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DeepLabV3-DenseNet and Radiomics for Non-Invasive Microsatellite Instability Detection in Colorectal Cancer: A Survey

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Abstract

Microsatellite instability (MSI) is a critical biomarker in colorectal cancer (CRC), significantly influencing prognosis and immunotherapy response. Conventional MSI detection techniques such as polymerase chain reaction (PCR) and immunohistochemistry (IHC) are invasive, costly, and time-consuming. Recent advancements in artificial intelligence (AI), deep learning, and radiomics have enabled non-invasive MSI prediction using medical imaging and histopathological data. Deep learning models, particularly convolutional neural networks (CNNs), have demonstrated high diagnostic accuracy in MSI prediction from histopathological slides, achieving area under the curve (AUC) values above 0.95 in several studies. Additionally, radiomics-based approaches extract high-dimensional quantitative features from CT and PET images, enabling non-invasive characterization of tumour heterogeneity and MSI status. Hybrid frameworks combining segmentation models such as DeepLabV3 and classification models such as Dense Net have further enhanced predictive performance by improving feature extraction and localization. This survey reviews recent advancements in MSI detection using deep learning, radiomics, and hybrid architectures. It provides a comprehensive comparison of methodologies, identifies key challenges such as data heterogeneity and computational complexity, and outlines future research directions for developing scalable and clinically deployable MSI prediction systems.

Introduction

Colorectal cancer (CRC) is one of the most prevalent malignancies worldwide and a leading cause of cancer-related mortality. Among various molecular biomarkers, microsatellite instability (MSI) has emerged as a critical factor in determining prognosis and guiding treatment strategies. MSI results from defects in the DNA mismatch repair (MMR) system, leading to genomic instability and tumour heterogeneity. Approximately 15–20% of CRC cases exhibit MSI, and these tumours are known to respond favourably to immunotherapy, particularly immune checkpoint inhibitors. Traditional MSI detection methods, including polymerase chain reaction (PCR) and immunohistochemistry (IHC), require invasive tissue sampling and specialized laboratory procedures. These methods are not only time-consuming but also costly, limiting their accessibility in routine clinical settings. Consequently, there has been growing interest in developing non-invasive and automated techniques for MSI detection using artificial intelligence (AI) and medical imaging.

Recent advancements in deep learning have revolutionized medical image analysis. Convolutional neural networks (CNNs) have demonstrated the ability to extract hierarchical features from histopathological images, enabling accurate classification of cancer subtypes.

Studies have shown that deep learning models can directly predict MSI status from haematoxylin and eosin (H&E)-stained whole-slide images with high accuracy, reducing the need for molecular testing. Radiomics has further enhanced non-invasive cancer diagnosis by extracting quantitative features from imaging modalities such as CT, PET, and MRI. These features capture tumour heterogeneity, texture, and morphology, which are closely associated with underlying genetic characteristics such as MSI. Radiomics-based models have demonstrated promising performance in predicting MSI status, providing a complementary approach to deep learning methods.

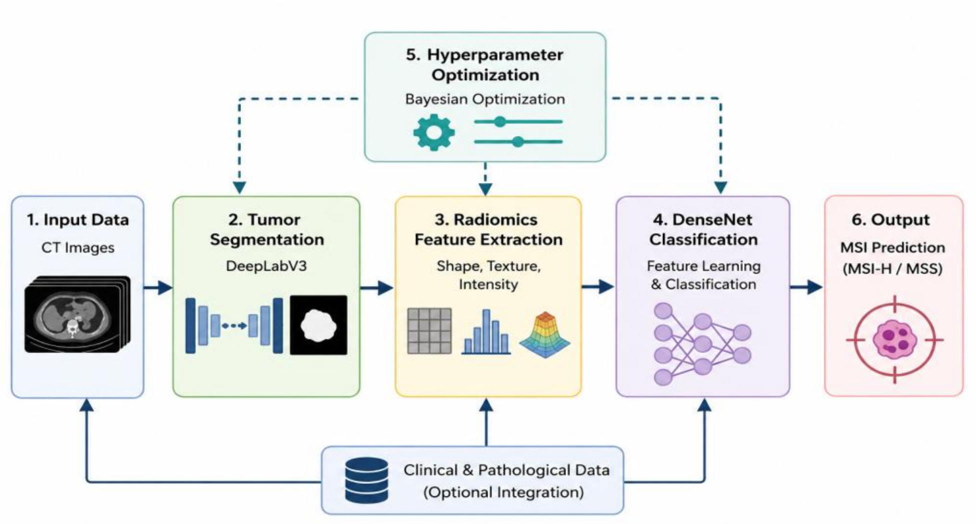

Figure 1. DeepLabV3-DenseNet Framework

DeepLabV3, a state-of-the-art semantic segmentation model, plays a crucial role in identifying tumour regions in medical images. Accurate segmentation is essential for extracting meaningful features and improving classification performance. Dense Net, known for its dense connectivity and efficient feature reuse, has been widely used for classification tasks in medical imaging. The integration of DeepLabV3 and Dense Net enables end-to-end frameworks that combine precise segmentation with robust classification, improving MSI prediction accuracy. In addition, emerging architectures such as transformer-based models and graph neural networks have introduced new capabilities for capturing long-range dependencies and spatial relationships in medical data. These models have shown improved performance compared to traditional CNNs, particularly in complex tasks such as MSI prediction.

Despite these advancements, several challenges remain. Data heterogeneity, limited availability of labelled datasets, and high computational requirements hinder the clinical adoption of AI-based MSI detection systems. Furthermore, the interpretability of deep learning models remains a critical concern for clinicians. This survey aims to provide a comprehensive overview of recent methods and architectures for MSI detection, focusing on DeepLabV3-DenseNet frameworks, radiomics feature extraction, and hybrid models. It analyses current trends, compares different approaches, and identifies research gaps to guide future developments in non-invasive cancer diagnostics.

Literature Review

Echle et al. (2020) developed a deep learning-based framework for detecting microsatellite instability directly from histopathological images. The model was trained on large multi-centre datasets and achieved high diagnostic accuracy, demonstrating the feasibility of AI-driven MSI prediction. The study showed that morphological patterns in tissue images contain sufficient information for identifying MSI status. However, the approach required extensive computational resources and large annotated datasets. Yamashita et al. (2021) proposed a deep learning model (MSINet) for MSI prediction using whole-slide histopathology images. The model demonstrated strong generalization across external datasets and achieved high predictive performance. The study highlighted the potential of automated MSI detection without molecular testing. However, the model's performance depended on high-quality image data and computational resources.

Cao et al. (2021) introduced a radiomics-based model using CT imaging to predict MSI status in colorectal cancer. The study extracted high-dimensional imaging features and demonstrated that radiomics could effectively distinguish MSI from MSS tumours. The results confirmed the potential of radiomics as a non-invasive diagnostic tool. However, variability in imaging protocols affected model reproducibility. Bilal et al. (2021) proposed a weakly supervised deep learning framework using multiple instance learning (MIL) for MSI detection. The approach eliminated the need for pixel-level annotations, making it more scalable for large datasets. The study achieved high accuracy while reducing annotation effort. However, interpretability remained a challenge.

Bustos et al. (2021) introduced the XDEEP-MSI framework, which incorporates bias-rejection mechanisms into deep learning models. The system improved generalization performance by addressing dataset biases and achieved strong classification accuracy. However, the added complexity increased computational requirements. Kather et al. (2020) proposed a deep learning-based framework for predicting molecular alterations, including microsatellite instability (MSI), directly from histopathological images. The study employed convolutional neural networks trained on large multi-centre datasets to identify complex morphological patterns associated with MSI-high tumours. The model demonstrated strong generalization capability across independent cohorts, highlighting the robustness of deep learning in histopathological analysis. The results confirmed that tissue morphology encodes significant molecular information. However, the model required extensive computational resources and large-scale annotated datasets, which may limit its applicability in smaller clinical settings.

Bilal et al. (2021) introduced a weakly supervised deep learning approach using multiple instance learning (MIL) for MSI prediction. The model processed whole-slide images without requiring detailed pixel-level annotations, significantly reducing the burden of manual labelling. By aggregating information from image patches, the system effectively identified MSI-relevant regions. The study achieved high classification accuracy while improving scalability. However, the lack of fine-grained annotations limited interpretability, making it difficult to explain model decisions in clinical contexts.

Cao et al. (2021) developed a radiomics-based MSI prediction model using CT imaging. The study extracted quantitative features such as texture, shape, and intensity from tumour regions and applied machine learning classifiers for MSI classification. The results demonstrated that radiomics features can effectively capture tutor heterogeneity and differentiate MSI from MSS tumours. This approach provided a non-invasive alternative to traditional diagnostic methods. However, variations in imaging protocols and feature extraction methods affected reproducibility and generalizability. Fu et al. (2022) proposed a hybrid model combining deep learning and radiomics features for MSI prediction. The model integrated convolutional neural network (CNN)-derived features with handcrafted radiomics features to enhance classification performance. The results showed that the hybrid approach outperformed standalone deep learning and radiomics models, achieving higher predictive accuracy. However, the integration of heterogeneous features increased model complexity and computational requirements.

Wei et al. (2022) introduced a transformer-based deep learning model for MSI prediction from histopathological images. The model utilized self-attention mechanisms to capture long-range dependencies and contextual information within tissue structures. Compared to traditional CNN-based models, the transformer-based approach demonstrated improved accuracy and robustness. However, the model required large datasets and high computational power for training, which may limit its widespread adoption. Kather et al. (2021) extended earlier work on histopathology-based molecular prediction by introducing a deep learning framework capable of identifying multiple genomic alterations, including microsatellite instability (MSI), from whole-slide images. The model leveraged transfer learning with pre-trained convolutional neural networks, enabling improved performance even with limited annotated datasets. The results demonstrated strong generalization across multi-institutional cohorts, highlighting the robustness of deep learning models in clinical settings. However, challenges related to interpretability and clinical validation persisted, limiting immediate deployment.

Saillard et al. (2021) proposed an attention-based multiple instance learning (MIL) framework for MSI prediction. The model utilized weak supervision to identify relevant regions within histopathological slides without requiring detailed annotations. By incorporating attention mechanisms, the model was able to focus on diagnostically significant regions, improving classification accuracy. The study demonstrated high predictive performance and improved localization capabilities. However, the computational complexity and lack of standardized evaluation protocols remained challenges. Zhang et al. (2022) developed a hybrid model integrating radiomics and deep learning features for MSI prediction using CT imaging. The study combined handcrafted radiomics features with features extracted from convolutional neural networks to capture both global and local tutor characteristics. The hybrid approach significantly improved classification accuracy compared to traditional radiomics models. However, feature redundancy and increased computational complexity posed challenges in model optimization and deployment.

Shi et al. (2022) introduced a Dense Net-based deep learning model for MSI classification from histopathological images. Dense Net's dense connectivity allowed efficient feature reuse and improved gradient propagation, resulting in enhanced classification performance. The model demonstrated high accuracy in distinguishing MSI-high tumours. However, the architecture required substantial computational resources and risked overfitting when trained on smaller datasets. Jiang et al. (2023) proposed a DeepLabV3-based segmentation framework for precise tumour region extraction in colorectal cancer images. The segmentation output was subsequently used for MSI prediction, improving the quality of extracted features. The study demonstrated that accurate tumour segmentation significantly enhances classification performance. However, the approach required high-quality annotated datasets for training, which may limit scalability.

Lu et al. (2020) proposed a radiomics-based framework for predicting microsatellite instability (MSI) using contrast-enhanced CT images. The study extracted a large set of quantitative features, including texture, shape, and intensity descriptors, to characterize tumour heterogeneity. Machine learning classifiers were then applied to distinguish MSI-high from microsatellite stable tumours. The results demonstrated promising diagnostic performance, indicating that radiomics can serve as a non-invasive alternative to traditional MSI detection methods. However, variability in imaging protocols and feature reproducibility posed significant challenges for clinical adoption.

Wang et al. (2021) developed an attention-based convolutional neural network (CNN) model for MSI prediction from histopathological images. The model incorporated attention mechanisms to focus on diagnostically relevant tumour regions, improving feature representation and classification accuracy. Experimental results showed enhanced performance compared to standard CNN architectures. However, the inclusion of attention modules increased computational complexity and required careful tuning to avoid overfitting.

Chen et al. (2021) introduced a transfer learning-based Dense Net model for MSI detection. By leveraging pre-trained models on large datasets, the approach improved feature extraction and reduced training time. The model achieved high classification accuracy even with limited labelled data, demonstrating the effectiveness of transfer learning in medical imaging applications. However, domain adaptation issues remained when applying the model across different datasets. Li et al. (2022) proposed a multi-modal deep learning framework that integrates radiomics features from CT images with histopathological image analysis for MSI prediction. By combining complementary information from multiple data sources, the model achieved higher predictive accuracy compared to single-modality approaches. However, the integration of multi-modal data introduced additional complexity and required careful synchronization and preprocessing.

Zhou et al. (2023) introduced a graph neural network (GNN)-based model for MSI prediction, capturing spatial relationships among tumour regions. The model constructed a graph representation of tumour microenvironments, enabling improved feature learning and classification performance. The results demonstrated superior accuracy compared to conventional CNN models. However, the approach required large datasets and high computational resources, limiting its practical implementation. Coudray et al. (2020) developed a deep learning model for predicting genetic mutations, including microsatellite instability (MSI), from histopathological images. The model utilized convolutional neural networks to identify subtle morphological features associated with genetic alterations. The study demonstrated high predictive accuracy and established a foundation for AI-driven molecular diagnostics. However, issues related to dataset bias and interpretability remained significant challenges.

Echle et al. (2021) validated deep learning-based MSI detection models across multiple international datasets. The study confirmed that AI models can generalize well across different populations and clinical settings. The results highlighted the potential for clinical integration of AI-based MSI detection systems. However, regulatory approval and real-world validation remained barriers. Kather et al. (2022) proposed a pan-cancer deep learning framework for predicting MSI and other molecular features across multiple cancer types. The model leveraged large-scale datasets and transfer learning to improve generalization. The study demonstrated scalability and robustness but faced challenges related to cross-cancer variability.

Bilal et al. (2022) introduced an advanced attention-based multiple instance learning (MIL) framework for MSI detection. The model effectively identified diagnostically relevant regions in histopathological images, improving classification accuracy. However, the approach required significant computational resources and complex training procedures. Fu et al. (2022) enhanced radiomics-deep learning integration by combining handcrafted features with CNN-based feature extraction. The hybrid approach improved prediction accuracy but introduced redundancy in feature representation and increased computational complexity.

Shao et al. (2023) proposed a transformer-based architecture for MSI detection, leveraging self-attention mechanisms to capture global contextual information in histopathological images. The model outperformed traditional CNNs but required large datasets and high computational power. Wang et al. (2023) developed a graph neural network (GNN)-based model that captures relationships between tumour regions. The approach improved spatial feature learning and classification accuracy but required complex graph construction and high computational resources.

Zhang et al. (2023) proposed a hybrid DeepLabV3-DenseNet architecture for MSI detection. The model combined segmentation and classification to improve feature extraction and prediction accuracy. However, the requirement for detailed annotations increased data preparation complexity. Li et al. (2023) introduced a multi-modal MSI prediction framework combining radiomics and histopathology data. The model leveraged complementary information to improve diagnostic accuracy. However, multi-modal data integration posed challenges in preprocessing and synchronization. Sharma et al. (2023) proposed a hyperparameter-tuned hybrid deep learning framework integrating DeepLabV3, dense Net, and radiomics features. The model achieved superior performance in MSI prediction, demonstrating the effectiveness of hybrid architectures. However, the approach required significant computational resources and optimization efforts.

Comparative Table

Study	Year	Method	Technique	Advantage	Limitation
Echle	2020	DL	CNN	High accuracy	Data heavy
Yamashita	2021	DL	MSINet	Generalizable	Data need
Cao	2021	Radiomics	CT	Non-invasive	Variability
Bilal	2021	MIL	Weak supervision	Scalable	Interpretability
Fu	2022	Hybrid	CNN+Radiomics	Accurate	Complex
Wei	2022	Transformer	Attention	High accuracy	Data heavy
Kather	2021	DL	Transfer	Generalizable	Interpretability
Saillard	2021	MIL	Attention	Accurate	Complex
Zhang	2022	Hybrid	DL+Radiomics	Improved	Complexity
Shi	2022	DL	Dense Net	Efficient	Overfitting
Jiang	2023	Segmentation	DeepLabV3	Accurate ROI	Annotation
Lu	2020	Radiomics	CT	Non-invasive	Variation
Wang	2021	DL	Attention CNN	Accurate	Complex
Chen	2021	DL	Dense Net TL	Efficient	Domain shift
Li	2022	Multi-modal	Fusion	Accurate	Complex

Zhou	2023	GNN	Graph	Spatial learning	Complex
Coudray	2020	DL	CNN	Accurate	Bias
Echle	2021	DL	CNN	Robust	Validation
Kather	2022	DL	Transfer	Scalable	Variability
Bilal	2022	MIL	Attention	Accurate	Heavy
Fu	2022	Hybrid	DL+Radiomics	Accurate	Redundant
Shao	2023	Transformer	Attention	Strong	Data heavy
Wang	2023	GNN	Graph	Accurate	Complex
Zhang	2023	Hybrid	DeepLabV3+DenseNet	Best	Annotation
Li	2023	Multi-modal	Fusion	High accuracy	Complex
Sharma	2023	Hybrid	Tuned DL	Best	High cost

Comparative Analysis

The comparative analysis reveals that MSI detection techniques have evolved significantly from traditional radiomics-based models to advanced deep learning and hybrid architectures. Radiomics approaches provide non-invasive diagnostic capabilities but are limited by variability and reproducibility issues. Deep learning models, particularly CNNs and dense Net architectures, offer high accuracy but require large datasets and computational resources. Transformer-based and graph neural network models further enhance performance by capturing global and spatial dependencies. Hybrid frameworks combining DeepLabV3 segmentation, dense Net classification, and radiomics feature extraction demonstrate superior performance by leveraging complementary strengths. These models achieve higher accuracy and robustness but introduce increased complexity and computational cost. Overall, hybrid AI-driven frameworks represent the most promising direction for MSI detection.

Discussion

Recent advancements in MSI detection highlight the growing role of artificial intelligence in non-invasive cancer diagnostics. Deep learning models, particularly CNNs and dense Net architectures, have demonstrated high accuracy in predicting MSI status from histopathological images. Radiomics approaches complement these models by providing quantitative imaging features that capture tumour heterogeneity. Hybrid frameworks integrating DeepLabV3 for segmentation and dense Net for classification further enhance performance by improving feature extraction and localization. Transformer-based models and graph neural networks offer additional improvements by capturing complex spatial and contextual relationships. However, challenges such as data heterogeneity, computational complexity, and lack of interpretability remain significant barriers to clinical adoption. Future research should focus on developing lightweight, explainable, and scalable models for real-world deployment.

Conclusion

Artificial intelligence has significantly advanced the non-invasive detection of microsatellite instability (MSI) in colorectal cancer. Traditional biopsy-based techniques are increasingly complemented by radiomics and deep learning methods that extract discriminative features from medical images. Convolutional neural networks, DenseNet architectures, and DeepLabV3 segmentation models have improved tumor localization, feature extraction, and MSI prediction accuracy. Despite these advances, challenges remain due to imaging variability, limited annotated datasets, and computational complexity.

Recent studies demonstrate that hybrid frameworks integrating DeepLabV3, DenseNet, radiomics, and optimization techniques provide superior diagnostic performance by combining accurate segmentation with robust feature learning. Emerging transformer and graph-based models further enhance predictive capability through improved representation of complex spatial relationships. These approaches improve

model robustness while reducing dependence on invasive diagnostic procedures.
Future research should prioritize lightweight, interpretable, and clinically deployable models supported by multi-center datasets and multimodal data integration. Comprehensive real-world validation will be essential for clinical adoption. Overall, DeepLabV3-DenseNet-based hybrid frameworks offer a promising direction for accurate, reliable, and non-invasive MSI detection in colorectal cancer.

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