# CASE REVIEW

# Changing patterns in interventional bronchoscopy

NIKOLAOS ZIAS, ALEXANDRA CHRONEOU, ANNE V. GONZALEZ, ANTHONY W. GRAY, CARLA R. LAMB, DAVID R. RIKER AND JOHN F. BEAMIS Jr

Department of Pulmonary and Critical Care Medicine, Lahey Clinic Medical Center, Tufts University School of Medicine, Burlington, Massachusetts, USA

#### ABSTRACT

Background and objective: Many interventional tools for airway disorders can now be delivered via flexible bronchoscopy (FB), including neodymium-yttrium aluminium garnet laser, electrocautery, argon plasma coagulation, cryotherapy, balloon dilatation and metal or hybrid stents. Comparison of outcomes for patients undergoing rigid bronchoscopy (RB) with those treated using FB highlights the usefulness of the FB approach. Methods: A retrospective medical record review of all interventional bronchoscopy procedures performed at Lahey Clinic over the past 8 years was conducted. Patients were categorized into two groups according to the procedure used, that is, RB (251 patients), and FB (161 patients) groups. Patients with malignancies were included as a separate subgroup, comprising 178 RB and 117 FB patients. For every procedure, the location of the lesion, patient survival from the first interventional procedure performed, and in patients with malignancy, additional treatments received such as chemotherapy and radiation were recorded.

*Results:* Ninety per cent of RB procedures were performed in patients with tracheal or main stem lesions, while over half the patients undergoing FB had more distal lesions. A trend towards increasing use of FB for interventional procedures in recent years was noted. *Conclusions:* FB is a valuable alternative to RB for treating less advanced malignant disease or distal airway lesions.

Key words: bronchoscopy, laser, stent, survival.

# INTRODUCTION

Interventional bronchoscopy encompasses a broad range of diagnostic and therapeutic techniques. These therapeutic procedures are most frequently used in the palliative management of malignant airway obstruction, although they also have indications in the treatment of benign airway diseases.

Rigid bronchoscopy (RB) is a core procedure of interventional pulmonology. From the time that Gustav Killian performed the first RB in 1897, it was mostly used as a tool for foreign body removal. Nearly 100 years later, Toty *et al.*<sup>1</sup> and Dumon *et al.*<sup>2</sup> performed neodymium-yttrium aluminium garnet (Nd : YAG) laser via RB for malignant airway obstruction and renewed interest in the use of this instrument.

While RB retains a central role in the interventional armamentarium, flexible bronchoscopy (FB), utilizing Nd : YAG laser photocoagulation, has offered an alternative for the relief of obstructing endotracheal or endobronchial malignancies in patients in whom RB could not be performed.<sup>3</sup> In recent years, many interventional tools have been delivered through the FB working channel, including electrocautery, argon plasma coagulation (APC), cryotherapy, brachy-therapy, photodynamic therapy, balloon dilatation and metal or hybrid stents, achieving optimal results in the treatment of tracheobronchial lesions. Given the increasing availability of therapeutic tools that can be delivered via the FB, we sought to review the Lahey Clinic experience.

This report is a retrospective review of all interventional bronchoscopy procedures performed at Lahey Clinic Medical Center over a recent 8-year period. We examined the range of procedures performed by RB compared with FB during this time period, compared diagnostic indications for the various interventions, and determined whether outcomes differed between patients treated by RB or FB.

### **METHODS**

Lahey Clinic has a well-established and recognized interventional pulmonology programme, and serves as a referral centre for Massachusetts and neighbouring states. The medical records of all patients who underwent interventional bronchoscopy procedures at this institution between January 1999 and January

Correspondence: John F. Beamis Jr, Department of Pulmonary and Critical Care Medicine, Lahey Clinic Medical Center, 41 Mall Road, Burlington, MA 01803, USA. Email: john.f.beamis@lahey. org

Received 16 June 2008; invited to revise 3 August 2008, 26 September 2008; revised 5 August 2008, 30 September 2008; accepted 14 October 2008 (Associate Editor: Philip Eng).

2007 were retrospectively reviewed. Patients were followed for at least 10 months after the interventional procedure.

## **Patient groups**

Patients were identified from the bronchoscopy suite and operating room logbooks, and were included in the study if they underwent an interventional bronchoscopy procedure. Of 4839 bronchoscopy procedures, 769 (15.8%) were classified as 'interventional cases', performed in 412 patients. Patients were divided into RB (251 patients) or FB (161 patients) groups according to the procedure performed (Fig. 1). Patients with malignancies were included as a separate subgroup comprising 178 RB and 117 FB patients.

#### Parameters recorded

For every patient, the following were recorded: (i) the indication for the interventional procedure; (ii) the location of the lesion in the tracheobronchial tree; (iii) the various treatment modalities used; and (iv) survival from the time of the first interventional procedure. For patients with non-small cell lung cancer (NSCLC), the stage of the disease at the time of the first procedure and, for all patients with malignancy, other treatments provided (chemotherapy, radiation, brachytherapy) were recorded. Survival was calculated only for patients with malignant disease. Survival was determined using patients' charts, and the Social Security death index website (http:// ssdi.genealogy.rootsweb.com/). This retrospective study was approved by the Lahey Clinic Institutional **Review Committee.** 

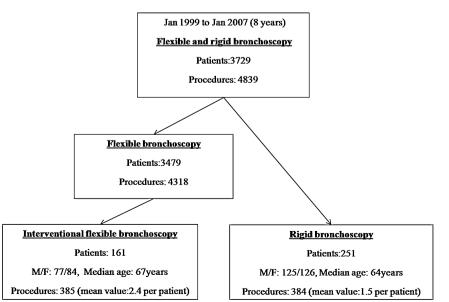
#### Indications

Indications for interventional bronchoscopy treatment included central airway stenosis >50%, patent airways distal to the obstruction, potential for functioning distal lung tissue and severe respiratory symptoms resulting from the airway obstruction primarily dyspnoea. Every patient underwent a standard preoperative assessment, consisting of laboratory investigations (including coagulation parameters), diagnostic FB and chest CT. Cardiovascular risks, increased respiratory demands, unresolved co-agulopathies and haemodynamic instability were all considered in making the decision to proceed with an interventional procedure.

#### Interventional procedures

The equipment used included the Dumon Series II rigid broncoscopes (Bryan Corporation Inc., Woburn, MA, USA) with optical system, probes, stent introducer, stenting forceps and flexible bronchoscopes (Pentax, Lifecare Division and Olympus Medical Systems Corp., Tokyo, Japan). The interventional procedures were performed by an experienced interventional pulmonary physician, with the assistance of an interventional pulmonary fellow. RB was performed under general anaesthesia in the operating room, while FB was performed under moderate sedation with midazolam and fentanyl in the bronchoscopy suite. Patients were placed in the supine position and during laser treatment fraction of inspired oxygen (Fi $O_2$ ) was maintained at <40% to avoid endobronchial combustion. The techniques used were: resection (electrocautery, cryotherapy, Nd : YAG laser photoresection, photodynamic therapy, brachytherapy), dilatation (rigid dilatorsbougies, rigid bronchoscope, balloon dilatation) and maintenance (photodynamic therapy, airway stents, brachytherapy).

Nd : YAG laser, electrocautery, cryotherapy, APC and balloon dilatation were performed using both rigid and flexible bronchoscopes. Silicone stents were placed only by RB, while metal and hybrid stents were



**Figure 1** Total numbers of procedures performed and characteristics of the patients in each of the two groups investigated. placed by both RB and FB. Nd : YAG laser was set to low power settings (30–40 W) with a pulse duration of 1 s. The brachytherapy method used was the high dose rate technique. Using an Ir192 source, 700 cGy were usually deliver weekly for three applications.

#### **Statistical analysis**

Data are presented as mean and SD (or median and range) and were compared using the *t*-test, or the Mann–Whitney test for data that was not normally distributed. Survival rates were computed using Kaplan–Meier survival curves. Patients were followed until death, or data were censored at the study closure date (November 2007) if patients were still alive. Statistical analyses were performed using SPSS version 14 for Windows (SPSS Inc., Chicago, IL, USA).

 Table 1
 Number of times a technique was used for the procedures performed<sup>†</sup>

Technique	FB procedures $(n = 385)$	RB procedures (n = 384)
Nd : YAG laser	78	139
Stent	76	129
Electrocautery	118	36
APC	65	3
Balloon dilatation	35	35
Cryotherapy	11	2
Brachytherapy	35	0
Photodynamic therapy	2	0
Mechanical debulking	0	97
Bronchoscopic dilatation	0	139

<sup>†</sup> Multiple techniques may have been used during the same procedure.

APC, argon plasma coagulation; FB, flexible bronchoscopy; Nd : YAG, neodymium-yttrium aluminium garnet; RB, rigid bronchoscopy.

Table 2	Descriptive statistics for patients with malignant
lesions	

	Flexible bronchoscopy n (%)	Rigid bronchoscopy n (%)
Number of patients <sup>†</sup>	117	178
Chemotherapy	89 (76.7)	99 (56.9)
External radiation	82 (70.6)	99 (56.9)
NSCLC patients	86	135
Stage		
IV	22 (24.5)	25 (18.5)
IIIB	44 (51.1)	103 (76.2)
IIIA	6 (6.9)	5 (3.7)
IIB	11 (12.7)	2 (1.4)
IIA	3 (3.4)	0

<sup>+</sup> All patients with malignancy.

NSCLC, non-small cell lung cancer.

597

A *P*-value of <0.05 was considered statistically significant.

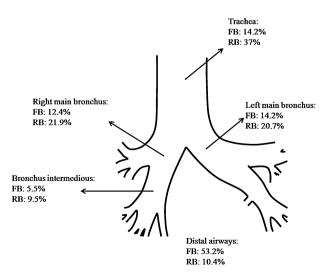
#### RESULTS

The total numbers of procedures performed are presented in Figure 1. There were no age or gender differences between patient groups. Table 1 details the therapeutic modalities delivered via the RB or FB approaches. When FB was performed, electrocautery was the most frequently used therapeutic intervention, followed by Nd : YAG laser, APC and stent placement. In contrast, when RB was used, Nd : YAG laser and stent placement were the most frequently performed interventions.

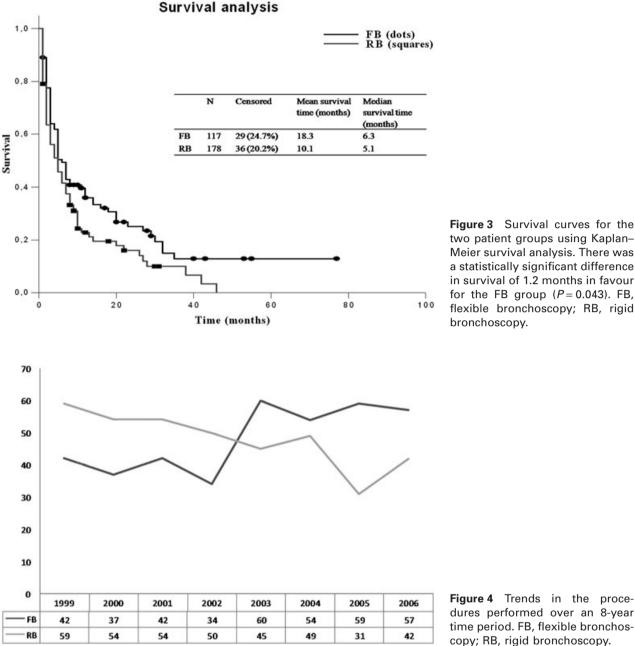
Figure 2 shows the distribution of lesions within the tracheo-bronchial tree in the two treatment groups. In patients treated by FB, lesions were located in the distal airways in over half the cases. In contrast, for patients treated by RB, the trachea and main stem bronchi were involved in over 90% of cases.

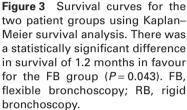
The most common diagnoses of malignancy among patients in both groups were NSCLC, followed by small cell lung cancer (SCLC) and metastatic malignancies (oesophageal cancer  $\rightarrow$  colon cancer  $\rightarrow$  breast cancer  $\rightarrow$  renal cell carcinoma, etc.). Squamous cell carcinoma was the most frequent histological type diagnosed in NSCLC patients, followed by adenocarcinoma. Bronchial carcinoid, a low grade malignancy that can be treated by interventional bronchoscopy,<sup>4,5</sup> was also very common in this series. The list of benign diagnoses included tracheal stenosis (idiopathic, tracheomalacia or post-intubation), followed by polypoid benign lesions, vascular lesions, amyloidosis, hamartomas, etc.

In both groups, most patients with NSCLC had stage IIIB or stage IV disease (Table 2). Less advanced disease (stages IIA and IIB) was noted in 14 patients (16.1%) in the FB group and in only 2 patients (1.4%) in the RB group.



**Figure 2** Location of lesions in the tracheo-bronchial tree for the two patient groups. FB, flexible bronchoscopy; RB, rigid bronchoscopy.





Survival rates are depicted in Figure 3. There was a statistically significant difference (P = 0.043) in survival rates between patients who underwent FB (6.3 months) compared with patients treated by RB (5.1 months), with a median difference in survival of 1.2 months.

Figure 4 shows the number of interventional RB and FB procedures performed during the study period.

# DISCUSSION

With an institutional experience in interventional bronchoscopy that spans nearly 30 years we have had the opportunity to witness the evolution of interventional pulmonology as applied to patients

with tracheobronchial lesions. The indications for interventional bronchoscopy procedures are numerous. Tracheal stenosis, tracheomalacia, hamartomas, amyloidosis are some of the benign diseases that are treatable by interventional bronchoscopy. NSCLC, SCLC and metastatic malignancies, however, comprise the majority of tracheobronchial lesions treated by interventional bronchoscopy. Tracheal stenosis after intubation seems to be increasing as an indication for interventional bronchoscopy.<sup>6-8</sup> This may be due to the fact that in recent years treatment in the intensive care unit has been offered to more patients,<sup>9</sup> resulting in more

patients undergoing endotracheal intubation and tracheostomy. This can lead eventually to granuloma formation around the tracheal stoma and/or web-like stenosis at the site of the endotracheal tube cuff.<sup>10,11</sup>

Rigid bronchoscopy provides excellent control of the airways, better visualization, better suction and safe control of possible haemorrhage.<sup>12</sup> However, the use of RB has been limited by the number of bronchoscopists trained in RB techniques, the limited availability of operation rooms and the expense of Nd: YAG laser equipment. Laser treatment combined with mechanical dilatation and 'scooping' of endoluminal masses have been the RB interventions most frequently performed over the last three decades. In recent years it has become possible to deploy most new treatments through FB, thus avoiding general anaesthesia and providing more options for the patient. Techniques such as electrocautery, APC, cryotherapy, balloon dilatation, self-expandable metal stents (covered or uncovered), photodynamic therapy and brachytherapy catheters were applied primarily by FB, while Nd : YAG laser therapy was delivered mostly by RB. In addition, silicone stents can only be deployed using RB and this is the recommended stent for benign lesions.

On average 1.5 procedures were performed per patient in the RB group, and this was similar to the series reported by Cavaliere *et al.*,<sup>13</sup> Chan *et al.*,<sup>12</sup> Moghissi and Dixon<sup>14</sup> and Noppen *et al.*,<sup>15</sup> in which 1.6-1.9 procedures were performed per patient. In the FB group a mean of 2.4 procedures per patient was required in order to complete treatment. There was an inverse relationship between the number of RB procedures, which declined over the years, from 60 to 40, and the number of FB procedures that substituted for RB procedures. This finding can be viewed in relation to the previously published Lahey Clinic experience, in which RB was the main interventional procedure performed, with an average of around 60 procedures per year.<sup>16</sup> Although the numbers of interventional procedures have remained the same over time, FB has been used more frequently in recent years.

The present data demonstrated the value of FB as an alternative modality for the treatment of distal lesions in the tracheobronchial tree. More than half the treatments in the FB group were performed for peripheral lesions, while in the RB group 90% of the lesions were located in the trachea or main stem bronchi. Other case series also showed that the less bulky or peripheral lesions could be treated using FB and non-laser techniques.<sup>3,12,17,18</sup> The techniques used have varied according to the location of the lesions. Hujala et al.<sup>19</sup> reported that the most common factor contributing to treatment failure during RB procedures was an unfavourable location of the tumour. In their series, the location of 18% of tumours was too distal in the bronchial tree for effective therapy. The trachea, carina and main bronchi were the most favourable locations, whereas both upper lobe bronchi were the most difficult tumour sites to treat. The use of FB through RB is an approach that overcomes the limitations of RB for reaching peripheral lesions. This is an especially valuable approach when both central and distal lesions are encountered in the bronchial tree. Patients with more subtle disease, especially after other treatments have been provided (chemotherapy, radiotherapy, surgery), may benefit from the less interventional nature of the FB approach. However, RB is usually the only choice in patients with suffocating lesions and excessive dyspnoea.

Several studies<sup>17,19–24</sup> have reported median survival rates after interventional bronchoscopy ranging from 3.7 to 8.4 months. Survival is a misleading parameter as it does not take into account the palliative effect of therapy and is not based on randomized controlled trials.13<sup>13</sup> However, survival has been reported in every published case series on interventional bronchoscopy, to demonstrate the utility and justify the use of interventional procedures. In the present series, survival rates for patients with malignant disease were best for the FB group (6.3 months), followed by the RB group (5.1 months). The reason for the better survival in the FB group may be that these patients had less advanced disease (stage IIB or IIA) compared with those in the RB group. Another factor could be that the peripheral location of the lesion played a role in the final outcome, allowing a longer time interval before the lesion caused major symptoms.

Prospective studies addressing improvement in symptoms, complications, performance status, survival and quality of life are required to better demonstrate the efficacy and palliative effect of interventional bronchoscopy procedures. The conclusions from our study are limited by its retrospective nature. Controlled, prospective studies comparing various therapies using interventional bronchoscopy have been problematic because of the often critical nature of airway obstruction that requires urgent therapy. As a consequence, biases such as bronchoscopist preference, patient performance status and comorbidities may affect results.

Rigid bronchoscopy remains an important tool for treating tracheobronchial lesions. It offers an excellent view, facilitates management of central airway conditions and is the only approach providing the capacity for mechanical debulking and dilatation of central lesions, along with silicone stenting. FB can be used for less advanced malignancies, the majority of benign lesions and lesions in the peripheral bronchial tree, although more procedures are required per patient to complete the treatment. In recent years we have performed an increasing number of interventional bronchoscopy procedures and, in particular, procedures performed by FB. Interventionists with a preference for the FB approach should also be adequately trained in RB procedures to deal with possible complications that can be serious.

### REFERENCES

- 1 Toty L, Personne C, Colchen A, Vourc'h G. Bronchoscopic management of tracheal lesions using the neodynium yttrium aluminium garnet laser. *Thorax* 1981; **36**: 175–8.
- 2 Dumon JF, Reboud E, Garbe L, Aucomte F, Meric B. Treatment of tracheobronchial lesions by laser photoresection. *Chest* 1982; **81**: 278–84.

- 3 Castro DJ, Saxton RE, Ward PH, Oddie JW, Layfield LJ *et al.* Flexible Nd : YAG laser palliation of obstructive tracheal metastatic malignancies. *Laryngoscope* 1990; **100**: 1208–14.
- 4 Brokx HA, Kunst PW, van Diest PJ, Postmus PE, Sutedja TG. Bronchial typical carcinoid tumors: histological study of intraversus extraluminal growth pattern. *Lung Cancer* 2004; 44: 129– 30.
- 5 Brokx HA, Risse EK, Paul MA, Grunberg K, Golding RP *et al.* Initial bronchoscopic treatment for patients with intraluminal bronchial carcinoids. *J. Thorac. Cardiovasc. Surg.* 2007; **133**: 973–8.
- 6 Kastanos N, Estopa Miro R, Marin Perez A, Xaubet Mir A, Agusti-Vidal A. Laryngotracheal injury due to endotracheal intubation: incidence, evolution, and predisposing factors. A prospective long-term study. *Crit. Care Med.* 1983; 11: 362–7.
- 7 Koshkareva Y, Gaughan JP, Soliman AM. Risk factors for adult laryngotracheal stenosis: a review of 74 cases. *Ann. Otol. Rhinol. Laryngol.* 2007; **116**: 206–10.
- 8 Norwood S, Vallina VL, Short K, Saigusa M, Fernandez LG *et al.* Incidence of tracheal stenosis and other late complications after percutaneous tracheostomy. *Ann. Surg.* 2000; **232**: 233–41.
- 9 Goldenberg D, Esclamado R, Flint P, Cummings CW. Surgical management of upper airway stenosis. In: Cummings CW, Haughey BH, Thomas JR (eds) *Cummings Otolaryngology— Head and Neck Surgery*, 4th edn. Mosby, St Louis, 2005; 2103–28.
- 10 Grillo HC, Donahue DM. Post intubation tracheal stenosis. Semin. Thorac. Cardiovasc. Surg. 1996; 8: 370–80.
- 11 Weymuller EA Jr. Laryngeal injury from prolonged endotracheal intubation. *Laryngoscope* 1988; **98**: 1–15.
- 12 Chan AL, Tharratt RS, Siefkin AD, Albertson TE, Volz WG et al. Nd : YAG laser bronchoscopy. Rigid or fiberoptic mode? *Chest* 1990; **98**: 271–5.
- 13 Cavaliere S, Venuta F, Foccoli P, Toninelli C, La Face B. Endoscopic treatment of malignant airway obstructions in 2008 patients. *Chest* 1996; **110**: 1536–42.

- 14 Moghissi K, Dixon K. Bronchoscopic NdYAG laser treatment in lung cancer, 30 years on: an institutional review. *Lasers Med. Sci.* 2006; 21: 186–91.
- 15 Noppen M, Meysman M, D'Haese J, Schlesser M, Vincken W. Interventional bronchoscopy: 5-year experience at the academic hospital of the vrije universiteit brussel (AZ-VUB). *Acta Clin. Belg.* 1997; **52**: 371–80.
- 16 Beamis JF Jr, Vergos K, Rebeiz EE, Shapshay SM. Endoscopic laser therapy for obstructing tracheobronchial lesions. Ann. Otol. Rhinol. Laryngol. 1991; 100: 413–19.
- 17 Lee CM, Wu JL. Fiberoptic bronchoscopic Nd-YAG laser therapy in obstructive airway diseases. *Zhonghua Yi Xue Za Zhi (Taipei)* 1994; **53**: 135–40.
- 18 Asimakopoulos G, Beeson J, Evans J, Maiwand MO. Cryosurgery for malignant endobronchial tumors: analysis of outcome. *Chest* 2005; **127**: 2007–14.
- 19 Hujala K, Sipila J, Grenman R. Endotracheal and bronchial laser surgery in the treatment of malign and benign lower airway obstructions. *Eur. Arch. Otorhinolaryngol.* 2003; 260: 219– 22.
- 20 Cavaliere S, Foccoli P, Farina PL. Nd : YAG laser bronchoscopy. A five-year experience with 1396 applications in 1000 patients. *Chest* 1988; **94**: 15–21.
- 21 Chhajed PN, Baty F, Pless M, Somandin S, Tamm M *et al.* Outcome of treated advanced non-small cell lung cancer with and without central airway obstruction. *Chest* 2006; **130**: 1803–7.
- 22 Han CC, Prasetyo D, Wright GM. Endobronchial palliation using Nd : YAG laser is associated with improved survival when combined with multimodal adjuvant treatments. *J. Thorac. Oncol.* 2007; **2**: 59–64.
- 23 Santos RS, Raftopoulos Y, Keenan RJ, Halal A, Maley RH *et al.* Bronchoscopic palliation of primary lung cancer: single or multimodality therapy? *Surg. Endosc.* 2004; 18: 931–6.
- 24 Shea JM, Allen RP, Tharratt RS, Chan AL, Siefkin AD. Survival of patients undergoing Nd : YAG laser therapy compared with Nd : YAG laser therapy and brachytherapy for malignant airway disease. *Chest* 1993; **103**: 1028–31.