·综述·

New applications of MRI in rectal mucinous adenocarcinoma

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[**Abstract**] Rectal mucinous adenocarcinoma (RMAC) is a relatively rare but highly aggressive type of tumour, and its early diagnosis and accurate staging are highly important for disease prognosis. With the continuous development of medical imaging technology, MRI, a noninvasive imaging tool, is increasingly being used to diagnose rectal cancer. Although there have been several studies on the application of MRI in rectal cancer, there is still a lack of systematic summaries regarding the specific types, imaging characteristics, diagnostic challenges, and potential solutions for RMAC. In this review, we aim to summarize the MRI characteristics of RMAC, explore the current research status and application prospects of emerging technologies in this field, and provide references for clinical practice.

[**Key words**] Rectal mucinous adenocarcinoma; Magnetic resonance imaging; Diagnostic imaging
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磁共振成像在直肠黏液腺癌中的新应用

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[**摘要**] 直肠黏液腺癌(RMAC)是一种相对少见但侵袭性极强的肿瘤类型,其早期诊断和准确分期对患者的预后具有重要意义。随着医学影像技术的不断发展,MRI 作为一种无创成像工具,越来越多地应用于直肠癌的诊断。虽然目前已有多项关于 MRI 在直肠癌中应用的研究,但对于 RMAC 的具体类型、影像特点、诊断挑战和潜在的解决方案仍缺乏系统总结。本综述旨在总结 RMAC 的 MRI 特点,探讨目前该领域新兴技术的研究现状和应用前景,以期为临床实践提供参考。

[**关键词**] 直肠黏液腺癌;磁共振成像;诊断成像

Rectal mucinous adenocarcinoma (RMAC) is a distinct type of adenocarcinoma characterized by tumour tissue containing at least 50% mucus components[1]. The current study indicates that RMAC constitutes approximately 10% of all rectal cancers[2]. Epidemiological studies have demonstrated that the incidence of mucinous adenocarcinoma (MAC) varies significantly with geographic, ethnic, sex, and age. Geographically, MAC accounts for 6.9%-8.9% of relevant malignancies in China and 2.8%-3.82% in Japan, whereas Western populations such as the United States have higher proportions (10%-11.6%)[1,3]. Ethnic analyses revealed that while colorectal cancer subtypes were similarly distributed among Caucasians, African Americans, and other groups in the United States, Chinese Americans displayed a markedly lower MAC incidence (7.5%) than Caucasians (9.3%) and African American populations (9.4%), suggesting genetic and lifestyle influences[1]. Gender disparities have emerged in Western cohorts, with

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German and American studies reporting higher female proportions [Germany, 47% vs 41% nonmucinous adenocarcinoma (NMAC); American, 52.1% vs 48.6%], although no significant sex-based differences are observed in Chinese patients[1]. Age-related patterns further diverge as German data show no age distinction between MAC and NMAC cases, and American studies indicate elevated MAC rates in patients over 65 years old. In comparison, Chinese cohorts demonstrate a younger onset predominance (< 50 years)[3].

Clinically, the symptoms of RMAC are similar to those of other forms of rectal cancer, including changes in bowel habits, abdominal pain, and bloody stools. The symptoms of RMAC are difficult to distinguish from those of regular adenocarcinoma, which presents major diagnostic problems for medical practitioners. Moreover, as patients with RMAC are usually diagnosed with more advanced disease, their general prognosis is rather negative[1]. Numerous studies have shown that several factors influence the survival rate of patients with RMAC, including tumour differentiation, lymph node metastasis, and the clinical stage of the tumour[4]. Moreover, RMAC has a certain level of resistance to chemoradiotherapy, which further worsens its already poor prognosis. It has a poorer correlation with tumour downstaging and tumour regression grading[2]. Lee et al[5] reported, for example, that patients with RMAC had less favourable treatment outcomes and a worse disease prognosis among stage II or III colorectal cancer patients receiving FOLFOX (chemotherapy regimen) adjuvant chemotherapy. Shin et al[6] reported that following the first round of chemoradiotherapy, patients with RMAC had a worse disease prognosis and a lower T-stage downstaging rate than did patients with NMAC.

Currently, the diagnosis of RMAC primarily relies on tissue biopsy. However, conventional biopsy techniques may not accurately reflect the true characteristics of the tumour, particularly in larger or more deeply situated lesions, which could lead to false-negative results[7]. Furthermore, the processing and analysis of biopsy samples may be impacted by technical and expertise-related constraints, consequently influencing diagnostic accuracy[8].

MRI is a valuable noninvasive imaging technique for evaluating RMAC. It can visualize the mesorectal fascia, distinguish between the rectal wall layers, and reveal local lymph node involvement[1]. Preoperative staging of rectal cancer, surgical planning, and evaluation following neoadjuvant chemoradiotherapy all rely on MRI, which has some useful capacity. MRI is the present reference standard imaging modality for restaging rectal cancer and guides clinical care decisions, especially following neoadjuvant chemoradiotherapy[9,10]. To investigate the predictive elements of the response to chemoradiotherapy, MRI can also be used to precisely evaluate the number of mucin pools (MPs) in primary cancer tissue and compare it with the histological findings of resected samples[11].

This article comprehensively reviewed the MRI characteristics of RMAC, compared the advantages and disadvantages of MRI with those of other examination methods, analyzed its limitations in diagnosing RMAC, and explored the research status and application prospects of emerging MRI technologies. RMAC has different characteristics from NMAC on MRI, such as high signals on T2-weighted imaging (T2WI) and unique enhancement patterns. Emerging MRI technologies, such as diffusion-weighted imaging (DWI), diffusion kurtosis imaging (DKI), and dynamic contrast-enhanced MRI (DCE-MRI), provide important information for tumour diagnosis, staging, and treatment response prediction at the micro level, but they also face some challenges. In the future, the integration of MRI technology with artificial intelligence (AI) and radiomics is expected to lead to breakthroughs in the diagnosis and treatment of RMAC, improve the accuracy of clinical decision-making and the level of personalized treatment, and ameliorate the prognosis of patients.

1. MRI imaging characteristics of RMAC

RMAC exhibits distinctive MRI features in comparison with NMAC, reflecting their fundamental pathological differences. On T2WI, the MAC typically demonstrate hyperintense signals due to abundant extracellular mucin-containing water-rich mucoproteins, which contribute to the elevated T2 signal intensity. In contrast, NMAC predominantly displays intermediate T2 signals owing to its cellular composition of tightly packed tumour cells and fibrous stroma with minimal mucin content. The contrast-enhancement patterns further delineate these subtypes,

MACs frequently exhibit hypoenhancement during contrast-enhanced MR images, which is attributed to tumour cells dispersed within mucin pools that hinder the diffusion of contrast agents, whereas NMACs display significant enhancement due to their dense cellular structure and enhanced vascular supply. Additionally, MACs may display calcifications, likely resulting from dystrophic calcification secondary to tumour cell degeneration and mucin concentration, a feature rarely observed in NMAC. These MRI disparities, including signal intensity, enhancement characteristics, and calcification frequency, provide essential diagnostic criteria for distinguishing MAC from NMAC, ultimately enhancing preoperative diagnostic accuracy and guiding tailored therapeutic strategies (Fig. 1)[11].

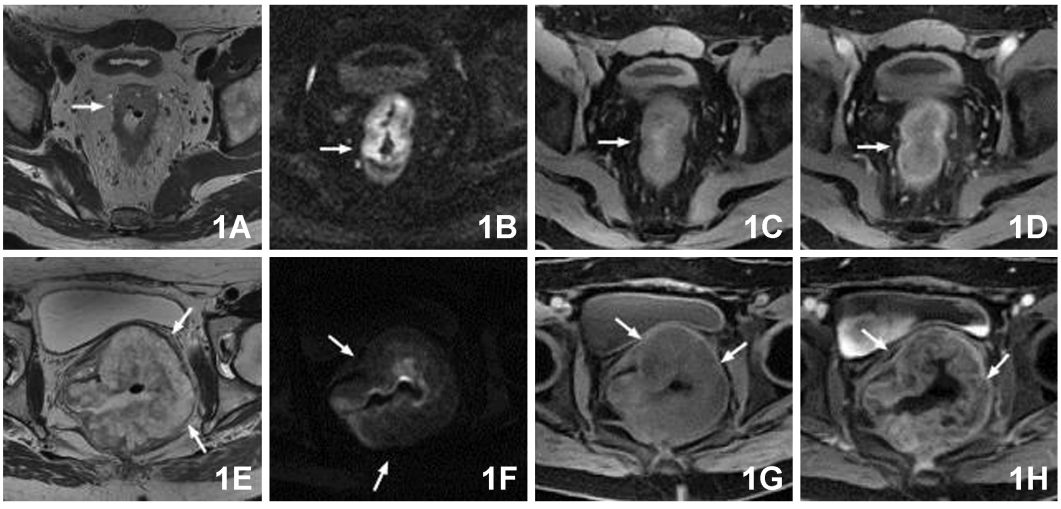

Fig. 1 MRI image comparison between rectal adenocarcinoma and mucinous adenocarcinoma [1]
A-D, Rectal adenocarcinoma(arrows); A, Axial non-fat suppressed T2WI illustrating irregular circumferential thickening of the rectal wall with a T2WI signal that was slightly elevated compared to fat; B, DWI revealing a high signal within the lesion; C, Axial T1-weighted imaging (T1WI) demonstrating low signal intensity; D, Axial contrast-enhanced T1WI showing moderate to high enhancement of the tumor; E-H, RMAC(arrows); E, Axial non-fat suppressed T2WI depicting wall thickening of the rectum, encompassing approximately three-quarters of the circumference, with a predominantly high signal on the left wall, interspersed with low signal regions adjacent to fatty tissue exhibiting T2 high signal; F, DWI primarily illustrating a high signal within the lesion; G, Regular T1WI presenting low signal intensity; H, Axial enhanced T1WI indicating enhanced tumor borders with low internal enhancement

In addition to the typical MRI features of RMAC, RMAC reveals notable variations from conventional adenocarcinoma on imaging. Particularly at the pathological T3 and pathological T4 stage, studies have shown that the tumour length of a RMAC is often longer than that of a traditional adenocarcinoma[12]. Furthermore, the lymph node metastasis properties of RMAC differ from those of typical adenocarcinoma. Compared with conventional adenocarcinoma, RMAC usually results in smaller maximum lymph node diameters in patients without lymph node involvement (pN0). Moreover, in patients with lymph node involvement(pN+), RMAC is associated with a greater degree of internal lymph node heterogeneity[12]. This may indicate a greater malignant potential and risk of metastasis[13]. These imaging disparities help clinicians distinguish between RMAC and classic adenocarcinoma during diagnosis and affect the creation of treatment plans. Therefore, understanding the differences in imaging characteristics between RMAC and other types of rectal cancer is highly important for clinical practice.

2. Applications of emerging MRI technologies in the diagnosis of RMAC

In the field of rectal cancer diagnosis and treatment, MRI technology plays an increasingly important role, especially in the diagnosis of RMAC, which has attracted much attention. Currently, conventional MRI methods such as T1WI and T2WI can provide doctors with information about the basic morphology and location of tumours. Emerging technologies, including DWI, DKI, DCE-MRI, amide proton transfer (APT) imaging, magnetization transfer imaging (MTI), and magnetic resonance spectroscopy (MRS), can be used to analyse tumour characteristics at the microscopic level and are highly important for

tumour diagnosis, staging, and treatment response prediction.

2.1 DWI: DWI assesses the movement of water molecules within tissues, providing valuable insights into tumour cell density and microenvironmental changes. DWI has diverse applications in rectal cancer management. The routine use of DWI is included in the European Society for Radiotherapy and Oncology (ESTRO) guidelines for initial staging and reassessment after neoadjuvant therapy (NAT)[14]. However, the role of DWI in tumour detection and staging is limited, and it has no additional value in the T staging of rectal cancer[14].

DWI depicts RMAC as a low-intensity signal compared with adenocarcinoma because the mucinous component results in reduced cellularity. Measuring the apparent diffusion coefficient (ADC) (used to describe the speed and range of molecular diffusion motion in different directions in the DWI sequence) allows for differentiation between various rectal types of tumours and RMAC, with the latter exhibiting a greater ADC[15].

In RMAC, these parameters are intimately linked to tumour progression and biological characteristics, rendering DWI a valuable modality for tumour assessment. The diagnosis RMAC and differentiating it from tubular adenocarcinoma may be difficult. The mucinous elements in both tumour types typically demonstrate high signal intensity on T2WI, complicating differentiation[16]. Nonetheless, DWI may provide supplementary value. Compared with tubular adenocarcinoma, RMAC has increased DWI signal intensity and reduced overall signal uniformity[16]. Moreover, studies have indicated that ADC values may assist in distinguishing mucinous carcinoma from adenocarcinoma because of its distinct diffusion properties[15].

2.2 DKI: The traditional approach utilized in DWI assumes that the displacement of water molecules adheres to a Gaussian distribution pattern. However, owing to the intricate microenvironment of biological tissues, nonGaussian diffusion movements of water molecules also occur[17]. Consequently, DKI, a novel nonGaussian diffusion model, has been developed. In the field of rectal cancer diagnosis, numerous studies have focused on DKI technology, delving into its value in diagnosing rectal cancer. These investigations investigating its role in evaluating pathological prognostic factors, predicting responses to neoadjuvant chemoradiotherapy, determining lymph node metastasis, differentiating mismatch repair (MMR) status, and preoperative grading.

Song et al[18] utilized multiple DWI techniques, including DKI, for the preoperative grading of rectal cancer. The results revealed significant differences in the DKI-derived parameter mean kurtosis (MK) (used to quantify the degree to which water molecule diffusion behaviour deviates from a Gaussian distribution, reflecting the complexity and heterogeneity of tissue microstructure) between low-grade and high-grade rectal cancers. Furthermore, a logistic regression-based machine learning model incorporating multiple DWI-derived metrics, including DKI, exhibited robust diagnostic efficacy in preoperative grading [area under the curve (AUC), 0.902, 95% *CI*, 0.754-1.000; specificity, 0.856; sensitivity, 0.925; Youden index, 0.781]. These findings further underscore the diagnostic potential of DKI in the preoperative grading of rectal cancer[18].

Among the DKI parameters used to evaluate pathological prognostic factors, the MK is significantly associated with histological differentiation, lymph node metastasis (LNM), and extramural vascular invasion (EMVI) in patients with rectal cancer. Multivariate *logistic* regression analysis revealed that a higher MK and lower ADC were independently associated with poorly differentiated tumours; A higher perfusion fraction (f) and MK were correlated with LNM, and a higher f, MK, lower mean diffusivity (MD) (used to represent the nonGaussian deviation-corrected diffusion coefficient, reflecting the diffusion capacity of water molecules within tissues), and lower ADC were independently linked to EMVI. When these pathological prognostic factors were assessed, MK demonstrated superior diagnostic efficacy compared with parameters such as ADC, with higher AUC values for evaluating histological differentiation, LNM, and EMVI. This study revealed that DKI parameters can serve as imaging biomarkers for the preoperative assessment of pathological prognostic factors in patients with rectal cancer[17]. Yin et al[19] reached similar conclusions by comparing the efficacy of DKI with that of other imaging techniques in evaluating LNM in patients with rectal cancer. The MK value in the LNM-

positive group was significantly greater than that in the LNM-negative group, whereas the MD value was significantly lower. Furthermore, the diagnostic performance of DKI (MD + MK) significantly surpassed that of conventional DWI and restricted spectrum imaging, achieving an AUC of 0.908, a sensitivity of 87.10%, and a specificity of 86.96%. These findings highlight the substantial value of DKI in assessing lymph node metastasis in patients with rectal cancer.

Synthetic DKI images generated via a multitask reconstruction network combined with radiomic methods can be used to predict pathological complete response (pCR) to neoadjuvant chemoradiotherapy (nCRT) in patients with locally advanced rectal cancer[20]. Radiomics models constructed from real and synthetic DKI images demonstrated similar performance in predicting pCR, with AUC values of 0.825 and 0.807, respectively[20]. These findings indicated that synthetic DKI images exhibit comparable efficiency to real DKI images in predicting the nCRT response, suggesting a novel approach for the clinical assessment of treatment efficacy.

Chen et al[21] performed DKI scans and histogram analysis on patients with rectal cancer and revealed that among the quantitative DKI parameters, the apparent diffusion coefficients for non-Gaussian distributions (D) values (D10th, D25th, and D50th) of the deficient mismatch repair (dMMR) group were lower than the proficient mismatch repair (pMMR) group (P=0.031, 0.001, and 0.002, respectively), with AUC of 0.687, 0.773, and 0.808, respectively. In comparison, dMMR group presented a greater kurtosis coefficient (K) values (K75th, K90th, and Kskewness) than did the pMMR group, and the K kurtosis was lower than the pMMR group (P<0.05), and the AUC were 0.712, 0.788, 0.835, and 0.684, respectively. These findings suggest that DKI-derived parameters can help differentiate the MMR status in patients with rectal cancer, offering new opportunities for guiding personalized clinical treatment strategies.

These efforts provide critical foundations for the precise diagnosis and treatment of rectal cancer. However, research specifically targeting RMAC is scarce. Nonetheless, existing findings establishes a strong foundation for further exploration into the application of DKI in diagnosing RMAC.

2.3 DCE-MRI: DCE-MRI is a sophisticated imaging modality capable of providing quantitative pharmacokinetic metrics. It has demonstrated significant clinical applicability in the assessment of tumour vasculature and perfusion across a variety of organs[22], which is highly important for the biological behaviour of RMAC.

To further investigate the predictive value of DCE-MRI, Katja et al[23] carried out a prospective study and carried out MRI examinations on 95 patients who had rectal cancer (21 of whom had MAC) both before and after they received neoadjuvant chemotherapy and radiation therapy. According to previous findings, the contrast agent exchange rate (K21) of NMAC was significantly greater than that of MAC prior to treatment. This is primarily attributable to a significant number of extracellular mucin pools in the MAC, which leads to a decrease in the relative capillary surface area. K21 has become an important indicator for evaluating tumour microvessel density and vascular function, providing a key basis for gaining insight into the vascular characteristics of RMAC. It is closely related to factors such as the surface area, permeability and interstitial space of tumour blood vessels. K21 is also closely related to the interstitial space. The findings of the present study also demonstrated that neoadjuvant chemotherapy and radiation therapy had a more significant influence on dynamic magnetic resonance parameters in NMAC, which also demonstrated a more favourable response to treatment. According to multivariate analysis, mucinous histology was a predictor of poor response. However, patients with a K21 value at or above the 75th percentile had a more favorable treatment respense. The results of this study suggest that K21 can serve as an efficient biomarker to identify patients who are more likely to have a favourable response to neoadjuvant therapy, making it easier to make individualized decisions regarding therapeutic treatment.

In a separate study, Maria et al[22] investigated additional DCE-MRI parameters, including Ktrans (the forwards volume transfer constant representing influx between plasma and the extracellular-extravascular compartment) and Kep (the rate constant representing exchange between the extracellular-extravascular space and plasma). Their findings indicated that the pretreatment Ktrans values were

elevated in patients who achieved a pCR relative to those who did not, whereas Kep values were diminished in the pCR cohort. Despite the lack of statistically significant changes in posttreatment Ktrans, the notable reduction in posttreatment Kep within the pCR group indicates that Kep may serve as a superior marker for residual tumour burden and treatment effectiveness.

These findings emphasize the potential of DCE-MRI parameters, particularly Kep, in assessing the tumour response and predicting the pCR. Integrating these biomarkers into clinical protocols could improve treatment stratification, optimize therapeutic strategies, and enhance patient outcomes.

2.4 APT Imaging: APT imaging is a molecular MRI technique derived from chemical exchange saturation transfer (CEST) imaging[24]. CEST operates as an imaging modality that exploits endogenous proton groups within biological tissues—including amide, amine, and aliphatic protons—to generate image contrast[24].

In the pursuit of diagnostic and prognostic biomarkers, Li et al[25] reported that the mean APT signal intensity exhibited greater diagnostic capacity than did the ADC in predicting distinct p53 and Ki-67 expression statuses in patients with rectal adenocarcinoma, with AUC values of 0.757 and 0.920, respectively. In a prospective study involving 61 rectal adenocarcinoma patients who underwent 3D amide proton transfer-weighted (APTw) imaging, Chen et al[26] identified a significant positive correlation ($r=0.550$) between the mean APTw value and WHO histological grade. Furthermore, the mean APTw value demonstrated superior performance compared with other imaging biomarkers in distinguishing low-grade from high-grade rectal adenocarcinomas, attaining 92.31% sensitivity and 79.17% specificity[26]. Consistent findings were reported in the study by Li et al[27]. Their results revealed markedly higher APT signal intensity in WHO high-grade rectal adenocarcinomas than in low-grade rectal adenocarcinomas [(2.668 ± 0.638)% vs (2.226 ± 0.347)%]. Moreover, a marked disparity in APT signal intensity was observed between conventional adenocarcinomas and RMACs [(3.192 ± 0.661)% vs (2.333 ± 0.471)%][27].

2.5 MTI: MTI is an advanced MRI technique that exploits interactions between free protons and macromolecularly bound protons to assess tissue composition. An analysis of the correlation between the magnetization transfer ratio (MTR) and the histological tumour regression grade (TRG) demonstrated that the MTI is crucial for assessing therapeutic response in the context of RMAC. The 95th percentile MTR, with an AUC of 0.88, effectively distinguishes between positive and negative treatment responses. This enhanced diagnostic performance addresses the shortcomings of conventional imaging in differentiating residual tumours from fibrosis[28]. Moreover, histogram-based analysis of MTI data offers quantitative insight into tumour heterogeneity, enabling more precise delineation of residual disease and treatment responsiveness[28]. When combined with DWI, MTI offers a more comprehensive appraisal of treatment effectiveness by combining anatomical and functional imaging biomarkers, thus enhancing the distinction between viable tumour and post-treatment changes. Nonetheless, current research remains constrained by limited cohort sizes, variability in therapeutic protocols, and insufficient pathological validation, potentially impacting the generalizability of the results. Future research should focus on standardizing imaging protocols, the inclusion of larger study populations, and improving histopathological correlation to improve the clinical utility of MTI.

2.6 MRS: MRS is a noninvasive imaging modality that provides comprehensive metabolic insights about biological tissues. It holds significant potential in diagnosis and monitoring of tumours[29,30]. Through metabolic profiling encompassing alterations in mucin, phospholipid, choline, and lipid concentrations, MRS facilitates tumour classification and biological characterization[29,30]. This technique is particularly valuable for distinguishing RMAC from other subtypes of rectal cancer because it highlights mucin and phospholipid features, offering important novel perspectives on tumour biology and treatment responsiveness.

3. Comparison of MRI with other common examination methods

In the diagnostic evaluation of RMAC, selecting an appropriate diagnostic method is crucial because it directly influences the accuracy of disease assessment of the disease, the formulation of therapeutic

strategies, and the prognosis of the disease. Although MRI remains highly valuable in RMAC diagnosis, it is not the sole option. Clinically, several other diagnostic techniques are employed, such as endorectal ultrasound (ERUS), computed tomography (CT), positron emission tomography-computed tomography (PET-CT), and histopathological biopsy. Each modality possesses distinct advantages and limitations and serves differing functions across various clinical contexts. Comparing MRI with these standard diagnostic methods allows clinicians to develop a more holistic understanding of the characteristics of each approach. On the basis of individual patient factors, including the stage of the disease, physical condition, and financial situation, the most appropriate diagnostic tool can be chosen, thereby facilitating accurate diagnosis and forming a robust basis for subsequent personalized treatment. Table 1 presents an overview of the advantages and disadvantages of these investigative approaches in the diagnosis of rectal cancer and their specific roles in the context of RMAC.

Table 1 Comparison of different examination methods

method	advantage	disadvantage	clinical role in RMAC	reference
MRI	1. Excellent soft tissue resolution 2. Accurately visualizes mesorectal fascia, circumferential resection margin (CRM), EMVI, and mucin pools 3. High sensitivity/specificity in T/N staging 4. No radiation exposure	1. Not applicable to patients with metal implants in the body 2. High cost and longer examination time 3. Limited availability in some settings 4. May overestimate fibrosis post-chemoradiotherapy (CRT)	1. Preferred modality for local staging 2. Distinguishes mucinous vs. non-mucinous subtypes 3. Monitors response to CRT	[11-13, 16, 22, 23, 27-33]
ERUS	1. High resolution for superficial and distal lesions 2. Superior for early T staging (T1/T2) 3. Cost-effective and widely available	1. Limited depth penetration 2. Poor performance for high or complex lesions 3. Ineffective in post-CRT assessment or for mucinous content	1. Adjunct tool for early-stage tumors 2. Limited utility in RMAC due to mucin pool interference	[34, 35]
CT	1. Fast and widely accessible 2. Effective for detecting distant metastases 3. Good spatial resolution	1. Low soft tissue contrast 2. Inaccurate CRM assessment 3. Ionizing radiation exposure	1. Useful for systemic staging 2. Limited role in assessing local invasion in RMAC	[34, 36-38]
PET-CT	1. Detecting distant and small metastases 2. Evaluating metabolic activity 3. Altering treatment plan in advanced disease.	1. Low sensitivity for mucinous tumors 2. Expensive, limited access 3. Inferior to MRI for local staging	1. Adjunct for metastasis detection 2 Limited utility in RMAC due to low fludeoxyglucose (FDG) uptake in mucinous tissue	[11, 33, 39-41]
pathological biopsy	1. Gold standard for diagnosis 2. Providing cellular/molecular details 3. Confirming histological subtype	1. Risk of sampling error, especially in deep/large lesions 2. Invasive 3. Expertise-dependent	1. Essential for definitive diagnosis 2. Limited by sampling and cannot represent whole-tumor heterogeneity	[7, 8]

3.1 ERUS: ERUS is a highly accurate, noninvasive imaging modality for evaluating early rectal cancers, particularly low-lying tumours, due to its superior spatial resolution[35]. After studies using endorectal coilare excluded, ERUS exibits superiority in overall T staging T1/T3 substaging and N staging, while MRI is more suitable for T2 staging[35]. Both modalities showed comparable performance in N staging (ERUS AUC = 0.90 vs. MRI AUC = 0.86, $P = 0.11$). When studies using endorectal coils are excluded, ERUS maintains superiority in overall T staging, T1/T3 substaging, and N staging, whereas MRI remains preferable for T2 staging [35]. ERUS is limited in its ability to assess high rectal tumours, large/complex lesions, and critical prognostic factors (e.g., extramural depth, mesorectal fascia involvement, and EMVI). ERUS struggles in differentiating T3a (minimal extramural invasion) from T3b (significant invasion with extramural vascular invasion, EMVI), achieving a diagnostic accuracy of 67.4%-79.1%, sensitivity of 60%-66.7%, and specificity of 82.1%-85.7%, whereas MRI shows greater sensitivity and specificity, although there is no statistically significant difference in overall accuracy ($P > 0.05$)[42]. It also fails to distinguish tumour infiltration from peritumoral fibrosis, hindering post-chemoradiotherapy

evaluation[42]. In RMAC, MRI markedly outperforms ERUS owing to its T2WI proficiency, which distinctly identifies mucin pools as hyperintense regions. Although studies utilizing ultrasound for RMAC are scarce, recent research has revealed the unique sonographic characteristics of RMAC through three-dimensional ultrasound. This encompasses extended segmental involvement, a prevalence of flat-type lesions, and well-preserved multilayer intestinal wall components observable in longitudinal sections[34]. A concentric ring sign in the transverse section has been identified as a possible diagnostic characteristic. The therapeutic value of ERUS in RMAC is unsatisfactory because the increased mucin content obscures lesion borders and impacts staging accuracy[34].

In summary, ERUS is a valuable method for assessing the rectal cancer stage, particularly in cases involving tumours in distal organs. ERUS has the highest accuracy for precise staging evaluation when the tumour is located 3 to 6 cm above the anal canal[43]. Despite its accessibility and low cost, the ERUS examination has certain limitations. It should not be utilized as the sole imaging modality for rectal cancer; instead, it serves as a useful adjunct in the diagnostic and therapeutic process.

3.2 CT: CT plays a crucial role in the diagnosis of rectal cancer, particularly in tumour staging and metastasis detection. It demonstrates high accuracy in both local and systemic staging of rectal cancer. For example, a study revealed that the overall accuracy of T staging by CT in the tumor node metastasis classification(TNM) classification of rectal cancer was 76.9%[44]. In particular, in distinguishing between T3 and T4a stages, the sensitivity and specificity are 70.6% and 100%, respectively[36]. Owing to its unique ability to identify distant tumour metastases, it may vividly show the size, location, and depth of lesions as well as the degree of invasion into nearby tissues and organs[31]. The ability of CT to visualize internal tissue layers, particularly in terms of soft tissue contrast, is limited[34]. Consequently, clearly delineating the boundary between the tumour and adjacent normal tissues is challenging, particularly when evaluating the involvement of the CRM, as the accuracy of CT imaging is relatively low in this context[45]. When the CRM is less than 1 mm, it is challenging to detect using CT; However, MRI can accurately assess it through high-resolution imaging[46,47]. In evaluating lymph node metastasis, a study demonstrated that the sensitivity of CT alone for detecting lymph node metastasis was 55.2%, whereas the specificity was 67.0%[48]. In comparison, MRI has a sensitivity of 72% and a specificity of 80% in detecting lateral lymph node metastasis[49]. The most significant disadvantage of CT, meanwhile, is that it uses ionizing radiation, which might endanger some groups, pregnant women in particular[37]. CT is also prone to overlooking minor mucosal lesions since it has reduced sensitivity in identifying early and mild lesions[38]. Furthermore, CT usually shows eccentric thickening of the bowel wall with peripheral enhancement in the imaging examination of RMAC (Fig. 2)[34,38]. Although CT is useful in determining distant metastases, its restrictions in tumour staging make it not the recommended imaging modality for analysing RMAC invasion[34].

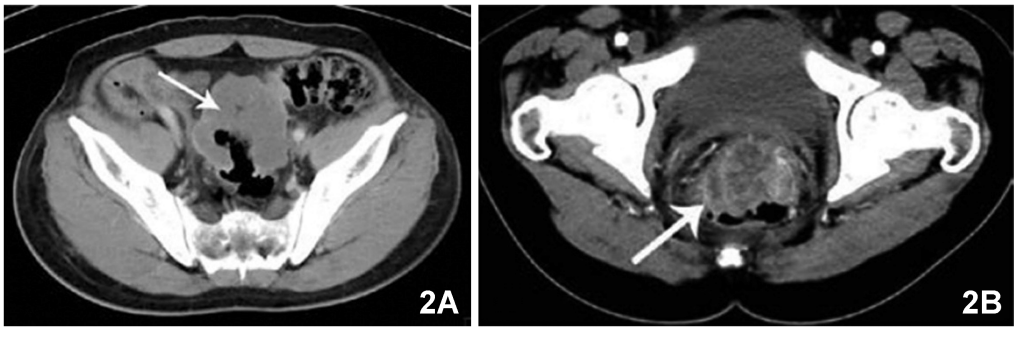

Fig. 2 CT of RMAC and NMAC[45]

A, CT of a 52-year-old male with RAMC, CT scan showing severe thickening of the rectal wall and a large area of low attenuation (arrow); B, CT of a 55-year-old male with NMAC, CT scan showing thickening of the rectal wall due to mass formation with heterogeneous enhancement (arrow)

3.3 PET-CT: PET-CT is a crucial imaging modality for detecting small metastatic lesions and quantitatively assessing tumour metabolic activity at the molecular level. It serves as a supplement to traditional imaging in informing treatment decisions, especially when a definitive diagnosis is unattainable[39]. PET-CT has high accuracy in the preoperative staging of rectal cancer, particularly in detecting lymph node and distant metastases. Studies have shown that PET-CT can identify small metastatic lesions that are often difficult to detect using traditional imaging modalities such as CT or MRI, thereby providing more comprehensive information for treatment decisions[50,51]. In one study, PET-CT detected additional lesions in 45% of patients that were not identified by conventional imaging, resulting in a change in staging for 30% of these patients[51]. PET-CT, when combined with deep learning and radiomics features, can effectively predict the lymph node metastasis status in patients with rectal cancer. For example, one investigation developed a predictive model integrating deep learning, radiomics, and clinical features, achieving AUC values of 0.934, 0.902, and 0.836 in the training, validation, and test cohorts, respectively, thereby indicating robust predictive capability[50]. These findings indicate that PET-CT is highly valuable in the preoperative assessment of lymph node metastasis. In guiding therapeutic decision-making, PET-CT has had a considerable impact on the surgical management of patients with rectal cancer. For example, one study reported that PET-CT influenced surgical plans in 14% of patients with liver metastases, 20% of those with lung metastases, and 23% of those with locoregional recurrence[52]. Additionally, PET-CT contributes to the identification of resectable metastatic lesions, thereby potentially enabling curative surgical intervention[52]. Although PET-CT offers several benefits in the assessment of rectal cancer, it also has certain limitations. For example, PET-CT has relatively low sensitivity (15.3%) in detecting small lymph node metastases measuring less than 7 mm[53]. Compared with conventional imaging techniques such as CT and MRI, PET-CT has distinct advantages in detecting distant metastases[51]. However, regarding local tumour staging (e.g. T staging), PET-CT does not exhibit significantly superior accuracy compared with MRI. Consequently, PET-CT is typically employed as a diagnostic tool complementary to conventional imaging modalities rather than as a replacement.

The accuracy of assessing RMAC is still controversial. The reduced cellular density of extensive extracellular mucin reservoirs in mucinous tumours causes either a whole or partial decrease in glycolytic activity[40]. This increases the likelihood of false-negative PET-CT results. Research has demonstrated that tumours with substantial mucinous content have markedly decreased FDG uptake, hence compromising the diagnostic precision of PET-CT. In contrast, tumours with a greater cellular component may display moderate ^{18}F-fluorodeoxyglucose (^{18}F-FDG) absorption[11]. Some recent investigations revealed no appreciable differences in metabolic ^{18}F-FDG PET parameters [e.g., maximum standard uptake value (SUV) and SUV_{mean}] between RMAC and NMAC (Fig. 3)[33,41]. PET-CT alone may be insufficient for accurate RMAC diagnosis because of the diverse nature

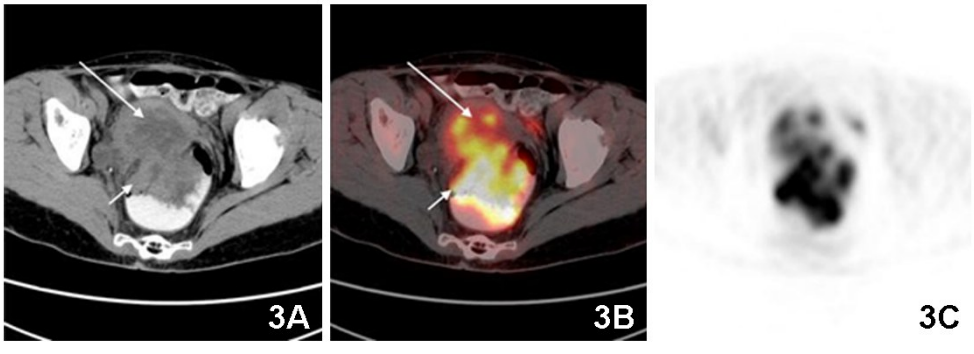

Fig. 3 Axial images obtained from ^{18}F-FDG PET/CT in a 65-year-old female patient diagnosed with RMAC[49]
A, B, CT image and PET-CT fusion image, iodinated contrast-enhanced CT of the rectal region reveals notable thickening of the rectal wall accompanied by a substantial zone of decreased attenuation (long arrow), which demonstrates reduced metabolic activity in comparison to the more solid area identified by the short arrow; C, PET image

of mucinous tumours. In challenging circumstances, adjunct imaging techniques, such as MRI with diffusion-weighted imaging, may enhance diagnostic precision.

3.4 Pathological biopsy: Pathological biopsy remains the principal approach for diagnosing RMAC, but it has certain limitations. For tumours in larger or deeper locations, conventional biopsy techniques may fail to accurately capture the tumour's true pathological features, resulting in false-negative results[7]. In addition, the processing and analysis of biopsy specimens are vulnerable to the limitations of technology and professional knowledge, affecting the accuracy of diagnosis[8]. MRI, as a noninvasive imaging modality, allows for comprehensive visualisation of the morphology, anatomical positioning, and invasion range of the tumour as a whole without causing damage to the patient, offering valuable adjunctive information for clinical diagnosis. Although MRI cannot supplant histopathological assessment entirely, it can complement pathological methods to improve the accuracy and reliability of diagnosis. Before surgery, MRI can help doctors better understand the tumour situation and formulate more targeted and effective biopsy strategies. After surgery, MRI can be used to assess the therapeutic efficacy and detect potential tumour recurrence, whereas histological examination can be used to provide detailed insights into the cellular architecture, providing a basis for further treatment.

4. Limitations and deficiencies of MRI technology in RMAC diagnosis

RMAC is a unique subtype of rectal cancer in which precise staging and infiltration evaluation are essential for treatment strategy formulation. Advancements in imaging technology have rendered MRI the principal instrument for RMAC assessment, owing to its exceptional soft tissue resolution. MRI facilitates an accurate evaluation of tumour infiltration depth, intestinal wall stratification, tumour engagement with the mesorectal fascia (MRF), and pelvic lymph node involvement, offering critical imaging data for surgical decision-making and neoadjuvant therapy planning. Furthermore, MRI has excellent sensitivity and specificity in the diagnosis of RMAC, accurately delineating the degree of local tumour invasion[9]. Therefore, the application of MRI in RMAC assessment has become a clinical standard, facilitating personalized treatment strategies with greater precision.

4.1 Tumour staging: MRI evaluation of RMAC depends on the TNM staging system and American Joint Committee on Cancer (AJCC) recommendations. Precise T staging is essential, as it dictates therapeutic approaches. Research indicates that 3T MRI attains significant diagnostic precision for RMAC staging, 97.6% for T1, 92.1% for T2, 89% for T3, and 90% for T4[13], establishing it as the recommended imaging modality for preoperative evaluation[9]. Currently, the treatment for RMAC is the same as that for ordinary adenocarcinoma, but different T stages require different treatment approaches. Local excision procedures may be employed for tumours in the T1 stage. At the T2 stage, more extensive surgical procedures, such as low anterior resection or abdominoperineal resection, are needed. In instances of locally advanced rectal carcinoma, it is imperative to perform an entire mesorectal excision subsequent to neoadjuvant therapy. Thus, precise identification of the T stage is highly important[32]. Moreover, RMAC is far more prone to cause peritoneal spread than conventional adenocarcinoma[10]. Although discontinuous mucinous implants are generally inconspicuous, they are more prevalent than conventional adenocarcinomas are. In the absence of fat saturation, they often exhibit T2-weighted signal intensities akin to those of fat and fluid (Fig. 4)[12]. Identifying these deposits is crucial since their existence elevates the patient's status to T4a if the peritoneal reflection is involved and to stage IV if tumour cells are found in more distant areas of the peritoneum.

4.2 Lymph node staging: MRI-based criteria have been established to assess the likelihood of malignancy in lymph nodes during initial rectal imaging. The criteria encompass lymph node dimensions, signal intensity, border attributes, and morphology. In RMAC, lymph nodes with mucin should be regarded as suspicious, irrespective of their size[54] In RMAC, insufficient lymph node staging presents a concern, as lymphatic vessels may allow tumour cells to disseminate into the peritoneal cavity[55]. This infiltration hinders the identification and assessment of metastatic lymph nodes[55]. Current research indicates that the attributes of lymph node metastasis in RMAC differ from those in traditional adenocarcinoma. The internal heterogeneity

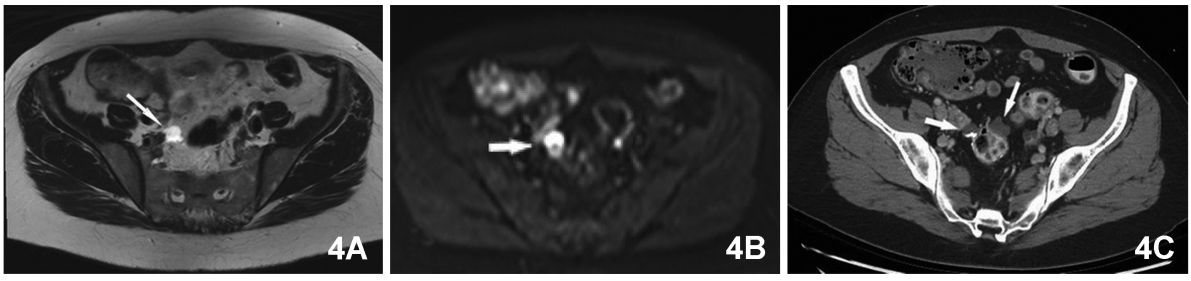

Fig. 4 A 40-year-old female patient presenting with a documented history of polycystic ovarian syndrome is presented[12]
A, An axial T2-weighted MRI image revealing the presence of a mucin pool adjacent to the peritoneal lining (white arrow); B, Image displaying the aforementioned pool (white arrow) as observed on an axial diffusion-weighted imaging MRI; C, Image illustrating the pools (white arrows) identified on an axial contrast-enhanced CT scan

is more pronounced, and MRI assessments indicate that the best cut-off values for the short diameter of malignant lymph nodes differ between the two types (6.05 mm for RMAC and 8.05 mm for traditional adenocarcinoma)[12]. Fig. 5 illustrates exemplary instances of lymph node metastasis in both RMAC and conventional rectal adenocarcinoma. MRI has the ability to detect the mesenteric fascia and identify patients with unresectable lymph nodes. It can also be used to comprehensively evaluate tumour dissemination, its association with adjacent structures, and mesorectal infiltration. Accurate diagnosis of regional lymph nodes is essential in the context of neoadjuvant treatment, as it prevents misjudgement prior to treatment and enables the development of personalized treatment strategies. Given the aforementioned factors, doctors must remain attentive to lymph node status while diagnosing RMAC and should construct definitive assessment criteria to ascertain lymph node metastases of RMAC.

4.3 Evaluating the invasion of adjacent organs: MRI is essential for evaluating the spatial relationship and extent of invasion between the tumour and surrounding tissues. This is especially beneficial for assessing tumour infiltration into the mesentery, bladder, vaginal wall, and adjacent tissues. The RMAC tends to increase fistula development and infiltration into adjacent tissues, a trait similar to that noted in MACs originating from various source sites[10]. This aggressive local invasion is mainly attributed to the abundance of extracellular mucin, which promotes tumour dissemination outside the rectal wall. Likewise, rectal invasion by neighbouring appendiceal or cervical MACs may have the same imaging characteristics on MRI (Fig. 6)[10]. These tumours often appear as ill-defined masses with T2-hyperintense mucin pools and irregular margins and tend to infiltrate locally and extensively.

4.4 Evaluating extramural vascular infiltration: MRI has become a widely endorsed modality for assessing EMVI in invasive rectal carcinoma. Evidence suggests that MRI has high sensitivity and specificity, with

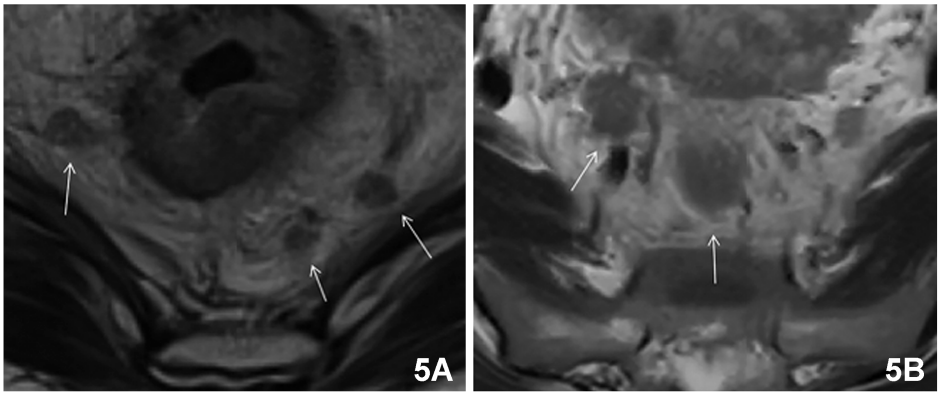

Fig. 5 MRI of lymph node metastasis in RMAC and conventional rectal adenocarcinoma[15]
A, A 37-year-old female patient with T3N2 RMAC, the metastatic lymph nodes did not exhibit a signal-intense mucin pool, the maximum short diameter observed in the lymph nodes was 6 mm, and at least one lymph node displayed internal heterogeneity (indicated by arrows); B, A 52-year-old female with classic rectal adenocarcinoma accompanied by a T3N2 tumor, the maximum short diameter of the lymph nodes measured 14 mm, exhibiting a round shape with an irregular peripheral contour (indicated by arrows)

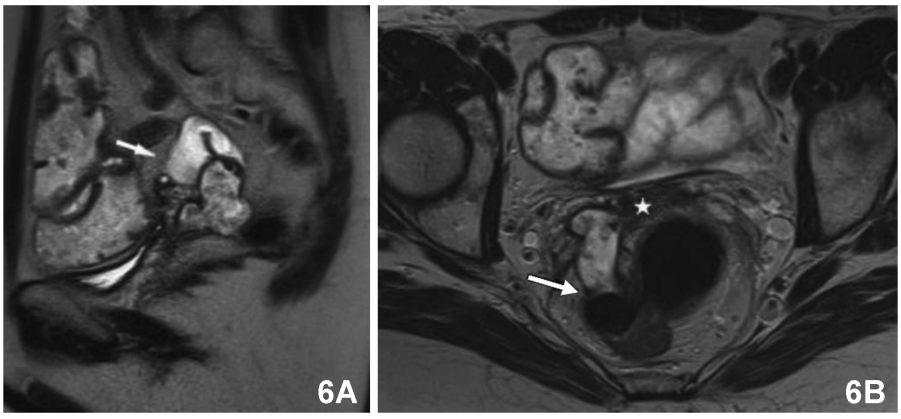

Fig. 6 MRI of appendiceal mucinous adenocarcinoma invading the vagina and rectum[12]
A, T2-weighted sagittal MRI, a 67-year-old female patient exhibited symptoms of vaginal discharge, with an initial suspicion of rectal carcinoma extending into the vaginal area, a comprehensive staging evaluation revealed an appendiceal mucinous adenocarcinoma (indicated by the white arrow); B, Axial MRI, appendiceal mucinous adenocarcinoma infiltrating the apex of the vagina (marked by the white star) and the rectum (noted by the white arrow)

detection accuracy reaching up to 95%[13]. This is particularly significant because the presence of EMVI correlates with an adverse prognosis, even in patients with rectal cancer who exhibit a favourable response to preoperative chemoradiotherapy[10]. The precise identification of EMVI is critical for informing therapeutic decisions, as it is frequently linked to decreased disease-free survival. DWI, a complementary MRI technique, offers valuable insights into tumour cellularity and aids in evaluating the extent of tumour infiltration[32]. However, it is imperative to exercise caution when using DWI to detect small lesions, as the restricted diffusion that potentially attributable to sluggish intravascular flow can yield false-positive results. Patients exhibiting EMVI may necessitate more intensive therapeutic strategies to optimise clinical outcomes, given the predictive significance of EMVI. The accurate evaluation of EMVI and tumour spread via MRI is indispensable for the development of individualised treatment protocols in RMAC.

5. Future directions

With the continuous development of AI, the deep integration of MRI-based radiomics and AI will lead to revolutionary changes in the diagnosis and treatment of RMAC. Radiomics can extract massive quantities of quantitative features from MR images. Given its robust data analysis and pattern recognition capabilities, AI can deeply mine and analyse these features with minimal human intervention[56]. Machine learning (ML) is another field of AI. Mathematical models can be developed using convolutional neural networks (CNNs) and deep learning (DL)[3]. Radiomics and ML can be used in combination to improve the accuracy of results[14]. By leveraging AI, multiomics integration enhances the understanding of tumour heterogeneity, supporting accurate diagnosis and personalized therapy. Advanced supercomputing systems enable the combination of the world's largest clinical image dataset with clinical and omics information, providing a robust computational environment for data analysis[57]. While MRI-based radiomics provides valuable data mined from medical images, significant limitations still impede its clinical translation, including technical requirements, standardization, model reproducibility, and a lack of clinical validation[58]. Future perspectives may involve combining clinical data, validating imaging biomarkers, and using radiomics, which appears to be a more feasible approach for clinical practice.

6. Conclusion

RMAC is a rare subtype of rectal adenocarcinoma that differs from regular adenocarcinoma in genetics and spread patterns. For the management of diseases, accurate staging is thus quite important. The use of MRI encompasses several difficulties. For example, initial disease staging is challenging since the signal intensity of mucin on T2-weighted sequences resembles that of fat and liquid[11]. The peritoneal dissemination is widespread in RMAC and is also easily missed during diagnosis. And, correctly identifying EMVI and significant metastatic lymph nodes in RMAC is equally important for treatment planning. Additionally, the imaging staging methods for RMAC have limitations.

They are not conducive to doctors accurately assessing and implementing targeted therapy and may even lead to misjudgment of poor prognosis owing to relatively high TNM staging at the time of diagnosis[1,59]. However, the use of new MRI techniques is expected to provide more disease characteristics and accurate staging results for the diagnosis and treatment of RMACs and MACs in other locations, thus offering doctors more comprehensive decision-making support and promoting the formulation of precise individualized treatment strategies. Although current MRI techniques have made specific progress, several challenges remain. In the future, it is necessary to strengthen research and cooperation to promote technological advancements and ultimately achieve the goal of providing patients with more effective early diagnoses, which means improving the disease prognosis and the patients' quality of life.

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