**Name of Journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 63169

**Manuscript Type:** REVIEW

**Artificial intelligence in small intestinal diseases: Application and prospects**

Yang Y *et al*. Artificial intelligence in small intestinal diseases

Yu Yang, Yu-Xuan Li, Ren-Qi Yao, Xiao-Hui Du, Chao Ren

**Yu Yang, Yu-Xuan Li, Xiao-Hui Du,** Department ofGeneral Surgery, Chinese People’s Liberation Army General Hospital, Beijing 100853, China

**Ren-Qi Yao, Chao Ren,** Trauma Research Center, The Fourth Medical Center and Medical Innovation Research Division of the Chinese People‘s Liberation Army General Hospital, Beijing 100048, China

**Ren-Qi Yao,** Department of Burn Surgery, Changhai Hospital, Naval Medical University, Shanghai 200433, China

**Author contributions:** Yang Y searched the literature for recent advances in the field and wrote the manuscript; Yang Y, Li YX, Yao RQ and Du XH edited and revised the manuscript; Ren C designed the study; all authors approved the final version to be published.

**Supported by**theNational Natural Science Foundation of China, No. 81871317.

**Corresponding author: Chao Ren, MD, PhD,** Trauma Research Center, Fourth Medical Center and Medical Innovation Research Division of the Chinese People’s Liberation Army General Hospital, No. 51 Fucheng Road, Beijing 100048, China. rc198@sina.com

**Received:** January 25, 2021

**Revised:** April 9, 2021

**Accepted:** May 8, 2021

**Published online:**

**Abstract**

The small intestine is located in the middle of the gastrointestinal tract, so small intestinal diseases are more difficult to diagnose than other gastrointestinal diseases. However, with the extensive application of artificial intelligence in the field of small intestinal diseases, with its efficient learning capacities and computational power, artificial intelligence plays an important role in the auxiliary diagnosis and prognosis prediction based on the capsule endoscopy and other examination methods, which improves the accuracy of diagnosis and prediction and reduces the workload of doctors. In this review, a comprehensive retrieval was performed on articles published up to October 2020 from PubMed and other databases. Thereby the application status of artificial intelligence in small intestinal diseases was systematically introduced, and the challenges and prospects in this field were also analyzed.

**Key Words:** Artificial intelligence; Machine learning; Deep learning; Prognosis prediction; Small intestinal diseases

Yang Y, Li Y, Yao R, Du X, Ren C. Artificial intelligence in small intestinal diseases: Application and prospects. *World J Gastroenterol* 2021; In press

**Core Tip:** Artificial intelligence has been widely used in the management of small intestinal diseases, which has greatly improved the diagnostic efficiency of capsule endoscopy and other examination methods, and at the same time, beneficial progression has also been obtained in the prognosis prediction of small intestinal diseases. Although AI still faces risks such as overfitting and black box effects, its stability and efficiency give it great potential in the management of small intestinal diseases. This article reviews the current application status of AI in small intestinal diseases. In addition, challenges and prospects in this field are discussed.

**INTRODUCTION**

The small intestine is located in the middle of the gastrointestinal digestive system, with a total length of 5 m to 7 m, including the duodenum, jejunum and ileum, and is the longest organ of the digestive system. Small intestinal diseases (SIDs) mainly include celiac disease (CD), small intestinal Crohn’s disease (SICD), primary small intestinal tumor (PSIT), obscure gastrointestinal bleeding and so on. The traditional examination methods include X-ray barium enterography, computed tomography (CT), magnetic resonance imaging (MRI), balloon-assisted enteroscopy, deep enteroscopy and so on. In recent years, the emergence of capsule endoscopy (CE) has brought a revolutionary breakthrough for the diagnosis of SIDs. However, because of the special anatomical position of the small intestine (far away from the oral cavity and anus, overlap and peristalsis), there are still many problems in the diagnosis of SIDs, such as high technical requirements, low positive rate of diagnosis, inaccurate qualitative location of the disease, patient intolerance and so on. In addition, the onset of SIDs is insidious, the specificity of clinical symptoms is low, and the lesion site is not easy to explore, so the clinical diagnosis of SIDs has always been a difficult problem. With the emergence of artificial intelligence (AI) and its wide application in the medical field, it also provides new methods for the whole management process of SIDs and greatly improves the efficiency of SIDs management.

AI is a concept put forward in the 1950s. It is a frontier cross discipline developed on the basis of computer science, neuropsychology, philosophy, linguistics, cybernetics, information theory and so on[1]. The research fields of AI include expert system, machine learning (ML), fuzzy logic, natural language processing and so on. Research methods are also developing continuously, from ML to deep learning and then to convolutional neural network (CNN), promoting the rapid development of research in various fields. The research of AI in the medical field is mainly focused on auxiliary diagnosis. This series of methods of AI has become a hot implementation tool in the field of medical imaging and digestive endoscope[2,3]. Taking the experiment of the breast cancer AI detection system established by Google as an example, the computer-aided diagnosis system based on AI can help doctors reduce the misdiagnosis rate of breast cancer by 5.7%[4]. Researchers at Houston Methodist Hospital also said in their study that they have developed AI software that parses breast X-ray images 30 times faster than ordinary doctors, with an accuracy of 99%[5]. AI is widely used in the study of digestive fields such as gastric cancer[6], colorectal cancer[7], esophageal cancer[8] and so on. AI has also been extensively researched in the field of SIDs, which will be introduced in this paper.

This study used the keywords of “artificial intelligence” and “small intestine” to search the relevant literature in the databases of PubMed, Embase, Web of Science and Cochrane Library up to October 2020. Studies included in our review were required to meet the following inclusion criteria: (1) full-text paper available in English; and (2) studies that associated AI with the small intestinal diseases. We excluded descriptive papers without validation of methods. The application status of AI in SIDs was summarized, and the challenges and prospects in this field were discussed.

**AI IN SMALL INTESTINE ANATOMY**

***Organ segmentation of the small intestine***

With the advent of AI, it is possible to perform computer-assisted organ segmentation in CT, MRI, endoscopy and other examination methods and has shown good application potential in the fields like assisted localization of radiotherapy. The following will introduce the research progress of this aspect in the field of the small intestine especially the duodenum (Table 1).

**CT**: Some studies had used the CNN method to automatically segment duodenum and other abdominal organs from CT images, with clinically acceptable accuracy and efficiency[9,10]. Tong *et al*[11] proposed an end-to-end segmentation network for improving multiorgan segmentation performance using the ML method. The dice similarity coefficient and average surface distance were quantitatively evaluated, and the results confirmed this network had good accuracy and timeliness in the anatomical segmentation of abdominal organs including the duodenum.

**MRI**: Fu *et al*[12] conducted a retrospective analysis on 3D MR images of 120 patients and proposed a CNN model, which has been verified to accurately segment the abdominal organs including the duodenum and expedite the contouring process for MRI-guided adaptive radiotherapy. Chen *et al*[13] also conducted a similar study, and in their study, the inference process was completed within 1 min, indicating an obvious advantage of timeliness. The length of the small intestine is an important factor in the management of patients with short bowel syndrome. Some scholars designed a special software algorithm to calculate the length of small intestine based on magnetic resonance enterography images in mice. Compared with the measured results of anatomical specimens, the mean absolute difference between the two methods was 1.8 ± 3.8 cm (*P* = 0.24), and the mean percentage difference was 9.4% ± 6.0%[14].

**Endoscopy:** In a Japanese study based on GoogLeNet architecture, a CNN diagnostic program was constructed, using 27335 esophagogastroduodenoscopy (EGD) images for the training set and using 17081 EGD images for the independent validation set. The results showed that the CNN has a good effect to classify the anatomical location of EGD images for stomach and duodenum images, with an area under the curve of 0.99[15]. Igarashi *et al*[16] used AlexNet (a deep learning framework) to retrospectively analyze 85246 original images of EGD images in 441 patients with gastric cancer and developed an anatomical organ classifier. The accuracy rates of the training and validation sets were 0.993 and 0.965, respectively.

***Diagnosis of small intestinal mucosal lesions***

With the emergence of CE in 2000[17], it has revolutionized our understanding of small intestinal mucosa[18-20], enabling doctors to detect small intestinal mucosal erosion, ulcers, vascular disease, bleeding, polyps, parasite and other lesions more efficiently. However, reliable and rapid reading of video is still a challenge, but more and more studies have shown that the combination of AI and CE can greatly improve the efficiency of our evaluation of small intestinal mucosal lesions; the detection accuracy was above 90% in most studies[21-27].

**Ulcer**: Previous studies have confirmed that applying a CNN system of deep learning to the reading process of CE can reduce the reading time without decreasing the detection rate of erosion and ulcer lesions[28-32].

**Angioectasias and bleeding:** Intestinal angioectasias cause more than 8% of all gastrointestinal bleeding episodes[33]. Different studies have applied ML, CNN and computer algorithms to the differential diagnosis of intestinal angioectasias and have achieved high sensitivity and specificity[34-39]. AI is also applied to the direct examination of intestinal mucosal bleeding by CE, which can directly calculate the blood content in the digestive tract and infer whether there is active bleeding in the small intestinal mucosa[40-44].

**Protruding lesions:** There are a variety of small intestinal mucosal protruding lesions. CNN can help doctors describe their shape features, help analyze their nature and distinguish polyps, epithelial tumors, submucosal tumors, *etc.*[34,45,46].

**Villous atrophy:** Villous atrophy is a defining symptom of some digestive tract diseases such as CD. Some scholars combined AI methods with CE for the detection and measurement of villous atrophy and successfully mapped the extent of the diseased small intestine[47].

AI is also used in risk prediction and clinical treatment decisions of small intestinal mucosal lesions. For example, one study used CNN for the risk prediction of acute intestinal bleeding[48], and another study applied CNN to risk prediction and therapeutic tactics selection for duodenal ulcers[49]. Wong *et al*[50] built a ML model, based on data from 22854 patients with gastroduodenal ulcer including six clinical parameters to identify patients at high risk for recurrent ulcer bleeding within 1 year. Gastrointestinal bleeding is a common complication of left ventricular assist device treatment. Axelrad *et al*[51] developed an endoscopic algorithm. Compared with conventional cohorts, the implementation of the algorithm increased endoscopic diagnostic efficiency by 68%, treatment efficiency by 113%, the number of procedures per patient decreased by 27%, the length of hospital stay decreased by 33%, and the estimated cost decreased by 18%.

In addition, the interference of intestinal contents to CE can also be reduced by AI. Combined with support vector machine, Bashar *et al*[52] designed a classifier for separating useless frames that are highly contaminated by turbid fluids, fecal materials and/or residual foods. The accuracy of this classifier was more than 80%. Pietri *et al*[53] developed a computer algorithm to automatically evaluate the demeanor of small intestinal bubbles in CE images. The specificity of this algorithm was 95.79%, the sensitivity was 95.19%, and the calculation time was 0.037 s per frame. It can be used to reduce the interference of bubbles in CE images. Klein *et al*[54] created a computed algorithm based on the pixels in the color bar to score and classify the preparation of the small intestine for CE, and this automatic scoring method has a concordance rate of more than 90% with the assessment of clinicians.

**AI IN COMMON SMALL INTESTINAL DISEASES**

***AI in celiac disease***

CD is a complex autoimmune disease. Patients who ingest foods containing gluten will develop an autoimmune response that causes damage to the small intestine. CD is one of the most common chronic digestive diseases, with a prevalence rate of 1% worldwide[55]. Duodenal biopsy is the gold standard for diagnosis[56]. Noninvasive methods such as endoscopy and clinical features analysis are also widely used in diagnosis, but the diagnostic rate of CD is only 15%–20% through current strategies[57]. However, with the increasing application of AI in the diagnosis of CD, the accuracy and efficiency of diagnosis are greatly improved[58] (Table 2 ).

Previous studies have confirmed that AI-assisted duodenoscope images analysis can greatly improve the diagnostic efficacy of CD, with the accuracy between 80% and 100% and specificity and sensitivity over 80%[59-61]. In the diagnosis of CD, the combination of AI and CE is closer, which can improve the accuracy of diagnosis and significantly save the diagnosis time[62-65]. AI was also used in the analysis of duodenal mucosa biopsy, which can help with qualitative analysis and play an important role in quantitative analysis[66,67]. At the same time, the application of AI with X-ray images[68], peripheral blood mononuclear cells[69] and clinical features[60,70] in the diagnosis and classification of CD have also achieved progress.

***AI in small intestinal Crohn’s disease***

Crohn’s disease is a chronic nonspecific inflammatory bowel disease that affects the entire gastrointestinal tract, in which 30% of patients are confined to the small intestine, commonly known as small intestinal Crohn‘s disease[71]. SICD most often involves the distal ileum as well as the jejunum and the digestive tract above and has a higher incidence of intestinal strictures than colonic Crohn‘s disease[72,73]. The application of AI in the management of SICD is comprehensive, including diagnosis, risk prediction, extra-intestinal manifestation (EIM) prediction and so on (Table 3).

**Diagnosis:** Lamash *et al*[74,75] used CNN to analyze MRI images and construct an assessment model for SICD. Their model could effectively distinguish active and inactive inflammatory segments, distinguish segments with strictures and segments without strictures and could be used to measure the length of intestinal strictures. Parfеnov *et al*[76] used a software diagnostic algorithm to analyze the CE images of 25 SICD patients, preliminarily confirming that CE could be used to diagnose early SICD with intestinal mucosal inflammation. Klang *et al*[77] performed automatic analysis of CE images of 49 SICD patients using a CNN method, achieving diagnostic accuracy of more than 95% and significantly reducing reading time. Yang *et al*[78] also attempted to combine CNN with a microultrasound system for early diagnosis of SICD in mice and achieved good effectiveness in the identification of early inflammation.

**Risk prediction of SICD:** Taylor *et al*[79] used ML classifiers (elastic network and random forest) to classify small intestine inflammation in asymptomatic first-degree relatives of patients with SICD. They found that genetic variants associated with SICD, family history and fecal calprotectin together identified individuals with presymptomatic intestinal inflammation who are therefore at risk for SICD. Shen *et al*[80] developed a web-based SICD hazard stratification tool. Predicting high-risk populations for SICD based on altered bowel habit, abdominal pain, white blood cell count, albumin and platelet count abnormalities allowed clinicians to identify potential SICD earlier.

**Risk prediction of EIMs:** AI is controversial in the evaluation of the EIMs of SICD. In the study of Bottigliengo *et al*[81], based on Bayesian machine learning technology evaluation combined with genetic factors to predict the occurrence of EIMs in Crohn’s disease, it has no advantage over traditional statistical tools. Whereas Menti *et al*[82] used Bayesian machine learning technology to predict the risk of occurrence of EIMs in Crohn’s disease, and the prediction accuracy was 82% when considering only clinical factor and 89% combined with genetic factors, which was outperforming other prediction techniques.

***AI in primary small intestinal tumor***

The incidence of PSIT is about 5% of gastrointestinal tumors and 0.2% of all kinds of tumors[83,84]. The main site of PSIT is the duodenum, followed by the jejunum and ileum[85]. There are a variety of pathological types of malignant PSIT. Adenocarcinoma is the most common pathological type, up to 40%, followed by neuroendocrine tumors (25%), malignant lymphomas (10%-15%) and malignant stromal tumors (9%)[86]. PSIT lacks specific manifestations in the early stage, and they are faced with many problems in the clinic, such as difficult diagnosis, high misdiagnosis rate, nonstandard treatment and so on[87]. AI has been applied in the field of auxiliary diagnosis and prognostic analysis of PSIT, and has an important impact on the management (Table 4).

**Diagnosis**: Inoue *et al*[88] used CNN to analyze EGD images for the diagnosis of superficial nonampullary duodenal epithelial tumors. The overall diagnosis accuracy of CNN was 94.7%, including 94% for adenomas and 100% for high-grade dysplasias, and it only took 12-31 s for analysis. The method of support vector machine was applied to the automatic analysis of CE images, which greatly improved the accuracy and efficiency of diagnosis[89-92]. In addition, Barbosa *et al*[93] used the CNN to automatically analyze CE images for the diagnosis of PSIT, which also had high sensitivity and specificity, reaching 98.7% and 96.6%, respectively.

**Risk stratification and prognosis prediction:** In different studies, ML was used to analyze the pathological tissue samples, plasma protein multibiomarker and miRNA markers of patients with small intestinal neuroendocrine tumors[94-96]. Their studies provided some new and effective methods for early diagnosis, treatment strategy selection, prognosis prediction and recurrence risk prediction of small intestinal neuroendocrine tumors. In the study of Yan *et al*[97], random forest models were performed to evaluate the correlation of risk stratification for small intestinal stromal tumors. Their study suggested multidetector CT texture analysis may become an important comprehensive tool for preoperative risk stratification of small intestinal stromal tumors.

***AI in other small intestinal diseases***

**Small intestinal obstruction:** Cheng *et al*[98,99] used CNN to analyze abdominal radiographs to assist in the diagnosis of small intestinal obstruction (SIO). The sensitivity and specificity of the CNN diagnostic system were 83.8% and 68.1%, respectively, based on the training set of 2210 abdominal radiographs. When the training set was expanded to 7768 abdominal radiographs, the diagnostic sensitivity and specificity were increased to 91.4% and 91.9%, respectively. Their study suggests that the accuracy of detection of SIO by CNN improves significantly with the increasing number of training radiographs. Lucas *et al*[100] explored the development of an ML tool for SIO detection based on CT images. They evaluated the accuracy of eye tracking in image centerline annotation of the small intestine as the first step in the development of an ML tool for SIO. Their results showed that the eye tracking-based annotation was accurate and precise enough for application in ML-based small intestinal centerline annotation.

**Small intestinal motor dysfunction:** Small bowel intestinal dysfunction (SIMD) can occur during the development of many diseases, so the evaluation of small intestinal motor function is an important means for the auxiliary diagnosis and severity evaluation of these diseases. AI is widely used to evaluate small intestinal motor function through CE images. Using intraintestinal manometry as the gold standard for the diagnosis of SIMD, Malagelada *et al*[101] proved that an ML model was reliable to evaluate CE images for the diagnosis of SIMD. Applying this model, they found that 29% of patients with functional intestinal disorders had SIMD, significantly higher than that of the healthy population (3%), confirming the pathophysiological changes in the intestine of functional intestinal disorders[102]. Furthermore, a classification method for classifying functional intestinal disorders according to small intestinal motor function was also proposed[103].

De Iorio *et al*[104] also demonstrated that ML can reliably detect reduced intestinal muscle activity and motion by CE images through the method of injecting intestinal muscle inhibition (glucagon) into healthy subjects. Moreover, the study of Seguí *et al*[105] suggested that CNN was also reliable in the description and classification of small intestine motor characteristics with the classification accuracy reaching 96%. Malagelada *et al*[106] also used ML to analyze CE and abdominal MRI images of patients with cystic fibrosis and confirmed that the delay in small bowel and colonic transit times in patients with cystic fibrosis is associated with known endocrine dysfunction and with SIMD.

**Small intestinal ischemia-reperfusion injury:** Intraoperative evaluation of intestinal viability in patients with acute intestinal ischemia is a critical factor for surgical decision making. In the pig jejunum experiment, Strand-Amundsen *et al*[107] attempted to apply ML to the analysis of multivariate time-series of bioimpedance sensor data to analyze intestinal viability after intestinal ischemia-reperfusion. The results suggested that the measurement should be made before the onset of reperfusion, and the prediction effect was better when the measurement was repeated continuously during ischemia and reperfusion. The detection accuracy of irreversible damage may be close to 100%.

**Enteropathies associated with undernutrition:** There is a significant histopathological overlap in duodenal biopsies of enteropathies associated with undernutrition such as environmental enteropathy and CD. Syed *et al*[108] used CNN to establish a histopathological analysis model, which can effectively distinguish environmental enteropathy, CD and normal intestinal mucosa. The detection accuracy was 93.4%, and the false-negative rate was 2.4%.

**CHALLANGES AND PROSPECTS**

At present, in order to promote the application of AI in the field of SIDs, we still need to solve some problems and challenges: (1) insufficiency of training sample size. The incidence of most SIDs is not high. For example, the incidence of PSIT is much lower than that of gastric tumors and colorectal tumors, which affects the amount of data in the training set. Measurement errors are easy to occur when the sample size is small[109], and as suggested by the continuity study of Cheng *et al*[98,99], expanding the sample size of the training set can significantly improve the inspection accuracy of AI model; (2) lack of prospective data. Most of the studies used retrospective data, which have been artificially screened before AI model training and lack prospective studies; (3) single source of data. Most of the training sets and verification sets used in the study come from single-center data, so it is still necessary to further improve the repeatability and stability of the model through multicenter data. As in Alzheimer‘s disease research, each single center should be encouraged to share data in anticipation of establishing large-scale and open databases[110]; (4) the interpretation of the results. Due to the inevitable problems of AI, like overfitting of training set data[111] and the “black box” characteristic of the algorithm[112], the accuracy and interpretation of the AI model are inconsistent, which may have a negative impact on clinical application[113]. More intensive basic research and extensive verification are needed to improve this deficiency; (5) ethical and legal issues. Can we trust the results of AI? Once the AI diagnosis and treatment prediction fails, it will give rise to a series of social, ethical and legal problems[114,115]. It is necessary to combine human supervision with AI tools more reliably; and (6) AI has been widely researched in various fields. We should attach importance to learning experience from different research fields and try to carry out related research in the field of SIDs, so as to promote the continuous progress of AI research in the field of SIDs.

**CONCLUSION**

The advantages of AI in the diagnosis and prognosis analysis of SIDs have been increasingly recognized, and the high accuracy and efficiency of AI detection greatly reduce the workload of doctors. Although there are still various challenges in the application of AI, the potential of AI in improving the management efficiency of diseases cannot be ignored. Clinicians should work together with experts in various fields to promote the development of AI in SIDs.

**REFERENCES**

1 **Hamet P**, Tremblay J. Artificial intelligence in medicine. *Metabolism* 2017; **69S**: S36-S40 [PMID: 28126242 DOI: 10.1016/j.metabol.2017.01.011]

2 **Lee JG**, Jun S, Cho YW, Lee H, Kim GB, Seo JB, Kim N. Deep Learning in Medical Imaging: General Overview. *Korean J Radiol* 2017; **18**: 570-584 [PMID: 28670152 DOI: 10.3348/kjr.2017.18.4.570]

3 **He YS**, Su JR, Li Z, Zuo XL, Li YQ. Application of artificial intelligence in gastrointestinal endoscopy. *J Dig Dis* 2019; **20**: 623-630 [PMID: 31639272 DOI: 10.1111/1751-2980.12827]

4 **McKinney SM**, Sieniek M, Godbole V, Godwin J, Antropova N, Ashrafian H, Back T, Chesus M, Corrado GS, Darzi A, Etemadi M, Garcia-Vicente F, Gilbert FJ, Halling-Brown M, Hassabis D, Jansen S, Karthikesalingam A, Kelly CJ, King D, Ledsam JR, Melnick D, Mostofi H, Peng L, Reicher JJ, Romera-Paredes B, Sidebottom R, Suleyman M, Tse D, Young KC, De Fauw J, Shetty S. International evaluation of an AI system for breast cancer screening. *Nature* 2020; **577**: 89-94 [PMID: 31894144 DOI: 10.1038/s41586-019-1799-6]

5 **Bozkurt S**, Gimenez F, Burnside ES, Gulkesen KH, Rubin DL. Using automatically extracted information from mammography reports for decision-support. *J Biomed Inform* 2016; **62**: 224-231 [PMID: 27388877 DOI: 10.1016/j.jbi.2016.07.001]

6 **Niu PH**, Zhao LL, Wu HL, Zhao DB, Chen YT. Artificial intelligence in gastric cancer: Application and future perspectives. *World J Gastroenterol* 2020; **26**: 5408-5419 [PMID: 33024393 DOI: 10.3748/wjg.v26.i36.5408]

7 **Wang KW**, Dong M. Potential applications of artificial intelligence in colorectal polyps and cancer: Recent advances and prospects. *World J Gastroenterol* 2020; **26**: 5090-5100 [PMID: 32982111 DOI: 10.3748/wjg.v26.i34.5090]

8 **Zhang YH**, Guo LJ, Yuan XL, Hu B. Artificial intelligence-assisted esophageal cancer management: Now and future. *World J Gastroenterol* 2020; **26**: 5256-5271 [PMID: 32994686 DOI: 10.3748/wjg.v26.i35.5256]

9 **Kim H**, Jung J, Kim J, Cho B, Kwak J, Jang JY, Lee SW, Lee JG, Yoon SM. Abdominal multi-organ auto-segmentation using 3D-patch-based deep convolutional neural network. *Sci Rep* 2020; **10**: 6204 [PMID: 32277135 DOI: 10.1038/s41598-020-63285-0]

10 **Peng Z**, Fang X, Yan P, Shan H, Liu T, Pei X, Wang G, Liu B, Kalra MK, Xu XG. A method of rapid quantification of patient-specific organ doses for CT using deep-learning-based multi-organ segmentation and GPU-accelerated Monte Carlo dose computing. *Med Phys* 2020; **47**: 2526-2536 [PMID: 32155670 DOI: 10.1002/mp.14131]

11 **Tong N**, Gou S, Niu T, Yang S, Sheng K. Self-paced DenseNet with boundary constraint for automated multi-organ segmentation on abdominal CT images. *Phys Med Biol* 2020; **65**: 135011 [PMID: 32657281 DOI: 10.1088/1361-6560/ab9b57]

12 **Fu Y**, Mazur TR, Wu X, Liu S, Chang X, Lu Y, Li HH, Kim H, Roach MC, Henke L, Yang D. A novel MRI segmentation method using CNN-based correction network for MRI-guided adaptive radiotherapy. *Med Phys* 2018; **45**: 5129-5137 [PMID: 30269345 DOI: 10.1002/mp.13221]

13 **Chen Y**, Ruan D, Xiao J, Wang L, Sun B, Saouaf R, Yang W, Li D, Fan Z. Fully automated multiorgan segmentation in abdominal magnetic resonance imaging with deep neural networks. *Med Phys* 2020; **47**: 4971-4982 [PMID: 32748401 DOI: 10.1002/mp.14429]

14 **Wilson NA**, Park HS, Lee KS, Barron LK, Warner BW. A Novel Approach to Calculating Small Intestine Length Based on Magnetic Resonance Enterography. *J Am Coll Surg* 2017; **225**: 266-273.e1 [PMID: 28445795 DOI: 10.1016/j.jamcollsurg.2017.04.009]

15 **Takiyama H**, Ozawa T, Ishihara S, Fujishiro M, Shichijo S, Nomura S, Miura M, Tada T. Automatic anatomical classification of esophagogastroduodenoscopy images using deep convolutional neural networks. *Sci Rep* 2018; **8**: 7497 [PMID: 29760397 DOI: 10.1038/s41598-018-25842-6]

16 **Igarashi S**, Sasaki Y, Mikami T, Sakuraba H, Fukuda S. Anatomical classification of upper gastrointestinal organs under various image capture conditions using AlexNet. *Comput Biol Med* 2020; **124**: 103950 [PMID: 32798923 DOI: 10.1016/j.compbiomed.2020.103950]

17 **Iddan G**, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. *Nature* 2000; **405**: 417 [PMID: 10839527 DOI: 10.1038/35013140]

18 **Kopylov U**, Seidman EG. Diagnostic modalities for the evaluation of small bowel disorders. *Curr Opin Gastroenterol* 2015; **31**: 111-117 [PMID: 25635667 DOI: 10.1097/MOG.0000000000000159]

19 **Eliakim R**. Video capsule endoscopy of the small bowel. *Curr Opin Gastroenterol* 2008; **24**: 159-163 [PMID: 18301265 DOI: 10.1097/MOG.0b013e3282f3d946]

20 **Kopylov U**, Seidman EG. Clinical applications of small bowel capsule endoscopy. *Clin Exp Gastroenterol* 2013; **6**: 129-137 [PMID: 23983481 DOI: 10.2147/CEG.S48005]

21 **Oh DJ**, Kim KS, Lim YJ. A New Active Locomotion Capsule Endoscopy under Magnetic Control and Automated Reading Program. *Clin Endosc* 2020; **53**: 395-401 [PMID: 32746536 DOI: 10.5946/ce.2020.127]

22 **Beg S**, Wronska E, Araujo I, González Suárez B, Ivanova E, Fedorov E, Aabakken L, Seitz U, Rey JF, Saurin JC, Tari R, Card T, Ragunath K. Use of rapid reading software to reduce capsule endoscopy reading times while maintaining accuracy. *Gastrointest Endosc* 2020; **91**: 1322-1327 [PMID: 31981645 DOI: 10.1016/j.gie.2020.01.026]

23 **Pérez-Cuadrado-Robles E**, Pinho R, Gonzalez B, Mão de Ferro S, Chagas C, Esteban Delgado P, Carretero C, Figueiredo P, Rosa B, García Lledó J, Nogales Ó, Ponte A, Andrade P, Juanmartiñena-Fernández JF, San-Juan-Acosta M, Lopes S, Prieto-Frías C, Egea-Valenzuela J, Caballero N, Valdivieso-Cortazar E, Cardoso H, Gálvez C, Almeida N, Borque Barrera P, Gómez-Rodríguez BJ, Sánchez Ceballos F, Bernardes C, Alonso P, Argüelles-Arias F, Mascarenhas Saraiva M, Pérez-Cuadrado-Martínez E. Small Bowel Enteroscopy - A Joint Clinical Guideline from the Spanish and Portuguese Small Bowel Study Groups. *GE Port J Gastroenterol* 2020; **27**: 324-335 [PMID: 32999905 DOI: 10.1159/000507375]

24 **Gomes C**, Pinho R, Ponte A, Rodrigues A, Sousa M, Silva JC, Afecto E, Carvalho J. Evaluation of the sensitivity of the *Express View* function in the Mirocam® capsule endoscopy software. *Scand J Gastroenterol* 2020; **55**: 371-375 [PMID: 32150486 DOI: 10.1080/00365521.2020.1734650]

25 **Oumrani S**, Histace A, Abou Ali E, Pietri O, Becq A, Houist G, Nion-Larmurier I, Camus M, Florent C, Dray X. Multi-criterion, automated, high-performance, rapid tool for assessing mucosal visualization quality of still images in small bowel capsule endoscopy. *Endosc Int Open* 2019; **7**: E944-E948 [PMID: 31367673 DOI: 10.1055/a-0918-5883]

26 **Ding Z**, Shi H, Zhang H, Meng L, Fan M, Han C, Zhang K, Ming F, Xie X, Liu H, Liu J, Lin R, Hou X. Gastroenterologist-Level Identification of Small-Bowel Diseases and Normal Variants by Capsule Endoscopy Using a Deep-Learning Model. *Gastroenterology* 2019; **157**: 1044-1054.e5 [PMID: 31251929 DOI: 10.1053/j.gastro.2019.06.025]

27 **Karargyris A**, Bourbakis N. Detection of small bowel polyps and ulcers in wireless capsule endoscopy videos. *IEEE Trans Biomed Eng* 2011; **58**: 2777-2786 [PMID: 21592915 DOI: 10.1109/TBME.2011.2155064]

28 **Hwang Y**, Lee HH, Park C, Tama BA, Kim JS, Cheung DY, Chung WC, Cho YS, Lee KM, Choi MG, Lee S, Lee BI. Improved classification and localization approach to small bowel capsule endoscopy using convolutional neural network. *Dig Endosc* 2020 [PMID: 32640059 DOI: 10.1111/den.13787]

29 **Otani K**, Nakada A, Kurose Y, Niikura R, Yamada A, Aoki T, Nakanishi H, Doyama H, Hasatani K, Sumiyoshi T, Kitsuregawa M, Harada T, Koike K. Automatic detection of different types of small-bowel lesions on capsule endoscopy images using a newly developed deep convolutional neural network. *Endoscopy* 2020; **52**: 786-791 [PMID: 32557474 DOI: 10.1055/a-1167-8157]

30 **Aoki T**, Yamada A, Aoyama K, Saito H, Fujisawa G, Odawara N, Kondo R, Tsuboi A, Ishibashi R, Nakada A, Niikura R, Fujishiro M, Oka S, Ishihara S, Matsuda T, Nakahori M, Tanaka S, Koike K, Tada T. Clinical usefulness of a deep learning-based system as the first screening on small-bowel capsule endoscopy reading. *Dig Endosc* 2020; **32**: 585-591 [PMID: 31441972 DOI: 10.1111/den.13517]

31 **Aoki T**, Yamada A, Aoyama K, Saito H, Tsuboi A, Nakada A, Niikura R, Fujishiro M, Oka S, Ishihara S, Matsuda T, Tanaka S, Koike K, Tada T. Automatic detection of erosions and ulcerations in wireless capsule endoscopy images based on a deep convolutional neural network. *Gastrointest Endosc* 2019; **89**: 357-363.e2 [PMID: 30670179 DOI: 10.1016/j.gie.2018.10.027]

32 **Fan S**, Xu L, Fan Y, Wei K, Li L. Computer-aided detection of small intestinal ulcer and erosion in wireless capsule endoscopy images. *Phys Med Biol* 2018; **63**: 165001 [PMID: 30033931 DOI: 10.1088/1361-6560/aad51c]

33 **Fan GW**, Chen TH, Lin WP, Su MY, Sung CM, Hsu CM, Chi CT. Angiodysplasia and bleeding in the small intestine treated by balloon-assisted enteroscopy. *J Dig Dis* 2013; **14**: 113-116 [PMID: 23216888 DOI: 10.1111/1751-2980.12021]

34 **Aoki T**, Yamada A, Kato Y, Saito H, Tsuboi A, Nakada A, Niikura R, Fujishiro M, Oka S, Ishihara S, Matsuda T, Nakahori M, Tanaka S, Koike K, Tada T. Automatic detection of various abnormalities in capsule endoscopy videos by a deep learning-based system: a multicenter study. *Gastrointest Endosc* 2021; **93**: 165-173.e1 [PMID: 32417297 DOI: 10.1016/j.gie.2020.04.080]

35 **Leenhardt R**, Li C, Le Mouel JP, Rahmi G, Saurin JC, Cholet F, Boureille A, Amiot X, Delvaux M, Duburque C, Leandri C, Gérard R, Lecleire S, Mesli F, Nion-Larmurier I, Romain O, Sacher-Huvelin S, Simon-Shane C, Vanbiervliet G, Marteau P, Histace A, Dray X. CAD-CAP: a 25,000-image database serving the development of artificial intelligence for capsule endoscopy. *Endosc Int Open* 2020; **8**: E415-E420 [PMID: 32118115 DOI: 10.1055/a-1035-9088]

36 **Vezakis IA**, Toumpaniaris P, Polydorou AA, Koutsouris D. A Novel Real-time Automatic Angioectasia Detection Method in Wireless Capsule Endoscopy Video Feed. *Annu Int Conf IEEE Eng Med Biol Soc* 2019; **2019**: 4072-4075 [PMID: 31946766 DOI: 10.1109/EMBC.2019.8857445]

37 **Tsuboi A**, Oka S, Aoyama K, Saito H, Aoki T, Yamada A, Matsuda T, Fujishiro M, Ishihara S, Nakahori M, Koike K, Tanaka S, Tada T. Artificial intelligence using a convolutional neural network for automatic detection of small-bowel angioectasia in capsule endoscopy images. *Dig Endosc* 2020; **32**: 382-390 [PMID: 31392767 DOI: 10.1111/den.13507]

38 **Vieira PM**, Silva CP, Costa D, Vaz IF, Rolanda C, Lima CS. Automatic Segmentation and Detection of Small Bowel Angioectasias in WCE Images. *Ann Biomed Eng* 2019; **47**: 1446-1462 [PMID: 30919139 DOI: 10.1007/s10439-019-02248-7]

39 **Leenhardt R**, Vasseur P, Li C, Saurin JC, Rahmi G, Cholet F, Becq A, Marteau P, Histace A, Dray X; CAD-CAP Database Working Group. A neural network algorithm for detection of GI angiectasia during small-bowel capsule endoscopy. *Gastrointest Endosc* 2019; **89**: 189-194 [PMID: 30017868 DOI: 10.1016/j.gie.2018.06.036]

40 **Aoki T**, Yamada A, Kato Y, Saito H, Tsuboi A, Nakada A, Niikura R, Fujishiro M, Oka S, Ishihara S, Matsuda T, Nakahori M, Tanaka S, Koike K, Tada T. Automatic detection of blood content in capsule endoscopy images based on a deep convolutional neural network. *J Gastroenterol Hepatol* 2020; **35**: 1196-1200 [PMID: 31758717 DOI: 10.1111/jgh.14941]

41 **Arieira C**, Monteiro S, Dias de Castro F, Boal Carvalho P, Rosa B, Moreira MJ, Cotter J. Capsule endoscopy: Is the software TOP 100 a reliable tool in suspected small bowel bleeding? *Dig Liver Dis* 2019; **51**: 1661-1664 [PMID: 31281069 DOI: 10.1016/j.dld.2019.06.008]

42 **Xiao Jia**, Meng MQ. A deep convolutional neural network for bleeding detection in Wireless Capsule Endoscopy images. *Annu Int Conf IEEE Eng Med Biol Soc* 2016; **2016**: 639-642 [PMID: 28268409 DOI: 10.1109/EMBC.2016.7590783]

43 **Han S**, Fahed J, Cave DR. Suspected Blood Indicator to Identify Active Gastrointestinal Bleeding: A Prospective Validation. *Gastroenterology Res* 2018; **11**: 106-111 [PMID: 29707077 DOI: 10.14740/gr949w]

44 **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]

45 **Saito H**, Aoki T, Aoyama K, Kato Y, Tsuboi A, Yamada A, Fujishiro M, Oka S, Ishihara S, Matsuda T, Nakahori M, Tanaka S, Koike K, Tada T. Automatic detection and classification of protruding lesions in wireless capsule endoscopy images based on a deep convolutional neural network. *Gastrointest Endosc* 2020; **92**: 144-151.e1 [PMID: 32084410 DOI: 10.1016/j.gie.2020.01.054]

46 **Li B**, Meng MQ, Xu L. A comparative study of shape features for polyp detection in wireless capsule endoscopy images. *Annu Int Conf IEEE Eng Med Biol Soc* 2009; **2009**: 3731-3734 [PMID: 19965014 DOI: 10.1109/IEMBS.2009.5334875]

47 **Ciaccio EJ**, Bhagat G, Lewis SK, Green PH. Extraction and processing of videocapsule data to detect and measure the presence of villous atrophy in celiac disease patients. *Comput Biol Med* 2016; **78**: 97-106 [PMID: 27673492 DOI: 10.1016/j.compbiomed.2016.09.009]

48 **Das A**, Wong RC. Prediction of outcome in acute lower gastrointestinal hemorrhage: role of artificial neural network. *Eur J Gastroenterol Hepatol* 2007; **19**: 1064-1069 [PMID: 17998830 DOI: 10.1097/MEG.0b013e3282f198f7]

49 **Nemytin IuV**, Petrov VP, Zuev VK, Osipov VV, Esin SV, Baryshev SS. [The use of artificial neuronal networks in the treatment of peptic ulcer]. *Voen Med Zh* 2000; **321**: 40-44, 96 [PMID: 10929514]

50 **Wong GL**, Ma AJ, Deng H, Ching JY, Wong VW, Tse YK, Yip TC, Lau LH, Liu HH, Leung CM, Tsang SW, Chan CW, Lau JY, Yuen PC, Chan FK. Machine learning model to predict recurrent ulcer bleeding in patients with history of idiopathic gastroduodenal ulcer bleeding. *Aliment Pharmacol Ther* 2019; **49**: 912-918 [PMID: 30761584 DOI: 10.1111/apt.15145]

51 **Axelrad JE**, Faye AS, Pinsino A, Thanataveerat A, Cagliostro B, Pineda MFT, Ross K, Te-Frey RT, Effner L, Garan AR, Topkara VK, Takayama H, Takeda K, Naka Y, Ramirez I, Garcia-Carrasquillo R, Colombo PC, Gonda T, Yuzefpolskaya M. Endoscopic Algorithm for Management of Gastrointestinal Bleeding in Patients With Continuous Flow LVADs: A Prospective Validation Study. *J Card Fail* 2020; **26**: 324-332 [PMID: 31794863 DOI: 10.1016/j.cardfail.2019.11.027]

52 **Bashar MK**, Kitasaka T, Suenaga Y, Mekada Y, Mori K. Automatic detection of informative frames from wireless capsule endoscopy images. *Med Image Anal* 2010; **14**: 449-470 [PMID: 20137998 DOI: 10.1016/j.media.2009.12.001]

53 **Pietri O**, Rezgui G, Histace A, Camus M, Nion-Larmurier I, Li C, Becq A, Ali EA, Romain O, Chaput U, Marteau P, Florent C, Dray X. Development and validation of an automated algorithm to evaluate the abundance of bubbles in small bowel capsule endoscopy. *Endosc Int Open* 2018; **6**: E462-E469 [PMID: 29616238 DOI: 10.1055/a-0573-1044]

54 **Klein A**, Gizbar M, Bourke MJ, Ahlenstiel G. Validated computed cleansing score for video capsule endoscopy. *Dig Endosc* 2016; **28**: 564-569 [PMID: 26716407 DOI: 10.1111/den.12599]

55 **Ludvigsson JF**, Card TR, Kaukinen K, Bai J, Zingone F, Sanders DS, Murray JA. Screening for celiac disease in the general population and in high-risk groups. *United European Gastroenterol J* 2015; **3**: 106-120 [PMID: 25922671 DOI: 10.1177/2050640614561668]

56 **Oberhuber G**, Granditsch G, Vogelsang H. The histopathology of coeliac disease: time for a standardized report scheme for pathologists. *Eur J Gastroenterol Hepatol* 1999; **11**: 1185-1194 [PMID: 10524652 DOI: 10.1097/00042737-199910000-00019]

57 **Molder A**, Balaban DV, Jinga M, Molder CC. Current Evidence on Computer-Aided Diagnosis of Celiac Disease: Systematic Review. *Front Pharmacol* 2020; **11**: 341 [PMID: 32372947 DOI: 10.3389/fphar.2020.00341]

58 **Gadermayr M**, Wimmer G, Kogler H, Vécsei A, Merhof D, Uhl A. Automated classification of celiac disease during upper endoscopy: Status quo and quo vadis. *Comput Biol Med* 2018; **102**: 221-226 [PMID: 29739614 DOI: 10.1016/j.compbiomed.2018.04.020]

59 **Gadermayr M**, Kogler H, Karla M, Merhof D, Uhl A, Vécsei A. Computer-aided texture analysis combined with experts’ knowledge: Improving endoscopic celiac disease diagnosis. *World J Gastroenterol* 2016; **22**: 7124-7134 [PMID: 27610022 DOI: 10.3748/wjg.v22.i31.7124]

60 **Tenório JM**, Hummel AD, Cohrs FM, Sdepanian VL, Pisa IT, de Fátima Marin H. Artificial intelligence techniques applied to the development of a decision-support system for diagnosing celiac disease. *Int J Med Inform* 2011; **80**: 793-802 [PMID: 21917512 DOI: 10.1016/j.ijmedinf.2011.08.001]

61 **Wimmer G**, Vécsei A, Häfner M, Uhl A. Fisher encoding of convolutional neural network features for endoscopic image classification. *J Med Imaging (Bellingham)* 2018; **5**: 034504 [PMID: 30840751 DOI: 10.1117/1.JMI.5.3.034504]

62 **Chetcuti Zammit S**, Bull LA, Sanders DS, Galvin J, Dervilis N, Sidhu R, Worden K. Towards the Probabilistic Analysis of Small Bowel Capsule Endoscopy Features to Predict Severity of Duodenal Histology in Patients with Villous Atrophy. *J Med Syst* 2020; **44**: 195 [PMID: 33005996 DOI: 10.1007/s10916-020-01657-9]

63 **Li BNN**, Wang X, Wang R, Zhou T, Gao R, Ciaccio EJ, Green PH. Celiac Disease Detection from Videocapsule Endoscopy Images Using Strip Principal Component Analysis. *IEEE/ACM Trans Comput Biol Bioinform* 2019; **PP** [PMID: 31751282 DOI: 10.1109/TCBB.2019.2953701]

64 **Vicnesh J**, Wei JKE, Ciaccio EJ, Oh SL, Bhagat G, Lewis SK, Green PH, Acharya UR. Automated diagnosis of celiac disease by video capsule endoscopy using DAISY Descriptors. *J Med Syst* 2019; **43**: 157 [PMID: 31028562 DOI: 10.1007/s10916-019-1285-6]

65 **Zhou T**, Han G, Li BN, Lin Z, Ciaccio EJ, Green PH, Qin J. Quantitative analysis of patients with celiac disease by video capsule endoscopy: A deep learning method. *Comput Biol Med* 2017; **85**: 1-6 [PMID: 28412572 DOI: 10.1016/j.compbiomed.2017.03.031]

66 **Wei JW**, Wei JW, Jackson CR, Ren B, Suriawinata AA, Hassanpour S. Automated Detection of Celiac Disease on Duodenal Biopsy Slides: A Deep Learning Approach. *J Pathol Inform* 2019; **10**: 7 [PMID: 30984467 DOI: 10.4103/jpi.jpi\_87\_18]

67 **Das P**, Gahlot GP, Singh A, Baloda V, Rawat R, Verma AK, Khanna G, Roy M, George A, Singh A, Nalwa A, Ramteke P, Yadav R, Ahuja V, Sreenivas V, Gupta SD, Makharia GK. Quantitative histology-based classification system for assessment of the intestinal mucosal histological changes in patients with celiac disease. *Intest Res* 2019; **17**: 387-397 [PMID: 30996219 DOI: 10.5217/ir.2018.00167]

68 **Virta J**, Hannula M, Tamminen I, Lindfors K, Kaukinen K, Popp A, Taavela J, Saavalainen P, Hiltunen P, Hyttinen J, Kurppa K. X-ray microtomography is a novel method for accurate evaluation of small-bowel mucosal morphology and surface area. *Sci Rep* 2020; **10**: 13164 [PMID: 32753621 DOI: 10.1038/s41598-020-69487-w]

69 **Sangineto M**, Graziano G, D’Amore S, Salvia R, Palasciano G, Sabbà C, Vacca M, Cariello M. Identification of peculiar gene expression profile in peripheral blood mononuclear cells (PBMC) of celiac patients on gluten free diet. *PLoS One* 2018; **13**: e0197915 [PMID: 29795662 DOI: 10.1371/journal.pone.0197915]

70 **Pastore RL**, Murray JA, Coffman FD, Mitrofanova A, Srinivasan S. Physician Review of a Celiac Disease Risk Estimation and Decision-Making Expert System. *J Am Coll Nutr* 2019; **38**: 722-728 [PMID: 31063433 DOI: 10.1080/07315724.2019.1608477]

71 **Feuerstein JD**, Cheifetz AS. Crohn Disease: Epidemiology, Diagnosis, and Management. *Mayo Clin Proc* 2017; **92**: 1088-1103 [PMID: 28601423 DOI: 10.1016/j.mayocp.2017.04.010]

72 **Nóbrega VG**, Silva INN, Brito BS, Silva J, Silva MCMD, Santana GO. THE ONSET OF CLINICAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASE PATIENTS. *Arq Gastroenterol* 2018; **55**: 290-295 [PMID: 30540094 DOI: 10.1590/S0004-2803.201800000-73]

73 **Lazarev M**, Huang C, Bitton A, Cho JH, Duerr RH, McGovern DP, Proctor DD, Regueiro M, Rioux JD, Schumm PP, Taylor KD, Silverberg MS, Steinhart AH, Hutfless S, Brant SR. Relationship between proximal Crohn’s disease location and disease behavior and surgery: a cross-sectional study of the IBD Genetics Consortium. *Am J Gastroenterol* 2013; **108**: 106-112 [PMID: 23229423 DOI: 10.1038/ajg.2012.389]

74 **Lamash Y**, Kurugol S, Warfield SK. Semi-Automated Extraction of Crohns Disease MR Imaging Markers using a 3D Residual CNN with Distance Prior. *Deep Learn Med Image Anal Multimodal Learn Clin Decis Support (2018)* 2018; **11045**: 218-226 [PMID: 30450491 DOI: 10.1007/978-3-030-00889-5\_25]

75 **Lamash Y**, Kurugol S, Freiman M, Perez-Rossello JM, Callahan MJ, Bousvaros A, Warfield SK. Curved planar reformatting and convolutional neural network-based segmentation of the small bowel for visualization and quantitative assessment of pediatric Crohn’s disease from MRI. *J Magn Reson Imaging* 2019; **49**: 1565-1576 [PMID: 30353957 DOI: 10.1002/jmri.26330]

76 **Parfеnov АI**, Аkopova АО, Shcherbakov PL, Мikcheeva ОМ. Role of video capsulе endoscopy in the diagnostic algorithm of small bowel Crohn’s disease. *Ter Arkh* 2019; **91**: 37-42 [PMID: 31094474 DOI: 10.26442/00403660.2019.04.000079]

77 **Klang E**, Barash Y, Margalit RY, Soffer S, Shimon O, Albshesh A, Ben-Horin S, Amitai MM, Eliakim R, Kopylov U. Deep learning algorithms for automated detection of Crohn’s disease ulcers by video capsule endoscopy. *Gastrointest Endosc* 2020; **91**: 606-613.e2 [PMID: 31743689 DOI: 10.1016/j.gie.2019.11.012]

78 **Yang S**, Lemke C, Cox BF, Newton IP, Nathke I, Cochran S. A Learning-Based Microultrasound System for the Detection of Inflammation of the Gastrointestinal Tract. *IEEE Trans Med Imaging* 2021; **40**: 38-47 [PMID: 32881684 DOI: 10.1109/TMI.2020.3021560]

79 **Taylor KM**, Hanscombe KB, Prescott NJ, Iniesta R, Traylor M, Taylor NS, Fong S, Powell N, Irving PM, Anderson SH, Mathew CG, Lewis CM, Sanderson JD. Genetic and Inflammatory Biomarkers Classify Small Intestine Inflammation in Asymptomatic First-degree Relatives of Patients With Crohn’s Disease. *Clin Gastroenterol Hepatol* 2020; **18**: 908-916.e13 [PMID: 31202982 DOI: 10.1016/j.cgh.2019.05.061]

80 **Shen EX**, Lord A, Doecke JD, Hanigan K, Irwin J, Cheng RKY, Radford-Smith G. A validated risk stratification tool for detecting high-risk small bowel Crohn’s disease. *Aliment Pharmacol Ther* 2020; **51**: 281-290 [PMID: 31769537 DOI: 10.1111/apt.15550]

81 **Bottigliengo D**, Berchialla P, Lanera C, Azzolina D, Lorenzoni G, Martinato M, Giachino D, Baldi I, Gregori D. The Role of Genetic Factors in Characterizing Extra-Intestinal Manifestations in Crohn’s Disease Patients: Are Bayesian Machine Learning Methods Improving Outcome Predictions? *J Clin Med* 2019; **8** [PMID: 31212952 DOI: 10.3390/jcm8060865]

82 **Menti E**, Lanera C, Lorenzoni G, Giachino DF, Marchi M, Gregori D, Berchialla P; Piedmont Study Group on the Genetics of IBD. Bayesian Machine Learning Techniques for revealing complex interactions among genetic and clinical factors in association with extra-intestinal Manifestations in IBD patients. *AMIA Annu Symp Proc* 2016; **2016**: 884-893 [PMID: 28269885]

83 **Mellouki I**, Jellali K, Ibrahimi A. [Tumors of the small bowel: about 27 cases]. *Pan Afr Med J* 2018; **30**: 13 [PMID: 30167041 DOI: 10.11604/pamj.2018.30.13.5407]

84 **Sarosiek T**, Stelmaszuk M. [Small intestine neoplasms]. *Pol Merkur Lekarski* 2018; **44**: 45-48 [PMID: 29498365]

85 **Tran TB**, Qadan M, Dua MM, Norton JA, Poultsides GA, Visser BC. Prognostic relevance of lymph node ratio and total lymph node count for small bowel adenocarcinoma. *Surgery* 2015; **158**: 486-493 [PMID: 26013988 DOI: 10.1016/j.surg.2015.03.048]

86 **Zhang Y**, Zulfiqar M, Bluth MH, Bhalla A, Beydoun R. Molecular Diagnostics in the Neoplasms of Small Intestine and Appendix: 2018 Update. *Clin Lab Med* 2018; **38**: 343-355 [PMID: 29776634 DOI: 10.1016/j.cll.2018.03.002]

87 **Zhao Z**, Guan X, Chen Y, Wang X. [Progression of diagnosis and treatment in primary malignant small bowel tumor]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2017; **20**: 117-120 [PMID: 28105627]

88 **Inoue S**, Shichijo S, Aoyama K, Kono M, Fukuda H, Shimamoto Y, Nakagawa K, Ohmori M, Iwagami H, Matsuno K, Iwatsubo T, Nakahira H, Matsuura N, Maekawa A, Kanesaka T, Yamamoto S, Takeuchi Y, Higashino K, Uedo N, Ishihara R, Tada T. Application of Convolutional Neural Networks for Detection of Superficial Nonampullary Duodenal Epithelial Tumors in Esophagogastroduodenoscopic Images. *Clin Transl Gastroenterol* 2020; **11**: e00154 [PMID: 32352719 DOI: 10.14309/ctg.0000000000000154]

89 **Vieira PM**, Ramos J, Lima CS. Automatic detection of small bowel tumors in endoscopic capsule images by ROI selection based on discarded lightness information. *Annu Int Conf IEEE Eng Med Biol Soc* 2015; **2015**: 3025-3028 [PMID: 26736929 DOI: 10.1109/EMBC.2015.7319029]

90 **Liu G**, Yan G, Kuang S, Wang Y. Detection of small bowel tumor based on multi-scale curvelet analysis and fractal technology in capsule endoscopy. *Comput Biol Med* 2016; **70**: 131-138 [PMID: 26829705 DOI: 10.1016/j.compbiomed.2016.01.021]

91 **Vieira PM**, Freitas NR, Valente J, Vaz IF, Rolanda C, Lima CS. Automatic detection of small bowel tumors in wireless capsule endoscopy images using ensemble learning. *Med Phys* 2020; **47**: 52-63 [PMID: 31299096 DOI: 10.1002/mp.13709]

92 **Li BP**, Meng MQ. Comparison of several texture features for tumor detection in CE images. *J Med Syst* 2012; **36**: 2463-2469 [PMID: 21523427 DOI: 10.1007/s10916-011-9713-2]

93 **Barbosa DJ**, Ramos J, Lima CS. Detection of small bowel tumors in capsule endoscopy frames using texture analysis based on the discrete wavelet transform. *Annu Int Conf IEEE Eng Med Biol Soc* 2008; **2008**: 3012-3015 [PMID: 19163340 DOI: 10.1109/IEMBS.2008.4649837]

94 **Panarelli N**, Tyryshkin K, Wong JJM, Majewski A, Yang X, Scognamiglio T, Kim MK, Bogardus K, Tuschl T, Chen YT, Renwick N. Evaluating gastroenteropancreatic neuroendocrine tumors through microRNA sequencing. *Endocr Relat Cancer* 2019; **26**: 47-57 [PMID: 30021866 DOI: 10.1530/ERC-18-0244]

95 **Drozdov I**, Kidd M, Nadler B, Camp RL, Mane SM, Hauso O, Gustafsson BI, Modlin IM. Predicting neuroendocrine tumor (carcinoid) neoplasia using gene expression profiling and supervised machine learning. *Cancer* 2009; **115**: 1638-1650 [PMID: 19197975 DOI: 10.1002/cncr.24180]

96 **Kjellman M**, Knigge U, Welin S, Thiis-Evensen E, Gronbæk H, Schalin-Jäntti C, Sorbye H, Joergensen MT, Johanson V, Metso S, Waldum H, Søreide JA, Ebeling T, Lindberg F, Landerholm K, Wallin G, Salem F, Schneider MDP, Belusa R. A plasma protein biomarker strategy for detection of small intestinal neuroendocrine tumors. *Neuroendocrinology* 2020 [PMID: 32721955 DOI: 10.1159/000510483]

97 **Yan J**, Zhao X, Han S, Wang T, Miao F. Evaluation of Clinical Plus Imaging Features and Multidetector Computed Tomography Texture Analysis in Preoperative Risk Grade Prediction of Small Bowel Gastrointestinal Stromal Tumors. *J Comput Assist Tomogr* 2018; **42**: 714-720 [PMID: 30015796 DOI: 10.1097/RCT.0000000000000756]

98 **Cheng PM**, Tejura TK, Tran KN, Whang G. Detection of high-grade small bowel obstruction on conventional radiography with convolutional neural networks. *Abdom Radiol (NY)* 2018; **43**: 1120-1127 [PMID: 28828625 DOI: 10.1007/s00261-017-1294-1]

99 **Cheng PM**, Tran KN, Whang G, Tejura TK. Refining Convolutional Neural Network Detection of Small-Bowel Obstruction in Conventional Radiography. *AJR Am J Roentgenol* 2019; **212**: 342-350 [PMID: 30476452 DOI: 10.2214/AJR.18.20362]

100 **Lucas A**, Wang K, Santillan C, Hsiao A, Sirlin CB, Murphy PM. Image Annotation by Eye Tracking: Accuracy and Precision of Centerlines of Obstructed Small-Bowel Segments Placed Using Eye Trackers. *J Digit Imaging* 2019; **32**: 855-864 [PMID: 31144146 DOI: 10.1007/s10278-018-0169-5]

101 **Malagelada C**, De Iorio F, Azpiroz F, Accarino A, Segui S, Radeva P, Malagelada JR. New insight into intestinal motor function via noninvasive endoluminal image analysis. *Gastroenterology* 2008; **135**: 1155-1162 [PMID: 18691579 DOI: 10.1053/j.gastro.2008.06.084]

102 **Malagelada C**, De Lorio F, Seguí S, Mendez S, Drozdzal M, Vitria J, Radeva P, Santos J, Accarino A, Malagelada JR, Azpiroz F. Functional gut disorders or disordered gut function? Small bowel dysmotility evidenced by an original technique. *Neurogastroenterol Motil* 2012; **24**: 223-228, e104-e105 [PMID: 22129212 DOI: 10.1111/j.1365-2982.2011.01823.x]

103 **Malagelada C**, Drozdzal M, Seguí S, Mendez S, Vitrià J, Radeva P, Santos J, Accarino A, Malagelada JR, Azpiroz F. Classification of functional bowel disorders by objective physiological criteria based on endoluminal image analysis. *Am J Physiol Gastrointest Liver Physiol* 2015; **309**: G413-G419 [PMID: 26251472 DOI: 10.1152/ajpgi.00193.2015]

104 **de Iorio F**, Malagelada C, Azpiroz F, Maluenda M, Violanti C, Igual L, Vitrià J, Malagelada JR. Intestinal motor activity, endoluminal motion and transit. *Neurogastroenterol Motil* 2009; **21**: 1264-e119 [PMID: 19614865 DOI: 10.1111/j.1365-2982.2009.01363.x]

105 **Seguí S**, Drozdzal M, Pascual G, Radeva P, Malagelada C, Azpiroz F, Vitrià J. Generic feature learning for wireless capsule endoscopy analysis. *Comput Biol Med* 2016; **79**: 163-172 [PMID: 27810622 DOI: 10.1016/j.compbiomed.2016.10.011]

106 **Malagelada C**, Bendezú RA, Seguí S, Vitrià J, Merino X, Nieto A, Sihuay D, Accarino A, Molero X, Azpiroz F. Motor dysfunction of the gut in cystic fibrosis. *Neurogastroenterol Motil* 2020; **32**: e13883 [PMID: 32475007 DOI: 10.1111/nmo.13883]

107 **Strand-Amundsen RJ**, Tronstad C, Reims HM, Reinholt FP, Høgetveit JO, Tønnessen TI. Machine learning for intraoperative prediction of viability in ischemic small intestine. *Physiol Meas* 2018; **39**: 105011 [PMID: 30207981 DOI: 10.1088/1361-6579/aae0ea]

108 **Syed S**, Al-Boni M, Khan MN, Sadiq K, Iqbal NT, Moskaluk CA, Kelly P, Amadi B, Ali SA, Moore SR, Brown DE. Assessment of Machine Learning Detection of Environmental Enteropathy and Celiac Disease in Children. *JAMA Netw Open* 2019; **2**: e195822 [PMID: 31199451 DOI: 10.1001/jamanetworkopen.2019.5822]

109 **Loken E**, Gelman A. Measurement error and the replication crisis. *Science* 2017; **355**: 584-585 [PMID: 28183939 DOI: 10.1126/science.aal3618]

110 **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]

111 **Chartrand G**, Cheng PM, Vorontsov E, Drozdzal 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]

112 **Lawrence DR**, Palacios-González C, Harris J. Artificial Intelligence. *Camb Q Healthc Ethics* 2016; **25**: 250-261 [PMID: 26957450 DOI: 10.1017/S0963180115000559]

113 **Cabitza 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]

114 **Yu KH**, Beam AL, Kohane IS. Artificial intelligence in healthcare. *Nat Biomed Eng* 2018; **2**: 719-731 [PMID: 31015651 DOI: 10.1038/s41551-018-0305-z]

115 **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 DOI: 10.1002/rcs.1968]

**Footnotes**

**Conflict-of-interest statement:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**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/

**Manuscript source:** Invited manuscript

**Peer-review started:** January 25, 2021

**First decision:** March 29, 2021

**Article in press:**

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** China

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

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Chen CH, Jiang Y, Orhan K, Pons-Beltrán V **S-Editor:** Zhang H **L-Editor:** Filipodia **P-Editor:**

**Table 1 Applications of artificial intelligence in organ segmentation of the small intestine**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Diagnostic method** | **AI technology** | **Training set** | **Validating set** | **Outcomes** |
| Tong *et al*[11] | CT  | ML | 90 images |  -  | DSC of duodenum: 69.26% |
| Kim *et al*[9] | CT | CNN | 80 images | 40 images | DSC of duodenum: 0.595 |
| Peng *et al*[10] | CT | CNN | 43 images |  -  | DSC of duodenum: 0.61 |
| Fu *et al*[12] | MRI | CNN | 100 images | 20 images | Dice coefficient of duodenum: 65.50% ± 8.90% |
| Dice coefficient of bowel: 86.60% ± 2.69% |
| Chen *et al*[13] | MRI | DL | 66 images | 36 images | DSC of duodenum: 0.80 |
| Takiyama *et al*[15] | EGD | CNN | 27335 images | 17081 images | AUCs: 0.99 |
| Igarashi *et al*[16] | EGD | ML | 49174 images | 36072 images | Accuracy (Ts: 0.993, Vs: 0.965) |

AI: Artificial intelligence; AUCs: Area under the curves; CNN: Convolutional neural network; CT: Computed Tomography; DL: Deep learning; DSC: Dice similarity coefficient; EGD: Esophagogastroduodenoscopy; ML: Machine learning; MRI: Magnetic resonance imaging; Ts: Training set; Vs: Validating set.

**Table 2 Applications of artificial intelligence in celiac disease**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Diagnostic method** | **AI technology** | **Training set** | **Testing set** | **Outcomes** |
| Chetcuti *et al*[62] | CE | ML | 81 patients |  -  | Accuracy: 75.3% |
| Li *et al*[63] | CE | Computer-assisted recognition | Ep: 240, Cp: 220 |  -  | Accuracy: 93.9% |
| Vicnesh *et al*[64] | CE | Computerized algorithm | 21 patients |  -  | Accuracy: 89.82% |
| Zhou *et al*[65] | CE | CNN | Ep: 6, Cp: 5 | Ep: 5, Cp: 5 | Accuracy: 100% |
| Gadermayr *et al*[59] | EGD | Computer-assisted | 290 patients (2835 images) |  -  | Accuracy: 94%-100% |
| Das *et al*[67] | Mucosal biopsies | Computer-assisted | Ep: 124, Cp: 137 | Ep: 120, Cp: 105 | Sen: 90.3%, Spe: 93.5%, AUCs: 96.2% |
| Wei *et al*[66] | Mucosal biopsies | DL | 212 images |  -  | Accuracy: 95.3%, AUCs > 0.95 |
| Pastore *et al*[70] | Clinical data | Computer-assisted | 100 patients |  -  | Reliability: 0.813 |
| Tenório *et al*[60] | Clinical data | Decision trees, Bayesian inference, k-nearest neighbor algorithm, support vector machines, artificial neural networks | 178 patients | 38 patients | Accuracy: 80.0%, Sen: 0.78, Spe: 0.80, AUCs: 0.84 |
| Virta *et al*[68] | Micro-CT | Computer-assisted point cloud analysis | 81 patients |  -  | Accuracy: 100% |
| Sangineto *et al*[69] | Gene expression in PBMCs | ML, random forest algorithm | Ep: 17, Cp: 20 |  -  | Accuracy: 100% |

AI: Artificial intelligence; AUCs: Area under the curves; CE: Capsule endoscopy; CNN: Convolutional neural network; Cp: Control group; DL: Deep learning; EGD: Esophagogastroduodenoscopy; Ep: Experimental group; ML: Machine learning; micro-CT: X-ray microtomography; PBMCs: Peripheral blood mononuclear cells; Sen: Sensitivity; Spe: Specificity.

**Table 3 Applications of artificial intelligence in small intestinal Crohn’s disease**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Diagnostic method** | **AI technology** | **Training set** | **Testing set** | **Outcomes** |
| Yang *et al*[78] | Microultrasound | CNN | 43 mice |  -  | AUCs: 0.8831 |
| Shen *et al*[80] | Clinical data | Computerized algorithm | Ep1: 61, Cp1: 78 | Ep2:42, Cp2: 57; Ep3:84, Cp3: 495 | AUCs: 0.92 |
| Bottigliengo *et al*[81] | Clinical data | BMLTs (NB, BN, BART) | 152 patients |  -  | AUCs without genetic variables (NB: 0.71, BN: 0.50, BART: 0.76), AUCs with genetic variables (NB: 0.75, BN: 0.67, BART: 0.78) |
| Taylor *et al*[79] | Clinical data | ML (elastic net and random forest) | 480 first-degree relatives  |  -  | AUCs (elastic net): 0.80, AUCs (random forest): 0.87 |
| Menti *et al*[82] | Clinical data | BMLTs | 152 patients |  -  | Accuracy without genetic variables: 82%, accuracy with genetic variables: 89% |
| Klang *et al*[77] | CE | DL | 49 patients (17640 images) |  -  | AUCs: 0.94-0.99, accuracy: 95.4%-96.7% |
| Parfеnov *et al*[76] | CE | Computerized algorithm | 25 patients |  -  | 44% patients confirmed only with the help of AI |
| Lamash *et al*[74,75] | MRI | CNN | 15 patients | 8 patients | Dice coefficients: 75%-97% |

AI: Artificial intelligence; AUCs: Area under the curves; BART: Bayes additive return trees; BMLTs: Bayesian machine learning techniques; BN: Bayesian network; CE: Capsule endoscopy; DL: Deep learning; CNN: Convolutional neural network; Cp: Control group; Ep: Experimental group; ML: Machine learning; MRI: Magnetic resonance imaging; NB: Naive Bayes.

**Table 4 Applications of artificial intelligence in primary small intestinal tumor**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Diagnostic method** | **AI technology** | **Training set** | **Testing set** | **Outcomes** |
| Inoue *et al*[88] | EGD | CNN | 531 images | 1080 images | Accuracy: 94.7%-100% |
| Liu *et al*[90] | CE | SVM | 89 patients |  -  | Sen: 97.8%, Spe: 96.7% |
| Vieira *et al*[89,91] | CE | SVM | 29 patients (936 images) |  -  | This SVM outperforms others by more than 5% |
| Barbosa *et al*[93] | CE | CNN | Ep: 104, Cp: 100 | Ep: 92, Cp: 100 | Sen: 98.7%, Spe: 96.6% |
| Panarelli *et al*[94] | MicroRNA sequencing  | ML | 84 samples |  -  | Accuracy (Ts: 98.5%, Vs: 94.4%) |
| Drozdov *et al*[95] | Gene expression profiling | ML | 73 samples |  -  | Differentiated from normal cells (Sen: 100%, Spe: 92%), metastases prediction (Sen: 100%, Spe: 100%) |
| Kjellman *et al*[96] | Plasma protein multibiomarker  | Random forestmodel | Ep:135, Cp: 143 |  -  | AUCs: 0.97 |
| Yan *et al*[97] | CT | Random forestmodel | 213 patients |  -  | AUCs: 0.943 |

AI: Artificial intelligence; AUCs: Area under the curves; CE: Capsule endoscopy; CNN: Convolutional neural network; CT: Computed tomography; Cp: Control group; EGD: esophagogastroduodenoscopy; Ep: Experimental group; ML: Machine learning; SVM: Support vector machine; Sen: Sensitivity; Spe: Specificity; Ts: Training set; Vs: Validating set.