while the benign ones were composed of inflammation nodules, inflammatory granuloma, fungal infection, and fibrosis. Density of malignant nodules included solid (n=10), mGGN (n=11) and pGGN (n=5), while that of benign ones included solid (n=19) and mGGN (n=4). The most frequent mutations detected were EGFR and TP53. Differentially methylated positions (DMPs) were filtered using the following criteria: 1). With adjusted p-value less than 0.05; 2). Locate in the promoter region of cancer-driving genes. 3). Correlated with the expression of the corresponding gene in the TCGA-LUAD dataset. Afterward, features composed of 285 DMPs and the mutation status of EGFR or TP53 were further filtered by recursive feature elimination using a random-forest classifier, and 6 features produced the highest nested-cross-validation score in the training set were selected. A random-forest classifier based on them generated a performance of 95.83% in the training set. Genes where the 6 features locate in were *PREX1, GGTLC1, MEST, CLEC14A*, and *LTC4S*. As the enrolled patients were all nodule harboring, our foremost goal is to identify the benign ones, i.e. to improve the specificity of the classifier. So we evaluated the prediction probability threshold in an independent validating set, which demonstrated the default threshold (probability $>$ 0.5) created the best specificity. The random-forest classifier was then tested in an independent testing set, resulting in an accuracy of 87.10%, a sensitivity of 81.25%, and a specificity of 93.33%. **Conclusion:** We identified 6 CpGs and created a random-forest classifier using them, which could distinguish early-stage lung adenocarcinomas from benign pulmonary nodules with a sensitivity of 81.25% under a specificity of 93.33%. As all of them locate in promoter regions of cancer-driving genes, the 6 CpGs are well worth further validating in blood. **Keywords:** Early-stage lung adenocarcinomas, Benign pulmonary nodules, Random-Forest classifier

P38 PATHOLOGY - PATHOLOGY/STAGING

P38.01
The Role of Pathology in The Proposed Subdivided N Descriptors of The TNM Staging System For Lung Cancer— A Single Center Experience

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Introduction: IASLC has proposed to subdivide N descriptors of TNM Staging for lung cancer into N1a (single N1 station), N1b (multiple N1 stations), N2a1 (skip metastases), N2a2 (single N2 with N1 involvement) and N2b (multiple N2 stations). The lymph nodes (LNs) on resection specimens have been dissected and reported separately according to their stations in our department over the years. The aim of this study is to evaluate the survival differences between pathologically confirmed subdivided N descriptors and to examine the value of other parameters related to N1 LNs such as the number of metastasis in a single LN station, size of the largest metastasis, extranodal invasion, and metastasis defined by direct infiltration of the primary tumor. **Methods:** The analysis was conducted on data from 630 NSCLC patients who underwent surgical treatment between 2008-2019. The IASLC nodal map and anatomical definitions were used to describe regional lymph node stations. Survival analysis was done with Kaplan Meier method. **Results:** Among 630 patients, 193 showed pathological nodal involvement (128 N1, 65 N2). The distribution of cases into the subdivided N categories were as follows: 437 were N0, 88 were N1a, 40 were N1b, 13 were N2a1, 42 were N2a2, and 10 were N2b. The mean number of LNs dissected by pathologists was 12.10±7.31, sampled by surgeons was 7.56±5.84. Overall survival (OS) rates of the subdivided N descriptors- regardless of T stage, histologic type, adjuvant therapy- were significantly different: 85.9% for N0, 77.2% for N1a, 66.1% for N1b, 76.2% for N2a1, 33.5% for N2a2 and 44.4% for N2b ($p<0.001$). Multiple LN station involvement is found to be an unfavorable prognostic sign both for N1 and N2 cases (N1a vs N1b) (N2a1 vs N2a2, N2b). Patients with only single N2 involvement (skip metastasis) had a better OS then multiple N1 involvement (N2a1 vs N1b) ($p<0.001$). Among N1 cases (n:128) the number of involved LNs in a single station (1 LN/ $>$1 LN), extracapsular invasion (absent/ present), and the size of the largest metastasis did not show any significant difference in survival rates ($p>0.005$). Patients having metastases in distally located N1 stations (13, 14), and metastasis defined by direct extension of the primary tumor into the lymph nodes showed a favorable survival; all patients were alive. However, statistical analysis could not be done for these groups due to the limited number of cases. **Conclusion:** Evaluation of N1 LNs is under the responsibility of pathologists; they should be dissected and reported according to their stations. As proposed by IASLC, single or multiple N1 station involvement shows a survival difference. In contrast, presence of one or more metastatic lymph nodes in a single N1 station does not seem to have a prognostic value. Distal or proximal LN involvements, LN metastasis caused by direct infiltration of the primary tumor may have an effect on survival. Studies in larger multi-institutional series should be conducted. In addition, the favorable prognosis of N2a1 cases in our series is remarkable and should further be evaluated in detail. **Keywords:** Lung cancer staging, 8th TNM classification, lymph node sampling

P38.02
Reproducibility and Accuracy of Intra-Operative Assessment on Tumor Spread Through Air Spaces in Stage 1 Lung Adenocarcinomas

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Introduction: STAS has been associated with worse prognosis in patients with early-stage lung adenocarcinoma, particularly those undergoing sublobar resection. Intra-operative consultation (IC) of STAS has been advocated by some surgeons to guide surgical management. However, to date, information regarding the reproducibility and accuracy of frozen section (FS) for STAS diagnosis is limited. Thus, we assessed inter-observer (IOA) and intra-observer agreement among pathologists evaluating STAS in FS, and its diagnostic yield for detecting STAS. Preliminary data were previously presented at a conference and we now report the results of more detailed analyses with a larger study cohort. **Methods:** We retrospectively evaluated 100 T1 lung adenocarcinoma resections assessed by IC and with ample non-neoplastic lung parenchyma in FS slides. A consensus panel of 3 pathologists jointly reviewed all histology slides, documented the diagnosis on STAS (+/-) and artifacts (+/-) per published criteria (Kadota, 2015), and recorded several histological parameters in each case. Five pulmonary pathologists blinded to clinicopathologic data, independently reviewed FS slides in each case on two separate rounds, and recorded the presence of STAS and artifacts per same criteria. The second round occurred after a consensus conference in which selected cases with low IOA were discussed. IOAs on STAS were assessed using the *Fleiss-kappa* statistics and were correlated with several pathologic features including the presence of artifacts. Diagnostic yield was determined by comparing consensus diagnoses made by $\geq$3 observers in the FS slide with the final diagnosis of the consensus panel, and assessed by receiver operating characteristic curves (ROC). **Results:** There was a high variability in the