

# British Thoracic Society guideline for advanced diagnostic and therapeutic flexible bronchoscopy in adults

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► An additional appendix 4 is published online only. To view this file please visit the journal online (<http://thorax.bmj.com>).

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Membership of the Committee with their conflicts of interest are shown in Appendix 1 and a list of stakeholders is given in Appendix 5.

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## SUMMARY OF RECOMMENDATIONS

### Diagnosis of mediastinal/hilar lymph nodes and peribronchial masses

#### Conventional transbronchial fine needle aspiration (TBNA)

- B ► Conventional transbronchial needle aspiration (TBNA) is a safe technique and should be used to sample mediastinal and hilar lymphadenopathy during initial diagnostic bronchoscopy where a pre-procedure CT scan has demonstrated significant adenopathy.
- Conventional TBNA is a safe technique for sampling hilar and mediastinal lymph nodes in cases of suspected sarcoidosis and may be used in conjunction with endobronchial and transbronchial biopsies.
- ✓ ► Depending upon the clinical setting, a non-diagnostic conventional TBNA result may warrant further investigation. Real-time endobronchial ultrasound-guided TBNA (EBUS-TBNA) or surgical lymph node sampling should be considered.

#### Endobronchial ultrasound-guided transbronchial fine needle aspiration (EBUS-TBNA)

- B ► EBUS-TBNA is a safe and effective technique for the assessment of hilar and mediastinal lymph nodes in cases of confirmed or suspected lung cancer.
- EBUS-TBNA is a safe and effective technique for sampling hilar and mediastinal lymph nodes in cases of suspected sarcoidosis and may be used in conjunction with endobronchial and transbronchial biopsies.
- D ► EBUS-TBNA is a safe and effective technique for sampling paratracheal and peribronchial intraparenchymal lung masses.
- At present there is insufficient evidence to recommend EBUS-TBNA for routine use in the diagnosis of lymphoma.
- ✓ ► In cases where EBUS-TBNA results are negative for malignancy, a confirmatory surgical biopsy should be performed where appropriate.

### Therapeutic procedures for malignant disease

#### Malignant airway obstruction

##### 1. Endobronchial debulking of tumours

- D ► In patients with central airway obstruction (CAO) due to intraluminal tumour, endobronchial tumour debulking should be considered.
- ✓ ► When undertaking endobronchial debulking of tumours, a laryngeal mask or uncuffed endotracheal tube is recommended to achieve airway control.

##### 2. Endobronchial electrocautery or diathermy

- D ► Endobronchial electrocautery may be considered for use with curative intent in benign disease of the airway including incising web-like stenosis, benign tumours and granulation tissue. It may also be considered for primary treatment of early stage non-invasive lung cancer.
- Endobronchial electrocautery may be considered for palliation of malignant CAO, with or without critical airway narrowing.
- ✓ ► When undertaking snare resection, intermittent bursts of electrocautery of not more than 2 s duration should be used while carefully closing the snare until resistance is felt.
- Avoid an Fio<sub>2</sub> of >0.4 when undertaking electrocautery to reduce the risk of airway fire.

##### 3. Argon plasma coagulation (APC)

- D ► APC may be considered for the debulking of obstructing endobronchial tumour.
- APC may be considered for tumour debulking in patients without acute critical airway narrowing.
- APC may be considered for the treatment of haemoptysis in patients with endobronchial abnormalities.

##### 4. Thermal laser

- D ► In patients with CAO due to intraluminal tumour, relief of obstruction using Nd-YAG laser may be considered.
- ✓ ► The power setting should be limited to 40 W

##### 5. Cryotherapy and cryoextraction

- B ► Cryobiopsy may be considered for diagnostic endobronchial tissue sampling to provide large-volume specimens without crush artefact.
- D ► Cryotherapy may be considered for tumour debulking in patients without critical airway narrowing.
- Cryorecanalisation/cryoextraction may be considered for tumour debulking.

##### 6. Photodynamic therapy (PDT)

- D ► PDT may be considered for tumour debulking in patients without critical airway narrowing.
- ✓ ► The technique should be available for carefully selected patients on a regional basis.

##### 7. Brachytherapy

- C ► Brachytherapy should not be used first-line in preference to external beam radiotherapy for the palliation of lung cancer.
- D ► Brachytherapy should be considered for the palliation of haemoptysis or CAO in locally advanced central lung cancer.

#### Airway support with stents

- D ► The use of self-expanding metallic stents may be considered for the treatment of malignant CAO due to extrinsic disease.
- Self-expanding metallic stents may be used to maintain airway patency following endobronchial debulking techniques.
- Self-expanding metallic stents can be used to restore or maintain airway patency in conjunction with other treatments such as external beam radiotherapy.

- ✓ ▶ Patients require careful specialist follow-up after stent insertion.
  - ▶ Stents should be used with caution in non-malignant disease, considering their long-term complications. Self-expanding metallic stents may be difficult to remove following long-term placement.
  - ▶ Self-expanding metallic stents should only be used in benign disease after all other therapeutic options have been exhausted.
  - ▶ A risk-benefit assessment should be performed, incorporating immediate and long-term implications, prior to selecting any particular type of stent.
- Treatment with curative intent for early lung cancer
- C ▶ Fractionated brachytherapy should also be considered for the curative treatment of early central lung cancer, especially if performance or cardiorespiratory status precludes surgery or radical external beam radiotherapy. The success of brachytherapy for radical treatments requires accurate local staging to exclude extrabronchial tumour extension.
- D ▶ PDT can be considered for the curative treatment of early central lung cancer, especially for tumours 1 cm or less in diameter and provided there is no imaging evidence of extrabronchial involvement.
- ▶ PDT can be considered for the curative treatment of recurrent lung cancer where there is localised endobronchial disease in patients who are not fit for surgery or radical radiotherapy.
- Emerging applications for flexible bronchoscopy**
- Electromagnetic navigation bronchoscopy
- D ▶ Electromagnetic bronchoscopy may be considered for the biopsy of peripheral lesions or to guide TBNA for sampling mediastinal lymph nodes.
- Endobronchial valves in emphysema
- B ▶ Endobronchial valves may be considered in the treatment of selected patients with severe emphysema and hyperinflation with heterogeneous disease in the absence of significant collateral ventilation or who have a complete fissure on CT scanning.
- ✓ ▶ Patients should be enrolled into clinical trials until more robust data of clinical benefit is available.
- Bronchial thermoplasty in asthma
- A ▶ Bronchial thermoplasty is a possible treatment option in selected patients with severe persistent asthma already on maximal therapy, although its place in the treatment of asthma remains to be established.
- ✓ ▶ Long-term safety and efficacy remain unclear. Hence, treatment should be limited to a few specialist centres in carefully selected patients. Longer-term follow-up of treated patients is recommended.

## INTRODUCTION

### Clinical context and need for a guideline

Interventional bronchoscopy has rapidly evolved in recent years. The field includes the use of more complex diagnostic procedures such as endobronchial ultrasound, the use of bronchoscopic interventions for the relief of central airway obstruction (CAO) due to malignancy and, more recently, the development of therapeutic interventions for non-malignant disease.<sup>1</sup> Many practitioners may feel that this is a highly specialist field and that the techniques are experimental, only for tertiary centres. Perhaps they feel that they do not have the expertise to undertake these procedures. The fact is that some of these techniques such as transbronchial needle aspiration (TBNA) really should be part of every bronchoscopist's practice. Others such as endobronchial ultrasound (EBUS) are rapidly becoming standard practice and should be available to all patients, and some such as bronchial thermoplasty and airway valves are yet to establish their role in routine practice. There are also a large variety of methods of tumour debulking, and it is clearly not easy for a practitioner outside the field to know what are the indications, contraindications, potential benefits and complications of each technique, or which technique to consider learning. This guideline therefore aims to help all those who undertake flexible bronchoscopy to understand more about this important and rapidly developing area.

In August 2007 the Standards of Care Committee of the British Thoracic Society (BTS) invited the Interventional Pulmonology Specialist Advisory Group of the BTS to produce an evidence-based update of the guideline on bronchoscopy and agreed this should now include interventional bronchoscopy. The Working Party decided to start with this new guideline on interventional bronchoscopy.

### Target audience of the guideline

This guideline is aimed primarily at practitioners within the UK but may be of relevance to other healthcare systems. It is intended to inform those who undertake or intend to undertake the procedures within the guideline, and also to inform others as

to what may be available for patients under their care and the indications, likely response and complications of such procedures. Not all of the procedures may be available in all areas, including some tumour debulking procedures, but at least one of the tumour debulking modalities should be available in each cancer network.

### Scope of the guideline

This guideline was formulated following consultation with stakeholders from the medical and nursing professions, patient groups and healthcare management. Advanced diagnostic and therapeutic procedures in adults using a flexible bronchoscope are included in the guideline.

### Topics covered in the guideline

- ▶ Transbronchial needle aspiration (TBNA) and endobronchial ultrasound-guided (EBUS) TBNA
- ▶ Electrocautery/diathermy
- ▶ Argon plasma coagulation (APC)
- ▶ Laser
- ▶ Cryotherapy
- ▶ Cryoextraction
- ▶ Photodynamic therapy (PDT)
- ▶ Brachytherapy
- ▶ Tracheobronchial stents
- ▶ Electromagnetic navigation bronchoscopy (ENB)
- ▶ Endobronchial valves for emphysema
- ▶ Bronchial thermoplasty for asthma

### Topics not covered in the guideline

- ▶ Rigid bronchoscopy
- ▶ Autofluorescence bronchoscopy

### Rigid or flexible bronchoscopy for interventional procedures?

This guideline covers interventional procedures performed using flexible bronchoscopy. In many units, however, rigid bronchoscopy alone would be used for such procedures. Most UK respiratory physicians lack training in rigid bronchoscopy, and most

bronchoscopy units outside thoracic surgery centres do not have ready access to rigid bronchoscopy as a back-up for, or as an alternative to, flexible bronchoscopy.

The main advantages of flexible bronchoscopy are:

1. It is widely available
2. The majority of respiratory physicians are trained to use flexible bronchoscopy
3. It does not require a general anaesthetic
4. It provides access to more distal airways and good access to the upper lobe bronchi

The main advantages of rigid bronchoscopy are:

1. A general anaesthetic is more comfortable for the patient
2. It allows control of ventilation and oxygenation during interventional procedures
3. It permits the removal of large volumes of tumour
4. It provides more control in cases of massive haemoptysis
5. It permits silicon stent insertion
6. Obstructing airway lesions can be cored out
7. Large centrally-placed foreign bodies can be removed

Most interventional procedures, however, can be undertaken via flexible or rigid bronchoscopy, including removal of many foreign bodies, metallic stent insertion and tumour debulking with diathermy, argon plasma, cryoextraction and photodynamic therapy (PDT). Although thermal lasers can be used with either scope, most practitioners of this technique prefer to use rigid bronchoscopy. Silicone and Y-stents are inserted via rigid bronchoscopy.

## METHODOLOGY

This guideline is based on the best available evidence. The methodology used to write the guideline adheres strictly to the criteria as set by the AGREE collaboration in the document, which is available online <http://www.agreecollaboration.org/1/agreeguide/>.

### Clinical questions and literature search

Clinical questions were gathered in the PICOT (Patient, Intervention, Control, Outcome and Time) format to define the scope of the guideline and inform the literature search.

Systematic electronic database searches were conducted in order to identify potentially relevant studies for inclusion in the guideline. For each topic area the following databases were searched: Ovid MEDLINE (from 1988) (including MEDLINE In Process), Ovid EMBASE (from 1988), Ovid CINAHL (from 1982) and the Cochrane Library (from 1992) (including the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials, the Health Technology Assessment database and the NHS Economic Evaluation Database).

The searches were first run in January 2008 and updated in September 2010. Searches were saved and run on a monthly basis to identify newly published literature to date. Searches included a combination of indexed terms and free text terms and were limited to English language publications only. The initial search identified 3751 potential papers.

### Appraisal of the literature

Appraisal was performed using the criteria stipulated by the AGREE collaboration. Each paper was appraised by a pair of reviewers. One individual (IDR) read the title and abstract of each article retrieved by the literature searches and decided whether the paper was definitely relevant, possibly relevant or not relevant to the project. Criteria formulated for categorising the abstracts into these three groups were:

- Whether the study addressed the clinical question.
- Whether the appropriate study type was used to produce the best evidence to answer the clinical question.
- Abstract was in English.
- Studies where exclusively rigid bronchoscopy was used were not evaluated.
- Abstracts were not rejected on the basis of the journal of publication, country in which the research was performed or published nor the date of publication.

The full paper was obtained for all relevant or possibly relevant abstracts and allocated to the relevant section(s) which were broadly grouped as argon plasma, brachytherapy, cryotherapy, diathermy, EBUS, TBNA, endobronchial valves, general interventional bronchoscopy, laser, photodynamic therapy, stents, thermoplasty and virtual bronchoscopy with electromagnetic navigation.

The first screening process identified 1022 of the initial 3751 reference abstracts to be definitely or possibly relevant to the guideline. Two guideline reviewers independently reviewed the abstracts to identify papers to be appraised for the guideline.

Three hundred and eighty-seven papers were critically appraised. The two leads for each section independently appraised each paper assigned to them using the Scottish Intercollegiate Guidelines Network (SIGN) critical appraisal checklists. A web-based guideline development tool (<http://www.bronchoscopy-guideline.org>) enabled each pair of reviewers to collaborate online. The reliability of the evidence in each individual study was graded using the SIGN critical appraisal check lists and is shown in the evidence tables (+++, ++ or –). The body of evidence for each recommendation was summarised into evidence statements and graded using the SIGN grading system (see table 1). Disagreements were resolved by discussion with the section partner.

### Considered judgement and grading of evidence

The Guideline Group used the online-derived evidence tables to judge the body of evidence and grade recommendations for this guideline. Evidence tables are shown in online Appendix 4 available online. Where evidence was lacking to answer the formulated clinical questions, expert opinions were obtained for formal consensus statements using the Delphi method. The following were considered in grading of the recommendations:

- The available volume of the body evidence.
- How applicable the obtained evidence was in making recommendations for the defined target audience of this guideline.

**Table 1** Revised grading system for recommendations in evidence based guidelines

Grade	Evidence
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews or RCTs, or RCTs with a high risk of bias
2++	High quality systematic reviews of case-control or cohort studies or High quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytic studies, for example, case reports, case series
4	Expert opinion

RCT, randomised controlled trial.

- ▶ Whether the evidence was generalisable to the target population for the guideline.
- ▶ Whether there was a clear consistency in the evidence obtained to support recommendations.
- ▶ What the implications of recommendations will be on clinical practice in terms of resources and skilled expertise.
- ▶ Cost-effectiveness was not reviewed in detail as in-depth economic analysis of recommendations fall beyond the scope of this guideline.

Recommendations were graded from A to D as indicated by the strength of the evidence as shown in table 2. Important practical points lacking any research evidence were highlighted as 'Good Practice Points' (GPP).

### Drafting of the guideline

The Guideline Committee corresponded regularly by email and meetings of the full group were held in December 2007, June 2008, December 2008, March 2009, June 2009 and October 2009. The guideline was discussed at an open session at the BTS Winter Conference in December 2009. A revised draft guideline document was circulated to all the relevant stakeholders for consultation in May 2010 followed by a period of online consultation. The BTS Standards of Care Committee reviewed the draft guideline in July 2010. Further revision was made in September 2010 following the incorporation of suggestions by international experts in interventional bronchoscopy. The guideline was reviewed by the BTS Standards of Care Committee in November 2010 and submitted for publication.

The Guideline Group members adhered to the BTS policy for the Declaration of Interests and, where appropriate, specific interests are declared in Appendix 1.

The guideline will be reviewed and updated in 2015.

### Audit, research and training recommendations

#### Audit

- ▶ All those undertaking any interventional procedure are advised to maintain records of each procedure including indication, outcome and complications for audit purposes.
- ▶ It is recommended that a database should be kept of all those in the UK undertaking interventional procedures and numbers being treated.
- ▶ The database should include details of current training in interventional procedures available in the UK.

#### Research

- ▶ A randomised controlled trial (RCT) comparing symptom relief and survival in patients with malignant CAO receiving

airway intervention in combination with conventional anticancer therapy versus conventional anticancer therapy alone.

- ▶ An RCT comparing EBUS with surgical staging of the mediastinum in lung cancer.
- ▶ An RCT comparing EBUS-TBNA with standard bronchoscopic techniques for the diagnosis of sarcoidosis.
- ▶ An RCT comparing outcomes including quality of life of treatment by debulking for CAO followed by conventional anticancer treatment with anticancer treatment alone.
- ▶ Defining the population or phenotype of disease that benefits from the bronchoscopic lung volume reduction techniques available.
- ▶ Further RCTs on the techniques available for bronchoscopic lung volume reduction with improved patient selection.
- ▶ Longer-term evaluation of safety and efficacy of bronchial thermoplasty.

Recommended standards of care based on the recommendations in this guideline can be found on the BTS website at: <http://www.brit-thoracic.org.uk/>.

### Training

It is clear from a survey of respiratory trainees in the UK that, by the final year of training, few consider themselves to be competent to undertake interventional diagnostic or therapeutic procedures; 36% felt competent to undertake simple TBNA but only 2.8% felt competent to undertake EBUS-TBNA or endo-bronchial diathermy.<sup>2</sup> To be competent in any specialised technique it is useful to have attended a course and undertaken the procedure on a model, but it is also necessary to have received experience in a centre undertaking the procedure and also to have hands-on experience. Evidence on training requirements is sparse.

There are published recommendations for training by the American College of Chest Physicians<sup>3</sup> and also in the ERS/ATS statement on interventional pulmonology.<sup>4</sup> The Guideline Group has decided not to quote specific numbers of procedures required to be performed before an individual is deemed competent as these numbers are usually arbitrary. Individuals have different learning curves and hence focus should be towards monitoring an individual's performance and outcomes.<sup>5</sup> Standards for particular procedures need to be determined and agreed. These can then be used for outcome-based assessment of competency.

### DIAGNOSIS OF MEDIASTINAL/HILAR LYMPH NODES AND PERIBRONCHIAL MASSES

#### Conventional TBNA

##### Principles

Transbronchial lymph node sampling can be used both for diagnosis and for staging of lung cancer and can be performed at initial diagnostic bronchoscopy.

TBNA entails inserting a fine (usually 19–22 gauge) needle through the wall of the airway into a lymph node in order to obtain a specimen for cytological, histological or microbiological analysis. The technique can also be used to sample parenchymal lung masses that lie adjacent to the trachea or major airways. The procedure can be performed with or without the use of ultrasound guidance.

##### Technique

In conventional TBNA a needle is passed through the working channel of a standard bronchoscope to puncture the airway wall at the site of the target lymph node or lung mass, whose

**Table 2** Grades of recommendations

Grade	Type of evidence
A	At least one meta-analysis, systematic review or RCT rated as 1++ and directly applicable to the target population <i>or</i> A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results <i>or</i> Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results <i>or</i> Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4 <i>or</i> Extrapolated evidence from studies rated as 2+
✓	Important practical points for which there is no research evidence nor is there likely to be any research evidence. The Guideline Committee wishes to emphasise these as Good Practice Points.

RCT, randomised controlled trial.

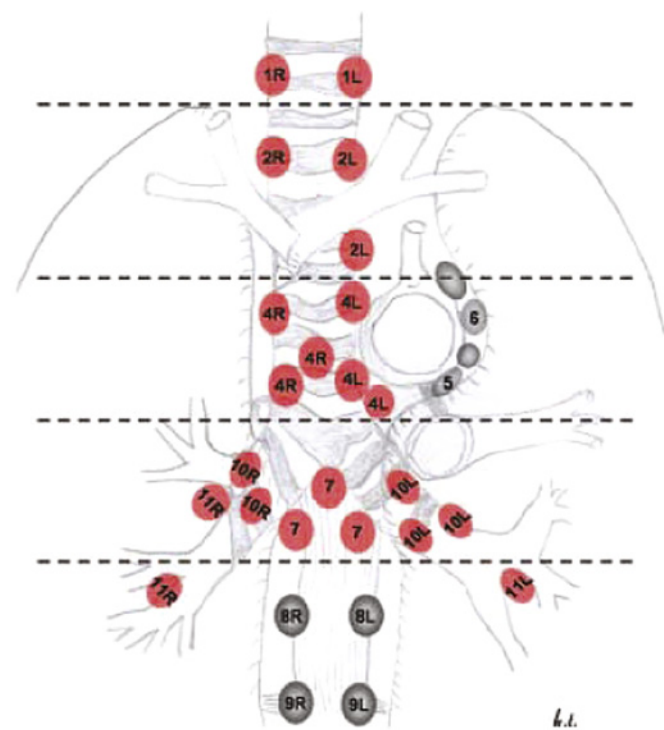
position is determined from study of a pre-procedure CT. Virtual bronchoscopy using CT reconstructions has recently been described and can be used to help identify suitable positions for TBNA. Lymph nodes stations that can be accessed in this way are 2R, 2L, 3P, 4R, 4L, 7, 10R, 10L, 11R and 11L (figure 1).

Ultrasound guidance may be used to locate lymph nodes for TBNA. In early descriptions a radial ultrasound miniprobe introduced through the working channel of a conventional bronchoscope was used to locate lymph nodes. The miniprobe was then removed and a TBNA needle was introduced to puncture the node at the predetermined position. This technique did not allow for real-time ultrasound visualisation of the TBNA. More recently, real-time EBUS-TBNA has been described which involves use of a convex array linear ultrasound bronchoscope. The use of real-time ultrasound imaging during TBNA allows specific nodes to be targeted and permits accurate biopsy of multiple lymph node stations when necessary for staging. Lymph nodes as small as 4 mm in the short axis have been sampled.

The technique of TBNA is simple. Diagnostic yield is dependent upon operator experience, the position and the size of the lymph node. The use of rapid on-site cytopathology improves yield. A guide on how to perform TBNA is available in Appendix 2.

### Indications

TBNA is mainly used to sample hilar and mediastinal lymph nodes. It can also be used to sample paratracheal and peribronchial lung masses.



**Figure 1** Lymph node stations accessible by transbronchial fine needle aspiration (TBNA) are shown in red. Precise localisation of lymph nodes for TBNA may be assisted by real-time endobronchial ultrasound guidance. Nodes that cannot be sampled by TBNA are shown in dark grey. The dotted lines indicate anatomical borders that are important for identification of the different lymph node stations using endobronchial ultrasound. Station 3a/p nodes are not indicated on this image. Stations 5 and 6 nodes may be seen during endobronchial ultrasound but sampling is usually not possible due to the interposition of the great vessels. Figure reproduced from Tournoy *et al*<sup>6</sup> with permission of the publishers.

### Complications

Conventional (non-ultrasound-guided) TBNA is safe with few reported complications. In a meta-analysis by Holty *et al* the pooled complication rate was 0.3%.<sup>7</sup> The complications most commonly reported are pneumomediastinum and pneumothorax, minor and self-limiting bleeding and puncture of adjacent structures.

### Evidence

The majority of papers on conventional TBNA are case series. One meta-analysis by Holty *et al* has been reported.<sup>7</sup> The reported sensitivities for this approach vary considerably. In their analysis Holty *et al* divided studies according to whether or not they had surgically confirmed all TBNA results and enrolled at least 10 patients with and without mediastinal metastasis.<sup>7</sup> In six studies that met these entry criteria, pooled sensitivity and specificity for diagnosis of malignancy were 39% (95% CI 17% to 61%) and 99% (95% CI 96% to 100%), respectively. However, the prevalence of mediastinal metastases in these studies was only 34%. Analysis of another group of studies in the review by Holty *et al* in which the prevalence of mediastinal metastases was 81% had a pooled sensitivity for the detection of malignancy of 78% (95% CI 71% to 84%).<sup>7</sup> A similar figure was reported by Detterbeck *et al*.<sup>8</sup> In their review of the literature they reported a pooled TBNA sensitivity of 78% and specificity of 99%. The prevalence of disease in this pooled analysis was 75%.<sup>8</sup>

Two studies have demonstrated that 5–7 aspirates per node are required before a plateau in diagnostic accuracy is achieved.<sup>9 10</sup> The success rate is highest in lymph nodes >20 mm in the short axis<sup>7</sup> and in the station 4R and 7 lymph node locations (figure 1).

Rapid on-site cytology may improve the success rate and reduce the number of needle aspirates and the number of lymph node stations sampled.<sup>10</sup>

The role of TBNA in the diagnosis of sarcoidosis has been reported.<sup>11 12</sup> Considering TBNA alone, the diagnostic yield in stage I disease (61–82%) was higher than in stage II (42–75%). However, most operators use TBNA in this setting in conjunction with endobronchial and transbronchial biopsies and diagnostic yields of around 90% are achievable in stage I and II disease.

### Evidence statement

- Conventional TBNA is a safe technique to sample mediastinal and hilar lymphadenopathy at initial diagnostic bronchoscopy in cases of either suspected malignant involvement or sarcoidosis. (Evidence level 2++)

### Recommendations

- Conventional TBNA is a safe technique and should be used to sample mediastinal and hilar lymphadenopathy at initial diagnostic bronchoscopy where a pre-procedure CT scan has demonstrated adenopathy. (Grade B)
- Conventional TBNA is a safe technique for sampling hilar and mediastinal lymph nodes in cases of suspected sarcoidosis and may be used in conjunction with endobronchial and transbronchial biopsies. (Grade B)

### Good practice points

- Depending upon the clinical setting, a non-diagnostic conventional TBNA result may warrant further investigation. Real-time EBUS-TBNA or surgical lymph node sampling should be considered. (✓)

## Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)

EBUS-TBNA provides images of the mediastinal structures immediately surrounding the tracheobronchial tree.

### Indications

EBUS-TBNA is mainly used to sample hilar and mediastinal lymph nodes. It can also be used to sample paratracheal and peribronchial lung masses.

### Complications

In most centres the procedure is performed under moderate sedation. No advantage has been demonstrated by performing the technique under general anaesthesia.<sup>13</sup> The reported safety profile is excellent. In their meta-analysis, Gu *et al* reported only two complications in 1299 patients (0.15%).<sup>14</sup>

### Evidence

In 2009, two meta-analyses and one systematic review reported the sensitivity and specificity of EBUS-TBNA. Adams *et al* and Gu *et al* reported that the pooled sensitivity for EBUS-TBNA was 88% (95% CI 70% to 94%) and 0.93 (95% CI 91 to 944), respectively.<sup>14 15</sup> In their systematic review Varela-Lema *et al* reported that sensitivity for the diagnosis of malignancy ranged from 85% to 100%.<sup>16</sup> In all three reports the specificity was 100%, but this figure is artificial as positive TBNA results were not confirmed by surgical resection. It should be noted, however, that many of the published case series upon which the systematic reviews are based come from a relatively small group of investigators and further experience is needed to see if these results can be widely replicated.

Although in case series the reported sensitivity for the detection of malignancy in mediastinal lymph nodes is similar to that of mediastinoscopy,<sup>17</sup> there are no reported prospective studies comparing the accuracy of EBUS-TBNA and mediastinoscopy for staging of lung cancer.

Tournoy *et al* reported on the sensitivity of EBUS-TBNA for diagnosis of malignancy from intraparenchymal lung masses.<sup>18</sup> In this study of 60 patients they reported a sensitivity of 82% (95% CI 69% to 91%). A similar study by Nakajima *et al* reported a sensitivity of 94% in 35 patients.<sup>19</sup>

One US-based study has reported the use of EBUS-TBNA in the diagnosis of lymphoma. In a retrospective review of 25 patients who underwent EBUS-TBNA for suspected lymphoma, 10 of 11 patients with a final diagnosis of lymphoma were correctly identified, giving a sensitivity of 90.9% and a specificity of 100%.<sup>20</sup> Despite these impressive results, the applicability of EBUS-TBNA for the diagnosis of lymphoma in the UK is unclear, given that histopathology is often required for the final diagnosis.

Four studies have assessed the clinical usefulness of EBUS-TBNA in the diagnosis of sarcoidosis. In these case series EBUS-TBNA was diagnostic in 88–93% of patients. However, it should be noted that the pre-test probability of a final diagnosis of sarcoidosis in these series was high.<sup>21–24</sup> At present there is no evidence to indicate that EBUS-TBNA sampling of lymph nodes is any more or less effective for identifying non-caseating granulomas than transbronchial/endobronchial lung biopsies combined with bronchoalveolar lavage. A clinical trial addressing this issue is currently underway (<http://Clinicaltrials.gov/NCT00872612>). At present some operators combine transbronchial biopsies and EBUS-TBNA lymph node sampling during a single procedure.

### Evidence statements

- ▶ EBUS-guided TBNA has high sensitivity and specificity for identifying malignancy in mediastinal and hilar lymph nodes in patients with lung cancer. (Evidence level 2++)
- ▶ EBUS-TBNA has high sensitivity for identifying malignancy when used for sampling paratracheal and peribronchial parenchymal lung masses. (Evidence level 3)
- ▶ EBUS-TBNA has a high sensitivity for identifying non-caseating granulomas in hilar and mediastinal lymph nodes in cases of suspected sarcoidosis. (Evidence level 2++)
- ▶ The complication rate of TBNA under EBUS guidance is very low, indicating that it is a safe procedure. (Evidence level: 2++)

### Recommendations

- ▶ EBUS-TBNA is a safe and effective technique for the assessment of hilar and mediastinal lymph nodes in cases of confirmed or suspected lung cancer. (Grade B)
- ▶ EBUS-TBNA is a safe and effective technique for sampling paratracheal and peribronchial intraparenchymal lung masses. (Grade D)
- ▶ EBUS-TBNA is a safe and effective technique for sampling hilar and mediastinal lymph nodes in cases of suspected sarcoidosis and may be used in conjunction with endobronchial and transbronchial biopsies. (Grade B)
- ▶ At present there is insufficient evidence to recommend EBUS-TBNA for routine use in the diagnosis of lymphoma. (Grade D)

### Good practice point

- ▶ In cases where EBUS-TBNA results are negative for malignancy, a confirmatory surgical biopsy should be performed where appropriate. (✓)

## THERAPEUTIC PROCEDURES FOR MALIGNANT DISEASE: MALIGNANT AIRWAY OBSTRUCTION

### Endobronchial debulking of tumours

Most new diagnoses of lung cancer are made at an advanced disease stage with 50% of patients having involvement of the central airways either due to endobronchial disease, extrinsic compression or both.<sup>13</sup> Endotracheal or endobronchial obstruction by malignant disease may lead to cough, breathlessness and obstructive pneumonia.

Endobronchial therapy may result in improvement of symptoms and quality of life. There are a number of treatment options available for relieving such symptoms including external beam radiotherapy. However, endobronchial debulking of tumours using rigid and flexible bronchoscopy is commonly used in some centres, especially when such techniques are readily available. There is a need to know the frequency of use of the various debulking techniques, and for more studies to compare the response to other forms of symptom palliation including external beam radiotherapy.

Rigid bronchoscopic procedures under general anaesthesia combine the ability to maintain adequate ventilation, to remove large volume tumour and safely control large volume haemorrhage, but the widespread availability of, and increasing experience in, flexible bronchoscopy has led to an increasing use of flexible bronchoscopic procedures for debulking.

Available procedures for debulking endobronchial tumours via flexible bronchoscope include:

1. Electrocautery/diathermy
2. Argon plasma coagulation (APC)
3. Thermal laser
4. Cryotherapy

5. Cryoextraction/cryorecanalisation
6. Photodynamic therapy (PDT)
7. Brachytherapy

Some of these procedures offer immediate relief of symptoms and in others the benefit is delayed. Where there is extrinsic compression of the airway, insertion of a stent may be more appropriate. When these procedures are performed, there should be adequate airway control since they carry significant risks of haemorrhage, respiratory failure and cardiac arrhythmias.<sup>25</sup> A secure airway such as an endotracheal tube or laryngeal mask should be considered since this allows rapid and repeated insertion of the bronchoscope, high volume suction and the deployment of a balloon bronchial blocker. An example of a malignant airway obstruction flow diagram is shown in Appendix 3.

#### Recommendation

- ▶ In patients with CAO due to intraluminal tumour, endobronchial tumour debulking should be considered. (Grade D)

#### Good practice point

- ▶ When undertaking endobronchial debulking of tumours, a laryngeal mask or uncuffed endotracheal tube is recommended to achieve airway control. (✓)

### Electrocautery or diathermy

#### Principles

Electrocautery (also known as diathermy) uses high-frequency electric current to cause heating which leads to coagulation at lower temperatures or tissue vaporisation at higher temperatures. The current is delivered endobronchially via a probe, snare or needle knife. The degree of tissue destruction depends on the power used, the duration and surface area of contact, and the density and moisture content of the tissue.<sup>26</sup> A monopolar technique is used in the airways. The current passes from the applicator device, through the body to a return electrode usually applied to a limb. Low voltage, low power and high current settings will cause coagulation, while high voltage and low current will cause carbonisation ('cutting'). Most electrocautery devices used via the bronchoscope use a blend of cut and coagulation waveforms.

#### Technique

The equipment required for electrocautery is a high-frequency electrocautery generator and a selection of devices for endobronchial application. These may include a wire snare, probe, needle knife and 'hot' or punch biopsy forceps. The passage of an uncuffed endotracheal tube over the flexible bronchoscope at the beginning of the procedure can facilitate repeated removal of resected tissue. The initial energy setting (around 20 W) should be tested on normal mucosa before treating the lesion. Duration of treatment will affect the depth of tissue damage. Van Boxem *et al* showed that, at a power setting of 30 W, the depth of tissue necrosis increased with duration of application, from 0.1 mm after 1 s progressively to 1.9 mm after 5 s.<sup>27</sup> Longer duration of coagulation (3–5 s) caused damage to underlying cartilage. It is necessary to continuously remove mucus, debris and blood to avoid current leakage.

The probe may be used to vaporise superficial tumours. The snare is useful for debulking large volumes, especially of polypoid tumours. It may be necessary to take a number of separate sections of tumour before the airway is opened up. Removal of large volume tumour from the airway can be achieved in a variety of ways including suction, grasping or

biopsy forceps, or use of a cryoprobe. The knife is particularly useful for resecting benign webs.

#### Indications

Electrocautery has been used for treating benign and malignant disease, and with both curative and palliative intent. The prospective management of benign stenoses using electrocautery<sup>28</sup> is effective. It has also been used for removal of granulation tissue and removal with curative intent of both benign and early stage malignant tumours with a visible distal margin and <3 mm invasion of the bronchial mucosa and no invasion of the cartilage.<sup>27</sup> Radiographically occult lung cancer can be treated with bronchoscopic electrocautery. Electrocautery has principally been used for the palliation of malignant CAO. It appears to be as effective in achieving tumour debulking as the neodymium-yttrium-aluminium-garnet (Nd:YAG) laser and can provide immediate relief of symptoms.<sup>29</sup>

#### Complications

The main complication of diathermy is bleeding. In the largest series this occurred in 1:56 cases.<sup>29</sup> Airway fire has been described.<sup>30–32</sup> To avoid this complication, a fractional inspired oxygen (Fio<sub>2</sub>) of 0.4 or less is recommended, and some groups recommend switching off supplemental oxygen during diathermy use.<sup>33</sup>

Careful application of the patient plate and the use of insulated bronchoscopes reduce the risk of current leakage causing burns. Use in patients with pacemakers should be avoided if possible but, if use is unavoidable, guidelines for reducing risk are available from the Medicines and Healthcare products Regulatory Agency (MHRA).<sup>34</sup> It is recommended that the skin surface overlying a metallic joint prosthesis be avoided when placing return electrodes for electrocautery.

#### Evidence

The evidence for palliation of airway obstruction from both primary and metastatic lung tumour comes from case series alone.<sup>29–31 33 35–38</sup> The results are consistent, with successful outcomes in 39/56 patients,<sup>35</sup> 27/32 patients<sup>36</sup> and 35/37 patients.<sup>33</sup> A safety study undertaken by Horinouchi *et al*<sup>33</sup> concluded that electrocautery is a safe and reliable procedure when used according to strict guidelines, which include a power output not exceeding 30 W for punch biopsy and snare resection, 20 W for probe, and 10 W for needle knife. To prevent airway fire the authors allowed supplemental oxygen only when electrical current was not being applied.

#### Evidence statements

- ▶ Endobronchial electrocautery has an acceptable safety profile in experienced hands provided appropriate device settings are employed. (Evidence level 3)
- ▶ Endobronchial electrocautery is effective for endobronchial tumour debulking, with or without critical airway narrowing. (Evidence level 3)
- ▶ Endobronchial electrocautery is effective in the treatment of early stage lung cancer. (Evidence level 3)
- ▶ Endobronchial electrocautery is effective in the treatment of benign tumours and stenoses of the airways. (Evidence level 3)

#### Recommendations

- ▶ Endobronchial electrocautery may be considered for use with curative intent in benign disease of the airway including incising web-like stenosis, benign tumours and granulation tissue. It may also be considered for primary treatment of early stage non-invasive lung cancer. (Grade D)

- ▶ Endobronchial electrocautery may be considered for palliation of malignant CAO, with or without critical airway narrowing. (Grade D)

#### Good practice points

- ▶ When undertaking snare resection, intermittent bursts of electrocautery of not more than 2 s duration should be used while carefully closing the snare against resistance. (✓)
- ▶ Avoid an  $\text{FiO}_2$  of  $>0.4$  when undertaking electrocautery to reduce the risk of airway fire. (✓)

### Argon plasma coagulation (APC)

#### Principles

APC is a non-contact mode of electrocautery that can be delivered using flexible bronchoscopy. It causes desiccation and coagulation of exophytic endobronchial tumours, and can provide rapid haemostasis when used to treat haemoptysis arising from visible endobronchial lesions.<sup>39–43</sup>

#### Technique

The technique requires a suitable high-frequency current generator, a source of argon, a return electrode and a flexible delivery catheter containing a monopolar treatment electrode. The treatment catheter is made from a Teflon tube, typically of 1.5 mm or 2.3 mm in diameter, which contains a thin wire. The wire conducts the high-frequency current to the tip of the catheter where it ends in a tungsten electrode. The computer-controlled high-frequency generator sends high-voltage high-frequency current to the electrode, while argon is delivered along the catheter at a flow rate of 0.3–2.0 l/min. Argon plasma is produced at the tip and emerges from the catheter as a ‘spray’ of coagulating current, which seeks the path of least electrical resistance to the return electrode through the patient. It is recommended that the skin surface overlying a metallic joint prosthesis be avoided when placing return electrodes for APC. As the current passes through the bronchial mucosa, resistance within the tissue leads to heating, coagulation and desiccation. Increasing electrical resistance in the coagulated tissue in turn limits current flow and therefore the depth of coagulation, which is about 2 mm after a 2 s application. This self-limiting effect of APC is a useful feature for endobronchial application, reducing the risk of bronchial perforation.

#### Indications

APC is principally used for:

- ▶ The treatment of haemoptysis caused by lesions within the central airways.
- ▶ Debulking of exophytic endobronchial tumours, both benign and malignant.
- ▶ Debulking of granulation tissue arising as a complication of tracheobronchial stent insertion.

The published studies of APC do not permit the identification of patients most likely, on clinical or radiological grounds, to benefit from the procedure.

#### Contraindications

In common with other ablation procedures performed using flexible bronchoscopy, APC should not normally be used for the treatment of lesions causing significant tracheal obstruction unless facilities are immediately available for securing the airway in the event of complications. Such lesions can more safely be treated by flexible bronchoscopy under general anaesthesia with endotracheal intubation or by rigid bronchoscopy. As with laser or electrocautery, APC is contraindicated where there is a requirement for a  $\text{FiO}_2$  of  $>0.4$  because of the theoretical risk of

endobronchial fire, although this complication has not been described in the literature. Most modern implantable cardiac pacemakers or defibrillators are compatible with diathermy/APC, but advice should be sought from the patient’s cardiologist prior to the procedure.

#### Complications

No procedure-related complications were described in the studies of Morice *et al*, Crosta *et al* and Okada *et al*.<sup>39 41 42</sup> One patient died within 48 h of the procedure but this was ascribed to neutropenic sepsis. In the study by Reichle *et al*, 5/364 patients (1.4%) developed bronchial or tracheal perforations, all of which resolved on treatment.<sup>40</sup> Three patients developed temporary post-procedural neurological complications and two patients died (myocardial infarction, hypovolaemic shock). The neurological and cardiac complications in these five patients may have been caused by intracardiac gas embolism. This has also been described by Reddy *et al*<sup>44</sup> who reported three cases of intracardiac gas embolism (two fatal) occurring after APC over a period of 3 years, an estimated incidence of 1.3–2%. All were treated using rigid bronchoscopy and it is not clear whether gas embolism arose as a complication of APC or of jet ventilation. The overall incidence of significant complications appears therefore to be approximately 2%.

#### Evidence

The use of APC to treat CAO or haemoptysis using flexible bronchoscopy was examined in four retrospective case series involving 123 patients.<sup>39 41–43</sup> In a much larger retrospective analysis of 364 prospectively collected cases,<sup>40</sup> rigid bronchoscopy was used in more than 90%, but a flexible bronchoscope was passed through the rigid bronchoscope to deliver the treatment.

The studies used different outcome measures for relief of CAO, retrospectively specified in all except the study by Reichle *et al*.<sup>40</sup> The outcome measure used for haemoptysis was consistent—namely, non-recurrence during follow-up.

In treating CAO, APC consistently improved symptoms and airway patency in all studies. In the only study with predefined outcomes, APC produced complete or partial success in reopening the treated airway in two-thirds of patients (124/186).<sup>40</sup> The treatment of haemoptysis was described as being completely successful in 149/150 patients. The evidence is from case series alone but the outcomes are consistent.

#### Evidence statements

- ▶ APC is effective in the treatment of CAO. (Evidence level 3)
- ▶ APC is effective in the treatment of haemoptysis due to endobronchial disease. (Evidence level 3)
- ▶ APC delivered via flexible bronchoscopy for the treatment of CAO or haemoptysis due to endobronchial lesions has a major complication rate of 2%. (Evidence level 3)

#### Recommendations

- ▶ APC may be considered for the debulking of obstructing endobronchial tumour. (Grade D)
- ▶ APC may be considered for tumour debulking in patients without acute critical airway narrowing. (Grade D)
- ▶ APC may be considered for the treatment of haemoptysis in patients with endobronchial abnormalities. (Grade D)

### Thermal laser

#### Principles

Laser therapy for the relief of endobronchial obstruction was first described in 1974 using the  $\text{CO}_2$  laser. The majority of

publications report use of the Nd-YAG laser. In laser therapy the heat energy from laser light is used to coagulate and vaporise endobronchial tissue.

### Technique

The technique can be delivered via rigid or flexible bronchoscopy. Low-power laser is used initially to coagulate tissue to reduce the risk of bleeding. The laser fibre tip should be at least 3 mm from the target tissue to avoid the tissue being vaporised. Continuous suction is used during the procedure to remove smoke from the airways, and continuous inspection of non-obstructed airways is performed to remove any debris and to optimise ventilation. Inspired oxygen is limited to 40% to reduce the risk of airway fire. Laser exposure should be kept to a minimum.

### Indications

The main indication for laser therapy is the immediate relief of endobronchial obstruction due to primary lung cancer or metastatic disease.

### Complications

Complications include massive haemorrhage (1%), pneumothorax (0.4%) and pneumomediastinum (0.2%).<sup>45</sup> The peri-procedural death rate is 2–3%.<sup>46–48</sup> Thermal laser causes more airway scarring and subepithelial fibrosis than other immediate debulking techniques such as diathermy, argon plasma and cryoextraction.<sup>49</sup> With the Nd-YAG laser the literature suggests that the complication rate can be reduced by limiting the power setting to a maximum of 40 W.<sup>45</sup>

### Evidence

Data are almost entirely from case series<sup>45 50–53</sup> and, although outcome data in many of these series are poorly documented, laser therapy appears to be effective in providing rapid relief of endobronchial obstruction with symptomatic improvement in around 70–80%.<sup>47 48 54</sup> One-year survival following treatment was around 30%.<sup>45 46</sup> There is some evidence that outcomes are better if the airway is not totally occluded prior to treatment. Laser therapy has no role in airway occlusion due to extrinsic compression.

Nd-YAG laser is a technique with considerable set-up and maintenance costs. Coulter *et al* and Boxem *et al* reported that electrocautery was as effective as laser in the palliation of endobronchial tumour, but is less expensive.<sup>55 56</sup>

### Evidence statements

- ▶ Nd-YAG laser is effective for endobronchial tumour debulking, with or without critical airway narrowing. (Evidence level 3)
- ▶ There is no role for laser therapy in endobronchial obstruction caused by extrinsic compression. (Evidence level 3)

### Recommendation

- ▶ In patients with CAO due to intraluminal tumour, relief of obstruction using Nd-YAG laser may be considered. (Grade D)

### Good practice point

- ▶ Limit power setting to 40 W. (✓)

## Cryotherapy and cryoextraction

### Principles

Cryotherapy uses extreme cold to cause delayed local destruction of tissue. It is applied in cycles of freezing and thawing, causing tissue necrosis.

### Technique

Cryotherapy is currently used in two different ways. Standard cryotherapy uses a cryoprobe inserted through the instrument channel of a bronchoscope and applied directly to the target tissue. The tissue is frozen and then allowed to thaw, and repeated freeze-thaw cycles lead to tissue necrosis. One disadvantage of standard cryotherapy is the need to repeat bronchoscopy 3–7 days later to remove necrotic material.

A newer form of cryotherapy, 'cryoextraction', is performed with probes which have an improved join between gas channel and probe in order to withstand much greater forces. The probe is applied to the tissue and the freeze cycle activated for 3–7 s (depending on the tissue composition). The bronchoscope is then removed with the cryoprobe and attached tumour tissue. The tissue is allowed to thaw once it is removed from the airway. This technique is undertaken using an endotracheal airway to facilitate repeated removal and reinsertion of the bronchoscope.

### Indications

Cryotherapy—and, in particular, cryoextraction—is mainly indicated as a palliative measure in malignant airway obstruction. Cryoextraction can also be effectively applied to remove foreign objects and blood clots from the airways. There may be an indication for the treatment of low-grade malignant lesions such as adenoid cystic carcinoma and early cancer such as carcinoma in situ.<sup>4</sup> The quality of specimens obtained using cryoextraction with absence of crush artefact has led to its use for endobronchial and transbronchial lung biopsy.

### Complications

Cryotherapy appears to be safe in the treatment of malignant endobronchial obstruction. In case series,<sup>57–63</sup> the complications observed were haemoptysis (4–10%), bronchospasm (4.5%), cardiac arrhythmia (11%) and death (1.3%).

One case series reported on cryoextraction for recanalisation (cryorecanalisation) with a 10% rate of significant bleeding (six patients) managed with conservative measures and APC; no deaths were reported in the series.<sup>64</sup> Another recent case series reported significant bleeding requiring APC or blocking devices in 8%.<sup>65</sup>

### Evidence

In the largest case series comprising 521 patients, cryotherapy appeared effective in the treatment of malignant endobronchial obstruction.<sup>58</sup> Technical success as judged by restoration of airway patency was 61% and improvement occurred in symptoms such as haemoptysis (61–76.4%), cough (69%) and dyspnoea (59–81%). One- and two-year survivals were 38.4% and 15.9%, respectively.<sup>58</sup> Another series of 225 patients showed airway patency restoration (complete or partial) in 91%.<sup>65</sup> A lot of the evidence base is from one centre which performed the procedure with a combination of rigid bronchoscopy and a flexible bronchoscope. The reviewers felt it was still important evidence that could be included in this guideline for flexible bronchoscopy, particularly as the technique can just as easily be performed by flexible bronchoscopy.

In one series where 57 patients with malignant tracheal bronchial obstruction were managed by bronchoscopy and cryoextraction, complete recanalisation was observed in 61% and partial restoration of patency in a further 22%.<sup>64</sup>

Since cryoextraction produces immediate results (unlike conventional cryotherapy), it may be used for the management of acute tracheal or bronchial obstruction.<sup>64–66</sup> Eighty-five per

cent of patients with endobronchial stenosis could be treated with immediate response. Application of this technique is possible at the lobar or segmental level.

In a recent multicentre trial, cryobiopsy sensitivity was 95% compared with forceps sensitivity of 85%.<sup>67</sup> The use of cryobiopsy for transbronchial lung biopsy has also been described. In a trial of 41 patients the mean specimen diameter was 15.11 mm with the cryoprobe compared with 5.82 mm with conventional forceps. Pneumothorax occurred in two patients.<sup>67</sup>

### Evidence statements

- ▶ Cryotherapy has an acceptable safety profile in the treatment of malignant endobronchial obstruction. (Evidence level 3)
- ▶ Cryotherapy is effective in the treatment of malignant endobronchial obstruction without critical airway narrowing. (Evidence level 3)
- ▶ Cryorecanalisation/cryoextraction is effective in the treatment of malignant endobronchial obstruction both with and without critical airway narrowing. (Evidence level 3)

### Recommendations

- ▶ Cryotherapy may be considered for tumour debulking in patients without critical airway narrowing. (Grade D)
- ▶ Cryobiopsy may be considered for diagnostic endobronchial tissue sampling to provide large-volume specimens without crush artefact. (Grade B)
- ▶ Cryorecanalisation/cryoextraction may be considered for tumour debulking. (Grade D)

## Photodynamic therapy (PDT)

### Principles

PDT uses a systemic photosensitiser, most commonly a haematoporphyrin derivative, selectively retained and concentrated in tumour tissue to render the tumour sensitive to light of a given wavelength. The sensitised tumour is then illuminated by laser light of that wavelength, usually 630 Nm at the red end of the spectrum. In the presence of sensitiser and oxygen, laser light illumination causes tumour cell death by a complex pathway triggered by the release of singlet oxygen.

### Technique

PDT requires a photosensitiser, a diode laser and a flexible light-guide, at the end of which is either a radial diffuser or a forward-projecting microlens. The photosensitiser most often used has been intravenous porfimer sodium administered in a dose of 200 mg/kg. The laser with its calibration device is a compact desktop instrument. Forty-eight hours after the administration of photosensitiser the tumour is illuminated by laser light using a flexible light-guide passed down the working channel of a standard flexible bronchoscope. The use of PDT lasers requires standard laser safety precautions, principally to address the risk of ocular damage. There are no thermal risks.

### Indications

PDT has been used for the treatment of:

- ▶ Early central lung cancer, defined as visible endoscopically but not on imaging.
- ▶ The palliative treatment of malignancy causing endobronchial large airway obstruction.

### Complications

Hematoporphyrin derivatives are taken up by skin, causing sensitivity to sunlight or bright direct light for up to 8 weeks. Protection of exposed areas is necessary, but indoor light is safe

and some light exposure is required to photobleach the sensitiser from the skin. In one series of nine patients there was one massive haemoptysis and one bronchopleural fistula.<sup>68</sup> Complications may arise from delayed necrosis of treated tissue.

Compared with electrocautery, more airway scarring and more subepithelial fibrosis were seen after treatment with PDT.<sup>49</sup>

### Organisation and cost

PDT requires the purchase or loan of a diode laser. Intravenous PDT sensitisers are expensive. Light-guides are reusable, being deployed inside a disposable plastic sheath.

### Evidence

In the treatment of early central lung cancer, complete responses have been reported in 30–100% of patients and at least 80% in most series.<sup>69–71</sup> Around a third of patients have required two treatments and a few have needed three treatments. Partial responders can be considered for other treatments including resection or radiotherapy if appropriate. Better responses have been reported for tumours 1 cm or less in diameter. Overall 5-year survival rates have been around 50%, cancer-specific survival up to 90%.

There are only a few series reporting the effect of PDT in palliating the endobronchial symptoms of advanced lung cancer, but it has been shown to be effective for palliation before or after other treatments. Moghissi *et al* reported experience of 100 cases, 82% of whom had been pretreated.<sup>72</sup> Mean endoluminal obstruction (estimated bronchoscopically) fell from 86% to 17.5% with significant increases in forced expiratory volume in 1 s (FEV<sub>1</sub>). All patients had symptomatic relief and 20% had a complete endoscopic response for 3–19 months. There was no treatment-related mortality in this series.

In a review of 12 papers comprising 636 patients with advanced lung cancer, almost all patients had some relief in cough and dyspnoea.<sup>73</sup> Comparisons with YAG laser treatment suggests more prolonged symptomatic relief with PDT,<sup>74</sup> but it has also been used in combination with YAG laser and with endobronchial radiotherapy, with some evidence of a better response to combined treatments.

### Evidence statements

- ▶ PDT is effective in tumour debulking and palliation of symptoms in tracheobronchial obstruction from non-small cell lung carcinoma. (Evidence level 1–)
- ▶ PDT is effective in the palliation of advanced tracheobronchial lung cancer, although adverse events including haemoptysis can occur. (Evidence level 2+)
- ▶ PDT is effective in the curative treatment of early stage lung cancer. (Evidence level 2+)

### Recommendations

- ▶ PDT may be considered for tumour debulking in patients without critical airway narrowing. (Grade D)
- ▶ PDT can be considered for the curative treatment of early central lung cancer, especially for tumours 1 cm or less in diameter and provided there is no imaging evidence of extrabronchial involvement. (Grade D)
- ▶ PDT can be considered for the curative treatment of recurrent lung cancer, for localised endobronchial disease in patients who are not fit for surgery or radical radiotherapy. (Grade D)

### Good practice point

- ▶ The technique should be available for carefully selected patients on a regional basis, administered by physicians or

surgeons with a particular interest and expertise in lung cancer, bronchoscopy and airway management. (✓)

## Endobronchial brachytherapy

### Principles

The word derives from the Greek 'Brachis' meaning 'close to'. It refers to the placement of radioactive sources within or alongside tumours, enabling an effective local dose to be administered but sparing surrounding tissues from the effects of radiation. The use of brachytherapy for lung tumours has been made possible by the development of high dose rate sources enabling treatment to be administered in minutes rather than hours. The technique is suitable for the relief of large airway obstruction and the relief of haemoptysis and other symptoms caused by endobronchial tumour. It can also be used with curative intent for tumours which are small enough to be encompassed by the limited field of radiation.

### Technique

Most centres have used iridium-192, an artificially manufactured isotope. The treatment source consists of a series of iridium pellets housed in a stainless steel capsule approximately the size of a rice grain. It is welded to a drive cable and housed in a safe. A flexible bronchoscope is used to place an applicator (a blind-ending catheter) within or alongside an intraluminal tumour. The bronchoscope is then removed over a long guidewire, leaving the applicator in situ. The guidewire is removed and replaced by a radiodense graduated metal insert. A chest x-ray is taken and the treatment length planned using the insert and its relationship to the main carina to localise the area to be treated. The insert is then removed and the applicator connected to the safe. The radioactive source is then delivered by its drive cable to preplanned positions inside the applicator. The treatment length is determined by the number of positions selected and the diameter of the treatment field is determined by the dwell time at each position. Typically, in a sausage-shaped field, some 10×2 cm is administered. The treatment takes only a few minutes and is therefore suitable for outpatient or day case use. Most centres have used fractionated regimes, typically three fractions of 5–7.5 Gy,<sup>75 76</sup> but the treatment is also effective as a single fraction of 15 Gy.<sup>77</sup>

### Indications

The technique is suitable for the primary and secondary palliation of symptoms caused by large airway obstruction including cough, shortness of breath, haemoptysis and obstructive collapse. It is effective for the treatment of endobronchial tumour and submucosal/peribronchial infiltration. It is not suitable for the treatment of extrinsic compression. It offers flexibility in a number of situations such as bilateral or multiple tumours, or in patients who have been pre-treated with other techniques including external beam radiotherapy. It may be considered for the attempted cure of early central lung cancer subject to accurate local staging to confirm that there has not been extrabronchial spread of tumour.

### Complications

Some patients develop radiation bronchitis and occasionally stenosis. The principal serious risk is of massive haemoptysis, often occurring as a late complication in good responders, and more likely to occur with a higher local radiation dosage—that is, in patients who have also received external beam radiation either sequentially or concurrently.

### Organisation and cost

The equipment is expensive to purchase but can also be used to treat other organ sites and is usually available in major radio-

therapy centres. It requires the availability of flexible bronchoscopy, preferably within the radiotherapy treatment area, and needs good collaboration between physician/endoscopist and clinical oncologist. Health economics comparisons are not straightforward, but it compares favourably with multifraction external beam treatments in terms of cost and patient convenience and avoids the side effects of external beam radiation, especially oesophagitis. It should be available to cancer networks as a treatment option for selected patients.

### Evidence

Brachytherapy has been shown to be effective in the palliation of previously untreated inoperable lung cancer, relieving cough in 20–70% of patients, dyspnoea in 25–80% and haemoptysis in 70–90%.<sup>75 76 78 79</sup> The relief of obstructive collapse has been reported in around 25% of patients.<sup>80</sup> Endoscopic evidence of tumour regression has been observed in most patients, with some complete responses.<sup>75</sup>

Brachytherapy has also been reported to be effective in the palliation of previously treated lung cancer, with symptom relief and endoscopic improvement.<sup>77 80–82</sup>

There are few comparative studies available, but Stout *et al* compared a single fraction of brachytherapy with fractionated palliative external beam radiotherapy, reporting comparable symptom relief but a slightly better duration of response for the external beam arm and also a slightly longer survival.<sup>83</sup>

No survival benefit has been demonstrated for palliative treatments. Survival has been related, unsurprisingly, to performance status.

Brachytherapy has been used to treat radiologically-occult early-stage lung cancer.<sup>75 84</sup> Complete endoscopic responses have been reported in 65–90% of patients, with partial responses in the remainder and 5-year survival of around 80%.

Brachytherapy has been shown to be safe and well tolerated, but massive haemoptysis has been reported in up to 7% of patients and is more likely with higher local dosage, combined or re-treatments, or following laser therapy.<sup>77</sup>

### Evidence statements

- ▶ Brachytherapy is effective in the palliation of inoperable lung cancer. (Evidence level 1)
- ▶ Brachytherapy is safe but massive haemoptysis has been reported in up to 7% of patients. (Evidence level 3)
- ▶ Brachytherapy may be used to treat early stage lung cancer (Evidence level 3)

### Recommendations

- ▶ Brachytherapy should be considered for the palliation of haemoptysis or CAO in locally advanced central lung cancer. (Grade D)
- ▶ Brachytherapy should not be used first-line in preference to external beam radiotherapy for the palliation of lung cancer. (Grade C)
- ▶ Fractionated brachytherapy can be considered for the curative treatment of early central lung cancer, especially if performance or cardiorespiratory status precludes surgery or radical external beam radiotherapy. The success of brachytherapy for radical treatments requires accurate local staging to exclude extrabronchial tumour extension. (Grade C)

## Tracheobronchial stents

### Principles

Tracheal and bronchial stents can be used to maintain airway patency and integrity. Plastic (ie, silicone) stents<sup>85 86</sup> and metal

stents are available. Silicone stents are deployed using rigid bronchoscopy under general anaesthesia. The majority of the published case series regarding outcomes and complications of stent deployment are for deployment by rigid bronchoscopy only.<sup>87</sup> Stent deployment using rigid bronchoscopy is not addressed in this guideline. A recent review offers further information.<sup>88</sup>

Flexible bronchoscopy is an alternative to rigid bronchoscopy to deploy metallic airway stents. The current standard is the Self-Expanding Metallic Airway Stent (SEMAS), made from the alloy NITINOL (Nickel Titanium National Ordnance Laboratories).

### Technique

SEMAS are used to treat airway stenosis or aerodigestive fistulae due to malignant disease. Their use is not advised in benign disease because of the high incidence of severe complications with prolonged use.

Before embarking upon a stenting procedure, a stent of the correct diameter, length and type must be chosen. The availability of modern multislice CT scans with multiplanar reformats has considerably facilitated this process, making it possible accurately to estimate the length and minimum diameter of the luminal stenosis and the diameter of the adjacent normal lumen. Where a main bronchus is extensively narrowed, the opposite main bronchus can be used to estimate the premorbid airway diameter. The length of the stent should be chosen to provide at least 0.5–1.0 cm of overlap at each end of the stenosed segment where possible. The diameter of the stent should be 1–2 mm greater than the estimated normal diameter of the airway. Stent sizing is usually 12–14 mm in diameter for main bronchi, 18–20 mm for the trachea, with lengths of 40 mm for the left main bronchus, 30–40 mm for the right main bronchus and 60–80 mm for the trachea. Where the lesion is exclusively extrabronchial, an uncovered stent is favoured because ventilation of side-branching bronchi can be maintained. For lesions with both extrinsic compression and endobronchial tumour, a stent incorporating a covering membrane ('covered stent') is favoured to prevent tumour in growth through the stent after deployment. A selection of stent sizes should be available prior to the procedure in case bronchoscopic inspection leads to a change of chosen stent size.

Some operators favour the insertion of an uncuffed endotracheal tube over the bronchoscope to protect the airway during the procedure. This may reduce trauma to the vocal cords from repeated bronchoscopic intubation and withdrawal during the procedure. After airway inspection a guidewire is introduced through the working channel of the bronchoscope and positioned beyond the distal extent of the lesion. The bronchoscope is then withdrawn leaving the guidewire in place. The bronchoscope is reintroduced next to the guidewire. The stent is placed over the guidewire and introduced. The distal end of the stent is advanced beyond the stenosed airway segment. The precise positioning of the proximal and distal ends of the stent can be checked either bronchoscopically or fluoroscopically. When these are satisfactory, the stent can be deployed.

A number of stent deployment devices are available. These all have the stent held compressed radially onto a delivery catheter and held down by a restraining mechanism which may be a silk thread or an external catheter. More recently, metallic carinal Y-stents have become available whose deployment is complex and better performed during rigid bronchoscopy.

### Indications

SEMAS are used principally for the relief of CAO due to malignant disease. Other indications include malignant airway

fistulas and post-anastomosis bronchial strictures following lung transplantation.

### Organisation

The expertise to deliver airway stenting should exist within each cancer network. It may be provided by thoracic surgeons or respiratory physicians, but should form part of multimodality treatment supervised by a properly constituted cancer multidisciplinary team. It is essential that the team performing the procedures should have appropriate expertise in managing airway complications, should they occur. Safe airway stenting requires the presence of at least two experienced practitioners, one to visualise the endobronchial appearances and one to deploy the stent.

### Complications

The use of self-expanding metallic stents for the treatment of CAO is associated with a number of complications including stent malposition, migration or fracture, haemorrhage, mucus impaction, overgrowth by granulation tissue or tumour, infection, aerodigestive fistula formation and bronchospasm. Early stent-associated deaths have been reported due to complications such as hypoxia following stent migration, severe sepsis<sup>89</sup> and bronchospasm.<sup>90</sup> Complications may necessitate stent removal, which can be complex and hazardous where there has been a stent fracture. In benign airway conditions where life expectancy is greater, metallic stents are not recommended because of the longer-term risk of stent fracture.

### Evidence

The absence of RCTs of airway stenting makes evaluation of its true effectiveness difficult. Nine case series (349 patients) have described the efficacy and safety of stent insertion by flexible bronchoscopy for malignant and benign airway conditions. SEMAS appear effective in improving breathlessness and cough.<sup>90–93</sup> A visual increase in airway patency has been documented.<sup>93</sup> In a series of 40 patients with malignancy-associated CAO, the severe dyspnoea index improved in 34/39 patients within 24 h of stent insertion.<sup>90</sup>

In CAO due to benign causes, stents improve symptoms. In a series of 40 patients this improvement was evident in stridor in 73% of cases, breathlessness in 71%, cough in 79% and in sputum clearance in 75%.<sup>91</sup> In five series where a proportion of patients had lung function assessed before and after stent insertion,<sup>89 91–94</sup> FEV<sub>1</sub>, forced vital capacity (FVC) and airway resistance (where measured) improved.

In patients with acute respiratory failure due to malignant CAO requiring mechanical ventilation, stenting is associated with weaning from ventilatory support. In one series this was achieved in 14 of 26 patients with CAO, 21 of whom had malignancy.<sup>95 96</sup> These case series data do not permit the identification of stenting as the cause of weaning success.

RCTs are needed to compare the addition of airway stenting to conventional anticancer treatments versus conventional treatment alone in patients with CAO due to malignancy.

### Evidence statements

- Self-expanding metallic stents are effective in the treatment of malignant CAO following endobronchial debulking techniques. (Evidence level 3)
- Self expanding metallic stents are effective in the treatment of extrinsic malignant CAO. (Evidence level 3)

## Recommendations

- ▶ The use of self-expanding metallic stents may be considered for the treatment of malignant CAO due to extrinsic disease. (Grade D)
- ▶ Self-expanding metallic stents may be used to maintain airway patency following endobronchial debulking techniques. (Grade D)
- ▶ Self-expanding metallic stents can be used to restore or maintain airway patency in conjunction with other treatments such as external beam radiotherapy. (Grade D)

## Good practice points

- ▶ Patients require careful specialist follow-up after stent insertion. (✓)
- ▶ Stents should be used with caution in non-malignant disease because of their long-term complications. Self-expanding metallic stents may be difficult to remove following long-term placement. (✓)
- ▶ Self-expanding metallic stents should only be used in benign disease after all other therapeutic options have been exhausted. (✓)
- ▶ A risk-benefit assessment should be performed, incorporating immediate and long-term implications, before selecting any particular type of stent. (✓)

## EMERGING APPLICATIONS FOR FLEXIBLE BRONCHOSCOPY

The following applications have been developed for use with the flexible bronchoscope but are yet to have established a clear place in routine practice.

### Electromagnetic navigation bronchoscopy (ENB)

#### Principles

ENB is an image-guided localisation system to aid biopsy of lesions that are not visible endobronchially. It combines CT-generated virtual bronchoscopy and electromagnetic tracking of a steerable probe within the bronchial tree.

#### Technique

A multi-slice thin-section CT scan of the thorax is performed and used to create a 3-D virtual bronchoscopy. During virtual bronchoscopy, specific bronchial landmarks such as the main and segmental carinae are identified and the target lesion is marked. At bronchoscopy the patient lies in a magnetic field created by an electromagnetic board placed below the chest. A magnetic locatable probe, passed through the bronchoscope, is used to mark the same sites in the bronchial tree as were previously identified on virtual bronchoscopy. The two sets of data are then merged to co-register the CT data on the bronchoscopic spatial points. This allows the data from the virtual bronchoscopy to direct the bronchoscopic probe to the lesion. Once the desired location is reached, the locatable guide is exchanged for biopsy forceps or bronchial brushes and sampling is performed.

#### Indications

- ▶ Peripheral nodule sampling
- ▶ Targeted biopsy in patients with diffuse lung disease
- ▶ Mediastinal lymph node sampling
- ▶ Insertion of fiducial markers for radiotherapy
- ▶ Implantation of brachytherapy seeds or catheters
- ▶ Dye marker placement for surgical resection of peripheral mass

#### Complications

ENB appears to be safe, with pneumothorax as the most commonly reported complication. The rates of pneumothorax reported in three studies using ENB were 3.5–7.5%,<sup>97–99</sup> which

are lower than reported rates of pneumothorax following CT-guided percutaneous needle biopsy.<sup>100–102</sup> However, RCTs comparing the techniques have not been performed.

## Evidence

The evidence comes from six case series<sup>97–99 103–105</sup> with a total of 231 patients. In these studies a diagnostic rate of 59–80% was achieved. The results indicate that diagnostic accuracy is related to the size of the pulmonary opacity, with greater accuracy for masses >40 mm in diameter.

In a randomised study, Eberhardt *et al* achieved a higher diagnostic rate by combining ENB with radial EBUS than with ENB alone (88% vs 59%).<sup>106</sup> In a separate study they achieved a higher diagnostic rate using suction catheter aspiration (90%) compared with forceps biopsy (50%).<sup>107</sup>

Studies using virtual bronchoscopy alone to guide peripheral lung biopsy have found similar diagnostic rates,<sup>108–110</sup> and there is currently a lack of evidence that ENB provides additional sensitivity.

ENB appears to be a safe and effective but expensive modality for the sampling of peripheral lung lesions.

## Recommendation

- ▶ Electromagnetic bronchoscopy may be considered for the biopsy of peripheral lesions or to guide TBNA for sampling mediastinal lymph nodes. (Grade D)

## Valves in the treatment of emphysema

### Principles

Patients with severe emphysema who are on maximal medical treatment are often very disabled. Treatment options other than lung transplantation and, in selected cases, lung volume reduction surgery are limited. This group of patients has significant morbidity with repeated hospitalisations and increased health-care utilisation. In the UK over 20% of patients with emphysema have severe disease, and in 2004 chronic obstructive pulmonary disease accounted for 1.4 million consultations with over 100 000 hospital admissions.

Endobronchial valves may be used in the treatment of patients with emphysema with severe hyperinflation. The valves are inserted into the target area of the lungs via flexible bronchoscopy under conscious sedation or general anaesthesia. Two different valves systems are available. The Zephyr valve is a one-way duck-billed valve and the intrabronchial valve (IBV) is an umbrella-like device. Both valves act by reducing gas inflow to the treated segment while allowing air and secretions to exit.

### Technique

The procedure may be performed under conscious sedation or general anaesthesia. The insertion of an endotracheal tube at the beginning of the procedure is recommended. Under direct vision the size of the target airway is estimated. For the Zephyr valve, an appropriately-sized device on its catheter is inserted through the instrument channel of the bronchoscope and the valve is partly deployed. The valve is then wedged onto a carina in the target area to prevent distal or incorrect placement. Once appropriately positioned, the valve is fully deployed. Further valves are placed in order to achieve complete occlusion of the target lobe. Placement of the IBV is similar but requires accurate airway sizing with a calibrated balloon catheter.

### Indications

- ▶ Heterogeneous (ie, >10% variation) in emphysematous destruction between adjacent lobes on CT scanning

- ▶ Moderate to severe airflow obstruction ( $FEV_1 < 50\%$  predicted)
- ▶ Severe dyspnoea ( $MRC \geq 2$ )
- ▶ Hyperinflation (total lung capacity  $\geq 100\%$  predicted, residual volume  $\geq 150\%$  predicted)
- ▶ Optimum treatment of chronic obstructive pulmonary disease for at least 6 weeks

### Contraindications

- ▶ Carbon monoxide transfer factor  $< 15\%$  predicted and  $FEV_1 < 15\%$  predicted
- ▶ Oxygen tension on air  $< 6.0$  kPa
- ▶ Production of purulent sputum more often than not ( $> 50\%$  of days)
- ▶ Lung nodule requiring surgery

### Evidence

The evidence consists of open-label cohort studies<sup>111–117</sup> in 222 patients with severe emphysema and one randomised study has recently been published.<sup>118</sup>

Two devices have been used differently. The Zephyr valve has been used to produce atelectasis by unilateral treatment of a whole lobe. The IBV has been used in a strategy of airflow redirection by treating both upper lobes but leaving at least one sub-segment in each lobe open.<sup>119</sup> Quantitative CT has shown that treatment of patients with emphysema with bronchial valves results in changes in regional volumes with a significant decrease in treated upper lobe volumes and a significant increase in the non-treated non-upper lobe volumes.<sup>120</sup>

Treatment has been complicated by exacerbations and some pneumothoraces but is generally safe. In the randomised study there were eight deaths (2.7%) and the incidence of other key adverse events was distal pneumonia (0.5%), pneumothorax requiring an intercostal drain for  $> 7$  days (1.4%) and respiratory failure (1.8%).<sup>118</sup> There have been small improvements in lung function and variable improvements in quality of life depending on treatment strategy. The randomised study with Zephyr valves<sup>118</sup> has shown only modest improvements in  $FEV_1$  of about 5.8%. There were no consistent improvements in the 6 min walk test and quality of life measures.

The open-label study with the IBV demonstrated improvements in quality of life but no significant change in pulmonary function.<sup>119</sup> However, the changes in subjective measures such as quality of life in an open-label study should be interpreted with caution. The place of endobronchial valves in patients with emphysema remains to be established.

### Evidence statements

- ▶ Endobronchial valves in the treatment of emphysema appear to be safe in patients with severe disease. (Evidence level 1)
- ▶ Endobronchial valve insertion in patients with severe emphysema and hyperinflation leads to small improvements in lung function. (Evidence level 2–)

### Recommendation

- ▶ Sufficient efficacy has not been demonstrated with endobronchial valves to recommend their use currently. However, they may be considered in the treatment of selected patients with severe emphysema and hyperinflation with heterogeneous disease in the absence of significant collateral ventilation or in those who have a complete fissure on CT scanning. (Grade B)

### Good practice point

- ▶ Patients should be enrolled into clinical trials until more robust data of clinical benefit are available. (✓)

### Other procedures in emphysema

A number of bronchoscopic procedures are being developed for emphysema that include airway stents (bypass procedure) in homogeneous emphysema, coils which lead to infolding of the lung, hydrofoam gel and steam instillation to induce localised fibrosis.

### Bronchial thermoplasty for asthma

#### Principle

The prevalence of asthma is increasing and ranges from 10% to 13% in the UK. It is associated with a high admission rate of around 200 per 100 000 of the population per annum, and approximately 18% of patients in the UK have severe persistent asthma. Some symptoms are due to airflow obstruction as a direct result of airway smooth muscle contraction. Airway smooth muscle may also have a role in the pathogenesis of asthma by secreting proinflammatory cytokines and promoting airway remodelling. The goal of bronchial thermoplasty is to reduce airway smooth muscle.

#### Technique

The treatment is performed via flexible bronchoscopy under conscious sedation. Microwave energy is delivered to the bronchial wall via a flexible catheter from a radiofrequency generator. The treatment catheter is passed through the bronchoscope and is navigated to the distal target airway. A wire array at the distal end of the catheter is expanded and the radiofrequency generator activated. This heats the airway wall to about 65°C and selectively ablates the concentric smooth muscle. The airways are treated in a systematic manner from distal to proximal. The right lower lobe is treated first followed by the left lower lobe 3 weeks later, then the upper lobes.

#### Indications

Thermoplasty may be indicated in patients with severe persistent asthma receiving high-dose combination inhalers ( $> 1000$  µg beclometasone equivalent) plus long-acting bronchodilators or long-term oral corticosteroids. The  $FEV_1$  should be  $> 50\%$  predicted.

#### Complications

Patients may experience post-procedure respiratory exacerbations. Limited long-term safety data for this procedure are available.

#### Evidence

The evidence base includes preliminary studies demonstrating feasibility and safety in 25 patients,<sup>121</sup> two randomised controlled studies in 146 patients and one randomised sham controlled study in 297 patients.<sup>123–125</sup> The studies have consistently demonstrated a transient increase in asthma-related adverse events in the short term during the bronchoscopic treatment, but are associated with a significant reduction in adverse events, asthma-related symptoms and hospitalisations in the longer term. The AIR2 randomised sham controlled study demonstrated a 32% reduction in exacerbations and a decrease of  $> 80\%$  in emergency room visits. There were improvements in quality of life and asthma control symptoms; the mean change in the Asthma Quality of Life Questionnaire (AQLQ) was 1.35 from baseline and 79% of patients had a clinically meaningful improvement in the AQLQ score. There was a reduction of 66% in days lost from work, school and other activities due to asthma.<sup>125</sup>

However, despite some evidence for the use of thermoplasty in asthma, the studies are selective and the outcomes are only

positive in some aspects. This is a treatment which might be useful for some selected cases of difficult asthma. The final place of thermoplasty in cases of difficult asthma remains to be established.

### Evidence statements

- ▶ Bronchial thermoplasty in patients with moderate to severe asthma has been associated with a short-term increase in asthma-related symptoms. (Evidence level 1)
- ▶ Bronchial thermoplasty in patients with moderate to severe asthma leads to a reduction in adverse events from 6 weeks after their final treatment. (Evidence level 1)
- ▶ Treatment with bronchial thermoplasty in patients with moderate to severe asthma has been shown to reduce the frequency of respiratory exacerbations, days lost from school or work due to asthma and to improve the quality of life. (Evidence level 1)

### Recommendation

- ▶ Bronchial thermoplasty is a possible treatment option in selected patients with severe persistent asthma already on maximal therapy, although its place in the treatment of asthma remains to be established. (Grade A)

### Good practice point

- ▶ Long-term safety and efficacy remains unclear. Hence, treatment should be limited to a few specialist centres in carefully selected patients. Longer term follow-up of treated patients is recommended. (✓)

### CONCLUSION

This guideline provides an evidence-based overview of advanced diagnostic and therapeutic techniques, some of which are widely available and some of which are only available in specialist centres. It is clear that TBNA and EBUS are becoming standard practice in all regions. Tumour ablation is not routinely available via flexible bronchoscopy in all regions, and there are insufficient trainees who feel competent to undertake these procedures at the end of their training. There is therefore a need to identify those centres which provide hands-on training and to increase the availability of that training.

In this rapidly developing field, new techniques and more evidence are going to become available so it is planned to review this guideline in 2015. There is also a need provide the evidence for patients, other practitioners and commissioners of the benefits of these techniques in the UK, so it will be important for centres using advanced bronchoscopy techniques to keep careful records and undertake audit.

Not all techniques described here will be used in all centres or even every region. Some centres may continue, for example, to refer all patients for stenting or tumour ablation to surgical units. However, there is a need for all practitioners to be aware of what is available and to know when to consider referring patients for procedures they do not undertake themselves.

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## APPENDIX 1 Committee membership and declared conflict of interest

Contributor	Sections contributed	Conflict of interest
Professor RA Lewis Chairman of the British Thoracic Society Interventional Bronchoscopy Guideline Group. Consultant Respiratory Physician with a special interest in lung cancer Worcestershire Royal Hospital Worcester	Development of the Guideline Electromagnetic Navigation Bronchoscopy Photodynamic Therapy Endobronchial Valves Diathermy Evidence tables	Professor Lewis has been in receipt of loan and prototype equipment from Olympus Ltd. Professor Lewis has no financial interest in Olympus Ltd. He is a faculty member of an interventional bronchoscopy course that is sponsored by Olympus, Erbe, Cook Medical, Superdimension, Taewoong medical, Alveolus & Emphysis. Prof Lewis has no financial interest in any of these companies and there is no conflict of interest in relation to the guideline.
Dr IA Du Rand Specialist Registrar in Respiratory Medicine West Midlands Deanery Completing MSc Oxford University in Evidence Based Medicine Dr PV Barber Consultant Respiratory Physician with a special interest in lung cancer University hospital of South Manchester, Manchester	Development of the Guideline Developed website for on-line appraisal General Interventional Bronchoscopy Evidence tables Appendix 3 Photodynamic Therapy Brachytherapy Evidence tables Appendix 3	None     Dr Barber has used diode laser equipment loaned by Axcant Ltd. He has no financial interest in Axcant Ltd.
Dr J Goldring Specialist Registrar in Respiratory Medicine London deanery Dr S Mandal Specialist Registrar in Respiratory Medicine London deanery	General Interventional Bronchoscopy Diathermy Evidence tables General Interventional Bronchoscopy Diathermy Evidence tables	None   None

Continued

## Continued

Contributor	Sections contributed	Conflict of interest
Dr M Munavvar Consultant Respiratory Physician with a special interest in lung cancer Lancashire Teaching Hospitals Preston	Endobronchial Ultrasound Argon Plasma Coagulation Evidence tables	Dr M Munavvar has been involved in prototype evaluation of interventional bronchoscopy/thoracoscopy related equipment for Olympus, Boston Scientific, Cook and Spiration. He organises Interventional Bronchoscopy/Thoracoscopy and Basic Bronchoscopy courses, which are sponsored by numerous companies including Olympus, ERBE, Wolf, Sonosite, Rocket, UK Medical, Nucletron, Pentax, Fujinon, Conmed, Cook, Spiration and others. Dr Munavvar has no financial interest in any of these companies and there is no conflict of interest in relation to the guidelines.
Dr RC Rintoul Consultant Respiratory Physician with a special interest in lung cancer Papworth Hospital Papworth Everard Cambridge CB23 3RE	Endobronchial Ultrasound Electromagnetic navigation Laser therapy Cryotherapy General Interventional bronchoscopy Evidence tables	Dr Rintoul is in receipt of loan equipment from Olympus Ltd and Hitachi Pentax and Papworth Hospital acts as a reference centre for the technique of EBUS-TBNA. Olympus Ltd has provided educational grants to support courses about EBUS. Dr Rintoul has no financial interest in either Olympus Ltd or Hitachi Pentax.
Dr PL Shah Chairman of the BTS Interventional Pulmonology SAG Consultant Respiratory Physician with a special interest in lung cancer Royal Brompton Hospital and the Chelsea and Westminster Hospital, London	Laser Cryotherapy Endobronchial valves Thermoplasty Brachytherapy Photodynamic therapy Evidence tables	Dr PL Shah is a principle investigator for a number of clinical trials and the host institutions for the trials (Royal Brompton Hospital and the Chelsea & Westminster Hospital have been reimbursed for clinical trial expenses by Asthmatx, Boehringer Ingelheim, Broncus, Olympus & PneumRx. He is the course director for an interventional bronchoscopy course which has been sponsored by Olympus, Erbe, Cook Medical, Superdimension, Taewoong medical, Alveolus & Emphysis. Dr Shah has no financial interest in any commercial entity whose interests are in any way connected with this guideline.
Dr S Singh Secretary of the BTS Interventional Pulmonology SAG Consultant Respiratory and Intensive Care Physician Chelsea and Westminster Hospital, London	Stenting Thermoplasty Evidence tables	Dr S Singh is a co investigator for interventional bronchoscopy trials in bronchial thermoplasty and lung coils. He is a faculty member of an interventional bronchoscopy course that is, sponsored by Olympus, Erbe, Cook Medical, Superdimension, Taewoong medical, Alveolus & Emphysis. He has previously received Speaker fees from Cook Medical. Dr Singh has no financial interest in any company associated with this guideline.
Dr MG Slade Consultant Respiratory Physician with a special interest in lung cancer Papworth Hospital Papworth Everard Cambridge CB23 3RE	Argon plasma coagulation Stenting Evidence tables Appendix 2	Dr Slade is clinical director of thoracic services at Papworth Hospital, which is or has been in receipt of loan equipment from Olympus UK Ltd and Hitachi Medical Ltd. Olympus UK, Pentax UK, Boston Scientific UK, Erbe Medical UK, Richard Wolf UK and Storz UK have sponsored educational courses on interventional pulmonology run by Dr Slade in Oxford and Cambridge. Dr Slade has no financial interest in any commercial entity whose interests are in any way connected with this guideline.
Dr A Woolley Consultant Respiratory Physician Worcestershire Royal Hospital Worcester	Electromagnetic Navigation Bronchoscopy Evidence tables	None

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Nicholas Smith BA(Hons) MSc, Information Support Librarian.  
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Rowlands Library, Worcestershire Royal Hospital.

## APPENDIX 2

## A step-by-step practical guide for performing transbronchial needle aspiration (TBNA)

## Initial considerations

TBNA requires very few additional resources to implement, and is therefore readily available to all practitioners. Bronchoscopists have, however, frequently found that 'real-world' results do not equal those in the published literature. This guide is intended to help shorten the learning curve.

TBNA is best viewed as a team effort. Optimal results depend upon

- (i) Familiarity with the needle for both the bronchoscopist and the assisting staff.
- (ii) Collaboration with colleagues in cytopathology to ensure optimal specimen preparation.
- (iii) Careful pre-procedure discussion with a radiologist to ensure that the bronchoscopist knows where the targets are endobronchially.

## The needle

There are several different TBNA needles available and choice between them is clearly a matter of personal preference and cost. It is recommended that demonstration needles are obtained of different types. Needles with a clear plastic outer sheath have the advantage that the aspirated material can be viewed during sampling, which helps the operator to know that the sample will be adequate. The whole team should practise with the chosen needle so that everyone knows what instructions will be given for advancing and retracting the needle, how and when to apply and release suction, and so on.

## Tuition

There are a number of courses available on advanced techniques in bronchoscopy, which offer hands-on training in TBNA technique. It is strongly recommended that a new operator attends such a course, ideally together with bronchoscopy assisting staff.

## The procedure

- (i) The procedure described is for lymph node sampling. TBNA can also be used to sample extrabronchial tumour, or to take specimens from deep within necrotic lesions.
- (ii) Target lymph nodes are identified from prior CT or PET scanning. If the procedure is being performed for lung cancer staging, a plan is made to sample the highest-station nodes first (i.e., N3 before N2 before N1).
- (iii) The bronchoscopy is begun as usual. Once the bronchoscope is within the trachea, lymph node sampling is performed before any other inspection or sampling. If possible suctioning within the airways is avoided, lest any exfoliated malignant cells enter the working channel and contaminate the TBNA sample. If the view is obscured by mucus or blood, the injection of a small quantity of saline is used to clear the optic.
- (iv) The bronchoscope is positioned over the first target site, and the needle sheath advanced through the working channel. Approximately 5 mm of needle sheath is allowed to protrude from the distal end of the channel.
- (v) The bronchoscope is flexed so that the tip of the needle sheath lies against the airway wall, between the cartilaginous rings, and directed towards the target.
- (vi) The needle sheath is anchored within the working channel by one of two methods: operators with large hands may be able to use the little finger to apply gentle pressure to the sheath against the wall of the working channel, while still directing the

bronchoscope. Others may prefer to ask an assistant to anchor the needle sheath. An advantage for the operator of anchoring the needle oneself is that subtle tactile feedback occurs as the sheath tip moves up and down the airway, 'bumping over' the cartilage rings. This may facilitate precise, correct positioning of the sheath tip between the rings.

(vii) The assistant is then asked to advance the needle, using some agreed instruction (eg, 'needle out'). If the needle is of a type that has a reasonably stiff wire running down it, and if the tip of the sheath is correctly positioned between the airway cartilages, the needle will often pass directly through the airway wall. This is known as the 'Hub against the wall' method. If the needle does not penetrate the airway and instead causes the sheath and bronchoscope to recoil, the operator can advance the bronchoscope, with the needle sheath still anchored within the working channel, to attempt penetration with the 'Piggy back' method.

(viii) Once the needle has passed through the airway wall, it may be necessary to advance the needle sheath, while carefully withdrawing the bronchoscope, so that more of the needle sheath is visible before sampling begins. Otherwise, as the needle sheath is drawn back to begin the cycle of to-and-fro motion through the lymph node, the airway wall may simply recoil forwards towards the bronchoscope, obscuring the view, before any relative motion between the needle and the lymph node has occurred.

(ix) The bronchoscopist then asks that suction be applied to the needle.

(x) The bronchoscopist then begins to-and-fro motion of the needle sheath, and observes carefully the motion of the needle as it enters the airway wall. It is important to be able to observe definite motion in and out, though care should be taken not to withdraw the needle completely from the airway wall. This takes considerable practice.

(xi) During the sampling process it is helpful if an assistant holds the bronchoscope stationary at the nose or mouth.

(xii) With some experience it is possible for the operator to know whether a lymph node is being successfully sampled. If it is, then gooeey material, looking a little like

pink toothpaste or raspberry ripple ice-cream, is seen entering the needle sheath. If the needle appears to be well-positioned, and satisfactory passes are being performed, but no such aspirate is obtained, it is worth slowly withdrawing the needle and then advancing it rapidly in a jabbing motion. This is because some lymph nodes have a relatively tough capsule that deforms steadily as the needle is advanced, without permitting penetration. A jabbing action can overcome this effect and allow the needle to enter the node, which then yields "goo" as above.

(xiii) Once a satisfactory specimen is obtained, the needle is withdrawn by the assistant, in response to a clear and previously agreed instruction from the operator. The needle sheath is withdrawn and the specimen prepared by the assistant.

(xiv) The way that specimens are prepared will depend upon the preference of the local cytopathologist. The options are direct smears, air-dried or fixed with cytological fixative, or both; or simple flushing of the sample into liquid, which may be either saline, cytological fixative or media suitable for RNA extraction or flow cytometry. The best results, in the author's experience, are always obtained by giving the cytopathology department what it wants.

(xv) Further samples are then taken from the same lymph node station, before moving on to further, lower-stage sites. It is recommended that up to 5 passes are obtained through each node.

### Golden rules

There are a few rules that will help to avoid complications and promote success.

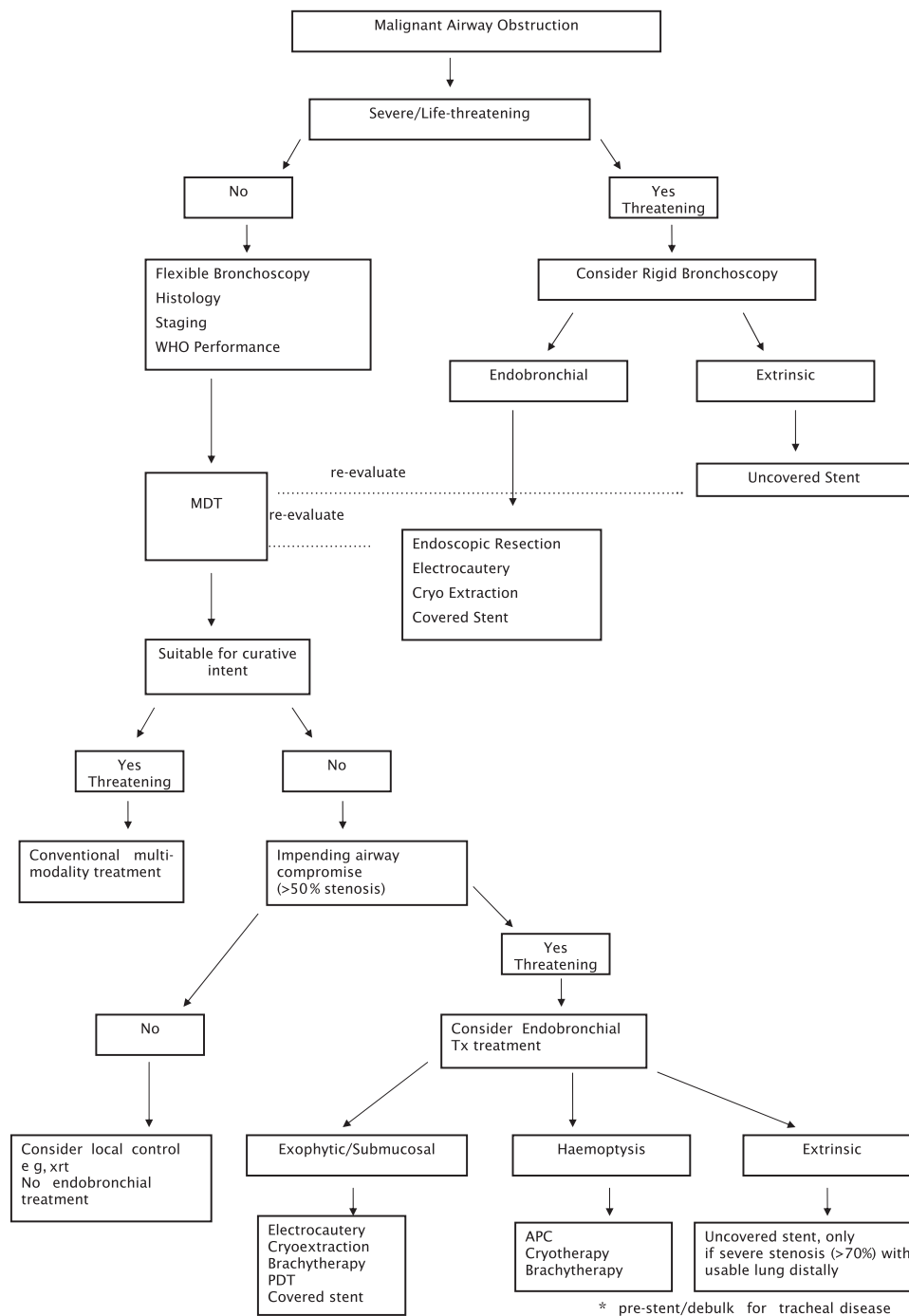
(i) The needle should never be advanced unless the tip of its sheath is clearly visible, otherwise the needle may perforate the working channel.

(ii) Always sample the highest-station nodes first.

(iii) Don't give up if the first few nodes sampled give non-diagnostic results. The learning curve for TBNA is not flat.

(iv) Aim for large (>2 cm short axis) nodes for your first few procedures.

**APPENDIX 3**  
**An example of a malignant airway obstruction flow**  
**diagram (local facilities may determine the**  
**approach used)**



	Time to onset of action	Contra-indications	Advantages	Disadvantages	Effectiveness to palliate symptoms (% patients)	Effectiveness to open airway (% patients)	Complications
PDT	Within 48 h, <sup>3</sup> often much quicker	Tracheal disease requires pre-stent or debulk Porphyria Allergy to haematoporphyrin	Effective palliative measure for endobronchial airway obstruction.	Delayed onset of action. Debulking often required after palliative treatment Skin photosensitivity for 6–8 weeks	100% <sup>126</sup>	80% <sup>3</sup>	Skin Burn if not protected Initial airway oedema/obstruction Late stricture Occasional major bleeding
Brachytherapy	Gradual over days or weeks, occasionally months	Prior high-dose radiation or thermal laser Tracheal disease may require pre-stent or debulk	Long-term palliation of symptomatic endobronchial malignancy	Requires specialised equipment and radiotherapist collaboration	69–90% <sup>81 126 127</sup>	78–85% <sup>81 126 127</sup>	Radiation bronchitis Late stenosis Late massive haemoptysis
Original Cryotherapy	1–2 weeks		Can be used to remove foreign objects or mucus plugs	Multiple bronchoscopies required	70–93% <sup>60 126 128 129</sup>	77–79% <sup>60 126 128 129</sup>	Bleeding Initial hyperaemia of tumour, with temporary increase in airway obstruction. Bleeding following tumour extraction
Cryo-extraction	Immediate effect		Effective palliation of central airway obstruction.	Requires specialist equipment	>90%	83–91%	
Thermal Laser	Immediate	If exclusive extrinsic airway compression	Rapid therapeutic effect. Extensive experience worldwide	Not well established as a flexible bronchoscopy technique; poorly tolerated with conscious sedation. Difficult to treat upper lobe lesions	63–94% <sup>45 56 130</sup>	>90% in trachea <sup>3</sup> 60–70% for more distal lesions <sup>3 45 56 130</sup>	Smoke Haemorrhage Hypoxia Airway perforation Airway fire risk with >40% FiO <sub>2</sub>
Diathermy/ Electrocautery	Immediate effect	Caution with pacemaker	Inexpensive Good safety profile	Time-consuming probe in contact with tissue, needs frequent cleaning	70–97% <sup>35 56 131</sup>	88% <sup>35 56 131</sup>	Airway fire Contact burns Airway perforation
APC	Immediate effect	Caution with pacemaker	Effective in haemoptysis and for larger areas of superficial cancer	Ineffective for major debulking	100% in haemoptysis <sup>42</sup>	91% <sup>42 126</sup>	Bleeding Fire Late stenosis

## APPENDIX 4

### Evidence Tables

Available on-line on the BTS Website and at <http://thorax.bmjgroup.com>

## APPENDIX 5

### List of Stakeholders

#### Name of College/Society

Royal College of Physicians  
Royal College of Physicians, Edinburgh  
Royal College of Surgeons of England  
Royal College of Surgeons of Edinburgh  
Royal College of Physicians and Surgeons of Glasgow

Royal College of Anaesthetists  
British Geriatrics Society  
Society for Acute Medicine  
TSANZ  
Endoscopy UK  
NICE  
Royal College of General Practitioners  
Royal College of Nursing  
Royal college of Pathologists  
British Society of Clinical Cytology  
British Oncological Association  
Royal College of Radiologists  
Society for Cardiothoracic Surgery in GB and Ireland  
KeyMed Olympus Pentax—commercial stakeholders contacted only upon completion of the guideline for comments

## **Appendix 4**

### *Evidence Tables*

# Cryotherapy Evidence Tables

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Moghissi, K	Treatment of Endotracheal or Endobronchial Obstruction by Non-Small Cell Lung Cancer: Lack of patients in an MRC Randomised Trial Leaves Key Questions Unanswered	1999 Clinical Oncology	RCT	plus plus	75 patients were randomised out of 200, 75 radiotherapy (n=38) endobronchial treatment (n=37)	Radiotherapy age 72.2 years. Male n= 23, female n= 15. Endobronchial radiotherapy age 71 years. Male n= 24, female n= 13. All had partial or complete obstruction of trachea, main bronchi or lobar bronchus by confirmed NSCLC. Disease had to be too advanced for surgical resection or radical radiotherapy with curative intent. All patients had to be thoracic radiotherapy naive.	Radiotherapy versus endobronchial treatments ( cryotherapy, laser or brachytherapy)	Radiotherapy versus endobronchial treatments ( cryotherapy, laser or brachytherapy)	Up to 3 years	Site of obstruction; severity of breathlessness; cough; haemoptysis; chest pain; stridor; FEV1; FVC; PEFR; QoL measurements; dyspnoea score WHO performance status radiotherapy performance status symptoms and 1 year survival	Relief of dyspnoea: radiotherapy 32%, endobronchial therapy 28%. Palliation of symptoms: radiotherapy 27%, endobronchial therapy 22%. Improvement in WHO performance status: radiotherapy 14%, endobronchial therapy 38%. 1 year survival: radiotherapy 26%, endobronchial therapy 29%	Medical Research Council UK	The study was discontinued before full recruitment but does show that endobronchial treatments and radiotherapy all appear as effective in palliation of symptoms in patients with endobronchial obstruction from non small cell lung cancer.
Homasson, J. P.; Renault, P.; Angebault, M.; Bonniot, J. P.; Bell, N. J.	Bronchoscopic cryotherapy for airway strictures caused by tumors	1986 Chest	Qualitative research	minus	27 patients -22 with malignant obstruction and 5 benign granulomas.	Mean age = 60 years (range 39 to 88)	Effect of cryotherapy on airway narrowing caused by tumours.	No comparison group.	Not reported	Key outcome measures: local tumour control, (biopsy and radiological results) and safety of cryotherapy.	Disappearance or regression of the tumour leading to improved ventilation of a lobe or lung and cessation of haemoptysis = 61.9% (13/21). Technical failures (probe was too short) = 18.5% (5/27). Residual tumour identified on biopsy = 4.5% (1/22) Complications: Death due to major myocardial ischaemia = 3.7% (1/27); Change in heart rhythm during procedure = 11.1% (3/27); Mild fever = 7.4% (2/27).	Not recorded	Cryotherapy is safe and effective at treating endobronchial tumours from cancer and benign granulomas not amenable to other treatments.
Bertoletti, L.	Bronchoscopic Cryotherapy Treatment of Isolated Endoluminal Typical Carcinoid Tumor	2006 Chest	Qualitative research	plus	18 patients with endobronchial typical carcinoid	Average age 47 years. 11 F: 7 M	Effect of cryotherapy on endobronchial typical carcinoids	Recurrence rates and safety	Abstract reports 55 months median as does discussion. Results reports 44.5 months.	Recurrence rates and safety	Recurrence rates: 2 patients had local recurrence (after more than 5 years). 1 patient had atypical carcinoid and developed contralateral lung recurrence. Safety: 1 episode of minor bleeding requiring local vasopressin, 1 episode of pneumomediastinum which resolved spontaneously.	Not reported	Cryotherapy is a safe and effective treatment in endoluminal typical carcinoid. Only 2 patients developed local Recurrence more than 5 years after treatment. Overall safe and worthwhile treatment option in patients with disease co-morbidity where lung preservation is crucial.
Hetzel, M.; Hetzel, J.; Schumann, C.; Marx, N.; Babiak, A.	Cryorecanalization: A new approach for the immediate management of acute airway obstruction	2004 Journal of Thoracic and Cardiovascular Surgery	Qualitative research	plus	60 patients: 57 malignant tracheobronchial cancer, 3 granulomatous tissue and tracheal stents. 60 patients recruited prospectively. They had either: 1)high grade stenosis in trachea or main bronchus due to exophytic tumours or 2) complete obstruction of a lobe or segment. Patients who had stenosis due to extrinsic compression	Age 19-81years. Of the 60 patients, 23 had complete bronchial obstruction and 37 had high grade airway stenoses. Of those with complete obstruction 17 had segmental or lobar atelectasis. 51/60 had lung cancer. Others were a mixture of metastases or benign disease.	The ability to be able to open an airway with a cryoprobe.	No comparison group.	Up to 71 week.	Safety, the main outcome measure was the degree of recanalisation. Three degrees of recanalisation were distinguished:- Successful; no residual stenosis detected. Partial; residual stenosis evident in endoscopy but stenosis passable. Unsuccessful; persistent non-passable stenosis or closure.	Complete recanalisation in 61% of patients. 22% had partial recanalisation. 17% of cases were unsuccessful. Of 57 patients, 14 presented again. Safety: None died. 6 large bleeds but all controlled.	Not stated	Cryorecanalisation or cryoextraction is safe in patients with tracheobronchial malignancy with good success rates (over 80%) with some restoration of their airways. Large series demonstrating that cryorecanalisation with a new cryoprobe works in the majority of patients with intrinsic bronchial obstruction.

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Maiwand, MO	Cryosurgery for Lung Cancer: Clinical Results and Technical Aspects	2004 Technology in Cancer Research & Treatment	Qualitative research	plus	521 patients	Mean age = 67.9 years (range 22 to 88). Male to female 1.8:1. Mean no. of treatments = 2.4	Effect of cryotherapy on patients with obstructive tracheobronchial malignancy.	Between patients who had had standard cryosurgery and those who had had direct intrathoracic cryosurgery performed intraoperatively.	Mean follow up 18 months (range 4-84 months)	Pulmonary function tests, performance status, symptom quantification and complication rate.	Improvement in one or more symptoms = 86% (448/521). Cough = 69.0% (318/461). Dyspnoea = 59.2% (300/507). Haemoptysis = 76.4% (154/202). Chest pain = 42.6% (71/167). Mean FEV1 before cryosurgery = 1.39L and post cryosurgery = 1.51L, p < 0.05; mean FVC before cryosurgery = 1.93L and post cryosurgery = 2.13L, p < 0.05. Mean Karnofsky performance status before cryosurgery = 60 and post cryosurgery = 75, p < 0.05. Mean WHO performance status before cryosurgery = 3.04 and post cryosurgery = 2.20, p < 0.05. One-year survival = 38.4%, two-year survival = 15.9%. Median survival (Kaplan-Meier) = 8.2 months. Complications: in-hospital mortality (all due to respiratory failure) = 1.3% (7/521); haemoptysis = 4% (21/521); postoperative atrial fibrillation = 2% (12/521); respiratory distress and poor gas exchange = 3% (16/521).	Not reported	In patients with advanced obstructive tracheobronchial malignancy treatment with cryotherapy improved: lung function, symptoms, quality of life and performance status. The complication rate was low with respiratory exacerbation in 3% of patients and in hospital mortality of 1.3%.
Asimakopoulou, G.	Cryosurgery for Malignant Endobronchial Tumors: Analysis of Outcome	2005 Chest	Qualitative research	plus plus	172 patients who underwent at least 2 sessions of cryosurgery and 157 who underwent 1 round of cryosurgery. 329 patients with malignant endobronchial tumours	All had malignant primary or metastatic obstructive lung carcinoma. Groups matched for age (68), sex, histological type and stage. More patients received radiotherapy in group A.	Effect of cryotherapy	Between patients who had at least two sessions of cryotherapy in comparison to patients who only had one treatment session.	Not specifically stated although mean survival in group A was 15 months and group B 8.3 months.	Dyspnoea, cough, haemoptysis, lung function, survival and performance Status	Cough, dyspnoea, haemoptysis were significantly reduced in both groups after cryosurgery (p<0.001). Group A benefited more than group B. Lung function tests improved significantly in group A. Mean survival in group A was 15 months and 8.3 months in group B.	Not reported	Well presented paper showing cryosurgery is beneficial.
Marasso, A.	Cryosurgery in bronchoscopic treatment of tracheobronchial stenosis. Indications, limits, personal experience.	1993 Chest	Qualitative research	minus	234 patients with malignant and non-malignant tracheobronchial stenosis.	1979-1988. 183/234 had malignant tumours. 7 carcinoids/cylindroma. 44 non-malignant stenoses.	Ability of cryotherapy to relieve symptoms	None	Not stated	Resolution of atelectasis; reduction in haemoptysis; improvement in dyspnoea; oxygenation. And sepsis.	Key outcome measures: respiratory function tests and symptom quantification. Resolution of lung atelectasis = 57% (30/52). Resolution of lobe atelectasis = 76% (48/63). Resolution or reduction of haemoptysis = 93% (58/62). Dyspnoea improvement = 81% (87/107). PaO2 improvement = 71% (120/168). Sepsis improvement = 40% (26/65)	Equipment funded by FIAT Enterprise REsearch centre.	See 3.10
Maiwand, MO	Cryotherapy for advanced carcinoma of the trachea and bronchi	1986 British Medical Journal	Qualitative research	plus	75 patients with advanced carcinoma of trachea or bronchi.	54 men and 21 women. Mean age 63 years (range 29-80). All had advanced lung cancer who had failed surgical resection, radiotherapy or who had had no previous treatment.	Cryotherapy to debulk endobronchial tumour	None	> 12 months > 12 months	Improvement in symptoms.	Improvement in stridor 20/33, dyspnoea 23/31 and in haemoptysis 11/11.	Not stated	Cryotherapy improves key symptoms such as stridor, dyspnoea and haemoptysis in patients treated with cryotherapy for advanced carcinoma involving trachea and main bronchi. Another case series. Need to consider Maiwand papers carefully there is a concern that there may be patient overlap between reports..

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Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Praveen, N.	Fibreoptic Bronchoscopic Cryotherapy in the Managemnet of Tracheobronchial Obstruction.	1996 Chest	Qualitative research	plus	22 patients. 20 malignant tracheobronchial obstruction and 2 stenosis in lung transplant patients.	All had endobronchial lesions at prior bronchoscopy. 20 malignant lesions; 2 granulomatous tissue. Inoperable. Mean age 62 years. Male:female 11:11.	Effect of cryotherapy in symptomatic endobronchial lesions not suitable for surgery	No comparator group	Not stated	Clinical response and endoscopic appearance. Safety and complication rate. No objective measurements taken.	Key outcome measures: endoscopic appearance and symptom quantification. All intrinsic tumour removed = 90% (18/20). Failure to remove tumour = 5% (1/20). Died before re-evaluation = 5% (1/20). Improvement in dyspnoea = 70.6% (12/17). Improvement in haemoptysis = 100% (5/5). Complications: bronchospasm during bronchoscopy, necessitating premature abortion of procedure = 9.1% (2/22) (these patients were subsequently treated successfully after pre-treatment with bronchodilator or steroids); cardiopulmonary arrest during procedure = 4.5% (1/22).	Not stated	In patients with tracheobronchial malignant obstruction cryotherapy is a useful and effective treatment in patients not amenable to surgery. It can safely be performed with conscious sedation. There is a small risk of bronchospasm and one patient developed a cardiopulmonary arrest during the procedure.
Vergnon, JM.	Initial combined cryotherapy and irradiation for unresectable non-small cell lung cancer; Preliminary results.	1992 Chest	Qualitative research	plus	38 patients with unresectable non small cell lung cancer.	35 males, 3 females. Age range 37 -9 years	Effect of cryotherapy and radiotherapy	none	up to 4 years	Safety, survival and volume reduction of tumour	Safety: none related to cryotherapy, 2 deaths from radiation induced pneumonitis, 1 tracheobronchial fistula. Cryotherapy reduced the volume of treatment in 26/38 patients. In this group after radiotherapy 17 had no residual tumour. Survival: 560 days, in group where there was insufficient volume reduction, all patients had residual tumour survival 144 days.	Not reported	Cryotherapy is safe and effective in the treatment of unresectable non small cell lung cancer. Cryotherapy followed by radiotherapy is also safe and effective. Those patients with a volume reduction of their tumour appear to have a better response with the additional radiotherapy.

# EBUS TBNA Evidence Tables

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Herth, Felix; Becker, Heinrich D.; Ernst, Armin	Conventional vs Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration: A Randomised Trial	2004 Chest	RCT	plus plus	200 were included, 100 in each arm	Age- Group A- 55.7 and 55.8 years in EBUS and conventional respectively. Group B- 57.5 and 58.8 years respectively. There were 75 women and 125 men. Regional hospital based study. Ethnic origin, co morbidity and disease status were not mentioned, although they were all referred with undiagnosed mediastinal lymphadenopathy	EBUS guided TBNA was compared with conventional (non-ultrasound guided) TBNA. In this paper EBUS guidance involved localisation of the LN by radial EBUS followed by TBNA. TBNA was not performed in real-time.	Comparisons were made between conventional TBNA and EBUS guided TBNA.	There is no duration of follow up as this is a diagnostic study. However, all patients with inconclusive TBNA had a surgical biopsy	Outcome measures were either a positive diagnosis e.g. malignant cells or a lymphocyte positive specimen, indicating that a lymph node had been sampled.	For subcarinal LNs, the yield from conventional TBNA was 74% compared to 86% for EBUS guided. This was significant (p<0.05). For LNs 2,3,4 the figures were 58% and 84% respectively (p<0.001). Combined data were 71% versus 80% (p<0.05).	None stated	Overall, the data is quite convincing and not surprising. However, this study has not been reported very well. In general, detail is sparse. For example, there were no details of inclusion and exclusion criteria, nor a power calculation. The information from the study is useful, although this technique has been superseded by real time EBUS guided TBNA, which has been proven to provide superior results.
Varela-Lema, L.	Effectiveness and safety of endobronchial ultrasound-transbronchial needle aspiration: a systematic review	ERJ 2009	Systematic Reviews and Meta-analyses	plus plus			Staging of lung cancer or suspected lung cancer: Sensitivity ranged 85-100%; NPV 11-97.4% Diagnosis of sarcoidosis: sensitivity 88-93% Diagnosis of lymphoma: insufficient evidence to support this at present Safety of EBUS-TBNA is very good.			No confidence intervals or p-values reported. The ranges given for sensitivity etc are the highest/lowest reported in the papers that the authors included. This was a systematic review article rather than a meta-analysis.	Main one was sensitivity for diagnosis of malignancy. Negative predictive value was considered and it is clearly stated that due to the relatively low NPV in some papers, that surgical staging should be used to confirm negative results if clinical suspicion persists.		EBUS-TBNA is a safe and highly accurate procedure for diagnosing and staging hilar and mediastinal lymph nodes for patients with suspected or confirmed malignancy. Evidence for sarcoidosis is promising but it is not sufficient to recommend for routine diagnosis of lymphoma.
Varela-Lema, L.	Effectiveness and safety of endobronchial ultrasound-transbronchial needle aspiration: a systematic review	ERJ 2009	Systematic Reviews and Meta-analyses	plus plus			Staging of lung cancer or suspected lung cancer: Sensitivity ranged 85-100%; NPV 11-97.4% Diagnosis of sarcoidosis: sensitivity 88-93% Diagnosis of lymphoma: insufficient evidence to support this at present Safety of EBUS-TBNA is very good.			No confidence intervals or p-values reported. The ranges given for sensitivity etc are the highest/lowest reported in the papers that the authors included. This was a systematic review article rather than a meta-analysis.	Main one was sensitivity for diagnosis of malignancy. Negative predictive value was considered and it is clearly stated that due to the relatively low NPV in some papers, that surgical staging should be used to confirm negative results if clinical suspicion persists.		EBUS-TBNA is a safe and highly accurate procedure for diagnosing and staging hilar and mediastinal lymph nodes for patients with suspected or confirmed malignancy. Evidence for sarcoidosis is promising but it is not sufficient to recommend for routine diagnosis of lymphoma.

# PDT Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Diaz-Jimenez JP	Efficacy and safety of photodynamic therapy versus Nd-YAG laser resection in NSCLC with airway obstruction.	1999 European Respiratory Journal	RCT	plus plus	31 patients with trachea-bronchial obstruction from non small cell lung cancer 14 Photodynamic therapy 17 ND-YAG laser	Inoperable NSCLC, unsuitable for radical Tx due to poor pulmonary function or adverse staging All male, mean age 67 and 64 respectively all male mean age 65+/-7 years	Effect of PDT and ndYAG laser for the treatment of tracheo-bronchial obstruction from non small cell lung cancer	PDT therapy versus nd-YAG laser	500 days	Symptom relief (cough, sputum, haemoptysis, dyspnoea) and reduction of airway obstruction. Length of time to tumour recurrence at treated site, response of tumour size at bronchoscopy and CT scanning, measure QOL (Karnovsky), time to next local recurrence tumour response, survival and safety.	PDT vs Nd-YAG time to treatment failure: 50 vs 38 days p=0.03. Reasons for stopping treatment: -no response 36 pts; Objective tumour progression n=54, systemic progression n=11; worsening of symptoms n=23; death n=13. Response at one week 43% vs 53%. Response at 1 month 38.5% vs 23.5% (not significant). Adverse events; bronchitis 41 pts photosensitivity 4 n/a 2 events in 16 pts, usually cough & photosensitivity. Symptom relief: similar in both groups. Airway obstruction improved from 79%	Lederle Pharmaceutical Co	A reasonably conducted randomised study showing effective palliation with PDT and some indication of a more prolonged effect than thermal laser PDT is as effective in the management of endobronchial airway obstruction from malignant disease as laser. PDT is better than laser in terms of duration of response but greater side effects particularly skin photosensitivity.
Moghissi, K.	Endoscopic laser therapy in malignant tracheo-bronchial obstruction using sequential Nd-YAG laser and photodynamic therapy.	1997 Thorax	Qualitative research	plus	17	Inoperable carcinoma causing >50% endoluminal obstruction.	Effect of sequential Nd YAG laser and PDT Nd YAG 40-60 watt pulses for 4 seconds in non-contact mode; PDT 4-6 weeks later, poly-HpD 2mg/Kg, light at 630 Nm, 0.5-2cm cylindrical diffuser, 400mW/cm Mainly Squamous and adeno-carcinoma, 1 renal metastasis, 1 large cell, 1 adenoid cystic.	None	Up to 39 months	Symptom relief, performance, pulmonary function. Endoscopic/histological response.	Mean % increase in lumen 66% (range 40-90%). Complete pathological response in 7 patients, for -3-6 months. All patients had symptomatic improvement. FEV1 improvement 25% (range 0-70%), FVC 28% (range 0-90%). 11 survived 1 year, 8 for 2 years. Median survival 18.5 months (5-39), 95% CI 9.9-29.5.	Supported by the Yorkshire Cancer Research Campaign and the Laser Trust (Moghissi) Appeal	Illustrates potential for palliation in major occlusive disease, including some complete histologic remissions, one with adenoid cystic carcinoma.
Ono, R.	Hematoporphyr in derivative photodynamic therapy in roentgenographically occult carcinoma of the tracheo-bronchial tree.	1992 Cancer	Qualitative research	plus	36	XR occult carcinoma of the tracheo- bronchial tree, unsuitable for conventional treatment for various reasons: poor respiratory function (12), cardiac disease (10), multiple lesions (5), age>80 (2), experimental treatment (7).	HpD PDT 2.5mg/Kg, light at 72 hours, 360-1800 Joules.	None	No patients lost to follow up. Complete responders followed up from 13 to 72 months, less than complete responders followed up from 37 to 109 months.	Survival, endoscopic response.	Survival: 1 yr 92%, 2 yr 81%, 3 yr 74.5%, 4 yr 58% 5 yr 43%. 11 had apparent complete response (12 lesions), only 1 after a single course, 8 after 2 courses, 3 after 3-4 courses. 8 complete remissions had no local recurrence at 13-72 months. 4 had local recurrence at 43-54 months. 25 patients (27 lesions) had partial response. 19 had XRT, 6 had surgery. 10 alive at 37-109 months. All partial responders subsequently died but most of unrelated causes. No significant treatment morbidity.	Not specified	Lots of data on each patient in tabulated form. Only 5 of 20 deaths were from recurrent disease. Authors refer to the need for better staging/depth assessment to plan suitable choice of treatment but suggest combined PDT/XRT might give the best outcome.
Furukawa, K.	Locally recurrent central-type early stage lung cancer < 1cm in diameter after complete remission by photodynamic therapy	2005 Chest	Qualitative research	plus	93 patients with 114 lesions. Distinction drawn between lesions <1cm and those greater.	Early central lung cancer	Effect of HpD PDT	Comparison of response, recurrence, and survival between lesions above and below 1cm diameter	Up to 65 months	Complete response (CR), partial response (PR), recurrence rates and cytological characteristics of the primary tumour and recurrences in relation to depth of initial lesion.	Lesions < 1cm: CR 93%, 5-year survival 58%, =>1cm CR 58% >1cm 59% (p<0.001, re CR). Recurrence after CR in 12 of 95 lesions, 9 of 77 lesions <1cm (11.7%), 3 of 18 => 1cm (16.7%). PR in 18 patients, 19 lesions -> surgery 13, Cth 5, XRT 1. Most had recurrence within 12 months.	Not specified	The cytological data is not very coherent but the opinion expressed is that depth assessment is important in treatment selection; a system of cytologic classification is attempted (types 1-3) which is said to reflect tumour depth ?if this has been validated elsewhere.

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Okunaka, T.	Lung cancers treated with photodynamic therapy and surgery	1999 Diagnostic & Therapeutic Endoscopy	Qualitative research	plus	26	Patients being considered for surgery for NSCLC. PDT used to increase resectability or to reduce the extent of required surgery, Stage IA n=1, IB n=2, IIA n=1, IIB n=6, IIIA n=6, IIIB n=5, IV n=1.	Effect of pre-op PDT on resectability.	An attempt is made to compare with similar patients undergoing surgery alone, but not randomised.	60 months	Inoperable to operable reduction in required surgery	Inoperable to operable: 4 Pneumonectomy to sleeve lobectomy: 11 to lobectomy: 7 no change. 4 5-year survival of 5 T3 (main bronchus) patients receiving PDT/surgery calculated at 60%, compared with 50.9% for 11 similar patients receiving surgery alone. The survival curves showing several deaths at 0-20 months in the latter group.	Not specified	In addition, the increase in resectability, there is a suggestion that survival compared to equivalent cases undergoing surgery alone may be improved - remarkable if the PDT group have been downstaged by PDT to surgical 'comparability', but not quite clear; can only be regarded as 'observation', but the illustrated example also appears to show a case where lobectomy was successfully achieved in an apparently inoperable situation (by UK standards) even by pneumonectomy, PDT eradicating disease from lateral wall of RMBR and distal trachea, enabling RUL resection.
Kato, H.	Photodynamic therapy (PDT) of lung cancer. Experience of the Tokyo medical university.	2004 Photodiagnosis and Photodynamic Therapy	Qualitative research	plus	321 curative intent, 81 palliation of obstructing tumours, 32 pre-operative	Patients with lung cancer in the named categories.	Effect of PDT in the above categories.	None	Curative: 243 months palliative: not specified pre-op: not specified.	Curative: complete response rates and recurrence rates. Palliative: >50% relief of large A/W obstruction. Pre-op: - increase in resectability rates; reduction of extent of resection	Curative: CR 86.4%, recurrence 10%, 5 year overall survival 57.6%, 5 year lung-cancer specific s. 92.5%, 90 patients disease-free at up to 243 months, 6 patients died from lung cancer. Palliative: >50% opening in 75%, pre-op: 4 of 5 rendered operable, 23/27 reduced from pneumonectomy, lobectomy or sleeve lobectomy.	Not specified	Part review, part results of authors' own work. Substantial numbers of patients. Data in each group rather sketchy, general style is discursive but clearly a reflection of large PDT experience.
Usuda J	Photodynamic therapy for lung cancers based on novel photodynamic diagnosis using talaporfin sodium and autofluorescence	2007 Lung Cancer	Qualitative research	plus	29 patients with 38 lesions.	Centrally located early lung cancer defined as in-situ or limited invasion, not beyond bronchial cartilage, endoscopically accessible, XR occult, no evidence of metastasis. All male patients, mean age 72.3years, with stage 0 or stage 1 endobronchial squamous cell carcinomas assessed with EBUS.	PDT using NPe6 and a diode laser detection system. IV Talaporphyryn Sodium, 40mg/M sq. Laser, 'SAFE-3000', 408 Nm to define tumour margin. Treatment laser: 664 Nm, 4 hours later, 100 Joule/cm sq Histol and cytol and 1,2 and 3 months post-Tx + fluorescence re-assessment Autofluorescence bronchoscopy to define tumour margin, and PDT (NPe6 and AIGalnP diode laser)	None	Not clearly stated, but at least 21 months.	CR, PR, recurrence rate, Cytological and histological confirmation of response at 1,2,3,6,9,12 months post treatment and then at 6 month intervals.	CR: 35 of 38 lesions., 33<10mm, 5>10mm, 7 recurrences after CR, at 8-21 months. 1 had surgery, 6 rePDT, only 2 CR, 2 then had XRT, 2 had Chemotherapy. No detailed survival data: all patients were alive. Complete response 93.9% with 9.7% later recurrence for tumours = or < than 1cm (31 pts) and 80% CR if >1cm with 100% recurrence.	Supported in part by a Grant-in-Aid for Young Scientists (B) from the Ministry of Education, Culture, Sports, Science and Technology, Japan (MEXT). KAKENHI 18791002	Substantial discussion of fluorescence findings and recurrent disease in terms of different morphology - 'thickened', 'polypoid' and 'nodular' types, e.g. thickened type most unobtrusive to white light, and all recurrent disease was also of this type. Study of 29 pts (38 lesions) of stage 0 or 1 squamous carcinoma assessed with autofluorescence and then treated with PDT. 35/38 lesions showed complete response. Study concluded that PDD system using SAFE-3000 and NPe6 improved the quality and efficacy of PDT and avoided misjudgement of the dose of the photosensitiser or laser irradiation in PDT.

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Moghissi, K.	Photodynamic therapy in early central lung cancer: a treatment option for patients ineligible for surgical resection	2007 Thorax	Qualitative research	plus	21	Patients with Early Central Lung Cancer (bronchoscopically visible, radiologically occult, no evidence of lymphadenopathy or metastasis). Retrospective cohort extracted from a total of 200 PDT-treated patients between 1991 and 2005	PDT effect on ECLC	None	Up to 82 months	Endoscopic response Disease-free and overall survival.	29 treatments in 21 patients, 6 had 2 treatments, 1 had 3 treatments. Complete response in 100% of patients. 2 months- 5 years + 7 had local recurrence at 6-15 months after first treatment, 15 patients alive at 12-82 months, 5-year survival 50.6%	Supported by Laser Trust Fund (Moghissi)	Retrospective and 'subset' study design, difficult to critically assess but endoscopic remission rates well demonstrated. Survival data hard to interpret in early-stage disease due to lead-time bias, but these were T1-2 tumours, not 'dysplasia' (5 were reported as Ca in situ however).
Edell, E.S.	Photodynamic therapy in the management of early superficial squamous cell carcinoma as an alternative to surgical resection.	1992 Chest	Qualitative research	plus	13	Operable squamous-cell cancers - patients elected to have PDT	Effect of HpD PDT in early superficial lung cancer	None	7-49 months	Endoscopic response, confirmed by biopsy/cytology. Confirmation that X-Ray occult.	12 CR, 10 after a single treatment (71%), no recurrence at 7-49 months, 3 required 2 treatments, 1 of these had local recurrence and went on to have pneumonectomy, still stage 1 disease. One pt had 2 cancers, one recurred at 4 months, successfully re-treated. No significant adverse events. Three had mild burns to hands and face.	Not specified	Suggests results comparable with surgery, avoiding the loss of large amounts of lung tissue for what are small tumours, and with no apparent morbidity
Freitag L.	Sequential photodynamic therapy (PDT) and high dose brachytherapy for endobronchial tumour control in patients with limited bronchogenic carcinoma	2004 Thorax	Qualitative research	plus	32	Technically inoperable primary bronchogenic lung cancer, including some patients with recurrent airway tumours.	Combined PDT/HDR brachytherapy in the treatment of bulky endobronchial tumours limited to the airways. PDT 200 Joules/cm, 1-3cm or micro-lens, Photofrin 2mg/Kg Brachy 4Gy x 5 treatments at weekly intervals.	No direct comparisons	3-46 months, mean 24	Endoscopic response, visual/histological.	CR 24 (75%) after initial PDT. CR increased to 97% after sequential brachytherapy, only one patient with residual histological positivity, who received an additional 8 Gy - tumour still present but A&W at 37 months recurrence in 6(19%) at 6,9,11,12,24,26 months after PDT, 5 at original site, one 2cm distal. Disease eradicated in three by various 2ry Tx. LN mets in 1 pt at 3 months, 1 pulmonary met at 11 months. All pts A&W @ 3-46 months. No severe adverse events, usual acute local effects and a few with late scarring, none requiring intervention; no sig. burns with PDT.	None specified	No comparative data for this rather unusual combination treatment, but results appear to compare favorably with historical experience of conventional treatments such as radical XRT. Clear potential for randomised comparisons, e.g. with either modality alone or even a three-arm study.
Magro, C.M.	The application of photodynamic therapy in the treatment of metastatic endobronchial disease	2006 Lasers in Surgery and Medicine	Qualitative research	plus	9	Endo bronchial metastasis from various primary sites.	Effect of PDT	None	Up to 24 months	Endoscopic response, radiology and symptom relief	Haemoptysis in 3 patients. Progressive dyspnoea and obstructive collapse in 7 patients. Relief of symptoms in 100% of patients. Complete endoscopic response in 7. 7 patients required 2 treatments, 2 required 3 treatments. One massive haemoptysis during debridement. One BP fistula, 8 died at 2 days - 13 months. Mean survival 6.38 months, median 4.2 months, 1 alive at 24 months	Not specified	Small numbers but lots of information.
Moghissi, K.	The place of bronchoscopic photodynamic therapy in advanced unresectable lung cancer. Experience of 100 cases.	1999 European Journal of Cardio-Thoracic Surgery	Qualitative research	plus	100	Advanced inoperable bronchial carcinoma with endoluminal obstruction, 80% pre-treated with chemo/XRT, 9% YAG.	Effect of PDT on symptoms, performance, pulmonary function and bronchoscopic/histologic status	None	Up to 75 months	Change in bronchial lumen, relief of dyspnoea and haemoptysis, pulmonary function, histological response and survival.	Mean endoluminal obstruction fell from 86% to 17.5%. Mean increase in FEV1 280ml, FVC 430ml All patients had symptomatic relief. 20% had complete response, for 3-19 months. Median survival 5 months, 2-year survival 19%. Only significant influence on survival was PS. No treatment-related mortality. Some mild skin reactions.	Supported by the Laser Trust Fund (Moghissi) Appeal and the Yorkshire Cancer Research Campaign	Suggests PDT under-used in a salvage setting for the palliation of malignant airway obstruction.

# Thermoplasty Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Cox, Gerard; Thomson, Neil C.; Rubin, Adalberto S.; Niven, Robert M.; Corris, Paul A.; Siersted, Hans Christian; Olivenstein, Ronald; Pavord, Ian D.; McCormack, David; Chaudhuri, Rekha; Miller, John D.; Laviolette, Michel	Asthma control during the year after bronchial thermoplasty	2007 New England Journal of Medicine	RCT	plus	Total patients = 112. 56 treatment group 56 control group	Inadequately controlled chronic persistent asthma. Mean age 39.4 +/- 11.2 years treatment group and 41.7 +/- 11.4 years control group. Sex: treatment group M 24: 31 F and control group M23 : 31F. 93% white race.	The effect of bronchial thermoplasty	Bronchial thermoplasty and combination inhalers vs combination inhalers alone.	1 YR	Mild exacerbations, severe exacerbations, ACQ, lung function, symptom scores, symptom free days, adverse effects, rates of exacerbations, peak flow AQLQ asthma quality of life questionnaire, ACQ asthma control questionnaire.	The mean rate of mild exacerbations, as compared with baseline, was reduced in the bronchial-thermoplasty group but was unchanged in the control group (change in frequency per subject per week, -0.16±0.37 vs. 0.04±0.29; p = 0.005). At 12 months, there were significantly greater improvements in the bronchial-thermoplasty group than in the control group in the morning peak expiratory flow (39.3±48.7 vs. 8.5±44.2 liters per minute), scores on the AQLQ (1.3±1.0 vs. 0.6±1.1) and ACQ reduction, (1.2±1.0 vs. 0.5±1.0), the percentage of symptom-free days (40.6±39.7 vs. 17.0±37.9), and symptom scores (reduction, 1.9±2.1 vs. 0.7±2.5) while fewer puffs of rescue medication were required. Values for airway responsiveness and forced expiratory volume in 1 second did not differ significantly between the two groups. Adverse events immediately after treatment were more common in the bronchial-thermoplasty group than in the control group but were similar during the period from 6 weeks to 12 months after treatment.	Sponsor - ASTHMAT x	Bronchial-thermoplasty in subjects with moderate or severe asthma results in a marginal but clear improvement in asthma control, at the expense of short term adverse events. Bronchial-thermoplasty is safe in patients with moderate to severe asthma and improves asthma control. it appears to reduce the frequency of mild exacerbations, improves quality of life and reduces asthma symptoms. There was also an improvement in symptom free days.
Cox, Gerard; Thomson, Neil C.; Rubin, Adalberto S.; Niven, Robert M.; Corris, Paul A.; Siersted, Hans Christian; Olivenstein, Ronald; Pavord, Ian D.; McCormack, David; Chaudhuri, Rekha; Miller, John D.; Laviolette, Michel	Asthma control during the year after bronchial thermoplasty	2007	RCT	plus	Total patients = 112. 56 treatment group 56 control group	Inadequately controlled chronic persistent asthma. Mean age 39.4 +/- 11.2 years treatment group and 41.7 +/- 11.4 years control group. Sex: treatment group M 24: 31 F and control group M23 : 31F. 93% white race.	The effect of bronchial thermoplasty	Bronchial thermoplasty and combination inhalers vs combination inhalers alone.	1 YR	Mild exacerbations, severe exacerbations, ACQ, lung function, symptom scores, symptom free days, adverse effects, rates of exacerbations, peak flow AQLQ asthma quality of life questionnaire, ACQ asthma control questionnaire.	The mean rate of mild exacerbations, as compared with baseline, was reduced in the bronchial-thermoplasty group but was unchanged in the control group (change in frequency per subject per week, -0.16±0.37 vs. 0.04±0.29; p = 0.005). At 12 months, there were significantly greater improvements in the bronchial-thermoplasty group than in the control group in the morning peak expiratory flow (39.3±48.7 vs. 8.5±44.2 liters per minute), scores on the AQLQ (1.3±1.0 vs. 0.6±1.1) and ACQ reduction, (1.2±1.0 vs. 0.5±1.0), the percentage of symptom-free days (40.6±39.7 vs. 17.0±37.9), and symptom scores (reduction, 1.9±2.1 vs. 0.7±2.5) while fewer puffs of rescue medication were required. Values for airway responsiveness and forced expiratory volume in 1 second did not differ significantly between the two groups. Adverse events immediately after treatment were more common in the bronchial-thermoplasty group than in the control group but were similar during the period from 6 weeks to 12 months after treatment.	Sponsor - ASTHMAT x	Bronchial-thermoplasty in subjects with moderate or severe asthma results in a marginal but clear improvement in asthma control, at the expense of short term adverse events. Bronchial-thermoplasty is safe in patients with moderate to severe asthma and improves asthma control. it appears to reduce the frequency of mild exacerbations, improves quality of life and reduces asthma symptoms. There was also an improvement in symptom free days.

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Castro M, Rubin AS, Laviolette M, Fiterman J, De Andrade Lima M, Shah PL, Fiss E, Olivenste in R, Thomson NC, Niven RM, Pavord ID, Simoff M, Duhamel DR, McEvoy C, Barbers R, Ten Hacken NH, Wechsler ME, Holmes M, Phillips MJ, Erzurum S, Lunn W, Israel E, Ja	Effectiveness and Safety of Bronchial Thermoplasty in the Treatment of Severe Asthma: A Multicenter, Randomized, Double-Blind, Sham-Controlled Clinical Trial.	2009 American Journal of Respiratory and Critical Care Medicine	RCT	plus plus	297 patients randomised; 101 to sham and 196 to thermoplasty	Adults 18-65 with chronic persistent asthma, using inhaled corticosteroids at >1000ug/day (beclomethasone equivalent), and LABA >100ug/day. Upto 10mg/day of oral corticosteroids. Stable medications for 4 weeks pre entry, FEV1 >60%, pc20 <8mg/ml, AQLQ <6.25. Thirty Multicentre sites in 6 countries. Average age 40 years. Sex: in BT group 81 males & 109 females and in the sham group 38 males & 60 females. FEV1 BT group 77.8 +/- 15.65, sham group 79.7 +/- 15.4	The effect of bronchial thermoplasty	Comparison between treatment with bronchial-thermoplasty and sham treatment	one year	The primary outcome was the difference between study groups in the AQLQ score change from baseline to the average of the 6-, 9-, and 12-month scores (integrated AQLQ). Safety was assessed by reviewing all adverse events occurring during the treatment and post-treatment periods. Secondary outcomes included changes in: AQLQ (absolute and individual domains), ACQ scores, percentage of symptom-free days, symptom scores, morning peak expiratory flow (PEF), rescue medication use, and FEV1. Additional outcomes included severe asthma exacerbations (exacerbations requiring systemic corticosteroids or doubling of ICS dose), percentage of subjects experiencing severe exacerbations, respiratory-related unscheduled physician office visits, emergency department (ED) visits, hospitalizations, and days missed from work/school or other activities due to asthma.	The mean change in integrated AQLQ score in the ITT population was greater in the BT group (1.35, 6 1.10) than in 3 the sham group (1.16, 6 1.23; ppsuperiority, 96.0%). During the short term period (i.e. during bronchoscopy) there was an increase in adverse events in the treated group (mainly asthma exacerbations). All expected and self limiting. In the post treatment period a significant reduction in adverse events was observed in thermoplasty group. During the post-treatment period, there was a 32% reduction in the rate of severe exacerbations in the BT group compared with the sham group (0.48 vs. 0.70 exacerbations/subject/yr, respectively; ppsuperiority, 95.5%). Of the BT subjects, 26.3% (50/190) experienced severe exacerbations, compared with 39.8% (39/98) of sham subjects (ppssuperiority 99.0%). In the post-treatment period, subjects in the BT group reported fewer days lost from work/school or other activities due to asthma (1.32 +/- 0.36 d/yr) compared with sham (3.92 +/- 1.55 d/yr; ppsuperiority, 99.3%). Secondary endpoint measures of morning PEF, symptom-free days, symptom score, and rescue medication use showed an improvement over baseline in both BT and sham groups, although the differences between the groups were not statistically significant.	Asthmatx (industry)	Well conducted MCRCT - the first of its kind for mechanical devices in asthma control. There is an overall beneficial effect in AQLQ and ED visits, although the severe exacerbation rate was only slightly better for BT than sham (1.02 v 0.91 (pps superiority 25.8%) for the whole 52 weeks. The study design and patient perceptions of likely benefit may have reduced the difference of the therapeutic impact. It will have a role in severe asthma management alongside other modalities, although this needs to be defined further. Bronchial thermoplasty in patients with moderate to severe asthma is associated with short term increase in adverse events. These usually consists of an increase in asthma related symptoms. Bronchial thermoplasty in patients with moderate to severe asthma is associated with a reduction in adverse events in the longer term (six weeks after last bronchoscopy onwards). Treatment with bronchial thermoplasty in patients with moderate to severe asthma reduces the frequency of respiratory exacerbations. Treatment with bronchial thermoplasty in patients with moderate to severe asthma reduces the number of days lost from school or work due to asthma. Treatment with bronchial thermoplasty in patients with moderate to severe asthma improves quality of life.
Miller, John D.;Cox, Gerard;Vincic, Lydia;Lombard, Charles M.;Loomas, Bryan E.;Danek, Christopher J.	A prospective feasibility study of bronchial thermoplasty in the human airway	2005 Chest	Qualitative research	plus	8	8 white patients (4 male), pre lung resection.  mean age, 65 ± 8.3 years range 52-78).	Safety and feasibility of bronchial thermoplasty to reduce airway smooth muscle	2 groups - 55 and 65 centigrade. Bronchoscopic appearance before and after BT and histological appearance of resected airways after BT	5-20 days	Bronchoscopic airway calibre and appearance.  Safety  Histological analysis to assess changes in airway mucosa and airway smooth muscle composition	Descriptive. No statistical analysis of effects.  Well tolerated with no adverse events.  Treatment sites : slight erythema, oedema for 2 weeks and then normal. No airway scarring and reduction in airway smooth muscle	Asthmatx (industry)	Delivery of radifrequency energy and heating the airways to 65 centigrade reduces the amount of airway smooth muscle. There is transient epithelial damage which recovers within two weeks. Minor cartilage necrosis which also quickly recover. The procedure is safe and well tolerated in human subjects.

Thermoplasty

Evidence

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Cox, Gerard;Miller, John D.;McWilliams, Annette;FitzGerald, J. Mark;Lam, Stephen	Bronchial thermoplasty for asthma	2006 American journal of respiratory and critical care medicine	Qualitative research	plus	18  Only 16 had procedure as 2 withdrew consent.	<p>Mean age 39 years (range 24-58) 6 male 10 female.</p> <p>FEV<sub>1</sub> 82% predicted ± 13.9.</p> <p>All subjects were 18 yr of age or older and had stable asthma, as indicated by no change in their asthma condition or medication needs in the previous 6 wk.</p> <p>Primary exclusion criteria included respiratory tract infection within the last 6 week; a history of two or more lower respiratory tract infections per year requiring antibiotic treatment; and the use of more than four puffs in a 24-h period of a short-acting 2-adrenergic agonist, such as albuterol 100 µg/puff or equivalent, except for exercise.</p>	effect of bronchial thermoplasty on safety and asthma symptoms	timescale effects (upto 2 y) on: 1. safety 2. efficacy 3. bronchoscopic surveillance 4. Asthma control - AQLQ, Asthma control	2 years	timescale effects (upto 2 y) on: 1. safety 2. efficacy 3. bronchoscopic surveillance 4. Asthma control - AQLQ, SAEs, hospitalisations	<p>Prebronchodilator FEV<sub>1</sub> (% predicted) was maintained after BT, with no significant change from baseline (82.2 ± 14.0, n = 16) at the 2-yr follow-up (85.7 ± 13.1, n = 15). There were significant increases observed at 12 wk (88.6 ± 16.1, n = 15, p = 0.043) and 1 yr (88.3 ± 17.1, n = 16, p = 0.030). Post-bronchodilator FEV<sub>1</sub> (% predicted) was maintained throughout the period, with no significant change from baseline. The prebronchodilator FEV<sub>1</sub> /FVC ratio was statistically significantly higher at 1 yr (75.8%) than at baseline (72.7%; p = 0.049). This change was not significant at 12 wk (72.8%) or 2 yr (74.5%) post-treatment. There was no significant increase in the mean postbronchodilator FEV<sub>1</sub> /FVC ratios after treatment.</p>	asthma tx - industry	BT is well tolerated in patients with mild-moderate asthma and results in decreased airway hyperresponsiveness that persists for at least 2 yr. Baseline and 12-wk post-treatment measurements included spirometry, methacholine challenge, daily diary recordings of peak flow, symptoms, and medication usage.

# General IB Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Hautman n, Hubert; Gamarra, Fernando; Henke, Markus; Diehm, Stephanie ; Huber, Rudolf M.	High frequency jet ventilation in interventional fiberoptic bronchoscopy	2000 Anesthesia and Analgesia	Cohort	plus	123 patients who had 161 procedures using high-frequency jet ventilation fiberoptic bronchoscopy	Average age 60.7+/- 11.2. Other demographic characteristics not given in the paper. FEV1 57% predicted (1.75L) pO2 9.27 pCO2 4.67. 61% chronic bronchitis, 39% on bronchodilators, 46% NSCLC, 8% SCLC and 20% benign stenoses	The use of high-frequency jet ventilation in fiberoptic bronchoscopy for the management of main airway stenosis	Nil	<24hrs	Incidence of complications, duration of anaesthetic, duration of ventilation and duration of time spent in recovery unit	None	Not reported	This could have been a good paper; however, of indeterminate usefulness..
Lunn, William; Garland, Robert; Ashiku, Simon; Thurer, Robert L.; Feller, Kopman David ; Ernst, Armin	Microdebrider bronchoscopy: A new tool for the interventional bronchoscopist	2005 Annals of Thoracic Surgery	Cohort	plus	23	Age range: 29-79. Male: 10; female: 13. Inpatients (all 'critical illness'): 7; outpatients: 16 Diagnoses: * tracheal granulation tissue: 14 * subglottic stenosis: 6 * tracheal & mainstem malignancy: 3	The effect of a microdebrider via a rigid bronchoscope	Nil	1-24 months	Requirement of re-evaluation / intervention for airway obstruction	Not specified, but no patient needed further re-evaluation / intervention during follow-up (unclear what happened to patients at the 'end' of follow-up).	No financial support received; "equipment used has not been donated for the purposes of this study."	A microdebrider may be used to remove central tracheobronchial malignant and benign lesions through a rigid bronchoscope or suspension laryngoscope. It is a rapid procedure and in a small case series, symptoms improved and it did not result in any immediate complications.
Perrin, G.; Colt, H. G.; Martin, C.; Mak, M. A.; Dumon, J. F.; Gouin, F.	Safety of interventional rigid bronchoscopy using intravenous anesthesia and spontaneous assisted ventilation; A prospective study	1992 Chest	Cohort	minus	This was a cross sectional survey and not a cohort study. 83 patients included.	Mean age 48 (range 9-85), 63% male. 16% had cardiovascular comorbidity and 13% double Lung Transplant.	Not applicable	No comparisons	Not reported	Complications peri and post-operatively.	Not applicable	Not reported	This study only provides information on how one centre performs rigid bronchoscopy and their complication rate.
Pastis, Nicholas J.; Nietert, Paul J.; Silvestri, Gerard A.	Fellows' perspective of their training in interventional pulmonary procedures	2005 Journal of Bronchology	Qualitative research	minus	304 respiratory trainees (only 32% response rate hence results may not be representative)	23 respiratory only trainees, 2 cardiothoracic trainees, 277 respiratory/critical care trainees. 31% penultimate year fellows, 30% final year fellows, 22% first year post fellowship and 17% second year post fellowship	Not applicable	Satisfaction of training in programs with and without interventional bronchoscopy trainers.	Not applicable	Percentage of respondents offered interventional training. Percentage of respondents who achieved recommended competency numbers, satisfaction with procedural training.	Not applicable	Not reported	Respiratory trainees were mostly satisfied with training in simple fibre-optic bronchoscopy and TBNA and were able to achieve numbers required for competency. However, training for interventional and advanced diagnostic procedures was less satisfactory with few trainees being able to achieve the required numbers for competence. Half the trainees have suggested a further year in interventional training would be helpful.
Pastis, Nicholas J.; Nietert, Paul J.; Silvestri, Gerard A.	Variation in training for interventional pulmonary procedures among US pulmonary/critical care fellowships: A survey of fellowship directors	2005 Chest	Qualitative research	minus	122 pulmonology & critical care program directors were surveyed	As 3.1	The number of training programs offering various bronchoscopic, pleural and critical care procedures, and the proportion of fellows achieving the ACCP minimum numbers for competency	Between procedures and programs, and whether the program has an interventional pulmonologist.	Not applicable	As 3.3	All programs offer flexible bronchoscopy; 96% of trainees achieve the minimum 100 procedures (range 80-400). Tube thoracostomy and TBNA are the only others achieved by 2/3 of trainees.	Not reported	A useful study which is sure to mirror the UK experience.

# Argon Plasma Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Morice, R. C.; Ece, T.; Ece, F.; Keus, L.	Endobronchial argon plasma coagulation for treatment of hemoptysis and neoplastic airway obstruction	2001 Chest	Qualitative research	minus	60	43 male, 17 female. Median age 63 (range 29-84). Diagnoses NSCLC42, SCLC 1, renal cell ca 12, thyroid ca 1, melanoma 1, benign 3. Median time from diagnosis to APC treatment 7.3 months (range 0-62 mo). Number of patients with an airway lesion in each location: trachea=10, RMB=20, LMB=23, RUL 17, RBI 9, RML 2, RLL 2, LUL 18, LLL 16. Thirty-one patients had haemoptysis which was severe (>200ml/d) in 6, moderate (50-200 ml/d) in 23 and mild (<50ml/d but persistent for > 1 week) in 27.	Use of argon plasma coagulation (APC) delivered via flexible bronchoscopy (FB) to treat haemoptysis or symptomatic airway obstruction	Comparison of airway cross-sectional area pre and post treatment (means of measurement not stated).	Median 53 days (range 18-321 days)	For patients presenting with haemoptysis: mean duration of haemoptysis-free follow-up after treatment. For patients presenting with central airway obstruction; 'symptomatic improvement in dyspnoea' (means of measurement not described) and change in airway cross sectional area expressed as a percentage of healthy airway luminal area (means of measurement not described)	Haemoptysis: mean haemoptysis-free follow-up 97 days (sd 91.9 days). Three patients required second treatments at 53, 87 and 101 days. Central airway obstruction: 'symptoms improved immediately in all patients except 1'. 'excellent' improvement in dyspnoea in 37 cases (53%) and moderate in 32 (46%).	Not stated	This is simply a consecutive case series, of the use of APC. There were no clear objective measures of improvement, such as dyspnoea scale, spirometry or radiological demonstration. Nevertheless, demonstrates the safety and benefit of this simple technique, performed with the flexible bronchoscope, under conscious sedation.
Crosta, C.; Spaggiari, L.; De Stefano, A.; Fiori, G.; Ravizza, D.; Pastorino, U.	Endoscopic argon plasma coagulation for palliative treatment of malignant airway obstructions: Early results in 47 cases	2001 Lung Cancer	Qualitative research	minus	47 patients underwent APC treatment for malignant neoplasms of the tracheobronchial system causing obstruction and/or recurrent bleeding.	41 male, 6 female. All with malignant airway obstruction: squamous carcinoma 32, adenocarcinoma 4, large cell 3, metastatic cancer 8. Median age 69 years (range 39-86). 21 patients (47%) had already received treatment with other modalities. In 26 (53%) APC was considered only suitable treatment.	Treatment with APC via flexible bronchoscopy (FB) under conscious sedation.	Not applicable	Average 6.7 months (range 0-21)	Maintenance of lumen patency, haemostasis, reduction of tumour tissues, desiccation or control of tissue overgrowth in the silicon stent	'Aims of treatment achieved in 41/47 cases (91%). No clear definition of this term. Mean treatment time was approximately 30 minutes (range 15-40). 126/166 treatments performed as outpatient or day cases, and 40/166 during hospital admission There were 'no complications or side effects caused by the treatment'.	Not stated	Outcome measures very poorly defined. No side effects or adverse events of any kind reported - seems implausible.

# Brachytherapy Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Gejerman , Glen; Mullokandov, Eduard A.; Bagarella, Emilia; Blaivas, Allen; Beitler, Jonathan J.	Endobronchial brachytherapy and external-beam radiotherapy in patients with endobronchial obstruction and extrabronchial extension	2002 Brachytherapy	Qualitative research	plus	41 patients	Locally advanced primary or secondary lung cancer. Age range 36-94. Obstructive symptoms due to endobronchial disease, some also with extrabronchial extension.	The effect of brachytherapy with external beam radiation	Comparisons of outcomes based on: - symptom relief; endoscopic response and performance status	Up to 30 months	Safety, bronchoscopic response, symptomatic response and survival	In 50% there was endoscopic clearance and KPS score change. Median survival: 11.0 vs 4.2 months if there was endoscopic response, p=0.01 7.8 vs 1.5 months if there was symptom resolution, p=0.001. KPS 78.5 vs 54 re symptom resolution or not. Only KPS associated with significant survival benefit, RR=0.92, 95%CI (0.88-0.95)	Not reported	A good quality observational study with some useful statistics on what benefits can be achieved, and in which patients. No survival benefit demonstrated. KPS is key to survival and treatment benefit, unsurprising but nevertheless confirmed. No significant adverse effects in this poor-prognosis group. Brachytherapy in combination with external beam irradiation is safe with improvement in symptoms and reduction in degree of endobronchial obstruction in patients with endoluminal obstruction from cancer
Susnerwalla, S. S.; Sharma, S.; Deshpande, D. D.; Dinshaw, K. A.; Viswanathan, P. S.	Endobronchial brachytherapy: a preliminary experience	Journal of Surgical Oncology	Qualitative research	plus	14 patients with malignant airway obstruction	Malignant airway obstruction, median age 56 years, 11 male and 3 females	The effect of brachytherapy	none	Up to 10 months	Safety, subjective appearance: bronchoscopic appearance in 5 patients and radiologically in 9 patients, symptom response	Safety: transient haemoptysis and catheter dislodged in 1 patient. Subjective appearance: bronchoscopic appearance assessed in 5 patients - 1 near total regression, 3 partial regression. Radiological appearance assessed in 9 patients - 3 near total regression and 3 partial regression. 50% symptom response.	Not reported	Brachytherapy is safe with regression of tumour in the majority of patients and some symptomatic benefit.
Fuwa, N	External irradiation and intraluminal irradiation using middle-dose-rate iridium in patients with roentgenographically occult lung cancer.	2001 International Journal of Radiation Oncology Biology Physics	Qualitative research	plus	39 patients with radiologically occult lung cancer	Radiographically occult lung cancer, 38 males and 1 female. Age range 54-82 years, median 64.5 years.	The effect of 'middle dose-rate' brachytherapy (28Gy) and external beam irradiation (45Gy)	No direct comparisons	Up to 5 years	Complete response, partial response, relapse-free survival and safety.	39 patients - 38 complete response and 1 partial response. Local relapse 4 out of 39 patients. 3 year survival 87%. 5 year survival 87%. Safety; erosion in 1 patient, stenosis in 1 patient and obstruction in 1 patient	Not stated	Interesting dosage, 'Iridium thin wires', 4-6Gy per fraction over 2.5 hours approx, total 20-40Gy, higher in patients with poor lung function to compensate for a lower external beam radiation dose (30-40Gy vs 40-50Gy). External beam radiotherapy and brachytherapy is safe and effective treatment option in radiologically occult lung cancer in patients who are not suitable or refuse surgery.
Hernandez, P	High dose rate brachytherapy for the local control of endobronchial carcinoma following external irradiation.	1996 Thorax	Qualitative research	plus plus	29 patients with in-operable lung cancer treated with radiotherapy	Recurrent or residual disease following external radiotherapy. 19 males, 10 females, average age 65 years, (range 36-80).	High dose rate brachytherapy after external beam radiotherapy.	Pre and post therapy	To death, up to 19 months	Cough, haemoptysis, dyspnoea, performance, functional level (ECOG), symptoms, assessment of chest radiographs for atelectasis/pneumonitis, bronchoscopic appearance and safety.	Percentage better, worse or same (at 8 weeks). Endobronchial appearance: 42%, 8% and 50% respectively (>25% var). Atelectasis: 28%, 28%, 44% respectively. Haemoptysis: 69%, 19%, 12% respectively. Pneumonitis: 25%, 59%, 16% respectively. Dyspnoea: 24%, 28%, 48% respectively. Cough: 24%, 21%, 55%. ECOG (PS) 24%, 34%, 42% respectively. 118 placements, in 81 treatments; functional level (ECOG) 7 (24%) improved. Symptoms: haemoptysis 11 (69%); improved dyspnoea in 7 (24%); improved cough in 7 (24%) and improved assessment of chest radiographs for atelectasis in 5	not stated	Few major complications. High dose brachytherapy following external beam radiotherapy is generally safe and may palliate symptoms from lung cancer particularly haemoptysis

# Brachytherapy Evidence Table

											(28%). Improved bronchoscopic appearance 11 (42%), improved safety in massive haemoptysis (non-fatal), 5 minor haemoptysis and 1 pneumothorax.		
Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Ozkok, S.	High dose rate endobronchial brachytherapy in the management of lung cancer: Response and toxicity evaluation in 158 patients.	2008 Lung Cancer	Qualitative research	plus	158 patients with endobronchial lung cancer	Group A curative treatment n=43, 43 males 0 females median age 58 years (39-73). Group B Palliative treatment=74, 73 males, 1 female median age 60.5 years (35-77). Group C recurrence n=41, 37 males, 4 females median age 53.5 (35-82) years.	The effect of external beam (EB) and high dose rate (HDR) brachytherapy. Group A: 60Gy EB and 3x 5Gy HDR brachytherapy. Group B: 30Gy EB and 7.5Gy HDR brachytherapy. Group C 3 x 7.5Gy HDR brachytherapy.	Response between groups	up to 5 years	Survival, performance status, symptom relief, overall and complete endoscopic response rates and toxicity.	Safety: fatal haemoptysis 18; radiation bronchitis 8; oesophagitis 2; tracheal malacia 1; persistent cough 2; mycosis 1 and bronchospasm 3. Symptomatic improvement: cough 58% (30 complete); dyspnoea 77% (76 complete); haemoptysis 100 (92% complete). Bronchoscopic response: curative group A 86% (67% complete response); palliative group B 77% (39% complete response); recurrent Group C 72% (28% complete). Group A: complete response 67%, overall response 86%, 2 and 5-year survivals 25.5% and 9.5% respectively. Relief of cough 58%, dyspnoea 77%, haemoptysis. 100%. Group B: complete response 39%, overall response 77%, symptom relief 57%, 90%, and 78%; median survival 7 months. Group C: complete response 28%, overall response 72%; ss: 55%, 78%, 77%; Median survival 6 months. Prognostic factors: treatment intent, total BED, No. of brachytherapy fractions, all p<0.001.	not stated	A detailed and informative study of outcomes in three categories of patient, with good data on response, survival and toxicity. External beam radiotherapy and brachytherapy is effective at palliating symptoms and reduces airway obstruction in patients with lung cancer for patients treated with curative intent through to palliation and treatment for disease recurrence. Fatal haemoptysis is the main complication and related to total radiotherapy dose and multiple brachytherapy applications.
Gustafson , G.	High dose rate endobronchial brachytherapy in the management of primary and recurrent bronchogenic malignancies.	1995 Cancer	Qualitative research	plus	Recurrent/progressive endobronchial obstruction. KP > 60. 46 patients	Various prior treatments, 12 XRT, 22 primary lung cancer, 17 recurrent lung cancer, 7 metastatic tumours	HDRBr, 1-4 fractions, 7Gy @ 1cm. (3 fractions protocol) Multiple catheters in 11 patients effect of brachtherapy (3x 7GY depth 1 cm)	None	17.5 months	Safety, radiographic response, symptomatic response.	28/38 symptomatic patients had a significant clinical response, including 6 complete responses and 3 for duration of life. Symptom control for a median of 6.5 months (1.5-23). 69% reduction of atelectasis or decrease in tumour size, radiographically. Endoscopic: 36% complete response, 22% > 50% reduction, 33% 25-50% reduction. 8 bronchoscopies after treatment was completed, 5 improved, 3 progressed. MFH 3 (7%) 2,12 and 20 weeks all had prev/concurrent radiotherapy. Safety: 4% dysphagia, 4% transient increased symptoms, 2% persistent cough, 8% radiation pneumonitis and 7% fatal haemoptysis. Radiographic response 25/36 (69% partial response); symptomatic response 28/38 (74%); bronchoscopic response 33/36.	Not stated	Brachytherapy is safe and effective at relieving endobronchial obstruction from malignant tumours. It is also safe and effective in patients already treated with radiotherapy. Fatal haemorrhage is the most concerning adverse event (7%).

# Brachytherapy Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Anacak, Y.	High dose rate endobronchial brachytherapy in combination with external beam radiotherapy for stage 3 non-small cell lung cancer.	2001 Lung Cancer	Qualitative research	plus	30 patients with stage III NSCLC	Median age 58 years (41-73). All male. Stage IIIA 13, stage IIIB 17. Karnofsky score> 60	External beam radiotherapy (XRT) 50Gy, 2Gy daily fractions, + 10Gy local booster. Brachytherapy: 5Gy after every 10 XRT fractions, total 15Gy, mean length 9 +/- 2.68cm.	Historical comparisons with previous regimes on survival.	Up to 5 years	Symptomatic response, objective response, disease free survival and safety.	Symptomatic response: cough 12/28 (43%), haemoptysis 20/21 (95%), chest pain 15/17 (88%), dyspnoea 12/15 (80%). Objective response: complete response 16 (53.3%), partial response 7 (23.3%), disease free survival 9+/-4 months. Safety: radiation bronchitis 21 (70%), oesophagitis 2 (6.6%), bronchial fistula 4 (25%), oesophageal fibrosis 2 (12.5%), fatal haemoptysis 2 (10.5%).	Not stated	Good control with combination external beam radiotherapy and brachytherapy. Generally safe and provides effective palliation of symptoms. However, it does not appear to prolong disease free interval or survival.
Kelly, J.F.	High-dose-rate endobronchial brachytherapy effectively palliates symptoms due to airway tumors: The 10-year M.D. Anderson Cancer Center experience.	2000 International Journal of Radiation Oncology Biology Physics	Qualitative research	plus	175 patients with lung cancer.	Patients with endobronchial or tracheal tumour. 160 previously treated with XRT. Males 56, females 119. Mean age 60 years (range 28-79). 9% tracheal obstruction, 40% main stem obstruction and 66% lobar obstruction.	5 Gy at 6mm x 2 treatments. Effect of high dose endobronchial brachytherapy.	None	54 months maximum	Survival, complication,s including MFH, symptom, response and bronchoscopic response	Symptom response: 115 patients had symptomatic benefit - 56 considerably better (32%), 59 slight improvement (34%) and 29 no better (17%). 18 felt worse (10%). Bronchoscopic response: 14 complete response (12%), 76partial response (66%), 23 no response (20%) and 2 progression (2%). Safety: 4 major fatal bleed, 1 fistula, 1 necrosis, 1 stenosis, non fatal haemoptysis 2, necrosis 2 and oesophageal stricture 1. Patients who improved had a better survival 7 vs 4 months (p=0.003)	Not reported	High dose brachytherapy is safe and effective at improving symptoms. There is a survival benefit in responders. Fatal haemoptysis event rate is about 5%. Two fractions of HDRBr can palliate symptoms and achieve endoscopic remission even in previously irradiated patients. Study claims a survival benefit however it is not clear on what basis.
Raju, P. I.; Roy, T.; McDonal d, R. D.; Harrison, B. R.; Crim, C.; Hyers, T. M.; Marshall, S. J.; Ohar, J. A.; Naunheim, K. S.	IR-192, low dose rate endobronchial brachytherapy in the treatment of malignant airway obstruction	1993 International Journal of Radiation Oncology Biology Physics	Qualitative research	plus	39 patients (study period 1986 to 1989); 38 recurrent lung cancer, 1 metastatic renal cancer	Advanced lung cancer with malignant airway obstruction, many previously irradiated, some prior laser treatments	Effect of brachytherapy	No direct comparisons. Some drawn in the discussion	Until death, maximum 31 months	Radiological re-expansion, safety, bronchoscopic response, symptomatic benefit and survival.	Safety: minor only, sore throat, nose bleeds. Bronchoscopic response (assessed in 72% of patients): 46% complete response, 43% partial response. Symptomatic benefit: dyspnoea improved in 82%, haemoptysis improved in 89%, cough improved in 79%, post obstructive pneumonia improved in 92%. Median survival 5 months	Not reported	As 3.10
Ofiara, L.	Local determinants of response to endobronchial high-dose rate brachytherapy in bronchogenic carcinoma.	1997 Chest	Qualitative research	plus	30 patients with bronchogenic carcinoma.	20 endoluminal disease; 10 submucosal disease; 27/30 completed treatment	High Dose-rate effect of brachytherapy	Endoluminal versus submucosal/extinsic disease and central versus peripheral disease.	8 weeks	Chest radiograph changes, symptom scores, ECOG performance status and bronchoscopic response.	Improvement: total: endoluminal vs submucosal, central vs peripheral. Haemoptysis: 11/14, 7/10 vs 4/4, 4/6 vs 7/8. Cough: 11/24, 6/16 vs 5/8, 3/10 vs 8/14. Dyspnoea: 8/24, 6/16 vs 2/8, 3/10 vs 5/14. Pneumonitis: 1/5, 0/4 vs 1/1, 0/2 vs 1/3. Atelectasis: 9/21, 6/15 vs 3/6, 2/8 vs 7/13. Bronchoscopic response: 15/24, 10/16 vs 5/8, 5/10 vs 10/14. Cough and haemoptysis were significantly improved only in peripheral group. Haemoptysis was significantly improved in endoluminal and submucosal groups and cough only in submucosal group.	not stated	Better response for cough in submucosal disease. Brachytherapy improves symptoms in patients with both endobronchial and submucosal disease. Slightly better symptom control was observed in patients with peripheral disease in comparison to central disease.
Lo, TCM.	Low dose rate versus high dose rate intraluminal brachytherapy for malignant endobronchial tumors.	1995 Radiotherapy and Oncology	Qualitative research	plus	169 patients with malignant endobronchial tumours. 110 LDR and 59 HDR.	95% recurrent/Tx failures or metastatic disease with a poor outlook. Low dose n=110, male=71, females=39. Median age 64 years (range 35-82). high dose n=59, 39 males, 20 females.	The effect of low dose versus, (1Gy/h) high dose rate intraluminal brachytherapy (>10 Gy/hr)	Effect of low dose rate versus high dose intraluminal brachytherapy	Up to 75 months	Safety, clinical response and bronchoscopic response	LDR HDR Clinical response: 72% and 85 % respectively. Endoscopic improvement 82% and 93 % respectively. Median survival 5 and 3 months. MFH: 2, Fistula: 2 all in LDR group Prior laser: no outcome difference. Safety: low dose rates 2 patients developed fistula, 2 patients died from haemoptysis. High dose	Not stated	A very poor-prognosis group. Wordy discussion, wide ranging and quite interesting but not focused on the main issue. Includes a brief summary table of other LDR and HDR series.

Brachytherapy Evidence Table

						Median age 66 years (range 35-83).					rate group no complications.		
Kishi, K.; Yoshimasu, T.; Shirai, S.; Minakata, Y.; Kimura, M.; Sonomura, T.; Shiroyama, Y.; Sato, M.	Usefulness of mini-tracheostomy and torque controlled insertion of applicator in fractionated endobronchial brachytherapy	2006 British Journal of Radiology	Qualitative research	plus	8 patients tracheobronchial cancer, 3 tracheal cancers, 3 lung cancers, 1 mediastinal and 1 metastatic cancer	Advanced endobronchial lung cancer, 6 males, 2 females. Median age 55.9 years (range 51-70).	Use of mini-tracheostomy for brachtherapy	None	Up to 31 months	Symptomatic and endoscopic response	'Improvement, unquantified.	Not reported	The only justification for using this study would be as a reference for other techniques of brachytherapy, source placement and the potential avoidance of repeat bronchoscopies.

# Endobronchial Valve Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Wood, DE.	A Multicenter trial of an intrabronchial valve for treatment of severe emphysema.	2007 The Journal of Thoracic and Cardiovascular Surgery	Qualitative research	plus	30 patients	Age (y) 64, sd 10 range 42-78. Male/female 19/11. FEV1 (L) 0.86 sd 0.28, TLC (L) 7.74 sd 1.53, RV (L) 5.10 sd 1.20, Work (W) 43.80 sd 24.76, SGRQ total scores 59.7 sd 13.7.	Effect of endobronchial valves.	None. No comparative group.	28 patients for at least 6 months, 6 patients for 12 months	Safety SGRQ FEV1 and 6MWT.	Safety of procedure: bronchospasm 4 (6%), arrhythmia, cardiovascular 6 (9%), PaCO2 retention 2 (3%) haemoptysis 1 1%, post procedure ie after 30 days, pneumonia 4 (6%). SGRQ change from baseline change compared with baseline at 1 month - 8.1 sd 9.6 (p=0.0001), at 3 months - 6.9 sd 12.9 (p=0.01) at 6 months - 6.8 sd 14.3 (p=0.05). FEV1 no significant change 6MWT no significant change.	Spiration (industry)	Endobronchial valves with bilateral treatment in patients with emphysema improves quality of life. There were small but not significant improvements in proportion of patients who had meaningful clinical improvement in FEV1 & exercise capacity.
Wan, Innes Y. P.; Toma, Tudor P.; Geddes, Duncan M.; Snell, Greg; Williams, Trevor; Venuta, Federico; Yim, Anthony P. C.	Bronchoscopic lung volume reduction for end-stage emphysema: Report on the first 98 patients.	2006 Chest	Qualitative research	plus	98 patients	Age: yr 63 sd 10, FEV1(L): 0.9 sd 0.3 (30.1% sd 10.7), RV(L) 5.1 sd 1.3 (244.3% sd 60.3), TLC (L) 7.8 sd 1.5 (128.4% sd 17.1). 6MWT: 303 sd 118 DLCO (mL/min/mm Hg) 9.6 sd 5.4 (32.7% sd 16.3).	Effect of endobronchial valves	Between unilateral and bilateral treatment complete lobar exclusion versus incomplete lobar exclusion	90 days	Safety, FEV1, RV, exercise tolerance and DLCO.	Safety and complications: 8 serious complications; (1 death from lung cancer, 7 pneumothorax. Other 2 pneumothoraces with drains for less than 7 days and 17 COPD exacerbations). FEV1 improvement 4.5% (- 3.5 to 17.3%) p=0.007. FVC improvement 4.0% (- 7.3 to 18.6%) p=0.024. RV 3.2% (- 15.6 to 5.4%) p=0.025. Exercise tolerance 10.4% (- 2.8 to 29.3%) p= 0.001. DLCO 6.4% (- 8.5 to 30.5%) p= 0.063.	Emphasys (industry)	Multicentre experience of endobronchial valve placement in 98 patients with heterogeneous emphysema significantly reduced RV by 4.9%, increased FEV1 by 9.0%, and 6MWT by 23%. Effect on DLCO did not reach significance. Serious complications in 8 of 98 patients studied including one death.
Venuta, Federico; De, Giacomo Tiziano; Rendina, Erino A.; Ciccone, Anna Maria; Diso, Daniele; Perrone, Alessandro; Parola, Daniela; Anile, Marco; Coloni, Giorgio F.	Bronchoscopic lung-volume reduction with one-way valves in patients with heterogenous emphysema	2005 Annals of Thoracic Surgery	Qualitative research	plus	13 patients	Median age 56 years (range 32-71). 12 males, 1 female. FEV1 22% predicted (15-52). RV 233% predicted (178-329). Heterogeneous emphysema	Feasibility, and short term functional outcome of endobronchial valve lung volume reduction	Pre and post valve insertion assessment of lung function and MRC scale	3 months	FEV1, RV, ITGV, TLC, FVC, DLCO, Suppl O2, PaO2, 6MWT, MRC scale.	59 valves place (median 4 per patient range 2-6). Safety: 6 complications in 3 patients (2 bilateral pneumothorax, 1 contralateral pneumothorax and 2 episodes of bronchospasm). FEV1 from 22% (15-52) to 29% (18-58) at 3 months, p= 0.01. RV residual volume from 233% (178-329) to 207% (144-278) p=0.01. 6MWT 223 m (120-460) to 410 (245-520) p=0.005.	Emphasys (industry)	Longitudinal study on 13 pts with heterogeneous emphysema following endobronchial valve placement. Main complications were pneumothoraces (3 in 2 pts). Significant increase in FEV1, RV, 6MWT, use of supplemental oxygen and MRC grade dyspnoea
Toma, Tudor P.; Hopkinson, Nicholas S.; Hillier, James; Hansell, David M.; Morgan, Clifford; Goldstraw, Peter G.; Polkey, Michael I.; Geddes,	Bronchoscopic volume reduction with valve implants in patients with severe emphysema	2003 Lancet	Qualitative research	plus	8 patients with severe emphysema.	7 male, 1 female with severe emphysema, and severe dyspnoea despite maximal medical therapy, heterogeneous disease on CT and V/Q scans. Median age 59 years (43-69). Median FEV1 0.79L (0.61-1.07) 23% predicted (18.4-35.7%). Residual volume + 272.8% (219-321). Excluded isolated bullae, alpha 1 antitrypsin deficiency, >75ys and current smokers, CO2 >7.3kPa, FEV >10% predicted.	Effect of valves	Lung function, CT scan, shuttle distance and SGRQ score pre and post valve insertion.	4 weeks	Feasibility, safety, FEV1, residual volume shuttle distance and SGRQ score.	Feasibility 25 valves inserted. Safety: 2 ipsilateral pneumothoraces, 3 exacerbations of COPD. FEV1 significant improvement 0.79 (0.61-1.07) to 1.06 (0.75 -1.22) (p=0.025). RV no change p=0.093. Shuttle distance (p=-.337). SGRQ score (p=0.26)	Grant from Royal Brompton Emphysema Research Trust Fund and Emphasys (industry)	Early study of endobronchial valve placement in 8 patients with heterogeneous emphysema showing improvement in FEV1 and TLCO but not shuttle distance, TLC, RV or SGRQ. 2 pneumothoraces complicated procedure.

# Endobronchial Valve Evidence

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Hopkinson, Nicholas S.; Tudor P.; Hansell, David M.; Goldstraw, Peter; Moxham, John; Geddes, Duncan M.; Polkey, Michael L.	Effect of bronchoscopic lung volume reduction on dynamic hyperinflation and exercise in emphysema	2005 American journal of respiratory and critical care medicine	Qualitative research	plus	19 patients	19 patients (16 males:3 females). Mean age 58.7 years, (sd 8.7). FEV1 predicted 28.4 (11.9). RV 260.5 (68.4) peak V02 0.84 (0.22).	Effect of endobronchial valve placement on physiological and functional measures	Pre and post valve insertion measurements	4 weeks	Complications, radiological assessment, mean cycle endurance exercise time, static lung function (FEV1, VC, PEFR, TLC, RV, FRC, TLCO, VA, KCO, Pinsp max, Pexp max WMEP. Pn, sn, Pes, sn, Cough Pgas, Pdi, tw) Static lung compliance and respiratory muscle strength.	Safety: 2 pneumothoraces, 5 exacerbation of symptoms, clostridium difficile diarrhea. Exercise 39% improvement in mean cycle endurance from 227 (sd 129) to 315 (sd 195) seconds. FEV1 predicted 28.4 (sd 11.9) to 31.5 (sd 13.2) p=0.047. RV 260.5 (68.4) to 240.4 (64.5) p=0.24.	Wellcome Trust and European Union grants, Emphasys provided valves and educational grant for partial funding of salary	Study of placement of endobronchial valves in 19 patients with extensive measurement of lung function and exercise endurance. Endobronchial valve placement can improve lung volumes and gas transfer in patients with COPD and prolong exercise time by reducing dynamic hyperinflation in the short term (up to 4 weeks).
Fraioli, Francesco ; Calabrese, F. A.; Venuta, F.; Anile, M.; Bertoletti, L.; Carbone, I.; Catalano, C.; Passariello, R.	MDCT assessment of lung volume in patients undergoing bronchial stenting for treatment of pulmonary emphysema: Correlation with respiratory tests and personal experience	2006 Radiologia Medica	Qualitative research	plus	9 patients, only 4 finally treated	9 male, age 60-70 years with severe limitation in daily activity despite adequate medical therapy, severe dyspnoea and radiological evidence of heterogeneous emphysema, FEV1 <35%, RV >180%. Excluded homogenous emphysema, smoking PaCO2 >50mmHg, DLCO <20%	MDCT assessment of lung volume after endobronchial valve placement	Pre and post treatment lung volume	30 days	Volume assessment of upper lobes of the lung, FEV1, RV and 6MWT.	Limited data presented, only lung volumes reduced in 3 out of 4 patients. FEV1 improved in only 1 patient. RV reduced in 3 out of 4 patients and 6MWT improved in all 4 patients	Not reported	Very small study, hence limited information except for endobronchial valves reduced upper lobe lung volumes and residual volumes. MDCT assessment of lung volume was studied in 9 patients, 4 of whom had endobronchial valve placement.
Toma, Tudor P.; Kon, Onn Min; Oldfield, William; Sanefuji, Reina; Griffiths, Mark; Wells, Frank; Sivasothy, Siva; Dusmet, Michael; Geddes, Duncan M.; Polkey, Michael I	Reduction of persistent air leak with endoscopic valve implants	2007 Thorax	Qualitative research	plus	2	2 females, aged 35 & 32 years 1) post single lung transplant with lymphangioleiomyomatosis 2) bilateral pneumothoraces following severe pneumonia and ARDS.	Effect of endobronchial valve placement on air leak	none	5 days in patient one (died) and 22 months in patient two	Procedural success in controlling pneumothorax	Patient 1; first procedure unsuccessful, second procedure partial success but patient died. Patient 2; successful and well at 22 months.	Valves provided by Emphasys, and educational grant from Royal Brompton Hospital	Report of only two cases where endobronchial valve insertion was used to control persistent air leaks. Needs much more extensive study to confirm preliminary findings.

# Endobronchial Valve Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
De, Oliveira Hugo G.; Macedo, Neto Amarilio V.; John, Angela B.; Jungblut, Sandra; Trola, João Carlos; Menna, Barreto Sérgio S.; Fortis, Elaine A. F.	Transbronchoscopic pulmonary emphysema treatment: 1-Month to 24-month endoscopic follow-up	2006 Chest	Qualitative research	plus	19 patients	19 patients, 13 male with severe COPD. 13 men, 6 female. Mean age 67.6 years (sd 8.71), bode index 7-10 in 10 patients bode index 5-6 in 9 patients. DLCO < 45%, RV >130%	Functional and objective response to insertion of endobronchial valves for lung volume reduction in the treatment of emphysema	Historical, pre and post insertion of valves	3 month follow up completed in 18 patients. 6 month follow up completed in 14 and 12 month follow up completed in 11. 24 month follow up completed in 5 patients.	Bronchoscopic follow up for valve position, safety, visual effects on valve (development of granulation tissue). Functional outcomes: SGRQ, 6MWT, BODE index, FEV1 and FVC, TLC and blood gases.	Safety: 2 pneumothoraces, 1 mucus hyper-secretion, 2 bronchospasm short term. Long term: 4 bronchopneumonia, 2 DVT, 1 CCF. Visual effects on valve: 64 valves inserted (development of granulation tissue), 1 valve displacement, granuloma formation in majority. FEV1: 12% improvement up to 3 months but no improvement at 12 and 24 months. SGRQ improvements at 3 and 6 months only.	Valves provided by Emphasys Emphasys provided salary grant to the Medical Foundation of Rio Grande de Sul	Insertion of endobronchial valves in patients with emphysema is safe with few short term complications. Increased incidence of pneumonia seen in longer term. It provides short to medium term (up to 6 months) benefits in pulmonary function and quality of life but overall effect appears to have subsided by 12 months.
Anile, Marco; Venuta, Federico; De, Giacomo Tiziano; Rendina, Erino Angelo; Diso, Daniele; Pugliese, Francesco; Ruberto, Franco; Coloni, Giorgio Furio.	Treatment of persistent air leakage with endobronchial one-way valves	2006 Journal of Thoracic and Cardiovascular Surgery	Qualitative research	plus	3 patients	Age range 29 -82 years. Varying clinical indications (metastatic breast cancer with pleural effusion & air leak; leukaemia with pneumothorax; emphysema and lung cancer post thoracotomy)	Role of endobronchial valves.	Historical comparison with previous conventional treatment in same patients	3 weeks	Success in stopping air leaks	All patients had air leak stopped and chest drain removed within 48 hours	Not reported	3 case reports. Endobronchial valves are safe and may be used to treat persistent air leaks from a pneumothorax.
Travaline, JM	Treatment of persistent Pulmonary Air Leaks Using Endobronchial Valves	2009 Chest	Qualitative research	plus	n= 40 with prolonged air leak	15 females, 25 males age 60+/- 14 years, recurrent spontaneous pneumothorax 21, post operatively 7, iatrogenic 6, first spontaneous pneumothorax 4, bronchoscopic volume reduction 1, trauma 1. Duration of leak median 20 days	Effect of valves on air leak	None (pre and post therapy)	5 to 1109 days	Safety, cessation or reduction of air leak	Resolution of air leak 19 (47.5%). Complete resolution 18 patients (45%), reduction in air leak 2 (5%). No change in time to valve placement and chest tube removal median 7.5 days). Safety: 1 valve displacement, 1 hypoxia, 1 pneumonia and 1 malposition of valve.	Industry (Emphasys)	Restrospective study of the use of endobronchial valve placement in 40 patients with prolonged airleak. The procedure completely resolved the airleak in 47.5% and reduced the leak in 45%. Endobronchial valves are a safe alternative method of treatment for patients with persistent air leaks.

# Laser Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Brutinel, W. M.; Cortese, D. A.; McDouga II, J. C.	A two-year experience with the neodymium-YAG laser in endobronchial obstruction	1987 Chest	Qualitative research	plus	116 patients treated 176 times	Median age 60 years. 78 male (67%) 38 female (33%). 107 malignant disease and 9 benign lesions. 104 GA and 12 conscious sedation. All patients were referred for endoscopic management and palliation of significant symptomatic airway obstruction due to a malignant or benign process. In all cases conventional treatment had failed or the patient was considered ineligible for it. 61% primary lung cancer. 15% metastatic cancer. 24% benign.	Use of Nd:YAG laser for relief of endobronchial obstruction.	No comparison group	Median length of survival was estimated at 216 days. 36% of patients were alive at one year and 17% at 2 years.	Safety, survival at 1 year and 2 years. Assessment of improvement in dyspnoea, haemoptysis, hypoxaemia, cough, atelectasis or obstructive pneumonitis.	Safety: haemorrhage 10, fever 7, prolonged mechanical ventilation 7, death 3, airway obstruction 2 and pneumothorax 1. Survival: 36% patients alive at 1 year; 17% alive at 2 years. Symptom relief: dyspnoea 70%, hypoxia 32%, haemoptysis 63%, cough 40%, atelectasis 40%, and obstructive pneumonia improved in 7%.	Not stated	Good, well conducted review of 116 patients undergoing laser treatment for endobronchial obstruction. Outcomes clearly stated. Data should be included although it should be noted that data was from early 80s.
Jung, S. S.; Weiman, T. J.	Endobronchial Nd:YAG laser surgery	1989 The Journal of the Kentucky Medical Association	Qualitative research	plus	40 patients with endobronchial lesions: 36 malignant and 4 benign	30 male, 10 females. Average age 60 years. Dyspnoea in 29/40 and haemoptysis 21/40	Effect of Nd:YAG laser	None	11 months	Safety, Karnofsky performance status.	2 deaths (MI, resp failure) Karnofsky performance status score increased from 30 pre treatment to 60 post treatment.	Not reported	Outcome data presented poorly but safety data useful. Laser treatment is safe and improves performance status of patients.
Kiriyama, Masanobu; Fujii, Yoshitaka; Yamakawa, Yosuke; Fukai, Ichiro; Yano, Motoki; Kaji, Masahiro;	Endobronchial neodymium:yttrium-aluminum garnet laser for noninvasive closure of small proximal bronchopleural fistula after lung resection	2002 Annals of Thoracic Surgery	Qualitative research	plus	8 patients with tracheo-bronchial fistula after lung resection	7 males, 1 female. Mean age 53.1 years (37- 68 years) all of whom had a small bronchopleural fistula (BPF).	Effect of YAG laser in treatment of broncho-pleural fistula	None	Up to 36 days	Resolution of broncho-pleural fistula	Resolution in 4 out of 8 patients where broncho-pleural fistula at the resection stump was less than 2 mm in size. Failed in further 3 who had residual tumour or infection at the BPF.	Not reported	Only helpful in small BPFs. It is more a large case report of YAG laser treatment of adjacent mucosa where broncho-pleural fistula at the resection stump was less than 2 mm in size may be a useful treatment option.
Beamis, Jr J. F.; Rebeiz, E. E.; Vergos, K.; Shapshay, S. M.	Endoscopic laser therapy for obstructing tracheobronchial lesions	1991 Annals of Otolaryngology	Qualitative research	plus	269 patients	Obstructing lesions due to malignant or benign disease. Lung cancer 200; metastatic cancer 36; benign tumours 6; stenosis 27. Main symptoms dyspnoea, haemoptysis, cough, post-obstructive pneumonitis. Average age 63.5 years. Male 168, female 101.	Ability of CO <sub>2</sub> laser or Nd:YAG laser to treat tracheal or bronchial obstruction	None	Up to 90 weeks	Safety, complication rate, relief of symptoms.	Of 400 procedures in 269 patients, significant relief was reported after 313 (78%). No improvement after 87 (21.8%) of procedures. Pre-op x-ray showed partial or total atelectasis in 137 patients. Post op x-ray showed improvement in 70 (51%). One death intra-operatively; 11 died within one week of procedure. For benign disease, 81% got relief and there were no deaths.	Not reported	Outcome data is not well reported. Safety data useful. Nd:YAG laser treatment under general anesthesia or conscious sedation is safe with symptomatic benefit.
Moghissi K	Endoscopic laser therapy in malignant tracheobronchial obstruction using sequential Nd-YAG laser and photodynamic therapy.	1997 Thorax	Qualitative research	plus	17 patients with tracheobronchial obstruction	9 males, 8 females. Average age 69 years (range 45-79). All had inoperable primary (16/17) or secondary (1/17) tracheobronchial lesions causing more than 50% endoluminal obstruction. Stage IIIA or IIIB.	Nd:YAG laser for relief of endobronchial obs followed by PDT 4-6 weeks later	None. All patients received laser and then PDT.	up to 48 months	Relief of symptoms, WHO PS, subjective degree of improvement. PFTs, changes in CXR, percentage bronchial opening and path response were also recorded.	Survival: 65% at one year; 47% at two years. Median survival was 18.5 months. Improvement in airway obstruction in all patients; mean change in luminal opening 66% (40-90%). Mean FEV1 25% (0-90%) increase. Mean FVC 28% (0-70%) increase. All patients had symptomatic improvement and at least a partial response and 7 had a complete response for 3-6 months.	Yorkshire Cancer Research Campaign and Laser Trust (Moghissi) appeal.	As with most of these studies all patients in this study received active treatment - there was no control group. However, the size of the benefit and survival suggests that they would have done better than a control group had there been one. The survival times with combined approach (laser and PDT) seem to be better than other series of laser alone.

# Laser Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Colt, H. G.; Janssen, J. P.; Dumon, J. F.; Noirclerc, M. J.	Endoscopic management of bronchial stenosis after double lung transplantation	1992 Chest	Qualitative research	plus	6 patients with double lung transplants and bronchial stenosis.	Cystic fibrosis patients with double lung transplant, mean age (14.3+/- 5.5) years	Use of laser and balloon dilatation	None	1 year	Treatment success and safety.	Treatment success but no objective measures quoted.	Not reported	Treatment success but no objective measures quoted
Katic, M. R.; Burick, A. J.; Lucchino, D. B.	Experiences with laser bronchoscopy	1991 Pennsylvani a medicine	Qualitative research	plus	58 patients, 56 with malignant endobronchial disease and 2 benign design.	41 (71%) males, 17 females (29%). Age range 37 to 81 years.	Effect of Nd YAG laser	None	Unclear	Safety and symptomatic response	Safety: 2 deaths (2.3%); 8 complications (9.2%); bleeding 5; pneumothorax 1; hypotension 1; Co2 retention 1. Improvement in dyspnoea 83%; and improvement of haemoptysis 100%.	Not reported	Laser treatment is generally safe with a 2% mortality. It also results in an improvement in symptoms.
Gelb, AF	Laser in treatment of lung cancer.	1984 Chest	Qualitative research	plus	46 patients, (27 patients incomplete obstruction and 19 patients complete obstruction).	Incomplete obstruction: 1. male, 8 female, average age 63+/- 15 years. Complete obstruction: 8 male, 11 female, average age 64 +/- 10 years. Group 1: All had incomplete obstruction of tracheobronchial tree due to NSCLC. 16 patients previously treated with surgery, RT or chemotherapy. Group 2: Complete obstruction of part of the tracheobronchial tree.	Ability of Nd:YAG laser to relieve symptoms in lung cancer.	Efficacy in between the two groups i.e. those with complete versus incomplete obstruction	Not stated	Safety, improvement of airway obstruction, FEV1, FVC, Karnofsky score, dyspnoea score.	Incomplete obstruction: safety- 3 deaths (2 fatal haemorrhage); 7 needed rigid bronchoscopy. Palliative benefit 23/27 patients FEV1 52+/- 19 to 74+/- 27. FVC 64+/-23 to 77+/-26. Karnofsky score 41+/-15 to 51+/-18. Dyspnoea score 3.7+/-0.6 to 2.8+/-0.7. Complete obstruction: safety - 2 deaths. Palliative benefit 6/19 patients. FEV1 44+/- 13 to 48+/-13. FVC 46+/-14 to 59+/-18. Karnofsky score 30+/-10 to 34+/-16. Dyspnoea score 3.7+/-0.5 to 3.4+/-0.5. Following laser treatment, 23/27 patients with incomplete obstruction had immediate palliative relief compared with only 6/19 in the group with complete obstruction.	Not stated	Laser treatment with flexible bronchoscopy is safe and effective and improves airway patency. Success rates are greater in patients with incomplete obstruction. Treatment improves symptoms, Karnofsky score and dyspnoea. This is one of the earlier studies using laser and illustrates the higher morbidity/mortality rate. In the partial obstruction group 3/27 patients died peri-procedure or within 2 weeks and in the total obstruction group 2/19 died one associated with an airway fire.
Hetzel, MR	Laser therapy in 100 tracheobronchial tumours.	1985 Thorax	Qualitative research	plus plus	100 patients with tracheobronchial tumours	60 males, 40 females. Average age 65 years (27-83). 84 local anesthesia and flexible bronchoscopy. 21 cases general anesthesia with rigid bronchoscope. All had histologically proven and inoperable tracheal or bronchial tumours causing symptoms. 64 previous RT, 11 chemotherapy, 12 surgery with relapse of symptoms. 96/100 had lung tumours and 4 metastatic disease.. 59 had partial obstruction of trachea or bronchus, 17 complete obstruction and 24 recurrent haemoptysis.	Nd:YAG or Argon laser	Pre and post therapy partial obstruction versus complete obstruction	Up to 115 weeks or to death.	Patient's reported symptoms, PFTs. 6MWT. Haemoptysis diary charts and complications	Safety: 2 deaths (0.69% procedure mortality or 2% overall mortality) in patients with partial obstruction. Symptomatic response: 76% objective response (63%) in patients with complete obstruction. Symptomatic response 38%; objective response 29%. Haemoptysis: symptomatic response 67%, objective response 58%.	Part funded by Office of Chief Scientist, DHSS.	Although 68% had symptomatic improvement and 56% had objective improvement there was no control group in this study so it is difficult to say exactly how much effect laser has. Main complication was peri-procedural death (2%) of patients - both due to treatment of tumours causing near complete obstruction of the airway.

# Laser Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Antypas, G.; Baltayanis, N.; Bolanos, N.; Anagnostopoulos, D.; Tsourelis, L.; Kavoukas, J.	Nd: YAG laser in the palliative treatment of tracheal diseases	2000 Journal of B.U.ON.	Qualitative research	plus	484 patients between 1987-1998	All were referred for endoscopic management and palliation of significant symptomatic airway obstruction due to malignant or benign process. Previous treatments had failed or patient was considered ineligible. Mean age 68 (range 38-72). 138 women; 246 men. 350 were due to bronchial carcinoma, 67 metastatic endobronchial carcinoma, 59 benign tumours & cicatricial lesions of the trachea in 8	The effect of Nd:YAG laser for relieving bronchial obstruction.	None. No comparisons are made. The study reports a cohort of patients who were treated.	Not clearly reported. Follow up data was not available in 253 patients. Cumulative survival percentages for 350 pts was 55% at 6 months and 28% at 1 year.	Restoration of airway patency, safety and reduction of symptomatic haemoptysis.	653 procedures under GA; 318 (91%) successful treatment with restoration of airway patency. 86% of patients (30/35) reduction in dyspnoea; 90% (36/40) re-expansion of collapsed lobe. Safety: deaths 3, respiratory failure 6, haemorrhage 5, pneumothorax 4, MI 2 (both died), mediastinal emphysema 1.	Not stated	Laser treatment for endobronchial tumours is technically safe and feasible with high success rate for restoration of airway patency.
Cavaliere, S.; Foccoli, P.; Farina, P. L.	Nd:YAG laser bronchoscopy. A five-year experience with 1,396 applications in 1,000 patients	1988 Chest	Qualitative research	plus	1000 patients between 1982-87.	649 malignant tumours of which 593 were lung cancer, 139 non-malignant stenoses and 89 miscellaneous.	Ability of Nd:YAG laser to relieve endobronchial obstruction.	Outcomes from those with malignant tumours was compared with those with benign tumours.	A sub-group were followed for up to 1 year	Safety, improvement in airway caliber, observational improvement in ventilation, no objective measurement. Survival	Safety: 10 patients (1%) haemorrhage; mediastinal emphysema 2 patients (0.2%); pneumothorax 4 patients (0.4%); 5 deaths (0.5%). Airway calibre improved in 925 of patients treated. Survival 50% at 6 months and 26% at one year	Not stated	Laser treatment is safe under both general with rigid bronchoscopy and local anesthesia with flexible bronchoscopy. There were improvements in airway calibre. The outcomes are presented with little objective data to support conclusions. Airway lumen is subjective as is improvement in dyspnoea.
Chan, AL.	Nd:YAG laser bronchoscopy. Rigid or fiberoptic mode?	1990 Chest	Qualitative research	plus	79 patients had 124 procedures performed. 42 patients had procedures undertaken by rigid bronchoscope, 32 had procedures performed by FOB and 12 had combined procedures.	All had symptoms of dyspnoea and majority had haemoptysis. Those with lung cancer had had previously had surgery or chemotherapy or RT or considered unsuitable for these treatments. Mean age for those having rigid bronchoscopy was 64.5 years (range 25-82) and those having FOB 63.9 (range 32-86). Those having combined RB/FOB were older mean 71.9 yrs (p<0.05). No difference in sex distribution Majority of cases treated were malignant. 8 were benign granulomas (no diff between RB or FOB approach). Significantly more cases with RB were proximal and right sided compared with FOB which had a distal/left sided predominance.	Ability of Nd:YAG LASER therapy to open an occluded airway using either FOB or Rigid bronch or combination.	Rigid versus flexible bronchoscopy; general anesthesia versus conscious sedation.	At least 1 year	Estimated survival using each approach; complication profile; percentage improvement in endobronchial obstruction post laser therapy; duration of procedure; mean total number of pulses used; total power applied per procedure.	Complication rate: rigid bronchoscopy group- haemorrhage (>50ml) 4; MI 2; cardiac arrhythmia 2; flexible bronchoscopy- haemorrhage 3; cardiac arrhythmia 2; bronchopulmonary fistula 1; mediastinitis 1. Percentage improvement in endobronchial obstruction (rigid vs flexible) trachea 56% vs 47%; R proximal 53% vs 36%; R distal 13% vs 56%; L proximal 56% vs 38%; L distal 3% vs 31%. In RB group majority of cases were right proximal and distal (sig diff p<0.001) from FOB group. Mean duration 2.5 hours with RB and 3.5 with FOB. Mean total number of pulses per procedure was significantly higher for RB group compared with FOB group (p<0.001). Total power applied showed no difference. Use of RB significantly improved airway calibre when right or left proximal lesions were involved (p<0.05) and FOB sig improved airway calibre for Right (p<0.05) and left distal lesions (p<0.05). No difference in complications. Survival in RB group 25% alive at 6/12 and 14% at 1 year compared with 19% and 6% respectively in FOB group. Median length of survival in RB group was 15 weeks compared to 9 months for FOB group. No significant survival differences between any group.	Not stated	No difference in complication rates between rigid versus flexible bronchoscopy groups. Better restoration of airway patency in patients with central tumours with rigid bronchoscopy and better restoration with flexible bronchoscopy when obstruction was more distal.

# Laser Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
McDouga II, J. C.; Cortese, D. A.	Neodymium-YAG laser therapy of malignant airway obstruction. A preliminary report	1983 Mayo Clinic Proceedings	Qualitative research	plus	22 patients with tracheo-bronchial obstruction.	12 males, 10 females. Cancer 19, carcinoid 1, Hodgkins disease 1 and benign stricture 1.	Effect of laser treatment.	None	Unclear	Safety	2 deaths from fatal heamorrhage during procedure.	Not reported	YAG laser treatment is feasible in patients with tracheo-bronchial obstruction but at higher power settings (50-90 watts) has a higher risk of fatal haemorrhage.
Parr, G. V. S.; Unger, M.; Trout, R. G.; Atkinson, W. G.	One hundred neodymium-YAG laser ablations of obstructing tracheal neoplasms	1984 Annals of Thoracic Surgery	Qualitative research	plus	40 patients with tracheo-bronchial obstruction.	34 primary lung cancer; 4 metastatic malignancy and 2 benign	Ability of Nd:YAG laser to relieve endobronchial obstruction.	None	Unclear	Patency of previously obstructed bronchus and bleeding during procedure. Clinical and symptomatic improvement, safety and effectiveness	Simply described as 'excellent' or 'fair' or 'poor'. No quantification. 22 excellent; 10 fair; 8 poor. Safety: no deaths, 1 unassociated pneumothorax, 1 bradycardia. Effectiveness: no objective measures described, success in 22 patients, limited or poor benfit in 8 patients.	Not reported	Nd YAg appears to be safe in the treatment of tracheo-bronchial obstruction. Inadequate objective data to judge benefit in this paper.
Livingston, D. R.; Mehta, A. C.; Golish, J. A.	Palliation of malignant tracheo-bronchial obstruction by Nd-YAG laser: An update of experience at The Cleveland Clinic Foundation	1987 Journal of the American Osteopathic Association	Qualitative research	plus	74 patients	48 men; 26 women. Age 44-86 years. Underwent 88 procedures with ND:YAG laser for malignant endobronchial obstruction.	Effect of Nd-YAG laser treatment for restoration of airway patency	None	Not reported	Subjective improvement. Safety. Flow-volume loops; V/Q scan.	Safety: 5 events, 3 deaths (2 assoc with haemorrhage and 1 with MI), swelling of vocal cords, hypotension, respiratory failure. Symptomatic benefit in most patients.	Not stated	Treatment with laser is safe with symptomatic benefit but outcome evidence is reported poorly.
Ross DJ	Survival characteristics after neodymium: YAG laser photoresection in advanced stage lung cancer	1990 Chest	Qualitative research	plus	69 patients with tracheo-bronchial obstruction from cancer. Two excluded from survival analysis as lost to follow up. Split into 2 groups: Successful photoresection (55 cases) if at least 75% of lumen was restored and unsuccessful (14 cases) if not.	Limited info: mean age 63 years in successful and 61 years in unsuccessful group. All patients needed resection for haemoptysis, dyspnoea, obstructive pneumonitis, atelectasis.	Effect of Nd Yag laser therapy	Between successful and unsuccessful therapy; 75% restoration of luminal calibre was classed as successful.	32 months	Survival: improved survival in patients treated successfully (p>0.5). Karnofsky index successful 41+/-13 to 60+/-17 unsuccessful 45+/-8 to 54+/-5.	Survival, Karnofsky index.	Not reported	Suggestion that patients successful treated with laser for endobronchial obstruction from cancer have a better survival than patients with unsuccessful treatment.
Andrews, Brian T.; Graham, Scott M.; Ross, Alan F.; Barnhart, William H.; Ferguson, J. Scott; McLenna, Geoffrey	Technique, utility, and safety of awake tracheoplasty using combined laser and balloon dilation	2007 Laryngoscope	Qualitative research	minus	18 patients	14 females, 4 males, average age 49 years (range 28-74). Aetiology; 10 idiopathic, 4 tracheostomy, 2 wegners, 1 radiation, 1 inhalation injury.	Effect of laser tracheoplasty in conjunction with balloon dilatation.	None	22 months (3-55 months)	Procedure success and safety.	Success in all patients apparently, although very poorly addressed. Other than saying how many procedures were required, there is no other objective measure given - inadequate data: 44% one procedure; 28% two procedures; 17% three procedures; 6% four procedures; 6% five procedures. No complications.	Not reported	Do not include in guideline Success in all patients apparently, although very poorly addressed.

# Laser Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Ward, R. F.	Treatment of tracheal and endobronchial lesions with the potassium titanyl phosphate laser	1992 Annals of Otolaryngology	Qualitative research	minus	18 patients; 15 paediatric group (age range newborn to 13 years)	Age range newborn to 44 years. 15 paediatric, 3 adults. Predominantly granulomatous disease, granulation tissue, cysts and tracheal stenosis.	Effect of potassium titanyl phosphate laser.	None	Not stated	Safety, clearance of granulomatous lesions	Unable to assess from information provided.	Not reported	Do not include in guideline
Dumon, J.F.	Treatment of tracheo-bronchial lesions by laser photoresection.	1982 Chest	Qualitative research	plus	111 patients with tracheo-bronchial lesions.	Age 5 to 85; 22 female, 89 male. Procedures performed for inoperable tracheo-bronchial tumours; correction of tracheal stenosis; removal of surgical sutures; haemoptysis.	Ability of Nd:YAG LASER to open airways.	Flexible versus rigid bronchoscopy; conscious sedation versus general anesthesia.	Up to 11 months for a proportion of patients.	Few objective measurements are given. Mainly subjective for those with tumours. Complications. Safety.	Safety: no serious complications. Proportion of patients who improved: excellent 37 /63, improved 22/63, poor result 4/63. Most had good/excellent immediate improvement Tracheal stenosis; all improved or had 'excellent' outcome (trachea fully reopened or by at least 7.5 mm) Dilatations were co-performed. Tracheal granulomas - very good results. No complications.	Not stated	Large retrospective review; good results. Clearly define type of patients that can be treated. Lack of objective measurement of outcomes. Good safety apparently although data limited. Laser treatment is safe and effectively restores airway patency in tracheo-bronchial obstruction. Treatment is equally effective with rigid or flexible bronchoscopy and with conscious sedation or general anaesthesia.

# Stents Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Chan, Andrew L.;Juarez, Maya M.;Allen, Roblee P.;Alberts on, Timothy E.	Do airway metallic stents for benign lesions confer too costly a benefit?	2008 BMC Pulmonary Medicine	Qualitative research	plus	35	<p>35 adult patients (17 female) deemed unsuitable for surgery or declining surgery and presenting with central airway obstruction from benign causes resulting in the placement of 82 self-expanding metallic stents.</p> <p>Mean age 59.5 +/- 14.3 years.</p> <p>Underlying disease: tracheobronchial malacia n=23; postintubation stenosis n=17; lung transplant anastomotic stenosis n=4; other n=8.</p> <p>Co-morbidities: COPD n=14; pneumonia n=10; lung transplant, ILD (n=4 each); CVA n=3; ARDS n=2 and other n=8.</p>	Treatment with a self-expanding metal airway stent for central airway obstruction of benign cause.	None.	<p>Median follow-up 473 days.</p> <p>Mean duration of stent survival within patient = 616 days (range 1- 3205 days).</p>	<p>Improvement in symptoms of stridor, respiratory distress cough and secretion clearance (none of these further defined in the paper).</p> <p>Complications: major (requiring an intervention or having a significant clinical impact) and minor; early (less than 24 hours after stent placement) and late.</p> <p>Type of stent deployed.</p>	<p>Improvement in stridor (73%), respiratory distress (71%), cough (79%) and secretion clearance (75%).</p> <p>One or more complications occurred in 28 patients (80%). There was at least one major complication in 16 patients (46%) and at least one minor complication in 27 (77%).</p> <p>Early complications occurred in 3 patients (9%): Temporary glottic oedema n=1 Sustained hypoxia requiring CPAP n=1 Stent migration n=1.</p> <p>Late complications occurred in n=27 (77%) of patients Major late complications in 13 (37%) Obstructive granuloma in 20 (24.4%) stents in 10 (28.6%) patients Stent fracture in 16 (19.5%) stents in 6 (17.1) patients Stent migration in 10 (12.2%) stents in 6 (17.1%) patients</p>	Not described.	Self expanding metallic stents can be used in inoperable benign airway stenosis with caveats based on this single centre case series opinion.
Hautman n, Hubert;B auer, Martin;Pf eifer, Klaus J.;Huber, Rudolf M.	Flexible bronchoscopy: A safe method for metal stent implantation in bronchial disease	2000 Annals of Thoracic Surgery	Qualitative research	plus	51	<p>51 patients attending a teaching hospital.</p> <p>Mean age 58.8+/-12.3 years.</p> <p>Indications: dyspnoea 53%; retention pneumonia 17%; secretions 15%, dyspnoea and stridor 12%, lung abscess 3%. Malignant disease in 84%, benign collapse in 16%.</p> <p>65 stents placed (28% under topical anaesthesia, 72%=48 patients with IV sedation).</p> <p>73% of malignant obstructions were extrinsic, remainder were exophytic or combination.</p>	Efficacy and safety of metallic stent placement through a flexible bronchoscope	None	<p>median follow-up 39 days (range 1- 1561 days).</p>	<p>Lung function parameters (FEV<sub>1</sub>, PEF, Raw, FEV<sub>1</sub>/FVC %) and blood gases before and 72 hours after stent insertion.</p> <p>Clinical improvement (not otherwise defined).</p> <p>Complications of stent insertion.</p>	<p>FEV<sub>1</sub> improvement 1.57 to 1.99 p=0.019; PEF 2.9 L/S - 4.1L/S p=0.001; Raw 0.64kpa/Ls<sup>-1</sup> to 0.39 P=0.004; pO<sub>2</sub> 69.7mmhg to 69.4 p=ns; pCO<sub>2</sub> 34.7mmhg to 32.9 p=ns.</p> <p>Clinical improvement following 52 out of 65 stent implantations.</p> <p>Complications occurred following 20/65 stent insertion procedures, 3 fatal and 17 non-fatal. 3 deaths between 24 hours and 30 days post implantation: 1 at 24 hours due to displaced stent causing asphyxia, 1 from septic shock complicating stent occlusion by mucus, and 1 due to massive haemoptysis. Non-fatal complications: poor stent positioning 7 cases, wrongly sized stent 3 cases, leading to stent migration in 2, stent migration in 8 other cases, hypotension 2 cases.</p>	No information supplied	Reasonably sized retrospective review of earlier metallic stents at a single centre. Metallic stents can be placed safely by flexible bronchoscopy in malignant and benign airway stenoses/collapse, with demonstrable efficacy immediately. It also addresses the use of anaesthesia, high frequency jet ventilation and type of stents.
Miyazawa, T.;Yamakido, M.;Ikeda, S.;Furukawa, K.;Takiguchi, Y.;Tada, H.;Shirakusa, T.	Implantation of Ultraflex nitinol stents in malignant tracheobronchial stenoses	2000 Chest	Qualitative research	minus	<p>34</p> <p>54 stents</p> <p>19 emergency procedures.</p>	<p>34 patients (30 male) prospectively collected in 6 Japanese centres over 1 year.</p> <p>Mean age 63 ± 10 years.</p> <p>Underlying diagnosis: bronchogenic carcinoma 25 (squamous 11, adeno</p>	Implantation of an Ultraflex stent.	Measurements of dyspnoea index, FEV <sub>1</sub> , FVC, PEF, and 'obstruction of airway diameter' (not defined) before and after Ultraflex stent implantation.	1 year	<p>Measurements of dyspnoea index, FEV<sub>1</sub>, FVC, PEF, and 'obstruction of airway diameter (not defined) before and after Ultraflex stent implantation.</p>	<p>Lung function data available in 16 patients (47%). Improvement in VC from 1.97±0.54L to 2.46±0.60L (p&lt;0.01), FEV<sub>1</sub> from 1.40±0.51 L to 1.74 ± 0.52 L (p&lt;0.001) and in PEF from 2.9 ±1.4 L/s to 3.6 ± 1.2 L/s (p&lt;0.05).</p> <p>Improvement in dyspnoea index, reported as percentage of patients with DI 0-2. Prior to treatment 32%, day 1 79%, day 30 85%, day 60</p>	No information provided	Small case series without comment of selection/exclusion of cases. Provides safety and efficacy data for inoperable cancer with symptomatic central airway obstruction. A good number of cases in the institute, with 1 year survival data, allowing a reasonable comment regarding the potential

# Stents Evidence Table

						8, small cell 5, adenoid cystic 1; oesophageal carcinoma 4; mediastinal tumour 3; metastatic disease 2.  Type of obstruction: intraluminal tumour 22; extrinsic compression 12.					79%. (p<0.001 before vs day 1, day 30, day 60).  Improvement in obstruction of airway diameter (81±15% before vs 14±17% on day 1, 12±12% on day 30 and 22±28% on day 60, p<0.001).  Complications: tumour ingrowth 8 patients (24%), tumour overgrowth 7 (21%), granulation tissue ingrowth 1 (3%), retained secretions 3 (9%), stent migration 0. Death occurred in 21 patients. 15 from cachexia, 5 from bleeding, and 1 from respiratory insufficiency. There were no deaths attributed to stent-related complications.  Median survival 3 months, 1-year survival 25.4%.		value of metallic airway stents for relief of symptoms in this setting.  However, in 8/34 patients (24%), additional radiotherapy/chemotherapy was given after stent placement which may have influenced symptomatic outcomes, lung function and survival. The outcome data are not reported separately for patients who did or did not have supplementary treatments.
Lin, S. M.; Lin, T. Y.; Chou, C. L.; Chen, H. C.; Liu, C. Y.; Wang, C. H.; Lin, H. C.; Yu, C. T.; Lee, K. Y.; Kuo, H. P.	Metallic stent and flexible bronchoscopy without fluoroscopy for acute respiratory failure	2008 The European Respiratory Journal	Qualitative research	minus	26	26 patients (19 male) mechanically ventilated and with central airway obstruction or tracheo-oesophageal fistula.  Mean age 63.6 ±15.8 years.  Mean APACHE II score 17.4±4.1 29 stents placed.  Causes of airway lesion: malignancy 21 (80.8%) (oesoph ca 11, lung cancer 5, buccal cancer 2, thyroid cancer 1, mediastinal schwannoma 1, mediastinal carcinoid 1, Benign 6 (19.2%) - dynamic collapse right main bronchus 2, post intubation tracheal stenosis 1, tracheal stenosis 1.	Self-expanding metallic tracheobronchial stent insertion using flexible bronchoscopy without fluoroscopy.	Requirement for mechanical ventilation before and after stenting.	median follow-up 30.5 days (range 1-473).	Requirement for mechanical ventilation and duration of mechanical ventilation. Complications. Survival.	After stent implantation, 14 (53.8%) were successfully liberated from ventilator. Of these 13 were liberated within 1 day.  Overall mortality rate was 58% (83% for successfully liberated and 36% for unsuccessful).  Median length of survival was 30.5 days (3-473) (34.5 for successfully liberated and 21.0 for unsuccessful)	No information provided	Retrospective study in ventilated ICU patients  This suggests its use is effective, although it cannot imply that these patients will be extubatable as a result of stent placement.
Lonchyna, Vassyl A.; Arcidi, Jr Joseph M.; Garrit y, Jr Edward R.; Simpson, Kevin; Al ex, Charles; Y eldandi, Vijay; Bak hos, Mamdou h	Refractory post-transplant airway strictures: Successful management with wire stents	1999 European Journal of Cardio-thoracic Surgery	Qualitative research	minus	18	18 Lung transplant recipients presenting with anastomotic strictures of the bronchi (14 male).  Mean age range 18-65, median 45.  Underlying diagnosis: Cystic fibrosis 8; COPD 5; Idiopathic pulmonary fibrosis 3; Primary pulmonary hypertension 1; Alpha 1 anti-trypsin deficiency 1.	Tracheobronchial stenting with wire stents.  Silicone stents were used in the early stages.	Symptoms and FEV <sub>1</sub> before and after stent insertion.	6 months for spirometry in 12 patients. Otherwise, no range of follow up provided.	FEV <sub>1</sub> pre and post stenting.  Need for further procedures.  Complications.	Pre stent FEV <sub>1</sub> 1.19L (±0.64L) vs post-stent 2.06L (±0.7L) p<0.0001. Data available in 12/18 patients (3 patients unable to provide FEV <sub>1</sub> because ventilated, 3 patients incomplete data).  Complications: Bronchial dehiscence requiring re-operation n=3 (17%); severe bleeding requiring thoracotomy 1/18 (6%); granulation tissue formation n=1; acute stent occlusion by mucus n=1	not stated	A well described experiential series for a specific type of need for stents. Suggestion of early use of SEMAS being positive vs traditional silicone, whilst highlighting potential problems

# Stents Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Dasgupta, Asok;Dol match, Bart L.;Abi, Saleh Wajdy J.;Mathur , Praveen N.;Mehta, Atul C.	Self-expandable metallic airway stent insertion employing flexible bronchoscopy: Preliminary results	1998 Chest	Qualitative research	minus	37	<p>37 patients (24 male) and 52 stents placed.</p> <p>Mean age 56 years (range 31-94).</p> <p>Indications:tracheobronchomalacia (TBM, n=13); neoplasia n=20; tracheal stenosis n=6. For TBM patients, causes were lung transplantation in 6, relapsing polychondritis in 3, post tracheostomy in 2 and idiopathic in 2.</p> <p>Stents were inserted in trachea (n=19), left main bronchus (n=20) right main bronchus/bronchus intermedius (n=13).</p> <p>8 patients had 2 stents, 2 had 3 stents and 1 had 4 stents.</p>	Insertion of self-expanding metallic stents for the treatment of large airway obstruction, using flexible bronchoscopy.	Symptoms, lung function and requirement for ventilatory assistance before and after stent placement	Median follow-up 21 weeks (range 1-128 weeks)	<p>Symptoms, FEV<sub>1</sub>, FVC.</p> <p>Need for ventilatory support.</p> <p>Complications</p>	<p>Symptomatic improvement described in 36/37 patients.</p> <p>TBM: 9/13 patients had lung function results. Mean improvement in FEV<sub>1</sub> 45% (range 0-211%), FVC 35% (-4 to 227%), PEF 32% (1-86). 1/2 patients weaned from ventilation. 1 patient died of CVA.</p> <p>Neoplasia: 4/5 patients successfully weaned from mechanical ventilation.</p> <p>Tracheal stenosis: mean increase in FEV<sub>1</sub> of 17%, FVC 9% measured in 4 patients.</p> <p>Complications: 19 complications occurred: granulation tissue in 6 (4 obstructing, 2 non-obstructing); Infection in 2 patients, one requiring stent removal.</p>	Not stated	Small cohort experience shows effectiveness and safety in malignant and benign inoperable lesions.
Hsu, L. H.;Liu, C. C.;Lin, C. Y.;Yen, K. L.;Chan, K. Y.	Self-expandable metallic tracheobronchia 1 stent insertion and endobronchial electrocautery with flexible bronchoscopy: Preliminary results at a cancer center	2002 Journal of the Formosan Medical Association	Qualitative research	plus	12	<p>12 patients (10 Male).</p> <p>Mean age 53.3 years (range 33-79).</p> <p>Indications: malignant central airway obstruction 9; tracheo-oesophageal fistula due to oesophageal cancer 1; benign airway stenoses 2 (1 tracheal and 1 subglottic) after intubation and tracheostomy.</p>	Insertion of a covered Ultraflex distal-release self-expanding metallic stent placed using flexible bronchoscopy, for relief of large airway obstruction.	Breathlessness score and subjective assessment before and after stent placement.	Median follow-up 11 weeks (range 5-38 weeks)	<p>Subjective symptom assessment, breathlessness score, FEV<sub>1</sub>.</p>	<p>Symptoms reportedly improved in 12/12 patients.</p> <p>FEV<sub>1</sub> measured in 6 and improved by mean of 696.7 mL (range 470-1140 mL).</p> <p>Median dyspnoea score before stent placement = IV, after = I</p> <p>Complications: stent removal after 4 weeks due to tumour relapse in 1 patient; stent misplacement n=1. Retained secretions described as the most common complication but frequency not specified.</p>	not addressed	Stents with optional debulking may alleviate dyspnoea in malignant central obstruction, and may improve lung function.
Herth, F	Successful Bronchoscopic Placement of Tracheobronchial Stents Without Fluoroscopy	2001 Chest	Qualitative research	minus	96	<p>96 patients (60 male)</p> <p>Mean age 59.8 (range 26-92).</p> <p>Indications for procedure: large airway obstruction n=90; airway fistula n=10.</p> <p>Underlying disease: NSCLC 40; oesophageal cancer 20; post intubation tracheal stenosis 18; SCLC 6; thyroid cancer 6; metastasis to thorax 5; goitre 2; lymphoma 2; benign disease NOS 1.</p> <p>Sites of airway obstruction trachea 60, LMB 17, RMB 13, BI 7, LUL 2, RML 1.</p>	Insertion of a metallic Ultraflex stent without fluoroscopic guidance using flexible bronchoscopy under conscious sedation (n=52) or rigid bronchoscopy under general anaesthesia (n=48). 100 stents were inserted.	None	Not stated	<p>Satisfactory positioning of stent.</p> <p>Need for repositioning.</p> <p>Use of fluoroscopy.</p> <p>Complications</p>	<p>All stents (n=100) satisfactorily placed without repositioning or fluoroscopy. No complications.</p>	Not stated.	<p>This study in 96 patients with airway obstruction showed that bronchoscopic placement of metallic airway stents can be achieved effectively and safely through endoscopic visualisation by experienced operators without fluoroscopy.</p> <p>It did not look at other stents nor any follow up data to discuss stent complications or patient outcomes.</p>

# Stents Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Monnier, Philippe;Mudry, Albert;Stanzel, Franz;Haeussinger, Karl;Heitz, Markus;Probst, Rudolf;Bolliger, Chris T.	The use of the covered Wallstent for the palliative treatment of inoperable tracheobronchial cancers: A prospective, multicenter study	1996 Chest	Qualitative research	minus	40	<p>40 patients (male 29) with malignant tracheobronchial obstruction were recruited into a prospective multicentre audit of outcomes.</p> <p>Mean age 62 (range 36-83).</p> <p>Underlying diagnosis: squamous cell carcinoma of trachea or bronchus 25; small cell lung cancer 3; oesophageal cancer 3; other cancer 9.</p> <p>50 stents placed.</p>	Insertion of a Wallstent	Dyspnoea index and subjective assessment of bronchial lumen before and 1, 30 and 90 days after Wallstent insertion.	90 days	<p>Dyspnoea index and subjective assessment of bronchial lumen before and 1, 30 and 90 days after Wallstent insertion.</p> <p>Performance status change (Karnofsky index)</p> <p>Complications - immediate (misplacement, extent of tumour coverage, migration, anaesthetic) and late (regrowth, granulation, retained secretions)</p>	<p>Before insertion, 30/40 patients had dyspnoea index 3 or 4 and 10/40 DI 0-2. At day 1, 5/39 had DI 3-4 and 24/39 had DI 0-2. At day 30 4/22 had DI 3-4 and 18/22 DI 0-2. At day 90 2/13 had DI 3-4 and 11/13 DI 0-2.</p> <p>Prior to insertion, 3/40 patients have &lt;50% bronchial obstruction and 37/40 &gt;50%. At day 1, 39/39 have obstruction of 0-25%. At day 30 12/19 patients have airway 0-50% obstruction.</p> <p>Mean Karnofsky index 40-70</p> <p>Complications: One patient died of bronchospasm during the procedure. Prolonged postoperative laryngeal oedema 1; incorrect stent sizing requiring removal 3; stent migration 3; sputum retention within stent 15.</p> <p>3 month survival 13/40 - no stent related deaths.</p>	No information provided.	<p>Well reported prospective multi center trial of a single stent type in palliative cancer associated stenoses Prospective a priori outcomes defined (efficacy, safety, tolerance). Detailed reporting of pre,intra and post procedure events, including 'failures'.</p> <p>However, the analysis of dyspnoea index into two groups, DI 0-2 and DI 3-4 was not pre-specified in the methods and no statistical tests of the outcomes are reported in the paper.</p> <p>Additionally, it's expensive and there is poorer accuracy of placement with fluoroscopy (telestep device) than endoscopically (Rigidstep - Rigid bronch). From this, wallstent was an important utility in specific circumstances probably for more proximal lesions (rigid deployment), with improvements in dyspnoea, diameter (in more severe), performance index - less so in more severe.</p>

# Diathermy Evidence Table

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Sutedja G	Endobronchial Electrocautery is an Excellent Alternative for Nd: YAG Laser to Treat Airway Tumors	Journal of Bronchology 1997	Qualitative research	minus	56 patients with intraluminal tumours suitable for debulking with Nd:YAG were recruited	45 men, 11 women, median age 64 (range 20-90). 37 patients had intraluminal NSCLC, 19 had other tumours including carcinoid and hamartomas.	Could electrocautery be used for intraluminal tumour clearance.	These would have been cases that would normally have been treated by Nd:YAG, the study assessed whether electrocautery could be used instead.	Not documented	Successful clearance of intraluminal tumour, the need to convert procedure to Nd:YAG.	N/A	Not reported	This is a case series of 56 patients with visible intraluminal tumour who would normally be laser candidates. Instead they had diathermy with conscious sedation (apart from 9 patients with carcinoid who were done under GA) and tumour clearance was achieved in 70%. The remainder proved to have extraluminal disease. 1 patient required laser to achieve deeper necrosis. Complications- 1 patient required rigid bronchoscopy to control haemorrhage. Good qualitative data demonstrating, electrocautery is equally effective as Nd:YAG laser in intraluminal tumour clearance. The authors also suggest that electrocautery is a more cost-effective technique.
Sutedja G	Fibreoptic bronchoscopic electrosurgery under local anaesthesia for rapid palliation in patients with central airway malignancies: a preliminary report	Thorax 1994	Qualitative research	minus	17 patients with intraluminal tumour.	17 patients with a median age of 65 (range 48-85) years. All patients had advanced inoperable tumour and had a poor performance status.	Is fibreoptic bronchoscopic electrocautery an effective mode of rapid symptom relief in patients with intraluminal tumour.	N/A	Survival data recorded up to 11 months. treatment session continued until >75% reopening of lumen or 30 minutes treatment time. Patients asked about symptoms prior to discharge (2-5 days post treatment)	Restoration of >75% of lumen diameter, improvement in symptoms of dyspnoea and haemoptysis, lung function and ABGs.	N/A	Not reported	Clearance of tumour to improve luminal diameter to >75% was achieved in all patients with intraluminal obstruction. Physiological measures were not available in all the patients, however there was no major deterioration in lung function. Electrocautery appears to be a safe and effective method of palliating symptoms of obstruction due to tumour.
Horinouchi H	Safety study of endobronchial electrosurgery for tracheobronchial lesions: Multicenter prospective study	Journal of Bronchology 2008	Qualitative research	plus	37 patients	31 males and 6 females aged 16-83 years were recruited. All had endobronchial lesions, which could be directly visualised in the tracheobronchial tree. 12 primary lung cancer, 10 recurrent lung cancer, 6 tracheal malignancy, 5 other tumours, 4 inflammatory granulomas	This was safety and reliability study of endobronchial electrosurgery.	N/A	Not recorded	resolution of airway stenosis and /or resection of intraluminal tumour with minimal bleeding.	N/A	Not reported	A good qualitative study demonstrating the safety of endobronchial electrosurgery. Can be used from subglottis to subsegmental bronchi for resection of intraluminal tumour. No mortality or morbidity observed in the 37 patients enrolled in this study.

## Diathermy Evidence Table

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De La Cruz LI	Use of endobronchial electrocautery for the palliation of airway obstruction due to metastases from nonpulmonary malignancies	Journal of Bronchology 2006	Qualitative research	plus	13 patients in total and a total of 26 procedures.	8 male and 5 female participants, median age 67 years (range 39-88). All participants had metastatic non-pulmonary malignancy causing endobronchial obstruction. Symptomatic airway metastases Indications: atelectasis (42%), haemoptysis (31%), both (27%) Primary malignancy: renal cell cancer 6, melanoma 2, uterine 1, bladder 1 breast 1, ovarian 1, squamous cancer of epiglottis 1. Site of tumour: main stem bronchi and all lobar bronchi	A retrospective review of electrocautery procedures to evaluate efficacy and safety in symptomatic airway metastases.	Not applicable	Not specified	Side effects of treatment and percentage of endoluminal patency post-procedure. A complete response was defined by a 75% patent lumen after procedure and a partial response 50% patency.	Complete response in 27% of procedures, partial in 58% of procedures	Listed as no financial support	Too many study limitations in a very small study population (12), half of whom were renal cell carcinomas and therefore not generalisable.
Hooper, RG and Jackson	Endobronchial electrocautery	Chest 1988	Qualitative research	minus	18 patients with endobronchial lesions.	Not stated	The use of endobronchial electrocautery in endobronchial lesions as a diagnostic and therapeutic tool.	None	Not fully documented, up to 36 months.	Diagnostic utility of electrocautery, recanalisation of the bronchial lumen.	N/a	Not reported	Endobronchial electrocautery can be used as a diagnostic and therapeutic tool in those with endobronchial lesions. Side effects are minimal, however there is a risk of tracheal fire.
Gerasin VA	Endobronchial electrosurgery	Chest 1988	Qualitative research	minus	14 patients, 10 males, 4 females	Patients aged 23-68. Patients presenting with endobronchial/endotracheal tumours (both benign and malignant) causing obstruction of the airway, noted on previous fiberoptic bronchoscopy.	Use of endobronchial electrosurgery and diathermic snare to remove endobronchial tumour.	No comparisons made	1 to 4 years	Complete/partial tumour removal.	Not applicable	Not reported	Endobronchial electrocautery is safe to use in the palliation of malignant tumours causing obstruction and as radical management in benign tumours.

# Virtual Bronchoscopy Evidence

Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Asano, Fumihiro; Matsuno, Yoshihiko; Shinagawa, Naofumi; Yamazaki, Koichi; Suzuki, Toshitaka; Ishida, Takashi; Moriya, Hiroshi	A virtual bronchoscopy navigation system for pulmonary peripheral lesions	2006 Chest	Qualitative research	plus	37 patients with 38 pulmonary lesions	37 patients (23 male).  Median age 72.5 (30-85).  All with small peripheral pulmonary lesions ≤30mm. 5 lesions 0-1cm, 21 1-2cm and 12 > 2cm. Lesions in RUL (14), RML (4), RLL (9), LUL (7), LLL (4)	N/A	Diagnostic accuracy of ultrathin bronchoscopic biopsy using virtual bronchoscopic navigation. Confirmation of diagnosis by other method not reported, except 10 cases of inflammation which shrank or disappeared during follow-up.	N/A	Sensitivity / specificity / PPV / NPV / accuracy	Ultrathin bronchoscope guided to planned route 94.7%.  Forceps advanced to lesion 86.8%.  Diagnostic rate 81.6% .  For fully diagnosed lesions (37 of 38): sensitivity 81.8%, specificity 100%, negative predictive value 78.9%, positive predictive value 100%, accuracy for malignant disease 89.2%.	Not reported, but navigation system is Olympus prototype.	In 37 patients with small peripheral lesions virtual bronchoscopic navigation can be used to guide forceps to the site of a lesion in 86.8% of cases with a diagnostic rate of 81.6%.  No comparison attempted with conventional techniques. Historical comparison from literature only. RCT needed.  Exam time median 24.9 mins (range 11.6-58.2)
Moorthy, K.; Smith, S.; Brown, T.; Bann, S.; Darzi, A.	Evaluation of virtual reality bronchoscopy as a learning and assessment tool	2003 Respiration	Qualitative research	plus	No patients. The study used a virtual reality bronchoscopy simulator as a learning and assessment tool. 9 bronchoscopy novices and 9 experienced bronchoscopists .	9 Novices without bronchoscopic experience were compared to 9 experienced bronchoscopists (200 to 1000 bronchoscopies)	Not applicable	Measures of knowledge (% of bronchial segments visualised) and technical skill (time taken, wall collisions, economy = %/time), comparing first attempt of novices with subsequent attempts (up to 10) and with experienced bronchoscopists (after 2 attempts).	Not applicable	Percentage of segments visualised, time taken, wall collisions, economy (= %/time)	Differences between novices and experts disappeared after 3 sessions (percentage of segments visualised and economy) or 5 sessions (number of wall collisions). Novices improved after 5 sessions: percent segment visualised 74.7 (±17.8) to 95.2 (±4.7) time taken 797.2 (±381) to 603 (±124.5) secs wall collisions 55.2 (±19.4) to 40 (±12.48) economy 0.1 (±0.03) to 0.15 (±0.04)	Loan of equipment VB system provided by HT Medical Systems	This paper shows value of virtual reality bronchoscopy in training of novice bronchoscopists with rapid learning curve. Should be referenced in 'training' section of guideline. Study demonstrates improvement in skills within 5 sessions. Assessment not made with real patients.
Merritt, Scott A.; Gibbs, Jason D.; Yu, Kun Chang; Patel, Viral	Image-Guided Bronchoscopy for Peripheral Lung Lesions: A Phantom Study	2008 Chest	Qualitative research	plus	No patients 12 bronchoscopists localising 10 synthetically created lesions	No population. Phantom model with 10 synthetic lesions.  6 pulmonary fellows, 6 faculty members. Mean 8 ±9 years of training (range 1-23, median 3).  Bronchoscopists had performed average 175 ±97 bronchoscopies (range 20-350, median 175).	N/A	Comparison of standard bronchoscopic practice with real time virtual bronchoscopy image guided system. Accuracy of peripheral lesion localisation for biopsy using std ultrafine bronchoscopy or VB-guided ultrafine bronchoscopy, tested on phantom patient.	N/A	Biopsy-site position error (distance from forceps contact point to ground-truth lesion boundary) Localisation success (site identification with biopsy-site error ≤5mm)	Localisation success rate 43 ±16% for standard bronchoscopy, 94 ±7.9% for image-guided method. Biopsy site position error 9.7 ±9.1mm for standard practice, 2.2 ±2.3mm for image-guided method.	NIH National Cancer Institute grants R01-CA07432 and R44-CA091534	This was a study showing that ability to localize 10 lesions in a test phantom by 12 bronchoscopist doubled by use of virtual bronchoscopic real time image guidance 43% to 94%.

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McGuire, Franklin R.;Michael, Kerley J.;Ochran, Timothy;Bedekar, Ajay R.;Swafford, Rachelle;McLemore, Theodore L.	Radiotherapy monitoring device implantation into peripheral lung cancers: A therapeutic utility of electromagnetic navigational bronchoscopy	2007 Journal of Bronchology	Qualitative research	minus	None	Not applicable	None	None	No follow up	None	None	Not mentioned	A description study of the possible use of electromagnetic navigation to perform biopsies and implant radiotherapy monitoring devices. No patient data is given!
Asano, Fumihiko;Matsuno, Yoshihiko;Matsushita, Tomomichi;Konno, Hirohito;Saito, Yoshio;Seko, Akira;Ishihara, Yoichiro	Transbronchial diagnosis of a pulmonary peripheral small lesion using an ultrathin bronchoscope with virtual bronchoscopy navigation	2002 Journal of Bronchology	Qualitative research	plus	One	83 year old man with cough, sputum and peripheral small pulmonary lesion (18 x 14mm), and emphysema on CT, pO <sub>2</sub> 69mmHg, pCO <sub>2</sub> 50mmHg.	NA	None	Not stated. Lesion disappeared after antibiotics.	None	NA	Not stated.	Case report of use of ultrathin bronchoscopy (external diameter 2.8mm, working channel 1.2mm) with virtual bronchoscopy guidance to biopsy small peripheral pulmonary lesion (18 x 14mm) in right segment 3. Production of VB images took 15 mins (1mm CT collimation, 0.5mm reconstruction). Images produced up to 11th bronchus. Bronchoscopy took 15 mins, biopsy obtained. Diagnosis of pneumonia confirmed by resolution after antibiotics. Study followed/superseded by case series of 38 lesions (Asano et al)
Davoudi, Mohsen;Osann, Kathryn;Colt, Henri G.	Validation of two instruments to assess technical bronchoscopic skill using virtual reality simulation	2008 Respiration : international review of thoracic diseases	Qualitative research	plus	22 subjects 7 novice, 8 trainees, 8 experienced bronchoscopists	3 groups: bronchoscopy novices (medical students, interns or medical observers with no prior hands-on experience of bronchoscopy), trainees, faculty (attendings) sex, age,gender not relevant.	None	Comparison of two instruments to assess technical bronchoscopic skill BSTAT and BSET Test for interrater and test-retest reliability	NA	Reliability of two instruments to assess bronchoscopic skill Performance scores by level of experience Performance scores over time Performance skill compared by ANOVA Reproducibility and validity	Significant learning effect present only for novices (p,0.056 and 0.050) otherwise tests reproducible (reliable) Both tests show inter and intrasubject reproducibility. Test - retest reliability by ICC 0.86 for BSTAT and 0.85 for BSET. Test detect increase skill with increased experience (p<0.0005)	Part funded with grant support from UC Irvine C3REST (Centre for Research and Education)	Study confirming reproducibility (reliability) of 2 tests of bronchoscopic skill BTEST and BSTAT in 3 groups of subjects at different levels of training, although
Galia, Massimo;Lo, Casto Antonio;Midiri, Massimo;Bellia, Maria;Bartolotta, Tommaso Vincenzo;Cademartiri, Filippo;De, Maria Marcello;Lagalla, Roberto	Virtual bronchoscopy in patients with central endobronchial stenosing lesions. Technique optimisation with single slice spiral CT	2004 Radiologia Medica	Qualitative research	minus	10	10 patients (6 male)  Aged 22-60.  All with obstructing bronchopulmonary disease diagnosed by fiberoptic bronchoscopy: 3 adenocarcinomas; 3 small cell carcinomas; 2 squamous cell carcinomas; 1 haemangioma, 1 benign stricture.	To determine an original protocol for single slice CT virtual bronchoscopy in the evaluation of patients with central airway stenoses compared to fiberoptic bronchoscopy	Virtual reality bronchoscopy based on single slice CT compared to fiberoptic bronchoscopy in 10 individual case descriptions	Not stated.	Descriptive comparison of virtual bronchoscopy versus fiberoptic bronchoscopy	Not possible to assess	None stated	A protocol is described to adequately visualise virtual bronchoscopic images from single slice CT and is validated by comparison with the findings from fiberoptic bronchoscopy in 10 cases. Not blinded. Study found acceptable VB images, able to visualise lesions seen at bronchoscopy and able to visualise airways distal to obstructing lesions. Main emphasis of study was setting most appropriate parameters for CT in order to construct VB images.

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Authors	Title	year journal	Study type	Quality rating	numbers	characteristics	Intervention	Comparison	Follow up	Outcomes	Effect size	Funding	Comments
Kagadis, G. C.;Patrinou, V.;Kalogeropoulos, C. P.;Karnabatidis, D.;Petsas, T.;Nikiforidis, G. C.;Dougenis, D.	Virtual endoscopy in the diagnosis of an adult double tracheal bronchi case	2001 European Journal of Radiology	Qualitative research	minus	1 single case report	Patient with ipsilateral double tracheal bronchi	Use of virtual bronchoscopy in the diagnosis of this anatomical variant.	Virtual endoscopy compared with bronchoscopy.	Not stated.	VB findings confirmed by bronchoscopy.	Single case study therefore N/A.	Not stated.	Single case study of use of virtual bronchoscopy and bronchoscopy in the diagnosis of adult double tracheal bronchi and its value in planning surgery on the trachea.
Crawford, Stephen W.;Colt, Henri G.	Virtual reality and written assessments are of potential value to determine knowledge and skill in flexible bronchoscopy	2004 Respiration	Qualitative research	minus	12 pulmonary and critical care trainees undertaking a bronchoscopy simulator test and a theoretical knowledge test.	All were trainee pulmonologists in the investigators department.	NA	Comparison of ability to enter 5 named segments on a bronchoscopy simulator with year of training and results of test of theoretical knowledge	NA	% of named bronchoscope segments correctly identified.  Accuracy of response to a 50 question MCQ (not independently tested or evaluated).  Subjective assessment of training tool by trainees.	71% of bronchial segments identified correctly (said not to be associated with years of training but n = 12 and not possible to conclude this).  Only 51% of questions answered correctly, not related to ability to identify bronchial segments , number of bronchoscopies or years of training.	Not stated.	Very poor study with only 12 trainees in which technical ability and theoretical knowledge is assessed in relation to years of training. Only notable finding of this study is that only 3/12 trainees could enter a specified bronchial segment! Assessors were pulmonary and critical care trainees. Outcome was subjective views of assessors about the training tool, and relationship between technical skill, theoretical knowledge, bronchoscopy experience and stage of training. Results suggest tool may be potentially useful for training. Theoretical knowledge not related to number of procedures carried out, or years of training. Technical skills not related to theoretical knowledge. Unclear how free trainees were to express honest views - not clear whether responses were anonymous.
Jones, Catherine M.;Athanasίου, Thanos;Nair, Sujit;Aziz, Omer;Purkayastha, Sanjay;Konstantinos, Vlachos;Paraskeva, Paraskevas;Casula, Roberto;Glenville, Brian;Darzi, Ara	Do technical parameters affect the diagnostic accuracy of virtual bronchoscopy in patients with suspected airways stenosis?	2005 European Journal of Radiology	Systematic Reviews and Meta-analyses	plus plus	Overall diagnostic performance, pooled sensitivity and specificity, AUC and odds ratio. Results are meaningful. Virtual bronchoscopy performs well in the investigation of patients with suspected airway stenosis with high overall sensitivity, specificity and odds ratio for diagnosis. Diagnostic power for stenotic lesions using virtual bronchoscopy compared to		Pooled sensitivity 85% (95%CI: 77-91%) Pooled specificity 87% (95%CI: 81-92%) AUC 0.947			VB is accurate for diagnosis of stenotic lesions. Technical parameters within range of studies make no significant difference to accuracy. Relevant to professionals and policy-makers.			Second meta-analysis from same group published in 2005 with very slight differences in study selection, and slightly different focus (studies of patients with suspected airway stenoses, focusing on importance of technical CT parameters). Studies of patients with known bronchial stenoses excluded unless blinded comparison with control groups. Adult population. Included if data given on technical CT parameters: pitch, collimation, reconstruction interval, rendering method and scanner type. 3 additional studies (Lacasse, 2004, Hooppe 2004, Polverosi 1998) not included in first meta-analysis. Study adds little to previous meta-analysis, but confirms accuracy for stenotic lesions and shows no effect of technical CT parameters

					flexible bronchoscopy, using ROC analysis.								on accuracy.
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