

Digital Pathology Is a Measurement System

Five studies on low-frequency variants, slide aging, AI calibration, Ki67 method effects, and cytology biomarker concordance.

Saturday, September 26, 2026

Digital PCR | HER2 stability | Steatosis | Ki67 | Claudin 18.2

FIVE SIGNALS WORTH YOUR BENCH TIME

01 / MOLECULAR PATHOLOGY / BRAF V600E

Digital PCR found low-frequency BRAF variants missed by ARMS-PCR

Finding. In 252 thyroid samples, digital PCR and ARMS-PCR agreed in tumor and benign tissue overall, but digital PCR detected seven additional low-frequency calls in adjacent tissue, a lymph node, and aspirates; discrepant findings were re-reviewed and confirmed by sequencing.

Why it matters. Higher analytical sensitivity changes the pathology feedback loop. Discordant molecular findings may justify slide review, tumor-content assessment, and an orthogonal method rather than automatic acceptance or rejection.

Limits. This was retrospective and focused on one variant. Perfect internal diagnostic metrics are vulnerable to case mix, small discrepant counts, and verification design and require external validation.

Evidence label: Peer-reviewed retrospective diagnostic-accuracy study; open access at verification.

02 / PREANALYTICS / HER2 SLIDES

HER2 antigen survived two months at room temperature, not years

Finding. Block-matched slides showed significant long-term HER2 antigen loss at room temperature but not at -80 C. Over two months, degradation in either condition was small relative to tumor heterogeneity and inter-run variation; frozen slides retained a shelf life of at least one year.

Why it matters. Archived-slide studies need storage metadata and a defined staining window. A control block or freshly cut section can separate true biology from post-sectioning epitope loss.

Limits. The study addressed HER2 under specific sectioning, storage, staining, and quantification conditions. It does not establish universal shelf lives for other antibodies or laboratories.

Evidence label: Peer-reviewed analytical slide-stability study; full text may require subscription.

03 / LIVER PATHOLOGY / MEASUREMENT DEFINITION

Visual steatosis estimates ran 1.4 to 3.6 times higher than AI measurements

Finding. Ten liver pathologists assessed 20 whole-slide cases and selected fields using different definitions. Whether they estimated steatosis area or hepatocytes containing fat drove much of the spread; visual estimates exceeded corresponding AI measurements, especially in small-droplet-rich cases.

Why it matters. Human-AI disagreement may start with the measurand, not the observer. A laboratory must define droplet size, denominator, and reporting scale before validating reproducibility or decision thresholds.

Limits. The reader and slide sets were limited. Calibration equations were exploratory and require independent validation before clinical use; the AI measurement is not automatically ground truth.

Evidence label: Peer-reviewed multi-reader comparative study; full text may require subscription.

Ki67 method choice reclassified one quarter of luminal-like tumors

Finding. In 389 invasive breast cancers, eyeballing produced lower Ki67 estimates than digital analysis in low-grade tumors below 20%. Digital reassessment moved 28 of 62 luminal-A-like and 16 of 109 luminal-B-like cases, an absolute classification discordance of 25.7%.

Why it matters. A cutoff has no stable meaning without a counting method. Manual image counting aligned more closely with digital analysis and may offer a controlled option where full digital analysis is unavailable.

Limits. The study compared methods within one specimen set and surrogate molecular groups. Reclassification does not establish which method better predicts treatment response or outcomes.

Evidence label: Peer-reviewed comparative pathology study; full text may require subscription.

Cytology supported Claudin 18.2 testing, with a site-dependent caution

Finding. In 37 paired gastric or gastroesophageal cases, cytology and surgical specimens were concordant in 86%. At the 75% cutoff, cytology sensitivity was 77% and specificity 92%; agreement was perfect for paired gastric-primary samples but lower when metastatic sites were involved.

Why it matters. Cytology can expand access when surgical tissue is absent, but specimen origin belongs in validation and discrepant-result rules because spatial heterogeneity can cross a treatment threshold.

Limits. Only 37 pairs were studied, and subgroup estimates were smaller still. The results are assay-, cutoff-, preparation-, and tumor-site-specific and need larger external validation.

Evidence label: Peer-reviewed paired-specimen concordance study; full text may require subscription.

Verified source trail

1. Yu, Zhang, Jiang, et al. Improving the Accuracy of Papillary Thyroid Cancer Pathological Evaluation With Digital PCR Detection of the BRAF V600E Mutation. Journal of Clinical Laboratory Analysis. 2026. DOI: 10.1002/jcla.70323.

2. Scott, Benanto, Robbins, et al. Temperature-Dependent Long-term and Short-term Stability of Human Epidermal Growth Factor Receptor 2 Antigenicity on Pathology Slides. Archives of Pathology & Laboratory Medicine. 2026. DOI: 10.5858/arpa.2025-0447-oa.

3. Nazli, Shaaban, Patil, et al. Visual steatosis assessment: method-dependent variation and systematically higher estimates compared with AI measurement. Histopathology. 2026. DOI: 10.1111/his.70272.

4. Ojha, Agrawal, Verma, et al. Quantifying Ki67 for characterising molecular subtypes in breast cancer: a comparative study of visual assessment and digital image analysis. Journal of Clinical Pathology. 2026. DOI: 10.1136/jcp-2026-210651.

5. Yang, Kaur, Wang, et al. Claudin 18.2 Expression Concordance in Paired Cytology and Surgical Specimens of Gastric and Gastroesophageal Junction Adenocarcinomas. Archives of Pathology & Laboratory Medicine. 2026. DOI: 10.5858/arpa.2025-0466-oa.

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