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## 465. Biology and diagnosis of thoracic tumours

### E4686

#### Telomerase vs CD34 and MIB1 in non small cell lung cancer

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In lung cancer telomerase adds DNA sequences (TTAGGG) to telomeres giving the cell unlimited proliferative capacity. The expression of telomerase may be a critical step in tumor progression. In our study we compared the telomerase activity with CD34 and MIB1 (both associated with cell proliferation) in 60 resected non small cell lung cancer (NSCLC) to evaluate the diagnostic role of this enzyme. Internationally recognised cut off values were adopted for CD34 and MIB1. Telomerase enzyme activity was evaluated by immunohistochemical analysis counting the number of positive cells per standard number of 250 cells. We considered telomerase-positive patients those with five positive cells and highly positive those with at least ten cells. All CD34 positive patients (11/60 = 18.3%) showed an important telomerase activity (100% > 10 cells). Among the 50/60 (83.3%) MIB1 positive patients only 14/50 (28%) showed positive telomerase activity. In conclusion our data indicate that telomerase activity was correlated only with CD34, no tight correlation between MIB1 and the enzyme activity. Telomerase could have an important diagnostic role in NSCLC being perhaps more specific than tumor markers commonly used in clinical practice.

### E4687

#### Akt induced cytoplasmic mislocalization of p27<sup>Kip1</sup> protein and correlated with poor prognosis in lung adenocarcinoma

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**Introduction:** The aims of this study were to investigate the expression of Akt and p27<sup>Kip1</sup> proteins in lung adenocarcinoma tissues and cells, to clarify their relations and to evaluate the prognostic factors in lung adenocarcinoma patients.

**Methods:** 59 consecutive lung adenocarcinoma patients were retrospective reviewed and followed up. Immunohistochemistry was performed to examine lung adenocarcinoma tissue samples for the expression of Akt and p27<sup>Kip1</sup>. Kaplan-Meier survival analysis and Cox's proportional hazards model were used for statistical analysis. Meanwhile, H1299 cells were cultured *in vitro* and transfected with expression constructs encoding the active form of p27 or/and Akt for 32hr. Immunofluorescence assay was detected in H1299 cells under fluorescence microscope.

**Results:** Constitutive activation of Akt (phosphorylated Akt, P-Akt) and positive

p27<sup>Kip1</sup> staining were observed in cytoplasmic and nuclei of lung adenocarcinoma cells. Poor differentiation, high TNM stage and lymph node metastasis were strongly associated with P-Akt over-expression ( $P < 0.05$ ). Three-year survival rate of patients with P-Akt positively expressed was lower than those with P-Akt negative patients (0% vs 33%). Both P-Akt and nuclear p27<sup>Kip1</sup> can be referred as an independent prognostic factor in Cox model ( $P < 0.05$ ). The *in vitro* results showed p27<sup>Kip1</sup> protein mainly localizes in the nuclei of H1299 cells and cytoplasmic mislocalization of p27<sup>Kip1</sup> was significantly associated with the constitutive phosphorylation of Akt.

**Conclusions:** Akt was overexpressed and activated in lung adenocarcinoma. Akt signaling pathway play a pivotal role in the tumorigenesis of lung adenocarcinoma.

### E4688

#### The effects of dalteparin, a kind of low molecular weight heparin, on lung adenocarcinoma A549 cell line *in vitro*

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Unfractionated heparin and low molecular weight heparin play their anticoagulant roles by activating the physiological coagulation inhibitor antithrombin. Besides the anticoagulant effects, a wide variety of biological activities of them have been discovered. Recently, their beneficial roles on cancer progression have been reported. Several underlying mechanisms by which heparin and low molecular weight heparin affect tumor have been proposed. It is unknown whether the growth and proliferation of tumor cell could be inhibited or delayed by heparin and low molecular weight heparin directly. In this study, we interfered with the normal growth of A549 cells with dalteparin, observed the alteration of cell viability, cell cycle progression, cell apoptotic status and the expressions of p21<sup>WAF1</sup> and p27<sup>KIP1</sup>. It was observed the viability of A549 cells were inhibited by dalteparin dose-dependently and time-dependently. More cells were arrested in G1 phase and induced to early apoptosis. Dalteparin enhances the expression of p21<sup>WAF1</sup> and p27<sup>KIP1</sup> protein, but does not affect the mRNA of p21<sup>WAF1</sup> and p27<sup>KIP1</sup>. Silencing of the gene expression of p21<sup>WAF1</sup> or p27<sup>KIP1</sup> causes the attenuation of the effects of dalteparin on cell cycle progression and apoptosis. It was concluded the inhibitive effect of dalteparin on A549 cells is associated with the cell cycle arrest in G1 phase and the induction to early apoptosis. The alterations of cell cycle progression and apoptosis status were partly attributed to the increases of p21<sup>WAF1</sup> and p27<sup>KIP1</sup> proteins. The changes of p21<sup>WAF1</sup> and p27<sup>KIP1</sup> proteins in dalteparin-treated A549 cells occurred at posttranscriptional levels.

### E4689

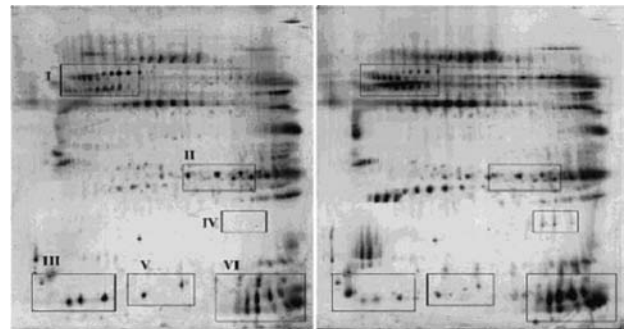
#### Identification of tumor-associate proteins in stage-I lung squamous cancer by proteomics

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**Objective:** To establish the differential protein express spectra of the stage-I squamous lung cancer (SLC) by proteomics.

**Methods:** Collect 30 pairs of surgical specimens of stage-I SLC patients, analyze the proteins by the comparative proteomic techniques, including 2-DE atlas and Image Master elite 3.10 software, identified the protein ID by MALDI-TOF-MS and database matching.

**Results:** L was cancer tissue, R was adjacent tissue.



Protein ID	Area	Mr/pl	Lung cancer (%vol)	Adjacent normal tissue (%vol)	Fold difference
HSP60	I	65kD/5.2-5.5	0.320±0.203	0.162±0.144	2
ATP synthase β chain	I	56kD/5.0-5.4	0.372±0.329	0.840±0.563	-2.3
HSP27	II	30kD/5.8-6.5	1.153±0.397	0.790±0.260	1.5
Galectin 1	III	12-13kD/4.9-5.3	1.981±0.971	1.308±0.289	1.5
Crystallin α B	IV	22-23kD/6.7-7.3	0.345±0.362	0.994±0.328	-2.9
Nuclear FMRP					
interacting protein 1	V	15kD/6.3	1.096±0.366	0.647±0.319	1.7
Calgranulin B	V	14kD/5.5	0.774±0.398	0.546±0.140	1.5
Hemoglobin	VI	15.9kD/8.2	6.336±4.259	3.041±2.068	2.1

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8 proteins were identified. 6 were up-regulated in the cancer tissue, including the heat shock protein 60(HSP60), heat shock protein 27 (HSP27), galectin 1, nuclear FMRP interacting protein 1, calgranulin B, hemoglobin; 2 proteins were down-regulated: ATP synthase and crystallin  $\alpha$ B.

**E4690****Small cell lung cancer Xenografts can be successfully grafted from bronchoscopy derived samples: model for lung cancer translational research**

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Lung Cancer Xenografts offer many advantages in Translational Research of cancer biology over cancer cell lines. Most xenografts are grown from portions of resected cancers. Small Cell Lung Cancer (SCLC) are seldom resected, and therefore few xenografts exist. We report on the successful grafting of small cell xenografts from samples retrieved during diagnostic and therapeutic bronchoscopies, that is a good model for translational lung cancer research.

**Methods:** Between 4-2004 and 12-2007, 12 patients with cytology/histology proven SCLC had extra "waste" specimen collected for xenograft growth per IRB approved protocols. These include rinse-out of trans-bronchial needle aspiration of mediastinal tumor, needle aspiration, endobronchial biopsies, tumor debriement by biopsy or mechanical microdebrider removal of visible endobronchial tumor. Aspirates are mixed with 1-3 ml Matrigel; biopsies are homogenized and then placed in Matrigel, and then injected in flanks of Athylic Nude mice. Animals observed for tumor implant and growth, eventually sacrificed for characterization of tissue and further passaging in additional animals.

**Results:** 5/12 patients' samples resulted in successful xenografting with follow-up confirmation of SCLC. 3 of these 5 successfully passaged. 3/12 attempted grafts pending. Cells from xenografts can generate cell lines and are used in translational characterization of molecular and genetic profiles, and in development of targeted therapeutic trials.

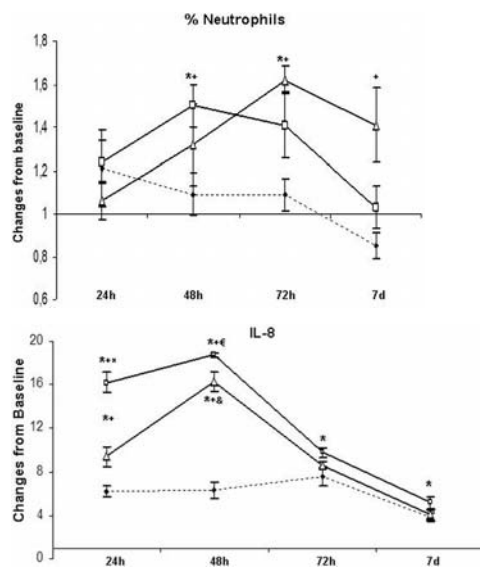
**Conclusion:** Successful SCLC xenografts can be grown from bronchoscopy samples, including TBNA. This can be a useful model for lung cancer translation research.

**E4691****Low doses of silver nitrate induce pleurodesis with a limited systemic response in rabbits**

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**Rationale:** This study describes the systemic effects induced by a new technique of pleurodesis using repeated doses of 0.1% SN in comparison to single intrapleural injections of 0.5% SN or talc.

**Methods:** Rabbits were injected intrapleurally with 0.1% SN repeatedly at times 0, 24 and 48 hours. Two other groups received a single dose of 0.5% SN nitrate or talc 400mg/kg. After 24, 48, 72 hours and 7 days blood samples were assayed for leukocytes, neutrophils, LDH, IL-8, VEGF and TGF- $\beta$  levels. Macroscopic pleural adhesions (scores 0-4) were evaluated after 28 days.



**Results:** Both talc and 0.5% SN led to a significant increase in neutrophils, LDH, IL-8 and TGF- $\beta$  in comparison to control, whereas 0.1% SN increased only LDH and TGF- $\beta$ . Of note, the 0.1% SN group had a significant lower neutrophil response than other groups. Neutrophils, IL-8 and VEGF in talc and 0.5% SN groups peaked between 24 and 48 hours and tended to decrease with time. All groups had an efficient pleurodesis.

**Conclusion:** Sequential doses of 0.1% SN produced an efficient pleurodesis in rabbits, with a low systemic inflammatory response in comparison to talc or 0.5% SN.

**E4692****Diagnostic accuracy of CT-guided coaxial cutting needle lung biopsy of lung nodules**

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Percutaneous cutting needle biopsies achieve a better diagnostic accuracy for benign lung lesions and comparable high diagnostic accuracy for malignant lung lesions, compared to fine needle aspiration biopsies. Factors that affect diagnostic accuracy, are size of the nodules and the nodules being of benign character.

The goal of our study is to evaluate the accuracy of CT-guided percutaneous coaxial cutting needle biopsies of lung nodules larger than 10 mm. To analyse the variables affecting the diagnostic accuracy and at the same time record the complication rate.

The study is a retrospective study on 217 percutaneous consecutive needle tissue-core biopsies were performed with a coaxial cutting needle under CT- guidance. The biopsies were performed from February 2002 until February 2004. There were 190 patients which had taken 217 biopsies. The procedure was done on an out-patient basis. The biopsy procedure was standardized and the nodules were  $\geq 10$  mm in diameter.

The overall diagnostic accuracy of CT-guided percutaneous coaxial cutting needle biopsy of lung lesions was 94%. Sensitivity was 93%, specificity 100%, negative predictive value 84% positive predictive value 100%. False positive rate 0% and false negative rate was 16%.

The factors affecting diagnostic accuracy, in this study were final diagnosis of benign aetiology and thickness of the thorax wall.

Pneumothorax in 27% of the cases. 8% were in need of pleural drainage. One patient had a hemoptysis more than 30 ml.

**Conclusion:** CT-guided percutaneous cutting needle biopsy of a lung nodule, provides a high degree of diagnostic accuracy. The procedure can be conducted safely on an out-patient basis.

**E4693****Could <sup>18</sup>F-FDG PET repeated within cycle 1 predicts objective response to chemotherapy in advanced non-small cell lung cancer (NSCLC)? A pilot study results**

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**Background:** <sup>18</sup>F-FDG-PET already showed to be an early and sensitive assessment of the effectiveness of anticancer treatment in different solid tumours after the first cycle of chemotherapy. Aim of the study was to test if PET scan repeated 2 weeks after the start of chemotherapy is predictive of the subsequent response and survival in patients with advanced NSCLC.

**Patients and methods:** 22 patients, stage IIIB-IV NSCLC, were enrolled. All patients underwent PET scan at baseline (PET1), 15 days after the beginning (PET2), at the end of chemotherapy. Assessment of the disease by CT was performed at baseline and every other cycle. Response was evaluated according to RECIST criteria and analysis of PET scans.

**Results:** Patients were dichotomized in 2 groups (responders, non-responders) based on the PET changes in all visible lesions between PET1 and PET2 (including the SUV change between baseline and subsequent PET in the primary tumour (DSUV) and the overall assessment of all visible lesions). Among responders, CT scan performed after 2 cycles showed objective response in 55% of the cases, while only 1 OR in non-responders (Fisher exact test, p=0.04). Overall PET response overestimate CT response in 6/21 cases while underestimate it in 3/21 cases. Adopting different cut-off values for baseline SUV or DSUV of the primary lesion no correlation was found with progression-free (PFS) or overall survival. A non significant trend for improved PFS was found in responders vs non. Data on OS are still immature.

**Conclusion:** This study indicates that early PET restaging during cycle 1 may predicts an objective response to CT scan after 2 cycles.

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**E4694****Evaluation of pleural fluid clot histology in the diagnosis of pleural malignancy**

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**Introduction:** Cytological analysis of pleural fluid is one of the initial investigations to identify the cause of an exudative pleural effusion. Potentially the diagnostic yield could be enhanced by the histological examination of pleural fluid clots. Centrifuged pleural fluid is combined with thrombin and plasma to form a clot, fixed in formalin and set in a wax block. This condenses the cellular material and allows immunostaining.

**Aim:** To evaluate whether the analysis of pleural fluid clots, in addition to pleural fluid cytology increases diagnostic yield.

**Method:** 90 patients who had examination of both pleural fluid cytology and clot histology over a 2 year period were reviewed (2005-7). All histology and cytology results were recorded including those of further investigations e.g. pleural biopsies. Final diagnoses were documented.

**Results:** A histological diagnosis of malignancy was made in 44(49%). Most diagnoses were made from biopsies (48%, n=21). 18 (41%) diagnoses came from both fluid cytology and clot histology. Clot alone and pleural fluid alone accounted for 2 and 3 diagnoses respectively. 7 had two pleural samples examined; the second sample confirmed the diagnosis in 3. In 6 the clot examination confirmed a diagnosis which was reported as showing either suggestive or suspicious cells from fluid cytology. Therefore, clot histology was required to make an exact diagnosis in 8 (18%).

**Conclusion:** Our series shows that pleural clot histology does increase the diagnostic yield of pleural fluid examination by a small amount. It also helps clarify a cytological diagnosis by allowing immunostaining. Larger series would be needed to establish whether it is more useful in certain situations.

**E4695****The role of PET-CT in mediastinal lymph node staging in NSCLC**

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**Purpose:** To determine the role of PET-CT in mediastinal lymph node staging in NSCLC.

**Material and methods:** 83 NSCLC cases who are possibly operable were taken into the study. Flexible bronchoscopy, thorax CT, PET-CT and mediastinoscopy were applied to all cases. In addition three cases went through mediastinotomy and eight went through extended mediastinoscopy. Thoracotomy and systemic mediastinal sampling was performed in 55 cases.

**Findings:** Findings regarding thorax CT, PET-CT and mediastinoscopy are shown in the table.

	CT	PET-CT	Mediastinoscopy
Sensitivity	54.5	84.8	84.6
Spesificity	72	72	100
Accuracy	65	77.1	92.7
PPV	56.2	66.6	100
NPV	70.8	87.3	88

**Results:** It has been observed that PET-CT has higher PPV and NPV than thorax CT in mediastinal lymph node staging. However, in our study, false positivity rate of PET-CT was found to be 33.4%. For this reason, in patients considered for surgery, mediastinal lymph node positivity detected in PET-CT should not exclude surgical treatment; invasive staging should be performed.

**E4696****PET-CT, NSCLC staging and surgery: an audit of current experience**

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**Aims:** To determine the accuracy of PET-CT staging in NSCLC patients referred for curative surgical resection.

**Methods:** The records of 40 patients considered for radical therapy referred for PET-CT assessment between January and November 2007 were analysed retrospectively.

**Results:** 4 patients declined PET-CT imaging. When compared to conventional CT 13 patients retained the same radiological stage, 9 were downstaged, 12 upstaged and 3 derived a non-cancerous diagnosis (n=36) (median wait for imaging 8 days).

Of the 31 potential surgical candidates, 14 (45%) avoided a non-therapeutic surgical intervention as a result of PET-CT. 17 patients were referred for resection. The PET-CT results in 4 patients had the same corresponding pathological stage while 4 were pathologically downstaged and 6 upstaged [CT equivalent in 7, 3, 4 patients respectively] (n=14 exclusions: 1 non NHS, 1 declined PET-CT, 1 non lung primary).

The PET-CT mediastinal lymph node status in the included patients was concordant with pathological stage in 8, false negative in 3 (all adenocarcinomas) and false positive in 3 (all squamous cell carcinoma (SCC)) [CT equivalent in 11, 1, 2 patients respectively].

**Conclusions:** Our experience indicates that conventional CT staging through the filter of PET-CT is a good predictor of pathological stage. Preventing unnecessary operative procedures confirms the incremental cost effectiveness per QALY gained using a PET-CT NSCLC assessment strategy. However, PET-CT can incorrectly both over and under represent nodal status. This small audit affirms that surgery with mediastinal sampling should be the default position in fit patients with equivocal PET-CT mediastinal nodes, especially with proven SCC.

**E4697****Usefulness of various diagnostic techniques during fiberoptic bronchoscopy for endoscopically visible lung lesions**

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**Objectives:** The aim of the present study was to evaluate the value of various diagnostic techniques, following fiberoptic bronchoscopy, in the diagnosis of visible lung lesions.

**Material and Methods:** A retrospective study was based on 284 patients who underwent bronchoscopy in Sismanoglio General Hospital during a 12-month period and found to have endoscopically visible pulmonary lesions. Histologic examination of forceps biopsy (FB) specimens was performed in 180 (63.3%) patients. Cytological evaluation on bronchial brushing (BB), bronchial washings (BW) and post-bronchoscopic sputum smears were performed in 192 (67.6%), 280 (98.59%) and 238 (83.8%) cases respectively.

**Results:** Two hundred thirty one patients had at least one of the techniques positive for lung malignancy (81.33%). Mean age 66.37; range 20-89 years. Of the above 231 tumors, 72 were diagnosed as squamous cell carcinoma (31.17%), 38 as adenocarcinoma (16.45%), 1 as BAC (0.4%), 46 as small cell lung carcinoma (16.2%), 55 as non- small cell lung carcinoma (19.9%), 3 as mixed (1.3%), 3 as metastatic (1.3%), 4 as carcinoids (1.73%) 1 as lymphoma (0.4%) and 8 as suspicious for malignancy (3.46%). FB gave positive results in 106 (58.9%), BB in 126 (65.6%), BW in 151 (53.9%) and post-bronchoscopic sputum in 62 (26.8%) cases. The addition of the combination of the three cytological techniques to the FB increased the diagnostic yield from 40.49% to 81.33% (p<0.0001).

**In conclusion:** the combination of the cytohistological techniques results in a statistical significant increase in the diagnostic yield of visible lung lesions.

**E4698****Is invasive staging necessary for NSCLC cases with no mediastinal N2 in PET/CT and thorax CT imaging?**

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Need of invasive staging in potentially resectable NSCLC patients with no pathological sized lymph nodes seen in thorax CT and Fluorodeoxyglucose F-18 labeled integrated positron emission tomography-computed tomography (PET-CT) imaging was researched. Between January 2006 and December 2007 84 patients (3 women, 81 men; mean age 57.4±8.1 years) with PET-CT images who have undergone at least one of the invasive surgical mediastinal staging procedures were evaluated. 48 patients (57%) were negative for mediastinal N2 according to both PET-CT and thorax CT imaging; in 13 (15.5%) thorax CT was negative and PET-CT positive, in 8 (9.5%) thorax CT was positive and PET-CT negative. 48 patients with thorax CT and PET-CT negative imaging (3 women, 45 men; mean age 57.3±8 years) were evaluated with mediastinoscopy and thoracotomy results and N2 disease were determined in 6 (12.5%) of them. Among them 4 had one (1 with number 5, 2 with number 7, 1 with 2R numbered stations) and 2 had more than one pathological stations. Last consensus implies that invasive evaluation may not be done in mediastinal invasion negative patients according to thorax CT and PET-CT. Our results showed that N2 was determined in 12.5% of these cases. Therefore, although both imaging techniques are negative, need for surgical mediastinal staging procedures should be evaluated according to the patient.

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**E4699****Two-pore domain K<sup>+</sup> channel TASK-1 maintains the membrane potential in non-small cell lung cancer (NSCLC) cells**

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**Rationale:** Survival in lung cancer is poor, partly due to chemotherapy failure. Hypoxia is present in solid tumors and may lead to chemotherapy resistance. It is well accepted, that changes in ion channel conductance are associated with cell survival. Members of the recently described background two-pore domain K<sup>+</sup> channel family like TASK-1 are blocked by hypoxia. However, the role of TASK-1 in cancer cells is largely unknown. The aim of this study was to analyze the function of TASK-1 in NSCLC cell lines.

**Methods:** A549 cells were cultured at 1% O<sub>2</sub> or ambient oxygen for 72 h and investigated with the whole-cell patch-clamp technique. Expression of TASK-1 was confirmed by RT-PCR.

**Results:** TASK-1 is present in A549 cells. The resting membrane potential under normoxic conditions was  $-37 \pm 2$  mV. The K<sup>+</sup> current, active around the resting membrane potential was non-inactivating, anandamide- and acidosis-sensitive. The specific TASK-1 inhibitor anandamide significantly reduced the K<sup>+</sup> current and led to membrane depolarization ( $-23 \pm 2$  mV,  $p < 0.01$ ). In chronic hypoxia, the anandamide-sensitive K<sup>+</sup> current was completely abolished and the cells were depolarized to  $-27 \pm 3$  mV ( $p = 0.01$ ).

**Conclusions:** TASK-1 plays an important role for maintaining the membrane potential in A549 lung cancer cells. Hypoxia blocks K<sup>+</sup> current and leads to membrane depolarization largely due to the block of TASK-1 current.

C. Wohlkoenig and C. Nagaraj are supported by the Medical University of Graz (PhD Program Molecular Medicine).

**E4700****Videothoracoscopy in diagnosis and palliative treatment of malignant pleural mesothelioma**

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**Introduction:** malignant pleural mesothelioma is characterized by quick spread and asymptomatic course of disease, and therefore demands novel highly effective and minimally invasive diagnostics methods.

**Objectives:** the aim of the study was to assess the efficiency of videothoracoscopy in diagnosis and palliative treatment of malignant pleural mesothelioma.

**Patients and methods:** 700 videothoracoscopies were performed in the thoracic oncology department of the Petrov Research Institute of Oncology between 1994 and 2008. 34 patients (4.8%) underwent thoracoscopy for diagnosis and palliative treatment of malignant mesothelioma of pleura, including 23 males and 11 females, mean age 52 years. Chest X-ray showed diffuse pleural thickening or pleural nodules in 17 cases (50%); and isolated pleural effusion in other patients. Videothoracoscopy revealed epithelial type malignant pleural mesothelioma in all patients. Disease was local in 3 cases and radical surgery was performed. Other 31 patients received palliative care: pleurodesis (talc – 4, argon plasma coagulation – 21, combined pleurodesis with photodynamic therapy – 6) and argon plasma coagulation of tumor for cytoreduction – 14 cases (41%).

**Results:** The reduction of pain and cancer intoxication as well as the permanent stop of pleural effusion was reached in all patients. Mean Karnofsky index increased from 60 to 70% within 6 month after procedure. Relapse-free period was 9 month (from 6 to 13) for 14 patients with full clinical response, and 5 month (from 3 to 8) for other patients with partial response.

**Conclusion:** videothoracoscopy is the method of choice for both diagnosis and palliative treatment of common malignant pleural mesothelioma.

**E4701****Combined radiation therapy in treatment of tracheal cancers**

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Malignant tumors of the trachea are uncommon. Patients who presents with symptomatic airway malignant obstruction often have limited therapeutic options. Intraluminal irradiation has been used in attempt to obtain sustained palliation.

**Purpose:** To assess the results of high-dose rate (HDR) intraluminal brachytherapy (ILBT) in combination with external beam radiation treatment (EBRT) in patients with unresectable tracheal cancers.

**Patients and methods:** We reviewed the treatment outcomes between 1993 and 2006 in 12 patients with tracheal cancers (9 squamous cell carcinoma, 2 adenoid cystic carcinoma, 1 mucoepidermoid carcinoma), age 37-71, median 58), who underwent HDR ILBT + EBRT. Most patients received HDR ILBT of 2100cGy in 3 fractions (one per week) was delivered at a distance 10 mm from the mid-

source. Prior or during HDR ILBT all patients underwent EBRT to a total dose of 3000-4500 cGy in 10-22 fractions/4 fractions per week.

**Results:** Disease-related symptoms like dyspnoea, cough, haemoptysis and chest pain significantly improved 2 month after completion of therapy in 75% patients. Objective responses (complete-CR and partial-PR) evaluated by tracheo-bronchoscopy and by CT, X-ray chest, was confirmed in 66,6% of the treated patients. The average actuarial survival was 13.6 months (the range 2-64 months). Complications occurred in 5 patients (1 fistula, 1 haemoptysis, 1 oesophagitis, 2 fibrosis pulmonum).

**Conclusion:** HDR ILBT in combination with EBRT effectively palliates most symptoms caused by the malignant obstruction of trachea, and in that way contributes improvement in the quality of life.

**E4702****How do lung cancer patients die?**

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**Background:** Lung cancer remains the commonest cancer related death in the western world. About 36,000 patients die of Lung cancer in the UK every year. There is very scarce data on the actual cause of death in Lung cancer patients. Mortality among these patients remains high due to late presentation and significant co-morbidities.

**Aim:** We studied the cause of death in lung cancer patients referred to our hospital. Data of patients with lung cancer were collected from hospital death registry and lung cancer database. The cause of death was taken from the death certificate.

**Results:** 97 patients (Males-53%) died over a period of 18 months. The mean age was 69 years. The median survival was 58 days (Mean 163 days). The main cause of death as documented in the death certificate is as listed in Table 1.

Table 1. Cause of death

Cause of death	Number
Lung cancer	54 (56%)
Pneumonia	21 (22%)
Congestive cardiac failure	3 (3%)
Myocardial infarction	3 (3%)
Pulmonary embolism	3 (3%)
Neutropenic sepsis	2 (2%)
Renal failure	2 (2%)
Others	9 (9%)

Perforated bowel, Respiratory failure due to COPD, cerebro vascular disease, gastrointestinal bleeding, sepsis and Ischaemic bowel are the other main causes of death recorded. 44% of the patients died due to other causes not directly related to lung cancer. Nearly 30% of patients had significant co-morbidities like diabetes, heart disease, hypertension, etc.

**Conclusion:** Patients with lung cancer often have other co-morbidities. There is inadequate data looking specifically at the cause of death in lung cancer patients. We postulated lung cancer death is multifactorial. This small study shows that only just above half of patients die from the lung cancer itself. Patients often succumb due to other coexisting illnesses or complications of treatment.

**E4703****Detection of lung malignancy using 99mTc/Tektrotyd**

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**Aim:** 99m-Tc-Tektrotyd is a radiopharmaceutical indicated for diagnosis of tumors with overexpression of somatostatin receptors.

**Patients and Methods:** Whole body scintigraphy (WBS) and single photon emission computed tomography (SPECT) was performed in 27 patients (pts) with ECAM (Mediso) gamma camera 2 hours after i.v. administration of 740 MBq of 99mTc-Tektrotyd. In case of positive findings, ROI was drawn around each lesion and compared to the contralateral position, and tumor to non tumor (T/NT) ratio was calculated.

**Results:** In 6 pts with squamous cell lung cancer, 1 adenocarcinoma, 12 primary lung carcinoid, 5 lung metastases from neuroendocrine tumors of different origin, 3 tuberculosis and pneumonia and 1 with echinococcal cysts, 31 pulmonary lesions were detected on Rtg and CT. Among the true positive (TP) findings there were 20 lesions (6 squamous cell tumors, 1 adenocarcinoma, 8 primary lung carcinoids and 5 lung metastases from neuroendocrine tumors). In 4 pts false negative (FN) findings were found (2 poorly differentiated and 2 small neuroendocrine tumors). Among 4 true negative (TN) pts there were 2 pts after successful surgery, 1 with tuberculosis and 1 with hydatid cysts. Two pts with pneumonia were false positive (FP). The mean T/NT ratio in group with TP findings was  $1.86 \pm 0.24$  on WBS and  $2.8 \pm 0.19$  on SPECT ( $p < 0.05$ ). Because of the high uptake of radiopharmaceutical, and widespread metastases, five pts were indicated for radionuclide therapy with 90-Y-DOTA TATE, and three of them received it.

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**Conclusion:** Preliminary results show that scintigraphy with  $^{99m}\text{Tc}$ -Tektrotyd is useful method in diagnosis, staging and follow-up of pts suspected to have lung carcinoids and other lung cancer.

**E4704****The inhibitory effect of peroxisome proliferator-activated receptor- $\gamma$  ligands on malignant pleural mesothelioma cell growth**

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**Background** Peroxisome proliferator-activated receptor- $\gamma$  (PPAR- $\gamma$ ) is a member

of the nuclear hormone receptor superfamily. PPAR- $\gamma$  ligands have been shown growth inhibition of several cancer cells.

**Objectives:** The aim of this study was to investigate the inhibitory effect of PPAR- $\gamma$  ligands on malignant pleural mesothelioma (MPM) cell growth.

**Methods:** Human MPM cell line, EHMES-10 was cultured in the presence or absence of PPAR- $\gamma$  ligands such as 15-deoxy- $\Delta^{12,14}$ -prostaglandin  $\text{J}_2$  (15d-PG $\text{J}_2$ ) and troglitazone (TGZ). WST-1 assay was used to detect cell proliferation. Apoptotic cells were detected by ANNEXIN V-FITC/7-Amino-Actinomycin-D staining.

**Results:** 15d-PG $\text{J}_2$  and TGZ inhibit EHMES-10 cell growth in dose- and time-dependent manners. In addition, 15d-PG $\text{J}_2$  and TGZ increased apoptotic cells in dose- and time-dependent manners.

**Conclusions:** These results suggested that 15d-PG $\text{J}_2$  and TGZ inhibit EHMES-10 cell growth via induction of apoptosis.