Review Article

Artificial intelligence applications in computed tomography in gastric cancer: a narrative review

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Background and Objective: Artificial intelligence (AI) is a revolutionary technique which is deeply impacting and reshaping clinical practice in oncology. This review aims to summarize the current status of the clinical application of AI-based computed tomography (CT) for gastric cancer (GC), focusing on diagnosis, genetic status detection and risk prediction of metastasis, prognosis and treatment efficacy. The challenges and prospects for future research will also be discussed.

Methods: We searched the PubMed/MEDLINE database to identify clinical studies published between 1990 and November 2022 that investigated AI applications in CT in GC. The major findings of the verified studies were summarized.

Key Content and Findings: AI applications in CT images have attracted considerable attention in various fields such as diagnosis, prediction of metastasis risk, survival, and treatment response. These emerging techniques have shown a high potential to outperform clinicians in diagnostic accuracy and time-saving.

Conclusions: AI-powered tools showed great potential to increase diagnostic accuracy and reduce radiologists' workload. However, the goal of AI is not to replace human ability but to help oncologists make decisions in their practice. Therefore, radiologists should play a predominant role in AI applications and decide the best ways to integrate these complementary techniques within clinical practice.

Keywords: Artificial intelligence (AI); radiomics; machine learning (ML); computed tomography (CT); gastric cancer (GC)

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Introduction

Gastric cancer (GC) is the fifth most common malignancy and the fourth reason for cancer-related deaths (1). Furthermore, in several South-Central Asian countries, GC is the most common and fatal cancer in men (1). Attributed to the endoscopic screening, the mortality of GC decreased in some countries. However, the overall 5-year survival rate remains poor due to asymptomatic onset and delayed diagnosis (2).

Artificial intelligence (AI) is a revolutionary technique which is deeply impacting and reshaping clinical practice in oncology (3). It is an umbrella term that describes computing techniques for simulating human intelligence (4).

Machine learning (ML) is a domain branch of AI. It is defined as computing algorithms that enable self-learning of input data patterns without explicit instruction (5). Deep learning (DL) is an important subset of ML. DL is defined as a learning algorithm that can automatically learn unknown features, maximizing classification with limited supervision through multiple layers of artificial neural network (6,7). As an advanced ML method, DL has received widespread attention and made breakthroughs in various fields such as computer vision tasks and clinical applications by simulating the human brain for analysis, learning, and data analysis. DL performs representation learning on data, using multiple processing layers composed of multiple non-linear transformations to achieve high-level abstractions of the data (8,9). The biggest characteristic of DL is its ability to autonomously learn through multi-layer neural networks, approximating complex functions through deep non-linear network structures and directly obtaining features associated with the data. DL has revolutionized the algorithmic design approach in many domains including speech recognition, image classification, and text understanding, gradually forming a new paradigm that uses end-to-end models to directly output final results from training data (10). Compared to traditional data feature extraction processes, DL reduces the need for manual preprocessing steps and enables autonomous ML and feature extraction (8). The features obtained by DL thus provide a more fundamental characterization of the data and exhibit significant advantages in terms of classification and visualization. Additionally, due to the robustness of DL, it can typically avoid unexpected variables that researchers may not anticipate, such as inter-observer variability and different clinical conditions and scanning parameters (11,12). With the advancement of computing power and graphic processing technologies, AI techniques such as segmentation, detection and classification are being increasingly utilized to the field of medical imaging (11,13,14). AI has demonstrated the potential to outperform clinicians in diagnostic accuracy and time-saving (14).

Although endoscopy is the most effective tool for early detection of GC, it cannot identify metastatic lesions, which may lead to mismanagement of patients (15). The diagnostic accuracy is mainly dependent on the experience of endoscopists (16). Biopsy specimens and pathological slices are difficult to capture the heterogeneity over the whole tumor. Therefore, computed tomography (CT) is currently the most commonly used and convenient tool for diagnosing, preoperative staging, and treatment efficacy evaluation for GC (17). However, the consistency and accuracy of image interpretation vary largely, which may not improve with training and experience (9). The analysis of CT images mainly relies on morphological features, which provide limited information underlying tumor development and progression (18). These problems present inevitable challenges for radiologists in personalized and precision medicine. Due to the desire to solve these problems, AI applications in CT images attracted considerable attention in various fields such as image segmentation, diagnosis, prediction of metastasis risk, survival, and treatment response (9). AI techniques provide new methods to process images and translate them into quantitative data, allowing the identification of microscopic features of tumors invisible to human eyes (14). Nevertheless, promising results of AI-assisted CT analysis have been reported. Several concerns have also accompanied the surge of AI applications in clinical practice.

In this review, we will summarize the current status of the clinical application of AI-based CT for GC, focusing on diagnosis, genetic status detection and risk prediction of metastasis, prognosis and treatment efficacy. The challenges and prospects for future research will also be discussed. We present this article in accordance with the Narrative Review reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-201/rc).

Methods

We searched the PubMed database to identify studies investigating AI applications in CT in GC. The latest search time was 1/11/2022. The search terms used were: "gastric cancer" and ("artificial intelligence" or "machine learning" or "deep learning" or "radiomics") and "computed tomography". The secondary references cited in articles obtained from the MEDLINE and PubMed search were also retrieved. We only considered research articles written in English. Two authors read the potential studies and wrote the draft. The search strategy is summarized in *Table 1*. The characteristics of key studies are summarized in *Table 2*.

Diagnosis and differential diagnosis

Accurate T-staging is essential for selecting appropriate patients for neoadjuvant chemotherapy (NAC) (55). However, 22.8% of T1/2 GC were misdiagnosed as stage T3/4 by a combination of endoscopy and CT preoperatively (56). Wang and colleagues reported a CT-

Table 1 The search strategy summary

Items	Specification
Date of search	1/11/2022
Databases and other sources searched	PubMed/MEDLINE
Search terms used	"gastric cancer" and ("artificial intelligence" or "machine learning" or "deep learning" or "radiomics") and "computed tomography"
Timeframe	From 1/1990 to 1/11/2022
Inclusion and exclusion criteria	Restricted to articles published in English; without predefined restriction as to the study
Selection process	Two authors independently screened data sources. A third author mediated the process when disagreements occurred

Table 2 Summary of characteristics of key studies

References	Application	Number of patients	Machine learning algorithm	Feature type	Optimal results
Diagnosis					
Wang 2020 (19)	T staging	244	RF	Radiomics	AUC, 0.899
Sun 2020 (20)	T staging	572	SVM, ANN	Radiomics, DL	AUC, 0.900
Ma 2017 (21)	Differentiating Borrmann type IV GC from PGL	70	LASSO	Radiomics	AUC, 0.903
Feng 2022 (22)	Differentiating Borrmann type IV GC from PGL	438	Transfer learning	DL	AUC, 0.990
Wang 2021 (23)	Differentiating gastric neuroendocrine carcinomas from adenocarcinomas	126	LASSO	Radiomics	AUC, 0.821
Chen 2022 (24)	Differential diffuse-type from signet ring cell GC	693	SVM	Radiomics	AUC, 0.918
Metastasis prediction					
Gao 2020 (15)	Lymph node metastasis	768	LASSO	Radiomics	AUC, 0.920
Chen 2020 (18)	Lymphovascular invasion	160	LASSO	Radiomics	AUC, 0.856
Dong 2020 (25)	Lymph node metastasis	730	SVM, ANN, RF	Radiomics, DL	AUC, 0.822
Wang 2020 (26)	Lymph node metastasis	247	RF	Radiomics	AUC, 0.886
Li 2020 (27)	Lymph node metastasis	204	SVM, ANN	Radiomics	AUC, 0.840
Jin 2021 (28)	Lymph node metastasis	1,699	CNN	DL	AUC, 0.876
Fan 2022 (29)	Lymphovascular invasion	101	Adaptive boosting, linear discriminant analysis, logistic regression	Radiomics	AUC, 0.944
Liu 2020 (30)	Peritoneal metastasis	233	SVM	Radiomics	AUC, 0.762
Dong 2019 (31)	Peritoneal metastasis	554	SVM, ANN, LASSO	Radiomics	AUC, 0.958
Huang 2020 (32)	Peritoneal metastasis	955	LASSO	Radiomics	AUC, 0.870

Table 2 (*continued*)

Table 2 (*continued*)

References	Application	Number of patients	Machine learning algorithm	Feature type	Optimal results
Mirniaharikandehei 2021 (33)	Peritoneal metastasis	159	Gradients boosting machine	Radiomics	AUC, 0.69
Chen 2021 (34)	Peritoneal metastasis	239	RF	Radiomics	AUC, 0.981
Liu 2021 (35)	Peritoneal metastasis	599	LR	Radiomics	AUC, 0.873
Huang 2020 (36)	Peritoneal metastasis	544	CNN	DL	AUC, 0.900
Jiang 2021 (37)	Peritoneal metastasis	1,225	CNN	DL	AUC, 0.946
Genetic status and molecular subtypes					
Zhao 2021 (38)	Epstein-Barr virus status	133	LASSO	Radiomics	AUC, 0.955
Zhang 2022 (39)	Epstein-Barr virus status	54	Decision tree	Radiomics	AUC, 0.870
Wang 2021 (40)	Human epidermal growth factor 2	132	RF	Radiomics	AUC, 0.830
Prognosis prediction					
Li 2019 (41)	OS	181	LASSO	Radiomics	HR, 2.72
Jiang 2018 (42)	OS, DFS	1,591	LASSO	Radiomics	HR, 3.308 (OS); HR, 1.742 (DFS)
Jin 2021 (43)	OS, DFS	428	LASSO	Radiomics	AUC, 0.965 (OS); AUC, 0.824 (DFS)
Shin 2021 (44)	RFS	410	LASSO	Radiomics	AUC, 0.719
Jiang 2021 (45)	OS, DFS	1,615	S-Net	DL	HR, 0.159 (OS); HR, 0.318 (DFS)
Zhang 2021 (46)	OS	640	Multi-focus and multi-level fusion feature pyramid network	DL	HR, 9.46
Treatment response prediction					
Jiang 2020 (47)	Chemotherapy response	1,778	LASSO	Radiomics	HR, 0.591
Li 2020 (48)	Chemotherapy response	739	SVM	Radiomics	HR, 1.526
Li 2022 (49)	Chemotherapy response	855	U-net	Radiomics, DL	AUC, 0.797
Xu 2021 (50)	Neoadjuvant chemotherapy	292	SVM	Radiomics	AUC, 0.922
Liu 2021 (51)	Neoadjuvant chemotherapy	69	LASSO	Radiomics	AUC, 0.934
Wang 2021 (52)	Neoadjuvant chemotherapy	155	LASSO	Radiomics	AUC, 0.953
Tan 2020 (53)	Chemotherapy response	86	RF	Delta-radiomics	AUC, 0.828
Liang 2022 (54)	PD-1 inhibitor	87	Logistic regression, SVM	Radiomics	AUC, 0.865

RF, random forest; AUC, area under the curve; SVM, support vector machine; ANN, artificial neural network; DL, deep learning; GC, gastric cancer; PGL, primary gastric lymphoma; LASSO, least absolute shrinkage and selection operator; CNN, convolutional neural network; LR, logistic regression; HR, hazard ratio; OS, overall survival; DFS, disease-free survival; RFS, recurrence-free survival; PD-1, programmed cell death-1.

based radiomics model accuracy for differentiation of T2 and T3/4 stage GC, with an optimal area under the curve (AUC) of 0.899 (19). Sun *et al.* extracted handcrafted DL features from three phase contrast-enhanced CT (CECT) and built a radiomics signature using ML methods (20). Unlike traditional radiomics analysis, this study did not only used handcraft features, but also features extracted from DL neural networks, which provided more diagnostic information beyond a visual interpretation. Their radiomics nomogram, combined with radiomics signature and conventional CT signs, performed well in identifying T4a stage GC, with an optimal AUC of 0.90 (20).

Primary gastric lymphoma (PGL) is one of the most diagnosed gastric malignancies, difficult to differentiate from Borrmann type IV GC using conventional CT (21). The treatment options for the two diseases are different (57). Surgery is the main treatment option for GC, while chemo and radiotherapy are the best options for PGL (57). Ma *et al.* reported a radiomics based model differentiating Borrmann type IV GC from PGL. The model showed favorable accuracy with an AUC of 0.903 (21). DL algorithms typically require a substantial amount of data for effective training. Therefore, this requirement often leads to the challenge of data scarcity under ideal circumstances (58). Transfer learning is an ML technique that enhances the performance of a target task by leveraging knowledge acquired from a related source task. This approach enables the reduction of data requirements for the target task, making it less reliant on a large amount of data (59). Feng *et al.* proposed a transfer learning model based on CT and whole slide images. The model achieves high accuracy for distinguishing PGL from Borrmann type IV GC, with AUCs ranging from 0.92 to 0.99 (22).

Recently, Wang and colleagues constructed a radiomics nomogram with radiomics signature, lymph node metastasis (LNM), and tumor margin. This nomogram revealed a moderate accuracy for differentiating gastric neuroendocrine carcinomas from adenocarcinomas (23). Chen *et al.* reported a radiomics-based nomogram for differential diagnosis for diffuse-type and signet ring cell GC (24).

Risk prediction of metastasis

LNM prediction

LNM is one of the most important hazard factors for the unfavorable outcome of GC (60). Although CT is the most commonly used tool for preoperative assessment of LNM, conventional CT mostly relies on morphological characteristics with unsatisfactory sensitivity for LNM (61). Huang *et al.* firstly revealed the value of radiomics for predicting LNM in colorectal cancer (62). In this study, 150 radiomics features were extracted from CT images and reduced to 24 optimal predictors by using the least absolute shrinkage and selection operator (LASSO) model with 10-fold cross-validation. Then, a radiomics signature was established with linear combination of selected features. The radiomics signature demonstrated significant association with LNM status. Since then, radiomics and DL approaches have attracted great interest for LNM prediction in GC (15,25,26,28,63,64). Several studies developed radiomic models by extracting features from CECT images and found promising results (15,25,63,65,66). Dong *et al.* enrolled 730 locally advanced GC (AGC) patients from five independent centers and proposed a DL radiomic nomogram based on multiphase CT. The nomogram showed good predictive ability for N-staging with best AUC of 0.822 (25). Dual-energy CT (DECT) provides quantitative information on material concentration and improves the ability of tumor characterization. Li *et al.* extracted DL and radiomics features from three monochromatic images for arterial phase (AP) or portal venous phase (VP) image of CECT (27). They found that AP and VP radiomics showed significant association with LNM. The nomogram incorporated the two radiomics signatures, and CT-reported LNM achieved better performance in both cohorts with AUCs of 0.84 and 0.82 (27). For GC confined to the mucosa and submucosa, patients without LNM can receive endoscopic resection in order to avoid complication of lymphadenectomy. Nevertheless, up to 25% of T1b (submucosa) patients suffer LNM. Endoscopic resection for EGC with LNM may delay the detection of LNM and prevent early management of patients. Thus, accurate preoperative diagnosis of LNM is of particular significance for patients with early-stage GC. Gao *et al.* proposed a radiomics signature with 6 features and revealed favorable accuracy for LNM prediction for early-stage GC (17).

While most LNM prediction models were based on images of primary gastric lesions, Gao *et al.* proposed a faster region-based convolutional neural network (CNN) model by labeling perigastric metastatic lymph nodes. The recognition accuracy of their model achieved 95.4% (64). Jin *et al.* proposed a CNN-based model for predicting 11 lymph node stations. The model showed excellent prediction accuracy with an AUC of 0.88. Furthermore, by

visualizing subnetworks, they found that imaging features related to intratumoral heterogeneity and invasive seem to be most valuable for predicting LNM (28).

Lymphovascular invasion (LVI)

LVI, which refers to lymphatic and/or blood vessel invasion, is an independent risk factor for LNM and early recurrence in GC patients (67,68). Chen *et al.* developed a radiomics signature based on AP and VP images to predict LVI (18). The radiomics signature combined with AP and VP features achieved good predictive accuracy with an optimal AUC of 0.865. Fan *et al.* constructed a radiomics model integrating CECT- and PET-based features for predicting LVI in GC. Three ML classifiers (adaptive boosting, linear discriminant analysis, and logistic regression) were used for model construction. A combined model with 10 radiomics features and 8 clinical factors showed the best performance with AUCs of 0.92–0.94 (29). Li *et al.* developed two LVI prediction models for GC using radiomics and the transfer learning method (69). The two models showed similar prediction performances. They further constructed a nomogram incorporating the radiomics model, histologic grade, radiological T, and N stage. The nomogram also revealed good predictive ability for progression-free survival (PFS) and overall survival (OS).

Peritoneal metastasis (PM)

The peritoneum is one of the most common sites of metastasis in GC (70). However, occult PM, which shows no positive signs on CT images, occurs in 10–30% of GC patients (71). Therefore, tools for detecting occult PM are an urgent need. Several studies have evaluated the value of CT-based ML methods for predicting occult PM (30-34). In contrast to conventional radiomics workflow, which only extracts features from the primary tumor area, Dong *et al.* built two radiomics signatures by features extracted from the tumor area and peritoneal area. Their results showed that radiomics features from both areas could provide useful information on PM. The nomogram incorporated the radiomics signatures and Lauren types achieved an extremely high accuracy for predicting PM with (31). In another study conducted by Chen and his colleagues, iodine uptake (IU) and 120-kV equivalent mixed (M) images were acquired for feature extraction by using DECT (34). They found that IU-derived radiomics features provide useful information for predicting PM. Since adjacent nontumor tissues may also provide a wealth of information of tumorigenesis, Liu and colleagues applied the bounding box annotation method, which contained both the tumor and peritumoral area, to develop a radiomics-based model for the prediction of PM (35). Unlike traditional label methods of lesions, bounding box method can encompass both the tumor and peritumoral area. This allows for the inclusion of more information compared to traditional annotation methods, making it more convenient and time-saving (72,73).

Huang *et al.* first investigated the value of DL model for identifying occult PM for AGC. Their proposed deep CNN model based on 2D CECT images revealed promising accuracy with an AUC of 0.90 (36). In a multicenter study that enrolled 1,978 GC patients, Jiang developed a deep CNN model with long-short connections for predicting occult PM (37). In contrast to a conventional CNN, their model incorporates a long connection that facilitates the extraction of multilevel tumor features. These features are then integrated into the final fully connected layer for prediction (37). Their model achieved better performance with best AUCs of 0.946.

Genetic status and molecular subtypes

With the development of high-throughput sequencing techniques, several genomic classification systems reflecting the complicated genomic mechanisms underlying GC have been proposed. The Cancer Genome Atlas (TCGA) has proposed a molecular classification including four subgroups: Epstein-Barr virus (EBV) status, microsatellite instable, genome stable and chromosomal instability. This system has been incorporated into the World Health Organization (WHO) classification (74,75). Epithelial-to-mesenchymal transition and TP53 mutation are key players in the development and progression of tumor. Based on these two mechanisms, the Asian Cancer Research Group categorized GC into four molecular subtypes, which correlate well with the progression and outcome of GC (76). The molecular subtypes showed better stratification ability for adjuvant chemotherapy (AC) and immunotherapy response (77,78). Thus, preoperative identification of molecular subtypes is of great significance for treatment management for GC patients. However, researches focusing on the association between AI methods and genetic information of GC are still rare. EBV-positive GC is related to better survival and response of chemotherapy. By utilizing the public database of TCGA and The Cancer

Imaging Archive, Zhao and colleagues constructed two radiomics models based on 2D or 3D features (38). Both models showed a good discriminating ability of EBV expression status. Zhang *et al.* developed a 9-feature radiomics model for predicting EBV status (39). The model also showed favorable accuracy with a sensitivity of 80% and a specificity of 84%.

The overexpression of human epidermal growth factor 2 (HER2) associates with a poor clinical outcome and plays a crucial role in tumorigenesis in GC (79,80). The ToGA trial demonstrated that anti-HER2 monoclonal antibody trastuzumab with chemotherapy prolonged survival of $HER2^+$ AGC patients (81). Therefore, trastuzumab is recommended as the first-line treatment for AGC patients with HER2 overexpression by National Comprehensive Cancer Network guidelines. However, GC is a highly heterogeneous disease. In contrast to breast cancer, which generally exhibits homogenous HER2 overexpression, intratumoral heterogeneity of HER2 status has been observed in GC (82,83). Therefore, an accurate evaluation of HER2 status is of great importance for predicting the treatment efficacy of HER2 target therapy. Wang *et al.* developed two radiomics models based on the AP and VP images for HER2 expression status in GC (40). Both models showed moderate accuracy for discriminating HER2-negative GC with AUCs ranging from 0.72 to 0.83.

Prognosis prediction

As GC is highly heterogeneous with significant clinical characteristics variations even within the same stage, the commonly used tumor-node-metastasis (TNM) staging system offers insufficient information for outcome prediction. Moreover, the TNM stage can only be precisely confirmed postoperatively. Therefore, several studies have investigated the potential and their added value of radiomics- and DL-based approaches for prediction of survival and recurrence risk of GC (41-44).

Li *et al.* found that radiomics features could effectively predict the OS of GC patients undergone radical resection (41). Jiang and colleagues built a radiomics signature with 19 features related to disease-free survival (DFS) and OS (42). Jin *et al.* proposed a radiomics signature for predicting DFS and OS for GC patients. In addition, the radiogenomics analysis showed that some of the radiomics features might be associated with genes involved in drug metabolisms and chemokine regulation (43). Shin *et al.* have explored the association between CT-based radiomics features and reccurence-free survival (RFS) in 420 locally AGC patients. A merged model consisting of the radiomics signature and significant clinical parameters showed better accuracy than the radiomics signatures and clinical parameters alone (44).

Jiang *et al.* utilized a novel deep neural network named "S-net" that integrated comprehensive multi-scale image features to predict the DFS and OS of GC patients (45). Unlike conventional CNN architectures, the S-net model integrates the idea of multi-level feature stream fusion. This design choice is based on the understanding that both low-level features from shallow layers and high-level features from deep layers contain valuable information for survival analysis. By incorporating this approach, the S-net model can effectively extract and integrate comprehensive multi-scale image features, enabling a thorough understanding of complex tumor phenotypes (45). While S-net leverages various high-level features for survival prediction (45), it overlooks the valuable shallow information due to the repeated pooling and convolution operations. Therefore, Zhang *et al.* further proposed a multi-focus fusion feature pyramid network which unified separate lower-level and fused higher-level features. In this model, a new designed strategy of cascade connection which extracts single and fused lower-level features maps in shadow bottom-top pathway. The model showed better performance than radiomics and conventional DL approaches (46).

Treatment response prediction

Chemotherapy is a routine treatment for improving the survival of GC patients. However, the overall efficacy rate of most regimens is less than 40% (84). Recently, conversion therapy, defined as a surgical treatment aimed at R0 resection after NAC for initially unresectable or marginally resectable tumors, emerged as another treatment opinion for metastatic AGC patients (82). Nevertheless, only 20–40% of patients show sensitivity to NAC (85,86). In addition, 40–60% of patients suffered recurrence after R0 surgery (87). Therefore, it is of great importance for identifying optimal candidates who could benefit from AC/NAC and thus avoid unnecessary toxicity. Several teams have investigated the potential of CT-based radiomics and DL methods for predicting AC/NAC response.

Jiang *et al.* developed a radiomics signature for evaluating tumor infiltrated lymphoid and myeloid cells. Their proposed radiomics signature could also serve as an AC response prediction tool (47). Li *et al.* built a radiomics

signature by extracting features from intratumoral and peritumoral regions of CT images. The radiomics signature showed good predictive ability for DFS and AC response for stage II/III GC (48). Li *et al.* developed an DL model which consisted of clinical, handcrafted radiomics and DL features for differential diagnosis of signet-ring cell carcinoma (49). The reported AUCs for predicting NAC response for AGC ranged from 0.68 to 0.89 (50,88-92). A significant portion of AGC patients do not achieve pathological downstaging after NAC. Thus, early and precise patient stratification would be beneficial in identifying suitable candidates for NAC. Xu and colleagues proposed a radiomics signature by utilizing restaging CT images for early detection of pathological downstaging with NAC for AGC. The model showed a promising prediction ability with an optimal AUC of 0.96, outperforming the routinely used Response Evaluation Criteria in Solid Tumors (RECIST) system (50).

Liu *et al.* developed a multi-energy radiomics model by extracting radiomic features from three different sets of monochromatic images derived from DECT. Their findings revealed that high-energy features achieved the best performance for AC response prediction. The predictive ability of the multi-energy model outperformed all the monochromatic radiomics models (51). Similarly, Wang *et al.* developed a radiomics model based on IU and M images to differentiate serosal invasion after NAC. The model showed great accuracy with AUCs of 0.95 and 0.91 (52).

Recently, analysis of the alteration of radiomics features pre- and post-treatment, refer as delta radiomics, has shown potential for predicting treatment response (93,94). Delta-radiomics is a radiomics-based approach that focuses on the analysis of changes or differences in radiomic features before and after treatment. It aims to capture and quantify the temporal changes in tumor characteristics. By comparing radiomic features extracted from pre- and post-treatment images, delta-radiomics can provide valuable information about treatment response, tumor progression, or the effectiveness of interventions (92). Tan *et al.* reported a delta radiomics model, revealing moderate predictive accuracy for AC response for AGC patients with an average AUC of 0.75 (53). However, in the study conducted by Chen and colleagues, radiomics features were extracted from 8 image series acquired by DECT, including VP-IU, VP-M, delayed IU, and delayed M images pre- and post-NAC. The pre-NAC IU-based model performed better than the delta radiomics model for predicting DFS and OS for AGC patients who received NAC (95). This result implies that the pretreatment images might provide more information for prognosis.

Immunotherapy, represented by inhibitors of programmed cell death-1 (PD-1), has shown encouraging efficacy in AGC patients. However, effective biomarkers for identifying beneficiary patients are still lacking. We developed and validated a radiomics signature for evaluating tumor-infiltrating regulatory T cells, which contributed to hyperprogression disease after PD-1 treatment (96). Liang *et al.* recently proposed a radiomics nomogram to predict PD-1 inhibitor response for AGC (54). The model showed good accuracy for identifying responders of anti-PD-1 therapy with AUCs of 0.87 and 0.78. Moreover, the model could also accurately predict the PFS of patients.

Challenges and future perspective

There are still some intractable limitations yet to be addressed in translating AI techniques from bench to bedside.

First and foremost, explainability is the biggest obstacle in translating AI models into routine clinical practice. The explainability in AI refers to the question of whether we can understand the reasoning and decision-making process behind the predictions or decisions made by ML and DL models (97). Due to the complex nature of DL models, which consist of numerous parameters and intricate non-linear functions, their internal workings are often difficult to intuitively interpret. Explainability is crucial for the application of AI, especially in domains where scrutiny, validation, and trust in the model's predictions are required, such as medical diagnosis (98). Currently, for most ML-based models, especially DL models, it is difficult to explain how the models made certain decisions, which refers to the "black box". However, transparency and explainability are essential for legal and ethical reasons in clinical medicine. Understanding how an ML-based model comes to its predictions is important to ensure fairness and increase the confidence of clinical practitioners when using it. In addition, AI models can be influenced by data biases, leading to unfair predictions for specific groups or attributes (98). Thus, better explainability can allow developers and end-users to identify potential biases of models and find ways to improve them. Recently, explanatory artificial intelligence (XAI) has drawn great attention from researchers. XAI aims to provide more transparent, explainable decisions for AI models. There are mainly three approaches for improving the explainability of ML models, including proxy models, visualization of CNN, importance estimators (5). Although

all these methods have not yet been widely used in the area of medical imaging, further advancement of XAI will possibly help the clinical application of AI models.

Secondly, repeatability and reproducibility are also crucial issues that need to be resolved. Only part of the studies reported the images acquisition, procession, and ML methodology in sufficient detail (15,19,20,22,24-26,29,31,33,36,37,44,47). The scanner parameter and the image pre-processing methods, target area delineation, feature extraction, and model building algorithm varied dramatically among studies. This underlines the need for a standardized methodology for CT acquirement protocol and AI analysis workflow. The Standards for Reporting of Diagnostic Accuracy Studies (STARD) statement recommends structured reporting for studies (99). A team promoted the Image Biomarker Standardization Initiative (IBSI) and provided standardized radiomics features to calibrate different software (100). These initiatives may help to improve the repeatability and reproducibility of research.

Thirdly, most of the current studies were retrospective and carried out in a single-center, which may also lead to the overfitting of the models. Prospective multicenter studies are needed to establish well-curated datasets and ensure the generalizability of the models. However, collecting and harmonizing imaging data from different centers are complex tasks technically. Most of the radiomic features are highly sensitive to the diversity of scanner manufacturers, acquisition protocols, and reconstruction algorithms. Therefore, it is difficult to draw direct comparisons and harmonization of results from different centers. The current standardization of imaging procedures is insufficient to overcome variations in radiomic feature distributions among centers. One popular method is resampling images to a unified voxel size and filtering images to get similar spatial resolution before feature extraction. However, this method may be insufficient to remove the center effect and can be harmful to texture analysis (7,101). DL networks are recently used to synthesize images with similar properties to obtain comparable features. Li *et al.* proposed a generative adversarial network-based normalization method which could reduce the variability of features obtained by different CT protocols and centers (102). The results showed that radiomic features extracted from harmonized images could effectively improve the accuracy of the LASSO classifier. In another study, by using a public CT texture phantom dataset, DL networks were trained to transform image features to improve their stability across varying CT devices and parameters (103). ComBat is a method for removing batch effects, initially used for genomic analysis. Recently, this method has been used in several multicenter studies for harmonization of radiomic features extracted from different scanners and institutions. The results showed that ComBat could effectively improve the predictive accuracy and stability of models (104-106).

Conclusions

AI-powered tools showed great potential to increase diagnostic accuracy and reduce radiologists' workload. However, the goal of AI is not to replace human ability but to help oncologists make decisions in their practice. Therefore, radiologists should play a predominant role in AI applications and decide the best ways to integrate these complementary techniques within clinical practice.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-201/rc

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