

Endobronchial Ablative Therapies

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KEYWORDS

• Ablative therapy • Airway lesions • Endobronchial therapy • Bronchoscopy

KEY POINTS

- Patients with symptomatic airway lesions may receive significant clinical improvement after treatment with endobronchial ablative therapies.
- There are several airway ablative therapies—the choice of ablative technique depends on the lesion and the clinical situation.
- Blending ablative techniques together may enhance patient outcomes.
- Ablative techniques require additional training to master their use.
- Ablative techniques can be used with flexible and rigid bronchoscopy.

INTRODUCTION

A variety of benign and malignant diseases may result in endoluminal lesions. Depending on the extent and location of an endoluminal lesion, patients may exhibit significant symptoms of dyspnea, cough, postobstructive atelectasis, post-obstructive pleural effusion, and hemoptysis.^{1,2} Removing or decreasing the overall size of the endobronchial lesion may improve a patient's symptoms, quality of life, and life expectancy.¹⁻⁷ There are a variety of endobronchial ablative therapies available to treat endoluminal lesions.^{1,2} The choice among different endobronchial ablative therapies depends on the size of the lesion, location of the lesion, characteristics of the lesion, availability of the different therapies at the practicing institution, and the training and skill of the bronchoscopist.¹ Many of the different ablative therapies are blended together to provide additional benefit.⁸⁻¹⁰ This article presents a review of common endobronchial ablative therapies used in interventional pulmonology.

INDICATIONS AND CONTRAINDICATIONS FOR ENDOBRONCHIAL ABLATIVE THERAPIES

Endobronchial ablative therapies are indicated for endoluminal lesions, which are associated with a variety of respiratory symptoms (**Box 1**). Lesions that occupy more than 50% of the airway lumen and are associated with respiratory symptoms generally improve with ablation of the lesion.^{1,11} Lesions within the lumen of the airway can lead to a chronic cough due to airway irritation and ineffective mucociliary clearance.^{1,2} Altered mucociliary clearance can also lead to atelectasis and recurrent pneumonia. Endoluminal lesions can lead to abnormal airway physiology, resulting in ventilation and perfusion mismatching. Finally, lesions within the airway can be friable and associated with hemoptysis.¹²

There are few contraindications for ablation of abnormal endobronchial lesions (see **Box 1**). An absolute contraindication to endobronchial ablative therapies is the presence of extrinsic airway compression.^{1,11,12} A lesion that extrinsically

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Box 1**Indications and contraindications for endobronchial ablative therapies***Indications*

1. Lesion occupying greater than 50% of the airway with symptoms of dyspnea
2. Hemoptysis
3. Recurrent pneumonia
4. Intractable cough

Absolute contraindication

1. Extrinsic compression of airway^a

Relative contraindication

1. Inability to lower FiO_2 to less than 40%^b
2. Distal airway obstructions
3. Airway obstruction present for more than 4 weeks
4. Length of obstruction more than 4 cm^c

^a Brachytherapy can deliver radiotherapy to lesions externally compression the airway.

^b Laser, Electrocautery, and APC can be associated with airway fires, reducing the FiO_2 reduces this risk.

^c Brachytherapy can deliver radiotherapy to lesions longer than 4 cm.

compresses the airway cannot be addressed by most ablative technologies. Ablative techniques render therapy through a physical contact or interaction with the abnormal endoluminal tissue. Lesions that are associated with extrinsic airway compression of the airway lumen have normal endobronchial or endotracheal tissue. Brachytherapy is the only technique used to address lesions extrinsic to the airway.^{13,14} The field of radiation effect rendered by brachytherapy includes tissues up to and beyond 1 cm from the brachytherapy catheter.^{13,14}

Relative contraindications include distal airway obstructions, airway obstructions present for more than 4 weeks, obstructions longer than 4 cm, and patients who require more than 40% fraction of inspired oxygen (FiO_2) during bronchoscopy.¹¹ Obstructions in small distal airways may be futile to treat. The amount of functional lung distal to the point of obstruction may not warrant the risk associated with attempting to ablate a lesion in a distal airway.¹¹ The distal airway wall is thinner than larger proximal airways. The thinner airway wall is associated with an increased risk of airway perforation.

Atelectasis and lobar collapse due to airway obstructions that have been present for more than

4 weeks may not improve with the ablation of an endoluminal lesion.⁹ The pathophysiology behind persistent alveolar collapse and atelectasis after removal of an obstructing luminal lesion is not entirely known. It is assumed that prolonged alveolar collapse and atelectasis lead to loss of surfactant, abnormal mucus collection and inspissation, airway wall inflammation, and malacia, each of which contributes to the limited or no expansion of previously atelectatic lung tissue.

Long endoluminal airway lesions can be difficult to manage.¹¹ Extensive tumor debulking is associated with prolonged surgical times, increased risk of airway perforations, increased risk of bleeding, and residual airway wall malacia. When used alone, endobronchial ablative techniques are associated with poor outcomes and limited symptomatic improvement. Brachytherapy is a therapeutic option that may be beneficial for long or complicated airway lesions.^{13,14} Using ablative therapies with airway stenting and balloon bronchoplasty may provide a suitable treatment strategy to address long airway lesions while minimizing complications.^{10,12}

Endobronchial ablative therapies that generate heat, high temperatures, or electrical currents are associated with airway fires.^{1,12,15} To minimize the risk of airway fires, bronchoscopists should limit the inspired oxygen concentration to no more than 40% and extend the ablative device at least 4 mm to 5 mm from the end of the bronchoscope and at least 1 cm from the end of the endotracheal tube.^{11,12} To further limit the risk of airway fires, consideration could be given to the use of a rigid bronchoscope.

ENDOBONCHIAL ABLATIVE THERAPIES

There are several types of endobronchial ablative therapies available (**Table 1**). Commonly these therapies are divided into hot and cold therapies. Hot therapies refer to light amplification by simulated emission of radiation (laser), electrocautery, and argon plasma coagulation (APC). These therapies in general use some form of heat energy transfer to provide the therapeutic intervention. Cold therapy refers to the use of cryotherapy. Additional therapies that are not classified within a hot or cold category include brachytherapy and photodynamic therapy (PDT). Brachytherapy uses the placement of radioactive material within the airway to provide therapeutic benefit. PDT refers to the use of an infused photoporphyrin molecule that is taken up by malignant tumor cells and then activated during bronchoscopy using a light source at a specific wavelength. Each of these therapies has unique risks, benefits, and indications.

Table 1
Comparison of endobronchial ablative therapies

	Laser	Electrocautery	Argon Plasma Coagulation	Cryotherapy	Brachytherapy	Photodynamic
Time to improvement	Immediate	Immediate	Immediate to days	Days to weeks	Days to weeks	Days to weeks
Control of bleeding	Excellent	Excellent	Excellent	None	None	None
Tumor specific	No	No	No	No	Yes	Yes
Depth of penetration	Variable, dependent on power settings	Variable, dependent on power settings	3 mm	3 mm	Variable, dependent on radiation dose	3 mm
Expense	+++	+	++	++	++++	++++

The relative expense of each therapy is represented by “+” – one “+” correlates with the least expensive therapy whereas “++++” correlates with the most expensive therapy.

LASER

Laser therapy uses light energy transmitted through fibers to desiccate endoluminal tissue.^{1,12} There are several types of lasers (potassium titanyl phosphate, yttrium aluminum pevroskite, carbon dioxide, and Nd:YAG).¹ Each laser is unique in that each medium (for example, Nd:YAG) used for light generation emits light at a specific wavelength. Nd:YAG, potassium titanyl phosphate, and yttrium aluminum pevroskite lasers are commonly used during bronchoscopy given that they emit light energy transmitted through optical fibers.¹² Laser therapy is a commonly used endobronchial ablative therapy due to predictable tissue effects, precise area of treatment effect, rapid and immediate results, repeatability of treatments, and the ability to blend laser airway interventions with other airway interventions.^{11,16}

Laser therapy destroys tissue through thermal activity. Thermal activity is generated as a result of the transfer of light energy to tissue.^{1,11} Lasers are used in many different settings. Lasers are used to coagulate superficial bleeding lesions or to ablate endoluminal tissues.^{1,11,12} At low-power settings, lasers have a shallow effect and coagulate tissue.¹² At higher-power settings, lasers penetrate deeper and result in carbonization and vaporization of tissue.¹² In addition to modifying the power settings, bronchoscopists adjust the distance from the tip of the laser fiber to modify the effect at the level of the tissue.¹⁷ Holding the fiber 1 cm away from the lesion results in a shallow penetration whereas holding the fiber 3 mm to 4 mm away from the lesion results in deeper penetration. This variation in effect allows bronchoscopists to adjust the focus of the procedure according to the characteristics of the lesion and

may provide individualized treatments for different areas of the lesion.

Laser therapy provides a precise and effective treatment. Given the ability to carbonize and vaporize tissue, the effects of laser therapy are immediate.¹² The immediate effects often result in dramatic improvements in a patient's complaints or symptoms. The tissue surrounding the target tissue is also affected. There is some degree of heat transfer to adjacent tissues. The cells within the adjacent tissue absorb heat energy. The absorption of heat energy results in some degree of thermal injury and cell death of surrounding tissue. The adjacent thermal energy and cell death are responsible for the delayed effect of laser therapy. The delayed effects of laser therapy are seen 48 to 96 hours after the bronchoscopy and result in a further improvement in airway lumen size. **Fig. 1** depicts the use of laser ablative therapy in a malignant airway obstruction. In this case, the ablative technique was followed by the placement of a fully covered self-expandable metallic stent.

Electrocautery

Electrocautery uses the flow of electricity to generate heat. Electrical current flows from the probe into the target tissue adjacent to the tip of the probe. Heat generation occurs in target tissues given the differences in resistance.¹ The heat generation results in cell death. The effects of electrocautery depend on several variables, including the nature of the lesion, current waveform properties, and the power setting, machine mode, and type of probe used.^{1,12,18,19} The electrical current waveforms are adjusted to achieve different results. Waveforms with high frequency result in a cut mode whereas waveforms with a low

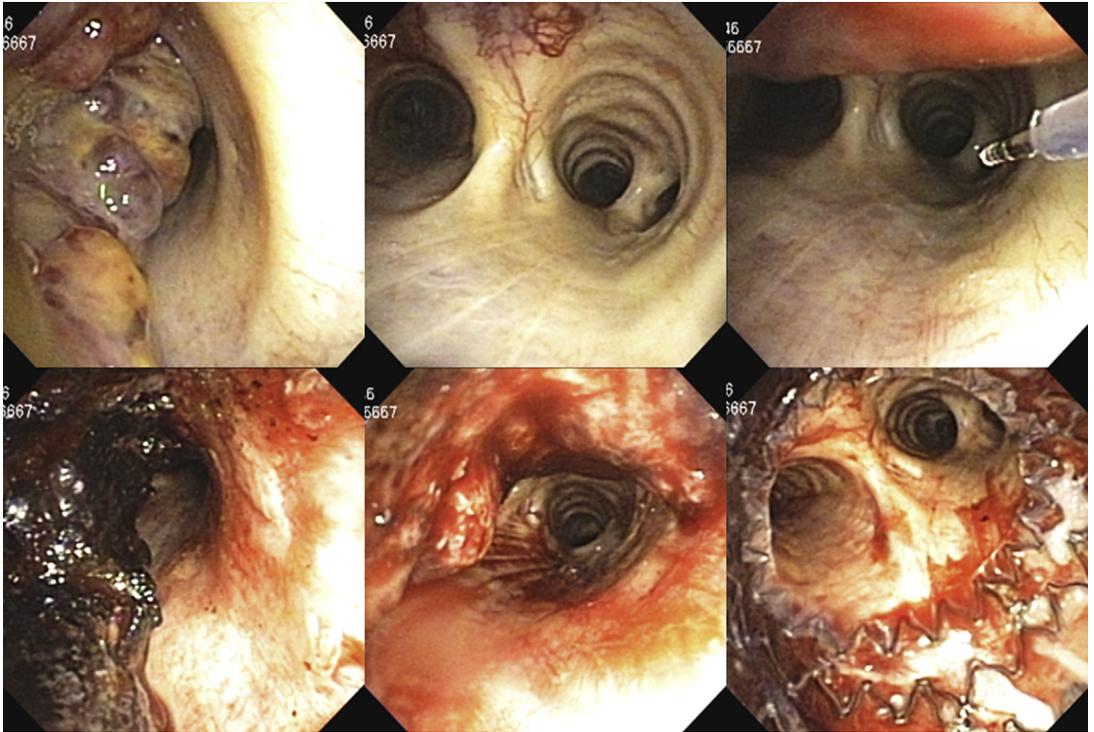


Fig. 1. This series of photos depicts the use of laser ablative therapy. The upper-left tile demonstrates a large malignant lesion in the midtrachea. The upper-middle tile depicts lower trachea and bilateral proximal mainstem bronchi that are free of malignant disease. The upper-right tile shows the laser fiber in the distal trachea. The lower-left tile depicts the midtrachea after laser ablation—note the large eschar. The lower-middle tile depicts the midtrachea after eschar débridement—note the significant improvement in airway patency. The lower-right tile depicts the midtrachea to low trachea after deployment of a fully covered self-expandable metallic stent. This is an example of blending therapies to maximize clinical benefit.

frequency result in a coagulation mode.^{18,19} The frequency is modified to achieve a blended effect. High-power settings vaporize and carbonize tissue whereas low-power settings are used for coagulation.^{12,18,19} Similarly, high-power settings penetrate deep into tissue whereas low-power settings have a shallow effect.^{18,19} Depending on the probe used, the treatment effect is precise or more diffuse. Electrocautery results in an immediate ablative effect due to tissue carbonization and vaporization.^{12,18,19} As with laser therapy, there is also a delayed effect. The delayed effect is due to the cytotoxic effect of heat generation in adjacent tissue. The cost associated with electrocautery is minimal because most health care centers have electrocautery machines available.^{19,20} In addition, the specialized probes and instruments can be purchased as needed, thereby decreasing lofty instrument fees.^{19,20}

There are many instruments available for use with electrocautery. Common instruments include a probe, snare, knife, and forceps. The variety of instruments allows for variability in addressing

endobronchial lesions.¹⁹ Given that most of the instruments require close proximity to the lesion treated, the probes tend to require frequent cleaning and lead to longer procedure times compared with laser therapy. **Fig. 2** depicts the use of an electrocautery knife and probe used to ablate a simple benign subglottic stenosis due to prolonged endotracheal intubation. **Fig. 3** depicts the use of an electrocautery snare and probe to remove and ablate an endobronchial lesion.

Argon Plasma Coagulation

APC works similarly to electrocautery.¹ APC uses argon gas as the medium through which the electrical current flows to the tissue treated.^{1,18,21} Argon gas emanates from a port on the tip of the APC catheter. The tip of the catheter has an electrode that generates an electrical current. When activated, electrical current flows from the tip of the catheter to the target tissue.

APC has superficial effects on tissue and is an excellent option for coagulation.^{1,12,18,21} Given



Fig. 2. The left tile depicts a narrow simple benign subglottic stenosis due to prolonged endotracheal intubation. The middle tile depicts the same lesion after electrocautery knife treatment. The incisions allow the tissue to relax and increase the size of the airway. The right tile depicts the same lesion treated with the electrocautery probe to remove the redundant stenotic tissue.

the shallow effects, it is not optimal for debulking endobronchial tissue because carbonization and vaporization are unlikely.¹¹ APC lacks precision because the argon gas emanates from the tip of the catheter and flows in all directions.^{11,12} This nonspecific spray of gas also allows for treating lesions in unusual locations or at right angles to the tip of the probe.¹⁸ As with laser and electrocautery, there is an immediate tissue ablative effect as well as a delayed cytotoxic effect of heat transmission.

Cryotherapy

Cryotherapy refers to the use of extreme cold to treat airway lesions.¹ Cryotherapy uses a special probe through which a rapidly expanding gas (nitrous oxide or liquid nitrogen are 2 gases that are commonly used) flows to the tip of the catheter and cools it to a temperature of -40°C .^{1,22} The

probe is applied to the target lesion (physical contact is made with the tissue) and cooled to its target temperature.^{1,22} Active cooling occurs for 30 to 60 seconds followed by a period of passive rewarming. The freeze-and-thaw cycle is repeated 2 to 3 times for maximal effect. The probe is then repositioned to treat adjacent areas.

Cryotherapy has several issues that make it less desirable than laser, electrocautery, or APC. Cryotherapy lacks precision, has a shallow treatment effect, and has no immediate effect.^{1,22} Malignant tissue is particularly sensitive to cryotherapy given the water content of malignant cells whereas cartilage and normal respiratory tissue tends to be resistant to cryotherapy.²² Maximal tissue destruction occurs 1 to 2 weeks after cryotherapy and requires repeat treatments to achieve the desired effect.²² In addition, cryotherapy is time consuming given the multiple repeat freeze-and-thaw cycles.



Fig. 3. The left tile depicts a polypoid mass lesion in the distal left mainstem bronchus. The middle tile depicts an electrocautery snare being placed over the polypoid mass lesion. The right tile depicts the distal left mainstem after removal of the polypoid lesion. The base of the polypoid lesion required treatment with the electrocautery probe. Patency was restored to the left mainstem.

Brachytherapy

Brachytherapy refers to the use of radiation to treat malignant lesions.¹ Typically, a bronchoscopy is performed and the target airways are identified. Then, a specialized catheter is inserted through the working channel of a standard flexible bronchoscope and placed under direct visualization or with the assistance of fluoroscopy or ultrasound.^{13,14,22} Depending on the type or location of the lesion, multiple catheters may be used.¹³ Once secured, radiation seeds are advanced through the catheter and into the desired location.^{13,22} Once the treatment has been rendered, the probe and seeds are removed.

Brachytherapy is not used for lesions that are associated with acute complaints of dyspnea.^{1,22} There are no immediate effects with radiation therapy.^{1,22} Maximal effect is seen several weeks after the treatment.²² Brachytherapy is generally used for long lesions growing into airways or lesions compressing the airways.^{13,14,22} High doses of radiotherapy are delivered to selected areas, allowing for excellent treatment response. In addition, it can be offered to patients who have already received maximal external beam radiation and who are not candidates for more conventional endobronchial ablative techniques such as laser, electrocautery, or photodynamic therapy.^{13,22} Brachytherapy is expensive and requires specialized facilities to render the treatments.

Photodynamic Therapy

PDT refers to the application of light energy to tissues that have been pretreated with a photosensitizer.^{1,11,22,23} Patients receive an intravenous injection of a photosensitization agent (such as Photofrin) 2 to 3 days before their planned bronchoscopy.^{22,23} The photosensitization agent is

taken up by actively metabolizing cells and to a higher degree by malignant tissues.^{22,23} A standard bronchoscope is then used to survey the airway and to advance the light probe into position.^{22,23} Once in position, the light probe is activated and emits light at a specific frequency to activate the photosensitizing agent.^{22,23} Once activated, the photosensitizing agent results in the generation of reactive oxygen species that damage cellular structures and leads to cell death.^{22,23} PDT does not result in immediate effects.^{1,11} The maximal effect is seen several days after PDT.^{22,23} Patients generally undergo repeat bronchoscopy 2 to 4 days after PDT treatment to remove sloughed tissue.^{22,23} PDT is repeated as necessary to reach deeper tissue as layers of malignant tissue are removed.^{22,23}

COMPLICATIONS OF ENDOBRONCHIAL ABLATIVE THERAPIES

Most complications are similar to those experienced with routine flexible bronchoscopy (**Table 2**). Rare complications of routine bronchoscopy, such as respiratory failure, myocardial infarction, cardiac arrhythmia, and death, may occur more frequently with these advanced techniques.^{15,16,24} The reason that the incidence may be increased is due to prolonged sedation given during the procedure and the need for decreased fractional inspired oxygen levels (in laser, electrocautery, and APC), which may allow transient or prolonged hypoxia during the procedure.^{15,16,24} In addition, each of the endobronchial ablative therapies has unique risks specifically related to the technology of the therapy.

Airway perforation is a potential complication related to laser, electrocautery, and, to a lesser extent, APC.^{1,11,12,15,16,24} These hot therapies immediately ablate and dissect tissue. With dissection

Table 2
Complications of endobronchial ablative therapies

Type of Endobronchial Therapy	Airway Perforation	Hemorrhage	Airway Fire	Air Embolism	Respiratory Failure	Myocardial Infarction, Arrhythmia	Death
Laser	Possible	Possible	Possible	Very rare	Possible	Rare	Very rare
Electrocautery	Possible	Possible	Possible	No	Possible	Rare	Very rare
APC	Unlikely	Unlikely	Possible	No	Possible	Rare	Very rare
Cryotherapy	No	No	No	No	Possible	Rare	Very rare
PDT	No	No	No	No	Possible	Rare	Very rare
Brachytherapy	No	Unlikely	No	No	Possible	Rare	Very rare

Rates of complication vary significantly among pulmonologists, airway centers, and patients. Precise estimates of risk are difficult to site as such qualitative estimates are commonly described.

into deeper levels of tissue or when the angle of the instrument is perpendicular to the airway wall, it is possible that the airway wall is perforated, leading to pneumomediastinum, pneumothorax, and hemorrhage. To reduce the risk of these severe complications, bronchoscopists should deploy the therapy parallel to the airway wall and frequently re-evaluate the tissue planes dissected to prevent dissection into deeper tissue or through the airway wall. Additionally, power settings, modes, or different instruments are used to minimize the depth of penetration and potentially reduce the risk of airway perforation.^{1,11,12} Cryotherapy, PDT, and brachytherapy are unlikely to cause airway perforation because they do not actively ablate tissue and do not dissect through the airway wall.²²

Endobronchial ablative therapies are commonly used to address bleeding endoluminal lesions; however, they also cause bleeding.^{1,12,15} Electrocautery and laser are excellent therapies to

address bleeding airway lesions; however, both of these therapies dissect through airway walls and into bronchial vessels, causing massive hemoptysis.^{11,15} Given the shallow effects of APC, it is unlikely to cause massive bleeding.^{1,18,21} Cryotherapy, PDT, and brachytherapy are unlikely to cause massive hemoptysis because they do not actively ablate or dissect through tissue.²² PDT and brachytherapy are associated with delayed hemoptysis due to mucosal tissue breakdown and ulceration as a result of the therapy.²²

Airway fires are a potentially catastrophic complication of laser, electrocautery, and APC ablative therapies. If high oxygen levels are present within the airway during activation of these technologies, the bronchoscope, endotracheal tube, or the tissue itself could be ignited.^{11,12} To limit this dreaded complication, oxygen concentration should be kept to below 40% and preferably below 30% as long as feasibly possible.^{11,12} If optimal oxygen levels cannot be

Box 2

Practical considerations of endobronchial ablative therapies

Hot therapies (laser, electrocautery, and APC)

- FiO_2 must stay below 40% to reduce the risk of airway fires.
- When advanced airways are needed, a laryngeal mask airway instead of an endotracheal tube should be considered to reduce the risk for airway fires.
- Using a rigid bronchoscope should be considered, when available and appropriate to the situation, to reduce the risk for airway fires.
- Ideal interventions often are associated with immediate clinical improvement.

Electrocautery and APC

- Due to the electrical current, caution should be used in patients with pacemakers.
- Wide array of specialized instruments that allow for unique interventions (for electrocautery).
- Electrocautery achieves similar results to laser and is more economical.

Cryotherapy

- Results are delayed.
- It is able to be performed with any inspired level of oxygen.
- It is time consuming.

Photodynamic therapy

- Associated with intense photosensitivity to sunlight.
- Results may take days to weeks.
- Repeat bronchoscopy is required to remove sloughed tissue.
- Applicable only in patients with tumors that have significant blood flow.

Brachytherapy

- Additional radiation may be delivered to areas that have received maximal external beam radiation.
- It can be delivered to long lesions or lesions that are external to and compressing the airway.
- It is expensive and requires special facilities.

achieved, then the procedure should be aborted and an alternate ablative technique used. In addition, the tip of the laser fiber or the electrocautery instrument should be at least 1 cm away from the end of the bronchoscope and several centimeters away from the endotracheal tube. Limiting the use of endotracheal tubes may reduce the risk of airway fires. Laryngeal mask airways, which remain above the vocal cords, provide excellent ventilation and control of the airway while limiting ignitable material in the airway. Finally, in high-risk airways, consideration is given to the use of a metallic rigid bronchoscope as an alternative to a flexible bronchoscope, thus further limiting the presence of ignitable material in the airway.

Air embolism is a rare complication of laser therapy. The cause is believed a result of bronchial wall blood vessel disruption in the setting of positive pressure ventilation and the use of a gas cooled laser fiber.^{25,26} Air embolism can result in cerebral infarction. This complication is limited by using noncontact laser fibers and non-gas-cooled fibers.^{25,26}

PRACTICAL CONSIDERATIONS OF ENDOBRONCHIAL ABLATIVE THERAPIES

Endobronchial ablative therapies are used to treat several malignant and nonmalignant airway lesions. Choosing among the different endobronchial ablative therapies can be difficult. Optimal therapy depends on the type of lesion, location of the lesion, whether a lesion is malignant or benign, amount of inspired oxygen needed to maintain safe oxygen saturations, availability of the ablative therapies, training and experience of the practitioner rendering the therapy, and whether immediate effects are desired (**Box 2**).

Laser and electrocautery result in immediate relief of airway stenosis and are commonly deployed in patients who have critical airway narrowing and require immediate intervention.^{12,19,20} These airway interventions are commonly used in conjunction with other advanced airway techniques (such as balloon bronchoplasty and stenting) to enhance airway patency and to improve the duration of effect.¹⁰ Although there are different technologies, they achieve similar results.^{19,20} In addition, electrocautery is more economical because most health care institutions have the necessary electrocautery device and are only required to purchase new probes or instruments.²⁰

Using endobronchial ablative therapies in practice requires additional training. Additional training

is necessary to determine the optimal therapy for patients as well as to use the therapy safely, limit complications, and manage complications if they occur. The knowledge gained through additional training maximizes patient benefit while reducing risks to patients.

SUMMARY

There are many endobronchial ablative therapies. Each endobronchial therapy is unique and has distinct risks and benefits associated with its use. Patients with endoluminal disease may receive significant benefit through endobronchial intervention, and patients with benign airway disease may receive lifelong relief. The choice of optimal endobronchial ablative therapy depends on several patient factors and technical issues. The decision to blend the ablative techniques with other airway interventions should be considered and depends on the clinical situation. Bronchoscopists using endobronchial ablative therapies should be experienced and well trained with the therapy used.

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