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**Ultrasound-based artificial intelligence in gastroenterology and hepatology**

Liu JQ *et al.* Ultrasound AI in gastroenterology and hepatology

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**Abstract**

Artificial intelligence (AI), especially deep learning, is gaining extensive attention for its excellent performance in medical image analysis. It can automatically make a quantitative assessment of complex medical images and help doctors to make more accurate diagnoses. In recent years, AI based on ultrasound has been demonstrated very helpful in diffuse liver diseases and focal liver lesions, such as analyzing the severity of non-alcoholic fatty liver and the stage of liver fibrosis, identifying benign and malignant liver lesions, predicting the microvascular invasion of hepatocellular carcinoma, curative transarterial chemoembolization effect, and prognoses after thermal ablation. Moreover, AI based on endoscopic ultrasonography has been applied in some gastrointestinal diseases, such as distinguishing gastric mesenchymal tumors, detection of pancreatic cancer and intraductal papillary mucinous neoplasms, and predicting the preoperative tumor deposits in rectal cancer. This review focuses on basic technical knowledge about AI and the above clinical application in the ultrasound of liver and gastroenterology. Lastly, we discuss the challenges and future perspectives of AI.

**Key Words:** Artificial Intelligence; Ultrasound; Liver; Gastroenterology; Deep learning

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**Core Tip:** Recently, artificial intelligence (AI) based on ultrasound has been confirmed helpful in diffuse liver diseases and focal liver lesions, such as analyzing the severity of non-alcoholic fatty liver and the stage of liver fibrosis, identifying benign and malignant liver lesions, predicting the microvascular invasion of hepatocellular carcinoma, curative transarterial chemoembolization effect, and prognoses after thermal ablation. Moreover, AI based on endoscopic ultrasonography has been applied in some gastrointestinal diseases. This review focuses on basic technical knowledge about AI and the above clinical application in the ultrasound of liver and gastroenterology. Additionally, we discuss the challenges and future perspectives of AI.

## INTRODUCTION

Liver disease causes 2 million deaths per year in the world among which cirrhosis is the 11<sup>th</sup> leading cause of death in the world and liver cancer is the 16<sup>th</sup> leading cause of death<sup>[1]</sup>. The prevalence of nonalcoholic fatty liver disease (NAFLD) is 25% and is estimated to be 33.5% by 2030<sup>[2]</sup>. Gastrointestinal diseases affect an estimated 60 to 70 million American citizens annually. It is reported that pancreatic cancer is one of the top 5 causes of death from cancer and colorectal cancer accounts for 8.5% of cancer-related death<sup>[3-5]</sup>. Therefore, it is of great importance to pay attention to these diseases.

In clinical practice, many imaging techniques such as X-ray, computed tomography, magnetic resonance imaging and ultrasound have played a vital part in the detection and treatment of diseases<sup>[6]</sup>. Ultrasound, a noninvasive and real-time diagnostic technique, is the most commonly used method for detecting and diagnosing human digestive diseases<sup>[7]</sup>. However, the interpretation and analysis of ultrasound images depend deeply on the subjective judgment and experience of human experts.

Radiologists may make mistakes due to exhaustion when dealing with large amounts of images<sup>[8]</sup>.

Artificial intelligence (AI) is defined as computer algorithms created by humans and improved with analogs of the thoughts, judgments, and reactions that take place in the human brain. In recent years, radiologists have increasingly embraced to the aid of AI-powered diagnoses. AI can make a quantitative analysis by recognizing the information of images automatically, and is widely applied in the medical images of ultrasound in diffuse liver diseases, focal liver lesions, pancreatic cancer, and colorectal cancer. In this paper, we plan to describe an overview of the development in AI-based ultrasound in the above applications. In addition, we also discuss the future opportunities and challenges of the AI-based ultrasound.

## AI

Currently, the algorithms of AI used in medical images mainly include traditional machine learning algorithm (MLA) and deep learning.

### <sup>8</sup>*Machine learning*

Machine learning is described as a kind of data science which offers computers with the capacity to study without being programmed with specific rules<sup>[9]</sup>. It focuses on computer algorithms which are studied from the training model and give predictions on another model<sup>[10]</sup>. Machine learning depend mainly on the predefined characteristics which display the regular patterns inherent in model acquired from regions of interest with explicit parameters on the basis of expert experience. Then, other medical image features can be quantified, such as various mass shape, size, and echo.

Radiomics which belongs to traditional machine learning is a popular field of study related to the acquisition and assessment of patterns within medical images, including CT, MRI, and ultrasound. These patterns include complicated patterns which are hard to recognize or analyze by human eyes<sup>[11]</sup>.

### *Deep learning*

Deep learning is at the leading edge of AI and is developing rapidly. Deep learning is described as a group of artificial neural network (ANN) algorithms which include many hidden layers. Namely, deep learning depends on a subset of algorithms that try to model high-level abstractions in modal<sup>[12]</sup>.

Recently, convolutional neural networks (CNNs) are the most favorite kind of deep learning architectures in the assessment of medical images<sup>[13]</sup>. CNNs consist of an input layer, multiple hidden layers and an output layer (Figure 1). The hidden layers include convolutional layers, pooling layers, connected layers, and normalization layers. Convolutional layers and pooling layers can complete feature extraction and aggregation<sup>[9]</sup>.

## APPLICATION OF ULTRASOUND-BASED AI IN HEPATOLOGY

### *Diffuse liver diseases*

Diffuse liver diseases display a failure in the metabolic and synthesis processes of liver<sup>[14]</sup>. Liver biopsy is the gold standard for the diagnosis of fibrosis and nonalcoholic fatty liver disease (NAFLD). However, liver biopsy is an invasive process which has many complications such as hemorrhage, biliary peritonitis, and pneumothorax<sup>[15]</sup>. In addition, liver biopsy is not feasible for the long-term management of patients with chronic liver diseases. Noninvasive liver imaging methods such as CT, MRI and ultrasound have been extensively studied. Ultrasound is one of most common methods to diagnose liver diseases due to its non-invasiveness, cheap price, and real time ability. MLAs based on ultrasound have been applied for analysis of steatosis and the staging of liver fibrosis.

Table 1 shows the application of ultrasound-based AI in diffuse liver disease.

**Fatty liver diseases:** An excess amount of fat in the liver cells is found in fatty liver diseases (FLD). The main causes of FLD include obesity, alcoholism, diabetes, nonalcoholic steatohepatitis, drugs, toxins<sup>[16,17]</sup>. FLD is related to the growing risk of cirrhosis and liver cancer. The most common cause of FLD is NAFLD which the

prevalence ranges from 25% to 45% in many researches<sup>[18]</sup>. Several noninvasive imaging methods such as CT, MRI, and ultrasound can diagnose the NAFLD<sup>[19]</sup>. Thereinto, while hepatic steatosis is greater than 33%, ultrasound is the cheapest diagnostic method with 93% sensitivity<sup>[18]</sup>.

Conventional ultrasound is commonly used for NAFLD evaluation but its qualitative nature, doctor dependency, and unsatisfactory accuracy limits the application. Moreover, the ultrasound images of fatty liver and early cirrhosis have many common features, it is hard to identify the two diseases by human eyes<sup>[20]</sup>.

In recent years, ultrasound-based AI has demonstrated high accuracy for detection of steatosis and represented excellent reproducibility and reliability.

Byra *et al*<sup>[21]</sup> created a CNN model to acquire features from B-mode ultrasound image. It was reported that they could assess the amount of steatosis present in the liver with the AUC of 0.98 and their approach may assist the doctors in automatically assessing the amount of fat in the liver clinically<sup>[21]</sup>.

Biswas *et al*<sup>[22]</sup> revealed that deep learning-based algorithm reached a superior performance for fatty liver disease identification and risk stratification with 100% accuracy, and 1.0 AUC when compared with conventional machine learning system support vector machine (SVM) (accuracy: 82%, AUC: 0.79) and extreme learning machine (ELM) (accuracy: 92%, AUC: 0.92).

Deep learning has also been applied to quantitatively evaluate NAFLD. The radiofrequency data of ultrasound displays much more information of hepatic microstructure than that of gray-scale B-mode images<sup>[23]</sup>. Han *et al*<sup>[24]</sup> developed a deep learning algorithm that use radiofrequency data for NAFLD assessment. The results revealed that the sensitivity, specificity and the positive predictive value for NAFLD diagnosis were 97%, 94% and 97%, respectively. They confirmed that the quantitative analysis of raw radiofrequency ultrasound signals showed the potential of identifying NAFLD and quantifying hepatic fat fraction<sup>[24]</sup>.



**Liver fibrosis and cirrhosis:** Patients with chronic liver disease (CLD) may have no clinical symptoms within a long time, or may develop to fibrosis and cirrhosis<sup>[25]</sup>. The activation of the resting hepatic stellate cell into an activated myofibroblast plays an important role in the progress of liver fibrosis. The activated myofibroblast expresses abundant  $\alpha$ -smooth muscle actin and collagens<sup>[26]</sup>.

Cirrhosis which is full with various nodules and gets harder than the normal liver is the advanced period of fibrosis<sup>[27]</sup>. Liver fibrosis and early cirrhosis are confirmed to be partly reversible. Therefore, the precise diagnosis of liver fibrosis is vital for the treatment and management of CLD patients.

In clinical practice, liver biopsy is the gold standard for the diagnosis of liver fibrosis. Various noninvasive modalities such as ultrasound and elastography have been used as alternatives to liver biopsy. Some studies suggest that AI models based on ultrasound and elastography have great potential for the classification of liver fibrosis.

AI based on conventional ultrasound: AI based on conventional ultrasound have been applied to improve their performance for the diagnosis and grade of liver fibrosis.

Yeh *et al*<sup>[28]</sup> built an SVM model to analyze liver fibrosis. B-mode images of 20 fresh postsurgical human liver were used to assess ultrasound capacity in evaluating the stage of fibrosis. The study indicated the best classification accuracy of two, three, four, and six classes were 91%, 85%, 81% and 72%, respectively<sup>[28]</sup>. The results confirmed that the SVM model may be suggested to assess diverse liver fibrosis stage.

Other than the B-mode ultrasound, duplex ultrasound has also been applied to diagnose liver fibrosis. Using an ANN model based on duplex ultrasound, Zhang *et al*<sup>[29]</sup> demonstrated that their model reached the accuracy, sensitivity and specificity were 88.3%, 95.0% and 85.0%, respectively. The ANN model included five ultrasonographic parameters: thickness of spleen, liver vein waveform, the hepatic parenchyma, liver artery pulsatile index and hepatic damping index. The study suggested that their ANN model has the potential to diagnose liver fibrosis noninvasively<sup>[29]</sup>.

Studies have been confirmed<sup>1</sup> that radiomics show great performance in the grade of liver fibrosis. By the use of texture analysis to analyze ultrasound liver images, the study found the accuracies of S0-S4 were 100%, 90%, 70%, 90% and 100%, respectively<sup>[30]</sup>.

It is reported that deep learning has great potential for liver fibrosis evaluation. Lee *et al*<sup>[31]</sup> built a deep convolutional neural network (DCNN) and trained four-class model (F0 vs F1 vs F2 vs F4) to predict METAVIR scores. 13608 ultrasound images of 3446 patients who accepted surgery, liver biopsy, or transient elastography (TE) were selected to train the DCNN model. The model achieved a higher AUC of 0.857 for the classification of cirrhosis compared with five radiologists (AUC range, 0.656-0.816;  $P < 0.05$ ) using the external test set<sup>[31]</sup>.

AI based on ultrasound elastography: ultrasound elastography has been performed to acquire quantitative assessment of liver tissue stiffness which is related to the grades of fibrosis. These technologies include strain elastography (SE) and shear wave elastography (SWE)<sup>[32]</sup>.

Recently, some studies confirmed that the AI based on SWE has great value to identify and stage liver fibrosis.

Compared to conventional radiomics, a multiparametric ultrasonic model using MLAs demonstrated better manifestation in fibrosis assessment<sup>[33]</sup>. By quantifying color information from SWE images, Gatos *et al*<sup>[34,35]</sup> created an SVM model which could differentiate patients with liver diseases from controls with the accuracy, sensitivity, and specificity were 87.3%, 93.5% and 81.2%, respectively.

Deep learning has also been applied in the assessment of liver fibrosis. A multicenter research used deep learning radiomics on 2D-SWE ultrasound images (DLRE) for the classification of liver fibrosis<sup>[36]</sup>. DLRE got higher AUCs of 0.97 for F4, 0.98 for  $\geq$  F3 and 0.85 for  $\geq$  F2 fibrosis when compared with standard 2D-SWE.

It is necessary to contain a large training dataset for deep learning. However, it is hard and expensive to get abundant medical images in clinics. One method to solve this problem is the employment of transfer learning (TL) which can enhance the



performance by TL from other areas to ultrasound area<sup>[37]</sup>. A study developed a CNN model by TL radiomics to assess ultrasound <sup>1</sup>images of gray-scale modality (GM) and elastogram modality (EM) for the grade of accurate liver fibrosis. TL in GM and EM revealed much higher diagnostic accuracy of AUCs compared with non-TL. Multimodal GM + EM was confirmed to be the most precise diagnostic model with the AUCs were 0.930, 0.932, and 0.950 for classifying  $\geq S2$ ,  $\geq S3$ , and  $S4$ , respectively. It is suggested that this TL model had excellent performance in liver fibrosis staging in clinical applications<sup>[38]</sup>.

### *Focal liver lesion*

Focal liver lesions (FLLs) are described as an abnormal part of the liver mainly coming from hepatocytes, biliary epithelium and mesenchymal tissue<sup>[39]</sup>. Due to its cheap price, non-invasiveness and real-time imaging, ultrasound is the preferred method for the diagnosis of FLLs. Based on this trend, the AI models using ultrasound images have more advantages over CT and MRI in routine clinical applications<sup>[40]</sup>. Table 2 shows the application of ultrasound-based AI in FLLs.

**The application of AI in diagnosis of benign and malignant FLLs:** <sup>1</sup>Hepatocellular carcinoma (HCC) is the fifth most common malignancy worldwide and accounts for the second leading cause of cancer-related death<sup>[41]</sup>. It is vital to identify benign and malignant FLLs for patients in the early stage.

AI based on conventional ultrasound: Deep learning based on B-mode ultrasound has been demonstrated helpful in the diagnosis of benign and malignant FLLs.

A CNN model was performed to distinguish benign and malignant FLLs and achieved a higher accuracy than two experts<sup>[42]</sup>. Yang *et al*<sup>[43]</sup> developed a multicenter study to improve the B-mode ultrasound diagnostic performance for FLLs. The CNN of ultrasound performed high sensitivity and specificity in detecting FLLs and it may be helpful for less-experienced doctors to enhance their judgment in liver cancer diagnosis.

AI based on B-mode ultrasound images has also been applied for the diagnosis of primary or secondary malignant liver tumors. A study proposed <sup>2</sup> the machine learning for discriminating HCC and metastatic liver tumors using SVM. The results revealed a <sup>23</sup> classification accuracy of 91.6% with sensitivity of 90% for HCCs and 93.3% for metastatic liver tumors<sup>[44]</sup>.

AI based on contrast-enhanced ultrasound (CEUS): Recently, CEUS is a commonly ultrasound modality for the detection of FLLs<sup>[45]</sup>. Many studies have indicated that CEUS images had better sensitivity and specificity for the differentiation of malignant and benign tumors compared with B-mode images. One of the advantages of CEUS is that the images can be analyzed quantitatively. Time intensity curve (TIC) is a common quantitative analysis tool for CEUS<sup>[46]</sup>. Recently, AI based on CEUS images was reported to have great performance for the discrimination of FLLs.

Gatos *et al*<sup>[47]</sup> created a pretrained SVM algorithm to distinguish benign and malignant FLLs. In this model, a complex segmentation method based on TIC is used to detect lesions and process contours of 52 CEUS images. <sup>2</sup> The accuracy, sensitivity, and specificity were reported 90.3%, 93.1%, and 86.9%, respectively<sup>[47]</sup>. Another study using SVM revealed that <sup>25</sup> the sensitivity, specificity and accuracy of benign and malignant grading were 94.0%, 87.1% and 91.8% while the classification accuracy of HCC, metastatic liver tumor and the benign were 85.7%, 87.7%, and 84.4%, respectively<sup>[46]</sup>.

In addition to the TIC, extracting features except TICs from region of interest of CEUS images and videos was also applied in AI. A two-stage multi-view learning framework which was the integration of deep canonical correlation analysis (DCCA) and multiple kernel learning (MKL) for CEUS-based computer-aided diagnosis was proposed to identify liver tumors. The DCCA-MKL framework achieved performance for discriminating benign from malignant liver tumors with the accuracy, sensitivity, specificity was 90.4%, 93.6%, 86.8%, respectively<sup>[48]</sup>.

**The application of AI for the differential diagnosis of FLLs:** AI based on conventional ultrasound: With the development of AI, AI based on B-mode ultrasound images has

great performance on the diagnosis of different FLLs. Hwang *et al*<sup>[49]</sup> extracted hybrid textural features from ultrasound images and used an ANN to diagnose FLLs. They indicated that the model revealed enormous potential with the diagnosis accuracy of over 96% among all FLLs groups (hemangioma *vs* malignant, cyst *vs* hemangioma and cyst *vs* malignant)<sup>[49]</sup>.

Deep learning was also applied in the distinction of different FLLs. Schmauch *et al*<sup>[50]</sup> created an algorithm that simultaneously detected and characterized FLLs. Although the amount of training data was relatively small, the average ROC-AUC score of FLL detection and characterization was 0.935 and 0.916.

A CNN model was developed and validated for tumor detection and 6-class discrimination (HCCs, focal fatty sparing, focal fatty infiltration, hemangiomas and cysts)<sup>[51]</sup>. This model reached 87.0% detection rate, 83.9% sensitivity and 97.1% specificity in the internal evaluation. In external validation groups, the model achieved 75.0% detection rate, 84.9% sensitivity and 97.1% specificity.

AI based on CEUS: CEUS also had excellent potential for AI to distinguish different FLLs.

An ANN was applied to study the role of TIC analysis parameters of 4-class discrimination of liver tumors. The neural network had 94.45% training accuracy and 87.12% testing accuracy. The automatic classification process registered 93.2% sensitivity and 89.7% specificity<sup>[52]</sup>.

Căleanu *et al*<sup>[53]</sup> reported the 5-class classification of liver tumors using deep neural networks (DNN) with an accuracy of 88%. In this study, DNN algorithms are compared with state-of-the-art architectures, and a novel leave-one-patient-out evaluation procedure was presented.

All these studies indicated that AI based on conventional ultrasound and CEUS played a vital part for the detection and distinction of FLLs.

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**The application of AI in the management of HCC patients:** Because of the development of new treatments, the management of HCC patients has become much

more complicated. Radiomics can offer accurate assessment of great numbers of image features from medical images. These features which is difficult for human eyes can be detected by machine learning or deep learning. AI model based on radiomics has also been reported applicable for the management of HCC, such as prediction of microvascular invasion (MVI), curative transarterial chemoembolization (TACE) effect, recurrence after thermal ablation and prognosis.

Predicting MVI: MVI is described as the invasion of tumor cells within a vascular space lined by endothelium. It has been proven that MVI is a predictor of early recurrence of HCC and poor survival outcomes<sup>[54]</sup>. The only way to confirm MVI is *via* histopathology after surgery. It is of great benefit for HCC patients to make noninvasive and accurate identification of MVI before surgery<sup>[55]</sup>. The application of AI based on gray-scale ultrasound images and CEUS indicated good performance in predicting preoperative MVI.

A study indicated that the radiological features of gray scale ultrasound images of gross-tumoral area predicted preoperative MVI of HCC with 0.81 AUC<sup>[56]</sup>. A CEUS-based radiomics score was built for preoperative prediction of MVI in HCC<sup>[57]</sup>. The radiomics nomogram revealed great potential in the detection of MVI with 0.731 AUC compared with the clinical nomogram with 0.634 AUC. It was indicated that the radiomics data based on ultrasound was a single predictor of MVI in HCC. Our group created a radiomics model based on CEUS to evaluate MVI of HCC patients before surgery. The model revealed a better detection in the primary group with the AUC: 0.849 *vs* 0.690 as well as the validation group with the AUC: 0.788 *vs* 0.661 when compared with the clinical model. We confirmed that the portal venous phase, delay phase, tumor size, rad-score, and alpha-fetoprotein level were single predictors related to MVI<sup>[58]</sup>.

Predicting curative TACE effect: Pathways participated in important cancer related progress such as cell proliferation and angiogenesis are major goals for the treatment of HCC patients. Additionally, transcription factors and cell cycle regulators are also considered to be interesting for anti-HCC drugs<sup>[59]</sup>.



TACE is a widely used first-line therapy for HCC patients diagnosed at the intermediate stage. The tumor response to the first TACE is highly different and obviously related to the subsequent therapies as well as the patients' survival<sup>[60]</sup>. Hence, the exact prediction of HCC responses after first TACE is vital for patients.

The prediction of tumor responses to TACE heavily depends on MRI and serological biomarkers<sup>[61,62]</sup>. But these methods achieved unsatisfactory accuracy of prediction. The application of AI based on both B mode ultrasound and CEUS demonstrated better prediction efficacy.

An AI-based radiomics was established and validated to predict the personalized responses of HCC to the first TACE session. The deep learning radiomics-based CEUS model (R-DLCEUS) showed better performance compared with the machine learning radiomics-based B mode model (R-B Mode) and machine learning radiomics-based time intensity curve of CEUS model (R-TIC) with the AUC were 0.93, 0.80 and 0.81 respectively<sup>[63]</sup>. They suggested that the deep learning-based radiomics could benefit TACE candidates in clinical work.

Predicting recurrence after thermal ablation: Thermal ablation has been confirmed to be an available therapy for early-stage HCC patients who are unsuitable for operation or recurrence occurred after surgery<sup>[64]</sup>. In addition, the recent two-year recurrence rates of HCC patients who underwent thermal ablation were reported 2%-18%<sup>[65]</sup>. The accurate preoperative prediction of the thermal ablation outcomes is of great importance for HCC patients. Compared with other imaging modalities, CEUS is radiation-free and with better temporal resolution when revealing the blood supply of tumor. The application of AI based on CEUS could be performed on the preoperative prediction of the thermal ablation outcomes.

A radiomics model was created to predict the early and late recurrence of HCC patients who accepted thermal ablation<sup>[66]</sup>. The combined model including CEUS, US radiomics, and clinical factors showed better performance for early recurrence with AUC of 0.89 and for late recurrence prediction with C-index of 0.77.



Predicting the prognoses: Surgical resection (SR) and radiofrequency ablation (RFA) are common curative strategies for HCC patients diagnosed at the early stage<sup>[64]</sup>.

Some studies have been reported to compare the long-term survivals of RFA and SR for early-stage HCC patients<sup>[67,68]</sup>. However, the conclusions were sharply different. Hence, it is necessary to find useful predictive means to select the optimal patients who are suitable for RFA or SR before surgery. AI models based on CEUS had great performance for the prediction of progression-free survival.

A deep learning-based radiomics from CEUS images was built to predict the progression-free survival (PFS) of SR and RFA for HCC patients. Both SR and RFA models achieved high prediction accuracy of two-year PFS. They also identified that a higher average probability of two-year PFS may be acquired while some RFA and SR patients exchange their choices<sup>[69]</sup>.

By utilizing conventional ultrasound images and CEUS, these AI prediction models can be applied in the individualized management of HCC patients.

## **APPLICATION OF ULTRASOUND-BASED AI IN UPPER GASTROINTESTINAL DISEASE**

### ***Gastric mesenchymal tumors***

The majority of gastric mesenchymal tumors are occasionally found during routine esophagogastroduodenoscopy examinations. The incidence of gastric mesenchymal tumors is uncertain, but the prevalence of subepithelial tumors identified under endoscopy in Korea was reported 1.7%<sup>[70]</sup>. Most gastric mesenchymal tumors are gastrointestinal stromal tumors (GISTs), which may metastasize to the liver and peritoneum after surgery<sup>[71,72]</sup>. Hence, distinguishing GISTs from benign mesenchymal tumors such as leiomyomas or schwannomas is of great importance in clinic practice. Endoscopic ultrasonography (EUS) is a common method to assess gastric mesenchymal tumors. It helps doctors evaluate the detailed size, shape, origin and border of the lesions<sup>[73-75]</sup>. But the interpretation of EUS images by the endoscopists is subjective and in poor interobserver agreement. Recently, EUS images interpretation using AI has

developed rapidly, and is applied to distinguish GISTs from benign mesenchymal tumors.

A convolutional neural network computer-aided diagnosis (CNN-CAD) model based on EUS images was developed to assess gastric mesenchymal tumors. They reported the model distinguished GISTs from non-GIST tumors with the 83.0% sensitivity, 75.5% specificity, and 79.2% accuracy<sup>[76]</sup>. The CNN-CAD model had the potential to provide diagnostic assistance to endoscopists in the future.

### *Pancreatic diseases*

EUS is currently a common tool to diagnose pancreatic diseases in clinical practice. However, the specificity for the diagnosis of pancreatic diseases using EUS images is low and deeply depends on the subjective judgment of endoscopists. Studies have confirmed that AI based on EUS improves their performance for the diagnosis of pancreatic diseases. Recently, AI using EUS images has been applied in the differential diagnosis of pancreatic cancer, distinguishing intraductal papillary mucinous neoplasms (IPMNs) and detecting pancreatic segmentation.

**Pancreatic cancer:** Pancreatic cancer (PC) is relatively uncommon, with an incidence of 8-12 per 100000 per year. Pancreatic cancer attributes to hereditary germline or somatic acquired mutations in some genes such as tumor suppressor genes and cell cycle genes. These mutations are also associated with the progression and metastasis of pancreatic cancer. Moreover, shortened telomerase, cell turnover, and genomic instability take an important part in the development of pancreatic cancer<sup>[77]</sup>.

The early diagnosis and surgery of PC, especially the lesions size less than 1 cm, can achieve long-term prognoses with a five-year survival rate of 80.4%<sup>[78]</sup>. However, PC is most frequently detected at an advanced stage and the five-year survival rates remain as low as 3%-15%<sup>[79]</sup>. Hence, early detection is vital for the treatment of PC patients. Studies have reported that AI based on EUS has great performance for the diagnosis of PC.

AI based on B-mode EUS: AI models based on B-mode EUS have been applied to improve their performance for the diagnosis of PC.

Norton *et al*<sup>[80]</sup> first reported the use of CAD utilizing EUS images in pancreatic diseases in 2001. The study included 14 patients with focal chronic pancreatitis and 21 with PC. They showed the diagnostic sensitivity of the two diseases was 89% and the overall accuracy was 80%<sup>[80]</sup>. However, this study cannot be referred to as AI-CAD in current applications as the number of patients was limited and the resolution of images were very low.

With the development of AI, ANN and SVM presented good performance in the diagnosis of PC<sup>[81-83]</sup>.

Das *et al*<sup>[81]</sup> developed an ANN model to distinguish chronic pancreatitis from PC. The results achieved 93% sensitivity, 92% specificity, 87% positive predictive value (PPV), 96% negative predictive value (NPV) and 0.93 ROC<sup>[81]</sup>. By using a multi-layered neural network, the study confirmed the first machine learning results for the EUS images of the pancreas. But the sample size was small and lacked pathological evidence in chronic pancreatitis and normal pancreas groups.

By selecting better texture features which included multifractal dimensional features, a quantitative measure of fractality (self-similarity), and complexity from EUS images, a SVM prediction model was created to identify PC and non-PC patients<sup>[83]</sup>. The model reached 97.98% accuracy, 94.32% sensitivity, 99.45% specificity, 98.65% PPV, and 97.77% NPV. The study demonstrated that SVM using EUS images is a useful tool for diagnosing PC and pancreatic diseases.

It is reported that AI was also applied for the age-dependent pancreatic changes on EUS images of PC cases.

Ozkan *et al*<sup>[84]</sup> suggested a high-performance computer-aided diagnostic model applying ANN to discriminate PC and noncancer patients in three age groups. In the under-40-year-old group, the accuracy, sensitivity and specificity were 92%, 87.5%, and 94.1%, respectively. In the 40-to-60-year-old group, the accuracy, sensitivity and specificity were 88.5%, 85.7% and 91.7%, respectively. In the > 60-year-old group, the

<sup>6</sup> accuracy, sensitivity and specificity were 91.7%, 93.3% and 88.9%, respectively. The total performance of this model showed the accuracy, sensitivity and specificity were 87.5%, 83.3% and 93.3%, respectively.

Besides the machine learning, deep learning has been applied to B-mode EUS images for analysis of pancreatic cancer. A CNN model using EUS images was developed for the detection of PC<sup>[85]</sup>. The sensitivity, specificity, PPV, and NPV were reported 90.2%, 74.9%, 80.1%, and 88.7%, respectively. The CNN model included six normalization layers, seven convolution layers, four max-pooling layers and six activation layers. The EUS-CNN application was first reported to have the potential to detect PC from EUS images.

AI based on EUS elastography: Real-time EUS elastography can provide more information about the features of pancreatic masses by the use of strain assessment. It is reported that EUS elastography has been applied in the differential diagnosis of pancreatic lesions. However, the accuracy and reproducibility were unstable<sup>[86,87]</sup>.

<sup>10</sup> The application of AI improves their performance in the diagnosis of pancreatic cancer. A prospective, blinded, multicentric study using EUS elastography by ANN was performed in focal pancreatic lesions<sup>[88]</sup>. They demonstrated the sensitivity, specificity, PPV, and NPV values for the diagnosis of PC were 87.59%, 82.94%, 96.25%, and 57.22%, respectively. The study suggested that the ANN model may provide fast and accurate diagnoses in clinicals.

AI based on contrast-enhanced EUS: Contrast-enhanced EUS has been used to enhance the detection of pancreatic lesions<sup>[89]</sup>. AI based on contrast-enhanced EUS has great performance for the diagnosis of pancreatic cancer.

An ANN model based on the TIC analysis from contrast-enhanced EUS images was designed to diagnose PC and chronic pancreatitis. The study reached 94.64% sensitivity, 94.44% specificity, 97.24% PPV, and 89.47% NPV<sup>[90]</sup>. The study suggested that the model could provide additional diagnostic value to CEUS interpretation and EUS-FNA results.

**IPMNs:** IPMNs are considered to be precursor lesions of pancreatic adenocarcinoma. Early surgical resection of IPMNs can provide a survival benefit for patients<sup>[91]</sup>. EUS is often used to assess the malignancy of IPMNs in clinics. Several predictive techniques were used to diagnose the malignancy of IPMNs with no satisfactory results (70%-80%)<sup>[92,93]</sup>.

Compared with human diagnosis and conventional EUS features, AI *via* deep learning algorithms was confirmed to be a more exact and objective way for the differential diagnosis of malignant IPMNs.

Kuwahara *et al*<sup>[94]</sup> performed a predictive CNN model using EUS images to detect the malignant IPMNs. The model reached the 95.7% sensitivity, 94.0% accuracy and 92.6% specificity. The accuracy was higher compared with the diagnosis of radiologist (56.0%). The author suggested that the application of AI can evaluate malignant IPMNs before surgery.

**Pancreatic segmentation:** AI using EUS images has also been applied in the pancreatic segmentation.

A deep learning-based classification system was created to utilize the “station approach” in the EUS of pancreas<sup>[95]</sup>. The system got 90.0% accuracy in classification, and 0.77 and 0.813 dice in blood vessel and pancreas segmentation. The results were similar to that of EUS experts. Thus, this study revealed that AI has the feasibility to detect the station and segmentation of the pancreas.

## APPLICATION OF ULTRASOUND-BASED AI IN LOWER GASTROINTESTINAL DISEASE

### *Colorectal tumors*

Colorectal cancer is the third most common cancer worldwide and accounts for the second leading cause of cancer related death. Moreover, a growing number of patients were diagnosed rectal cancer patients under 50 years old<sup>[96]</sup>. Colorectal cancer attributes to the gene mutations of epithelial cells, such as oncogenes, tumor suppressor genes and



genes associated with DNA repair. The specific molecular mechanisms implicated in this type of cancer may include the instability of chromosomes and microsatellite<sup>[97]</sup>.

Recently, some researchers pay more attention to tumor deposits (TDs) of rectal cancer. TDs are described as focal aggregates of adenocarcinoma located in the surrounding fat of colon or rectum. They are discontinuous with the primary tumor and unrelated to a lymph node<sup>[98,99]</sup>.

It is reported that patient with TD-positive have more malignant tumors, with less disease-free survival and overall survival<sup>[100]</sup>. However, TDs are often diagnosed by pathology only after surgery. Hence, the non-invasive preoperative prediction of TDs is of great scale for rectal cancer patients. EUS is currently a common tool to detect rectal masses. Recently, ultrasound-based radiomics have been applied to predict the status of TDs.

Chen *et al*<sup>[101]</sup> developed an ANN system using ultrasound radiomics and clinical factors to predict TDs. Endorectal ultrasound and SWE examinations were conducted for 127 patients with rectal cancer. The accuracy was 75.0% in the validation group. The model reached 72.7% sensitivity, 75.9% specificity, and 0.743 AUC. The study suggested that ultrasound-based radiomics has the potential for the prediction of TDs before treatment.

Table 3 shows the application of ultrasound-based AI in gastrointestinal disease.

## **CONCLUSION**

In recent years, AI models using ultrasound images have developed rapidly. They can offer a more precise and efficient diagnosis and ease the burden of doctors.

AI based on ultrasound has been confirmed helpful in diffuse liver diseases and focal liver lesions, such as assessing the severity of NAFLD and the grade of liver fibrosis, distinguishing benign and malignant liver lesions, predicting the MVI of HCC, curative TACE effect and prognoses after thermal ablation. In addition, AI based on EUS has great performance in gastrointestinal diseases, such as distinguishing gastric

mesenchymal tumors, differential diagnosis of pancreatic cancer, distinguishing IPMNs, and predicting the status of TDs in rectal cancer.

However, the application of AI based on ultrasound in clinical practice has some limitations. The main reason may due to the high instability of radiologist in ultrasound image acquisition and interpretation<sup>[102]</sup>. Hence, it is necessary to unify the ultrasonic image acquisition process as well as the standard of ultrasonic data measurement during the ultrasound examination.

In addition, some studies of AI-powered ultrasound were retrospective and trained on limited data offered by a single hospital with potential data selection bias and the amount of data in the training set was not enough. Abundant prospective studies from multi-center recruitments should assure the efficiency and stability of these AI models. Additionally, deep learning needs a large number of images, it is necessary to establish abundant database with common collaborative efforts.

In addition, the application of AI based on EUS has some limitations. The number of EUS examinations is overwhelmingly low compared to other examinations such as endoscopy and CT, especially in gastrointestinal diseases.

In the future, AI based on ultrasound may be used to develop highly accurate and more efficient models for more digestive diseases such as peptic ulcers, stomach neoplasms, inflammatory bowel disease, and so on. These models may heavily reduce the workload for doctors by automatic identification of disease on radiologic and histopathologic images. Moreover, the application of AI can enable building individual management for patients as well as predicting disease progression and complications in clinics. Additionally, AI may improve distance teaching by remote monitoring and enhance medical service in undeveloped areas.

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