

## **ABSTRACT (ENGLISH)**

In this thesis new applications of bronchoscopic techniques are described. In the first and main part of this thesis the potential use of this technique for early detection of lung cancer and the possible improvements of it are evaluated in a number of studies. In the second part some other aspects for bronchoscopic use in specific situations are described. The most important reason to detect lung cancer at an early stage is its poor outcome in general however the tool(s) to screen need to be sensitive to have impact on survival. In Chapter 2 a review of these aspects is given and the practical aspects are discussed. A new technique, autofluorescence bronchoscopy (AFB), that might have more promise than sputum cytology for early central airway lesions, is discussed. It has much higher specificity than white light bronchoscopy (WLB) and the advantage that it might be combined with treatment of the occult endobronchial cancers. The most important disadvantage is the character of the procedure: it is invasive. AF is superior over WL bronchoscopy in the detection of airway dysplasia but has difficulty distinguishing bronchitis, previous biopsy and airway fibrosis from pre-invasive lesions, resulting in longer procedural time and need for additional sedation which may compromise patient safety, increase the risk of bronchospasm, and bleeding from multiple endobronchial biopsies. In chapter 3, we used the dual system with simultaneous WLB and AFB. This resulted in shorter procedure time and the bronchoscopist is targeting the appropriate sites reflected in better sensitivity and specificity for detecting preneoplastic lesions.

In chapter 4 AFB was used in a group of patients with a high risk of developing lung cancer. Field cancerization is a well-known phenomenon in head and neck cancer patients. Although secondary primary lung cancers were mainly found in the parenchyma (71%) in this group of 51 patients the use of AFB affected the management in 1/3 of the cases. It detected 5 radiologically occult lung cancers and changed the surgical approach in 2 others.

In chapter 5 a new approach to improve AFB is described. AFB is more sensitive than WLB for detecting early (pre-)neoplastic lesions but the low specificity still makes it necessary that an excessive number of biopsies has to be taken. By adding the color fluorescence ratio R/G to AFB at 0.54 the sensitivity and specificity became 85% and 80% respectively for detecting early preneoplastic lesions. Adding this R/G ratio during the procedure to the visual score improved the specificity further to 88%.

AFB is more sensitive than WLB for detecting early neoplastic and pre-neoplastic lesions. WLB performed in these studies was by fiberoptic bronchoscopes, however these have during the last decade been replaced by videobronchoscopes. Whether the superiority of

AFB over white light detection with fiberoptic bronchoscopes is also applicable to videobronchoscopes was investigated in chapter 6. It was found that the videobronchoscope mode of AFB, the autofluorescence-reflectance imaging, was comparable to white light videobronchoscopy (WLVB) for detection of the early neoplastic and preneoplastic lesions. WLVB detected better bronchitis and by that prevented unnecessary biopsies of those areas.

In chapter 7 an overview of available techniques and future developments for bronchoscopic detection are described.

New techniques with widespread applications in lung cancer and pulmonary diseases have become on the market. In chapter 8 a rather old approach, transbronchial needle aspiration (TBNA), was used in patients for restaging after chemoradiotherapy prior to surgery. For 71% of the patients this technique achieved the correct diagnosis and made further staging of the mediastinum unnecessary. Critical for the success of TBNA is proper training and preparation of the obtained material.

In chapter 9, we set out to determine if conventional TBNA yield could be improved with training of bronchoscopists and assistants, standardization of technique, TBNA needle and specimen preparation. Post intervention TBNA yield was further compared against endobronchial ultrasound (EBUS) guided sampling with linear or radial probe EBUS. Conventional TBNA yield doubled from 43% (without intervention) to 82% (post-intervention). For lymph nodes measuring less than 2cm, EBUS was found to be more useful. Although EBUS is primarily used for the detection of lymph nodes it may have a role in other situations. In chapter 10 an example of this is described. Tracheomalacia due to chronic compression by a vascular ring was found which might be helpful for preoperative evaluation and decision making in this situation.

Bronchoscopy is a technique with extensive challenges and potential for improvement as is outlined in chapter 11.