INTRODUCTION:

Lung cancer is the leading cause of cancer-related deaths of both men and women in the United States. The World Health Organization divides lung cancer into two types: non-small cell lung cancer (NSCLC) as discussed in this guideline and small cell lung cancer (SCLC). The most common lung cancer, NSCLC, includes various histologies: squamous carcinoma, adenocarcinoma, and large cell carcinoma. These are grouped together for purposes of diagnosis, staging, prognosis, and treatment. In general, tissue diagnosis is used to classify patients into one of three groups reflecting the extent of the disease and the treatment approach: surgically resectable disease, locally and/or regionally advanced disease, and metastatic disease.

Surgery alone has been the standard treatment for patients with resectable NSCLC for many years. However, patients with completely resected disease have disappointing survival rates. In some cases, relapse occurs at distant sites which suggest that NSCLC may be a systemic disease when diagnosed. Chemotherapy and radiation therapy are now treatment considerations in both the preoperative and postoperative settings.

Prognosis and treatment of NSCLC are based on the staging of the cancer which documents the extent of cancer growth and spread. The initial goal of staging is to determine if the tumor is surgically resectable. Some patients with resectable disease may be cured by surgery while others, due to contraindications to surgery, may be candidates for radiation therapy for curative intent or for local control.

GOAL OF THE GUIDELINE:

This guideline outlines several methods suitable for the delivery of radiation therapy to treat lung cancer. These include the use of external beam radiation therapy such as three-dimensional conformal radiation therapy (3D-CRT), endobronchial brachytherapy, postoperative radiation therapy (PORT) and stereotactic body radiation (SBRT). Endobronchial brachytherapy and SBRT are aggressive approaches justified, in part, for non-resectable tumors. While these advances in treatment offer a range of regimens, the goal of this guideline is to guide diagnosis and treatment to the most efficient, comparatively effective, diagnostic and treatment pathway. With the exception of medically inoperable tumors and extreme palliative circumstances, radiation treatment is performed, in most cases, in conjunction with surgical intervention.

GENERAL CONSIDERATIONS:
Surgical resection is the preferred treatment for early stage NSCLC. Assessment of the patient’s overall medical condition, including pulmonary reserve, is important in considering the potential benefits of surgery, especially since an immediate post-operative mortality rate of 3% to 5% can be expected.

Radiation therapy with curative intent is an acceptable alternative to surgery for patients presenting with inoperable stage I and II disease. These patients may either be unable to tolerate a surgical resection or they may refuse surgery based on risk considerations. Patients with stage IIIA disease are a relatively heterogeneous group. Some patients present with resectable tumors and microscopic metastases to lymph nodes, while others present with bulky, unresectable local-regional disease. Therapeutic approaches require consideration of the extent of disease; radiation, surgery and chemotherapy in various combinations are considered for treatment. Subsets of patients have been reported with 5-year survivals of up to 25% Reported studies suggest that postoperative radiation therapy (PORT) may be associated with an increase in survival in patients with N2 nodal disease but not in patients with N0 and N1 nodal disease.

Patients with locally advanced, unresectable stage III disease may benefit from radiation therapy administered sequentially with chemotherapy. However, the combination of thoracic radiotherapy delivered concurrently with cisplatin-based chemotherapy has been shown to provide the greatest survival benefit.

Patients with stage II and stage III disease may present with Pancoast tumors that form at the extreme apex, in the superior sulcus of the lung. The tumors may invade pleura, chest wall, brachial plexus, subclavian vessels, and vertebral bodies. Treatment options for these patients include aggressive treatment for cure with a combination of preoperative radiation and surgical resection.

MEDICALLY NECESSARY INDICATIONS FOR RADIATION THERAPY AND TREATMENT OPTIONS:

- **Post Operative**
  - T1-2,N0 with margins positive
    - 3D-CRT +/- chemotherapy
  - T1-2,N1 or T3,N0
    - 3D-CRT + chemotherapy
  - T1-3,N2 or T3,N1
    - 3D-CRT + chemotherapy

- **Pre Operative**
  - T3-4, N0-N1 or Superior Sulcus Tumors
    - Preoperative 3D-CRT + concurrent chemotherapy
  - Stage IIA (T4,N0,M0 or T3-4N1,M0 or T1-3N2,M0)
    - 3D-CRT + concurrent chemotherapy followed by resection

- **Inoperable – Definitive**
  - Stage I disease (T1-2a,N0,M0)
    - 3D-CRT/chemoradiation
• Stereotactic body radiation therapy (SBRT) is an option for inoperable Stage I disease located in the peripheral lung. Typical dose fractionation schemes:
  - 30-34 Gy x 1 (< 2 cm tumor, > 1 cm from chest wall)
  - 15-20 Gy x 3 (< 5 cm tumor, > 1 cm from chest wall)
  - 12-12.5 Gy x 4-5 (< 5 cm tumor, < 1 cm from chest wall, < 2 cm from central structures)
  - 10-12 Gy x 5 (< 5 cm tumor, < 1 cm from chest wall, < 2 cm from proximal bronchial tree)
  - Stage II and Stage III disease (T2b-T4,N0,M0 or T1-4,N1-3,M0)
    - 3D-CRT/chemoradiation
  - Stage IIIA - locally advanced (T4,N0,M0 or T3-4,N1,M0 or T1-3,N2,M0)
    - 3D-CRT + concurrent chemotherapy

• Palliative Radiation Therapy
  - Stage IV
    - 3D External radiation as palliative therapy to relieve pain, airway or endobronchial obstruction, and other symptoms.
  - Post Operative Radiation Dose Guidelines (based on margin status)
    - Negative margins: 50-54 Gy
    - Gross positive margin: 60-70 Gy
    - Microscopic positive margin/extracapsular nodal extension: 54-60 Gy
  - Pre Operative Radiation Therapy Dosage Guidelines
    - 45-50 Gy
  - Definitive Radiation Therapy Guidelines
    - 60-74 Gy

  *Unless otherwise indicated standard radiation fractionation consists of 1.8 Gy to 2.0 Gy per day*

• Endobronchial Brachytherapy
  - Patients with primary tumors who are not otherwise candidates for surgical resection or externalbeam radiation therapy due to comorbidities or location of the tumor
  - Palliative therapy for airway obstruction or severe hemoptysis in patients with primary, metastatic, or recurrent tumors.

TREATMENT OPTIONS REQUIRING ADDITIONAL CLINICAL REVIEW:

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 non 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 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**
Stereotactic Body Radiation Therapy (SBRT) is not considered a standard form of treatment for NSCLC except for inoperable Stage I disease. Other requests for SBRT will require a peer review to make a medical necessity determination. Documentation from the radiation oncologist must include the clinical rationale for performing SBRT rather than 3-D conformal treatment.
REFERENCES:


Cerfolio RJ, Bryant AS, Jones VL, Cerfolio RM. Pulmonary resection after concurrent chemotherapy and high dose (60Gy) radiation for non-small cell lung cancer is safe and may provide increased survival. *Eur J Cardiothorac Surg* 2009: 35:718-723.


