Medical Coverage Policy

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Wide-Area Transepithelial Tissue Sampling with Computer-Assisted 3D Analysis (WATS3D)

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Oral Cancer Screening Systems

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Overview

This Coverage Policy addresses wide-area transepithelial tissue sampling with computer-assisted three-dimensional (3D) analysis (WATS3D) which is proposed as an endoscopic method of sampling tissue from the esophagus for detection and surveillance of Barrett's esophagus.

Coverage Policy

The use of wide-area transepithelial tissue sampling with computer-assisted three-dimensional (3D) analysis (WATS3D) is considered experimental, investigational or unproven.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

General Background

Wide-area transepithelial sampling with three-dimensional sampling (WATS/ WATS3D/ WATS-3D / WATS^{3D}) (CDx Diagnostics, Suffern, NY) is proposed as an endoscopic method of sampling tissue from the esophagus for detection and surveillance of Barrett's esophagus (BE). It is proposed to be used in addition to the standard biopsy protocol during endocsopy. The first-generation WATS^{3D} system was formerly known as EndoCDx. WATS^{3D} is a novel method that uses an abrasive brush to sample larger surface areas of the esophagus. These specimens allow for analysis of large sheets of cells while maintaining the 3-dimensional aspects of the tissue. The tissue is analyzed by software that uses algorithm to identify abnormal cells, which are confirmed by an expert pathologist.

The current gold standard for screening in BE is the 'Seattle protocol' which includes detailed endoscopic examination with 4 quadrant nontargeted mucosal forceps biopsies every 1 to 2 cm in the BE segment, combined with direct sampling of any visible lesions or "targeted" biopsies.

U.S. Food and Drug Administration (FDA)
No information on EndoCDx or WATS^{3D} (CDx Diagnostics) is found on FDA website search.

Professional Societies/Organizations
National Comprehensive Cancer Network® (NCCN): NCCN clinical guideline for esophageal and esophagogastric junction cancers (Version 4.2024 — July 30, 2024) notes that the use of wide-area transepithelial sampling with computer-assisted 3-dimensional analysis (WATS3D) is a relatively new sampling technique combining an abrasive brush biopsy of the Barrett esophagus mucosa with computer-assisted pathology analysis to highlight abnormal cells, may help increase the detection of esophageal dysplasia in patients with Barrett esophagus (MS-8). It does not include this test in the screening/testing recommendations for esophageal cancer (ESOPH-D, 2 OF 2). It is noted in the guideline, "the utility and accuracy of WATS for detecting HGD/adenocarcinoma in patients with Barrett's esophagus needs to be evaluated in larger phase III randomized trials" (MS-8) (NCCN, 2024).

American Gastroenterological Association (AGA): The AGA Clinical Practice Update on High-Quality Upper Endoscopy: Expert Review document includes 'The Biopsy Protocols for the Evaluation of Selected Upper Gastrointestinal Conditions' (Table 1) specific to Barrett's esophagus. It states:

- Four-quadrant biopsy specimens for every 1-2 cm of Barrett's esophagus (Seattle protocol), along with targeted biopsy specimens of mucosal abnormalities.
- Avoid routine biopsy specimens of a normal or irregular Z-line.
- Diagnostic yield is improved significantly if at least 8 biopsy specimens are taken, even if patients have only 1-2 cm of Barrett's esophagus (AGA/ Nagula, 2024).

American College of Gastroenterology (ACG): The 2022 ACG Updated Guideline on the Diagnosis and Management of Barrett's Esophagus makes 21 recommendations. They are broken up by:

- Diagnosis
- Screening
- Surveillance
- Treatment (Medical)
- Treatment (Endoscopic).

Diagnosis-specific Recommendations	Quality of evidence	Strength of recommendation
3.We suggest at least 8 endoscopic biopsies be obtained in screening examinations with endoscopic findings consistent with possible BE, with the Seattle protocol followed for segments of longer than 4 cm	Low	Conditional
4. We recommend that dysplasia of any grade detected on biopsies of BE be confirmed by a second pathologist with expertise in GI pathology	Low	Strong

Surveillance-specific Recommendations	Quality of evidence	Strength of recommendation
8. We recommend both white light endoscopy and chromoendoscopy in patients undergoing endoscopic surveillance of BE.	Moderate	Strong

Surveillance-specific Recommendations	Quality of evidence	Strength of recommendation
9. We recommend a structured biopsy protocol be applied to minimize detection bias in patients undergoing endoscopic surveillance of BE.	Low	Strong
10. We suggest endoscopic surveillance be performed in patients with BE at intervals dictated by the degree of dysplasia noted on previous biopsies.	Very low	Conditional
11. We recommend that length of BE segment be considered when assigning surveillance intervals with longer intervals reserved for those with BE segments of <3 cm.	Moderate	Strong
12. We could not make a recommendation on the use of wide-area transepithelial sampling with computer-assisted 3-dimensional analysis in patients undergoing endoscopic surveillance of BE.	n/a	n/a
13. We could not make a recommendation on the use of predictive tools (p53 staining and TissueCypher) in addition to standard histopathology in patients undergoing endoscopic surveillance of BE (Shaheen, et al., 2022).	n/a	n/a

American Gastroenterology Association (AGA): The AGA 2022 Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review states the following:

- Best Practice Advice 7: Wide-area transepithelial sampling (WATS-3D) may be used as an adjunctive technique to sample the suspected or established Barrett's segment (in addition to the Seattle biopsy protocol)

Further prospective studies directly comparing WATS-3D and Seattle protocol are needed to understand if WATS-3D sampling might be as or more effective (Muthusamy, et al., 2022).

American Society for Gastrointestinal Endoscopy (ASGE): ASGE published guidelines on the screening and surveillance of Barrett's esophagus (ASGE, 2019).

- In patients with known or suspected BE, we suggest using WATS-3D in addition to Seattle protocol biopsy sampling compared with white-light endoscopy with Seattle protocol biopsy sampling (Strength of recommendation: conditional, Quality of evidence: low).

Strength of recommendations-conditional:

- Patients: Most individuals in this situation would want the suggested course of action, but many would not.
- Clinicians: Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their values and preferences.
- Policymakers: Policymaking will require substantial debate and involvement of various stakeholders.

Quality of evidence- low:

- Meaning: Our confidence in the estimate of the effect is limited; the true effect may be substantially different from the estimate of the effect.
- Interpretation: Further research is very likely to have an impact on our confidence in the estimate of the effect and is likely to change the estimate.

Literature Review

DeMeester et al. (2021) conducted a multicenter, randomized controlled trial to compare the frequency of Intestinal metaplasia (IM) detection during upper endoscopy by forceps biopsy sampling (FB) versus wide area transepithelial sampling (WATS) brush. Patients presenting for upper endoscopy for foregut symptoms or surveillance of Barrett's esophagus (BE) at nine centers in the United States were randomized to either FB or WATS. The study included 1,002 patients with FB was done in 505 and WATS in 497. The overall frequency of finding IM was 21% and was similar with FB (19.6%) and WATS (22.7%, P = .2). Low-grade dysplasia was found in eight patients and no patient had high-grade dysplasia. There was no difference in detection of dysplasia between FB and WATS. In patients with no history of IM, WATS found significantly more IM compared with FB when a columnar-lined esophagus (CLE) was present (32.4% with WATS vs 15.2% with FB, P = .004). In 184 patients with known BE, FB and WATS found IM with similar frequency (38.5% FB vs 41.9% WATS, P = .6) with no difference in short- or long-segment BE. The authors concluded that overall, FB and WATS detected a similar frequency of IM and dysplasia with WATS was twice as likely as FB to find IM in patients without a history of BE who had CLE on endoscopy. In patients with known BE, WATS and FB showed IM and dysplasia with similar frequency. Limitations of this study noted by the authors include most patients were women with no history of intestinal metaplasia (IM), and this influenced the frequency of finding IM. Another cited limitation is only 30 patients with long-segment BE underwent surveillance. In these patients, 14 had FB and16 had WATS, and although both techniques found IM and dysplasia with a similar frequency, this should be studied further in a larger group of patients given the potential for a Type II error. The authors noted in this series there was a paucity of patients with dysplasia, and future studies in a larger group of patients with dysplasia may allow better assessment of WATS versus FB in this setting.

Van Munster et al. (2023) conducted a randomized trial including 17 participating medical centers to evaluate WATS^{3D} (WATS) as a substitute for four-quadrant random forceps biopsies (FB). A total of 172 patients scheduled for a regular imaging endoscopy for BE, with a history of BE-associated neoplasia were included. They had either:

- BE in the absence of visible lesions with either low grade dysplasia (LGD) or high-grade dysplasia (HGD) diagnosed on FBs; or,
- flat BE after prior endoscopic resection (ER) for a visible lesion with the resection specimen showing LGD, HGD, or mucosal esophageal adenocarcinoma (EAC) with good-to-moderate differentiation, without lymphovascular invasion, and with negative resection margins.

Exclusion criteria for participation included: age <18 years; BE length < 2cm circumferential extent or > 10 cm maximum extent; prior ablation therapy; and history of esophageal surgery other than fundoplication. Patients were randomized by a computer-generated system into two groups: FB sampling followed by WATS; or WATS followed by FB. The minimum time between endoscopic resection (ER) and randomization was 6 weeks. WATS and FB were performed during the same endoscopy.

- Allocated to FB, then WATS (n = 81) but 71 analyzed. Inadequate WATS specimen, n = 9; Inadequate FB specimen, n = 1.
- Allocated to WATS, then FB (n = 91) but 76 analyzed. Inadequate WATS specimen, n = 14; Inadequate FB specimen, n = 1.

Results demonstrated no statistically significant difference between WATS and FB for the detection of HGD/EAC as single modality. However, using WATS as an adjunct to FB significantly increased the detection of HGD/ EAC vs. FB alone (absolute increase 10%) in a population of BE patients enriched for dysplasia.

Of the 172 patients were included, of whom 21 had high grade dysplasia (HGD)/esophageal adenocarcinoma (EAC) detected by both modalities, 18 had HGD/EAC detected by WATS but missed by FB, and 12 were detected by FB but missed by WATS. The detection rate of HGD/EAC did not differ between WATS and FB (P = 0.36). No complications related to the procedure

occurred. The authors concluded they did not find a statistically significant difference between WATS and FB for the detection of HGD/EAC as single modality.

Vennalaganti et al. (2018) conducted a randomized non-controlled trial of referred Barrett's esophagus (BE) patients undergoing surveillance at 16 medical centers. The study included 160 patients (mean age, 63.4 years; 76% men; 95% white) who received either biopsy sampling followed by WATS or WATS followed by biopsy sampling. The primary outcome was rate of detection of high-grade dysplasia/esophageal adenocarcinoma (HGD/EAC) using WATS in conjunction with biopsy sampling compared with biopsy sampling alone using standard histopathologic criteria. Secondary aims included evaluating neoplasia detection rates based on the procedure order (WATS vs biopsy sampling first), of each procedure separately, and the additional time required for WATS. The median circumferential and maximal BE extents were 1.0 cm (interquartile range: .0-5.0) and 4.0 cm (interquartile range, 2.0-8.0), respectively. The diagnostic yield for biopsy sampling alone was as follows: HGD/EAC, 7 (4.4%); low-grade dysplasia (LGD), 28 (17.5%); nondysplastic BE (NDBE), 106 (66.25%); and no BE, 19 (11.9%). The addition of WATS to biopsy sampling yielded an additional 23 cases of HGD/EAC (absolute increase, 14.4%; 95% confidence interval, 7.5%-21.2%). Among these 23 patients, 11 were classified by biopsy sampling as NDBE and 12 as LGD/indefinite for dysplasia (IND); 14 received biopsy sampling first and nine WATS first (not significant) and most (n = 21; 91.7%) had a prior dysplasia history. WATS added an average of 4.5 minutes to the procedure. The authors concluded that results of this multicenter, prospective, randomized trial demonstrate that the use of WATS in a referral BE population increases the detection of HGD/EAC. The authors noted that at the time of the trial WATS specimens were evaluated only by pathologists at a single central laboratory and that in the study population (20%) were enriched with BE patients with a known history of dysplasia or referred for endoscopic therapy, and the results may not be generalizable to a low-risk BE surveillance population.

Shaheen et al. (2024) reported on a cohort of 23,933 consecutive patients enrolled in a prospective observational registry. The registry began in April 2021 and is ongoing (CDx Diagnostics, Suffern, NY). Study patients were selected from an initial cohort of 36,355 patients who fulfilled the following inclusion criteria:

- the indication for the endoscopic procedure was screening due to GERD.
- patient did not have a history of Barrett’s esophagus (BE), intestinal metaplasia (IM), or dysplasia in esophageal mucosa.
- no history of esophageal surgery, endoscopic ablation, or endoscopic mucosal resection (EMR) at any time before entrance into the study.
- WATS-3D and forcep biopsy (FB) were both used in the same endoscopic session.

While all patients underwent both WATS-3D and (FB) at the time of endoscopy, the sequence was determined at the endoscopist’s discretion. FBs were performed first in 79% of patients, whereas the remainder had WATS-3D performed first. At the time of endoscopy, the location and characteristics of the Z line were noted and categorized into 1 of 4 groups:

1. regular
2. irregular (defined as <1 cm of esophageal columnar-lined epithelium [CLE] extending into the tubular esophagus)
3. potential short-segment BE ([SSBE], defined as ≥1 cm but <3 cm of CLE extending into the tubular esophagus)
4. potential long-segment BE ([LSBE], defined as ≥3 cm of CLE extending into the tubular esophagus)

Shaheen et al. evaluated the efficacy of adjunctive use of WATS-3D in consecutive patients with GERD who were being screened for BE. Shaheen et al. reported:

- Overall, WATS-3D diagnostic yield for IM was significantly higher than FB in the entire study cohort (25.6% vs 16.3%, P< 0.0001 and in each of the 4 endoscopic subgroups separately.

- Of the 6,829 patients with ≥1 cm of esophageal columnar mucosa (fulfilling endoscopic criteria for BE), 2,878 (42.1%) had IM identified by either FB or WATS-3D and thus fulfilled both the endoscopic and histological criteria for BE. This included 1,317 patients (19.3% of those fulfilling endoscopic criteria for BE) detected by WATS-3D only, but not by FB
- A total of 19.3% (1,317/6,829) of patients who demonstrated endoscopic findings consistent with BE had their diagnosis confirmed solely on the basis of the WATS-3D findings.
- No significant differences were detected between the diagnostic yields of FB compared with WATS-3D regarding detection of any grade of dysplasia, nor in any of the individual diagnostic categories of dysplasia when each of those were evaluated separately.
- Shaheen reported that among patients with positive WATS-3D but negative FB, the care plan changed in 90.7%.

The authors noted as a registry study, the use of electronic or dye-based chromoendoscopy was not a mandate, and the routine use of these modalities may have affected our results. There was no central pathology review; thus, confirmation of the FB diagnosis could not be performed. Similarly, there was no central review of endoscopic findings, such as the appearance of the Z line. Also, a small percentage of patients (1% overall) had dysplasia and given the lack of confirmatory reads of these patients, miscategorization could have affected reported adjunctive yields.

Smith et al. (2019) conducted a multicenter, prospective trial to investigate the benefit of wide area transepithelial sampling with 3-dimensional computer-assisted analysis (WATS) used adjunctively to the combination of random and targeted forcep biopsy (FB) in the detection of esophageal dysplasia (ED), and as a secondary outcome, Barrett's esophagus (BE). The study included 12,899 patients ages 18 years and older undergoing screening for suspected BE as well as those with known BE undergoing surveillance for dysplasia. Of these, 14% of patients had a history of known BE. Patients with a suspicious lesion concerning for invasive cancer on endoscopy and requiring endoscopic resection were excluded from the study. Investigators were instructed to use both WATS and FB to sample suspected BE only in patients displaying salmon-colored mucosa in the tubular esophagus. Community endoscopists at 21 sites utilized WATS as an adjunct to both targeted and random FB in patients undergoing BE screening and surveillance. The investigators alternated taking FB and WATS samples first. WATS specimens were analyzed at CDx Diagnostics (Suffern, NY) while FB samples were analyzed by each site's regular pathologists. FB identified 88 cases of ED, and WATS detected an additional 213 cases missed by FB. These 213 cases represented an absolute increase of 1.65%, raising the yield from 0.68% to 2.33%. Adding WATS to FB increased the overall detection of ED by 242% (95% CI: 191%-315%). Fewer than 61 patients needed to be tested with WATS to identify an additional case of ED. The combination of random and targeted FB identified 1,684 cases of BE, and WATS detected an additional 2,570 BE cases. The absolute incremental yield of adding WATS to FB is 19.9%, increasing the rate of detection from 13.1% to 33%. Adding WATS to FB increased the overall detection of BE by 153% (95% CI: 144-162%). The number needed to test with WATS in order to detect an additional case of BE was 5. Whether FB or WATS was done first did not impact the results. The authors concluded that these results underscore the shortcomings of FB in detecting BE-associated neoplasia, which can potentially impact the management and clinical outcomes of these patients. The authors noted that although routine screening for BE in women is not recommended, women accounted for 61% of patients in the study and data regarding females in our study who would be potential candidates for BE screening by exhibiting multiple risk factors for BE or EAC (age >50 years of age, Caucasian race, chronic or frequent GERD, central obesity, waist circumference >88 cm, waist to hip ratio >0.8, current or past history of smoking, a confirmed family history of BE or EAC) was not collected.

Gross et al. (2018) conducted a multicenter, prospective trial to determine if wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS) used

adjunctively with forceps biopsy (FB) can increase the detection of Barrett's esophagus (BE) and esophageal dysplasia (ED). The study included 4,203 patients, that were screened for suspected BE and undergoing surveillance for BE. The patients at 25 community-based practices underwent WATS adjunctively to targeted FB and random four-quadrant FB. Findings included that 594 were diagnosed with BE by FB alone, and 493 additional cases were detected by adding WATS, increasing the overall detection of BE by 83% (493/594, 95% CI 74%–93%). Low-grade dysplasia (LGD) was diagnosed in 26 patients by FB alone, and 23 additional cases were detected by adding WATS, increasing the detection of LGD by 88.5% (23/26, 95% CI 48%–160%). It was noted in the study that there were 288 cases of BE and 16 cases of ED identified by FB that were undetected by WATS. These discrepant results are not unexpected as FB was used both to target any visible mucosal abnormality and to obtain random four-quadrant biopsy samples and WATS was used only to test large segments of the esophagus that would have remained untested by both targeted and random FB. The authors note that the study was not designed to address the question of whether WATS is more or less effective than FB in identifying BE and ED. The authors concluded that the study demonstrates that the increased adjunctive use of WATS to FB increases the detection of BE and ED.

Johanson et al. (2010) prospectively evaluated 1,183 patients (from original cohort of 1,266 pts) to determine if and by how much the detection of BE and esophageal dysplasia can be increased by the addition of EndoCDx to a standard esophageal biopsy protocol. Included patients were over age 18, scheduled for mucosal forceps biopsies for screening or surveillance of BE and dysplasia including with symptoms of gastroesophageal reflux and suspected BE as well as those with known BE undergoing surveillance for dysplasia. Patients were excluded if inadequate brush biopsy or forceps biopsy results or those with missing pathology reports. Each patient had two brush biopsies (BB) and then random four-quadrant FB every 1–2 cm of the esophagus. Among the 1,183 patients, BE was diagnosed in 363 patients by FB and in 340 patients by BB. Of the 340 patients with BE detected by the BB, 146 had negative FB results. The authors note the addition of two brush biopsies to the standard multiple forceps biopsy protocol increased the detection of BE by 39.8% (146/363, 95% confidence interval 32–48%). This added detection of BE in 11.5% of all patients tested with the BB (146/1,266) resulted in a number of patients needed to test (NNT) to obtain each additional positive finding of Barrett's esophagus of 8.7.
Esophageal dysplasia was diagnosed in 16 patients by forceps biopsy and in 19 patients by brush biopsy. Of the
19 patients diagnosed with esophageal dysplasia by brush biopsy, 14 had negative forceps biopsy results. It is unknown if there were adverse events or complications.

Trindade et al. (2023) reported a retrospective analysis from a pooled analysis of two registry studies to assess WATS^{3D} (WATS) performance based on BE segment length. A total of 8471 participants were enrolled if

A) they were either being screened for BE, or
B) were in a BE surveillance protocol and had visible columnar-lined epithelium (CLE) in the tubular esophagus (any length) at the time of endoscopy.

Participants were excluded if they had incomplete records, prior esophageal surgery, endoscopic mucosal (or submucosal) resection or prior ablation, did not have CLE, or did not undergo FB at the same session. All participants underwent both WATS and FB. A total of:

- 457 (5%) participants had <1 cm of esophageal columnar-lined epithelium (CLE)
- 6262 (74%) participants had short columnar segments (1-2.9 cm)
- 1752 (21%) participants had long segments (at least 3 cm).

The author reported that the overall adjunctive yield of WATS for a diagnosis of any BE was 47.6% (absolute yield, 17.5%). Separated into the various length categories, the adjunctive yield of WATS-3D for a diagnosis of "Any BE" was:

- 64% in the <1 cm length category,
- 59.8% in the short-segment category,

- 22.7% in the long-segment category.

The difference between short and long segments was significant (P = .001). With respect to finding "any dysplasia," the overall adjunctive yield of WATS was 139.3% (absolute yield, 2.4%). Adverse events / complications were not reported.
The authors summarized that when WATS is added as an adjunct to FB, it is effective at increasing the diagnostic yield of detection of BE, as well as additional dysplasia in participants with both short- and long-segment esophageal columnar-lined mucosa. They noted that further prospective studies should be conducted to determine if WATS can be used potentially as a replacement to FB to detect nondysplastic BE (NDBE) and dysplasia in participants with either suspected or known BE, given the known limitations and frequent lack of adherence to the Seattle protocol method of FB tissue sampling in current gastroenterology practice.

Shaheen et al. (2022) retrospectively analyzed a prospective registry to evaluate the outcome, measured in terms of progression to high-grade dysplasia (HGD) or EAC, of a cohort of 4545 BE patients diagnosed with either no dysplasia, BE-associated crypt dysplasia (CD), or low-grade dysplasia (LGD) by WATS3D.The primary outcome was the crude progression rate, defined as the proportion of patients per patient-year who demonstrated progression on forceps biopsy sampling to either HGD or EAC, stratified by baseline WATS3D histologic grade. Crude progression rate was calculated by dividing the number of patients progressing to HGD/EAC by the total patient-years of observation for each baseline disease stage (NDBE, CD, and LGD).
Shaheen et al. defined a cohort of 4545 patients undergoing a WATS3D procedure for either screening or surveillance of BE, with no prior history of esophageal dysplasia or endoscopic eradication therapy, fulfilling the following criteria:

1. Initial endoscopy demonstrating ≥1 cm of columnar-lined mucosa in the esophagus.
2. Forceps biopsy sampling of the esophageal columnar metaplasia showing intestinal metaplasia.
3. WATS3D sampling of the esophagus demonstrating intestinal metaplasia and either nondysplastic BE (NDBE), CD, or LGD. Patients with WATS3D findings considered indefinite for dysplasia were excluded.
4. At least 1 additional follow-up endoscopy with WATS3D administration, separated by a minimum of 12 months from the index endoscopy.

The 4545 patients had 2 WATS3D separated by ≥12 months. The mean follow-up was 1.97 years. Reported results included but are not limited to the following: Overall, .33% of patients progressed to HGD/EAC, as diagnosed by forceps biopsy sampling, over the follow-up period. Overall, 55% of the baseline WATS3D samples had accompanying forceps biopsy sampling data available for analysis, and of these, over 98% of the forceps biopsy samples were diagnosed as nondysplastic BE (NDBE). No patient was diagnosed with CD or HGD on forceps biopsy sampling. In patients with baseline NDBE, progression was .08% per patient-year (95% confidence interval [CI], .02%-.14%). Progression of baseline CD was significantly higher, at 1.42% per patient-year (95% CI, 0%-3.01%). For baseline LGD, progression was 5.79% per patient-year (95% CI, 1.02%-10.55%). Other risk factors for progression were increasing age and BE segment length. Adverse events are unknown as they were not reported.

Corbett et al. (2022) retrospectively analyzed two prospective registries, defining a cohort of 1114 patients.
The analysis purpose was to determine the "adjunctive and absolute yield of WATS3D for detection of post ablation IM". Specifically, Corbett et al. evaluated the diagnostic efficacy of WATS3D for detection of intestinal metaplasia (IM) and dysplasia / esophageal adenocarcinoma (EAC) in Barrett's esophagus (BE) patients who have undergone endoscopic eradication therapy (EET).
The characteristics of the included cohort are unclear. Corbett et al. reports including patients who had undergone radiofrequency ablation (77.7%) and had a preablation history of nondysplastic BE (NDBE) (47.9%), high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) (18.7%), or

indefinite dysplasia, crypt dysplasia, low-grade dysplasia, and/or unspecified dysplasia (33.4%) on prior preablation endoscopies. Most patients also had a hiatus hernia (60.3%). Patients were included if they were being surveyed for BE after endoscopic eradication therapy (EET) (≥1 EET session) and did not have prior esophageal surgery other than endoscopic mucosal resection (EMR). The cohort included patients whose baseline diagnosis preablation was nondysplastic BE (NDBE), most of whom were derived from 2 large studies specifically looking at this group as well as patients with dysplasia. Additionally, the cohort included patients who had not yet completed EET as well as some deemed refractory to EET. Patients were excluded if information regarding endoscopy or histology were incomplete or unavailable for analysis. All patients underwent both WATS-3D and FB sampling at the time of postablation endoscopy.IM adjunctive yield of WATS was defined as the number of IM cases added by WATS (that were negative for IM by FB sampling) divided by the number of IM cases detected by FB sampling (including dysplasia cases).The absolute yield of WATS was defined as the number of cases that WATS detected (that were not detected by FB sampling) divided by the total number of cases.
Reported results from the cohort analysis include but are not limited to the following: the WATS-3D adjunctive yield for detection of residual/recurrent IM or dysplasia was 52.5% and 91.5%, respectively. The absolute yield for IM and dysplasia detection was 16% and 4.4%, respectively. Of 29 patients with high-grade dysplasia or esophageal adenocarcinoma detected by WATS3D, FB sampling missed 11, including 7 where FB sampling did not detect any IM. The added yield of detection of BE was found to be greater in patients with either no endoscopic evidence of residual BE (260%) or in those with short segments of residual BE (66.9%) compared with long-segment BE (21.1%). However, for dysplasia, no differences were noted according to either the presence or length of visible BE at endoscopy. Adverse events are unknown as they were not reported. Most patients were white (88%). A limitation of this study is the potentially conflicting reported inclusion criteria.

Kaul et al. (2020) conducted a retrospective review to evaluate the clinical utility of WATS3D and its impact on the management of patients with BE and dysplasia. The study included 432 consecutive patients who had a WATS3D positive and an accompanying forcep biopsy (FB) negative result. Physicians were contacted to determine if the WATS3D result impacted their decision to enroll patients in surveillance or increase the frequency of surveillance, recommend ablation, and/or initiate or increase the dose of proton pump inhibitors (PPIs). WATS3D directly impacted the management of 97.8% of 317 BE patients; 96.2% were enrolled in surveillance and 60.2% were started on PPIs or their dose was increased. WATS3D impacted the management of 94.9% and 94.1% of the 98 low-grade dysplasia and 17 high-grade dysplasia patients, respectively. As a result of WATS3D, 33.7% of low-grade dysplasia and 70.6% of high-grade dysplasia patients underwent endoscopic therapy. More than 37% of all dysplasia patients were enrolled in a surveillance program, and nearly 30% were scheduled to be surveilled more frequently. PPIs were either initiated, or the dose was increased in more than 54% of all dysplasia patients.

Agha et al. (2021) conducted a retrospective observational cohort study and included 108 patients who underwent screening for BE with WATS3D and forceps biopsy (FB) between across three endoscopy centers. The FB specimens were reviewed by community pathologists, while the WATS3D samples were sent to CDX technology labs, NY. The review included 108 patients that were screened for BE using both modalities concurrently.
FB and WATS3D detected 62 (57.4%) and 83 (76%) cases of BE, respectively. The absolute difference of 21 cases (18.6%) of BE was attributed to the addition of WATS3D. The number needed to test with WATS3D was 5. The samples were divided into four groups to compare the agreement across all groups: (FB−; WATS3D+), (FB−; WATS3D−), (FB+; WATS3D+), and (FB+ and WATS3D−). Overall agreement by kappa statistic was 0.74. The authors concluded that WATS3D identified 21 cases of BE missed by FB. Using WATS3D in addition to FB increased the yield of BE during surveillance endoscopy, with no increase in complications.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No Determination found	
LCD		Numerous LCDs	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven when used to report wide-area transepithelial tissue sampling with computer-assisted 3D analysis (WATS3D):

CPT®* Codes	Description
88104	Cytopathology, fluids, washings or brushings, except cervical or vaginal; smears with interpretation
88112	Cytopathology, selective cellular enhancement technique with interpretation (eg, liquid based slide preparation method), except cervical or vaginal
88305	Level IV - Surgical pathology, gross and microscopic examination
88312	Special stain including interpretation and report; Group I for microorganisms (eg, acid fast, methenamine silver)
88361	Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; using computer-assisted technology

***Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.**

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Review	• No clinical policy statement changes. Content moved from Omnibus Codes CP 0504.	11/15/2024

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