DECEMBER PULMONARY PATHOLOGY JOURNAL CLUB

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3. Molecular Analysis of Peripheral Lung Adenocarcinoma in Brush Cytology Obtained by EBUS Plus Fluoroscopy-Guided Bronchoscopy. Sánchez-Font A et al. Cancer Cytopathol 2018; 126:860

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11. Targeted Sequencing Analysis of Pulmonary Adenocarcinoma with Multiple Synchronous Ground-Glass/Lepidic Nodules. Park E et al. JTO 2018; 13:1776

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14. Optimization and validation of PD-L1 immunohistochemistry staining protocols using the antibody clone 28-8 on different staining platforms. Koppel et al. Mod Pathol 2018; 31:1630

<u>Non-neoplastic</u>
1. Lung histopathology of non-infectious pulmonary complications after allogeneic haematopoietic stem cell transplantation. Meignin V. Histopathology 2018; 73:832

2. Local vs. systemic pulmonary amyloidosis—impact on diagnostics and clinical management. Baumgart JV et al. Virchows Archiv 2018; 473:627-637

Case Report

1. Primary tracheal hyalinizing clear cell carcinoma. Icard et al. Lung Cancer 2018; 125:100.

Review articles

The Seminars in Diagnostic Pathology is dedicated to lung pathology including several reprints of prior articles from 2007

1. Reprint of: Pathologic manifestations of Immunoglobulin(Ig)G4-related lung Disease. Yi ES, Sekiguchi H, Peikert T, Ryu JH, Colby TV. Semin Diagn Pathol 2018; 35:347

2. Reprint of: Unusual non-neoplastic lesions of the lung. Moran CA, Suster S. Semin Diagn Pathol 2018; 35:339

3. Reprint of: Nonspecific interstitial pneumonia: pathologic features and clinical implications. Myers JL. Semin Diagn Pathol 2018; 35: 334

4. Reprint of: The pathology of pulmonary sarcoidosis: update. Ma Y, Gal A, Koss M. Semin Diagn Pathol 2018; 35:324

5. The utility of bronchoalveolar lavage in the evaluation of interstitial lung diseases: A clinicopathological perspective. Gharsallia H, Mlikab M, Sahnouna I, Maaleja S, El Gharbia LD, El Meznib F. Semin Diagn Pathol 2018; 35: 280

6. Interstitial lung disease: Elementary lesions and diagnosis. Mlika M, Braham E, Mezni F. Semin Diagn Pathol 2018; 35: 288

7. Interstitial lung diseases: Imaging contribution to diagnosis and elementary radiological lesions. Nejia H, Attiaa M, Affes M, Baccouchea I, Miled-M'rada KB, Hantous-Zannada S. Semin Diagn Pathol 2018; 35:297

8. Clonality assessment of multifocal lung adenocarcinoma by pathology evaluation and molecular analysis. Sun W et al. Human Pathol 2018; 81:261

9. Pulmonary disorders that are potentially associated with anti- neutrophilic cytoplasmic antibodies: A brief review. Mark R. Wick. Semin Diagn Pathol 2018; 35:304

I. ARTICLES FOR DISCUSSION

1. Current and Future Management of Malignant Mesothelioma: A Consensus Report from the National Cancer Institute Thoracic Malignancy Steering Committee, International Association for the Study of Lung Cancer, and Mesothelioma Applied Research Foundation. Tsao AS et al. JTO 2018; 13:1655

This article reviews existing data on the current knowledge of genomics, therapies in early-stage and unresectable MPM, identifying gaps and proposing areas standardization for future clinical trials.

Pertinent to us includes need for:

- Standardization in pathology reporting and definition of core panel of biomarkers
- Translational studies in early and unresectable MPM
- Need to standardized what biospecimens should be collected and how in the era of NGS
    - All future trials should have translational correlates, pre-, during and post- and with progression
    - Specimens should include blood, pleural effusion, tumor tissue (1ary and metastasis)
    - SOPs for collection techniques for all specimens
- Also need to standardize how to process and store biospecimens, and what additional information to add.

Several consensus manuscripts to be published in these various areas of gap and for us, 2 planned manuscripts: 1) Pathology manuscript for the standardization of specimen collection and reporting, and 2) Translational correlate manuscript for the standardization of research specimen collection and use.

2. Pathologic Grading of Malignant Pleural Mesothelioma: An Evidence-Based Proposal. Pelosi et al. JTO 2018; 13:1750

Aim

Develop an innovative and reproducible grading score using only parameters that are common and reproducible, readily accessible to clinicians.

Material and methods

- Multicenter (5 centers) in Italy, retrospective, divided into training set of 328 patients and validation set of 612 patients.
- Clinical charts abstracted for demography, OS, staging, type of treatments and type of specimen
- Dx confirmed by 2 pathologists and various parameters recorded: %necrosis, subtype, cell atypia (mild, mod, severe), nucleoli (inconspicuous, disctinct, macro), mitotic count/mm2, Ki-67 hotspot. These parameters were compared between the 2 pathologists in 128 cases for interobserver variability.
- Various statistics to build a Pathologic Grossing System (PGS) predicting outcome

Results

- Mostly older males, with tumor staging in 39%, and difference in palliative chemo between the training and validation set. *Differences between training and validation set but no p values to see if significant or not*
- Epithelioid or biphasic with predominant epithelioid most common subtype
- 1/3 cases with necrosis, mod to severe atypia in >50%, with Ki-67 >30% and >3 mitosis/mm2
- Ultimately, based on interobserver variability, excluded cell atypia and nucleoli from the PGS.
- Based on the multivariate analysis, necrosis (absent vs present), subtype (epithelioid/biphasic versus sarcomatoid), Ki-67 <30% versus $\geq$ 30%, and mitosis (1-2, 3-5, 6-9, $\geq$10) were included in the PGS score
- Predicting 12 month mortality with AUC of > 0.7, better than Ki-67 or mitotic count alone.
- PGS 0 vs 1-3 vs 4+ that created 3 distinct survival curves in testing (median 26.2 mos vs 12.8 vs 3.7) and validation (med 26.9 vs 14.4 vs 7.7) although PGS although in validation the difference a little smaller for 1-3 vs 4+

Conclusion

Overall good study that creates a potentially useful grading score, not unlike other developed grading score in other tumor types. It should be tested in a large independent cohort to see if it stands as providing these parameters are not part of our routine practice and not included in our synoptic reports.

3. A combination of MTAP and BAP1 immunohistochemistry is effective for distinguishing sarcomatoid mesothelioma from fibrous pleuritic. Kinoshita Y et al. Lung Cancer 2018; 125:198

Aim

To study MTAP, instead of FISH for 9p21, in association with BAP1 in the differential diagnosis of fibrosing pleuritic versus sarcomatoid MM

Material and methods

- 30 cases of MM biphasic or sarcomatoid and 17 cases of pleuritic (proven clinically/radiologically to have no progression over 1 year of FU).
- IHC for BAP1 and MTAP and FISH for 9p21
- Statistical analysis

Results

	MM	PLEURITIS	Sensitivity/Specificity
	Loss	Loss	
MTAP IHC	24	0	80/100
BAP1 IHC	11	0	36.7/100
FISH 9p21	28	0	93.3/100
MTAP-BAP1	27	0	90/100
FISH- BAP1	30	0	100/100

Conclusion

In our practice, FISH has proven not useful and takes 2 weeks if not more for a result. So based on their result, would look at adding MTAP to our battery of IHC

4. IMP3 as a prognostic biomarker in patients with malignant peritoneal mesothelioma.
Hui S et al. Human Pathol 2018; 81:138
Background and aim
- IMP3 (insulin growth factor mRNA-binding protein 3) expressed in several malignant tumor and high expression would be associated with poor prognosis.
- Fli-1 regulates expression of genes involved in vessel formation, invasion and metastasis and its expression has not been not studied in mesothelioma
- Study aims at assessing expression of IMP3 and Fli-1 in Peritoneal MM (PMM) and assess their prognostic role and correlation with proliferation activity.

Methods
- 44 patients with diagnosis of PMM over 4 years
    - Determined the T stage using a peritoneal carcinomatosis index (PCI) as previously published based on size and extent (Cancer 2011) with T1= score 0-10, T2= score 11-20, T3= score 21-30 and T4= score 31-39

- IHC for IMP3, Fli-1, Ki67
    - IMP3 and Fli-1 scored as 0 (<5%+ cells), to 3 + (>50%+ cells) in increment of 25%, with 0 being negative, 1-3+ positive
    - Division into 4 groups, both IHC neg, IMP3 only +, Fli1 only + and both +
    - Ki-67 divided into low (10% or less), and high >10%

Results
- Median OS was 7 months
- Almost all cases (42/44) were positive for Fli-1 versus 23 (of 44) for IMP3
- No correlation between age and sex and IMP3 and Fli-1
- Correlation between Epithelioid versus non epithelioid, low and high Ki67 and higher score of IMP3 and Fli-1
- In a multivariate analysis, the only variables that indicated poor prognosis was treatment and IMP3 (as negative versus positive); not PCI, stage, Fli-1, combo IMP3 and Fli-1 or Ki67

Conclusion
Another biomarker to add to a list of potential prognostic biomarkers.

5. Malignant peritoneal mesothelioma in patients with endometriosis. Butnor KJ et al. J Clin Pathol 2018; 71:971

Aim

To report on 6 women with peritoneal MM in the setting of endometriosis

Methods

- Retrospective review searching for diagnosis of PMM and endometriosis.
- DX of MM was based on the WHO criteria and the DX of endometriosis was based on clinical data and/or pathologic confirmation.
- If lung tissue was available, asbsestos fiber content was performed

Results

- 6 women identified
  - 1 from the surgical files of one institution
  - 5 from consult practice of 231 women with MM over 7 year period
- Med age at dx was lower with patients with endometriosis than without
  - 44.5 yrs (29-55 yrs) versus 58.0 yrs
- 5 epithelioid and 1 biphasic
- Classic immunoprofile with only 1 case of faint ER/PR and 1 case of weak MOC-31
- 3 cases of MM dx concurrently with endometriosis; 3 had prior dx of endometriosis (5-30 yrs).
- 2 with possible history of asbestos exposure and lung analyzed in another case which did not show asbestos fibers
- Information on treatment outcome from records incomplete
- Outcome was based on a search of the Social Security Death Index
  - 1 death at 1 yr
  - 5 others not recorder as dead, 4 months to 12 years following diagnosis

Conclusion

Endometriosis is a possible risk factor for PMM in women

6. Investigating unilateral pleural effusions: the role of cytology. Arnold DT et al. Eur Respir J 2018; 52: 180

Aim

To assess the ability of using cytology on pleural effusions for the diagnosis of malignancy in a larger prospective cohort using modern ancillary testing

Methods

- Cohort
    - Consecutive patients, single-center, undiagnosed unilateral pleural effusion
    - All underwent a diagnostic thoracentesis
    - 12 months FU or until death
- Pleural fluid analysis (transudate versus exudate)
- Cytology and IHC if suspicious (EMA, BerEp4, CK5/6, calretinin- if AD,CK7/20, TTF-1, ER/PR, Ca125), flow for lymphoma.
    - "non-dx" if clinically suspicious for malignancy with a neg cytology and required additional procedure.
- Malignancy defined as
    - Positive cytology or biopsy
    - Histologically confirmed pulm/extrathoracic malignancy with radiographic evidence of met to ipsilateral pleura
    - Radiologic changes c/w progression to malignancy
    - Autopsy confirming pleural malignancy

Results

- 8 year period, 921 consecutive patients, male predominant, mean age 70.2 yrs
- 515 (56%) with confirmed diagnosis of malignancy in the 12 month FU
    - Lung 166, 32%; Mesothelioma 148, 29%
    - Sensitivity of pleural effusion for diagnosing malignancy varied between 0 (sarcoma/melanoma) to 94.7% (ovarian carcinoma) according to primary tumor site and cell type, with a mean sensitivity of 46.4%
        - Lung AD 82%, Lung SQCC 14.3%, SCLC 43.8%
        - Mesothelioma 6.1% - 94% therefore required a biopsy for definitive diagnosis (*BAP-1 or other not included as part of their panel)
    - 276 non-diagnostic effusions, 248 had follow-up tissue confirmation of malignancy
- Information that added value for risk of malignancy included exudative effusion, female sex, male with prior history of cancer or asbestos exposure.

Conclusions

Their results are on par with prior reports and explain the variability of the sensitivity as it is much influenced by the proportion of various primary tumor sites and cell types.

II. Articles for notation

Neoplastic

1. Identification of Grossing Criteria for Intraoperative Evaluation by Frozen Section of Lung Cancer Resection Margins. Gagné A et al. Am J Surg Pathol 2018; 41:1495

In the background, the authors state that there is a lack of standardized approach and evidence based recommendation for when to do frozen sections to assess margins. In this retrospective study, the authors studied margins, bronchial or parenchymal, from 2299 specimens from 1903 consecutive specimens and assessed clinical impact from positive margins. This was followed by a validation study. There was a low incidence (4%) of positive margins, higher for parenchymal than bronchial but in almost half, a new resection margin was performed, which decreased the incidence of positive margin to 2%. ROC curves confirmed that the tumor-margin distance was the best indicator of positive margin. Based on sensitivity and false negative rates, only gross margin of 2 cm or less for both parenchymal and bronchovascular margins could be assessed on frozen with a risk of missing a margin in 0.6%. Well done study, worth considering for our practice.

2. Correlation Between Programmed Death Receptor-1 Expression in Tumor-Infiltrating Lymphocytes and Programmed Death Ligand-1 Expression in Non–Small Cell Lung Carcinoma. del C. Monroig-Bosque P et al. Arch Pathol Lab Med 2018; 142:1388

The authors focused the study of the expression of PD-1 and PD-L1, the correlation with TILs and prognostic significance in Stage I NSCLC of 161 patients identified between 1975 and 1991. 42% of NSCLC were PD-L1 TC$\geq$ 50% and 47% with PD-1$\geq$ 1%, with positive correlation between PD-1 in TILs with PD-L1 TC expression and for the most part with PD-L1 in ICs. There was no association with disease-specific survival with PD-1/PD-L1 score.

3. Molecular Analysis of Peripheral Lung Adenocarcinoma in Brush Cytology Obtained by EBUS Plus Fluoroscopy-Guided Bronchoscopy. Sánchez-Font A et al. Cancer Cytopathol 2018; 126:860

The goal of this prospective study is to assess feasibility of testing for *KRAS* and *EGFR* mutations on brush cytologies for peripheral lesions obtained from radial- miniprobe endobronchial ultrasound transbronchial biopsy and correlating the results to those obtained from histological samples. In the 43 cytology samples, molecular testing was feasible in all and a mutation in either gene was identified in 16 patients, with correlation to biopsy being 87% with 2 false negative on cytology. These results are comparable to other molecular cytology studies.

4. Molecular Genetic Alterations in Thyroid Transcription Factor 1–Negative Lung Adenocarcinoma in Cytology Specimens: A Subset With Aggressive Behavior and a Poor Prognosis. Rodriguez EF et al. Cancer Cytopathol 2018; 126:853

The authors assessed the prognosis and molecular alterations in cytology specimens of 50 TTF-1 negative AD and contrasted the results to 210 TTF-1 positive AD. There was a change in the molecular testing during the span of this retrospective study which resulted in a subset of AD having an expanded gene panel tested. TTF-1 neg AD had a worse prognosis (although there was no multivariate analysis done) and has fewer mutations in EGFR and KRAS but more rearrangements in ALK. These results are comparable to other studies.

5. TERT promoter mutations in solitary fibrous tumour. Demicco EG et al. Histopathol 2018; 73:843
TERT mutation occurs in up to 20% of SFT and studies have suggested TERT mutation to be prognostic. The authors assessed TERT mutation in the setting of their risk prognostication score. They studied 216 tumors (189 of which could be sequenced) stratified according to their risk prediction model. 30% were intrathoracic and more commonly mutated (30%). TERT mutation did not add value to their risk model except for intermediate risk tumors which had a shorter time to metastasis if mutated.

6. Histomorphometric evaluation of the Ki-67 proliferation rate and CD34 microvascular and D2-40 lymphovascular densities drives the pulmonary typical carcinoid outcome. de Vilhena AF et al. Hum Pathol 2018; 81:201
The authors studied the role of Ki-67, angiogenesis through CD34 and lymphangiogenesis through D2-40 in the prognosis (using overall survival) of 128 typical carcinoid tumors, as defined by the WHO. Morphometry was used to quantify all 3 IHC. The results of the IHC correlated with stage and its various parameters. Based on multivariate, CD34-MVD of <7% seems to distinguish longer versus shorter term survival.

7. Roles of human epidermal growth factor receptor family in pulmonary lymphangioleiomyomatosis. Kobayashi K et al. Hum Pathol 2018; 81:121
The aim of this study is to assess the status of the various HER, which are upstream receptors of mTOR, as potential therapeutic targets for LAM, on 34 explants. RKT signaling antibody array was performed in 4 cases, IHC for EGFR, HER2, HER3 and HER4 in all, and qRT-PCR in 8. They did not look for mutations in EGFR. Results are underwhelming and not very convincing. Expression by the array and some by qRT-PCR (not for Her2) and the IHC pictures they show is mostly cytoplasmic staining.

8. Clonality assessment of multifocal lung adenocarcinoma by pathology evaluation and molecular analysis. Sun W et al. Human Pathol 2018; 81:261
The authors look at the role of lepidic growth pattern, along with the comprehensive histologic assessment, EGFR/KRAS mutations and using CGH array as gold standard to distinguish independent primaries from intrapulmonary metastasis. The problem is CGH array is a flawed method as gold standard, EGFR and KRAS mutations well known to be too prevalent to be used for clonality. And confirmed the reason IASLC determined LPA/MIA and AIS should have a separate staging as these are all likely to be independent by definition.

9. Analysis of a large cohort of non-small cell lung cancers submitted for somatic variant analysis demonstrates that targeted next-generation sequencing is fit for purpose as a molecular diagnostic assay in routine practice. Moore DA et al. J Clin Pathol 2018; 71:1001
The authors studied the clinical impact of using NGS for the detection of molecular abnormalities in a retrospective study of 2796 samples of NSCLC over 3 years. NGS analysis was performed using the Oncomine Solid Tumour Panel (22 gene panel) for DNA mutations only. 8% rejected for insufficient tumor content, another 5% with failure, TAT of 7 working days and a little more than 60% with an identified driver mutation. Study confirms the feasibility of current practice in most institutions, and in US, even broader panels commonly used. No discussion on cost and since NHS in UK.

10. An Integrative Analysis of Transcriptome and Epigenome Features of ASCL1–Positive Lung Adenocarcinomas. Miyashita N et al. JTO 2018; 13:1676
This study focused on ASCL1+ AD, a group of AD with NE differentiation. The authors performed extensive molecular and functional studies that suggest that ASCL1 would be a master transcriptional regulator and ASCL1+ AD have a distinct molecular phenotype.

11. Targeted Sequencing Analysis of Pulmonary Adenocarcinoma with Multiple Synchronous Ground-Glass/Lepidic Nodules. Park E et al. JTO 2018; 13:1776
There were 2 goals to this study 1- Compare molecular profile of synchronous AAH/AIS/MIA/LPA and 2- Assess these profiles as part of step wise progression. Only looked at mutations with a targeted panel. No major surprises. EGFR was the most frequently mutated gene and same mutation commonly shared amongst the synchronous lesions. Mutations were identified in AAH and the average mutation rate increased between AAH and LPA. There was intratumoral heterogeneity between the lepidic and invasive components within a tumor but the driver mutations remained the same.

12. Clinicopathological and genomic comparisons between different histologic components in combined small cell lung cancer and non-small cell lung cancer. Lung Cancer 2018; 125:282
The background of the study is based on reports of Adenocarcinoma transforming into SCLC after chemotherapy or therapy with EGFR inhibitors. Furthermore, there has been no study looking at the mutational statuses of these tumors. The authors studied 4 combined SCLC and 4 cases of AD transforming into SCLC after treatment. IHC and sequencing for mutations and fusions and analyzed each components in the case of combined and each tumor AD/SCLC in cases of transformation. The results show that when detected, *EGFR, p53, RB1* mutations were detected, they were identical between both components/tumors. Same for *PIK3 and PTEN*. There were additional mutations in the SCLC of the combined cases and transformation in the *TSC1* gene, as well as *MYC and TERT* amplification. Interesting results supporting same cell giving rise to 2 different components.

13. Comparative study of programmed cell death ligand-1 immunohistochemistry assays using 22C3 and 28-8 antibodies for non-small cell lung cancer: Analysis of 420 surgical specimens from Japanese patients. Saito et al. Lung Cancer 2018; 125-230
Using a cohort of 420 NSCLC, the authors compared the overall percent agreement, positive and negative percent agreement between PD-L1 clones 22C3 and 28-8 at cut-offs of 1, 25 and 50%. Overall percent agreement was high, 89% and above but there was discordance for the positive percentage agreement such that 22C3 was more sensitive and resulted in having more cases positive at various cut-offs compared to 28-8 clone. Results difficult to understand but seems like all platforms performed in a similar way.\

14. Optimization and validation of PD-L1 immunohistochemistry staining protocols using the antibody clone 28-8 on different staining platforms. Koppel et al. Mod Pathol 2018; 31:1630
The authors assessed PD-L1 clone 28-8 using 4 different platforms 1- Dako Autostained Link 48, Dako Omins, Leica Bond-III and Ventana BenchMark ULTRA) on NSCLC, melanoma,

H&N cancers. Control tissues were used for specificity and sensitivity. They assessed inter- and intra-assay reliability at cut-offs of 1, 5, 10 and 50%.

Non-neoplastic

1. Lung histopathology of non-infectious pulmonary complications after allogeneic haematopoietic stem cell transplantation. Meignin V. Histopathology 2018; 73:832

The authors looked at the histologic patterns of non-infectious pulmonary complications following allogenic hematopoietic stem cell transplant in 61 patients. A little more than half had airway disease, including bronchiololectatis and obliterative bronchiolitis. 41% had both airway and interstitial lesions, classifiable as OP (8), NSIP (10), DAD (6), LIP (1) and PPFE (3). Overall good article to reference. The only question would be can PPFE be considered a complication of stem cell transplant.

2. Local vs. systemic pulmonary amyloidosis—impact on diagnostics and clinical management. Baumgart JV et al. Virchows Archiv 2018; 473:627-637

In this retrospective study, the authors studied 207 bronchial and lung specimens (biopsies or resections) from 205 patients with proven amyloid, assessing the different types of amyloid between localized and diffuse amyloidosis, the clinical correlation and prognosis. Their method of amyloid typing was IHC, which is the main limitation of this study. AL was the most prevalent type seen in 88% of cases (Lambda 68%, Kappa 13% and indeterminate in 7%). ATTR was seen in 10% and AA in 1%, mixed amyloid with more than 1 stain in 0.5%. The demographics, clinical and radiologic information, histologic distribution, prognosis was similar to previous reports. So nothing new from this study.

Case Report

1. Primary tracheal hyalinizing clear cell carcinoma. Icard et al. Lung Cancer 2018; 125:100.

First case report of a clear cell carcinoma arising in the trachea, confirmed with FISH for *EWSR1.* Another salivary-type carcinoma to add to our list of those arising in the trachea-bronchial tree.

Review articles

The Seminars in Diagnostic Pathology is dedicated to lung pathology including several reprints of prior articles from 2007

1. Reprint of: Pathologic manifestations of Immunoglobulin(Ig)G4-related lung Disease. Yi ES et al. Semin Diagn Pathol 2018; 35:347

Comprehensive review of the clinical, radiologic and pathologic manifestations of IgG4 disease in the lung. A must have!

2. Reprint of: Unusual non-neoplastic lesions of the lung. Moran CA, Suster S. Semin Diagn Pathol 2018; 35:339

Questionable inclusion of inflammatory pseudotumor in this review but it was 2007. Also discusses placental transmogrification, pulmonary alveolar microlithiasis, and metastatic calcification.

3. Reprint of: Nonspecific interstitial pneumonia: pathologic features and clinical implications. Myers JL. Semin Diagn Pathol 2018; 35: 334
Everything you need to know about NSIP.

4. Reprint of: The pathology of pulmonary sarcoidosis: update. Ma Y et al. Semin Diagn Pathol 2018; 35:324
An update is relative but some topics are timeless.

5. The utility of bronchoalveolar lavage in the evaluation of interstitial lung diseases: A clinicopathological perspective. Gharsallia H et al. Semin Diagn Pathol 2018; 35: 280
Excellent review on the role of BALs in the diagnosis of ILD. Clinicians routinely use BAL to narrow their differential diagnosis. Although it often remains broad in some instances can be relatively specific. Nice tables providing the necessary information. In the future, BALs can be used to apply genomics and proteomics promising added value.

6. Interstitial lung disease: Elementary lesions and diagnosis. Mlika M et al. Semin Diagn Pathol 2018; 35: 288
Well written review using an algorithmic approach to diffuse lung diseases, with localization of histologic abnormalities, patterns of injuries and types of infiltrates. Good article to share with trainees.

7. Interstitial lung diseases: Imaging contribution to diagnosis and elementary radiological lesions. Nejia H et al. Semin Diagn Pathol 2018; 35:297
Excellent review. The authors first review the normal anatomy on CT Scan, then explain the various abnormalities individually, like honeycombing, GGO, reticulation etc and how to diagnose these and the inherent challenges, and finally they go in the radiologic findings of different ILDs.

8. Pathologic features of smoking-related lung diseases, with emphasis on smoking-related interstitial fibrosis and a consideration of differential diagnoses. Mark R. Wick. Semin Diagn Pathol 2018; 35: 315
This review goes beyond smoking related diseases and emphasis Smoking-related Interstitial Fibrosis, with an attempt at clarifying the concept of SIRF.

9. Pulmonary disorders that are potentially associated with anti- neutrophilic cytoplasmic antibodies: A brief review. Mark R. Wick. Semin Diagn Pathol 2018; 35:304
Overall nice review. The focus is on the ANCA-vasculitis's and there are several comprehensive tables for the differential diagnosis of vasculitis, ANCA positive entities and other.