Endobronchial management of central cancers

F.J.F. Herth

Most of the estimated 215,020 new cases of lung cancer diagnosed in the USA in the year 2008 will be in an advanced stage [1]. More than 50% of these patients will have involvement of the central airways [2]. This can be in the form of bulky endobronchial disease, endobronchial extension or extrinsic compression of the airways by the tumour or by lymphadenopathy. Many of these patients have respiratory symptoms due to their disease. Shortness of breath, haemoptysis and cough are often the complaints that bring patients to a physician and to the complex treatment programmes currently used for the management of lung cancer. Some of these patients may benefit from endobronchial intervention as part of the management of their disease [3].

Standard management techniques of lung cancer (surgery, radiation therapy and chemotherapy) measure treatment response, 5-yr survival and recurrence rates. When treating endobronchial disease, the concepts of symptom-free survival, dyspnoea indices and quality-of-life scores also need to be evaluated. Obstruction of the central airways (trachea and mainstem bronchi) can cause worrisome symptoms such as dyspnoea, cough and haemoptysis and, when significant (>50% obstruction), cannot be tolerated for any length of time. This may be either intrinsic or extrinsic to the airway [3].

Some patients become incapacitated by their symptoms of dyspnoea. Many studies not only demonstrate improvement in clinical symptoms and quality of life, but also suggest increased overall survival with the use of endobronchial management techniques [4–8].

Not all endobronchial disease causes complete obstruction of the airways. Sometimes patients have partial obstruction, which often has a less severe symptom complex. As these patients enter treatment programmes, the endobronchial component of their disease, in response to these treatments, can lead to more complicated concerns. External-beam radiotherapy can induce endobronchial inflammation and swelling, further compromising the airways. Radiation or chemotherapy can lead to necrosis of the endobronchial component of the cancer. The inflammation and necrotic tissue can cause further airway compromise by inducing airway obstruction, lung collapse and possible post-obstructive pneumonia. Therefore, endobronchial techniques should be considered throughout the management of lung cancer patients [7, 8].

Lastly, when all management options have been used, end-stage patients will often develop compromise of their airways as the cancer continues to progress. Endobronchial management options may help to relieve some of their symptoms, allowing them freedom from shortness of breath as they go home, in conjunction with hospice or other palliative therapies [3, 9, 10].

Most endobronchial techniques are performed on an outpatient basis. Unless a patient presents with respiratory failure, many of the procedures performed provide
immediate relief of symptoms. This rapid symptomatic improvement allows patients to return home with an improved quality of life or better prepares them to continue treatment at their local programmes. Although interventional procedures are not definitive therapies, they often provide partial to total relief of the strangling sensation produced by complete airway occlusion.

Interventional pulmonary programmes that include endobronchial procedures need an armamentarium of therapeutic modalities rather than a single invasive approach to manage patients with complicated lung cancer. As each patient’s anatomy differs, the manner in which the patient’s cancer leads to symptoms varies. Several procedures used in conjunction (e.g. laser and stenting) may be necessary to provide the most efficacious management of the disease. Offering a multitude of modalities allows the best selection of approaches for the patient [7, 8].

The following sections discuss a variety of techniques and tools available to the interventionalist. In many cases, no one technique is better than the others and some combination of these techniques often offers the greatest benefit to the patient. The current author suggests that patients with central airway obstruction be managed by specialised centres that offer multiple modalities of therapy and where experts from multiple specialties work as a team [7–9].

Bronchoscopy

Since the inception of flexible fibreoptic bronchoscopy in the late 1960s in Japan and in 1970 in the USA, the flexible bronchoscope has become the most widespread tool for evaluating and diagnosing diseases of the airways and lungs [11]. The rigid bronchoscope, the flexible bronchoscope’s predecessor, was in many regards forgotten as a tool until interventional pulmonology evolved in the 1980s. Interventional pulmonologists re-evaluated this tool and found its properties advantageous to the procedures that are currently performed. A survey in 1991 by the American College of Chest Physicians reported that only 8% of responding pulmonologists used a rigid bronchoscope [12].

Overall, the concurrent use of the flexible bronchoscope with the rigid bronchoscope is necessary for the practice of interventional pulmonology. The rigid bronchoscope offers many advantages to the interventional pulmonologist, one of which is the superior control of the airway achieved with its use. Ventilation is performed through the scope itself rather than around the flexible bronchoscope. The larger-bore rigid bronchoscopes allow optical systems, large calibre suction catheters and the laser to pass through the scope simultaneously. Large biopsy forceps are used through the rigid bronchoscope, which can provide more significant tissue biopsies as well as assist in mechanical debulking of lesions. However, the rigid bronchoscope is a more difficult tool to use, which requires additional training. In addition, rigid bronchoscopy is most commonly performed in the operating room with general anaesthesia. Overall, in difficult airway conditions, rigid bronchoscopy is an excellent technique for the management of endobronchial disease [3, 10].

The rigid bronchoscope itself can be used as a tool in the management of endobronchial disease (fig. 1). The distal end of the bronchoscope has a bevelled end. This edge can be used to shear large sections of endobronchial tumour away from the airway wall in a technique often referred to as coring out. In a report on 56 patients with endobronchial obstruction from the trachea to the distal mainstem bronchi, MATHISEN and GRILLO [13] described improvement in 90% of their patients. Only three out of the 56 patients had more than minor bleeding with this procedure. Although this procedure
is technically difficult, coring out combined with the use of larger biopsy forceps allows tumour to be quickly resected from the obstructed airway.

**Functional evaluation in interventional bronchoscopy**

As interventional bronchoscopy moves towards becoming a specialty in its own right, it is essential that global leaders in the field work together to develop standard approaches to the pre-interventional evaluation. These tests and procedures will allow better selection of patients for particular interventions and, potentially, better predictions of outcomes.

In addition, standard protocols, decision trees and management algorithms need to be developed and investigated as they pertain to many post-intervention issues. Studies of outcome measures, in addition to survival, should be well designed and implemented so that practitioners can further justify the performance of these expensive but often life-saving procedures to hospital administrators who are often unwilling to invest in the necessary equipment, as well as to physician groups and third-party payers who may be reluctant to approve patient referrals because of cost-of-care concerns.

**Mechanical removal of obstruction**

In cases of life-threatening central airway obstruction, rapid mechanical resection of intraluminal, exophytic tumour tissue by rigid bronchoscopy “curettage” and/or forceps resection is a well established technique [10, 14] (fig. 2). Provided functional lung parenchyma can be recruited and the pulmonary artery is open, this procedure may provide instant relief. However, because bleeding is inevitable, which may compromise gas exchange, coagulation methods should be applied prior to mechanical removal. Neodymium:yttrium-aluminium-garnet (Nd:YAG) laser, electrocautery, cryotherapy or other techniques may be used for this purpose. Immediate haemostasis can often be obtained by mechanical airway wall compression using the rigid bronchoscope shaft.

---

Fig. 1. – Different types of rigid scopes and lenses.
Laser therapy

Laser, an acronym coined from light amplification by stimulated emission of radiation, has many medical uses, including the endobronchial management of lung cancer. Several laser types are currently used within the bronchi: Nd:YAG, potassium-titanyl-phosphate (KTP) and carbon dioxide (CO₂). The most common laser used endoscopically is the Nd:YAG, which delivers energy at a wavelength of 1,064 nm. The laser energy can be conducted via a quartz monofilament and, thus, can be easily used with either the rigid or flexible bronchoscope. Normally, Nd:YAG is used at 30–60 W, but it has a wide range of power outputs, up to 100 W. Depending on the energy level used, the laser can affect tissue several millimetres to several centimetres in depth [15].

The predominant tissue effects of Nd:YAG lasers are thermal necrosis and photocoagulation. Thermal necrosis uses higher energy levels to destroy tissue. The problem with this approach is the significant vascularity of most lung cancers. In destroying tissue with laser energy, large blood vessels can also be destroyed. These blood vessels can be perforated with the tissue destruction, leading to significant haemorrhage and an increase rather than a decrease in morbidity and mortality with this procedure.

The most commonly used effect of laser energy is photocoagulation. Using lower energy levels, the surface of the tumour is heated, causing shrinkage of the tumour and diminishing the blood flow to that region. By devascularising the tumour, more rapid mechanical debulking can be performed with improved control of bleeding.

Laser therapy can be performed via either flexible or rigid bronchoscopy (fig. 3). The majority of interventionalists use rigid bronchoscopy as the predominant tool for the performance of laser procedures when possible. Nd:YAG laser fibres can be passed through the working channel of most flexible bronchoscopes. Using the flexible bronchoscope, laser energy can be delivered to areas that cannot be reached with the rigid bronchoscope [16, 17].

The reported success rate of symptom palliation using laser energy in the endobronchial management of lung cancer is high. Reports of clinical improvement rates range 84–92% following laser bronchoscopy [18–20]. Brutinel et al. [21] compared 25 historical controls (i.e. patients who would have been candidates for laser management but did not receive it due to the unavailability of the procedure at
the time of their management) with 71 patients treated with laser bronchoscopy as part of the treatment programme. The authors reported 76 and 100% mortality rates at 4 and 7 months, respectively, in the control population. In the group treated with laser bronchoscopy, survival rates at 7 months and 1 yr were 60 and 28%, respectively. Although no definitive randomised studies are available, review of historical studies would suggest improved survival in patients treated with endobronchial techniques.

**Cryotherapy**

Cryotherapy is another modality for the endobronchial destruction of malignant tissue that obstructs the tracheobronchial tree. This technique uses cold instead of the heat used in laser-based technologies. A probe is placed onto or into an obstructing tumour mass. Liquid nitrogen (-196°C) or nitrous oxide (-80°C) cools the probe tip when performing cryotherapy. This tissue freezing leads to the destruction of all cells in an area of ~1 cm in diameter around the probe tip. Vascular thrombosis occurs with the super-cooling of tissue, minimising the bleeding during resection of the tumour.

The limiting factor to using cryotherapy is that the tissues destroyed with the freezing procedure take time to die and necrose. This requires returning to the lesion to remove the necrosed arterial and, in some cases, repeating treatments. Although cryotherapy is effective at tumour destruction and management, the necessity of repeated procedures makes this a more time-consuming procedure to perform, limiting its usefulness in management of bulky endobronchial disease [22, 23].

**Electrocautery**

In recent years, the use of electrocautery to treat endobronchial obstruction of central airways has become more popular because the equipment is much less expensive than laser, is available in most hospitals, and the electrocautery probes can be passed through rigid or flexible bronchoscopes. Sutedja et al. [24] reported 17 patients with central airway obstruction treated with electrocautery *via* a flexible bronchoscope. 15 of the 17 patients had an immediate reopening of the airway. Although physiological parameters
did not improve in 11 patients, airway calibre >75% normal was achieved and dyspnoea was relieved. Haemoptysis was also effectively palliated. There were no deaths in this series. The authors comment on the simplicity of the technique and the ability of electrocautery to produce rapid palliation and immediate tumour debulking. VAN BOXEM et al. [25] described the tissue effects of bronchoscopic electrocautery and showed that this technique can produce superficial airway damage but also has the potential of damaging deeper cartilaginous layers. The amount of damage seems to correlate with the duration of the coagulation therapy. COULTER and MEHTA [26] also found excellent success rates of 89% in a series of 38 patients who underwent 47 endobronchial electrocautery procedures using flexible bronchoscopy. These authors state that endobronchial electrosurgery has the potential of eliminating the need for laser photo resection in more than one third of patients presenting with central airway obstruction.

The argon plasma coagulator (APC) is a variant of endobronchial electrocautery that uses argon gas passed through a small catheter to act as an electrical conducting medium. This is a noncontact technique that has excellent coagulation properties. The APC machine is much less expensive to purchase than a laser. It has been used to relieve endobronchial obstruction with good results. The instrument is particularly helpful for the palliation of haemoptysis and is said to be relatively safe when treating granulation tissue around airway stents. MORICE et al. [27] achieved 100% palliation of haemoptysis in cancer patients using the APC. Patients presenting with airway obstruction had improvement in the degree of airway lumen obstruction, decreasing from a pretreatment average obstruction of 76 ± 24.9% to 18.4 ± 22.1% after APC debulking using flexible bronchoscopy. FREITAG and REICH [28] recently reviewed their experience with the APC and state that APC is the instrument of choice for treating haemoptysis from lesions visible by bronchoscopy.

Endobronchial prosthesis

Endobronchial prosthesis involves stents, which can be used in several clinical situations: intrinsic, extrinsic or mixed endobronchial obstruction. Stents work well in conjunction with other modalities, such as laser and mechanical debulking of tumours. Currently, stents are composed of silastic rubber and metal alloys. Advantages and disadvantages of each are noted in tables 1 and 2.

Silicon stents

Many of the silicon stents in use evolved from the Montgomery T-tube, which was first used in the early 1960s. This T-shaped stent supports the entire trachea with an arm that extends through a permanent tracheostomy. In patients with a patent

<table>
<thead>
<tr>
<th>Table 1. – Advantages and disadvantages of silicon stents</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Removable and replaceable</td>
</tr>
<tr>
<td>No growth through stent</td>
</tr>
<tr>
<td>Low cost</td>
</tr>
<tr>
<td>Low likelihood of granulation tissue formation</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>Potential for migration/dislodgement</td>
</tr>
<tr>
<td>Rigid bronchoscopy needed for placement</td>
</tr>
<tr>
<td>Possible secretion adherence</td>
</tr>
</tbody>
</table>
tracheostomy, the Montgomery T-tube remains an excellent tool for the management of endotracheal disease [29].

In 1990, Dumon [30] reported the use of what is now referred to as the Dumon stent (Bryon Corporation, Woburn, MA, USA). Developed in 1987, it is a silastic stent with evenly spaced studs along its outside walls (fig. 4). These studs not only assist in maintaining the placement of the stent in the airway, but also allow the clearance of secretions around the walls of the stent. Although the use of expandable wire mesh stents is increasing, the Dumon stent probably is currently the most common stent used by interventionalists.

The Dumon stent is effective in maintaining the structural integrity when placed endobronchially. Its solid walls prevent tumour growth from re-obstructing airways. Endobronchial tumours are often debulked and then a stent is placed prior to the initiation of radiotherapy or chemotherapy or both. Another advantage of the Dumon stent is the ease of removal. This can be significant when endobronchial procedures are used early in the management of cancer patients. After definitive therapies have been used (radiation or chemotherapy), re-evaluation of the airway can be performed, and the stent can be left in place, removed (if deemed of no further clinical advantage) or replaced with a larger stent that would further improve the calibre and stability of the airway. The disadvantages of the Dumon stent are the potential for migration and the need for a rigid bronchoscope for placement. The migration issue, although often referred to, occurs less often when the stent is placed by an experienced interventional endoscopist [30–34].

Other silastic stents include the Hood stent (Hood Laboratories, Decatur, GA, USA) and the hybrid Rüsch Y stent (Rüsch Inc., Duluth, GA, USA). The Hood stent is similar

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy to place</td>
<td>Permanent</td>
</tr>
<tr>
<td>Good wall/internal diameter relationship</td>
<td>Tumour regrowth (noncovered stents)</td>
</tr>
<tr>
<td>Powerful radial force</td>
<td>Possible migration of covered stents</td>
</tr>
<tr>
<td>Excellent conformity for irregular tracheal or bronchial walls</td>
<td>Significant granulation tissue stimulation</td>
</tr>
<tr>
<td>Good epithelialisation</td>
<td>Epithelialisation affecting wall mechanics and secretion clearance</td>
</tr>
<tr>
<td></td>
<td>Radial force causing necrosis of bronchial wall, erosion, fistulas and perforation</td>
</tr>
</tbody>
</table>

Fig. 4. – The Dumon stent.
Metal stents

Metal stents have been used in the endobronchial management of lung cancer. The advantage of metal stents is the relative ease for placement via a flexible bronchoscope with fluoroscopic assistance. This ease of placement allows some bronchoscopists to use these stents as their sole modality in the management of endobronchial disease. However, this practice limits the options to patients that may otherwise be available if all interventional modalities were offered. The wire mesh design of many of the original metal stents did not prevent the tumour from growing through the stent over time. A wrap is applied to the outside of the wire mesh to prevent tumour invasion through the stent. Data that support the use of both of these stents for the endobronchial management of lung cancer is available [35–38].

Most of the metallic stents are made of nitinol, a titanium and nickel alloy, which has little bioreactivity. These stents have excellent inner to outer diameter and conform well to various airway shapes, maintaining an equal pressure along the entire length of the stent. They are available in a variety of lengths and diameters. Overall, the covered versions of the stents are excellent for use in palliation of airway obstruction (fig. 5).

Metal stents epithelialise, as they remain in the airways, thereby becoming incorporated into the wall of the bronchus. The epithelialisation changes the mechanics of the airways with time by making them stiffer, which may lead to further airway complications [39, 40]. Another consideration with the use of metal stents is the fact that, once they are endoscopically placed, their removal is difficult and often impossible. Although uncommon, the risk with the use of metal stents is the erosion that can occur through bronchial/tracheal walls. This is particularly serious when erosion occurs into blood vessels, leading to massive uncontrollable haemoptysis.

Stents are effective tools for the endobronchial management of lung cancer. The choice of stent to use should be made carefully, weighing advantages and disadvantages of each, so that the proper tool is used in all situations. Multiple stent types need to be available to the endoscopist to allow the proper choice for the clinical situation.

Although several new prototypes are being studied, there have been relatively few advances in stent technologies in recent years. BOLLIGER et al. [4] described an improvement in the Polyflex stent (Rüsch AG, Kernen-Rommelshausen, Germany) by the addition of studs on the outer surface to reduce the chance of migration. This silicon stent has some advantages over the Dumon stent, including a thinner stent wall and a better ability to mould to airways of varying diameter.

Photodynamic therapy

Photodynamic therapy (PDT) has received increased attention in recent years. PDT is an important adjunctive modality to the management of endobronchial disease, but it
does not replace Nd:YAG lasers, stents and rigid bronchoscopy. PDT also can be used with bulky disease, but most interventionalists feel that it is of limited benefit in this role [41, 42]. The most suitable lesions for PDT are in situ carcinomas or those limited to 4–5 mm of microinvasion [43].

A photosensitising drug is intravenously administered to the patient 48–72 h prior to the procedure. Porfimer sodium (Photofrin) is the most common agent currently used for this. This photosensitiser penetrates all cells systemically. It is not cleared as quickly in cancer cells as in other cells and is, therefore, found in higher concentrations in cancer cells as opposed to the endothelium surrounding the tumour [43, 44]. An argon dye laser is then used to provide the 630-nm wavelength light energy required to activate the intracellular porfimer sodium. The laser energy is transmitted via a flexible quartz fibre, which can be used through either a flexible or rigid bronchoscope. The fibre tip can be placed in close proximity to the tumour mass or it can be imbedded into the tumour to provide the energy needed to start the intracellular activation of the porfimer sodium. This reaction leads to cellular destruction by a variety of mechanisms. Tissue necrosis then ensues as the cancer cells die [43–45].

As the neoplastic tissue necrotises, it must be removed by repeated bronchoscopies. Flexible bronchoscopy is commonly performed daily or every other day for up to 1 week to remove the necrotic tissue. The necrosis of a bulky tumour can be dangerous to the patient if the necrotic tissue separates from the bronchial wall and occludes the airway. In some programmes that use only PDT, patients remain intubated following the procedure for 1–2 days due to this concern. If necrotic tissue is removed over the first 24–48 h, a second laser application to the cancer can be performed, thus improving the cancer tissue destruction. PDT is an excellent therapeutic modality for patients with early-stage cancers. It destroys neoplastic tissue effectively and is an outstanding therapeutic modality in carcinoma in situ and microinvasive cancers. PDT is a necessary tool in our armamentarium of endobronchial treatments, but the time delays and multiple steps of management make it a more cumbersome therapy for the management of late-stage endobronchial lung cancer [45].
**Endoluminal brachytherapy**

Brachytherapy means the direct placement of a highly radioactive source inside a tumour mass. This can be done either by implanting the source directly into the tumour, via the natural route (endoluminal brachytherapy) or by placing the source into the tumour bed during tumour resection. Endoluminal brachytherapy employing the afterloading technique with iridium-192 high dose rate (HDR) is largely applied for the curative and palliative treatment of endobronchial tumours due to its tumour-specific and long-lasting effect. Endoluminal brachytherapy using flexible bronchoscopy and an HDR regimen can be performed on an outpatient basis and is not more strenuous for the patient than a diagnostic bronchoscopy. Symptomatic improvement can be achieved in 70–80% of patients and sometimes small tumours can even be cured. The afterloading procedure can be combined with all other modalities of tumour therapy. It can be used as a boost to conventional external irradiation and as a local treatment modality in patients on systemic chemotherapy or as the only local treatment. HDR treatment is usually delivered with 1–6 fractions at an interval of 1–3 weeks and a dose of 3–20 Gy per fraction (at 1 cm from the source axis). In patients previously treated with external beam radiation therapy and in the palliative setting, a regimen of 7–10 Gy (HDR) per fraction and a total of 2–3 fractions per treatment is recommended. However, the optimal dosage and fractionation schemes for the tumour therapy are still unknown and there is need for further studies. In about 10% of the patients, radiation bronchitis occurs, and there may be fatal haemorrhage, possibly related to the therapy and often occurring weeks to months after the actual treatment. This complication could perhaps be avoided through scheduling and dosing of the HDR brachytherapy [46]. Overall, endobronchial brachytherapy is a well tolerated, not very aggressive treatment option, especially in patients with reduced performance status [46]. Endoluminal brachytherapy is therefore a permanent interdisciplinary challenge with the need for a close contact between radiation oncologists and chest physicians.

**Conclusion**

Modern interventional pulmonology techniques have evolved during the last 25 yrs. These techniques are now mainstream therapies for central airway obstruction resulting from malignant and benign conditions. Recent literature confirms the efficacy and safety of endobronchial therapies developed in the 1980s and 1990s. Although the Nd:YAG laser remains the prototypic therapy for endoluminal disease, there is a trend toward the use of less expensive, more readily available techniques such as electrocautery. A variety of stents are available for management of central airway obstruction resulting from external compression or loss of cartilage support. Whether these techniques should be performed by all pulmonologists or be limited to centres of excellence remains controversial. Certainly all pulmonologists should become familiar with the indications and contraindications of these procedures so that they can be made available to appropriate patients.
Summary

The field of interventional pulmonary medicine is a relatively new area in pulmonary medicine, resulting from technological advances as well as the increasing need for palliative and curative treatment modalities for patients with tracheobronchial, parenchymal and pleural disease. This chapter reviews the advances in endoscopic techniques aimed at the tracheobronchial tree, laser photo destruction, electrosurgery, argon plasma coagulation, stent placement, brachytherapy and others, in patients suffering from lung cancer.

Keywords: Bronchoscopy, cryotherapy, electrocautery, interventional pneumology, laser therapy, stents.

Statement of interest

F.J.F. Herth has received travel support to the European Respiratory Society (ERS) Congress from the ERS, and an honorarium to speak at the Postgraduate courses.

References


