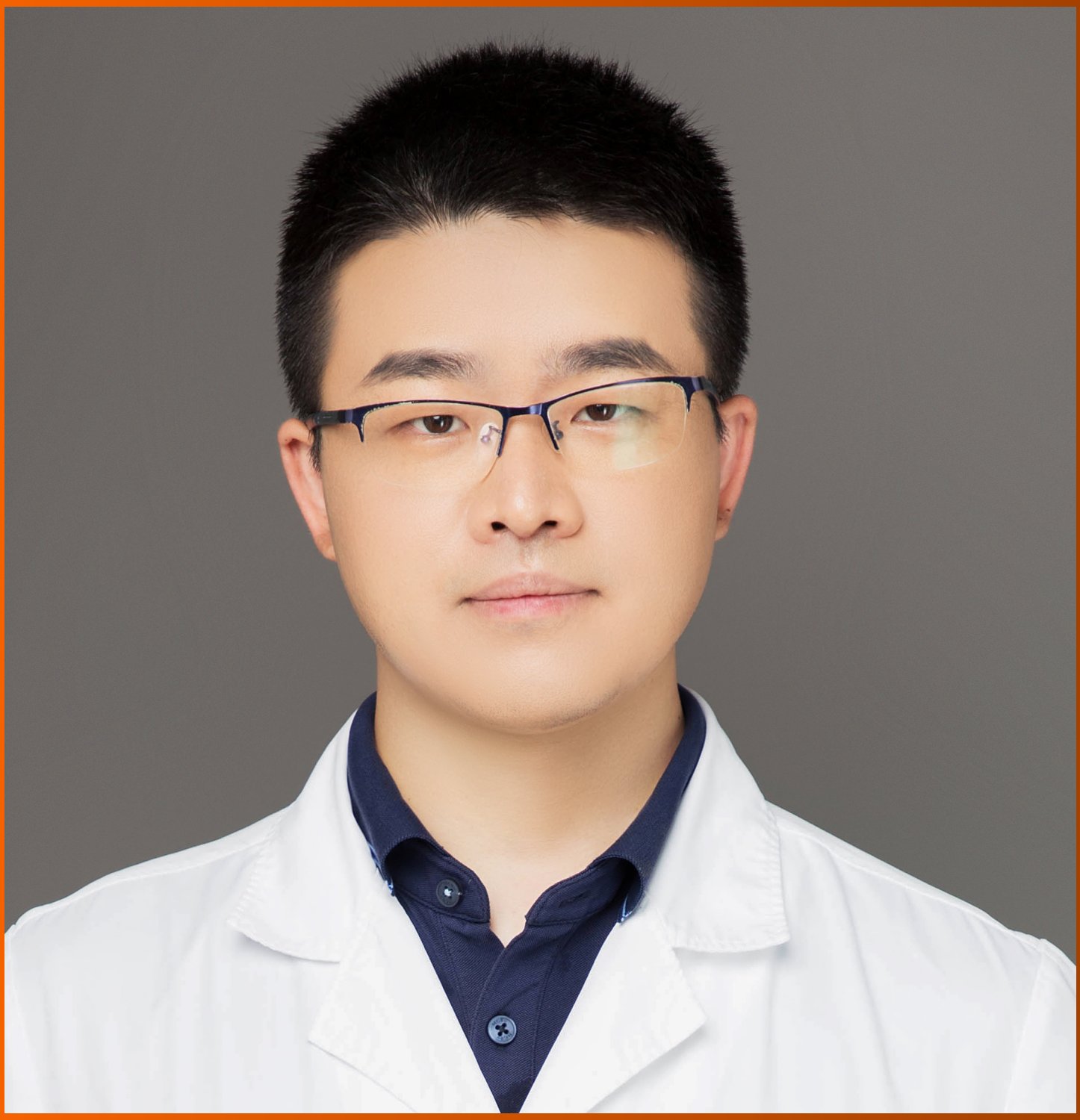
ISSN 1948-5190 (online)

World Journal of *Gastrointestinal Endoscopy*

World J Gastrointest Endosc 2024 September 16; 16(9): 502-544



Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Endoscopy

Contents

Monthly Volume 16 Number 9 September 16, 2024

World Journal of Gastrointestinal Endoscopy

Monthly Volume 16 Number 9 September 16, 2024

Contents

NAME OF JOURNAL
World Journal of Gastrointestinal Endoscopy

ISSN
ISSN 1948-5190 (online)

LAUNCH DATE
October 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Bing Hu, JooYoung Cho

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5190/editorialboard.htm

PUBLICATION DATE
September 16, 2024

PUBLISHING PARTNER
Digestive Endoscopy Center of West China Hospital, SCU

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

PUBLISHING PARTNER's OFFICIAL WEBSITE
http://www.cd120.com/index.html

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2024 September 16; 16(9): 540-544

DOI: 10.4253/wjge.v16.i9.540

ISSN 1948-5190 (online)

LETTER TO THE EDITOR

Confocal laser endomicroscopy for gastric neoplasm

Arkadeep Dhali, Rick Maity, Roger B Rathna, Jyotirmoy Biswas

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade B

Novelty: Grade B, Grade B

Creativity or Innovation: Grade B, Grade B

Scientific Significance: Grade A, Grade A

P-Reviewer: Ji Y; Wakatsuki T

Received: March 13, 2024

Revised: August 22, 2024

Accepted: August 28, 2024

Published online: September 16, 2024

Processing time: 182 Days and 8.4 Hours

Arkadeep Dhali, Department of Gastroenterology, Sheffield Teaching Hospitals NHS Foundation Trust, Royal Hallamshire Hospital, Sheffield S10 2JF, United Kingdom

Arkadeep Dhali, School of Medicine and Population Health, University of Sheffield, Sheffield S10 2HQ, United Kingdom

Rick Maity, General Medicine, Institute of Post Graduate Medical Education and Research, Kolkata 700020, India

Roger B Rathna, Department of Internal Medicine, University Hospitals Leicester NHS Trust, Leicester Royal Infirmary, Leicester LE1 5WW, United Kingdom

Jyotirmoy Biswas, General Medicine, College of Medicine and Sagore Dutta Hospital, Kolkata 700058, India

Co-first authors: Arkadeep Dhali and Rick Maity.

Corresponding author: Arkadeep Dhali, MBBS, MPH, PGCert Clin Ed, FRSPH, NIHR Academic Clinical Fellow, Department of Gastroenterology, Sheffield Teaching Hospitals NHS Foundation Trust, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, United Kingdom. arkadipdhali@gmail.com

Abstract

Confocal laser endomicroscopy (CLE) is a novel endoscopic modality that provides real-time histological information *via* high-resolution magnified view of the mucosa. CLE has a higher sensitivity, specificity, and diagnostic accuracy in detecting atrophic gastritis as compared to chromoendoscopy and narrow-band imaging. It can even predict low-grade and high-grade intraepithelial neoplasia by analyzing gastric pit patterns. CLE may have some advantages over the standard biopsy protocol, such as higher diagnostic yield and fewer biopsy requirements. Its diagnostic accuracy in detecting superficial gastric cancer is higher than that of white-light endoscopy. Inherent limitations, such as a narrow field of vision, can be surpassed by technological advancements and integration with other detection methods. Artificial intelligence holds promise in automated analysis of histopathological images. Thus, CLE can be helpful in screening for early gastric cancer and may help reduce the risk of complications from repeated biopsies, such as mucosal damage, bleeding, and infection.

Key Words: Confocal laser endomicroscopy; Gastric cancer; Narrow band imaging; Diagnostic yield

Core Tip: Confocal laser endomicroscopy is a new imaging technique used during endoscopy procedures to evaluate the mucosa in vivo. Diagnosing and monitoring early cancer in the upper gastrointestinal tract can be effectively achieved through the use of this tool. Minimizing the number of biopsies required is one of the main benefits of this technology, while still maintaining a high diagnostic sensitivity rate. This helps to reduce the risk of complications, such as mucosal damage, bleeding, and infection, that may be caused by repeated biopsies.

Citation: Dhali A, Maity R, Rathna RB, Biswas J. Confocal laser endomicroscopy for gastric neoplasm. *World J Gastrointest Endosc* 2024; 16(9): 540-544
URL: https://www.wjgnet.com/1948-5190/full/v16/i9/540.htm
DOI: https://dx.doi.org/10.4253/wjge.v16.i9.540

TO THE EDITOR

Confocal laser endomicroscopy (CLE) is a novel endoscopic modality that provides real-time histological information *via* high-resolution magnified view of the mucosa. CLE is based on the principle of confocal microscopy, wherein a low-power laser beam is focused at a specific plane in the tissue and the fluorescence emitted is detected, enabling the functional reconstruction of an image. Since CLE relies upon tissue fluorescence, intravenous and/or topical contrast agents are utilized. There are two kinds of CLE systems that can be used for gastrointestinal (GI) endoscopy. The first one is endoscope-based CLE (eCLE), which is a combination of a miniature confocal scanner and a unique flexible endoscope tip. However, this system is not frequently utilized in clinical practice. The other system is known as probe-based CLE (pCLE), which has a flexible confocal microprobe that can easily pass through the working channels of most traditional endoscopes. In comparison to eCLE, pCLE can capture images more quickly. However, its resolution and preset fixed plane depth are limited[1,2].

COMPARISON OF CLE WITH ENDOCYTOSCOPY

Both CLE and endocytoscopy are high-definition imaging modalities that are designed to provide *in vivo* histological information of GI mucosa and have endoscope-integrated as well as probe-based devices. However, the latter is based on white-light microscopy by using tissue stains (such as methylene blue, crystal violet, or toluidine blue), meaning that visualization and magnification of subepithelial layers is not possible with endocytoscopy[2]. There are few studies comparing the diagnostic accuracies of CLE and endocytoscopy; Zhou *et al*[3] and Pirogov *et al*[4] showed that CLE had a sensitivity, specificity, and diagnostic accuracy of 90%, 87%, and 95.6%, respectively, in detecting early gastric cancer, while Abad *et al*[5] found that endocytoscopy had a sensitivity, specificity, and accuracy of 84.8%, 90%, and 87.2%, respectively, in diagnosing early gastric cancer.

CLINICAL DATA

Gastric cancer has various stages of progression, including chronic gastritis, chronic atrophic gastritis (AG), gastric intestinal metaplasia, gastric intraepithelial neoplasia, and early gastric carcinoma (EGC). A study by Zhang *et al*[6] used eCLE to classify the morphology of gastric pits into seven types based on different pathological conditions. They performed eCLE on 132 consecutive patients and 10 gastric samples and found that the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of type E gastric pit pattern for predicting AG were 83.6%, 99.6%, 96.6%, and 97.6%, respectively[6]. Another study by Wallace *et al*[7] presented the Miami classification for pathological conditions using pCLE.

Li *et al*[8] improved this classification by adding an index of vascular structure, which allows for a more valuable and complete assessment of gastric mucosa. It includes three types of pit patterns and seven subtypes with three kinds of vessel architecture. By combining vascular changes in neoplastic gastric mucosa with gastric pit patterns, this classification has the ability to predict high-grade intraepithelial neoplasia (HGIN) as well as low-grade intraepithelial neoplasia (LGIN). The study results support this statement, with sensitivity, specificity, and diagnostic accuracy for LGIN being 84%, 99.78%, and 99.57%, respectively, and for HGIN being 88.89%, 99.89%, and 99.84%, respectively[8].

Liu *et al*[9] did a study that compared the effectiveness of narrow-band imaging (NBI), CLE, and chromoendoscopy (CE) in detecting AG. NBI and CE are both effective techniques for visualizing precancerous lesions, but they differ significantly from CLE in terms of their working principles. The vascular structures and mucosal features are enhanced by both NBI and CE *via* different mechanisms; NBI utilizes blue and green wavelengths of light, and CE employs staining agents to detect dysplastic and malignant lesions in the GI tract. Both NBI and CE provide visualization of the superficial

mucosal details and vasculature, whereas CLE constructs images at the cellular and subcellular levels, detecting different grades of cellular atypia with a high accuracy[10]. While the diagnostic accuracies of CE and NBI were comparable, the sensitivity, specificity, and accuracy of CLE (92.31%, 86.18%, and 89.33%, respectively) were significantly higher than CE (83.85%, 78.86%, and 81.42%, respectively). The research discovered that CLE has effective sensitivity (91.94%), specificity (96.86%), and NPV (97.37%) in detecting metaplastic AG. This type of AG has unique features, including goblet cells, brush borders, columnar absorptive cells, and villiform foveolar epithelium[11]. These results underline the benefits of using CLE to differentiate between metaplastic AG and non-metaplastic AG.

The biopsy protocol recommended by the Sydney System comprises five parts. Two parts are taken from the antrum, located 3 cm from the pylorus at the greater or lesser curvature. Another two parts are taken from the corpus, one from the lesser curvature, which is located 4 cm proximal to the incisura, and one from the middle of the greater curvature. The final part is taken from the incisura[12]. CLE has some advantages over the standard biopsy protocol, such as higher diagnostic yield and fewer biopsy requirements. Large-scale studies, including multicentric randomized trials, are required for validation of CLE as a potential alternative to standard biopsy protocols.

EGC is detected primarily through histological examination, but this method has limitations. One such area for improvement is the consistency of results from biopsies taken before and after surgery, which can lead to erroneous clinical decision-making[13]. In addition, repeated biopsy can cause mucosal fibrosis, leading to complications like perforation, bleeding, and partial removal of affected mucosa[14,15].

Li *et al*[16] carried out a study to address some of the limitations of the Miami classification. They examined the eCLE images of 182 patients with stomach disease in the first phase and developed a new two-tiered CLE classification for superficial gastric cancer. This classification categorizes gastric mucosa into non-cancerous or cancer/HGIN lesions based on various characteristics such as their cells, architecture, and microvessels. For cancer, glands become irregular in shape and size, pits and glands become disorganized or destroyed, and cells become disordered and lose polarity. The microvessels also exhibit irregular shape and calibre[16]. Lou *et al*[17] used CLE and pathological results to arrive at a diagnosis of poorly differentiated adenocarcinoma of the small curvature of the stomach. The second phase of the study involved examining the effectiveness of that classification in diagnosing gastric lesions, with histological results serving as the benchmark. Compared to white-light endoscopy (WLE), eCLE was found to have higher sensitivity, specificity, PPV, NPV, and accuracy in detecting EGC/HGIN lesions using the two-tiered CLE classification. Specifically, eCLE had a sensitivity of 88.9% compared to 72.2% for WLE and a specificity of 99.3% compared to 95.1% for WLE. The PPV for eCLE was 85.3% compared to 41.6% for WLE, while the NPV was 99.5% compared to 98.6% for WLE. Lastly, the accuracy of eCLE was 98.8% compared to 94.1% for WLE[17].

LIMITATIONS OF CLE

Despite providing high-resolution functional imaging of the GI mucosa, CLE has certain limitations. The primary limitation is the narrow field of vision, due to which the entire GI mucosa cannot be visualised[18]. Although fluorescein is safe to use, there is limited data on the safety profiles of other contrast agents such as acriflavin and cresyl violet[1]. As fluorescent dyes do not stain the nuclei, the nuclear structures cannot be assessed by CLE, making it a distant possibility as a standalone screening test for cancer[18]. Scanning systems at the proximal end of the instrument are often bulky and limit the ability to control the focus. Instead, miniature distal scanning mechanisms, such as the microelectromechanical systems (MEMS) scanner, offer more flexibility in controlling the focus and provide comprehensive assessment of the mucosa with aberration-free scanning over a large field-of-view[19]. Other limitations hindering the widespread adoption of CLE are the requirement of high capital investment and specialized training. Despite its limitations, CLE exhibits substantial potential as an imaging technique for detecting tumors in the upper digestive tract. By making further technological advancements and integrating it with other detection methods, we can overcome its inherent limitations[1].

FUTURE INTEGRATION WITH ARTIFICIAL INTELLIGENCE

Artificial intelligence (AI), which has shown promise in analyzing histologic images such as hematoxylin and eosin images and immunohistochemical staining images, may be useful in evaluating images obtained by CLE[20]. Since diagnosis relies on good-quality histopathological images, which are often difficult to obtain in clinical practice, AI models can assist in real-time, automated interpretation of histopathological images and can supplement the pathologist's interpretation[1,20].

CONCLUSION

CLE is a new imaging technique used during endoscopy procedures to evaluate the mucosa in vivo. Diagnosing and monitoring early cancer in the upper GI tract can be effectively achieved through the use of this tool. Minimizing the number of biopsies required is one of the main benefits of this technology, while still maintaining a high diagnostic sensitivity rate. This helps to reduce the risk of complications, such as mucosal damage, bleeding, and infection, that may be caused by repeated biopsies. The inherent limitations of CLE can be surpassed by integrating it with other imaging modalities. AI has a promising role in real-time automated interpretations of histopathological images obtained by CLE.

Multicentric randomized trials are required for validation of CLE as a screening test for gastric cancer and as a potential alternative to standard histological diagnoses *via* biopsies.

FOOTNOTES

Author contributions: Dhali A conceptualized the article, conducted literature review and wrote the primary manuscript; Maity R conducted literature review and wrote the primary manuscript; Rathna R conducted literature review and wrote the primary manuscript; Biswas J conducted literature review and wrote the primary manuscript. All authors agreed with the final version of the manuscript.

Conflict-of-interest statement: All authors declare no conflicts of interest.

Country of origin: United Kingdom

ORCID number: Arkadeep Dhali 0000-0002-1794-2569; Rick Maity 0009-0003-5316-2329.

S-Editor: Liu JH
L-Editor: A
P-Editor: Cai YX

REFERENCES

1 **Pilonis ND**, Januszewicz W, di Pietro M. Confocal laser endomicroscopy in gastro-intestinal endoscopy: technical aspects and clinical applications. *Transl Gastroenterol Hepatol* 2022; **7**: 7 [PMID: 35243116 DOI: 10.21037/tgh.2020.04.02]
2 **Goetz M**, Malek NP, Kiesslich R. Microscopic imaging in endoscopy: endomicroscopy and endocytoscopy. *Nat Rev Gastroenterol Hepatol* 2014; **11**: 11-18 [PMID: 23897286 DOI: 10.1038/nrgastro.2013.134]
3 **Zhou YW**, Zhang LY, Ding SN, Zhang AL, Zhu Y, Chen YX, Zhang QC, Sun LT, Yu JR. Hesitate between confocal laser endomicroscopy and narrow-band imaging: how to choose a better method in the detection of focal precancerous state of gastric cancer. *Am J Transl Res* 2022; **14**: 55-67 [PMID: 35173829]
4 **Pirogov SS**, Sokolov VV, Karpova ES, Pavlov PV, Volchenko NN, Kaprin AD. [Early gastric cancer and precancerous conditions diagnostics with confocal laser endomicroscopy]. *Eksp Klin Gastroenterol* 2014; 18-24 [PMID: 25518478]
5 **Abad MRA**, Inoue H, Ikeda H, Manolakis A, Rodriguez de Santiago E, Sharma A, Fujiyoshi Y, Fukuda H, Sumi K, Onimaru M, Shimamura Y. Utilizing fourth-generation endocytoscopy and the 'enlarged nuclear sign' for in vivo diagnosis of early gastric cancer. *Endosc Int Open* 2019; **7**: E1002-E1007 [PMID: 31404432 DOI: 10.1055/a-0957-2866]
6 **Zhang JN**, Li YQ, Zhao YA, Yu T, Zhang JP, Guo YT, Liu H. Classification of gastric pit patterns by confocal endomicroscopy. *Gastrointest Endosc* 2008; **67**: 843-853 [PMID: 18440377 DOI: 10.1016/j.gie.2008.01.036]
7 **Wallace M**, Lauwers GY, Chen Y, Dekker E, Fockens P, Sharma P, Meining A. Miami classification for probe-based confocal laser endomicroscopy. *Endoscopy* 2011; **43**: 882-891 [PMID: 21818734 DOI: 10.1055/s-0030-1256632]
8 **Li Z**, Zuo XL, Li CQ, Liu ZY, Ji R, Liu J, Guo J, Li YQ. New Classification of Gastric Pit Patterns and Vessel Architecture Using Probe-based Confocal Laser Endomicroscopy. *J Clin Gastroenterol* 2016; **50**: 23-32 [PMID: 25751373 DOI: 10.1097/MCG.0000000000000298]
9 **Liu T**, Zheng H, Gong W, Chen C, Jiang B. The accuracy of confocal laser endomicroscopy, narrow band imaging, and chromoendoscopy for the detection of atrophic gastritis. *J Clin Gastroenterol* 2015; **49**: 379-386 [PMID: 25485568 DOI: 10.1097/MCG.0000000000000164]
10 **Trivedi PJ**, Braden B. Indications, stains and techniques in chromoendoscopy. *QJM* 2013; **106**: 117-131 [PMID: 23097386 DOI: 10.1093/qjmed/hcs186]
11 **Guo YT**, Li YQ, Yu T, Zhang TG, Zhang JN, Liu H, Liu FG, Xie XJ, Zhu Q, Zhao YA. Diagnosis of gastric intestinal metaplasia with confocal laser endomicroscopy in vivo: a prospective study. *Endoscopy* 2008; **40**: 547-553 [PMID: 18618938 DOI: 10.1055/s-2007-995633]
12 **Dixon MF**, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. *Am J Surg Pathol* 1996; **20**: 1161-1181 [PMID: 8827022 DOI: 10.1097/00000478-199610000-00001]
13 **Chung IK**, Kim SP, Lee S, Lee CK, Kim S, Kim H, Park S, Lee TH, Park J. Importance of Diagnostic Endoscopic Resection to Compensate Histological Discrepancy Between Endoscopic Forceps Biopsy and Resected Specimens in Superficial Gastric Neoplasms. *Gastrointest Endosc* 2009; **69**: AB112 [DOI: 10.1016/j.gie.2009.03.093]
14 **Jeon SR**, Cho WY, Jin SY, Cheon YK, Choi SR, Cho JY. Optical biopsies by confocal endomicroscopy prevent additive endoscopic biopsies before endoscopic submucosal dissection in gastric epithelial neoplasias: a prospective, comparative study. *Gastrointest Endosc* 2011; **74**: 772-780 [PMID: 21802680 DOI: 10.1016/j.gie.2011.05.005]
15 **Gotoda T**. Endoscopic resection of early gastric cancer. *Gastric Cancer* 2007; **10**: 1-11 [PMID: 17334711 DOI: 10.1007/s10120-006-0408-1]
16 **Li WB**, Zuo XL, Li CQ, Zuo F, Gu XM, Yu T, Chu CL, Zhang TG, Li YQ. Diagnostic value of confocal laser endomicroscopy for gastric superficial cancerous lesions. *Gut* 2011; **60**: 299-306 [PMID: 21193460 DOI: 10.1136/gut.2010.223586]
17 **Lou JX**, Wu Y, Huhe M, Zhang JJ, Jia DW, Jiang ZY. Diagnosis of poorly differentiated adenocarcinoma of the stomach by confocal laser endomicroscopy: A case report. *World J Clin Cases* 2024; **12**: 1481-1486 [PMID: 38576802 DOI: 10.12998/wjcc.v12.i8.1481]

18 **Han W**, Kong R, Wang N, Bao W, Mao X, Lu J. Confocal Laser Endomicroscopy for Detection of Early Upper Gastrointestinal Cancer. *Cancers (Basel)* 2023; **15** [PMID: 36765734 DOI: 10.3390/cancers15030776]

19 **Lee M**, Li G, Li H, Duan X, Birla MB, Chang TS, Turgeon DK, Oldham KR, Wang TD. Confocal laser endomicroscope with distal MEMS scanner for real-time histopathology. *Sci Rep* 2022; **12**: 20155 [PMID: 36418439 DOI: 10.1038/s41598-022-24210-9]

20 **Cho H**, Moon D, Heo SM, Chu J, Bae H, Choi S, Lee Y, Kim D, Jo Y, Kim K, Hwang K, Lee D, Choi HK, Kim S. Artificial intelligence-based real-time histopathology of gastric cancer using confocal laser endomicroscopy. *NPJ Precis Oncol* 2024; **8**: 131 [PMID: 38877301 DOI: 10.1038/s41698-024-00621-x]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com