An update on advances in interventional bronchoscopy

October 01, 2006 | Lung Cancer [1]  
By David Tzeng, MD [2] and Andrew Chan, MD [3]  

Abstract: Because of recent advances, more patients may potentially benefit from a variety of interventional bronchoscopic techniques. Nd:YAG laser phototherapy is the most widely used modality and is the treatment of choice for patients with endobronchial malignancies who have large-central airway obstruction. Cryotherapy may be superior to Nd:YAG phototherapy for more distal airways lesions because of the lower risk of airway perforation, but it may be suboptimal for bulky airways disease that requires quick relief of obstruction. Brachytherapy relieves symptoms, such as cough, dyspnea, and hemoptysis, in many patients who have locally invasive airway malignancies. Endobronchial ultrasonography appears to be a safe and sensitive method for staging lung cancer. In select patients with emphysema, a 1-way endobronchial valve can be used to reduce lung volumes. Bronchial thermoplasty is being studied as a potential treatment for asthma. (J Respir Dis. 2006;27(10):415-428)

The role of interventional bronchoscopy continues to expand and now encompasses both malignant and some of the more common nonmalignant respiratory indications. It continues to play an integral part in the multimodality, multidisciplinary management of unresectable endobronchial tumors. In the case of primary lung cancer, such a multimodality approach may prolong survival. Shea and associates, for example, demonstrated improved survival in patients who had unresectable endobronchial squamous cell cancer. However, Cavaliere and Dumon have suggested that quality of life may be a more immediate and suitable criterion for assessing the value of an interventional bronchoscopic approach.

Recently, lung volume reduction using the endobronchial route has been described, with some promising--albeit early--findings. Endobronchial ultrasonography to guide transbronchial needle aspiration appears safe and can augment the diagnostic yield. In one study, bronchial thermoplasty resulted in reduction of airway smooth muscle mass, which may be of relevance in the treatment of asthma.

In this article, we review the following techniques in greater detail: Nd:YAG laser phototherapy, argon plasma coagulation and other electrocautery devices, photodynamic therapy, cryotherapy, stents and bronchoplasty, autofluorescence bronchoscopy, endobronchial ultrasonography, endobronchial lung volume reduction techniques, and bronchial thermoplasty. Nd:YAG laser phototherapy

Because 75% or more of patients with lung cancer have metastatic spread at the time of diagnosis, interventional bronchoscopy should be considered in patients who have endobronchial extension of their disease. These endobronchial tumors tend to be underdiagnosed, at least in part because fiberoptic bronchoscopy is not a routine procedure in patients who have lung metastases.

The unique properties of laser permit its use to heat the endobronchial tumor tissue, resulting in vaporization of or coagulation and hemostasis in this tissue. The Nd:YAG laser is currently the most widely used modality in interventional bronchoscopy.

Compared with the carbon dioxide laser, the Nd:YAG laser provides deeper tissue penetration (up to 5 mm), superior photocoagulation, and hemostasis. Although the carbon dioxide laser allows for greater precision, its use is hampered by a shallow tissue penetration of 0.5 mm and the requirement of a rigid bronchoscope. Furthermore, the wavelength of the carbon dioxide laser (10,600 nm) precludes its transmission via flexible quartz fiber, necessitating the use of a cumbersome articulated arm system.

The wavelength of the Nd:YAG laser (1064 nm) gives rise to its versatility. Because it is transmissible via a flexible quartz fiber, the Nd:YAG laser can be used via either a flexible or a rigid bronchoscope. While rigid bronchoscopy is superior to flexible bronchoscopy for proximal airway endobronchial lesions, flexible bronchoscopy is better for distal lesions. Nevertheless, rigid bronchoscopy remains the treatment of choice in patients with respiratory distress and severe endobronchial obstruction by bulky tumors.

Rigid bronchoscopy provides the added benefit of allowing simultaneous laser use and suctioning, a
significant advantage when dealing with vascular lesions, such as renal cell metastases. The bevel of the rigid bronchoscope can also be used to "core" a tumor. Unfortunately, only a minority of pulmonologists are trained in or familiar with its use.13

Local control of endobronchial tumors by bronchoscopic laser phototherapies can be highly successful. Some centers report a success rate of greater than 90%.14,15 Effective control is reduced in cases of peripheral lesions, concomitant extrinsic airway compression, and complete obstruction and as the duration of airway obstruction increases.14-16 In addition to the control of endobronchial lesions, Mantovani and colleagues37 reported improved quality of life in patients who had undergone laser therapy for palliative treatment of surgically unresectable or recurrent endobronchial lung cancer.

Complications resulting from Nd:YAG laser phototherapies include hemorrhage, pneumothorax, pneumomediastinum, airway perforation, cardiac arrhythmia, and myocardial infarction.12,14,15,18

Airway fire within the major airways is rare, with increased risk in patients with endotracheal tubes or silicone stents and in those receiving high fractions of inspired oxygen.11,19 **Photodynamic therapy**

The use of photodynamic therapy requires the intravenous infusion of photosensitizing agents that are preferentially retained in the tumor tissue for the treatment of malignant lesions. Tumor cell death from membrane injury and vascular damage results from the formation of singlet oxygen species20 subsequent to the activation of these drugs by light of an appropriate wavelength.21,22 Timing of light activation depends on the agent used. Bronchoscopic debridement of the necrotic tissue is necessary 1 to 2 days following activation.23 A variety of photosensitizing agents have been studied. However, the only agent currently approved by the FDA is porfimer sodium, which belongs to the family of porphyrin-based agents.24 Light application usually occurs between 48 and 72 hours after administration of this agent. Although the peak absorption of porfimer sodium is at 405 nm, a monochromatic light at 630 nm is used in photodynamic therapy, because this wavelength allows greater depth penetration.24

In a study of patients with microinvasive squamous cell carcinoma, Cortese and associates25 reported a 71% complete response rate using photodynamic therapy. This effect was sustained after 12 months in 52% of the patients. Kato and associates26 found response rates of 94% when target lesion lengths were less than 1 cm, but the response rates were only about 38% when the tumors were more than 2 cm in length.

Patients who undergo photodynamic therapy may experience increased light sensitivity for up to 6 weeks. Massive hemoptysis and formation of a tracheoesophageal fistula can result from extensive tumor necrosis.

While photodynamic therapy has been reported to be effective in the management of endobronchial malignancies, Nd:YAG remains the treatment of choice in patients who have obstruction of the large central airway.23,27,28 Nevertheless, photodynamic therapy may still play a role in patients who have inoperable endobronchial non-small-cell lung cancer. **Cryotherapy**

The development of a thin, flexible cryoprobe has allowed endobronchial malignancies to be managed via both rigid and flexible bronchoscopy.29 It is inexpensive to use, is safe, and does not have the risk of airway fires that is associated with laser phototherapies.30

Using cryotherapy, repeated cycles of freezing followed by thawing causes tumor cell death. Depending on whether nitrous oxide, carbon dioxide, or nitrogen is used, temperatures of 280°C to 2160°C are achieved at the probe tip (Figure 1). Cellular destruction of about 1 cm occurs via intracellular and extracellular crystallization and thrombosis.31

In 35 patients with early superficial bronchogenic carcinoma, Deygas and colleagues32 performed cryotherapy through a rigid bronchoscope. They achieved a complete response rate of 91% at 1 month and at 1 year. However, 28% of the patients had a recurrence at 4 years.32 Others have found a synergistic response using cryotherapy with external beam radiation33 and chemotherapy.34

Cryotherapy may be superior to Nd:YAG phototherapy for more distal airways lesions because of the lower risk of airway perforation.35 However, maximal effect requires 2 to 4 weeks of repeated procedures.36 As a result, cryotherapy may be suboptimal for bulky airways disease that requires quick relief of obstruction.37 Nevertheless, more recently, Hetzel and coworkers38 reported immediate success in at least partially relieving acute airway obstruction using a novel cryoprobe in 83% of patients. **Electrocoagulation techniques**

Selection of patients for electrocautery is similar to that for cryotherapy. Using high-frequency alternating current (10^5 to 10^7 Hz), the probe tip either coagulates, vaporizes, or resects the tumor depending on the amount of power used. In contrast to cryotherapy, maximal effect is achieved when minimal contact ("kissing" the probe to the lesion) is made between the probe and the tissue,
since this concentrates the conductance and thermal effects.\textsuperscript{38}

Argon plasma coagulation is a newer form of noncontact electrocoagulation.\textsuperscript{39} As the name implies, this modality uses ionized argon gas to transmit the electric current. Because of its noncontact nature, it offers the advantage of treating tumors at acute angles from the electrode tip (Figure 2). Morice and associates\textsuperscript{39} reported that argon plasma coagulation achieved complete control of hemoptysis and symptomatic improvement in all but 1 patient with endobronchial obstruction. Reichle and associates\textsuperscript{40} reported a 67% success rate in recanalizing obstructive lesions. Electrocautery devices are monopolar and thus require the patient, bronchoscope, and generator to be grounded to complete the circuit. Similar to laser phototherapy, electrocautery techniques carry a risk of airway fires. Other potential complications include hemorrhage and airway perforation, although argon plasma coagulation may offer more effective hemostasis.\textsuperscript{41}\textbf{Endobronchial stents and bronchoplasty}

The treatment of endobronchial stenosis by balloon dilatation can be performed via flexible or rigid bronchoscopy. Bronchoplasty can be performed independently or often as a precursor to endobronchial stent placement. Balloon pressures of 6 to 15 atm for 1 to 2 minutes are used to dilate the stenosed airway. A potential complication of bronchoplasty is tracheobronchial laceration or rupture, although this is rare. Effective management of airway stenoses often necessitates the placement of endobronchial stents in addition to bronchoplasty. Patient selection is important, because endobronchial stents are more effective in proximal lesions, such as tracheal or main-stem stenoses.\textsuperscript{41}

Currently, endobronchial stents are made of silicone, metal, or a combination of the two. Rigid bronchoscopy under general anesthesia is required for placement of silicone stents.\textsuperscript{15,42} In contrast, metal stents can be placed via flexible bronchoscopy. In a retrospective review of 11 patients who had undergone silicone stent placement for tracheal or main bronchial obstruction from inoperable esophageal cancer, Chan and associates\textsuperscript{43} reported that all patients had immediate relief of symptoms and 4 patients were successfully weaned from mechanical ventilation. Hsu and colleagues\textsuperscript{44} reported symptom relief in all 12 patients who underwent stent placement with self-expandable metal stents. Nine of the patients had stent placement for malignant airway obstruction; 2, for benign airways obstruction; and 1, for a tracheoesophageal fistula associated with esophageal cancer. They reported that 5 patients died during follow-up, with a median survival of 44 days; the remaining 6 patients survived after 23 weeks.\textsuperscript{44}

Although most stents are well tolerated, complications can occur in up to 25% of cases\textsuperscript{45} and include stent migration, granulation tissue buildup, airway wall perforation, or stent fracture. Erosion through the tracheobronchial wall resulting in massive hemorrhage can also occur.\textsuperscript{46} During a 1-year follow-up, Madden and associates\textsuperscript{47} found that halitosis affected 5 of 15 patients who had undergone expandable metal stent placement for various pathologies. When performing Nd:YAG laser phototherapy on patients who have silicone stents, particular care should be taken to reduce the risk of airway fire. Scherer\textsuperscript{48} found that maintaining oxygen concentrations of less than 40% minimized this risk.\textbf{Brachytherapy}

Endobronchial radiation therapy, or brachytherapy, is used to treat locally invasive airway malignancies. When used in patients who have received maximal doses of external beam radiation, this palliative procedure allows localized endoluminal delivery of radiation of about 3000 rads. Under the guidance of flexible bronchoscopy, the afterloading catheter is placed into the lumen of the endobronchial lesion. Both low-dose (less than 2 Gy/h) and high-dose (more than 10 Gy/h) radiation use \textsuperscript{192}Ir.\textsuperscript{41}

Brachytherapy is effective in relieving symptoms, such as cough, dyspnea, and hemoptysis, in 50% to 100% of patients.\textsuperscript{49,50} Escobar-Sacristán and colleagues\textsuperscript{51} reported that 85% of symptoms resolved after brachytherapy in patients with inoperable malignant endobronchial tumor or residual bronchial surface tumor after surgical resection. Complete endoscopic response, characterized as tumor disappearance and negative biopsy result, was achieved in 57% of the patients.\textsuperscript{51}

In patients with inoperable non-small-cell lung cancer, Mantz and associates\textsuperscript{52} found improved local disease control at 5 years using combined brachytherapy and external beam radiation compared with external beam radiation alone (58% vs 32%). This benefit was seen in patients with T1 or T2 disease.\textsuperscript{52} When high-dose brachytherapy was used at the time of endobronchial wall stenting, Allison and colleagues\textsuperscript{53} found rapid improvement in Karnofsky status in 10 patients at 1 week postprocedure.

The potential complications of brachytherapy include hemoptysis and fistula formation.\textsuperscript{54} High-dose brachytherapy appears to increase the risk of hemoptysis.\textsuperscript{55}\textbf{Autofluorescence bronchoscopy}
Lung carcinoma in situ generally has an excellent prognosis, and recognition at this stage could improve survival.\textsuperscript{56} Autofluorescence bronchoscopy potentially allows earlier detection using light-induced fluorescence. Endobronchial lesions as small as 1 mm\textsuperscript{3} can be detected.\textsuperscript{27} While porfimer sodium can also be used for tumor localization, autofluorescence bronchoscopy offers several advantages. In addition to lower costs, autofluorescence bronchoscopy is not associated with the adverse effect of skin photosensitivity and does not require a waiting period between drug administration and bronchoscopy. Using light in the blue or violet range (405 to 442 nm), malignant bronchial tissue has reduced fluorescence intensity at least 10-fold.\textsuperscript{27} However, autofluorescence bronchoscopy currently remains a research tool for which further data are needed to assess its usefulness in diagnosing early lung carcinoma and its effect on mortality. \textbf{Endobronchial ultrasonography}

This modality has been widely available for more than 5 years and consists of 2 main techniques: the miniprobe and the transbronchial needle aspiration/endobronchial ultrasound bronchoscope (EBUS). Miniaturized ultrasound probes can now be inserted through the 2.8-mm working channel of a bronchoscope. The probe tip consists of a rotating piezoelectric crystal within a water-filled balloon. As the latter is inflated, a 360-degree view of the airway is obtained. The standard frequency of EBUS is 20 MHz, with the crystal acting as both a signal generator and a receiver. The penetration depth at this frequency is about 4 to 5 cm, with a resolution of less than 1 mm.\textsuperscript{57} Not only does EBUS visualize airway wall layers well, but it can also be used to guide biopsy of mediastinal and hilar lymph nodes and peripheral lung lesions. Paone and associates\textsuperscript{58} found a sensitivity of 0.79 in patients with lung cancer who underwent EBUS and transbronchial biopsy, compared with 0.55 in those who underwent transbronchial biopsy alone. The accuracy was 0.85 and 0.69, respectively. In lesions smaller than 3 cm, transbronchial biopsy sensitivity and accuracy declined to 0.31 and 0.5, respectively, while EBUS with transbronchial biopsy maintained a sensitivity of 0.75 and an accuracy of 0.83.

The use of EBUS-guided transbronchial needle aspiration significantly increased the yield of transbronchial needle aspiration in all lymph node stations except in the subcarinal region. The overall success rate was 86\%,\textsuperscript{59} irrespective of lymph node size or location. EBUS with transbronchial needle aspiration appears to be a safe and sensitive method for staging lung cancer. It can potentially spare invasive staging procedures that may affect patient management\textsuperscript{60} and, possibly, health care economics.

EBUS also appears to be more sensitive than CT scanning of the chest in detecting tumor invasion in the airway wall.\textsuperscript{61} Herth and colleagues\textsuperscript{62} found that no fatal hemoptysis occurred during the use of thermal ablation techniques, because EBUS allowed the visualization intraoperatively of adjacent blood vessels.\textsuperscript{57} \textbf{Endobronchial lung volume reduction techniques}

Interventional bronchoscopy may now benefit patients with emphysema. In select patients with heterogeneous disease, lung volumes may be reduced via the blockage of targeted airways with 1-way, endoscopically placed endobronchial valves (Figure 3). Such valves prevent air from entering the target area of the lung but allow air and distal bronchial secretions to escape, with the intent of promoting collapse at the target site.\textsuperscript{63,64} This process may reduce both hyperinflation and dead space and may improve ventilation-perfusion matching by allowing expansion of previously compressed, less damaged regions of lung.\textsuperscript{65} This procedure appears to be relatively safe, but complications include pneumothorax, exacerbation of chronic obstructive pulmonary disease, pneumonia, and hemoptysis.\textsuperscript{63,65}

Up to one third of patients have shown improvement in lung function and quality of life.\textsuperscript{63} In a multicenter report, Wan and colleagues\textsuperscript{66} showed significant increases in forced expiratory volume in 1 second, forced vital capacity, and 6-minute walk tests and a significant decrease in residual volume in patients with emphysema who underwent endobronchial lung volume reduction. Unilaterally treated patients tended to show greater improvement than bilaterally treated ones. A further clinical trial for this experimental procedure is now under way. Patients who have homogeneous emphysema, however, may benefit from the experimental use of a radiofrequency catheter placed endoscopically to create extra-anatomic bronchopulmonary passages. This is followed by the insertion of an expandable stent through each passage. This procedure may improve expiratory flow and thus reduce dynamic hyperinflation.\textsuperscript{67} Further investigations continue regarding this technique. \textbf{Bronchial thermoplasty}

The delivery of controlled therapeutic radiofrequency to the airways causes coagulation of bronchial tissue and can reduce the amount of airways smooth muscle in its wall.\textsuperscript{68} It appears to be well-tolerated, with no significant adverse events occurring acutely or during a 20-day follow-up.\textsuperscript{8,69} Such a procedure may benefit select patients with asthma and promote a sustained reduction in
airway responsiveness to methacholine. For example, Cox and colleagues demonstrated that bronchial thermoplasty resulted in significant improvement in airway responsiveness that persisted for at least 2 years. This new approach for the treatment of asthma appears to have significant potential, and the results of further studies are awaited.

References: REFERENCES


Source URL: http://www.cancernetwork.com/update-advances-interventional-bronchoscopy

Links:
[2] http://www.cancernetwork.com/authors/david-tzeng-md
[3] http://www.cancernetwork.com/authors/andrew-chan-md