candidates for cystectomy, concurrent chemoradiotherapy may be considered as a potentially curative alternative to radical cystectomy, which is the standard treatment by NCCN guidelines.³

Treat the whole bladder with or without pelvic nodal radiotherapy at 39.6 Gy to 50.4 Gy using conventional or accelerated hyperfractionation. Elective treatment to the lymph nodes is optional and comorbidities of the patient should be considered as well as the risks of toxicity to the adjacent critical structures prior to treatment.

A boost can be considered of either the whole or partial bladder between 60 Gy to 70 Gy. For node-positive disease, consider boosting grossly involved nodes to the highest achievable dose that does not violate dose-volume histogram (DVH) parameters based on the clinical scenario. Reasonable alternatives to conventional fractionation include taking the whole bladder to 55 Gy in 20 fractions or using simultaneous integrated boosts to sites of gross disease. When irradiating the bladder only or bladder tumor boost, consider daily image guidance.

Concurrent chemoradiotherapy is recommended for added tumor cytotoxicity and can be given without significant increased toxicity over RT alone. Concurrent 5-FU and mitomycin C or low-dose gemcitabine can be used instead of cisplatin-containing regimens in patients with low or moderate renal function. Such therapy is optimally given by dedicated multidisciplinary teams.

Concurrent chemoradiotherapy (preferred) or RT alone should be considered as potentially curative therapy for medically inoperable patients. Concurrent chemoradiotherapy or RT alone should be considered for local palliation in patients with metastatic disease.

There is growing evidence that using a hypofractionated schedule in locoregional control using 55 Gy in 20 fractions over 4 weeks to treat patients with locally advanced bladder cancer was noninferior to a schedule of 64 Gy in 32 fractions over 6.5 weeks regarding both invasive locoregional control and toxicity.⁴

NCCN[®] also indicates “optimal candidates for bladder preservation with chemoradiotherapy include patients with tumors that present without hydronephrosis, are without concurrent extensive or multifocal Tis, and are <6 cm. Ideally, tumors should allow a visually complete or maximally debulking TURBT.”³

The Use of Radiation Therapy in the Postoperative Setting

Recent NCCN Guidelines[®] recommend consideration of postoperative pelvic radiation for patients with pT3/pT4 pN0-2 positive lymph nodes and/or positive surgical margins.³

Palliative Radiation Therapy

Recent NCCN guidelines recommend that palliative radiation should be given in the metastatic or recurrent setting. Hypofractionated regimens, that is, more than 2 Gy per fraction, are usually preferred for the convenience of patients.³

DEFINITIONS

- **Adjuvant radiation therapy** - Additional radiation therapy given after the primary treatment to lower the risk of cancer recurrence.
- **Brachytherapy (BT)** - Brachytherapy is a procedure that involves placing radioactive material inside your body. Brachytherapy is sometimes called internal radiation.
- **Definitive radiation** - radiation therapy used with curative intent.
- **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** - 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.
- **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 bladder cancer radiation treatments. Definitive radiation management patients receive concurrent chemotherapy. 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.

Bladder Cancer			
Definitive with or without Chemotherapy	Number of Fractions	Total Dose	Technique
		20	55 Gy
	22-35	39.6-70 Gy	IMRT, 3D, IGRT
Adjuvant (Post-operative)	25-35	45-70 Gy	IMRT, 3D, IGRT
Palliative	1-15	8-37.5 Gy	3D

REFERENCES

1. Radiation therapy for bladder cancer. American Cancer Society (ACS). <https://www.cancer.org/cancer/bladder-cancer/treating/radiation.html>. Accessed May 2, 2022.
2. Sanli O, Dobruch J, Knowles MA, et al. Bladder cancer. *Nat Rev Dis Primers*. 2017;3:17022. Published 2017 Apr 13.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer. (Version 1.2022). Available at https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. ©National Comprehensive Cancer Network, 2022.
4. Choudhury A, Porta N, Hall E, et al. Hypofractionated radiotherapy in locally advanced bladder cancer: an individual patient data meta-analysis of the BC2001 and BCON trials. *Lancet Oncol*. 2021;22(2):246.

Please see all related radiation therapy treatment policies for additional information on the treatment modalities. (3D-CRT, 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
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder

Code	Description
C67.9	Malignant neoplasm of bladder, unspecified
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:	5/5/2022, 5/13/2022, 5/16/2022, 5/18/2022, 5/31/2022, 7/20/2022,8/17/2022
3	Policy Revision Dates:	5/5/2022, 5/13/2022, 5/16/2022, 5/18/2022, 5/31/2022, 7/20/2022, 8/17/2022
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	5/18/2022, 5/31/2022, 8/31/2022
6	Revision Changes:	8/17/2022- Per NCCN, Minimum dosing for Adjuvant changed from 28 to 25 fx and from 50 Gy to 45 Gy Definitive dosing changed from 25-33 fx, 50-66 Gy to 22-35 fx, 39.6 Gy -70 Gy