

# Artificial Intelligence in *Gastroenterology*

*Artif Intell Gastroenterol* 2020 November 28; 1(4): 60-85





# Artificial Intelligence in Gastroenterology

## Contents

Bimonthly Volume 1 Number 4 November 28, 2020

### MINIREVIEWS

- 60 Artificial intelligence: A new budding star in gastric cancer  
*Wang WA, Dong P, Zhang A, Wang WJ, Guo CA, Wang J, Liu HB*
- 71 Artificial intelligence in gastrointestinal cancer: Recent advances and future perspectives  
*Kudou M, Kosuga T, Otsuji E*

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The primary aim of *Artificial Intelligence in Gastroenterology* (AIG, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

**INDEXING/ABSTRACTING**

There is currently no indexing.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Yu-Jie Ma*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lai Wang*.

**NAME OF JOURNAL**

*Artificial Intelligence in Gastroenterology*

**ISSN**

ISSN 2644-3236 (online)

**LAUNCH DATE**

July 28, 2020

**FREQUENCY**

Bimonthly

**EDITORS-IN-CHIEF**

Rajvinder Singh, Ferruccio Bonino

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2644-3236/editorialboard.htm>

**PUBLICATION DATE**

November 28, 2020

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**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>



## Artificial intelligence: A new budding star in gastric cancer

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**Author contributions:** Wang WA and Liu HB contributed to the conceptualization of this study; Wang WA, Wang WJ, and Guo CA contributed to the methodology; Wang WA, Dong P, Zhang A, and Wang J contributed to the investigation; Wang WA and Wang WJ contributed to the data classification; Wang WA wrote the manuscript.

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

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### Abstract

The pursuit of health has always been the driving force for the advancement of human society, and social development will be profoundly affected by every breakthrough in the medical industry. With the arrival of the information technology revolution era, artificial intelligence (AI) technology has been rapidly developed. AI has been combined with medicine but it has been less studied with gastric cancer (GC). AI is a new budding star in GC, and its contribution to GC is mainly focused on diagnosis and treatment. For early GC, AI's impact is not only reflected in its high accuracy but also its ability to quickly train primary doctors, improve the diagnosis rate of early GC, and reduce missed cases. At the same time, it will also reduce the possibility of missed diagnosis of advanced GC in cardia. Furthermore, it is used to assist imaging doctors to determine the location of lymph nodes and, more importantly, it can more effectively judge the lymph node metastasis of GC, which is conducive to the prognosis of patients. In surgical treatment of GC, it also has great potential. Robotic surgery is the latest technology in GC surgery. It is a bright star for minimally invasive treatment of GC, and together with laparoscopic surgery, it has become a common treatment for GC. Through machine learning, robotic systems can reduce operator errors and trauma of patients, and can predict the prognosis of GC patients. Throughout the centuries of development of surgery, the history gradually changes from traumatic to minimally invasive. In the future, AI will help GC patients reduce surgical trauma and further improve the efficiency of minimally invasive treatment of GC.



**Manuscript source:** Invited manuscript

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** China

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): 0  
Grade C (Good): C  
Grade D (Fair): D, D, D  
Grade E (Poor): 0

**Received:** June 30, 2020

**Peer-review started:** June 30, 2020

**First decision:** September 14, 2020

**Revised:** October 15, 2020

**Accepted:** November 28, 2020

**Article in press:** November 28, 2020

**Published online:** November 28, 2020

**P-Reviewer:** Cianci P, Filippou D, Yarema R, Yeh HZ

**S-Editor:** Wang JL

**L-Editor:** Filipodia

**P-Editor:** Li X



**Key Words:** Gastric cancer; Artificial intelligence; Gastroscopy; Lymph node; Robotic surgery; Minimally invasive

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**Core Tip:** Artificial intelligence (AI) is an important part of the information technology revolution. AI can be used in the following three aspects: (1) Gastroscopy for gastric cancer (GC) can improve the diagnostic accuracy of early GC and reduce the missed diagnosis of atypical parts of advanced GC; (2) Imaging doctor determination of the location of the lymph nodes. More importantly, it can more effectively determine lymph node metastasis of GC; and (3) Improving robotic surgical systems and further reducing patient injuries, by advancing from minimally invasive to nearly non-invasive surgery.

**Citation:** Wang WA, Dong P, Zhang A, Wang WJ, Guo CA, Wang J, Liu HB. Artificial intelligence: A new budding star in gastric cancer. *Artif Intell Gastroenterol* 2020; 1(4): 60-70  
**URL:** <https://www.wjgnet.com/2644-3236/full/v1/i4/60.htm>  
**DOI:** <https://dx.doi.org/10.35712/aig.v1.i4.60>

## INTRODUCTION

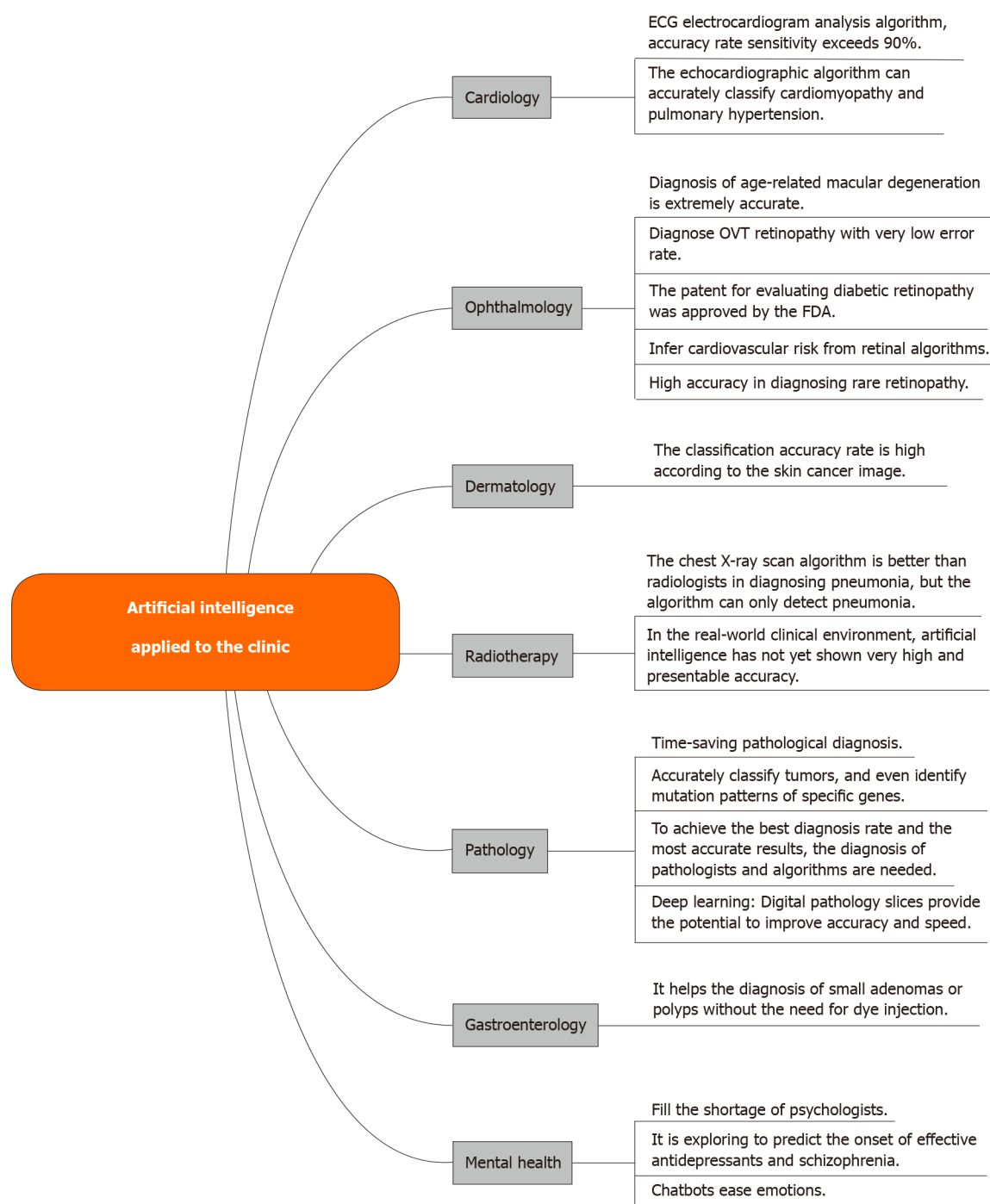
Gastric cancer (GC) is the fifth most common cancer and the third leading cause of cancer death worldwide. The incidence of GC in East Asia has increased significantly in recent years<sup>[1]</sup>, ranking second in incidence in China, representing the most common cause of cancer death<sup>[2]</sup>. In recent years, with the transformation of information technology, AI (AI) technology is gradually becoming an alternative to traditional technology or an integral part of an integrated system. AI has been used to solve complex practical problems in various fields and is becoming more and more popular today<sup>[3]</sup>. AI can learn from examples, has certain fault tolerance, can deal with noisy data and incomplete data, can deal with nonlinear problems, and can be predicted and summarized at high speed once it has been trained. AI-based systems are being widely developed and deployed worldwide, mainly because of their symbolic reasoning, flexibility, and interpretation capabilities. Thanks to the rapid development of large amounts of labeled data and computers, AI, especially deep learning, has begun to penetrate the medical field. AI is of great significance to medicine and has been partially applied in clinic. Topol<sup>[4]</sup> enumerates and analyzes the main aspects and functions of AI in clinical application at present (refer to **Figure 1** for details). AI can make accurate judgments on diseases through large-scale learning, and can assist clinicians in the diagnosis and treatment of GC. As such, AI-assisted diagnosis has become an important direction for the diagnosis of GC.

## APPLICATION OF AI IN GASTROSCOPE

Gastrointestinal endoscopy is the most important and potential direction for AI-assisted diagnosis. In previous studies, much of the initial work of endoscopic AI technology has focused on the detection and optical diagnosis of colonic polyps<sup>[5]</sup>. Esophagogastroduodenoscopy (EGD) is widely regarded as one of the standard methods for diagnosing gastric diseases. However, a study<sup>[6]</sup> has shown that the missed rate of endoscopy in the 3 years before diagnosis of gastrointestinal tumors is 11.3%. Two other studies<sup>[7,8]</sup> showed that the proportion of missed GCs was 9.4% and 25.8%. AI-based detection's potential usefulness in GC was first reported by Hirasawa *et al*<sup>[9]</sup>. For gastroenterology, AI is another important direction for the diagnosis of GC.

### *Application of AI in the diagnosis of early GC by endoscopy*

Topol<sup>[4]</sup> thinks that AI can help make clinical diagnosis fast and accurate, optimizing processes in the health-care system to reduce diagnostic errors and malpractice. More than this, it can benefit the patient's daily life, helping in observing



**Figure 1 Artificial intelligence applied to the clinic.**

and analyzing their health data to accelerate rehabilitation. Gastrointestinal endoscopy is an important and rapidly developing research field in the application of AI in gastrointestinal surgery, specifically in the diagnosis and treatment of early cancer. Endoscopic submucosal dissection (referred to as ESD) and endoscopic mucosal resection (referred to as EMR) are considered to be the most beneficial procedures for patients with early GC (EGC), and surgical treatment is considered when endoscopic treatment is not possible. The risk of lymph node metastasis in the mucosal layer (referred to here as “M”)/shallow submucosal layer (referred to here as “SM1”; < 500 mm from the muscularis mucosa) is very low but the potential of metastasis in the deep submucosal layer (referred to here as “SM2”; > 500 mm invasion) is quite high. As usual, for patients with EGC and an infiltration depth greater than 500 mm, surgery is considered the first choice. However, for patients with EGC whose depth of

invasion is limited to the M or superficial submucosa (~ 500 mm from the muscularis mucosa), ESD/EMR should be provided.

The accuracy of endoscopists in using endoscopy, endoscopic ultrasonography, or both to predict the depth of invasion was only 69% to 85% in previous studies<sup>[10]</sup>. Therefore, it is an important clinical problem to accurately predict the invasion depth of EGC. Research has shown that machine vision can interpret specific medical images more accurately and faster than humans using high magnification<sup>[11]</sup>. In a separate study that is more accurate, Zhu *et al*<sup>[12]</sup> report significant progress in the use of endoscopy in EGC. They developed and validated an AI system model that uses deep learning algorithms to determine the depth of invasion of EGC. The model is called a convolutional neural network computer-aided detection (CNN-CAD) system, which can determine whether the intrusion depth is "M/SM1" and "SM2" or deeper. In the research results of Zhu *et al*<sup>[12]</sup>, the AI machine learned a total of 790 GC images and tested 203 GC images, which are different and independent of the learning images. The result is that when the threshold of CNN-CAD system is 0.5, the sensitivity is 76.47%, the specificity is 95.56%, and the accuracy is 89.16%. The positive and negative predictive values were 89.66% and 88.97%, respectively. The sensitivity of the endoscopist was 87.80%, the specificity was 63.31%, the accuracy was 71.49%, and the positive and negative predictive values were 55.86% and 91.01%, respectively.

For experienced endoscopists, the CNN-CAD system has once again achieved higher accuracy and specificity. High specificity of 96% will help to enhance the accurate diagnosis of the depth of invasion, distinguishing EGC from deeply invasive submucosal layer cancer. However, there are still some limitations in the research of Zhu *et al*<sup>[12]</sup>. First there are relatively few materials for deep learning. Second, in AI learning algorithms, only high resolution and clear images are selected as learning and testing materials. These two points lead to a serious defect whereby AI models may show excellent performance in clean and clear images of GC, but the diagnostic accuracy may be greatly affected when faced with poor quality images which endoscopists often encounter in clinical practice. This disadvantage can be overcome by enabling AI to learn a large number of images which are common among clinical gastroscopic pictures, such as mucus on the surface of the lesion, the lesion not being concentrated, or the location being too narrow to be seen clearly.

On colonoscopy, it is considered very difficult to find small adenoma or pedicleless polyps. In a first prospective clinical trial of AI, in a real-time routine colonoscopy, a total of 466 images of 466 tiny polyps were analyzed, with an accuracy of 94% and a negative predictive value of 96%. The speed of AI optical diagnosis is 35 s, which is faster than that of clinical endoscopists<sup>[11]</sup>. The algorithm is equally effective for novices and gastroenterologists and does not require dye injection. This study and Zhu *et al*<sup>[12]</sup> reached similar conclusions and revealed the application potential of AI in gastrointestinal endoscopy.

With AI, it's like opening a third eye to an endoscopist. AI for the diagnosis of disease, especially for EGC, is not only reflected in high accuracy but also in the quick training of junior doctors, improved diagnosis rate of EGC, and reduced missed cases.

### **Application of AI in endoscopic diagnosis of advanced GC**

Gastroscopy easily detects advanced GC but there is also a certain risk of missed diagnosis. Korean scholars<sup>[13]</sup> prospectively collected undiagnosed cases of advanced GC with recent endoscopies, from 1997 to 2008, and reviewed the medical records of advanced GC diagnosed before 1991 to 1996. In total, 2310 cases of GC were analyzed. In that study, more than one-third of patients with advanced GC were not found in the previous endoscopy and they were located around the cardia.

Wu *et al*<sup>[14]</sup> has developed a new deep (D)CNN for endoscopic vision. This DCNN system is used to screen for EGC without blind spots during gastroenteroscopy (*i.e.* EGD). As a result, DCNN identified EGC from non-malignant tumors with an accuracy of 92.5%, sensitivity of 94.0%, specificity of 91.0%, positive predictive value of 91.3%, negative predictive value of 93.8%; these results were better than any achieved by an endoscopist. The accuracy of EGC detection by endoscopists is surpassed by the DCNN system of Wu *et al*<sup>[14]</sup>, and that can better identify the location of the stomach. The advantage of the system is that it can detect EGC actively and track suspicious cancer lesions during EGD. Although the above study was aimed at EGC, we can see that an AI system has great potential for accurate diagnosis of advanced GC. The accuracy of GC diagnosis will be improved because of the intervention of an AI system. The high rate of missed diagnosis of advanced GC in the cardia will also be overcome by an AI system.

The prevalence and incidence rates of advanced stage GC are high, and the diagnosis rate is about 2/3. This has prompted doctors and researchers from all over

the world not only to improve the detection rate of EGC but also to optimize the clinical management of advanced GC<sup>[15]</sup>.

### Perspectives

Ishioka *et al*<sup>[16]</sup> believe that the application of a CNN system in video should be expanded, and the image is expected to improve the standard of early detection of GC. Luo *et al*<sup>[17]</sup> developed a gastrointestinal-AI diagnostic system. Seven validation sets were used in their multicenter study, with accuracy ranging from 91.5% to 97.7%. The diagnostic sensitivity of “griaids” was higher than that of endoscopists (85.8%) and interns (72.2%). Kanesaka *et al*<sup>[18]</sup> collected and randomly selected 66 EGC magnifying narrow-band imaging (m-Nbi) images and 60 non cancer m-Nbi images as training sets, and 61 EGC m-Nbi images and 20 non cancer m-Nbi images as test sets. The test shows that the cadx system has great potential in the real-time diagnosis and sketching of EGCS in m-Nbi images. The study by Horiuchi *et al*<sup>[19]</sup> also supports this conclusion.

Whether it is EGC or advanced GC, the invasion depth of the tumor is related to the prognosis of the patients. Accurate determination of the invasion depth is beneficial to the patients. The overall accuracy rate of using “WLis” to evaluate the invasion depth of Zhu *et al*<sup>[12]</sup> was 89.16%, which was significantly higher than that of endoscopists.

Many research studies on AI and the stomach have been focused on Japan, China and South Korea. At present, the combination of GC and AI mainly focuses on the detection and diagnosis of GC. In addition, AI systems may have potential applications in other areas. There are also many research studies on the application of AI technology in the detection and diagnosis of GC.

AI has great potential in the field of digestive diseases. Using AI for accurate diagnosis can make more accurate optical biopsy and reduce unnecessary biopsy or endoscopic resection, which is beneficial to patients. This can reduce the risk of bleeding, the incidence of complications, and the economic expenditure caused by the disease.

## APPLICATION OF AI IN LYMPH NODE METASTASIS OF GC

Just as AI is gradually changing gastroenterology and endoscopy, it has also changed imaging doctors greatly. Preoperative localization diagnosis of lymph nodes is an ongoing and substantial challenge for radiologists. At present, the detection of lymph nodes is mainly achieved by imaging methods, which extracts a variety of diagnostic features. Some feature extraction methods are used to extract the effective diagnosis features, and then to realize the diagnosis of lymph node metastasis. Lymph node metastasis is an important independent factor affecting the prognosis of GC. Before medical and surgical treatment, lymph nodes must be understood as accurately as possible to determine treatment options and evaluate prognosis. Lymph node metastasis is an important independent factor affecting the prognosis of GC. Some studies have shown that the diagnosis of lymph node metastasis is of great significance<sup>[20-22]</sup>. AI and the diagnosis of GC lymph nodes can be divided into two aspects. The former is the application of AI in the diagnosis of lymph nodes, and the latter is the application of AI in the diagnosis of lymph node metastases. Because artificial detection is time-consuming and laborious, AI detection of abdominal lymph nodes is considered to be one of the development trends.

Barbu *et al*<sup>[23]</sup> propose an automatic detection method based on learning, which can detect and segment axillary and pelvic lymph nodes at the same time. First, the learning-based method is used to detect the suspected lymph nodes; then, the segmentation model is used to extract the boundary of each suspected lymph node. Finally, some features of the lymph nodes are used to score all the suspected lymph nodes; ultimately, the portion with the highest score is the lymph nodes. Although there has been some work to achieve automatic or semi-automatic detection of lymph nodes, so far few have detected gastric lymph nodes in the treatment of GC. Due to the different structure of different parts of the gastric system, it is difficult to detect gastric lymph nodes, so it is necessary to use AI technology to detect gastric lymph nodes.

### Application of AI in lymph node detection

Lymph nodes are mainly detected by the observation of radiologists. Although this method has high clinical value, it takes a lot of time to detect every lymph node, so it is difficult to detect every lymph node in clinical application. In addition, radiologists need continuous training to detect lymph nodes accurately. In order to improve the efficiency of imaging doctors, it is a potential direction to detect lymph nodes with the

help of computer.

In the treatment of GC, it is necessary to resect the metastasis and the lesion at the same time. The abdominal lymph node is one of the main metastasis routes of GC. It is very important for the prognosis of patients to accurately determine the resection area.

AI can learn to distinguish lymph nodes better and greatly reduce the work burden of imaging doctors. There are few reports about the use of AI technology to locate lymph nodes in GC. However, lung cancer, breast cancer, prostate cancer<sup>[24-28]</sup> and other reports are more common.

### **Application of AI in detection of lymph node metastasis**

The medical decision-making method mainly depends on the clinical practice experience of doctors, their own medical knowledge, and various kinds of doctors. The therapeutic instrument diagnoses the patient's examination results. On the one hand, this traditional decision-making method depends on the professional level and subjective factors of doctors, which will lead to misdiagnosis, missed diagnosis, and other wrong decisions. On the other hand, modern diseases usually have the characteristics of multi-attribute, instability, complexity and time-varying, which require the information in medical diagnosis to have the characteristics of timeliness, accuracy, acceptability and traceability. With the development of computer technology and the production of a large amount of medical data, it is imperative to use computers to realize auxiliary decision-making, which has a positive role in improving the accuracy of medical diagnosis, reducing missed diagnosis and improving work efficiency.

The most common path of GC metastasis is lymph node metastasis, which is due to the abundance of lymphatic vessels and lymph nodes around the stomach<sup>[29]</sup>. In most studies, lymph node metastasis has been judged by size alone<sup>[30,31]</sup>. However, large lymph nodes may be caused by inflammation, and small lymph nodes may also have metastases. In addition, some studies have shown that lymph node metastasis is related to multiple characteristics<sup>[32-34]</sup>. However, it is difficult for doctors to make final diagnosis with multiple features at the same time, so it is necessary to introduce a clinical decision support system<sup>[35]</sup>.

According to National Comprehensive Cancer Network (commonly known as NCCN) guidelines<sup>[36]</sup>, preoperative evaluation of metastatic lymph nodes is considered to be an indication of neoadjuvant chemotherapy. In our opinion, surgery is still the most effective way to treat GC. Radical resection of metastatic lymph nodes is recommended by NCCN guidelines and Japanese GC guidelines as the key to the success of radical gastrectomy<sup>[36,37]</sup>. In this regard, accurate standard dissection and dissection of metastatic lymph nodes can greatly improve the 5-year survival rate of patients<sup>[38]</sup>. Until now, enhanced computer tomography (CT) has been used to judge gastric lymph node metastasis and tumor stage, which is the most reliable and commonly used method for evaluating lymph nodes in GC<sup>[39]</sup>. However, for the CT diagnosis of GC lymph nodes, the false negative and false positive of perigastric metastatic lymph nodes are inevitable technical problems<sup>[40]</sup>. Gao *et al*<sup>[41]</sup> found that, through in-depth study, faster region-based CNNs have higher judgment efficiency and recognition accuracy for CT diagnosis of perigastric metastatic lymph nodes.

### **Perspectives**

The number of gastric lymph node dissections has been shown to be an independent predictor of the prognosis of GC by most studies. Many guidelines and studies have recognized that the minimum standard is to clear more than 15 lymph nodes during operation<sup>[42-44]</sup>. An AI system is helpful to reduce the imbalance of image source distribution, to the diagnosis and treatment of GC, and to determining the location of lymph nodes and lymph node metastasis.

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## **AI AND ROBOTIC SURGERY**

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During the operation of the robotic surgery system, the doctor controls the bedside robotic arm system through the console. There are a total of three robotic arms through which the surgery is completed; the imaging system follows the robotic arm to enter the body for imaging, providing a field of vision for the doctor's surgery. Compared with traditional surgical operations, the surgical trauma performed by surgical robots is less invasive and basically minimally invasive. In recent years, with the rise of rapid rehabilitation surgery and the popularization and application of the Leonardo da Vinci robotic surgery operating system in China, many medical institutions have carried out



robotic surgery. For example, minimally invasive robotic surgery is used increasingly in interventional therapy of urinary tumors<sup>[45,46]</sup>. In the field of gastrointestinal surgery, robotic radical gastrectomy has also become one of the minimally invasive radical methods commonly used in central hospitals specializing in GC<sup>[47]</sup>. The implementation of robotic surgery emphasizes the concept of "precise surgery"<sup>[48]</sup>. Robotic surgery uses a technologically advanced platform, with the chief knife doctor sitting at the console and operating in the operating room or by remotely controlling the robot. With the increasing complexity of mechanical surgery technology, the accuracy and proficiency of robotic surgery will be increased only by developing advanced training modes<sup>[49,50]</sup>.

### **AI in Da Vinci robotic GC surgery**

Traditional laparotomy, laparoscopic surgery and robotic surgery are considered as three surgical treatments for GC. Laparoscopic surgery was first performed in 1991<sup>[51]</sup> because it caused less trauma to patients than traditional surgery, gradually replacing the former. Robotic surgery has the advantages of using wristed instruments, tremor filtering, and high-resolution 3D images over laparoscopic surgery<sup>[52]</sup>, which were also reported in another article first<sup>[53]</sup>.

Robot-assisted applications in minimally invasive surgery were first described in 1985, and this technology has evolved to its current state in the form of a Da Vinci surgical system (Intuitive Surgery, Sunnyvale, CA, United States)<sup>[54]</sup>. Studies have shown that prediction by deep learning systems combined with diagnosis by human pathologists has reduced the error rate by about 85%. It was demonstrated that medical professionals and machine deep learning significantly improved decision-making<sup>[55]</sup>.

Machine learning (ML) is widely used in many fields, such as communication and engineering manufacturing, but rarely be used in medicine, especially in surgery<sup>[56]</sup>. The efficiency of doctors can be improved by ML. With the continuous development of medicine, efficiency is also increasingly valued by the public<sup>[57]</sup>. Before the birth of the laparoscopic technique, the surgeon's operation often brought great trauma to the patient, and it is a long process for a young doctor to accumulate experience and learn through laparotomy. Especially in some operations with high accuracy requirements, although the surgeons have undergone long professional training and repeated operations, there is also a risk of errors and the efficiency of doctors' diagnosis and treatment is a little low. However, after the birth of endoscopic technology, traditional laparotomy was gradually replaced because of its high trauma, and after learning the endoscopic surgical technology, the surgeon's clinical treatment efficiency has been greatly improved. The robotic surgery technology born after the endoscopic technology is even more so. Robotic surgery technology can greatly enhance the surgical efficiency of doctors who are lacking surgical experience and further reduce the trauma suffered by patients.

In addition to the above points, the robot can also be combined with AI in the following aspects. First of all, the level of operator can be distinguished by AI combined with robot. Fard *et al*<sup>[57]</sup> extracted eight global motion features for surgeons at novice and expert levels. The ability of AI to automatically classify experts and novice surgeons has been proved by research. Dai *et al*<sup>[58]</sup> developed and validated an integrated system to alert operators before suture breaks. The results show that this system can improve the results related to knotting tasks in robotic surgery and can reduce suture failure without reducing the quality of the resulting knots. Iranian scholars<sup>[59]</sup> used the Cox proportional hazard model and artificial neural network model to predict the survival rate of Iranian GC patients, and found that the prediction accuracy of the neural network was 83.1%, and that of the Cox regression model was 75.0%. Compared with the Cox proportional hazard regression model, the neural network model was deemed a more powerful statistical tool to predict the survival rate of GC patients.

### **Perspectives**

Robotic surgery provides a good platform for the application of AI in surgical systems (gastrointestinal surgery). It is possible for a large number of clinical data to be evaluated and interpreted by ML methods. The rapid acquisition of surgical technology by junior doctors, the efficiency of a surgeons' operation, and the small trauma to patients are the results of the combination of ML method and robotic operation for the prognosis judgment and prediction of GC patients. However, there is a big flaw in this, which is the standardization of data.

AI affects and narrows the training growth cycle of robotic GC surgeons, reduces patient injury, changes the surgical results, and may even make GC surgery a robotic

automated surgery in the future. To be honest, it is still difficult to do this, but we firmly believe that when surgeons, GC patients, robotic engineers and AI programmers cooperate in multiple disciplines, advanced robotic AI surgery for GC will be realized.

## CONCLUSION

The problem of population aging has been increasing in East Asian countries in recent years, especially in China, where the incidence of cancer has increased year by year. As a new and comprehensive subject, AI will become an important means to promote the development of the medical industry. The application of AI in GC is mainly focused on digestive endoscopy, lymph node image positioning diagnosis, and working in combination with a robotic surgery system. In terms of gastrointestinal endoscopy, AI can detect EGC earlier and faster, with higher accuracy than clinical endoscopists. For advanced GC, AI can increase the detection rate of cancers in areas where gastroscopy is performed, such as pump-door cancer, which reduces the missed diagnosis rate. In the face of GC lymph nodes, the intervention of AI not only reduces the burden of radiologists, but also increases the accuracy of lymph node localization. Just as for the location of lymph nodes, it is also of great significance for detection of lymph node metastasis with higher accuracy. It also has important potential for robotic surgery of GC. AI has further revolutionized GC surgery by training young doctors to perform robotic GC surgery, improving surgical trauma of patients and predicting patient prognosis in timely and accurate manners - precision surgery was gradually promoted by AI to improve the relevant outcomes of GC disease and surgery without affecting patient survival and safety.

In addition to gastroscopic detection of GC or precise localization of lymph nodes, as well as use of Da Vinci robotic surgery to improve the patient's intraoperative experience and prognosis, the aim is to minimize trauma suffered by patients. The development of technology is constantly being updated, and the invention of laparotomy has saved the lives of many patients with GC but also brought great trauma to these patients. After the advent of endoscopic techniques, the concept of minimally invasive surgery began to gain popularity, and laparoscopic surgery gradually replaced open surgery because of its smaller damage. However, in the development of technology and times, the limitations of its operation are also increasingly exposed.

With the arrival of the big data era, AI technology has gradually matured, and its combination with robotic surgical systems has become a research hotspot. Robotic surgery, boasting accuracy that laparoscopic surgery does not have, is an emerging surgical system for the future. Through the deep integration of this system with AI, the trauma of the patient's operation is further reduced. In the future, there may even be a fully automated robotic surgical system controlled by AI, in which case the trauma of GC surgery will be very small and can be considered noninvasive. In other words, the change that AI will bring to GC is that the surgical treatment of GC will change from greater trauma to minimally invasive, and from minimally invasive to nearly noninvasive.

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## Artificial intelligence in gastrointestinal cancer: Recent advances and future perspectives

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**Author contributions:** Kudou M performed the research, analyzed the data, and wrote the manuscript; Kosuga T made contributions to conception and supervision of the study; Otsuji E critically revised the article; and all authors have read and approved the final manuscript.

**Conflict-of-interest statement:** The authors declare no conflicts of interests for this article.

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**Manuscript source:** Invited manuscript

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### Abstract

Artificial intelligence (AI) using machine or deep learning algorithms is attracting increasing attention because of its more accurate image recognition ability and prediction performance than human-aid analyses. The application of AI models to gastrointestinal (GI) clinical oncology has been investigated for the past decade. AI has the capacity to automatically detect and diagnose GI tumors with similar diagnostic accuracy to expert clinicians. AI may also predict malignant potential, such as tumor histology, metastasis, patient survival, resistance to cancer treatments and the molecular biology of tumors, through image analyses of radiological or pathological imaging data using complex deep learning models beyond human cognition. The introduction of AI-assisted diagnostic systems into clinical settings is expected in the near future. However, limitations associated with the evaluation of GI tumors by AI models have yet to be resolved. Recent studies on AI-assisted diagnostic models of gastric and colorectal cancers in the endoscopic, pathological, and radiological fields were herein reviewed. The limitations and future perspectives for the application of AI systems in clinical settings have also been discussed. With the establishment of a multidisciplinary team containing AI experts in each medical institution and prospective studies, AI-assisted medical systems will become a promising tool for GI cancer.

**Key Words:** Artificial intelligence; Gastric cancer; Colorectal cancer; Endoscopy; Pathology; Radiology

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**Specialty type:** Gastroenterology and Hepatology

**Country/Territory of origin:** Japan

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**Received:** September 19, 2020

**Peer-review started:** September 19, 2020

**First decision:** October 17, 2020

**Revised:** October 28, 2020

**Accepted:** November 13, 2020

**Article in press:** November 13, 2020

**Published online:** November 28, 2020

**P-Reviewer:** Cabezuelo AS, Gao F

**S-Editor:** Wang JL

**L-Editor:** A

**P-Editor:** Ma YJ



**Core Tip:** Artificial intelligence (AI) is attracting increasing attention because of its more accurate image recognition ability and prediction performance than human-aid analyses. The application of AI models to gastrointestinal clinical oncology has been investigated, and the findings obtained indicate its capacity for automatic diagnoses with similar accuracy to expert clinicians and the prediction of malignant potential. However, limitations in the evaluation of gastrointestinal tumors by current AI models have yet to be resolved. The limitations of and future perspectives for the application of AI-assisted systems to clinical settings have been discussed herein.

**Citation:** Kudou M, Kosuga T, Otsuji E. Artificial intelligence in gastrointestinal cancer: Recent advances and future perspectives. *Artif Intell Gastroenterol* 2020; 1(4): 71-85

**URL:** <https://www.wjgnet.com/2644-3236/full/v1/i4/71.htm>

**DOI:** <https://dx.doi.org/10.35712/aig.v1.i4.71>

## INTRODUCTION

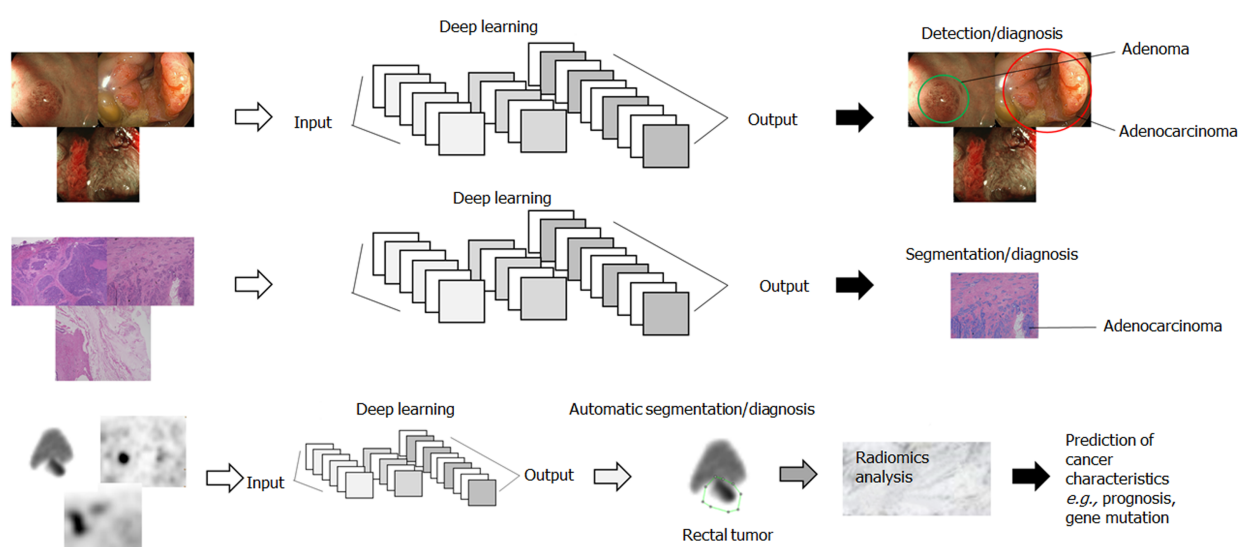
Recent advances in diagnostic technology and treatment strategies for gastrointestinal cancer have improved clinical outcomes. Even with the development of novel imaging modalities with high accuracy and resolution, image reading, and novel biomarkers, such as the genetic screening of tumors, circulating tumor DNA, and micro RNA, the diversity and quantity of data on tumor malignant potential is beyond the limits of human interpretation<sup>[1-8]</sup>. Therefore, the establishment of more accurate diagnostic methods with high objectivity using computer-aided diagnosis systems (CAD), such as technologies involving artificial intelligence (AI), is needed in clinical settings<sup>[9-11]</sup>.

AI is defined by the intelligence of machines in contrast to the natural intelligence of humans. It is generally applied when a machine mimics the cognitive functions of humans, such as learning and problem solving<sup>[12]</sup>. The concept of AI was initially advocated in 1956 by McCarthy *et al.*<sup>[13]</sup>, and the development of machines with the ability to think like humans with intelligence was anticipated. However, machines or computer programs that function as classifiers or detectors, such as image classification and recognition and the prediction of characteristics in populations, are currently regarded as AI.

Recent AI technologies were developed due to technical advances in machine learning and deep neural network algorithms<sup>[14-17]</sup>. Convolutional neural networks (CNN) are one of the deep neural networks that are useful for image analyses. Algorithms using CNN models have been applied to many research fields in gastrointestinal cancer, such as the automatic endoscopic detection of tumors, the automatic diagnosis of cancer in pathological specimens, and image analyses of radiological modalities<sup>[10,18]</sup>. In endoscopic research, CNN are trained using thousands of endoscopic images to detect tumors, differentiate between benign and malignant tumors, and predict tumor invasion depth<sup>[9,19-22]</sup>. In recent years, a real-time CAD endoscopic system was developed using trained CNN. In the area of pathology, deep learning has been performed using non-cancerous and cancer images to automatically identify and segment the cytoplasm, nucleus, and stromal cells. CNN and machine learning models with image analyses, such as a texture analysis, were subsequently built to identify cancerous regions or diagnose cancer<sup>[23]</sup>. In the field of radiology, a CAD system of image modalities, such as X-ray, computed tomography (CT), and magnetic resonance images (MRI), was developed using a deep learning model constructed using cancer and non-cancer images to recognize anatomy and detect and segment tumors<sup>[24]</sup>. The malignant potential of tumors has been analyzed using a radiomics approach, which aims to quantitatively assess tumor heterogeneity by an analysis of medical images through the deep or machine learning of histograms, textures, and shapes<sup>[25-27]</sup>. AI models of gastrointestinal cancer are summarized in Figure 1.

AI with strong analytical power has attracted the attention of many researchers; therefore, the number of studies on diagnostic AI systems in gastrointestinal cancer has rapidly increased in the past decade. We herein investigate recent advances and future perspectives through a review of the literature.

In this minireview, the bibliographic search was performed using the database MEDLINE (through PubMed) for identifying studies published on AI technology in



**Figure 1 Clinical research using artificial intelligence in gastrointestinal cancer.** Deep learning based on convolutional neural networks showing the input layer with raw data of the image, such as endoscopic, pathological, and radiological images, the hidden layer with a series of convolutions computed for each layer and the classification of the image, the prediction of malignant potentials, and the segmentation of tumor in the output layer.

the endoscopy, pathology, and radiology of gastric and colorectal cancer between 2016 and 2020. We summarized the application of AI in each area according to the extracted 49 Literatures; subsequently, the consideration about current issues and future perspectives of AI in gastrointestinal cancer was stated with some literature review.

## APPLICATION OF AI TO ENDOSCOPY IN GASTROINTESTINAL CANCER

Previous studies on the endoscopic diagnosis of gastric cancer (GC) and colorectal cancer (CRC) using AI between 2016 and 2020 were summarized in Tables 1 and 2.

### Gastric cancer

The purposes of the studies reviewed on AI for GC were (1) tumor detection; (2) the diagnosis of malignancy; (3) real-time detection; and (4) the prediction of tumor invasion depth. The basic method of these studies was as follows: Endoscopic images of GC, gastritis, and non-cancerous mucosae, which were diagnosed pathologically or by an expert endoscopist, were captured and CNN was subsequently trained using these images. Diagnostic and detection accuracy were then assessed using the constructed CNN models.

Yoon *et al*<sup>[28]</sup> attempted to develop CNN models with the ability to detect early GC and predict invasion depth. The areas under the curves of receiver operating characteristic curves (AUC) for early GC detection and depth prediction were 0.981 and 0.851, respectively. Moreover, the diagnostic accuracy of invasion depth was lower for undifferentiated GC than for differentiated GC<sup>[28]</sup>. Zhu *et al*<sup>[29]</sup> also trained a CNN model to predict the invasion depth of GC. The AUC, positive predictive value (PPV), and negative predictive value (NPV) of their model were 0.94, 89.6%, and 88.9%, respectively. The CNN-CAD system achieved significantly higher accuracy and specificity than a human endoscopist. Li *et al*<sup>[30]</sup> also developed CNN models for the detection of GC with high diagnostic accuracy (sensitivity: 91.1%, specificity: 90.6%, and PPV: 90.9%). Hirasawa *et al*<sup>[31]</sup> reported that CNN models exhibited difficulties distinguishing between differentiated-type intramucosal cancers with a diameter of 6 mm or less and gastritis. Ishioka *et al*<sup>[32]</sup> examined the detection accuracy of a real-time endoscopic diagnosis of GC using CNN models that they had constructed; the detection rate of GC using these models was 94.1%. CNN identified the region of GC that had been difficult to distinguish from background gastritis, even by experienced endoscopists. Luo *et al*<sup>[33]</sup> developed a gastrointestinal AI diagnostic system (GRAIDs) and compared its diagnostic accuracy with that of expert and trainee endoscopists. PPV was 0.814 for GRAIDs, 0.932 for the expert endoscopist, and 0.824 for the trainee endoscopist, while NPV was 0.978 for GRAIDs, 0.980 for the expert endoscopist, and

**Table 1 Previous studies on upper endoscopy of gastric cancer using artificial intelligence**

Ref.	Targets	Sample sizes	Inputs	Tasks	Analysis method	Diagnostic performance
Yoon <i>et al</i> <sup>[28]</sup>	GC (ESD/surgery)	800 cases	GC/non-GC images in close-up and distant views	Detection and invasion depth prediction	CNN	AUC: detection, 0.981; depth, 0.851
Zhu <i>et al</i> <sup>[29]</sup>	GC	993 images	GC images	Diagnosis of invasion depth	CNN	Sensitivity: 76.4%, PPV: 89.6%
Li <i>et al</i> <sup>[30]</sup>	GC and healthy	386 GC and 1702 NC images	NBI images	Diagnosis of GC	CNN	Sensitivity: 91.1%, PPV: 90.6%
Hirasawa <i>et al</i> <sup>[31]</sup>	GC	13584 training and 2296 test images	GC images	Diagnosis of GC	CNN	Sensitivity: 92.2%, PPV: 30.6%
Ishioka <i>et al</i> <sup>[32]</sup>	EGC	62 cases	Real-time images	Detection	CNN	Detection rate: 94.1%
Luo <i>et al</i> <sup>[33]</sup>	GC	1036496 images	GC images	Detection	CNN	PPV: 0.814, NPV:0.978
Horiuchi <i>et al</i> <sup>[34]</sup>	GC and gastritis	1492 GC and 1078 gastritis images	NBI images	Detection	CNN	Sensitivity: 95.4%, PPV: 82.3%

GC: Gastric cancer; CNN: Convolutional neural network; AUC: Area under the curve; PPV: Positive predictive value; NC: Non-cancer; NBI: Narrow-band image; EGC: Early gastric cancer.

**Table 2 Previous studies on colonoscopy using artificial intelligence**

Ref.	Targets	Sample sizes	Inputs	Tasks	Analysis method	Diagnostic performance
Akbari <i>et al</i> <sup>[35]</sup>	Screening endoscopy	300 polyp images	Polyp images	Auto segmentation of polyps	CNN	Accuracy: 0.977, Sensitivity: 74.8%
Jin <i>et al</i> <sup>[36]</sup>	Screening endoscopy	Training: 2150 polyps, test: 300 polyps	NBI images	Differentiation of adenoma and hyperplastic polyps	CNN	The model reduced the time of endoscopy and increased accuracy by novice endoscopists
Urban <i>et al</i> <sup>[37]</sup>	Screening endoscopy	8641 polyp images and 20 colonoscopy videos	Polyp images	Detection of polyps	CNN	AUC: 0.991, Accuracy: 96.4%
Yamada <i>et al</i> <sup>[38]</sup>	Screening endoscopy	4840 images, 77 colonoscopy videos	Real-time images	Differentiation of the early signs of CRC	CNN	Sensitivity: 97.3%, Specificity: 99.0%

CNN: Convolutional neural network; NBI: Narrow-band image; AUC: Area under the curve.

0.904 for the trainee endoscopist. These findings demonstrated that the diagnostic accuracy of GRAIDs for the detection of GC was similar to that of the expert endoscopist and superior to that of the trainee endoscopist. CNN models of narrow-band imaging (NBI) for GC have been reported, with sensitivity and PPV of 91.1-95.4% and 82.3-90.6%, respectively<sup>[34]</sup>.

### Colorectal cancer

The purposes of the studies reviewed on AI for CRC were (1) the segmentation and detection of polyps; and (2) the diagnosis of polyp pathology. In the development of efficient automatic diagnostic models, models need to automatically segment polyps and extract their features. Akbari *et al*<sup>[35]</sup> attempted to construct CNN models of colonoscopy for automatic segmentation and feature extraction. The accuracy, specificity, and sensitivity of the model for automatic segmentation were 0.977, 0.993, and 0.758, respectively. An ideal CAD system of colonoscopy needs to have the ability to predict the pathological diagnosis of an automatically detected tumor and subsequently recommend appropriate treatment strategies for lesions. Jin *et al*<sup>[36]</sup> reported a CNN model for predicting the pathological diagnosis of small lesions ( $\leq 5$  mm) using NBI data from colonoscopy. The accuracy, sensitivity, specificity, PPV, and NPV of their model for predicting the pathological diagnosis of polyps, adenoma *vs* hyperplasia were 86.7%, 83.3%, 91.7%, 93.8%, and 78.6%, respectively. On the other hand, the accuracies of polyp diagnoses by novices, experts, and NBI-trained expert endoscopists were 73.8%, 83.8%, and 87.6%, respectively. Using CNN-processed

results, overall accuracy by novice endoscopists significantly increased to 85.6%. A real-time diagnostic system in colonoscopy was developed using CNN models. Urban *et al*<sup>[37]</sup> constructed CNN models to identify polyps, which were subsequently adapted to colonoscopy videos, and these models exhibited the ability to detect either type of polyp equally well and identify polyps with an ROC value of 0.991 and accuracy of 96.4%. Yamada *et al*<sup>[38]</sup> applied their CNN model, which was developed to detect early signs of CRC, to colonoscopic videos. The sensitivity and specificity of their AI system for detecting the regions of CRC were 97.3% and 99.0%, respectively, while the sensitivity and specificity of endoscopists were 87.4% and 96.4%; respectively. Therefore, the AI system may be used to alert endoscopists in real-time to overlooked abnormalities, such as non-polypoid polyps, during colonoscopy, thereby increasing the early detection of this disease.

## APPLICATIONS OF AI TO THE PATHOLOGICAL DIAGNOSIS OF GASTROINTESTINAL CANCER

Previous studies on the pathological diagnosis of GC and CRC using AI between 2016 and 2020 are summarized in Tables 3 and 4. An automatic pathological diagnosis of gastrointestinal cancer generally involves the following processes: (1) Automatic segmentation: Distinguishing various structures, such as the cytoplasm, nuclei, and stoma, and the recognition of atypia; (2) The diagnosis and grading of carcinoma; (3) The diagnosis of malignant potential, such as invasion depth and lymphovascular invasion; and (4) The prediction of survival. Therefore, previous studies aimed to develop a CAD system with the ability to perform these processes.

### Gastric cancer

Qu *et al*<sup>[39]</sup> attempted to develop CNN models for (1) and (2), proposed a novel stepwise fine-tuning-based deep learning scheme for gastric pathology image classification, and established a novel protocol to further boost the performance of state-of-the-art deep neural networks and overcome the insufficiency of well-annotated data. In their proposed two-stage method, CNN was initially trained using tissue-wise data on the background, epithelium, and stoma as well as cell-wise data on nuclei and the cytoplasm, and was then tuned using well-annotated data from benign or malignant data sets. The diagnostic accuracy of their constructed two-stage CNN models was higher than that of one-stage models. Yoshida *et al*<sup>[40]</sup> attempted to develop CNN models for (1) and (2) with the ability to automatically segment malignant regions in full-slide images of biopsy samples and subsequently diagnose histological classifications through a nuclear analysis at high magnification. In negative biopsy specimens, the concordance rate between their AI system and expert pathologists was 90.6%; however, the concordance rate for positive biopsy specimens was less than 50%. Mori *et al*<sup>[41]</sup> trained CNN models for (3) to discriminate the tumor invasion depth of gastric signet-ring cell carcinoma. Their models exhibited the ability to diagnose intramucosal or advanced histological characteristics with an accuracy of 85%, sensitivity of 90%, specificity of 81%, and AUC of 0.91. The prediction of survival in GC patients using the deep learning method has also been examined. Jiang *et al*<sup>[42]</sup> investigated the efficacy of deep learning models for (4) using a support vector machine (SVM). They classified GC patients into two groups using SVM based on patient characteristics and immunohistochemistry (IHC) data on the following immunomarkers: CD3, CD8, CD45RO, CD45RA, CD57, CD68, CD66b, and CD34. The findings obtained revealed that the classifier of SVM was a stronger prognostic factor than the TNM stage or CA19-9.

### Colorectal cancer

Numerous studies on the pathology of CRC using AI were reported compared to GC, are classified as follows.

**Studies on AI models for automatic segmentation:** Van Eycke *et al*<sup>[43]</sup> and Graham *et al*<sup>[44]</sup> developed CNN models to segment the glandular epithelium. The F1 values of these models ranged between 0.9 and 0.912. Abdelsamea *et al*<sup>[45]</sup> developed tumor parcellation and quantification (TuPaQ), which is a tool for refining biomarker analyses through the rapid and automated segmentation of the tumor epithelium. Tissue microarray (TMA) cores from CRC were manually annotated and analyzed to provide the ground truth, epithelial or non-epithelial tissue. CNN (TuPaQ) was trained using these data. The accuracy, sensitivity, and specificity of TuPaQ were



**Table 3 Previous studies on the pathology of gastric cancer using artificial intelligence**

Ref.	Targets	Sample size	Input	Task	Analysis method	Diagnostic performance
Qu <i>et al</i> <sup>[39]</sup>	GC	15000 images	Pathological images	Evaluation of stepwise methods	CNN	AUC: 0.828-0.920
Yoshida <i>et al</i> <sup>[40]</sup>	GC	3062 biopsy samples	Pathological images stained by H&E	Automatic segmentation, diagnosis of carcinoma	CNN	Sensitivity: 89.5%, specificity: 50.7%
Mori <i>et al</i> <sup>[41]</sup>	GC (surgery)	516 images from 10 GC cases	Pathological images stained by H&E	Diagnosis of invasion depth in signet cell carcinoma	CNN	Sensitivity: 90%, Specificity: 81%
Jiang <i>et al</i> <sup>[42]</sup>	GC (surgery)	786 cases	IHC (CD3, CD8, CD45RO, CD45RA, CD57, CD68, CD66b, and CD34)	Prediction of survival	SVM	The immunomarker SVM was useful for predicting survival

GC: Gastric cancer; AUC: Area under the curve; H&E: Hematoxylin eosin staining; CNN: Convolutional neural network; IHC: Immunohistochemistry; SVM: Support vector machine.

0.939, 0.779, and 0.946, respectively. Yan *et al*<sup>[46]</sup> examined the diagnostic accuracy of their AI models for the classification, segmentation, and visualization of large-scale tissue histopathology images. The accuracies of their models ranged between 81.3 and 93.2%. Haj-Hassan *et al*<sup>[47]</sup> attempted to develop CNN models for the automatic segmentation of benign hyperplasia, intra-epithelial neoplasms, and carcinoma, and the findings obtained showed that the models segmented tumors with a high accuracy of 99.1%.

**Diagnosis and grading of carcinoma:** Rathore *et al*<sup>[48]</sup> reported deep learning models for cancer detection and grading. The features of CRC biopsy samples were extracted based on pink-colored connecting tissues, purple-colored nuclei, and white-colored epithelial cells and lumina. The extracted features, particularly white-colored epithelial cells and lumina, were classified using SVM and classification performance was subsequently assessed. The accuracies of cancer detection and grading by their model were 95.4 and 93.4%, respectively. Yang *et al*<sup>[49]</sup> proposed a combination of SVM and color histograms to classify pathological images. The AUC of the model for diagnosing carcinoma was 0.891. Chaddad *et al*<sup>[50]</sup> reported that the classification of images using a texture analysis effectively diagnosed carcinoma (accuracy: 98.9%). Yoshida *et al*<sup>[51]</sup> showed that a CAD system using a previously described CNN model for GC was useful for diagnosing adenoma and carcinoma (undetected rate of carcinoma and adenoma: 0-9.3% and 0-9.9%, respectively).

**Diagnosis of malignant potential:** Takamatsu *et al*<sup>[52]</sup> reported the prediction of lymph node metastasis using a machine learning analysis of morphological parameters (such as shape and roundness) in cytokeratin-stained T1 CRC images. The AUC of the model was 0.94. The automatic evaluation of tumor budding in IHC with CNN and machine learning was previously performed<sup>[53]</sup>. Models were constructed to assess tumor budding using TMA on pan-cytokeratin-stained tumors, and the  $R^2$  value of the correlation of the models with manual counting for the diagnosis of tumor budding was 0.86.

**Prediction of survival:** Bychkov *et al*<sup>[54]</sup> proposed AI models for the automatic prediction of survival in CRC patients using the TMA of CRC pathological images. The automatic detection of tumors was initially achieved using CNN; CNN cases were subsequently classified by a recurrent neural network. Predicted survival by their model correlated with actual clinical outcomes. Kather *et al*<sup>[55]</sup> reported automatic models for discriminating structures in tissue samples and then predicting survival. Their models predicted the survival of CRC more accurately than the TNM stage or manual evaluations of cancer-associated fibroblasts. Moreover, survival prediction SVM models using immunomarkers evaluated by IHC, such as CD3 and CD8, have been developed<sup>[56]</sup>, and the classifier correlated with patient survival.

**Table 4** Previous studies on the pathology of colorectal cancer using artificial intelligence

Ref.	Targets	Sample size	Input	Task	Analysis method	Diagnostic performance
Van Eycke <i>et al</i> <sup>[43]</sup>	CRC		H&E staining, IHC image	Segmentation of the glandular epithelium	TMA, CNN	F1 value: 0.912
Graham <i>et al</i> <sup>[44]</sup>	CRC		H&E staining	Differentiation of intratumor glands	CNN	F1 values: 0.90
Abdelsamea <i>et al</i> <sup>[45]</sup>	CRC	333 samples	H&E staining, IHC (CD3)	Differentiation of the tumor epithelium	TMA, CNN	Accuracy: 0.93-0.94
Yan <i>et al</i> <sup>[46]</sup>	CRC		H&E staining	Tumor classification, segmentation of tumors,	CNN	Accuracy: Classification, 97.8%; segmentation, 84%
Haj-Hassan <i>et al</i> <sup>[47]</sup>	CRC		Multispectral images	Segmentation of carcinoma	CNN	Accuracy: 99.1%
Rathore <i>et al</i> <sup>[48]</sup>	CRC	Biopsy samples	H&E staining	Detection and grading of tumors	Texture and morphology patterns, SVM	Recognition rate: Detection, 95.4%; grading, 93.4%
Yang <i>et al</i> <sup>[49]</sup>	CRC	180 samples	H&E staining	Diagnosis of benign tumors, neoplasms, and carcinoma	SVM, histogram, texture	AUC: 0.852
Chaddad <i>et al</i> <sup>[50]</sup>	CRC	30 cases	H&E staining	Diagnosis of carcinoma, adenoma, and benign tumors	Automatic segmentation, texture	Accuracy: 98.9%
Yoshida <i>et al</i> <sup>[51]</sup>	CRC	1328 samples	H&E staining	Diagnosis of benign tumors, neoplasms, and carcinoma	CNN, automatic analysis of structure	Undetected rate of carcinoma and adenoma: 0-9.3% and 0-9.9%, respectively
Takamatsu <i>et al</i> <sup>[52]</sup>	CRC surgery	397 samples	H&E staining	Prediction of lymph node metastasis	LR, shape analysis	AUC: 0.94
Weis <i>et al</i> <sup>[53]</sup>	CRC	596 cases	IHC (AE1/AE3)	Automatic evaluation of tumor budding	TMA, CNN	Correlation; R2 value: 0.86
Bychkov <i>et al</i> <sup>[54]</sup>	CRC surgery	420 cases	H&E staining	Prediction of survival	TMA, CNN	Good biomarker for predicting survival
Kather <i>et al</i> <sup>[55]</sup>	CRC	973 slides	H&E staining	Prediction of survival	Stromal pattern, CNN	Good biomarker for predicting survival
Reichling <i>et al</i> <sup>[56]</sup>	CRC surgery	1018 cases	HE, IHC (CD3, CD8)	Prediction of survival	RF, monogram	Good biomarker for predicting survival

CRC: Colorectal cancer; H&E: Hematoxylin eosin staining; IHC: Immunohistochemistry; TMA: Tissue microarray; CNN: Convolutional neural network; SVM: Support vector machine; AUC: Area under the curve; LR: Linear regression.

## APPLICATIONS OF AI TO A RADIOLOGICAL DIAGNOSIS OF GASTROINTESTINAL CANCER

Previous studies on the radiological diagnosis of GC and CRC using AI between 2016 and 2020 were summarized in Tables 5 and 6.

### Gastric cancer

Regarding GC, many researchers have attempted to develop AI models using (1) a radiomics approach; or (2) CNN models predicted malignant potential, such as survival, lymph node metastasis, and post-operative recurrence, through analyses of the radiological image features of GC.

**Radiomics approach:** Li *et al*<sup>[57]</sup> developed a survival prediction model involving a general radiomics analysis of CT. The region of interest was manually drawn along the margin of the tumor on CT images, and radiological features were extracted. After manual image segmentation, the heterogeneity of the extracted feature was quantified using an image analysis, such as texture and histogram analyses. Analyzed cases were then classified based on the risk score (R-signature) evaluated using the least absolute shrinkage and selection operator method. The performance of a radiomics nomogram, including factors correlating with survival, was then evaluated. The findings obtained showed that the R-signature correlated with the survival of GC patients. Furthermore, the prediction of survival by the radiomics monogram including the R-signature was

**Table 5 Previous studies on the radiological diagnosis of gastric cancer using radiomics or artificial intelligence**

Ref.	Targets	Sample size	Input	Task	Analysis method	Diagnostic performance
Li <i>et al</i> <sup>[57]</sup>	GC, radical surgery	181 cases	Primary tumor, preoperative CT	Prediction of survival	Manual segmentation, radiomics, Nomograms	The TNM stage and radiomics signature were good biomarkers
Zhang <i>et al</i> <sup>[58]</sup>	GC, radical surgery	669 cases	Primary tumor, preoperative CT	Predication of early recurrence	Manual segmentation, radiomics, Nomograms	AUC: 0.806-0.831
Li <i>et al</i> <sup>[59]</sup>	GC, radical surgery	204 cases	Primary tumor, pre-operative dual-energy CT	Pre-operative diagnosis of LNM	Manual segmentation, radiomics, Nomogram	AUC; 0.82--0.84
Li <i>et al</i> <sup>[60]</sup>	GC, radical surgery	554 cases	Primary tumor, preoperative CT	Prediction of a pathological status, survival	Semi-automatic segmentation, radiomics	AUC for prediction of the pathological status: 0.77, the TNM stage and radiomics signature were good biomarkers
Wang <i>et al</i> <sup>[61]</sup>	GC, radical surgery	187 cases	Primary tumor, preoperative dynamic CT	Pre-operative prediction of intestinal-type GC	Manual segmentation, radiomics, Nomograms	AUC: 0.904
Jiang <i>et al</i> <sup>[62]</sup>	GC, surgery	214 cases	Primary tumor, preoperative PET-CT	Prediction of survival	Manual segmentation, radiomics, Nomograms	C-index: DFS, 0.800; OS, 0.786
Chen <i>et al</i> <sup>[63]</sup>	GC, surgery	146 cases	Primary tumor, preoperative MRI	Pre-operative diagnosis of lymph node metastasis	Manual segmentation, radiomics analysis	AUC: 0.878
Gao <i>et al</i> <sup>[64]</sup>	GC, surgery	627 cases, 17340 images	Lymph nodes, preoperative CT	Pre-operative diagnosis of lymph node metastasis	Manual segmentation, deep learning	AUC: 0.9541.
Huang <i>et al</i> <sup>[65]</sup>	GC, surgery		Primary tumor, preoperative CT	Pre-operative diagnosis of peritoneal metastasis	Manual segmentation, CNN	Ongoing, retrospective cross-sectional study

GC: Gastric cancer; CT: Computed tomography; AUC: Area under the curve; LNM: Lymph node metastasis; DFS: Disease-free survival; MRI: Magnetic resonance imaging; CNN: Convolutional neural network.

more accurate than that by normal nomograms (T and N stages and differentiation). Previous studies investigated the prediction of malignant potential using a radiomics approach. Zhang *et al*<sup>[58]</sup> evaluated the diagnostic accuracy of CT radiomics models for predicting post-operative recurrence in GC patients, and the AUC of the models were 0.806-0.831. Li *et al*<sup>[59]</sup> reported CT radiomics models for predicting lymph node metastasis, with an AUC of 0.82-0.84. Li *et al*<sup>[60]</sup> also developed CT radiomic models with the ability to predict the pathological status and survival with high accuracy. Wang *et al*<sup>[61]</sup> analyzed primary tumors on CT images of the arterial phase, portal phase, and delay phase for the discrimination of intestinal-type GC by a radiomics approach. The AUC of their model was 0.904. Jiang *et al*<sup>[62]</sup> described a radiomics model of PET-CT for predicting survival. The C-indexes of this model for overall survival and disease-free survival were 0.786 and 0.800, respectively. A radiomics analysis of MRI for GC has also been conducted. Chen *et al*<sup>[63]</sup> examined the heterogeneity of primary tumors on MRI using a radiomics approach, and showed that the model was useful for predicting the N stage.

**CNN model:** Gao *et al*<sup>[64]</sup> developed a CNN model of CT for predicting lymph node metastasis. Radiologists initially labeled upper abdominal-enhanced CT images of metastatic lymph nodes. CNN models were then constructed using the labeled image data, and the AUC of the model was 0.954. Huang *et al*<sup>[65]</sup> described a protocol for predicting peritoneal metastasis using CNN models, and this research is ongoing.

### Colorectal cancer

Treatment strategies for lower rectal cancer (LRC) have recently been attracting increasing attention because of the difficulties associated with achieving curative treatment. Therefore, many researchers have targeted LRC patients for the development of AI models for radiological diagnoses. The aims of a recent AI study on CRC were (1) the automatic detection or segmentation of primary tumors; (2) the

**Table 6 Previous studies on the radiological diagnosis of colorectal cancer using radiomics or artificial intelligence**

Ref.	Targets	Sample size	Input	Task	Analysis method	Diagnostic performance
Trebeschi <i>et al</i> <sup>[66]</sup>	LRC	140 cases	Primary tumor, MRI	Automatic detection, segmentation	CNN	DSC: 0.68-0.70, AUC: 0.99
Wang <i>et al</i> <sup>[67]</sup>	LRC	568 cases	Primary tumor, MRI	Automatic segmentation	CNN	DSC: 0.82
Wang <i>et al</i> <sup>[68]</sup>	LRC	93 cases	Primary tumor, MRI	Automatic segmentation	Deep learning	DSC: 0.74
Men <i>et al</i> <sup>[69]</sup>	LRC	278 cases	Primary tumor, CT	Automatic segmentation	CNN	DSC: 0.87
Shayesteh <i>et al</i> <sup>[70]</sup>	LRC, NCRT followed by surgery	98 cases	Primary tumor, pre-treatment MRI	Prediction of CRT responses	Manual segmentation, radiomics, machine learning	AUC: 0.90
Shi <i>et al</i> <sup>[71]</sup>	LRC, NCRT followed by surgery	45 cases	Primary tumor, pre-treatment MRI, mid-radiation MRI	Prediction of CRT responses	Manual segmentation, CNN	AUC: CR, 0.83; good response, 0.93
Ferrari <i>et al</i> <sup>[72]</sup>	LRC, NCRT followed by surgery	55 cases	Primary tumor, MRI before, during and after CRT	Prediction of CRT responses	Manual segmentation, radiomics, RF	AUC: CR: 0.86, non-response: 0.83
Bibault <i>et al</i> <sup>[73]</sup>	LRC, NCRT followed by surgery	95 cases	Primary tumor, pre-operative CT	Prediction of CRT responses	Manual segmentation, radiomics, CNN	80% accuracy
Dercle <i>et al</i> <sup>[74]</sup>	CRC, FOLFIRI with/without cetuximab	667 cases	Metastatic tumor, CT	Prediction of tumor sensitivity to chemotherapy	Manual segmentation, radiomics, machine learning	AUC: 0.72-0.80
Ding <i>et al</i> <sup>[75]</sup>	LRC, radical surgery	414 cases	Lymph nodes, pre-operative MRI	Pre-operative diagnosis of lymph node metastasis	Manual segmentation, CNN	AI system > radiologist
Taguchi <i>et al</i> <sup>[76]</sup>	CRC	40 cases	Primary tumor, CT	Prediction of the KRAS status	Manual segmentation, radiomics	AUC: 0.82

LRC: Lower rectal cancer; MRI: Magnetic resonance imaging; CNN: Convolutional neural network; DSC: Dice similarity coefficient; AUC: Area under the curve; NCRT: Neoadjuvant chemoradiotherapy; CR: Complete response; RF: Random forest; CT: Computed tomography; CRC: Colorectal cancer.

prediction of treatment responses; and (3) the prediction of malignant potential.

**Automatic detection or segmentation of primary tumors:** Trebeschi *et al*<sup>[66]</sup> reported a CNN model for the automatic segmentation of primary tumors on MRI. CNN models were trained using T2-weighted images (T2WI) and diffusion-weighted images with primary tumor labeling by expert radiologists. The CNN model showed high segmentation accuracy, with a dice similarity coefficient (DSC) of 0.68-0.70. The AUC of the resulting probability maps was 0.99. Two CNN models were also developed for the automatic segmentation of primary tumors on T2WIs, with DSC of 0.82 and 0.74, respectively<sup>[67,68]</sup>. Men *et al*<sup>[69]</sup> attempted to develop CNN models for automatic segmentation on CT images with an application to the delineation of the clinical target volume (CTV) and surrounding organs for radiotherapy. The mean DSC values of the models were 87.7% for the CTV, 93.4% for the bladder, 92.1% for the left femoral head, 92.3% for the right femoral head, 65.3% for the intestines, and 61.8% for the colon.

**Prediction of treatment responses:** Shayesteh *et al*<sup>[70]</sup> reported radiomics models predicting treatment responses to neo-adjuvant chemoradiotherapy. Primary tumors on MRI T2WI were manually segmented and an image analysis of the data, shape, texture as well as a histogram analysis were performed. The relationship between the pathological features and treatment responses to CRT was assessed by a machine learning approach, which revealed that the AUC and accuracy of the model were 95 and 90%, respectively. Shi *et al*<sup>[71]</sup> and Ferrari *et al*<sup>[72]</sup> also described the efficacy of radiomics models for predicting CRT responses using pre-treatment, mid-radiation, post-treatment MRI (AUC for predicting a complete response (CR): 0.83 and 0.86, respectively). Bibault *et al*<sup>[73]</sup> compared the diagnostic accuracy of several models, Cox's regression, CNN, and SVM for predicting CR in pre-operative CRT using CT data. CNN exhibited the ability to predict CR with the highest accuracy (80%). A radiomics model for predicting chemotherapeutic responses has also been reported. Dercle *et al*<sup>[74]</sup> demonstrated that their radiomic model using CT images successfully predicted sensitivity to anti-EGFR therapy (AUC: 0.80).

**Prediction of malignant potential:** Ding *et al*<sup>[75]</sup> developed AI models to predict lymphatic node metastasis using pre-operative MRI. CNN models were constructed using MRI lymph node images manually labeled by radiologists. They compared the diagnostic accuracy of CNN and a radiologist for predicting lymph node metastasis. As a result, CNN was more accurate than radiologists in identifying pelvic metastatic lymph nodes. A model for predicting gene profiles was also reported. These research methods are generally called radiogenomics. Taguchi *et al*<sup>[76]</sup> showed that a machine learning model using a texture analysis of CT images and SUV values of PET-CT predicted KRAS mutations with high accuracy (AUC: 0.82).

## CURRENT ISSUES AND FUTURE PERSPECTIVES

### *AI research for endoscopy*

The majority of studies previously reported that a CAD system using AI for endoscopy had the ability to diagnose gastrointestinal tumors with high accuracy; however, there were many limitations. Researchers were more likely to use high-quality endoscopic images to construct AI models, which cannot always be acquired in clinical settings<sup>[9]</sup>. Furthermore, outcome indicators for clinical applications have not yet been defined. Therefore, parameters to assess the functional performance of AI models need to be established<sup>[19]</sup>. In addition, the majority of studies have been retrospective in nature using still images from non-clinical settings. These conditions do not mimic real-time clinical settings, in which endoscopists often encounter difficult-to-analyze images in daily practice. Moreover, it currently remains unclear whether AI models will enhance medical performance, reduce medical costs, and increase the satisfaction of patients and medical staff in clinical settings. Another limitation is that many clinicians and clinical researchers do not have sufficient knowledge to understand AI systems; therefore, non-AI experts as well as medical journal reviewers may encounter difficulties when assessing research on AI and its applications. Furthermore, the number of medical staff with the skill to educate physicians on AI is very limited<sup>[19]</sup>.

Nevertheless, once these limitations are resolved, CAD systems using AI will markedly improve diagnostic quality in endoscopic examinations. CAD systems for endoscopy are expected to serve as a second observer during real-time endoscopy, facilitating the detection of more neoplasms by endoscopists. Some CAD systems may also provide “optical biopsies” to differentiate the types of colon polyps<sup>[9]</sup>. Therefore, CAD systems have a promising future in the effective training of junior endoscopists as assistant observers.

### *AI research for pathology*

Previous studies reported that AI models distinguish structures in tissues and detect cancerous regions with high accuracy. Furthermore, survival may be predicted using image analyses by AI. However, there are also a number of limitations in research. AI models are educated using pathological images of cancer tissue labeled by pathologists. However, interobserver disagreement in pathological diagnoses commonly occurs between pathologists<sup>[77,78]</sup>. Therefore, the quality of teaching data varied in each study. Furthermore, the majority of AI models were constructed using a small cohort. It might be possibility non-reproducible laboratory-specific machine learning methods. In addition, the clinical use of AI models requires a digital slide scanner, image storage, maintenance contracts, image analysis software, and IT support systems, which may be expensive in clinical settings. Moreover, many pathologists and technicians do not have sufficient knowledge to understand AI systems. Therefore, the recruitment of AI experts to introduce AI systems into clinical settings is needed for education and the adjustment of systems to different clinical settings.

Despite these limitations, whole-slide scanning using AI models, such as the TMA method, is advantageous for pathologists and clinicians. This method may be a second observer in the prevention of false diagnoses by pathologists and the teaching of trainees. Furthermore, the heterogeneities of cancer tissue cannot be precisely evaluated by the human eyes of pathologists. Therefore, the assessment of cancer tissue using AI models is a novel research method beyond human cognition that is expected to predict proteomics, genomics, and the molecular signaling pathways of tumors as precision medicine by cancer genome sequencing.



### AI research for radiology

Previous studies reported the efficacy of automatic segmentation or diagnosis in solid malignant tumors<sup>[77-79]</sup>. However, difficulties are associated with automatic segmentation by AI models in the field of gastrointestinal cancer because of large individual differences in imaging features of the gastrointestinal tract, except for the rectum. The radiomics approach represents an attractive method for detecting malignant potential and imaging biomarkers for precision medicine through image analyses of intratumor heterogeneity. However, a number of limitations need to be considered. The manual or semi-automatic segmentation of tumors is generally needed in the radiomics approach. Interobserver variability in manual segmentation often occurs in this process, resulting in the poor reproducibility of data by the radiomics model. Furthermore, previous studies demonstrated that radiomic features may be affected by a number of parameters, such as the scanning equipment<sup>[80]</sup>, image pre-processing<sup>[81]</sup>, acquisition protocols<sup>[82,83]</sup>, image reconstruction algorithms<sup>[84,85]</sup>, and delineation. In addition, although researchers of radiology or AI experts are knowledgeable about radiomics and AI models, they often cannot target the clinical task that needs to be improved for clinicians or patients in clinical settings. However, clinicians are not sufficiently aware of AI, and few reviewers of scientific literature on clinical medicine often are developing AI models or are able to judge research involving AI. Therefore, a multidisciplinary team needs to be introduced into research and medical teams to promote AI-supported medicine.

Despite these limitations, radiomic models for the image diagnosis or prediction of malignancy have the potential to support clinical teams for more accurate and rapid diagnoses. These models may increase patient satisfaction levels for homogenized diagnostic accuracy. Moreover, radiogenomics may have a major impact on precision medicine. Non-invasive assessments of the entire tumor tissue may be possible, without having to rely on a single biopsy to represent all cancer lesions within a patient. As further information becomes available on these imaging markers, the characteristics of cancers will be elucidated in more detail. Therefore, the radiomics approach will enhance the treatment effects of molecular biological approaches for oncological precision medicine.

## DISCUSSION

AI will be an important component of diagnostic methods to diagnosis patient disease, determine most appropriate treatments, and predict prognosis and drug resistance. A lot of research methods have been developed with the aims and found to have varying levels of performance. For clinical use of disease diagnosis, AI seems valuable for use in endoscopy, where it could increase detection of benign polyp and malignant tumor. Meanwhile, AI may be useful to analysis intratumor heterogeneity of radiological and pathological images in order to predict malignant potentials, such as the prognosis of patients and therapeutic effects. Our minireview covered only articles listed in MEDLINE, and might have missed some literatures in medical image analysis journals and computer science. Despite of the limitation, AI has become an important part of clinical cancer research in recent years.

There is no turning back for the development of AI in gastrointestinal cancer, and future implications are large. However, some limitations that require caution should be recognized. Most studies were performed using low-quality datasets from pre-clinical studies. Furthermore, AI algorithms are often considered to be black-box models. The difficulty in understanding the process of AI decision may prevent physicians from finding the potential confounding factors. Ethical challenge is one of the problems to be considered. In the present AI system, AI is not aware of the human preferences or legal liabilities. Therefore, medical staff will have to make decisions for patients according to their preferences, environment, and ethics. AI will not completely replace doctors, and computer technology and medical staff will always have to work together. However, the diagnostic accuracy of AI systems has markedly increased and may detect novel biomarkers that cannot be identified by the human eye or in human-aid analyses. AI systems will be introduced into general hospitals in the near future under the management of multidisciplinary teams consisting of medical staff and AI experts.

## CONCLUSION

We reviewed the recent published literatures on AI in gastrointestinal cancer, suggesting that AI may be used to accurately diagnose clinical images, identify new therapeutic targets, and process clinical data from large patient datasets. Although the physicians must recognize the limitations of AI diagnostic system, AI-assisted medical systems will become a promising tool for gastrointestinal cancer.

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