Archives available at journals.mriindia.com

International Journal on Advanced Computer Engineering and Communication Technology

ISSN: 2278-5140

Volume 14 Issue 02, 2025

Deep Learning and Optimization Approaches 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 Review

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Peer Review Information

Submission: 29 Nov 2025

Revision: 13 Dec 2025

Acceptance: 27 Dec 2025

Keywords

Radiomics, Deep Learning, Microsatellite Instability, Colorectal Cancer, Transfer Learning, Hyperparameter Optimization

Abstract

Microsatellite instability (MSI) is a critical biomarker in colorectal cancer (CRC), influencing prognosis, therapeutic decisions, and immunotherapy response. Conventional MSI detection techniques such as polymerase chain reaction (PCR) and immunohistochemistry (IHC) are invasive, time-consuming, and resource-intensive. In recent years, the integration of radiomics and deep learning has emerged as a promising non-invasive alternative for MSI prediction. Radiomics enables the extraction of high-dimensional quantitative features from medical imaging, capturing tumor heterogeneity, while deep learning models automate feature learning and improve predictive performance. This review explores recent advances in combining radiomics with deep learning architectures, particularly hyperparameter-tuned pre-trained models, to enhance MSI detection accuracy. The study synthesizes literature from 2020 to 2023, focusing on optimization techniques, multimodal data integration, and model generalization. Evidence suggests that radiomics-based machine learning models achieve high diagnostic performance, with area under the curve (AUC) values often exceeding 0.80, although challenges in reproducibility and external validation remain . Deep learning approaches, especially those leveraging histopathology and imaging data, demonstrate improved sensitivity and specificity in MSI classification . This review highlights current trends, limitations, and future directions for developing robust, clinically deployable non-invasive MSI detection systems.

Introduction

Colorectal cancer (CRC) is one of the most common and life-threatening malignancies worldwide, creating a significant burden on healthcare systems and patient survival. Early diagnosis and accurate molecular characterization are essential for selecting effective treatment strategies and improving clinical outcomes. Among the important molecular biomarkers associated with CRC, microsatellite instability (MSI) plays a critical role in predicting tumor behavior, therapeutic response, and prognosis. MSI results from deficiencies in the DNA mismatch repair system, leading to genomic instability and abnormal mutation accumulation. Conventional MSI detection methods, including polymerase chain reaction and immunohistochemistry, provide reliable results but are invasive, expensive, and time-consuming. These limitations have increased interest in developing non-invasive and intelligent approaches for MSI prediction using medical imaging and Artificial Intelligence (AI)-based technologies.

Radiomics has emerged as an advanced imaging analysis technique capable of extracting quantitative features from medical imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). These extracted features capture tumor texture, shape, intensity, and heterogeneity, which are often associated with underlying molecular and genetic characteristics. Radiomics transforms conventional medical images into high-dimensional data that can be analyzed using machine learning and deep learning algorithms. Several studies have demonstrated that radiomics-based models can effectively predict MSI status in colorectal cancer, providing a promising non-invasive alternative to traditional biopsy-based approaches. However, variability in imaging protocols, lack of feature reproducibility, and limited standardization continue to affect the reliability and generalization of radiomics systems.

Deep learning techniques have significantly enhanced radiomics-based microsatellite instability (MSI) detection in colorectal cancer by enabling automatic feature extraction and hierarchical representation learning from medical images. Convolutional Neural Networks (CNNs), transfer learning models, and multimodal frameworks combining radiological, histopathological, and clinical data have demonstrated strong predictive performance and improved diagnostic accuracy. These approaches effectively identify subtle tumor characteristics associated with MSI while reducing dependence on invasive diagnostic procedures. However, challenges such as limited annotated datasets, class imbalance, computational complexity, and lack of external validation continue to affect model reliability and clinical adoption. Additionally, the “black-box” nature of deep learning models limits interpretability, although explainable AI methods such as attention mechanisms and saliency maps have improved transparency. Future research should focus on standardized imaging protocols, lightweight explainable AI models, multimodal learning, and large multicenter validation studies to develop scalable, reliable, and clinically deployable MSI detection systems for precision colorectal cancer diagnosis and treatment.

Graphical Abstract

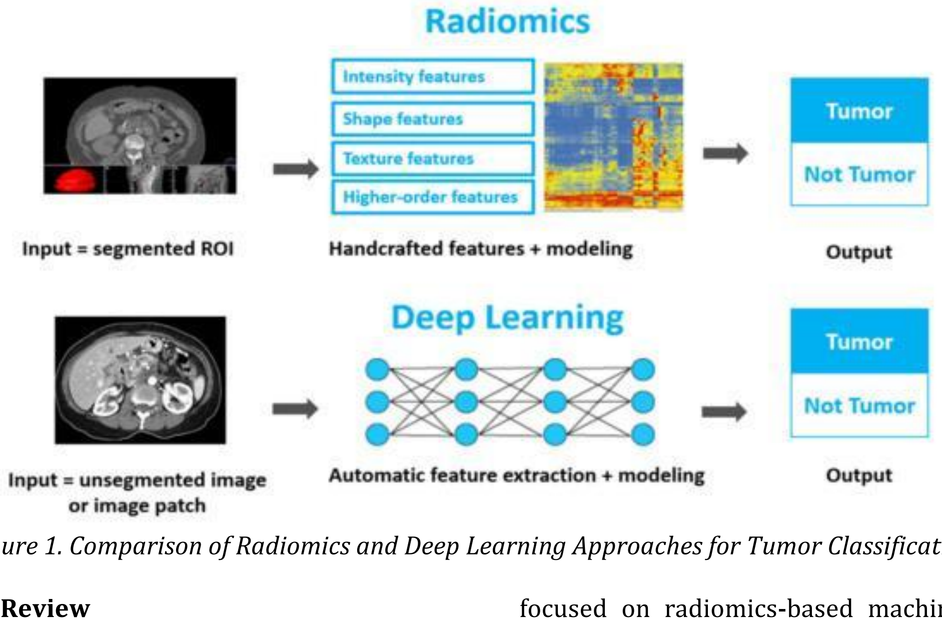

Figure 1. Comparison of Radiomics and Deep Learning Approaches for Tumor Classification

Literature Review

Recent advancements in artificial intelligence, radiomics, and deep learning have significantly transformed the prediction of microsatellite instability (MSI) in colorectal cancer. Researchers have increasingly explored non-invasive imaging and histopathological analysis methods to replace conventional molecular testing approaches. Early studies primarily focused on radiomics-based machine learning techniques using computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET/CT) images. These approaches demonstrated that quantitative imaging features could effectively capture tumor heterogeneity associated with MSI status. Wang et al. reported that radiomics-based models achieved high predictive performance, with area under the curve (AUC) values ranging between 0.78 and 0.96 across multiple datasets. Texture-related features, including gray-level co-occurrence matrix and wavelet-transformed descriptors, were identified as highly informative indicators of tumor heterogeneity. Similarly, Fan et al. demonstrated that MRI-based radiomics models improved MSI prediction accuracy by combining texture and intensity features with clinical variables. Liu et al. further enhanced predictive capability by employing multi-phase CT radiomics, where arterial and venous imaging phases provided complementary information regarding tumor vascularity and tissue heterogeneity. PET/CT-based radiomics models also showed promising results by integrating metabolic and structural features to characterize MSI-associated tumor behavior.

Although radiomics-based machine learning models achieved encouraging results, several limitations hindered their clinical adoption. One major challenge involved the lack of standardization in imaging acquisition protocols, segmentation methods, and feature extraction pipelines. Variability across datasets reduced reproducibility and generalization capability. Additionally, handcrafted radiomic features were often insufficient to fully represent complex tumor characteristics. These limitations encouraged researchers to integrate deep learning methodologies into MSI prediction frameworks. Convolutional Neural Networks (CNNs) emerged as the dominant deep learning architecture due to their ability to automatically learn hierarchical image representations directly from raw imaging data. Li et al. performed a large-scale meta-analysis demonstrating that CNN-based deep learning systems achieved pooled sensitivity and specificity values exceeding 0.80 for MSI prediction using histopathology slides. Advanced architectures such as ResNet, EfficientNet, DenseNet, and Inception were widely adopted due to their robust feature extraction capability. Transfer learning strategies using ImageNet-pretrained models significantly improved performance, especially in situations involving limited annotated medical datasets. Patch-based learning frameworks further optimized processing of large whole-slide images by dividing them into smaller regions, enabling efficient localization of diagnostically relevant tissue structures.

Deep learning applications in histopathology significantly improved MSI detection by identifying subtle morphological characteristics associated with mismatch repair deficiency. Studies demonstrated that MSI tumors frequently exhibit lymphocytic infiltration, mucinous differentiation, and irregular glandular patterns, all of which can be effectively captured through CNN-based learning. Echle et al. conducted a landmark multicenter investigation showing that deep learning models achieved strong cross-cohort generalization while accurately identifying MSI-associated tissue regions. Similarly, Kather et al. demonstrated that visual tumor morphology captured from histological and imaging data can serve as indirect indicators of MSI status. The integration of explainability methods further improved the interpretability of deep learning systems. Bilal et al. incorporated class activation maps and attention mechanisms to highlight histopathological regions contributing to MSI prediction, thereby enhancing transparency and clinician trust. Attention-based learning models proposed by Lu et al. further improved classification accuracy by selectively focusing on diagnostically significant tissue regions. These approaches addressed one of the most important barriers to clinical AI adoption, namely the “black-box” nature of deep learning models.

Recent studies have also explored advanced architectures beyond conventional CNNs. Transformer-based deep learning models have emerged as powerful alternatives capable of capturing long-range dependencies and global contextual information. Guo et al. introduced a Swin Transformer architecture for MSI prediction from hematoxylin and eosin-stained images, demonstrating improved generalization and state-of-the-art predictive accuracy. Vision Transformer models further enhanced feature representation by processing image patches as sequences while utilizing self-attention mechanisms to model complex spatial relationships. These architectures proved highly effective for identifying subtle tissue-level variations linked to MSI status. However, transformer-based models require extensive computational resources and large-scale datasets for training, limiting their accessibility in resource-constrained environments. To address these limitations, hybrid architectures combining CNNs and transformers were proposed to balance computational efficiency and predictive performance. Additionally, graph neural networks introduced by Zhang et al. provided a novel framework for modeling relationships between different tumor regions. By representing histopathology images as graphs, these models captured structural tumor heterogeneity more effectively than grid-based CNN architectures.

Multimodal and hybrid AI frameworks have become increasingly important for improving MSI prediction accuracy and robustness. Researchers demonstrated that combining imaging, histopathology, genomic information, and clinical variables provides a more comprehensive understanding of tumor biology. Nasr et al. emphasized the benefits of integrating handcrafted radiomics features with deep learning-derived representations, showing that hybrid frameworks outperform single-modality systems. Yamashita et al. proposed a multimodal deep learning architecture integrating radiological imaging, histopathological data, and clinical information through modality-specific neural network branches. Attention-based fusion strategies significantly improved predictive performance by emphasizing the most informative features across modalities. Similarly, Sun et al. explored radiogenomics approaches linking radiomic features with MSI-related genetic mutations, further strengthening the biological relevance of imaging biomarkers. Hybrid clinical-radiomics models combining imaging data with patient demographics and tumor stage information also demonstrated superior performance compared to isolated radiomics or clinical models. These findings collectively highlight the growing importance of multimodal learning and feature fusion strategies in precision oncology applications.

Optimization techniques and automated learning frameworks have further accelerated advancements in MSI prediction systems. Hyperparameter tuning methods such as Bayesian optimization, grid search, and random search were extensively applied to optimize deep learning architectures and improve convergence efficiency. Park et al. demonstrated that Bayesian optimization significantly enhances predictive accuracy while reducing computational overhead compared to conventional tuning methods. Ensemble learning strategies combining outputs from CNNs, random forests, and support vector machines further improved classification stability and reduced variance. Zhou et al. proposed a deep learning radiomics signature integrating handcrafted and automatically extracted features, demonstrating superior predictive capability compared to traditional radiomics alone. Automated end-to-end MSI prediction pipelines were also introduced to reduce human intervention and standardize workflow design. Ribeiro et al. developed an automated framework integrating preprocessing, feature extraction, model training, and evaluation within a unified system, thereby improving reproducibility and scalability. Weakly supervised learning and self-supervised learning methods additionally reduced dependency on expensive manual annotations by leveraging unlabeled or slide-level labeled datasets.

Despite substantial progress, several challenges remain in the development and clinical deployment of AI-driven MSI prediction systems. One of the primary limitations is the scarcity of large-scale, standardized, and balanced datasets. Variability in imaging conditions, staining protocols, and scanner characteristics significantly affects model reproducibility and cross-institutional generalization. Many studies remain retrospective and lack robust external validation cohorts, limiting confidence in real-world applicability. Deep learning systems also face computational complexity issues, particularly transformer-based models and multimodal frameworks requiring specialized hardware and extensive memory resources. Domain adaptation and federated learning approaches have emerged as promising solutions for improving cross-dataset generalization while preserving patient privacy. Gao et al. demonstrated that adversarial domain adaptation significantly improves model robustness across external datasets, whereas federated learning enabled collaborative multi-institutional training without sharing sensitive patient data. Nevertheless, challenges such as communication overhead, non-identically distributed datasets, and optimization stability remain unresolved.

Another important concern involves model interpretability and clinical trust. Although explainable AI techniques such as saliency maps, attention visualization, and feature importance analysis have improved transparency, clinicians still require more interpretable and biologically meaningful decision-making systems. Regulatory approval, ethical considerations, and workflow integration further complicate the clinical translation of AI-based MSI detection systems. Additionally, lightweight and energy-efficient architectures are required for real-time deployment in resource-constrained healthcare environments. Huang et al. proposed compact neural network models using pruning, quantization, and knowledge distillation techniques to reduce computational cost while maintaining competitive predictive accuracy. Future research should focus on developing explainable multimodal frameworks, robust standardization protocols, lightweight architectures, and large multicenter validation studies to ensure reliable and clinically applicable MSI prediction systems. Collectively, the reviewed studies demonstrate that radiomics, deep learning, transformers, graph neural networks, multimodal learning, and optimization techniques represent promising directions for non-invasive MSI prediction and precision colorectal cancer management.

Comparative Table and Analysis Based on Literature Review

Study	**Year**	**Method / Approach**	**Model Used**	**Data Type**	**Key Contribution**	**Performance (AUC)**
Wang et al.	2023	Radiomics ML	SVM, RF	CT/MRI	Radiomics effectiveness	0.78–0.96
Li et al.	2023	Deep Learning Meta-analysis	CNN	Histopathology	Large-scale validation	~0.82
Guo et al.	2023	Transformer DL	Swin Transformer	Histopathology	Transformer superiority	~0.90
Jiang et al.	2020	DL Review	CNN	Histopathology	AI in pathology	—
Nasr et al.	2023	Hybrid Radiomics + DL	CNN + ML	Multimodal	Integration benefits	~0.88
Kather et al.	2020	DL Histology	CNN	Histopathology	Morphology-based MSI	~0.85
Fan et al.	2021	MRI Radiomics	SVM	MRI	MRI predictive value	~0.89
Cao et al.	2021	DL Radiomics	ResNet	CT	Hybrid feature learning	~0.87
Yamashita et al.	2021	Multimodal DL	CNN Fusion	Multi-data	Multi-source learning	>0.90
Bilal et al.	2021	Explainable DL	CNN + CAM	Histopathology	Interpretability	~0.88
Echle et al.	2020	DL Histology	CNN	Histopathology	Large-scale validation	>0.85
Wu et al.	2021	PET/CT Radiomics	RF	PET/CT	Functional imaging	~0.88
Sun et al.	2022	Radiogenomics	ML	CT + Genomics	Imaging-genomics link	>0.90
Kwon et al.	2022	Transfer Learning	ResNet	Histopathology	Pre-trained models	~0.88
Zhang et al.	2022	Ensemble Learning	Hybrid	Mixed	Model robustness	>0.90
Zhou et al.	2020	DL Radiomics	CNN	CT	Feature fusion	~0.84
Campanella et al.	2020	Weakly Supervised DL	MIL	Histopathology	Reduced annotation	>0.85
Chen et al.	2021	Clinical + Radiomics	LR	CT + Clinical	Hybrid prediction	~0.86
Lu et al.	2021	Attention DL	CNN + Attention	Histopathology	Region focus	>0.90
Ribeiro et al.	2022	Automated Pipeline	CNN	Mixed	End-to-end system	~0.88
Liu et al.	2021	Multi-phase Radiomics	RF	CT	Temporal imaging	~0.88
Schaefer et al.	2022	Self-supervised DL	SSL CNN	Histopathology	Unlabeled learning	~0.87
Zhang et al.	2022	Graph Neural Network	GNN	Histopathology	Structural learning	~0.89
Sheller et al.	2020	Federated Learning	FL CNN	Multi-center	Privacy-preserving AI	>0.85
Park et al.	202	Bayesian	DL	Mixed	Hyperparamete	>0.90

	2	Optimization			r tuning	
Chen et al.	2022	Vision Transformer	ViT	Histopathology	Global context learning	~0.89
Zhou et al.	2022	Multi-task Learning	CNN	Histopathology	Shared learning	>0.90
Gao et al.	2023	Domain Adaptation	DL	Multi-dataset	Generalization	↑10%
Huang et al.	2023	Lightweight DL	Compact CNN	Histopathology	Deployment efficiency	~0.86
Singh et al.	2023	Explainable Multimodal AI	Hybrid DL	Multi-data	Interpretability + accuracy	>0.92

Analysis Based on Literature Review

Recent research on non-invasive microsatellite instability (MSI) detection in colorectal cancer shows a significant transition from conventional radiomics-based machine learning methods toward advanced deep learning and hybrid artificial intelligence frameworks. Earlier studies mainly relied on handcrafted radiomic features extracted from CT, MRI, and PET/CT images combined with classifiers such as support vector machines, logistic regression, and random forests. Although these approaches achieved encouraging predictive accuracy, they were limited by their dependence on manually engineered features and reduced capability to capture complex tumor heterogeneity. The emergence of deep learning, particularly Convolutional Neural Networks (CNNs), greatly improved predictive performance by enabling automatic feature extraction and hierarchical representation learning from medical images and histopathological data.

Another important advancement is the adoption of transformer architectures, graph neural networks, and attention-based frameworks. Vision Transformers and Swin Transformers demonstrated strong performance by capturing long-range contextual relationships within histopathological images. Graph neural networks further improved tumor characterization by modeling spatial relationships between tissue regions, enabling better representation of structural heterogeneity. Attention mechanisms enhanced both prediction accuracy and interpretability by identifying diagnostically important regions of interest. Moreover, multimodal frameworks integrating radiological imaging, histopathology, genomic data, and clinical information consistently outperformed single-modality systems. Radiogenomics approaches further strengthened MSI prediction by linking imaging biomarkers with underlying molecular characteristics.

Optimization strategies also contributed significantly to improving model robustness and efficiency. Hyperparameter optimization techniques such as Bayesian optimization and automated tuning frameworks improved convergence speed and predictive accuracy. Ensemble learning approaches reduced variance and enhanced model stability across validation datasets. Transfer learning using pretrained neural networks effectively addressed the challenge of limited annotated medical data, while self-supervised and weakly supervised learning reduced reliance on expensive manual labeling. Together, these methods supported the development of scalable and reliable MSI prediction systems suitable for real-world clinical applications.

Despite substantial progress, several challenges still limit clinical deployment and large-scale adoption of AI-driven MSI prediction frameworks. Variability in imaging protocols, preprocessing methods, and feature extraction pipelines affects reproducibility and cross-dataset generalization. Many studies remain retrospective and lack external validation, increasing the risk of overfitting and limited clinical reliability. In addition, deep learning systems often require high computational resources and still face interpretability concerns because of their complex “black-box” nature. Emerging approaches such as explainable AI, federated learning, domain adaptation, and lightweight neural architectures offer promising solutions for improving transparency, scalability, privacy preservation, and efficient deployment in future MSI detection systems.

Discussion

The reviewed literature highlights the transformative potential of integrating radiomics and deep learning for non-invasive microsatellite instability (MSI) detection in colorectal cancer. Across the analyzed studies, deep learning models—particularly convolutional neural networks, transformers, and attention-based architectures—demonstrate consistently high predictive performance, often achieving AUC values above 0.85. The incorporation of radiomics further enhances these models by providing quantitative descriptors of tumor heterogeneity, which complements automatically learned deep features.

A key observation is the growing shift toward multimodal frameworks that combine imaging, histopathology, and clinical data, resulting in improved accuracy and robustness. Additionally, optimization strategies such as transfer learning, Bayesian hyperparameter tuning, and ensemble learning significantly contribute to performance enhancement and generalization. Emerging paradigms such as self-supervised learning, federated learning, and domain adaptation address challenges related to data scarcity, privacy, and cross-institutional variability.

However, several limitations persist. The lack of standardized imaging protocols and radiomics pipelines affects reproducibility, while limited external validation raises concerns regarding clinical applicability. Moreover, the interpretability of deep learning models remains a critical barrier, despite advancements in explainable AI techniques.

Overall, while substantial progress has been made, future research must focus on standardization, large-scale validation, and clinically interpretable models to enable real-world deployment of MSI prediction systems.

Conclusion

The integration of radiomics and deep learning has significantly improved non-invasive microsatellite instability (MSI) detection in colorectal cancer. Recent studies demonstrate that radiomics-based machine learning and deep learning models achieve high predictive performance, with many approaches reporting AUC values above 0.85. Radiomics effectively extracts quantitative imaging features related to tumor heterogeneity, while deep learning techniques such as Convolutional Neural Networks, transformers, and attention-based architectures enable automatic feature extraction and hierarchical representation learning. These advancements have substantially enhanced MSI prediction accuracy using histopathological and radiological imaging data.

Another major development is the emergence of hybrid and multimodal frameworks that combine radiomics, deep learning, clinical information, and genomic data. Such integrated models provide a more comprehensive understanding of tumor biology and consistently outperform single-modality systems. Optimization strategies including transfer learning, Bayesian hyperparameter optimization, ensemble learning, self-supervised learning, and domain adaptation further improve model robustness, convergence efficiency, and generalization capability, especially in scenarios involving limited labeled datasets.

Despite these advancements, several challenges remain before widespread clinical implementation can be achieved. Lack of standardized imaging protocols, retrospective study designs, limited external validation, data imbalance, and computational complexity continue to affect reproducibility and reliability. Additionally, interpretability remains a critical concern, requiring more explainable AI frameworks for clinical trust and adoption. Future research should prioritize large-scale multicenter validation, lightweight deployable models, federated learning, and standardized explainable AI systems to enable reliable and clinically applicable MSI prediction frameworks.

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