Lung 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

Lung cancer has the highest prevalence of cancer deaths in the United States among both men and women. There are two major types of lung cancer: small cell and non-small cell. Non-small cell lung cancer is the most common type of lung cancer, with small cell appearing most often in heavy smokers.

Treatment options for lung cancer depend on the type and stage, with non-small cell treated with surgery, chemotherapy, radiation therapy (RT), and/or targeted therapy. Small cell lung cancer is usually treated with chemotherapy and RT. Although lung cancer is the deadliest type of cancer in the United States, it is only the second-most diagnosed cancer in both men and women.[1]

Radiotherapy is an important modality used for the treatment of lung cancer. Seventy-seven percent of all patients with lung cancer have an evidence-based indication for radiotherapy, although it is often underutilized. RT can be used as curative or palliative treatment across all stages of disease. Technological advances have allowed better RT targeting of tumors and reduced incidental irradiation of surrounding normal tissues. This has expanded the indications for RT in lung cancer and improved outcomes both in terms of increasing survival and reducing toxicity.[2]

Non-Small Cell Lung Cancer (NSCLC)

For NSCLC, radiation may be used as an adjunct to surgery. RT may also serve as definitive therapy in unresectable disease. For unresectable stage II and III disease, concurrent chemoradiotherapy is the standard of care. Determination of the appropriateness of RT should be made by radiation oncologists who perform lung cancer RT as a prominent part of their practice.

Radiation oncology input as part of a multidisciplinary evaluation or discussion should be provided for all patients with stage III NSCLC, with early-stage disease who are medically inoperable, who refuse surgery, or who are high-risk surgical candidates, and with stage IV disease that may benefit from local therapy.

Nonrandomized comparisons of using advanced technologies demonstrate reduced toxicity and improved survival versus older techniques. In a prospective trial of definitive/consolidative chemo/RT for patients with stage III NSCLC, IMRT was associated with a nearly 60% decrease (from 7.9% to 3.5%) in high-grade radiation pneumonitis and similar survival and tumor control outcomes. Therefore, IMRT is preferred over 3DCRT in this setting.[3]

General Treatment Information

Early-Stage NSCLC (Stage I, Selected Node-Negative Stage IIA)

SABR (also known as stereotactic body radiation therapy or SBRT) has achieved good primary tumor control rates and overall survival, higher than conventionally fractionated radiotherapy. Although SABR is not proven equivalent to lobectomy, some prospective series have demonstrated similar overall and cancer-specific survival.[3]

SABR is also an appropriate option for patients with high surgical risk (able to tolerate sublobar resection but not lobectomy, for example, age greater than or equal to 75 years, or poor lung function). More modestly hypofractionated or dose-intensified conventionally fractionated 3DCRT regimens are less preferred alternatives and may be considered if referral for SABR is not feasible. Close follow-up and salvage therapy for isolated and/or locoregional recurrence after SABR have been shown to improve overall survival in a large retrospective study. [3]

SABR is most commonly used for tumors up to 5 cm in size, though selected larger, isolated tumors can be treated safely if normal tissue constraints are respected. Prescription doses incompletely describe the actual delivered doses, which also strongly depend on how the dose is prescribed (to the isocenter vs. an isodose volume cover a proportion of the PTV), the degree of dose heterogeneity, whether the tissue density heterogeneity corrections are used, and the type of dose calculation algorithm. All of these must be considered when interpreting or emulating regimens from prior studies. [3]

Locally Advanced NSCLC (Stage II-III)

Concurrent chemotherapy/RT is recommended for patients with inoperable stage II (node-positive) and stage III NSCLC. Sequential chemotherapy/RT or RT alone is appropriate for frail patients unable to tolerate concurrent therapy. Accelerated RT regimens may be beneficial, particularly if concurrent chemotherapy would not be tolerated (that is, in sequential or RT-only approach).

Preoperative concurrent chemotherapy/RT is an option for patients with resectable stage IIIA (minimal N2 and treatable with lobectomy) NSCLC and is recommend for resectable superior sulcus tumors. RT should be planned in advance such that it continues to a definitive dose without interruption if the patient does not proceed to surgery as initially planned ("Non-Small Cell Lung Cancer," 2022). Preoperative chemotherapy and postoperative RT are an alternative for patients with resectable stage IIIA disease. The optimal timing of RT in trimodality therapy (preoperative with chemotherapy or postoperative) is not established and is controversial. [3]

The determination of resectability in trimodality therapy should be made prior to initiation of all treatment. Upfront multidisciplinary consultation is particularly important when considering surgical treatment for patients with stage III NSCLC. [3]

In patients with clinical stage I/II upstaged surgically to N2+, post-operative radiotherapy (PORT) appears to improve survival significantly as an adjunct to postoperative chemotherapy in non-randomized analyses. Although the optimal sequence is not established, PORT is generally administered after postoperative chemotherapy in parallel with chemotherapy for positive resection margins. [3]

Small Cell Lung Cancer (SCLC)

RT has a potential role in all stages of SCLC, as part of either definitive or palliative therapy. Radiation oncology input, as part of a multidisciplinary evaluation or discussion, should be provided for all patients early in the determination of the treatment strategy.[4]

General Treatment Information
Limited Stage
For limited-stage SCLC, the optimal dose and schedule of RT have not been established. Based on the randomized phase III trial, INT 0096, 45 Gy in 3 weeks (1.5 Gy twice daily [BID]) is superior (category 1) to 45 Gy in 5 weeks (1.8 Gy daily). When BID fractionation is used, there should be at least a 6-hour fractionation interval to allow repair of normal tissue.[4]

Retrospective and randomized phase II studies suggest that similarly accelerated dose of 40-42 Gy in three weeks but given in once-daily fractionation produced similar outcomes as 45 Gy in three weeks BID fractionation. If using once-daily conventionally fractionated RT, use higher doses of 66 Gy to 70 Gy. Two randomized phase II trials did not demonstrate superiority of 66 Gy in 6.5 weeks/2 Gy daily (the European CONVERT trial) or 70 Gy in 7 weeks/2 Gy daily (CALGB 30610/RTOG 0538) over 45 Gy in three weeks/1.5 Gy BID, but overall survival and toxicity were similar.[4]

Extensive Stage

Consolidative thoracic RT is beneficial for selected patients with extensive stage small cell lung cancer (ES-SCLC) with complete or good response to systemic therapy, especially with residual thoracic disease and low-bulk extra thoracic metastatic disease. Studies have demonstrated that consolidative thoracic RT up to definitive doses is well-tolerated, results in fewer symptomatic chest recurrences, and improved long-term survival in some patients.

Prophylactic Cranial Irradiation

In patients with limited stage small cell lung cancer (LS-SCLC) who have a good response to initial therapy. Prophylactic cranial irradiation (PCI) decreases brain metastases and increases overall survival.

In patients with ES-SCLC that have responded to systemic therapy, PCI decreases brain metastases. A randomized trial conducted by the EORTC found improved overall survival with PCI. However, a Japanese randomized trial found that in patients who had no brain metastases on baseline MRI, PCI did not improve overall survival compared with routine surveillance MRI and treatment of asymptomatic brain metastases upon detection. [4]

Surveillance imaging for brain metastases is recommended for all patients regardless of PCI status.[5]
The preferred dose for PCI to the whole brain is 25 Gy in 10 daily fractions. A shorter course (for example, 20 Gy in 5 fractions) may be appropriate in selected patients with extensive-stage disease. In a large, randomized trial (PCI 99-01), patients receiving a dose of 36 Gy had higher mortality and higher chronic neurotoxicity compared to patients treated with 25 Gy. [4]

DEFINITIONS

- **Brachytherapy (BT) -** Brachytherapy is a procedure that involves placing radioactive material inside your body. Brachytherapy is sometimes called internal radiation.
- **Definitive radiation treatment** – 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 is used to aim 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.
- **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.
- **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 lung 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.

Non-Small Cell Lung Cancer			
Early-Stage Lung Cancer (Node Negative)	**Number of Fractions**	**Total Dose**	**Technique**
	1-5	25-60 Gy	SBRT
	8-10	60-70 Gy	IMRT, 3D, IGRT
Definitive Radiotherapy with or without Chemotherapy	30-35	60-70 Gy	IMRT, 3D, IGRT
Preoperative Radiotherapy	25-30	45-54 Gy	IMRT, 3D, IGRT
Postoperative Radiotherapy	25-35	50-70 Gy	IMRT, 3D, IGRT
Palliative Radiotherapy	1-15	8-45 Gy	3D, IGRT

Small Cell Lung Cancer			
Limited Stage with or without Chemotherapy	**Number of Fractions**	**Total Dose**	**Technique**
	30 (delivered twice a day)	45 Gy	IMRT, 3D, IGRT
	28	45 Gy	IMRT, 3D, IGRT
	30-35	60-70 Gy	IMRT, 3D, IGRT
Extensive Stage	1-15	8-45 Gy	3D, IGRT
Prophylactic Cranial Radiation	5-10	20-30 Gy	IMRT, 3D, IGRT

REFERENCES

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2. Vinod SK, Hau E. Radiotherapy treatment for lung cancer: Current status and future directions. *Respirology*. 2020;25(S2):61-71.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer. (Version 3.2022). Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. ©National Comprehensive Cancer Network, 2022.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Small Cell Lung Cancer. (Version 2.2022). Available at https://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf. ©National Comprehensive Cancer Network, 2022.

5. Daly ME, Ismaila N, Decker RH, et al. Radiation Therapy for Small-Cell Lung Cancer: ASCO Guideline Endorsement of an ASTRO Guideline. *J Clin Oncol*. 2021;39(8):931-939.

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, 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 available through the AMA.

Code	Description
C34.00 - C34.92	Malignant neoplasm of bronchus and lung
C78.00 - C78.02	Secondary malignant neoplasm of lung
D02.20 - D02.22	Carcinoma in situ bronchus and lung
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, single treatment area, single port or parallel opposed ports, simple blocks or no blocks: 20 MeV or greater
G6007	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: up to 5 MeV
G6008	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: 6-10 MeV
G6009	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: 11-19 MeV
G6010	Radiation treatment delivery, 2 separate treatment areas, 3 or more ports on a single treatment area, use of multiple blocks: 20 MeV or greater
G6011	Radiation treatment delivery, 3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; up to 5 MeV
G6012	Radiation treatment delivery, 3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 6-10 MeV
G6013	Radiation treatment delivery, 3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 11-19 MeV
G6014	Radiation treatment delivery, 3 or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, electron beam; 20 MeV or greater
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
G0339	Image-guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session or first session of fractionated treatment
Z51.5	Encounter for palliative care

Code	Description
Z53.09	Surgery contraindicated
Z92.3	Personal history of irradiation

REVISION AND REVIEW HISTORY

No.	Description	Metadata
1	Original Effective Date:	5/2022
2	Policy Review Dates:	5/9/2022, 5/16/2022, 5/17/2022, 5/31/2022, 7/20/2022
3	Policy Revision Dates:	5/9/2022, 5/16/2022, 5/17/2022, 5/31/2022, 7/20/2022
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval:	5/17/2022, 5/31/2022
6	Revision Changes:	7/20/22- Prophylactic Cranial Irradiation- IMRT from 10 to 5-10 fractions and 25 Gy to 20-30 Gy