

# Anatomic pathology selected abstracts

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## **Automated artificial intelligence for HER2 IHC scoring in breast cancer**

September 2025—The efficacy of human epidermal growth factor receptor 2 antibody-drug conjugate therapy for treating HER2-low breast cancers necessitates more accurate and reproducible HER2 IHC scoring. The authors conducted a study to validate the performance and utility of a fully automated artificial intelligence (AI) solution for interpreting HER2 IHC in breast carcinoma. In the two-arm multireader study of 120 HER2 IHC whole slide images from four sites, four surgical pathologists assessed HER2 scoring with and without the aid of an AI solution. Both arms of the study were compared with high-confidence ground truth established by agreement of at least four of five breast pathology subspecialists according to the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) 2018 and 2023 guidelines. The mean interobserver agreement among the ground truth pathologists across all HER2 scores was 72.4 percent (n=120). The AI solution demonstrated high accuracy for HER2 scoring, with 92.1 percent agreement on slides with high confidence ground truth (n=92). Use of the AI tool improved reader performance. Interobserver agreement increased from 75 percent for digital manual read to 83.7 percent for AI-assisted review, and scoring accuracy improved from 85.3 to 88 percent. For distinguishing HER2 0 from 1+ cases (n=58), pathologists supported by AI showed significantly higher interobserver agreement (69.8 percent without AI versus 87.4 percent with AI) and accuracy (81.9 percent without AI versus 88.8 percent with AI). This study demonstrated the utility of a fully automated AI solution to aid in scoring HER2 IHC according to ASCO/CAP 2018 and 2023 guidelines. Pathologists showed improvements in HER2 IHC scoring consistency and accuracy with the use of AI, especially for distinguishing HER2 0 from 1+ cases. The authors concluded that this AI solution could be used by pathologists as a decision-support tool for enhancing the reproducibility and consistency of HER2 scoring, particularly for identifying HER2-low breast cancers.

Krishnamurthy S, Schnitt SJ, Vincent-Salomon A, et al. Fully automated artificial intelligence solution for human epidermal growth factor receptor 2 immunohistochemistry scoring in breast cancer: A multireader study. *JCO Precis Oncol.* 2024. [doi.org/10.1200/PO.24.00353](https://doi.org/10.1200/PO.24.00353)

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## **P53-abnormal oral epithelial dysplasias: evaluation of progression and local recurrence**

Grading of oral epithelial dysplasia can be challenging due to considerable intraobserver and interobserver variability. Abnormal immunohistochemical staining patterns in the tumor-suppressor

protein p53 recently have been shown to potentially be associated with progression of oral epithelial dysplasia (OED). The authors conducted a retrospective longitudinal study to determine whether p53-abnormal OED, p53-conventional OED, and p53-human papillomavirus (HPV) OED have a statistically significant difference in progression among low-grade lesions and local recurrence/malignant transformation among high-grade lesions. For the study, they identified 214 oral biopsies from 203 patients who participated in a longitudinal study between 2001 and 2008 and had a diagnosis of reactive or nondysplastic lesions, low-grade lesions (mild or moderate OED), or high-grade lesions (severe OED or carcinoma in situ). Tissue microarrays were constructed from the most representative area of the pathology. Three consecutive sections were sectioned and stained with hematoxylin and eosin, p53 IHC, and p16 IHC. The staining results were reviewed by two pathologists blinded to clinical outcome. Samples were categorized into p53-abnormal (overexpression or null type) OED (n=46), p53-conventional (p53 wild type, HPV independent) OED (n=118), and p53-HPV (p53 wild type, HPV associated) OED (n=12) using a previously published pattern-based approach. P16 expression was scored positive when there was diffuse, block-like staining involving at least the lower two-thirds of the epithelium. Discordant p53 or p16 cases were re-reviewed by both pathologists and reconciled by consensus. All cases of p53-HPV (HPV associated) OED were identified in high-grade lesions. In contrast, cases of p53-abnormal OED were observed in mild OED (9.5 percent), moderate OED (23 percent), and severe OED or carcinoma in situ (51 percent). None of the 27 reactive or nondysplastic lesions showed abnormal p53 staining patterns. Among the 135 low-grade lesions, 23 (17 percent; two mild OEDs and 21 moderate OEDs) progressed to a high-grade lesion or squamous cell carcinoma, with 11 cases showing progression during the first three years. Eighty-two percent (nine of 11) of those that progressed faster showed abnormal p53 patterns. Survival analysis revealed that p53-abnormal OED had poorer progression-free probability ( $P < .0001$ ; hazard ratio, 11.24; 95 percent confidence interval, 4.26-29.66) compared with p53-conventional OED. Furthermore, p53-abnormal OED had poorer local recurrence-free survival compared with p53 wild-type OED ( $P = .03$ ). The authors concluded that this study indicates that OED with a p53-abnormal pattern is at high risk for progression and recurrence independent of dysplasia grade.

Ko YCK, Liu KYP, Chen E, et al. p53 abnormal oral epithelial dysplasias are associated with high risks of progression and local recurrence—a retrospective study in a longitudinal cohort. *Mod Pathol*. 2024;37. [doi.org/10.1016/j.modpat.2024.100613](https://doi.org/10.1016/j.modpat.2024.100613)

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### **Characterization of clear cell stromal tumor of lung**

Clear cell stromal tumor is a recently described mesenchymal neoplasm of the lung that is characterized by spindle cells with variably clear to pale eosinophilic cytoplasm and prominent vascularity. It also has a recurrent *YAP1::TFE3* gene fusion in most cases. Fewer than 20 cases had been reported at the time of this study, and data on clinical behavior of the tumor are limited. Most tumors appear to be benign, and aggressive behavior rarely has been reported. The authors conducted a study involving a large multi-institutional series of clear cell stromal tumors comprising eight cases (five men and three women; median age, 59 years [range, 35-48 years]). They investigated the tumor's clinicopathologic and genomic features and assessed the diagnostic use of IHC for YAP1 C-terminus. All tumors appeared as well-delineated round nodules and were a median size of 3.4 cm (range, 0.7-7.5 cm). They involved conductive airways, frequently in proximity to a pulmonary artery branch. An apparent sharp interface at low power was typical. However, at higher power, the respiratory epithelium was present toward the periphery and lining and occasionally invaginated the tumor nodule,

imparting a biphasic appearance. Distinctive thin-walled or staghorn-shaped vessels, or both, were present in all tumors. The neoplastic cells formed focal polypoid projections within the lumen of thin-walled vessels. Five of eight cases demonstrated foci of intratumoral vascular thrombosis. A chronic inflammatory cell infiltrate was characteristically present. In all cases, a predominantly lymphocytic infiltrate was present as scattered cells and occasional small aggregates. A few cases showed prominent eosinophils and others showed aggregates of foamy histiocytes (six of eight cases). The tumors were primarily made up of histiocytoid, ovoid- to spindle-shaped cells with indistinct cell borders, and the cells formed sheets with occasional loose nests and whorls. Despite the name clear cell stromal tumor, clear cytoplasm was not a prominent finding. More commonly, the tumor cells exhibited variably clear and pale eosinophilic cytoplasm. The cells generally had relatively uniform nuclei with inconspicuous nucleoli and no significant atypia. Bizarre nuclei with degenerative atypia were focally identified in seven of eight cases. Mitotic activity was absent or very low. No tumors had areas of necrosis. In all cases, a *TFE3* rearrangement was demonstrated by FISH or DNA/RNA sequencing. The *YAP1::TFE3* fusion was identified by sequencing in seven tumors. The authors concluded that the combination of YAP1 C-terminus loss and TFE3 overexpression using IHC reliably predicts an underlying *YAP1::TFE3* fusion in these neoplasms and may be more sensitive than *TFE3* FISH. All patients pursued a benign clinical course, with no recurrences or metastases. This study provides further characterization of this novel entity, supporting its wider recognition.

Odintsov I, Isaacson A, Fritchie KJ, et al. Clear cell stromal tumor of the lung: Clinicopathologic, immunohistochemical, and molecular characterization of eight cases. *Mod Pathol*.  
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