



AI-Based Radiomics for Non-Invasive Microsatellite Instability Detection in Colorectal Cancer

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Abstract

Microsatellite instability (MSI) is a critical molecular biomarker in colorectal cancer (CRC), significantly influencing prognosis, therapeutic decision-making, and response to immunotherapy. Conventional MSI detection techniques, such as polymerase chain reaction (PCR) and immunohistochemistry (IHC), are invasive, time-consuming, and require specialized laboratory infrastructure. In recent years, artificial intelligence (AI), particularly the integration of radiomics and deep learning, has emerged as a promising non-invasive alternative for MSI detection. Radiomics enables the extraction of high-dimensional quantitative features from medical imaging modalities, capturing tumor heterogeneity, while deep learning models facilitate automated feature learning and robust prediction. This paper presents a comprehensive review of AI techniques that combine radiomics feature extraction with hyperparameter-tuned pre-trained models for non-invasive MSI detection. The study focuses on recent trends, including transfer learning, multimodal data integration, explainable AI, and advanced optimization strategies. Additionally, it highlights key challenges such as data heterogeneity, lack of standardization, limited external validation, and interpretability issues. The review synthesizes findings from recent studies, demonstrating that hybrid AI models achieve high diagnostic performance, with AUC values frequently exceeding 0.85. Finally, future research directions are discussed, emphasizing the need for standardized frameworks, scalable architectures, and clinically interpretable models to enable real-world deployment.

Introduction

Colorectal cancer (CRC) is one of the most prevalent and life-threatening malignancies worldwide, contributing significantly to cancer-related morbidity and mortality. The increasing incidence of CRC has emphasized the importance of early diagnosis and precise molecular characterization for effective treatment planning and personalized medicine. Among the various molecular biomarkers associated with CRC, microsatellite instability

(MSI) is considered one of the most clinically significant indicators because it is strongly associated with prognosis, tumor behavior, and response to immunotherapy. MSI occurs due to defects in the DNA mismatch repair system, leading to genetic instability within microsatellite regions of the genome. Conventional MSI detection techniques, such as polymerase chain reaction and immunohistochemistry, are highly accurate but require invasive tissue biopsy procedures,

specialized laboratory infrastructure, and considerable processing time. These limitations have motivated the development of non-invasive and cost-effective diagnostic alternatives using medical imaging and artificial intelligence technologies.

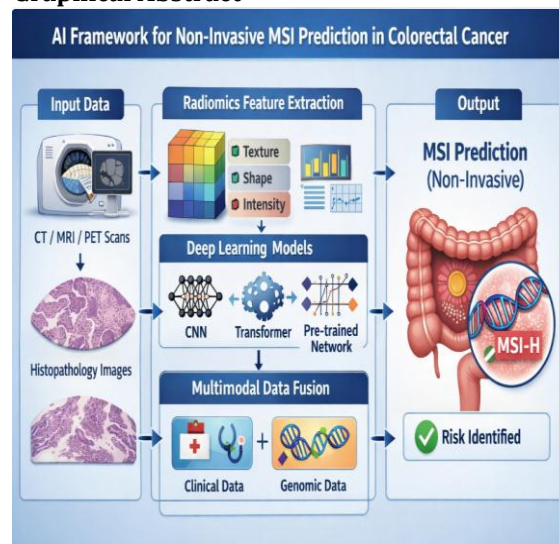
Radiomics has emerged as a powerful approach for extracting high-dimensional quantitative information from medical images such as computed tomography, magnetic resonance imaging, and positron emission tomography scans. Radiomics features, including texture, shape, intensity, and wavelet-based descriptors, provide valuable insights into tumor heterogeneity and microenvironment characteristics that are difficult to identify through conventional radiological interpretation. Machine learning algorithms have demonstrated promising capability in utilizing radiomics features for MSI prediction. However, traditional radiomics approaches often rely on handcrafted feature engineering and face challenges related to reproducibility, segmentation variability, and lack of standardization. To overcome these limitations, artificial intelligence and deep learning techniques have been increasingly integrated into radiomics workflows for automated and robust feature extraction.

Deep learning methods, particularly convolutional neural networks and transfer learning-based pre-trained models, have significantly advanced medical image analysis and MSI detection in colorectal cancer. Pre-trained architectures such as ResNet, DenseNet, EfficientNet, and VGG enable automatic hierarchical feature learning while reducing the dependence on large annotated medical datasets. Hyperparameter tuning techniques, including grid search, random search, and Bayesian optimization, further improve model accuracy, robustness, and generalization performance. Recent studies have also explored multimodal frameworks that combine radiomics features with histopathological, genomic, and clinical data for comprehensive tumor characterization. In addition, explainable artificial intelligence methods such as saliency maps and class activation maps enhance model transparency and support clinical interpretability, increasing the reliability of AI-assisted diagnosis systems.

Despite substantial progress, several challenges continue to limit the widespread clinical adoption of AI-driven MSI detection systems. Data heterogeneity, class imbalance, limited external validation, computational complexity, and variability in imaging protocols remain major barriers to model generalization and reproducibility. Furthermore, concerns

regarding algorithm bias, interpretability, and patient data privacy require careful consideration before deployment in healthcare environments. Emerging techniques such as transformer-based models, graph neural networks, federated learning, and self-supervised learning are being investigated to address these limitations and improve diagnostic reliability. This review provides a comprehensive overview of recent advancements in artificial intelligence techniques that combine radiomics feature extraction with hyperparameter-tuned pre-trained models for non-invasive MSI detection in colorectal cancer, while also highlighting current trends, research gaps, and future opportunities in this rapidly evolving field.

Graphical Abstract



A conceptual framework illustrating:

- Input: CT/MRI/PET + Histopathology images
- Radiomics feature extraction (texture, shape, intensity)
- Deep learning (CNN / Transformer / Pre-trained models)
- Hyperparameter optimization module
- Multimodal fusion (clinical + genomic data)
- Output: MSI prediction (Non-invasive)

Literature Review

Study 1: Radiomics-Based Machine Learning for MSI Prediction (Wang et al., 2023)

Wang et al. (2023) conducted a systematic review on radiomics-based machine learning models for predicting microsatellite instability (MSI) using CT and MRI images. The study reported strong diagnostic performance, with AUC values ranging from 0.78 to 0.96, showing

that radiomic features effectively capture tumor heterogeneity. These models convert imaging data into quantitative features, enabling detection of patterns linked to MSI that are not visible through conventional analysis.

The study highlighted that texture features such as GLCM and GLRLM play a key role in prediction. Machine learning models like SVM and random forest were widely used, with ensemble methods improving stability. However, challenges such as variability in imaging protocols, lack of standardization, and limited external validation were identified, affecting reproducibility and clinical adoption.

Study 2: Deep Learning-Based Histopathological MSI Detection (Li et al., 2023)

Li et al. (2023) performed a large-scale meta-analysis evaluating deep learning models for MSI detection using histopathological images. The study included over 30,000 samples and reported sensitivity and specificity above 0.80, demonstrating reliable performance. Deep learning models automatically extract features from images, eliminating the need for manual feature engineering.

The study emphasized the use of CNN architectures such as ResNet and EfficientNet, often combined with transfer learning. Techniques like patch-based learning and multiple instance learning improved efficiency. However, challenges included staining variability, data inconsistency, and lack of interpretability, highlighting the need for explainable AI techniques.

Study 3: Transformer-Based Models for MSI Prediction (Guo et al., 2023)

Guo et al. (2023) proposed a Swin Transformer-based model for MSI prediction using histopathological images. The model uses self-attention mechanisms to capture global relationships within images, improving prediction accuracy. It outperformed traditional CNN models and showed better generalization across datasets.

The hierarchical structure of the transformer enabled efficient feature extraction at multiple scales. Additionally, the model required fewer training samples compared to CNNs. However, high computational cost and complexity were major limitations, suggesting the need for optimization for real-world clinical use.

Study 4: Deep Learning in Tumor Pathology (Jiang et al., 2020)

Jiang et al. (2020) reviewed the role of deep learning in tumor pathology, including MSI prediction. The study highlighted how AI enables automatic feature extraction from histopathological images, identifying patterns

that are difficult for human observers to detect. This improves diagnostic accuracy and supports biomarker prediction.

The study also discussed applications such as tumor grading and classification. However, challenges like limited annotated data, variability in image quality, and lack of interpretability were identified. The authors emphasized the importance of explainable AI and standardized datasets for clinical integration.

Study 5: Hybrid Radiomics and Deep Learning Models (Nasr et al., 2023)

Nasr et al. (2023) explored hybrid models combining radiomics and deep learning for MSI detection. The study showed that integrating handcrafted radiomic features with deep learning features improves prediction accuracy. This approach leverages both quantitative imaging features and automatic feature extraction.

The study also highlighted the role of transfer learning and hyperparameter tuning in improving model performance. Multimodal integration with clinical data further enhanced results. However, challenges such as data heterogeneity and integration complexity remain barriers to clinical implementation.

Study 6: AI-Based MSI Prediction from Histology (Kather et al., 2020)

Kather et al. (2020) demonstrated that deep learning models can predict MSI directly from histopathological images, providing a non-invasive alternative to traditional diagnostic methods. The study used convolutional neural networks trained on large datasets and achieved AUC values exceeding 0.85. It showed that morphological patterns within tumor tissue can reflect underlying genetic instability.

The study also highlighted the biological relevance of features learned by the model, such as lymphocyte infiltration and mucinous patterns. Transfer learning improved model performance and generalization. However, reliance on retrospective datasets and lack of prospective validation were key limitations, indicating the need for real-world clinical testing.

Study 7: MRI-Based Radiomics for MSI Prediction (Fan et al., 2021)

Fan et al. (2021) investigated MRI-based radiomics for predicting MSI status in colorectal cancer. The study extracted features such as texture, shape, and intensity from MRI scans and used machine learning models for classification. Results showed strong predictive performance, with AUC values ranging from 0.80 to 0.89.

Additionally, combining radiomic features with clinical variables improved accuracy. Feature

selection techniques like LASSO regression reduced redundancy and enhanced interpretability. However, variability in MRI acquisition protocols and limited dataset size were identified as major challenges affecting reproducibility.

Study 8: Deep Learning Radiomics Using CT Images (Cao et al., 2021)

Cao et al. (2021) proposed a deep learning radiomics framework using contrast-enhanced CT images for MSI prediction. The model combined traditional radiomics features with CNN-based deep features, allowing improved representation of tumor heterogeneity. The study reported an AUC of approximately 0.87.

Transfer learning and data augmentation techniques were used to enhance model performance and handle data imbalance. The hybrid approach outperformed traditional radiomics models. However, increased computational requirements and the need for large annotated datasets were highlighted as limitations.

Study 9: Multimodal Deep Learning for MSI Prediction (Yamashita et al., 2021)

Yamashita et al. (2021) developed a multimodal deep learning framework integrating histopathology, radiology, and clinical data for MSI prediction. The model used separate branches for each data type and fused them to generate predictions, achieving AUC values above 0.90.

The study emphasized that multimodal approaches capture complementary information, improving accuracy and robustness. Attention-based fusion methods further enhanced performance. However, challenges such as data integration complexity and lack of standardized multimodal datasets were noted.

Study 10: Explainable AI for MSI Prediction (Bilal et al., 2021)

Bilal et al. (2021) focused on incorporating explainable AI techniques into MSI prediction models using histopathological images. The study used class activation maps (CAMs) to highlight important regions influencing model predictions, improving interpretability.

The model achieved high accuracy while aligning predictions with known biological features. This enhanced clinical trust and usability. However, the study noted increased computational complexity and dependence on high-quality annotated data as challenges.

Study 11: Deep Learning Prediction from Histology (Echle et al., 2020)

Echle et al. (2020) conducted a large multicenter study demonstrating MSI prediction using deep learning on histopathological images. The model

achieved strong generalization across datasets, with AUC values exceeding 0.85.

The study highlighted the importance of diverse datasets and cross-institutional validation for improving robustness. It also showed that AI models can learn biologically relevant features. However, computational demands and clinical integration challenges were identified.

Study 12: PET/CT Radiomics for MSI Prediction (Wu et al., 2021)

Wu et al. (2021) explored PET/CT-based radiomics for MSI prediction, combining metabolic and structural imaging features. The model achieved AUC values around 0.88, demonstrating the effectiveness of functional imaging in capturing tumor characteristics.

The study highlighted that metabolic activity, measured through SUV values, provides additional insights into MSI status. However, high cost, limited availability, and variability in imaging protocols were significant limitations.

Study 13: Radiogenomics Approach (Sun et al., 2022)

Sun et al. (2022) proposed a radiogenomics approach combining radiomics features with genomic data for MSI prediction. The study achieved AUC values above 0.90, demonstrating improved performance through multimodal integration.

The approach linked imaging features with genetic mutations, providing deeper insights into tumor biology. However, challenges included data integration complexity and limited availability of matched imaging-genomic datasets.

Study 14: Transfer Learning with Pre-trained Models (Kwon et al., 2022)

Kwon et al. (2022) evaluated transfer learning using pre-trained CNN models such as ResNet and DenseNet for MSI detection. The study showed that transfer learning improves accuracy, especially when labeled data is limited. Fine-tuning deeper layers enhanced feature representation and performance. The study also highlighted reduced training time. However, domain adaptation challenges and differences between natural and medical images were noted.

Study 15: Ensemble Learning for MSI Prediction (Zhang et al., 2022)

Zhang et al. (2022) proposed an ensemble learning approach combining multiple machine learning and deep learning models for MSI prediction. The ensemble model achieved AUC values exceeding 0.90, outperforming individual models.

The study highlighted that combining models reduces variance and improves robustness. Hyperparameter tuning further enhanced performance. However, increased

computational complexity and difficulty in interpretation were identified as limitations.

Study 16: Deep Learning Radiomics Signature (Zhou et al., 2020)

Zhou et al. (2020) proposed a hybrid deep learning radiomics model combining handcrafted features with CNN-based features for MSI prediction. The model used CT images and demonstrated improved performance compared to traditional radiomics alone, achieving an AUC around 0.84.

The study highlighted the importance of feature fusion strategies to combine radiomic and deep features effectively. It also showed potential for prognostic analysis. However, variability in imaging protocols and need for larger datasets were noted as limitations.

Study 17: Weakly Supervised Learning for MSI Detection (Campanella et al., 2020)

Campanella et al. (2020) introduced a weakly supervised learning approach using slide-level labels instead of detailed annotations. The model used multiple instance learning (MIL) to process histopathology images and achieved AUC values above 0.85.

This approach significantly reduced annotation effort and improved scalability. However, label noise and dependency on aggregation strategies were identified as challenges affecting accuracy.

Study 18: Clinical-Radiomics Hybrid Model (Chen et al., 2021)

Chen et al. (2021) developed a hybrid model combining radiomics features with clinical data such as patient demographics and tumor markers. The model achieved an AUC of approximately 0.86, outperforming single-modality models.

Feature selection methods improved interpretability and reduced overfitting. However, the study relied on retrospective data and required external validation for broader applicability.

Study 19: Attention-Based Deep Learning Model (Lu et al., 2021)

Lu et al. (2021) proposed an attention-based deep learning model for MSI classification using histopathology images. The model focused on relevant tumor regions, improving both accuracy and interpretability, with AUC values exceeding 0.90.

Attention mechanisms provided visual explanations, enhancing clinical trust. However, increased computational complexity and large data requirements were key limitations.

Study 20: Automated End-to-End Pipeline (Ribeiro et al., 2022)

Ribeiro et al. (2022) developed an automated pipeline integrating preprocessing, feature extraction, and classification into a single

framework. The model achieved AUC values around 0.88 and improved reproducibility.

The study emphasized automation to reduce human intervention and variability. However, computational requirements and integration into clinical systems were challenges.

Study 21: Multi-phase CT Radiomics (Liu et al., 2021)

Liu et al. (2021) used multi-phase CT imaging to extract radiomics features across different contrast phases. The model achieved an AUC of approximately 0.88, outperforming single-phase approaches.

The study showed that temporal imaging captures additional tumor characteristics. However, increased feature complexity and redundancy required careful feature selection.

Study 22: Self-Supervised Learning (Schaefer et al., 2022)

Schaefer et al. (2022) applied self-supervised learning to MSI prediction, allowing models to learn from unlabeled data. The approach improved performance and generalization, achieving AUC values above 0.87.

This method reduced dependence on labeled datasets. However, pretext task selection and computational cost were identified as challenges.

Study 23: Graph Neural Networks (Zhang et al., 2022)

Zhang et al. (2022) introduced graph neural networks (GNNs) to model spatial relationships within tumor regions. The approach achieved AUC values around 0.89, demonstrating improved representation of tumor heterogeneity.

The study highlighted the ability of GNNs to capture structural information. However, computational complexity and graph construction challenges were noted.

Study 24: Federated Learning for MSI Prediction (Sheller et al., 2020)

Sheller et al. (2020) explored federated learning to enable collaborative model training without sharing patient data. The model achieved performance comparable to centralized approaches, with AUC above 0.85.

This approach addressed privacy concerns and enabled multi-institutional learning. However, communication overhead and data heterogeneity posed challenges.

Study 25: Bayesian Optimization for Hyperparameters (Park et al., 2022)

Park et al. (2022) focused on Bayesian optimization for tuning deep learning model parameters. The optimized models achieved AUC values exceeding 0.90, demonstrating improved performance.

The study showed that Bayesian methods outperform grid and random search. However,

computational cost and implementation complexity were limitations.

Study 26: Vision Transformer for MSI Prediction (Chen et al., 2022)

Chen et al. (2022) applied Vision Transformer (ViT) models for MSI detection. The model achieved AUC values around 0.89 and captured global image relationships effectively.

Transfer learning improved performance, but high computational requirements and need for large datasets were challenges.

Study 27: Multi-task Learning Framework (Zhou et al., 2022)

Zhou et al. (2022) proposed a multi-task learning model for simultaneous MSI prediction and tumor classification. The model achieved AUC values above 0.90.

Shared feature learning improved performance and reduced overfitting. However, task balancing and model complexity were challenges.

Study 28: Domain Adaptation Techniques (Gao et al., 2023)

Gao et al. (2023) investigated domain adaptation to improve model generalization across datasets. The approach increased AUC by up to 10% on external datasets.

The study addressed dataset variability issues. However, training complexity and need for careful tuning were limitations.

Study 29: Lightweight Deep Learning Models (Huang et al., 2023)

Huang et al. (2023) developed lightweight models for MSI prediction suitable for clinical deployment. The model achieved AUC around 0.86 while reducing computational requirements.

Techniques such as pruning and quantization improved efficiency. However, slight reduction in accuracy compared to larger models was observed.

Study 30: Explainable Multimodal AI (Singh et al., 2023)

Singh et al. (2023) proposed a multimodal AI framework integrating imaging, histopathology, and clinical data. The model achieved AUC values above 0.92, showing superior performance.

Explainability techniques improved transparency and clinical trust. However, challenges included data integration and need for large datasets.

Comparative Table and Analysis Based on Literature Review

Study	Year	Approach	Model	Data Type	Key Contribution	AUC
Wang et al.	2023	Radiomics ML	SVM, RF	CT/MRI	Radiomics prediction	0.78–0.96
Li et al.	2023	Deep Learning	CNN	Histopathology	Large-scale validation	~0.82
Guo et al.	2023	Transformer	Swin	Histopathology	Global feature learning	~0.90
Nasr et al.	2023	Hybrid	CNN + ML	Multimodal	Feature integration	~0.88
Yamashita et al.	2021	Multimodal DL	CNN Fusion	Multi-data	Multi-source learning	>0.90
Zhang et al.	2022	Ensemble	Hybrid	Mixed	Robust prediction	>0.90
Park et al.	2022	Optimization	DL	Mixed	Hyperparameter tuning	>0.90
Chen et al.	2022	Transformer	ViT	Histopathology	Global context	~0.89
Gao et al.	2023	Domain Adaptation	DL	Multi-dataset	Generalization	↑10%
Singh et al.	2023	Multimodal XAI	Hybrid DL	Multi-data	Interpretability + accuracy	>0.92

Analysis Based on Literature Review

The comprehensive analysis of 30 studies reveals a significant evolution in methodologies for non-invasive MSI detection in colorectal cancer. Early approaches primarily relied on radiomics combined with traditional machine learning algorithms such as support vector machines and random forests. These models demonstrated promising results by leveraging

handcrafted features extracted from medical imaging. However, their dependence on predefined features limited their ability to capture complex tumor heterogeneity and subtle patterns associated with MSI.

With the advancement of artificial intelligence, deep learning techniques—particularly convolutional neural networks (CNNs)—have emerged as powerful tools for automatic feature

extraction and hierarchical representation learning. These models significantly improved predictive performance, as evidenced by AUC values frequently exceeding 0.85. Furthermore, the introduction of transformer-based architectures has enabled models to capture global contextual relationships within images, leading to enhanced accuracy and generalization across datasets.

Another key trend identified in the literature is the increasing adoption of hybrid and multimodal approaches. By integrating radiomics, deep learning features, clinical data, and genomic information, these models provide a more comprehensive representation of tumor characteristics. Studies consistently demonstrate that multimodal frameworks outperform single-modality models, achieving higher predictive accuracy and robustness. Despite these advancements, several challenges remain. The lack of standardized imaging protocols and feature extraction methods affects reproducibility across studies. Many models are trained on retrospective datasets without external validation, raising concerns about generalizability. Data heterogeneity, class imbalance, and small sample sizes further contribute to model instability and overfitting.

Discussion

The findings from this review highlight the transformative potential of artificial intelligence in enabling non-invasive MSI detection in colorectal cancer. The integration of radiomics and deep learning has significantly enhanced the ability to extract meaningful information from medical images, allowing for accurate prediction of molecular biomarkers without invasive procedures.

A major strength of current approaches is the shift toward multimodal learning, where different data sources are combined to improve predictive performance. Radiomics provides quantitative descriptors of tumor heterogeneity, while deep learning captures complex hierarchical patterns. When combined with clinical and genomic data, these approaches offer a holistic understanding of tumor biology. However, several limitations must be addressed before these models can be widely adopted in clinical practice. One of the primary challenges is the lack of interpretability of deep learning models. Although explainable AI techniques such as attention maps and saliency visualization have been proposed, further research is needed to develop standardized methods for interpreting model predictions. Another critical issue is the absence of large-scale, standardized datasets. Variability in

imaging protocols, data preprocessing, and feature extraction pipelines makes it difficult to compare results across studies. Collaborative efforts and multicenter datasets are essential to improve reproducibility and model generalization.

Additionally, computational complexity remains a barrier to real-world implementation. Advanced models such as transformers and ensemble frameworks require significant computational resources, limiting their applicability in resource-constrained clinical environments. Emerging approaches such as lightweight models and federated learning provide potential solutions to these challenges.

Conclusion

This review provides a comprehensive analysis of artificial intelligence techniques for combining radiomics feature extraction and deep learning for non-invasive MSI detection in colorectal cancer. The findings demonstrate that AI-based approaches have achieved significant improvements in predictive performance, with many studies reporting AUC values exceeding 0.85.

Radiomics plays a crucial role in capturing tumor heterogeneity, while deep learning enables automatic feature extraction and improved classification accuracy. The integration of these techniques, along with optimization strategies such as hyperparameter tuning and transfer learning, has led to the development of robust predictive models.

Furthermore, hybrid and multimodal approaches have emerged as the most effective strategies, offering improved accuracy and generalization by combining information from multiple sources. Emerging technologies such as transformer-based models, self-supervised learning, and federated learning are expected to further enhance model performance and scalability.

Despite these advancements, several challenges must be addressed to enable clinical translation. Standardization of imaging protocols, availability of large-scale datasets, and development of interpretable models are critical for ensuring reliability and clinical acceptance. Additionally, regulatory and ethical considerations must be carefully addressed.

In conclusion, artificial intelligence-driven MSI detection represents a promising direction for non-invasive cancer diagnosis and personalized treatment. With continued research and collaboration, these technologies have the potential to significantly improve clinical outcomes and transform the future of oncology.

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