Chapter 11

Diagnostic and Therapeutic Approaches in Respiratory Endoscopy

R. Peric, M. de Mol, N. van Walree and J.G. Aerts

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/52740

1. Introduction

The field of respiratory endoscopy has developed over the last decade. Endoscopy is now used for early detection, diagnostic procedures, endoscopic ultrasound and endobronchial interventions. Bronchoscopy is a standard procedure for endoscopists but recently new techniques like autofluoresence bronchoscopy have been introduced. It is not known how these techniques should be incorporated in standard clinical care. Autofluorescence bronchoscopy can be used for detection of premalignant lesions but it is known that the used histological classification does not correlate to biological behaviour. Premalignant lesions may regress or very early abnormal lesions may progress into tumor. Therefore the work up of these lesions is not known. To overcome this problem new techniques are introduced like optical coherence tomography or incorporation of spectroscopy. The value of these techniques for daily practice and research will be reviewed. We will discuss all the presently available techniques and there indications.

Endobronchial ultrasound is a new technique used for staging in lung cancer or diagnostics purposes. This technique offers impressive opportunities for endoscopists to perform minimal invasive staining of the mediastinum and lung lesions adjacent to the bronchus. However the exact role of the endobronchial ultrasound in staging of lung cancer has to be established. Also although quite limited the technique can have complications which should be kept in mind before performing this procedure. The indications and major drawbacks of this technique will be discussed.

Endobronchial interventions have proven to be of mostly palliative value for individual patients. As large randomised trials are lacking, lots of techniques are applied mostly depending on local habits. However from published data some guideline can be given. We will review the main endoscopic interventions and advise which technique to be used in which indication.

2. EUS and EBUS in non-small cell lung cancer

The development of transesophageal endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) and transbronchial ultrasound real time guided needle aspiration (EBUS-TBNA) have drastically altered lung cancer staging algorithms. Both are minimally invasive techniques that enable ultrasound controlled tissue sampling in addition or as an alternative to surgical procedures. Tissue proof of presumed mediastinal spread is mandatory for accurate diagnosis and staging as well as treatment planning. Imaging modalities such as computed tomography (CT), positron emission tomography (PET) provide information regarding size and metabolic activity, respectively, but are not accurate enough to be used in clinical practice. Consequently, tissue diagnosis remains necessary. Mediastinoscopy is considered the standard method for mediastinal lymph node staging, however drawbacks are its invasiveness, requirement for general anesthesia, clinical admission and costs. The role of endosonography is evolving rapidly, the aim of the following is to present the status of E(B)US based on a literature survey.

2.1. EUS-FNA

Linear echo-endoscopes were originally developed for gastrointestinal diseases [1]. In 1995 it became apparent that a considerable part of the middle and posterior mediastinum could be reached and sampled [2] including lymph nodes paratracheal on the left (station 4L), in the aortopulmonary window (station 5), para-aortal (station 6), subcarinally (station 7), lower paraesophageal (station 8), pulmonary ligament (station 9), as well as the left adrenal gland. Levels 2 and 4R are not always accessible. Specific sonographic features of lymph nodes (short axis size >1cm, round shape, distinct margins, homogeneous echogenicity, absent central hilar structure, coagulation necrosis) are more likely to contain metastasis [3] for which EUS has a sensitivity, specificity, positive and negative predictive value of 78%, 71%, 75% and 79% respectively [4]. EUS in combination with FNA however is more accurate, with a pooled sensitivity of 83% and a pooled specificity of 97% [5]. Rapid on site evaluation by a cytopathologist (ROSE) has been shown to improve the diagnostic yield [6], if however on- site cytology isn't available, the optimal number of needle passes needed to obtain an optimal yield is three [7]. EUS-FNA is usually performed in an ambulatory setting under local anaesthesia and conscious sedation using midazolam. The procedure is considered safe as no serious complications have been reported. FNA of a cystic lesion, however, should be avoided due to the risk of mediastinitis [8, 9].

2.2. EBUS-TBNA

Sampling mediastinal lymph nodes through the tracheal carina using a rigid bronchoscope was first described in 1949 [10]. In 1983 Wang reported the use of TBNA for lung cancer staging [11]. The sensitivity varies between 39% and 78% depending on the prevalence of mediastinal metastasis [12]. Despite being an available technique for over 50 years, TBNA has been underused. The main reason for its limited use is the lack of real time needle visualization causing numerous false negative results and complications [13]. Radial endobronchial

http://dx.doi.org/10.5772/52740

ultrasound first described in 1992 has been shown to increase the yield of TBNA, however, due to the nature of the probe it does not allow real time needle visualization [14]. Conversely, the linear endobronchial ultrasound developed in 2002 could reach and sample para-tracheal (stations 2 and 4), subcarinal (station 7), hilar and intrapulmonary nodes (stations 10 and 11) [15]. Specific sonographic features of lymph nodes (short axis size >1cm, round shape, distinct margins, homogeneous echogenicity, absent central hilar structure, coagulation necrosis) are more likely to contain metastasis [16] for which EBUS-TBNA has a pooled sensitivity of 88% and a pooled specificity of 100% [17]. Optimal results can be obtained in three aspirations per lymph node. When at least one tissue core aspiration is obtained, two aspirations per lymph node can be acceptable [18]. EBUS-TBNA is generally performed in a ambulatory setting under local anaesthesia and conscious sedation using midazolam. To date, no major complications have been reported.

2.3. Comparison of staging methods

Non-invasive methods such as CT and PET have limited sensitivity (57%) and specificity (82%), with a positive predictive value of only 79% for detection of mediastinal lymph node metastasis [4]. The combination of lymph node size and metabolic activity with PET/CT improves accuracy, but does not eliminate the need for invasive testing [19]. For primary mediastinal lymph node staging, the American College of Chest Physicians (ACCP) and the European Society of Thoracic Surgery (ESTS) consider mediastinoscopy the gold standard with a sensitivity of 78% and a negative predictive value of 88% [20, 21]. Although considered a standard, there are limitations to its diagnostic reach. Stations 5, 6, posterior part of 7, 8 and 9 are not accessible by cervical mediastinoscopy. Further limitations are the requirement for general anesthesia, clinical admission, costs, as well as a reported 2% risk morbidity [22]. Less invasive methods have emerged such as TBNA, EUS-FNA and EBUS-TBNA. TBNA has a variable yield, is a 'blind' technique, and the results depend on the size of the lymph node. In contrast, real-time ultrasound-guided nodal aspiration by EUS or EBUS has a higher sensitivity for mediastinal metastasis. In a comparison of EUS-FNA and mediastinoscopy, both methods are just as accurate (91% versus 90%), but due to their complementary reach, the combination of EUS-FNA and mediastinoscopy detect significantly more patients with lymph node metastasis than either method alone [23]. EUS-FNA prevented 50-70% of scheduled surgical procedures [24, 25]. Furthermore, in combining EUS-FNA and EBUS-TBNA a near complete minimally invasive mediastinal staging can be achieved with a higher sensitivity (93%) and negative predictive value (97%) compared with either method alone [26]. Strategies with an EBUS-TBNA bronchoscope placed first in the airway and then in the oesophagus can be just as useful with a sensitivity of 96% and a negative predictive value of 95% [27]. Finally, a staging strategy combining endosonography and surgical staging compared with surgical staging alone resulted in greater sensitivity (94% versus 79%) for mediastinal metastasis and fewer unnecessary thoracotomies [28]. Cost–minimization models for assessment of mediastinal nodal metastasis demonstrate that the pretest probability of nodal metastasis determines the most cost effective strategy. EUS alone or combined with EBUS is less costly compared with surgical staging [29]. In a strategy using PET, EUS-FNA reduced staging costs by 40% by

preventing surgical staging [30]. Given that the sensitivity of EUS-FNA and EBUS-TBNA is similar to that of mediastinoscopy and that endosonography is less invasive, safe, and more cost- effective, endosonography is now regarded as the initial staging procedure of choice and incorporated in guidelines.

2.4. Conclusion

EUS-FNA and EBUS-TBNA enable complete ultrasound controlled mediastinal tissue sampling in addition or as an alternative to surgical procedures and as such have drastically altered lung cancer staging algorithms.

3. Therapeutic bronchoscopy in thoracic malignancies: Endobronchial interventions

In the last decades multiple endobronchial intervention techniques have been developed for the treatment of various pulmonary conditions and regaining airway patency. Especially in patients with pulmonary malignant diseases and significant partial airway obstruction, ensuring an open airway on a short notice is mandatory due to an increased risk of complete obstruction and suffocation. A surgical approach is usually not feasible in these patients, as it is mostly a palliative intervention. Also, significant comorbidities (i.e. COPD, heart failure) often do not permit a surgical approach as such a procedure is accompanied with an increased risk of severe complications. Therefore techniques are required that ensure a patent airway with a minimal risk of complications.

Obstruction of the airways in patients with thoracic malignancies is caused by three mechanisms: 1. endoluminal growth of neoplasms, 2. compression of the airway by a malignant process, and 3. a combination of these two. Interventions in patients are aimed at debulking of tumorous tissue and regaining an open airway. This can be best performed with rigid or flexible bronchoscopy and offers in most cases instant relief for the patient. Beneficial features of flexible bronchoscopy compared to rigid bronchoscopy are the lack of general anaesthesia and the easy access of the distal bronchi and the airways of the upper lobes. However, rigid bronchoscopy enables control of ventilation during the procedure, the removal of large fragments of tumorous tissue and stenting of the affected airways [31]. Examples of the applied techniques during these interventions are laser therapy, diathermia, argon plasma coagulation and the application of endobronchial stents. Application of brachytherapy, cryotherapy and photodynamic therapy are in most cases contraindicated for the treatment of lesions obstructing the airways, since they require time to achieve their effects.

We will discuss the different advantages and disadvantages of each technique and also their indications and contraindications. We will review their use in a palliative setting, but also evaluate their potential as a curative intervention.

http://dx.doi.org/10.5772/52740

3.1. Interventional techniques

3.1.1. Electrocautery

Electrocautery uses an electrical current to achieve its effects. The voltage difference between probe and target tissue generates a flow of electrons. Due to resistance of the target tissue for the electrons, heat is generated which is used for coagulation and tissue necrosis. The extend of the effect of electrocautery on the target tissue depends of several factors [32]. First, the smaller the contact area between probe and tissue, the more the current density is increased and thereby the effect on the tissue. Second, the time the electrons are allowed to flow through the tissue. Longer duration of application results in an increased effect. Third, the wattage or voltage difference between probe and tissue. An increased wattage corresponds with an increased flow of electrons and thus an increased effect. Reduction of the effect of electrocautery is due to the leakage of electrons via fluids and the metallic segments of the bronchoscope.

Compared with the YAG laser, electrocautery combines low costs [33] with easy to use features in daily practice and a lower risk of airway perforation [34]. Contact of the probe with the target tissue results in a similar effect as the YAG laser, although the extent of the effect is different. As with argon plasma coagulation (see below), the electrons do not reach the deeper tissue layers as compared with the photons of the YAG laser and therefore cause superficial necrosis. Due to these properties, electrocautery is very suitable for regaining airway patency in combination with mechanical debulking and stenting.

Since electrocautery causes superficial necrosis, it may be useful for the treatment of endobronchial carcinoma in situ and endoluminal superficial lung cancer [35]. Electrocautery should also be considered for the treatment of granulomatous tissue and various other benign lesions [36, 37].

Complications of electrocautery are endobronchial fires, especially when the fraction of inspired oxygen is more than 0.4 and high wattage settings are used, and perforation of the bronchial wall [34]. Contraindications for electrocautery are the same as for lasertherapy (see below) [32].

3.1.2. Argon plasma coagulation

Argon plasma coagulation allows coagulation without making contact with tissue. It uses ionised argon gas (plasma) to conduct electrons. These electrons do not reach the deeper layers of tissue, in contrast with the scattering photons emitted by the Nd-YAG laser, and thereby cause superficial coagulation/necrosis. A similar effect is achieved by the carbon dioxide laser. Argon plasma coagulation can be used for coagulation, vaporisation and cutting. In patients with airway obstruction by endobronchial tumour growth it should be combined with mechanical debulking. Since its effect is superficial, it minimizes the risk of bleeding in areas of the bronchial tree were major vessels rally just beneath the surface of the airway.

Due to its ability in achieving superficial necrosis, Argon plasma jet coagulation may be used in a curative setting for the treatment of superficial lungcancer [38, 39].

Complications of argon plasma coagulation are the same as with electrocautery. They include endobronchial fires and bronchial wall perforation [40]. Contraindications are comparable with the ones for laser surgery and electrocautery.

3.1.3. Laser resection

Laser resection of endobronchial lesions can be performed using rigid or flexible bronchoscopy. To date, the neodymium- yttrium aluminium garnet (Nd-YAG) laser is the most commonly applied laser. Toty et al were one of the firsts to describe the use of the Nd-YAG laser for patients with tracheal and bronchogenic cancer [41]. Since then several studies have evaluated its role as an instrument to relieve obstruction and achieve haemostasis [42, 43].

During procedures the power setting should be limited to 40 W to prevent complications [31]. The tumorous tissue is first devascularised after which it can be removed. In relatively small lesions a good strategy may be vaporisation of the whole lesion.

In contrast with the Nd-YAG laser the carbon dioxide laser has limited coagulation abilities. Its most important advantage lies in its quality as a precise cutting instrument.

When laser surgery is performed during flexible bronchoscopy, general anaesthesia is in most cases not required.

Advantages of the Nd-YAG laser are its ability to vaporise tissue and its excellence in coagulation. It disadvantages are the increased risk of perforation and the costs [33, 42]. Also localisation of the tumor, especially in the upper bronchi, has a negative influence on the success of the procedure [42].

Complications associated with endobronchial laser surgery are perforation, intraoperative ventilation problems, post and intraoperative bleeding, postoperative infections, fistula formation, endobronchial fire and even death [32, 42].

It is clear that laser therapy offers excellent opportunities for palliative care. Rapid relief of dyspnoea and haemoptysis can be achieved in patients with endobronchial growth of a malignancy. The only contraindication is external compression of the airways. Relative contraindications are coagulopathy and hypoxemia [32]. Laser surgery can also be considered in multiple non-malignant conditions [36]. Examples are stenosis due to trauma, sarcoidosis, radiation therapy, granulation tissue and benign tumors.

3.1.4. Endobronchial stenting

To date, endobronchial and tracheal stent placement is being performed for already multiple decades [44]. In these years various new stents have been developed ranging from bare metal stents to covered metal stents and silicone stents. Due to the high rate of complications associated with the use of bare metal stents, covered metal stents and silicone stents are now being preferred by most interventional pulmonologists [45]. Unfortunately, comparative data of the different stents is lacking. In almost all cases the choice of the applied stent is made by the personal experience of the performing interventional pulmonologist.

http://dx.doi.org/10.5772/52740

Some of the silicone stents, such as the Dumon stent [46], need to be placed by rigid bronchoscopy. This procedure requires general anestheisa. The self-expanding metal stents however, do not require general anaesthesia and can be inserted during flexible bronchoscopy.

Stents are being used for ensuring an open airway in cases with extrinsic compression due to neoplasms or after debulking of endobronchial malignancies. Furthermore, they can be applied to cover malignant fistulas or iatrogenic fistulas after surgery and for fistulas between the oesophagus and trachea.

Complications associated with endobronchial stenting are the increased production of mucoid secretions, migration of the stent, the development of granulation tissue and the increased chance of respiratory tract infections. Applying endobronchial stents is contraindicated if non-viable lung is present beyond the obstruction [45].

4. Conclusion

We summarised the different endobronchial interventional tools for patients with pulmonary malignancy. All the discussed methods have in common that they offer rapid relief of symptoms. Differences exist in the costs and the ease of use of the various methods. Unfortunately, no comparing data is available. Therefore the level of expertise of the interventional pulmonologist with a certain tool, the nature of the lesion and the associated risks should determine which tool to use. When not available and intervention is mandatory, patients should be referred to hospitals in which these procedures are being performed. It is clear that in the group of patients with malignancies, the risk of severe complications exists. Patients should be accordingly informed about these risks with in mind that in some cases time does not permit less radical interventions.

Author details

R. Peric, M. de Mol, N. van Walree and J.G. Aerts

Department of Pulmonary Diseases Erasmus MC Rotterdam and Amphia Hospital Breda, The Netherlands

References

[1] Wiersema MJ, Vilmann P, Giovannini M et al. Endosonography-guided fine-needle aspiration biopsy: diagnostic accuracy and complication assessment. Gastroenterology 1997; 112: 1087-1095

[2] Pedersen BH, Vilmann P, Milman N et al. Endoscopic ultrasonography with guided fine needle aspiration biopsy of a mediastinal mass lesion. Acta Radiol 1995; 36: 326-328

[3] Bhutani MS, Hawes RH, Hoffman BJ. A comparison of the accuracy of echo features during endoscopic ultrasound (EUS) and EUS-guided fine- needle aspiration for diagnosis of malignant lymph node invasion. Gastrointest Endosc 1997; 45: 474-479

[4] Toloza EM, Harpole L, McCrory DC. Noninvasive staging of non-small cell lung cancer: a review of the current evidence. Chest 2003; 123(Suppl): 137S-146S

[5] Micames CG, McCrory DC, Pavey DA et al. Endoscopic ultrasound-guided fine- needle aspiration for non-small cell lung cancer staging: a systematic review and metaanalysis. Chest 2007; 131: 539-548

[6] Tournoy KG, Praet MM, Van Maele G et al. Esophageal endoscopic ultrasound with fine-needle aspiration with an on-site-cytopathologist: high accuracy for the diagnosis of mediastinal lymphadenopathy. Chest 2005; 128(4): 3004-3009

[7] Leblanc JK, Ciaccia D, Al Assi MT et al. Optimal number of EUS-guided fine needle passes needed to obtain a correct diagnosis. Gastrointest Endosc 2004; 59: 475-481

[8] Annema JT, Veselic M, Versteegh MI et al. Mediastinitis caused by EUS-FNA of a bronchogenic cyst. Endoscopy 2003; 35:791-793

[9] Aerts J.G, Kloover J, Los J et al. EUS-FNA of enlarged necrotic lymph nodes may cause infectious mediastinitis. J Thorac Oncol. 2008; 3: 1191-1193

[10] Schieppati E. Mediastinal lymph node puncture through the tracheal carina. Surg Gynecol Obstet 1958; 107: 243-246

[11] Wang KP, Terry PB. Transbronchial needle aspiration in the diagnosis and staging of bronchogenic carcinoma. Am Rev Respir Dis 1983; 127: 344-347

[12] Holty JEC, Kuschner WG, Gould MK. Accuracy of transbronchial needle aspiration for mediastinal staging of non-small cell lung cancer: a meta-analysis. Thorax 2005; 60: 945-955

[13] Haponik EF, Sture D. Underutilization of transbronchial needle aspiration: experience of current pulmonary fellows. Chest 1997; 112: 251-253

[14] Hurter T, Hanrath P. Endobronchial sonography: feasibility and preliminary results. Thorax 1992; 47: 565-567

[15] Yasufuku K, Chiyo M, Sekine Y et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. Chest 2004; 126(1): 122-128

[16] Fujiwara T, Yasufuku K, Nakajima T. et al. The utility of sonographic features during endobronchial ultrasound-guided transbronchial needle aspiration for lymph node staging in patients with lung cancer. Chest 2010; 138(3): 641-647

[17] Adams K, Shah PL, Edmonds L et al. Test performance of endobronchial ultrasound and transbronchial needle aspiration biopsy for mediastinal staging in patients with lung cancer: systematic review and meta-analysis. Thorax 2009; 64: 757-762

[18] Lee HS, Lee GK, Hwangbo B et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration in mediastinal staging of non-small cell lung cancer. Chest 2008; 134: 368-374

[19] Tournoy KG, Maddens S, Gosselin R et al. Integrated FDG-PET/CT does not make invasive staging of the intrathoracic lymph nodes in non-small cell lung cancer redundant: a prospective study. Thorax 2007; 62: 696-701

[20] Detterbeck FC, Jantz MA, Wallace MB et al. Invasive mediastinal staging of lung cancer: ACCP evidence based clinical practice guidelines (2nd edn). Chest 2007; 132: 202S-220S

[21] De Leyn P, Lardinois D, Van Schil PE et al. ESTS guidelines for preoperative lymph node staging for non-small cell lung cancer. Eur J Cardiothorac Surg 2007; 32:1-8

[22] Hammoud ZT, Anderson RC, Meyers BF et al. The current role of mediastinoscopy in the evaluation of thoracic disease. J Thorac Cardiovasc Surg 1999; 118(5):894-899

[23] Annema JT, Versteegh MI, Veselic M et al. Endoscopic ultrasound added to mediastinoscopy for preoperative staging of patients with lung cancer. JAMA 2005; 294: 931-936

[24] Tournoy KG, De Ryck F, Vanwalleghem LR et al. Endoscopic ultrasound reduces surgical mediastinal staging in lung cancer: a randomized trial. Am J Respir Crit Care Med 2008; 177: 531-535

[25] Annema JT, Versteegh MI, Veselic M et al. Endoscopic ultrasound guided FNA in the diagnosis and staging of lung cancer and its impact on surgical staging. J Clin Oncol 2005; 23: 8357-8361

[26] Wallace MB, Pascual JM, Raimondo M et al. Minimally invasive endoscopic staging of suspected lung cancer. JAMA 2008; 299: 540-546

[27] Herth FJ, Krasnik M, Kahn N et al. Combined endoscopic-endobronchial ultrasound-guided fine-needle aspiration of mediastinal lymph nodes through a single bronchoscope in 150 patients with suspected lung cancer. Chest 2010; 138: 790-794

[28] Annema JT, van Meerbeek JP, Rintoul RC et al. Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial. JAMA 2010; 304: 2245-2252

[29] Harewood GC, Pascual J, Raimondo M et al. Economic analysis of combined endoscopic and endobronchial ultrasound in the evaluation of patients with suspected non-small cell lung cancer. Lung Cancer 2010; 67: 366-371

[30] Kramer H, van Putten JW, Post WJ et al. Oesophageal endoscopic ultrasound with fine needle aspiration improves and simplifies the staging of lung cancer. Thorax 2004; 59: 596-601

[31] Du Rand IA, Barber PV, Goldring J, Lewis RA, Mandal S, Munavvar M, Rintoul RC, Shah PL, Singh S, Slade MG, Woolley A; British Thoracic Society Interventional Bronchoscopy Guideline Group. Britisch Thoracic Society guideline for advanced diagnostic and therapeutic flexible bronchoscopy in adults. Thorax, 2011; 66(3); iii1-21

[32] Bolliger CT, Sutedja TG, Strausz J, Freitag L.Therapeutic bronchoscopy with immediate effect: laser, electrocautery, argon plasma coagulation and stents. Eur Respir J, 2006; 27; 1258-1271

[33] Van boxem T, Muller M, Venmans B, Postmus P, Sutedja T, Nd-YAG laser vs bronchoscopic electrocautery for palliation of symptomatic airway obstruction : A cost-effectiveness study., 1999; 116(4):1108-12

[34] Tremblay A, Marquette C. Endobronchial electrocautery and argon plasma coagulation: A practical approach. Can Respir J, 2004; 11;305- 310

[35] Van Boxem T, Venmans BJ, Schramel FM, et al. Radiographically occult lung cancer treated with fiberoptic bronchoscopic electrocautery: A pilot study of a simple and inexpensive technique. Eur Respir J, 1998; 11; 169-172

[36] Marel M, Pekarek Z, Spasova I, Pafko P, Schutzner J, Betka J, Pospisil R. Management of benign stenoses of the large airways in the university hospital in Prague, Czech republic, in 1998-2003. Respiration, 2005; 72(6); 622-628

[37] Wahidi MM, Unroe MA, Adlakha N, Beyea M, Shofer SL. The use of electrocautery as the primary ablation modality for malignant and benign airway obstruction. J Thorac Oncol, 2011; 6(9); 1516-1520

[38] Sutedja TG, van Boxem AJ, Postmus PE. The curativepotential of intraluminal bronchoscopic treatment forearly-stage non-small-cell lung cancer. Clin Lung Cancer, 2001; 2; 264–270

[39] Mathur PN, Edell E, Sutedja G, Vergnon JM. Treatment of early stage non-small cell lung cancer. American College of Chest Physicians. Chest 2003; 123: Suppl. 1, 176S–180S

[40] Reichle G, Freitag H, kullmann J, Prenzel R, Macha HN, Farin G. Argon plasma coagulation in bronchology: A new method – alternative or complementary? J Bronchol, 2000; 7; 109-117

[41] Toty L, Personne C, Colchen A. Vourc'h G. Bronchoscopic management of tracheal lesions using the neodynium yttrium aluminium garnet laser. Thorax, 1981; 36(3); 175-178

[42] Hujala K, Sipilä J, Grenman R. Endotracheal and bronchial laser surgery in the treatment of malignant and benign lower airway obstructions. Eur Arch Otorhinolaryngol, 2003; 260(4); 219-222

[43] Han CC, Prasetyo D, Wright GM. Endobronchial palliation using Nd:YAG laser is associated with improved survival when combined with multimodal adjuvant treatment. J Thorac Oncol, 2007; 2; 59-64

[44] Montgomery WW. T-tube tracheal stent. Arch otolaryngol, 1965; 82; 320-321

[45] Bolliger CT, Mathur PN, Beamis JF, Becker HD, Cavaliere S, Colt H, Diaz-Jimenez JP, Dumon JF, Edell E, Kovitz KL, Macha HN, Mehta AC, Marel M, Noppen M, Strausz J, Sutedja TG; European Respiratory Society/American Thoracic Society. ERS/ATS statement on interventional pulmonology. European Respiratory Society/American Thoracic Society. Eur Respir J, 2002 Feb; 19(2) ; 356-73

[46] Dumon JF, Cavaliere S, Diaz-Jimenez JP, et al. Seven-year experience with the Dumon prosthesis. J. Bronchol, 1996; 3; 6-10

[47] References by our group related to the subject:

[48] Optical detection of preneoplastic lesions of the central airways. van der Leest C, Amelink A, van Klaveren RJ, Hoogsteden HC, Sterenborg HJ, Aerts JG.

[49] ISRN Oncol. 2012;2012:957835. Epub 2012 Mar 22

[50] Endoscopic ultrasound fine needle aspiration in the diagnosis of lymphoma. Creemers K, van der Heiden O, Los J, van Esser J, Newhall D, Djamin RS, Aerts JG. J Oncol. 2011;2011:785425. Epub 2011 Apr 10.

[51] Characterization of mediastinal lymph node physiology in vivo by optical spectroscopy during endoscopic ultrasound-guided fine needle aspiration. Kanick SC, van der Leest C, Djamin RS, Janssens AM, Hoogsteden HC, Sterenborg HJ, Amelink A, Aerts JG. J Thorac Oncol. 2010 Jul;5(7):981-7.

[52] Integration of single-fiber reflectance spectroscopy into ultrasound-guided endoscopic lung cancer staging of mediastinal lymph nodes. Kanick SC, van der Leest C, Aerts JG, Hoogsteden HC, Kascáková S, Sterenborg HJ, Amelink A. J Biomed Opt. 2010 Jan-Feb;15(1):017004.

[53] EUS-FNA of enlarged necrotic lymph nodes may cause infectious mediastinitis. Aerts JG, Kloover J, Los J, van der Heijden O, Janssens A, Tournoy KG. J Thorac Oncol. 2008 Oct;3(10):1191-3.

[54] Endoscopic ultrasound reduces surgical mediastinal staging in lung cancer: a randomized trial. Tournoy KG, De Ryck F, Vanwalleghem LR, Vermassen F, Praet M,

Aerts JG, Van Maele G, van Meerbeeck JP. Am J Respir Crit Care Med. 2008 Mar 1;177(5):531-5. Epub 2007 Oct 25.

[55] HIF1a expression in bronchial biopsies correlates with tumor microvascular saturation determined using optical spectroscopy. Aerts JG, Amelink A, van der Leest C, Hegmans JP, Hemmes A, den Hamer B, Sterenborg HC, Hoogsteden HC, Lambrecht BN. Lung Cancer. 2007 Sep;57(3):317-21. Epub 2007 May 7.

[56] Optical spectroscopy for the classification of malignant lesions of the bronchial tree. Bard MP, Amelink A, Skurichina M, Noordhoek Hegt V, Duin RP, Sterenborg HJ, Hoogsteden HC, Aerts JG. Chest. 2006 Apr;129(4):995-1001.

[57] Measurement of hypoxia-related parameters in bronchial mucosa by use of optical spectroscopy. Bard MP, Amelink A, Hegt VN, Graveland WJ, Sterenborg HJ, Hoogsteden HC, Aerts JG. Am J Respir Crit Care Med. 2005 May 15;171(10):1178-84.

[58] Improving the specificity of fluorescence bronchoscopy for the analysis of neoplastic lesions of the bronchial tree by combination with optical spectroscopy: preliminary communication.

[59] Bard MP, Amelink A, Skurichina M, den Bakker M, Burgers SA, van Meerbeeck JP, Duin RP, Aerts JG, Hoogsteden HC, Sterenborg HJ. Lung Cancer. 2005 Jan; 47(1): 41-7.