TissueCypher published clinical validation and utility studies

TissueCypher
▸ Barrett's Esophagus

STUDY	REFERENCE	KEY FINDINGS
Technical feasibility study	Prichard JW, Davison JM, Campbell BB, et al. TissueCypher: A systems biology approach to anatomic pathology. *J Pathol Inform*. 2015;6(1):48.	• Demonstrated that assessing Barrett's esophagus tissue for epithelial cell abnormalities and cellular changes in the lamina propria may serve as an adjunct to conventional pathology in the assessment of BE.
GAPP1 study	Critchley-Thorne RJ, Duits LC, Prichard JW, et al. A tissue systems pathology assay for high-risk Barrett's esophagus. *Cancer Epidemiol Biomarkers Prev*. 2016 Jun;25(6):958-968.	• Clinical validation demonstrating TissueCypher predicts risk of future progression to HGD or EAC in patients with BE who have baseline histologic diagnosis of ND, IND or LGD.
GAPP2 study	Critchley-Thorne RJ, Davison JM, Prichard JW, et al. A tissue systems pathology test detects abnormalities associated with prevalent high-grade dysplasia and esophageal cancer in Barrett's esophagus. *Cancer Epidemiol Biomarkers Prev*. 2017 Feb;26(2):240-248.	• Clinical validation of locked assay to detect prevalent HGD/EAC missed by standard white light endoscopy and histology in patients with Barrett's esophagus.
CC/UP study	Davison JM, Goldblum J, Grewal US, et al. Independent blinded validation of a tissue systems pathology test to predict progression of patients with Barrett's esophagus. *Am J Gastroenterol*. 2020;115:843-852.	• Independently validated the ability of TissueCypher to predict risk of future progression to HGD/EAC within 5 years in BE patients with ND, IND or LGD. • Demonstrated that TissueCypher identifies an "at-risk" subset of patients with NDBE who progress at a higher rate than patients with expert-confirmed LGD.
CE study	Hao J, Critchley-Thorne RJ, Diehl DL, et al. A cost-effectiveness analysis of an adenocarcinoma risk prediction multi-biomarker assay for patients with Barrett's esophagus. *Clinicoecon Outcomes Res*. 2019;11:623-635.	• Demonstrated cost-effectiveness of TissueCypher-directed management versus standard of care-directed surveillance and treatment. • Indicated change in healthcare utilization and potential improvement in patient outcomes associated with TissueCypher-directed management.
AMC spatial and temporal study	Frei NF, Konte K, Bossart EA, et al. Independent validation of a tissue systems pathology assay to predict future progression in non-dysplastic Barrett's esophagus: A spatial-temporal analysis. *Clin Transl Gastroenterol*. 2020; Oct 11(10):e00244.	• Confirmed ability of TissueCypher to predict incident progression in NDBE patients. • Confirmed ability of TissueCypher to identify NDBE patients that progress at a higher rate than patients with expert-confirmed LGD. • Demonstrated that evaluation of additional spatial and temporal specimens increases the predictive performance of TissueCypher.
SURF biomarker study	Frei NF, Khoshiwal AM, Konte K, et al. Tissue systems pathology test objectively risk stratifies Barrett's esophagus patients with low-grade dysplasia. *Am J Gastroenterol*. 2021 Apr; 116(4)675-682.	• Retrospective analysis of completed prospective randomized clinical trial[1]. • Independently validated the ability of TissueCypher to predict risk of progression to HGD/EAC in patients with community practice diagnosis of LGD.
Geisinger decision impact study	Diehl DL, Khara HS, Akhtar N, Critchley-Thorne RJ. TissueCypher Barrett's esophagus assay impacts clinical decisions in the management of patients with Barrett's esophagus. *Endosc Int Open*. 2021; 09(03): E348-E355.	• TissueCypher changed the management plan for 55% of BE patients studied at an expert center. • TissueCypher led to upstaging of management plan in 21.7% of patients, indicating potential to improve outcomes. • TissueCypher led to downstaging of management plan in 33.4% of patients, supporting surveillance rather than therapy.

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STUDY	REFERENCE	KEY FINDINGS
Mayo pooled analysis study	Iyer PG, Codipilly DC, Chandar AK, et al. Prediction of progression in Barrett's esophagus using a tissue systems pathology test: A pooled analysis of international multicenter studies. *Clin Gastroenterol Hepatol*. 2022 Dec;20(12):2772-2779.e8.	• Across all analyses, TissueCypher was the strongest and most significant predictor of progression to HGD or EAC. • Predictive performance of clinicopathologic factors was significantly improved by the inclusion of the TissueCypher risk classes. • In the NDBE patient cohort, a TissueCypher high risk score predicted an 18-fold increased risk of progression vs. TissueCypher low risk score and identified 52% of the NDBE progressors, all of whom were missed by the standard of care.
SURF utility study	Duits LC, Khoshiwal, AM, Frei, NF et al. An automated tissue systems pathology test can standardize the management and improve health outcomes for patients with Barrett's esophagus. *Am J Gastroenterol*. 2023; 118(11):p 2025-2032.	• Incorporating TissueCypher into the standard of care can increase the early detection of progressors who can receive therapeutic interventions or short-interval surveillance, while also increasing the percentage of non-progressors who can avoid unnecessary therapy and be managed by surveillance alone. • TissueCypher guidance clinically and statistically improved the standard of care by increasing the likelihood of appropriate management decisions for all patients and decreasing the variability in management that results from basing care solely on the diagnoses of dysplasia.
Expanded SURF biomarker study	Khoshiwal AM, Frei NF, Pouw RE et al. A tissue systems pathology test outperforms pathology review in risk stratifying patients with low-grade dysplasia. *J. Gastroenterol*. 2023; 165(5):p 1168-1179.E6.	• The study confirmed that TissueCypher is an objective test that outperformed a group of 16 generalist and 14 expert pathologists. • Compared with known patient outcomes, pathologists showed weak agreement in diagnoses. One group of pathologists tended to over-diagnose and another group tended to under-diagnose.
Enhanced pooled analysis study	Davison JM, Goldblum JR, Duits LC, et al. A tissue systems pathology test outperforms the standard of care variables in predicting progression in patients with Barrett's esophagus. *Clin Transl Gastroenterol*. 2023; 14(11):p e00631.	• TissueCypher is superior to clinicopathologic features in risk stratifying BE patients, has significantly higher sensitivity than pathology, identifies majority of progressors at the NDBE stage. • TissueCypher risk stratifies in all clinically relevant subsets of BE patients, including those considered low risk per current clinical variables, e.g. female patients, short segment.
QURE utility study	Peabody JW, Cruz JDC, Ganesan D, et al. A randomized controlled study on clinical adherence to evidence-based guidelines in the management of simulated patients with Barrett's esophagus and the clinical utility of a tissue systems pathology test: results from Q-TAB. *Clin Transl Gastroenterol*. 2024; 15(1) e00644.	• Use of TissueCypher significantly improved physician adherence to clinical guidelines for surveillance and treatment of both BE patients at high and low risk for disease progression. • Use of TissueCypher can enable physicians to make risk-aligned management decisions, leading to improved patient health outcomes.
Clinical experience study	Villa NA, Ordonez-Castellanos M, Yodice M, et al. The tissue systems pathology test objectively risk-stratifies patients with Barrett's esophagus results from a multicenter US clinical experience study. *J Clin Gastroenterol*. 2024 Jul 2. doi: 10.1097/MCG.0000000000002040. Online ahead of print.	• Across 8,080 patients, TissueCypher provided objective risk stratification within all clinically relevant patient subsets. • Even in patient populations with low-risk clinical features (i.e. female, short-segment), TissueCypher identified patients with a higher risk of progression to HGD/EAC.

List of Abbreviations Used in the Table: Barrett's esophagus (BE), esophageal adenocarcinoma (EAC), high-grade dysplasia (HGD), indefinite for dysplasia (IND), low-grade dysplasia (LGD), non-dysplastic (ND), non-dysplastic Barrett's esophagus (NDBE)

1 Phoa et al., Radiofrequency ablation vs endoscopic surveillance for patients with Barrett esophagus and low-grade dysplasia: a randomized clinical trial. *JAMA*. 2014;311:1209-17.

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