

# Artificial Intelligence in *Gastroenterology*

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# Artificial Intelligence in Gastroenterology

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*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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## Artificial intelligence in rectal cancer

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### Abstract

Accurate and rapid diagnosis is essential for correct treatment in rectal cancer. Determining the optimal treatment plan for a patient with rectal cancer is a complex process, and the oncological results and toxicity are not the same in every patient with the same treatment at the same stage. In recent years, the increasing interest in artificial intelligence in all fields of science has also led to the development of innovative tools in oncology. Artificial intelligence studies have increased in many steps from diagnosis to follow-up in rectal cancer. It is thought that artificial intelligence will provide convenience in many ways from personalized treatment to reducing the workload of the physician. Prediction algorithms can be standardized by sharing data between centers, diversifying data, and creating big data.

**Key Words:** Rectal cancer; Artificial intelligence; Deep learning; Machine learning

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**Core Tip:** There is a growing interest in the application of artificial intelligence in healthcare to improve disease diagnosis, management, and the development of effective treatments. Considering the large number of patients diagnosed with rectum cancer and a significant amount of data, artificial intelligence is an important tool to improve diagnosis and treatment, follow-up in rectal cancer, develop personalized medicine, improve the quality of life of patients, and reduce unnecessary health expenses.

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## INTRODUCTION

Artificial intelligence (AI) is the computer science that tries to imitate human-like intelligence in machines by using computer software and algorithms to perform certain tasks without direct human stimuli<sup>[1,2]</sup>. Machine learning (ML) is a subset of AI that uses data-driven algorithms that learn to imitate human behavior based on the previous example or experience<sup>[3]</sup>. Deep learning (DL) is an ML technique that uses deep neural networks to create a model. Increasing computing power and reducing financial barriers led to the emergence of the DL field<sup>[4]</sup>.

AI has entered our lives as support in every field. In medicine, it helps clinical processes and management of medical data and information. AI applications assist physicians in diagnosis, research, treatment, and prognosis evaluation of the disease<sup>[5]</sup>. Cancer is the most common cause of death in developed countries, and it is estimated that the number of cases will increase even more in aging populations<sup>[6,7]</sup>. Therefore, cancer research will continue to be the top priority for saving lives in the next decade.

In oncology, there are typical clinical questions such as 'Which patients have the highest risk of toxicity?' and 'What is the probability of local control and survival in this patient?'. Although clinical studies exist as the gold standard for answers to these questions, clinical studies are costly, slow, and limited to reachable patients. By using the available data, future clinical studies can be better planned, and new findings can be obtained. Evidence-based medicine is based on randomized controlled trials designed with a large patient population. However, the number of clinical and biological parameters that need to be investigated to obtain precise results is increasing day by day<sup>[8]</sup>.

New and separate approaches are required for all patient subpopulations. Clinicians should use all diagnostic tools (radiological imaging, metabolic imaging, blood and genetic testing, *etc.*) to decide on the appropriate combination of therapy (radiotherapy, chemotherapy, targeted therapy, and immunotherapy). In oncology, AI, a new methodology that provides information using the large data available, has begun to be used to support clinical decisions<sup>[9]</sup>. It is important to combine a large and heterogeneous amount of data and create accurate models. Today, AI in oncology has entered our lives in early detection, diagnosis, treatment, and patient follow-up.

Although AI can take place in every step from patient consultation to patient follow-up in rectal cancer and can contribute to the clinician and the society, there are still many challenges and problems to be solved. Big data sets should be created for AI first, and these data sets should be improved. The development of prediction tools with a wide variety of variables and models limits the comparability of existing studies and the use of standards. Prediction algorithms can be standardized by sharing data between centers, diversifying data, and creating big data. In addition, the models can be made clinically applicable by updating the models by entering new data into the models. Today, the accuracy and quality of the data is also of great importance, as no AI algorithm can fix the problems in training data.

Colorectal cancer is the fourth most common type of cancer worldwide, with approximately 800000 new cases diagnosed each year and accounting for approximately 10% of all cancers<sup>[10]</sup>. Determining the optimal treatment plan for a patient with rectal cancer is a complex process. In addition to decisions regarding the purpose of rectal cancer surgery, the possible functional consequences of treatment, including the possibility of preserving normal bowel function and genitourinary function, should be considered. Achieving treatment goals and minimal impact on the quality of life can be challenging at the same time, especially for patients with distal rectal cancer. Careful patient selection in terms of specific treatment options and the use of sequential multimodality therapy combining chemoradiotherapy (CRT), chemotherapy (ChT), and surgical treatment are recommended for most patients<sup>[11]</sup>.

In this review, the role of AI in the diagnosis, treatment, and follow-up of rectal cancer is discussed.



## AI IN DIAGNOSIS OF RECTAL CANCER

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

Rectal cancers constitute the majority of gastrointestinal tumors. Among the metastatic spreading routes of rectal cancer, lymph node (LN) metastasis is the most important due to its high risk of local recurrence, which leads to poor prognosis<sup>[12]</sup>. LN metastasis is an important factor in treatment selection and in predicting prognosis. Preoperative evaluation of metastatic LNs is critical in determining the optimal treatment strategies of rectal cancer cases. Magnetic resonance (MR) imaging is widely used in clinical practice for the diagnosis of metastatic LNs in rectal cancer. MR is considered superior to computed tomography (CT) for better separation of soft tissue. Radiologists often evaluate their shape, boundaries, and signal intensities to identify metastatic LN<sup>[13]</sup>. However, correct evaluation in a short time is a great challenge, especially when considering clinics with a high number of cases. Also, when the same MR image is evaluated by different radiologists, very different results can be obtained, which weakens the sensitivity of LN staging<sup>[14-17]</sup>. As a result, it is often difficult to accurately determine the presence of LN metastasis. In recent years, the development of DL technology has greatly improved image recognition capability, making it possible to identify specific target areas within an image and allow images to be classified according to specified target features<sup>[18]</sup>.

According to some studies, although the AI system is more successful than senior physicians in the diagnosis of solid tumors, such as lung, breast, prostate, and thyroid cancer, few studies have yet been reported on the determination of metastatic LN<sup>[19-25]</sup>. In the literature, there are studies in which LN metastases have been detected with AI in some cancers such as lung, oral cavity, breast, stomach, and thyroid cancer<sup>[26-30]</sup>.

In the study conducted by Ding *et al*<sup>[18]</sup> enrolling 414 cases diagnosed with rectal cancer by collecting data from six centers, MR images of the cases were evaluated. Faster region-based convolutional neural network (Faster R-CNN), a new AI algorithm, was evaluated in the study. Patients who underwent surgery with a diagnosis of rectal cancer, whose patient data could be accessed, who did not receive preoperative RT or ChT, and who had MR images at the stage of diagnosis, were included in the study. Radiologist-based diagnosis and pathologist-based diagnosis were compared with the Faster R-CNN system. The number of metastatic LNs diagnosed between two of the three groups was evaluated using the pair-wise correlation analysis. A statistically significant correlation was found in the comparison of both groups [radiologist - Faster R-CNN ( $P < 0.001$ ), pathologist - radiologist ( $P = 0.011$ ), and pathologist - Faster R-CNN ( $P < 0.001$ )]. In Faster R-CNN, radiologist, and pathologist LN staging, consistency control was performed between groups, and the highest consistency was found among the Faster R-CNN - radiologist diagnosis ( $P = 0.018$ ). Among the Faster R-CNN - pathologist diagnosis, the  $P$  value was 0.039. Among the radiologist - pathologist diagnosis, the  $P$  value was 0.043<sup>[18]</sup>.

In another study by Ding *et al*<sup>[13]</sup>, Faster R-CNN was evaluated for metastatic LN prediction, and it aimed to create mathematical nomograms for preoperative metastatic LN prediction. In the prediction of metastatic LN with Faster R-CNN, the MR images of 545 rectal cancer cases who did not receive preoperative RT or ChT were divided into training and validation groups at the rate of 2:1. While creating the nomogram, 183 cases were used as an outcome variable for the presence of LN metastasis, and 153 cases were used as validation for the level of LN metastasis (N1 or N2). Variables were age, gender, preoperatively differentiate grade, metastatic LN obtained by MR, metastatic LN obtained by postoperative pathology, carcinoembryonic antigen (CEA), carbohydrate antigen 19-9. Important variables in predicting metastatic LN positivity with Faster R-CNN in univariate analysis were tumor differentiation grade and CEA level ( $P < 0.05$ ) and age and tumor differentiation gradient in multivariate analysis ( $P < 0.001$ ). Variables determined as important variables in multivariate analysis in MR-based and Faster R-CNN-based metastatic LN prediction were used in nomogram formation; in the MR-based nomogram and the Faster R-CNN-based nomogram, area under curve (AUC) and 95% confidence interval (CI) were found to be 0.856 (0.808-0.905) and 0.862 (0.816-0.909), respectively. According to this study, the Faster R-CNN nomogram appears to be suitable and reliable for predicting the presence of metastatic lymph nodes preoperatively<sup>[13]</sup>.

Lu *et al*<sup>[31]</sup> evaluated 28080 MR images of 351 rectal cancer cases with Faster R-CNN in their study. Radiologist diagnosis and Faster R-CNN diagnosis were compared using receiver operating characteristic curves (ROC), and the Faster R-CNN ROC was found to be 0.912. It was accepted as a more effective and more objective method. According to the study, the diagnosis was made in 20 s per case with Faster R-CNN, while radiologists made the diagnosis in 600 s per case<sup>[31]</sup>.

The diagnosis of metastatic LN in rectal cancer is very important for treatment decisions and prognosis. The diagnosis of metastatic LN by MR is largely based on the subjective interpretation of the radiologist. Therefore, it lacks objectivity and reproducibility, although it has a variable diagnostic accuracy. Therefore, using AI systems in the diagnosis phase can contribute to the ability of radiologists to diagnose metastatic LN correctly and in a shorter time and to make a more accurate treatment decision with more accurate tumor, node, metastasis (TNM) staging.

### **AI in the detection of *t* stage and tumor differentiation**

Choosing the most appropriate treatment is important in rectal cancer. A correct preoperative stage is important for the surgical and neoadjuvant CRT decision. Generally, pathological type, tumor differentiation, infiltration depth, and presence of lymph node metastasis determine the prognosis of the tumor. Therefore, understanding the pathological features of the tumor is very important for the clinical treatment decision<sup>[32]</sup>. Radiomic analysis is a tool developed to assess tumor heterogeneity. Radiomics is a noninvasive method that includes high-quality image acquisition, high-throughput quantitative feature extraction, high-dimensional feature extraction, and diagnostic, prognostic, or predictive model generation. Radiomic models using medical images and clinical data have potential in making clinical decision<sup>[33]</sup>. The MRI-based radiomic model has been used to differentiate cancer from benign tissue and reflect the histological features of rectal cancer<sup>[34]</sup>.

In the study conducted by Ma *et al*<sup>[35]</sup> with 152 rectal cancer cases, it aimed to predict the pathological characteristics of the tumor from the MR-based radiomic model. Tumor delineation was performed using 3T MR and high resolution T2-weighted images, and 1029 radiomic features were extracted. Multilayer perceptron, logistic regression (LR), support vector machine (SVM), decision tree (DT), random forest, and K-nearest neighbor (KNN) have been trained and used five-fold cross-validation to create prediction models. The best performance of the radiomics model for the degree of differentiation, T stage, and N stage was obtained by SVM (AUC, 0.862; 95%CI: 0.750–0.967; sensitivity, 83.3%; specificity, 85.0%), multilayer perceptron (AUC, 0.809; 95%CI: 0.690–0.905; sensitivity, 76.2%; specificity, 74.1%), and random forest (AUC, 0.746; 95%CI: 0.622–0.872; sensitivity, 79.3%; specificity, 72.2%). This study demonstrated that the high-resolution T2-weighted images-based radiomics model could serve as pretreatment biomarkers in predicting pathological features of rectal cancer<sup>[35]</sup>.

### **AI in detection of distant metastasis**

Although advances in treatment strategies and multidisciplinary treatment modalities have reduced local recurrences, distant metastasis continues to be the main cause of treatment failure in patients with rectal cancer<sup>[6]</sup>. The most common metastasis site is the liver, and liver metastasis develops in 26.5% of cases within 5 years from diagnosis<sup>[36]</sup>. At the stage of diagnosis, there is no liver metastasis in staging, but metachronous liver metastasis (MLM) that develops after initial staging and treatment is thought to be caused by occult metastases and micrometastases<sup>[37,38]</sup>.

The main treatment strategy for early detected MLM is surgical resection, providing better prognosis and survival as well as a chance for cure compared to other treatments. However, a significant portion of patients with MLM may have lost their surgical chances by the time it is detected<sup>[39]</sup>. Although studies are reporting that some variables increase the risk of MLM, there is still no definite marker that can be used to predict the cases that will develop MLM<sup>[40]</sup>. Radiomics, which have come to the forefront recently, are obtained by using automated high-throughput extraction of many quantitative properties, offering the chance to capture intratumoral heterogeneity in a noninvasive manner<sup>[41]</sup>.

Liang *et al*<sup>[42]</sup> predicted MLM by using MR radiomics with ML in a total of 108 rectal cancer cases with 54 MLM and 54 nonmetastatic patients. Radiomics were obtained from venous phase and T2-weighted MR images, and 2058 radiomic properties were evaluated by two separate ML techniques (SVM; LR). After determining the optimal radiomic properties, four groups of models were created: A model containing five radiomic features from T2 weighted MR images (Model<sub>T2</sub>), a model containing eight radiomic features from venous phase images (Model<sub>VP</sub>), a model containing the sum of these radiomics, *i.e.* 13 radiomics (Model<sub>combined</sub>), and a model containing 22 optimal radiomics (Model<sub>optimal</sub>). Model<sub>optimal</sub> was determined as the best prediction model with the LR algorithm, and its accuracy, sensitivity, specificity, and AUC were 0.80, 0.83, 0.76, and 0.87, respectively<sup>[42]</sup>.

Peritoneal carcinomatosis (PC) has a poor prognosis and is considered a terminal stage. PC is present at diagnosis in 5%-10% of the cases diagnosed with colorectal cancer and in 25%-44% of recurrent disease. While a median survival of 33 mo can be achieved with cytoreductive surgery and hyperthermic intraperitoneal ChT, it is < 10 mo if incomplete cytoreductive surgery and diffuse PC are present<sup>[43]</sup>. Survival rates can also be high with minimally invasive surgery if PC can be detected early. To predict synchronous PC cases, Yuan *et al*<sup>[44]</sup> evaluated 19814 tomography images obtained from 54 PC and 76 non-PC cases in training, and 7837 images obtained from 40 cases as the test group. Using the ResNet-three dimensional (3D) algorithm + SVM algorithm, an accuracy rate of 94.1% was obtained, AUC: 0.92 (0.91-0.94), sensitivity 93.7%, specificity 94.4%, positive predictive value 93.7%, and the negative predictive value was found to be 94.4%. The performance of the algorithm was determined to be better than routine contrast-enhanced CT (AUC: 0.791 *vs* AUC: 0.92)<sup>[44]</sup>.

Distant metastasis detection can be made more accurately in the earlier period by supporting the physician with the prediction models having high accuracy and this can reduce the cost of treatment while increasing survival rates.

## AI IN RECTAL CANCER TREATMENT AND RESPONSE TO TREATMENT

### Contouring in radiotherapy

Contouring is an important step that is routinely performed in RT to determine the treatment target and organs at risk (OAR). In a typical clinical workflow, the radiation oncologist needs to contour this target volume and OAR on the simulation images. Contouring is generally performed on CT and less commonly on MR images in clinics where MR guided RT is applied. This contouring process can take hours per patient<sup>[45]</sup>. AI can be used both to minimize the differences between physicians and to shorten the duration of this step in RT planning.

**Target volume contouring:** MR plays an important role in the diagnosis and treatment of rectal cancer<sup>[46]</sup>. It guides the physician in identifying the primary tumor, especially in RT planning. Also, MR-based planning increases local control and complete response rates, with the potential to facilitate individualized treatment plans for dose escalation<sup>[47,48]</sup>. Also, defining and contouring gross tumor volume (GTV) is time-consuming, and differences in target volume contouring among physicians may cause variability in treatment and different oncological results<sup>[49]</sup>. Although the application of Atlas-based automatic segmentation algorithms can reduce the identification time, these methods have low performance in rectal cancer<sup>[50]</sup>. The main advantage of DL methods is that they automatically create the most suitable model from the training data sets. In recent years, DL methods have also started to be used in RT steps. Tumor contouring with CNNs has been extensively studied in lung and head and neck cancers and a reduction in contouring time per patient of up to 10 min was observed compared to the contouring time of the physician<sup>[51-53]</sup>.

In rectum cancer, contouring of GTV and clinical target volume (CTV) were performed using MR and CT images. Wang *et al*<sup>[54]</sup> created a DL-based autosegmentation algorithm for GTV delineation using MR (3 Tesla, T2-weighted) images of 93 locally advanced rectal cancer cases. The model was trained in two phases that are tumor recognition and tumor segmentation. Data is divided into 90% training and 10% validation groups for 10-fold cross-validation. Hausdorff distance (HD), average surface distance (ASD), Dice index (DSC), and Jaccard index (JSC) were used to compare and evaluate automatic and manual contouring. For the validation data set, DSC, JSC, HD and ASD (mean  $\pm$  SD) were  $0.74 \pm 0.14$ ,  $0.60 \pm 0.16$ ,  $20.44 \pm 13.35$ , and  $3.25 \pm 1.69$  mm, respectively. In the manual contouring of two radiation oncologists, DSC, JSC, HD and ASD (mean  $\pm$  SD) were  $0.71 \pm 0.13$ ,  $0.57 \pm 0.15$ ,  $14.91 \pm 7.62$ , and  $2.67 \pm 1.46$  mm, respectively. There was no statistically significant difference between the DL-based autosegmentation and manual contouring in terms of DSC ( $P = 0.42$ ), JSC ( $P = 0.35$ ), HD ( $P = 0.079$ ), and ASD ( $P = 0.16$ ) values. Before postprocess (erosion and dilation), that is, correction of contours and removing small isolated points, a statistically significant difference ( $P = 0.0027$ ) was found only in HD. According to this study, results close to manual contouring can be obtained with DL-based algorithms using T2-weighted MR images<sup>[54]</sup>.

In another study by Trebeschi *et al*<sup>[55]</sup>, tumor contouring was performed using multiparametric MR images. The study included 140 locally advanced rectal cancer cases, and each case was contoured by two experienced radiologists. In this study, the CNN algorithm was used to function as a voxel classifier. CNN was trained using the



voxel values of the region with and without tumor in MR. In the independent validation data set, the DSC value was determined as 0.68 and 0.70 according to CNN and both radiologists. The AUC value for both radiologists was found to be 0.99. This study showed that DL can perform the correct localization and segmentation of rectal cancer in MRI in most patients<sup>[55]</sup>.

Song *et al*<sup>[56]</sup> evaluated CTV contouring with CNN in 199 rectal cancer cases. For training, validation, and testing, 98 cases, 38 cases, and 63 cases were used, respectively. While volumetric DSC showed the volumetric overlap between automatic segmentation and manual contouring, surface DSC showed the overlap between automatic segmentation and manual contouring surfaces. Two CNN techniques were used in the present study that were DeepLabv3 + and ResUNet, and the volumetric DSC and surface DSC of CTV were 0.88 *vs* 0.87 ( $P = 0.0005$ ) and 0.79 *vs* 0.78 ( $P = 0.008$ ), respectively. According to this study, high quality and shorter CTV contouring can be performed with CNNs<sup>[56]</sup>. Target volume contouring studies with AI in rectum cancer are summarized in [Table 1](#).

**Contouring of OAR:** In radiotherapy, it is necessary to make the contouring of OAR correctly to protect them and to evaluate the toxicity correctly. To fully benefit from the advantages of technological developments in RT planning and devices, OAR must be defined correctly. This step can become a rate limiting step in clinics with a high number of patients. Also, there may be differences among the practitioners, and due to significant anatomical changes (edema, tumor response, weight loss, *etc.*) during the treatment, it may be necessary to make a new plan with new contouring during the treatment. AI, particularly CNN, is a potential tool to reduce the physician's workload and set a standard in contouring. In recent years, DL methods have been widely used in medical applications, and CNN has been used in contouring OAR in head-neck, lung, and prostate cancer<sup>[57-59]</sup>. There are also studies on this subject in rectal cancer.

OAR contouring was also evaluated in the study performed by Song *et al*<sup>[56]</sup> for CTV contouring. As OAR, small intestine, bladder, and femoral heads were contoured. With ResUNet, both volumetric and surface DSC values in femoral head contouring and surface DSC values in bladder contouring were found to be statistically more significant, and contouring performance was better. Higher volumetric and surface DSC were obtained with DeepLabv3 + for the small intestine<sup>[56]</sup>.

Men *et al*<sup>[60]</sup> conducted a segmentation study using deep dilated CNN based DL technique in both CTV and OAR (bladder, femoral heads, small intestine, and colon). CT images of 278 rectal cancer cases were included in the study. Images of 218 randomly selected cases were used for training, and images of the remaining 60 cases were used for validation. In this study, DSC was also evaluated and for CTV, bladder, left femoral head, right femoral head, small intestine, and colon as 87.7%, 93.4%, 92.1%, 92.3%, 65.3%, and 61.8%. CTV and OAR contouring time per case was found to be 45 s on average<sup>[60]</sup>.

In another study conducted by Men *et al*<sup>[61]</sup>, the effect of the patient's position on segmentation accuracy was investigated with CNN. The study included 50 supine and 50 prone cases with planning CT, and three different models were trained: Patients in the same position, patients in different positions, and patients in both positions. Performance evaluation regarding segmentation was performed using DSC and HD for CTV, bladder, and femurs. While the model trained in different positions compared to the model trained in the same position was statistically significantly better for CTV and bladder ( $P < 0.05$ ), it was found to be  $P > 0.05$  in femur segmentation. DSC values were 0.84 *vs* 0.74, 0.88 *vs* 0.85, and 0.91 *vs* 0.91 for CTV, bladder, and femurs, respectively. The accuracy rates for the model trained in both positions were similar ( $P > 0.05$ ). The DSC was 0.84, 0.88, and 0.91 for CTV, bladder, and femur, respectively. According to this study, while the patient position is important for CTV and bladder in segmentation with the CNN model, it was not found to be an important factor for the femur<sup>[61]</sup>. Studies are summarized in [Table 1](#).

In RT, while providing effective treatment for the tumor, protection of OAR is very important in terms of acute and late side effects. For this, it is an important step to define the tumor volume and OAR correctly and accurately. However, this step requires intensive labor and time and can be rate-limiting. Creating models with DL and using them in clinical practice will ensure standardization among physicians in contouring and accelerate this step.

### Radiotherapy planning

Treatment planning is an important step in the RT workflow. Treatment planning has become more sophisticated over the past few decades with the help of computer science, allowing for the minimization of normal tissue damage while providing

**Table 1 Target volume and organs at risk contouring with artificial intelligence**

Ref.	Number of patients	Imaging method	Contouring	Artificial intelligence method	Results
Wang <i>et al</i> <sup>[54]</sup> , 2018	93	MR (3 Tesla, T2 - weighted)	GTV, CTV	CNN	Between deep learning-based autosegmentation and manual contouring DSC ( $P = 0.42$ ), JSC ( $P = 0.35$ ), HD ( $P = 0.079$ ), and ASD ( $P = 0.16$ ); Before postprocess process only in HD ( $P = 0.0027$ ).
Trebeschi <i>et al</i> <sup>[55]</sup> , 2017	140	Multiparametric MRI (1.5 Tesla, T2-weighted)	GTV	CNN	According to CNN and both radiologists in independent validation data set DSC: 0.68 and 0.70; For both radiologists AUC: 0.99.
Song <i>et al</i> <sup>[56]</sup> , 2020	199	CT (3 mm section thickness)	CTV and OAR	CNNs (DeepLabv3+ and ResUNet)	CTV segmentation better with DeepLabv3+ than ResUNet (volumetric DSC, 0.88 <i>vs</i> 0.87, $P = 0.0005$ ; surface DSC, 0.79 <i>vs</i> 0.78, $P = 0.008$ ); DeepLabv3+ model segmentation was better in the small intestine, with the ResUNet model, bladder and femoral heads segmentation results were better. In both models, the OAR manual correction time was 4 min.
Men <i>et al</i> <sup>[60]</sup> , 2017	278	CT (5 mm section thickness)	CTV and OAR	CNN (DDCNN)	DSC values; CTV: 87.7%, bladder: 93.4%, left femoral head: 92.1%, right femoral head: 92.3%, small intestine: 65.3%, colon 61.8%.
Men <i>et al</i> <sup>[61]</sup> , 2018	100	CT (3 mm section thickness)	CTV and OAR	CNN	CTV and bladder contouring were better in the model trained in the same position than the model trained in a different position ( $P < 0.05$ ). No statistically significant difference between femoral heads ( $P > 0.05$ ). No statistical difference between accuracy rates in CTV, bladder, and femoral heads segmentation in the model trained in both positions ( $P > 0.05$ ).

AUC: Area under the curve; ASD: Average surface distance; CNN: Convolutional neural network; CT: Computed tomography; CTV: Clinical target volume; DDCNN: Deep dilated convolutional neural network; DSC: Dice similarity coefficient; GTV: Gross tumor volume; HD: Hausdorff distance; JSC: Jaccard index; MRI: Magnetic resonance imaging; OAR: Organs at risk.

adequate tumor dose. As a result, treatment planning has become more labor-intensive and takes hours and sometimes even days for planners. In RT planning, many algorithms have been developed to support planners, and these algorithms focus on automating the planning process and/or optimizing dosimetric changes. These algorithms have contributed to the improvement of treatment planning efficiency and quality<sup>[62]</sup>. Planning workflow starts with determining dosimetric requirements regarding target volume and OARs and makes decisions about basic planning parameters, including beam energy, number, and angles, *etc.*, based on the needs of each case. While creating a minimally acceptable plan can be quick, improving a plan is much more difficult. Also, the plan may need to be improved according to the mid-plan result evaluation of the physicians, which causes increased effort and time. Automatic treatment planning systems, from simple automation to AI, are gradually taking their place in planning systems.

The knowledge-based planning system helps to use the previous planning information in the database with ML methods in obtaining the best dose distribution for target volume and OAR. Knowledge-based treatment planning algorithms use geometric and dosimetric information to estimate doses for new patients using the information found in training data. The dose volume histogram prediction model was created by using a knowledge-based treatment planning system, using 80 plans in training, and evaluating 70 plans in the test with simultaneous integrated boost and VMAT techniques. Using this model, the multileaf collimator sequences of 70 clinically validated plans were re-optimized. While doing this, parameters such as field geometry and photon energy were not changed. Dosimetric results were evaluated by comparing dose volume histogram data as homogeneity index, conformal index, hot spots (volumes taking more than 107% of the prescribed dose), mean dose, femoral heads, and bladder mean ( $D_{mean\_mesane}$ ,  $D_{mean\_femoralhead}$ ) and 50% of the dose ( $D_{50\%bladder}$ ,  $D_{50\%femoralhead}$ ). Similar conformal index was obtained when comparing the original plan ( $1.00 \pm 0.05$  for planning target volume (PTV)<sub>boost</sub> and  $1.03 \pm 0.02$  for PTV) and the knowledge-based plan ( $0.99 \pm 0.04$  for PTV<sub>boost</sub> and  $1.03 \pm 0.02$  for PTV). Better homogeneity index values were obtained in the knowledge-based plan ( $0.05 \pm 0.01$  for PTV<sub>boost</sub> and  $0.26 \pm 0.01$  for PTV) compared to the original plan ( $0.06 \pm 0.01$  for PTV<sub>boost</sub> and  $0.26 \pm 0.01$  for PTV) ( $P < 0.05$ ). It has been shown that  $V_{107\%}$  values in the original plan were higher than the knowledge-based plan. The knowledge-based plan achieved a statistically significant decrease in  $D_{50\%femoralhead}$ ,  $D_{mean\_femoralhead}$ ,  $D_{50\%}$

bladder<sup>r</sup> and Dmean<sub>mesane</sub> values. According to this study, the knowledge-based planning system provided a statistically significant advantage in some dosimetric data compared to the original plans<sup>[63]</sup>.

Zhou *et al*<sup>[64]</sup> aimed to develop a DL model for intensity-modulated RT, which provides an estimation of 3D voxel-wise dose distribution. Of the 122 post-op intensity-modulated RT treated cases, the plans of 100 cases were used for training-validation, and the plans of 22 cases were used for testing. To estimate 3D dose distributions, a 3D-DL model named U-Res-Net\_B was created<sup>[60]</sup>. No statistically significant difference was found between the original plans and the DL model named U-Res-Net\_B in terms of dosimetric parameters (homogeneity index, conformal index, V50, and V45 for PTV and OARs). The DSC value of the model was higher than 0.9 for most isodose volumes, and the ratio of 3D gamma passing ranged from 0.81 to 0.90 for PTV and OAR. This study has developed a DL model by considering beam configuration input; this model has shown that it has potential in terms of automated planning for easier clinical evaluation of more comprehensive cases<sup>[64]</sup>.

### Evaluation of chemoradiotherapy response

In locally advanced rectal cancer, neoadjuvant CRT improves local control, disease-free survival, and sphincter preservation rates<sup>[65]</sup>. However, tumor regression patterns after neoadjuvant CRT vary widely, from the pathological complete response (pCR) to disease progression. Although cases with pCR have the best survival and tumor control, neoadjuvant CRT can provide pCR in only 10%-30% of cases in locally advanced rectal cancer<sup>[66]</sup>. Some studies have shown that cases with pCR have low recurrence rates, and therefore less invasive alternative surgical treatments, such as sphincter-sparing local excision or a watch-and-wait approach, may be more appropriate<sup>[67-70]</sup>. Therefore, it is very important to determine the cases that are likely to have a complete clinical response before surgery.

MR, which enables the evaluation of the therapeutic response noninvasively, is promising in the early prediction of pCR. MR images taken at different times of the CRT, including before, during, and after treatment, can be analyzed separately or in combination to provide anatomical and functional information. With the advancement of MR imaging technology, several different sequences can be included in the MR protocol within a reasonable imaging time (< 30 min), and this multiparametric MR can provide comprehensive information to facilitate quantitative radiomic analysis for prediction of tumor response<sup>[71]</sup>. Radiomics extracts hundreds of quantitative image features and then uses advanced statistical analysis to classify different groups. Nie *et al*<sup>[72]</sup> predicted patients with pCR after CRT was completed with 80%-90% prediction accuracy of pretreatment multiparametric MRI-based radiomic analysis.

Shi *et al*<sup>[71]</sup> predicted the treatment response with DL from the radiomics they obtained from the MR images taken before treatment and in the middle of treatment (3-4 wk after the start of treatment) in CRT cases with a diagnosis of locally advanced rectal cancer. Of the 51 cases included in the study, 45 cases pre-treatment, 41 cases mid-treatment, and 35 cases both pre-treatment and mid-treatment MR images were available, and the MR protocol was specified as T2, diffusion-weighted imaging with b-values of 0 and 800 s/mm<sup>2</sup> and dynamic contrast-enhanced. In the surgical specimen performed after CRT, the response of the case depending on the tumor regression grade was determined. Total tumor volume and mean apparent diffusion coefficient (ADC) were measured on MRI. Using Haralick's Gray Level Co-occurrence Matrix was used to distinguish cases with and without pCR, cases with and without good response by applying radiomics using texture, and histogram parameters and CNN. Tumor volume decreased in mid-treatment MRI compared to before, and ADC increased. In predicting the cases with and without pCR with their radiomic features, AUC values were found to be 0.80, 0.82, and 0.86 when the pre-treatment MR, mid-treatment MR, and both MR, respectively, were evaluated together. In cases that respond well and those that do not, these rates were 0.91, 0.92, and 0.93, respectively. When MRIs before and during treatment were evaluated together, AUC was found to be 0.83 in DL prediction of cases with and without pCR<sup>[71]</sup>.

A study conducted by Fu *et al*<sup>[73]</sup> aimed to obtain and compare handcrafted and DL-based radiomic features from pre-treatment diffusion-weighted imaging-MR images. Forty-three cases that underwent CRT with the diagnosis of locally advanced rectal cancer were included in the study. MRI was taken before treatment in all patients, and total mesorectal excision was applied 6-12 wk after the CRT. GTV from MR images was contoured by an experienced radiation oncologist. Postsurgical cases were grouped as responsive (*n* = 22) and unresponsive (*n* = 21). Handcrafted and DL-based radiomic features were extracted from diffusion-weighted imaging ADC map using traditional computer-aided diagnostic methods and pretrained CNN, respectively. The

ROC curve (AUC) of the model created with handcrafted radiomic features was 0.64, while that of the DL-based model was 0.73. Its statistical significance was found to be better ( $P < 0.05$ ). According to this study, radiomic features obtained from MR images and the algorithm created using DL were shown to be better in predicting CRT response<sup>[73]</sup>.

In another study by Shayesteh *et al*<sup>[74]</sup>, 98 cases diagnosed with rectal cancer were included in the study, and MRI was performed 1 wk before the CRT. Radiomics such as density, shape, and texture features were extracted from MR images. For training and validation, 53 and 45 cases, respectively, were used. SVM, Bayesian network, neural network, and KNN algorithms were used one by one and together for predicting response to CRT. Prediction performance was evaluated by AUC. When the algorithms were evaluated separately, the best result was obtained with the Bayesian network algorithm, and the AUC and accuracy rate were 0.75 and 80.9%, respectively. When the algorithms (SVM, neural network, Bayesian network, KNN) were evaluated together, the AUC and accuracy rate were 0.97 and 92.8%, respectively. According to this study, the prediction process can be improved when algorithms are used together<sup>[74]</sup>.

In another study conducted with 89 cases diagnosed with locally advanced rectal cancer, 66 cases were included in the training group and 23 cases were included in the test group, and resistance prediction to CRT was evaluated. Radiomics obtained from pre-treatment MR, ADC images, and clinical features of the cases were evaluated with the Random Forest Classifier (RFC) algorithm. Of 133 radiomic features and nine clinical features (entropy<sub>mean</sub>, inverse variance energy<sub>mean</sub>, small area emphasis, ADC<sub>min</sub>, ADC<sub>mean</sub>, sd Ga02, small gradient emphasis, age, and size) were determined as ten important variables. With the RFC algorithm, cases resistant to CRT were estimated with an accuracy rate of 91.3% (88.9% sensitivity and 92.8% specificity, AUC: 0.83)<sup>[75]</sup>. According to this study in predicting the response to CRT, when the radiomic and clinical parameters are evaluated together, predictions with high accuracy rates can be obtained. If these resistant cases can be predicted, treatment strategies can be changed, and oncological outcomes can be improved.

In another study conducted with 55 cases diagnosed with locally advanced rectal cancer, radiomics obtained from MRI images taken before, during, and after CRT were evaluated by the RFC algorithm for treatment response prediction. Images of 28 cases from 55 cases were used in the training, and images of 27 cases were used to evaluate the performance of the algorithm. pCR was obtained in 16 cases from all cases, and good results were obtained with the RFC algorithm in predicting pCR with AI (AUC: 0.86, 95% CI: 0.70-0.94). In the prediction of unresponsive cases, AUC was 0.83 (95% CI: 0.71-0.92) with the RFC algorithm<sup>[76]</sup>.

In the study conducted by Bibault *et al*<sup>[77]</sup> with 95 cases diagnosed with T2-4N0-1 rectal cancer, radiomics (1683 radiomic features per case) obtained from CT images before CRT were evaluated together with clinical and treatment data, and the response prediction was made with AI. While radiomics were used with deep neural network and SVM, prediction models were created using only TNM staging in linear regression. pCR was obtained in a total of 23 cases. In prediction with deep neural network, SVM, and LR algorithms, the accuracy rates were 80.0%, 71.5%, and 69.5%, respectively<sup>[77]</sup>. In another study, artificial neural network, Naïve Bayes Classifier, KNN, SVM, and multiple LR models were evaluated in the response prediction of 270 locally advanced rectal cancer patients who underwent CRT. The most important factors affecting pCR were post CRT CEA level, the time between CRT and surgery, ChT regimen, clinical nodal status, and nodal stage. The accuracy rates for artificial neural network, KNN, SVM, Naïve Bayes Classifier, and multiple LR were 88%, 80%, 71%, 80%, and 77%, respectively<sup>[78]</sup>. Studies evaluating the CRT response with AI in rectal cancer are summarized in Table 2.

Shen *et al*<sup>[79]</sup> predicted response to CRT in 169 rectal cancer cases using positron emission tomography (PET)-CT radiomics. A total of 68 features were excluded from the metabolic active tumor site. Estimation was made with the RF algorithm, and the ROC algorithm was used to evaluate the performance. After CRT, pCR was obtained in 22 (13%) cases, and 42 radiomics features were included in the algorithm. Accordingly, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 81.8%, 97.3%, 81.8%, 97.3%, and 95.3%, respectively<sup>[79]</sup>.

While the correct classification of cases in which pCR is provided helps to identify less invasive therapeutic strategies such as mucosectomy or wait-and-watch, early prediction of cases that do not respond to CRT will also allow these cases to be directed to more effective treatments.



**Table 2 Studies of chemoradiotherapy response prediction with artificial intelligence**

Ref.	Number of patients	Parameters evaluated	Imaging method	Technique used	Results
Shi <i>et al</i> <sup>[71]</sup> , 2019	51 (90% cases for training and the remaining 10% for testing)	Tumor volume, mean ADC, radiomic	MRI (Pre-CRT and mid-CRT) (T2-DWI, DCE)	CNN	(1) pCR response prediction: (a) Pre-CRT with MR AUC: 0.80; (b) Mid-CRT with MR AUC: 0.82; and (c) Pre- and mid-CRT MR together AUC: 0.86; and (2) Good response to CRT: predicting yes/no: (a) Pre-CRT with MR AUC: 0.91; (b) Mid-CRT with MR AUC: 0.92; and (c) Pre- and mid-CRT MR together AUC: 0.93.
Fu <i>et al</i> <sup>[73]</sup> , 2020	43	Radiomic	MRI (Pre-CRT, DWI)	Handcrafted traditional computer-aided diagnostic method <i>vs</i> deep learning	Deep learning model with handcrafted model CRT response prediction AUC values: 0.64 <i>vs</i> 0.73 ( $P < 0.05$ )
Shayesteh <i>et al</i> <sup>[74]</sup> , 2019	98 (53 training and 45 validation set)	Radiomic	MRI (1 wk before CRT) (3 Tesla, T2W-weighted)	Machine learning (SVM, BN, NN, KNN)	AUC for the BN algorithm: 74%, accuracy: 79%; When four algorithms were used together, AUC: 97.8% and accuracy rate 92.8%.
Yang <i>et al</i> <sup>[75]</sup> , 2019	89 (66 training and 23 testing)	Radiomic and clinical features	MRI (Pre-CRT) (3 Tesla, T2W, 3 mm section thickness)	RFC	Predicting the accuracy of tumor resistance with RFC 91.3%, AUC: 0.83.
Ferrari <i>et al</i> <sup>[76]</sup> , 2019	55 (28 training, 27 validation)	Radiomic	MR (Pre, Mid, Post RT) (3 Tesla, T2W, 2 mm section thickness)	RFC	(1) Prediction of cases with pCR by RFC; AUC: 0.86; and (2) Prediction of unresponsive cases with RFC; AUC 0.83.
Bibault <i>et al</i> <sup>[77]</sup> , 2018	95	Radiomic, clinical variables	CT	DNN, SVM, LR	CRT response prediction accuracy rates; DNN: 80%; SVM: 71.5% LR: 69.5%.
Huang <i>et al</i> <sup>[78]</sup> , 2020	270 (236 training, 34 validation)	Clinical variables	-	ANN, KNN, SVM, NBC, MLR	pCR prediction accuracy rates and AUC values; ANN: 88%, 0.84 KNN: 80%, 0.74 SVM: 71%, 0.76 NBC: 80%, 0.63 MLR: 83%, 0.77.

ADC: Apparent diffusion coefficient; ANN: Artificial neural network; AUC: Area under the curve; BN: Bayesian network; CNN: Convolutional neural network; CRT: Chemoradiotherapy; CT: Computed tomography; DCE: Dynamic contrast-enhanced; DNN: Deep neural network; DWI: Diffusion-weighted imaging; KNN: K-nearest neighbors; LR: Linear regression; MLR: Multiple logistic regression; MRI: Magnetic resonance imaging; NBC: Naïve bayes classifier; NN: Neural network; pCR: Pathological complete response; RFC: Random forest classifier; SVM: Support vector machine.

### Prediction of KRAS mutation in rectal cancer

Kirsten rat sarcoma (KRAS) mutations, which occur in approximately 30%–40% of colorectal cancer, have been indicated as a highly specific negative biomarker for the antibody-targeted therapies to the epidermal growth factor receptor<sup>[80]</sup>. Metastatic colorectal cancers with KRAS mutations are resistant to anti-epidermal growth factor receptor targeted therapy. Therefore, the KRAS mutation test has been recommended by the National Comprehensive Cancer Network guidelines to guide targeted therapy for cases diagnosed with metastatic colorectal cancer<sup>[81]</sup>.

Determination of the KRAS mutation is usually made by pathological examination of the tumor tissue. However, intratumor heterogeneity or heterogeneity of KRAS mutation that can occur between different tumor regions limits histological approaches<sup>[82]</sup>. Moreover, the inability to determine mutation status due to poor DNA quality of biopsy samples, difficult to access tissue samples from metastatic colorectal cancers, repeated tumor sampling, and relatively high costs also limit the feasibility of molecular tests to monitor targeted therapy<sup>[83]</sup>. Therefore, a relatively simple and noninvasive method for KRAS mutations can be helpful for personalized treatment strategies.

In a study by Cui *et al*<sup>[84]</sup>, 304 cases with rectal cancer diagnosis from center I (training dataset,  $n = 231$ ; internal validation dataset,  $n = 91$ ) and 86 cases from center II were included as an external validation dataset. It aimed to predict KRAS mutation from T2-weighted image-based radiomics. Subsequently, three classification methods, *i.e.* LR, decision tree, and SVM algorithm, were applied to develop the radiomics signature for KRAS prediction in the training dataset. The predictive performance was evaluated by ROC analysis. A total of seven radiomics properties were accepted as important variables for KRAS prediction, and the best predictor was determined as the SVM. The AUC was found to be 0.722 (95%CI: 0.654–0.790)<sup>[84]</sup>.



## AI IN FOLLOW-UP IN RECTAL CANCER

### Treatment toxicity

Effective toxicity estimation and evaluation schemes are required to limit RT-related side effects. High-tech devices and planning systems provide submillimetric precision. However, while giving the desired dose to the target volume, the OARs in its immediate neighborhood may be affected, leading to RT-induced toxicity. Acute toxicity occurs during treatment or within 3 mo of completion of treatment and usually, full recovery takes weeks to months. Late side effects such as fibrosis or RT-induced oncogenesis are generally irreversible and considered progressive over time. When planning RT, its potential benefits should be weighed against the possibility of damaging healthy organs and tissues to maximize the curative response while minimizing the possibility of normal tissue complications. On the other hand, the target volume should not be compromised to preserve OARs. In addition to complex dosimetric data, AI provides the clinician with the ability to predict complications by integrating higher-level information such as detailed clinical and comorbidity data into a more comprehensive and quantitative model<sup>[85]</sup>.

Dosimetric parameters include dose volume histogram parameters and threshold doses such as maximum point doses. Nondosimetric factors include other variables such as age, gender, and histopathology. Normal tissue complication probability and tumor control probability prediction models focused on using dosimetric parameters alone<sup>[86,87]</sup>. Also, the necessity of using nondosimetric parameters has been emphasized in the Quantitative Analysis of Normal Tissue Effects in the Clinic<sup>[88]</sup>. Data-driven approaches, on the other hand, aim to determine the model that best fits the input data (called properties or independent variables) and output data (called the response or dependent variable). Toxicity predictors can be examined roughly in three parts as dosimetric, clinical, and image-based.

In rectum cancer RT, toxicity can be predicted in advance with AI-based models, and appropriate dose-area restrictions, additional treatment planning (simultaneous CT, *etc.*), and prophylactic medical support treatments can be reviewed. There are AI studies that predicted rectal toxicity in prostate and cervical cancer radiotherapy, but there are no studies predicting toxicity with AI in rectal cancer radiotherapy<sup>[89-91]</sup>. Oyaga-Iriarte *et al*<sup>[92]</sup> conducted a study to predict irinotecan toxicity in metastatic colorectal cancer with ML models, and leukopenia was estimated with 76% accuracy, neutropenia 75%, and diarrhea 91%.

The development of prediction tools with a wide variety of variables and models limits the comparability and standard use of existing toxicity studies. Toxicity estimation algorithms can be standardized by sharing data between centers and creating big data. The application of such models is valuable in many different ways for both patients and clinicians.

### Survival

In oncological treatments, forecasting is very important in the treatment decision-making process because accurate survival prediction is critical in making palliative/curative treatment decisions. Also, the prediction of remaining life expectancy can be an incentive for patients to live a fuller or more fulfilling life. Survival statistics assist oncologists in making treatment decisions, but these are data from large and heterogeneous groups and are not well suited to predict what will happen to a specific patient. AI algorithms for the prediction of RT and ChT response have received considerable attention recently. In cases diagnosed with cancer, predicting survival is important in improving treatment and providing information to patients and clinicians. Considering the data set of rectal cancer patients with specific demographic, tumor, and treatment information, it is an important issue whether the patient's survival or recurrence can be predicted by any parameter. Today, many hospitals store data in digital media. By evaluating these large data sets with AI techniques, it may be possible to predict treatment outcomes of patients, plan personalized medicine, improve corporate performance, and regulate health insurance.

In a study conducted by Zhao *et al*<sup>[93]</sup>, survival prediction was made with an ML method in cases with metastatic rectal cancer, and 4098 cases were used in training and 3107 cases were used as test data. A survival prediction nomogram was created. While creating the prediction model, lasso (least absolute shrinkage and selection operator), an ML technique that can lead to superior performance compared to traditional multivariate regression, was used. The model was designed to predict 3-year overall survival. The ML model formed the basis of the nomogram. Important

variables used in the nomogram were age, Charlson-Deyo score, tumor grade, pre-op CEA, liver metastasis, bone metastasis, brain metastasis, lung metastasis, peritoneal metastasis, presence of primary surgery, surgery for the metastatic area, the number of metastatic lymph nodes, and the presence of ChT. The c-index was used to evaluate the performance of the ML technique. Internally validated c-index values were 0.816 (95%CI: 0.813-0.818), 0.789 (95%CI: 0.786-0.790), and 0.778 (95%CI: 0.775-0.780) for 1-, 2-, and 3-year survival, respectively. External validated c-index was 0.811, 0.779, and 0.778 for 1-, 2-, and 3-year survival, respectively<sup>[93]</sup>. There was great variation in overall survival times in cases diagnosed with metastatic rectal cancer. Accurate models with ML methods can assist patients and clinicians in setting expectations and clinical decisions in this challenging patient group.

Pham *et al*<sup>[94]</sup> used AI to discover DNp73 expression in terms of 5-year overall survival and prognosis in their study with 143 cases diagnosed with rectal cancer. Ten different CNN algorithms were used, and each immunochemical image was resized. For the algorithm, 90% of these images were used in training and 10% as test data, and the accuracy rates of ten algorithms varied between 90%-96%<sup>[94]</sup>.

Li *et al*<sup>[95]</sup> conducted a study with 84 patients diagnosed with locally advanced rectal cancer and predicted survival with radiomics obtained from PET, CT, and PET-CT images with CNN. They compared the CNN method evaluated in the study with the Cox proportional-hazards model and random survival forests method. C-index was used in the performance evaluation of the methods. C-indexes of models created with radiomics obtained from PET, CT, and PET-CT images for Cox proportional-hazards, random survival forests, and CNN were 0.53-0.58-0.60 *vs* 0.58-0.61-0.58 and 0.62-0.60-0.64 respectively, and the best performance was obtained when CNN and PET-CT were used together<sup>[95]</sup>.

In the study conducted by Oliveira *et al*<sup>[96]</sup> to predict the 1-, 2-, 3-, 4-, and 5-year survival of cases with rectal and colon cancer, they evaluated 2221 cases in the test for colon cancer, 20061 cases in training, 551 cases in the test for rectal cancer, and 4962 cases in training. Important variables for colon cancer were determined as age, CEA, CS site-specific factor 2, TNM stage, localization of the primary tumor, and regional lymph nodes. For rectal cancer, important variables were age, tumor extension, tumor size, TNM staging, surgery of the primary tumor, and gender. ML performance was evaluated by the accuracy rate and AUC. Accuracy rates and AUC for predicting survival for colon cancer for 1-, 2-, 3-, 4-, and 5-years were 95.6% (AUC: 0.980), 96.2% (0.984), 96.4% (0.988), 96.6% (0.988), and 96.4% (0.985), respectively, and their mean was 96.2% (0.984). Accuracy rates and AUC for predicting 1-, 2-, 3-, 4-, and 5-year survival for rectal cancer were 94.4% (AUC: 0.957), 94.4% (0.960), 94.0% (0.961), 93.8% (0.963), and 94.5% (0.971), respectively, with a mean of 94.1% (0.960)<sup>[96]</sup>.

Accurate survival prediction in cancer patients remains a problem due to the increasing heterogeneity and complexity of cancer, treatment options, and different patient characteristics (age, Karnofsky Performance Status Scale, comorbid diseases, *etc.*). If reliable predictions can be achieved with AI, it can help with personalized care and medicine. Studies on AI-based survival prediction are increasing day by day in the literature, and there is still no standard algorithm.

## CONCLUSION

In recent years, the increasing interest in AI in all fields of science has led to the development of innovative tools in oncology. The development of prediction tools with a wide variety of variables and models limits the comparison of existing studies and the use of standards.

In order to improve long-term prognosis, it is important to predict the overall survival of patients with a diagnosis of rectal cancer and progression of the disease receiving multimodal treatment. With the evaluation of clinical, radiological, genetic, dosimetric, and epidemiological factors using AI, it is possible to perform accurate predictions to achieve personalized treatment. Given high treatment costs, potential serious toxicity, harms of early progression, and low survival in cases of ineffective treatment, predictive systems with AI are promising. Multicenter studies with large data sets can provide algorithms with higher accuracy rates.

AI technology develops day by day in the realization of human behaviors in oncology and offers more efficient, faster, and lower cost solutions. Both AI and robotic potential are enormous in the follow-up and treatment of rectal cancer. AI and robotics are on the way to becoming a part of our health ecosystem.

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