Application of artificial intelligence in gastrointestinal endoscopy

Short title: AI in gastrointestinal endoscopy

Changjiang Zhou[1], Wei Zhang[2], Chunyang Niu[1], Qing Yang[1,2] and Liqiang Wang[1,2,*]

[1]Research Center for Intelligent Sensing, Zhejiang Lab, Hangzhou, 311100, China.
[2]State Key Laboratory of Modern Optical Instrumentation, College of Optical Science and Engineering, Zhejiang University, Hangzhou, 310027, China.

* Correspondence： Prof. Liqiang Wang

State Key Laboratory of Modern Optical Instrumentation, College of Optical Science and Engineering, Zhejiang University, Hangzhou, 310027, China.
E-mail:wangliqiang@zju.edu.cn

ABSTRACT

Endoscope is an important tool for the diagnosis and treatment of gastrointestinal diseases. With the development of artificial intelligence (AI), especially deep learning (DL) technology, more and more endoscopic AI systems are being studied for the detection and diagnosis of gastrointestinal diseases. The literature shows that AI has many applications in clinical practice, and shows great potential in improving detection accuracy, efficiency, and adenoma detection rate. In this review, we introduce the current application of AI technology in gastrointestinal endoscopy in the esophagus, stomach and colorectum, and sort out the AI systems that successfully obtained the regular approval. Finally, we discuss the opportunities and challenges of the AI-based endoscopic system in clinical applications, and provide insights into the future.

Keywords： Artificial intelligence, Gastrointestinal endoscopy, Deep learning,

Computer-aided detection, Computer-aided diagnosis

INTRODUCTION

Gastrointestinal (GI) disease is one of the most common diseases that affects human health seriously. The emergence of GI endoscopy opens a new era in the diagnosis and treatment of digestive tract diseases.[1] Doctors can directly observe various diseases of the digestive cavity, and take biopsy for pathological examination with the help of GI endoscope.

In recent years, artificial intelligence (AI), with its unique advantages, has made important breakthroughs in the application of medicine, which has attracted widespread attention.[2] AI-assisted GI endoscopy has also become a research hotspot.[3-5] Traditional machine learning approaches like support vector machine (SVM) needs to extract features manually (such as color and anatomical grain), which can easily cause related features to be incomplete, thereby reducing the accuracy.[6] And they require experts to preset parameters, which may lead to inefficient. Driven by big data and high-performance computers, deep learning (DL) extracts image features through a multi-layer neural network automatically.[7] Convolutional neural network (CNN) is a deep feedforward neural network that has been developed in recent years, which is particularly well-suited to computer vision problems.[8] Recently, given the breakthrough of transformer in image analysis, transformer-based approaches have also been gradually applied to GI endoscopy analysis.[9]

The tasks of AI in image analysis mainly include classification, detection and segmentation.[10] In specific clinical applications, most endoscope AI systems are defined as computer-aided detection (CADe) and diagnosis (CADx).[11] They mainly focuse on the identification of early cancer and precancerous lesions of the GI tract, such as the identification of early cancers in esophagus and stomach, and the detection of colon polyps.[12] Based on the mucosal surface glandular duct opening and neovascularization status of these lesions, combined with endoscopic image parameters such as high definition white light imaging (WLI) endoscopy, narrow-band imaging (NBI) technology, and magnified endoscopy, several AI systems for identifying early cancers of the GI tract have been published in major academic journals.[13-14]

Endoscopy AI Challenge has also been held over the years.[15] According to the actual clinical requirements of GI endoscopy, the sponsor constructed corresponding scenarios, proposed AI analysis tasks, and provided high-quality datasets and annotations. The challengers from various countries actively participated and put forward various solutions, which achieved satisfying results. EAD2019, for example, provides a multicenter, multimodal endoscopy dataset for detecting artifacts generated during endoscopic surgery.[16] EDD2020 aims to assess localization of disease regions using bounding boxes and exact pixel-level segmentation. Because clinical applicability by assessing real-time monitoring and offline performance evaluations of algorithms for improved accuracy and better quantitative reporting is required today.[17] These challenges, to some extent, promote the application of AI in digestive endoscopy analysis.

We performed a systematic research for original publications on the subject of AI in the field of GI endoscopy, and classified them by different parts. At the same time, we counted the AI endoscopy products that had been approved. The purpose is to summarize the current situation and future perspectives of AI in both research and clinical practice of GI endoscopy.

CURRECT STATUS OF AI IN GI ENDOSCOPY

Esophagus

Esophageal cancer is one of the most common malignant tumors of the upper GI tract, ranking seventh in the incidence and sixth among the death of malignant tumors worldwide.[18] Most patients have reached the moderate or advanced stages of cancer when they go to the hospital. Endoscopic treatment of early esophageal cancer and precancerous lesions can achieve a cure rate of more than 90%, which can significantly improve the prognosis of patients.

It is difficult to detect Barrett's neoplasia and superficial esophageal squamous cell carcinoma (SCC), because that early lesions have subtle visual changes on endoscopy.[19] AI can help to aid in esophageal cancer detection and diagnosis. Table 1 shows the studies that AI applied in the field of esophagus. Van der Sommen *et al*.[20] used SVM to identify early neoplastic lesions on a per-patient basis with 86% sensitivity and 87% specificity. It was first reported for early neoplastic lesions. Additionally, more and more studies[21-24] have reported on Barrett's neoplasia with DL methods. For example, Hashimoto R *et al*.[25] reported that they used 1374 images to train CNN model. It could detect the Barrett's neoplasia with 96.4% sensitivity, 94.2% specificity, and 95.4% accuracy. Additionally, Ebigbo A *et al*.[26] developed a CNN-based model for th prediction of submucosal invasion in Barrett's cancer with 77% sensitivity, 64% specificity, and 74% diagnostic accuracy. Several studies have also reported on Esophageal SCC.[27-29] Cai SL *et al*.[29] collected 746 patients and developed a CNN-based model with 97.8% sensitivity, 85.4 % specificity, and 91.4% diagnostic accuracy. Guo *et al*.[30] trained CNN models for real-time automated detection of SCC via NBI with 98.0% sensitivity and 95.0% specificity.

Table 1. Summary of AI applied in the field of esophagus

Ref	Published year	Aim of study	Study design	Number of subjects	Type of AI	Endoscopic modality	Sensitivity	Specificity	Accuracy
van der Sommen F[20]	2016	Barrett's esophagus	Retrospective	44 patients	SVM	WLI	86	87	
Sehgal V,[21]	2018	Barrett's esophagus	Retrospective	40 patients	Decision trees	WLI	97	88	92

Groof JD[22]	2019	Barrett's esophagus	Retrospective	60 patients	SVM	WLI	95	85	91.7
Horie Y,[28]	2019	outcomes of esophageal cancer	Retrospective	384 patients	CNN	WLI/ NBI	98		98
Cai SL[29]	2019	early esophageal squamous cell carcinoma	Retrospective	746 patients	CNN	WLI	97.8	85.4	91.4
Kumagai Y[31]	2019	esophagus	Retrospective	240 patients	CNN	WLI	92.6	89.3	
Groof AJ[24]	2020	Barrett's esophagus	Retrospective	669 patients	CNN	WLI	90	88	89
Groof AJ[23]	2020	Barrett's esophagus	Retrospective	689 patients	CNN	WLI	91	89	90
Ebigbo A[25]	2020	Barrett's oesophagus	Retrospective	129 patients	CNN	WLI	83.7	100	89.9
Ebigbo A[26]	2020	Barrett's cancer	Retrospective	230 patients	CN	WLI	77	64	71

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Hashimoto R[27]	2020	Barrett's esophagus	Retrospective	1374 images	CNN	WLI	96.4	94.2	95.4
Guo L[30]	2020	Early esophageal squamous cellcarcinoma	Retrospective	549 patients	CNN	NBI	98	95	
Tokai Y[32]	2020	esophageal squamous cell carcinoma	Retrospective	1751 images	CNN	WLI/NBI	84.1	73.3	80.9
Wang, Y. K.[33]	2021	esophageal neoplasms	Retrospective	936 images	CNN	WLI/NBI	92.6	70.4	90.9

Stomach

Gastric cancer has a high incidence and poor prognosis all over the world. Research data indicate that in 2018, there were about 1,033,000 new cases and 783,000 deaths of gastric cancer worldwide.[18] The 5-year survival rate of patients with early diagnosis of gastric cancer can reach more than 90%, and studies have found that the false negative rate of traditional GI endoscopy screening for early cancer can reach 4.6%-25.8%.

Helicobacter pylori infection is an independent risk factor for gastric cancer. Table 2 shows the researches of AI used in the field of stomach. Several studies[34-36] have reported on Helicobacter pylori infection. Shichijo *et al.*[34] collected 1768 patients and developed a CNN-based model for the prediction of H. pylori gastritis. The sensitivity, specificity, and accuracy for diagnosing H. pylori infection were 88.9%, 87.4%, and 87.7%, respectively. Nakashima *et al.*[36] used the training images of WLI, blue laser imaging (BLI), and linked color imaging (LCI) from 162 patients for diagnosing H. pylori infection with 96.7% sensitivity and 86.7% specificity. Besides, there are also several studies[37-38] are reported for gastric cancer. Wu L *et al.*[39] reported that they used 9151 images to train CNN model. It could detect the gastric cancer with 94.0% sensitivity, 91.0% specificity, and 92.5% accuracy.

Table 2. Summary of AI applied in the field of stomach

Ref	Published year	Aim of study	Study design	Number of subjects	Type of AI	Endoscopic modality	Sensitivity	Specificity	Accuracy
Shichijo S[34]	2017	Helicobacter pylori infection	Retrospective	1768 patients	CNN	WLI	88.9	87.4	87.7
Itoh T [35]	2018	Helicobacter pylori infection	Retrospective	149 patients	CNN	WLI	86.7	86.7	
Nakashima	2018	Helicobacter pylori	Retrospective	162 patients	CNN	WLI\BLI\CLI	96.7	86.7	

H[36]		infection							
Zheng W[40]	2019	Helicobacter pylori infection	Retrospective	1507 images	CNN	WLI	81.4	90.1	84.5
Hirasawa T[37]	2018	gastric cancer	Retrospective	2639 lesions	CNN	WLI	98		98
Wu L [39]	2019	gastric cancer	Retrospective	9151 images	CNN	WLI	94.0	91.0	92.5
Cho BJ[38]	2020	gastric cancer	Retrospective	1066 patients	CNN	WLI			84.6
Wu, L[41]	2021	gastric cancer	Retrospective	37 EGCs and 63 noncancerous lesions	CNN	WLI/NBI			87.81
Zhao X[42]	2021	Gastrointestinal tract location classification		113 videos	Transformer	WLI			94.5

Colorectum

Colorectal cancer is one of the malignant tumors with the highest incidence and mortality in the world. In recent years, the incidence of colorectal cancer has shown an upward trend. Regular colonoscopy can effectively reduce the incidence and mortality.[43] Colon polyp detection using AI has always been an interesting application scenario for researchers.

The primary role of the CADe system is to help doctors reduce the missed diagnosis of polyps, thereby reducing ADRs, and it has been verified in multiple prospective clinical studies.[44] Misawa *et al.*[45] built a real-time CADe system through CNN, using 135 videos to evaluate the detection ability. The sensitivity, specificity, and accuracy for the frame-based analysis, were 90.0%, 63.3%, and 76.5%, respectively. Yamada *et al.*[46] developed a real-time CADe model based on CNN for the early automatic detection of colorectal tumors, including polypoid and non-polypoid lesions. The sensitivity of the model for detecting lesions is 97.3%, and the specificity is 99.0%.

In the CADx system, AI is mainly used to identify the characteristics of polyps. AI has been applied to the endoscopic diagnosis of many optical modalities such as WLI, LCI, autofluorescence endoscope, M-NBI, magnifying endoscope and so on.[47] Sánchez-Montes *et al.*[48] constructed a CADx system that used SVM for automated optical diagnosis and achieved high diagnostic abilities with 92.3% sensitivity, 89.2% specificity, and 91.1% accuracy. Chen *et al.*[49] designed a DNN CAD system to characterize diminutive polyps using NBI with optical magnification. They compared the polyp's characterization between the NBI based CADx and novel and expert endoscopists. AI was faster (0.45 ± 0.07 sec) than experts (1.54 ± 1.30 sec) and novel endoscopists (1.77 ± 1.37 sec). It correctly classified the neoplastic histology with 96.3% sensitivity and 78.1% specificity. The accuracy was 90.1%. The system was able to better characterize the polyps than novel endoscopists and was comparable to the experts.

In addition, AI has other applications in colonoscopy, such as the detection of inflammatory bowel disease. Gottlieb *et al.*[50] collected 947 full endoscopic videos of 249 patients from 14 countries, with a total of 19.5 million images. The study found that DL algorithms can be trained to predict the severity of ulcerative colitis (UC). In this study, using video rather than still images, it was found that DL algorithms could be trained to predict the severity of ulcerative UC, and that the performance of AI algorithms met or exceeded previously published indicator for the severity of UC score. Maeda *et al.*[51] developed and evaluated a CAD system that uses endoscopy to predict histological inflammation. It obtained data on 187 UC patients who received biopsy samples after endoscopy, including six colorectal sites from the cecum, ascending colon, transverse colon, descending colon, sigmoid colon and rectum. Endoscopic images and biopsy samples of each patient were collected, and all endoscopic images were labeled with reference to the histological activity of biopsy samples. A total of 12900 endoscopic images from 87 patients were used for training to construct CAD, and 525 independent segments from the remaining 100 patients were collected for validation. The main evaluation of the CAD system was the ability to predict histological inflammation. The results showed that the accuracy of CAD system was up to 91.0%, and it could completely automatically identify persistent histological inflammation associated with UC.

Other Field

Capsule endoscopy is a safe, non-invasive, and highly accepted diagnosis tool for GI diseases. Because of a large amount of video data, capsule endoscopy is an ideal field for AI research, which can help doctors identify different lesions and regions of interest.[52] As newer generations of high-definition capsules emerge, richer data are available for training a CNN to detect masses or sources of occult bleeding. Leenhardt *et al.*[53] developed a CNN to detect GI angioectasias in the small bowel. This model is proved to have 100% sensitivity for detecting angioectasias, with a specificity of 96%. This approach assesses a full-length study in 39 min. Lui *et al.*[54] obtained data from 439 capsule videos and trained a CNN model to identify multiple types of lesions and their positions on the capsule endoscopic images. The model recognizes arteriovenous malformations, erythema, varicose veins, swelling, masses, ulcers, erosions, blood, red villi, diverticula, polyps and xanthomas with an accuracy rate of

97%. Aoki *et al.*[55] developed an AI diagnosis system for the diagnosis of erosions and ulcers in capsule endoscopy. The system used 5,360 images of erosion and ulcers for deep CNN training and tested on 10,440 small intestine endoscopic images. The test was completed in 233 seconds, and the area under the receiver operating characteristic curve for the diagnosis of erosion and ulcer was 0.958. The sensitivity, specificity and accuracy were 88.2%, 90.9% and 90.8%, respectively.

The binocular endoscope has the features of three-dimensional (3D) imaging and measurement, which can provide depth information to assist endoscopists operate the endoscope more accurately, efficiently and safely.[56] Traditional binocular matching algorithms such as semi-global block matching algorithm (SGBM), for the texture less and high gloss endoscopic images, will generate disparity maps with holes and mismatch problems. Researchers began to explore binocular disparity prediction based on DL. Some proposed models, such as MCCNN, GC-Net, GA-Net, can effectively improve the accuracy of disparity prediction in the above-mentioned difficult areas.[57] In addition, binocular reconstruction will also spend a lot of time for left and right images matching. For this reason, many monocular endoscopic AI models are put forward for real-time 3D reconstruction and measurement of the GI tract.[58]

FRONTIER RESEARCH

There are still many new types of endoscopes used in clinical practice, including endocytoscopy (EC), endoscopic ultrasound (EUS), electronic choledochoscope. AI technology is also used in image analysis of these endoscopes. Compared with traditional endoscopes, the application of AI technology is still a cutting-edge research because of the small amount of dataset and the complicated structure of the observed objects of these new endoscopes.

EC is a new kind of endoscope with ultra-high magnification, which can magnify digestive tract mucosal epithelium 520× to observe and evaluate in vivo cells, to improve cytological diagnosis efficiency and realize the so-called "optical biopsy".[59-61] This technique was first released by Olympus and observed in vivo esophageal squamous cell nuclei in the clinic.[62] However, the recognition and interpretation of EC images close to pathology have put forward high requirements for endoscopists. Therefore, the combination of EC and AI has gradually become a new research focus.[60] Kumagai *et al.* trained 4715 (1141 malignant and 3574 non-malignant images) esophageal EC images based on GoogLeNet and achieved 90.9% diagnostic accuracy on the independent test set. It showed that AI has the potential to assist endoscopists in real-time diagnosis of esophageal cancer without reference to histological biopsy.[31] Mori *et al.* diagnosed small colorectal adenomas (< 5 mm) in 791 patients based on Olympus colonoscopy (CF-H290ECI) and Cybernet CAD system (trained on 61,925 EC images). The results showed that the sensitivity and specificity of NBI mode or staining mode were about 90%.[63-64] With the development of EC and AI technology, real-time pathological diagnosis in vivo by endoscopists is expected to become a reality shortly.

Electronic choledochoscope is an endoscope that can directly observe the bile duct. Bile duct pathologies ranging from benign choledocholithiasis to malignant biliary strictures cholangiocarcinoma constitute the majority of the volume of pancreatobiliary endoscopy. Indeterminate bile duct strictures, with uncertainty for the presence of malignancy, have remained an Achilles' heel for a biliary endoscopist.[65]There are few kinds ofresearch on the application of AI in choledochoscope because of low resolution of SpyGlass cholangioscopy relative to colonoscopy and the infrequency incidence of such indeterminate bile duct strictures.[66] However, the application of AI in pancreaticobiliary endoscopy is of great potential, and it is expected to reduce inter-operator variability, enhance the accuracy of diagnosis, and assist in accurate therapeutic decision-making in real-time, thereby essentially mimicking the presence of an expert in every endoscopy suite.

In EUS, AI is used for detecting anatomical features, differential pancreatic tumors, and cysts. Kuwahara T[67] collected 4000 EUS images to train a DL architecture (ResNet50) for the malignancy of IPMN classification with an accuracy of 94%. Zhang JJ *et al*.[68] used Unet++ and ResNet50 for semantic segmentation and classification for EUS stations with accuracy of 82.4% in station classification and

0.715 dice in segmentation. Seven *et al*.[69] collected a total of 685 images of GISTs from 55 retrospectively included patients to predict the malignant potential of gastric gastrointestinal stromal tumors (GISTs) based on DL models. The overall sensitivity, specificity, and accuracy of the DL model for predicting malignancy risk were 83%, 94%, and 82% in the training dataset, and 75%, 73%, and 66% in the validation cohort, respectively.

CLINICAL PRACTICE

AI products in Endoscopy must undergo rigorous review to obtain regulatory approval before they can be commercialized. Meanwhile, the large number of endoscopic images used for AI model training requires the agreement of hospitals, patients, and industry. Therefore, the development cycle of endoscopic AI products is usually long. Currently, there are only a few AI products in endoscopy, which have obtained regulatory approval. These products mainly focus on CADe and CADx of colorectal lesions, aiming to improve the ADR and diagnostic accuracy. Some of them were developed by the major endoscopy companies based on their endoscopes and clinical images, such as Endo-AID,[70] CAD EYE[71-72] and DISCOVERY.[73-74] In this way, the software and hardware of products were better matched. The other part comes from software companies that often support multi-band endoscopes, such as GI-Genius,[75-77] EndoBRAIN,[78-79] ENDOANGEL.[80-81] Table 3 summarized these AI products and their performance.

Table 3. Summary of AI products

Product	Year	Manufacturer	Function	Performance
ENDO-AID[70]	2020	Olympus Corp., Tokyo, Japan	Colon CADe	integrated into the latest EVIS X1 endoscopy system
CAD EYE[71-72]	2020	Fujifilm Corp., Tokyo, Japan	Colon CADe & CADx	100 polyps in 25 patients; CADe ADR: 85%

				(WLI), 89% (LCI); CADx: 88.8% (non-magnified BLI-LASER/LED), 87.8% (magnified BLI-LASER/LED)
DISCOVERY[73-74]	2020	Pentax Medical, Tokyo, Japan	Colon CADe	ADR: n = 803, 48.0% (CADe) vs 37.5% (standard)
GI-Genius[75-77]	2019	Medtronic, Minneapolis, MN, USA	Colon CADe	ADR: n = 685, 54.8% (CADe) vs 40.4% (standard) The reaction time was faster by AI system as compared with endoscopists in 82% of cases (n = 277/337; difference 1.27+3.81 s)
EndoBRAIN[78-79]	2018/2020	Cybernet Corp., Tokyo, Japan	Colon CADe & CADx	trained using 69,142 endocytoscopic images and identified colon lesions with 96.9% sensitivity, 100% specificity, 98% accuracy, a 100% positive-predictive value, and a 94.6%

				negative-predictive
ENDOANGEL[80-81]	2020	EndoAngel Crop., WuHan, China	CADe & CADx & improving endoscopy quality	ADR: n = 704, 16.0% (CADe) vs 8.0% (standard) A per-lesion accuracy of 84.7%, sensitivity of 100%, and specificity of 84.3% for detecting gastric cancer (n = 1050)

CONCLUSIONS

After training with a large number of endoscopic images or videos, the endoscopy AI systems can reach the diagnosis level of general doctors or experts, so they have many potential clinical applications, such as detection of precancerous lesions, identification of lesions based on mucosal or vascular patterns, risk stratification before/during treatment, and assessment of key performance indicators. The main advantages of AI-assisted endoscopy systems are to reduce the workload of doctors, reduce missed diagnoses, and improve diagnosis efficiency and accuracy, so AI will become more and more important in clinical practice in the future. AI technology will provide a good way to obtain top-notch medical technology in areas with a lack of medical resources and low-level medical resources, and benefit the local people to realize the sharing of high-quality medical resources. The AI-assisted diagnosis system can be used as an important auxiliary method for physicians to complete accurate diagnoses under endoscopy, and it also provides an effective tool for training low-age endoscopists in the future.

However, there are still many problems and challenges. First of all, researchers tend to collect high-quality endoscopic images to construct training sets and exclude common low-quality and unanalyzable images (eg, obscure images, those containing mucus, stained images, or those with partial views of lesions), which may lead to poor generalization in models in clinical practice.[82] In this case, the accuracy of the AI system may be exaggerated, as its good performance when using static, high-quality images does not guarantee that recognition will be successful when using dynamic videos. Secondly, the model is only tested in a small number of data sets, while the data used for clinical testing is huge. It is impossible to guarantee the real effect of the AI system in clinical application, even for products already on the market. Finally, there are ethical issues. AI products can only be used for auxiliary analysis while it is the doctor who really makes the judgment and assumes the responsibility. Therefore, no matter how high the accuracy of the system is, the doctor cannot rely too much on it.

In summary, AI technology has made important achievements in GI endoscopy analysis research, while there are also many challenges and limitations. With further improvement of AI technology, it is expected that AI will have a routine application in endoscopic clinical practice in the future.

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Conflicts of Interest

The authors declare no conflicts of interest.

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