TissueCypher published clinical validation and utility studies

TissueCypher ▸ Barrett's Esophagus®

STUDY	KEY FINDINGS
Technical feasibility study Prichard JW, et al. J *Pathol Inform*. 2015.	• 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, et al. *Cancer Epidemiol Biomarkers Prev*. 2016.	• 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, et al. *Cancer Epidemiol Biomarkers Prev*. 2017.	• 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, et al. *Am J Gastroenterol*. 2020.	• Independently validated the ability of TissueCypher to predict risk of future progression to HGD/EAC within 5 years in patients with BE 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, et al. *Clinicoeconomics Outcomes Res*. 2019.	• 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, et al. *Clinical and Translational Gastroenterol*. 2020.	• Confirmed ability of TissueCypher to predict incident progression in patient with NDBE. • Confirmed ability of TissueCypher to identify patients with NDBE 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, et al. *Am J Gastroenterol*. 2021.	• 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, et al. *Endosc Int Open*. 2021.	• TissueCypher changed the management plan for 55% of patients with BE studied at an expert center. • TissueCypher led to escalation of management plan in 21.7% of patients, indicating potential to improve outcomes. • TissueCypher led to de-escalation of management plan in 33.4% of patients, supporting surveillance rather than therapy.

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STUDY	KEY FINDINGS
Mayo pooled analysis study Iyer PG, et al. Clin *Gastroenterol Hepatol.* 2022.	• 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, et al. *Am J Gastroenterol.* 2023.	• 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, et al. *J. Gastroenterol.* 2023.	• 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, et al. *Clin Transl Gastroenterol.* 2023.	• TissueCypher is superior to clinicopathologic features in risk stratifying patients with BE, has significantly higher sensitivity than pathology, identifies majority of progressors at the NDBE stage. • TissueCypher risk stratifies in all clinically relevant subsets of patients with BE, including those considered low risk per current clinical variables, e.g. female patients, short-segment.
QURE utility study Peabody JW, et al. *Clin Transl Gastroenterol.* 2024.	• Use of TissueCypher significantly improved physician adherence to clinical guidelines for surveillance and treatment of both patients with BE 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, et al. *J Clin Gastroenterol*. 2024.	• 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.
Systematic review and meta-analysis Houghton CC, et al. *J Clin Gastroenterol.* 2025.	• Six clinical validity studies met eligibility criteria for a systematic review and meta-analysis, comprising 699 patients. • Common and Random effects models of ORs and HRs showed that patients who scored TSP-9 High/Int risk were 6.6 or 6.7 times more likely to progress to HGD/EAC, respectively, within 5 years versus patients with low-risk results.

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.

FULL BIBLIOGRAPHY

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