

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2020 September 28; 26(36): 5387-5533



**OPINION REVIEW**

- 5387 COVID-19 pandemic and challenges in pediatric gastroenterology practice  
*Kriem J, Rahhal R*

**MINIREVIEWS**

- 5395 Treatment of eosinophilic esophagitis with swallowed topical corticosteroids  
*Nennstiel S, Schlag C*
- 5408 Artificial intelligence in gastric cancer: Application and future perspectives  
*Niu PH, Zhao LL, Wu HL, Zhao DB, Chen YT*

**ORIGINAL ARTICLE****Basic Study**

- 5420 Granulocyte-macrophage colony-stimulating factor protects mice against hepatocellular carcinoma by ameliorating intestinal dysbiosis and attenuating inflammation  
*Wu YN, Zhang L, Chen T, Li X, He LH, Liu GX*

**Retrospective Study**

- 5437 Transitioning patients with inflammatory bowel disease from hospital-based to rapid home-based infliximab: A stepwise, safety and patient-orientated process towards sustainability  
*Bohra A, Rizvi QAA, Keung CYY, Vasudevan A, van Langenberg DR*
- 5450 Histopathological validation of magnifying endoscopy for diagnosis of mixed-histological-type early gastric cancer  
*Ozeki Y, Hirasawa K, Kobayashi R, Sato C, Tateishi Y, Sawada A, Ikeda R, Nishio M, Fukuchi T, Makazu M, Taguri M, Maeda S*

**Observational Study**

- 5463 Major gastrointestinal bleeding and antithrombotics: Characteristics and management  
*Bouget J, Viglino D, Yvetot Q, Oger E*
- 5474 Pediatric non-alcoholic fatty liver disease and kidney function: Effect of HSD17B13 variant  
*Di Sessa A, Umamo GR, Cirillo G, Passaro AP, Verde V, Cozzolino D, Guarino S, Marzuillo P, Miraglia del Giudice E*
- 5484 Motility index measured by magnetic resonance enterography is associated with sex and mural thickness  
*Månsson S, Ekberg O, Ohlsson B*
- 5498 Impact of B-mode-ultrasound-guided transhepatic and transperitoneal cholecystostomy tube placement on laparoscopic cholecystectomy  
*Liu P, Liu C, Wu YT, Zhu JY, Zhao WC, Li JB, Zhang H, Yang YX*

**Prospective Study**

- 5508** Effects of early oral feeding after radical total gastrectomy in gastric cancer patients  
*Lu YX, Wang YJ, Xie TY, Li S, Wu D, Li XG, Song QY, Wang LP, Guan D, Wang XX*

**CASE REPORT**

- 5520** SMARCB1/INI1-deficient pancreatic undifferentiated rhabdoid carcinoma mimicking solid pseudopapillary neoplasm: A case report and review of the literature  
*Hua Y, Soni P, Larsen D, Zreik R, Leng B, Rampisela D*
- 5527** Solitary peritoneal metastasis of gastrointestinal stromal tumor: A case report  
*Sugiyama Y, Shimbara K, Sasaki M, Kouyama M, Tazaki T, Takahashi S, Nakamitsu A*

**ABOUT COVER**

Editorial board member of *World Journal of Gastroenterology*, Dr. José M Ramia is Head of Department (Surgery) in Hospital General Universitario de Alicante (Spain), since June 2020. Dr. Ramia undertook his surgical residency program at Hospital 12 de Octubre (Madrid) (1991-1995), receiving his PhD in 1999 (Universidad Complutense, Madrid). He has published 310 articles in medical journals and 25 books chapters. His research interests involve every surgical topic of liver, bile duct and pancreas diseases and liver transplantation. He is the current President of the Spanish Chapter of International Hepato-pancreato Biliary Association (HPBA), member of the Educational Committee and Scientific and Research Committee of European-African HPBA, and examiner for the HPB FEBS Board. Dr Ramia is a fellow of the American College of Surgeons, Royal College of Surgeons (England) and European Board of Surgery-HPB. (L-Editor: Filipodia)

**AIMS AND SCOPE**

The primary aim of *World Journal of Gastroenterology* (*WJG, World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

**INDEXING/ABSTRACTING**

The *WJG* is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2020 edition of Journal Citation Report® cites the 2019 impact factor (IF) for *WJG* as 3.665; IF without journal self cites: 3.534; 5-year IF: 4.048; Ranking: 35 among 88 journals in gastroenterology and hepatology; and Quartile category: Q2.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Yan-Liang Zhang; Production Department Director: Yun-Xiaojuan Wu; Editorial Office Director: Ze-Mao Gong.

**NAME OF JOURNAL**

*World Journal of Gastroenterology*

**ISSN**

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

**LAUNCH DATE**

October 1, 1995

**FREQUENCY**

Weekly

**EDITORS-IN-CHIEF**

Andrzej S Tarnawski, Subrata Ghosh

**EDITORIAL BOARD MEMBERS**

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

**PUBLICATION DATE**

September 28, 2020

**COPYRIGHT**

© 2020 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>

## Artificial intelligence in gastric cancer: Application and future perspectives

Peng-Hui Niu, Lu-Lu Zhao, Hong-Liang Wu, Dong-Bing Zhao, Ying-Tai Chen

**ORCID number:** Peng-Hui Niu 0000-0003-0114-1625; Lu-Lu Zhao 0000-0001-8344-0498; Hong-Liang Wu 0000-0002-3757-8610; Dong-Bing Zhao 0000-0002-3011-5277; Ying-Tai Chen 0000-0003-4980-6315.

**Author contributions:** Niu PH, Zhao LL, and Wu HL contributed equally to this work; All authors made substantial contributions to the intellectual content of this paper.

**Supported by** National Key R&D Program of China, No. 2017YFC0908300.

**Conflict-of-interest statement:** All the authors have no conflict of interest related to the manuscript.

**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/>

**Peng-Hui Niu, Lu-Lu Zhao, Dong-Bing Zhao, Ying-Tai Chen**, Department of Pancreatic and Gastric Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

**Hong-Liang Wu**, Department of Anesthesiology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100021, China

**Corresponding author:** Ying-Tai Chen, MD, Professor, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No.17 Panjiayuan Nanli, Beijing 100021, China. [yingtaichen@126.com](mailto:yingtaichen@126.com)

### Abstract

Gastric cancer is the fourth leading cause of cancer-related mortality across the globe, with a 5-year survival rate of less than 40%. In recent years, several applications of artificial intelligence (AI) have emerged in the gastric cancer field based on its efficient computational power and learning capacities, such as image-based diagnosis and prognosis prediction. AI-assisted diagnosis includes pathology, endoscopy, and computerized tomography, while researchers in the prognosis circle focus on recurrence, metastasis, and survival prediction. In this review, a comprehensive literature search was performed on articles published up to April 2020 from the databases of PubMed, Embase, Web of Science, and the Cochrane Library. Thereby the current status of AI-applications was systematically summarized in gastric cancer. Moreover, future directions that target this field were also analyzed to overcome the risk of overfitting AI models and enhance their accuracy as well as the applicability in clinical practice.

**Key Words:** Gastric cancer; Image-based diagnosis; Prognosis prediction; Artificial intelligence; Machine learning; Deep learning

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Recently, several applications of artificial intelligence have emerged in the gastric cancer field based on its efficient computational power and learning capacities,

**Manuscript source:** Invited manuscript

**Received:** May 24, 2020

**Peer-review started:** May 24, 2020

**First decision:** July 29, 2020

**Revised:** August 2, 2020

**Accepted:** August 29, 2020

**Article in press:** August 29, 2020

**Published online:** September 28, 2020

**P-Reviewer:** Ishizawa K, Kinami S, Srivastava M

**S-Editor:** Gao CC

**L-Editor:** Filipodia

**P-Editor:** Wang LL



such as image-based diagnosis and prognosis prediction. In this review, we searched the relevant works published up to April 2020 from the databases of PubMed, Embase, Web of Science, and the Cochrane Library, thus comprehensively summarizing the current status of artificial intelligence applications in gastric cancer. In addition, challenges and future directions that target the field are also discussed to improve the accuracy and applicability of artificial intelligence models in clinical practice.

**Citation:** Niu PH, Zhao LL, Wu HL, Zhao DB, Chen YT. Artificial intelligence in gastric cancer: Application and future perspectives. *World J Gastroenterol* 2020; 26(36): 5408-5419

**URL:** <https://www.wjgnet.com/1007-9327/full/v26/i36/5408.htm>

**DOI:** <https://dx.doi.org/10.3748/wjg.v26.i36.5408>

## INTRODUCTION

Gastric cancer has long been believed to be an aggressive malignancy with a 5-year survival rate of less than 40%<sup>[1]</sup>. Despite the decrease in incidence and mortality over the past few decades in some countries, gastric cancer is still the sixth most common malignancy and remains the fourth leading cause of cancer-related deaths across the globe<sup>[2-4]</sup>. Due to the early atypical symptoms of gastric cancer and its advanced aggressive behaviors, reducing recurrence and prolonging survival are increasingly dependent on advanced screening, diagnosis, treatment, prognosis prediction, and other new technologies. Artificial intelligence (AI), with its efficient computational power and learning capacity, has caught considerable attention in the field of gastric cancer.

Contrary to human intelligence, AI is the intelligence displayed by machines, which first emerged in 1956. The term “artificial intelligence” was commonly used to describe machines (or computers) that imitate human “cognitive” functions (*e.g.*, learning and problem solving) related to human thinking<sup>[5]</sup>. As a subset of AI, machine learning (ML) can be defined as the computer algorithms that can automatically improve through experience<sup>[6]</sup>. Based on training data, the learner utilizes ML algorithms to build models with which the predictions or decisions can be made without explicit programming. In the last few years, ML algorithms, including random forest and support vector machines (SVM), were applied in various domains, especially in medicine. As of 2020, in the field of ML, deep learning (DL) had become the primary approach adopted in much ongoing work. DL is a type of ML algorithm that uses multiple layers to extract higher-level features from the original input gradually. Briefly, ML is a significant branch of AI, and DL is performed to implement ML. Recent developments of efficient hardware and computational power led to several AI models emerging in the field of gastric cancer<sup>[7-43]</sup>. AI-assisted diagnosis mainly included pathology, endoscopy, and computed tomography (CT)<sup>[7-33]</sup>, while related researchers in prognosis focused on recurrence, metastasis, and survival prediction<sup>[36-43]</sup>.

In this review, we searched the relevant works published up to April 2020 from the databases of PubMed, Embase, Web of Science, and the Cochrane Library, thus comprehensively summarizing the current status of AI-applications in gastric cancer. In addition, challenges and future directions that target the field were also discussed to improve the accuracy and applicability of AI-models in clinical practice.

## AI IN THE DIAGNOSIS OF GASTRIC CANCER

Gastric cancer was mostly diagnosed at advanced stages because of their latent and nonspecific symptoms, which led to poor prognosis. It was reported that early accurate detection of gastric cancer could increase the overwhelming 5-year survival rate by approximately 90%<sup>[44,45]</sup>. However, an early gastric cancer diagnosis was mainly limited to the number of experienced imaging experts. Furthermore, the diagnostic accuracy largely depended on the clinical experience of experts and was vulnerable to multiple factors. It is impossible for qualified experts to avoid all misdiagnoses and missed diagnoses. AI methods, which imitated human cognitive function *via* a computer, were adept at processing and analyzing large amounts of data and thus could assist gastroenterologists in clinical diagnosis and decision making. To date, AI

has been applied in many medical imaging fields, such as endoscopy, pathology as well as CT imaging. AI-assisted endoscopic diagnosis included the extraction of image features<sup>[7,8]</sup>, the detection of early gastric cancer<sup>[9-14]</sup>, the detection of precancerous conditions<sup>[15]</sup>, the optimization of magnifying endoscopy with narrow-band imaging (M-NBI)<sup>[16-19]</sup> and the application of Raman endoscopy<sup>[20,21]</sup>. AI-assisted pathologic diagnosis involved the automatic identification of gastric cancer<sup>[22]</sup>, the detection of gastric cancer based on the whole slide imaging (WSI)<sup>[23-26]</sup>, the automatic detection of tumor-infiltrating lymphocytes (TILs)<sup>[27]</sup> and the segmentation of lesion regions<sup>[28-31]</sup>, while AI-assisted CT diagnosis focused on the identification of preoperative peritoneal metastasis<sup>[32]</sup>, the detection of perigastric metastatic lymph nodes<sup>[33]</sup> and two other new imaging techniques<sup>[34,35]</sup>. Under certain conditions, the diagnostic performance of these AI models was not inferior to human experts.

### **AI-assisted diagnosis in endoscopy**

Endoscopy has played an essential role in the detection of gastric cancer because it enables endoscopists to observe cancerous sites directly. Accurate diagnosis of early gastric cancer by using endoscopic images is an urgent need to improve the patient's poor prognosis. However, recent studies showed that the detection accuracy of conventional endoscopy only ranged from 69% to 79%<sup>[46]</sup>. Due to the heavy workload of medical image analysis, it was inevitable for experienced endoscopists to run into misdiagnosis and missed diagnosis. Recent efforts in endoscopy focused on adopting AI techniques to enhance the inspection and diagnosis of gastric cancer (summarized in [Table 1](#)).

The key to obtaining high detection accuracy lies in the extraction of discriminative features, which can significantly distinguish the lesion images from standard images. Liu *et al*<sup>[7]</sup> designed an algorithm of ML, which was called joint diagonalization principal component analysis for the dimension reduction of endoscopic images. Then, a novel AI-assisted method was presented to detect early images of gastric cancer by combining joint diagonalization principal component analysis and conventional algorithms without learning, which revealed a better performance than traditional related methods. Ali *et al*<sup>[8]</sup> presented a novel texture extraction method named Gabor-based gray level co-occurrence matrix to detect the abnormal frames from the whole chromoendoscopy sequence. Then, the authors combined the SVM classifier and Gabor-based gray level co-occurrence matrix texture features to screen for early gastric cancer. The detection accuracy, specificity, sensitivity and the area under the curve (AUC) value were 87%, 82%, 91% and 0.91, respectively, which were higher than those results obtained by the SVM classifier combined with other texture extraction methods.

A study conducted by Luo *et al*<sup>[9]</sup> constructed the Gastrointestinal Artificial Intelligence Diagnostic System to detect upper gastrointestinal cancer in real time automatically. They used 1036496 endoscopy images with standard white light from 84424 cases across China for training and testing. In the different large-scale validation and prospective sets, the diagnostic accuracy was satisfactory as it ranged from 0.915 to 0.977. Moreover, the experimental results demonstrated that the Gastrointestinal Artificial Intelligence Diagnostic System attained sensitivity comparable to that of the human experts (0.942 *vs* 0.945). Sakai *et al*<sup>[10]</sup> introduced a convolutional neural network (CNN)-based automatic detection model with high accuracy and believed that the model could enhance the diagnostic capabilities of endoscopists. Yoon *et al*<sup>[11]</sup> adopted a lesion-based model for the accurate detection and depth prediction of early gastric cancer and evaluated the significant factors associated with AI-assisted diagnosis.

Nakahira *et al*<sup>[12]</sup> described that the analysis system of AI-assisted endoscopic images could effectively stratify the risk of gastric cancer and further evaluated the consistency of the AI model with the consensus diagnoses of three endoscopists. Zhu *et al*<sup>[13]</sup> also constructed a CNN computer-aided detection system to determine the invasion depth of early gastric cancer. Their proposed model achieved substantially higher specificity and accuracy compared to endoscopists with an AUC of 0.94. Another study suggested a multicolumn CNN to improve gastric cancer screening<sup>[14]</sup>. The novelty of their method lies in combining electronic gastroscopy with the analysis tools of cloud-based endoscopic images. Experimental results revealed that the proposed multicolumn CNN method dramatically outperformed the other CNN models (including AlexNet<sup>[47]</sup>, GoogLeNet<sup>[48]</sup> and VGGNet<sup>[49]</sup>) and non-DL methods (including kNN<sup>[50]</sup> and SVM-based<sup>[51]</sup> classifiers).

Chronic atrophic gastritis is a common precancerous gastric condition that might lead to the appearance and development of gastric cancer<sup>[52]</sup>. Conventional endoscopy had high variability among different endoscopists for distinguishing of precancerous

Table 1 Applications of artificial intelligence in endoscopy based on different study population

Ref.	Year	Country/region	Number of cases	Study population	Methods	Results
Liu <i>et al</i> <sup>[7]</sup>	2016	China	400 images	Hospital	JDPCA	AUCs (0.9532), accuracy (90.75%)
Ali <i>et al</i> <sup>[8]</sup>	2018	Pakistan	176 images	Public images dataset	G2LCM	AUC (0.91), accuracy (87%)
Luo <i>et al</i> <sup>[9]</sup>	2019	China	1036496 images	Hospital	GRAIDS	Accuracy (up to 97.7%)
Sakai <i>et al</i> <sup>[10]</sup>	2018	Japan	29037 images	Hospital	CNN	Accuracy (87.6%)
Yoon <i>et al</i> <sup>[11]</sup>	2019	South Korea	11539 images	Hospital	VGG model	AUCs (0.981 for detection), AUCs (0.851 for depth prediction)
Nakahira <i>et al</i> <sup>[12]</sup>	2019	Japan	107284 images	Cancer Institute	Deep neural network	Kappa value (0.27)
Zhu <i>et al</i> <sup>[13]</sup>	2019	China	993 images	Hospital	CNN-CAD system	AUCs (0.94), accuracy (89.16%)
Wang <i>et al</i> <sup>[14]</sup>	2019	China	104864 images	Hospital	MCNN	Sensitivity (79.622%), specificity (78.48%)
Guimarães <i>et al</i> <sup>[15]</sup>	2020	Germany	270 images	Medical center	DL	AUCs (0.98), accuracy (93%)
Miyaki <i>et al</i> <sup>[16]</sup>	2015	Japan	100 cases	Hospital	SVM	Average output value (0.846 ± 0.220)
Liu <i>et al</i> <sup>[17]</sup>	2018	China	1120 M-NBI images/3068 images	Hospital	Deep CNN	Top accuracy (98.5%)
Horiuchi <i>et al</i> <sup>[18]</sup>	2019	Japan	2828 images	Hospital	CNN	Accuracy (85.3%)
Li <i>et al</i> <sup>[19]</sup>	2019	China	2088 images	Hospital	CNN	Accuracy (90.91%)
Bergholt <i>et al</i> <sup>[20]</sup>	2011	Singapore	1063 <i>in vivo</i> Raman spectra	Hospital	ACO-LDA algorithms	Sensitivity (94.6%), specificity (94.6%)
Duraipandian <i>et al</i> <sup>[21]</sup>	2012	Singapore	2748 <i>in vivo</i> Raman spectra	Hospital	PLS-DA algorithms	Accuracy (85.6%), specificity (86.2%)

JDPCA: Joint diagonalization principal component analysis; AUC: Area under the curve; G2LCM: Gabor-based gray-level co-occurrence matrix; GRAIDS: Gastrointestinal Artificial Intelligence Diagnostic System; CNN: Convolutional neural network; VGG model: Visual geometry group; CNN-CAD system: Convolutional neural network computer-aided detection; MCNN: Multicolumn convolutional neural network; DL: Deep learning; SVM: Support vector machine; M-NBI: Narrow-band imaging; ACO-LDA: Ant colony optimization integrated with linear discriminant analysis; PLS-DA: Partial least squares-discriminant analysis.

conditions. Therefore, Guimarães *et al*<sup>[15]</sup> developed and trained a DL approach by using 200 real-world endoscopic images to diagnose atrophic gastritis. The DL model achieved a diagnostic accuracy of 93% and an AUC of 0.98, outperforming the combined results of expert endoscopists.

Given the rapid advances of narrow-band imaging, magnifying endoscopy with M-NBI had been given great attention to the diagnosis in early gastric cancer, which showed a more conspicuous accuracy than that by general white light imaging<sup>[53]</sup>. However, interobserver variability was a limitation for the diagnosis of the lesions using M-NBI, and it was difficult for endoscopists to master the diagnostic technology in a short time<sup>[54]</sup>. Given that the advance of AI may offer such a solution, several studies related to AI-assisted image diagnosis have emerged in recent years. Miyaki *et al*<sup>[16]</sup> developed the SVM system to quantitatively identify gastric cancer based on magnifying endoscopy with blue-laser imagery. Liu *et al*<sup>[17]</sup> first applied transfer learning of fine-tuning deep CNN features to classify the gastric mucosal lesions of M-NBI images. Horiuchi *et al*<sup>[18]</sup> and Li *et al*<sup>[19]</sup> adopted a CNN system to boost the capability to distinguish early gastric cancer from noncancerous lesions efficiently and obtained excellent diagnostic performances. Their results suggested that the diagnostic sensitivity of the CNN model with M-NBI was superior compared to that of endoscopists.

Furthermore, a previous report suggested that M-NBI was still inadequate to effectively and accurately diagnose grossly invisible lesions due to the lack of sufficient biochemical information<sup>[55]</sup>. Raman spectroscopy, as a novel point-wise spectroscopic technique, could comprehensively display the surface and subsurface

cellular structures from diagnostic tissue. It was suggested that Raman endoscopy had the promising potential for the diagnosis of early gastric cancer. Bergholt *et al.*<sup>[20]</sup> first combined the real-time Raman endoscopy with AI-based algorithms to distinguish neoplastic and normal gastric tissues. Later, another study devised an automated Raman spectroscopy diagnostic framework named PLS-DA algorithms to detect gastric cancer with a diagnostic accuracy of 85.6%<sup>[21]</sup>.

### **AI-assisted diagnosis in pathology**

The traditional diagnosis of gastric cancers was to identify morphological features of the malignant cells by using histopathological biopsy specimens, and manual pathological inspection of gastric slices was time-consuming and laborious. The need for automatic image analysis and histological classifications of gastric cancer has been increasing. Li *et al.*<sup>[22]</sup> proposed a novel DL-based framework, called GastricNet, to automatically identify gastric cancers. The classification accuracy of the proposed framework was 100% on gastric pathological slices, which was substantially higher than other existing networks, including DenseNet<sup>[56]</sup> and ResNet<sup>[57]</sup>.

In addition, the WSI, as a virtual counterpart of glass slides<sup>[58]</sup>, was considered to be comparable to optical microscopy for the diagnosis of gastric cancers. The advances of WSI led to the emergence of several AI applications in pathological diagnosis. Sharma *et al.*<sup>[23]</sup> described that the CNN architecture could efficiently analyze pathological images with an accuracy of 0.6990 for cancer classification and 0.8144 for necrosis detection. Leon *et al.*<sup>[24]</sup> assessed the application of deep CNN in the automatic detection of gastric cancer pathological images. Two approaches based on deep CNN were presented: One was performed to analyze the morphological features from the whole images, while the other independently investigated the local characteristic properties. Experiment results showed an average accuracy of up to 89.72%, which demonstrated the excellent performance of the proposed model in the detection of gastric cancers. Iizuka *et al.*<sup>[25]</sup> trained CNNs and recurrent neural networks to distinguish stomach adenocarcinoma, adenoma and non-neoplastic. On three independent test sets of biopsy histopathology WSI, DL applications achieved AUCs up to 0.97 for the classification of gastric adenocarcinoma. Yoshida *et al.*<sup>[26]</sup> compared the classification results of experienced pathologists with that of the e-Pathologist constructed by NEC Corporation. Although the overall concordance rate between the two methods was only 55.6% (1702/3062), the concordance rate for the negative biopsy specimens was as high as 90.6% (1033/1140). Furthermore, current evidence revealed that TILs were associated with the prognosis of gastric cancer<sup>[59]</sup>. A related study presented the CNN model to automatically detect TILs on histopathological WSI with an acceptable accuracy of 96.88%<sup>[27]</sup>.

The automatic segmentation of lesion regions was a challenge in the AI-assisted pathological diagnosis of gastric cancer. To alleviate the shortage of well-annotated pathology image data, Liang *et al.*<sup>[28]</sup> firstly applied the DL method to segment the pathological images. They presented a new neural network architecture and algorithm named as an overlapped region forecast for the detection of gastric cancers. An intersection over union coefficient (IoU) of 88.3% and 91.1% accuracy indicated that the model had reached the standard of supervised learning. Qu *et al.*<sup>[29]</sup> presented a novel type of intermediate dataset and developed a stepwise fine-tuning-based scheme to improve the classification performance of deep neural networks. Sun *et al.*<sup>[30]</sup> also demonstrated that the proposed DL model was a powerful image segmentation tool with 91.60% for the mean accuracy and 82.65% for the mean IoU. Another study also demonstrated that the Mask R-CNN model was an effective method to target the field of medical image segmentation<sup>[31]</sup>.

Hence, these satisfactory results of AI-assisted applications highlighted the enormous potential benefit to help the pathologists and support the pathological detection of gastric cancer, especially for improving the efficiency of image segmentation and reducing the diagnostic time (summarized in [Table 2](#)).

### **AI-assisted diagnosis in CT imaging**

Attributable to the noninvasiveness and convenience, CT was widely used for the clinical diagnosis of gastric cancer<sup>[60,61]</sup>. However, the diagnostic accuracy was mainly dependent on the clinical experience of radiologists. When interpreting large amounts of CT images, the radiologist's diagnostic accuracy would inevitably decrease, and errors were more prone to occur. Several approaches based on ML and DL reported that they could effectively extract valuable information on CT images (summarized in [Table 3](#)). For example, Huang *et al.*<sup>[32]</sup> applied the DL method on diagnostic analysis and created a deep CNN model to identify the preoperative peritoneal metastasis in advanced gastric cancer.

**Table 2 Applications of artificial intelligence in pathology and computerized tomography based on different study population**

Ref.	Year	Country/region	Number of cases	Study population	Methods	Results
Li <i>et al.</i> <sup>[22]</sup>	2018	China	700 slices	Publicly gastric slice dataset	GastricNet	Accuracy (100%)
Sharma <i>et al.</i> <sup>[23]</sup>	2017	Germany	454 cases	Hospital	CNN	Accuracy (0.6990 for cancer classification), accuracy (0.8144 for necrosis detection)
Leon <i>et al.</i> <sup>[24]</sup>	2019	Colombia	40 images	Department of pathology	Deep CNN	Accuracy (up to 89.72%)
Iizuka <i>et al.</i> <sup>[25]</sup>	2020	Japan	1746 biopsy histopathology WSIs	Hospital, TCGA	CNN, RNN	AUCs (up to 0.98), accuracy (95.6%)
Yoshida <i>et al.</i> <sup>[26]</sup>	2018	Japan	3062 gastric biopsy specimens	Cancer center	ML	Overall concordance rate (55.6%)
Garcia <i>et al.</i> <sup>[27]</sup>	2017	Peru	3257 images	-	Deep CNN	Accuracy (96.88%)
Liang <i>et al.</i> <sup>[28]</sup>	2019	China	1900 images	-	DL	IoU (0.883), accuracy (91.09%)
Qu <i>et al.</i> <sup>[29]</sup>	2018	Japan	9720 images/19440 images	Hospital	DL	AUCs (up to 0.965)
Sun <i>et al.</i> <sup>[30]</sup>	2019	China	500 pathological images	Hospital	DL	IoU (0.8265), accuracy (91.60%)
Cao <i>et al.</i> <sup>[31]</sup>	2019	China	1399 pathological sections	-	the Mask R-CNN	AP value (61.2)

GastricNet: The deep learning framework; CNN: Convolutional neural networks; WSIs: Whole slide images; TCGA: The Cancer Genome Atlas; RNN: Recurrent neural networks; AUC: Area under the curve; ML: Machine learning; DL: Deep learning; IoU: Intersection over union coefficient; AP: Average precision.

**Table 3 Applications of artificial intelligence in computerized tomography based on different study population**

Ref.	Year	Country/region	Number of cases	Study population	Methods	Results
Huang <i>et al.</i> <sup>[32]</sup>	2020	China	-	Hospital	Deep CNN	-
Gao <i>et al.</i> <sup>[33]</sup>	2019	China	32495 images	Hospital	FR-CNN	AUCs (0.9541)
Li <i>et al.</i> <sup>[34]</sup>	2015	China	26 cases	Hospital	KNN algorithm	Accuracy (76.92%)
Li <i>et al.</i> <sup>[35]</sup>	2012	China	38 lymph node datasets	Hospital	ML	Accuracy (96.33%)

CNN: Convolutional neural networks; FR-CNN: Faster region-based convolutional neural networks; AUCs: Area under the curve; KNN algorithm: K-nearest neighbor algorithm; ML: Machine learning.

Compared to the current status of poor CT depiction in lymph node metastasis and low detection sensitivity, the novel DL-based model was expected to obtain an excellent performance of CT imaging. Gao *et al.*<sup>[33]</sup> developed and validated faster region-based CNN based on CT images. The experimental results showed that faster region-based CNN obtained a high accuracy for the diagnosis of perigastric metastatic lymph nodes with the mean average precision value of 0.7801 and AUC value of 0.9541.

Moreover, dual-energy spectral CT (DEsCT), as a new imaging technique, could easily switch between high-energy and low-energy datasets, which enabled the precise creation of virtual images based on monochromatic spectra. The recent improvement of DEsCT made it available for routine clinical practice. However, it was difficult for radiologists to take full advantage of more quantitative data obtained by the DEsCT system. A recent study introduced the AI-assisted utility of DEsCT imaging for the stages and characteristics of gastric cancer<sup>[34]</sup>. The authors used a new multiple instance learning method to determine the invasion depth of gastric cancer and achieved a gross accuracy of 0.7692 after optimization. Also, it was reported that gemstone spectral imaging could provide more valuable image information to radiologists than conventional CT<sup>[62]</sup>. Li *et al.*<sup>[35]</sup> proposed the ML-based gemstone spectral imaging analysis for lymph node metastasis in gastric cancer, which achieved a higher accuracy of detection. The feasibility and the effectiveness of gemstone spectral imaging-CT to

diagnose lymph node metastasis outperformed traditional detection methods, such as endoscopic ultrasound and the multidetector-row CT.

---

## AI IN PROGNOSIS PREDICTION OF GASTRIC CANCER

---

Accurate prognosis prediction of gastric cancer was of significance for both clinicians and patients. Such information could assist clinicians in decision-making and improve management over patients. It was appreciated that the demographics, pathological indicators, physiological states and even social contacts had an impact on the prognosis of gastric cancer patients. However, conventional statistical methods, such as the tumor-node-metastasis staging system and nomogram, could hardly analyze the complicated internal connections among these characteristics. Based on its excellent computational power and integration capability, AI models had been applied to improve the survival rates of gastric cancer patients.

In the last few years, the applications of AI in prognosis involved the predictions of survival time<sup>[36-38]</sup>, recurrence risk<sup>[39,40]</sup> and metastasis<sup>[41-43]</sup> (summarized in Table 4). Jiang *et al.*<sup>[36]</sup> applied SVM to survival analysis and developed a prognostic classifier. The results showed a higher predictive accuracy of overall survival and disease-free survival than the tumor-node-metastasis staging system defined by the American Joint Committee on Cancer. Besides, the proposed gastric cancer-SVM classifier was also used to predict adjuvant chemotherapeutic benefit, which was able to facilitate the individualized treatment for gastric cancer. Combining demographics, pathological indicators and physiological characteristics of 939 cases, Lu *et al.*<sup>[37]</sup> created a novel multimodal hypergraph learning framework to improve the accuracy of survival prediction. The result showed that the proposed approach outperformed random forest and SVM in overall survival prediction. Another study compared the value of artificial neural network and Bayesian neural networks (BNN) in survival prediction of gastric cancer patients, and the findings indicated BNN was superior to the artificial neural network method<sup>[38]</sup>.

Recurrence was one of the leading causes of death for gastric cancer patients<sup>[63]</sup>, thereby the accurate evaluation of recurrence risk was relevant in routine clinical work. Recent reports indicated that the AI-assisted recurrence prediction system achieved better performances than traditional statistical methods. Zhang *et al.*<sup>[39]</sup> used ML methods to extract radiomic signatures from CT images of 669 consecutive patients diagnosed with advanced gastric cancer. Then they constructed a CT-based radiomic model to predict the recurrent risk of advanced gastric cancer. Liu *et al.*<sup>[40]</sup> trained the SVM classifier to predict the recurrence in patients with gastric cancer. Using the gene expression profiling dataset GSE26253<sup>[64]</sup>, they discovered that a set of feature genes (including *PLCG1*, *PRKACA* and *TGFBR1*) potentially correlated with gastric cancer recurrence.

Lymph node metastasis was a significant prognostic indicator for gastric cancer<sup>[65]</sup>. The lack of accurate methods to predict gastric cancer metastasis has led to the application of AI-assisted prediction techniques to evaluate the metastasis risk better. Bollschweiler *et al.*<sup>[41]</sup> demonstrated that artificial neural networks could broadly enhance the predictive accuracy of lymph node metastasis. Hensler *et al.*<sup>[42]</sup> proposed a novel artificial neural network approach for the preoperative prediction of lymph node metastasis. Compared with the Maruyama Diagnostic System developed at the National Cancer Center in Tokyo, the proposed model showed higher accuracy and better reliability. Also, it was shown that liver metastases could severely diminish the long-term survival of gastric cancer patients. Jagric *et al.*<sup>[43]</sup> presented a learning vector quantization networks to predict postoperative liver metastasis in patients suffering from gastric cancer and obtained a reasonably high predictive value.

---

## CHALLENGES AND FUTURE PERSPECTIVES

---

Despite the reported great success of AI in medical image-based diagnosis and prognosis prediction, several barriers must be removed before widespread clinical practice occurs.

A flexible AI model requires a large amount of well-annotated data for training, validating and testing, while the related research with small sample sizes is prone to have measurement errors<sup>[66]</sup>. With advances in medical-based imaging, such as endoscopy and pathology, numerous data is generated continuously to help physicians in clinical diagnosis and decision making. However, such data are rarely

Table 4 Applications of artificial intelligence in gastric cancer prognosis based on different study population

Ref.	Year	Country/region	Number of cases	Study population	Methods	Results
Jiang <i>et al</i> <sup>[36]</sup>	2018	China	786 cases	Hospital	SVM classifier	AUCs (up to 0.834)
Lu <i>et al</i> <sup>[37]</sup>	2017	China	939 patients	Hospital	MMHG	Accuracy (69.28%)
Korhani Kangi <i>et al</i> <sup>[38]</sup>	2018	Iran	339 patients	Hospital	ANN, BNN	Sensitivity (88.2% for ANN, 90.3% for BNN), specificity (95.4% for ANN, 90.9% for BNN)
Zhang <i>et al</i> <sup>[39]</sup>	2019	China	669 cases	Hospital	ML	AUCs (up to 0.831)
Liu <i>et al</i> <sup>[40]</sup>	2018	China	432 GC tissue samples	Hospital	SVM classifier	Accuracy (up to 94.19%)
Bollschweiler <i>et al</i> <sup>[41]</sup>	2004	Germany, Japan	135 cases	Cancer center	ANN	Accuracy (93%)
Hensler <i>et al</i> <sup>[42]</sup>	2005	Germany, Japan	4302 cases	Cancer center	QUEEN technique	Accuracy (72.73%)
Jagric <i>et al</i> <sup>[43]</sup>	2010	Slovenia	213 cases	Clinical center	Learning vector quantization neural networks	Sensitivity (71%), specificity (96.1%)

SVM: Support vector machine; AUC: Area under the curve; MMHG: Multimodal hypergraph learning framework; ANN: Artificial neural networks; BNN: Bayesian neural network models; ML: Machine learning; GC: Gastric cancer; QUEEN technique: Quality assured efficient engineering of feedforward neural networks with supervised learning.

labeled or annotated, which are not suitable for algorithm training. Hence, the availability of high-quality data is a significant challenge for the development and optimization of AI. A meaningful way to access these qualified data sets is to establish large-scale open-access databases. Moreover, existing data resources should also be utilized effectively. Single hospitals and institutions are encouraged to share validated data to improve the applicability of AI in gastric cancer, which is similar to previous research related to Alzheimer's disease<sup>[67]</sup>.

An additional hurdle to the improvement of robust algorithms for gastric cancer is the interpretability of AI. In some studies, the applications of ML and DL revealed higher sensitivity and fewer false positives than radiologists<sup>[68,69]</sup>. However, they also inevitably ran into the risk of overfitting, leading to a tradeoff between accuracy and interpretability. In addition, the "black box" feature of algorithms may cause clinician's suspicion of ML applications. Cabitza *et al*<sup>[70]</sup> offered that the "black box" of ML may bring the unintended negative consequences in clinical practice. Fortunately, recent advances in data visualization tools deepened the visual understanding of algorithm decision making<sup>[71]</sup> thus contributing to the promotion of the optimization algorithms and widespread clinical acceptance.

Given its advantages of computational power and learning capacity, AI will appear in various gastric cancer fields. Increasingly, it is appreciated that the characteristics of diseases, the physiological, psychological states of patients and even social communication have an impact on the prognosis of gastric cancer patients. It is difficult for physicians to integrate complex data manually. An AI model is adept at integrating much information from the vast majority of data, which has the potential to reduce the workload of clinicians substantially. However, due to some ethical and safety issues, the predictions that are generated by AI require further evaluation and interpretation by professional physicians. Thereby, AI techniques will not wholly replace physicians in future clinical practice and combining human beings with AI can achieve the ideal state of higher efficiency.

## CONCLUSION

AI techniques, especially ML and DL, are making remarkable progress in the field of gastric cancer. The current status and future perspectives of AI-assisted diagnosis and prognosis were comprehensively introduced in this review. Numerous related researchers reported the impressive performance of AI, which was superior to the standard statistical methods. Despite several limitations and hurdles that exist in AI, such as the lack of well-annotated data and the interpretability of models, based on its

efficient computational power and learning competence, AI will revolutionize the diagnosis and prognosis of gastric cancer in the foreseeable future.

## REFERENCES

- Jemal A**, Ward EM, Johnson CJ, Cronin KA, Ma J, Ryerson B, Mariotto A, Lake AJ, Wilson R, Sherman RL, Anderson RN, Henley SJ, Kohler BA, Penberthy L, Feuer EJ, Weir HK. Annual Report to the Nation on the Status of Cancer, 1975-2014, Featuring Survival. *J Natl Cancer Inst* 2017; **109**: djx030 [PMID: 28376154 DOI: 10.1093/jnci/djx030]
- Islami F**, DeSantis CE, Jemal A. Incidence Trends of Esophageal and Gastric Cancer Subtypes by Race, Ethnicity, and Age in the United States, 1997-2014. *Clin Gastroenterol Hepatol* 2019; **17**: 429-439 [PMID: 29902641 DOI: 10.1016/j.cgh.2018.05.044]
- Steevens J**, Botterweck AA, Dirx MJ, van den Brandt PA, Schouten LJ. Trends in incidence of oesophageal and stomach cancer subtypes in Europe. *Eur J Gastroenterol Hepatol* 2010; **22**: 669-678 [PMID: 19474750 DOI: 10.1097/MEG.0b013e32832ca091]
- Ferlay J**, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, Znaor A, Bray F. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer* 2019; **144**: 1941-1953 [PMID: 30350310 DOI: 10.1002/ijc.31937]
- Russel S**, Norvig P. Artificial Intelligence: A Modern Approach. 2th ed. Pearson Education, 2003
- Christian R**. Machine Learning, a Probabilistic Perspective. *Chance* 2014; **27**: 62-63 [DOI: 10.1080/09332480.2014.914768]
- Liu DY**, Gan T, Rao NN, Xing YW, Zheng J, Li S, Luo CS, Zhou ZJ, Wan YL. Identification of lesion images from gastrointestinal endoscope based on feature extraction of combinational methods with and without learning process. *Med Image Anal* 2016; **32**: 281-294 [PMID: 27236223 DOI: 10.1016/j.media.2016.04.007]
- Ali H**, Yasmin M, Sharif M, Rehmani MH. Computer assisted gastric abnormalities detection using hybrid texture descriptors for chromoendoscopy images. *Comput Methods Programs Biomed* 2018; **157**: 39-47 [PMID: 29477434 DOI: 10.1016/j.cmpb.2018.01.013]
- Luo H**, Xu G, Li C, He L, Luo L, Wang Z, Jing B, Deng Y, Jin Y, Li B, Tan W, He C, Seeruttun SR, Wu Q, Huang J, Huang DW, Chen B, Lin SB, Chen QM, Yuan CM, Chen HX, Pu HY, Zhou F, He Y, Xu RH. Real-time artificial intelligence for detection of upper gastrointestinal cancer by endoscopy: a multicentre, case-control, diagnostic study. *Lancet Oncol* 2019; **20**: 1645-1654 [PMID: 31591062 DOI: 10.1016/S1470-2045(19)30637-0]
- Sakai Y**, Takemoto S, Hori K, Nishimura M, Ikematsu H, Yano T, Yokota H. Automatic detection of early gastric cancer in endoscopic images using a transferring convolutional neural network. *Conf Proc IEEE Eng Med Biol Soc* 2018; **2018**: 4138-4141 [PMID: 30441266 DOI: 10.1109/EMBC.2018.8513274]
- Yoon HJ**, Kim S, Kim JH, Keum JS, Oh SI, Jo J, Chun J, Youn YH, Park H, Kwon IG, Choi SH, Noh SH. A Lesion-Based Convolutional Neural Network Improves Endoscopic Detection and Depth Prediction of Early Gastric Cancer. *J Clin Med* 2019; **8**: 1310 [PMID: 31454949 DOI: 10.3390/jcm8091310]
- Nakahira H**, Ishihara R, Aoyama K, Kono M, Fukuda H, Shimamoto Y, Nakagawa K, Ohmori M, Iwatsubo T, Iwagami H, Matsuno K, Inoue S, Matsuura N, Shichijo S, Maekawa A, Kanesaka T, Yamamoto S, Takeuchi Y, Higashino K, Uedo N, Matsunaga T, Tada T. Stratification of gastric cancer risk using a deep neural network. *JGH Open* 2020; **4**: 466-471 [PMID: 32514455 DOI: 10.1002/jgh3.12281]
- Zhu Y**, Wang QC, Xu MD, Zhang Z, Cheng J, Zhong YS, Zhang YQ, Chen WF, Yao LQ, Zhou PH, Li QL. Application of convolutional neural network in the diagnosis of the invasion depth of gastric cancer based on conventional endoscopy. *Gastrointest Endosc* 2019; **89**: 806-815.e1 [PMID: 30452913 DOI: 10.1016/j.gie.2018.11.011]
- Wang H**, Ding S, Wu DS, Zhang YT, Yang SL. Smart connected electronic gastroscope system for gastric cancer screening using multi-column convolutional neural networks. *Int J Prod Res* 2019; **57**: 6795-6806 [DOI: 10.1080/00207543.2018.1464232]
- Guimarães P**, Keller A, Fehlmann T, Lammert F, Casper M. Deep-learning based detection of gastric precancerous conditions. *Gut* 2020; **69**: 4-6 [PMID: 31375599 DOI: 10.1136/gutjnl-2019-319347]
- Miyaki R**, Yoshida S, Tanaka S, Kominami Y, Sanomura Y, Matsuo T, Oka S, Raytchev B, Tamaki T, Koide T, Kaneda K, Yoshihara M, Chayama K. A computer system to be used with laser-based endoscopy for quantitative diagnosis of early gastric cancer. *J Clin Gastroenterol* 2015; **49**: 108-115 [PMID: 24583752 DOI: 10.1097/MCG.000000000000104]
- Liu XQ**, Wang CL, Hu Y, Zeng Z, Bai JY, Liao GB. Transfer learning with convolutional neural network for early gastric cancer classification on magnifying narrow-band imaging images. ICIP 2018: Proceedings of the 25th IEEE International Conference on Image Processing; 2018 Oct 07-10; Athens, Greece. New York: IEEE, 2018: 1388-1392 [DOI: 10.1109/ICIP.2018.8451067]
- Horiuchi Y**, Aoyama K, Tokai Y, Hirasawa T, Yoshimizu S, Ishiyama A, Yoshio T, Tsuchida T, Fujisaki J, Tada T. Convolutional Neural Network for Differentiating Gastric Cancer from Gastritis Using Magnified Endoscopy with Narrow Band Imaging. *Dig Dis Sci* 2020; **65**: 1355-1363 [PMID: 31584138 DOI: 10.1007/s10620-019-05862-6]
- Li L**, Chen Y, Shen Z, Zhang X, Sang J, Ding Y, Yang X, Li J, Chen M, Jin C, Chen C, Yu C. Convolutional neural network for the diagnosis of early gastric cancer based on magnifying narrow band imaging. *Gastric Cancer* 2020; **23**: 126-132 [PMID: 31332619 DOI: 10.1007/s10120-019-00992-2]
- Bergholt MS**, Zheng W, Lin K, Ho KY, Teh M, Yeoh KG, Yan So JB, Huang Z. *In vivo* diagnosis of gastric cancer using Raman endoscopy and ant colony optimization techniques. *Int J Cancer* 2011; **128**: 2673-2680 [PMID: 20726002 DOI: 10.1002/ijc.25618]
- Duraipandian S**, Sylvest Bergholt M, Zheng W, Yu Ho K, Teh M, Guan Yeoh K, Bok Yan So J, Shabbir A, Huang Z. Real-time Raman spectroscopy for *in vivo*, online gastric cancer diagnosis during clinical

- endoscopic examination. *J Biomed Opt* 2012; **17**: 081418 [PMID: 23224179 DOI: 10.1117/1.JBO.17.8.081418]
- 22 **Li YX**, Li XC, Xie XP, Shen LL. Deep learning based gastric cancer identification. ISBI 2018: Proceedings of the 15th IEEE International Symposium on Biomedical Imaging; 2018 Apr 04-07; Washington, DC. New York: IEEE, 2018: 182-185 [DOI: 10.1109/ISBI.2018.8363550]
  - 23 **Sharma H**, Zerbe N, Klempert I, Hellwich O, Hufnagl P. Deep convolutional neural networks for automatic classification of gastric carcinoma using whole slide images in digital histopathology. *Comput Med Imaging Graph* 2017; **61**: 2-13 [PMID: 28676295 DOI: 10.1016/j.compmedimag.2017.06.001]
  - 24 **Leon F**, Gelvez M, Jaimes Z, Gelvez T, Arguello H. Supervised Classification of Histopathological Images Using Convolutional Neuronal Networks for Gastric Cancer Detection. STSIVA 2019: Proceedings of the 22nd Symposium on Image, Signal Processing and Artificial Vision; 2019 Apr 24-26; Bucaramanga, Colombia. New York: IEEE, 2019 [DOI: 10.1109/STSIVA.2019.8730284]
  - 25 **Iizuka O**, Kanavati F, Kato K, Rambeau M, Arihiro K, Tsuneki M. Deep Learning Models for Histopathological Classification of Gastric and Colonic Epithelial Tumours. *Sci Rep* 2020; **10**: 1504 [PMID: 32001752 DOI: 10.1038/s41598-020-58467-9]
  - 26 **Yoshida H**, Shimazu T, Kiyuna T, Marugame A, Yamashita Y, Cosatto E, Taniguchi H, Sekine S, Ochiai A. Automated histological classification of whole-slide images of gastric biopsy specimens. *Gastric Cancer* 2018; **21**: 249-257 [PMID: 28577229 DOI: 10.1007/s10120-017-0731-8]
  - 27 **Garcia E**, Hermoza R, Castanon CB, Cano L, Castillo M, Castaneda C. Automatic Lymphocyte Detection on Gastric Cancer IHC Images using Deep Learning. CBMS 2017: Proceedings of the 30th IEEE International Symposium on Computer-Based Medical Systems; 2017 Jun 22-24; Thessaloniki, Greece. New York: IEEE, 2017: 200-204 [DOI: 10.1109/CBMS.2017.94]
  - 28 **Liang Q**, Nan Y, Coppola G, Zou K, Sun W, Zhang D, Wang Y, Yu G. Weakly Supervised Biomedical Image Segmentation by Reiterative Learning. *IEEE J Biomed Health Inform* 2019; **23**: 1205-1214 [PMID: 29994489 DOI: 10.1109/JBHI.2018.2850040]
  - 29 **Qu J**, Hiruta N, Terai K, Nosato H, Murakawa M, Sakanashi H. Gastric Pathology Image Classification Using Stepwise Fine-Tuning for Deep Neural Networks. *J Healthc Eng* 2018; **2018**: 8961781 [PMID: 30034677 DOI: 10.1155/2018/8961781]
  - 30 **Sun MY**, Zhang GH, Dang H, Qi XQ, Zhou XG, Chang Q. Accurate Gastric Cancer Segmentation in Digital Pathology Images Using Deformable Convolution and Multi-Scale Embedding Networks. *IEEE Access* 2019; **7**: 75530-75541 [DOI: 10.1109/ACCESS.2019.2918800]
  - 31 **Cao GT**, Song WL, Zhao ZW. Gastric Cancer Diagnosis with Mask R-CNN. IHMSC 2019: Proceedings of the 11th International Conference on Intelligent Human-Machine Systems and Cybernetics; 2019 Aug 24-25; Hangzhou, China. New York: IEEE, 2019: 60-63 [DOI: 10.1109/IHMSC.2019.00022]
  - 32 **Huang Z**, Liu D, Chen X, Yu P, Wu J, Song B, Hu J, Wu B. Retrospective imaging studies of gastric cancer: Study protocol clinical trial (SPIRIT Compliant). *Medicine (Baltimore)* 2020; **99**: e19157 [PMID: 32080093 DOI: 10.1097/MD.00000000000019157]
  - 33 **Gao Y**, Zhang ZD, Li S, Guo YT, Wu QY, Liu SH, Yang SJ, Ding L, Zhao BC, Li S, Lu Y. Deep neural network-assisted computed tomography diagnosis of metastatic lymph nodes from gastric cancer. *Chin Med J (Engl)* 2019; **132**: 2804-2811 [PMID: 31856051 DOI: 10.1097/CM9.0000000000000532]
  - 34 **Li C**, Shi C, Zhang H, Chen Y, Zhang S. Multiple instance learning for computer aided detection and diagnosis of gastric cancer with dual-energy CT imaging. *J Biomed Inform* 2015; **57**: 358-368 [PMID: 26319541 DOI: 10.1016/j.jbi.2015.08.017]
  - 35 **Li C**, Zhang S, Zhang H, Pang L, Lam K, Hui C, Zhang S. Using the K-nearest neighbor algorithm for the classification of lymph node metastasis in gastric cancer. *Comput Math Methods Med* 2012; **2012**: 876545 [PMID: 23150740 DOI: 10.1155/2012/876545]
  - 36 **Jiang Y**, Xie J, Han Z, Liu W, Xi S, Huang L, Huang W, Lin T, Zhao L, Hu Y, Yu J, Zhang Q, Li T, Cai S, Li G. Immunomarker Support Vector Machine Classifier for Prediction of Gastric Cancer Survival and Adjuvant Chemotherapeutic Benefit. *Clin Cancer Res* 2018; **24**: 5574-5584 [PMID: 30042208 DOI: 10.1158/1078-0432.CCR-18-0848]
  - 37 **Lu F**, Chen ZK, Yuan X, Li Q, Du ZD, Luo L, Zhang FY. MMHG: Multi-modal Hypergraph Learning for Overall Survival After D2 Gastrectomy for Gastric Cancer. DASC/PiCom/DataCom/CyberSciTech 2017: Proceedings of the 15th Intl Conf on Dependable, Autonomic and Secure Computing, 15th Intl Conf on Pervasive Intelligence and Computing, 3rd Intl Conf on Big Data Intelligence and Computing and Cyber Science and Technology Congress; 2017 Nov 6-10; Orlando, FL, USA. California: IEEE Computer Society, 2017: 164-9 [DOI: 10.1109/DASC-PICom-DataCom-CyberSciTec.2017.40]
  - 38 **Korhani Kangi A**, Bahrapour A. Predicting the Survival of Gastric Cancer Patients Using Artificial and Bayesian Neural Networks. *Asian Pac J Cancer Prev* 2018; **19**: 487-490 [PMID: 29480983 DOI: 10.22034/APJCP.2018.19.2.487]
  - 39 **Zhang W**, Fang M, Dong D, Wang X, Ke X, Zhang L, Hu C, Guo L, Guan X, Zhou J, Shan X, Tian J. Development and validation of a CT-based radiomic nomogram for preoperative prediction of early recurrence in advanced gastric cancer. *Radiother Oncol* 2020; **145**: 13-20 [PMID: 31869677 DOI: 10.1016/j.radonc.2019.11.023]
  - 40 **Liu B**, Tan J, Wang X, Liu X. Identification of recurrent risk-related genes and establishment of support vector machine prediction model for gastric cancer. *Neoplasia* 2018; **65**: 360-366 [PMID: 29788739 DOI: 10.4149/neo\_2018\_170507N326]
  - 41 **Bollschweiler EH**, Mönig SP, Hensler K, Baldus SE, Maruyama K, Hölscher AH. Artificial neural network for prediction of lymph node metastases in gastric cancer: a phase II diagnostic study. *Ann Surg Oncol* 2004; **11**: 506-511 [PMID: 15123460 DOI: 10.1245/ASO.2004.04.018]
  - 42 **Hensler K**, Waschulzik T, Mönig SP, Maruyama K, Hölscher AH, Bollschweiler E. Quality-assured Efficient Engineering of Feedforward Neural Networks (QUEEN) -- pretherapeutic estimation of lymph node status in patients with gastric carcinoma. *Methods Inf Med* 2005; **44**: 647-654 [PMID: 16400373 DOI: 10.1055/s-0038-1634021]
  - 43 **Jagric T**, Potrc S, Jagric T. Prediction of liver metastases after gastric cancer resection with the use of learning vector quantization neural networks. *Dig Dis Sci* 2010; **55**: 3252-3261 [PMID: 20186483 DOI: 10.1111/j.1365-2035.2010.04441.x]

- 10.1007/s10620-010-1155-z]
- 44 **Amin MB**, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR, Winchester DP. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more “personalized” approach to cancer staging. *CA Cancer J Clin* 2017; **67**: 93-99 [PMID: 28094848 DOI: 10.3322/caac.21388]
  - 45 **Sano T**, Coit DG, Kim HH, Roviello F, Kassab P, Wittekind C, Yamamoto Y, Ohashi Y. Proposal of a new stage grouping of gastric cancer for TNM classification: International Gastric Cancer Association staging project. *Gastric Cancer* 2017; **20**: 217-225 [PMID: 26897166 DOI: 10.1007/s10120-016-0601-9]
  - 46 **Choi J**, Kim SG, Im JP, Kim JS, Jung HC, Song IS. Comparison of endoscopic ultrasonography and conventional endoscopy for prediction of depth of tumor invasion in early gastric cancer. *Endoscopy* 2010; **42**: 705-713 [PMID: 20652857 DOI: 10.1055/s-0030-1255617]
  - 47 **Krizhevsky A**, Sutskever I, Hinton GE. ImageNet classification with deep convolutional neural networks. *Commun ACM* 2017; **60**: 84-90 [DOI: 10.1145/3065386]
  - 48 **Szegedy C**, Vanhoucke V, Ioffe S, Shlens J, Wojna Z. Rethinking the Inception Architecture for Computer Vision. CVPR 2016: Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition; 2016 JUN 27-30; Seattle, WA, USA. New York: IEEE, 2016: 2818-2826 [DOI: 10.1109/CVPR.2016.308]
  - 49 **Simonyan K**, Zisserman A. Very Deep Convolutional Networks for Large-Scale Image Recognition; 2014. Preprint. [cited 10 April 2015]. Available from: 1409.3301
  - 50 **Ding JR**, Cheng HD, Xian M, Zhang YT, Xu F. Local-weighted Citation-kNN algorithm for breast ultrasound image classification. *Optik* 2015; **126**: 5188-5193 [DOI: 10.1016/j.ijleo.2015.09.231]
  - 51 **Shen D**, Wu G, Suk HI. Deep Learning in Medical Image Analysis. *Annu Rev Biomed Eng* 2017; **19**: 221-248 [PMID: 28301734 DOI: 10.1146/annurev-bioeng-071516-044442]
  - 52 **Correa P**, Piazzuelo MB. The gastric precancerous cascade. *J Dig Dis* 2012; **13**: 2-9 [PMID: 22188910 DOI: 10.1136/gut.2003.034629]
  - 53 **Pimentel-Nunes P**, Dinis-Ribeiro M, Soares JB, Marcos-Pinto R, Santos C, Rolanda C, Bastos RP, Areia M, Afonso L, Bergman J, Sharma P, Gotoda T, Henrique R, Moreira-Dias L. A multicenter validation of an endoscopic classification with narrow band imaging for gastric precancerous and cancerous lesions. *Endoscopy* 2012; **44**: 236-246 [PMID: 22294194 DOI: 10.1055/s-0031-1291537]
  - 54 **Nakanishi H**, Doyama H, Ishikawa H, Uedo N, Gotoda T, Kato M, Nagao S, Nagami Y, Aoyagi H, Imagawa A, Kodaira J, Mitsui S, Kobayashi N, Muto M, Takatori H, Abe T, Tsujii M, Watari J, Ishiyama S, Oda I, Ono H, Kaneko K, Yokoi C, Ueo T, Uchita K, Matsumoto K, Kanesaka T, Morita Y, Katsuki S, Nishikawa J, Inamura K, Kinjo T, Yamamoto K, Yoshimura D, Araki H, Kashida H, Hosokawa A, Mori H, Yamashita H, Motohashi O, Kobayashi K, Hirayama M, Kobayashi H, Endo M, Yamano H, Murakami K, Koike T, Hirasawa K, Miyaoka Y, Hamamoto H, Hikichi T, Hanabata N, Shimoda R, Hori S, Sato T, Kodashima S, Okada H, Mannami T, Yamamoto S, Niwa Y, Yashima K, Tanabe S, Satoh H, Sasaki F, Yamazato T, Ikeda Y, Nishisaki H, Nakagawa M, Matsuda A, Tamura F, Nishiyama H, Arita K, Kawasaki K, Hoppo K, Oka M, Ishihara S, Mukasa M, Minamino H, Yao K. Evaluation of an e-learning system for diagnosis of gastric lesions using magnifying narrow-band imaging: a multicenter randomized controlled study. *Endoscopy* 2017; **49**: 957-967 [PMID: 28637065 DOI: 10.1055/s-0043-111888]
  - 55 **Mirabal YN**, Chang SK, Atkinson EN, Malpica A, Follen M, Richards-Kortum R. Reflectance spectroscopy for *in vivo* detection of cervical precancer. *J Biomed Opt* 2002; **7**: 587-594 [PMID: 12421125 DOI: 10.1117/1.1502675]
  - 56 **Huang G**, Liu Z, van der Maaten L, Weinberger KQ. Densely Connected Convolutional Networks. CVPR 2017: Proceedings of the 30th IEEE/CVF Conference on Computer Vision and Pattern Recognition; 2017 Jul 21-26; Honolulu, HI, USA. New York: IEEE, 2017: 2261-2269 [DOI: 10.1109/CVPR.2017.243]
  - 57 **He K**, Zhang X, Ren S, Sun J. Deep Residual Learning for Image Recognition. CVPR 2016: IEEE Conference on Computer Vision & Pattern Recognition. 2016 Jun 27-30; Seattle, WA, United States. New York: IEEE, 2016: 770-778 [DOI: 10.1109/CVPR.2016.90]
  - 58 **Mukhopadhyay S**, Feldman MD, Abels E, Ashfaq R, Beltaifa S, Cacciabeve NG, Cathro HP, Cheng L, Cooper K, Dickey GE, Gill RM, Heaton RP Jr, Kerstens R, Lindberg GM, Malhotra RK, Mandell JW, Manluco ED, Mills AM, Mills SE, Moskaluk CA, Nelis M, Patil DT, Przybycin CG, Reynolds JP, Rubin BP, Saboorian MH, Salicru M, Samols MA, Sturgis CD, Turner KO, Wick MR, Yoon JY, Zhao P, Taylor CR. Whole Slide Imaging Versus Microscopy for Primary Diagnosis in Surgical Pathology: A Multicenter Blinded Randomized Noninferiority Study of 1992 Cases (Pivotal Study). *Am J Surg Pathol* 2018; **42**: 39-52 [PMID: 28961557 DOI: 10.1097/PAS.0000000000000948]
  - 59 **Amedei A**, Della Bella C, Silvestri E, Prisco D, D'Elisio MM. T cells in gastric cancer: friends or foes. *Clin Dev Immunol* 2012; **2012**: 690571 [PMID: 22693525 DOI: 10.1155/2012/690571]
  - 60 **Wang FH**, Shen L, Li J, Zhou ZW, Liang H, Zhang XT, Tang L, Xin Y, Jin J, Zhang YJ, Yuan XL, Liu TS, Li GX, Wu Q, Xu HM, Ji JF, Li YF, Wang X, Yu S, Liu H, Guan WL, Xu RH. The Chinese Society of Clinical Oncology (CSCO): clinical guidelines for the diagnosis and treatment of gastric cancer. *Cancer Commun (Lond)* 2019; **39**: 10 [PMID: 30885279 DOI: 10.1186/s40880-019-0349-9]
  - 61 **Muro K**, Van Cutsem E, Narita Y, Pentheroudakis G, Baba E, Li J, Ryu MH, Zamaniah WIW, Yong WP, Yeh KH, Kato K, Lu Z, Cho BC, Nor IM, Ng M, Chen LT, Nakajima TE, Shitara K, Kawakami H, Tsuchida T, Yoshino T, Lordick F, Martinelli E, Smyth EC, Arnold D, Minami H, Tabernero J, Douillard JY. Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with metastatic gastric cancer: a JSMO-ESMO initiative endorsed by CSCO, KSMO, MOS, SSO and TOS. *Ann Oncol* 2019; **30**: 19-33 [PMID: 30475956 DOI: 10.1093/annonc/mdy502]
  - 62 **Chandra N**, Langan D A. *Gemstone Detector: Dual Energy Imaging via Fast kVp Switching*. In: Johnson T, Fink C, Schönberg S, Reiser M. (eds) Dual Energy CT in Clinical Practice. Medical Radiology. Springer, Berlin, Heidelberg 2011; 35-41 [DOI: 10.1007/174\_2010\_35]
  - 63 **Li F**, Zhang R, Liang H, Liu H, Quan J. The pattern and risk factors of recurrence of proximal gastric cancer after curative resection. *J Surg Oncol* 2013; **107**: 130-135 [PMID: 22949400 DOI: 10.1002/jso.23252]
  - 64 **Lee J**, Sohn I, Do IG, Kim KM, Park SH, Park JO, Park YS, Lim HY, Sohn TS, Bae JM, Choi MG, Lim DH, Min BH, Lee JH, Rhee PL, Kim JJ, Choi DI, Tan IB, Das K, Tan P, Jung SH, Kang WK, Kim S. Nanostring-

- based multigene assay to predict recurrence for gastric cancer patients after surgery. *PLoS One* 2014; **9**: e90133 [PMID: 24598828 DOI: 10.1371/journal.pone.0090133]
- 65 **Siewert JR**, Böttcher K, Stein HJ, Roder JD. Relevant prognostic factors in gastric cancer: ten-year results of the German Gastric Cancer Study. *Ann Surg* 1998; **228**: 449-461 [PMID: 9790335 DOI: 10.1097/00000658-199810000-00002]
- 66 **Loken E**, Gelman A. Measurement error and the replication crisis. *Science* 2017; **355**: 584-585 [PMID: 28183939 DOI: 10.1126/science.aal3618]
- 67 **Jack CR Jr**, Bernstein MA, Fox NC, Thompson P, Alexander G, Harvey D, Borowski B, Britson PJ, L Whitwell J, Ward C, Dale AM, Felmlee JP, Gunter JL, Hill DL, Killiany R, Schuff N, Fox-Bosetti S, Lin C, Studholme C, DeCarli CS, Krueger G, Ward HA, Metzger GJ, Scott KT, Mallozzi R, Blezek D, Levy J, Debbins JP, Fleisher AS, Albert M, Green R, Bartzokis G, Glover G, Mugler J, Weiner MW. The Alzheimer's Disease Neuroimaging Initiative (ADNI): MRI methods. *J Magn Reson Imaging* 2008; **27**: 685-691 [PMID: 18302232 DOI: 10.1002/jmri.21049]
- 68 **Chartrand G**, Cheng PM, Vorontsov E, Drozdal M, Turcotte S, Pal CJ, Kadoury S, Tang A. Deep Learning: A Primer for Radiologists. *Radiographics* 2017; **37**: 2113-2131 [PMID: 29131760 DOI: 10.1148/rg.2017170077]
- 69 **Lan K**, Wang DT, Fong S, Liu LS, Wong KKL, Dey N. A Survey of Data Mining and Deep Learning in Bioinformatics. *J Med Syst* 2018; **42**: 139 [PMID: 29956014 DOI: 10.1007/s10916-018-1003-9]
- 70 **Cabita F**, Rasoini R, Gensini GF. Unintended Consequences of Machine Learning in Medicine. *JAMA* 2017; **318**: 517-518 [PMID: 28727867 DOI: 10.1001/jama.2017.7797]
- 71 **Selvaraju RR**, Cogswell M, Das A, Vedantam R, Parikh D, Batra D. Grad-CAM: Visual Explanations from Deep Networks via Gradient-Based Localization. ICCV 2017: Proceedings of the 16th IEEE International Conference on Computer Vision; 2017 Oct 22-29; Venice, Italy. New York: IEEE, 2017: 618-626 [DOI: 10.1109/ICCV.2017.74]



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](mailto:bpgoffice@wjgnet.com)

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

<https://www.wjgnet.com>

