

Corporate Medical Policy

Confocal Laser Endomicroscopy

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Description of Procedure or Service

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 biopsy in patients with inflammatory bowel disease and Barrett's esophagus.

Background

CLE allows *in vivo* microscopic imaging of the mucosal epithelium during endoscopy. According to the American Society for Gastrointestinal Endoscopy (ASGE), with CLE, light from a low-power laser illuminates 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 spatial resolution of CLE images.

To date, 2 types of CLE systems have been cleared by the Food and Drug Administration (FDA). One is an endoscope-based system in which 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 μm with the endoscopic system and about 120 μm with the probe-based system. A limited area can be examined; no more than 700 μm in the endoscopic-based system and less with the probe-based system. As pointed out in review articles, the limited viewing area emphasizes the need for careful conventional endoscopy to target the 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 ophthalmological imaging of blood vessels when used with a laser scanning ophthalmoscope.

Unlike techniques such as chromoendoscopy (see policy Chromoendoscopy as an Adjunct to Colonoscopy) which are primarily intended to improve the sensitivity of colonoscopy, CLE is unique in that it is designed to immediately characterize the cellular structure of lesions. 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 left in place rather than removed and sent for histological evaluation. This would reduce risks associated with biopsy and reduce the number of biopsies and histological evaluations.

Another key potential application of CLE technology is targeting areas for biopsy in patients with Barrett's esophagus undergoing surveillance endoscopy. This is an alternative to the current standard approach recommended by the American Gastroenterological Association which is that individuals with Barrett's Esophagus who do not have dysplasia undergo endoscopic surveillance every 3 to 5

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years. 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 previously, 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 not currently an internationally accepted classification system for colorectal lesions, 2 systems have been developed that have been used in a number of studies conducted in different countries. These 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 potential issue 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 limited to colorectal applications of CLE.

Regulatory Status

Two confocal laser endomicroscopy devices have been cleared for marketing by the FDA through the 510(k) process. These include:

Cellvizio® (Mauna Kea Technologies) is a confocal microscopy with a fiber optic probe (i.e., 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 the FDA in 2006, can be used with any standard endoscope with a working channel of at least 2.8mm. According to FDA, the device is intended for confocal laser imaging of the internal microstructure of tissues in the anatomical 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 of the internal microstructure of tissues and for visualization of body cavities organs and canals during endoscopic and laparoscopic surgery. In 2018, the CranioFlex™ Confocal Miniprobe (Mauna Kea Technologies) was cleared to “provide visualization within the central nervous system during cranial diagnosis and therapeutic procedures such as tumor biopsy and resection.”

Confocal Video Colonoscope (Pentax Medical) is an endoscopy-based CLE system. The EC-3S7OCILK system, cleared by the FDA in 2004, is used with a Pentax Video Processor and with a Pentax Confocal Laser System. According to FDA materials, the intended use of the device is to provide optical and microscopic visualization of and therapeutic access to the lower gastrointestinal tract.

Related Policy

Chromoendoscopy as an Adjunct to Colonoscopy

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Use of confocal laser endomicroscopy is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When it is covered

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Not applicable.

When it is not covered

Use of confocal laser endomicroscopy is considered investigational.

Policy Guidelines

The evidence for confocal laser endomicroscopy (CLE) as an adjunct to colonoscopy in patients who have suspected or known colorectal lesions, includes multiple diagnostic accuracy studies. Relevant outcomes are overall survival, disease-specific survival, test 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 about the use of this technology in practice (eg, the learning curve, interpretation of lesions). The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for CLE with targeted biopsy in patients who have Barrett esophagus and are undergoing surveillance includes several randomized controlled trials (RCTs) and a meta-analysis. Relevant outcomes are overall survival, disease-specific survival, test validity, and resource utilization. Evidence from RCTs suggests CLE is more sensitive than white-light endoscopy for identifying areas of dysplasia. However, a 2014 meta-analysis found that the pooled sensitivity, specificity, and negative predictive value of available studies are 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.

The evidence for patients who have gastrointestinal lesions and have had endoscopic treatment and received CLE, includes 1 RCT and a systemic review. Relevant outcomes are overall survival, disease-specific survival, test validity, and resource utilization. The single RCT, which compared high definition (HD) white light endoscopy with HD white-light endoscopy plus CLE, was stopped early because 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.

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

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: 43206, 43252, 88375, 0397T

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 1/10/13

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Specialty Matched Consultant Advisory Panel 10/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 1/9/14

Specialty Matched Consultant Advisory Panel 11/2014

Senior Medical Director review 12/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 1/15/15

Specialty Matched Consultant Advisory Panel 11/2015

Medical Director review 11/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 11/12/15

Specialty Matched Consultant Advisory Panel 11/2016

Medical Director review 11/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 11/2016

Specialty Matched Consultant Advisory Panel 11/2017

Medical Director review 11/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 11/2017

Specialty Matched Consultant Advisory Panel 11/2018

Medical Director review 11/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 11/2018

Specialty Matched Consultant Advisory Panel 11/2019

Medical Director review 11/2019

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.87, 11/2019

Policy Implementation/Update Information

2/26/13 New policy issued. Use of confocal laser endomicroscopy is considered investigational. Medical Director review 1/2013. Notification given 2/26/13. Policy effective 5/28/13. (sk)

11/12/13 Specialty Matched Consultant Advisory Panel review 10/16/13. No change to Policy statement. (sk)

4/1/14 Reference added. No change to Policy statement. (sk)

1/13/15 References updated. Specialty Matched Consultant Advisory Panel review 11/2014. Senior Medical Director review 12/2014. No change to policy intent. (td)

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- 2/24/15 References updated. Policy Guidelines section updated. Policy Statement unchanged. (td)
- 5/26/15 Description section updated to remove archived Evidence Based Guideline. Policy Statements unchanged. (td)
- 12/30/15 Billing/Coding section updated to add code 0397T effective 1/1/16. References updated. Specialty Matched Consultant Advisory Panel review 11/18/2015. Medical Director review 11/2015. (td)
- 1/26/16 Policy Guidelines section revised. References updated. (td)
- 12/30/16 Regulatory Status and Policy Guidelines updated with minor revisions. Specialty Matched Consultant Advisory Panel review 11/2016. Medical Director review 11/2016. (jd)
- 12/15/17 References updated. Specialty Matched Consultant Advisory Panel 11/2017. Medical Director review 11/2017. (jd)
- 12/14/18 Minor revisions. References updated. Specialty Matched Consultant Advisory Panel 11/2018. Medical Director review 11/2018. (jd)
- 12/31/19 References updated. Specialty Matched Consultant Advisory Panel 11/2019. Medical Director review 11/2019. (jd)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.