Cancer Screening and Prevention **2026** | Epub
DOI: 10.14218/CSP.2026.00022

Consensus

Expert Consensus on the Clinical Application of Probe-based Confocal Laser Endomicroscopy in Colorectal Cancer, Precancerous Lesions, and Inflammatory Bowel Disease

Peng Pan[1,2#], Cheng-Long Wang[1#], Sheng-Bing Zhao[1], Xiuli Zuo[3], Zhen-Dong Jin[1], Zhuan Liao[1*] and Yu Bai[1*]

[1]*Department of Gastroenterology, National Clinical Research Center for Digestive Diseases, the First Affiliated Hospital of Naval Medical University, Shanghai, China;* [2]*Department of Gastroenterology, the 958th Army Hospital of the Chinese People's Liberation Army, Chongqing, China;* [3]*Department of Gastroenterology, Qilu Hospital of Shandong University, Jinan, Shandong, China*

[#]*These authors contributed equally to this work.*

Received: September 15, 2026 | **Revised:** October 08, 2026 | **Accepted:** October 20, 2026 | **Published online:** November 03, 2026

Abstract

Colorectal diseases pose a serious threat to human health, and conventional endoscopy has limitations in lesion characterization. This consensus aims to clarify the indications, operational specifications, image interpretation criteria, and quality control requirements for probe-based confocal laser endomicroscopy (pCLE) in lower gastrointestinal diseases, particularly colorectal cancer, precancerous lesions and polyps, and inflammatory bowel disease (IBD). A systematic literature search covered PubMed, Embase, the Cochrane Library, CNKI, and Wanfang Database through August 2026. Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation system. Forty-eight experts participated in two rounds of discussion and online voting, with agreement ≥80% required for consensus. Eight recommendations were finalized: five strong and three weak. Strong recommendations address colorectal lesion differentiation, targeted biopsy, mucosal barrier assessment, ulcerative colitis mucosal healing and relapse prediction, and IBD-associated colorectal neoplasia surveillance. Weak recommendations address distal resection margin assessment during radical surgery for low rectal cancer, irritable bowel syndrome research, and adjunctive IBD diagnosis and differentiation. Evidence for endoscopic resection margin assessment remains insufficient, and pCLE is not recommended for routine diagnosis of irritable bowel syndrome. pCLE provides adjunctive microscopic information for colorectal lesion characterization, targeted biopsy, and IBD assessment and surveillance; in IBD diagnosis, it does not replace conventional endoscopic and histopathological evaluation. This consensus provides evidence-based guidance for standardized clinical application.

Introduction

The spectrum of colorectal diseases is broad, encompassing colorectal cancer (CRC), colorectal polyps, inflammatory bowel disease (IBD), and other conditions, all of which pose a serious threat to human health. CRC is the third most common malignancy worldwide, and its early screening and timely intervention are key to reducing the disease burden.[1] In recent years, with advances in digestive endoscopy technology, high-definition colonoscopy has become the standard modality for CRC screening and early cancer diagnosis and treatment. However, traditional white-light endoscopy still has certain limitations in distinguishing small lesions and determining their nature; nontargeted biopsy not only increases patient costs but may also lead to missed diagnoses or overdiagnosis.[2] IBD mainly includes ulcerative colitis (UC) and Crohn's disease (CD), and its long-term follow-up management imposes higher requirements for the prevention of complications and cancer surveillance.[3] In addition, intestinal barrier dysfunction is closely related to the pathogenesis of various lower gastrointest-

Keywords: Consensus; Colorectal cancer; Precancerous lesions; Inflammatory bowel disease; Probe-based confocal laser endomicroscopy; Colorectal polyps.
***Correspondence to:** Yu Bai and Zhuan Liao, Department of Gastroenterology, the First Affiliated Hospital of Naval Medical University, 168 Changhai Road, Yangpu District, Shanghai 200433, China. ORCID: https://orcid.org/0000-0002-7577-6001 (YB); https://orcid.org/0000-0001-8506-8159 (ZL). Tel: +86-13564665324 (YB); +86-13061921980 (ZL), E-mail: md.baiyu@foxmail.com; Zhuanleo@126.com
How to cite this article: Pan P, Wang CL, Zhao SB, Zuo X, Jin ZD, Liao Z, *et al*. Expert Consensus on the Clinical Application of Probe-based Confocal Laser Endomicroscopy in Colorectal Cancer, Precancerous Lesions, and Inflammatory Bowel Disease. *Cancer Screen Prev*. Published online: Nov 03, 2026. DOI: 10.14218/CSP.2026.00022.

© 2026 The Author(s). This article has been published under the terms of Creative Commons Attribution-Noncommercial 4.0 International License (CC BY-NC 4.0), which permits noncommercial unrestricted use, distribution, and reproduction in any medium, provided that the following statement is provided. "This article has been published in *Cancer Screening and Prevention* at https://doi.org/10.14218/CSP.2026.00022 and can also be viewed on the Journal's website at https://www.xiahepublishing.com/journal/csp".

inal diseases, but effective real-time assessment methods are still lacking in clinical practice.[4] Therefore, exploring high-resolution imaging technologies to address these clinical needs is important.

Confocal laser endomicroscopy (CLE) is an *in vivo* microscopic imaging technology that combines confocal laser scanning microscopy with digestive endoscopy, enabling real-time acquisition of high-resolution optical images of superficial tissue microstructures, thereby providing auxiliary information for lesion identification, real-time assessment, and targeted biopsy.[5] According to the integration mode of the imaging component with the endoscope, CLE can generally be classified into endoscope-based confocal laser endomicroscopy (eCLE), probe-based confocal laser endomicroscopy (pCLE), and needle-based confocal laser endomicroscopy (nCLE). eCLE integrates the confocal imaging component into the tip of the endoscope; its commercial product appeared relatively early, but due to limitations in technical maturity and clinical applicability, it is now rarely used. pCLE uses an independent flexible fiber-optic imaging probe that can be delivered to the target area through an endoscope working channel compatible with its size; nCLE is even finer and, because it can pass through an endoscopy-guided puncture needle, may have additional clinical applications.[6] pCLE technology uses intravenous or topical application of fluorescent contrast agents (such as sodium fluorescein) to visualize specific tissue components; combined with laser excitation at a specific wavelength, it can visualize microscopic features such as mucosal epithelial cells, crypt structures, and vascular morphology.[7]

Since CLE technology was first applied in clinical practice in 2004, considerable clinical evidence has accumulated in the field of digestive disease diagnosis.[8] However, pCLE technology has not yet been widely applied, mainly due to high equipment costs, inconsistent operator training standards, and incomplete image interpretation criteria.[6] To promote the standardized application of pCLE technology, the consensus working group formulated this expert consensus based on a systematic search and analysis of domestic and international literature, combined with the current status of clinical practice in China. This consensus aims to clarify the indications, operational specifications, image interpretation criteria, and quality control requirements for pCLE in lower gastrointestinal diseases, particularly CRC, precancerous lesions and polyps, and IBD, provide evidence-based medical guidance for clinicians, and promote coordinated development of technological innovation and clinical application.[9]

Methods

This expert consensus was formulated by the Digestive Endoscopy Society of the Chinese Medical Association. A systematic search strategy was adopted for literature retrieval, and the databases searched were PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), and Wanfang Database. The search covered each database from inception through August 2026. Search terms included: confocal laser endomicroscopy, probe-based confocal laser endomicroscopy, lower gastrointestinal diseases, CRC, IBD, CLE, etc. The search combined subject headings and free-text terms; for example, the PubMed strategy was: ("confocal laser endomicroscopy"[MeSH Terms] OR "confocal laser endomicroscopy" OR "pCLE" OR "CLE") AND ("colorectal" OR "colon" OR "rectal" OR "inflammatory bowel disease" OR "irritable bowel syndrome"). A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of study selection is provided in the Supplementary Material (Supplementary Fig. 1). Illustrative search expressions for PubMed, Embase, the Cochrane Library, CNKI, and Wanfang Database, including the applied filters and study-selection summary, are provided in the Supplementary Material (Supplementary Table. 1); the PRISMA flow diagram summarizes the reported selection counts. Eligible designs included randomized controlled trials, cohort studies, case-control studies, and cross-sectional studies involving the clinical application of CLE in lower gastrointestinal diseases; studies were limited to those published in Chinese or English. Consensus statements, guidelines, reviews (including systematic reviews and meta-analyses), and editorials were not eligible for evidence grading; such publications were cited only as background or contextual references within the 52-publication consensus synthesis. The certainty of evidence was graded using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system,[9] divided into four levels: high, moderate, low, and very low. Two panel members independently graded the quality of evidence for each recommendation, and any disagreement was resolved through discussion with a third methodologist until consensus was reached. A GRADE evidence profile summarizing the evidence base, the quality rating, and the reasons for any downgrading for each of the eight statements is provided in the Supplementary Material (Supplementary Table. 2).

Methodological experts: The consensus panel included two methodologists specializing in epidemiology, statistics, and GRADE methodology (Jinfang Xu and Qian He from the Department of Military Health Statistics, Navy Medical University). They were responsible for designing the literature search strategy, training the panel in GRADE, supervising the evidence-grading process, and adjudicating grading disagreements; they did not vote on the recommendations. They served as non-voting methodological experts and are listed separately from the 48 voting experts in the consensus expert roster.

The consensus was developed using a conference-based approach, with two rounds of discussion and online voting. In the first offline meeting, experts reviewed the recommendations and content item by item and conducted detailed discussion; in the second round, conducted online, experts were invited to carefully review the draft consensus opinions and propose revisions; after revision, online voting was conducted again. Forty-eight experts from 39 medical institutions participated in the final online voting. The consensus attainment rate of each recommendation is reported together with the corresponding statement, and a complete record of the comments received and the revisions made during the consensus rounds is kept by the consensus working group and is available from the corresponding author upon reasonable request. Experts rated agreement on six levels according to the degree of agreement with the consensus: ① completely agree; ② basically agree, with minor reservations; ③ tend to agree, with major reservations; ④ tend to disagree, with minor objections; ⑤ partially disagree, with major objections; ⑥ completely disagree. Items for which the proportion of agreement levels ① + ② was ≥ 80% were listed as final recommended items; otherwise, they were not recommended. No topic-specific abstentions or recusals

occurred during the voting process; all 48 voting experts cast valid votes on each recommendation, and the agreement rate of each recommendation is reported with 48 as the denominator.

Conflicts of interest: All voting experts completed a conflict-of-interest declaration form before the consensus process. Experts who declared a potential conflict related to a specific topic would abstain from voting on the corresponding recommendations. The development of this consensus received no commercial funding or industry involvement.

This consensus divided recommendation strength into two levels: "strong recommendation" and "weak recommendation." A strong recommendation indicates that a statement is recommended for clinical practice when benefits clearly outweigh risks; a weak recommendation indicates that the statement may be considered for adoption, but the balance between benefits and risks remains uncertain. The strength of the statement was determined comprehensively based on factors such as evidence quality, balance of benefits and risks, patient values and preferences, and health economics considerations.[9,10]

pCLE equipment and pre-examination preparation

Equipment types and principles

Different pCLE systems and probe models differ in outer diameter, effective working length, field of view, imaging depth, lateral resolution, and image frame rate. The probe can be delivered to the target area through an endoscope working channel compatible with its outer diameter. The outer diameter of digestive tract pCLE probes is usually less than 2.8 mm, allowing them to pass through the working channel of a digestive endoscope to enter the target area, with good flexibility.[11,12]

pCLE uses a focused laser beam to scan tissue, collecting only fluorescence signals from the focal plane (depth-limited plane), thereby obtaining an optical section of that plane. Through point-by-point scanning and synchronous reconstruction, a two-dimensional microscopic image sequence approximately parallel to the tissue surface is formed in real time.[5] Fluorescent contrast agents are important for pCLE imaging: intravenous injection of sodium fluorescein can display vascular morphology and extracellular matrix; topical application of sodium fluorescein or cresyl violet (CV) can enhance the visualization of epithelial cells.[7,13] An intravenous dose of 2.5–5 mL of 10% sodium fluorescein (250–500 mg) is commonly used, and lower doses (e.g., 2 mg/kg) may also yield evaluable images while reducing skin yellowing.[7] Given the heterogeneity of existing studies, there is currently no universally accepted optimal dose, and the regimen should be individualized according to the patient's condition, the applicable product labeling, equipment requirements, and institutional standards.

Patient preparation and indications

Patient preparation before pCLE examination is similar to that for routine endoscopy. Bowel preparation is required the day before the examination, and fasting for 6–8 h is required on the day of the examination; for lower gastrointestinal examinations, adequate bowel cleanliness must be ensured. Patients should report their allergy history accurately, especially allergy to sodium fluorescein and other fluorescent dyes. The main indications for pCLE include:[9] real-time qualitative diagnosis of suspicious colorectal lesions; classification of colorectal polyps and decision-making regarding resection; assessment of mucosal healing and neoplasia surveillance in IBD; assessment of intestinal barrier dysfunction in selected cases. In accordance with the approved labeling of sodium fluorescein and relevant clinical guidance, a known history of hypersensitivity to sodium fluorescein is a contraindication to its administration; in patients with severe hepatic or renal impairment, pregnancy or lactation, allergic constitution or asthma, recent uncontrolled cardiovascular, metabolic, or respiratory diseases, or unstable general condition, pCLE should be performed with caution after individualized assessment of benefits and risks.

Operational specifications and safety of examination

pCLE examination should be performed on the basis of routine endoscopy. When white-light or enhanced endoscopy identifies suspicious lesions, pCLE-targeted examination can be performed to obtain real-time *in vivo* microscopic structural information, assist in lesion assessment and targeted biopsy, and thereby obtain microscopic information that may support diagnosis.[6] The operator should slowly deliver the pCLE probe compatible with the endoscope working channel to the target area, visualize the probe under direct endoscopic view, bring the distal end of the probe into gentle and stable contact with the mucosa, and adjust the contact position, contact angle, and contact pressure to obtain clear images. Probe movement should be slow and orderly, avoiding excessive compression of the mucosa. For each target area, a continuous stable video of sufficient duration should be obtained, and representative images should be saved.

Regarding safety, pCLE technology has a generally favorable safety record.[14] After intravenous injection of sodium fluorescein, transient skin yellowing, nausea, and other mild adverse reactions may occur; severe allergic reactions are extremely rare. For patients with known fluorescein allergy, fluorescein should be avoided; the use of an alternative dye such as CV requires a separate safety assessment. Existing evidence shows that CV can simultaneously achieve chromoendoscopy and confocal endomicroscopy imaging in the lower gastrointestinal tract and stomach, and can achieve negative visualization of nuclei through cytoplasmic enrichment. Studies have shown that its sensitivity and specificity for differentiating neoplastic from non-neoplastic lesions of the lower gastrointestinal tract are 98% and 100%, respectively[15]; in the diagnosis of gastric intestinal metaplasia, reported accuracy was 93.01%.[13] Based on existing data, topical application of CV may offer an alternative imaging approach in selected settings, subject to appropriate safety assessment. Before use, the pCLE probe should be strictly inspected, and forceful advancement under excessive bending angles should be avoided to prevent probe damage. Reported procedure-related complication rates are low, but standardized complication management procedures still need to be established.

pCLE image interpretation criteria and training

Normal and abnormal microscopic image features

Understanding and mastering normal pCLE image features supports interpretation of abnormal changes.[16] Normal colorectal mucosa under pCLE shows regular crypt structures, with each

crypt opening round or oval, uniform crypt spacing, goblet cells distributed between epithelial cells, regular epithelial cell arrangement, and clear cytoplasmic boundaries. Mucosal microvessels run straight, with uniform diameter and good fluorescence filling.

Abnormal image features can be classified according to lesion type.[8] In colorectal neoplastic lesions, typical features include: disordered crypt structure with irregular morphology; increased crypt spacing; reduced or absent goblet cells; slit-like or stellate glandular openings; increased cellular atypia with increased nuclear-to-cytoplasmic ratio; and abnormal vascular morphology with tortuous course and uneven diameter.[17] In inflammatory lesions, characteristic changes include: crypt abscesses; irregular crypt structure; vascular dilation and increased permeability with fluorescein leakage; widened epithelial intercellular spaces; and inflammatory cell infiltration in the mucosal lamina propria.[18,19] In intestinal barrier dysfunction, a key feature is leakage of fluorescein from blood vessels into the pericryptal stroma, with a fluorescence "halo" sign visible around crypt openings.[20]

Operator training, qualifications, and process requirements

The diagnostic accuracy of CLE depends in part on operator experience; therefore, establishing a standardized training system is crucial for promoting this technology.[14] Training content should cover theoretical instruction, simulation practice, mentored clinical cases, and continuing education. Domestic pCLE-related research has shown that after several hours of online learning and two days of offline training, the average sensitivity, specificity, and accuracy of endoscopists in diagnosing gastric cancerous lesions were each reported to reach 85%, supporting the feasibility of short-term training for gastric lesion assessment.[21]

Regarding training volume requirements, one study found no significant accuracy difference between the first and last 50 pCLE assessments.[22] The same study also found that image quality is a key factor affecting diagnostic accuracy; the diagnostic accuracy of high-quality images (95%) was significantly higher than that of average-quality images (86%) and low-quality images (45%), suggesting that operators should strive to obtain high-quality images.[22] In addition, studies have shown that validated classification criteria and training can improve interobserver consistency, with κ values reaching 0.64–0.73.[17]

It is recommended that CLE operators meet the following qualification requirements: possess qualifications for digestive endoscopy practice; complete at least 20 supervised CLE training cases as the minimum entry requirement, with additional supervised experience recommended before independent interpretation; be familiar with pCLE image features of common lesions; and be able to independently perform routine white-light endoscopy and identify suspicious lesions.[9]

Regarding the pCLE examination process, suspicious lesions should first be located by routine white-light or enhanced endoscopy, then the pCLE probe should be delivered to the target site through the working channel to obtain continuous dynamic images; analysis should be performed according to the corresponding interpretation criteria, targeted biopsy or treatment should be performed when necessary, and representative videos and images should be saved for subsequent review.[16]

Core statements of the expert consensus

Statement 1: pCLE can be used for real-time in vivo diagnosis and differentiation of CRC and precancerous lesions, achieving precise classification of colorectal adenomatous and non-adenomatous polyps.

Strong recommendation, high-certainty evidence (expert voting agreement rate: 91.7%).

Multiple high-quality studies have confirmed that pCLE demonstrates promising diagnostic performance in the real-time diagnosis of colorectal neoplastic lesions.[8,17,23] This rating is supported by direct evidence from dedicated pCLE validation studies that used histopathology as the reference standard,[17,24] which demonstrated consistent diagnostic performance across independent cohorts, rather than by extrapolation from broader CLE reviews or small case series. pCLE can clearly display the crypt structure, goblet cell distribution, and vascular morphology of the colorectal mucosa, thereby helping to distinguish normal mucosa, hyperplastic polyps, adenomas, and cancerous tissue.[17] Hyperplastic polyps are non-neoplastic lesions; under pCLE, the crypt structure is mildly irregular, the openings are stellate or slit-like, and goblet cells and normal microvessels are visible (Fig. 1). Adenomatous polyps are neoplastic lesions; pCLE images show disordered epithelial structure, irregular villous or tubular structures, thickened and dark epithelium, significantly reduced or even absent goblet cells, dilated and irregularly shaped vessels, and fluorescein leakage (Fig. 1). A two-phase study developed pCLE criteria using 28 videos and externally validated them using 36 additional colorectal polyp videos. The results showed that the overall accuracy of pCLE interpretation reached 84.9%, and in high-confidence predictions, the accuracy reached 91%, with sensitivity 83%, specificity 100%, positive predictive value of 98%, negative predictive value of 87%, and good interobserver agreement ($\kappa = 0.73$).[17] This study established key pCLE diagnostic criteria including epithelial surface regularity, goblet cell number, glandular axis, and glandular shape, providing a reproducible interpretive basis for differentiating adenomatous from non-adenomatous polyps. A validation study including 75 patients compared the classification performance of pCLE and virtual chromoendoscopy (Narrow Band Imaging, NBI, and Flexible Spectral Imaging Color Enhancement, FICE) for colorectal polyps. The results showed that the sensitivity of pCLE was significantly superior to virtual chromoendoscopy (91% *vs.* 77%, $P = 0.010$), while there was no significant difference in specificity (76% *vs.* 71%, $P = 0.77$); subgroup analysis further showed that the diagnostic sensitivity of pCLE was significantly superior to FICE (93% *vs.* 73%, $P = 0.003$), but there was no statistically significant difference compared with NBI (88% *vs.* 84%, $P = 1.00$).[24] These results suggest that pCLE has high sensitivity in the *in vivo* differentiation of colorectal polyps and may provide an additional tool for real-time optical diagnosis of colorectal polyps.

A review reported CLE sensitivity exceeding 90% for early gastrointestinal cancers and precancerous lesions.[23] After white-light endoscopy or electronic chromoendoscopy identifies suspicious lesions, CLE can further evaluate malignant features such as the degree of epithelial structural irregularity, abnormal vascular morphology, and disordered crypt openings, thereby supporting real-time optical characterization.[6] This real-time characterization may inform clinical decisions while histopathological confirma-

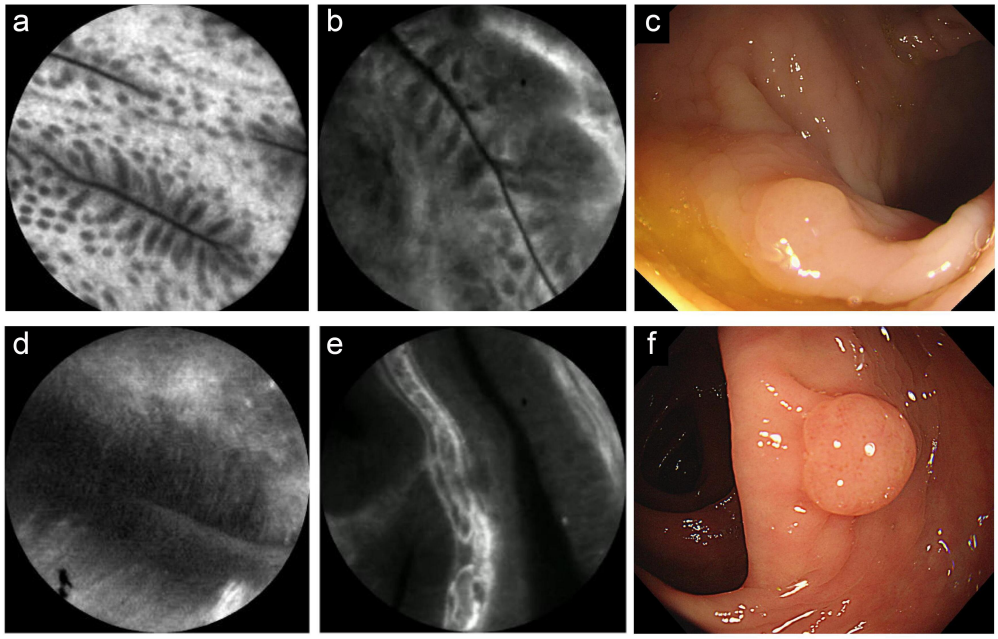


Fig. 1. Typical white-light endoscopic images and corresponding pCLE images of colorectal polyps. (a), (b), (d), and (e), pCLE images; (c) and (f), white-light endoscopic images. pCLE, probe-based confocal laser endomicroscopy.

tion remains important.

Statement 2: Chromoendoscopy-guided pCLE targeted biopsy can improve the detection of colorectal neoplasia in patients with long-standing ulcerative colitis and reduce the number of biopsies.

Strong recommendation, moderate-certainty evidence (expert voting agreement rate: 89.6%).

Traditional random biopsy has problems of sampling error and low efficiency, whereas CLE-guided targeted biopsy may improve lesion detection and reduce unnecessary biopsies.[10] A randomized controlled trial included 161 patients (153 analyzed) with long-standing ulcerative colitis, randomly assigned 1:1 to a conventional colonoscopy group (73 cases) and a chromoendoscopy combined with CLE group (80 cases), comparing the detection performance for intraepithelial neoplasia between the two groups. The results showed that the number of neoplasias detected in the chromoendoscopy-guided CLE group was 4.75 times that in the conventional group ($P = 0.005$), while the number of biopsies was reduced by 50% ($P = 0.008$). Among 134 localized lesions, the sensitivity, specificity, and accuracy of CLE in predicting neoplasia were 94.7%, 98.3%, and 97.8%, respectively. These results suggest that chromoendoscopy-guided CLE may improve the efficiency of UC neoplasia detection while reducing unnecessary biopsies.[25]

A study involving 22 patients with colorectal lesions preliminarily evaluated the diagnostic value of pCLE in determining the depth of lesion invasion.[26] The results showed that the sensitivity, specificity, and accuracy of pCLE for diagnosing SM2 or deeper invasion were 80%, 94%, and 91%, respectively, comparable to magnifying narrow-band imaging and magnifying chromoendoscopy. More importantly, pCLE may assist in estimating invasion depth before endoscopic resection, providing information to support treatment decisions.[26] Another study confirmed that pCLE combined with a fluorescently labeled fatty acid analog can improve the consistency ($\kappa = 0.68$) and overall effectiveness (74.65%) of colorectal tumor diagnosis, superior to traditional intravenous sodium fluorescein staining ($\kappa = 0.43$, 55.88%).[27]

Statement 3: pCLE can be used for intraoperative real-time assessment of the distal resection margin during radical surgery for low rectal cancer, whereas its value in determining lesion and resection margins during endoscopic mucosal resection (EMR)/endoscopic submucosal dissection (ESD) for early CRC remains to be validated in future studies.

Weak recommendation, low-certainty evidence (expert voting agreement rate: 83.3%).

The supporting evidence for this statement was mainly derived from studies performed during radical rectal surgery rather than during EMR or ESD. Current evidence therefore does not directly support the routine use of pCLE for margin determination during endoscopic resection.

In radical surgery for low rectal cancer, CLE/pCLE has been used for intraoperative real-time assessment of the distal margin to assist in selecting the surgical approach or assessing the likelihood of R0 resection. Liu *et al.*[28] performed real-time *in vivo* CLE "optical biopsy" before rectal transection in 18 patients with low rectal cancer to evaluate the distal margin and selected Dixon or Miles surgery based on the image results; all patients achieved R0 resection. Tan *et al.*[29] prospectively applied pCLE to determine the distal margin in real time in 43 patients with low rectal cancer undergoing transanal total mesorectal excision; the sensitivity,

specificity, and accuracy were 90.00%, 86.96%, and 88.37%, respectively, with a blinded re-interpretation accuracy of 86.05% and good interobserver agreement (κ = 0.767). All cases achieved R0 resection, with a median distal margin of 7 mm (interquartile range 5–10 mm). However, the setting of the above studies was radical surgery, which is not completely consistent with margin assessment during EMR/ESD for early CRC, and their conclusions cannot be directly extrapolated to endoscopic resection.

In postoperative follow-up, the role of pCLE in assessing mucosal healing and detecting residual or recurrent lesions remains insufficiently established. For patients who have undergone EMR or ESD, pCLE may be investigated as a supplementary method during endoscopic follow-up, providing detailed assessment of suspicious recurrent areas and guiding targeted biopsy or secondary treatment. However, this application should be combined with white-light endoscopy, enhanced endoscopy, and routine biopsy for comprehensive judgment, and should not be used alone as the basis for follow-up decisions.

Statement 4: pCLE can be used to detect minimal intestinal mucosal inflammation and may serve as a research tool for exploring the pathophysiology of irritable bowel syndrome (IBS); however, as IBS is a functional disorder diagnosed according to the Rome IV criteria, pCLE is not recommended as a routine diagnostic tool for IBS.

Weak recommendation, low-certainty evidence (expert voting agreement rate: 81.2%).

IBS has traditionally been regarded as a functional bowel disorder, but some studies have identified microscopic mucosal changes.[30] pCLE can observe the microscopic inflammatory manifestations of the colonic mucosa in real time *in vivo*, providing a useful research tool for exploring its pathophysiology. However, according to the Rome IV criteria, IBS remains a symptom-based clinical diagnosis, and pCLE findings should not be used as standalone diagnostic evidence for IBS.

A prospective controlled study included 37 patients with IBS and 37 healthy controls. The results showed that the colonic mucosa of IBS patients exhibited obvious signs of microinflammation on pCLE images: 65.8% of pCLE images from IBS patients showed inflammatory changes, compared with 23.4% of images from healthy controls (odds ratio (OR) 6.28, 95% confidence interval (CI) 4.14–9.52, $P < 0.001$).[30] Among the 37 IBS patients, 20 had microinflammation detected in ≥ 3 colonic segments, compared with only 1 in the control group. The sensitivity of pCLE for detecting inflammatory changes was 76%, specificity 91%, positive predictive value 76%, negative predictive value 91%, overall diagnostic accuracy 86.5%, and interobserver Kappa value 0.668.[30] These results indicate that CLE can reveal microscopic mucosal changes in IBS patients that are not detected by routine endoscopy, suggesting that such changes may be involved in the pathophysiology of IBS; their diagnostic value, however, requires further validation.

Another study performed ultrastructural analysis of the rectosigmoid mucosa in patients with diarrhea-predominant IBS.[31] CLE examination did not find obvious epithelial injury or inflammatory changes, but transmission electron microscopy revealed ultrastructural abnormalities such as widened intercellular junctions and increased gaps (>20 nm), suggesting impaired mucosal barrier integrity. These findings are consistent with proposed mechanisms of IBS and suggest that CLE combined with electron microscopy analysis can more comprehensively evaluate the intestinal mucosal status of IBS patients.

Statement 5: pCLE can evaluate colorectal mucosal barrier function through the fluorescein leakage test.

Strong recommendation, moderate-certainty evidence (expert voting agreement rate: 81.2%).

Intestinal mucosal barrier dysfunction is closely related to various lower gastrointestinal diseases, including IBD and IBS.[20] pCLE combined with the fluorescein leakage test provides a real-time, minimally invasive method for evaluating mucosal barrier function.[20]

Under normal conditions, intravenously injected sodium fluorescein is confined within blood vessels or the extracellular matrix, and there should be no obvious fluorescence leakage at intestinal crypt openings or intercellular spaces. When the mucosal barrier is damaged, fluorescein can leak through damaged epithelial intercellular spaces into the intestinal lumen, manifesting as overflow of fluorescence signal on pCLE images. Researchers have developed various quantitative indicators to assess barrier function, including the degree of fluorescence leakage, changes in vascular morphology, and changes in epithelial cell morphology.[18]

A prospective study including 81 patients with UC evaluated the prognostic value of pCLE for assessing intestinal barrier function.[18] Multivariate analysis showed that altered colonic permeability (OR = 3.85, 95% CI 1.25–11.77, $P = 0.018$) and microscopic inflammation detected by pCLE (OR = 6.04, 95% CI 1.89–19.31, $P = 0.002$) were independently associated with relapse after endoscopic mucosal healing. Survival analysis showed that patients with impaired barrier in the terminal ileum or colon had a higher risk of clinical relapse (hazard ratios of 6.01 and 6.51, respectively, $P < 0.001$). Notably, 29 patients who achieved "triple healing" (histological healing with normal permeability in both the terminal ileum and colon) had no relapse during the 24-month follow-up period,[18] suggesting that barrier function assessed by pCLE may serve as a supplementary indicator for treatment targets and prognostic assessment in UC.

Another study compared mucosal barrier abnormalities between IBD patients in endoscopic remission after biological therapy and non-IBD individuals.[32] Mucosal barrier abnormalities such as fluorescence leakage, vascular dilation, and colonic crypt dilation were observed in both groups, but IBD patients had more intercellular spaces in the terminal ileum and more obvious fluorescence leakage in the splenic flexure of colon. The study also found that hypertension, dyslipidemia, female sex, selective serotonin reuptake inhibitor use, and family history of IBD or CRC were significantly associated with barrier abnormalities.[32]

Statement 6: pCLE can provide auxiliary microscopic information for the diagnosis of IBD and may assist in the differential diagnosis between CD and UC; however, current evidence is limited, and pCLE should not replace conventional endoscopic and histopathological evaluation.

Weak recommendation, moderate-certainty evidence (expert voting agreement rate: 83.3%).

Accurate diagnosis and classification of IBD are crucial for formulating treatment strategies.[33] CLE can observe microscopic structural changes of the intestinal mucosa in real time, providing complementary microscopic information for the differential diagnosis between CD and UC. It should be emphasized that the differentiation between CD and UC is complex, and pCLE should only be used as an adjunct to, rather than a substitute for, established clinical, endoscopic, and histopathological assessment.

CLE can clearly display intestinal crypt structure, epithelial integrity, fluorescein leakage, and inflammatory distribution patterns, and can detect hidden microscopic inflammation in mucosa that appears normal under conventional white-light endoscopy, potentially improving the detection of IBD-related inflammation. A 2015 prospective study including 79 patients with confirmed IBD (40 CD, 39 UC) confirmed significant differences in CLE features between CD and UC[34]: CD was characterized by segmental discontinuous lesions, with significantly higher incidences of discontinuous inflammation (87.5% *vs.* 5.1%), focal cryptitis (75.0% *vs.* 12.8%), and crypt architectural abnormality (87.5% *vs.* 10.3%) than UC ($P < 0.0001$); UC was mainly characterized by diffuse continuous lesions, manifesting as severe extensive crypt deformation (87.2% *vs.* 17.5%), decreased crypt density (79.5% *vs.* 22.5%), and obviously irregular surface morphology (89.7% *vs.* 17.5%), with statistically significant differences ($P < 0.0001$). Based on the above features, the IDEA scoring system was established, achieving standardization of the differential diagnosis between CD and UC, with an overall diagnostic accuracy of 93.7%, including sensitivity 97.4% and specificity 90.0% for diagnosing UC, and sensitivity 90.0% and specificity 97.4% for diagnosing CD, which may aid the classification of indeterminate IBD.

A retrospective study included 23 CD patients, 27 UC patients, and 9 control subjects and developed a computer-assisted pCLE image analysis method.[33] The researchers extracted 14 morphological and functional parameters and found that mean crypt spacing, wall thickness, and fluorescein leakage in IBD patients were significantly higher than those in control subjects (increased by 155%, 188%, and 297%, respectively, $P < 0.05$). The above parameters in UC patients were also higher than those in CD patients (increased by 109%, 117%, and 174%, respectively, $P < 0.05$). The scoring system constructed based on these parameters had reported sensitivity and specificity of 100% for IBD diagnosis, and 92% sensitivity and 91% specificity in the differential diagnosis between CD and UC.[33] This study suggests that computer-assisted CLE image analysis may provide an additional approach for IBD diagnosis and classification.

An animal study used CLE combined with magnetic resonance imaging and light-sheet fluorescence microscopy multiscale imaging technology to comprehensively evaluate acute and chronic changes in colitis.[35] CLE could observe fluorescently labeled epithelial cells and mucosal microvessels in real time, with a spatial resolution of approximately 1.4 μm, and was significantly correlated with histological scores and inflammatory activity indices ($P < 0.01$). This multimodal imaging strategy may improve understanding of the pathogenesis of IBD.

Statement 7: pCLE can evaluate UC mucosal healing and predict the risk of disease relapse.

Strong recommendation, moderate-certainty evidence (expert voting agreement rate: 85.4%).

The treatment goal of UC has gradually escalated from simple clinical remission to histological healing, and CLE shows potential benefits in evaluating UC mucosal healing.[19] A prospective study included 23 patients with active UC who underwent CLE before and after anti-tumor necrosis factor therapy and completed 3-year follow-up.[36] Based on four indicators—crypt number, crypt lumen morphological deformity, crypt lumen leakage, and perivascular leakage—an endomicroscopic mucosal healing score (eMHs) was established. The results showed that the sensitivity, specificity, and accuracy of eMHs in predicting mucosal healing were 100%, 93.75%, and 94.44%, respectively, suggesting that CLE may help assess UC mucosal healing. Another prospective study included 82 UC patients and, using the Robarts Histopathology Index as the gold standard,[37] compared the value of the Mayo endoscopic score, modified Paddington International Virtual Chromoendoscopy Score (PICaSSO), and pCLE in assessing mucosal healing. The results showed that the sensitivity, specificity, accuracy, and area under the receiver operating characteristic curve of pCLE in predicting histological healing were 94.9%, 91.3%, 93.9%, and 96.5%, respectively, further supporting the application of CLE in evaluating UC histological healing. However, adding pCLE did not further improve accuracy over the advanced endoscopic methods assessed in that study. Regarding relapse prediction, a prospective, blinded cohort study included 19 UC patients in clinical and endoscopic remission[38]; during 12 months of follow-up, it was found that a composite score constructed from fluorescein leakage combined with crypt diameter could effectively predict UC relapse ($P < 0.01$), suggesting that microscopic mucosal structural changes detected by pCLE in UC patients in remission have potential predictive value for UC relapse. Another prospective study included 58 IBD patients (47 UC, 11 CD)[39]; during 12 months of follow-up, it was found that IBD patients in clinical remission who had cell shedding with fluorescein leakage had a significantly increased risk of relapse ($P < 0.001$). The sensitivity, specificity, and accuracy of the CLE-based grading system in predicting disease flares were 62.5%, 91.2%, and 79%, respectively, indicating that intestinal barrier dysfunction detected by CLE may help predict IBD relapse.

The ENHANCE index is a UC histological disease activity assessment tool specifically designed for pCLE, constructed based on a prospective study conducted in 5 French centers including 100 UC patients in endoscopic remission.[19] In this study, more than 1000 pCLE video sequences were centrally interpreted, and it was found that vascular diameter > 20 μm, crypt lumen dilation, fluorescein leakage, and irregular crypt structure were independent predictors of histological inflammation (using the Nancy index as the gold standard). The ENHANCE index constructed based on these parameters had an overall accuracy of 79.6%, sensitivity 57.8%, and specificity 82.8%. When the ENHANCE index ≤ 1, the negative predictive value was as high as 93.1%, which was associated with a high probability of excluding active inflammation.[19] This study proposes a standardized tool for real-time histological assessment of UC.

Another study used pCLE to evaluate mucosal microcirculatory changes in UC patients in remission.[40] The results showed that compared with healthy controls, UC patients had obvious microcirculatory imbalance: the standard deviation of vascular diameter was significantly increased (2.68 ± 0.29 vs 2.23 ± 0.26, $P < 0.01$), and functional capillary density was significantly reduced (0.272 ± 0.034 vs 0.289 ± 0.030, $P < 0.01$). The researchers classified mucosal blood flow distribution into three types: surrounding type (type A), spider-web type (type C), and defective type (type D). Healthy controls were mainly type A (66.67%) and type C (33.33%), while UC patients were mostly type C (71.3%), and type D was seen only in UC patients (14.29%). More importantly, UC patients with type D blood flow had a significantly shortened relapse interval,[40] suggesting that the microcirculatory pattern assessed by pCLE may be associated with UC mucosal healing and relapse risk.

Statement 8: pCLE can be used for early surveillance of colorectal carcinogenesis in IBD patients and for differentiating benign from malignant lesions.

Strong recommendation, moderate-certainty evidence (expert voting agreement rate: 87.5%).

Due to long-term chronic inflammatory stimulation, IBD patients have a significantly increased risk of colorectal neoplasia, and regular surveillance is crucial for early detection of neoplasia.[2] CLE shows good application prospects in the detection and differentiation of IBD-related neoplasia.[41] High-definition chromoendoscopy combined with targeted biopsy is currently the recommended surveillance strategy for IBD neoplasia, but it has limitations such as long procedure time and high technical requirements.[42] CLE may serve as an adjunct to chromoendoscopy by real-time observation of epithelial structural abnormalities and vascular morphological changes, improving the detection rate of flat or small neoplasias.[43] In UC surveillance, a trial of chromoendoscopy-guided CLE reported approximately 4.75 times as many neoplasias detected with fewer biopsies; reported diagnostic performance varies across CLE studies.[6] This "optical biopsy" capability enables clinicians to characterize suspicious lesions during examination and guide targeted biopsy or treatment.

In the differentiation of benign and malignant IBD-related colorectal carcinogenesis, CLE may assist lesion assessment by observing the degree of glandular structural disorder, cellular atypia, and vascular abnormalities.[43] For indeterminate lesions, CLE-guided targeted biopsy can improve biopsy targeting and potentially increase diagnostic yield, providing reliable evidence for subsequent treatment decisions. IBD patients have a significantly increased risk of CRC, and their dysplasia often occurs in the context of chronic inflammation, with lesions often flat and scattered, making detection by traditional white-light endoscopy difficult. Compared with white-light endoscopy, CLE can significantly improve the detection rate of dysplasia, especially for flat lesions. A randomized controlled study showed that in UC cancer surveillance,[25] the number of dysplasia detected in the chromoendoscopy combined with CLE group was about 5 times that in the traditional white-light endoscopy group, and the number of biopsies was reduced by about 50%. In qualitative diagnosis, CLE may assist real-time differentiation between neoplastic and non-neoplastic lesions: non-adenomatous lesions mostly retain normal epithelial structure, crypt morphology, and regular vascular network, while adenomatous lesions show immature epithelial differentiation, crypt budding, abnormal vascular structure, and loss of cell polarity.[44] A prospective study confirmed that the sensitivity of pCLE microscopic features in differentiating UC-related neoplasia from regenerative lesions was 100%,[45] and the specificity was 83%. A systematic review pointed out that the sensitivity of traditional Kudo classification in diagnosing related neoplasia in the context of IBD inflammation was only about 83%,[46] with a certain risk of missed diagnosis; while the Mainz classification combined with CLE can more accurately identify early dysplasia in the context of inflammation. In addition, the "optical biopsy" capability of CLE may support localization and targeted sampling of suspicious areas, improve the positive rate of biopsy, and thereby optimize the surveillance strategy for IBD-related carcinogenesis.[47]

Controversies and unresolved issues

During the voting process, two statements with an expert voting agreement rate lower than 80% were not presented as formal statements, because the available clinical evidence was considered insufficient. Firstly, pCLE may aid in the selection of biological agents in patients with IBD and may inform individualized treatment decisions.[48-52] Secondly, pCLE may assist in diagnosing special intestinal lesions such as radiation enteritis, ischemic colitis, cap polyposis, and intestinal disease after stem cell transplantation, although the clinical utility of these applications remains insufficiently established.[6] Prospective studies are needed to clarify diagnostic accuracy, reproducibility, and clinical benefit in these indications.

Conclusions

pCLE provides complementary microscopic information for colorectal lesion characterization, targeted biopsy, and IBD assessment and surveillance; in IBD diagnosis, it does not replace conventional endoscopic and histopathological evaluation. This consensus provides evidence-based guidance for standardized clinical application.

The evidence underlying these recommendations is limited by small study populations, heterogeneous CLE platforms and interpretation criteria, and the indirect applicability of eCLE or combined chromoendoscopy-CLE findings to pCLE alone. Multicenter prospective research is needed to determine incremental clinical benefit and cost-effectiveness.

Looking ahead, with the continuous development of new technologies such as AI-assisted diagnosis and molecular imaging, pCLE may become a useful tool for precision diagnosis and treatment of lower gastrointestinal diseases. It is recommended to strengthen multicenter clinical research collaboration, improve the training and certification system, promote health economics evaluation, and facilitate the standardized and widespread application of this technology, with the aim of improving patient care.

Supporting information

Supplementary material for this article is available at https://doi.

org/10.14218/CSP.2026.00022.

Acknowledgments

The authors thank Jinfang Xu and Qian He (Department of Military Health Statistics, Navy Medical University) for methodological support in literature search design and GRADE evidence grading; both contributed as non-voting methodological experts and have consented to being named.

Funding

This work was supported by the National Key Research and Development Program of China (No. 2023YFC2413801).

Conflict of interest

Yu Bai serves as an editorial board member, and Zhuan Liao serves as an associate editor, of *Cancer Screening and Prevention*. The authors declare no other conflicts of interest.

Author contributions

Study conception (ZL, ZDJ, YB), study design (YB), literature review (PP, CLW, SBZ), evidence appraisal (CLW), data synthesis (PP), data interpretation (XZ), manuscript drafting (PP, CLW, SBZ), coordination of the revision (CLW), critical revision of the manuscript (XZ, ZL, ZDJ, YB), supervision (ZDJ, YB). All authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work.

Ethical statement

The formulation of this expert consensus adheres to the Helsinki Declaration of the World Medical Association and relevant Chinese healthcare laws and regulations. The content of the consensus is based on the best available evidence from evidence-based medicine and was reached through multiple rounds of discussions and revisions by the expert panel. This consensus aims to provide a reference for clinical practice and cannot replace the professional judgment of doctors. The clinical images included in this manuscript are completely anonymized and contain no identifiable patient information or distinctive features that could compromise patient privacy.

Consensus Expert Committee

Yu Bai (The First Affiliated Hospital of Naval Medical University), Zhenzhai Cai (The Second Affiliated Hospital of Wenzhou Medical University), Jin Chai (The First Affiliated Hospital of Army Medical University), Fenglin Chen (Union Hospital Affiliated to Fujian Medical University), Ping Chen (Affiliated Hospital of Inner Mongolia Medical University), Bin Cheng (Shanxi Bethune Hospital; Tongji Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology), Shigang Ding (Peking University Third Hospital), Feng Gao (People's Hospital of Xinjiang Uygur Autonomous Region), Yan Geng (The 923rd Hospital of Joint Logistics Support Force of Chinese People's Liberation Army), Xiaohua Hou (Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology), Zhendong Jin (The First Affiliated Hospital of Naval Medical University), Peng Li (Beijing Friendship Hospital Affiliated to Capital Medical University), Rui Li (The First Affiliated Hospital of Soochow University), Xiuling Li (Henan Provincial People's Hospital), Yanqing Li (Qilu Hospital of Shandong University), Zhaoshen Li (The First Affiliated Hospital of Naval Medical University), Yunxiao Liang (People's Hospital of Guangxi Zhuang Autonomous Region), Zhuan Liao (The First Affiliated Hospital of Naval Medical University), Rong Lin (Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology), Ling Liu (West China Hospital of Sichuan University), Xiaogang Liu (Sichuan Provincial People's Hospital), Qifeng Lu (Fuyang People's Hospital), Xu Shu (The First Affiliated Hospital of Nanchang University), Siyu Sun (Shengjing Hospital Affiliated to China Medical University), Shanyu Qin (The First Affiliated Hospital of Guangxi Medical University), Chengwei Tang (West China Hospital of Sichuan University), Xinjian Wan (Shanghai Sixth People's Hospital), Rong Wang (Shanxi Provincial People's Hospital), Dong Wang (The Ninth People's Hospital of Shanghai Jiao Tong University School of Medicine), Hongguang Wang (Jilin City People's Hospital), Yongjun Wang (Beijing Friendship Hospital Affiliated to Capital Medical University), Jun Wu (The Third Affiliated Hospital of Naval Medical University), Qi Wu (Peking University Cancer Hospital), Rui Xie (Guizhou Provincial People's Hospital), Guifang Xu (The First Affiliated Hospital of Anhui Medical University), Hongyu Xu (The First Affiliated Hospital of Harbin Medical University), Hongwei Xu (Shandong Provincial Hospital), Hongzhi Xu (Zhongshan Hospital Affiliated to Xiamen University), Shuchang Xu (Tongji Hospital Affiliated to Tongji University), Aiming Yang (Peking Union Medical College Hospital, Chinese Academy of Medical Sciences), Ling Yang (Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology), Jing Zhang (Peking University Third Hospital), Shutian Zhang (Beijing Friendship Hospital Affiliated to Capital Medical University), Qiu Zhao (Zhongnan Hospital of Wuhan University), Liang Zhong (Huashan Hospital Affiliated to Fudan University), Xianfei Zhong (Leshan People's Hospital Affiliated to Southwest Medical University), Duowu Zou (Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine), Xiuli Zuo (Qilu Hospital of Shandong University)

Methodological experts (non-voting): Jinfang Xu and Qian He (Department of Military Health Statistics, Navy Medical University).

References

[1] Expert Group on Early Diagnosis and Treatment of Cancer; Chinese Society of Oncology; Chinese Medical Association. Expert consensus on the early diagnosis and treatment of colorectal cancer in China (2023 edition) (in Chinese). Zhonghua Yi Xue Za Zhi 2023;103(48): 3896–3908. DOI: 10.3760/cma.j.cn112137-20230804-00164, PMID: 38129166.

[2] Ibraheim H, Dhillon AS, Koumoutsos I, Gulati S, Hayee B. Curriculum review: colorectal cancer surveillance and management of dysplasia in IBD. Frontline Gastroenterol 2018;9(4):271–277. DOI: 10.1136/

flgastro-2017-100919, PMID: 30245789.

[3] Zhao X, Liu S. Interpretation of "Chinese Expert Consensus on Endoscopic Diagnosis and Treatment of Inflammatory Bowel Disease (2024, Guangzhou)" (in Chinese). Chinese Journal of Digestive Endoscopy 2025;42(5):348–351. DOI: 10.3760/cma.j.cn321463-20250317-00018.

[4] Gastrointestinal Hormone and Mucosal Barrier Group; Chinese Society of Gastroenterology, Li J. Clinical Expert Consensus on Gastrointestinal Mucosal Protection (2021, Fuzhou) (in Chinese). Chinese Journal of Digestion 2021;41(12):798–811. DOI: 10.3760/cma.j.cn311367-20210930-00524.

[5] Moravčík P, Hlavsa J, Kunovsky L, Kala Z, Penka I, Dastych M. Confocal Laser Endomicroscopy in the Diagnostics of Malignancy of the Gastrointestinal Tract (in Czech). Klin Onkol 2017;30(4):258–263. DOI: 10.14735/amko2017258, PMID: 28832171.

[6] Ayyad M, Gala D, Albandak M, Goyal RM, Abboud Y, Al-Khazraji A, *et al*. Probe-based confocal laser endomicroscopy: progress, challenges, and emerging applications. Surg Endosc 2025;39(12):7958–7972. DOI: 10.1007/s00464-025-12297-w, PMID: 41184675.

[7] Inoki K, Abe S, Tanaka Y, Yamamoto K, Hihara D, Ichijima R, *et al*. Reduced Intravenous Fluorescein Dose for Upper and Lower Gastrointestinal Tract Probe-Based Confocal Laser Endomicroscopy. Clin Endosc 2021;54(3):363–370. DOI: 10.5946/ce.2020.058, PMID: 32894932.

[8] Gadour E, Miutescu B, Al-Lehibi A, Mohamed M, Aljahdli E, Albeshir M, *et al*. Confocal Laser Endomicroscopy: Real-Time Histology at the Fingertips: A Comprehensive Review of Current Applications of Endomicroscopy in Barrett Esophagus, Inflammatory Bowel Disease, and Colorectal Lesions. Medicina (Kaunas) 2026;62(2):415. DOI: 10.3390/medicina62020415, PMID: 41752813.

[9] Digestive Medical Imaging Collaboration Group; Chinese Society of Gastroenterology, Li Y. Chinese Consensus on Clinical Application of Endomicroscopy in Digestive System Diseases (in Chinese). Chinese Journal of Digestion 2023;43(1):3–17. DOI: 10.3760/cma.j.cn311367-20221126-00586.

[10] Zhang H, He Z, Jin Z, Yan Q, Wang P, Ye X. The development and clinical application of microscopic endoscopy for in vivo optical biopsies: Endocytoscopy and confocal laser endomicroscopy. Photodiagnosis Photodyn Ther 2022;38:102826. DOI: 10.1016/j.pdpdt.2022.102826, PMID: 35337998.

[11] Napoleon B, Krishna SG, Marco B, Carr-Locke D, Chang KJ, Ginès À, *et al*. Confocal endomicroscopy for evaluation of pancreatic cystic lesions: a systematic review and international Delphi consensus report. Endosc Int Open 2020;8(11):E1566–E1581. DOI: 10.1055/a-1229-4156, PMID: 33140012.

[12] Yi S, Lü F, Wu C, Li J, Chen M, Zhang JY, *et al*. Preliminary study of endoscopic ultrasound-guided domestic needle-based confocal laser endomicroscopy in diagnosing digestive tract and surrounding tumors (in Chinese). Chinese Journal of Digestive Endoscopy 2026;43(1):43–49. DOI: 10.3760/cma.j.cn321463-20250328-00008.

[13] Sun YN, Zhang MM, Li LX, Ji R, Wang X, Li P, *et al*. Cresyl violet as a new contrast agent in probe-based confocal laser endomicroscopy for in vivo diagnosis of gastric intestinal metaplasia. J Gastroenterol Hepatol 2020;35(3):453–460. DOI: 10.1111/jgh.14864, PMID: 31518444.

[14] Al-Mansour MR, Caycedo-Marulanda A, Davis BR, Alawashez A, Docimo S, Qureshi A, *et al*. SAGES TAVAC safety and efficacy analysis confocal laser endomicroscopy. Surg Endosc 2021;35(5):2091–2103. DOI: 10.1007/s00464-020-07607-3, PMID: 32405892.

[15] Goetz M, Toermer T, Vieth M, Dunbar K, Hoffman A, Galle PR, *et al*. Simultaneous confocal laser endomicroscopy and chromoendoscopy with topical cresyl violet. Gastrointest Endosc 2009;70(5):959–968. DOI: 10.1016/j.gie.2009.04.016, PMID: 19595315.

[16] Kollar M, Spicak J, Honsova E, Krajciova J, Vackova Z, Martinek J. Role of confocal laser endomicroscopy in patients with early esophageal neoplasia. Minerva Chir 2018;73(4):417–427. DOI: 10.23736/S0026-4733.18.07795-7, PMID: 29806759.

[17] Vennelaganti S, Vennalaganti P, Mathur S, Singh S, Jamal M, Kanakadandi V, *et al*. Validation of Probe-based Confocal Laser Endomicroscopy (pCLE) Criteria for Diagnosing Colon Polyp Histology. J Clin Gastroenterol 2018;52(9):812–816. DOI: 10.1097/MCG.0000000000000927, PMID: 28885303.

[18] Minea H, Sfarti C, Chiriac S, Sîngeap AM, Danciu M, Blaj M, *et al*. Integrated Assessment of Intestinal Barrier Function and Microscopic Inflammation Using Confocal Laser Endomicroscopy for Relapse Prediction in Ulcerative Colitis. United European Gastroenterol J 2026;14(2):e70181. DOI: 10.1002/ueg2.70181, PMID: 41820246.

[19] Rahmi G, Coron E, Perrod G, Levy M, Moreau J, Moussata D, *et al*. Probe-based Confocal Laser Endomicroscopy for In Vivo Assessment of Histological Healing in Ulcerative Colitis: Development and Validation of the ENHANCE Index. J Crohns Colitis 2021;15(6):994–999. DOI: 10.1093/ecco-jcc/jjaa255, PMID: 33336249.

[20] Rath T, Dieterich W, Kätscher-Murad C, Neurath MF, Zopf Y. Cross-sectional imaging of intestinal barrier dysfunction by confocal laser endomicroscopy can identify patients with food allergy in vivo with high sensitivity. Sci Rep 2021;11(1):12777. DOI: 10.1038/s41598-021-92262-4, PMID: 34140591.

[21] Pan P, Gao J, Zhang Y, Pan JY, Zhang WH, Wang NN, *et al*. Establishment and Evaluation of a Probe-Based Confocal Laser Endomicroscopy Training System for Gastric Cancerous Lesions Diagnosis: Evidence From a National Training Program. Clin Transl Gastroenterol 2026;17(9):e01074. DOI: 10.14309/ctg.0000000000001074, PMID: 42508426.

[22] Belderbos TDG, van Oijen MGH, Moons LMG, Siersema PD. Implementation of real-time probe-based confocal laser endomicroscopy (pCLE) for differentiation of colorectal polyps during routine colonoscopy. Endosc Int Open 2017;5(11):E1104–E1110. DOI: 10.1055/s-0043-117948, PMID: 29104910.

[23] Ruan W, Yang J, Hou Y, Yv A, Ding Q, Zhou Y. Clinical Application of Confocal Laser Endomicroscopy in the Diagnosis of Gastrointestinal Diseases. Digestion 2026;107(5):436–448. DOI: 10.1159/000548414, PMID: 40966172.

[24] Buchner AM, Shahid MW, Heckman MG, Krishna M, Ghabril M, Hasan M, *et al*. Comparison of probe-based confocal laser endomicroscopy with virtual chromoendoscopy for classification of colon polyps. Gastroenterology 2010;138(3):834–842. DOI: 10.1053/j.gastro.2009.10.053, PMID: 19909747.

[25] Kiesslich R, Goetz M, Lammersdorf K, Schneider C, Burg J, Stolte M, *et al*. Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. Gastroenterology 2007;132(3):874–882. DOI: 10.1053/j.gastro.2007.01.048, PMID: 17383417.

[26] Abe S, Saito Y, Oono Y, Tanaka Y, Sakamoto T, Yamada M, *et al*. Pilot study on probe-based confocal laser endomicroscopy for colorectal neoplasms: an initial experience in Japan. Int J Colorectal Dis 2018;33(8):1071–1078. DOI: 10.1007/s00384-018-3059-x, PMID: 29700599.

[27] Deng F, Fang Y, Shen Z, Gong W, Liu T, Wen J, *et al*. Use of confocal laser endomicroscopy with a fluorescently labeled fatty acid to dia-

gnose colorectal neoplasms. Oncotarget 2017;8(35):58934–58947. DOI: 10.18632/oncotarget.19515, PMID: 28938608.

[28] Liu Z, Luo X, Jiang W, Chen D, Chen W, Li K, *et al*. Real-time in vivo optical biopsy using confocal laser endomicroscopy to evaluate distal margin in situ and determine surgical procedure in low rectal cancer. Surg Endosc 2019;33(7):2332–2338. DOI: 10.1007/s00464-018-6519-z, PMID: 30386986.

[29] Tan J, Ji HL, Hu YW, Li ZM, Zhuang BX, Deng HJ, *et al*. Real-time in vivo distal margin selection using confocal laser endomicroscopy in transanal total mesorectal excision for rectal cancer. World J Gastrointest Surg 2022;14(12):1375–1386. DOI: 10.4240/wjgs.v14.i12.1375, PMID: 36632126.

[30] Robles-Medranda C, Oleas R, Valero M, Puga-Tejada M, Soria-Alcívar M, Ospina J, *et al*. Confocal laser endomicroscopy detects colonic inflammation in patients with irritable bowel syndrome: a prospective study. Endosc Int Open 2020;8(4):E550–E557. DOI: 10.1055/a-1119-6327, PMID: 32258379.

[31] Zhao DY, Qi QQ, Long X, Li X, Chen FX, Yu YB, *et al*. Ultrastructure of intestinal mucosa in diarrhea-predominant irritable bowel syndrome. Physiol Int 2019;106(3):225–235. DOI: 10.1556/2060.106.2019.20, PMID: 31560236.

[32] Trieu TH, Vieujean S, Delhougne N, Seidel L, Louis E, Loly JP. Confocal Endomicroscopy Intestinal Epithelial Barrier Abnormalities in Individuals Without Documented Gastro-Intestinal Disease. United European Gastroenterol J 2025;13(4):576–585. DOI: 10.1002/ueg2.12756, PMID: 39873272.

[33] Quénéhervé L, David G, Bourreille A, Hardouin JB, Rahmi G, Neunlist M, *et al*. Quantitative assessment of mucosal architecture using computer-based analysis of confocal laser endomicroscopy in inflammatory bowel diseases. Gastrointest Endosc 2019;89(3):626–636. DOI: 10.1016/j.gie.2018.08.006, PMID: 30120955.

[34] Tontini GE, Mudter J, Vieth M, Atreya R, Günther C, Zopf Y, *et al*. Confocal laser endomicroscopy for the differential diagnosis of ulcerative colitis and Crohn's disease: a pilot study. Endoscopy 2015;47(5):437–443. DOI: 10.1055/s-0034-1391226, PMID: 25521573.

[35] Li T, Hui H, Hu C, Ma H, Yang X, Tian J. Multiscale imaging of colitis in mice using confocal laser endomicroscopy, light-sheet fluorescence microscopy, and magnetic resonance imaging. J Biomed Opt 2019;24(1):1–8. DOI: 10.1117/1.JBO.24.1.016003, PMID: 30701723.

[36] Hundorfean G, Chiriac MT, Mihai S, Hartmann A, Mudter J, Neurath MF. Development and Validation of a Confocal Laser Endomicroscopy-Based Score for In Vivo Assessment of Mucosal Healing in Ulcerative Colitis Patients. Inflamm Bowel Dis 2017;24(1):35–44. DOI: 10.1093/ibd/izx012, PMID: 29272480.

[37] Iacucci M, Cannatelli R, Gui X, Zardo D, Bazarova A, Gkoutos GV, *et al*. Assessment of Endoscopic Healing by Using Advanced Technologies Reflects Histological Healing in Ulcerative Colitis. J Crohns Colitis 2020;14(9):1282–1289. DOI: 10.1093/ecco-jcc/jjaa056, PMID: 32201877.

[38] Buda A, Hatem G, Neumann H, D'Incà R, Mescoli C, Piselli P, *et al*. Confocal laser endomicroscopy for prediction of disease relapse in ulcerative colitis: a pilot study. J Crohns Colitis 2014;8(4):304–311. DOI: 10.1016/j.crohns.2013.09.005, PMID: 24094597.

[39] Kiesslich R, Duckworth CA, Moussata D, Gloeckner A, Lim LG, Goetz M, *et al*. Local barrier dysfunction identified by confocal laser endomicroscopy predicts relapse in inflammatory bowel disease. Gut 2012;61(8):1146–1153. DOI: 10.1136/gutjnl-2011-300695, PMID: 22115910.

[40] Tian Y, Zheng Y, Teng G, Li J, Wang H. Imbalanced mucosal microcirculation in the remission stage of ulcerative colitis using probe-based confocal laser endomicroscopy. BMC Gastroenterol 2019;19(1):114. DOI: 10.1186/s12876-019-1037-6, PMID: 31262270.

[41] Passos MAT, Chaves FC, Chaves-Junior N. The importance of colonoscopy in inflammatory bowel diseases. Arq Bras Cir Dig 2018;31(2):e1374. DOI: 10.1590/0102-672020180001e1374, PMID: 29972402.

[42] Huguet JM, Ferrer-Barceló L, Suárez P, Sanchez E, Prieto JD, Garcia V, *et al*. Colorectal cancer screening and surveillance in patients with inflammatory bowel disease in 2021. World J Gastroenterol 2022;28(5):502–516. DOI: 10.3748/wjg.v28.i5.502, PMID: 35316962.

[43] Iacucci M, Uraoka T, Fort Gasia M, Yahagi N. Novel diagnostic and therapeutic techniques for surveillance of dysplasia in patients with inflammatory bowel disease. Can J Gastroenterol Hepatol 2014;28(7):361–370. DOI: 10.1155/2014/825947, PMID: 25157526.

[44] Sanduleanu S, Driessen A, Gomez-Garcia E, Hameeteman W, de Bruïne A, Masclee A. In vivo diagnosis and classification of colorectal neoplasia by chromoendoscopy-guided confocal laser endomicroscopy. Clin Gastroenterol Hepatol 2010;8(4):371–378. DOI: 10.1016/j.cgh.2009.08.006, PMID: 19683597.

[45] Ohmiya N, Horiguchi N, Tahara T, Yoshida D, Yamada H, Nagasaka M, *et al*. Usefulness of confocal laser endomicroscopy to diagnose ulcerative colitis-associated neoplasia. Dig Endosc 2017;29(5):626–633. DOI: 10.1111/den.12853, PMID: 28244237.

[46] Cassinotti A, Parravicini M, Chapman TP, Balzarini M, Canova L, Segato S, *et al*. Endoscopic characterization of neoplastic and non-neoplastic lesions in inflammatory bowel disease: systematic review in the era of advanced endoscopic imaging. Ther Adv Gastroenterol 2023;16:17562848231208667. DOI: 10.1177/17562848231208667, PMID: 37954537.

[47] Lord R, Burr NE, Mohammed N, Subramanian V. Colonic lesion characterization in inflammatory bowel disease: A systematic review and meta-analysis. World J Gastroenterol 2018;24(10):1167–1180. DOI: 10.3748/wjg.v24.i10.1167, PMID: 29563760.

[48] Loly JP, Vieujean S, Reenaers C, Van Kemseke C, Seidel L, Louis E, *et al*. In-Depth Assessment of Endoscopic Remission in Inflammatory Bowel Disease Treated by Anti-TNF or Vedolizumab. Inflamm Bowel Dis 2024;30(2):240–246. DOI: 10.1093/ibd/izad066, PMID: 37042951.

[49] Udristoiu AL, Stefanescu D, Gruionu G, Gruionu LG, Iacob AV, Karstensen JG, *et al*. Deep Learning Algorithm for the Confirmation of Mucosal Healing in Crohn's Disease, Based on Confocal Laser Endomicroscopy Images. J Gastrointestin Liver Dis 2021;30(1):59–65. DOI: 10.15403/jgld-3212, PMID: 33723558.

[50] Atreya R, Neumann H, Neufert C, Waldner MJ, Billmeier U, Zopf Y, *et al*. In vivo imaging using fluorescent antibodies to tumor necrosis factor predicts therapeutic response in Crohn's disease. Nat Med 2014;20(3):313–318. DOI: 10.1038/nm.3462, PMID: 24562382.

[51] Rath T, Bojarski C, Neurath MF, Atreya R. Molecular imaging of mucosal α4β7 integrin expression with the fluorescent anti-adhesion antibody vedolizumab in Crohn's disease. Gastrointest Endosc 2017;86(2):406–408. DOI: 10.1016/j.gie.2017.01.012, PMID: 28137597.

[52] Iacucci M, Jeffery L, Acharjee A, Grisan E, Buda A, Nardone OM, *et al*. Computer-Aided Imaging Analysis of Probe-Based Confocal Laser Endomicroscopy With Molecular Labeling and Gene Expression Identifies Markers of Response to Biological Therapy in IBD Patients: The Endo-Omics Study. Inflamm Bowel Dis 2023;29(9):1409–1420. DOI: 10.1093/ibd/izac233, PMID: 36378498.