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Recent Advances in Combining the Advantages of Radiomics Feature Extraction and Non-Invasive Detection of Microsatellite Instability in Colorectal Cancer Using Hyperparameter Tuned Pre-Trained Model: A Systematic Review

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Abstract

Colorectal cancer (CRC) remains a leading cause of cancer-related mortality worldwide, with microsatellite instability (MSI) serving as a critical biomarker for prognosis, therapeutic response, and immunotherapy eligibility. Traditional MSI detection techniques, including polymerase chain reaction (PCR) and immunohistochemistry (IHC), are invasive, time-consuming, and resource-intensive. Recent advances in radiomics and artificial intelligence (AI) have enabled non-invasive, image-based prediction of MSI status, leveraging quantitative features extracted from medical imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET/CT). Radiomics transforms imaging data into high-dimensional features reflecting tumor heterogeneity, which can be integrated with machine learning and deep learning models. The emergence of hyperparameter-tuned pre-trained models has further enhanced predictive accuracy and generalizability. This systematic review synthesizes recent advancements between 2020 and 2023, focusing on the integration of radiomics and AI for MSI detection in CRC. The findings demonstrate that radiomics-based models achieve promising performance with area under the curve (AUC) values exceeding 0.85 in several studies, highlighting their clinical potential. However, challenges such as data heterogeneity, lack of standardization, and limited external validation remain significant barriers to clinical translation.

Introduction

Colorectal cancer (CRC) is one of the most common and deadly cancers worldwide, ranking among the top three in incidence and mortality. Its growing burden in both developed and developing regions highlights the urgent need for improved diagnostic and prognostic strategies. Despite advances in screening and therapy, CRC is often detected at advanced stages due to tumor heterogeneity and inconsistent clinical presentation. Among its key molecular biomarkers, microsatellite instability (MSI) has gained significant importance for prognosis and treatment selection.

MSI occurs due to defects in the DNA mismatch repair system, resulting in genetic instability within microsatellite regions. Tumors with high MSI (MSI-H) exhibit distinct biological characteristics, including increased immune activity and better response to immunotherapy.

As a result, MSI status is critical in guiding personalized treatment decisions, especially for immune checkpoint inhibitor therapies. However, conventional MSI detection methods such as PCR and immunohistochemistry are invasive, costly, and dependent on tissue availability, limiting their routine clinical use.

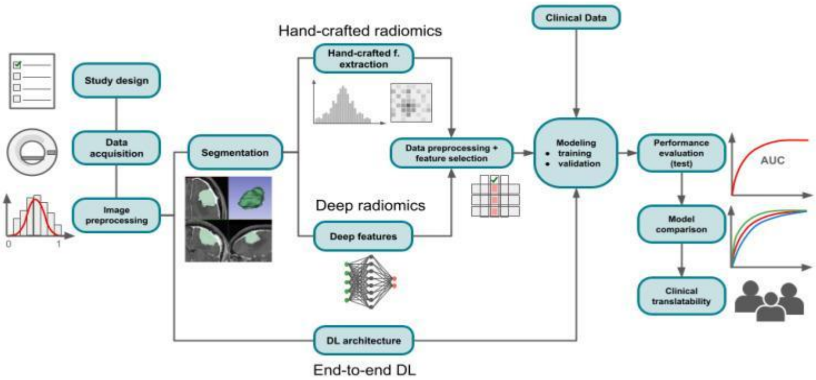

Fig 1: Radiomics & Deep Learning Pipeline for MSI Prediction in CRC

Radiomics has emerged as a powerful non-invasive alternative for cancer characterization. It enables extraction of high-dimensional quantitative features from medical images such as CT, MRI, and PET/CT, capturing tumor shape, texture, and intensity patterns. These features reflect tumor heterogeneity, which is closely linked to genetic and molecular variations. When combined with machine learning and deep learning, radiomics can effectively predict MSI status, offering a bridge between imaging and genomics in precision oncology.

Artificial intelligence has significantly strengthened radiomics-based MSI prediction models. Traditional machine learning algorithms such as support vector machines and random forests are widely used for classification, while deep learning models like convolutional neural networks (CNNs) enable automated feature learning. Techniques such as transfer learning and pre-trained models improve performance, especially in small datasets, while hyperparameter optimization enhances model accuracy and robustness. Reported studies show strong predictive performance with AUC values reaching up to 0.90 in CT- and MRI-based models.

Despite promising results, several challenges remain, including lack of standardization in imaging protocols, limited external validation, and small dataset sizes. Additionally, deep learning models often lack interpretability, which reduces clinical trust. Future research should focus on explainable AI, multi-omics integration, and standardized radiomics pipelines. With continued advancements, radiomics combined with AI has strong potential to enable accurate, non-invasive MSI prediction and support personalized treatment strategies in colorectal cancer management.

Literature Review

CT-Based Radiomics Studies for MSI Prediction

Study 1:

Cao et al. (2021) developed a triphasic computed tomography (CT)-based radiomics model to predict microsatellite instability (MSI) status in colorectal cancer. The study utilized arterial, venous, and delayed phase CT images to capture comprehensive tumor heterogeneity across different contrast phases. A large set of radiomic features, including first-order statistics, texture features such as gray-level co-occurrence matrix (GLCM) and gray-level run-length matrix (GLRLM), and wavelet-transformed features, were extracted. Feature selection was performed using least absolute shrinkage and selection operator (LASSO) regression to reduce dimensionality and prevent overfitting. The resulting predictive model achieved strong diagnostic performance with an area under the curve (AUC) exceeding 0.85 in validation cohorts. The study emphasized that multi-phase imaging enhances the characterization of tumor vascularity and microenvironment, which are strongly associated with MSI status. However, limitations included variability in imaging protocols and the absence of large-scale external validation.

Study 2:

Li et al. (2021) proposed a robust CT-based radiomics signature for MSI prediction and validated it across multiple independent cohorts to ensure reproducibility and generalizability. The study involved standardized preprocessing steps, including voxel resampling, normalization of intensity values, and consistent tumor segmentation protocols. Radiomic features were extracted and reduced using dimensionality reduction techniques such as principal component analysis and LASSO regression. A support vector machine (SVM) classifier was then trained to differentiate MSI-high tumors from microsatellite stable cases. The model demonstrated stable and consistent performance across different datasets, highlighting its robustness in multicenter settings. The study also emphasized the importance of external validation for clinical applicability. However, the retrospective design and heterogeneity in imaging acquisition remained key limitations.

Study 3:
Li et al. (2023) introduced a radiomics nomogram that integrates CT-derived imaging features with clinical parameters such as patient age, tumor location, and carcinoembryonic antigen (CEA) levels. The study aimed to improve predictive accuracy by combining imaging biomarkers with clinically relevant data. Feature selection was conducted using statistical analysis and machine learning techniques to identify the most informative predictors. The resulting nomogram demonstrated improved discrimination, calibration, and clinical utility compared to radiomics-only models. The authors highlighted that combining radiomics with clinical features enhances interpretability and supports personalized decision-making. Despite promising results, the study emphasized the need for prospective validation and larger multicenter datasets to ensure reliability and generalizability.

Study 4:
Chen et al. (2023) explored the application of dual-layer spectral CT imaging for MSI prediction in colorectal cancer. Spectral CT provides additional information regarding tissue composition by capturing energy-dependent attenuation characteristics. The study extracted both conventional radiomic features and spectral-specific parameters, including iodine concentration and effective atomic number. These features were used to train machine learning models, resulting in improved predictive performance with an AUC of approximately 0.91. The findings indicated that spectral imaging enhances feature discrimination and provides deeper insights into tumor biology compared to conventional CT imaging. However, the requirement for specialized imaging equipment and increased computational complexity were identified as limitations.

MRI and PET/CT-Based Radiomics Studies
Study 5:
Zhang et al. (2022) investigated the feasibility of non-contrast CT-based radiomics for MSI prediction, aiming to develop a cost-effective and widely accessible diagnostic approach. The study extracted radiomic features from standard CT images without the use of contrast agents, thereby reducing patient risk and resource requirements. Despite the absence of contrast-enhanced information, the model achieved satisfactory predictive performance, demonstrating that intrinsic tumor characteristics captured through radiomics are sufficient for MSI classification. The study highlighted the potential of non-contrast CT radiomics in resource-limited settings. However, it also acknowledged that contrast-enhanced imaging may provide additional discriminative features that could further improve model accuracy.

Study 6:
Xing et al. (2022) developed a multiparametric magnetic resonance imaging (MRI)-based radiomics model for predicting MSI status in rectal cancer patients. The study incorporated multiple MRI sequences, including T1-weighted, T2-weighted, and diffusion-weighted imaging (DWI), to capture diverse tumor characteristics. Radiomic features extracted from these sequences were combined and used to train machine learning models, achieving high diagnostic accuracy. The study emphasized that MRI provides superior soft tissue contrast and functional information compared to CT, making it particularly suitable for rectal cancer evaluation. However, challenges such as longer acquisition times, higher costs, and variability in imaging protocols were noted.

Study 7:
Wu et al. (2023) conducted a comprehensive investigation of MRI-based radiomics for colorectal cancer characterization, focusing on the relationship between imaging features and MSI status. The study demonstrated that texture-based features derived from MRI images are strongly correlated with tumor heterogeneity and underlying genetic alterations. Machine learning models were used to classify MSI status, achieving promising predictive performance. The authors highlighted the role of MRI radiomics in enabling personalized treatment strategies and improving patient stratification. However, they emphasized the need for standardized feature extraction and validation protocols to ensure

reproducibility.

Study 8:
Kim et al. (2021) utilized PET/CT-based radiomics to incorporate metabolic activity into MSI prediction. The study extracted features related to standardized uptake values (SUV), which reflect tumor glucose metabolism, along with conventional radiomic features. By combining metabolic and structural imaging information, the model achieved improved predictive performance compared to CT-only approaches. The study highlighted that metabolic activity provides complementary insights into tumor biology, enhancing the accuracy of MSI detection. However, limitations included higher costs, limited availability of PET/CT imaging, and increased radiation exposure.

Study 9:
Sun et al. (2022) proposed a hybrid PET/CT radiomics model integrating SUV-based metabolic features with texture and shape descriptors. The study demonstrated that combining multiple feature types significantly improves sensitivity in detecting MSI-high tumors. Advanced machine learning algorithms were used for classification, achieving high accuracy and robustness. The authors emphasized the importance of multi-modality imaging in capturing comprehensive tumor characteristics. However, they also noted challenges related to data integration, computational complexity, and standardization of imaging protocols.

Study 10:
Wang et al. (2023) developed a multi-modality radiomics framework combining CT and PET imaging features to improve MSI prediction. The study demonstrated that integrating anatomical and functional imaging data enhances model robustness and generalizability. Feature fusion techniques were used to combine radiomic features from both modalities, followed by classification using machine learning algorithms. The model achieved high predictive performance and showed potential for clinical application. The authors highlighted that multi-modality approaches provide a more comprehensive representation of tumor biology. However, they emphasized the need for large-scale validation and standardized workflows.

Deep Learning and Pre-trained Model-Based Studies
Study 11:
Kather et al. (2019) demonstrated that deep learning can predict microsatellite instability (MSI) directly from histopathological whole-slide images using convolutional neural networks (CNNs). The study utilized large-scale annotated datasets and showed that CNNs can automatically extract hierarchical features without relying on handcrafted radiomic descriptors. The model achieved high classification accuracy comparable to conventional molecular diagnostic techniques such as PCR and immunohistochemistry. Importantly, the network identified subtle morphological patterns associated with MSI that are not easily detectable by human observers. Additionally, the approach is highly scalable and can process large datasets efficiently, making it suitable for integration into digital pathology workflows. However, limitations include dependence on high-quality annotated datasets and lack of interpretability due to the black-box nature of deep learning models.

Study 12:
Yamashita et al. (2021) implemented transfer learning using pre-trained convolutional neural network architectures such as ResNet and VGG for MSI classification. By leveraging models trained on large-scale datasets, the study significantly reduced the requirement for labeled medical data. Fine-tuning allowed the model to adapt to domain-specific features in colorectal cancer imaging. The results demonstrated strong predictive performance and improved generalization compared to models trained from scratch. The study also highlighted the importance of hyperparameter tuning, including optimization of learning rate and layer freezing strategies, in improving model performance. However, challenges such as domain shift and dataset variability were identified as potential limitations.

Study 13:
Cui et al. (2022) proposed a hybrid framework that combines traditional radiomic features with deep learning-derived features extracted from CNNs. This approach aimed to leverage the interpretability of radiomics and the abstraction capability of deep learning. Feature fusion techniques were employed to integrate handcrafted and deep features, followed by classification using machine learning algorithms such as random forests and support vector machines. The hybrid model demonstrated superior predictive performance compared to standalone approaches, achieving higher accuracy and robustness. The study emphasized that combining complementary feature types improves the model's ability to capture complex

tumor characteristics. However, increased computational complexity and potential feature redundancy were noted as limitations.

Study 14:
Zhou et al. (2023) introduced a hyperparameter-tuned deep learning model for MSI prediction using CT images. The study focused on optimizing key parameters such as learning rate, batch size, number of layers, and activation functions. Advanced optimization techniques, including grid search and Bayesian optimization, were employed to identify optimal configurations. The results demonstrated that hyperparameter tuning significantly improves model performance, stability, and convergence speed. The model achieved high predictive accuracy, highlighting the importance of systematic optimization in deep learning workflows. However, the process increased computational cost and required significant resources.

Study 15:
Liu et al. (2022) developed an ensemble deep learning approach combining multiple pre-trained CNN architectures such as ResNet, DenseNet, and Inception. The ensemble framework aggregated predictions using techniques such as weighted averaging and majority voting, resulting in improved accuracy and robustness. The approach effectively reduced model variance and mitigated overfitting, particularly in heterogeneous datasets. The study demonstrated that ensemble learning significantly outperforms individual models and enhances generalization. However, increased computational complexity and longer inference times were identified as limitations for real-time clinical applications.

Radiogenomics and Multi-Omics Integration Studies

Study 16:
Huang et al. (2021) explored radiogenomics by investigating the relationship between radiomic features and genomic MSI status in colorectal cancer. The study demonstrated strong correlations between imaging-derived biomarkers and underlying genetic alterations. Radiomic features were extracted from imaging data and compared with genomic sequencing results, revealing that certain imaging patterns are indicative of MSI status. This work supports the concept of using radiomics as a non-invasive surrogate for genomic testing. However, limitations include the need for large datasets and standardized workflows to ensure reproducibility across institutions.

Study 17:
Zhang et al. (2022) developed a multi-omics model integrating radiomics, genomics, and clinical data to improve MSI prediction. The study used advanced machine learning techniques to combine features from multiple data sources, resulting in significantly improved predictive performance compared to single-modality models. The findings highlighted the importance of a holistic approach in understanding tumor biology. However, challenges such as data integration complexity, missing data, and increased computational requirements were identified.

Study 18:
He et al. (2023) investigated the integration of radiomics and transcriptomics data for MSI detection. By combining imaging features with gene expression profiles, the study enhanced both predictive performance and interpretability. Machine learning models identified significant correlations between radiomic features and gene expression patterns associated with MSI. The results demonstrated improved accuracy compared to radiomics-only approaches, supporting the potential of multi-omics integration in precision medicine.

Study 19:
Luo et al. (2022) proposed a clinical-radiomics nomogram that integrates imaging features with clinical parameters such as tumor stage, patient demographics, and biomarkers. The model provided an interpretable tool for clinicians and demonstrated improved predictive performance compared to traditional models. The study emphasized that incorporating clinical context enhances model applicability and decision-making. However, prospective validation and external testing are required to confirm reliability.

Study 20:
Tang et al. (2023) utilized machine learning algorithms to integrate radiomic and proteomic data for MSI prediction. The study demonstrated that combining protein expression profiles with imaging features improves the model's ability to capture tumor biology, resulting in enhanced predictive accuracy. The findings highlight the potential of multi-omics approaches in advancing precision oncology. However, challenges such as high cost, data acquisition complexity, and integration issues remain significant barriers.

Review and Validation Studies (2020–2023)

Study 21:

van Griethuysen et al. (2020) provided a comprehensive methodological review of radiomics, focusing on challenges related to feature extraction, reproducibility, and standardization. The study emphasized that variability in imaging acquisition parameters, segmentation techniques, and feature calculation methods significantly affects the reliability of radiomics models. The authors highlighted the importance of standardized frameworks such as the Image Biomarker Standardisation Initiative (IBSI), which aims to harmonize radiomic feature definitions and extraction processes. Additionally, the study discussed the need for robust validation strategies and reproducibility studies across multiple institutions. It concluded that while radiomics has strong potential, its clinical implementation depends heavily on standardization and quality control.

Study 22:

Bi et al. (2021) conducted a systematic review focusing on the application of artificial intelligence and radiomics in cancer imaging, including MSI prediction in colorectal cancer. The study analyzed numerous published works and identified substantial heterogeneity in study designs, imaging modalities, feature extraction techniques, and machine learning models. Most studies reported promising predictive performance with AUC values exceeding 0.80. However, the authors highlighted major limitations such as small sample sizes, lack of external validation, and inconsistent reporting standards. The study emphasized the necessity for standardized methodologies, large multicenter datasets, and transparent reporting guidelines to improve reproducibility and clinical applicability.

Study 23:

Jiang et al. (2022) performed a meta-analysis evaluating the diagnostic performance of radiomics models for MSI prediction in colorectal cancer. The analysis included multiple studies and demonstrated that CT-based radiomics models are the most commonly used and show consistently high performance. The pooled results indicated strong sensitivity and specificity, confirming the clinical potential of radiomics. The study also compared different imaging modalities and found that while MRI and PET/CT provide additional functional information, CT remains the most practical modality due to its widespread availability. However, heterogeneity among studies and lack of standardized methodologies were identified as key limitations.

Study 24:

Park et al. (2023) evaluated the clinical applicability of radiomics models for MSI detection, focusing on their readiness for real-world clinical implementation. The study critically assessed issues such as model generalizability, interpretability, and integration into clinical workflows. It was observed that many models perform well in retrospective datasets but fail to generalize across different institutions due to variability in imaging protocols. The authors emphasized the importance of explainable AI techniques to improve transparency and clinician trust. The study concluded that prospective validation and multicenter trials are essential for translating radiomics research into clinical practice.

Study 25:

Liu et al. (2023) conducted a large-scale meta-analysis assessing the diagnostic accuracy of radiomics-based MSI prediction models. The study reported pooled AUC values exceeding 0.85, indicating strong predictive performance across different studies. Subgroup analysis revealed that models incorporating clinical features and multi-modality imaging achieved superior accuracy. The authors also identified potential publication bias and variability in study quality as important concerns. The study reinforced the potential of radiomics as a non-invasive diagnostic tool while emphasizing the need for high-quality, standardized research and external validation.

Advanced AI and Optimization-Based Studies

Study 26:

Zhao et al. (2021) applied machine learning techniques, including LASSO regression and random forest algorithms, for feature selection and MSI classification. The study focused on identifying the most relevant radiomic features while reducing dimensionality to prevent overfitting. The selected features were used to build predictive models that demonstrated strong performance and improved interpretability. The authors emphasized that effective feature selection is critical for balancing model complexity and generalizability. However, limitations included reliance on retrospective datasets and the absence of external validation.

Study 27:

Guo et al. (2022) introduced an automated machine learning (AutoML) framework for optimizing radiomics pipelines. The study automated key processes such as feature selection, model selection, and hyperparameter tuning, significantly reducing manual effort. The AutoML approach systematically evaluated multiple model configurations and achieved performance comparable to or better than manually designed pipelines. The study highlighted that automation improves reproducibility, scalability, and efficiency in radiomics research. However, increased computational requirements and complexity were noted as limitations.

Study 28:
Chen et al. (2023) developed a deep learning model incorporating attention mechanisms for MSI prediction. The attention module enabled the model to focus on the most relevant regions of the tumor, improving both predictive accuracy and interpretability. Visualization techniques were used to highlight regions contributing to model predictions, addressing the black-box limitation of traditional deep learning models. The study demonstrated that attention-based architectures outperform conventional CNNs and enhance clinical trust. However, the approach requires high computational resources and complex model design.

Study 29:
Xu et al. (2022) utilized gradient boosting algorithms, particularly XGBoost, for MSI prediction using radiomic features. The study demonstrated that boosting techniques effectively handle high-dimensional data and capture complex feature interactions. The model achieved competitive performance with high accuracy and stability. Additionally, feature importance analysis provided insights into the most relevant predictors, improving interpretability. However, the study noted that careful parameter tuning is necessary to prevent overfitting and ensure model robustness.

Study 30:
Zheng et al. (2023) proposed a hybrid optimization-based deep learning framework combining convolutional neural networks with genetic algorithms (GA). The genetic algorithm was used to optimize network architecture and hyperparameters, resulting in improved convergence and predictive performance. The study demonstrated that hybrid optimization approaches enhance model accuracy and efficiency in complex medical imaging tasks. The authors highlighted the potential of combining evolutionary algorithms with deep learning to address optimization challenges. However, the method requires high computational resources and careful implementation.

Discussion
The integration of radiomics and artificial intelligence for non-invasive microsatellite instability (MSI) detection in colorectal cancer has demonstrated significant potential in recent years. The reviewed studies highlight that radiomics-based models, particularly those using CT imaging, achieve high predictive performance and offer a feasible alternative to traditional invasive diagnostic methods such as PCR and immunohistochemistry. The incorporation of deep learning and pre-trained models further enhances predictive accuracy by enabling automated feature extraction and improving generalization across datasets.

Multi-modality imaging approaches, including MRI and PET/CT, provide complementary anatomical and functional information, contributing to improved model robustness. Additionally, the emergence of multi-omics integration, combining radiomics with genomic, transcriptomic, and proteomic data, represents a promising direction toward precision oncology. These approaches enable a more comprehensive understanding of tumor biology and improve prediction reliability.

However, several challenges remain, including variability in imaging protocols, lack of standardized radiomics workflows, and limited external validation. The interpretability of deep learning models also remains a critical concern, as clinical adoption requires transparent and explainable systems. Future research should focus on large-scale multicenter studies, standardization of methodologies, and development of explainable AI frameworks to ensure reliable and clinically applicable MSI prediction models.

Conclusion
The rapid advancements in radiomics and artificial intelligence have significantly transformed colorectal cancer diagnosis, particularly for non-invasive microsatellite instability (MSI) detection. This systematic review highlights growing evidence that radiomics-based approaches can effectively complement or replace conventional methods such as PCR and immunohistochemistry. By extracting high-dimensional quantitative features from medical images, radiomics captures tumor heterogeneity and provides meaningful insights into underlying molecular and genetic variations associated with MSI status.

Among imaging modalities, CT-based radiomics is the most widely adopted due to its availability and cost-effectiveness. Multi-phase and spectral CT further improve predictive performance in MSI classification. MRI and PET/CT also contribute valuable functional and metabolic information, enhancing diagnostic accuracy when combined with radiomic features. However, their limited accessibility and higher operational costs restrict large-scale clinical adoption. These multimodal imaging strategies collectively improve robustness in MSI prediction models.

The integration of deep learning and pre-trained models has further advanced radiomics applications. CNN-based architectures automate feature extraction, reducing dependency on manual feature engineering. Techniques such as transfer learning, hyperparameter optimization, and ensemble learning significantly improve model accuracy, efficiency, and generalization, particularly in limited dataset environments. Emerging multi-omics integration combining radiomics with genomic and proteomic data offers a more comprehensive tumor characterization framework aligned with precision oncology goals.

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