WATS-3D brush biopsy for Barrett's esophagus

Clinical Policy ID: CCP.1472

Recent review date: 12/2025

Next review date: 4/2027

Policy contains: Barrett's esophagus, esophageal cancer, forceps biopsy, WATS-3D brush.

Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary..

Coverage policy

WATS-3D® brush biopsy (CDx Diagnostics®, Suffern, New York) for detection of Barrett's esophagus is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Conventional forceps biopsy.

Background

Barrett's esophagus is a condition that affects the cardiac sphincter in which the squamous cell mucosa that ordinarily lines the esophagus is replaced by metaplastic columnar cell mucosa, similar to that of the small intestine. Barrett's esophagus is thought to develop from chronic inflammation resulting from gastroesophageal reflux disease, affecting those who have had the disease for a long time or developed it at a young age. About 10% to 15% of persons with gastroesophageal reflux disease develop Barrett's esophagus, which is a major risk factor for the development of esophageal adenocarcinoma (Choi, 2022).

The prevalence of Barrett's esophagus in western nations ranges from 1.6% to 6.8%. A precancerous change in the tissue, called dysplasia, will develop in some cases. In 0.2% to 2.9% of Barrett's esophagus cases per year, the dysplasia will progress to esophageal adenocarcinoma (Lowe, 2022). Risk factors most strongly linked with progression of Barrett's esophagus without dysplasia or with low-grade dysplasia to high-grade dysplasia or esophageal adenocarcinoma include increasing age, male sex, ever-smoker status, increasing Barrett's segment length, and low-grade (versus no) dysplasia. Alcohol use and obesity did not raise risk (Krishnamoorthi, 2018).

Diagnosis of esophageal adenocarcinoma from endoscopic surveillance of Barrett's esophagus was associated with a 29% and 27%, respectively, lower mortality compared to carcinomas not detected by surveillance, based on a meta-analysis of eight studies (Ding, 2018) and a meta-analysis of 12 studies (Codipilly, 2018). Thus, effectiveness of surveillance is crucial for improving outcomes in esophageal cancer.

Detecting precancerous changes in patients with Barrett's esophagus can be challenging because of the flat and patchy distribution of the tissue. Four-quadrant cold forceps biopsies at intervals of every 1 to 2 cm throughout the columnar-lined esophagus has traditionally been the technique used to diagnose Barrett's esophagus. The "Seattle protocol", as it is called, can miss large portions of esophageal mucosa, underdiagnose dysplasia, and be laborious to perform (Smith, 2016).

WATS-3D brush biopsy is a device recently introduced to improve detection of Barrett's esophagus. WATS-3D stands for Wide Area Transepithelial Sampling with 3-Dimensional Analysis. It is a brush-based sampling technique combined with a computer-synthesized 3-dimensional image of resultant tissue to fill gaps from the standard cytology brush. Bristles are more rigid than earlier brushes, and the endoscopist pushes the brush against the epithelium in a zig-zag-like pattern (Smith, 2016). The WATS-3D brush biopsy is designed to overcome the limitations of forceps biopsy by sampling from a wider area within the esophagus and potentially increasing the yield during surveillance tissue sampling.

Findings

The European Society of Gastrointestinal Endoscopy does not recommend the routine use of the WATS-3D brush technique as an alternative or adjunct method to conventional biopsies during endoscopic Barrett's Esophagus (BE) surveillance. Although the WATS-3D technique allows deep transepithelial sampling and uses three-dimensional computer-assisted analysis for detecting dysplasia, there is uncertainty regarding the clinical relevance of dysplasia detected only through this method. Additionally, there is insufficient evidence to support its ability to replace traditional forceps biopsies (Weusten, 2023).

The American Gastroenterological Association recommends WATS-3D as an adjunctive technique to sample the suspected or established Barrett's segment (in addition to the Seattle biopsy protocol) based on evidence from a systematic review and meta-analysis demonstrating an incremental yield for dysplasia detection of 7.2% (Codipilly, 2022). Direct comparisons of WATS-3D and the Seattle protocol are needed to determine which sampling technique is superior (Muthusamy, 2022).

An American College of Gastroenterology guideline states patients with nondysplastic Barrett's esophagus should undergo endoscopic surveillance no more frequently than every three to five years, due to the small proportion that actually progress to esophageal cancer (Shaheen, 2016). The College was not able to make a recommendation on the use of WATS-3D analysis in patients undergoing endoscopic surveillance of Barrett's esophagus using white light endoscopy, as its incremental benefit is not clear (Shaheen, 2022).

In September 2019, the American Society for Gastrointestinal Endoscopy's Standards of Practice Committee issued a guideline on screening and surveillance of Barrett's esophagus. The panel initially made no recommendation for WATS-3D at the face-to-face meeting. After a review of additional published literature

(including data on adverse events) and an additional phone conference, the panel made a conditional recommendation for the use of WATS-3D, stating “In patients with known or suspected Barrett’s esophagus, we suggest using WATS-3D in addition to white light endoscopy with Seattle protocol biopsy sampling compared with white light endoscopy with Seattle protocol biopsy sampling alone.” The Committee based its decision on six studies with 6,271 Barrett’s endoscopy cases. Of these, white light endoscopy identified 125 dysplasia cases, while WATS-3D also identified the 125, plus 137 more cases (Qumseya, 2019).

The National Comprehensive Cancer Network noted that although the detection of dysplasia in those with Barrett’s esophagus is promising as demonstrated in smaller randomized controlled studies, they recommend the need for larger phase III randomized trials to assess the accuracy and utility of WATS-3D biopsy for detecting high grade dysplasia/adenocarcinoma in patients with Barrett’s esophagus. Their position remains that cytologic brushing and washings alone are rarely adequate for an initial diagnosis (National Comprehensive Cancer Network, 2023).

Current evidence from trials of low to moderate quality suggests WATS-3D added to forceps biopsies may improve the diagnostic yield of intestinal metaplasia and dysplasia within the Barrett’s esophagus segments during endoscopic surveillance, but it is unclear if improved diagnostic yield improves patient outcomes. Limitations in the evidence include a lack of gold standard for diagnosing high grade dysplasia or esophageal cancer, which may bias detection rates, a lack of follow up data, and WATS-3D diagnoses being derived from the manufacturer’s central laboratory. Notably, most cases of indefinite for dysplasia or low grade dysplasia detected only on WATS-3D were not confirmed by subsequent endoscopic forceps biopsies or follow up.

WATS-3D has the advantages of being easier to perform than four-quadrant forceps biopsies and involving fewer samples. However, further independent, prospective study that is sufficiently powered and takes into account the baseline risk for high grade dysplasia or esophageal cancer of the study population is needed to assess the independent role of WATS-3D as an alternative to forceps biopsy.

A study of 1,266 persons screened for Barrett’s esophagus and esophageal dysplasia found that 363 were diagnosed with Barrett’s by forceps biopsy alone, plus 146 additional cases by adding brush biopsy, an increase of 40%. In a subset of 848 patients with gastroesophageal reflux disease and no prior history of Barrett’s esophagus, adding brush biopsy increased the number diagnosed with esophageal dysplasia by 87.5% (another 14 in addition to the initial 16). All brush biopsies were conducted by pathologists at CDx laboratories (Johanson, 2011).

A study of 4,203 patients suspected to have Barrett’s esophagus revealed 594 were diagnosed by four-quadrant random forceps biopsy, and 493 additional cases were detected by adding WATS-3D, increasing the overall detection rate by 83%. Low-grade dysplasia was diagnosed in 26 patients by biopsy alone, and 23 additional cases were detected by adding WATS-3D, increasing the detection by 89% (Gross, 2018).

A study with 21 participating centers (n = 12,899) enrolled patients in a study of screening and surveillance for Barrett’s esophagus. Forceps biopsy identified 88 cases, and WATS-3D detected an additional 213 cases missed by forceps biopsy, an increase in detection of 142%. Combined random and targeted forceps biopsy identified 1,684 cases of Barrett’s esophagus, plus an additional 2,570 detected by WATS-3D, an increase of 153% (Smith, 2019).
The following tables illustrate findings of the prior three studies:

	# screened for Barrett’s	Cases found by standard biopsy	Other cases found by WATS-3D	% Additional Cases by WATS-3D
Johanson, 2011	1,266	363	146	+ 40%
Gross, 2018	4,203	594	493	+ 83%
Smith, 2019[1]	12,899	88	213	+142%

Smith, 2019[2]	12,899	1,684	2,570	+153%

[1]From forceps biopsy; [2]From random and targeted forceps biopsy

	# tested for dysplasia	Cases found by standard biopsy	Other cases found by WATS-3D	% Additional Cases by WATS-3D
Johanson, 2011	848	16	14	+ 88%
Gross, 2018	4,203	26	23	+ 89%
Smith, 2019	Not tested for dysplasia			

A systematic review/meta-analysis of 11 studies (n = 20,392) showed WATS-3D as adjunct to forceps biopsy, compared with forceps biopsy alone, resulted in 16% more detected cases of Barrett's esophagus, and 2% more detected cases of esophageal dysplasia, both statistically significant at $P < .00001$ and $P < .001$ (Suresh Kumar, 2020).

In a 2017-2018 study of upper endoscopy for foregut symptoms or Barrett's surveillance (n = 1,002), patients were randomized to either biopsies or WATS brush. No difference existed in detection of intestinal metaplasia (19.45% versus 22.72%, $P = .20$). WATS found significantly more intestinal metaplasia in patients with any endoscopically visible length of columnar-lined esophagus (Demeester, 2019).

A survey of 33 users of WATS-3D (all but one of whom were gastroenterologists), represented 4,881 total WATS-3D kits, 25.9% of the 18,828 used at that time. Serious adverse effects were reported in only .06% (three of 4,881) of the kits (Smith, 2014).

A study of slides obtained using the WATS-3D method from 149 patients with Barrett's esophagus (109 with no dysplasia, the other 40 with low-grade dysplasia, high-grade dysplasia, or esophageal adenocarcinoma) were evaluated by four blinded pathologists. The agreement between pathologists for all slides was high (mean kappa value = 0.86) (Vennalaganti, 2015).

In 2022 a randomized controlled clinical trial (ClinicalTrials.gov identifier NCT03859557) of 1,002 patients for surveillance or symptoms related to Barrett's esophagus at nine centers was performed comparing the forceps biopsy (n = 505) to the WATS technique (n = 497). The frequency of detecting intestinal metaplasia was 21% overall; forceps biopsy detected 19.6% and WATS detected 22.7% ($P = .2$). No significant difference in detection of low grade dysplasia with either technique, which was found in eight patients. No high grade dysplasia was found, but in patients with no history, WATS detected significantly more intestinal metaplasia (32.4%) than forceps biopsy (15.2%) when a columnar epithelial-lined esophagus was present (Demeester, 2022).

In 2023, we updated the references and guidelines and added new studies to the policy that confirm previous findings. No policy changes are warranted.

A systematic review and meta-analysis of found WATS-3D increased dysplasia detection over forceps biopsies alone, especially detection of indefinite for dysplasia and low grade dysplasia, by 7.2% (95% confidence interval 3.9% to 11.5%, seven studies) and increased high grade dysplasia/esophageal cancer detection by 2.1% (95% confidence interval 0.4% to 5.3%, six studies). Outcomes of dysplasia diagnosed solely on WATS-3D were confirmed in only 20 participants and the overall quality of included studies was graded as poor to moderate (Codipilly, 2022).

A prospective, multicenter randomized study (n = 172) compared the concordance and discordance between WATS-3D and four-quadrant random forceps biopsies for detection of high grade dysplasia and esophageal adenocarcinoma in participants under endoscopic surveillance for Barrett's esophagus and a recent history of dysplasia or mucosal adenocarcinoma. There was no significant difference in detection rates between the two techniques as single modalities ($P = .36$). WATS-3D detected an additional 18 cases high grade dysplasia and

esophageal adenocarcinoma that forceps biopsies missed, and WATS-3D missed 12 cases high grade dysplasia and esophageal adenocarcinoma detected by forceps biopsies (van Munster, 2023).

An analysis of two registry studies (n = 8,471) found WATS-3D added to forceps biopsy increased detection of intestinal metaplasia 47.6% and dysplasia 17.5% in participants regardless of the length of segments of esophageal columnar-lined epithelium (Trindade, 2023).

A single-institution retrospective study (n = 109) confirmed the improved detection of WATS-3D as an adjunct to forceps biopsy, although WATS-3D was unable to clearly discriminate low-grade dysplasia from an indefinite for dysplasia pathological diagnosis (Zhao, 2022).

In 2024, we found a new guideline from The European Society of Gastrointestinal Endoscopy that did not recommend the use of WATS-3D (Weusten, 2023). No policy changes are warranted.

In 2025, no new relevant literature found. No policy changes warranted.

References

On November 10, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Barrett’s esophagus,” “esophageal cancer,” “forceps biopsy,” “esophageal dysplasia,” “esophagitis,” and “WATS-3D.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Choi WT, Lauwers GY, Montgomery EA. Utility of ancillary studies in the diagnosis and risk assessment of Barrett's esophagus and dysplasia. *Mod Pathol.* 2022;35(8):1000-1012. Doi:10.1038/s41379-022-01056-0.

ClinicalTrials.gov. The evaluation of patients with esophageal and foregut disorders with WATS (Wide Area Transepithelial Sample With 3-Dimensional Computer-Assisted Analysis) vs. 4-quadrant forceps biopsy. https://www.clinicaltrials.gov/study/NCT03859557?term=NCT03859557&rank=1. Last updated March 11, 2019.

Codipilly DC, Chandar AK, Singh S, et al. The effect of endoscopic surveillance in patients with Barrett’s esophagus: A systematic review and meta-analysis. *Gastroenterology*. 2018;154(8):2068-2086.e5. Doi: 10.1053/j.gastro.2018.02.022.

Codipilly DC, Krishna Chandar A, Wang KK, et al. Wide-area transepithelial sampling for dysplasia detection in Barrett's esophagus: A systematic review and meta-analysis. *Gastrointestinal endoscopy*. 2022;95(1):51-59 e7. Doi: 10.1016/j.gie.2021.09.015.

Demeester S, Smith C, Severson P, Jobe B, Woodworth P, Dunst C. Multi-center randomized trial comparing standard forceps biopsies to wide-area transepithelial sampling brush for finding intestinal metaplasia and dysplasia in the esophagus and at the gastroesophageal junction. *Am J Gastroenterol*. 2019;114:S207-S208. Doi: 10.14309/01.ajg.0000590944.34704.3c.

Demeester S, Smith C, Severson P, et al. Hawaii Esophageal Course Study Group. Multi-center randomized controlled trial comparing forceps biopsy sampling with wide-area transepithelial sampling brush for detecting intestinal metaplasia and dysplasia during routine upper endoscopy. *Gastrointest Endosc*. 2022;95(6):1101-1110.e2. Doi: 10.1016/j.gie.2021.11.044.

Ding YE, Li Y, He XK, Sun LM. Impact of Barrett’s esophagus surveillance on the prognosis of esophageal adenocarcinoma: A meta-analysis. *J Dig Dis*. 2018;19(12):737-744. Doi: 10.1111/1751-2980.12682.

Gross SA, Smith MS, Kaul V, and the US Collaborative WATS^{3D} Study Group. Increased detection of Barrett's esophagus and esophageal dysplasia with adjunctive use of wide-area transepithelial sample with three-dimensional computer-assisted analysis (WATS). *United European Gastroenterol J*. 2018;6(4):529-535. Doi: 10.1177/2050640617746298.
Johanson JF, Frakes J, Eisen D, et al. EndoCDx Collaborative Group. Computer-assisted analysis of abrasive transepithelial brush biopsies increases the effectiveness of esophageal screening: A multicenter prospective clinical trial by the EndoCDx Collaborative Group. *Dig Dis Sci*. 2011;56(3):767-772. Doi: 10.1007/s10620-010-1497-6.
Krishnamoorthi R, Singh S, Ragunathan K, et al. Factors associated with progression of Barrett's esophagus: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol*. 2018;16(7):1046-1055.e8. Doi: 10.1016/j.cgh.2017.11.044.
Lowe D, Kudaravalli P, Hsu R. Barrett metaplasia. StatPearls [Internet]. https://pubmed.ncbi.nlm.nih.gov/29083678/. Last updated December 26, 2022.

Muthusamy VR, Wani S, Gyawali CP, Komanduri S. Aga clinical practice update on new technology and innovation for surveillance and screening in Barrett's esophagus: Expert review. *Clin Gastroenterol Hepatol*. 2022;20(12):2696-2706.e1. Doi: 10.1016/j.cgh.2022.06.003.

National Comprehensive Cancer Network. Esophageal and esophagogastric junction cancers. Version 2. 2023. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Last revised March 10, 2023.

Qumseya B, Sultan S, Bain P, et al. ASGE Standards of Practice Committee. ASGE guideline on screening and surveillance of Barrett's esophagus. *Gastrointest Endosc*. 2019;90(3):335-359.e2. Doi: 10.1016/j.gie.2019.05.012.
Shaheen NJ, Falk GW, Iyer PG, et al. Diagnosis and management of Barrett's esophagus: An updated ACG guideline. *Am J Gastroenterol*. 2022;117(4):559-587. Doi: 10.14309/ajg.0000000000001680.

Shaheen NJ, Falk GW, Iyer PG, Gerson LB, American College of Gastroenterology. ACG clinical guideline: Diagnosis and management of Barrett's esophagus. *Am J Gastroenterol*. 2016;111(1):30-50. Doi: 10.1038/ajg.2015.322.
Smith M, Iorio N, Walzer E, et al. Wide-area transepithelial sampling with computer-assisted 3-dimensional analysis (WATS^{3D}) safely evaluates a variety of esophageal disorders. *Am J Gastroenterol*. 2014;109:S24. https://journals.lww.com/ajg/Fulltext/2014/10002/Wide_Area_Transepithelial_Sampling_With.66.aspx.
Smith MS, Ikonomi E, Bhuta R, et al. and US Collaborative WATS Study Group. Wide-area transepithelial sampling with computer-assisted 3-dimensional analysis (WATS) markedly improves detection of esophageal dysplasia and Barrett's esophagus: analysis from a prospective multicenter community-based study. *Dis Esophagus*. 2019;32(3):doy099. Doi: 10.1093/dote/doy099.
Smith MS. The role of brush biopsy in the management of Barrett esophagus. *Gastroenterology & Hepatology.* 2016;12(11). https://www.gastroenterologyandhepatology.net/archives/november-2016/the-role-of-brush-biopsy-in-the-management-of-barrett-esophagus/.

Suresh Kumar VC, Harne P, Patthipati VS, et al. Wide-area transepithelial sampling in adjunct to forceps biopsy increases the absolute detection rates of Barrett's oesophagus and oesophageal dysplasia: A meta-analysis and systematic review. *BMJ Open Gastroenterol*. 2020;7(1):e000494. Doi: 10.1136/bmjgast-2020-000494.
Trindade AJ, Odze RD, Smith MS, Kaul V. Benefit of adjunctive wide-area transepithelial sampling with 3-dimensional computer-assisted analysis plus forceps biopsy based on Barrett's esophagus segment length. *Gastrointestinal endoscopy*. 2023;98(3):316-325. Doi: 10.1016/j.gie.2023.03.032.

van Munster SN, Leclercq P, Haidry R, et al. Wide-area transepithelial sampling with computer-assisted analysis to detect high grade dysplasia and cancer in Barrett's esophagus: A multicenter randomized study. *Endoscopy*. 2023;55(4):303-310. Doi: 10.1055/a-1949-9542.

Vennalaganti PR, Kanakadandi VN, Gross SA, et al. Inter-observer agreement among pathologists using wide-area transepithelial sampling with computer-assisted analysis in patients with Barrett's esophagus. *Am J Gastroenterol*. 2015;110(9):1257-1260. Doi: 10.1038/ajg.2015.116.

Weusten BLAM, Bisschops R, Dinis-Ribeiro M, et al. Diagnosis and management of Barrett esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy*. 2023. Doi:10.1055/a-2176-2440.

Zhao CL, Hossein-Zadeh Z, Dabiri B, et al. The concordance between wide-area transepithelial sampling with computer-assisted 3-dimensional analysis (WATS-3D) and standard endoscope biopsy in the detection of Barrett's esophagus and esophageal dysplasia. *Ann Diagn Pathol*. 2022;60:151982. Doi: 10.1016/j.anndiagpath.2022.151982.

Policy updates

10/2020: initial review date and clinical policy effective date: 11/2020

10/2021: Policy references updated.

10/2022: Policy references updated.

10/2023: Policy references updated.

10/2024: Policy references updated.

12/2025: Policy references updated.