

# Artificial Intelligence in *Gastroenterology*

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# Artificial Intelligence in Gastroenterology

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**ABOUT COVER**

Associate Editor of *Artificial Intelligence in Gastroenterology*, Dr. Xu Zhu is Chief Physician, Professor, and Doctoral Supervisor leading the Department of Interventional Therapy at Peking University Cancer Hospital (China). His over 20 years of research involve image-guided minimally invasive interventional and targeted therapies in tumoral diseases, investigating effects of transcatheter arterial chemoembolization, hepatic arterial infusion chemotherapy, and ablation therapy. He is currently Vice Chairman of the Oncology Interventional Professional Committee of the Chinese Anti-cancer Association, having won the association’s second prize Award for Science and Technology Progress in 2019; he is also Vice Chairman of the Liver Tumor Branch, China International Exchange and Promotive Association for Medical and Health Care, Vice Chairman of the Interventional Radiology Professional Committee, Chinese Society of Clinical Oncology, and Chairman of the Cryoablation and Targeted Therapy of Tumor Professional Committee, National Strategic Alliance of Industrial and Technology Innovation for Minimally Invasive Tumor Therapy of China. (L-Editor: Filipodia)

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The primary aim of *Artificial Intelligence in Gastroenterology* (AIG, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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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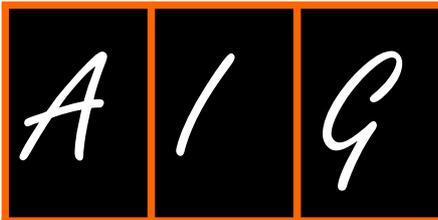
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## Diagnostic advances of artificial intelligence and radiomics in gastroenterology

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### Abstract

Traditional medical imaging, including ultrasound, computed tomography, magnetic resonance imaging, or positron emission tomography, remains widely used diagnostic modalities for gastrointestinal diseases at present. These modalities are used to assess changes in morphology, attenuation, signal intensity, and enhancement characteristics. Gastrointestinal tumors, especially malignant tumors, are commonly seen in clinical practice with an increasing number of deaths each year. Because the imaging manifestations of different diseases usually overlap, accurate early diagnosis of tumor lesions, noninvasive and effective evaluation of tumor staging, and prediction of prognosis remain challenging. Fortunately, traditional medical images contain a great deal of important information that cannot be recognized by human eyes but can be extracted by artificial intelligence (AI) technology, which can quantitatively assess the heterogeneity of lesions and provide valuable information, including therapeutic effects and patient prognosis. With the development of computer technology, the combination of medical imaging and AI technology is considered to represent a promising field in medical image analysis. This new emerging field is called "radiomics", which makes big data mining and extraction from medical imagery possible and can help clinicians make effective decisions and develop personalized treatment plans. Recently, AI and radiomics have been gradually applied to lesion detection, qualitative and quantitative diagnosis, histopathological grading and staging of tumors, therapeutic efficacy assessment, and prognosis evaluation. In this minireview, we briefly introduce the basic principles and technology of radiomics. Then, we review the research and application of AI and radiomics in gastrointestinal diseases, especially diagnostic advancements of radiomics in the differential diagnosis, treatment option, assessment of therapeutic efficacy, and prognosis evaluation of esophageal, gastric, hepatic, pancreatic, and colorectal diseases.

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**Core Tip:** This minireview summarizes the research and application of artificial intelligence (AI) technology, radiomics, and texture analysis in gastrointestinal diseases in detail and focuses on the diagnostic advances of AI and radiomics in lesion detection, differential diagnosis, decision of treatment plans, assessment of therapeutic efficacy and tumor response to treatment, and prognosis prediction of gastrointestinal diseases. This technology can provide more valuable information to allow clinicians and radiologists to understand and perform AI and radiomics in their clinical practice.

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## INTRODUCTION

In the 1980s, with the application of artificial neural network and computer-aided diagnosis and detection system software, artificial intelligence (AI) has gradually been integrated into the daily workflow of various fields<sup>[1]</sup>. Since the beginning of the 21<sup>st</sup> century, advances in computer technology have led to the rapid development of AI in medical applications. With the rapid development of AI, the combination of medical imaging and AI is considered a promising field in medicine and is primarily used for image data mining, extraction, searching, and applications, as well as image recognition and deep learning<sup>[2]</sup>. Currently, AI technology has been widely used in lung nodule, lung cancer, and breast cancer screening as well as prostate cancer, colorectal cancer, and head and neck cancer imaging<sup>[3-8]</sup>. In terms of gastroenterology, the main applications of AI are radiomics and texture analysis. The concept of radiomics was formally proposed in 2012 and refers to the process of converting digital medical images into mineable high-dimensional data by high-throughput extraction and analysis of innumerable quantitative imaging features from medical images obtained with imaging modalities, including ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET)<sup>[9,10]</sup>. Radiomics is a technology that combines multiple images and interdisciplinary techniques and primarily includes the following five imaging steps: (1) Image acquisition: Acquisition of high-quality, standardized medical images for diagnosis and evaluation; (2) Image segmentation: Manual, automatic, or semiautomatic segmentation and reconstruction of the image; (3) Feature extraction and quantification: This is the core process of radiomics to extract region of interest (ROI) texture feature parameters, including shape or size, first-order histogram or spherical statistical features, second-order histogram or texture, and higher-order statistics features and other special image features; (4) Feature selection: Screening of features based on repeatability, correlation with other features, and relationship with staging, prognosis, and gene expression; and (5) Model establishment: Incorporation of the selected radiomics features into a suitable prediction model<sup>[1,2,11]</sup>. By extracting high-throughput quantitative features, radiomics based on quantitative imaging can reflect not only certain components within the tumor but also intratumoral heterogeneity by providing supplementary information, thus helping to assess disease characteristics in detail<sup>[12]</sup>. The application of radiomics in gastroenterology is mainly focused on lesion recognition, clinical staging, and prognosis analysis. The purpose of this minireview is to provide a descriptive overview of diagnostic advances of AI and radiomics in gastroenterology.

## DIAGNOSTIC ADVANCES OF AI AND RADIOMICS IN ESOPHAGEAL CANCER

Esophageal cancer (EC) is the eighth most frequent malignant disease and the sixth most prevalent cause of disease-associated deaths worldwide<sup>[13]</sup>. The selection of a therapeutic approach and prognosis of EC are closely associated with preoperative tumor stage<sup>[14]</sup>. Therefore, accurate preoperative staging is of great importance for selecting an appropriate treatment plan and predicting prognosis. Traditionally, CT is a widely used modality for diagnosis and preoperative staging of EC; however, due to limited contrast resolution, CT cannot accurately identify early stage EC (T1-2) and is mainly used in the evaluation of regional spread and distance metastasis<sup>[15-17]</sup>. Recently, some studies have reported that radiomics and text analysis can improve the accuracy of preoperative tumor staging classification. In a study enrolling 73 patients with esophageal squamous cell carcinoma (ESCC), CT texture parameters based on unenhanced and contrast-enhanced CT images, kurtosis, entropy, and skew showed great potential in differentiating T stages (T1-2 *vs* T3-4), lymph node metastasis (N- *vs* N+), and overall stages of ESCC<sup>[18]</sup>. In a study of 154 patients with ESCC, the radiomics signature extracted from CT images was significantly associated with ESCC staging, yielding a better performance for discrimination of early stage (T1-2) and advanced stage (T3-4) ESCC compared to tumor volume, indicating the potential of radiomics in staging ESCC preoperatively<sup>[19]</sup>. F-18-fluorodeoxyglucose (<sup>18</sup>F-FDG) PET image-derived characteristics, including image textural features, standard unit value (SUV), and shape features, also allowed for better stratification of American Joint Committee on Cancer and tumor-node-metastasis (TNM) than F-18-fluorothymidine (<sup>18</sup>F-FLT) PET in ESCC patients<sup>[20]</sup>. Radiomics based on MR images (T<sub>2</sub>-TSE BLADE and contrast-enhanced Star VIBE) also more accurately distinguished metastatic lymph nodes compared with nonmetastatic lymph nodes, yielding an area under the receiver operating characteristic curve (AUC) of 0.821 (95% CI: 0.7042 to 0.9376) and 0.762 (95% CI: 0.7127 to 0.812), respectively<sup>[21]</sup>.

In addition to tumor staging, radiomics and textural analysis have also shown significant importance for efficacy and prognosis evaluation. Tixier *et al*<sup>[22]</sup> extracted gray level cooccurrence matrices (GLCM), gray-level size zone matrix, entropy, long-run matrix, and other texture features from PET images and found that these texture features were more effective (AUC: 0.82-0.89) than SUVmax and SUVmean (AUC: 0.59-0.7) in predicting the clinical response of chemoradiotherapy for patients with EC. In a study on prediction of response after chemoradiation for EC, an integrated model combining CT radiomic features and dosimetric parameters for 94 patients with EC permitted a prediction accuracy of 0.708 and AUC of 0.689, while using radiomic features alone permitted the best prediction accuracy of 0.625 and AUC of 0.412<sup>[23]</sup>. In total, 138 radiomics features extracted from MR T<sub>2</sub>WI in 68 patients with ESCC exhibited potential in distinguishing complete response (CR) from stable disease (SD), partial response (PR) from non-response (SD), and response (CR and PR) from SD. Moreover, using neural network and support vector machine prediction models, features extracted through spectral attenuated inversion-recovery T<sub>2</sub>WI exhibited better performance than those extracted from T<sub>2</sub>WI in predicting the response to chemoradiotherapy in EC<sup>[24]</sup>.

Radiomics also shows potential in the evaluation of disease prognosis. In a study of 239 patients with EC, a random forest (RF) model based on pretreatment CT radiomics features was used to predict 3-year overall survival (OS) following chemoradiotherapy. Compared to the model using standard clinical variables that yielded an AUC of 0.63 (95% CI: 0.54-0.71), the radiomics-based RF model yielded an AUC of 0.69 (95% CI: 0.61-0.77), demonstrating better prognostic power of the radiomics model compared with traditional clinical variables<sup>[25]</sup>. Yip *et al*<sup>[26]</sup> also analyzed the radiomics features extracted from enhanced CT images of 36 patients with T2 or above EC pre- and posttreatment of chemoradiotherapy and found that a posttreatment medium entropy of less than 7.356, a coarse of less than 7.116, and a median uniformity greater than 0.007 were associated with improved survival time. Moreover, the combination of pretreatment texture parameters (entropy and uniformity) with maximal wall thickness assessment in survival models performed better than morphologic tumor response alone with AUCs of 0.767 *vs* 0.487 and 0.802 *vs* 0.487<sup>[26]</sup>. In a study on the prediction of therapy response to neoadjuvant chemoradiotherapy in 97 EC patients, Beukinga *et al*<sup>[27]</sup> constructed a response prediction model based on pretreatment clinical parameters and <sup>18</sup>F-FDG PET/CT-derived textural features. Compared with the current most accurate prediction model with SUVmax, the constructed model had higher AUC (0.78 *vs* 0.58) and discrimination slope (0.17 *vs* 0.01). In another study of

31 patients with primary EC, a significant decrease in entropy and CT tumor heterogeneity and increase in uniformity were observed following neoadjuvant chemotherapy, indicating that CT texture analysis has the potential to assess prognosis and survival of patients with primary EC<sup>[28]</sup>. In another study of 61 ESCC patients who received radical radiation therapy, the survival rate was significantly correlated with the change of coarseness ( $P = 0.0027$ ) and strength ( $P = 0.0001$ ), which indicated that CT features (such as coarseness and strength) could be selected as outstanding imaging biomarkers for prediction of RT prognosis of ESC<sup>[29]</sup>.

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## DIAGNOSTIC ADVANCES OF AI AND RADIOMICS IN GASTRIC DISEASE

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Radiomics and texture analysis potentially aid radiologists in differential diagnosis of gastric tumors. In a study on the utility of texture features of CT images in differential diagnosis of gastric tumors, textural features derived from the arterial phase exhibited improved accuracy of differentiation between gastric adenocarcinoma (GC) and gastric lymphoma as well as gastric stromal tumor (GIST) and lymphoma; however, the textural features derived from the venous phase adequately distinguished between GC and GIST<sup>[30]</sup>. Similarly, in a study on the discrimination of Borrmann type IV gastric cancer and primary lymphoma, objective feature models including CT objective features (stomach wall thickness, infiltration degree, *etc.*) and clinical features (age, gender, *etc.*), texture feature models, and a combination of these two models were established to distinguish these two types of gastric malignancies. A sensitivity of 86.67% and specificity of 82.5% were found in the texture feature model, and a specificity of 100% was noted in the combination model with the highest AUC value (0.903), indicating the ability of radiomics in distinguishing gastric tumors from gastric primary lymphoma<sup>[31]</sup>.

In addition, radiomics and texture analysis are also helpful for detection of local and peritoneal metastases. In a study of 554 patients with advanced gastric cancer (AGC) who were initially diagnosed as having no peritoneal metastasis by CT, a nomogram of radiomics signatures was developed that reflected primary tumor phenotypes and peritoneum region metastasis and demonstrated the best diagnostic accuracy for occult peritoneal metastasis<sup>[32]</sup>. In another study, texture analysis of CT imaging was also verified as a useful predictor of occult peritoneal carcinomatosis in patients with AGC<sup>[33]</sup>.

Similar to its application in esophageal cancer, radiomics has also been reported to be helpful for tumor staging in many studies. CT texture parameters in the arterial phase and portal vein phase positively correlated with T stage, N stage, and overall stage ( $P < 0.05$ ) of GC and identified lymph node metastasis of GC<sup>[34]</sup>. All the entropy-related parameters derived from whole-volume ADC texture analysis exhibited a significant correlation with T, N, and overall stages. Furthermore, significant differences in these parameters were found between GCs with and without perineural invasion<sup>[35]</sup>.

Regarding preoperative prognosis evaluation, texture analysis has also demonstrated good application prospects. Giganti *et al*<sup>[36]</sup> analyzed the preoperative textural features based on multiple detector CT images of 56 patients with pathologically confirmed GC and found that texture parameters, namely, energy, entropy, maximum Hounsfield unit value, skewness, root mean square, and mean absolute deviation (filter 2), negatively correlated with the prognosis of GC. Moreover, these parameters could be used for risk stratification in GC and aid in assessment of aggressiveness of GC<sup>[36]</sup>. A radiomics signature based on CT imaging in the portal venous phase was used to predict survival of GC, add prognostic information to the TNM staging system, and predict patient benefit from chemotherapy<sup>[37]</sup>. Moreover, in another study of 26 patients with human epidermal growth factor receptor 2-positive AGC who received trastuzumab-based combination chemotherapy, heterogeneous texture features on contrast-enhanced CT images were associated with better survival, demonstrating the potential of an imaging biomarker to provide prognostic information on patient selection<sup>[38]</sup>.

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## DIAGNOSTIC ADVANCES OF AI AND RADIOMICS IN HEPATIC DISEASE

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Studies on radiomics in hepatic diseases mainly focus on the staging of hepatic fibrosis, differential diagnosis of tumor and nontumor lesions, treatment selection, and prognosis evaluation. Echegaray *et al*<sup>[39]</sup> performed enhanced CT texture analysis in 29

patients with hepatocellular carcinoma (HCC) and found that texture features of images obtained in the portal venous phase exhibited the lowest misdiagnosis rate (13.57%) in the differential diagnosis of focal liver lesions, demonstrating the superiority of radiomics compared with traditional imaging in distinguishing hepatic disease characteristics<sup>[39]</sup>. In a study of 164 hepatic lesions, Huang *et al.*<sup>[40]</sup> extracted the autocovariance texture features of lesions and proposed a support vector machine classifier system to identify benign lesions from malignant lesions. The system had an accuracy of 81.7% in identifying malignant hepatic lesions with a sensitivity of 75.0% and specificity of 88.1% and was useful in reducing the needs for iodinated contrast agent injection in CT examination<sup>[40]</sup>. Oyama *et al.*<sup>[41]</sup> assessed the accuracy for classification of HCC, metastatic tumors (MT), and hepatic hemangioma (HH) by characterization of non-contrast-enhanced fat-suppressed three-dimensional (3D) T<sub>1</sub>-weighted images by using texture analysis and topological data analysis using persistent homology. In the classification of HCC and MT, HCC and HH, and HH and MT, accuracies of 92%, 90%, and 73% were obtained by texture analysis, showing the potential application for computer-aided diagnosis with MR images<sup>[41]</sup>. In a study on the differential diagnosis of neoplastic or bland portal vein thrombosis in 109 patients, the mean value of positive pixels (without filtration), entropy (with fine filtration), and mean thrombus density values were helpful in the identification of neoplastic and bland thrombi with AUCs of 0.97, 0.93, and 0.91, yielding optimal cutoff values of 56.9, 4.50, and 54.0 HU, respectively ( $P < 0.001$ ); these findings indicated that CT texture analysis and CT attenuation values based on images obtained in the portal venous phase could be helpful in differentiating neoplastic thrombi from benign thrombi<sup>[42]</sup>.

In the evaluation of hepatic fibrosis and other nontumor lesions, radiomics also has shown good prospects. In a study on staging of hepatic fibrosis in 289 patients, CT texture parameters (mean gray-level intensity, kurtosis, and skewness) were helpful in the detection and staging of fibrosis<sup>[43]</sup>. In total, 41 texture features extracted from enhanced CT images of 83 patients with pathologically proven hepatic fibrosis offered a noninvasive assessment of liver fibrosis<sup>[44]</sup>. In a study on the texture features of non-contrast-enhanced CT images of 88 patients with pathologically confirmed nonalcoholic steatohepatitis (NASH), the mean texture parameters without a filter and skewness with a 2-mm filter were selected for the NASH prediction model for patients without suspected fibrosis, yielding an AUC of 0.94 and accuracy of 94% in the predictive model for the validation dataset. These results reveal the ability of the model to predict NASH<sup>[45]</sup>.

In addition, imaging texture analysis also shows good prospect in the evaluation of prognosis, optimization of treatment plans, and prediction of tumor response to treatment. Texture analysis exhibited potential in the assessment of prognosis and selection of appropriate patients with intermediate-advanced HCC treated by transcatheter arterial chemoembolization (TACE) and sorafenib<sup>[46]</sup>. In another study on the prediction of therapeutic response of HCC to TACE, textures derived from pretreatment dynamic CT imaging were analyzed in 96 patients with 132 HCCs, and increased arterial enhancement ratios and GLCM moments, smaller tumor size, and reduced tumor homogeneity were significant predictors of complete response (CR) after TACE<sup>[47]</sup>. A radiomics scoring system based on <sup>18</sup>F-FDG PET was generated in a study of 47 patients undergoing transcatheter arterial radioembolization using Yttrium-90 for unresectable HCC, and statistically significant differences in progression-free survival (PFS) and overall survival (OS) between low-risk patients and high-risk patients were detected, indicating that pretreatment <sup>18</sup>F-FDG PET-derived radiomics features served as an independent negative predictor of patient prognosis<sup>[48]</sup>. Similarly, preoperative skewness derived from images obtained in the portal venous phase was independently associated with OS in patients with resectable HCC and might be useful in the selection of patients for resection<sup>[49]</sup>. In a study focused on the prediction of OS and time to progression of 92 patients with advanced HCC treated with sorafenib, pretreatment CT texture feature entropy derived from images obtained in the portal venous phase was also identified as an independent predictor of OS in patients<sup>[50]</sup>.

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## DIAGNOSTIC ADVANCES OF AI AND RADIOMICS IN PANCREATIC DISEASES

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At present, the applications of radiomics analysis in pancreatic diseases mainly focus on the diagnosis and differential diagnosis of pancreatic tumors, biological stratification and grading of tumors, prognosis prediction, therapeutic assessment, and

efficacy evaluation. Radiomics analysis also aids in preoperative diagnostic accuracy and proper management decisions. In a study that enrolled 260 surgically resected pancreatic cystic neoplasms, the accuracy rate for serous cystic neoplasms (SCNs) before surgery was only 30.4% (102/260), indicating that greater than two-thirds of patients with SCN underwent unnecessary surgery. However, using a diagnostic model established based on dual-phase pancreatic CT imaging features, the accuracy rate of diagnosis significantly improved with an AUC of 0.767, sensitivity of 68.6%, and specificity of 70.9%<sup>[51]</sup>. In clinical practice, imaging findings of pancreatic neuroendocrine carcinoma (PNEC) and pancreatic ductal adenocarcinoma (PDAC) usually overlap, and the misdiagnosis of these two entities is common. In addition to traditional CT imaging features of tumor margin, parenchymal atrophy, and contrast ratio in the arterial and portal phases, Guo *et al.*<sup>[52]</sup> confirmed that texture parameters of entropy and uniformity were also valuable for distinguishing PNEC from PDAC. CT features and texture analysis were also useful for the classification of pancreatic neuroendocrine tumors (PNETs). In a study enrolling 101 patients with PNETs, entropy was predictive of Grades (G) 2 and 3 tumors with an accuracy of 79.3% for classifying G1, G2, and G3 tumors<sup>[53]</sup>. D'Onofrio *et al.*<sup>[54]</sup> also reported that parameters of kurtosis and entropy extracted from 3D CT-texture imaging analysis could predict the grade of PNETs, distinguishing G1 from G3, G2 from G3, and G1 from G2 tumors.

Promising results of radiomics and texture analysis were reported in the field of therapeutic assessment and prognosis prediction of PDAC. Texture parameters from preoperative CT images of pancreas head cancer in patients who underwent curative resection significantly differed between patients with and without recurrence, and this method could be used as an independent imaging tool for predicting prognosis<sup>[55]</sup>. In another study on patients with unresectable PDAC treated with chemotherapy, pretreatment CT quantitative imaging biomarkers based on texture analysis were associated with PFS and OS, and the combination of pretreatment texture parameters and tumor size performed better in survival models than imaging biomarkers alone<sup>[56]</sup>. Cozzi *et al.*<sup>[57]</sup> also reported that a CT-based radiomics signature correlated with OS and local control of PDAC after stereotactic body radiation therapy and allowed for identification of low- and high-risk groups of patients.

## DIAGNOSTIC ADVANCES OF AI AND RADIOMICS IN COLORECTAL DISEASES

At present, research on colorectal tumors mainly focuses on the extraction of texture features, identification of neoplastic and nonneoplastic lesions, preoperative staging of colorectal cancer (CRC), and evaluation of lymphatic metastasis. In a study on the efficiency of texture features by CT colonography in the differential diagnosis of colon lesions, combining high-order CT images with CT volumetric texture features yielded a significantly increased AUC of 0.85 in distinguishing neoplastic colon tumors from nonneoplastic lesions compared with the exclusive use of the parameter of image intensity<sup>[58]</sup>. A CT-based radiomics signature of patients with CRC before surgery might be a useful method for preoperative CRC tumor staging given its ability in the discrimination of stage I-II from stage III-IV CRC, yielding an AUC of 0.792 with a sensitivity of 0.629 and specificity of 0.874<sup>[59]</sup>.

The application of radiomics also showed efficacy in therapeutic evaluation of rectal cancer (RC). In a study on the response to neoadjuvant chemoradiation therapy (NCRT) in 51 patients with local advanced RC, radiomics based on pretreatment and early follow-up MRI could provide quantitative information to differentiate pathologic CR (pCR) from non-pCR and good response (GR) from non-GR<sup>[60]</sup>. Texture parameters derived from T<sub>2</sub>WI of RC also exhibited potential to assess the tumoral response to NCRT<sup>[61]</sup>.

Radiomics and texture analysis are also valuable for treatment decisions. In a study that enrolled 95 patients with T2-4 N0-1 RC treated with NCRT, a deep neural network was proposed to predict the CR of tumor to treatment. The model predicted CR with an increased accuracy of 80% compared with the linear regression model (69.5%) and support vector machine model (71.58%) after NCRT, demonstrating the potential of radiomics in the selection of patients for NCRT rather than radical resection<sup>[62]</sup>. In another study of 326 pathologically proven CRC patients, a radiomics nomogram incorporating both the radiomics signature and clinicopathologic risk factors for individual preoperative prediction of lymph node metastasis in patients with CRC was developed and facilitated the preoperative individualized prediction of lymph node metastasis<sup>[63]</sup>.

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## CONCLUSION

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In conclusion, AI and radiomics have been applied in routine clinical practice, including lesion detection, differential diagnosis, therapeutic assessment, prognosis prediction and so on (Figure 1). The incorporation of AI into current clinical radiology workflow has shown potential to help radiologists improve accuracy of diagnosis, evaluate therapeutic effect, and predict prognosis (Tables 1-3). However, at present these applications in clinical practice remain in their infancy, and many details of workflow need to be improved. First, there is no uniform standard for image acquisition at present. Different types of scanners and imaging acquisition protocols vary across institutions, and the image quality and stability of features also need to be improved. Second, although a majority of models could be built for radiomics analysis, it is still difficult to decide the best one for different clinical issues. Third, till now, most studies were retrospectively designed and the reliability of these research conclusions still needs to be tested. In order to overcome these barriers, it is of great importance to establish a unified labeling database, develop automatic standardized ROI mapping software, and select multiple machine learning methods for optimization. Moreover, for more applications and development of AI and radiomics in gastroenterology, multicenter cooperation is also an inevitable trend to verify large sample data from various institutions. Given the continuous accumulation of data, standardization of work processes, and continuous improvement of computer technology, AI and radiomics will make a major breakthrough in the field of precision medicine for gastroenterology in the future.

**Table 1 Application of radiomics in qualitative diagnosis in gastroenterology**

Classification of disease	Imaging modality	Features evaluated and methods	Outcomes	Ref.
<b>Gastric disease</b>				
AC; GIST; lymphoma	CECT	RLM; GLCM; absolute gradient; autoregressive model; wavelet transformation	Texture-based lesion classification in arterial phase differentiated between AC and lymphoma, and GIST and lymphoma, with misclassification rates of 3.1% and 0%, respectively Texture-based lesion classification in venous phase differentiated between AC and GIST, and different grades of AC with misclassification rates of 10% and 4.4%, respectively	[30]
Borrmann type IV GC; PGL	CECT	A total of 485 3D features, divided into four groups: First order statistics, shape and size based features, texture features, and wavelet features	The subjective findings model, radiomics signature, and combined model showed a diagnostic accuracy of 81.43% (AUC, 0.806; sensitivity, 63.33%; specificity, 95.00%), 84.29% (AUC, 0.886; sensitivity, 86.67%; specificity, 82.50%), and 87.14% (AUC, 0.903; sensitivity, 70.00%; specificity, 100%), respectively, in the differentiation of Borrmann type IV GC from PGL	[31]
<b>Hepatic disease</b>				
Neoplastic and bland portal vein thrombus	CECT	Mean; entropy; SD of pixel intensity; kurtosis; skewness	In the discrimination of neoplastic from bland thrombus, the AUCs were 0.97 for mean value of positive pixels, 0.93 for entropy, 0.99 for the model combining mean value of positive pixels and entropy, 0.91 for thrombus density, and 0.61 for the radiologist's subjective evaluation	[42]
HCC; MT; HH	MRI	GLCM; GLRLM; GLSZM; NGTDM	Texture analysis in differential diagnosis: HCC and MT: accuracy 92%, sensitivity100%, specificity 84%, AUC 0.95 HCC and HH: accuracy 90%, sensitivity 96%, specificity 84%, AUC 0.95 MT and HH: accuracy 73%, sensitivity74%, specificity72%, AUC 0.75	[41]
<b>Pancreatic disease</b>				
PSCN	CECT	A total of 385 radiomics high-throughput features: Intensity; wavelet; NGTDM	The accuracy rate of SCNs before surgery was only 30.4% (31/102) while the diagnostic model established based on dual-phase pancreatic CT imaging features had an improved accuracy rate of diagnosis, showing an AUC of 0.767, sensitivity of 68.6%, and specificity of 70.9%	[51]
PNEC; PDAC	CECT	Filtration-histogram approach and Laplacian-of-Gaussian band-pass filters (sigma values of 0.5, 1.5, and 2.5) were used and texture parameters under different filters, including: Kurtosis, skewness, entropy, and uniformity	PNEC showed a lower entropy and a higher uniformity compared to PDAC in the portal phase with an acceptable AUC of 0.71-0.72	[52]
<b>Colorectal disease</b>				
Neoplastic and non-neoplastic lesions	CECT	78 features for each lesion in total	Combining high-order CT images with CT volumetric texture features allowed a significantly higher AUC of 0.85 in distinguishing neoplastic colon tumors from non-neoplastic ones than only using the image intensity (AUC of 0.74)	[58]

CECT: Contrast-enhanced computed tomography; AC: Adenocarcinoma; GIST: Gastrointestinal stromal tumors; PGL: Primary gastric lymphoma; MT: Metastatic tumor; HH: Hepatic hemangioma; AUC: Area under the curve; GLCM: Grey level cooccurrence matrices; GLSZM: Gray-level size zone matrix; PSCN: Pancreas serous cystic neoplasms; SCN: Serous cystic neoplasm; PNEC: Pancreatic neuroendocrine carcinoma; PDAC: Pancreatic ductal adenocarcinoma.

Table 2 Application of radiomics in disease staging in gastroenterology

Classification of disease	Imaging modality	Features evaluated and methods	Outcomes	Ref.
<b>Esophageal disease</b>				
ESCC	Unenhanced CT and CECT	Six parameters based on HU values: Mean; 10 <sup>th</sup> percentiles; 90 <sup>th</sup> percentiles; kurtosis; entropy; skew	Kurtosis and entropy based on unenhanced CT were an independent predictor of T stages, lymph node metastasis (N- vs N+), and overall stages. Skew and kurtosis based on unenhanced CT images showed significant differences among N stages as well as 90th percentile based on contrast-enhanced CT images; entropy and 90th percentile based on CECT images showed significant correlations with N stage and overall stage	[18]
ESCC	CECT	A total of 9790 radiomics features were extracted including the following four categories: First-order histogram statistics, size and shape-based features, texture features, and wavelet features	The radiomics signature significantly associated with ESCC staging and yielded a better performance for discrimination of early and advanced stage ESCC compared to tumor volume	[19]
<b>Gastric disease</b>				
GC	MRI	Entropy-related parameters based on ADC maps including: (1) First-order entropy; (2-5) second-order entropies, including entropy(H) <sub>0</sub> , entropy(H) <sub>45°</sub> , entropy(H) <sub>90°</sub> , and entropy(H) <sub>135°</sub> ; (6) entropy(H) <sub>mean</sub> ; and (7) entropy(H) <sub>range</sub>	All the entropy-related parameters showed significant differences in gastric cancers at different T, N, and overall stages, as well as at different statuses of vascular invasion. Entropy, entropy(H) <sub>0</sub> , entropy(H) <sub>45°</sub> , and entropy(H) <sub>90°</sub> showed significant differences between gastric cancers with and without perineural invasion	[35]
GC	CECT	Mean; maximum frequency; mode; skewness; kurtosis; entropy	Maximum frequency in the arterial phase and mean, maximum frequency, mode in the venous phase correlated positively with T, N, and overall stage of GC; entropy in the venous phase also correlated positively with N and overall stage; skewness in the arterial phase had the highest AUC of 0.822 in identifying early from advanced GCs	[34]
<b>Hepatic disease</b>				
Hepatic fibrosis	CECT	Mean gray-level intensity; entropy; kurtosis; skewness	Mean gray-level intensity, mean, and entropy increased with fibrosis stage; kurtosis and skewness decreased with increasing fibrosis	[43]
<b>Pancreatic disease</b>				
PNET	CECT	Positive pixels; SD; kurtosis; skewness; entropy	Entropy was predictive of Grades 2 and 3 tumors with an accuracy rate for classifying G1, G2, and G3 tumors of 79.3%	[53]
PNET	CECT	Mean value; variance; skewness; kurtosis; entropy	Kurtosis was significantly different among the three G groups, giving an AUC value of 0.924 for the diagnosis of G3 with a sensitivity and specificity of 82% and 85%, respectively; entropy differed significantly between G1 and G3 and between G2 and G3 tumors, giving an AUC value of 0.732 for the diagnosis of G3 with a sensitivity and specificity of 82% and 64%, respectively	[54]
<b>Colorectal disease</b>				
CRC	CECT	The 16-feature-based radiomics signature was generated using LASSO logistic regression model	The 16-feature-based radiomics signature was an independent predictor for staging of CRC and could categorize CRC into stage I-II and stage III-IV. Compared with the clinical model, the radiomics signature showed significantly better performance either in the training dataset (AUC: 0.792 vs 0.632; <i>P</i> < 0.001) or in the validation dataset (AUC: 0.708 vs 0.592; <i>P</i> = 0.037)	[59]

ESCC: Esophageal squamous cell carcinoma; CECT: Contrast-enhanced computed tomography; GC: Gastric carcinoma; PNET: Pancreatic neuroendocrine tumor; CRC: Colorectal cancer; AUC: Area under the curve.

**Table 3 Application of radiomics in evaluation of therapeutic efficacy and prognosis in gastroenterology**

Classification of disease	Imaging modality	Features evaluated and methods	Outcomes	Ref.
<b>Esophageal disease</b>				
EC	<sup>18</sup> F-FDG PET	A total of 38 features (such as entropy, size, and magnitude of local and global heterogeneous and homogeneous tumor regions) extracted from 5 different textures	Tumor textural analysis provided non-responder, partial-responder, and complete-responder patient identification with a higher sensitivity (76%-92%) than any SUV measurement	[22]
ESCC	MRI	138 radiomic features were extracted from each image sequence based on three principal methods: Histogram-based (IH, GH), texture-based (GLCM, GLRLM, and NIDM), and transform-based (GWTF)	Radiomic analysis showed that CR <i>vs</i> SD, PR <i>vs</i> SD, and responders (CR and PR) <i>vs</i> non-responders could be differentiated by 26, 17, and 33 features, respectively; the prediction models (ANN and SVM) based on features extracted from SPAIR T2W sequence (SVM: 0.929; ANN: 0.883) showed higher accuracy than those derived from T2W (SVM: 0.893; ANN: 0.861)	[24]
<b>Gastric disease</b>				
GC	CECT	Histogram features: Kurtosis, skewness; GLCM: ASM, contrast, entropy, variance, correlation	Contrast, variance, and correlation showed fair accuracy for the prediction of good survival with all AUCs being over 0.7, and all were statistically significant	[38]
<b>Hepatic disease</b>				
HCC	CECT	21 textural parameters per filter were extracted from the region of interests delineated around tumor outline by application of a Gabor filter and wavelet transform with 3 band-width responses (filter 0, 1.0, and 1.5)	Texture analysis was observed to have potential in assessment of prognosis and selection of appropriate patients with intermediate-advanced HCC treated by TACE and sorafenib	[46]
HCC	CECT	First order statistics; geometry; texture analysis; GLCM	Textures derived from pretreatment dynamic CT imaging were analyzed, higher arterial enhancement ratio and GLCM moments, smaller tumor size, and lower tumor homogeneity were significant predictors of CR after TACE	[47]
<b>Pancreatic disease</b>				
Pancreas head cancer	CECT	Laplacian of the Gaussian band-pass filter was applied to detect intensity changes within the images smoothed by Gaussian distribution based on the filter sigma value of 1.0 (fine texture, filter width 4 pixels), 1.5 to 2.0 (medium texture, filter width 6-10 pixels), and 2.5 (coarse texture, filter width 12 pixels)	Texture parameters of average, contrast, correlation, and standard deviation with no filter, and fine to medium filter values, as well as the presence of nodal metastasis were significantly different between recurred and non-recurred patients; lower standard deviation and contrast and higher correlation with lower average value representing homogenous texture were significantly associated with poorer DFS, along with the presence of lymph node metastasis	[55]
PDAC	CECT	Mean gray-level; intensity; entropy; MPP; kurtosis; SD; skewness	Tumor size, tumor SD, and skewness were significantly and independently associated with PFS, while tumor size and tumor SD were significantly and independently associated with OS	[56]
<b>Colorectal disease</b>				
LARC	MRI	18 features extracted using the Haralick's GLCM and 12 parameters calculated for the histogram-based analysis	Radiomics based on pre-treatment and early follow-up MRI could provide quantitative information to differentiate pCR from non-pCR, and GR from non-GR.	[60]
Rectal cancer	MRI	Kurtosis; entropy; skewness; MPP	The change in kurtosis between midtreatment and pretreatment images was significantly lower in the PR + NR subgroup compared with the pCR subgroup; pretreatment AUROC to discriminate between pCR and PR + NR, was significantly higher for kurtosis (0.907, <i>P</i> < 0.001)	[61]

EC: Esophageal cancer; ESCC: Esophageal squamous cell carcinoma; PET: Positron emission tomography; MRI: Magnetic resonance imaging; CR: Complete response; SDs: Stable diseases; PRs: Partial responses; GLCM: Gray level cooccurrence matrices; GC: Gastric carcinoma; ASM: Angular second moment; AUC: Area under the curve; HCC: Hepatocellular carcinoma; CECT: Contrast enhanced computed tomography; TACE: Transcatheter arterial chemoembolization; DFS: Disease free survival; PFS: Progression-free survival; OS: Overall survival; PDAC: Pancreatic ductal adenocarcinoma; LARC: Local advanced rectal cancer; GR: Good response; MPP: Mean value of positive pixels.

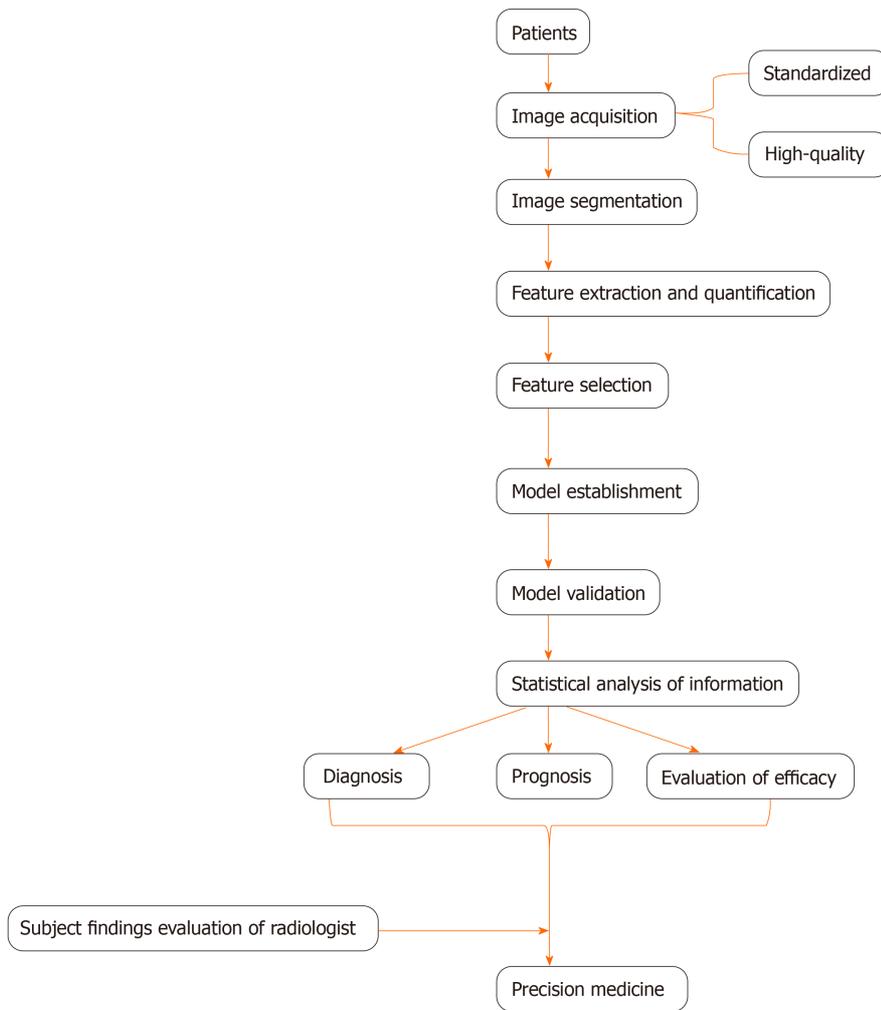


Figure 1 Overview of the workflow of artificial intelligence and radiomics in clinical practice.

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