FEP 2.01.84 Chromoendoscopy as an Adjunct to Colonoscopy

Effective Date: April 15, 2018

Related Policies:
2.01.87 Confocal Laser Endomicroscopy
6.01.32 Virtual Colonoscopy/CT Colonography

Chromoendoscopy as an Adjunct to Colonoscopy

Description

Chromoendoscopy refers to the use of dyes or stains during endoscopy to enhance tissue differentiation or characterization. When used with colonoscopy, the intent is to increase the sensitivity of the procedure by facilitating the identification of mucosal abnormalities. There are 2 types of chromoendoscopy: one involves actual spraying of dyes or stains through the working channel of an endoscope; the other, known as virtual chromoendoscopy, uses a computer algorithm to simulate different colors of light that result from dye or stain spraying.

FDA REGULATORY STATUS

In August 2014, the Fujifilm EPX-4440HD Digital Video Processor with Fujinon Intelligent Color Enhancement (FICE®) and Light Source was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The FDA documents stated that FICE® could be used to supplement white-light endoscopy but is not intended to replace histopathologic sampling as a means of diagnosis.

In April 2013, the i-SCAN™ (Pentax [Tokyo, Japan]), used for virtual chromoendoscopy, was cleared for marketing by FDA through the 510(k) process.[2] This digital image enhancement technology is part of the Pentax EPK-i5010 Video Processor. The i-SCAN™ has several modes that digitally enhance images in real time during endoscopy. The FDA documents stated that i-SCAN™ is intended as an adjunct following white-light endoscopy but not intended to replace histopathologic analysis.

FDA product code: GCT, PEA, FET (endoscopes and accessories).

No dye or stain product has been specifically approved by FDA for use in chromoendoscopy.

POLICY STATEMENT

Chromoendoscopy is considered **investigational** as an adjunct to diagnostic or surveillance colonoscopy.

Virtual chromoendoscopy is considered **investigational** as an adjunct to diagnostic or surveillance colonoscopy.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FEP 2.01.84 Chromoendoscopy as an Adjunct to Colonoscopy

RATIONALE

Summary of Evidence

Chromoendoscopy

For individuals who have an average risk of CRC who receive chromoendoscopy, the evidence includes an RCT focused on this population. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and change in disease status. The single RCT did not find that high-definition chromoendoscopy identified more clinically meaningful lesions than high-definition white-light colonoscopy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have an increased risk of CRC who receive chromoendoscopy, the evidence includes multiple RCTs, back-to-back colonoscopy studies, and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and change in disease status. A Cochrane systematic review of trials comparing chromoendoscopy with standard colonoscopy in high-risk patients (but excluding those with inflammatory bowel disease) found significantly higher rates of adenoma detection and rates of 3 or more adenomas with chromoendoscopy than with standard colonoscopy. The evidence for detecting larger polyps, defined as greater than 5 mm or greater than 10 mm, is less robust. While 1 study reported a significantly higher detection rate for polyps greater than 5 mm, no studies reported increased detection of polyps greater than 10 mm. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have inflammatory bowel disease who receive chromoendoscopy, the evidence includes observational studies and meta-analyses of observational data. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and change in disease status. The meta-analysis found a statistically significant higher yield of chromoendoscopy over white-light colonoscopy for detecting dysplasia. This evidence established that chromoendoscopy improves polyp detection rates; however, it is unclear whether the additional polyps detected are clinically important and, therefore, whether improved polyp detection rates will translate into improved health outcomes. Moreover, there are concerns about comparison groups used in some of these trials. It is uncertain whether the control groups received optimal colonoscopy; therefore, the improved detection rates by chromoendoscopy might have been a function of suboptimal standard colonoscopy. The evidence is insufficient to determine the effects of the technology on health outcomes.

Virtual Chromoendoscopy

For individuals who have an average risk of CRC who receive virtual chromoendoscopy, the evidence includes several RCTs and a meta-analysis. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and change in disease status. The available RCTs have not found that virtual chromoendoscopy improves the detection of clinically important polyps compared with standard white-light colonoscopy. Moreover, there is a lack of studies on the impact of virtual chromoendoscopy on CRC incidence or mortality rates compared with standard colonoscopy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have an increased risk of CRC who receive virtual chromoendoscopy, the evidence includes several RCTs and a meta-analysis. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and change in disease status. The available RCTs have not found that virtual chromoendoscopy improves the detection of clinically important polyps compared with standard white-light colonoscopy. Moreover, there is a lack of studies on the impact of virtual chromoendoscopy on CRC incidence or mortality rates compared with standard colonoscopy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have inflammatory bowel disease who receive virtual chromoendoscopy, the evidence includes an RCT and nonrandomized comparative study. Relevant outcomes are overall

survival, disease-specific survival, test accuracy and validity, and change in disease status. The RCT found a significantly greater likelihood that virtual chromoendoscopy would correctly identify the extent of disease inflammation than standard colonoscopy but no significant difference in the likelihood of identifying disease activity. A retrospective cohort study found that targeted biopsy resulted in a higher rate of neoplasia detection regardless of endoscopy method used. There is a lack of studies on the impact of virtual chromoendoscopy CRC incidence or mortality rates compared with standard colonoscopy. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Society for Gastrointestinal Endoscopy and American Gastroenterological Association

In 2015, the American Society for Gastrointestinal Endoscopy (ASGE) and the American Gastroenterological Association published the SCENIC consensus statement on surveillance and management of dysplasia in patients with inflammatory bowel disease (IBD).[23] The statement, developed by an international multidisciplinary group representing a variety of stakeholders, incorporated systematic reviews of the literature. Relevant recommendations included the following (see Table 1).

Table 1. Recommendations on Surveillance and Management of Dysplasia in Patients With IBD

Recommendation	LOA	SOR	QOE
"When performing surveillance with white-light colonoscopy, high definition is recommended rather than standard definition."	80%	Strong	Low
"When performing surveillance with standard-definition colonoscopy, chromoendoscopy is recommended rather than white-light colonoscopy."	85%	Strong	Moderate
"When performing surveillance with high-definition colonoscopy, chromoendoscopy is suggested rather than white-light colonoscopy."	84%	Conditional	Low

IBD: inflammatory bowel disease; LOA: level of agreement; QOE: quality of evidence; SOR: strength of recommendation.

Panelists did not reach consensus on the use of chromoendoscopy in random biopsies of patients with IBD undergoing surveillance.

Commentaries in 2 gastroenterology journals questioned whether the SCENIC guidelines would be accepted as the standard of care in IBD surveillance.[24,25] Both commentaries noted that the guidelines considered the outcome of detection of dysplasia and not disease progression or survival. Moreover, the authors noted the lack of longitudinal data on clinical outcomes in patients with dysplastic lesions detected using chromoendoscopy.

American Society for Gastrointestinal Endoscopy

In 2015, ASGE issued guidelines on endoscopy in the diagnosis and treatment of inflammatory bowel disease, which made the following recommendations about chromoendoscopy[26]: "Chromoendoscopy with pancolonic dye spraying and targeted biopsies is sufficient for surveillance in inflammatory bowel disease; consider 2 biopsies from each colon segment for histologic staging."

In 2015, ASGE also published a systematic review and meta-analysis assessing narrow-band imaging (NBI), i-SCAN, and Fujinon Intelligent Color Enhancement for predicting adenomatous polyp histology of small or diminutive colorectal polyps to determine whether they have met previously established criteria or thresholds to incorporate into clinical practice.[27] The ASGE assessment confirmed that:

> "…The thresholds have been met for narrow-band imaging with endoscopists who are experts in using these advanced imaging technologies and when assessments are made with high confidence. The ASGE Technology Committee endorsed the use of NBI for both the 'diagnose-and-leave'

strategy for diminutive (≤5 mm) rectosigmoid hyperplastic polyps and the 'resect-and-discard' strategy for diminutive (≤5mm) adenomatous polyps."

The report addressed the "trepidation" of patients, endoscopists, and pathologists with the "diagnose-and-leave" strategy, indicating there are challenges for implementation for the use of these strategies in clinical practice.

U.S. Multi-Society Task Force on Colorectal Cancer

The 2012 Multi-Society Task Force guidelines on colonoscopy surveillance after screening and polypectomy (consensus update) stated that chromoendoscopy and NBI might enable endoscopists to accurately determine if lesions are neoplastic and if there is a need to remove them and send specimens to pathology. The guidelines noted that these technologies currently do not have an impact on surveillance interval.[28]

U.S. Preventive Services Task Force Recommendations

The 2016 U.S. Preventive Services Task Force recommendations on screening for colorectal cancer do not mention chromoendoscopy.[29]

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

1. van Rijn JC, Reitsma JB, Stoker J, et al. Polyp miss rate determined by tandem colonoscopy: a systematic review. *Am J Gastroenterol.* Feb 2006;101(2):343-350. PMID 16454841
2. Food and Drug Administration (FDA). 510(k) Summary: Pentax EPK-i5010 Video Processor. 2013; http://www.accessdata.fda.gov/cdrh_docs/pdf12/K122470.pdf. Accessed November 1, 2017.
3. Pohl J, Schneider A, Vogell H, et al. Pancolonic chromoendoscopy with indigo carmine versus standard colonoscopy for detection of neoplastic lesions: a randomised two-centre trial. *Gut.* Apr 2011;60(4):485-490. PMID 21159889
4. Kahi CJ, Anderson JC, Waxman I, et al. High-definition chromocolonoscopy vs. high-definition white light colonoscopy for average-risk colorectal cancer screening. *Am J Gastroenterol.* Jun 2010;105(6):1301-1307. PMID 20179689
5. Brown SR, Baraza W. Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum. *Cochrane Database Syst Rev.* Oct 06 2010(10):CD006439. PMID 20927746
6. Brown SR, Baraza W, Din S, et al. Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum. *Cochrane Database Syst Rev.* Apr 07 2016;4:CD006439. PMID 27056645
7. Le Rhun M, Coron E, Parlier D, et al. High resolution colonoscopy with chromoscopy versus standard colonoscopy for the detection of colonic neoplasia: a randomized study. *Clin Gastroenterol Hepatol.* Mar 2006;4(3):349-354. PMID 16527699
8. Stoffel EM, Turgeon DK, Stockwell DH, et al. Chromoendoscopy detects more adenomas than colonoscopy using intensive inspection without dye spraying. *Cancer Prev Res (Phila).* Dec 2008;1(7):507-513. PMID 19139000
9. Subramanian V, Mannath J, Ragunath K, et al. Meta-analysis: the diagnostic yield of chromoendoscopy for detecting dysplasia in patients with colonic inflammatory bowel disease. *Aliment Pharmacol Ther.* Feb 2011;33(3):304-312. PMID 21128987
10. Wu L, Li P, Wu J, et al. The diagnostic accuracy of chromoendoscopy for dysplasia in ulcerative colitis: meta-analysis of six randomized controlled trials. *Colorectal Dis.* Apr 2012;14(4):416-420. PMID 21073646
11. Mooiweer E, van der Meulen-de Jong AE, Ponsioen CY, et al. Chromoendoscopy for surveillance in inflammatory bowel disease does not increase neoplasia detection compared with conventional colonoscopy with random biopsies: results from a large retrospective study. *Am J Gastroenterol.* Jul 2015;110(7):1014-1021. PMID 25823770

12. Freire P, Figueiredo P, Cardoso R, et al. Surveillance in ulcerative colitis: is chromoendoscopy-guided endomicroscopy always better than conventional colonoscopy? A randomized trial. *Inflamm Bowel Dis.* Nov 2014;20(11):2038-2045. PMID 25185683
13. Marion JF, Waye JD, Present DH, et al. Chromoendoscopy-targeted biopsies are superior to standard colonoscopic surveillance for detecting dysplasia in inflammatory bowel disease patients: a prospective endoscopic trial. *Am J Gastroenterol.* Sep 2008;103(9):2342-2349. PMID 18844620
14. Marion JF, Waye JD, Israel Y, et al. Chromoendoscopy is more effective than standard colonoscopy in detecting dysplasia during long-term surveillance of patients with colitis. *Clin Gastroenterol Hepatol.* May 2016;14(5):713-719. PMID 26656297
15. Gasia MF, Ghosh S, Panaccione R, et al. Targeted biopsies identify larger proportions of patients with colonic neoplasia undergoing high-definition colonoscopy, dye chromoendoscopy, or electronic virtual chromoendoscopy. *Clin Gastroenterol Hepatol.* May 2016;14(5):704-712 e704. PMID 26804384
16. Omata F, Ohde S, Deshpande GA, et al. Image-enhanced, chromo, and cap-assisted colonoscopy for improving adenoma/neoplasia detection rate: a systematic review and meta-analysis. *Scand J Gastroenterol.* Feb 2014;49(2):222-237. PMID 24328858
17. Chung SJ, Kim D, Song JH, et al. Comparison of detection and miss rates of narrow band imaging, flexible spectral imaging chromoendoscopy and white light at screening colonoscopy: a randomised controlled back-to-back study. *Gut.* May 2014;63(5):785-791. PMID 23853211
18. Chung SJ, Kim D, Song JH, et al. Efficacy of computed virtual chromoendoscopy on colorectal cancer screening: a prospective, randomized, back-to-back trial of Fuji Intelligent Color Enhancement versus conventional colonoscopy to compare adenoma miss rates. *Gastrointest Endosc.* Jul 2010;72(1):136-142. PMID 20493487
19. Pohl J, Lotterer E, Balzer C, et al. Computed virtual chromoendoscopy versus standard colonoscopy with targeted indigocarmine chromoscopy: a randomised multicentre trial. *Gut.* Jan 2009;58(1):73-78. PMID 18838485
20. Cha JM, Lee JI, Joo KR, et al. A prospective randomized study on computed virtual chromoendoscopy versus conventional colonoscopy for the detection of small colorectal adenomas. *Dig Dis Sci.* Aug 2010;55(8):2357-2364. PMID 19834809
21. Kiriyama S, Matsuda T, Nakajima T, et al. Detectability of colon polyp using computed virtual chromoendoscopy with flexible spectral imaging color enhancement. *Diagn Ther Endosc.* Apr 2012;2012:596303. PMID 22474404
22. Neumann H, Vieth M, Gunther C, et al. Virtual chromoendoscopy for prediction of severity and disease extent in patients with inflammatory bowel disease: a randomized controlled study. *Inflamm Bowel Dis.* Aug 2013;19(9):1935-1942. PMID 23839228
23. Laine L, Kaltenbach T, Barkun A, et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. *Gastroenterology.* Mar 2015;148(3):639-651 e628. PMID 25702852
24. Higgins PD. Miles to go on the SCENIC route: Should chromoendoscopy become the standard of care in IBD surveillance? [comment]. *Am J Gastroenterol.* Jul 2015;110(7):1035-1037. PMID 26148262
25. Marion JF, Sands BE. The SCENIC consensus statement on surveillance and management of dysplasia in inflammatory bowel disease: praise and words of caution [comment]. *Gastroenterology.* Mar 2015;148(3):462-467. PMID 25702851
26. Shergill AK, Lightdale JR, Bruining DH, et al. The role of endoscopy in inflammatory bowel disease. *Gastrointest Endosc.* May 2015;81(5):1101-1121 e1101-1113. PMID 25800660
27. Abu Dayyeh BK, Thosani N, Konda V, et al. ASGE Technology Committee systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting real-time endoscopic assessment of the histology of diminutive colorectal polyps. *Gastrointest Endosc.* Mar 2015;81(3):502.e501-502.e516. PMID 25597420
28. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology.* Sep 2012;143(3):844-857. PMID 22763141
29. U.S. Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for colorectal cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* Jun 21 2016;315(23):2564-2575. PMID 27304597

POLICY HISTORY

Date	Action	Description
September 2012	New Policy	
June 2013	Update Policy	Policy updated with literature search, No change to policy statements, References added, some renumbered or removed.
June 2014	Update Policy	Policy updated with literature review, no change in policy statements.
June 2015	Update Policy	References 10, 15, 18, and 20 added. Policy updated with literature review. Reference 11 and 13 added. Policy statements unchanged.
June 2016	Update Policy	Policy updated with literature review through October 7, 2015; references 11 and 21-23 added. Policy statements unchanged.
March 2018	Update Policy	Policy updated with literature review through September 14, 2017; reference 27 added. Policy statement changed to correct error: Chromoendoscopy and virtual chromoendoscopy considered investigational since Sept. 2012 but policy incorrected listed chrmoendoscopy as medically necessary; also not medically necessary language corrected to investigational due to 510k FDA status.