

Interventional Bronchoscopy Recent Advances

Dr Alok Nath
Department of Pulmonary Medicine
PGIMER
Chandigarh

Introduction

- ▶ An evolving field within pulmonary medicine that focuses on providing consultative and procedural services to patients with malignant and nonmalignant airway disorders
- ▶ Encompasses the following two main areas
 - malignant and nonmalignant airway disorders
 - artificial airways
- ▶ Extending to other lung diseases with therapies such as endoscopic lung volume reduction for emphysema and bronchial thermoplasty for asthma

Introduction

Flexible Bronchoscopy	Rigid Bronchoscopy	Artificial Airways
<p>Diagnostic</p> <ul style="list-style-type: none"> Endobronchial biopsy Transbronchial lung biopsy TBNA CT scan-guided FOB Endobronchial US AFB <p>Therapeutic</p> <ul style="list-style-type: none"> Balloon dilatation Endobronchial heat R_x Laser Argon plasma coagulation Electrocautery Photodynamic therapy Endobronchial cryotherapy Endobronchial brachyR_x Placement of metallic stents 	<ul style="list-style-type: none"> Balloon and rigid dilatation Mechanical debulking Endobronchial heat R_x Laser Argon plasma coagulation Electrocautery Photodynamic therapy Endobronchial cryotherapy Endobronchial brachyR_x Placement of metallic and silicone stents Placement of dynamic and Y stents Placement of Montgomery T-tubes 	<ul style="list-style-type: none"> Percutaneous tracheostomy Minitracheostomy Placement of transtracheal oxygen catheter

Introduction

- ▶ The main indication -presence of airway disorders resulting in central airway obstruction(CAO)
- ▶ The etiologies of CAO include
 - malignant airway disorders and
 - nonmalignant airway disorders
 - sarcoidosis
 - amyloidosis
 - relapsing polychondritis
 - infectious complications of tuberculosis, histoplasmosis
 - complications of lung transplantation
 - sequelae from the introduction of artificial airways

Therapeutic Bronchoscopy

- ▶ With the advent of accurate staging procedures diligent observation of the target tissues, i.e. in the pre-neoplastic and carcinoma in situ stage is possible
- ▶ Medically unfit patients with early stage cancer have been treated successfully with intraluminal bronchoscopic treatment (IBT)
- ▶ Superior cost-effectiveness ; minimally invasive; interventions and provides a solution for h early stage lung cancer and medically inoperable patient

Therapeutic Bronchoscopy

- ▶ RB is ideal for massive hemoptysis, tight airway stenosis, and a moderate-to-large tumor tissue burden in the airway
- ▶ Dilatation of airway stenoses can be achieved with controlled insertion of the barrel of the rigid bronchoscope, the sequential introduction of serially enlarging semi-rigid (Jackson) dilators, or balloon dilatation
- ▶ Mechanical debridement is accomplished by “coring” out the tissue with the barrel of the rigid bronchoscope or by grasping large pieces with rigid forceps

Therapeutic Bronchoscopy

- ▶ *“Therapeutic flexible bronchoscope”*, - large working channel (3.2 mm) and can accommodate large flexible forceps, making it feasible to remove medium sized endobronchial tissue growths during flexible bronchoscopy procedures in selected patents
- ▶ Tumor destruction can also be accomplished with a variety of endobronchial tools including heat therapy (eg, laser therapy, electrocautery, argon plasma coagulation), photodynamic therapy, cryotherapy, or radiotherapy (brachytherapy)

Laser therapy

- ▶ Laser energy delivered via rigid and/or flexible bronchoscopes in order to manage (palliate or cure) different endobronchial lesions
- ▶ Three main characteristics determine the suitability of a particular laser for therapeutic bronchoscopy
 - power density rating
 - ratio of absorption and scattering coefficients in soft tissue
 - the delivery system
- ▶ Lasers with high absorption coefficients and high scattering coefficients are good coagulators

Laser therapy

Type of laser	Wavelength nm	Biological effects	
		Vaporisation	Coagulation
Nd-YAG	1064	+++	+++
CO ₂	10600	+*	-
Argon	488–514	-	++
Dye	360–700	Activate photochemicals	
Diode	810	+	++
Excimer	193–351	Tissue destruction by mechanical effect	
YAP-Nd	1340	?	++

Nd-YAG: neodymium:yttrium aluminium garnet; CO₂: carbon dioxide; YAP-Nd: yttrium aluminium perovskite:neodymium. +: moderately good; ++: good; +++: excellent; ?: doubtful effect. *: precise cutting effect.

Laser therapy

The main indication for laser bronchoscopy comprises obstructive lesions of the trachea, the left and right main bronchi, the bronchus intermedius, and the lobar orifices

Most frequent indication being inoperable lung cancer with endobronchial manifestations

The main goal of the intervention is palliation

In most cases, laser bronchoscopy is combined with other treatment modalities, i.e. stenting, external beam irradiation and brachytherapy

It is contraindicated in extraluminal obstruction

Laser therapy

- ▶ Both rigid and flexible bronchoscope have been successfully used
- ▶ In addition to photocoagulation, mechanical dilation with rigid tubes of increasing diameter can also be performed
- ▶ The rigid technique is clearly favored for speed and safety by bronchoscopists skilled in both techniques

*Cortese DA J Bronchol 1994; 1: 72–75
Dumon JF Chest 1984; 86: 278–284*

Laser therapy

Clinical experience and results

- ▶ Restoration of airway Lumen has been achieved ranging from 83 to 93 % of patients in various studies
- ▶ Relief of symptoms has been reported in 63 to 94 % of patients

Cavaliere S. Chest 1988; 94:15–21

Brutinel WM. Chest 1987; 91:159–165

Cavaliere S. Chest 1996; 110:1536–1542

Venuta F. Ann Thorac Surg 2002; 74:995–998

Electrocautery and argon plasma coagulation

- ▶ The use of electrical current for tissue heating is called electrocautery or diathermy
- ▶ Argon plasma coagulation (APC) uses ionised argon gas jet flow (5plasma) to conduct electrons allowing a noncontact mode of treatment (lightning effect)
- ▶ The argon gas quite flexibly flows around bends and corners. Coagulated tissue has a higher resistance that automatically drives the argon gas flow away to nearby untreated tissue

Electrocautery and argon plasma coagulation

- ▶ APC is suitable for treating bronchial segments which take off at an acute angle from the major airways, such as apical and posterior segments of the upper lobes or the apical lower lobe segments
- ▶ Ultimate tissue effect depends on
 - voltage difference between probe and tissue
 - the surface area of contact
 - the duration of energy application
 - absence of leak

Electrocautery and argon plasma coagulation

Coagulation, cutting, fulguration, vaporisation and all combinations with mechanical debulking for quick airway recanalisation can be performed

Significant residual extraluminal stenosis or airway wall collapse can be managed by stent placement

Compared with Nd-YAG laser, the effect of electrocautery and APC are superficial but deep tissue coagulation is not always desirable

Electrocautery and argon plasma coagulation

- ▶ Maintenance cost is low, re-usable applicators are cheap, while the principle
- ▶ APC as a noncontact mode using an argon plasma jet also clears the pool of mucus and blood and conducts electrons around the corner
- ▶ It allows spraying of larger surface areas to obtain homogeneous and superficial necrosis
- ▶ Elegant for treating early stage superficial squamous cell cancer known to be several cell layers thick, is straightforward and easy to comprehend

Electrocautery and argon plasma coagulation

Clinical experience and results

- ▶ Restoration of airway Lumen has been achieved ranging from 88–89% of patients for electrocautery and 91% for APC in various studies
- ▶ Relief of symptoms has been reported in 70–97% of patients for electrocautery and in couple of studies 100% relief in hemoptysis has also been reported

Boxem T. Chest 1999; 116:1108–1112
Petrou M. Thorax 1993; 48:1156–1159
Sutedja G. Thorax 1994; 49:1243–1246
Crosta C. Lung Cancer 2001; 33:75–80

Electrocautery and argon plasma coagulation

- ▶ An attempt with curative approach has been advocated in various studies for early stages of lung malignancies
- ▶ Newer investigational techniques, combined with minimally invasive intralesional treatment, can provide a cost-effective early interventional management in the current screening area

McWilliams A. Oncogene 2002; 21: 6949–6959
Sutedja G. Eur Respir J 2003; 21: Suppl. 39, 57s–66s

- ▶ ACCP guidelines for treating early lesions have also advocated use of these modalities

Mathur PN. Chest 2003; 123: Suppl. 1, 176S–180

Cryotherapy

- ▶ This method offers delayed tumor destruction similar to PDT at a cost cheaper than electrocautery, and with the safety of not inducing collagen damage or bronchial wall perforation
- ▶ Cryotherapy is a unique method of destruction based on the cytotoxic effects of cold on living tissue
- ▶ Application of a low-temperature probe on a tissue first induces an immediate adherence between the probe and the tissue and then the appearance of intra- and extracellular ice crystals

Cryotherapy

- ▶ These crystals damage intracellular organelles, especially mitochondria
- ▶ In order to obtain a maximum lethal effect, it is necessary to have large ice crystals, especially at the intra-cellular level. This effect is achieved by rapid cooling of the tissue followed by slow thawing
- ▶ This physical and cellular phenomenon is coupled with a vascular effect: an initial vasoconstriction occurs, which is followed by a vasodilatation

Cryotherapy

- ▶ A complete vascular thrombosis appears 6–12 h later, thus completing the physical cytodestruction by induction of local infarction
- ▶ The area of destruction through cryotherapy has a diameter of ~1 cm when a 3-mm diameter probe is used. When in lateral contact with a bronchial wall, cytotoxicity can be considered complete to a depth of 3 mm
- ▶ Nonhaemorrhagic necrosis of the tissue occurs 8–15 days following the procedure. Collagen, cartilage or poorly vascularised tissues are very cryo-resistant

Cryotherapy

- ▶ Two types of probes are available: liquid nitrogen probes, and nitrous oxide (N₂O)-driven cryoprobes
- ▶ With flexible probes, each cycle of freezing and thawing lasts double the amount of time compared with a rigid probe cycle
- ▶ The rigid cryoprobe is more powerful than the flexible probe. A footpad or a trigger on the handle allows immediate and active thawing of the probe after cooling

Cryotherapy

- ▶ Once the lesion to be removed is found, the tip of the cryoprobe can be pushed into the protruding exophytic tumour or applied laterally onto infiltrative tumours and in situ carcinomas
- ▶ High oxygen concentration can be delivered without any restriction during cryotherapy. It is notable that cryotherapy is not a painful procedure
- ▶ Generally, three cycles of freezing and thawing are performed at each location. Each freezing period is short, at ,20 s

Cryotherapy

- ▶ At the end of the procedure, the tumor appears undamaged
- ▶ Cryothrombosis is delayed for several hours and it is dangerous to mechanically remove any part of the tumor at this stage
- ▶ For this reason, cryotherapy is not recommended when patients present with an acute dyspnea
- ▶ Necrotic sloughed tissue is eliminated by expectoration or removed by forceps between 8 and 10 days after cryotherapy

Cryotherapy

- ▶ Cryotherapy is very efficient on cellular and well-vascularised tumors such as bronchial carcinomas, carcinoids and adenoid cystic carcinomas or granulomas
- ▶ Cryotherapy alone is not indicated in benign strictures of the trachea or bronchi caused by fibromas, lipomas or post-intubation stenosis
- ▶ Cryotherapy is also not indicated in external compression of the bronchial tree

Cryotherapy

- ▶ Two side-effects of cryotherapy have been observed
 - A transient fever immediately following cryotherapy, this fever can be prevented by corticosteroid administration given during the procedure
 - Airway-sloughing material elimination after cryotherapy remains a problem
- ▶ A bronchial toilet with a flexible fiberoptic bronchoscope is recommended 8–10 days after cryotherapy

Cryotherapy

Clinical experience and results

- ▶ In a multicentre French study of 35 cases an 80% complete cure with a mean follow-up of 32 months was observed. The remarkable action of cryotherapy on tumor vascularisation also explains its effectiveness on hemoptysis
- ▶ Restoration of airway lumen has been achieved ranging from 77-97% of patients in various studies
- ▶ Relief of symptoms has been reported in 73–93% of patients

Walsh DA. Thorax 1990;45:509–513

Maiwand MO. Clin Chest Med 1995; 16:427–443

Marasso A. Chest 1993; 103:472–474

Brachytherapy

- ▶ Brachytherapy (brachys (Greek) meaning short) refers to the placement of a radioactive source (usually iridium-192 high dose rate (HDR)) within or near to an endobronchial or parabronchial malignancy to deliver local irradiation
- ▶ The primary radiation produced is gamma rays. The physical characteristics of these radioactive isotopes are characterized by the inverse square law
- ▶ The effects of irradiation are by single chain breaks of the DNA resulting in apoptosis and a decrease in cell proliferation

Brachytherapy

- ▶ To position the radiation source an after loading polyethylene probe is used, which is available in different diameters, usually 2–3 mm in external diameter
- ▶ A distinction between radiation with different energy levels can be made using the terms
 - Low dose rate (LDR), <2 Gy/h
 - medium dose rate 2–10 Gy/h
 - HDR > 20Gy/h (International Commission of Radiation)
- ▶ A HDR source with high activity of iridium-192 is usually used for endoluminal brachytherapy of thoracic malignancies

Brachytherapy

- ▶ Only one controlled, randomized study evaluated
 - the effect of dose rate,

There were no disadvantages for the shorter fractionation regimen

with a similar survival time (19 weeks) and local control time in both groups

- ▶ The complication rate was also similar (one fraction of 7.2 Gy at a weekly basis versus two fractions of 7.2 Gy at a 3 week interval) were compared

Brachytherapy

- ▶ In most cases, brachytherapy is applied in a palliative setting for alleviating dyspnea resulting from major airway obstruction by primary and secondary malignant tumors
- ▶ It is also indicated to palliate symptoms, such as cough, hemoptysis and dyspnea, in patients who have received their maximal dose of EBRT

- ▶ Brachytherapy can also be used as an endobronchial boost to EBRT

Saito M. Int J Radiat Oncol Biol Phys 1996; 34: 1029–1035

Huber RM. Int J Radiat Oncol Biol Phys 1997; 38: 533–540

Hernandez P. Thorax 1996; 51: 354–358.

Yokomise H. Respiration 1998; 65: 489–491

Aygun Cy. Int J Radiat Oncol Biol Phys 1992; 23: 127–132

Brachytherapy

- ▶ Incidentally detected occult CA by bronchoscopy - HDR brachytherapy, may be used with curative intent
- ▶ Good results, low morbidity, low cost and little inconvenience for the patient
- ▶ Nonmalignant tracheal and bronchial obstruction (recurrent granulation tissue formation in and around a stent or of granulation tissue at the bronchial anastomosis after lung transplantation)

Brachytherapy

Complications

- ▶ Severe coughing and increased bronchial secretion
- ▶ Temporary pleuritic pain or even pneumothoraces
- ▶ Radiation bronchitis and stenosis may occur days or weeks after therapy and can manifest with cough or wheezing
- ▶ Overall bronchial stenosis has been shown to occur in ~10% of patients after HDR EBRT for lung cancer
- ▶ The most important potential side-effects of brachytherapy are fatal hemoptysis and fistula formation. Such adverse outcomes are reported in 0–32% of patients, with an overall prevalence of ~10%

Brachytherapy

Complications

- ▶ The risk of hemorrhagic complications have been related to
 - The dose radiation administered
 - Histology of the neoplasm
- ▶ However, with usual dosages and fractionation, fatal hemorrhage seems to be correlated more with the natural course of a longer survival than with endoluminal brachytherapy itself

Brachytherapy

Clinical experience and results

- ▶ Relief of symptoms have reported to be 78–85% and restoration of airway patency has been seen in about 69–90% of patients

Kelly JF. Int J Radiat Oncol Biol Phys 2000; 48:697–702

Lo TC. Radiother Oncol 1995; 35:193–197
Petera J. Neoplasma 2001; 48:148–153

- ▶ Adding brachytherapy to Nd-YAG laser therapy improves the local control and seems to offer a significant survival advantage over either therapy alone

Chella A. Lung Cancer 2000; 27: 169–17

Mathur PN Chest 2003; 123: 176S–180S

Photodynamic therapy

- ▶ Bronchoscopic PDT began in 1982 at Tokyo Medical University when HAYATA et al. treated a patient who had an operable early lung cancer but refused surgical intervention
- ▶ The treatment was carried out with complete eradication of the tumor. After nearly 4 yrs the patient died from non cancer-related causes
- ▶ PDT is a treatment method which relies upon the excitation of a chemical photosensitiser (the drug) by an appropriate light whose wavelength matches the absorption band of the drug

Photodynamic therapy

- ▶ Oxygen is essential in PDT, since the photodynamic reaction, leading to cell necrosis, depends on the release of singlet oxygen and the generation of other oxygen-dependent cytotoxic agents
- ▶ Mechanism of PDT action appears to be mediated through the following
 - Generation of singlet oxygen and other toxic reactive oxygen species
 - Direct damage of subcellular and biomolecular structures of the cell
 - Indirect ischaemic effects and injuries resulting from vascular shut down of affected tissue
 - Indirect effects of the light-activated chemical and promotion of inflammatory and immune response
 - Apoptosis

Photodynamic therapy

- ▶ Bronchoscopic PDT for lung cancer is carried out as a two stage procedure, namely, “*photosensitization*” and “*illumination*”
- ▶ Photosensitization stage is achieved by an intravenous administration of a suitable photosensitiser (the drug) to the patient
 - The first photosensitiser used for bronchoscopic PDT was derived from the porphyrin family
 - At the present time, Photofrin1 is the most commonly used photosensitiser for bronchoscopic PDT
 - The recommended dose of Photofrin1 is 2 mg/kg body weight. At this dose, the drug is safe, reliable and nontoxic
 - One group has employed Foscan1 (meta- tetrachlorin) in a series of patients with apparent success and no major drawbacks

Photodynamic therapy

- ▶ Illumination consists of bronchoscopic exposure of the presensitized tumor to a light of a specific matching wavelength
 - The overall effect is necrosis of the tumor
 - There are essentially two methods of illumination: interstitial and surface illumination
 - In the former, the light exposure is from within the tumor mass; in the latter, the exposure is over the surface of the tumor
- ▶ The light which activates a porphyrin-based photosensitiser is within the red region of the spectrum (630 nm).

Photodynamic therapy

- ▶ The route of access for illumination of pre-sensitized endobronchial cancer is the biopsy channel of a flexible fibreoptic bronchoscope (FFB), which accommodates the light delivery optical fiber
- ▶ After administration of the photosensitizing drug, time is allowed for its absorption and its preferential retention in the tumor
 - For Photofrin1, this takes 24–72 h.
 - Following this period, bronchoscopic illumination is carried out as previously described
 - This is immediately followed by clearance of airways

Photodynamic therapy

- ▶ PDT is indicated in patients who are inoperable
 - Those with advanced stage disease (stages III and IV) at presentation. These patients are inoperable because they are oncologically unresectable
 - Those with early stage disease with oncologically and technically resectable cancer but who are, for a variety of reasons, unsuitable for surgical resection
- ▶ Success rates have been in the 90–100% range, translating itself to local cure due to the reported (very long) follow-up time of > 5 yrs. Tumor growth in the deeper layers and nodal disease are off limits for any local treatment

McWilliams A. Oncogene 2002; 21: 6949–6959
Sutedja G. Eur Respir J 2003; 21: Suppl. 39, 57s–66s

Photodynamic therapy

Mortality		Complications			
Operative	30-day	Skin burn %	Haemorrhage %	Respiratory	Other
0	1 (0.6)	4	0	8 (5)	0
0	10 (<0.9)	5–41 ⁺	2.4 FH 0.3	30 (29)	1 anaphylactic

Moghissi K. Eur Respir J 2003; 22: 535–541

Moghissi K. Eur J Cardiothorac Surg 1999; 15: 1–6

Moghissi K. Photodiagnosis and Photodynamic Therapy 2004; (In press)

Photodynamic therapy

- ▶ In some cases, bronchoscopic PDT has been carried out concomitant to chemotherapy or following chemo and or radiotherapy
- ▶ The Tokyo Medical University has shown a nearly 60% overall 5-yr survival and >90% cancer-specific survival in early lung cancer
- ▶ Another smaller series, has also shown comparable results
- ▶ A review of 12 articles from world literature involving 650 patients undergoing bronchoscopic PDT for early cancer shows that long survival of >5 yrs is achieved in >50% of cases

Kato H. J Photochem Photobiol B Biol 1998; 42: 96-99

Moghissi K. Eur Respir J 2003; 22: 535-541

Moghissi K. Eur J Cardiothorac Surg 1999; 15: 1-6

Moghissi K. Photodiagnosis and Photodynamic Therapy 2004; (In press)

Stents

- ▶ Stents are devices for the internal splinting of luminal structures
- ▶ In the airways, four major indications have been established
 - counteracting extrinsic compression from tumors or lymph nodes
 - stabilizing airway patency after endoscopic removal of intraluminally growing cancer
 - sealing malignant fistulas, e.g. stump dehiscences or fistulas between trachea and esophagus
 - treating benign strictures

Stents

- ▶ The first stents that were widely used were the T-tubes developed by *Montgomery*
- ▶ Though they require a tracheostomy, these silicone stents are still widely used by ENT surgeons and they are considered to be the safest approach in cases of very high tracheal stenoses
- ▶ *Dumon* developed the first stents that could be inserted through a bronchoscope without a tracheostomy
- ▶ At present, *Dumon* stents are still the most widely used worldwide

Stents

- ▶ Usually, *Dumon* stents are placed using rigid bronchoscopy under general anesthesia, which limits their use to centers where rigid bronchoscopy is practiced
- ▶ A few years after the Dumon stent, other polymer stents were developed and commercialized
- ▶ Considering the popularity of stent placement, there are very few multicentre studies and not a single randomized study comparing treated and untreated patients or individual type of stents

Stents

Name of Stent	Advantages	Disadvantages
Dumon stent	Most widely used Less chance of migration	Requires rigid bronchoscope and GA
Polyflex2 stent	Provide a bigger inner lumen	Migration common
Noppen stent	Less expensive	Requires rigid bronchoscope and GA
Wallstent Covered Ultraflex2 stent Alveolus Areo stent	Self expansible; Can be placed with Flexible bronchoscope	Expensive Migration
Dynamic stent Micro-tech bifurcation stent Bifurcated Dumon stent	Can be used for the sealing of oesophagotracheal fistulas and stump fistulas	Expensive

Stents

Clinical experience and results

- ▶ Although stents appear to be promising in alleviating symptoms of patients with malignant tracheobronchial obstruction but there are still many vexing issues
 - The efficacy regarding functional improvement and QoL appears to be proven
 - The expansion force of a stent that is necessary to cope with a malignant compression still remains unclear
 - Cost-effectiveness

Stents

- ▶ Following a lot of hype in the late 1990s, a growing number of articles deal with stent-associated complications
 - Retained secretions
 - Colonization of stent material
 - Migration
 - Stent fractures and development of granulation tissue
- ▶ Migration rates vary from 20–50%
- ▶ Obviously metal stents have a higher rate of migration than silastic stents
- ▶ Migration occurs more often in benign strictures than in malignant diseases

Stents

- ▶ Accumulation of secretions can be considered a slightly annoying problem or a severe complication
- ▶ Though colonisation and formation of biofilms in the prostheses does not necessarily mean that there is an infection, halitosis can be very compromising for a patient
- ▶ Granulation tissue formation at the edges of stents, even months after they have been inserted, can significantly narrow down the internal lumen

Therapeutic Bronchoscopy

Modality	Mechanism	Effect	Advantages	Disadvantages
Nd:YAG laser	Thermal energy produced by laser light	Coagulation and vaporization of tissue	Excellent debulking	Expensive; cumbersome setup
Electrocautery	Thermal energy produced by an electrical current	Coagulation of tissue but more superficial effect than laser	Excellent safety profile; multiple instrument designs; inexpensive	Contact mode requiring frequent cleaning of probe
Argon plasma coagulation	Thermal energy produced by the interaction between argon gas and an electrical current	Superficial coagulation of tissue	No undesired deep tissue effects	Ineffective for in-depth tissue coagulation or debulking
Photodynamic therapy	Injection of a photosensitizer followed by the destruction of presensitized tumor cells through illumination with nonthermal laser	Delayed destruction of tissue (24–48 h)	Relatively long-lasting effects	Expensive; need for multiple bronchoscopies; skin photosensitivity lasting up to 6 wk
Brachytherapy	Direct delivery of radiation therapy into the airway	Delayed and in-depth destruction of tissue	Long-lasting effect; synergistic with external beam radiation	Higher incidence of complications, particularly hemorrhage
Cryotherapy	Destruction of tissue by alternating cycles of freezing to extreme cold temperatures and thawing	Delayed destruction of tissue (1–2 wk)	Good tool for retrieval of foreign objects and removal of large mucus plugs or clots	Not suitable for debulking in acute airway obstruction; need for multiple bronchoscopies

Therapeutic bronchoscopy

Indications	Laser-assisted resection	High-frequency electrocautery	PDT	Cryotherapy	Silicone stents	Brachytherapy
Tracheal tumour with acute dyspnoea	++++	+++	NO	NO	NO	NO
Tracheal or bronchial tumour without acute dyspnoea	++++	++++	+	+++	NO	+++
Distal tumour	+ fibroscope	+++	+++	++	NO	+++
Infiltrative tumour	NO	++	++++	++++	NO	++++
Early stages	+	+++	+++	++++	NO	++++
Coagulation	+++ immediate	+++ immediate	+ / ++ delayed	++++ delayed	possible	++++ delayed
External compression	NO	NO	NO	NO	++++	++

PDT: photodynamic therapy; NO: not indication; +: slightly positive; ++: strongly positive; +++: very strongly positive; ++++: extremely strongly positive.

Therapeutic bronchoscopy

Results	Laser-assisted resection	High-frequency electrocautery	PDT	Cryotherapy	Silicone stents	Brachytherapy
Haemoptysis control	60	90	50-60*	65-86	Possible	80
Symptom improvement	80-90	50-60	70	66	90	85
PFT improvement	85	73	18-25 [†]	50	71	80
Airway clearance	90; immediate	84; immediate	50-60; delayed	75; delayed	90; immediate	80; delayed
Benefit duration months	2-3	ND	6-8	3-4	4	6.5
Ability to repeat	Yes	Yes	Yes	Yes	Yes	Yes*
Curative effects	Yes (selected cases)	Yes (80)	Yes (77-85)	Yes (81)	No	Yes (84)

Data are presented as %, unless otherwise indicated. PDT: photodynamic therapy; PFT: pulmonary functional tests; ND: not done. *: only when caused by submucosal vessels; [†]: in bronchial obstructive cases; * in selected cases.

Diagnostic bronchoscopy

- ▶ Two US Food and Drug Administration- approved innovations in diagnostic bronchoscopy are available to the interventional pulmonologist: auto fluorescence bronchoscopy (AFB) and EBUS
- ▶ It is arguable that both technologies can be performed by non-interventional pulmonologists, but the steep learning curve and the high cost of equipment make a dedicated practice of IP the ideal venue

Autofluorescence Bronchoscopy

- ▶ It utilizes differences in the biochemical, metabolic and structural composition of normal, preneoplastic and neoplastic tissues
- ▶ When the bronchial surface is illuminated by violet or blue light, normal tissues fluoresce strongly in the green
- ▶ As the bronchial epithelium changes from normal to dysplasia, and then to carcinoma *in situ* (CIS) and *invasive cancer*, there is a progressive decrease in the green autofluorescence but proportionately less decrease in red fluorescence intensity

Autofluorescence Bronchoscopy

- ▶ Increase in blood content results in a further decrease in the green autofluorescence in the lesion
- ▶ Preneoplastic and neoplastic lesions can appear to be brown, brownish red or red depending on the severity of the lesions, presence of endogenous porphyrins and the vascularity

Autofluorescence Bronchoscopy

- ▶ Two multicentre trials - sensitivity of detecting high-grade dysplasia, CIS or microinvasive cancer increases from 9–11% using WL examination alone to 56–66% using AFB

Lam et al Chest 1998 ,Ernst et al J. Bronchol.

2005

- ▶ Two prospective randomized trials also confirmed the improved sensitivity of AFB versus WL examination

Hirsch et al J. Natl. Cancer Inst. 2001 Häussinger et al

Thorax 2005

Autofluorescence Bronchoscopy

- ▶ The sensitivity in detecting dysplasia and CIS increased from 18% to 73% ¹
- ▶ Sensitivity in detecting dysplasia and CIS increased from 58% by WL alone was 82% by WL + AFB ²

Hirsch et al J. Natl. Cancer Inst. 2001 ¹, Häussinger et al

Thorax 2005²

Endobronchial ultrasound

- ▶ The integration of ultrasound technology and flexible fibreoptic bronchoscopy enables imaging of lymph nodes, lesions and vessels located beyond the tracheobronchial mucosa
- ▶ An ultrasound transducer with a frequency of 20 MHz is positioned at the tip of the probe
- ▶ The probe is positioned near the target area, where a balloon surrounding the probe has to be inflated with water in order to ensure coupling with the airway wall and transmission of the ultrasound waves

Endobronchial ultrasound

Once a target lymph node is identified, the transducer is removed and a needle is inserted through the working channel to obtain a sample

Endobronchial ultrasound

- ▶ A number of prospective studies have documented the high sensitivity (85 to 95.7%), high specificity (100%), and high accuracy (89 to 97%) of EBUS-transbronchial needle aspiration in the diagnosis of enlarged mediastinal lymph nodes

Rintoul RC. Eur Respir J 2005; 25:416– 421

Yasufuku K. Lung Cancer 2005; 50:347–354

Yasufuku K. Chest 2004; 126:122–128

- ▶ A large (n5200) randomized trail, between conventional TBNA and TBNA after EBUS localization, for mediastinal staging of enlarged nodes demonstrated that EBUS guidance significantly increased the yield of TBNA in all stations (84 versus 58%), except in the subcarinal region (86 versus 74%)

Herth F. Chest 2004; 125: 322–325

Endobronchial ultrasound

Largest study to date, 502 patients
572 lymph nodes were punctured and 535 (94%) resulted in a diagnosis

Biopsies were taken from all reachable lymph node stations (2L, 2R, 3, 4R, 4L, 7, 10R, 10L, 11R and 11L) and had a mean (range) diameter of 1.6 (0.8–3.2) cm

Sensitivity of 94% and a specificity of 100% for mediastinal staging was reported.

In contrast to all prior studies, which were performed in selected patients with enlarged mediastinal nodes on chest CT, EBUS-TBNA was evaluated in a prospective study in 100 patients with non small cell lung cancer without enlarged nodes at chest CT

Surgical verification was performed in all patients

In assessing mediastinal nodal status, EBUS-TBNA had a sensitivity of 92% a specificity of 100% and a negative predictive value of 96%

Herth FJ. Thorax 2006; 61: 795–798.

Herth FJ. Eur Respir J 2006; 28: 910–914.

Other newer developments

- ▶ Radiofrequency ablation is a thermal therapy that is traditionally applied percutaneously to treat primary or secondary malignancies of the lung.
- ▶ An interest in using this modality bronchoscopically has surfaced in the following three areas
 - its potential for use as an adjunct therapy in the removal of metallic stents by means of thermal destruction of granulation tissue
 - its role in ablative treatment for pulmonary nodules and masses
 - its possible therapeutic role in asthma
- ▶ The application in patients in asthma has recently gained attention

Other newer developments

- ▶ The hypothesis centers around the prospect of decreasing airway hyper responsiveness by reducing the smooth muscle mass with controlled low-energy radiofrequency ablation in the airways
- ▶ Two preliminary studies have demonstrated the safety and effectiveness of this treatment in patients with mild-to moderate asthma with significant reduction in airway responsiveness to methacholine challenge, and improvement in peak flows and number of symptom free days

*Miller JD. Chest 2005; 127:1999–2006
Cox G. Am J Respir Crit Care Med 2006;
173:965– 969*

Other newer developments

- ▶ Another promising application of therapeutic bronchoscopy in a common disease is bronchoscopic lung volume reduction in patients with emphysema
- ▶ By the placement of one-way valves in the upper lobe bronchi of patients with upper lobe predominant emphysema, upper lobe collapse can potentially be achieved, replicating the benefits of surgical lung volume reduction in a less invasive manner

Other newer developments

- ▶ Navigational bronchoscopy by electromagnetic guidance (superDimension; Plymouth, MN) is a groundbreaking concept in the diagnosis of peripheral lung lesions
- ▶ The patient is placed over an electromagnetic board and a micro sensor probe is inserted through the working channel of the bronchoscope into the airways
- ▶ Reference anatomic landmarks, such as the main and secondary carinae, as well as the target lesion are identified on a preacquired digitized chest CT scan and are loaded into the system

Other newer developments

- ▶ The same landmarks are then identified by the probe bronchoscopically, registered in the system, and aligned with data from the chest CT scan
- ▶ The sensor probe can now be directed in real time to the target lesion, and histologic sampling of tissue is conducted through an extended working channel
- ▶ Moreover, localized treatment such as radiofrequency ablation may be delivered directly to a malignant lesion in selected patients

Other newer developments

- ▶ Optical coherence tomography (OCT) is another evolving technology that brings the capability of a pathologist's microscope into the flexible bronchoscope.
- ▶ OCT is similar to US in the fact that both technologies collect backscattered signals from various structures and construct them into images; however, since OCT detects light waves rather than sound waves, the images are much clearer and have an exceptional spatial resolution.
- ▶ OCT images compared favorably and displayed with precision microstructures such as the epithelium, lamina propria, glands, and cartilage

Jung W. Lasers Surg Med 2004; 35:121–127
Han S. Respiration 2005; 72:537–541

Other newer developments

- ▶ An attractive future clinical application of OCT would be the detection and follow-up of submucosal *in situ histologic changes* without the need to obtain a biopsy

Thank you