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**Deep Learning and Optimization Approaches in DeepLabV3-DenseNet:
Leveraging Radiomics Feature Extraction and Non-Invasive Detection
of Microsatellite Instability in Colorectal Cancer with a
Hyperparameters-Tuned Pre-trained Model: A Review**

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Peer Review Information	Abstract
<p>Submission: 22 April 2025 Revision: 05 May 2025 Acceptance: 20 May 2025</p>	<p>Microsatellite instability (MSI) is a critical biomarker in colorectal cancer (CRC), influencing prognosis and response to immunotherapy. Traditional MSI detection methods rely on invasive biopsy and molecular testing, which are time-consuming and costly. Recent advancements in deep learning and radiomics have enabled non-invasive MSI prediction using medical imaging modalities such as CT, MRI, and histopathology slides. In particular, convolutional neural networks such as DeepLabV3 and dense Net have demonstrated superior performance in feature extraction and segmentation tasks. Radiomics-based approaches extract high-dimensional quantitative features from medical images, capturing tumour heterogeneity and underlying biological characteristics. Studies have shown that machine learning models using PET/CT radiomics can effectively predict MSI status with high accuracy. Furthermore, deep learning-based frameworks trained on histopathology images have achieved strong predictive performance with AUC values exceeding 0.9. Hybrid architectures combining DeepLabV3 for segmentation and dense Net for classification further enhance feature representation and model performance. This review explores recent advancements in deep learning and optimization-based MSI detection, focusing on radiomics, graph-based learning, and hyperparameter optimization. The study highlights the advantages of hybrid deep learning models and discusses current challenges, including data dependency, interpretability, and computational complexity.</p>
<p>Keywords</p> <p><i>Microsatellite Instability (MSI), Colorectal Cancer (CRC), DeepLabV3, Dense Net, Radiomics, Deep Learning.</i></p>	

Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide. Early detection and accurate characterization of tumour biomarkers are essential for improving patient outcomes and guiding personalized treatment strategies. One such biomarker is microsatellite instability (MSI), which results from defects in the DNA mismatch repair system.

MSI status plays a crucial role in determining the response to immunotherapy and is associated with better prognosis in certain CRC patients. Traditional methods for MSI detection involve polymerase chain reaction (PCR) testing and immunohistochemistry (IHC), both of which require invasive tissue sampling. These methods are time-consuming, costly, and may not fully capture tumour heterogeneity. As a result, there

is a growing interest in developing non-invasive approaches using medical imaging and artificial intelligence techniques.

Radiomics has emerged as a promising approach for extracting quantitative features from medical images such as CT and MRI scans. These features include texture, shape, and intensity patterns that are not visible to the human eye. Studies have demonstrated that radiomics can effectively capture tumour heterogeneity and predict clinical outcomes. For example, CT-based radiomics models have shown the ability to predict MSI status non-invasively, enhancing personalized treatment planning. Deep learning has further advanced the field by enabling automatic feature extraction and end-to-end learning. Architectures such as dense Net provide efficient feature reuse and improved gradient flow, making them suitable for classification tasks. Similarly, DeepLabV3, a semantic segmentation model, has shown strong performance in medical image segmentation tasks, including polyp detection in colonoscopy images. Combining segmentation and classification models allows for precise tumour localization and accurate MSI prediction.

Recent studies have also explored hybrid frameworks integrating radiomics and deep learning. These approaches leverage both handcrafted features and learned representations, improving model performance. Additionally, self-supervised learning and multiple instance learning techniques have been applied to histopathology images, achieving high MSI prediction accuracy with limited labelled data. Despite these advancements, several challenges remain. Deep learning models require large annotated datasets, which are often difficult to obtain in medical domains. Moreover, the lack of interpretability and high computational requirements limit their clinical adoption. Optimization techniques, including hyperparameter tuning and metaheuristic algorithms, play a crucial role in improving model performance and efficiency. This review aims to provide a comprehensive overview of deep learning and optimization approaches for MSI detection in colorectal cancer, with a focus on DeepLabV3-DenseNet architectures and radiomics-based feature extraction.

Literature Review

The application of deep learning and optimization techniques in colorectal cancer analysis, particularly for non-invasive prediction of microsatellite instability (MSI), has witnessed substantial advancement over recent years. MSI is a clinically significant biomarker associated with prognosis, immunotherapy response, and

treatment planning in colorectal cancer. Traditional diagnostic approaches such as polymerase chain reaction (PCR) and immunohistochemistry (IHC) are widely used but remain invasive, labor-intensive, and limited in capturing spatial tumour heterogeneity. Consequently, researchers have increasingly focused on computational pathology, radiomics, and artificial intelligence-based frameworks to develop accurate, scalable, and non-invasive MSI prediction models. The integration of convolutional neural networks (CNNs), graph-based learning, radiomics feature extraction, and optimization strategies has significantly enhanced diagnostic performance and opened new pathways for precision oncology.

Lian et al. (2020) presented one of the early deep learning frameworks for colorectal cancer histopathology analysis using CNN architectures. Their model demonstrated that deep networks can directly learn discriminative features from raw medical images without manual feature engineering, significantly improving classification accuracy. This study emphasized the strength of automated feature learning in medical imaging pipelines. However, the approach required extensive labeled datasets and suffered from limited interpretability, which remains a key challenge in clinical adoption.

Building upon this, Bustos et al. (2021) introduced the XDEEP-MSI framework for predicting MSI status from histopathology images. The model incorporated multi-scale feature extraction mechanisms along with bias reduction strategies, achieving high predictive accuracy with AUC values close to 0.90. The study highlighted the robustness of deep learning models in capturing complex histological patterns. Nevertheless, the framework required computationally intensive preprocessing and significant GPU resources, limiting scalability in resource-constrained environments.

Similarly, Schirris et al. (2021) proposed the Deep SMILE architecture, which leveraged self-supervised learning combined with multiple instance learning for MSI prediction from whole-slide images. This approach reduced dependency on large annotated datasets while maintaining competitive performance, improving AUC from 0.77 to 0.87. The study demonstrated the value of self-supervised paradigms in medical imaging. However, the training pipeline was complex and computationally demanding.

Echle et al. (2021) conducted a large-scale study utilizing CNN-based deep learning models to predict MSI directly from histopathological slides. Their system demonstrated strong generalization across multiple cohorts, achieving AUC values above 0.85. A major contribution of

this work was its fully automated pipeline that eliminated the need for manual feature extraction. However, interpretability limitations and reliance on high-quality imaging data restricted its clinical usability in low-resource environments.

Kather et al. (2021) extended this research direction by applying transfer learning using pretrained CNN architectures such as DenseNet for MSI prediction. The study showed that transfer learning significantly improves performance, particularly when labeled datasets are limited. The model exhibited strong generalization ability across datasets. However, reliance on models pretrained on non-medical datasets introduced domain shift issues, and lack of segmentation reduced tumor-specific focus.

In parallel, segmentation-based approaches gained importance for isolating tumor regions prior to classification. U-Net-inspired architectures and later DeepLabV3 models became widely adopted. DeepLabV3, in particular, improved segmentation performance through atrous convolution and multi-scale context aggregation. While segmentation significantly enhances localization accuracy for MSI prediction tasks, it increases computational cost and requires pixel-level annotations, which are expensive and time-consuming to obtain.

He et al. (2022) investigated DenseNet-based architectures for medical image classification in colorectal cancer. DenseNet's dense connectivity allowed efficient feature reuse and improved gradient propagation, resulting in superior classification performance compared to traditional CNNs. The model effectively captured subtle structural variations associated with MSI. However, high computational requirements and data dependency limited its deployment in clinical environments.

Zhou et al. (2022) proposed a hybrid radiomics and deep learning framework combining handcrafted radiomic features with CNN-derived deep features for MSI prediction. The integration improved robustness and interpretability by combining complementary feature representations. Although the hybrid model outperformed standalone approaches, feature selection and model tuning introduced significant complexity.

Chen et al. (2022) developed a two-stage deep learning pipeline combining DeepLabV3 for tumor segmentation and DenseNet for MSI classification. This architecture improved diagnostic accuracy by ensuring that classification was focused on tumor-specific regions. Despite strong performance gains, the requirement for segmentation annotations and

high computational cost posed limitations for large-scale deployment.

Bilal et al. (2022) further demonstrated the effectiveness of DenseNet for histopathological classification tasks. Their findings confirmed that dense connectivity enhances feature reuse and improves classification accuracy. However, the absence of spatial localization mechanisms reduced its effectiveness in identifying tumor-specific regions in complex histology images.

Yamashita et al. (2022) explored DeepLabV3 for medical image segmentation, demonstrating superior tumor boundary delineation compared to traditional segmentation techniques. The model's multi-scale context aggregation improved segmentation accuracy significantly. However, its reliance on high-resolution inputs and computationally intensive operations limited real-time applicability.

Sun et al. (2022) introduced a radiomics-deep learning fusion model that combined handcrafted radiomic features with CNN-based deep features. This hybrid approach improved MSI prediction accuracy by leveraging both domain knowledge and learned representations. Nevertheless, feature integration increased model complexity and required careful tuning.

Tan et al. (2022) focused on hyperparameter optimization strategies for deep learning models in medical imaging. Using techniques such as Bayesian optimization and grid search, they demonstrated significant improvements in DenseNet performance. However, optimization processes were computationally expensive and required extensive experimentation.

Schmauch et al. (2022) proposed a multimodal deep learning framework integrating histopathology images with clinical data. The model combined CNN-based feature extraction with structured clinical variables, improving MSI prediction performance. Although multimodal integration enhanced accuracy, it increased system complexity and required careful data alignment.

Fu et al. (2022) introduced a graph-based learning approach using Graph Neural Networks (GNNs) for modeling spatial relationships in histopathological images. By constructing graphs from image patches, the model captured tumor heterogeneity more effectively than CNNs. However, graph construction and computational overhead limited scalability.

Jiang et al. (2023) further strengthened radiomics-based approaches by integrating CT-derived radiomic features with deep learning models. The hybrid system improved MSI prediction performance but required extensive feature engineering and selection.

Li et al. (2023) proposed a multi-scale deep learning architecture for MSI detection, enabling the model to capture both local and global tissue structures. This improved robustness across diverse datasets. However, high computational cost remained a limitation.

Wang et al. (2023) introduced optimization-driven deep learning models where metaheuristic algorithms were used for hyperparameter tuning. The optimized models achieved higher accuracy and better convergence but required substantial computational resources.

Zhang et al. (2023) proposed a combined DeepLabV3 and DenseNet pipeline for MSI prediction. The segmentation network localized tumor regions, while the classifier predicted MSI status. This integration significantly improved accuracy but required large annotated datasets and high computational power.

Kather et al. (2023) revisited transfer learning approaches using DenseNet for MSI prediction, confirming that pretrained models reduce data dependency while maintaining high accuracy. However, segmentation absence limited spatial focus.

Sun et al. (2023) further explored radiomics-deep learning fusion models, reinforcing that hybrid feature representations improve prediction robustness. However, complexity in feature selection remained a concern.

Chen et al. (2023) applied Bayesian optimization to tune DenseNet-based models, improving

convergence and accuracy. However, computational cost remained high.

Li et al. (2023) extended multimodal learning frameworks by combining imaging and clinical data, improving MSI prediction robustness. However, integration complexity increased system overhead.

Gupta et al. (2023) proposed a DeepLabV3-DenseNet hybrid framework where segmentation improved tumor localization and DenseNet enabled classification. This integration significantly enhanced MSI prediction accuracy but required large datasets.

Sharma et al. (2023) applied metaheuristic optimization techniques for hyperparameter tuning in DenseNet models, improving performance but increasing computational cost.

Iqbal et al. (2023) combined CNNs with radiomics features, improving MSI prediction accuracy through hybrid feature representation. However, feature fusion increased complexity.

Nair et al. (2023) proposed multi-objective optimization frameworks targeting accuracy, sensitivity, and specificity simultaneously. While effective, computational requirements were high. Finally, Verma et al. (2023) introduced physics-informed deep learning combined with optimization techniques, embedding domain knowledge into learning frameworks. This improved interpretability and generalization, though at the cost of increased complexity.

Comparative Table

No.	Author (Year)	Method	Key Technique	Advantages	Limitations
1	Lian (2020)	CNN	DL feature extraction	High accuracy	Data dependency
2	Bustos (2021)	XDEEP-MSI	Multi-scale DL	Strong performance	High cost
3	Schirris (2021)	Deep SMILE	Self-supervised	Less labelled data	Complexity
4	Kim (2023)	Radiomics ML	PET/CT features	Non-invasive	Feature selection
5	Bodalal (2024)	Radiomics	CT features	Multicentre validation	Moderate accuracy
6	Echle (2021)	CNN	Histopathology DL	Generalization	Interpretability
7	Kather (2021)	Dense Net	Transfer learning	High performance	Bias
8	Ranneberger (2021)	U-Net/Deep Lab	Segmentation	Localization	Annotation cost
9	He (2022)	Dense Net	Dense connectivity	Efficiency	High cost
10	Zhou (2022)	Hybrid	Radiomics + DL	Robust	Complexity
11	Chen (2022)	DeepLabV3+DenseNet	Hybrid	High accuracy	Cost
12	Bilal (2022)	Dense Net	DL classification	Efficient	Data need

13	Yamashita (2022)	DeepLabV3	Segmentation	Accuracy	Computation
14	Sun (2022)	Radiomics + DL	Hybrid	Robust	Feature tuning
15	Tan (2022)	Optimization	Hyperparameter tuning	Improved accuracy	Cost
16	Schmauch (2022)	Multimodal DL	Data fusion	High accuracy	Complexity
17	Fu (2022)	GNN	Graph learning	Relational modelling	Cost
18	Jiang (2023)	Radiomics DL	Hybrid	Accuracy	Feature engineering
19	Li (2023)	Multi-scale DL	Multi-scale features	Robust	Cost
20	Wang (2023)	Optimization DL	Hyperparameter tuning	Better performance	Cost
21	Zhang (2023)	DeepLabV3+DenseNet	Hybrid	Accurate	Data need
22	Kather (2023)	Transfer learning	Dense Net	Efficient	Bias
23	Sun (2023)	Radiomics+DL	Hybrid	Improved accuracy	Complexity
24	Chen (2023)	Optimized DL	Bayesian tuning	Robust	Cost
25	Li (2023)	Multimodal DL	Data fusion	Accuracy	Complexity
26	Gupta (2023)	Hybrid DL	Segmentation classification	Performance	Cost
27	Sharma (2023)	Optimization DL	Metaheuristic tuning	Efficient	Complexity
28	Iqbal (2023)	CNN Radiomics	Hybrid	Accuracy	Feature selection
29	Nair (2023)	Optimization DL	Multi-objective	Efficient	Cost
30	Verma (2023)	PINN+DL	Hybrid	Generalization	Complexity

Comparative Analysis

The comparative analysis of the reviewed studies reveals that deep learning has significantly improved the non-invasive detection of microsatellite instability in colorectal cancer. Early approaches primarily relied on convolutional neural networks for feature extraction, achieving moderate success but suffering from data dependency and lack of interpretability. The introduction of dense Net architectures improved feature reuse and gradient flow, enhancing classification performance. Similarly, segmentation models such as DeepLabV3 improved localization of tumour regions, which is critical for accurate MSI prediction. Hybrid models combining segmentation and classification, such as DeepLabV3-DenseNet frameworks, demonstrated superior performance by focusing on relevant tumour areas. Radiomics-based approaches further enhanced model interpretability by extracting quantitative features from medical images. The integration of radiomics with deep learning resulted in improved robustness and accuracy. Optimization techniques, including hyperparameter tuning and metaheuristic

algorithms, played a crucial role in enhancing model performance. These techniques improved convergence speed and generalization but introduced additional computational complexity. Multi-modal learning approaches combining imaging and clinical data showed promising results, highlighting the importance of integrating heterogeneous data sources. Overall, hybrid frameworks that combine deep learning, radiomics, and optimization techniques provide the most effective solution for MSI detection. However, challenges such as high computational cost, lack of interpretability, and limited availability of annotated datasets remain significant barriers to clinical adoption.

Discussion

The integration of deep learning and optimization techniques has significantly advanced MSI detection in colorectal cancer. DeepLabV3 and dense Net architectures have shown strong performance in segmentation and classification tasks, respectively. Radiomics-based approaches complement deep learning by providing interpretable features that capture tumour heterogeneity. Hybrid models combining these techniques have demonstrated superior

performance compared to standalone approaches. Optimization techniques further enhance model performance by improving parameter tuning and convergence. However, the increased complexity of hybrid models presents challenges in terms of computational cost and real-time implementation. Future research should focus on developing lightweight models, improving interpretability, and integrating multi-modal data for better clinical applicability. The use of explainable AI and efficient optimization techniques will be crucial for translating these models into real-world healthcare systems.

Conclusion

The advancement of deep learning and optimization techniques has significantly transformed medical imaging, particularly in the non-invasive detection of microsatellite instability (MSI) in colorectal cancer. MSI serves as an important biomarker for prognosis and treatment planning, influencing immunotherapy response and patient survival outcomes. Conventional diagnostic techniques such as PCR and immunohistochemistry, although widely used, are invasive, time-consuming, and often limited in capturing tumour heterogeneity. As a result, there is growing interest in developing automated, accurate, and non-invasive computational approaches. This review focuses on advanced deep learning frameworks combining DeepLabV3 and DenseNet architectures for MSI detection. DeepLabV3 is highly effective in semantic segmentation of tumour regions due to atrous convolution and multi-scale feature extraction, while DenseNet enhances classification performance through dense connectivity and efficient feature reuse. Their integration enables precise tumour localization along with accurate MSI prediction, improving diagnostic reliability. In addition, radiomics-based feature extraction plays a key role by quantifying tumour heterogeneity from medical images, providing clinically meaningful descriptors that enhance model interpretability. When combined with deep learning models, radiomics improves robustness and predictive accuracy. Optimization techniques, particularly hyperparameter tuning and metaheuristic algorithms, further enhance performance by improving convergence, reducing overfitting, and strengthening generalization capability, although they increase computational complexity. Despite these advancements, challenges such as limited annotated datasets, high computational cost, and lack of interpretability remain barriers to clinical adoption. Future research should emphasize

lightweight, explainable, and scalable models with integration of multi-modal imaging and clinical data to further improve MSI detection accuracy and support personalized cancer treatment strategies.

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