# 11<sup>th</sup> Golnik Bronchoscopy Course

## PROGRAM

**Friday, 14 October 2011**

### 09.00 - 12.00 – Lectures

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<td>9.00 – 9.10</td>
<td>Opening</td>
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<td>How and why did we use bronchoscope – 60th anniversary</td>
<td>Nadja Triller</td>
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<td>Bronchoscopy – what’s the next step?</td>
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<td>EBUS mini-probe as a maxi-too</td>
<td>Aleš Rozman</td>
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<td>Precise tissue diagnosis for personalized treatment in lung cancer</td>
<td>Izidor Kern</td>
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<td>Strange bugs in bronchoscopy unit</td>
<td>Viktorija Tomič</td>
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<td>Strange bugs in bronchoscopy unit – Case report</td>
<td>Aleš Rozman</td>
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<td>LUNCH</td>
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### 14.00 - 18.30 - Workshops

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<td>Thoracoscopy</td>
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<td>4</td>
<td>Different biopsy techniques</td>
<td>Katarina Osońik, Nadja Triller</td>
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<td>Ralf Eberhardt</td>
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### 20.00 – GALA DINNER
### 09.00 - 13.00 – Lectures

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<td>Bronchoscopic LVR</td>
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<td>Medical thoracoscopy – advanced techniques</td>
<td>Aleš Rozman</td>
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<td>Rigid vs. semirigid thoracoscopy</td>
<td>Aleš Rozman</td>
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<td>9.55 – 10.10</td>
<td>Case report – interactive session (interstici)</td>
<td>Katarina Osolnik</td>
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<td>10.10 – 10.25</td>
<td>Case report – interactive session (EBUS)</td>
<td>Mateja Marc</td>
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<td>10.25 – 10.40</td>
<td>Case report- interactive session (torakoskopija)</td>
<td>Luka Camlek</td>
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<td>10.40 – 11.00</td>
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<td>11.00 – 13.00</td>
<td>Oral presentations</td>
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<td>13.00 – 13.30</td>
<td>Summary and certificates</td>
<td>Nadja Triller</td>
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**Coffee**

**COFFEE BREAK**
FACULTY

Ralf Eberhardt – Germany

Arthur Szulbowski - Poland

Stefano Gasparini - Italy

Nadja Triller - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia

Andrej Debeljak - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia

Izidor Kern - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia

Viktorija Tomič - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia

Aleš Rozman - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia

Katarina Osolnik - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia

Luka Camlek - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia

Mateja Marc Malovrh - University Clinic of Respiratory and Allergic Diseases Golnik Slovenia
How and why did we use the bronchoscope?  
Sixty years of bronchoscopy

Nadja Triller, Andrej Debeljak, Jurij Šorli  
University Clinic of Pulmonary Diseases and Allergy, Golnik

Bronchoscopy is one of the most commonly performed procedures in pulmonology. Although instruments for inspecting the body cavities (nose, ear, trachea, etc.) had been in use for ages, nobody looked into the trachea until suitable light sources, sufficient anesthesia, and a proper instrument for inspection were developed.

The rhinolaryngologist Gustav Killian (Fig. 1) from Freiburg University was the first to use bronchoscopy on tracheotomized patients. He used a modified Rosenheim esophagoscope and introduced it under local cocaine anesthesia into the trachea. He found that the trachea and bronchi were elastic and it was easy to introduce the rigid scope through the trachea to both main bronchi. After his first experiences on tracheotomized patients, he started to practice on cadavers and soon thereafter performed his first bronchoscopy in a volunteer. The first therapeutic bronchoscopy via the translaryngeal route was performed in 1897, when he removed the first foreign body, a pork bone, from the right main bronchi. Killian presented the new method at the meeting of the Society of South German Laryngologists in Heidelberg on 29 May 1898, and that same year his first publication on direct bronchoscopy was published. Killian’s bronchoscope attracted extensive interest. In 1907 Killian was invited to the U.S., where he met Chevalier Jackson. Jackson produced a bronchoscope with a small light bulb at its distal end that incorporated a suction device. However, the main emphasis of the method was on the retrieval of foreign bodies.

Figure 1. Gustav Killian performed the first rigid bronchoscopy, and Shigeto Ikeda performed the first flexible bronchoscopy.

The image quality was further improved by incorporating a telescopic lens system, which worked on the principle of a series of small lenses installed at various angles. This instrument opened up a new area of examination and expanded the applications
beyond foreign-body removal to the localization of hemoptysis and endobronchial diseases, mainly tuberculosis and other infections.

At the Ninth International Congress of Diseases of the Chest, held in Copenhagen in 1966, Shigeto Ikeda presented his new fiberbronchoscope. With this instrument, the depth of the bronchial tree could be reached to a much greater extent.

Figure 2. Stevan Goldman (a) performed the first rigid bronchoscopy (1951) and Jurij Šorli (b) performed the first flexible bronchoscopy in Slovenia (1974).

Fifty years after the inception of bronchoscopy, the first rigid bronchoscopy in Slovenia was performed at Golnik. The technique was introduced by Ivo Drinković and Stevo Goldman. The first rigid bronchoscope was brought from Paris and for the next few years it was the only such instrument in Slovenia. Bronchoscopic examinations were performed at Golnik and Topolšica, the two main hospitals for pulmonary diseases and tuberculosis at that time.

Because of the enthusiastic activities of both pioneers, bronchoscopy became the standard procedure in diagnosing the airways. Drinković and Goldman taught their skills, and in the following years their colleagues started performing diagnostic and therapeutic procedures. Judita Mešič, Leon Fink, Bojan Fortič, Marjan Komar, and Viktor Legiša used a rigid bronchoscope in everyday clinical practice.

The pulmonologist Jurij Šorli, trained by Judita Mešič, introduced flexible bronchoscopy in 1974. He performed the first bronchoscopic lung biopsy via flexible bronchoscope (Table 1). After Šorli introduced the flexible bronchoscope, he initially used it in combination with a rigid bronchoscope. In an era of expanding interventional procedures, this method of combining both bronchoscopes (flexible and rigid) has attracted new attention today. A new generation of bronchoscopists—Andrej Debeljak, Marija Zupančič, Janez Remškar, Marjan Fortuna, Marjeta Terčelj, Matjaž Turel, Nadja Triller, Katarina Osołnik, Damjan Eržen, Peter Kecelj, and others—introduced new diagnostic techniques (Table 1) and bronchoscopy became an integral part of respiratory medicine.

To date, five heads of the bronchoscopy department have overseen its organization, expanded knowledge, and promoted research (Figure 3).

Figure 3. Heads of the Bronchoscopy Department at Golnik Hospital.
Currently we are experiencing a new wave of new techniques in diagnostic and therapeutic procedures: endobronchial ultrasound, autofluorescence bronchoscopy, electromagnetic navigation, optical coherence tomography. Recent therapeutic advances include intrabronchial valve placement for nonsurgical treatment of emphysema and thermoplasty for difficult-to-treat asthma. Not all of these new techniques are used at the Chest Clinic at Golnik.

Diagnostic indications included tissue diagnosis, detection and staging of lung malignancy, evaluation of diffuse lung diseases such as sarcoidosis and idiopathic interstitial pneumonias, and identification of organisms infecting the respiratory tract. As a therapeutic modality, bronchoscopy has been used to place stents, to remove foreign bodies or masses, and to treat early stage endobronchial malignancy.

Today this top-level unit for diagnostics and therapeutic procedures brings together five medical doctors—Aleš Rozman (the head of the unit), Mateja Marc Malovrh, Luka Camlek, Katarina Osolnik, and Nadja Triller—and five nurse-assistants: Marija Primožič (the head of the nursing team), Štefan Duh, Martina Košnik, Slavi Mohorič, and Rudi Sluga (Fig. 4). They perform approximately 2,000 procedures per year. Most of these are bronchoscopies (1,400 to 1,500), but also include needle biopsies of the lung, closed pleural biopsies, and medical thoracoscopies. Their research findings and professional experience have helped prepare the guidelines and theoretical premises for respiratory endoscopy in Slovenia. This well-coordinated team keeps up to date with innovations in the field by regularly visiting and training at top-level European medical centers, especially in similar respiratory endoscopy units, such as Heidelberg, Hemer, and Berlin (Germany), Lille (France), Ancona (Italy), and Amsterdam (the Netherlands).
The unit is also a teaching center for specialists and their assistants from Slovenia and some other eastern and central European countries. The bronchoscopists’ research is mainly directed towards early diagnostics of lung cancer with autofluorescence bronchoscopy and endobronchial ultrasound. They have developed an excellent means to prepare patients for bronchoscopy. One of their achievements is an innovative method of reassuring patients during bronchoscopic examinations by playing music. Another major challenge for the staff is working in pure research projects.
Table 1. Introduction of new bronchoscopy techniques globally and at the Golnik endoscopy unit in the last 60 years.

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<tr>
<th>Year</th>
<th>Physician and technique</th>
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<tbody>
<tr>
<td>1897</td>
<td>Gustav Killian: father of bronchoscopy, first rigid bronchoscopy</td>
<td>1951</td>
<td>Ivo Drinković &amp; Stevo Goldman: fathers of bronchoscopy in Slovenia</td>
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<td>1947</td>
<td>Ian P. Stevenson: bronchoalveolar lavage</td>
<td>1982</td>
<td>Andrej Debeljak: bronchoalveolar lavage</td>
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<td>1955</td>
<td>H. E. Euler: transbronchial needle aspiration of mediastinal mass with rigid bronchoscope</td>
<td>1990</td>
<td>Andrej Debeljak: transbronchial needle aspiration of mediastinal mass with rigid bronchoscope</td>
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<tr>
<td>1956</td>
<td>Antonio O. Perez: catheter biopsy of the lung</td>
<td>1968</td>
<td>Leon Fink: catheter biopsy of the lung</td>
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<tr>
<td>1956</td>
<td>Eitaka Tsuboi: brushing in diagnosis of peripheral lung lesion</td>
<td>1974</td>
<td>Jurij Šorli: brushing in diagnosis of peripheral lung lesion</td>
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<td>1964</td>
<td>Eitaka Tsuboi,: transbronchial lung biopsy</td>
<td>1974</td>
<td>Jurij Šorli: transbronchial lung biopsy</td>
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<tr>
<td>1974</td>
<td>Georgios Nakratzas: endobronchial electrocautery</td>
<td>1999</td>
<td>Andrej Debeljak, Nadja Triller, Peter Kecelj, &amp; Saša Letonja: endobronchial electrocautery</td>
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<td>1978</td>
<td>Lucien Toty: Nd:YAG laser used through a bronchoscope</td>
<td>1992</td>
<td>Andrej Debeljak &amp; Marjeta Tečelj: transbronchial needle aspiration through flexible bronchoscope</td>
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<tr>
<td>1987</td>
<td>Fiberoptic video bronchoscopy</td>
<td>2000</td>
<td>Nadja Triller &amp; Andrej Debeljak: autofluorescence bronchoscopy</td>
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<tr>
<td>2002</td>
<td>Shigeo Tanaka: narrow band imaging bronchoscopy</td>
<td>2002</td>
<td>Nadja Triller: narrow band imaging electromagnetic navigation</td>
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<td>2002</td>
<td>James Fujimoto: endoscopic optical coherence tomography</td>
<td>2002</td>
<td>Never performed at Golnik</td>
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<td>2002</td>
<td>John D. Miller: bronchial thermoplasty</td>
<td>2002</td>
<td>Never performed at Golnik</td>
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<tr>
<td>2003</td>
<td>Yehuda Schwarz: electromagnetic navigation</td>
<td>2003</td>
<td>Never performed at Golnik</td>
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64. Triller N. Endobronchial ultrasound in the diagnosis of tracheobronchial and mediastinal lesions and in peripheral pulmonary tumours. Lijeć Vjesn, Supl 2003; 125(Suppl 2):12.


83. Osolnik K. Tehnična izvedba BAL. In: Kern I, ed. Proceedings of the bronchoalveolar lavage cytology course;
86. Šorič J. We were part of the revolution, but we did not realize this: A look at a participant’s role in the history of bronchology in Slovenia). In: Kadivec S, ed. Naslovni simpozij 2007. Zbornik predavanj Zdravstvena obravnava bolnika z obstruktivno boleznjo pljuč in alergijo: program za medicinske sestre in zdravstvene tehnike; 2007 Oct 3–4; Golnik, Bled. Golnik: Bolnišnica Golnik, Klinični oddelek za pljučne bolezni in alergijo, 2007;117–20. [Slovenian]
101 years of the Jacobaeus procedure: Our story

Andrej Debeljak
University Clinic of Pulmonary Diseases and Allergy, Golnik

Abstract
This article presents historical information about diagnostic thoracoscopy at Golnik Hospital. The following were determined: when the procedure was introduced into the diagnostic armamentarium, the medical staff that carried out the examinations, indications and contraindications for the procedure, the instruments that were used, the anesthesia methods, insufflation of pneumothorax, the introduction of the instrument, and biopsies. The results of thoracoscopy and the role of the therapeutic procedure (pleurodesis) are also shown. The titles of published lectures and articles on thoracoscopy in the last 20 years have been appended.

Introduction
In 1882 the Italian physician Carlo Forlanini introduced artificial pneumothorax, which became the most frequently applied method among the collapse therapies for pulmonary tuberculosis (1). The application of pneumothorax also enabled thoracoscopic endoscopy. Insufflation of air into the pleural cavity made its exploration possible, making the virtual cavity real.

The Swedish internist Hans Christian Jacobaeus is credited as the first to perform an endoscopic exploration of the thorax. In 1910 he described endoscopic exploration of the pleural cavity with a cystoscope, which he referred to as thoracoscopy, in two patients with tuberculous pleurisy (2). However, even before him in 1866 Samuel Gordon published a report on a thoracoscopy performed by Francis Richard Cruse from Ireland with a binocular endoscope in an 11-year-old girl with left-sided pleural empyema and thoracostoma (3).

Initially pneumothorax as a collapse therapy method was used to treat tuberculous caverns of the lungs. In patients with extensive pleural adhesions, the lungs could not be collapsed by pneumothorax. Thoracocautery (also known as “Jacobaeus’ operation”) was performed in these patients, and electrocautery was applied to the pleural adhesions through the thoracoscope to enable the lung to collapse.

The Golnik story
Thoracocautery was performed at Golnik for the first time in 1931 by Robert Neubauer. Through the thoracoscope, electrocautery was used to burn the pleural adhesions caused by tuberculosis (4).

Diagnostic thoracoscopy (i.e., endoscopic exploration of the pleural cavity with a thoracoscope to diagnose pleural disease) was the first invasive endoscopic examination used at Golnik Hospital. This procedure was developed because a thoracoscope had been used in previous years at Golnik Hospital to perform collapse therapy in patients with lung tuberculosis and pleural adhesions.

After that time, antituberculosis drugs made collapse therapy unnecessary. The number of consumptive patients declined. Golnik Hospital gradually became a hospital for nonspecific respiratory diseases.

In many centers in the world, thoracoscopy became a “forgotten art.” During that time, thoracic surgeons began to use the thoracoscope with increasing frequency for video-assisted thoracic surgery (VATS). They used general anesthesia and usually three ports: one for a video camera and two for operating instruments designed especially for thoracoscopic operations (5).
At Golnik, diagnostic thoracoscopy remained in the diagnostic armamentarium through the 1950s, 1960s, and 1970s. It was used in patients in whom malignant infiltration of the pleura was suspected. Our predecessors at Golnik, Leon Fink and Judita Mešič, performed diagnostic thoracoscopy. In 1985, Andrej Debeljak learned the procedure from his teacher Leon Fink. The instrument was a rigid Storz thoracoscope with Hopkins optics. The procedure was carried out under general anesthesia in an operating room. The day before the thoracoscopy, pneumothorax was insufflated with an Erka pneumothorax apparatus and confirmed with a chest X-ray. Before the introduction of the thoracoscope, the depth of pneumothorax was controlled by needle aspiration. The procedure was performed in the operating theatre. A specially designed operating table that could rotate the patient was used. A forceps biopsy with monopolar electrocautery was possible. The procedures were rarely performed, only three to five time a year. The most frequent diagnosis was mesothelioma or secondary malignant infiltration of the pleura.

In 1993, Andrej Debeljak visited the Clinic for Respiratory Diseases Hecheshorn in Berlin, where Hand-Jürgen Brandt and later Robert Loddenkemper were using thoracoscopy in the diagnostic workup of patients with pleural diseases. He wanted to assess the possibilities and usefulness of diagnostic thoracoscopy and its place in managing lung diseases, especially in relation to surgical thoracoscopy. Debeljak taught younger doctors how to perform thoracoscopy: Peter Kecelj, Matjaž Turel, Aleš Rozman, and Nadja Triller. Saša Letonja also carried out examinations. The number of thoracoscopies rose to 30 per year. In recent years Aleš Rozman has taught Mateja Marc and Luka Camlek how to perform thoracoscopies. The medical technicians that assisted in the procedures were the same as those that assisted in other endoscopic procedures: Marija Petrinec Primožič, Štefan Duh, Martina Košnik, Slavica Mohorič, Katica Zlatar, and Breda Papler.

Thoracoscopies were performed on the operating table in the bronchoscopy room. Generally, in addition to the operating physician, there was also an assistant physician. The indication for thoracoscopy was pleural exudate, suspicious malignant infiltration of the pleura, and previous failure of non-invasive diagnostic methods. An important indication was pleural exudate in patients with non–small-cell lung cancer that were considered otherwise resectable. An absolute contraindication was obliteration of the pleural space, and relative contraindications were bleeding disorders, hypoxemia, unstable cardiovascular status, and persistent uncontrollable cough.

Prior to thoracoscopy, systemic diseases, accompanied by pleural effusion, were excluded. Biochemical, bacteriological, and cytological examinations of the pleural effusion were carried out. If tuberculosis had been suspected, blind-needle biopsy of the pleura was performed. Today blind-needle biopsy of the parietal pleura is less important because of the lower incidence of consumptive patients in Slovenia (10/100,00).

In the first 5 years, general anesthesia was used. Marija Wolf from the Kranj maternity hospital administered the anesthesia. From 1990 onwards, we applied local anesthesia. We used local anesthesia with 30 ml of 1% lidocaine and analgesia with fentanyl 0.1 mg iv. As a premedication, 1 mg of atropine sulphas sc. was used. 26040E and 26172EB Storz rigid thoroscopes (Tuttlingen, Germany) were used, followed by an Olympus A5252A videothoroscope after 1999 and an Olympus videothoracoscope visera (Tokyo, Japan) after 2008. In recent years, from 2008
onwards, Aleš Rozman studied the usefulness of the semiflexible LFT 160 Olympus thoracoscope and carried out the majority of examinations using this instrument.

The day before thoracoscopy, we insufflated 1,200 ml (0–2,400 ml) of air using an Erka pneumothorax apparatus. Pneumothorax was confirmed by chest X-ray and before introducing thoracoscope by needle aspiration until 1990. We used Veress needles. Later, pneumothorax was insufflated on the operating table using an Erka pneumothorax apparatus immediately before thoracoscopy and confirmed with a chest X-ray, and from 1996 onwards by fluoroscopy with a Phillips BV 29 with a C arm. After 2008, pneumothorax was introduced by a B7050 CO₂ insufflator and 120 mm Surgineedle.

The typical point of entry was the sixth intercostal space in the mid-axillary line. If the disease was in the apical regions of the lung or pleura, the upper intercostal spaces were selected. We predominantly used the trocar technique to introduce the thoracoscope. When the pneumothorax was small, we used a blunt preparation to the pleura and entered the pleural cavity with the finger first. After aspiration of ca. 1,350 ml pleural effusion (range 0–5,000 ml), forceps biopsies of pleural and lung tissue were performed (11.5 samples on average, range 2–5), in addition to electrocautery, lysis of fibrinous adhesions, and talc insufflation for pleurodesis. In patients with large, usually malignant pleural effusions, or rarely recurrent pneumothorax and small emphysematous blebs, 3 to 5 g of talc were insufflated into the pleural cavity under direct optical control with a 26492 TH Storz insufflator.

Samples of pleura and pleural exudates were examined cytologically and histologically in the Pathology Department (Izidor Kern) and bacteriologically in the Bacteriology Department (Viktorija Tomič) and Mycobacteriology Department (Manca Žolnir Dovč).

A chi-square test was used to compare the sensitivity of thoracoscopy, needle pleural biopsy, and cytological examination in patients with malignant infiltration of the pleura. In the group of patients with malignant diseases, we determined accuracy, sensitivity, and positive and negative predictive value. Sensitivity was 94%. The procedure was most useful for diagnosing mesothelioma, secondary malignant infiltration of the pleura, pleural asbestosis and lymphoma, localized pleural tumors, and rarely peripheral lung tumors (6, 7, 8).

In patients with non–small-cell lung cancer and pleural effusion, medical thoracoscopy can exclude pleural carcinosis but it cannot be used for confirmation of tumor infiltration or sampling the mediastinal lymph nodes. Among 30 patients with non–small-cell bronchial carcinoma with pleural effusion without malignant cells, thoracoscopy confirmed malignant infiltration in 10 patients (33%). Talc pleurodesis was performed in two of them. In 20 patients (67%), non-specific inflammation was found. Four were not surgically treated because of local progression of the tumor or cardiorespiratory dysfunction. Successful resection was performed in 11 patients (37%). In two patients the N2 stage was found, and in two patients the T3 stage was found (9).

Pleurodesis with talc insufflation (3 to 5 grams of Luzenac talc) under visual control was equally successful as talc slurry instillation in 71 patients with malignant pleural effusion, success rate 81% and 93% (10). It was considered a success if pleural effusion did not reaccumulate in the first month after pleurodesis and the patient was not dyspneic.

The most frequent complications were subcutaneous emphysema and pain after talc insufflation, and the most serious complications were bronchopleural fistula and trapped lung. We did not observe other serious systemic complications or mortality.
Acute respiratory distress syndrome after talc pleurodesis killed 2.3% of patients in a cancer and leukemia group B study (11). This acute lung injury can be avoided by using large talc particle preparations (such as Lusenac talc). Such products are not readily available in many countries, including the United States. Instead of talc pleurodesis, a small indwelling tunneled pleural catheter that improves dyspnea and quality of life, with minimal intervention, minimal hospitalization and minimal complications, is gaining increasing popularity (12). In recent years at Golnik a small indwelling catheter has also been used for symptomatic therapy of malignant pleural effusions.

References:

Lectures and articles on thoracoscopy at Golnik Hospital 1991–2011


Peripheral pulmonary lesion (PPL)

- focal radiographic opacity, that may be characterised as nodule (<= 3cm) or mass (> 3cm)
- not visible by bronchoscopy (no findings of endobronchial lesion / extrinsic compression / submucosal infiltration / orifice narrowing)

PPL – prevalence of malignancy:

- 0.8 – 2 cm: 18% / > 2 cm: 50%
- 18 – 34% of lobectomies (without previous histological confirmation) in patients with benign lesions
- Accurate tissue diagnosis of PPL is strongly favoured before surgery.
**Equipment for EBUS miniprobe guided TBB**

- A miniature ultrasonic probe (20 MHz, mechanical-radial Type UM X20-20R (Olympus Optical, Tokyo, Japan)

**Endoscopic US system**

- Olympus EU-M30

**US-probe Catheter**

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**PPL – diagnostic methods:**

1. Bronchoscopic sampling
   - no guidance (sens. < 20%)
   - fluoroscopic guidance (sens. 20-84% mlg. / 35-56% ben.)
   - CT guidance + virtual bronchoscopy (65.4%)
   - EM – guidance (sens. 59%)
   - EM + EBUS guidance (sens. 88%)
   - EBUS guidance (sens. 49-88% mlg. / 73% overall sens.)

2. Percutaneous image – guided aspiration / biopsy
   - CT – guidance (sens. 90%)

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**Sensitivity of EBUS guided TBB**

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<th>Retrospective</th>
<th>Prospective</th>
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<th>EBUS guidance</th>
<th>Retrospective</th>
<th>Radiological</th>
<th>Video bronchoscopy</th>
<th>CT</th>
<th>MR</th>
<th>PET</th>
<th>EBUS guidance</th>
</tr>
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<tbody>
<tr>
<td>VATS + EBUS + TBB</td>
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</tr>
<tr>
<td>VATS + EBUS + TBB</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td></td>
<td></td>
<td></td>
<td>88%</td>
</tr>
<tr>
<td>VATS + EBUS + TBB</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td>88%</td>
<td></td>
<td></td>
<td></td>
<td>88%</td>
</tr>
</tbody>
</table>

Sensitivity of EBUS guided TBB

Endobronchial Ultrasonography-Guided Transbronchial Needle Aspiration Increases the Diagnostic Yield of Peripheral Pulmonary Lesions

A Randomized Trial

Table 1—Comparisons of Diagnostic Yields Among Three Different Procedures

<table>
<thead>
<tr>
<th>Variables</th>
<th>DW</th>
<th>TBB</th>
<th>TBAa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total samples, No.</td>
<td>58</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>Position samples, No.</td>
<td>55</td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td>yValue</td>
<td>1.88</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>Diagnostic sensitivity</td>
<td>14(24.13%)</td>
<td>18(32.10%)</td>
<td>30(53.57%)</td>
</tr>
<tr>
<td>yValue</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

Factors affecting the diagnostic yield:

- size of the lesion
- position of the mini-probe in relation to the lesion
- malignant / benign lesion
- bronchus sign
- operator
- additional guiding (fluoroscopy, EMN, guiding sheath)
- biopsy method (forceps, TBNA, brush, catheter aspirate, washing,...)
- number of biopsy samples (at least 5)
Position of the probe and sensitivity

Outside the lesion (sens. = 4%)
Adjacent to the lesion (sens. = 61%)
Within the lesion (sens. = 83%)

Yamada N et al. CHEST 2007; 132:603–608

Chao et al. Chest 2006;130:1191-1197

Benign vs. malignant lesion

- Continuous hyperechoic margin:
  - malignant disease
- Internal echoes:
  - homogeneous internal echo: benign lesions (rarely adenocarcinoma)
  - heterogeneous internal echo: malignant lesions
- Hyperechoic dots:
  - benign or malignant lesions
- Concentric circles:
  - benign lesions

Chen et al. Chest 2006;130:1191-1197
Benign vs. malignant lesion

- **Type I: Homogeneous Pattern**
  - Type Ia: with patent vesels and patent bronchioles: pneumonia
  - Type Ib: without vesels and bronchioles: organizing pneumonia, tuberculoma

- **Type II: Hyperechoic dots and linear arcs pattern**
  - Type IIa: without vesels: well differentiated adenocarcinoma
  - Type IIb: with patent vesels: well differentiated adenocarcinoma, lymphoma

- **Type III: Heterogeneous pattern**
  - IIIa: with hyperechoic dots and short lines: moderately differentiated adenocarcinoma, or squamous cell carcinoma (multiple cysts?)
  - IIIb: without hyperechoic dots and short lines: poorly differentiated adenocarcinoma


EBUS guided transbronchial lung biopsy in peripheral pulmonary lesions

Analysis 2011
Golnik University Clinic

Characteristics of the patients

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/Male</td>
<td>43/93</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>Median 67 (17-88)</td>
</tr>
<tr>
<td>No. of peripheral lesions</td>
<td>147</td>
</tr>
<tr>
<td>Peripheral lesions ≤ 3 cm</td>
<td>60</td>
</tr>
<tr>
<td>Peripheral lesions &gt;3 cm</td>
<td>87</td>
</tr>
</tbody>
</table>

Peripheral pulmonary lesions

- 579 patients / 136 pt’s with periph. lesion (23.5%)
- Mean (±SD) diameter 42 ± 21 mm (range 8-120mm)
### Malignant lesions

<table>
<thead>
<tr>
<th>Lesions</th>
<th>EBUS TBB</th>
<th>TBB</th>
<th>Fluoroscopy TBLB</th>
<th>CT guided TTNA</th>
<th>Metastasis NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>60</td>
<td>44</td>
<td>2</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Squamous cell ca</td>
<td>50</td>
<td>28</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Large cell ca</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Small cell ca</td>
<td>0</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non small cell ca</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoid</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic lung tu</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>E</strong></td>
<td><strong>115</strong></td>
<td><strong>52 (45%)</strong></td>
<td><strong>32 (2,6%)</strong></td>
<td><strong>13 (11,3%)</strong></td>
<td><strong>7 (6,1%)</strong></td>
</tr>
</tbody>
</table>

### Benign lesions

<table>
<thead>
<tr>
<th>Lesions</th>
<th>EBUS TBB</th>
<th>TBB</th>
<th>CT guided TTNA</th>
<th>Surgery</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organizing pneumonia</td>
<td>7</td>
<td>6</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>5</td>
<td></td>
<td>2 - cultures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess</td>
<td>4</td>
<td></td>
<td>1 - clin. response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamartoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>5</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other**</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>1 - follow up</td>
<td></td>
</tr>
<tr>
<td><strong>E</strong></td>
<td><strong>32</strong></td>
<td><strong>19 (59,4%)</strong></td>
<td><strong>1 (3,1%)</strong></td>
<td><strong>6 (18,8%)</strong></td>
<td><strong>5 (15,6%)</strong></td>
</tr>
</tbody>
</table>

*actinomycosis, aspergillus, lung infection, RA, undiagnosed

### False negative (24.5%) diagnostic procedures

- CT guided TTNA → 15
- Metastasis NA → 7
- Surgery → 6
- Fluoroscopy TBLB → 3
- Other → 5

**Complications:**

- 5 moderate bleedings after TBLB
- 1 PTHX
Diagnostic yield of EBUS guided TBB by location of the lesion:

- RS1-64%
- RS2-72%
- RS3-81%
- RS4-67%
- RS5-50%
- RS6-90%
- RS7-0
- RS8-50%
- RS9-67%
- RS10-56%
- LS1,2-89%
- LS3-67%
- LS4-100%
- LS5-50%
- LS6-86%
- LS8-100%
- LS9-100%
- LS10-89%

Diagnostic yield and the lesion size:
- ≤ 3 cm: > 3 cm: 60%-86%

Position of the probe and diagnostic yield:

- Outside the lesion (fluoroscopic guidance) (DG yield = 43.2%)
- Adjacent to the lesion (DB yield = 77.8%)
- Within the lesion, not at the end of the bronchus (DG yield = 80.0%)

Overall DG yield = 75.5%

Sensitivity of EBUS guided TBB

Conclusions

• EBUS is well tolerated and safe procedure
• diagnostic yield is high
• combination of guidance techniques improves DG yield
• take cytology specimen too
• radiation exposure for patients and medical personnel is reduced

Thank you.
Rigid versus semiflexible thoracoscopy in diagnosing pleural diseases.

Aleš Rozman

11th Bronchoscopy School Golnik
14 – 15 October 2011

University Clinic Golnik, Slovenia

Rozman A
Marc M
Malovrh M
Camlek L
Tollot K
Kern I

Thoracoscopy with semirigid instrument

- recent, successfully employed technique in DG of pleural diseases
- concerns about diagnostic adequacy of biopsy specimens obtained
- inferiority to rigid bronchoscopy?
The purpose of the study
... was to compare rigid and semiflexible instrument prospectively in randomized fashion to determine:
1. size of the samples
2. quality of the samples
3. diagnostic adequacy
4. complications / safety
in patients, who underwent thoracoscopy between 2008 and 2010.

Methods:
1. rigid thoroscope Olympus A5252A vs. semiflexible Olympus LTF-160
2. rigid 5mm forceps vs. flexible FB-55CD-1 Olympus forceps
3. local anaesthesia (lidocain) + i.v. Fentanyl analgesia / sedation
4. single point of entry

Patients:
1. n = 84
2. 60 (71.4%) male / 24 (28.6%) female
3. average age 63.5y (SD 10.1) from 41 to 78y
4. 29 (34.5%) patients had history of asbestos exposure

Biopsy sample quality:
1. area: program ImageJ 1.43u
2. sample quality:
   - easily interpretable - 1
   - interpretable with some difficulty - 2
   - interpretable with great difficulty - 3
   - non - interpretable - 4
3. amount of artefacts
   - no artefacts - 0
   - small amounts - 1
   - large amounts - 2
### Results:

<table>
<thead>
<tr>
<th></th>
<th>Rigid th.</th>
<th>Semiflexible th.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>38</td>
<td>41</td>
<td>79</td>
</tr>
<tr>
<td>Male</td>
<td>23</td>
<td>35</td>
<td>58</td>
</tr>
<tr>
<td>Female</td>
<td>15</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Age (SD)</td>
<td>63.3y (11.6y)</td>
<td>63.7y (8.7y)</td>
<td>63.5y (10.1y)</td>
</tr>
<tr>
<td>Number of biopsies</td>
<td>11.4 (SD 3.0)</td>
<td>10.8 (SD 2.3)</td>
<td>11.1 (SD 3.0)</td>
</tr>
<tr>
<td>Malignant disease</td>
<td>19 (50.0%)</td>
<td>28 (68.3%)</td>
<td>47 (59.5%)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>12</td>
<td>20</td>
<td>32</td>
</tr>
<tr>
<td>Secondary carcinoma</td>
<td>6</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Benign disease</td>
<td>19 (50.0%)</td>
<td>13 (30.7%)</td>
<td>32 (40.5%)</td>
</tr>
<tr>
<td>Asbestous pleuritis</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Non-specific pleuritis</td>
<td>13</td>
<td>9</td>
<td>22</td>
</tr>
<tr>
<td>Th. pneumonia</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Hernia</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Talc pleurodesis 8 8 16

Chest tube (days) 2.45 (SD 1.81) 3.47 (SD 2.84) 2.99 (SD 2.44)

Complications

- Severe bleeding after biopsy
- Empyema

### Sample Size:

#### Area (mm²)

<table>
<thead>
<tr>
<th></th>
<th>Semiflexible</th>
<th>Rigid</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>11.7 (SD 7.6)</td>
<td>24.7 (SD 12.6)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### Results - sample size:

![Box plot showing area comparison between semiflexible and rigid scopes]
Results – sample quality:

<table>
<thead>
<tr>
<th>Quality</th>
<th>Semiflexible</th>
<th>Rigid</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – easily interp.</td>
<td>30 (73.2%)</td>
<td>30 (78.9%)</td>
<td>60 (75.9%)</td>
</tr>
<tr>
<td>2 – interp. with some diff</td>
<td>10 (24.4%)</td>
<td>8 (21.1%)</td>
<td>18 (22.8%)</td>
</tr>
<tr>
<td>3 – interp. with great diff</td>
<td>1 (2.4%)</td>
<td>0 (0%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>4 – noninterpretable</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Chi-square = 1.110, sp=2
p=0.574

Rigid versus semiflexible thoracoscopy in diagnosing pleural diseases.

Conclusions:
1. Biopsy samples are smaller with semiflexible instrument.
2. Adequate biopsies and pleurodesis can be performed with semiflexible instrument.
3. The quality of samples according to diagnostic adequacy and artefacts doesn’t differ significantly.
4. Both procedures are safe.
Rigid versus semiflexible thoracoscopy in diagnosing pleural diseases.
Precise tissue diagnosis for personalized treatment in lung cancer

Izidor Kern
University Clinic Golnik

Historical perspective
1. to look
2. to sample
3. to treat
4. to diagnose on one cell

Quality & quantity matter
New step, switch in mentality

Benefits & limitations

Optimal specimen handling is essential for the accurate interpretation
**Bronchoscopic Specimens**

<table>
<thead>
<tr>
<th>Bronchial</th>
<th>Perihilar</th>
<th>Parenchymal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central, visible</td>
<td>Mediastinal, peribronchial</td>
<td>Peripheral, nonvisible</td>
</tr>
<tr>
<td>Aspirates</td>
<td>Transbronchial needle aspirations</td>
<td>Transbronchial biopsies</td>
</tr>
<tr>
<td>Lavates</td>
<td>Bronchial biopsies</td>
<td>Imprints of biopsies</td>
</tr>
<tr>
<td>Brushings</td>
<td>Imprints of biopsies</td>
<td>Bronchoalveolar lavage</td>
</tr>
<tr>
<td>Bronchial biopsies</td>
<td>Transbronchial needle aspirations</td>
<td>Transbronchial needle biopsies</td>
</tr>
<tr>
<td>Bronchial aspirations</td>
<td>Transbronchial needle aspirations</td>
<td>Transbronchial needle biopsies</td>
</tr>
</tbody>
</table>

**Biopsy - Tissue Sampling**

- **What to expect?**
  - Pretest probability
  - Do we need tissue diagnosis
- **Where to sample?**
- **How much?** - Size & number of biopsies
- Molecular biology
- Microbiological studies
- Research

**Biopsy**

- Bronchial
  - High diagnostic yield (~100% - >4 to 5 samples)
- Transbronchial
  - Histopathological detection of changes in lung parenchyma adjacent to bronchi (mLg, infection, sarcoidosis)
  - Value of negative results / nonspecific changes – to narrow differential diagnosis
  - Diagnostic yield of TBB? 30% → 60%
TRANSBRONCHIAL BIOPSY

- TBB – sufficient fragmented lung parenchymal tissue for the pathologist to reconstruct distribution and reaction pattern but with careful clinical and radiological correlation!
- No inflammation, no fibrosis – ILD not excluded
- Interstitial inflammation and fibrosis – nonspecific change - not necessarily ILD.
- TBB is not helpful in making the diagnosis of UIP.
- One of major diagnostic criteria of IPF is TBB showing no features to support an alternative diagnosis.

variety of cell specimens

- Classical exfoliative & FNAB cytopathology
- Lab processing depends on type of specimen and clinical information

BRONCHOALVEOLAR LAVAGE

- Insight in great volume of lung parenchyma - alveoli
- Parameters of good quality / specimen adequacy:
  1. $V_{recovered} / V_{instilled} > 30\%$
  2. < 40 red blood cells / 40x objective
  3. > 10% of epithelial cell (contamination)
  4. Cell viability > 60-70%
  5. TCC > $2 \times 10^6$
- Clinical information influence lab procedure (filtration!)
  - Infection
  - Alveolar lipoproteinosis
TRANSONBACHIAL NEEDLE BIOPSY & ASPIRATION

- "guided" sampling of lung masses (central or peripheral) and mediastinal lymph nodes (lung cancer staging) or tumours
- diagnostic yield up to 90%, also for benign lesions
- representativity of lymph node TBNA:
  - presence of lymphocytes ± malignant cells

sample processing

**TISSUE**
- cold ischemia
  - Time of fixation = time of sampling
  - Drying artifacts (prolonged exposure to air)
- Formalin fixation
  - 4% NBF = "10%" formalin, volume ratio 10:1
  - Formalin safety (special non-aldehyde fixatives)
- sterile transport medium for direct immunofluorescence (vasculitis, CTD)
- fresh (snap frozen)
- EM special fixative

**CELL**
- Do smears if possible
  - air dried
  - spray or ethanol fixed
- Rinse the needles
  - Fluid samples
  - BAL / sterile saline
  - ethanol fixative

transport

- immediate
  - fresh tissue specimen
  - BAL, non-fixed fluid cell specimens
- delayed
- request!!!
- safety
  - boxes, closed vials,...
ROSE
= to improve the yield of TBN
immediate evaluation of specimen adequacy

• on-site presence of cytopathologist
• telepathology system

1. representative (sufficient material, provisional dg)
   – positive – neoplastic cells
   – negative – lymphoid but no tumor cells
2. non representative
   – no lymphoid cells, necrosis, acellular specimen

ROSE
• rapid technique
  – toluidine blue
  – Diff Quick®
  – rapid HE, Papanicolaou
• quick answer (< 5 min)
• criteria of specimen representativity
  – enough, well preserved cells
  – diagnostic cells
  – presence of lymphatic cells (lymph nodes)

lung cancer
• major indication for bronchoscopy
• key advances in the therapeutic management
• substantial changes in the diagnostic pathway, including bronchoscopic techniques → improved acquisition of tumor tissue
  - accurate histological typing
  - tumor genotype & phenotype information
  - EGFR mutation testing
  - EGFR amplification?
  - EML4-ALK testing
  - ERCC1 IHK?
  - pemetrexed for nonSCC
  - gemcitabine for SCC
  - EGFR TKI for A, mu+
  - bevacizumab for nonSCC
  - crizotinib for A, ALK+
  - platinum for ERCC1+ nonplatinum for ERCC1-
IASLC/ATS/ERS proposed new classification of lung cancers for small biopsies and cytological specimens

A vs SCC

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>p63</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>TTF1</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CK7</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CK5/6</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

A: SPA+, napsin+, CK20-; SCC: 34betaE12+

NSCLC NOS < 10%

Tumor genotype & phenotype information

- Molecular markers
  - Diagnostic
  - Prognostic
  - Predictive

Progression-free survival in EGFR mutation positive and negative patients

Treatment by subgroup interaction test, p<0.001
EGFR testing requirements

1. quality of specimen, choose the best one
   • high % of tumour (>25 or 50%)
   • > 200-400 cells
   • does the tumour specimen represents the patient’s tumour
   • tissue > cell

2. specimen
   • BB (2-3)
   • TBB (4-5)
   • needle biopsies (>2)
   • cytological (TBNA, brushing, lavates,...)

quantity is essential

fate of one biopsy

1. H&E 5x
2. AB (mucin staining) 1x
3. IHC 5x (histo typing)
4. H&E first control
5. DNA extraction min 3x10μm (EGFR testing)
6. IHC (additional) 2x
7. ISH & IHC 2x (ALK testing)
8. H&E last control

What does influence the pathology result?

• sampling: “Was the lesion targeted?”
• Specimen quality: necrosis
• Experience of bronchoscopy team
• Processing & transport
• Acquisition of sample in lab, request
• Lab technique
• Pathology examination
• Clinical & radiologic information
• Limitations of pathology

Even a nonspecific dg is important in patient management.
precise tissue diagnosis for all

our team goal