# PULMONARY PATHOLOGY JOURNAL CLUB – November 2025
# (October 2025 print articles)
## November 24, 2025
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## Discussion Article

**Simon, AG, et al. Dedifferentiated Solitary Fibrous Tumor. A Clinicopathologic, Immunohistochemical, and Molecular Characterization of 25 Cases. American Journal of Surgical Pathology. 2025; 49:1015-1027.**

**Purpose:** This study aimed to investigate the clinicopathologic and molecular features of a large cohort of dedifferentiated solitary fibrous tumor (DDSFT) and to summarize previously reported cases through a comprehensive literature review.

**Methods:** The study cohort included 25 DDSFT cases. Immunohistochemical analysis was performed using antibodies against CD34, STAT6, TP53, and Rb. Targeted DNA sequencing was performed on dedifferentiated areas from 14 tumors using OncoPanel, which detects *NAB2::STAT6* fusion and secondary genetic alterations. A literature review of DDSFT cases published from 2009 to 2024 was also conducted.

**Results:**

**Clinical Features and Outcomes:** Table 1 summarizes the clinicopathologic features. The cohort included 13 males and 12 females, with a median age of 63 years. Most cases were primary tumors (84%). Tumor location included the pelvic cavity, thoracic cavity, and trunk. Based on the 3-variable model, 9 of 20 cases were classified as high risk.

**Pathologic Features:** All 25 cases contained areas of conventional SFT with an abrupt transition to a dedifferentiated component. DDSFT demonstrated highly variable morphology- including pleomorphic, epithelioid, spindle cell, and round cell patterns (Figure 1). Heterologous elements were present in 16% of tumors (Figure 2).

**Immunohistochemical Features:** STAT6 expression was identified in the conventional SFT component of all 19 tumors (100%). However, complete loss of nuclear STAT6 was observed in the dedifferentiated component of 36% of tumors, and reduced expression was observed in 9% (Figure 3).

**Molecular Features:** DNA sequencing revealed a *NAB2::STAT6* fusion leading to a truncated STAT6 transcript (STAT6-TAD) in 77% of tumors. Recurrent secondary alterations involved TP53 (71%), TERT (57%), and RB1 (21%) (Figure 4, 5).

**Literature Review:** Fifty-five additional DDSFT were identified in the literature (Table 3, Figure 6). STAT6 expression was present in 100% tumors of conventional components but was lost in 12.8% of dedifferentiated components. STAT6-TAD and STAT6-full length variants were the most common fusion types (Figure 5).

**Statistical Analysis:** Combined analysis of the study cohort and 55 published cases demonstrated that complete loss of STAT6 in DDSFT is associated with shorter disease-specific survival (HR 12.69, P= 0.023) (Figure 7, Table 4).

**Take home message:** Loss or reduction of STAT6 expression occurs in approximately one-third of DDSFT and represents an independent prognostic factor associated with shorter disease-specific survival.

**Comment:** These molecular findings improve our understanding of DDSFT progression. Loss of STAT6 may serve as a surrogate marker for genomic instability that contributes to the aggressive behavior of these tumors.

**Quaranta, A., et al. Loss of MTAP expression is not an accurate surrogate for CDKN2A homozygous deletions in peritoneal mesothelioma. *Histopathology* 2025;87:526–535.**

**Purpose**: Peritoneum is the 2nd most common anatomic site for mesothelioma after pleural mesothelioma. Homozygous deletion (HD) of CDKN2A, detected by FISH, is a recognized biomarker for distinguishing malignant mesothelioma from benign proliferations. Immunohistochemistry (IHC) for MTAP, a gene adjacent to CDKN2A, has been proposed as a surrogate for CDKN2A HD in pleural mesothelioma, but its diagnostic accuracy in peritoneal mesothelioma (PeM) remains underexplored. This study evaluates the reliability of MTAP IHC as a surrogate for CDKN2A HD in PeM.

**Methods**:

- Initially 50 PeM cases of either surgical resections or biopsies were selected. 14 benign mesothelial samples were selected as negative controls.
- FISH studies were performed on all 50 PeM. 11 cases were excluded because they did not meet the established quality criteria for FISH analysis.
- 39 PeM were included in the study cohort that was composed of 24 (61.5%) epithelioid, 12 (30.7%) biphasic, and 3 (0.8%) sarcomatoid PeMs.
- MTAP IHC was performed using antibody clone 2G4, with positivity assessed at both 1% and 30% cut-offs.
- Negative IHC result was defined by "faint"/weaker cytoplasmic expression than internal positive control or complete loss of cytoplasmic expression of MTAP.
- Concordance between MTAP IHC and CDKN2A FISH was evaluated using Cohen's Kappa statistic; diagnostic performance assessed via ROC curve analysis and McNemar's test.

**Results**:

- 69.2% (27/39) of PeM cases showed CDKN2A HD by FISH.
- MTAP IHC: Complete loss of MTAP observed in 33.3% (13/39) of cases (using 1% cut-off); applying a 30% cut-off, MTAP expression <30% was found in 56.41% (22/39) of cases. Intratumoral heterogeneity in MTAP staining was seen in 7 cases.
- Sensitivity of MTAP loss for CDKN2A HD was low (37%) and specificity moderate (75%) at the 1% cut-off; both decreased at the 30% cut-off (sensitivity 62%, specificity 50%).
- All control samples showed preserved MTAP expression and no CDKN2A HD.
- Concordance between MTAP IHC and CDKN2A FISH was low and not statistically significant (Cohen's Kappa < 0.1 for both cut-offs), indicating a lack of agreement of the two methods.
- ROC analysis indicated poor discriminatory value (AUC=0.569), i.e., MTAP IHC has limited predictive value for CDKN2A status.

**Take-home message**: MTAP IHC is not a sufficiently reliable surrogate for detecting CDKN2A HDs in PeM. While MTAP loss shows reasonable specificity using 1% cutoff, its low sensitivity and poor concordance with FISH-detected CDKN2A HD limit its diagnostic utility. Direct FISH analysis for CDKN2A remains advisable for routine diagnostics in PeM.

**Comment**: The data underscore the necessity of site-specific validation before extrapolating results from pleural to peritoneal mesothelioma. Notably, the study's conclusions are based on the use of a single MTAP antibody clone, and therefore may not be applicable to other MTAP antibody clones. Additionally, the study lacks detailed information about the FISH analysis, specifically whether it was conducted with a focus in regions exhibiting subclonal loss of MTAP by IHC.

**Ryerson CJ, et al. Standardized Clinical Terms and Definitions for Interstitial Lung Disease: A Consensus Statement from the Fleischner Society. American Journal of Respiratory and Critical Care Medicine. 2025;211(10):1756-1774.**

**Purpose**: The diagnosis and management of interstitial lung disease (ILD) is complicated by inconsistent and ambiguous terminology, leading to confusion for clinicians, researchers, and patients. This Fleischner Society Consensus Statement aims to define and standardize the clinical terminology for ILD diagnoses and major phenotypes, in order to improve communication and knowledge generation in the field.

**Methods**: The study design is illustrated in Figure 1. In detail, 10 ILD experts (including 3 thoracic pathologists) were interviewed to identify major clinical diagnoses and phenotypes, including preferred terms and rationales, with alternative terms noted. 60 ILD diagnoses were identified, which include 2 root terms (ILD and interstitial pneumonia) and another 8 terms with no alterative terms suggested in the literature or by the 10 committee members. A working Delphi group of 29 committee members (including 9 pulmonologists, 15 radiologists, 5 pathologists) evaluated the remaining 50 terms and rated agreement for preferred terms- as 5 (strongly agree), 4 (agree), 3 (neutral/unsure), 2(disagree), or 1 (strongly disagree). Terms with consensus (median score ≥4/5, interquartile range ≤1) were accepted. Terms lacking consensus were discussed via videoconference and reassessed in a follow-up survey.

**Results**:

- After Round 1, 47 out of 50 terms (94%) reached consensus on preferred terminology.
- The 3 terms that did not reach the threshold: alveolar macrophage pneumonia (AMP), idiopathic diffuse alveolar damage (DAD), and radiotherapy-associated lung injury.
- 3 additional terms were accepted on a second round of survey.
- Tables 1–9 list preferred and nonpreferred terms for each major category.
- Table 10 lists the terms with significant changes from previously used terminology.
    - iBIP replaces MDD diagnosis of HP in patients w/o an identifiable exposure
    - Alveolar macrophage pneumonia replaces DIP
    - iDAD replaces AIP
- Terms relevant to my daily clinical practice that I learned from this article include:
    - Interstitial lung abnormality: abnormal interstitial CT findings below the threshold for ILD
    - Progressive pulmonary fibrosis: need progression in at least 2 domains (clinical, physiologic, and radiologic), usually excluding IPF
    - Hypersensitivity pneumonitis is the preferred term over hypersensitivity pneumonia
    - iBIP, a provisional entity that replaces HP with no etiological exposure identified

**Take-home message**: This consensus statement provides standardized terminology for ILD clinical diagnoses and major phenotypes that should be used broadly in multidisciplinary care, clinical research, and communication.

**Comment**: The standardized clinical terms for ILD proposed here reflect the latest updates in the classification of interstitial pneumonia. While I agree with most of the changes introduced, I personally disagree with replacing "HP" with the less meaningful descriptive term "BIP/iBIP." This change contradicts the recently published 2020 guidelines on the diagnosis of HP and creates considerable confusion within the pulmonary community.

**Editorial: Oldham JM, Molyneaux PL. From Chaos to Clarity: Reassessing Interstitial Lung Disease Terminology. Am J Respir Crit Care Med. 2025;211(10):1733–1734.**

**Churg A, et al. A Brief Guide to Interpreting Transbronchial Cryobiopsies for Diffuse Parenchymal Lung Disease. Am J Surg Pathol. 2025;49(10):1068–1077.**

**Purpose**: Transbronchial cryobiopsies (CB) are increasingly used as an alternative to surgical lung biopsy (video-assisted thoracoscopic/VATS biopsy) for diagnosing diffuse parenchymal lung diseases (interstitial lung disease, ILD). The diagnostic criteria used in the interpretation of surgical (VATS) lung biopsies might not be suitable in the setting of CBs. This review article aims to propose a practical, structured approach for diagnosing ILD in CBs.

**Methods**: This is a review paper with no original data. The authors drew conclusions on their experience with over 1000 CBs and data from their recent studies totaling 240 patients with multidisciplinary diagnoses of UIP/ IPF, fibrotic HP, and CTD-ILD. They also included the reports of studies from Cooper et al (PMID: 33285079), Colby et al (PMID: 27588334), and Mehrad (PMID: 32320274).

**Results**: A stepwise approach is outlined in Figure 1:

- Step 1: Identify morphologically specific features (e.g., granulomas/sarcoidosis, Langerhans cell histiocytosis, aspiration, amyloidosis, and others) to make a specific diagnosis.
- Step 2: If absent, evaluate for characteristic architectural patterns, such as UIP and NSIP
    - Cooper et al (65 CB and VATS biopsies in the same patients): Fibroblast foci + patch old fibrosis, in the absence of alterative features, strongly favored a diagnosis of UIP/IPF (subpleural/paraseptal fibrosis or honeycombing had low sensitivity in CB as CB does not sample subpleural).
    - Churg et al (121 CB with MDD diagnosis of fibrotic HP (n=83) and IPF (n=38); 120 CB with MDD diagnosis of CTD-ILD): Expanded criteria: Fibroblast foci + patchy fibrosis/architectural distortion/honeycombing
    - Using either criteria, a UIP pattern in a CB is not specific to UIP/IPF but can be seen frequently in patients with fibrotic HP (53% of cases) and some patients with CTD-ILD (23% of cases).
    - If the initial section is nondiagnostic, deeper H&E levels are recommended to increase the chance to identify specific features (such as fibroblast foci and giant cells).
- Step 3: If there is no UIP pattern, look for NSIP pattern. The rules for diagnosing NSIP is similar to those for VATS biopsies.
    - NSIP pattern on CB strongly favored a diagnosis of CTD-ILD
    - NSIP+OP on CB predict a very high odds ratio for CTD-ILD
    - Lymphoid aggregates and plasma cell:lymphocyte ratio > 1:1 are of very limited use in CB and do not reliably separate IPF, fibrotic HP, and CTD-ILD.
    - Cellular NSIP + giant cells/granulomas strongly suggest a diagnosis of HP or drug reaction.
- CB pathology report:
    - Comment on how many pieces of lung parenchyma, bronchial wall alone, or bronchial wall and lung parenchyma have been sampled. This is important information to help the clinician to understand whether nondiagnostic CB is due to poor sampling or good sampling with no diagnostic features.
- Combining clinical and radiologic findings in the interpretation of CB is crucial.

**Comment**: This review provides much-needed practical guidance to pathologists working with transbronchial CBs in diffuse parenchymal lung disease. The proposed algorithm and discussion of pitfalls, strengths, and limitations fill an important knowledge gap.

**Articles for notation** (generated by ChatGPT with minimal human curation)

*Neoplastic*

**Suster DI, et al. Acantholytic squamous cell carcinoma of the lung with pseudoglandular features: clinicopathologic study of 14 cases. Virchows Archiv. 2025;487(5):619–628.**

**Summary**: This study reports 14 cases of acantholytic squamous cell carcinoma (SCC) of the lung with pseudoglandular features, a rare and diagnostically challenging histologic variant. These tumors exhibit a squamous phenotype by immunohistochemistry but mimic adenocarcinoma morphologically due to acantholysis (loss of intercellular cohesion) and formation of gland-like luminal spaces. These patterns sometimes coexist with entrapped alveolar structures, further complicating diagnosis. Molecular analysis (12/14 cases) revealed TP53 mutations in 66% of cases, with no mutations characteristic of adenocarcinoma. Other mutations included KIT, PIK3CA, IDH2, PTEN, and several copy number gains (e.g., FGFR1, KRAS) and losses (AR, ARAF).

**Take-home message**: Acantholytic SCC with pseudoglandular features is a rare but important diagnostic mimic of adenocarcinoma. Histologic overlap with adenocarcinoma or adenosquamous carcinoma can lead to misdiagnosis, especially in the absence of immunohistochemistry. p40 and CK5/6 positivity, along with negative TTF1/Napsin A, are key to proper classification.

**Takemura C, et al. Dynamic nature of hepatic differentiation in lung adenocarcinoma. Histopathology. 2025;87(4):565–572.**

**Summary**: This study investigates hepatic differentiation in lung adenocarcinoma, a rare phenomenon where tumor cells express hepatic markers such as HepPar1, glypican-3, and HNF4α. The authors were prompted by a lung adenocarcinoma case showing cytoplasmic TTF-1 expression, a feature characteristic of hepatocytes. Using two cohorts (123 resected tumors and 992 cases with multiple specimens over time), they examined the frequency, immunophenotype, and evolution of hepatic differentiation. In the tissue microarray cohort (123 tumors), only 1 adenocarcinoma (0.1%) exhibited hepatic marker expression (HepPar1+, HNF4α+, cytoplasmic TTF-1+), confined to specific tumor areas. Among the 992 cases, 8 tumors exhibited hepatic differentiation during disease progression. In 7 of 8 cases, hepatic marker expression (particularly HepPar1 and cytoplasmic TTF-1) emerged or increased during recurrence or metastasis, suggesting a dynamic and progressive nature rather than a static tumor subtype. Histologically, hepatic differentiation corresponded to areas with glandular or cribriform architecture, while solid areas lacked expression. SMARCA4 deficiency was present in 3 of the 8 cases, showing partial overlap with this phenotype.

**Take-home message**: The findings challenge the idea of lung hepatoid adenocarcinoma as a distinct entity, instead proposing that hepatic differentiation may evolve with disease progression or treatment. This also supports the concept of tumor evolution under therapeutic pressure, aligning with known transformations (e.g., to small cell or squamous cell carcinoma) seen in other NSCLC subtypes.

**Sugata K, et al. Impact of tumor cell burden beyond the elastic layer on prognosis in T2aN0M0 non-small cell lung cancer with visceral pleural invasion. Lung Cancer. 2025;208:108759..**

**Summary**: This study evaluated the prognostic impact of quantitative visceral pleural invasion (VPI) patterns in non-small cell lung cancer (NSCLC) staged as pT2aN0M0 with tumor size ≤4 cm and histologically confirmed pl1/pl2 VPI. The research focused on five measurable histological parameters: Total Tumor Cell Area (TCA) beyond the pleural elastic layer, Whole Tumor Area (WTA) beyond the elastic layer, Minimum Distance (min-DST) from pleural surface to tumor cell, Maximum Depth (max-DSI) of elastic layer invagination, and Tumor Cell Density (DTC). Using HE and Verhoeff–Van Gieson stains, the authors evaluated slides scanned with a digital pathology system and measured the parameters with image analysis

tools. Patients with higher TCA and WTA showed significantly worse recurrence-free survival (RFS) and overall survival (OS). Traditional VPI subclassifications (pl1 vs pl2) and other measurements (min-DST, max-DSI, DTC) did not show prognostic significance.

**Take-home message**: Total tumor cell area (TCA) beyond the elastic layer is a robust independent prognostic factor in pT2aN0M0 NSCLC with VPI. Quantifying pleural invasion may improve prognostic stratification, especially in tumors ≤4 cm. Traditional pl1 vs pl2 subclassification may be insufficient—TCA could supplement or improve upon current TNM descriptors in future iterations.

**Nambirajan A, et al. Baseline retinoblastoma transcriptional corepressor 1 (Rb1) functional inactivation is a pre-requisite but not sufficient for small-cell histological transformation in epidermal growth factor receptor (EGFR) mutant lung adenocarcinomas post-tyrosine kinase inhibitor therapy. Virchows Archiv. 2025;487(5):639–648.**

**Summary**: This ambispective study (2019–2023) from AIIMS, New Delhi, investigates whether Rb1 functional inactivation is sufficient to drive small-cell transformation in EGFR-mutant lung adenocarcinomas after tyrosine kinase inhibitor (TKI) therapy. Out of 84 post-TKI lung adenocarcinoma cases, 9 (10%) demonstrated histological transformation to small-cell carcinoma. All 9 small-cell transformation cases were found to be Rb1-deficient at baseline, confirmed either by Rb1 immunohistochemistry (IHC) loss or a $p16^{high}$/Cyclin $D1^{low}$ profile. These cases also harbored TP53 mutations. Interestingly, in a comparison cohort of 9 EGFR-mutant patients without transformation, only 1 was Rb1-deficient. The study underscores Rb1/p53 loss as a prerequisite but not the sole driver of histologic shift. Other mechanisms (e.g., lineage plasticity, APOBEC mutational processes) are likely contributors.

**Take-home message**: Rb1 loss is necessary but not sufficient for small-cell transformation in EGFR-mutant lung adenocarcinomas after TKI therapy. Routine Rb1 IHC at baseline may help flag patients at increased risk of transformation. Despite Rb1/p53 inactivation, other molecular drivers are likely required for full transformation. While baseline Rb1 IHC could potentially serve as a risk stratification tool, further prospective validation is needed. The study also reflects the growing relevance of functional IHC (p16, Cyclin D1) to complement mutation analysis, especially when RB1 mutations are not detected on sequencing.

**Pavlíčková K, et al. Correlation between p53 immunoexpression and TP53 mutation status in extrapulmonary small cell neuroendocrine carcinomas and its association with patient survival. Virchows Archiv. 2025;487(5):557–564.**

**Summary**: This multicenter study of 171 cases of extrapulmonary small cell neuroendocrine carcinoma (EP-SCNC) investigated the correlation between p53 immunoexpression and TP53 mutation status, and their impact on patient survival. There was strong concordance between p53 IHC and TP53 mutation status, though 17 discordant cases were identified. p53 immunohistochemistry (IHC) showed aberrant expression in 60.2% cases, whereas TP53 mutation detected by NGS was found in 73.6% cases. Notably, 14 tumors had TP53 mutations despite wild-type p53 expression. Conversely, 3 tumors showed p53 overexpression but had no TP53 mutation. TP53 mutations were associated with significantly shorter overall survival (median 8.9 vs. 16.2 months, $p = 0.041$). However, p53 IHC was not a reliable standalone prognostic marker in univariate analysis. TP53 mutations were less frequent than in pulmonary small cell carcinomas, where mutation rates exceed 90%.

**Bui J, et al. Extent of lymph node harvest in sublobar resections for early-stage non–small cell lung cancer: A population-based analysis. J Thorac Cardiovasc Surg. 2025;170(3):789–798.**

**Summary**: This population-based SEER-Medicare study assessed the adequacy of lymph node (LN) evaluation in patients undergoing sublobar resections for clinical stage IA non–small cell lung cancer (NSCLC). Study cohort includes 3,248 patients aged ≥66 who underwent sublobar resection (segmentectomy or wedge) from 2010–2019.Only 32.6% of patients had ≥6 lymph nodes examined, the threshold recommended by NCCN guidelines for adequate nodal staging. Segmentectomy patients had significantly higher median LN harvest (median 6 vs. 2 LNs) and more often met the ≥6 LN threshold. However, nearly half of segmentectomy cases still failed to meet adequate nodal sampling criteria. Predictors of higher LN count includes segmentectomy, academic center, and recent year of surgery (temporal improvement). The study emphasizes a disconnect between surgical practice and oncologic standards, especially in wedge resections.

**Take-home message**: For pulmonary pathologists, this underscores the importance of systematic LN retrieval and submission, particularly when grossing sublobar specimens. Histologic upstaging opportunities—and decisions about adjuvant therapy—depend on it. Close communication with surgeons may help improve LN yield, especially as segmentectomy becomes more common in early-stage disease.

**Commentary: Stiles BM, Vimolratana M. Commentary: Is it really that hard? J Thorac Cardiovasc Surg. 2025;170(4):924–925.**

**Altorki N, et al.** ***The extent of lymph node dissection is not associated with disease-free survival following lobar or sublobar resection: Results from Cancer and Leukemia Group B 140503 (Alliance)*****. J Thorac Cardiovasc Surg. 2025;170(4):933-942.**

**Summary**: This study presents a post hoc exploratory analysis of the CALGB 140503 phase III randomized trial, which assessed whether the extent of lymph node dissection (LAD)—categorized as simple sampling (S), systematic sampling (SS), or complete lymph node dissection (CLND)—impacted disease-free survival (DFS) and recurrence-free survival (RFS) in patients with peripheral clinical stage IA NSCLC ≤2 cm who had no nodal metastases confirmed intraoperatively. A total of 689 patients were analyzed: 182 underwent CLND, 349 had SS, and 158 had S. The trial found no statistically significant differences in 5-year DFS or RFS between the LAD groups, regardless of whether patients received lobar resection (LR) or sublobar resection (SLR). Recurrence patterns, including hilar, mediastinal, and distant metastases, were also similar across LAD types. Multivariable analysis revealed current smoking status as the only significant predictor of worse RFS. The study reinforces that in highly selected patients with robust nodal staging confirming node-negative status, more extensive LAD does not confer survival benefit. Histologically, adenocarcinoma was more common in SS (73.4%), while squamous cell carcinoma was more represented in the CLND group (24.2%).

**Take-home message**: In rigorously staged, node-negative patients with peripheral c-stage IA NSCLC ≤2 cm, the extent of lymph node dissection (simple, systematic, or complete) does not impact disease-free or recurrence-free survival. Either sampling or dissection is acceptable in this specific clinical context, potentially reducing operative time and morbidity without compromising oncologic outcomes..

**Commentary: Rocco G. Commentary: Cum grano salis. J Thorac Cardiovasc Surg. 2025;170(4):943–944.**

*Non-neoplastic*

**Tazelaar HD, et al.** ***Twenty-Four Years' Experience With a Pulmonary Pathology Journal Club: What Have We Learned?*** **Arch Pathol Lab Med. 2025;149(10):960–967.**

**Summary**: This article reflects on 24 years of experience running a monthly pulmonary pathology journal club initiated at Mayo Clinic in December 2000. The club was created to help pathologists stay current with

diagnostic thoracic pathology literature by distributing the task of literature review. Initially spanning 18 journals, later expanded to 23, the club eventually grew to involve multiple academic institutions and became a model of a multi-institutional, virtual, and collaborative journal club. Citation analysis (2007–2023) showed that articles selected for discussion were significantly more cited (mean 103 vs. 65; $P < .001$) than those only noted, indicating they were of greater impact. Website analytics (May–July 2024) showed that journal club materials (PDF summaries and audio files) were among the most accessed resources on the Pulmonary Pathology Society website, indicating wide external engagement. The article also describes the successful pilot use of a custom ChatGPT tool to assist with summary generation, which decreased preparation time but still required human review for context, nuance, and critical insight.

**Take-home message**: The Mayo Clinic–based pulmonary pathology journal club has succeeded in its goal of keeping subspecialists current in the field while evolving into a collaborative, multi-institutional model. Data support that articles chosen for discussion are more impactful. The use of AI tools (like ChatGPT) shows promise for easing preparation, though human curation remains essential. Broader dissemination via the Pulmonary Pathology Society website is valuable to the wider pathology community.

**Nan Y, et al.** ***Prognostication in patients with idiopathic pulmonary fibrosis using quantitative airway analysis from HRCT: a retrospective study.*** **Eur Respir J. 2025;66:2500981.**

**Summary**: This study introduces SABRE (Smart Airway Biomarker Recognition Engine), an AI-based quantitative CT tool designed to improve prognostication in idiopathic pulmonary fibrosis (IPF) by quantifying airway-related changes—specifically traction bronchiectasis—from high-resolution CT (HRCT) scans. SABRE employs a neural network to calculate airway volumes along the tracheobronchial tree, normalized to total lung volume. The tool distinguishes medium, small, and terminal airways and generates normalized airway volume (NAV) scores as a reproducible metric of airway dilation severity. The model was trained and validated on two large, independent cohorts: the Australian IPF Registry (training cohort; n=320) and the Open Source Imaging Consortium (OSIC) cohort (validation; n=540). Higher SABRE-derived NAV scores were significantly associated with worse transplant-free survival and disease progression, even after adjusting for established clinical predictors like age, sex, FVC, DLCO, and visual fibrosis scores. SABRE outperformed visual CT assessment in predictive modeling. SABRE may offer a more objective, quantitative, and reproducible biomarker for disease severity in IPF than traditional radiologic scoring.

**Take-home message**: SABRE is a novel AI-driven CT analysis tool that quantitatively measures traction bronchiectasis severity and adds independent prognostic value to established clinical and radiologic markers in IPF. It holds promise for improving risk stratification and potentially guiding therapeutic decision-making. However, clinical utility and workflow integration remain to be demonstrated prospectively. Regulatory pathways, cost, and infrastructure requirements will also influence its real-world impact. Still, this study firmly establishes SABRE as a leading candidate among emerging qCT prognostic tools in ILD.

**Editorial: Marinescu DC, Ryerson CJ. SABRE: a sharper tool for prognostication in pulmonary fibrosis. Eur Respir J. 2025;66(2501516.**

**Ryerson CJ, et al.** ***A fibrotic hypersensitivity pneumonitis pattern on CT may be associated with underlying connective tissue disease–associated ILD*****. Am J Respir Crit Care Med. 2025;212(3):299–308.**

**Summary**: This multicenter retrospective cohort study investigated the association between a fibrotic hypersensitivity pneumonitis (fHP) pattern on CT and the presence of underlying connective tissue disease–associated interstitial lung disease (CTD-ILD). Using high-resolution CT (HRCT) scans from 199 patients diagnosed with non-IPF fibrosing ILD, three thoracic radiologists scored the imaging as: typical HP pattern, compatible with HP, and indeterminate for HP. They specifically looked for features of fibrotic HP, such as upper and mid-lung predominant fibrosis, centrilobular nodules, and mosaic attenuation, and compared these

with the presence or absence of an established CTD. Among patients with CTD-ILD, 36% exhibited a fibrotic HP pattern. Fibrotic HP pattern was independently associated with a CTD diagnosis (adjusted OR 3.47, 95% CI 1.48–8.17). Rheumatoid arthritis and inflammatory myopathies were the most common CTDs in patients with fibrotic HP pattern. Histologic correlation was limited, but the study suggests that some radiologic fibrotic HP patterns may in fact represent manifestations of CTD-associated lung disease, especially in women and nonsmokers.

**Take-home message**: A fibrotic hypersensitivity pneumonitis pattern on CT—typically associated with environmental exposures—may be a radiologic mimic of CTD-ILD, particularly in patients with no clear exposure history. Radiologists and pathologists should consider a broader autoimmune workup when this pattern is seen, especially in women and nonsmokers. This study challenges the assumption that a fibrotic HP pattern on imaging always reflects exposure-related disease. For pulmonary pathologists, this raises important diagnostic and clinical implications, especially when histology overlaps (e.g., cellular interstitial infiltrates, bronchiolocentric fibrosis). A multidisciplinary approach, including serologic testing and rheumatologic consultation, may be warranted in these scenarios to avoid misclassification and ensure appropriate treatment pathways (e.g., immunosuppression vs. antigen avoidance).

**Editorial**: **Fernández Pérez ER, Travis WD, Lynch DA. Rethinking the computed tomography and histopathological nomenclature of hypersensitivity pneumonitis: Unveiling bronchiolocentric patterns of interstitial pneumonia. Am J Respir Crit Care Med. 2025;211(10):1738–1739.**

## Reviews

**Naidoo J, et al. 50 Years of Progress in NSCLC: A New Fellow's Guide in the Clinic. J Thorac Oncol. 2025;20(10):1392–1422.**

**Summary:** This extensive and multidisciplinary editorial traces five decades of advancement in non–small cell lung cancer (NSCLC), providing a chronological and thematic roadmap for new clinicians and trainees entering the field. Authored by an international team under the IASLC Communications Committee, it serves both as a historical overview and a practical clinical guide.

- Screening: Landmark trials (NLST, NELSON) validated low-dose CT screening. New eligibility models aim to reduce racial and sex-based disparities.
- Staging Evolution: From early TNM editions based on small US cohorts to recent IASLC-led revisions, especially the 9th edition's refined T/N/M subdivisions and incorporation of biologic markers under discussion.
- Pathology: Central to understanding NSCLC progression—major updates in WHO classifications, introduction of AIS, MIA, and histologic grading based on high-grade components. Seminal trials defined molecular classification, biomarker testing (EGFR, ALK, PD-L1), and response assessment post-neoadjuvant therapy (e.g., MPR, CPR).
- Diagnostics & Interventions: Introduction and evolution of bronchoscopy (EMN, robotic) and EBUS revolutionized staging and tissue acquisition, offering comparable diagnostic yield to TTNA with fewer complications.
- Therapeutics:
    - Chemotherapy: From alkylators and cisplatin to pemetrexed and taxanes—later combined with targeted or immune agents.
    - Targeted Therapy: Rapid evolution post-EGFR mutation discovery; now includes ALK, ROS1, MET, RET, KRAS, and others. Osimertinib and antibody-drug conjugates represent next-generation strategies.
    - Immunotherapy: PD-1/PD-L1 inhibitors are integrated into all stages. PACIFIC trial set new standards for stage III NSCLC.

- Radiation: SABR established for early-stage NSCLC; dose escalation refined; ongoing research into immunoradiotherapy synergy.
- Surgery: Shift from pneumonectomy to lobectomy to segmentectomy and VATS; latest trials (JCOG0802, CALGB140503) support sublobar resections in small tumors.

**Mascaux C, et al. *Advances in Lung Cancer Research: Non–Small Cell Lung Cancer.* J Thorac Oncol. 2025;20(10):1423–1442.**

**Summary:** This article presents a consensus-style review by leading experts from the IASLC Pathology, Staging, Screening, and Translational Research Committees, providing a sweeping update on key translational and clinical research advances in non–small cell lung cancer (NSCLC).

**Take-home message:** NSCLC research is rapidly converging toward integration of molecular, imaging, and immune profiling, reshaping diagnostics, staging, and therapy. This editorial stresses that personalized oncology is now multidimensional, and that interdisciplinary collaboration is essential to translate molecular and digital innovations into meaningful patient outcomes. This editorial serves as a state-of-the-science map for both researchers and clinicians. For pathologists, the emerging role of tumor budding, co-mutation signatures, and AI-assisted histologic interpretation offers rich areas for future involvement. It also urges the field to prepare for digital pathology and AI integration, not as distant aspirations but as imminent realities in clinical workflows.

**Pezzuto F, et al. Pulmonary plasma cell disorders: histopathology, diagnosis, and clinical perspectives. *Virchows Archiv*. 2025;487:573–586.**

**Summary:** This comprehensive review explores the spectrum of pulmonary plasma cell disorders, from benign reactive infiltrates (e.g., IgG4-related disease) to malignant neoplasms such as multiple myeloma and plasmacytoma. Four illustrative cases provide real-world insight into diagnostic complexity and histological subtleties.

**Take-home message:** Pulmonary plasma cell-rich lesions represent a heterogeneous group of diseases, requiring careful histologic and immunophenotypic analysis. Distinguishing reactive from neoplastic infiltrates hinges on light chain restriction and ancillary testing (IHC, ISH, molecular). IgG4-RD, while rare in the lung, presents key histologic clues and should be considered in relevant contexts. Pulmonary involvement by multiple myeloma, LCDD, or amyloidosis necessitates systemic evaluation.