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## OVERVIEW

Confocal laser endomicroscopy (CLE), also known as confocal fluorescent endomicroscopy and optical endomicroscopy, allows in vivo microscopic imaging of cells during endoscopy. CLE is proposed for a variety of purposes, especially as a real-time alternative to biopsy/polypectomy and histopathologic analysis during colonoscopy and for targeting areas to undergo biopsy in patients with inflammatory bowel disease or Barrett esophagus.

## MEDICAL CRITERIA

Not applicable

## PRIOR AUTHORIZATION

Not applicable

## POLICY STATEMENT

### BlueCHiP for Medicare

Use of confocal laser endomicroscopy is not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

### Commercial Products

Use of confocal laser endomicroscopy is considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

## COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

## BACKGROUND

Confocal laser endomicroscopy (CLE), also known as confocal fluorescent endomicroscopy and optical endomicroscopy, allows in vivo microscopic imaging of the mucosal epithelium during endoscopy. The process uses light from a low-power laser to illuminate tissue and, subsequently, the same lens detects light reflected from the tissue through a pinhole. The term *confocal* refers to having both illumination and collection systems in the same focal plane. Light reflected and scattered at other geometric angles that is not reflected through the pinhole is excluded from detection, which dramatically increases the resolution of CLE images.

To date, 2 CLE systems have been cleared by the U.S. Food and Drug Administration (FDA). One is an endoscope-based system with a confocal probe incorporated onto the tip of a conventional endoscope. The other is a probe-based system; the probe is placed through the biopsy channel of a conventional endoscope. The depth of view is up to 250  $\mu\text{m}$  with the endoscopic system and about 120  $\mu\text{m}$  with the probe-based system. A limited area can be examined - no more than 700  $\mu\text{m}$  in the endoscopic-based system and less with the probe-based system. As pointed out in systematic reviews, the limited viewing area emphasizes the need for careful conventional endoscopy to target areas for evaluation. Both CLE systems are optimized using a contrast agent. The most widely used agent is intravenous fluorescein, which is FDA-approved for ophthalmologic imaging of blood vessels when used with a laser scanning ophthalmoscope.

Unlike techniques such as chromoendoscopy, which are primarily intended to improve the sensitivity of colonoscopy, CLE is unique in that it is designed to characterize the cellular structure of lesions immediately. CLE can thus potentially be used to make a diagnosis of polyp histology, particularly in association with screening or surveillance colonoscopy, which could allow for small hyperplastic lesions to be overlooked rather than removed and sent for histologic evaluation. Using CLE would reduce risks associated with biopsy and reduce the number of biopsies and histologic evaluations.

Another potential application of CLE technology is targeting areas for biopsy in patients with Barrett esophagus undergoing surveillance endoscopy. This alternative to the current standard approach, recommended by the American Gastroenterological Association, is that patients with Barrett esophagus who do not have dysplasia undergo endoscopic surveillance every 3 to 5 years. The American Gastroenterological Association has further recommended that random 4-quadrant biopsies every 2 cm be taken with white-light endoscopy in patients without known dysplasia. Other potential uses of CLE under investigation include better diagnosis and differentiation of conditions such as gastric metaplasia, lung cancer, and bladder cancer.

As noted, limitations of CLE systems include a limited viewing area and depth of view. Another issue is standardization of systems for classifying lesions viewed with CLE devices. Although there is currently no internationally accepted classification system for colorectal lesions, 2 systems have been used in a number of studies conducted in different countries. They are the Mainz criteria for endoscopy-based CLE devices and the Miami classification system for probe-based CLE devices. Lesion classification systems are less developed for non-gastrointestinal lesions viewed by CLE devices (e.g., those in the lung or bladder). Another challenge is the learning curve for obtaining high-quality images and classifying lesions. Several recent studies, however, have found that the ability to acquire high-quality images and interpret them accurately can be learned relatively quickly; these studies were specific to colorectal applications of CLE.

#### REGULATORY STATUS

Two CLE devices have been cleared for marketing by FDA through the 510(k) process. Cellvizio® (Mauna Kea Technologies, Paris, France) is a confocal microscopy with a fiber optic probe (ie, a probe-based CLE system). The device consists of a laser scanning unit, proprietary software, a flat-panel display, and miniaturized fiber optic probes. The F-600 system, cleared by FDA in 2006, can be used with any standard endoscope with a working channel of at least 2.8 mm. According to FDA, the device is intended for confocal laser imaging the internal microstructure of tissues in the anatomic tract (gastrointestinal or respiratory) that are accessed by an endoscope. The 100 series version of the system was cleared by FDA in 2015 for imaging the internal microstructure of tissues and for visualization of body cavities organs and canals during endoscopic and laparoscopic surgery. FDA product code: GCJ.

Confocal Video Colonoscope (Pentax Medical, Montvale, NJ) is an endoscopy-based CLE system. The EC-3S7OCILK system, cleared by FDA in 2004, is used with a Pentax Video Processor and with a Pentax Confocal Laser System. According to FDA, the device is intended to provide optical and microscopic visualization of and therapeutic access to the lower gastrointestinal tract. FDA product code: GCJ/KOG (endoscope and accessories).

For individuals who have suspected or known colorectal lesions who receive CLE as an adjunct to colonoscopy, the evidence includes multiple diagnostic accuracy studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. While the reported sensitivity and specificity in these studies are high, it is uncertain whether the accuracy is sufficiently high to replace biopsy/polypectomy and histopathologic analysis. Moreover, issues remain concerning the use of this technology in clinical practice (eg, the learning curve, interpretation of lesions). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have Barrett esophagus who are undergoing surveillance who receive CLE with targeted biopsy, the evidence includes several RCTs and a meta-analysis. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. Evidence from RCTs has suggested CLE is more sensitive than standard endoscopy for identifying areas of dysplasia. However, a 2014 meta-analysis found that the pooled sensitivity, specificity, and negative predictive value of available studies were not sufficiently high to replace the standard surveillance protocol. National guidelines continue to recommend 4-quadrant random biopsies for patients with Barrett esophagus undergoing surveillance. The evidence is insufficient to determine the effects of the technology on health outcomes

For individuals who have gastrointestinal lesions and have had endoscopic treatment who receive CLE to assess adequacy of endoscopic treatment, the evidence includes an RCT and a systematic review. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. The single RCT, which compared high-definition white-light endoscopy with high-definition white-light endoscopy plus CLE, was stopped early because an interim analysis did not find a between group difference in outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a suspicion of a condition diagnosed by identification and biopsy of lesions (e.g., lung, bladder, or gastric cancer) who receive CLE, the evidence includes a small number of diagnostic accuracy studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. There is limited evidence on the diagnostic accuracy of CLE for these other indications. The evidence is insufficient to determine the effects of the technology on health outcomes.

#### **CODING**

The following codes are not covered for BlueCHiP for Medicare and not medically necessary for Commercial Products:

**43206** Esophagoscopy, flexible, transoral; with optical endomicroscopy

**43252** Esophagogastroduodenoscopy, flexible, transoral; with optical endomicroscopy

**88375** Optical endomicroscopic image(s), interpretation and report, real-time or referred,  
Each endoscopic session

**0397T** Endoscopic retrograde cholangiopancreatography (ERCP), with optical endomicroscopy  
(List separately in addition to code for primary procedure)

#### **RELATED POLICIES**

New Technology

#### **PUBLISHED**

Provider Update, August 2018

#### **REFERENCES:**

1. American Gastroenterological Association, Spechler SJ, Sharma P, et al. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. *Gastroenterology*. Mar 2011;140(3):1084-1091. PMID 21376940
2. Salvatori F, Siciliano S, Maione F, et al. Confocal laser endomicroscopy in the study of colonic mucosa in IBD patients: a review. *Gastroenterol Res Pract*. Apr 2012;2012:525098. PMID 22474440
3. Neumann H, Vieth M, Atreya R, et al. Prospective evaluation of the learning curve of confocal laser endomicroscopy in patients with IBD. *Histol Histopathol*. Jul 2011;26(7):867-872. PMID 21630216
4. Buchner AM, Gomez V, Heckman MG, et al. The learning curve of in vivo probe-based confocal laser endomicroscopy for prediction of colorectal neoplasia. *Gastrointest Endosc*. Mar 2011;73(3):556-560. PMID 21353852

5. Su P, Liu Y, Lin S, et al. Efficacy of confocal laser endomicroscopy for discriminating colorectal neoplasms from non-neoplasms: a systematic review and meta-analysis. *Colorectal Dis.* Jan 2013; 15(1): e1-12. PMID 23006609
6. Dong YY, Li YQ, Yu YB, et al. Meta-analysis of confocal laser endomicroscopy for the detection of colorectal neoplasia. *Colorectal Dis.* Sep 2013;15(9):e488-495. PMID 23810105
7. Wanders LK, East JE, Uitentuis SE, et al. Diagnostic performance of narrowed spectrum endoscopy, autofluorescence imaging, and confocal laser endomicroscopy for optical diagnosis of colonic polyps: a metaanalysis. *Lancet Oncol.* Dec 2013;14(13):1337-1347. PMID 24239209
8. Xie XJ, Li CQ, Zuo XL, et al. Differentiation of colonic polyps by confocal laser endomicroscopy. *Endoscopy.* Feb 2011;43(2):87-93. PMID 21038291
9. Buchner AM, Shahid MW, Heckman MG, et al. Comparison of probe-based confocal Laser endomicroscopy with virtual chromoendoscopy for classification of colon polyps. *Gastroenterology.* Mar 2010;138(3):834-842. PMID 19909747
10. Shahid MW, Buchner AM, Raimondo M, et al. Accuracy of real-time vs. blinded offline diagnosis of neoplastic colorectal polyps using probe-based confocal laser endomicroscopy: a pilot study. *Endoscopy.* Apr 2012; 44(4):343-348. PMID 22382851

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