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A Chronotherapy-Aware Multimodal Deep Learning Framework for Lung Cancer Risk Prediction

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***Abstract*—The high mortality rate associated with lung cancer worldwide emphasizes the importance of developing better risk prediction tools and personalized treatments. This paper presents a chronotherapy-aware multimodal deep learning framework that integrates histopathological imaging and clinical patient data for lung cancer risk prediction. A CNN-based model extracts discriminative image features, while an MLP processes structured clinical attributes, with class imbalance handled using SMOTE and class weighting. The learned representations are fused into a joint embedding space to estimate patient-level cancer risk probabilities. The results obtained from the experiments demonstrate that the multimodal fusion model outperforms unimodal approaches, achieving an accuracy of 89%, a macro-averaged F1-score of 0.65, and ROC-AUC of 0.81, compared to 34% accuracy for the image-only model and 69% accuracy for the clinical-only model. Additionally, a simulation-based chronotherapy-aware module models circadian rhythm–driven treatment efficacy using predicted risk scores, enabling personalized treatment-timing recommendations. The proposed framework demonstrates the effectiveness of multimodal learning combined with temporal treatment awareness for next-generation clinical decision-support systems.**

***Index Terms*—Lung Cancer Prediction, Multimodal Deep Learning, Histopathological Image Analysis, Clinical Data Modeling, Attention-Based Feature Fusion, Chronotherapy-Aware Decision Support, Risk Prediction, Public Medical Datasets**

I. Introduction

Lung cancer is a major public health challenge and one of the leading causes of cancer-related deaths worldwide. The high mortality rate is largely attributable to the late diagnosis of lung cancer and the rapid progression of the disease. Therefore, the development of robust lung cancer risk assessment tools to facilitate early detection is critically important. Conventional methods for the diagnosis of lung cancer are based on individual data sources, such as medical images. However, analyzing individual data sources may not be sufficient to capture the complex characteristics of the disease.

Advancements in deep learning techniques, particularly Convolutional Neural Network (CNN) based models for analyzing histopathology images, have shown strong potential in medical diagnostics. and machine learning models for structured clinical data, have shown promising results in lung cancer research [1]. However, most existing methods focus on single-modality analysis and do not fully exploit complementary information between data sources. Multimodal deep learning has emerged as an effective strategy for integrating heterogeneous data; however, its adoption is constrained by the limited availability of publicly accessible datasets containing both imaging and clinical information for the same patients [2]. In parallel, chronotherapy, aligning treatment with biolog-ical circadian rhythms, has gained attention for its potential to enhance treatment efficacy, yet it remains largely unexplored in AI-based lung cancer systems due to the lack of structured timing data [6].

In response to these issues, this work presents a multimodal deep learning approach that integrates histopathological image features and clinical data for lung cancer risk prediction using publicly available datasets. In addition, a chronotherapy-aware simulation module is introduced to demonstrate how predicted cancer risk scores can be combined with circadian rhythm modeling to support time-aware treatment interpretation.

The major contributions of the proposed work include the

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following,

- A chronotherapy-aware multimodal deep learning framework is proposed for lung cancer risk prediction by integrating histopathological imaging data with structured clinical features.
- An attention-based feature fusion strategy is developed to effectively combine complementary information from imaging and clinical modalities for improved prediction performance.
- A simulation-based chronotherapy-aware module is introduced to demonstrate how predicted cancer risk scores can be integrated with circadian rhythm modeling to support time-aware treatment interpretation.

The organization of this paper is outlined as follows. Section II presents the literature review, while Section III discusses the problem identification, Section IV describes the proposed methodology, Section V reports experimental results and analysis, Section VI presents visualization and interpretability, and Sections VII and VIII conclude the paper with future research directions.

II. Literature Review

Although deep learning has significantly improved medical diagnosis and cancer prediction, many existing studies rely on single-modality data, such as medical imaging or structured clinical records. Convolutional Neural Networks (CNNs) have demonstrated strong performance in histopathological image analysis [2], and recent studies have applied CNN-based models for lung cancer detection with improved accuracy [8]. However, image-based models often lack patient-specific clinical context, while clinical prediction models rely on demographic and medical history information but fail to capture detailed visual features from medical images [3].

To address these limitations, researchers have explored multimodal learning approaches that integrate imaging and clinical data. Early multimodal frameworks demonstrated the capability of learning joint representations from multiple modalities [4], and recent studies have shown improved prediction performance using multimodal medical data [9]. Nevertheless, limited availability of datasets containing both histopathological images and clinical information restricts the development of robust multimodal systems.

Furthermore, many AI-based lung cancer models focus only on diagnosis or survival prediction, although deep learning survival models such as DeepSurv have shown promising results for prognosis prediction [5]. In addition, chronotherapy, which aligns treatment with biological circadian rhythms, has demonstrated potential for improving treatment effectiveness [6], and recent studies have explored AI-based approaches for optimizing treatment timing [10]. However, this concept is rarely integrated into lung cancer prediction frameworks. Therefore, an integrated framework combining histopathological imaging, clinical data, multimodal fusion, and chronotherapy-aware interpretation is needed to improve lung cancer risk prediction and clinical decision support [11]

III. Problem Identification

Deep learning has significantly advanced lung cancer diagnosis and risk assessment; however, current approaches exhibit notable limitations. Most existing methods rely on a single type of information—either medical imaging or clini-cal data—leading to an incomplete understanding of disease characteristics. Image-based models often lack critical clinical context, while clinical-only approaches may fail to capture subtle morphological patterns present in histopathological images [3].

In addition, lung cancer diagnosis and prognostic assessment are often addressed as independent tasks, which limits the development of comprehensive decision-support systems. The scarcity of publicly available datasets containing paired histopathological images and structured clinical data further complicates the development of integrated multimodal models [2]. Chronotherapy, which aims to align treatment strategies with biological circadian rhythms, also remains largely unexplored in AI-based lung cancer systems due to the lack of structured temporal and treatment timing data [6].

Moreover, the absence of integrated AI-driven frameworks that simultaneously consider multimodal medical data and temporal treatment dynamics restricts the development of intelligent clinical decision-support systems capable of providing personalized and time-aware treatment recommendations.

Such challenges encourage the development of integrated multimodal learning models that integrates histopathological imaging and clinical data for improved lung cancer risk prediction, also exploring chronotherapy-aware risk interpretation as a complementary decision-support component [4].

IV. Proposed Methodology

This work proposes a multimodal deep learning framework for lung cancer risk prediction that integrates histopatholog-ical image data with clinical patient features. In addition, a chronotherapy-aware simulation module is introduced to demonstrate how predicted cancer risk scores can be combined with circadian rhythm modeling to support time-aware treatment planning. The framework is implemented using publicly available datasets and does not rely on genomic information; therefore, it is suitable for deployment in resource-constrained clinical settings. The overall pipeline consists of data acquisition and preprocessing, feature extraction from imaging and clinical modalities, multimodal feature fusion, lung cancer risk prediction, and chronotherapy-aware risk interpretation.

A. Data Acquisition and Preprocessing

The multimodal dataset is defined as:

$$D = \{(x_i^I, x_i^C, y_i)\}_{i=1}^{N} \quad (1)$$

where x_i^I denotes the histopathological image, x_i^C represents the corresponding clinical feature vector, and $y_i \in \{0, 1\}$ indicates the lung cancer risk label. Histopathological images are resized to a fixed resolution and normalized to ensure

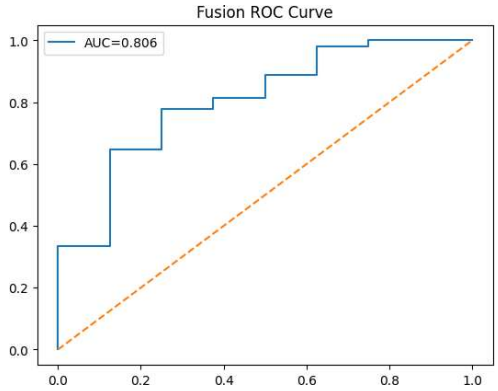


Fig. 4. ROC curve of the proposed multimodal fusion model for lung cancer risk prediction(AUC = 0.806).

D. Chronotherapy-Aware Treatment Optimization

Fig. 5 illustrates the variation in normalized predicted treatment efficacy over a 24-hour period based on a chronotherapy-aware simulation. The predicted efficacy follows a circadian pattern, reaching a peak value of approximately 1.0 at 06:00 h, indicating a potential optimal treatment time. The red dashed line denotes an efficacy threshold (0.8), above which treatment is considered optimal, resulting in a favorable treatment window from 03:00 to 09:00 h rather than a single time point. Following midday, efficacy gradually decreases, reaching a minimum near 18:00 h before rising again. This simulation demonstrates how AI-driven risk predictions can be integrated with circadian rhythm modeling to support time-aware treatment planning.

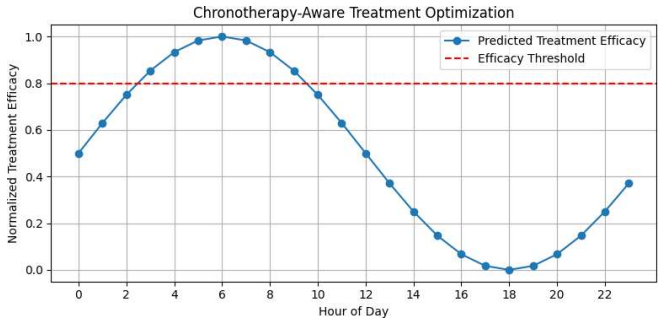


Fig. 5. Chronotherapy-aware simulation illustrating circadian modulation of predicted treatment efficacy over a 24-hour cycle.

VII. Conclusion

This work presents a chronotherapy-aware multimodal deep learning framework for lung cancer risk prediction using non-genomic data. By integrating histopathological image features with structured clinical patient information through an attention-based fusion strategy, the proposed approach addresses key limitations of unimodal diagnostic systems and provides a more comprehensive representation of lung cancer risk characteristics [1], [2].

Experimental analysis together with visualization results confirm that the framework maintains stable and scalable performance across public datasets, making it applicable for clinical decision-support applications. The results further indicate that effective lung cancer risk prediction systems can be developed without reliance on genomic information, improving feasibility in resource-constrained clinical settings [5].

Overall, the proposed framework demonstrates the capability of multimodal AI systems to assist in early detection and personalized treatment planning for lung cancer. Although the chronotherapy component is simulation-based, it illustrates the potential of integrating AI-driven risk prediction with circadian rhythm modeling to support future time-aware treatment planning.

VIII. Future Enhancements

Future work will focus on extending the proposed chronotherapy-aware multimodal framework by incorporating large-scale multi-center datasets containing paired histopathological images, clinical records, and longitudinal outcomes to improve robustness and generalizability. The current synthetic chronotherapy module can be replaced with real circadian biomarkers, treatment timing, and drug response data to enable clinically actionable treatment scheduling [6].

In addition, self-supervised and weakly supervised learning techniques can be explored to reduce dependence on labeled clinical data and improve representation learning from unlabeled medical images [7]. The integration of advanced explainable AI techniques, including attention visualization, feature-attribution methods, and Gradient-weighted Class Activation Mapping (Grad-CAM), may further enhance interpretability and clinical trust. Future extensions may also incorporate dynamic survival modeling, patient-specific threshold adaptation, and real-time clinical decision-support integration.

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