*Evolent	
Clinical guidelines: **SMALL CELL LUNG CANCER**	**Original Date: March 2011**
Radiation Oncology	**Last Revised Date: May 2023**
Guideline Number: Evolent_CG_123	**Implementation Date: January 2024**

GENERAL INFORMATION

- *It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.*
- *Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines and state/national recommendations.*

INDICATIONS FOR RADIATION THERAPY

Limited-Stage SCLC (T1-2, N1-N3 M0)[1]

- 2D or 3D Conformal Radiation Therapy (3DCRT)
- Two randomized phase III trials did not demonstrate superiority of 66 Gy in 6.5 weeks/2 Gy daily (the European CONVERT trial) or 70 G in 7 weeks/2 Gy daily (CALGB 30610/RTOG 0538) over 45 Gy in 3 weeks/1.5 Gy BID, but overall survival and toxicity were similar[2-4]

Dosage Guidelines:

  - Up to 30 fractions is medically necessary

Extensive-Stage SCLC (T any, N any, M1a/b)[1]

- Consolidative thoracic RT is beneficial for selected patients with ES-SCLC with complete response or good response to systemic therapy, especially with residual thoracic disease and low-bulk extrathoracic metastatic disease
- The Dutch CREST randomized trial of modest-dose thoracic RT (30 Gy in 10 fractions) in patients with ES-SCLC that responded to systemic therapy demonstrated significantly improved 2-year overall survival and 6-month progression-free survival. Benefit of consolidative thoracic RT is limited to the majority of patients who had residual thoracic disease after systemic therapy[5, 6]
- 2D or 3D Conformal Radiation Therapy (3DCRT) Radiation therapy to treat symptomatic sites or treatment of cord compression

Dosage Guidelines:

- 30 Gy in 10 daily fractions up to definitive dosing regimens in patients with a longer life expectancy.
- Up to 30 fractions is medically necessary

Prophylactic Cranial Irradiation (PCI)

- The benefit of PCI is unclear in patients who have undergone definitive therapy for very early LS-SCLC, i.e., pathologic stage I–IIA (T1–2, N0, M0)[7]
- However, PCI may have a benefit in patients who are found to have pathologic stage IIB or III SCLC after complete resection[7, 8]
- Routine PCI is not indicated for Extensive stage patients.
- PCI is not recommended in patients with poor performance status or impaired neurocognitive function[9]
- Brain MRI surveillance should be performed in patients not receiving PCI[7]

Hippocampal Sparing Intensity Modulated Radiation Therapy for PCI[1, 10, 11]
(Will be reviewed on a case-by-case basis)

- A phase III randomized trial of HA-WBRT versus conventional WBRT demonstrated improved cognitive preservation and patient-reported outcomes with HA-WBRT in patients with brain metastases from mixed histologies[10]
- For patients with a better prognosis (e.g., ≥4 months), hippocampal-sparing WBRT using IMRT plus memantine is preferred because it produces less cognitive function failure than conventional WBRT plus memantine[10]
- Hippocampal sparing whole brain IMRT (plus memantine) is considered medically necessary for individuals with all of the following:
  - Good performance status: ECOG rating is less than 3
  - Who have a prognosis of at least 4 months
  - No metastases within 5mm of the hippocampi
  - Have not had prior WBRT or external beam radiation to the brain
  - Do not have leptomeningeal disease

  2D or 3D Conformal Radiation Therapy (3DCRT) is indicated for in patients with poor performance status or impaired neurocognitive function.

  Dosage Guidelines
  - The preferred dose for PCI to the whole brain is 25 Gy in 10 daily fractions.

TREATMENT OPTIONS (to be reviewed on a case-by-case basis)

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 small cell lung cancer. 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**.** If IMRT is utilized, techniques to account for respiratory motion should be performed.

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.

Proton Beam Radiation Therapy

Proton beam is not an approved treatment option for small cell lung cancer. There are limited clinical studies comparing proton beam therapy to 3-D conformal radiation. Overall, studies have not shown clinical outcomes to be superior to conventional radiation therapy.

Stereotactic Body Radiation Therapy (SBRT)[1, 12-20]

SBRT is approvable for clinical stage I to IIA (T1-2,N0) Small Cell Lung Cancer who are medically inoperable or refuse surgery.

THE FOLLOWING APPLIES TO CMS (MEDICARE) MEMBERS ONLY:

For Proton Beam Radiation Therapy refer to Local Coverage Determination (LCD), if applicable.

BACKGROUND

The two major types of lung cancer are small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). SCLC differs significantly from NSCLC in that most patients with SCLC present with subclinical metastatic disease. Patients with SCLC are divided into those with limited- versus extensive-stage disease.[21] Although limited-stage disease is confined to the ipsilateral hemithorax, a third of these patients have subclinical systemic disease. Extensive-stage disease is defined as disease extending beyond the ipsilateral hemithorax, including positive pleural/pericardial effusion or distant metastases.[21] Systemic chemotherapy is an essential component of appropriate treatment for all SCLC patients, even those with limited-stage disease.

This guideline outlines methods suitable for the delivery of radiation therapy to treat SCLC. Radiation therapy may be delivered using conventional, accelerated fractionation, hyperfractionated regimens and prophylactic cranial irradiation. Three-dimensional conformal radiation therapy (3D-CRT) is the preferred technique. If image-guided radiation therapy is utilized, techniques to account for respiratory motion should be performed. The goal of this guideline is to guide diagnosis and treatment to the most efficient, comparatively effective, diagnostic and treatment pathway.

SCLC is highly sensitive to initial chemotherapy and radiation therapy; however, a cure is difficult to achieve because SCLC generally has a rapid doubling time, a high growth fraction, and early development of widespread metastases.

The treatment goal in patients with limited-stage disease is to achieve a cure with chemotherapy combined with thoracic radiation therapy. In patients with extensive-stage disease, this combined modality treatment does not improve survival compared with chemotherapy alone, but radiation therapy plays a role in palliation of symptoms. All patients with SCLC require systemic chemotherapy and where radiation therapy is utilized, it should be delivered concurrently with chemotherapy.[21] Patients with both limited- and extensive-stage disease may benefit from prophylactic cranial irradiation (PCI), decreasing the incidence of central nervous system metastases and prolonging survival. Two-dimensional, post lateral fields should be used in PCI treatment.

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POLICY HISTORY

Date	Summary
May 2023	• Added to Limited Stage SCLC: Two randomized phase III 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 3 weeks/1.5 Gy BID, but overall survival and toxicity were similar • Added to Extensive Stage SCLC: o Consolidative thoracic RT is beneficial for selected patients with ES-SCLC with complete response or good response to systemic therapy, especially with residual thoracic disease and low-bulk extrathoracic metastatic disease. o The Dutch CREST randomized trial of modest-dose thoracic RT (30 Gy in 10 fractions) in patients with ES-SCLC that responded to systemic therapy demonstrated significantly improved 2-year overall survival and 6-month progression-free survival. Benefit of consolidative thoracic RT is limited to the majority of patients who had residual thoracic disease after systemic therapy (17, 18). o Clarified/updated Dosage Guidelines under Extensive Stage SCLC • Added to PCI o The benefit of PCI is unclear in patients who have undergone definitive therapy for very early LS-SCLC, i.e., pathologic stage I–IIA (T1–2, N0, M0) o However, PCI may have a benefit in patients who are found to have pathologic stage IIB or III SCLC after complete resection o Routine PCI is not indicated for Extensive stage patients. o PCI is not recommended in patients with poor performance status or impaired neurocognitive function o Brain MRI surveillance should be performed in patients not receiving PCI • Moved Hippocampal sparing WBRT up under PCI • Clarified/updated Hippocampal sparing WBRT o A phase III randomized trial of HA-WBRT versus conventional WBRT demonstrated improved cognitive preservation and patient-reported outcomes with HA-WBRT in patients with brain metastases from mixed histologies o For patients with a better prognosis (e.g., ≥4 months), hippocampal-sparing WBRT using IMRT plus memantine is

	preferred because it produces less cognitive function failure than conventional WBRT plus memantine ○ Hippocampal sparing whole brain IMRT (plus memantine) is considered medically necessary for individuals with all of the following: (added "required physician review) ▪ Good performance status: ECOG rating is less than 3 ▪ Who have a prognosis of at least 4 months ▪ No metastases within 5mm of the hippocampi ▪ Have not had prior WBRT or external beam radiation to the brain ▪ Do not have leptomeningeal disease ○ 2D or 3D Conformal Radiation Therapy (3DCRT) is indicated for in patients with poor performance status or impaired neurocognitive function. • Deleted Additional Resources • Changed "Treatment options requiring physician review" to Treatment Options (will be reviewed on a case-by-case basis)
January 2022	• Added Hippocampal Sparing Intensity Modulated Radiation Therapy for PCI, including dosage guidelines • Updated SBRT as "approvable for clinical stage I to IIA (T1-2,N0) Small Cell Lung Cancer who are medically inoperable or refuse surgery" • Deleted "Stereotactic Body Radiation Therapy (SBRT) is not considered a standard form of treatment for SCL cancer. SBRT may be considered medically necessary to treat a previously irradiated field A request for SBRT will require a peer review to make a medical necessity determination."

Reviewed / Approved by Clinical Guideline Committee

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