

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2022 January 15; 14(1): 1-368



REVIEW

- 1 Molecular regulatory mechanism of ferroptosis and its role in gastrointestinal oncology: Progress and updates
Yang F, Sun SY, Wang S, Guo JT, Liu X, Ge N, Wang GX
- 19 Biomarkers for response to immune checkpoint inhibitors in gastrointestinal cancers
Li M, Kaili D, Shi L
- 38 Proteasome regulators in pancreatic cancer
Murugan NJ, Voutsadakis IA
- 55 Effects of *Helicobacter pylori* infection in gastrointestinal tract malignant diseases: From the oral cavity to rectum
Kuo YC, Yu LY, Wang HY, Chen MJ, Wu MS, Liu CJ, Lin YC, Shih SC, Hu KC
- 75 Bromodomain and extra-terminal inhibitors emerge as potential therapeutic avenues for gastrointestinal cancers
Sun HY, Du ST, Li YY, Deng GT, Zeng FR
- 90 Gastric cancer: An epigenetic view
Tang SY, Zhou PJ, Meng Y, Zeng FR, Deng GT
- 110 Statin as a therapeutic agent in gastroenterological cancer
Uemura N, Hayashi H, Baba H
- 124 Development of artificial intelligence technology in diagnosis, treatment, and prognosis of colorectal cancer
Liang F, Wang S, Zhang K, Liu TJ, Li JN

MINIREVIEWS

- 153 Impact of the microenvironment on the pathogenesis of mucosa-associated lymphoid tissue lymphomas
Uhl B, Prochazka KT, Fechter K, Pansy K, Greinix HT, Neumeister P, Deutsch AJ
- 163 Immunotherapy in liver transplantation for hepatocellular carcinoma: Pros and cons
Luo Y, Teng F, Fu H, Ding GS
- 181 Trimodality treatment in gastric and gastroesophageal junction cancers: Current approach and future perspectives
Charalampakis N, Tsakatikas S, Schizas D, Kykalos S, Tolia M, Fioretzaki R, Papageorgiou G, Katsaros I, Abdelhakeem AAF, Sewastjanow-Silva M, Rogers JE, Ajani JA
- 203 Radiofrequency ablation in the management of primary hepatic and biliary tumors
Hendriquez R, Keihanian T, Goyal J, Abraham RR, Mishra R, Girotra M

- 216 Immune evasion mechanisms and therapeutic strategies in gastric cancer

Ma ES, Wang ZX, Zhu MQ, Zhao J

- 230 Early-onset colorectal cancer: Current insights and future directions

Wu CWK, Lui RN

ORIGINAL ARTICLE

Basic Study

- 242 Hydrogen-rich water exerts anti-tumor effects comparable to 5-fluorouracil in a colorectal cancer xenograft model

Asgharzadeh F, Tarnava A, Mostafapour A, Khazaei M, LeBaron TW

- 253 Lnc524369 promotes hepatocellular carcinoma progression and predicts poor survival by activating YWHAZ-RAF1 signaling

Zheng W, Shen GL, Xu KY, Yin QQ, Hui TC, Zhou ZW, Xu CA, Wang SH, Wu WH, Shi LF, Pan HY

Retrospective Study

- 265 Characterization of E-cadherin expression in normal mucosa, dysplasia and adenocarcinoma of gastric cardia and its influence on prognosis

Wang HL, Zhao XK, Zhou FY, Song X, Li LY, Huang GR, Bao QD, Lei LL, Yang HJ, Li L, Xu RH, Li AL, Wang XZ, Han WL, Ren JL, Wang LD

Observational Study

- 278 Digestive cancer incidence and mortality among young adults worldwide in 2020: A population-based study

Li J

Prospective Study

- 295 Intertwined leukocyte balances in tumours and peripheral blood as robust predictors of right and left colorectal cancer survival

Cantero-Cid R, Montalbán-Hernández KM, Guevara J, Pascual-Iglesias A, Pulido E, Casavilla JC, Marcano C, Serrano CB, Valentín J, Bonel-Pérez GC, Avendaño-Ortiz J, Terrón V, Lozano-Rodríguez R, Martín-Quirós A, Marín E, Pena E, Guerra-Pastrián L, López-Collazo E, Aguirre LA

Randomized Controlled Trial

- 319 Effects of cognitive behavior therapy combined with Baduanjin in patients with colorectal cancer

Lin ZG, Li RD, Ai FL, Li S, Zhang XA

SYSTEMATIC REVIEWS

- 334 Exosomes as potential diagnosis and treatment for liver cancer

Wei XC, Liu LJ, Zhu F

META-ANALYSIS

- 348** Increased risk of colorectal neoplasia in inflammatory bowel disease patients with post-inflammatory polyps: A systematic review and meta-analysis

He DG, Chen XJ, Huang JN, Chen JG, Lv MY, Huang TZ, Lan P, He XS

LETTER TO THE EDITOR

- 362** Liquid biopsy: Precise diagnosis and therapy for cholangiocarcinoma

Wang SQ, Chai CX, Wang BR, Zhu F, Shang D, Li M

- 366** Comment on “Outcomes of curative liver resection for hepatocellular carcinoma in patients with cirrhosis”

Tang XL, Miao YD, Mi DH

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Oncology*, Esther Una Cidon, MD, MSc, PhD, Doctor, Department of Medical Oncology, Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust, Bournemouth BH7 7DW, United Kingdom. aunacid@hotmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (WJGO, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc.*

INDEXING/ABSTRACTING

The WJGO is now indexed in Science Citation Index Expanded (also known as SciSearch®), PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJGO as 3.393; IF without journal self cites: 3.333; 5-year IF: 3.519; Journal Citation Indicator: 0.5; Ranking: 163 among 242 journals in oncology; Quartile category: Q3; Ranking: 60 among 92 journals in gastroenterology and hepatology; and Quartile category: Q3. The WJGO's CiteScore for 2020 is 3.3 and Scopus CiteScore rank 2020: Gastroenterology is 70/136.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xiang Li*; Editorial Office Director: *Ya-Juan Ma*.

NAME OF JOURNAL

World Journal of Gastrointestinal Oncology

ISSN

ISSN 1948-5204 (online)

LAUNCH DATE

February 15, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-5204/editorialboard.htm>

PUBLICATION DATE

January 15, 2022

COPYRIGHT

© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Development of artificial intelligence technology in diagnosis, treatment, and prognosis of colorectal cancer

Feng Liang, Shu Wang, Kai Zhang, Tong-Jun Liu, Jian-Nan Li

ORCID number: Feng Liang 0000-0002-8798-0229; Shu Wang 0000-0002-8758-0508; Kai Zhang 0000-0002-4499-7186; Tong-Jun Liu 0000-0001-5712-4838; Jian-Nan Li 0000-0001-9744-7666.

Author contributions: Liang F wrote the paper; Liang F, Wang S, and Li JN performed the revision and approval of the final version; Zhang K and Liu TJ performed literature research; Wang S corrected the writing of the paper; Li JN designed the review; Liang F and Wang S contributed equally to this work.

Conflict-of-interest statement: The authors declare no conflict of interest for this article.

Supported by The Science and Technology Development Project of Jilin Province, No. 3D5197434429; and National Natural Science Foundation of China, No. 32000953.

Country/Territory of origin: China

Specialty type: Oncology

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

Peer-review report's scientific quality classification
Grade A (Excellent): A

Feng Liang, Kai Zhang, Tong-Jun Liu, Jian-Nan Li, Department of General Surgery, The Second Hospital of Jilin University, Changchun 130041, Jilin Province, China

Shu Wang, Department of Radiotherapy, Jilin University Second Hospital, Changchun 130041, Jilin Province, China

Corresponding author: Jian-Nan Li, PhD, Professor, Department of General Surgery, The Second Hospital of Jilin University, No. 218 Ziqiang Street, Changchun 130041, Jilin Province, China. jnli@ciac.ac.cn

Abstract

Artificial intelligence (AI) technology has made leaps and bounds since its invention. AI technology can be subdivided into many technologies such as machine learning and deep learning. The application scope and prospect of different technologies are also totally different. Currently, AI technologies play a pivotal role in the highly complex and wide-ranging medical field, such as medical image recognition, biotechnology, auxiliary diagnosis, drug research and development, and nutrition. Colorectal cancer (CRC) is a common gastrointestinal cancer that has a high mortality, posing a serious threat to human health. Many CRCs are caused by the malignant transformation of colorectal polyps. Therefore, early diagnosis and treatment are crucial to CRC prognosis. The methods of diagnosing CRC are divided into imaging diagnosis, endoscopy, and pathology diagnosis. Treatment methods are divided into endoscopic treatment, surgical treatment, and drug treatment. AI technology is in the weak era and does not have communication capabilities. Therefore, the current AI technology is mainly used for image recognition and auxiliary analysis without in-depth communication with patients. This article reviews the application of AI in the diagnosis, treatment, and prognosis of CRC and provides the prospects for the broader application of AI in CRC.

Key Words: Artificial intelligence; Colorectal cancer; Diagnosis; Treatment; Prognosis

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: The current artificial intelligence (AI) technology is mainly used for image

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

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Received: June 15, 2021

Peer-review started: June 15, 2021

First decision: August 8, 2021

Revised: August 19, 2021

Accepted: November 15, 2021

Article in press: November 15, 2021

Published online: January 15, 2022

P-Reviewer: Mitsala A, Morya AK

S-Editor: Yan JP

L-Editor: Wang TQ

P-Editor: Yan JP



recognition and auxiliary analysis without in-depth communication with patients. We here review the application of AI in the diagnosis, treatment, and prognosis of colorectal cancer (CRC) and look at the prospects for the broader application of AI in CRC.

Citation: Liang F, Wang S, Zhang K, Liu TJ, Li JN. Development of artificial intelligence technology in diagnosis, treatment, and prognosis of colorectal cancer. *World J Gastrointest Oncol* 2022; 14(1): 124-152

URL: <https://www.wjgnet.com/1948-5204/full/v14/i1/124.htm>

DOI: <https://dx.doi.org/10.4251/wjgo.v14.i1.124>

INTRODUCTION

With the invention of the computer, heavy scientific and engineering calculations have shifted from being done primarily by the human brain to being done more quickly and accurately by computers. Artificial intelligence (AI) has evolved rapidly with the continuous development of computer science and technology. AI is an umbrella term that helps humans perform tasks including computer simulation, decision-making, language understanding, problem-solving, voice and image recognition, and other “intelligent” tasks[1-3]. AI can be divided into machine learning (ML), deep learning (DL), anti-learning, quasi-supervised learning (QSL), and active learning (AL)[4-7]. ML is a subset of AI algorithm which uses statistical techniques to adjust and improve itself[1,3]. ML produces algorithms for analyzing data and learning to predict models, which means that ML is data-driven, with a little human intervention as possible in the decision-making process[4,8]. The model created by ML can be used as an independent executable system to predict the clinical phenotype[9]. The relevant technologies in ML include support vector machine (SVM), neural network (NN), random forest (RF), decision tree, and regression analysis[10]. Based on the association of class labels, ML is generally divided into supervised learning, unsupervised learning, and semi-supervised learning (SSL)[8,9]. Supervised learning is mainly used for solving classification and regression problems. Unsupervised learning is used for a cluster, density estimation, and dimensionality reduction[9]. SSL can significantly improve the learning accuracy when unlabeled data combined with a limited number of labeled data are used in SSL[11]. At present, supervised learning plays a leading role in AI and ML in the medical field[2]. Supervised learning provides more accurate results than other AI techniques because it considers the characteristics of the patients [10].

DL is a kind of developed ML based on an artificial NN (ANN)[2], which is inspired by the biological characteristics of the human brain, especially the connection of neurons[2,4]. DL can not only automatically find lesions, make recommendations for differential diagnosis, and write elementary medical reports, but can also be self-learning, *i.e.*, key characters and quantities can be extracted without a manual indication if the training data is provided[4]. Moreover, DL aims to copy the brain's learning process and process a large amount of high-dimensional data[12]. QSL is a statistical learning algorithm that avoids the manual marking of normal tissue and cancer tissue samples in traditional supervised learning and greatly reduces the intervention of experts[5]. ML usually needs a large number of annotated training sets, which are expensive to create. AI reduces the size of the required annotation set and generates a better classification model[7]. In some research, to predict the stage of colorectal cancer (CRC) from immune attributes, the anti-learning method has better performance than a series of ML algorithms[6].

CRC is the second reason for cancer death in males and the third reason for cancer death in females[13]. If colonic polyps, which may lead to at least 80%-95% of CRC [14], are detected by the screening procedure and resected in the precancerous stage, it can help prevent CRC development[15]. Although early and intensive screening can reduce cancer incidence and mortality, patients avoid CRC screening due to the complexity and cost of screening[15-17]. Generally, the methods of diagnosing CRC are divided into imaging diagnosis, endoscopy, and pathology diagnosis. Treatment methods are divided into endoscopic treatment, surgical treatment, and drug treatment. If lymph node metastasis is not confirmed preoperatively, lymph node

dissection is not required intraoperatively[18]. AI has great diagnostic potential because it can learn from a large data set. In the clinical image, AI is superior to medical experts and existing biomarkers[10]. This paper will describe the use of AI in the diagnosis, treatment, and prognosis of CRC. Web of Science and PubMed databases were searched using keywords “artificial intelligence” and “colorectal cancer”.

USE OF AI IN DIAGNOSIS OF CRC

DL in imaging diagnosis

The DL intelligent assistant diagnosis system can help the clinical diagnosis and treatment of CRC[19]. The computer-aided diagnosis (CAD) system usually analyzes the nature of the selected area (cancerous or noncancerous) through the informative characteristics of the known potential (cancerous) structure[20]. The CAD system can help radiologists diagnose CRC by visual cues (CAD marks) associated with potential pathology. In addition, CAD can help determine the location of the disease (computer-aided detection, CAdE) and determine whether the abnormality is benign or malignant. Regardless of the outcome, doctors must ultimately decide whether to “believe” the CAD mark[21]. The key for radiologists accepting the clinical use of CAD systems is to have a high detection sensitivity and a low false-positive rate (FP)[20]. Apart from polyps and cancer, other colorectal pathological morphologies are rare, which can explain why CAD solutions for computed tomography colonography (CTC) have developed so rapidly[22]. CAD of CTC has indeed improved sensitivity in finding polyps without disproportionately decreasing specificity, but the lesions mistaken for false-negative are significantly large and irregular[21-23]. Regge *et al*[21] believed that the difficulty of characterization (irregular and flat morphology) was the main determinant of radiologists’ rejection of true positive CAD indications.

Although the consequence of CRC misdiagnosis is much more severe than that of polyp misdiagnosis, the research of CAdE for CRC in CTC is still very limited[24]. The reason may be that the lack of literature on the detection characteristics of early CRC [25] and the fact that it remains a problem to effectively distinguish masses from normal colonic anatomy based on the design features of mathematical images[24]. Taylor *et al*[25] collected the morphological characteristics of flat tumors by locating tumors to distinguish tumors from normal tissue structure and found that the CAD system combined with CTC was relatively effective for detecting flat (non-polypoid) cancer. CAD can improve the speed of image interpretation, find out the polyps missed by experts, reduce the variability between observers, and improve the sensitivity of polyp detection[26,27]. However, the increase of FP generated by CAD may reduce the efficiency[22]. Deep transfer learning can greatly improve the accuracy of polyp detection in CTC[28]. Because the virtual intracavity images of polyp filtered by the CAdE system can be used to modify the deep convolutional NN (DCNN) trained by millions of non-medical images, the DCNN can identify polyps[28]. It can significantly improve the detection of polyps for inexperienced doctors using a visualization scheme in CTC. Combined with the CAD system, the visualization scheme can reduce radiologists’ interpretation time and improve the detection of colon tumors in CTC[29]. Van Wijk *et al*[30] presented a method by measuring the protrusion of candidate objects in a scale adaptive way to evaluate polyps larger than or equal to 6 mm, with a 95% sensitivity obtained. It was believed that identifying the size of polyps can reduce the risk of missed diagnosis of large polyps more than identifying the shape[30]. Kim *et al*[31] collected the CTC dataset interpreted by the CAD algorithm from polyp patients. The CTC dataset was designed to describe the lumpy structure extending into the lumen and could identify large polyps (> 6 mm) with a high sensitivity and acceptable FP. Based on the characteristics of volume and shape, Nappi *et al*[32] developed a CAdE method to detect the location of colonic polyps and used this method to evaluate the serrated polyps confirmed by colonoscopy and biopsy. The results showed that the detection accuracy of the method was much higher than that of the traditional CAdE system[32]. Therefore, the application of CAD diagnosis has a promising prospect. However, more data sets and effective annotations are still needed to enhance the accuracy of AI diagnosis[21].

The optimal portal venous phase timing recognition scan was selected for classifying the contrast enhancement time, which could help analyze the radiologic characteristics of the tumor and evaluate the efficacy of patients with advanced CRC [33]. Soomro *et al*[34] found that three-dimensional (3D) fully convolutional NNs combined with 3D level-set showed a higher sensitivity than 3D fully convolutional

NNs alone in the segmentation of CRC on magnetic resonance imaging (MRI), which helped for the diagnosis of CRC. In 3D-T2 weighted MRI, the 3D full collaborative network architecture based on DL could segment CRC more reasonably and effectively than other techniques[35]. In the high-resolution MRI image of rectal cancer, the use of a faster region-based convolution NN (Faster R-CNN) had a high accuracy in evaluating tumor boundaries[36,37]. Circumferential resection margin is one of the key factors affecting the treatment decision of CRC patients. Joshi *et al*[38] proposed an automatic calculation and visualization method of circumferential resection margin distance in MRI images of CRC to segment the middle rectal fascia, the corresponding tumor, and lymph node into different regions. The segmentation was used to analyze the shortest cut edge automatically, and the results obtained were almost identical to the experts' judgment[38].

DL in pathological diagnosis

If CRC is detected early, it is almost curable. However, in order to make a correct diagnosis, a double examination of biopsy and colonoscopy image is required, so the cost of diagnosis has increased[39]. Thus, the use of DL and automatic image analysis in pathology is increasing, which is called the third revolution of pathology[40]. Although the automatic coding in DL is considered helpful in extracting multi-layer image features and deep NNs can classify the features, it takes much time to train artificial neurons[41].

Convolutional NN (CNN) is a common method in pathological image analysis. Compared with other methods, CNN has the advantages of convenience for end-to-end learning (CNN learning parameters and representations are designed manually), flexibility, and high capacity[2]. The choice of color space is important for identifying cancer tissue because it deeply affects the performance of the classification model. CNN is used to analyze the tissue classification of different color spaces. Tiwari S proved that hue, saturation, value (HSV) color space was more suitable than any other color model for cancer tissue classification[42]. Because of the heterogeneity of the cells, texture, and cell contact complexity, it is challenging to detect and classify the nuclei in the pathological images of cancer tissues stained with hematoxylin and eosin (H&E)[43,44]. A space-constrained CNN based on DL was proposed for nuclear detection, which might provide a possibility for quantitative analysis of tissue components and clarify the tumor microenvironment. Moreover, the neighbor ensemble predictor combined with CNN could accurately predict the detected nuclear markers and classify the nuclei[43]. Although qualitative and quantitative analysis of histopathological images can clarify the tumor and explore various options for cancer treatment, it remains challenging due to cell heterogeneity. Zhang *et al*[45] proved that it had a good accuracy and lower cost of time when Faster R-CNN was used in feature extraction, providing a useful quantitative analysis group for pathological practice.

CNN, widely used to analyze histopathological images, only performs directly on the histopathological images, ignoring the histopathological images' stain decomposition. Xu *et al*[46] reported a new model based on DCNN to classify the H&E and immunohistochemistry images of epithelial and stromal cells in colon cancer. For distinguishing stromal from epithelial cells, the DCNN based model was always better than the traditional hand-made model. The morphology of glands and nuclei is used to evaluate the malignant degree of adenocarcinoma. As a necessity for quantitative diagnosis, the accurate detection and segmentation of the histological image are challenging due to its appearance variation, strong similarity, and tissue degradation. Chen *et al*[47] attempted to use a depth profile awareness network, which could output the accurate probability map of histological objects and draw clear contour lines, to improve the accuracy of detection and segmentation.

Digital pathology is a new field. The development of digital pathology may help pathologists to improve the quality of routine pathological operations[48]. The key to promoting the development of digital pathology is the CAD system, based on the principle of extracting histopathological features that pathologists consider important. Then, the existence of these features was explained quantitatively by computer calculation[49,50]. There are two important steps towards the CAD: Tumor segmentation of the whole section image in the histological section and the automatic segmentation of tumors in the H&E staining histological image[51]. Qaiser *et al*[51] found that tumor and non-tumor plaques had distinct homology, and proved the robustness and significance of persistent homology by exploring connectivity between nucleus. A method called persistent homology maps (PHPs) was proposed, which could distinguish tumor area from the normal area by simulating the atypical characteristics of tumor cell nucleus[51]. PHPs outperform other methods, including traditional CNN[51]. Two different tumor segmentation methods are proposed:

Targeting speed without affecting accuracy and targeting higher accuracy. The combination of PHPs and CNN features was shown to be better than competition algorithms[51].

DL in endoscopic diagnosis

Colonoscopy is a common method to screen polyps. The detection and removing of adenomatous polyps can reduce the incidence and mortality rates of CRC [13]. AI is necessary to improve machine performance and diagnosis accuracy, reducing the variability between operators and helping rapid treatment decision-making[3]. In addition, AI has a great potential to improve the detection rate of adenoma and reduce the cost of polypectomy[52]. The quality of intestinal preparation is an important factor influencing the effect of colonoscopy examination[53]. When the fecal residues are present in the colon, the rate of missed diagnosis of polyps will increase. Although the endoscopic image diagnostic program based on CNN has yielded good results, its diagnostic ability depends heavily on the quality and quantity of training data[4,54]. The use of CNN and colonoscopy procedure is expected to improve the detection rate and diagnosis accuracy of polyps[55]. Zhou *et al*[53] developed a CNN based system that was trained by collecting colonoscopy images. Through a human-machine competition, the system was found to be more reliable than endoscopic physicians in diagnosis of CRC. Taha *et al*[56] introduced a DL solution for polyps from colonoscopy, a pre-training architecture for feature extraction, used together with the classical SVM classifier. As the solution can avoid the high computational complexity and high resource requirements of CNN, it outperforms other models in the early screening of CRC[56]. Yao *et al*[57] proved that the features in red, green, blue (RGB) and HSV color space could well describe the frames in colonoscopy videos. It could improve the model's efficiency by integrating the prior knowledge based on vision into the data extracted by DL. Therefore, a feature extraction algorithm in HSV color space was designed to effectively improve the accuracy of diagnosis and reduce the cost[57]. McNeil *et al*[58] proposed an automatic quality control system based on DCNN, improving colonoscopy quality by cleaning the mucosal wall and reexamining the rushed segment. The system could increase the detection rate of polyps and have great significance for the early diagnosis and prevention of CRC.

The missed diagnosis rate of traditional colonoscopy approaches 25%[59,60], partly due to the lack of depth information, inter-observer variation, and contrast on the surface of the colon[60,61]. Computer-aided technology is important for polyp detection in endoscopic video. The method based on DL takes the lead in the evolution of algorithm performance[62]. It is a challenging task for CAD to minimize the FP of colonic polyps[63]. Mahmood *et al*[61] used a joint depth learning and graphics model-based framework to estimate depth from endoscopic images. At the same time, they used the texture-free colon model to generate training images and trained the model with those images[61]. The system could estimate the depth of virtual data with a relative error of 0.164, which was helpful to perfect the CAD system and identify lesions[61]. Komeda *et al*[64] believed that CNN had the advantage of learning from large data and led to high precision and fast processing time, and they designed a CNN-CAD system to study endoscopic images extracted from colonoscopy[64]. The analysis and cross-validation of 1200 cases of colonoscopy confirmed that the CNN-CAD system was helpful for the rapid diagnosis of colonic polyps and could simplify the decision-making process of colorectal polypectomy[64]. Compared with other algorithms, the CAD method (named RYCO) had the potential for rapid and accurate computer-aided polyp detection in colonoscopy. The fast target detection algorithm ResYOLO was pre-trained using a large non-medical image database, and the colonoscopy image was fine-tuned. At the same time, the time information was combined by a tracker named Efficient Convolution Operator to improve the detection results given by ResYOLO. RYCO could clarify the spatial characteristics of colorectal polyps directly and improve the detection efficiency of colorectal polyps[65]. In order to distinguish stage T1b and Tis/T1a CRC, the optical diagnostic system developed by CNN was proposed[66]. Zhu *et al*[66] selected the early CRC digital images without magnification and under a pure white light endoscope as the training dataset. At the end of the training process, 122 early CRC images were used to evaluate the diagnostic performance. The results showed that optical diagnoses by CNN had a high sensitivity but low specificity, which was different from humans[66]. Variations in polyp size and shape made the diagnosis of polyp in colonoscopy video challenging[67]. However, the Faster R-CNN could reduce the risk of polyp loss during colonoscopy[62]. Furthermore, Akbari *et al*[67] presented a fully convolutional network (FCN) method of polyp segmentation based on CNN. In the test phase, they did effective post-processing for the probability map generated by the network. The CVC-ColonDB

database was used to evaluate the method. The result showed that FCN could get more accurate segmentation results[67]. 3D-FCN could learn more representative spatiotemporal features from colonoscopy video and had stronger recognition ability than FCN[68].

The goal of the real-time endoscopic image diagnosis support system is to use AI during colonoscopy without interrupting the operation of any doctor[69]. Based on the DL method, the real-time optical detection and analysis of polyps can be carried out by white light endoscopy alone[70]. A real-time automatic polyp detection system can help endoscopists detect lesions that may correspond to adenomas quickly and reliably[13]. The accuracy of endoscopic differential diagnosis enables the “resection and discard” mode of small-scale colorectal polyps[71]. To relieve the high cost, long time consuming, and patients’ discomfort, Lund Henriksen *et al*[71] explored a system for automatic polyp detection to assist and automate the examination procedures. By comparing root mean square propagation, stochastic gradient descent, and adaptive moment estimation, when stochastic gradient descent was used as the training optimizer, the detection rate increased while the number of FP was relatively stable [71].

Although optical biopsy is a promising field, tissue biopsy remains the gold standard. Whether the surface microstructure accurately reflects the histological characteristics of lesions will affect the results of optical biopsy[3,13,72,73]. The widespread clinical use of microscopic technology, especially the combination of virtual chromoendoscopy and microscopic imaging, has brought more attention to the field of optical biopsy[74]. Endoscopists can reliably diagnose and differentiate microadenomatous and hyperplastic polyps using established optical evaluation criteria [75]. The development of CAD and AI algorithms may overcome the main obstacles of optical biopsy and change the treatment of colorectal lesions[74,76]. Endocytoscopy is an effective method for deep diagnosis of CRC because of the high resolution[73]. Kudo *et al*[77] developed an AI-based system called EndoBRAIN which could identify the colon tumor by analyzing the nucleus, crypt structure, and microvasculature in the endoscopic image. The initial training of EndoBRAIN was carried out using endoscopic images. The diagnostic efficiency of endoscopists and the diagnostic performance of EndoBRAIN were analyzed retrospectively. The result showed that EndoBRAIN could increase the accuracy of the diagnosis[77]. Mahmood *et al*[78] proposed a new monocular endoscope depth estimation and terrain reconstruction system, which took advantage of the joint training framework based on CNN and conditional random field. The system used the synthetic endoscope data for training and the colon model data for fine-tuning. It could be integrated into the endoscope system, which provided a basis for improving the CAD algorithm to detect, segment, and classify lesions[78].

ML in imaging diagnosis

ML has to extract the most relevant or predictive features from many tested features and use these to determine the categories of new image samples[79,80]. The features will help diagnose CRC in imaging. It is very important to segment colorectal tumors accurately in MRI images, while the manual or semi-manual method is very tedious, time-consuming, and operator-dependent[81]. CAD plays an important role in many medical analyses, especially in computed tomography (CT) image analysis. Although many methods are designed, there are still some deficiencies in structure segmentation [82]. Onder *et al*[5] reported that ML methods including SVM and logistic regression could achieve better classification performance and improve the accuracy of the baseline CAD system. The ideal colon segmentation effect could be achieved in a CT image using the NN algorithm to remove the turbid liquid of the large intestine[83]. Jian *et al*[81] proposed a segmentation method based on the FCN framework. The normalization method was used to reduce the difference between images. The segmentation method could extract features from standardized images and generate corresponding predictions for reference using the idea of transfer learning. Finally, all predictions were fused to determine the final tumor boundary[81]. Compared with manual segmentation of T2 weighted MRI images of CRC, the FCN based segmentation method had a higher accuracy. The FCN based segmentation method might replace the time-consuming manual method[81]. In order to achieve accurate segmentation, a regression NN-augmented lagrangian genetic algorithm (RNN-ALGA) based on ML was proposed. Using RNN-ALGA, an accuracy of 97% could be achieved under the condition of small error. RNN-ALGA was suitable for abdominal CT image slices and could improve structural segmentation accuracy and time efficiency in diagnosing colonic diseases[82].

ML in pathological diagnosis

Computational pathology based on AI and ML methods is most promising. The computer model has better image recognition ability than human experts[2]. Large-scale and high-quality training datasets are necessary for an ML-based image classifier to achieve high performance[84]. ML-based tissue classification is a valuable method for manual histological analysis. However, high-resolution image classification is a complex and computationally expensive task. In addition, the goal of many tissue analysis tasks is to identify rare areas in the tissue. In colon cancer, tumor budding (TB) exists in the front of the tumor-infiltrating area, which is an important sign of tumor invasiveness[85]. When the image is examined at a low resolution, the small objects are difficult or impossible to detect. Sun *et al*[85] provided a two-tier CNN classification method that was explored to identify the small and important tissue areas in the whole slice tissue. The processing time of the method is reduced by 43%. The two-tier classifier provided an effective tissue classification by reducing the task area and increasing the chance of tumor bud recognition[85]. A variety of serum tumor markers can be used in the diagnosis of CRC. There is a wide range of variability in the types and quantities of routinely used markers. The traditional single cut-off point also hinders the effective use of tumor markers. In order to improve the diagnosis accuracy and reduce the cost, it is important to optimize the inspection combination and make full use of the inspection value. Shi *et al*[86] proposed an AI algorithm called diagnosis strategy of serum tumor maker, which proved that two markers were enough for diagnosis. Compared with SVM and decision tree, the multiple tumor markers with multiple cut-off values (MVMTM) algorithm could greatly improve the diagnosis efficiency of CRC using carcinoembryonic antigen, carbohydrate antigen 19-9 (CA19-9), and CA50[87]. The establishment of an image database for colorectal tumor biopsy is an important step to detect the tumor. The automatic classification of tumor cells can improve the rapidity and accuracy of tumor diagnosis. Image processing and ML can be used to distinguish different cell types in digital biopsy sections. In addition to using conventional RGB/grayscale images, multispectral images often provide extensive information to support classification tasks. Kunthoth *et al*[88] used a multispectral image acquisition system to develop a colorectal biopsy section database divided into training sets and test sets. In order to avoid the deviation, 50 iterations were run, and the results of a single operation were averaged, which finally proved that the database had a high classification accuracy. The colorectal biopsy section database could help diagnose CRC[88].

ML in endoscopic diagnosis

With good results in computer vision and other fields, ML still requires certain manual guidance[4]. Removal of precancerous polyps is important for colon cancer prevention. However, the detection rate of adenomatous polyps is quite different among endoscopists[89]. By calculating the risk and difference of detecting polyps, adenomas, and CRC, Barua *et al*[90] compared colonoscopy with AI and colonoscopy without AI. It was found that an AI-based polyp detection system in colonoscopy could increase the detection rate of nonprogressive small adenomas and polyps but could not increase the detection rate of progressive adenomas[90]. Wang *et al*[89] developed the ENDOANGEL system and compared AI colonoscopy with colonoscopy without AI through random-control experiments. The results showed that AI significantly improved the detection rate of adenoma in colonoscopy[91]. Lui *et al*[92] suggested that the DL AI model could detect adenomas missed in routine colonoscopy in the real-time examination. They believed that the combination of AI and auxiliary equipment could eliminate the risk of missing lesions in colonoscopy when the intestine was well prepared[92]. Elastic scattering spectroscopy (ESS) for optical guided biopsy had a high accuracy in tumor detection. Rodriguez-Diaz *et al*[93] proposed two spectral classification frameworks, called ensemble classification and misclassification rejection, for clinical problems of non-tumor and tumor colorectal lesion classification based on ESS measurement. When the two frameworks were used to develop the diagnosis algorithm together, the classification effect would be better, and the medical cost would be reduced[93]. Near-infrared spectroscopy could also be used to diagnose CRC and differentiate malignant tumors. Kondepoti *et al*[94] collected the spectrum of cancer tissue and normal tissue from colonic tissue with an optical fiber probe. Major spectral differences could be observed. The spectrum was divided into cancer tissue and normal tissue with an accuracy of 89% using ANN, linear discriminant analysis, and other pattern recognition methods[94]. The method based on AL could perform real-time detection during colonoscopy and enhance detection performance at the same time. However, the possibility of increased FP

made the algorithm difficult to use in daily clinical practice[95]. Colon cancer might cause anemia as a common indication of colonoscopy. Hemoglobin concentration could be used as an indicator for the diagnosis of colon cancer, but it was not enough to diagnose colon cancer by hemoglobin concentration alone[96]. The AI-based ColonFlag™ might be an appropriate indicator, which used all indicators of whole blood count, age, and gender. At the same time, ColonFlag™ could provide appropriate treatment suggestions for patients who did not accept the fecal examination or colonoscopy[96]. Tian *et al*[97] believed that enhanced patient education (EPE) can be realized through visual aids, telephone, mobile and social media applications, multimedia education, and other software. EPE was used to guide the intestinal preparation of patients with colonoscopy and improve the detection rate of polyps, adenomas, and sessile serrated adenomas[97].

QSL and SSL in diagnosis

QSL eliminates the need for traditional supervised learning for manual labeling and reduces expert intervention. QSL texture labeling may be useful in the analysis and classification of pathological sections, but further research is needed[5]. The main purpose of analyzing millions of pixel histological images is to help pathologists predict cancer. At present, most methods are limited to the classification of tumors and stroma. Moreover, most of the existing methods are based on fully supervised learning and require many annotations that are difficult to obtain[98]. Javed *et al*[98] proposed a new group detection algorithm based on SSL, which could identify six different phenotypes in millions of pixels of image data. Two independent CRC datasets showed that the SSL algorithm was superior to the latest method[98]. ANNs are a class of models inspired by biological NNs, which are used to estimate functions that depend on a large number of general unknown inputs[99]. ANNs are usually shown as interconnected neuron systems, exchanging information with each other. Each connection has a digital weight, adjusted according to experience to make the input flexible and learn[4,9,99]. The establishment of diagnosis models based on ANN is helpful for clinicians to diagnose CRC, predicting postoperative outcomes, and screening high-risk prognosis subgroups[99]. ANNs have a good prospect in the general survey of CRC by establishing a clinical data model. This method is simple, low-cost, and non-invasive[100]. Other studies also described the application of AI in the diagnosis of CRC[101-107].

It is important to increase the sensitivity and specificity of early detection of CRC. First, massive endoscopic image datasets of early CRC should be set, with the early screening performed by colonoscopy and AI automatic recognition system. Second, early identification and timely warning for high-risk groups with a family history can be realized through new media and smartphone software. Third, with many pathological images and optical maps, we can identify whether the cutting edge is negative after endoscopic intervention in real time to adjust the treatment plan in time and avoid secondary surgery. Fourth, the government should establish a timely and effective national physical examination plan through AI to conduct early intervention and treatment for the high-risk population (Table 1).

USE OF AI IN TREATMENT OF CRC

AI in treatment decision

AI has become an irresistible trend in the medical field[108]. At present, oncologists are familiar with clinical practice guidelines (CPGs) and provide follow-up treatment for patients based on CPGs. On the contrary, physicians may not be familiar with the guidelines[109]. Passi *et al*[109] developed a decision support system (DSS) that used CRC follow-up data as a source of knowledge to generate appropriate follow-up recommendations for patients. Passi *et al*[109] designed and proposed the semantic framework of the web application, combining the current web technology and database storage with the designed ontology, and realized the unified development of DSS. Passi *et al*[109] also designed a web application interface to provide doctors with the functions of CPGs. DSS development could help physicians and nurses provide postoperative care for CRC patients[109]. Watson for Oncology provided oncologists with various cancer treatment suggestions, such as recommended, representing the preferred method; for consideration, not recommended. The absolute consistency of the treatment regimen with the recommendations of the multidisciplinary team of oncologists was studied. Lee *et al*[110] used Watson for Oncology to process cases and compared the results with the actual treatment received by patients. Key findings

Table 1 Artificial intelligence in diagnosis of colorectal cancer

Type of study	Ref.	No. of participants	Method	Control and interventions	Conclusion
Case control study	Yang <i>et al</i> [19], 2019	241	Depth-learning intelligent assistant diagnosis system	By comparing the accuracy of different algorithms on MRI images of patients with CRC, the algorithms that were conducive to the diagnosis of CRC were defined	T2-weighted imaging method had obvious advantages over other methods in differentiating CRC
Analytical research	Liu <i>et al</i> [20], 2011	429	SVM	Compared the performance of new and old classification methods in colorectal polyps CAD system	SVM could help CAD system get excellent classification performance
Review	Regge <i>et al</i> [21], 2013	NA	CAD system	NA	CAD system helped radiologists diagnose CRC with visual markers
Case control study	Summers <i>et al</i> [22], 2008	104	CAD system	The sensitivity of adenoma was measured by CAD system and compared with previous studies	CAD system had high accuracy in detecting and distinguishing adenoma
Descriptive research	Chowdhury <i>et al</i> [23], 2008	53	CAD-CTC system	The sensitivity of CAD-CTC system and manual CTC was compared through the image data of 53 patients	CAD-CTC system could effectively identify polyps and cancers with clinical significance in CT images
Case control study	Nappi <i>et al</i> [24], 2018	196	ResNets	Based on the clinical data of 196 patients, the classification performance of different models in distinguishing masses from normal colonic anatomy was compared	ResNets solved the practical problem of how to optimize the performance of DL
Case control study	Taylor <i>et al</i> [25], 2008	24	CAD system	The effectiveness of CAD system in detecting tumors was tested using the clinical data of 24 patients	CAD could effectively detect flat carcinoma by tumor morphology
Case control study	Summers <i>et al</i> [26], 2010	394	CAD-CTC system	The CTC data sets of 394 patients were trained in CAD system. It was confirmed that the experimental group could reduce the missed diagnosis rate of cancer	CAD-CTC system used advanced image processing and ML to reduce the occurrence of FP results
Case control study	Lee <i>et al</i> [27], 2011	65	CAD system	The CTC data sets of patient polyps were divided into a training data set and a test data set to compare the detection performance of CAD system	CAD system included colon wall segmentation, polyp specific volume filter, cluster size counting and thresholding, which had high detection performance of polyps and cancer tissue
Case control study	Nappi <i>et al</i> [28], 2015	154	DCNN	The clinical data were divided into a training data set and a test data set to compare the polyp detection performance of multiple classifiers	DCNN could greatly improve the accuracy of automatic detection of polyps in CTC
Case control study	Näppi <i>et al</i> [29], 2005	14	CAD system	The clinical data of 14 patients were used to test the effect of different staining methods on the effectiveness of polyp detection	CAD system helped to improve the ability to detect polyps in CTC
Case control study	van Wijk <i>et al</i> [30], 2010	84	CAD-CTC system	The polyp detection performance of different classification methods was tested through the clinical data of 84 patients	The sensitivity of the CAD-CTC system to distinguish polyps over 6 mm was very high
Case control study	Kim <i>et al</i> [31], 2007	35	CAD system	The sensitivity of CAD polyp detection was tested using colonoscopy data of 35 patients	CAD system helped to distinguish polyps and cancer tissue larger than or equal to 6 mm
Case control study	Nappi <i>et al</i> [32], 2017	101	CADe system	The polyp detection accuracy	CADe system could improve

				of novel and old CADe systems was compared by colonoscopy data of 101 patients	the accuracy of detecting serrated polyps or cancer tissues
Case control study	Ma <i>et al</i> [33], 2020	681	Portal venous phase timing algorithm	Training through 479 CT scan data sets; 202 CT scans were used for retrospective analysis and algorithm development and verification	It was helpful to quantitatively describe the characteristics of tumor enhancement
Case control study	Soomro <i>et al</i> [34], 2018	12	3D fully convolutional neural networks	The effects of polyp segmentation and recognition of different models were compared using MRI data of 12 patients	3D fully convolutional neural networks provided a more accurate segmentation result of colon MRI
Case control study	Soomro <i>et al</i> [35], 2019	43	DL	43 patients with CRC were evaluated by MRI. The data set was divided into 30 volumes for training and 13 volumes for testing	DL achieved better performance in colorectal tumor segmentation in volumetric MRI
Retrospective study	Wang <i>et al</i> [36], 2020	240	Faster R-CNN	The Faster R-CNN was trained using pelvic MRI images to establish an AI platform. The diagnosis results of AI platform were compared with those of senior radiologists	It was highly feasible to segment the circumcised positive margin with Faster R-CNN in MRI image of rectal cancer
Retrospective study	Wu <i>et al</i> [37], 2021	183	Faster R-CNN	The MRI data of 183 patients were collected as training objects. The platform was constructed using Faster R-CNN. The diagnostic accuracy was compared with that of radiologists	AI could effectively predict the T stage of rectal cancer
Case control study	Joshi <i>et al</i> [38], 2010	10	Non-parametric mixture model	Compared the accuracy of the algorithm and expert conclusions through the patient's MRI images	The algorithm could be used to distinguish T3 and T4 tumors accurately
Case control study	Shiraishi <i>et al</i> [40], 2020	314	CNN	The prognostic significance was evaluated by CNN based on the expression of tumor markers in 314 patients	CNN could help to evaluate the diagnosis and prognosis of tumor markers
Case control study	Pham[41], 2017	NA	DL	NA	DL could reduce training time and improve classification rate
Case control study	Tiwari[42], 2018	10	CNN	CNN was used to compare the accuracy of image classification methods for seven different tissue types	CNN determined the most suitable color for cancer tissue classification (HSV color space) by classifying tissues in different color spaces
Case control study	Sirinukunwattana <i>et al</i> [43], 2016	100	SC-CNN	Through the comparative evaluation on the image data set of 100 cases of CRC, SC-CNN was helpful to the quantitative analysis of tissue components	SC-CNN can help to predict the nuclear class tags more accurately
Case control study	Koohababni <i>et al</i> [44], 2018	NA	DL	NA	DL could combine the probability maps of a single nucleus to generate the final image, so as to improve the diagnostic performance of complex colorectal adenocarcinoma datasets
Case control study	Zhang <i>et al</i> [45], 2018	NA	Faster R-CNN	NA	Faster R-CNN provided quantitative analysis of tissue composition in pathological practice
Case control study	Xu <i>et al</i> [46], 2016	1376	DCNN	Compared the classification effects of AI and manual methods on the same pathological image dataset	DCNN can help to improve the accuracy of differentiation between epithelial and mesenchymal regions in digital tumor tissue microarray

Retrospective study	Chen <i>et al</i> [47], 2017	85	Deep contour-aware network	The classification performance of different segmentation methods on the same pathological image dataset was compared	Output accurate probability map of gland cells, draw clear outline to separate the originally gathered cells, and further improve the segmentation performance
Case control study	Yoshida <i>et al</i> [48], 2017	1328	An automated image analysis system	The classification results of the same dataset by human pathologists and electronic pathologists were compared	Compared with manual classification, the system had higher classification accuracy
Retrospective study	Saito <i>et al</i> [49], 2013	NA	CAD system	NA	CAD system could be used for quality control, double check diagnosis, and prevention of missed diagnosis of cancer
Descriptive research	Jin <i>et al</i> [50], 2019	NA	AI	NA	AI accelerated the transformation of pathology to quantitative direction, and provided annotation storage, sharing, and visualization services
Case control study	Qaiser <i>et al</i> [51], 2019	75	CNN	The segmentation and recognition effects of different methods on the same pathological dataset were compared	CNN and PHPs can more accurately and quickly distinguish tumor regions from normal regions by simulating the atypical characteristics of tumor nuclei
Retrospective study	Zhou <i>et al</i> [53], 2020	120	DCNN	In the man-machine competition of 120 images, the accuracy of AI and endoscopists was compared	DCNN helped to establish an objective and stable bowel preparation system
Case control study	de Almeida <i>et al</i> [54], 2019	NA	CNN	NA	CNN improved the accuracy of polyp segmentation. It can help to automatically increase the sample number of medical image analysis dataset
Case control study	Taha <i>et al</i> [56], 2017	15	DL	The effectiveness of the DL method for identifying polyps in colonoscopy images was verified on the public database	In the early screening of CRC, it was better than other single models
Case control study	Yao <i>et al</i> [57], 2019	NA	DL	NA	A DL algorithm in HSV color space was designed to effectively improve the accuracy of diagnosis and reduce the cost
Case control study	Bravo <i>et al</i> [59], 2018	NA	Supervised learning model	NA	Supervised learning model could help to detect polyps more than 5 mm automatically with high accuracy
Review	de Lange <i>et al</i> [60], 2018	NA	CAD system	NA	CAD system could eliminate the leakage rate of polyps, thus avoiding polyps from developing into CRC
Case control study	Mahmood <i>et al</i> [61], 2018	NA	CAD system	NA	CAD system combined with depth map could more accurately identify polyps or early cancer tissue
Retrospective study	Mo <i>et al</i> [62], 2018	16	DL	Compared the performance of multiple algorithms in the same dataset	DL was in the leading position in many aspects such as the performance of evolutionary algorithm, and was an effective clinical method
Case control study	Zhu <i>et al</i> [63], 2010	50	CAD system	Through the database of 50 patients, the performance differences of different segmentation strategies were compared	Initial polyp candidates could greatly facilitate the FP reduction process of CAD system
Case control study	Komeda <i>et al</i> [64], 2017	1200	CNN-CAD system	The efficiency of CNN-CAD system was evaluated by maintaining cross validation	CNN-CAD system can quickly diagnose colorectal polyp classification

				for 10 times	
Retrospective study	Zhang <i>et al</i> [65], 2018	18	CNN-CAD system	Through the video of 18 cases of colonoscopy, the efficiency of polyp detection between CNN-CAD system and existing methods was compared	CNN-CAD system can reduce the chance of missed diagnosis of polyps
Case control study	Zhu <i>et al</i> [66], 2019	357	CNN	The diagnostic performance of CNN was trained, fine-tuned, and evaluated using endoscopic data of 357 patients, and compared with that of manual diagnosis	The sensitivity of CNN optical diagnosis is higher than that of endoscopy, but the specificity is lower than that of endoscopy
Retrospective study	Akbari <i>et al</i> [67], 2018	300	FCN	The polyp segmentation method based on CNN was evaluated using CVC ColonDB database	FCN proposed a new method of image block selection and the probability map was processed effectively
Retrospective study	Yu <i>et al</i> [68], 2017	NA	3D-FCN	NA	3D-FCN could learn representative spatiotemporal features, and it had strong recognition ability
Case control study	Yamada <i>et al</i> [69], 2019	4395	AI	The AI system was trained through a large amount of data to make it sufficient to detect missed non polypoid lesions with high accuracy	AI could automatically detect the early features of CRC and improve the early detection rate of CRC
Retrospective study	Lund <i>et al</i> [71], 2019	20	DL	Polyp video dataset was used as training data. At the same time, a 5-fold cross validation method was used to evaluate the accuracy of the system	DL could improve the network training efficiency of polyp detection accuracy
Meta-analysis	Takamaru <i>et al</i> [73], 2020	NA	Endocytoscopy	NA	AI combined with endocytoscopy could greatly improve the efficiency of optical biopsy of CRC
Review	Djinbachian <i>et al</i> [76], 2019	NA	AI	NA	The sensitivity of optical diagnosis based on AI could be comparable to that of experienced endoscopists
Retrospective study	Kudo <i>et al</i> [77], 2019	69142	EndoBRAIN	A retrospective comparative analysis was performed between EndoBRAIN and 30 endoscopists on the diagnostic performance of endoscopic images in the same dataset	In the image of color cell endoscopy, EndoBRAIN could distinguish between tumor and non-tumor lesions accurately
Retrospective study	Mahmood <i>et al</i> [78], 2018	NA	CRF	NA	CRF estimated the depth of the colonoscopy image and reconstructed the surface structure of the colon
Case control study	Jian <i>et al</i> [81], 2018	2772	FCN	Quantitative comparison of manual and AI segmentation results of 2772 cases of CRC in MRI images	FCN was helpful for accurate segmentation of colorectal tumors
Case control study	Sivaganesan[82], 2016	20	RNN-ALGA	In the same database, milestone algorithms such as graph cut and level set were compared with RNN-ALGA algorithm	RNN-ALGA is suitable for abdominal slice of CT image, which can improve the accuracy and time efficiency of structure segmentation
Case control study	Gayathri <i>et al</i> [83], 2015	NA	NN	NA	NN can help to remove the colonic effusion and obtain the ideal colon segmentation effect
Retrospective study	Therrien <i>et al</i> [84], 2018	NA	SVM, CNN	NA	Using multiple datasets to train SVM and CNN could more accurately distinguish CRC staining tissue than single dataset
Case control study	Sun <i>et al</i> [85], 2019	NA	ML	NA	ML increased the chance of recognizing tumor bud by narrowing the region, thus

					providing effective tissue classification
Case control study	Shi <i>et al</i> [86], 2010	NA	DS-STM	NA	DS-STM could reduce the cost of diagnosis
Case control study	Su <i>et al</i> [87], 2012	212	MVMTM	The training set included 124 cases. The validation set included 88 cases. Compared the diagnostic efficiency of different methods for CRC	Compared with the traditional ML method, MVMTM has the advantages of low cost
Case control study	Kunhoth <i>et al</i> [88], 2017	80	Multispectral image acquisition system	A group of 20 samples were selected from 4 different types of colorectal cells. Compared the accuracy of different feature extraction methods	The database developed by this system had high classification accuracy
Case control study	Wang <i>et al</i> [89], 2018	1290	DL	Through the data of 1290 patients, an AI algorithm for real-time polyp detection was developed and verified	Compared with ML, DL could detect polyps in real time and reduce the cost
Meta-analysis	Barua <i>et al</i> [90], 2021	NA	AI	NA	AI based polyp detection system could increase the detection of small non-progressive adenomas and polyps
Randomized controlled study	Gong <i>et al</i> [91], 2020	704	ENDOANGEL system	704 patients were randomly assigned to use the ENDOANGEL system for colonoscopy or unaided (control) colonoscopy to compare the efficiency of ENDOANGEL system with conventional colonoscopy	The system significantly improved the detection rate of adenoma in colonoscopy
Meta-analysis	Lui <i>et al</i> [92], 2020	NA	AI	NA	AI system could improve the detection rate of adenoma and reduce the missed lesions in real-time colonoscopy
Case control study	Rodriguez-Diaz <i>et al</i> [93], 2011	134	A diagnostic algorithm with ESS	80 patients were randomly assigned to the training set, and the remaining 54 patients were assigned to the test set for prospective verification by the new algorithm	The algorithm with ESS reduced the risk and cost of biopsy, avoided the removal of non-neoplastic polyps, and reduced the operation time
Case control study	Kondepati <i>et al</i> [94], 2007	37	ANN	The tumor recognition accuracy of different algorithms was compared by collecting the spectra of cancer tissue and normal tissue	The spectrum was divided into cancer tissue group and normal tissue group by ANN, and the accuracy was 89%
Case control study	Angermann <i>et al</i> [95], 2016	NA	AL	NA	AL helped to realize real-time detection and distinguish between polyps and cancer tissues
Case control study	Ayling <i>et al</i> [96], 2019	619	ColonFlagTM	Through the clinical data of 619 patients, the performance of different systems in detecting CRC and high adenoma was compared	ColonFlagTM could help special patients establish an appropriate safety net
Meta-analysis	Tian <i>et al</i> [97], 2020	4560	EPE	Ten randomized controlled trials were included and 4560 participants were included for meta-analysis	EPE could guide the intestinal preparation of patients undergoing colonoscopy, and improve the detection rate of polyps, adenomas, and sessile serrated adenomas
Retrospective study	Javed <i>et al</i> [98], 2018	NA	QSL	NA	The prevalent communities found by QSL represented different tissue phenotypes with biological significance
Case control study	Wang <i>et al</i> [99], 2019	328	ANN	Different diagnostic models were established by back propagation and other	ANN combined with gene expression profile data could improve the diagnosis mode of

				methods, and the performance of each model was evaluated by cross validation test	CRC
Case control study	Battista <i>et al</i> [100], 2019	345	ANN	The diagnostic performance and FP of the new model were measured in the experimental group (patients with CRC) and the control group (patients with good health)	ANN could help to establish an easily available, low-cost mathematical tool for CRC screening
Review	Zhang <i>et al</i> [101], 2021	NA	ML	NA	ML based on cell-free DNA and microbiome data helped diagnose CRC
Case control study	Wang <i>et al</i> [102], 2021	9631	DCNN	The diagnostic accuracy of AI tools and experienced expert pathologists was compared through the same database	A novel strategy for clinic CRC diagnosis using weakly labeled pathological whole-slide image patches based on DCNN
Review	Jones <i>et al</i> [103], 2021	NA	AI	NA	Electronic health record type data combined with AI could help diagnose early cancer
Case control study	Lorenzovici <i>et al</i> [104], 2021	33	A computer aided diagnosis system	The accuracy of the system in diagnosing CRC was tested through a dataset of 33 patients	The system used ML to improve the accuracy of CRC diagnosis
Review and Meta-analysis	Xu <i>et al</i> [105], 2021	NA	CNN	NA	Through the comparative study of online database, CNN system had good diagnostic performance for CRC
Case control study	Öztürk <i>et al</i> [106], 2021	NA	CNN	NA	CNN was the most successful method that could effectively classify gastrointestinal image datasets with a small amount of labeled data
Review	Echle <i>et al</i> [107], 2021	NA	DL	NA	DL could directly extract the hidden information from the conventional histological images of cancer, so as to provide potential clinical information

NA: Not available; DL: Deep learning; ML: Machine learning; AL: Active learning; QSL: Quasi-supervised learning; CNN: Convolutional neural network; CRC: Colorectal cancer; SVM: Support vector machine; CAD: Computer-aided diagnosis; CTC: Computed tomography colonography; CT: Computed tomography; FP: False-positive rate; DCNN: Deep convolutional neural network; CADe: Computer-aided detection; 3D: Three-dimensional; MRI: Magnetic resonance imaging; AI: Artificial intelligence; R-CNN: Region-based convolutional neural network; SC-CNN: Space-constrained convolutional neural network; PHPs: Persistent homology maps; HSV: Hue, saturation, value; FCN: Fully convolutional network; CRF: Conditional random field; DS-STM: Diagnosis strategy of serum tumor maker; MVM: Multiple tumor markers with multiple cut-off values; ANN: Artificial neural network.

included an increased consistency rate after multiple disciplinary team implementation, a low consistency rate in elderly patients, and a high consistency rate in patients receiving chemotherapy. The results proved that Watson for Oncology might be helpful to simulate the effect of multiple disciplinary teams. Using evidence-based guidelines and simplifying treatment pathways, multidisciplinary care could provide best practices[110]. It is crucial to achieving personalized treatment since radiotherapy and chemotherapy are very painful. However, it is impossible to individualize patient treatment because the clinical situation of patients cannot easily link with DNA mutation[111]. Siddiqi *et al*[111] designed a MATCH system that provided a unique combination of clinical and genetic sequence data and constructed a database for all users. The MATCH system was currently providing hundreds of data samples, including clinical information, tumor markers, proteome sequences, gene inhibitors, *etc.* The importance of all data attributes and the corresponding processing information were modifiable[111]. Moreover, the system was developed with web services, which guaranteed interoperability among hospitals, pharmaceutical laboratories, and research centers, allowing them to access and exchange samples, information, and data models. The MATCH system helped identify the correlation between medical features so that oncologists could understand each patient's individual situation[111]. Nanorobots are expected to become intelligent drug delivery systems that respond to small molecular triggers[112]. Felfoul *et al*[113] developed a nanorobot that could deliver drugs to cancer cells. The robot sensed the concentration of hypoxia and

delivered drugs in the “anoxic area” generated by the active proliferation of cancer cells. The robot achieved an accurate effect of attacking cancer tumors[113]. Li *et al* [112] developed a nanorobot, which could kill cancer cells by releasing procoagulant substances in the cancer tissue, interrupting the blood supply to the cancer tissue. The greatest progress of robots is that it can significantly improve the targeting of chemotherapy drugs and reduce the killing effect of chemotherapy drugs on human normal tissues.

ML in immunotherapy pathway

Computational pathology can help obtain complete and repeatable datasets to promote individualized prediction of immunotherapy. ML can help evaluate the expression of immunohistochemical markers, tumor morphology, and the spatial distribution of tumor-infiltrating lymphocytes. The methylome group features queried by ML are proved to be suitable for predicting the response to immunosuppressive checkpoint inhibitors. Similar to image analysis, this method considers both tumor cells and reactive cells. The immune profiling is detected by spatial analysis and multiplexing of tumor immune cell interaction, and it is used as a predictor of patients’ response to cancer treatment[114]. ML can be used to inhibit the Wnt/beta-catenin signaling, which is beneficial in cancer therapy[115], and it has the potential to provide new therapeutic strategies for patients by recognizing the interaction of tumor cells [114].

AI in endoscopic and surgical therapy

The estimation of the invasion depth is an important step in successfully implementing endoscopic submucosal dissection[116]. At present, narrow-band imaging with magnifying endoscopy is a practical method to estimate the invasion depth of CRC. Lee *et al*[116] used AI to interpret the cell endoscope images. Processing thousands of images, the algorithm could diagnose more than 90% of invasive CRC in hundreds of images detected[116]. Although the incidence of lymph node metastasis is relatively low, most T1 CRCs still need to undergo colectomy and lymphadenectomy [117]. Ichimasa *et al*[117] used the data of hundreds of patients in the AI model. The model analyzed 45 clinical and pathological factors and predicted positive or negative lymph node metastasis. The operation specimen is the gold standard of lymph node metastasis. Model validation results showed that patients received many unnecessary surgeries without lymph node metastasis[117]. AI can reduce unnecessary surgeries after endoscopic resection of T1 CRCs by predicting the presence of lymph node metastasis[117].

Compared with open surgery, a minimally invasive one is superior in short-term prognosis and long-term efficacy[118]. With the increasing popularity of laparoscopic surgery, the number of robotic surgeries is also growing. Surgeons can control the robot system 100% and perform more accurate operations at any time[119]. Kim[119] reported an animal experiment in which the effect of using smart tissue autonomous robots was comparable or even superior to open surgery, laparoscopic surgery, or robotic surgery[119]. The smart tissue autonomous robot integrates the sewing tool, robot arm, force sensor, and camera in hardware and software. The robot has the ability to stitch soft tissue. The efficiency of the robot sutured on the plane was 5 times faster than that of the surgeons, and 9 times faster than that of the surgeons using laparoscopic manual tools. Experiments also showed that the stitching robot was more accurate and consistent[120]. Compared with the Da Vinci Si robot system, the new Da Vinci Xi increased more flexibility of operation, and it was expected to promote the performance of multi quadrant surgery[121]. The clinicopathological characteristics and perioperative outcomes of patients with two kinds of robot systems were analyzed. The results showed that the ileostomy rate of Xi group was low, the operation time was short, the amount of bleeding was small, and the recovery was fast [121]. Surgeons can input operation instructions, order medical robots to perform complicated operations, and constantly monitor the operation on the monitor. During the operation, the surgeon can see the anatomical structure without opening the abdomen. Because the fluorescent dye is injected before the operation, the malignant cells and tissues can be visible. As a result, doctors can remove lesions more precisely [119]. Because of the precise recognition and detailed operation of robotic surgery, the learning curve of robotic colorectal surgery is shorter than that of laparoscopic surgery.

Robotic surgeries are beneficial in minimally invasive surgery of tumors, such as high-resolution and stable 3D views, optimal *in situ* free movement, and elimination of natural tremors[118]. However, in the face of a real surgical suture, the robot exposes its limitations. The complex structure of the human body requires the robot to spend

much time processing information about the anastomosis, which is obviously not beneficial in the time-consuming operation. Therefore, improving the image recognition and processing ability of the robot is the right direction to improve and develop the robot's autonomous stitching[120]. Compared with traditional laparoscopic surgery, robot surgery has some benefits, such as less urinary and sexual dysfunction and less intraoperative blood loss. However, more powerful evidence is needed[122]. Due to the high cost of robot, it will take a while to collect the data of robot surgery. However, as competition can decrease the price of robotic surgical systems, its promotion will be accelerated in the future. In robotic CRC surgery, many limitations have presented, such as the lack of unified technical standards and excessive dependence on surgical robot equipment. The problems will be solved by establishing training system and integrating medicine, research, and production. During clinical studies and large data analysis, robotic surgery will be the new development trend of colorectal surgery[122]. Other studies also described the application of AI in the therapy of CRC[123-127] (Table 2).

USE OF AI IN PROGNOSIS EVALUATION OF CRC

As one of the most common cancers globally, CRC is a result of multi-step and multi-factor action. The key to early diagnosis and improving the overall survival rate is determining the high-risk population[128]. Some related risk factors may increase the possibility of CRC, such as age, lifestyle, personal disease history, and genetic syndrome[129]. In order to establish a risk prediction model of CRC, appropriate feature selection is needed. It is important to identify features with predictive power for taking appropriate interventions to address risks[130]. Each AI technology generates different important attributes to evaluate tumor prognosis based on potential biases and assumptions. Based on the accuracy and the minimum deviation, it is clear that the most significant tumor characteristics are lymphocyte infiltration, Dukes stage, age, and mitotic count[131]. Tumor invasiveness score is a new prognostic factor for predicting tumor stage in colon cancer patients[132]. It helps use ML to increase patient ethnicity in cancer survivability prediction and support personalized general medicine[133]. Most medical studies concentrate on treatment and etiology rather than prediction because prediction tends to be uncertain and risky. The decision tree classifier can predict recurrence or death according to various factors. It is beneficial for doctors to make further treatment decisions and avoid unnecessary treatments[134]. An accurate prognosis is a basis of making an appropriate treatment plan for cancer patients. Because of the heterogeneity of the disease and the inherent limitations of the pathological reporting system, the outcomes are very different for patients in similar stages of pathology. ML used different types of features that could be easily collected from immunofluorescence images to predict phase II mortality, and ML had more accuracy than current clinical guidelines[135].

ML in prognosis evaluation

The molecular subtype of CRC can be used as a prognostic indicator of relapse-free survival rate. The determination of molecular subtype depends on the analysis of hundreds of genes[136]. Popovici *et al*[136] proposed a method to recognize CRC molecular subtypes from conventional histological images based on an SVM classifier. They used the DCNN to extract the local descriptors and then construct the dictionary representation of each tumor sample. A set of SVM classifiers were trained to solve different binary decision problems. The combined output was used to predict the molecular subtype. The overall accuracy of the results was very high[136]. It was beneficial to improve the accuracy of prognosis prediction. Zhang *et al*[128] collected genetic variation and environmental information of CRC patients and cancer-free controls, trained the model with the large data, and established a multi-method integrated model. The model could effectively predict CRC risk[128]. The improved heterogeneous integrated learning model and generalized kernel recursive maximum correlation entropy algorithm had higher prediction ability than SVM[128]. ML is used to extract disease prediction models from electronic medical records[137]. ML can also solve many electronic medical record data, such as timeliness, imprecision, and integrity[129,138]. Hoogendoorn *et al*[137] could extract useful information from consulting notes, and the prediction performance of the ontology-based extraction method was significantly beyond the age and gender benchmark. It has been proved that the best way to predict CRC is by linking medical record texts with medical concepts[137].

Table 2 Artificial intelligence in treatment of colorectal cancer

Type of study	Ref.	Method	Conclusion
Retrospective study	Passi <i>et al</i> [109], 2015	DSS system	DSS system used follow-up data as a knowledge source to generate appropriate follow-up recommendations for patients receiving treatment
Retrospective study	Lee <i>et al</i> [110], 2018	Watson for Oncology	Watson for Oncology could provide evidence-based treatment advice for oncologists
Retrospective study	Siddiqi <i>et al</i> [111], 2008	MATCH system	MATCH system could provide hundreds of data samples to help doctors choose the most personalized treatment plan
Retrospective study	Li <i>et al</i> [112], 2018	Nanorobot	Nanorobots were relatively safe and immune inert. DNA nanorobots might represent a strategy for precise drug delivery in cancer treatment
Experimental study	Felfoul <i>et al</i> [113], 2016	Nanorobot	The robot achieved an accurate effect of attacking cancer tumors
Review	Koelzer <i>et al</i> [114], 2019	ML	The combination of ML and computational pathology could inform the clinical choice and prognosis stratification of CRC patients
Retrospective study	Lee <i>et al</i> [116], 2019	Narrow-band imaging	Narrow-band imaging helped doctors to predict the histology of colorectal polyps and estimate the depth of invasion
Meta-analysis, Case control study	Ichimasa <i>et al</i> [117], 2018	AI	AI could reduce unnecessary surgery after endoscopic resection of stage T1 CRC without loss of lymph node metastasis
Review	Kirchberg <i>et al</i> [118], 2019	Operation robot	Robotic surgery had great potential, but it still needed high-quality evidence-based medicine
Experimental study	Leonard <i>et al</i> [120], 2014	Smart tissue autonomous robot	Smart tissue autonomous robot was more accurate than surgeons using the most advanced robotic surgical system
Case control study	Huang <i>et al</i> [121], 2019	Operation robot	The operation robot had the advantages of short operation time, low estimated bleeding, and fast recovery after operation
Review	Zheng <i>et al</i> [122], 2020	Operation robot	There were some limitations, such as the disunity of technical standards and the excessive dependence on surgical robot equipment
Review	Mitsala <i>et al</i> [123], 2021	Computer-assisted drug delivery techniques	The technology could help to enhance the sensitivity and accuracy of targeted drugs
Case control study	Aikemu <i>et al</i> [124], 2020	AI	AI provided personalized and novel evidence-based clinical treatment strategies for CRC
Review	Hamamoto <i>et al</i> [125], 2020	AI	AI provided a variety of new technologies for the treatment of CRC, such as surgical robots, drug localization technology, and various medical devices
Review	Pritzker[126], 2020	AI	AI could screen individual biomarkers for comprehensive and individualized treatment of colon cancer with low toxicity
Experimental study	Ding <i>et al</i> [127], 2020	AI	The drug dose optimization technology based on AI could achieve more accurate individualized treatment than traditional methods

AI: Artificial intelligence; CRC: Colorectal cancer; DSS: Decision support system; ML: Machine learning.

The visual estimation of stroma ratio in microscopic images provides a strong predictor of survival rate in patients with CRC[139,140]. However, visual assessment is highly influenced by the observer and interstitial variation. Based on supervised learning, an objective quantitative method of tumor and stroma was established. Compared with the visual estimation of pathologists, the automatic tissue quantitative method was reliable and practical because it provided a new way to evaluate the prognosis and was crucial to predicting the tumor's survival ability[139]. Wang *et al* [141] developed a two-stage model to predict the survival of patients with advanced cancer. The first stage predicted whether patients could survive for more than 5 years. The second stage predicted the exact survival time of patients who could not survive for 5 years (in months). With low prediction error and good generalization performance, the two-stage model could help make treatment decisions, improve patient satisfaction, save medical resources, and reduce medical costs[141]. Based on the knowledge representation method of probability, Oliveira *et al*[142] designed a Clinical Decision Support System (CDSS) which, based on the cancer patients' records and the precise knowledge of experts, could propose an effective treatment scheme and solve the uncertainty of prognosis after surgery[142]. CDSS could complete four basic tasks: Data organization, data collection, the combination of various principles and specific data, and user-friendly display of analysis results. CDSS screened out appropriate

treatment methods from the aspects of curative effect, total survival rate, and side effect rate[143]. By comparing the treatment and prognosis of 250 cancer patients, Aikemu *et al*[124] found that Watson for Oncology could replace oncologists to provide patients with cutting-edge medical research and knowledge to a certain extent. It was also believed that the use of Watson for Oncology and other decision support tools could help achieve the promise of precision medicine[124].

Although resection of colon polyps can reduce the incidence rate and mortality of CRC by 75%, there is no individualized surveillance plan for polyp recurrence risk. Harrington *et al*[144] extracted polyp features from colonoscopy and pathological reports. The features extracted from these records and other demographic and anthropometric information were used to develop and compare ML models to predict polyp recurrence. The evaluation of the ML model further emphasized the important characteristics of predicting polyp recurrence from population and health records. RF model could detect patients with a high risk of recurrence and promote frequent follow-ups [144]. It is of great significance for individualized medical treatment. In order to improve the classification of polyps, Xie *et al*[145] proposed biometric modeling and ML methods to build polyp classifiers and screened the results of colonoscopy in a Chinese formation. The results showed that the RF model could improve the prediction performance compared with other methods[145]. Xie *et al*[145] also provided evidence that emotional state might be an influential factor in the early growth of CRC in China.

DL in prognosis evaluation

A deep network can directly predict the prognosis of CRC according to the morphological characteristics of tumor tissue samples[61]. Patients with CRC will benefit from the detection of TB, which is a reliable prognostic biomarker. DL can greatly reduce the number of FPs by detecting TB in H&E stained sections[146]. Zhao *et al*[147] proposed a DL model for automatic tumor-stroma ratio quantification using HE staining images of CRC. The model could eliminate the errors caused by traditional visual evaluation and reduce the work intensity of pathologists. Therefore, Zhao *et al* [147] believed that the model was suitable for clinical practice and might be helpful for clinical prognosis prediction and decision-making. Multimodal Deep Boltzmann Machine (DBM) is a DL structure used to predict patients' survival time. Syafiandini *et al*[148] integrated gene expression and clinical data into a new data form. The new data had few eigenvalues. In the multi-mode DBM architecture, these data were extracted from the joint hidden layer to identify gene subtypes, predict the response to a certain treatment, and find the most suitable treatment for patients[148]. Roadknight *et al*[149] described a dataset on the cellular and physical conditions of CRC patients who underwent surgical resection. These data provided unique immune status information for tumor resection, tumor classification, and postoperative survival[149]. Roadknight *et al*[149] studied the clustering and ML of these data to prove that the integrated method could predict the prognosis of patients. Compared with SVM, the better way to predict the tumor-node-metastasis stage from immunohistochemical markers is to use the anti-learning method[149]. Compared with other algorithms, the anti-learning method can more accurately predict cancer stage and survival rate from immune attributes[6].

SSL in prognosis evaluation

SSL methods use labeled or unlabeled data and graph regularization to predict patient survival and cancer recurrence[150,151]. The data of gene expression is transformed into the graph structure of SSL, and the data of protein interaction and gene expression are integrated to select gene pairs[151]. SSL methods can result in more accurate prediction than traditional SVM[11,150]. Recognition of cancer-related mutations is essential for understanding the cancer genomes that cause cancer gene activation or tumor suppressor gene inactivation[152]. Du *et al*[152] proposed a new feature selection method based on supervised learning that could identify gene mutations. The model was composed of the best features in candidate features' set with rotation forest. The method had a high accuracy and high prediction performance[152]. Chi *et al*[153] used the semi-supervised logistic regression method to establish the clinical prediction model of CRC survival risk. The performance of the model was strictly compared with that of other supervised learning models[153]. The model of CRC survival risk prediction established by the SSL method had good correction ability, popularization, interpretability, and clinical practicability. Other commonly used supervised learning methods, such as SVM, RF, and NN, showed poor calibration performance[153]. The SSL model might have more potential to develop a better risk prediction model in the actual clinical environment than the supervision model[153].

Other algorithms of AI in prognosis evaluation

The CRC recurrence support (CARES) system guided the prognosis by comparing the patients with new CRC and those with previous CRC to determine the high-risk group. As a result, only high-risk patients could receive more stringent examinations with reduced medical costs, while low-risk patients could be free from frequent and unnecessary examinations[154]. Immune cores could predict the prognosis of patients with colon cancer, and AI could detect additional prognostic markers on pathological sections. Digital tumor parameters (DGMate) were used to detect the digital parameters related to prognosis in tumor cells. The higher density of CD3+ tumor core, CD3+ invasive margin, and CD8+ tumor core was found, and the longer relapse-free survival was reported. CD3+ tumor core had a similar value to the classical CD3/CD8 immune core in prognosis. It was indicated that AI could help pathologists determine the prognosis of patients with colon cancer, which might improve patient treatments[155]. The existing methods describe the coordination among multiple genes by the additive representation of expression spectrum and use a fast heuristic method to identify the disjointed subnetworks. The methods may not be suitable for the potential combination of the disjointed genes[156]. Chowdhury *et al*[156] designed the Crane algorithm to solve this problem and proposed that the Crane algorithm was better than the addition algorithm in predicting CRC metastasis. In addition, AI could also be used to build CRC education software, whose menu contained an introduction, signs and symptoms, risk factors, preventive measures, and CRC screening procedures. The education software could achieve publicity and popularization of common sense through the communication between clinicians and patient representatives[157]. Other study also described the application of AI in the prognosis of CRC [158] (Table 3).

DISCUSSION

AI plays an important role in the fields of computer, internet, and vehicle engineering. The four main directions of future medical development are “personalization, precision, minimal invasion, and remoteness”[159]. In the field of medicine, first, AI gradually shows its advantages in disease diagnosis, treatment, and prognosis. CRC is one of the common human cancers, and its early diagnosis and standardized treatment have a profound impact on the prognosis. The development of AI for CRC has gone through the following stages: (1) Understanding cancer at the molecular and cellular levels through DL; (2) Assisting in the diagnosis of CRC according to images and pathological specimens; (3) Clinical drug designing and screening; and (4) Promoting the individualization of CRC diagnosis and treatment[159]. The diagnosis of CRC is mainly divided into imaging diagnosis and pathological diagnosis. Most of the imaging datasets are objective datasets with a high degree of information standardization. The CAD system based on DL realizes the automatic analysis and optimization of diversified images by extracting features from experts, extensive image training, making classification rules, and establishing mathematical models. Second, AI is beneficial to medical image analysis. Highly efficient image processing and analysis speed can quickly give auxiliary judgment results. Good sensitivity can reduce the missed diagnosis rate. Expert knowledge learning and quantitative data analysis can improve the quality of the basic inspection. Third, in clinical pathology, many digital sections of CRC have been accumulated, and some have been preliminarily developed with the technology of image recognition and DL. However, at present, AI cannot be separated from the auxiliary role. AI application at the functional level mainly includes disease diagnosis support and treatment decision support. The development of disease diagnosis support is active in treatment decision support. Advanced technologies are integrated with medicine and gradually play a necessary role in assisting diagnosis and early screening of major diseases.

Although AI is developing rapidly, it is still in the experimental stage and still faces many development bottlenecks. For example, first of all, the development of AI overemphasizes “probability association,” but diseases always exist in unknown areas. How to combine data and medical knowledge is the key to the development of image AI. Second, AI-based DL requires much label data for training. Although labeled data has more influence on training results than algorithms, high-quality data acquisition for training is a big problem. Third, the image data standardization is low. The level of image system interaction operation in different hospitals is low. Moreover, the datasets of each imaging system are scattered all over the country with a low level of interaction. Fourth, the difficulty of data annotation is great. The AI training requires a

Table 3 Artificial intelligence in prognosis evaluation of colorectal cancer

Type of study	Ref.	Method	Conclusion
Case control study	Zhang <i>et al</i> [128], 2017	Heterogeneous ensemble learning model	Heterogeneous ensemble learning model could use big data to identify high-risk groups of CRC patients
Retrospective study	Morgado <i>et al</i> [129], 2017	Decision support system	Decision support system could evaluate the risk of CRC by processing incomplete, unknown, or even contradictory data
Case control study	Anand <i>et al</i> [131], 1999	Intelligent hybrid system	Each AI technology produced a different set of important attributes. Intelligent hybrid system would be the trend of prognosis evaluation in the future
Case control study	Gupta <i>et al</i> [132], 2019	ML	ML could help to predict tumor stage and survival period
Case control study	Li <i>et al</i> [133], 2018	ML	Combining ML and database, clinicians might add race factor to evaluate prognosis
Case control study	Barsainya <i>et al</i> [134], 2018	Decision tree classifier	Decision tree classifier could predict recurrence and death according to various influencing factors
Cohort study	Dimitriou <i>et al</i> [135], 2018	ML	A framework for accurate prognosis prediction of CRC based on ML datasets
Case control study	Popovici <i>et al</i> [136], 2017	SVM	The accuracy of using SVM to distinguish CRC subtypes was very high
Experimental study	Hoogendoorn <i>et al</i> [137], 2016	AI	AI helped doctors to extract useful predictors from non-coding medical records
Experimental study	Kop <i>et al</i> [138], 2016	ML	The combination of ML and electronic medical records could help early detection and intervention
Case control study	Geessink <i>et al</i> [139], 2015	Supervised learning	Supervised learning helped to predict the survival ability of tumor, so as to accurately stratify the prognosis of tumor patients
Review	Wright <i>et al</i> [140], 2014	RF	RF could reduce the workload of pathologists by automatically calculating the area ratio of each slide
Meta-analysis	Wang <i>et al</i> [141], 2019	A two-stage ML model	Compared with the single-stage regression model, the two-stage model could obtain more accurate prediction results
Experimental study	Oliveira <i>et al</i> [142], 2013	CDSS	CDSS based on cancer patients records and knowledge could provide support for surgeons
Meta-analysis	Lo <i>et al</i> [143], 2000	CDSS	CDSS could select the appropriate treatment from the aspects of curative effect, overall survival rate, and side effect rate
Case control study	Harrington <i>et al</i> [144], 2018	ML	ML could be used to predict the risk of recurrence of colon polyps and cancer based on the pathological characteristics of medical records
Case control study	Xie <i>et al</i> [145], 2018	RF model	RF model helped to speculate the influencing factors of early CRC in China
Retrospective study	Bokhorst <i>et al</i> [146], 2018	DL	DL helped reduce FP by detecting tumor bud
Cohort study	Zhao <i>et al</i> [147], 2020	DL	The method allowed objective and standardized application while reducing the workload of pathologists
Retrospective study	Syafiandini <i>et al</i> [148], 2016	DBM	DBM helped to predict the survival time of cancer patients
Retrospective study	Roadknight <i>et al</i> [149], 2013	ML	ML helped predict the prognosis of patients according to the immune status and other information
Case control study	Cui <i>et al</i> [150], 2013	SSL	SSL improved the accuracy of predicting clinical results according to gene expression profile
Retrospective study	Park <i>et al</i> [151], 2014	SSL	SSL could improve the accuracy of predicting cancer recurrence
Retrospective study	Du <i>et al</i> [152], 2014	Supervised learning	Supervised learning could help to improve the accuracy of identifying cancer-related mutations
Case control study	Chi <i>et al</i> [153], 2019	Semi-supervised logistic regression method	Semi-supervised logistic regression method had better clinical prediction effect than supervised learning method
Review	Ong <i>et al</i> [154], 1997	CARES system	CARES system helped early detection of cancer recurrence in high-risk patients
Case control study	Reichling <i>et al</i> [155], 2020	DGMate	DGMate could judge the prognosis of tumor by detecting immunophenotype

Experimental study	Chowdhury <i>et al</i> [156], 2011	Crane algorithm	Crane algorithm helped to describe the coordination of multiple genes and effectively predicted the metastasis of CRC
Review	Mohamad <i>et al</i> [157], 2019	Nominal group technique	Nominal group technique was used in the content development of mobile app and the app used as a tool for CRC screening education
Retrospective study	Hacking <i>et al</i> [158], 2020	AI	AI could improve the prognosis of patients by increasing the diagnostic accuracy of slide images

CRC: Colorectal cancer; AI: Artificial intelligence; ML: Machine learning; SVM: Support vector machine; RF: Random forest; CDSS: Clinical Decision Support System; DBM: Deep Boltzmann Machine; SSL: Semi-supervised learning.

large amount of labeled image data, and the annotation needs to spend a lot of manual costs, which directly impacts the training results.

Meanwhile, the “black box” problem in ML raises several concerns clinically. ML can help read imaging and pathological pictures, recommend diagnosis and treatment options, and predict prognosis. However, due to the “black box” problem, the clinical application of AI tools progressed slowly. To further develop AI medicine, it is necessary to improve the interpretability of ML algorithms. The small steps of biological interpretation and clinical experience in ML algorithm can gradually solve the “black box” problem. In order to solve the above problems, data preprocessing is needed to complete the standardization, which requires the integration and fusion of heterogeneous data sets, such as images, physiological data, and information texts. At the same time, automatic software is used to analyze the medical image data quantitatively and extract a large number of features, including texture analysis, shape description, and other quantitative indicators.

The treatments for CRC are mainly surgery and chemotherapy. AI enables individual precision medicine by selecting appropriate treatment measures through big data analysis and comparison. At the same time, the development of robot technology provides a guarantee for the high accuracy of surgery and the high targeting of chemotherapy drugs. However, the quality of the data collection is still not enough to support AI to make treatment decisions independently. The complexity of the human body also reduces the speed of analysis and decision-making of AI in operations. In addition, robots cannot be widely used because of the high economic cost. Patients are often afraid of the unknown survival period after surgery, so giving a specific survival period can eliminate the psychological burden of patients. AI can predict the survival time and recurrence risk through patient information, surgery, and pathology and guide patients' prognosis and nursing. Therefore, high-quality, accurate data and standard operating specifications are required. In other words, the accuracy of prediction risk depends on the quality of the prognosis data, which in turn depends on the quality of data generated by diagnosis and treatment.

As diagnostic technology evolves, the information available to doctors is becoming more and more complex. In terms of treatment, new drugs are constantly developed, and new treatment schemes and methods are emerging. It is challenging for busy clinicians to have enough time and energy to obtain, screen, and use the information. With the continuous development of AI technology and image recognition, and the continued improvement of other aspects, AI will play an important role in CRC diagnosis and treatment. Therefore, the establishment of an AI standard system will be the top priority of future development. The standardization of images, features, medical record information, and other datasets will improve the accuracy of diagnosis and treatment. DL and ML will fully be combined to enable robots to complete surgery independently. Medical services include not only medical technology but also the guidance of patients' mental health. In the future, robots will provide nursing and adjust the psychological state of patients. However, moral and ethical issues must be well considered for the proper use of AI robots in today's medical environment.

Various countries have been trying to establish ethical, legal, and regulatory compliance standards for AI development. But there are many difficulties before fully accepting AI robots. First, patients' trust and acceptance will become an important factor in developing AI robotic surgery. The “black box” that has been used in many non-surgical applications has little theoretical transparency. In the medical field, lack of transparency impairs the doctors and patients' trust and acceptance of AI. Second, the safety of AI robot surgery is still an important issue to be concerned. The development of AI robot surgery involves a series of security problems, such as patient information protection, network security, robot autonomy, and machine failure. If the control of the AI robot is lost due to external factors such as network transmission delay and hacker attack, the immeasurable loss will happen. Third, the

responsibility attribution of medical malpractice remains a problem. Given the limitations of AI robots, the issues of medical malpractice responsibility will lead to a debate about the gray area of law. The solution of this problem will boost AI development[160].

CONCLUSION

Currently, AI is in the era of weak AI and does not have communication capabilities. Therefore, the current AI technology is mainly used for image recognition and auxiliary analysis without in-depth communication with patients. With the continuous development of AI technology, the role of AI in the diagnosis and treatment of CRC will continue to increase until the robot can complete surgery independently. At that time, AI will change the medical technologies and even the medical model.

ACKNOWLEDGEMENTS

We thank the anonymous referees for their useful suggestions.

REFERENCES

- 1 **Sivapalaratnam S.** Artificial intelligence and machine learning in haematology. *Br J Haematol* 2019; **185**: 207-208 [PMID: [30729496](#) DOI: [10.1111/bjh.15774](#)]
- 2 **Acs B, Rantalainen M, Hartman J.** Artificial intelligence as the next step towards precision pathology. *J Intern Med* 2020; **288**: 62-81 [PMID: [32128929](#) DOI: [10.1111/joim.13030](#)]
- 3 **El Hajjar A, Rey JF.** Artificial intelligence in gastrointestinal endoscopy: general overview. *Chin Med J (Engl)* 2020; **133**: 326-334 [PMID: [31929362](#) DOI: [10.1097/CM9.0000000000000623](#)]
- 4 **Min JK, Kwak MS, Cha JM.** Overview of Deep Learning in Gastrointestinal Endoscopy. *Gut Liver* 2019; **13**: 388-393 [PMID: [30630221](#) DOI: [10.5009/gnl18384](#)]
- 5 **Onder D, Sarioglu S, Karacali B.** Automated labelling of cancer textures in colorectal histopathology slides using quasi-supervised learning. *Micron* 2013; **47**: 33-42 [PMID: [23415158](#) DOI: [10.1016/j.micron.2013.01.003](#)]
- 6 **Roadknight C, Aickelin U, Qiu G, Scholefield J, Durrant L.** Supervised learning and anti-learning of colorectal cancer classes and survival rates from cellular biology parameters. Proceedings 2012 IEEE international conference on systems, man, and cybernetics. 2012: 797-802 [DOI: [10.1109/icsmc.2012.6377825](#)]
- 7 **Chen Y, Carroll RJ, Hinz ER, Shah A, Eyler AE, Denny JC, Xu H.** Applying active learning to high-throughput phenotyping algorithms for electronic health records data. *J Am Med Inform Assoc* 2013; **20**: e253-e259 [PMID: [23851443](#) DOI: [10.1136/amiajnl-2013-001945](#)]
- 8 **Le Berre C, Sandborn WJ, Aridhi S, Devignes MD, Fournier L, Smail-Tabbone M, Danese S, Peyrin-Biroulet L.** Application of Artificial Intelligence to Gastroenterology and Hepatology. *Gastroenterology* 2020; **158**: 76-94.e2 [PMID: [31593701](#) DOI: [10.1053/j.gastro.2019.08.058](#)]
- 9 **Jagga Z, Gupta D.** Machine learning for biomarker identification in cancer research - developments toward its clinical application. *Per Med* 2015; **12**: 371-387 [PMID: [29771660](#) DOI: [10.2217/pme.15.5](#)]
- 10 **Low SK, Nakamura Y.** The road map of cancer precision medicine with the innovation of advanced cancer detection technology and personalized immunotherapy. *Jpn J Clin Oncol* 2019; **49**: 596-603 [PMID: [31135897](#) DOI: [10.1093/jjco/hyz073](#)]
- 11 **Shi M, Zhang B.** Semi-supervised learning improves gene expression-based prediction of cancer recurrence. *Bioinformatics* 2011; **27**: 3017-3023 [PMID: [21893520](#) DOI: [10.1093/bioinformatics/btr502](#)]
- 12 **Gulati S, Patel M, Emmanuel A, Haji A, Hayee B, Neumann H.** The future of endoscopy: Advances in endoscopic image innovations. *Dig Endosc* 2020; **32**: 512-522 [PMID: [31286574](#) DOI: [10.1111/den.13481](#)]
- 13 **Wang P, Berzin TM, Glissen Brown JR, Bharadwaj S, Becq A, Xiao X, Liu P, Li L, Song Y, Zhang D, Li Y, Xu G, Tu M, Liu X.** Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. *Gut* 2019; **68**: 1813-1819 [PMID: [30814121](#) DOI: [10.1136/gutjnl-2018-317500](#)]
- 14 **Kang J, Gwak J.** Ensemble of instance segmentation models for polyp segmentation in colonoscopy images. *IEEE Access* 2019; **7**: 26440-26447 [DOI: [10.1109/access.2019.2900672](#)]
- 15 **Eisner R, Greiner R, Tso V, Wang H, Fedorak RN.** A machine-learned predictor of colonic polyps based on urinary metabolomics. *Biomed Res Int* 2013; **2013**: 303982 [PMID: [24307992](#) DOI: [10.1155/2013/303982](#)]
- 16 **Köküer M, Naguib RN, Jancovic P, Younghusband HB, Green RC.** Cancer risk analysis in families

- with hereditary nonpolyposis colorectal cancer. *IEEE Trans Inf Technol Biomed* 2006; **10**: 581-587 [PMID: [16871728](#) DOI: [10.1109/titb.2006.872054](#)]
- 17 **Bell CS**, Puerto GA, Mariottini G-L, Valdastrì P. Six DOF motion estimation for teleoperated flexible endoscopes using optical flow: A comparative study. 2014 IEEE international conference on robotics and automation. 2014: 5386-5392 [DOI: [10.1109/icra.2014.6907651](#)]
- 18 **Liu Z**, Wang S, Dong D, Wei J, Fang C, Zhou X, Sun K, Li L, Li B, Wang M, Tian J. The Applications of Radiomics in Precision Diagnosis and Treatment of Oncology: Opportunities and Challenges. *Theranostics* 2019; **9**: 1303-1322 [PMID: [30867832](#) DOI: [10.7150/thno.30309](#)]
- 19 **Yang T**, Liang N, Li J, Yang Y, Li Y, Huang Q, Li R, He X, Zhang H. Intelligent imaging technology in diagnosis of colorectal cancer using deep learning. *IEEE Access* 2019; **7**: 178839-178847 [DOI: [10.1109/access.2019.2958124](#)]
- 20 **Dalca A**, Danagouliau G, Kikinis R, Schmidt E, Golland P. Sparse classification for computer aided diagnosis using learned dictionaries. *Medical Image Computing and Computer-Assisted Intervention*, 2011: 537-545
- 21 **Regge D**, Halligan S. CAD: how it works, how to use it, performance. *Eur J Radiol* 2013; **82**: 1171-1176 [PMID: [22595503](#) DOI: [10.1016/j.ejrad.2012.04.022](#)]
- 22 **Summers RM**, Handwerker LR, Pickhardt PJ, Van Uitert RL, Deshpande KK, Yeshwant S, Yao J, Franaszek M. Performance of a previously validated CT colonography computer-aided detection system in a new patient population. *AJR Am J Roentgenol* 2008; **191**: 168-174 [PMID: [18562741](#) DOI: [10.2214/AJR.07.3354](#)]
- 23 **Chowdhury TA**, Whelan PF, Ghita O. A fully automatic CAD-CTC system based on curvature analysis for standard and low-dose CT data. *IEEE Trans Biomed Eng* 2008; **55**: 888-901 [PMID: [18334380](#) DOI: [10.1109/TBME.2007.909506](#)]
- 24 **Nappi JJ**, Hironaka T, Yoshida H. Detection of colorectal masses in CT colonography: Application of deep residual networks for differentiating masses from normal colon anatomy. *Medical imaging 2018: Computer-aided diagnosis*. Bellingham: Spie-Int Soc Optical Engineering, 2018 [DOI: [10.1117/12.2293848](#)]
- 25 **Taylor SA**, Iinuma G, Saito Y, Zhang J, Halligan S. CT colonography: computer-aided detection of morphologically flat T1 colonic carcinoma. *Eur Radiol* 2008; **18**: 1666-1673 [PMID: [18389248](#) DOI: [10.1007/s00330-008-0936-7](#)]
- 26 **Summers RM**. Current concepts in computer-aided detection for CT colonography. 2010 7th IEEE international symposium on biomedical imaging: From nano to macro. 2010: 269-272 [DOI: [10.1109/isbi.2010.5490363](#)]
- 27 **Lee JG**, Hyo Kim J, Hyung Kim S, Sun Park H, Ihn Choi B. A straightforward approach to computer-aided polyp detection using a polyp-specific volumetric feature in CT colonography. *Comput Biol Med* 2011; **41**: 790-801 [PMID: [21762887](#) DOI: [10.1016/j.combiomed.2011.06.015](#)]
- 28 **Nappi JJ**, Hironaka T, Regge D, Yoshida H. Deep transfer learning of virtual endoluminal views for the detection of polyps in CT colonography. *Medical imaging 2016: Computer-aided diagnosis*. Bellingham: Spie-Int Soc Optical Engineering, 2015 [DOI: [10.1117/12.2217260](#)]
- 29 **Näppi J**, Frimmel H, Yoshida H. Virtual endoscopic visualization of the colon by shape-scale signatures. *IEEE Trans Inf Technol Biomed* 2005; **9**: 120-131 [PMID: [15787014](#) DOI: [10.1109/titb.2004.837834](#)]
- 30 **van Wijk C**, van Ravesteijn VF, Vos FM, van Vliet LJ. Detection and segmentation of colonic polyps on implicit isosurfaces by second principal curvature flow. *IEEE Trans Med Imaging* 2010; **29**: 688-698 [PMID: [20199908](#) DOI: [10.1109/TMI.2009.2031323](#)]
- 31 **Kim SH**, Lee JM, Lee JG, Kim JH, Lefere PA, Han JK, Choi BI. Computer-aided detection of colonic polyps at CT colonography using a Hessian matrix-based algorithm: preliminary study. *AJR Am J Roentgenol* 2007; **189**: 41-51 [PMID: [17579150](#) DOI: [10.2214/AJR.07.2072](#)]
- 32 **Nappi JJ**, Pickhardt P, Kim DH, Hironaka T, Yoshida H. Deep learning of contrast-coated serrated polyps for computer-aided detection in CT colonography. *Medical imaging 2017: Computer-aided diagnosis*, 2017 [DOI: [10.1117/12.2255634](#)]
- 33 **Ma J**, Dercle L, Lichtenstein P, Wang D, Chen A, Zhu J, Piessevaux H, Zhao J, Schwartz LH, Lu L, Zhao B. Automated Identification of Optimal Portal Venous Phase Timing with Convolutional Neural Networks. *Acad Radiol* 2020; **27**: e10-e18 [PMID: [31151901](#) DOI: [10.1016/j.acra.2019.02.024](#)]
- 34 **Soomro MH**, De Cola G, Conforto S, Schmid M, Giunta G, Guidi E, Neri E, Caruso D, Ciolina M, Laghi A. Automatic segmentation of colorectal cancer in 3D MRI by combining deep learning and 3D level-set algorithm-a preliminary study. 2018 IEEE 4th middle east conference on biomedical engineering. 2018: 198-203 [DOI: [10.1109/mecbme.2018.8402433](#)]
- 35 **Soomro MH**, Coppotelli M, Conforto S, Schmid M, Giunta G, Del Secco L, Neri E, Caruso D, Rengo M, Laghi A. Automated Segmentation of Colorectal Tumor in 3D MRI Using 3D Multiscale Densely Connected Convolutional Neural Network. *J Healthc Eng* 2019; **2019**: 1075434 [PMID: [30838121](#) DOI: [10.1155/2019/1075434](#)]
- 36 **Wang D**, Xu J, Zhang Z, Li S, Zhang X, Zhou Y, Lu Y. Evaluation of Rectal Cancer Circumferential Resection Margin Using Faster Region-Based Convolutional Neural Network in High-Resolution Magnetic Resonance Images. *Dis Colon Rectum* 2020; **63**: 143-151 [PMID: [31842158](#) DOI: [10.1097/DCR.0000000000001519](#)]
- 37 **Wu QY**, Liu SL, Sun P, Li Y, Liu GW, Liu SS, Hu JL, Niu TY, Lu Y. Establishment and clinical application value of an automatic diagnosis platform for rectal cancer T-staging based on a deep

- neural network. *Chin Med J (Engl)* 2021; **134**: 821-828 [PMID: [33797468](#) DOI: [10.1097/CM9.0000000000001401](#)]
- 38 **Joshi N**, Bond S, Brady M. The segmentation of colorectal MRI images. *Med Image Anal* 2010; **14**: 494-509 [PMID: [20378393](#) DOI: [10.1016/j.media.2010.03.002](#)]
 - 39 **Dabass M**, Vashisth S, Vig R. Review of classification techniques using deep learning for colorectal cancer imaging modalities. 2019 6th International Conference on Signal Processing and Integrated Networks, 2019 [DOI: [10.1109/spin.2019.8711776](#)]
 - 40 **Shiraishi T**, Shinto E, Nearchou IP, Tsuda H, Kajiura Y, Einama T, Caie PD, Kishi Y, Ueno H. Prognostic significance of mesothelin expression in colorectal cancer disclosed by area-specific four-point tissue microarrays. *Virchows Arch* 2020; **477**: 409-420 [PMID: [32107600](#) DOI: [10.1007/s00428-020-02775-y](#)]
 - 41 **Pham TD**. Scaling of texture in training autoencoders for classification of histological images of colorectal cancer. *Advances in neural networks*, 2017: 524-532 [DOI: [10.1007/978-3-319-59081-3_61](#)]
 - 42 **Tiwari S**. An analysis in tissue classification for colorectal cancer histology using convolution neural network and colour models. *IJISMD* 2018; **9**: 1-19 [DOI: [10.4018/ijismd.2018100101](#)]
 - 43 **Sirinukunwattana K**, Ahmed Raza SE, Yee-Wah Tsang, Snead DR, Cree IA, Rajpoot NM. Locality Sensitive Deep Learning for Detection and Classification of Nuclei in Routine Colon Cancer Histology Images. *IEEE Trans Med Imaging* 2016; **35**: 1196-1206 [PMID: [26863654](#) DOI: [10.1109/TMI.2016.2525803](#)]
 - 44 **Koohababni NA**, Jahanifar M, Gooya A, Rajpoot N. Nuclei detection using mixture density networks. *Machine learning in medical imaging*, 2018: 241-248 [DOI: [10.1007/978-3-030-00919-9_28](#)]
 - 45 **Zhang X**, Chen G, Saruta K, Terata Y. An end-to-end cells detection approach for colon cancer histology images. 10th international conference on digital image processing, 2018 [DOI: [10.1117/12.2503067](#)]
 - 46 **Xu J**, Luo X, Wang G, Gilmore H, Madabhushi A. A Deep Convolutional Neural Network for segmenting and classifying epithelial and stromal regions in histopathological images. *Neurocomputing* 2016; **191**: 214-223 [PMID: [28154470](#) DOI: [10.1016/j.neucom.2016.01.034](#)]
 - 47 **Chen H**, Qi X, Yu L, Dou Q, Qin J, Heng PA. DCAN: Deep contour-aware networks for object instance segmentation from histology images. *Med Image Anal* 2017; **36**: 135-146 [PMID: [27898306](#) DOI: [10.1016/j.media.2016.11.004](#)]
 - 48 **Yoshida H**, Yamashita Y, Shimazu T, Cosatto E, Kiyuna T, Taniguchi H, Sekine S, Ochiai A. Automated histological classification of whole slide images of colorectal biopsy specimens. *Oncotarget* 2017; **8**: 90719-90729 [PMID: [29207599](#) DOI: [10.18632/oncotarget.21819](#)]
 - 49 **Saito A**, Cosatto E, Kiyuna T, Sakamoto M. Dawn of the digital diagnosis assisting system, can it open a new age for pathology? Medical imaging 2013: Digital pathology, 2013 [DOI: [10.1117/12.2008967](#)]
 - 50 **Jin Y**, Zhou C, Teng X, Ji J, Wu H, Liao J. Pai-wsit: An AI service platform with support for storing and sharing whole-slide images with metadata and annotations. *IEEE Access* 2019; **7**: 54780-54786 [DOI: [10.1109/access.2019.2913255](#)]
 - 51 **Qaiser T**, Tsang YW, Taniyama D, Sakamoto N, Nakane K, Epstein D, Rajpoot N. Fast and accurate tumor segmentation of histology images using persistent homology and deep convolutional features. *Med Image Anal* 2019; **55**: 1-14 [PMID: [30991188](#) DOI: [10.1016/j.media.2019.03.014](#)]
 - 52 **Chao WL**, Manickavasagan H, Krishna SG. Application of Artificial Intelligence in the Detection and Differentiation of Colon Polyps: A Technical Review for Physicians. *Diagnostics (Basel)* 2019; **9** [PMID: [31434208](#) DOI: [10.3390/diagnostics9030099](#)]
 - 53 **Zhou J**, Wu L, Wan X, Shen L, Liu J, Zhang J, Jiang X, Wang Z, Yu S, Kang J, Li M, Hu S, Hu X, Gong D, Chen D, Yao L, Zhu Y, Yu H. A novel artificial intelligence system for the assessment of bowel preparation (with video). *Gastrointest Endosc* 2020; **91**: 428-435.e2 [PMID: [31783029](#) DOI: [10.1016/j.gie.2019.11.026](#)]
 - 54 **de Almeida Thomaz V**, Sierra-Franco CA, Raposo AB. Training data enhancements for robust polyp segmentation in colonoscopy images. 2019 IEEE 32nd International Symposium on Computer-Based Medical Systems (CBMS), 2019: 192-197 [DOI: [10.1109/cbms.2019.00047](#)]
 - 55 **Azer SA**. Challenges Facing the Detection of Colonic Polyps: What Can Deep Learning Do? *Medicina (Kaunas)* 2019; **55** [PMID: [31409050](#) DOI: [10.3390/medicina55080473](#)]
 - 56 **Taha B**, Dias J, Werghi N, Ieee. Convolutional neural network as a feature extractor for automatic polyp detection. 2017 24th IEEE international conference on image processing, 2017: 2060-2064 [DOI: [10.1109/icip.2017.8296644](#)]
 - 57 **Yao H**, Stidham RW, Soroushmehr R, Gryak J, Najarian K. Automated Detection of Non-Informative Frames for Colonoscopy Through a Combination of Deep Learning and Feature Extraction. *Annu Int Conf IEEE Eng Med Biol Soc* 2019; **2019**: 2402-2406 [PMID: [31946383](#) DOI: [10.1109/EMBC.2019.8856625](#)]
 - 58 **McNeil MB**, Gross SA. Siri here, cecum reached, but please wash that fold: Will artificial intelligence improve gastroenterology? *Gastrointest Endosc* 2020; **91**: 425-427 [PMID: [32036947](#) DOI: [10.1016/j.gie.2019.10.027](#)]
 - 59 **Bravo D**, Ruano J, Gomez M, Romero E. Automatic detection of colorectal polyps larger than 5 mm during colonoscopy procedures using visual descriptors. 14th international symposium on medical information processing and analysis, 2018 [DOI: [10.1117/12.2511577](#)]

- 60 **de Lange T**, Halvorsen P, Riegler M. Methodology to develop machine learning algorithms to improve performance in gastrointestinal endoscopy. *World J Gastroenterol* 2018; **24**: 5057-5062 [PMID: [30568383](#) DOI: [10.3748/wjg.v24.i45.5057](#)]
- 61 **Mahmood F**, Durr NJ. Deep learning-based depth estimation from a synthetic endoscopy image training set. Medical imaging 2018: Image processing. Bellingham: Spie-Int Soc Optical Engineering, 2018 [DOI: [10.1117/12.2293785](#)]
- 62 **Mo X**, Tao K, Wang Q, Wang G. An efficient approach for polyps detection in endoscopic videos based on faster R-CNN. 2018 24th international conference on pattern recognition, 2018: 3929-3934 [DOI: [10.1109/icpr.2018.8545174](#)]
- 63 **Zhu H**, Fan Y, Lu H, Liang Z. Improving initial polyp candidate extraction for CT colonography. *Phys Med Biol* 2010; **55**: 2087-2102 [PMID: [20299733](#) DOI: [10.1088/0031-9155/55/7/019](#)]
- 64 **Komeda Y**, Handa H, Watanabe T, Nomura T, Kitahashi M, Sakurai T, Okamoto A, Minami T, Kono M, Arizumi T, Takenaka M, Hagiwara S, Matsui S, Nishida N, Kashida H, Kudo M. Computer-Aided Diagnosis Based on Convolutional Neural Network System for Colorectal Polyp Classification: Preliminary Experience. *Oncology* 2017; **93** Suppl 1: 30-34 [PMID: [29258081](#) DOI: [10.1159/000481227](#)]
- 65 **Zhang R**, Zheng Y, Poon CCY, Shen D, Lau JYW. Polyp detection during colonoscopy using a regression-based convolutional neural network with a tracker. *Pattern Recognit* 2018; **83**: 209-219 [PMID: [31105338](#) DOI: [10.1016/j.patcog.2018.05.026](#)]
- 66 **Zhu X**, Nemoto D, Mizuno T, Nakajima Y, Utano K, Aizawa M, Takezawa T, Sagara Y, Hayashi Y, Katsuki S, Yamamoto H, Hewett DG, Togashi K. Identification of deeply invasive colorectal cancer on non-magnified endoscopic images using artificial intelligence. *Gastrointest Endosc* 2019; **89**
- 67 **Akbari M**, Mohrekeh M, Nasr-Esfahani E, Soroushmehr SMR, Karimi N, Samavi S, Najarian K. Polyp Segmentation in Colonoscopy Images Using Fully Convolutional Network. *Annu Int Conf IEEE Eng Med Biol Soc* 2018; **2018**: 69-72 [PMID: [30440343](#) DOI: [10.1109/EMBC.2018.8512197](#)]
- 68 **Lequan Yu**, Hao Chen, Qi Dou, Jing Qin, Pheng Ann Heng. Integrating Online and Offline Three-Dimensional Deep Learning for Automated Polyp Detection in Colonoscopy Videos. *IEEE J Biomed Health Inform* 2017; **21**: 65-75 [PMID: [28114049](#) DOI: [10.1109/JBHI.2016.2637004](#)]
- 69 **Yamada M**, Saito Y, Imaoka H, Saiko M, Yamada S, Kondo H, Takamaru H, Sakamoto T, Sese J, Kuchiba A, Shibata T, Hamamoto R. Development of a real-time endoscopic image diagnosis support system using deep learning technology in colonoscopy. *Sci Rep* 2019; **9**: 14465 [PMID: [31594962](#) DOI: [10.1038/s41598-019-50567-5](#)]
- 70 **Allescher HD**, Weingart V. Optimizing Screening Colonoscopy: Strategies and Alternatives. *Visc Med* 2019; **35**: 215-225 [PMID: [31602382](#) DOI: [10.1159/000501835](#)]
- 71 **Lund Henriksen F**, Jensen R, Kvale Stensland H, Johansen D, Riegler MA, Halvorsen P. Performance of data enhancements and training optimization for neural network: A polyp detection case study. 2019 IEEE 32nd International Symposium on Computer-Based Medical Systems (CBMS), 2019: 287-293 [DOI: [10.1109/cbms.2019.00067](#)]
- 72 **Ahmad OF**, Soares AS, Mazomenos E, Brandao P, Vega R, Seward E, Stoyanov D, Chand M, Lovat LB. Artificial intelligence and computer-aided diagnosis in colonoscopy: current evidence and future directions. *Lancet Gastroenterol Hepatol* 2019; **4**: 71-80 [PMID: [30527583](#) DOI: [10.1016/S2468-1253\(18\)30282-6](#)]
- 73 **Takamaru H**, Wu SYS, Saito Y. Endocytoscopy: technology and clinical application in the lower GI tract. *Transl Gastroenterol Hepatol* 2020; **5**: 40 [PMID: [32632391](#) DOI: [10.21037/tgh.2019.12.04](#)]
- 74 **Rath T**, Morgenstern N, Vitali F, Atreya R, Neurath MF. Advanced Endoscopic Imaging in Colonic Neoplasia. *Visc Med* 2020; **36**: 48-59 [PMID: [32110657](#) DOI: [10.1159/000505411](#)]
- 75 **Shahidi N**, Rex DK, Kaltenbach T, Rastogi A, Ghalehjegh SH, Byrne MF. Use of Endoscopic Impression, Artificial Intelligence, and Pathologist Interpretation to Resolve Discrepancies Between Endoscopy and Pathology Analyses of Diminutive Colorectal Polyps. *Gastroenterology* 2020; **158**: 783-785.e1 [PMID: [31863741](#) DOI: [10.1053/j.gastro.2019.10.024](#)]
- 76 **Djinbachian R**, Dubé AJ, von Renteln D. Optical Diagnosis of Colorectal Polyps: Recent Developments. *Curr Treat Options Gastroenterol* 2019; **17**: 99-114 [PMID: [30746593](#) DOI: [10.1007/s11938-019-00220-x](#)]
- 77 **Kudo SE**, Misawa M, Mori Y, Hotta K, Ohtsuka K, Ikematsu H, Saito Y, Takeda K, Nakamura H, Ichimasa K, Ishigaki T, Toyoshima N, Kudo T, Hayashi T, Wakamura K, Baba T, Ishida F, Inoue H, Itoh H, Oda M, Mori K. Artificial Intelligence-assisted System Improves Endoscopic Identification of Colorectal Neoplasms. *Clin Gastroenterol Hepatol* 2020; **18**: 1874-1881.e2 [PMID: [31525512](#) DOI: [10.1016/j.cgh.2019.09.009](#)]
- 78 **Mahmood F**, Durr NJ. Topographical reconstructions from monocular optical colonoscopy images via deep learning. 2018 IEEE 15th international symposium on biomedical imaging, 2018: 216-219 [DOI: [10.1109/isbi.2018.8363558](#)]
- 79 **Vidyasagar M**. Machine learning methods in the computational biology of cancer. *Proc Math Phys Eng Sci* 2014; **470**: 20140081 [PMID: [25002826](#) DOI: [10.1016/j.arcontrol.2017.03.007](#)]
- 80 **Ebigbo A**, Palm C, Probst A, Mendel R, Manzeneder J, Prinz F, de Souza LA, Papa JP, Siersema P, Messmann H. A technical review of artificial intelligence as applied to gastrointestinal endoscopy: clarifying the terminology. *Endosc Int Open* 2019; **7**: E1616-E1623 [PMID: [31788542](#) DOI: [10.1055/a-1010-5705](#)]
- 81 **Jian J**, Xiong F, Xia W, Zhang R, Gu J, Wu X, Meng X, Gao X. Fully convolutional networks

- (FCNs)-based segmentation method for colorectal tumors on T2-weighted magnetic resonance images. *Australas Phys Eng Sci Med* 2018; **41**: 393-401 [PMID: 29654521 DOI: 10.1007/s13246-018-0636-9]
- 82 **Sivaganesan D.** Wireless distributive personal communication for early detection of collateral cancer using optimized machine learning methodology. *Wireless Personal Communicat* 2016; **94**: 2291-2302 [DOI: 10.1007/s11277-016-3411-9]
 - 83 **Gayathri Devi K, Radhakrishnan R.** Automatic segmentation of colon in 3D CT images and removal of opacified fluid using cascade feed forward neural network. *Comput Math Methods Med* 2015; **2015**: 670739 [PMID: 25838838 DOI: 10.1155/2015/670739]
 - 84 **Therrien R, Doyle S.** Role of training data variability on classifier performance and generalizability. *Medical imaging 2018: Digital pathology*, 2018 [DOI: 10.1117/12.2293919]
 - 85 **Sun CY, Liu W, Doyle S.** Two-tier classifier for identifying small objects in histological tissue classification: Experiments with colon cancer tissue mapping. *Medical imaging 2019: Digital pathology*, 2019 [DOI: 10.1117/12.2512973]
 - 86 **Shi J, Su Q, Zhang C, Huang G, Zhu Y.** An intelligent decision support algorithm for diagnosis of colorectal cancer through serum tumor markers. *Comput Methods Programs Biomed* 2010; **100**: 97-107 [PMID: 20346535 DOI: 10.1016/j.cmpb.2010.03.001]
 - 87 **Su Q, Shi J, Gu P, Huang G, Zhu Y.** An algorithm designed for improving diagnostic efficiency by setting multi-cutoff values of multiple tumor markers. *Expert Syst Appl* 2012; **39**: 5784-5791 [DOI: 10.1016/j.eswa.2011.11.089]
 - 88 **Kunhoth S, Al Maadeed S.** Building a multispectral image dataset for colorectal tumor biopsy. 2017 13th international wireless communications and mobile computing conference, 2017: 1745-1750 [DOI: 10.1109/iwcmc.2017.7986548]
 - 89 **Wang P, Xiao X, Glissen Brown JR, Berzin TM, Tu M, Xiong F, Hu X, Liu P, Song Y, Zhang D, Yang X, Li L, He J, Yi X, Liu J, Liu X.** Development and validation of a deep-learning algorithm for the detection of polyps during colonoscopy. *Nat Biomed Eng* 2018; **2**: 741-748 [PMID: 31015647 DOI: 10.1038/s41551-018-0301-3]
 - 90 **Barua I, Vinsard DG, Jodal HC, Løberg M, Kalager M, Holme Ø, Misawa M, Bretthauer M, Mori Y.** Artificial intelligence for polyp detection during colonoscopy: a systematic review and meta-analysis. *Endoscopy* 2021; **53**: 277-284 [PMID: 32557490 DOI: 10.1055/a-1201-7165]
 - 91 **Gong D, Wu L, Zhang J, Mu G, Shen L, Liu J, Wang Z, Zhou W, An P, Huang X, Jiang X, Li Y, Wan X, Hu S, Chen Y, Hu X, Xu Y, Zhu X, Li S, Yao L, He X, Chen D, Huang L, Wei X, Wang X, Yu H.** Detection of colorectal adenomas with a real-time computer-aided system (ENDOANGEL): a randomised controlled study. *Lancet Gastroenterol Hepatol* 2020; **5**: 352-361 [PMID: 31981518 DOI: 10.1016/S2468-1253(19)30413-3]
 - 92 **Lui TKL, Leung WK.** Is artificial intelligence the final answer to missed polyps in colonoscopy? *World J Gastroenterol* 2020; **26**: 5248-5255 [PMID: 32994685 DOI: 10.3748/wjg.v26.i35.5248]
 - 93 **Rodriguez-Diaz E, Castanon DA, Singh SK, Bigio JJ.** Spectral classifier design with ensemble classifiers and misclassification-rejection: application to elastic-scattering spectroscopy for detection of colonic neoplasia. *J Biomed Opt* 2011; **16**: 067009 [PMID: 21721830 DOI: 10.1117/1.3592488]
 - 94 **Kondepati VR, Oszinda T, Heise HM, Luig K, Mueller R, Schroeder O, Keese M, Backhaus J.** CH-overtone regions as diagnostic markers for near-infrared spectroscopic diagnosis of primary cancers in human pancreas and colorectal tissue. *Anal Bioanal Chem* 2007; **387**: 1633-1641 [PMID: 17205263 DOI: 10.1007/s00216-006-0960-x]
 - 95 **Angermann Q, Histace A, Romain O.** Active learning for real time detection of polyps in videocolonoscopy. 20th conference on medical image understanding and analysis, 2016: 182-187 [DOI: 10.1016/j.procs.2016.07.017]
 - 96 **Ayling RM, Lewis SJ, Cotter F.** Potential roles of artificial intelligence learning and faecal immunochemical testing for prioritisation of colonoscopy in anaemia. *Br J Haematol* 2019; **185**: 311-316 [PMID: 30714125 DOI: 10.1111/bjh.15776]
 - 97 **Tian X, Xu LL, Liu XL, Chen WQ.** Enhanced Patient Education for Colonic Polyp and Adenoma Detection: Meta-Analysis of Randomized Controlled Trials. *JMIR Mhealth Uhealth* 2020; **8**: e17372 [PMID: 32347798 DOI: 10.2196/17372]
 - 98 **Javed S, Fraz MM, Epstein D, Snead D, Rajpoot NM.** Cellular community detection for tissue phenotyping in histology images. *Computational pathology and ophthalmic medical image analysis*, 2018: 120-129 [DOI: 10.1007/978-3-030-00949-6_15]
 - 99 **Wang Q, Wei J, Chen Z, Zhang T, Zhong J, Zhong B, Yang P, Li W, Cao J.** Establishment of multiple diagnosis models for colorectal cancer with artificial neural networks. *Oncol Lett* 2019; **17**: 3314-3322 [PMID: 30867765 DOI: 10.3892/ol.2019.10010]
 - 100 **Battista A, Battista RA, Battista F, Cinquanta L, Iovane G, Corbisieri M, Suozzo A.** Development of a new mathematical tool for early colorectal cancer diagnosis and its possible use in mass screening. *J Int Math* 2019; **22**: 811-835 [DOI: 10.1080/09720502.2019.1649834]
 - 101 **Zhang W, Chen X, Wong KC.** Noninvasive early diagnosis of intestinal diseases based on artificial intelligence in genomics and microbiome. *J Gastroenterol Hepatol* 2021; **36**: 823-831 [PMID: 33880763 DOI: 10.1111/jgh.15500]
 - 102 **Wang KS, Yu G, Xu C, Meng XH, Zhou J, Zheng C, Deng Z, Shang L, Liu R, Su S, Zhou X, Li Q, Li J, Wang J, Ma K, Qi J, Hu Z, Tang P, Deng J, Qiu X, Li BY, Shen WD, Quan RP, Yang JT, Huang LY, Xiao Y, Yang ZC, Li Z, Wang SC, Ren H, Liang C, Guo W, Li Y, Xiao H, Gu Y, Yun JP, Huang D, Song Z, Fan X, Chen L, Yan X, Huang ZC, Huang J, Luttrell J, Zhang CY, Zhou W,**

- Zhang K, Yi C, Wu C, Shen H, Wang YP, Xiao HM, Deng HW. Accurate diagnosis of colorectal cancer based on histopathology images using artificial intelligence. *BMC Med* 2021; **19**: 76 [PMID: 33752648 DOI: 10.1186/s12916-021-01942-5]
- 103 **Jones OT**, Calanzani N, Saji S, Duffy SW, Emery J, Hamilton W, Singh H, de Wit NJ, Walter FM. Artificial Intelligence Techniques That May Be Applied to Primary Care Data to Facilitate Earlier Diagnosis of Cancer: Systematic Review. *J Med Internet Res* 2021; **23**: e23483 [PMID: 33656443 DOI: 10.2196/23483]
- 104 **Lorenzovici N**, Dulf EH, Mocan T, Mocan L. Artificial Intelligence in Colorectal Cancer Diagnosis Using Clinical Data: Non-Invasive Approach. *Diagnostics (Basel)* 2021; **11** [PMID: 33799452 DOI: 10.3390/diagnostics11030514]
- 105 **Xu Y**, Ding W, Wang Y, Tan Y, Xi C, Ye N, Wu D, Xu X. Comparison of diagnostic performance between convolutional neural networks and human endoscopists for diagnosis of colorectal polyp: A systematic review and meta-analysis. *PLoS One* 2021; **16**: e0246892 [PMID: 33592048 DOI: 10.1371/journal.pone.0246892]
- 106 **Öztürk Ş**, Özkaya U. Residual LSTM layered CNN for classification of gastrointestinal tract diseases. *J Biomed Inform* 2021; **113**: 103638 [PMID: 33271341 DOI: 10.1016/j.jbi.2020.103638]
- 107 **Echle A**, Rindtorff NT, Brinker TJ, Luedde T, Pearson AT, Kather JN. Deep learning in cancer pathology: a new generation of clinical biomarkers. *Br J Cancer* 2021; **124**: 686-696 [PMID: 33204028 DOI: 10.1038/s41416-020-01122-x]
- 108 **Araujo RL**, Linhares MM. Pushing the limits of liver surgery for colorectal liver metastases: Current state and future directions. *World J Gastrointest Surg* 2019; **11**: 34-40 [PMID: 30842810 DOI: 10.4240/wjgs.v11.i2.34]
- 109 **Passi K**, Zhao H. A decision support system (DSS) for colorectal cancer follow-up program via a semantic framework. *Int J Healthcare Informat Syst Informatics* 2015; **10**: 17-38 [DOI: 10.4018/ijhisi.2015010102]
- 110 **Lee WS**, Ahn SM, Chung JW, Kim KO, Kwon KA, Kim Y, Sym S, Shin D, Park I, Lee U, Baek JH. Assessing Concordance With Watson for Oncology, a Cognitive Computing Decision Support System for Colon Cancer Treatment in Korea. *JCO Clin Cancer Inform* 2018; **2**: 1-8 [PMID: 30652564 DOI: 10.1200/CC1.17.00109]
- 111 **Siddiqi J**, Akhgar B, Gruzdz A, Zaeafarian G, Ihnatowicz A. Automated diagnosis system to support colon cancer treatment: Match. 15th International Conference on Information Technology: New Generations, 2008: 201-205 [DOI: 10.1109/itng.2008.62]
- 112 **Li S**, Jiang Q, Liu S, Zhang Y, Tian Y, Song C, Wang J, Zou Y, Anderson GJ, Han JY, Chang Y, Liu Y, Zhang C, Chen L, Zhou G, Nie G, Yan H, Ding B, Zhao Y. A DNA nanorobot functions as a cancer therapeutic in response to a molecular trigger in vivo. *Nat Biotechnol* 2018; **36**: 258-264 [PMID: 29431737 DOI: 10.1038/nbt.4071]
- 113 **Felfoul O**, Mohammadi M, Taherkhani S, de Lanauze D, Zhong Xu Y, Loghin D, Essa S, Jancik S, Houle D, Lafleur M, Gaboury L, Tabrizian M, Kaou N, Atkin M, Vuong T, Batist G, Beauchemin N, Radzioch D, Martel S. Magneto-aerotactic bacteria deliver drug-containing nanoliposomes to tumour hypoxic regions. *Nat Nanotechnol* 2016; **11**: 941-947 [PMID: 27525475 DOI: 10.1038/nnano.2016.137]
- 114 **Koelzer VH**, Sirinukunwattana K, Rittscher J, Mertz KD. Precision immunoprofiling by image analysis and artificial intelligence. *Virchows Arch* 2019; **474**: 511-522 [PMID: 30470933 DOI: 10.1007/s00428-018-2485-z]
- 115 **Dzobo K**, Thomford NE, Senthane DA. Targeting the Versatile Wnt/ β -Catenin Pathway in Cancer Biology and Therapeutics: From Concept to Actionable Strategy. *OMICS* 2019; **23**: 517-538 [PMID: 31613700 DOI: 10.1089/omi.2019.0147]
- 116 **Lee BI**, Matsuda T. Estimation of Invasion Depth: The First Key to Successful Colorectal ESD. *Clin Endosc* 2019; **52**: 100-106 [PMID: 30914629 DOI: 10.5946/ce.2019.012]
- 117 **Ichimasa K**, Kudo SE, Mori Y, Misawa M, Matsudaira S, Kouyama Y, Baba T, Hidaka E, Wakamura K, Hayashi T, Kudo T, Ishigaki T, Yagawa Y, Nakamura H, Takeda K, Haji A, Hamatani S, Mori K, Ishida F, Miyachi H. Artificial intelligence may help in predicting the need for additional surgery after endoscopic resection of T1 colorectal cancer. *Endoscopy* 2018; **50**: 230-240 [PMID: 29272905 DOI: 10.1055/s-0043-122385]
- 118 **Kirchberg J**, Weitz J. Evidence for robotic surgery in oncological visceral surgery. *Chirurg* 2019; **90**: 379-386 [PMID: 30778607 DOI: 10.1007/s00104-019-0812-9]
- 119 **Kim YJ**. The Future Medical Science and Colorectal Surgeons. *Ann Coloproctol* 2017; **33**: 207-209 [PMID: 29354602 DOI: 10.3393/ac.2017.33.6.207]
- 120 **Leonard S**, Wu KL, Kim Y, Krieger A, Kim PC. Smart tissue anastomosis robot (STAR): a vision-guided robotics system for laparoscopic suturing. *IEEE Trans Biomed Eng* 2014; **61**: 1305-1317 [PMID: 24658254 DOI: 10.1109/TBME.2014.2302385]
- 121 **Huang YM**, Huang YJ, Wei PL. Colorectal Cancer Surgery Using the Da Vinci Xi and Si Systems: Comparison of Perioperative Outcomes. *Surg Innov* 2019; **26**: 192-200 [PMID: 30501567 DOI: 10.1177/1553350618816788]
- 122 **Zheng P**, Feng QY, Xu JM. Current status and consideration of robotic surgery for colorectal cancer in China. *Zhonghua Wei Chang Wai Ke Za Zhi* 2020; **23**: 336-340 [PMID: 32306599 DOI: 10.3760/cma.j.cn.441530-20200216-00056]
- 123 **Mitsala A**, Tsalikidis C, Pitiakoudis M, Simopoulos C, Tsaroucha AK. Artificial Intelligence in Colorectal Cancer Screening, Diagnosis and Treatment. A New Era. *Curr Oncol* 2021; **28**: 1581-

- 1607 [PMID: [33922402](#) DOI: [10.3390/curroncol28030149](#)]
- 124 **Aikemu B**, Xue P, Hong H, Jia H, Wang C, Li S, Huang L, Ding X, Zhang H, Cai G, Lu A, Xie L, Li H, Zheng M, Sun J. Artificial Intelligence in Decision-Making for Colorectal Cancer Treatment Strategy: An Observational Study of Implementing Watson for Oncology in a 250-Case Cohort. *Front Oncol* 2020; **10**: 594182 [PMID: [33628729](#) DOI: [10.3389/fonc.2020.594182](#)]
 - 125 **Hamamoto R**, Suvana K, Yamada M, Kobayashi K, Shinkai N, Miyake M, Takahashi M, Jinnai S, Shimoyama R, Sakai A, Takasawa K, Bolatkan A, Shozu K, Dozen A, Machino H, Takahashi S, Asada K, Komatsu M, Sese J, Kaneko S. Application of Artificial Intelligence Technology in Oncology: Towards the Establishment of Precision Medicine. *Cancers (Basel)* 2020; **12** [PMID: [33256107](#) DOI: [10.3390/cancers12123532](#)]
 - 126 **Pritzker KPH**. Colon Cancer Biomarkers: Implications for Personalized Medicine. *J Pers Med* 2020; **10** [PMID: [33066312](#) DOI: [10.3390/jpm10040167](#)]
 - 127 **Ding X**, Chang VHS, Li Y, Li X, Xu H, Ho C-M, Ho D, Yen Y. Harnessing an artificial intelligence platform to dynamically individualize combination therapy for treating colorectal carcinoma in a rat model. *Adv Ther* 2020; **3** [DOI: [10.1002/adtp.201900127](#)]
 - 128 **Zhang L**, Zheng C, Li T, Xing L, Zeng H, Yang H, Cao J, Chen B, Zhou Z. Building up a robust risk mathematical platform to predict colorectal cancer. *Complexity* 2017; **2017**: 1-14 [DOI: [10.1155/2017/8917258](#)]
 - 129 **Morgado P**, Vicente H, Abelha A, Machado J, Neves J. A case-based approach to colorectal cancer detection. Information science and applications, 2017: 433-442 [DOI: [10.1007/978-981-10-4154-9_50](#)]
 - 130 **Cueto-López N**, García-Ordás MT, Dávila-Batista V, Moreno V, Aragonés N, Alaiz-Rodríguez R. A comparative study on feature selection for a risk prediction model for colorectal cancer. *Comput Methods Programs Biomed* 2019; **177**: 219-229 [PMID: [31319951](#) DOI: [10.1016/j.cmpb.2019.06.001](#)]
 - 131 **Anand SS**, Smith AE, Hamilton PW, Anand JS, Hughes JG, Bartels PH. An evaluation of intelligent prognostic systems for colorectal cancer. *Artif Intell Med* 1999; **15**: 193-214 [PMID: [10082181](#) DOI: [10.1016/s0933-3657\(98\)00052-9](#)]
 - 132 **Gupta P**, Chiang SF, Sahoo PK, Mohapatra SK, You JF, Onthoni DD, Hung HY, Chiang JM, Huang Y, Tsai WS. Prediction of Colon Cancer Stages and Survival Period with Machine Learning Approach. *Cancers (Basel)* 2019; **11** [PMID: [31842486](#) DOI: [10.3390/cancers11122007](#)]
 - 133 **Li S**, Razzaghi T. Personalized colorectal cancer survivability prediction with machine learning methods. 2018 IEEE international conference on big data, 2018: 2554-2558 [DOI: [10.1109/bigdata.2018.8622121](#)]
 - 134 **Barsainya A**, Sairam A, Patil AP. Analysis and prediction of survival after colorectal chemotherapy using machine learning models. 2018 International Conference on Advances in Computing, Communications and Informatics, 2018 [DOI: [10.1109/icacci.2018.8554832](#)]
 - 135 **Dimitriou N**, Arandjelović O, Harrison DJ, Caie PD. A principled machine learning framework improves accuracy of stage II colorectal cancer prognosis. *NPJ Digit Med* 2018; **1**: 52 [PMID: [31304331](#) DOI: [10.1038/s41746-018-0057-x](#)]
 - 136 **Popovici V**, Budinská E, Dušek L, Kozubek M, Bosman F. Image-based surrogate biomarkers for molecular subtypes of colorectal cancer. *Bioinformatics* 2017; **33**: 2002-2009 [PMID: [28158480](#) DOI: [10.1093/bioinformatics/btx027](#)]
 - 137 **Hoogendoorn M**, Szolovits P, Moons LMG, Numans ME. Utilizing uncoded consultation notes from electronic medical records for predictive modeling of colorectal cancer. *Artif Intell Med* 2016; **69**: 53-61 [PMID: [27085847](#) DOI: [10.1016/j.artmed.2016.03.003](#)]
 - 138 **Kop R**, Hoogendoorn M, Teije AT, Büchner FL, Slottje P, Moons LM, Numans ME. Predictive modeling of colorectal cancer using a dedicated pre-processing pipeline on routine electronic medical records. *Comput Biol Med* 2016; **76**: 30-38 [PMID: [27392227](#) DOI: [10.1016/j.compbimed.2016.06.019](#)]
 - 139 **Geessink OGF**, Baidoshvili A, Freling G, Klaase JM, Slump CH, van der Heijden F. Toward automatic segmentation and quantification of tumor and stroma in whole-slide images of H&E stained rectal carcinomas. Medical imaging 2015: Digital pathology. Bellingham: Spie-Int Soc Optical Engineering, 2015 [DOI: [10.1117/12.2081665](#)]
 - 140 **Wright A**, Magee D, Quirke P, Treanor D. Towards automatic patient selection for chemotherapy in colorectal cancer trials. Medical imaging 2014: Digital pathology, 2014 [DOI: [10.1117/12.2043220](#)]
 - 141 **Wang Y**, Wang D, Ye X, Wang Y, Yin Y, Jin Y. A tree ensemble-based two-stage model for advanced-stage colorectal cancer survival prediction. *Informat Sci* 2019; **474**: 106-124 [DOI: [10.1016/j.ins.2018.09.046](#)]
 - 142 **Oliveira T**, Barbosa E, Martins S, Goulart A, Neves J, Novais P. A prognosis system for colorectal cancer. Proceedings of the 26th IEEE International Symposium on Computer-Based Medical Systems, 2013 [DOI: [10.1109/cbms.2013.6627846](#)]
 - 143 **Lo Bello L**, Pistone G, Restuccia S, Vinci E, Mazzoleni G, Malaguarnera M. 5-fluorouracil alone versus 5-fluorouracil plus folinic acid in the treatment of colorectal carcinoma: meta-analysis. *Int J Clin Pharmacol Ther* 2000; **38**: 553-562 [PMID: [11125868](#) DOI: [10.5414/cpp38553](#)]
 - 144 **Harrington L**, Suriawinata A, MacKenzie T, Hassanpour S. Application of machine learning on colonoscopy screening records for predicting colorectal polyp recurrence. Proceedings 2018 IEEE international conference on bioinformatics and biomedicine, 2018: 993-998 [DOI: [10.1109/BIOMED47090.2018.8452121](#)]

- 10.1109/bibm.2018.8621455]
- 145 **Xie X**, Xing J, Kong N, Li C, Li J, Zhang S. Improving colorectal polyp classification based on physical examination data-an ensemble learning approach. *EEE Robot Automat Lett* 2018; **3**: 434-441 [DOI: [10.1109/lra.2017.2746918](https://doi.org/10.1109/lra.2017.2746918)]
- 146 **Bokhorst JM**, Rijsternberg L, Goudkade D, Nagtegaal I, van der Laak J, Ciompi F. Automatic detection of tumor budding in colorectal carcinoma with deep learning. *Computational pathology and ophthalmic medical image analysis*, 2018: 130-138 [DOI: [10.1007/978-3-030-00949-6_16](https://doi.org/10.1007/978-3-030-00949-6_16)]
- 147 **Zhao K**, Li Z, Yao S, Wang Y, Wu X, Xu Z, Wu L, Huang Y, Liang C, Liu Z. Artificial intelligence quantified tumour-stroma ratio is an independent predictor for overall survival in resectable colorectal cancer. *EBioMedicine* 2020; **61**: 103054 [PMID: [33039706](https://pubmed.ncbi.nlm.nih.gov/33039706/) DOI: [10.1016/j.ebiom.2020.103054](https://doi.org/10.1016/j.ebiom.2020.103054)]
- 148 **Syafiandini AF**, Wasito I, Yazid S, Fitriawan A, Amien M. Cancer subtype identification using deep learning approach. 2016 International Conference on Computer, Control, Informatics and its Applications, 2016 [DOI: [10.1109/ic3ina.2016.7863033](https://doi.org/10.1109/ic3ina.2016.7863033)]
- 149 **Roadknight C**, Aickelin U, Scholefield J, Durrant L. Ensemble learning of colorectal cancer survival rates. 2013 IEEE international conference on computational intelligence and virtual environments for measurement systems and applications, 2013: 82-86 [DOI: [10.1109/civemsa.2013.6617400](https://doi.org/10.1109/civemsa.2013.6617400)]
- 150 **Cui Y**, Cai X, Jin Z. Semi-supervised classification using sparse representation for cancer recurrence prediction. 2013 IEEE international workshop on genomic signal processing and statistics, 2013: 102-105 [DOI: [10.1109/gensips.2013.6735949](https://doi.org/10.1109/gensips.2013.6735949)]
- 151 **Park C**, Ahn J, Kim H, Park S. Integrative gene network construction to analyze cancer recurrence using semi-supervised learning. *PLoS One* 2014; **9**: e86309 [PMID: [24497942](https://pubmed.ncbi.nlm.nih.gov/24497942/) DOI: [10.1371/journal.pone.0086309](https://doi.org/10.1371/journal.pone.0086309)]
- 152 **Du X**, Cheng J. Identification and analysis of driver missense mutations using rotation forest with feature selection. *Biomed Res Int* 2014; **2014**: 905951 [PMID: [25250338](https://pubmed.ncbi.nlm.nih.gov/25250338/) DOI: [10.1155/2014/905951](https://doi.org/10.1155/2014/905951)]
- 153 **Chi S**, Li X, Tian Y, Li J, Kong X, Ding K, Weng C. Semi-supervised learning to improve generalizability of risk prediction models. *J Biomed Inform* 2019; **92**: 103117 [PMID: [30738948](https://pubmed.ncbi.nlm.nih.gov/30738948/) DOI: [10.1016/j.jbi.2019.103117](https://doi.org/10.1016/j.jbi.2019.103117)]
- 154 **Ong LS**, Shepherd B, Tong LC, Seow-Choen F, Ho YH, Tang CL, Ho YS, Tan K. The Colorectal Cancer Recurrence Support (CARES) System. *Artif Intell Med* 1997; **11**: 175-188 [PMID: [9413605](https://pubmed.ncbi.nlm.nih.gov/9413605/) DOI: [10.1016/s0933-3657\(97\)00029-8](https://doi.org/10.1016/s0933-3657(97)00029-8)]
- 155 **Reichling C**, Taieb J, Derangere V, Klopfenstein Q, Le Malicot K, Gornet JM, Becheur H, Fein F, Cojocarasu O, Kaminsky MC, Lagasse JP, Luet D, Nguyen S, Etienne PL, Gasmi M, Vanoli A, Perrier H, Puig PL, Emile JF, Lepage C, Ghiringhelli F. Artificial intelligence-guided tissue analysis combined with immune infiltrate assessment predicts stage III colon cancer outcomes in PETACC08 study. *Gut* 2020; **69**: 681-690 [PMID: [31780575](https://pubmed.ncbi.nlm.nih.gov/31780575/) DOI: [10.1136/gutjnl-2019-319292](https://doi.org/10.1136/gutjnl-2019-319292)]
- 156 **Chowdhury SA**, Nibbe RK, Chance MR, Koyutürk M. Subnetwork state functions define dysregulated subnetworks in cancer. *J Comput Biol* 2011; **18**: 263-281 [PMID: [21385033](https://pubmed.ncbi.nlm.nih.gov/21385033/) DOI: [10.1089/cmb.2010.0269](https://doi.org/10.1089/cmb.2010.0269)]
- 157 **Mohamad Marzuki MF**, Yaacob NA, Bin Yaacob NM, Abu Hassan MR, Ahmad SB. Usable Mobile App for Community Education on Colorectal Cancer: Development Process and Usability Study. *JMIR Hum Factors* 2019; **6**: e12103 [PMID: [30990454](https://pubmed.ncbi.nlm.nih.gov/30990454/) DOI: [10.2196/12103](https://doi.org/10.2196/12103)]
- 158 **Hacking S**, Nasim R, Lee L, Vitkovski T, Thomas R, Shaffer E, Nasim M. Whole slide imaging and colorectal carcinoma: A validation study for tumor budding and stromal differentiation. *Pathol Res Pract* 2020; **216**: 153233 [PMID: [33068916](https://pubmed.ncbi.nlm.nih.gov/33068916/) DOI: [10.1016/j.prp.2020.153233](https://doi.org/10.1016/j.prp.2020.153233)]
- 159 **Wang Y**, He X, Nie H, Zhou J, Cao P, Ou C. Application of artificial intelligence to the diagnosis and therapy of colorectal cancer. *Am J Cancer Res* 2020; **10**: 3575-3598 [PMID: [33294256](https://pubmed.ncbi.nlm.nih.gov/33294256/)]
- 160 **O'Sullivan S**, Nevejans N, Allen C, Blyth A, Leonard S, Pagallo U, Holzinger K, Holzinger A, Sajid MI, Ashrafian H. Legal, regulatory, and ethical frameworks for development of standards in artificial intelligence (AI) and autonomous robotic surgery. *Int J Med Robot* 2019; **15**: e1968 [PMID: [30397993](https://pubmed.ncbi.nlm.nih.gov/30397993/) DOI: [10.1002/rcs.1968](https://doi.org/10.1002/rcs.1968)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: bpgoffice@wjgnet.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

