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Radiomics and Machine Learning for Predicting Metachronous Liver Metastasis in Rectal Cancer

Predicting Metachronous Liver Metastasis in Rectal Cancer

Abstract

A recent study by Long Z *et al.* used a predictive model to explore the efficacy of radiomics based on multiparametric magnetic resonance imaging (MRI) in predicting metachronous liver metastasis (MLM) in newly diagnosed rectal cancer (RC) patients. The machine learning (ML) algorithms, particularly the random forest model (RFM), appeared well-matched to the complex nature of radiomics data. The predictive capabilities of the RFM, as evidenced by the area under the curve (AUC) of 0.919 in the training cohort and 0.901 in the validation cohort, highlighted its potential clinical utility.

However, we highlighted several methodological limitations, including excluding genomic markers, potential biases from the retrospective design, limited generalizability due to a single-center study, and variability in image interpretation. We propose further investigation into integrating multi-omic data, conducting larger multicenter studies, and utilizing advanced imaging techniques. Additionally, we highlighted the importance of interdisciplinary collaboration to improve predictive model development and advocate for cost-effectiveness analyses to facilitate clinical integration. Overall, this predictive model may improve the early detection and management of MLM in RC patients, with promising avenues for future exploration. Ongoing research in this domain can potentially improve clinical outcomes and the quality of care for RC patients.

Key Words: Rectal cancer; Liver metastases; Neoplasm; Metastasis; Machine learning; Magnetic resonance imaging; Radiomics; Machine learning.

Krishnan A. Radiomics and Machine Learning for Predicting Metachronous Liver Metastasis in Rectal Cancer. *World J Gastrointest Oncol* 2025; In press

Core Tip: In a recent study by Long Z *et al.*, multiparametric magnetic resonance imaging and radiomics were utilized to anticipate the occurrence of metachronous liver metastasis (MLM) in individuals newly diagnosed with rectal cancer (RC). The random forest model (RFM), a predictive model component, demonstrated significant accuracy, achieving AUC values of 0.919 in the training cohort and 0.901 in the validation cohort, highlighting its potential for non-invasive risk assessment. By integrating radiomic features with clinical data, the model can support tailored treatment strategies and improve patient care. Nevertheless, it is important for future research to address methodological limitations, such as the exclusion of genomic markers, potential biases from the retrospective design, and the necessity for external validation across varied patient populations. Expanding the model to integrate multi-omic data and advanced imaging techniques has the potential to further its clinical significance and practicality.

TO THE EDITOR

With great interest, we read the research article from Long Z *et al.*[1]. In this study, the authors investigated the efficacy of radiomics based on multiparametric magnetic resonance imaging images of preoperative first-diagnosed rectal cancer in predicting metachronous liver metastasis (MLM) from rectal cancer (RC). This study is an important contribution to the growing area of predictive models in oncology, particularly in addressing the urgent requirement for dependable approaches to predict MLM in patients with RC. This study's findings can be important in pinpointing patients at high risk of liver metastasis and effectively managing their condition. It can

also improve long-term survival rates and prognosis for these patients. The authors' innovative use of radiomics in combination with ML to build a non-invasive prediction model has substantial promise for clinical potential.

The authors emphasized the significant impact of liver metastasis on the survival of patients with RC, highlighting the ongoing challenge of early detection. Using radiomics, the authors propose an innovative approach that promises to improve clinical outcomes by facilitating personalized monitoring and therapeutic interventions. The ML algorithms, particularly the random forest model (RFM), appear well-matched to the complex nature of radiomics data. The predictive capabilities of the RFM, as evidenced by the **area under the curve (AUC) of 0.919 in the training cohort and 0.901 in the validation cohort**, highlighted its potential clinical utility. We acknowledge the authors' efforts and valuable contributions as the study addresses a critical need for a predictive model. However, we offer some constructive suggestions based on several methodological limitations, confounders, and biases that may affect the results' accuracy and future studies to improve their study.

Areas for Further Investigation:

The study presented was innovative, but several areas require further investigation. Firstly, the authors note that the model did not include genomic markers like KRAS/NRAS mutations due to the invasive nature and cost of genomic testing[2]. However, future studies could benefit from incorporating non-invasive genomic or liquid biopsy markers to improve the model's predictive accuracy and clinical applicability as personalized oncology evolves to integrate multi-omic data[3]. A study by Di Sario *et al.* indicated that combining radiomics with liquid biopsy data could provide real-time insights into tumor biology. This integration could improve the interpretability of predictive models, potentially leading to better-informed clinical decisions[3]. Secondly, the retrospective study design may introduce selection or recall bias due to the limited control over variables. To address this, using a propensity score matching technique to balance baseline characteristics between groups (*e.g.*, patients

who develop MLM and those who do not) and conducting prospective validation of findings would be advantageous and reduce confounding[4]. Longitudinal studies that monitor changes in tumor characteristics through serial imaging and biomarker analysis can further explain the association between radiomic features and metastasis progression. Utilizing federated learning techniques to integrate datasets from various centers helps overcome issues related to data sharing, which could strengthen model robustness and protect the privacy and security of sensitive data. Thirdly, as the study only involved 301 rectal cancer patients from a single institution with a relatively homogeneous patient population, its generalizability to the larger population may be limited. Conducting multicenter studies involving more diverse populations is critical to improve the study's statistical power and generalizability.

Moreover, a larger, independent external validation cohort from multiple centers could further validate the reproducibility of the findings across diverse clinical settings. Fourth, the treatment and stage of cancer can vary among patients, which could affect the relationship between radiomic features and liver metastasis. Therefore, using multivariable models to account for these differences and to analyze the data based on patient characteristics such as cancer stage, age, and treatment history is important[5]. Fifth, when interpreting MRI images, the radiologist's expertise and the subjective nature of identifying features can lead to variations. It is recommended that multiple radiologists be involved in cross-checking findings or utilizing artificial intelligence (AI)-assisted image interpretation to minimize subjectivity. Lastly, the differences in follow-up time among patients, with a median follow-up time of 23.5 months, could impact the detection of metachronous liver metastasis outcomes. Standardizing the follow-up duration for all patients or adjusting for differences using time-dependent statistical models such as Kaplan-Meier survival curves or Cox regression models is recommended.

Future Research Directions:

The present study used a framework to predict MLM involvement in RC using imaging omics and ML algorithms. However, to improve the clinical applicability and accuracy of a predictive model, it is imperative to conduct comprehensive studies, and there are several promising directions for future exploration. While the current study had 301 patients, validating the predictive model in larger, multicenter cohorts will strengthen the reliability and applicability of the findings. Similarly, we need more understanding of diverse patient populations with various tumor characteristics and responses to treatment, and larger datasets would allow the evaluation of the model's predictive performance across different demographic and clinical settings[6].

Future research endeavors should consider integrating genomic, proteomic, and metabolomic data with imaging features to improve the model's predictive capability. Understanding the molecular support of RC and its metastasis could lead to identifying additional biomarkers and risk factors that may not be discernible through imaging alone[7]. Similarly, implementing longitudinal studies that monitor changes in tumor characteristics and treatment responses over time can facilitate the development of dynamic prediction models[7]. A study by Lipkova *et al.* showed that integrating proteomics and metabolomics data can potentially deepen our biological understanding of MLM. This combined approach could contribute to developing more reliable predictive models[6]. These models would enable real-time adjustments to risk assessments based on changes in radiomic features and clinical parameters, thereby improving personalized patient management.

Promoting collaboration among radiologists, oncologists, surgeons, and data scientists will augment the model's development and implementation. Interdisciplinary approaches will foster a comprehensive understanding of rectal cancer and its metastasis, ensuring that the predictive model is clinically relevant and effective[8]. Future studies could be explored using advanced imaging techniques such as functional MRI, PET/MRI, and AI-enhanced imaging techniques. These could yield further insights into tumor biology and metastatic potential and refine the prediction models by integrating more comprehensive imaging data. In addition, these imaging modalities

could offer additional insights into tumor microenvironments and their metabolic conditions. Importantly, conducting cost-effectiveness analyses of the proposed predictive model is necessary for its integration into clinical practice. Evaluating the financial implications of using this model for early detection and treatment planning would help justify its adoption into healthcare systems[9]. The authors proposed an innovative predictive model, but further exploration is required on its integration into clinical practice. It is important to consider the practical limitations of implementing this model in real-world settings, such as the requirement for additional resources and clinician training. Similarly, collaboration with health economists is important to evaluate the cost-effectiveness of integrating these models into routine clinical practice.

CONCLUSION

In conclusion, this study significantly contributes to the ongoing efforts to improve the early detection and management of metachronous liver metastasis in rectal cancer patients. The development of non-invasive predictive models like the one presented here has the potential to revolutionize clinical decision-making and improve patient outcomes. Nevertheless, further studies are required to address the challenges related to model standardization, multicenter validation, and cost-cogency. The suggestions aimed to address these challenges; future studies can refine predictive models. Ongoing research in this domain can potentially improve clinical outcomes and the quality of care for RC patients. We look forward to further advancements in this field and the eventual clinical integration of these predictive models.

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PRIMARY SOURCES

1 Xinyu Dou, Jiaona Xi, Gaozan Zheng, Guangming Ren et al. "A nomogram was developed using clinicopathological features to predict postoperative liver metastasis in patients with colorectal cancer", Journal of Cancer Research and Clinical Oncology, 2023 13 words — 1%

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