2. collapse with bronchioalveolar cell carcinoma (CwB), 3. adenocarcinoma cells (Cells), 4. fibroblasts (F), and 5. mucus (M). Areas of air-type adenocarcinomas (in 49 cases) demonstrated predominantly C and/or CwB (C/CwB type: in 46 cases). Areas of solid-type adenocarcinomas (in 69 cases), in comparison, demonstrated predominantly Cells and/or Cells/F (Cells/F type: in 66 cases). We noted a statistically significant difference between the histopathological findings of the areas of tumor opacity on mediastinal window images of air-type and solid-type tumors. In 34 cases, Cells/F type adenocarcinomas revealed microscopic evidence of metastasis (pleural involvement, vascular invasion, lymphatic permeation, or lymphnode metastasis). Whereas, no C/CwB type adenocarcinomas cases revealed any microscopic metastasis. The prognosis of C/CwB after resection is better than for Cells/F.

**Conclusion:** We found that ‘Air-type’ adenocarcinomas demonstrated C/CwB type, and that ‘Solid-type’ adenocarcinomas demonstrated Cells/F type. We concluded that the histopathological findings of small pulmonary adenocarcinomas could be classified into two groups: C/CwB type and Cells/F type. The prognosis of C/CwB is better than for Cells/F.

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**D04-02**  
Pathology, Thu, 12:30 - 14:15  

**Anceusomy by FISH analysis and histology as predictors of invasive lung cancer in bronchial biopsies from high risk subjects**


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**Background:** The development of Lung Carcinoma (LC) is accompanied by changes in histological and chromosomal abnormalities in the airway mucosa. Neither histological grade nor markers of chromosomal abnormalities in preneoplastic epithelial lesions have been adequately validated as predictors of invasive LC.

**Methods:** Histological dysplasia score and chromosomal aneusomy measured by FISH analysis were compared as correlates of invasive LC in a case-control study of 44 individuals with LC (cases) and 90 individuals without LC (controls). We used bronchial biopsy samples from subjects found by LIFE or white light bronchoscopy to have had moderate dysplasia (MD), severe dysplasia (SD) or carcinoma in situ (CIS). Tissue samples were reviewed by the study pathologist, the grades of preneoplastic change were verified and the appropriate areas in each histological slide were selected for FISH analysis. A 4-color FISH probe was used for aneusomy detection targeting centromere 6, 5p15.2, 7p12 (EGFR) and 8q24 (CMYC). Three or more copies for two or more of these DNA targets indicated an aneusomic cell. Premalignant lesions were classified as aneusomic when displaying aneusomic cells above the threshold defined in normal bronchial epithelium (mean + 3 SD).

**Results:** The population included 104 males and 30 females with a mean age of 64 years and a mean smoking history of 62 pack-years. There was no difference in mean age, sex distribution or pack-years of smoking between LC cases and controls, but cases had a higher frequency of current smokers (p=0.05). Thirty two had CIS as the highest histological grade of mucosal abnormality, 48 had SD and 54 MD. The strongest correlate with invasive LC was CIS by histological examination (OR=12.5, 95% CI 4.1 to 38.1). Chromosomal aneusomy was seen in 64% of the LC cases but in only 31% of the controls. (OR = 4.6, 95% CI 2.0 to 10.9). The proportion of subjects with chromosomal aneusomy increased from moderate dysplasia (22.2%) to severe dysplasia (41.7%) and CIS lesions (71.9%) and showed a similar trend for cases and controls. Presence of aneusomy slightly increased the risk for LC in MD (OR=1.91, 95% CI 0.26 to 13.8) but was a substantial impacting factor in subjects with SD (OR=7.06, 95% CI 0.82 to 60.1) and CIS (OR=5.93, 95% CI 0.5 to 69.7).

**Conclusions:** CIS on histological examination and abnormal FISH analysis are both associated with lung cancer cross-sectionally. Future studies need to examine these biomarkers prospectively, and to assess their interaction in predicting lung cancer risk.