# Bronchoscopic Therapies for Peripheral Lung Malignancies

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**KEYWORDS**

• Peripheral lung cancer • Bronchoscopy • Treatment • Ablation

**KEY POINTS**

- Guided bronchoscopy techniques allow for minimally invasive access to essentially the entire lung, providing a potential means to provide focal therapy for localized lung cancers.
- A variety of therapeutic ablation methods are in use for bronchoscopic treatment of central airway malignancies and percutaneous CT-guided interventions for peripheral lung cancer. These modalities are being adapted for use with guided bronchoscopy.
- Early studies of guided bronchoscopy ablation of early-stage lung cancers are promising but still investigational at this time.

## INTRODUCTION

The detection, diagnosis, and treatment of early lung cancer have been the focus of much recent attention in the medical literature, with good reason. Lung cancer has the second highest incidence of new cases and remains the most common cause of mortality from malignancy in the United States with an estimated 155,870 deaths in 2017. The Surveillance, Epidemiology, and End Results database shows that the 16% of lung cancers presenting as localized disease have the best 5-year relative survival of 55.6%. However, survival decreases dramatically to 28.9% for those with spread to regional lymph nodes and is far worse for metastatic disease.[1]

In an effort to identify early-stage lung cancer, the US Preventive Services Task Force recommends use of annual low-dose computed tomography (CT) screening in at-risk populations.[2] These and other similar professional society recommendations supporting screening with low-dose CT cite the 20.0% relative reduction in mortality from lung cancer and 6.7% all-cause mortality reduction demonstrated in the National Lung Screening Trial.[3] Because of efforts such as low-dose CT screening, the diagnosis of patients with early-stage lung cancer is likely to increase.

The current treatment paradigm for stage I and II non-small cell lung cancer (NSCLC) recommends surgical resection for patients without medical contraindications.[4] Lobectomy is the operative procedure of choice but, unfortunately, many patients may not tolerate surgery due to concurrent comorbidities or limited functional status. As a result, an ideal therapeutic option would be less invasive than surgical resection but with equitable outcomes.

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Recent advances in flexible bronchoscopy make this a potential method of accessing a parenchymal lung tumor and delivering a therapeutic intervention. Bronchoscopy has been long been used to treat malignant central airway obstructions and, more recently, therapeutic percutaneous transthoracic methods of tissue destruction are being used. These same methods of tissue destruction are now being used in conjunction with minimally invasive guided bronchoscopy techniques to directly treat peripheral lung tumors. Bronchoscopic therapies for peripheral lung malignancies remain experimental at this time. This article reviews therapeutic modalities currently under investigation or theorized to merit future evaluation (Table 1).

## GUIDED BRONCHOSCOPY AND ITS ROLE IN CURRENT TREATMENT PARADIGMS

Current recommendations for treatment of early-stage NSCLC include lobectomy with systematic lymph node evaluation, including mediastinal lymph node dissection for stage II disease.[4] Support for lobectomy stems from data demonstrating increased local recurrence with limited resection approaches compared with lobectomy.[5–7] However, surgical resection is not without inherent risks. Complication rates from lobectomy range from 1.6% to 2.3%; however, these rates increase many fold for patients with risk factors such as advanced age or concurrent pulmonary or cardiovascular disease.[8] As many as 25% of patients may not be able to undergo surgical resection due to other comorbid conditions.[9] In contrast, limited resection approaches have less impact on pulmonary function and quality of life.[10] Earlier studies demonstrated reduced survival with segmentectomy and wedgectomy compared with lobectomy; however, some subsequent retrospective studies suggest similar 5-year overall survival rates.[11–14] Although lobectomy remains the intervention of choice, it is possible that limited resection approaches may be able to offer similar overall survival with less impact on pulmonary function for high-risk surgical patients. However, all surgical interventions still subject patients to potential risk. Development of nonsurgical approaches may further limit complications or potentially be used in combination with other minimally invasive therapeutic interventions.

Historically, flexible bronchoscopy was limited in its ability to successfully and reliably navigate to peripheral lung lesions. Conventional diagnostic

**Table 1**
**Theoretic considerations for therapeutic methods**

| Therapy | Advantages | Disadvantages |
|---|---|---|
| Radiofrequency Ablation (RFA) | • Air limits damage to normal lung | • Heat sink effect from adjacent blood vessels |
| Microwave Ablation | • Generates a larger, more predictable ablation field than RFA<br>• Area of cell death not limited by heat sink effect from adjacent blood vessels | • Microwave ablation devices not yet tested in human trials |
| Photodynamic Therapy | • Minimal damage to surrounding normal tissue | • Limited light penetrance minimizes effectiveness for larger tumors<br>• Photosensitivity skin reactions |
| Brachytherapy | • Less radiation damage to surrounding tissue than with an external radiation source | • Repeated dosing requires leaving a delivery catheter in place |
| Vapor Ablation | • Rapid delivery of thermal energy to the target lung region | • Affects a larger region of lung parenchyma |
| Cryoablation | • Decreased damage to adjacent airways | • Effective freeze zone limits treatment of large lesions<br>• Heat sink effect from adjacent blood vessels |
| Direct Injection | • Can also target mediastinal lymph nodes<br>• Deliver higher concentrations of chemotherapeutics than systemic therapy | • Unclear toxicity of extravasated or spilled injectate |