

# Artificial Intelligence in *Gastroenterology*

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

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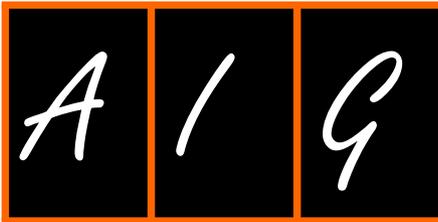
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## Colorectal cancer: Artificial intelligence and its role in surgical decision making

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### Abstract

Despite several advances in the oncological management of colorectal cancer (CRC), there still remains a lacuna in the treatment strategy, which differs from center to center and on the philosophy of the treating clinician that is not without bias. Personalized treatment is essential for the treatment of CRC to achieve better long-term outcomes and to reduce morbidity. Surgery has an important role to play in the treatment. Surgical treatment of CRC is decided based on clinical parameters and investigations and hence likely to have judgmental errors. Artificial intelligence has been reported to be useful in the surveillance, diagnosis, treatment, and follow-up with accuracy in several malignancies. However, it is still evolving and yet to be established in surgical decision making in CRC. It is not only useful preoperatively but also intraoperatively. Artificial intelligence helps to rectify the human surgical decision when clinical data and radiological and laboratory parameters are fed into the computer and may guide correct surgical treatment.

**Key Words:** Artificial Intelligence; Colorectal cancer; Clinical implications; Treatment strategy; Surgical treatment

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**Core Tip:** Treatment decision making in colorectal cancer significantly affects the outcome, which is a multidisciplinary team approach and is not without bias. Surgery plays a significant role in the treatment. Whether artificial intelligence may improve the outcome of surgery in colorectal cancer is not known. The present review focuses on its current role in surgical decision making and future impact.

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## INTRODUCTION

Mr. Alan Turing in 1950 hypothesized that a machine can also think like a human being in his book entitled "Computing Machinery and Intelligence"[1]. The term "artificial intelligence (AI)" was later coined by John McCarthy in a summer workshop[1,2]. AI has evolved from simple tasks to more complex tasks similar to a human brain[1].

AI has proven its worth in various day-to-day life and human requirements, including health care (health tracking devices)[3], automobiles (autopilot)[4], banking and finances (chatbots, robotraders)[5], surveillance (CCTV cameras), social media, entertainment, education, space exploration, industries (aluminum, dairy)[6-8], and disaster management[9,10]. One recent example is the efficient production of facemasks during the coronavirus disease 2019 pandemic[11] (Table 1). Its potential has been exploited in various fields of medicine, including online appointment scheduling, online check-in at hospitals, digitization of medical records, follow-up and immunization reminder, drug dosage algorithm, and adverse effect warnings during the prescription of multidrug combinations. Besides this, its application in the field of oncology is immense. AI is assisting in generating new approaches for cancer detection, screening of healthy subjects, diagnosis, classification of cancers using genomics, tumor microenvironment analysis, prognostication, follow-up, and new drug discovery[12-15].

Colorectal cancer (CRC) is one of the most common types of gastrointestinal (GI) tract malignancy and is the fourth most leading cause of cancer death globally[16,17]. AI has been used to facilitate screening, diagnosis (colonoscopy, advanced endoscopic modalities, imaging), genetic testing, and treatment (chemotherapy, radiotherapy, robotic assisted surgery)[18]. New research and developments are required for better patient management to improve the outcome.

In the past decade, several developments have taken place in the management of CRC, *e.g.*, revised anatomy of the rectum and concept of total mesorectal excision by Heald *et al*[19], concept of complete mesocolic excision and central vascular ligation by Hohenberger[20] for colon cancer, imaging and staging techniques, introduction of staplers[21], newer chemotherapeutic agents and biologicals, radiation therapy, and mode of surgery (laparoscopic and robotic surgery)[22,23] have significantly improved the outcome and sphincter preservation. However, there still remain numerous challenging issues like accurate preoperative diagnosis, staging, individualized and personalized treatment planning, and intraoperative challenges to minimize complications and improve the surgical outcome. Newer tools of AI have been used in various fields of medicine, including drug development, health monitoring, managing medical data, disease diagnostics, digital consultations, personalized treatment, analysis of health plans, and medical and surgical treatment[24] and is quickly finding a role in surgery and surgical decision making.

Two common fields of the AI used in medicine are: virtual and physical[25]. Virtual field is commonly used in medical imaging, clinical diagnosis, treatment, and drug research and development. Surgical and nursing robots are the part of physical fields. Because of ongoing innovations in AI, it is being used widely in medicine, both for diagnosis and management of tumors. AI has played a significant role in CRC at various stages and is reported to have improved the 5-year survival. The subsection of AI used in medicine is deep learning, which is responsible for widespread application of AI[26]. This method encompasses all the concepts of AI and is based on artificial neural networks (ANN), which is inspired by the neurons in a biological brain. Deep learning involves application of training a specific task on a larger data set, extracting information from them, and using them for future predictions about these tasks through flexible adaptation to the new data. Recently, deep learning has been used to predict cardiovascular risk based on retinal images[27], classification of skin lesions[28], mammogram-based breast cancer detection[29], and esophageal carcinoma[30]. However, application of AI in surgery is challenging, as unlike the use of static images, surgery includes dynamic procedural data like the patient clinical parameters, different devices used, and knowledge of clinical guidelines and from the experiences[31]. The uses and applications of various branches of AI in medicine as well as other fields are shown in Table 1.

In 2007, IBM began development of Deep QA technology (Watson). In 2017, Artery's medical imaging platform was the first Food and Drug Administration approved cloud-based deep learning application in healthcare for cardiac disorders, which was faster in giving results as compared to the professionals(15 s vs 30 s)[32]. The Food and Drug Administration-approved "GI genius" in the year 2019 is the first device based on machine learning to aid clinicians in detecting polyps or tumors during colonoscopy.

**Table 1 Subfields of artificial intelligence and its application in day-to-day human life**

S. No	Fields of AI	Description
1	Machine learning	Pattern identification and analysis where machine can help to improve based on past experiences provided from the given data set
2	Deep learning	Consists of multilayered neural networks called artificial neural network, which enables the computer to learn and make decisions on its own
3	Natural language processing	Ability of the computer to extract data from human language and make decisions
4	Computer vision	Potential to obtain information from a series of images or videos
5	Mixed-integer linear programming model[11]	It is helpful in finding the locational, supply, production, distribution, collection, quarantine, recycling, reuse, and disposal decisions within a multiperiod multiechelon multiproduct supply chain
6	Covering tour approach[9]	Optimizing the distribution and allocation of resources among individuals. It is useful at the time of crisis
7	Mixed-integer linear mathematical model[6]	This model optimizes economic, social, and environmental objectives simultaneously
8	Neural network with runner root algorithm[8]	Minimizing risk and maximizing return in industrial production
9	Meta-heuristic algorithms[7]	A comprehensive framework to predict the demand for dairy products
10	Hybrid shapley value and multimooora method[10]	An intelligent performance evaluation system for different supply chains in industries

AI: Artificial intelligence; S. No: Serial number.

This paper reviews the current status of AI in CRC surgical decision making and its future implications.

## USES OF AI IN GASTROINTESTINAL DISORDERS AND COLORECTAL CANCER

AI is progressively being used in the understanding of GI diseases[33-35]. Imaging such as X-ray, computed tomography scanning, magnetic resonance imaging, or endoscopic imaging is being used for diagnosis[36-39]. The application of AI has led to early detection of intestinal malignancies or premalignant lesions, and inflammatory or other non-malignant diseases or lesions[40].

With IBM Watson for oncology (WFO), AI has found its increasing role in oncology therapy. It has been used in several malignancies like breast carcinoma, lung carcinoma, gastric cancer, colon and rectal cancer, *etc.* Initially, Memorial Sloan Kettering Cancer Center (New York, United States) started the use of WFO machine learning. WFO uses natural language processing and clinical data from multiple resources (treatment guidelines, expert opinions, literature, and medical records) to formulate treatment recommendations[41]. A recent meta-analysis[42] had shown the highest concordance between WFO and Mass Detection Tool in breast carcinoma and the lowest in stomach carcinoma. The Manipal Comprehensive Cancer Centre (Bangalore, India) has implemented WFO for treatment in 250 CRC patients[43]. There was a concordance in 92.7% of rectal and 81.0% of colon cancer patients between WFO and Mass Detection Tool recommendations[43].

## AI IN COLORECTAL CANCER

AI is used in the diagnosis and treatment of colorectal polyps and cancer. In colorectal cancer, it helps in diagnosis, staging (lymph node or liver metastasis), preoperative treatment planning, response to treatment assessment, intraoperative assistance, postoperative prognostic information, *etc*[44-46].

### ***AI in preoperative surgical decision making: staging and planning***

After diagnosis of CRC is made, the most important consideration is staging to determine a further plan of management, whether upfront surgery, neoadjuvant treatment, or palliative treatment.

In locally advanced rectal cancer, preoperative chemoradiotherapy is known to reduce the local recurrence. However, selection of patients is essential to avoid unnecessary complications due to overtreatment. Therefore, there is a need for a system that can differentiate between T2 and T3 rectal cancers. Kim *et al*[47] used convolutional neural network models to distinguish T2 from T3 lesions from magnetic resonance imaging with an accuracy of 94%. Similarly, Wu *et al*[48] also used convolutional

neural network to stage rectal cancers.

In addition to its role in preoperative imaging, AI provides faster interpretation compared to radiologists (20 s vs 600 s) in the detection of lymph node metastasis in rectal cancer[49]. Preoperatively, positron emission tomography/computed tomography is commonly used in the case of indeterminate lesions on contrast-enhanced computed tomography to potentially find curable M1 disease (National Comprehensive Cancer Network guidelines version 3.2021). Recently, application of AI has improved the sensitivity and specificity of detection of pulmonary nodules[50]. AI can also be used to reconstruct the area of interest from two-dimensional data obtained from imaging and endoscopic findings to generate a three-dimensional structure for better delineation of the tumor in relation to the surrounding vital structures, which may be useful in preoperative surgical planning[51]. This is extremely useful in determining which patient will require a pelvic exenteration or which patient will require a lateral pelvic lymph node dissection. This is also useful to safeguard the important surrounding structures during surgery to reduce the postoperative morbidity and mortality related to it.

In colon cancer, clinical evidence of bulky nodal disease or T4b lesion entails neoadjuvant therapy (National Comprehensive Cancer Network guidelines version 3.2021). It is also recommended that the presence of nodal involvement in T1 cancer requires colectomy and lymphadenectomy. Kudo *et al*[52] applied machine learning ANN in 3134 patients with T1 CRC based on the patient's data on age, gender, tumor size, location, morphology, lymphatic and vascular invasion, and histologic grade to predict nodal involvement. ANN model was significantly better in lymph node metastasis detection compared to guidelines (area under the curve: 0.83 vs area under the curve: 0.73,  $P$  value = 0.005). Therefore, these patients can be subjected to upfront surgery and lymphadenectomy instead of endoscopic treatment. A meta-analysis by Bedrikovetski *et al*[53] using 17 studies (12 used radiomics models and 5 used deep learning models) concluded that AI was more efficient than radiologists in predicting lymph node metastasis. Similarly, AI was found to be better in detecting metastatic nodes as compared to conventional positron emission tomography/computed tomography imaging[54].

### **AI in intraoperative surgical decision making**

Execution of a surgery depends upon the operating skill and ability of decision making. In 1978, Dr. Spencer[55], a cardiovascular surgeon, mentioned that "a skilfully performed operation is about 75% decision making and 25% dexterity." The decision making can be both technical or non-technical, which impacts patient outcome. Studies of surgical errors have shown that over half of the adverse events are due to cognitive errors[56]. But surgical training is more focused on skill training rather than decision making as it is a challenging task to train[57]. Decision-making skills may vary with experience of operating surgeons[58]. Thus, improving the quality of surgical decision making could help to improve the outcome of surgery.

Decision making is a three-step process, *i.e.* assessment of the situation, action-taking, and re-evaluation of the action's consequences. AI has been used as a decision making aid in a variety of fields, both in medicine and in surgery[59,60]. AI can help surgeons to assess a given situation (*e.g.*, retrieving better data about a clinical situation), the types of actions taken (*e.g.*, through decision suggestion), and the process of re-evaluating the impact of the decision taken. Therefore, it can be achieved in three different ways: (1) Retrieving data and experience from similar clinical scenarios and to supplement sensory input during minimal access surgery, which are not available compared to open surgery; (2) Intraoperative pathology assessment, tumor margin mapping, tumor classification, and tissue identification; and (3) Suggestion of steps of surgery.

**Identification of surrounding structures:** Harangi *et al*[61] used an ANN model to distinguish ureter from uterine artery during laparoscopic hysterectomy with 94.2% accuracy. Similarly, Quelled *et al*[62] applied a system of retrieving related videos of retinal surgery, and subsequent steps were followed during surgery to minimize the risk of injury. AI made it possible to define dissection planes in the robotic gastrectomy and to identify the recurrent laryngeal nerve during thyroidectomy[63,64]. Various studies have shown improved detection of vital structures during laparoscopic cholecystectomy to prevent bile duct injury using AI (Madani *et al*[65], Mascagni *et al*[66], Tokuyasu *et al*[67]). **Table 2** highlights the studies where AI was used for identification of vital structures.

In CRC surgery, AI can be used to detect nearby vital structures (nerve plexus, presacral venous plexus, ureter, bladder, urethra, prostate, seminal vesicles), lymph node metastasis (lateral pelvic nodes, nodes near the root of inferior mesenteric artery), determination of the margin of resection, vascularity, and adequacy of anastomosis.

Augmented reality augments surgeons' intraoperative vision by providing a semi-transparent overlay of preoperative imaging on the area of interest[68]. It has been used in several GI surgical procedures like laparoscopic splenectomy[69] and pancreaticoduodenectomy[70]. Augmented reality can be applied to CRC surgeries to identify and preserve the nearby vital structures.

**Deciding the level of resection:** In CRC surgery, determination of margin status is important to decide the level of resection and consideration for the feasibility of an anastomosis or the creation of a stoma. Margin status can be obtained with "optical biopsy" (*in vivo* diagnostic imaging), which can avoid time-consuming resection and frozen section analysis. Fluorescence-guided surgery is evolving, and it has

**Table 2 Studies having found the role of artificial intelligence in identification of vital structures in surgery**

S. No	Primary aim	AI method used	Ref.
1	Recognition of ureter and uterine artery	Convolutional neural network	Harangi <i>et al</i> [61], 2017
2	Recognition of surgical steps of retinal surgery	Content-based video retrieval system	Quellec <i>et al</i> [62], 2011
3	To define safe dissection plane in robot assisted gastrectomy	Deep learning model based on U-net	Kumazu <i>et al</i> [63], 2021
4	Recurrent laryngeal nerve detection during thyroidectomy	Deep learning computer vision algorithm	Gong <i>et al</i> [64], 2021

AI: Artificial intelligence; S. No: Serial number.

shown promising results in determination of liver or peritoneal metastasis, anastomotic perfusion, detection of sentinel nodes, ureter, and nerves, and intraoperative detection of primary and recurrent lesions during colorectal cancer surgery[71]. Such a concept can be extrapolated on to AI for more efficient performance. Modalities used for intraoperative optical biopsy are confocal laser endomicroscopy, hyperspectral imaging, optical coherence tomography, and contrast-enhanced ultrasonography. There are several studies where these modalities have been used to distinguish abnormal epithelium from normal with the help of AI (Table 3). Using hyperspectral imaging, Jansen-Winkel *et al*[72] reported 94% accuracy in distinguishing carcinoma from adenoma and healthy mucosa using ANN on post-resection of colonic lesions during surgery. A couple of experimental studies have shown that laparoscopic hyperspectral imaging can be used to distinguish malignant tissue in CRC from normal tissue. These modalities can be used to help in surgical decision making in CRC as revisional surgery can be done intraoperatively rather than waiting for frozen sections or final histology avoiding another surgery[73,74]. AI has been effective in differentiating glioblastoma, parathyroid gland, and malignant lesions of the colon from adjacent normal tissues[75-77].

**Deciding the site of anastomosis:** Studies have shown the incidence of colocolic and colorectal anastomosis leak to be 3.3% and 8.6%, respectively[78] and has adverse clinical outcomes and economic burden[79]. It can lead to anastomotic site stricture, recurrence of malignancy, and poor evacuatory function. The literature has shown poor predictive value of surgeons' perceptions of possible anastomotic site leaks that led to investigating other methods like the use of indocyanine green[80]. The robotic platform provides an inbuilt near infrared camera for assessment of vascularity at the resection margin and to reduce anastomotic site leakage[81]. A study by Mazaki *et al*[82], where auto-artificial intelligence was used to develop a predictive model for anastomotic leakage, showed that triple-row staplers can decrease the leak rate. There is an ongoing study by Taha *et al*[83] known as the PANIC study (The Prediction of Anastomotic Insufficiency risk after Colorectal surgery), which utilizes machine learning principles to formulate an algorithm for prediction of anastomotic leak following colonic (PANIC-C) or colorectal (PANIC-R) anastomosis. The results of the study are expected to be available by December 2022.

**Helping in operative step suggestion:** Operative step suggestion in CRC is at a developmental stage. In the literature, AI has been used in cataract surgery and spinal cord surgery with satisfactory results. Tian *et al*[84] developed VeBIRD (Video-Based Intelligent Recognition and Decision system) to track and classify the cataract grade on videos of phacoemulsification surgeries. It helped to decide the amount of ultrasonic energy needed to emulsify a cataract based on the grade. Therefore, a less experienced surgeon can perform the procedure with as much efficiency as that of an experienced surgeon. Somatosensory evoked potential is used during spinal cord surgeries to detect spinal cord injury. A decrease in somatosensory evoked potential value needs to be confirmed with awakening the patient and checking spinal cord function and this decrease in somatosensory evoked potential can be due to the effect of anesthesia. Fan *et al*[85] applied support vector regression and multi-support vector regression to distinguish spinal cord injury from anesthetic effect. Similarly, in CRC surgery such methods can help to find the area of interest to formulate standardized resection and differentiate intraoperative lymphorrhea from ureter or bladder injury using AI.

Colorectal cancer surgery requires accurate and judicious preoperative decisions to optimize the outcome of surgery (personalized treatment). The decision can be augmented by the use of AI, which is expected to be precise and without errors. It can assist in imaging, tissue diagnosis, and staging before surgery. It can be used preoperatively to choose patients for neoadjuvant therapy and those requiring upfront surgeries. Intraoperatively, it helps in the identification of tumor tissue (to determine the margin of resection), metastatic lymph nodes (for the extent of lymphadenectomy), and important surrounding structures. Its assistance is also useful in assessing the adequate vascularity at the anastomotic site that can decrease the postoperative anastomotic leak and thereby reduce the morbidity and mortality.

**Table 3 Studies of artificial intelligence differentiating normal epithelium from abnormal or malignant cells**

S. No	Modality used	Primary aim of study	AI method used	Ref.
1	CEUS	To differentiate glioblastoma from normal tissue	Support vector machines	Ritschel <i>et al</i> [75], 2015
2	OCT	To distinguish parathyroid tissue from thyroid, lymph node, and adipose tissue	Texture feature analysis and back propagation artificial neural network	Hou <i>et al</i> [76], 2017
3	CLE	Normal colonic mucosa from malignant lesion	Fractal analysis and neural network modelling	Ștefănescu <i>et al</i> [77], 2016
4	Hyperspectral imaging	Differentiation of colonic carcinoma from adenoma and healthy mucosa	Artificial neural network	Jansen-Winkel <i>et al</i> [72], 2021

AI: Artificial intelligence; CEUS: Contrast-enhanced ultrasonography; OCT: Optical coherence tomography; CLE: Confocal laser endomicroscopy; S. No: Serial number.

Like the application of AI in several domains of medicine and health, it may play a significant role in surgical decision making, enhancing the outcome, in addition to diagnosis (imaging, endoscopy, tissue diagnosis).

## FUTURE IMPLICATIONS

The future is promising, where AI is likely to play a significant role in reducing the bias of the Mass Detection Tool in deciding the treatment strategy and reducing the diagnosis and planning time with uniformity and with no or minimum error. The day is not far when the surgical world may be able to find a personalized surgical treatment for each and every patient of CRC, with improved intraoperative technical execution and reduced complications. The overall time taken in the management of CRC will be reduced, the treatment will be standardized, and the outcome will be maximized.

## CONCLUSION

The role of AI in CRC is currently limited to preoperative staging and assessment of surgical resection margins and anastomotic sites. Its application to surgical decision making is still evolving, and the literature is very limited. However, the future is promising.

## FOOTNOTES

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