P1968
Bronchoscopic cryotechnique gains high diagnostic rate in submucosal tumor growth
Wolfram Grüning1, Sergej Grif2, Henrik Wurps1, Winnie Ammenwerth1, Torsten-Gerriet Blu1, Jens Kollmeier2, Nikolaus Schönfeld1, Christian Boch1, Susann Stephan-Falkenau2, Thomas Mairinger1, Torsten Bauer1.
1Department of Pneumology, HELIOS Klinikum Emil von Behring, Pulmonary Diseases Clinic Heckeshorn, Berlin, Germany; 2Department of Pathology, HELIOS Klinikum Emil von Behring, Pulmonary Diseases Clinic Heckeshorn, Berlin, Germany.

Introduction: The diagnostic yield of endoscopic biopsy in the central bronchial system is impaired when submucosal tumor growth is present. Conventional forceps biopsy fails to reveal conclusive histology even in cases of extrabronchial compression or other indirect tumor signs. Since endoscopic cryotechniques have increasing impact for diagnoses of malignant and inflammatory lung disease we compared the diagnostic rate of forceps and cryoprobe in patients with suspected submucosal tumor growth.

Methods: 116 patients with macroscopic submucosal tumor infiltration were investigated prospectively with forceps- and cryobiopsy from 05/2009 to 02/2011. In all cases 1-3 forceps and 1-2 cryoprobe biopsies were obtained, other biopsy methods were added as needed. Specimens underwent routine histopathological processing.

Results: Histological diagnosis was achieved with the following specimens: Forceps 4/116 pts. (3.5%), cryo 48 (41.4%), forceps/cryo 34 (29.3%), cryo/TBNA 2 (1.7%), cryo/EBUS 6 (5.2%), forceps/cryo/TBNA 2 (1.7%), forceps/cryo/EBUS 2 (1.7%), TBNA 4 (3.5%), EBUS 12 (10.3%). CT-guided biopsy 2 (1.7%). Hit ratio of forceps in contrast to cryoprobe in all combinations was 42 (36.2%) and 94 (81%) respectively. Severe hemorrhage (>3 min) as the only complication occurred in 8 (6.9%) cases.

Discussion: In case of endobronchial submucosal tumor growth we found a relevant difference of diagnostic yield and a decisive superiority of cryotechnique, which should be considered for routine use in diagnostic bronchoscopy.

P1969
Does routine use of EBUS-TBNA and EUS-FNA improve the accuracy of staging of non small cell lung cancer patients – A national tumor registry based study
Mark Krasnik, Anders Mellemgaard, Erik Jakobsen.

Department of Thoracic and Cardiovacular Surgery, Rigshospitalet, Copenhagen, Denmark Department of Oncology, Herlev Hospital, Copenhagen, Denmark Department of Thoracic and Cardiovacular Surgery, Odense University Hospital, Odense, Denmark.

Background: Evaluation of the extend of disease or stage (TNM) is a prerequisite for correct treatment of lung cancer. Several studies have showed that biopsies and fine needle aspirations obtained by EBUS-TBNA and EUS-FNA yield similar results as mediastinoscopy, which previously has been considered the gold standard for evaluation of mediastinal nodal involvement in NSCLC. Thus EBUS-TBNA and EUS-FNA should now be considered as procedures which are equally effective as mediastinoscopy in staging while at the same time being more gentle to the patient.

Material: We therefore used data from a population based lung cancer registry to evaluate the association between frequency of use of EBUS-TBNA/EUS-FNA and precision of mediastinal staging. EUS in diagnostics and staging of lung cancer have been used in several centres for more than a decade and since 2005 several centres have intergraded EBUS TBNA in their procedures.

Results: The material consisted of 7000 operated patients since 2003. The use of endoscopic ultrasound (EBUS-TBNA/EUS-FNA) were mostly used in one region and mediastinoscopy in another. The concordance between cN and pN were highest and equal in the regionally where mediastinoscopy were used and the region where Endoscopic Ultrasound were used.

Conclusion: For the first time it is possible to get an impression of the impact of the use of EBUS-TBNA and EUS-FNA in a national population of lung cancer patients. The were no difference in the cN/pN ratio in the areas where they used mediastinoscopy and where they used endoscopic Ultrasound.

P1970
Impact of endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) in the evaluation of mediastinal adenopathy in lung cancer
Niamh Coleman1, Amanda Lavan1, Killian Hurley2, Ross Morgan2.
1Internal Medicine, Beaumont Hospital, Dublin, Ireland; 2Respiratory Medicine, Beaumont Hospital, Dublin, Ireland.

Introduction: TBNA is an established technique for sampling mediastinal nodes in the diagnosis and staging of lung cancer. The advent of EBUS-TBNA has increased impact for diagnoses of malignant and inflammatory lung disease. In case of endobronchial submucosal tumor growth we found a relevant difference of diagnostic yield and a decisive superiority of cryotechnique, which should be considered for routine use in diagnostic bronchoscopy.

Methods: Data collected included patient characteristics, nodes sampled, pathological diagnosis and clinical outcome. Following EBUS introduction, this data was collected prospectively over a 6 month period.

Results: 63 TBNA procedures were performed in the months preceding EBUS introduction. The overall diagnostic yield was 71.43% (n=45) and 46.67% (n=21).
of these specimens were from station 7. Seven specimens were acquired via EBUS-TBNA in the first 6 months of the programme. The diagnostic yield was 83.3% (n=65), 42.3% (n=52) were samples from station 7, 28.1% (n=22) from 4R, 5.1% (n=4) from 4L and 9% (n=7) from 10R. Sensitivity for cancer improved from 80.65% in the cTBNA group to 83.3% in the EBUS-TBNA group despite a dip to 75% in the first 3 months of the programme when analysed separately. Specificity was 100%. There were no major complications.

**Conclusions:** EBUS-TBNA was associated with improvement in diagnostic yield and sensitivity for lung cancer nodal involvement when compared to conventional techniques. A clear learning curve was seen but overcome within 3 months. This improvement in yield and the ability to sample more nodal locations may reduce referral for surgical or repeat procedures.

---

**P1971**

Evaluation of endobronchial ultrasound-guided needle aspiration selected samples - The point of view of pathology

Rica Zinsky1, Rolf Henrich2, Boeluekbas Boeluekbas1, Joachim Schirren3, Huijun Li4, Maria Aliae Mohamed-Hussein1, Maha Elkouly1, Tarek Mahfouz1, I. Yochino2, H. Hoshino2, S. Yoshida2, M. Suzuki3, K. Hiroshima3, Y. Nakatani2, Alaa Mohamed-Hussein1, Maria Elkholy1, T. Makhoul1, I. Yochino2

**Methods:**

Samples – The point of view of pathology

Evaluation of endobronchial ultrasound-guided needle aspiration selected samples – The point of view of pathology

Rica Zinsky1, Rolf Henrich2, Boeluekbas Boeluekbas3, Joachim Schirren3, Huijun Li4, Maria Aliae Mohamed-Hussein1, Maha Elkouly1, Tarek Mahfouz1, I. Yochino2, H. Hoshino2, S. Yoshida2, M. Suzuki3, K. Hiroshima3, Y. Nakatani2, Alaa Mohamed-Hussein1, Maria Elkholy1, T. Makhoul1, I. Yochino2

Background: Mediastinal staging in non-small cell lung cancer with endosonography (EUS-FNA plus EBUS-TBNA) was associated with improvement in diagnostic yield and the ability to sample more nodal locations may reduce referral for surgical or repeat procedures.

**Conclusions:**

A negative endosonography should be followed by a mediastinoscopy if PET positive mediastinal nodes are present. In the absence of PET positive nodes, a mediastinoscopy following a negative endosonography can be omitted.

---

**P1974**

Risk of lung cancer in patients with preinvasive bronchial lesions followed by autofluorescence bronchoscopy and chest computed tomography


**Aim:** To assess risk of lung cancer (LC) in patients with preinvasive bronchial lesions and to identify factors associated with higher risk.

**Patients and methods:**

124 patients with one or more preinvasive bronchial lesions and normal chest computed tomography (CT) (mean age 66.7 years, 121 males and 3 females), followed-up by white light and autofluorescence bronchoscopy (AFB) every 4-6 mo and chest CT every 6-12 mo, end points were development of carcinoma in situ (CIS) or LC.

**Results:** Among 240 preinvasive bronchial lesions, 20 CIS or LC lesions were detected during follow-up in 20 (16%) patients, 7 were detected as new endobronchial lesions, 10 as new peripheral lesions and 3 as local progression from severe dysplasia to CIS. Mediastinal node disease was detected in 24 (range: 6-54 mo). The Cumulative risk of progression was 7% at one year, 20% at three years and 44% at 5 years. Among detected lung cancers, 80% were stage 0 or stage I and underwent treatment with curative intent. Diagnosis of new SD during follow-up (p<0.0001), chronic obstructive pulmonary disease (COPD) (p=0.01) or smoking index >52 packyear (p=0.042) was associated with higher risk. Even after controlling for other risk factors, COPD was associated with risk of progression. Baseline lesion grade was not predictive of patient outcome (p=0.146).

**Conclusions:**

Patients with preinvasive bronchial lesions, especially those with new SD during follow-up, COPD or smoking >52 packyear are at high risk of LC, AFB and CT follow-up facilitated early detection and treatment with curative intent.

---

**P1975**

Validation of diagnostic molecular markers in bronchial fluid for lung cancer

Maria Alia Mohamed-Hussein1, Nura Maruna1, Begona Ruiz-Arditiello2, Sandra Pedrero2, Larranz Garcia1, Maria Urribarri3, Sergio Carrera1, Jaime Algorta2, Guillermo Lopez-Vivanco1, Rafael Zalacain1,1 Pneumology, Cruces Hospital, Baracaldo, Spain; 2PROTEOMIKA, Technology Park in Vizcaya, Zamudio, Spain; 3Oncology, Cruces Hospital, Baracaldo, Spain

**Aim:** To set a diagnosis method in bronchial fluid to detect lung cancer (LC) with high sensitivity. For this, using proteomic techniques, we have identified some biomarkers which are increased in patients with LC.

**Material/Methods:** We have included bronchial aspirates samples from 204 patients diagnosed with lung cancer by biopsy 141 non-microscopic (NSCLC) (59

**Validation of diagnostic molecular markers in bronchial fluid for lung cancer**

Maria Alia Mohamed-Hussein1, Nura Maruna1, Begona Ruiz-Arditiello2, Sandra Pedrero2, Larranz Garcia1, Maria Urribarri3, Sergio Carrera1, Jaime Algorta2, Guillermo Lopez-Vivanco1, Rafael Zalacain1

**Aim:** To set a diagnosis method in bronchial fluid to detect lung cancer (LC) with high sensitivity. For this, using proteomic techniques, we have identified some biomarkers which are increased in patients with LC.

**Material/Methods:** We have included bronchial aspirates samples from 204 patients diagnosed with lung cancer by biopsy 141 non-microscopic (NSCLC) (59
P1974

Cytology of lung cancer: diagnosis and follow-up.

Yoshihiro Nishimura.

P1977

Clinical utility of EGFR gene mutation analysis with cytological materials from bronchoscopy not histological materials

Kyosuke Nakata, Yoshikazu Tomita, Hidetugu Tateno, Takaoy Iwasaki, Makoto Hayashi, Yutaka Tsuchiyu, Jun Yamashita, Yumiko Azuma, Fumio Koshima, Department of Respiratory Medicine, Showa University Fujigaoka Hospital, Yokohama, Japan; 2Department of Clinical Pathology, Showa University, Tokyo, Japan

Purpose: To review the usefulness of FOB obtained washings and brushings in the diagnosis of lung cancer.

Methods: Retrospective analysis of 23 suspected lung cancer cases undergoing bronchoscopy room has led to a significant reduction in the number and need of biopsies performed during this period to numbers performed prior to our in-room cytopathologist. We found that the availability of a cytopathologist within the bronchoscopy room has led to a significant reduction in the number of EBs performed while for PFS independent markers were VEGFR1 (r=0.004), VEGFR1/VEGFR2 (r=0.033) and VEGFR2 (r=0.007) in washing.

Conclusions: The circulating VEGF levels are controversial. Nevertheless, the prognostic value of cVEGF levels is correlated with T descriptors in TNM staging system (r=0.040 relatively). From those who were treated with chemotherapy, best responses were observed in lower concentrations of VEGF in serum and washing (r=0.001). Higher concentrations of wVEGF are correlated with worse overall survival (HR 2.208, 95%CI 1.132-4.308, P=0.020) and PFS (HR 2.265, 95%CI 1.405-3.634, P=0.001). Similar results for OS and PFS were observed with high values of the wVEGF/VEGFR2 ratio. Multivariate Cox analysis revealed as independent markers for overall survival VEGFR2 levels in serum and washing (p=0.017 and p=0.004 relatively), while for PFS independent markers were VEGFR1 (p=0.004), VEGFR1/VEGFR2 (p=0.033) and VEGFR2 (p=0.007) in washing.

P1978

Prognostic impact of angiogenesis factors in bronchoscopic washing fluid from patients with non-small cell lung cancer

Andriana Charalambou1, Christina Fountoulakis1, Marinos Zontanos2, Ioannis Danos3, Panos Demertzis3, Ioannis Gouzos4, Kostas Syrigos1. 1Oncology Unit, 3rd Dept. of Medicine, Athens School of Medicine, 29th Pulmonary Dept., 3rd Pulmonary Dept., St. Sophia General & Chest Hospital, Athens, Greece

Background: Angiogenesis has been proven to be a process related to the migration, proliferation and metastasis of cancer cells. The prognostic value of angiogenesis factors is still controversial.

Aim: The aim of this study is to define the VEGF, VEGFR1 and VEGFR2 and the ratios of VEGF/VEGFR1 and VEGF/VEGFR2 in the blood serum and the washing of patients with newly diagnosed non-small cell lung cancer (NSCLC).

Methods: 40 patients with NSCLC participated in this study. The measurement of the circulating (c) and washing (w) levels of VEGF, VEGFR1 and VEGFR2 was carried out with the ELISA method.

Results: vVEGF levels is correlated with T descriptors in TNM staging system (r=0.021), as well as the ratio VEGF/VEGFR2 in serum and washing (r=0.03 and r=0.040 relatively). From those who were treated with chemotherapy, best responses were observed in lower concentrations of VEGF in serum and washing (r=0.001). Higher concentrations of wVEGF are correlated with worse overall survival (HR 2.208, 95%CI 1.132-4.308, P=0.020) and PFS (HR 2.265, 95%CI 1.405-3.634, P=0.001). Similar results for OS and PFS were observed with high values of the wVEGF/VEGFR2 ratio. Multivariate Cox analysis revealed as independent markers for overall survival VEGFR2 levels in serum and washing (p=0.017 and p=0.004 relatively), while for PFS independent markers were VEGFR1 (p=0.004), VEGFR1/VEGFR2 (p=0.033) and VEGFR2 (p=0.007) in washing.

Conclusions: The circulating VEGF levels are controversial. Nevertheless, the definition of angiogenic markers in washing could recognize a high risk group of patients who could benefit from an aggressive initial therapeutic approach.
positive histology alone. 3 (20%) cases had positive cytology but negative histology in the context of an endobronchial lesion. All 7 patients without an endobronchial lesion had negative cytology and were subsequently found not to have cancer. Only 1 patient with an endobronchial lesion had both negative histology and cytology and was proven not to have cancer.

Conclusion: From this retrospective analysis we conclude that 20% of lung cancers would have been missed had cytological samples not been taken in addition to endobronchial biopsies. Therefore we suggest that any patient with an endobronchial lesion should have brushings and washings accompanying a biopsy. We cannot deduce from our small study whether, in the absence of a visible endobronchial lesion, brushings and washings are diagnostically valuable.

P1981
Relative contribution of cytological specimen type in the determination of lung cancer histologic identity – Analysis of one year’s comparative data
Stylianos Michaelides1, Aphrodite Emmanouelidou 2, George Goulas1, Ageliki Lazaratou1, Despina Melemeni1, Aikaterini Blana2, Vassilios Handrinios1, 11st Dept. of Thoracic Medicine, 2Dept. of Clinical Cytology, Sismanoglion General Hospital, Maroussi, Athens, Attiki, Greece

We retrospectively evaluated the relative contribution of cytological specimens in identifying the histologic type of lung cancer. Seventy-four patients (50 male & 24 female) aged 63±8.9 years (mean±SD), eventually diagnosed to have lung cancer were studied. Diagnosis was established by either bronchoscopic or surgical biopsy. The spectrum of cytological specimens included: simple sputum smear (SP), bronchial washings (BW), post-bronchoscopy secretions (PR), brushings (BS) and transbronchic fine needle aspirates (FNAs). The distribution of histologic types was as follows: Small Cell Lung Cancer (SCLC) 24 pts (32.4%), Squamous Cell Carcinoma 20 pts. (26%), Adenocarcinoma 14 pts. (18.9%), Undifferentiated Carcinoma 6pts. (12.3%), Large cell Carcinoma 2 pts. (0.28%). Analysis of data showed that simple sputum cytology was diagnostic in 24.3% (relative contribution 66.6% for SCLC and 33.4% for NSCLC). Success rate of BW was 42% (almost equally partitioned between SCLC & NSCLC 52% & 48% respectively). BS diagnosed 23% of lung cancer, of which 56.3% was the yield for adenocarcinoma. The contribution of FNA smears cannot be evaluated due to the very small sample size (only 2 patients which was successful in both). The overall contribution of cytology in the diagnosis among all types of lung cancer cases studied was 57 pts among a total of 74 (77%). We conclude that simple sputum cytology should not be neglected (having a diagnostic rate of 25% of patients) while the significance of BS in adenocarcinoma (56.3%) should be emphasized given its frequent peripheral location that does not allow obtaining tissue for histologic diagnosis.

P1982
Liquid-based cytology in the diagnosis of pulmonary malignancy in bronchial brushings and washings
Beata Olejniczak1, Anna Dzembjek1, Agneta Westman2, Noorén Lundebrokh2, 1Department of Medicine, Trelleborg Hospital, Trelleborg, Sweden; 2Department of Clinical Pathology and Cytology, University Hospital Malmo, Malmo, Sweden

Background and aims: Bronchial cytology (BC) is well established in the diagnosis of lung cancer but some cases remain equivocal. Liquid-based cytology (LBC) was developed to improve the diagnostic accuracy and increase the sensitivity for malignancy in BC. The study was conducted to compare the diagnostic performance of CytoRichRed (CRR) fixed Tripath preparations with conventional smears (CS) from bronchial brushings (BB) and bronchial washings (BW).

Methods: BB and BW from 61 patients, subjected to fiberoptic bronchoscopy, were studied. BB specimens were split into two equal parts, one part was fixed in CRR and the other in acid alcohol and stained according to Papanicolaou. BBs were smeared onto slides, air-dried and Giemsa-stained, then brushes were rinsed in CRR and the cellular suspensions were processed according to the TriPath technique. Slides were evaluated in a blinded fashion and cytological diagnoses were compared with "true" diagnoses, based on histology and clinical data.

Results: In all 575 and 244 CS and 61 and 61 CRR/Tripath slides were prepared from the BB and the BW, respectively. CS diagnoses agreed in 575/61 cases. In the four discrepant cases the conventional/CRR diagnoses were atypia/benign, benign/atypia (malignancy favoured), benign/equivocal, atypia (re- classified as benign. All four cases turned out to be malignant.

Conclusions: The diagnostic accuracy did not differ between conventional and CRR/Tripath preparations. Our results indicate that LBC using CRR/Tripath can replace CS, significantly reducing workload and cost.

P1983
Endobronchial ultrasound and fluoroscopy in the study of peripheral lung lesions
Albert Sánchez-Fourn1, Laia Giralt1, Rodrigo Alcántara2, Javier Gimeno1, Laura Pijuan1, Joan Vollmer1, Joaquim Geci1, Victor Curull1, 1Servei de Pneumologia, Hospital del Mar-Pare de Salut Mar, Barcelona, Spain; 2Servei de Radiodiagnostic, Hospital del Mar-Pare de Salut Mar, Barcelona, Spain; 3Servei d’Anatomia Patològica, Hospital del Mar-Pare de Salut Mar, Barcelona, Spain

Introduction: Endobronchial ultrasound (EBUS) is a minimally invasive tech-