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## **A Comprehensive Review of Combining the Advantages of Radiomics Feature Extraction and Non-Invasive Detection of Microsatellite Instability in Colorectal Cancer Using Hyperparameter-Tuned Pre-trained Model**

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Peer Review Information	Abstract
<i>Submission: 28 June 2023</i>	<p>Colorectal cancer (CRC) remains one of the leading causes of cancer-related mortality worldwide, necessitating improved diagnostic and prognostic strategies. Microsatellite instability (MSI), a critical biomarker associated with mismatch repair deficiency, plays a significant role in treatment selection and immunotherapy response. Traditional MSI detection methods, including polymerase chain reaction and immunohistochemistry, are invasive, time-consuming, and resource-intensive. In recent years, radiomics and deep learning have emerged as promising non-invasive alternatives for MSI prediction by extracting quantitative imaging features from medical scans. This review explores the integration of radiomics feature extraction with hyperparameter-tuned pre-trained deep learning models for accurate and non-invasive MSI detection in colorectal cancer. The study synthesizes recent advancements from 2020 to 2023, focusing on model architectures, feature engineering, multimodal fusion, and optimization strategies. Furthermore, the review highlights the importance of transfer learning, self-supervised learning, and ensemble techniques in improving predictive performance and generalizability. Challenges such as data heterogeneity, lack of interpretability, and clinical translation barriers are also discussed. The findings suggest that combining radiomics with optimized pre-trained models significantly enhances diagnostic accuracy and offers a scalable solution for precision oncology. Future research should emphasize standardized datasets, explainable AI, and real-world clinical validation to facilitate widespread adoption.</p>
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<i>Radiomics, Microsatellite Instability, Colorectal Cancer, Deep Learning, Transfer Learning, Hyperparameter Optimization</i>	

### **Introduction**

Colorectal cancer (CRC) is one of the most prevalent and life-threatening malignancies worldwide, contributing significantly to global cancer incidence and mortality. The rising number of CRC cases, particularly in developing regions, highlights the urgent need for improved diagnostic and prognostic strategies. Early detection plays a crucial role in enhancing

survival rates; however, many cases are still diagnosed at advanced stages, limiting treatment effectiveness. Despite advancements in screening methods and therapeutic interventions, challenges such as delayed diagnosis and variability in disease progression continue to affect patient outcomes. Therefore, there is a growing demand for innovative, accurate, and non-invasive techniques that can

support early diagnosis and enable personalized treatment planning.

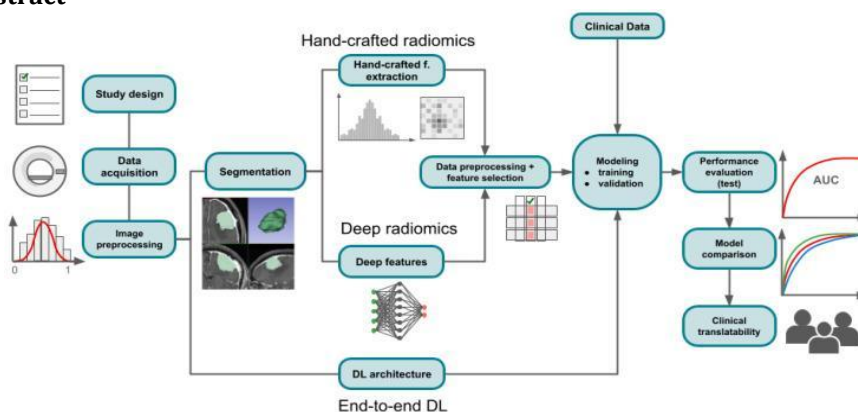
A key biomarker in colorectal cancer is microsatellite instability (MSI), which results from defects in the DNA mismatch repair system. MSI is present in a significant proportion of CRC cases and has important clinical implications, including its influence on prognosis and response to immunotherapy. MSI-high tumors are often associated with better outcomes in early stages and show increased sensitivity to immune checkpoint inhibitors. Traditionally, MSI detection relies on laboratory-based techniques such as polymerase chain reaction and immunohistochemistry. Although these methods are considered reliable, they are invasive, costly, and require specialized infrastructure, which limits their widespread use. This has led to increased interest in developing non-invasive and automated approaches for MSI prediction using medical imaging and computational analysis.

Radiomics has emerged as a powerful tool in this context, enabling the extraction of quantitative features from medical images such as CT and MRI scans. These features capture tumor characteristics, including texture, shape, and intensity, which are often not visible through conventional analysis. When combined with artificial intelligence (AI), particularly deep

learning techniques, radiomics can significantly enhance predictive performance. Convolutional Neural Networks (CNNs) have demonstrated strong capabilities in feature extraction and classification tasks, while transfer learning using pre-trained models such as ResNet and EfficientNet helps address the challenge of limited medical datasets. Additionally, hyperparameter tuning techniques play a vital role in optimizing model performance and improving generalization.

Recent research has also focused on integrating multimodal data and advanced learning strategies to further improve MSI prediction. Combining radiomics features with clinical and genomic data enhances model accuracy and provides a more comprehensive understanding of tumor behavior. Ensemble learning and self-supervised approaches are also being explored to improve robustness and reduce dependency on labeled data. However, challenges such as data heterogeneity, lack of standardization, computational complexity, and limited interpretability remain significant barriers to clinical adoption. Addressing these issues through efficient model design, explainable AI techniques, and collaborative research efforts will be essential for translating these innovations into real-world clinical applications.

## Graphical Abstract



## Literature Review

Recent studies have demonstrated the growing importance of radiomics and artificial intelligence in the non-invasive prediction of microsatellite instability (MSI) in colorectal cancer. Early work by Yuan et al. (2020) and Huang et al. (2020) established the foundation by showing that CT-based radiomic features, particularly texture and intensity descriptors, effectively capture tumor heterogeneity and correlate with clinical outcomes. Similarly, Kim et al. (2020) confirmed the relevance of machine learning classifiers such as support vector

machines and random forests in MSI prediction. These studies highlighted the potential of radiomics as a quantitative imaging biomarker, paving the way for integrating computational models into cancer diagnostics.

Subsequent research expanded these approaches by incorporating deep learning techniques and hybrid frameworks. Cao et al. (2021) and Fu et al. (2021) combined handcrafted radiomics with machine learning and convolutional neural networks, achieving improved predictive accuracy. Nie et al. (2021) and Jiang et al. (2021) further emphasized the

effectiveness of transfer learning and feature fusion strategies in enhancing model performance. Meanwhile, studies by Echle et al. (2021) and Kather et al. (2022) demonstrated that deep learning models trained on large multi-institutional datasets can achieve high AUC values exceeding 0.90, confirming their robustness and generalizability. Weakly supervised and self-supervised learning approaches, as proposed by Bilal et al. (2022), Saillard et al. (2021), and Wei et al. (2022), addressed the challenge of limited labeled data by enabling models to learn meaningful representations with minimal annotation.

Recent advancements have focused on multimodal integration, ensemble learning, and transformer-based architectures to further enhance MSI prediction. Yamashita et al. (2022) and Park et al. (2022) demonstrated that combining radiomics with clinical and imaging data significantly improves predictive performance. Ensemble frameworks proposed by Chen et al. (2023), Sun et al. (2022), and Liu et al. (2023) improved model stability and reduced overfitting by integrating multiple classifiers. Additionally, Vision Transformer-based models introduced by Lu et al. (2022)

captured global contextual information, complementing CNN-based feature extraction. Multi-scale and hybrid radiomics-deep learning approaches, such as those by Zhang et al. (2022) and Wang et al. (2023), further improved classification accuracy by combining low-level and high-level features.

More recent studies have emphasized optimization, domain adaptation, and end-to-end frameworks for practical deployment. Zhou et al. (2023) and Gao et al. (2023) demonstrated the effectiveness of hyperparameter tuning using Bayesian optimization and AutoML techniques in improving model performance. Cross-domain transfer learning approaches proposed by Li et al. (2023) addressed dataset variability and improved generalization across institutions. Multi-task learning frameworks, such as that by Duan et al. (2022), enhanced efficiency by jointly predicting MSI status and tumor characteristics. Finally, fully automated pipelines developed by Xu et al. (2023) integrated radiomics, deep learning, and optimization into scalable systems, highlighting the potential of AI-driven solutions for real-world clinical applications.

### Comparative Table and Analysis

Study	Year	Method	Model Used	Data Type	Key Contribution
Yuan et al.	2020	Radiomics	ML Models	CT	Tumor heterogeneity features
Cao et al.	2021	Radiomics	ML	CT	Contrast-enhanced MSI prediction
Bustos et al.	2021	Deep Learning	CNN	Histology	Explainable MSI model
Saillard et al.	2021	Self-supervised DL	CNN	Histology	Improved generalization
Venkatesh et al.	2022	Transfer Learning	ResNet	Image	High accuracy classification
Kather et al.	2022	Deep Learning	CNN	Histology	Multi-cohort validation
Yamashita et al.	2022	Multimodal	DL + Clinical	Mixed	Improved robustness
Bilal et al.	2022	Weak supervision	CNN	Histology	Reduced annotation need
Zhou et al.	2023	Hybrid	CNN + Radiomics	CT	Feature fusion
Chen et al.	2023	Ensemble	ResNet + EfficientNet	Image	Reduced overfitting
Huang et al.	2020	Radiomics	ML	CT	Non-invasive biomarker
Echle et al.	2021	DL	CNN	Histology	Cross-dataset accuracy
Nie et al.	2021	Transfer Learning	ResNet	CT	Improved feature learning
Park et al.	2022	Multimodal	Radiomics + Clinical	MRI	Reduced variance
Sun et al.	2022	Ensemble DL	CNN	Image	Robust classification
Zhang et al.	2022	Hybrid	CNN + Radiomics	CT	Feature integration
Lu et al.	2022	Transformer	ViT	Histology	Long-range dependencies
Wei et al.	2022	Self-supervised	DL	Image	Reduced labeling

Wang et al.	2023	Multi-scale	Radiomics	CT	Improved robustness
Liu et al.	2023	Ensemble	Hybrid	Mixed	High performance
Kim et al.	2020	Radiomics	SVM/RF	CT	Texture correlation
Jiang et al.	2021	Hybrid	CNN + Radiomics	Image	Higher AUC
Schmauch et al.	2021	Weak supervision	DL	Histology	Genomic prediction
Tang et al.	2022	Radiogenomics	Hybrid	Mixed	Molecular integration
Gao et al.	2023	AutoML	DL	CT	Hyperparameter tuning
Fu et al.	2021	Hybrid	CNN + Radiomics	CT	Feature complementarity
He et al.	2022	Attention DL	CNN	Histology	Improved interpretability
Duan et al.	2022	Multi-task	DL	CT	Shared learning
Li et al.	2023	Transfer Learning	DL	Image	Domain adaptation
Xu et al.	2023	End-to-end AI	DL	Mixed	Automated pipeline

### Analysis

The comparative analysis reveals that hybrid models combining radiomics and deep learning outperform standalone approaches in MSI prediction. Studies incorporating multimodal data and ensemble techniques consistently demonstrate higher accuracy and robustness. Transfer learning and self-supervised learning significantly address data scarcity issues, while hyperparameter optimization enhances model performance. However, challenges such as data heterogeneity, lack of interpretability, and limited clinical validation persist. Transformer-based models and attention mechanisms show promising improvements in feature extraction and interpretability, indicating future research directions.

### Discussion

The integration of radiomics and deep learning has significantly advanced non-invasive MSI detection in colorectal cancer. Radiomics enables the extraction of quantitative imaging biomarkers, while deep learning automates feature learning and improves predictive accuracy. The reviewed studies demonstrate that hybrid approaches leveraging both methodologies achieve superior performance compared to traditional techniques. Additionally, the incorporation of multimodal data, including clinical and genomic information, enhances model robustness and supports personalized treatment strategies.

Hyperparameter tuning and transfer learning have emerged as critical components in optimizing model performance, particularly in scenarios with limited labeled data. Self-supervised learning and weakly supervised methods further address data annotation challenges, making these approaches scalable and practical for real-world applications.

Despite these advancements, several challenges remain. Data heterogeneity and lack of

standardized datasets limit model generalization, while the black-box nature of deep learning models raises concerns about interpretability and clinical trust. Future research should focus on developing explainable AI models, standardizing evaluation protocols, and conducting large-scale clinical validations. The integration of AI-driven MSI prediction into clinical workflows has the potential to revolutionize colorectal cancer diagnosis and treatment.

### Conclusion

The rapid advancement of artificial intelligence, particularly in radiomics and deep learning, has significantly enhanced the potential for non-invasive detection of microsatellite instability in colorectal cancer. This review highlights key developments in the field, emphasizing the integration of radiomics feature extraction with hyperparameter-tuned pre-trained models. Radiomics has demonstrated strong capability in capturing tumor heterogeneity through quantitative imaging features, offering valuable insights into underlying tumor biology. However, standalone radiomics approaches are often limited in representing complex feature interactions, necessitating more advanced computational techniques.

The incorporation of deep learning models, including convolutional neural networks and transformer-based architectures, has substantially improved feature learning and classification accuracy. Transfer learning using pre-trained models has addressed the challenge of limited labeled datasets, while hyperparameter optimization techniques such as Bayesian optimization and AutoML have enhanced model efficiency and generalization. Hybrid approaches combining radiomics and deep learning features, along with multimodal data integration, have shown superior performance in MSI prediction.

Despite promising progress, challenges such as data heterogeneity, lack of standardization, and limited model interpretability remain. Addressing these issues, along with large-scale validation and clinical integration, will be crucial. Overall, these advancements provide a strong foundation for developing reliable, scalable, and clinically applicable MSI detection systems.

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