NSCLC 360

Leveraging Multi-Omics Data for a Holistic and Explainable Decision Support for Non Small Cell Lung Cancer Management

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***Abstract*—Non-Small Cell Lung Cancer (NSCLC) remains a leading cause of cancer-related mortality, with existing diagnostic and prognostic models often failing to capture the complexity of tumor biology. This study proposes a holistic and explainable decision support system that integrates multi-omics data—including genomics, transcriptomics, and proteomics—along with advanced machine learning (ML) and deep learning (DL) techniques to enhance NSCLC detection, prognosis prediction, complication forecasting, and recurrence assessment. To address the challenge of interpretability in AI-driven healthcare, we incorporate Explainable AI (XAI) methods such as SHAP and LIME, ensuring model transparency and clinical trust. Additionally, traditional statistical models like Cox proportional hazards regression are combined with ML approaches for robust survival analysis, while modern AI architectures, including Vision Transformers and multi-task learning models, improve tumor localization and TNM classification. By developing an interpretable and clinically meaningful AI-based decision support system, this research aims to advance personalized lung cancer management and improve patient outcomes through seamless integration into clinical workflows.**

Keywords— Non-Small Cell Lung Cancer, Multi-Omics, Machine Learning, Explainable AI, Prognosis, Decision Support System, Precision Oncology

I. INTRODUCTION

Non-Small Cell Lung Cancer (NSCLC) remains one of the leading causes of cancer-related deaths worldwide [1], with a high incidence and a poor prognosis when diagnosed at advanced stages. Despite advancements in medical technologies and therapeutic strategies, early diagnosis, effective prognosis prediction, and management of NSCLC remain significant challenges. Traditionally, the clinical management of NSCLC involves a combination of imaging techniques, histopathological analysis, and molecular profiling. However, these methods often fail to provide comprehensive insights due to their inability to fully capture the complexity of cancer biology.[2]

Recent developments in data science and artificial intelligence (AI) have opened new avenues for improving the management of NSCLC. The integration of multi-omics data—including genomics, transcriptomics, proteomics, and imaging data—into decision support systems promises to enhance the precision and accuracy of cancer diagnosis, prognosis, and treatment planning [3]. These multi-omics datasets hold the potential to provide a more holistic view of tumor behavior, patient health, and therapeutic responses. However, despite the promise of AI and machine learning (ML) in cancer care, challenges remain in making these systems both reliable and interpretable in clinical settings.[4]

The aim of this research is to leverage the power of multi-omics data in developing a comprehensive and explainable decision support system for NSCLC management. By incorporating advanced AI models, including deep learning and machine learning algorithms, along with clinical insights, this system seeks to address several key aspects of NSCLC management: detection, diagnostic analysis, prognosis prediction, complication forecasting, and recurrence assessment.

Furthermore, this study seeks to overcome the limitations of existing AI-driven models, such as the lack of transparency and reproducibility, by adopting explainable AI (XAI) approaches. These methods will not only improve the accuracy of predictions but also enhance their clinical interpretability, ensuring that healthcare providers can confidently make informed decisions. In doing so, we aim to provide a tool that can seamlessly integrate into clinical workflows, ultimately improving patient outcomes and advancing personalized cancer care.

II. LITRETURE REVIEW

The use of a decision support system is highly common in the medica field especially in the case of cancer, however major systems such as IBM Watson for Oncology [5],promised to be a powerful tool but severely failed with real-world applications For example, when tested in Korea to assess its decision support system the system demonstrated a concordance rate of only 0.48 [6], meaning its perfor-

mance was worse than random chance. This failure is largely attributed to a lack of transparency and modularization. This research aims to modernize decision support systems by adopting a stepwise approach, covering detection, diagnostic analysis, prognosis, complication prediction, and recurrence assessment. By integrating these components seamlessly, the proposed system will provide meaningful and interpretable insights to support clinicians effectively.

A. *Machine Learning-Based Tumor Localization and TNM Classification from PET/CT Imaging*

The application of machine learning (ML) and deep learning (DL) in DICOM PET/CT imaging has significantly advanced the automation of tumor localization and TNM pathology extraction, addressing critical challenges in lung cancer diagnosis. Early approaches relied on traditional feature engineering techniques, such as radiomics-based texture analysis and statistical models for tumor segmentation and staging. These methods often struggled with inter-observer variability and manual annotation complexity. However, after 2015, the emergence of CNNs, LSTMs, and hybrid models improved the accuracy of tumor detection by learning hierarchical feature representations from PET/CT scans [7]. Advanced techniques, including random forests and SVMs, were initially employed for classification tasks, but deep learning models such as ResNet and U-Net demonstrated superior performance in segmenting tumor regions and classifying TNM stages [8]. The introduction of Transformer-based architectures in 2017 marked a paradigm shift in medical imaging analysis, as self-attention mechanisms improved long-range dependency learning in multi-modal PET/CT datasets [9]. Recent research has explored Vision Transformers (ViTs) and Swin-Transformers, achieving higher accuracy in TNM classification and metabolic activity quantification by integrating anatomical and functional imaging data [10]. Furthermore, the integration of Large Language Models (LLMs) with PET/CT analysis has facilitated context-aware tumor staging, bridging radiological imaging with clinical pathology reports to enhance diagnostic decision-making. Despite these advancements, challenges such as limited labeled datasets, standardization of DICOM protocols, and high computational costs remain barriers to widespread clinical adoption . Future research should focus on multi-task learning architectures, domain-specific fine-tuning, and explainable AI frameworks to improve the clinical reliability and generalizability of AI-driven TNM staging models.

B. *Prognostic Analysis*

Recent advances in deep learning have significantly enhanced lung cancer prognosis prediction by integrating histopathological and molecular data. Various models, including convolutional neural networks (CNNs) and transformer-based architectures, have been applied to predict survival outcomes, recurrence risks, and therapy responses. Despite improvements in predictive accuracy, challenges related to clinical integration, interpretability, and generalizability persist. Liu et al [11]. highlighted the use of a novel deep learning-based model (MIM) for ADC prognosis prediction, achieving high accuracy in distinguishing infiltration patterns. Yu et al [12]. demonstrated the effectiveness of Transformer-guided MIL for aneuploidy-based prognosis classification. Guo et al [13]. integrated EfficientUnet and ResNet to enhance tumor and TILs staining predictions, improving overall survival assessment. Despite these advancements, limitations remain. Many models suffer from a lack of transparency, making clinical adoption difficult. Replicability across different datasets is often challenging due to variations in data sources and preprocessing techniques. Additionally, interpretability remains a key concern, as deep learning-based predictions are often considered black-box approaches, limiting their applicability in real-world clinical decision-making.

Given these concerns, this research prioritizes the use of the well-established and interpretable Cox proportional hazards model. Widely adopted in clinical prognostic studies, Cox regression provides a transparent framework for survival analysis, allowing for direct interpretation of feature importance and risk stratification. Guo Y et al. [14] demonstrated the effectiveness of Cox regression combined with LASSO for feature selection, achieving a validated C-index of 0.668. Additionally, the inherent explainability of the Cox model enabled N. Sun et al. [15] to identify two potential gene biomarkers, enhancing clinical decision-making and personalized treatment strategies.

By leveraging these robust statistical models, this research aims to develop an effective yet interpretable prognostic framework, ensuring both predictive accuracy and clinical usability. The integration of explainable methodologies will facilitate better decision support, ultimately improving patient outcomes.

C. *An Explainable AI Approach for Predicting Complications from Lung Cancer Diagnostic Workups Using Limited Clinical Data*

Lung cancer remains a leading cause of cancer-related mortality, often necessitating invasive diagnostic procedures such as biopsies, bronchoscopy, and thoracic surgery. These procedures pose significant risks, with complication rates reaching 38.5% in thoracic surgeries [16]. Traditional risk models rely on extensive datasets to predict these complications; however, real-world constraints, such as data availability and variability, often limit their generalizability and clinical applicability [17].

Machine learning (ML) techniques, including Logistic Regression, Random Forest, and XGBoost, have demonstrated superior accuracy in predicting diagnostic complications compared to conventional statistical models [18], [19]. Despite these advancements, the inherent "black-box" nature of many ML models poses challenges for clinical adoption, as clinicians require interpretability and transparency to trust model-driven predictions. This challenge has driven the adoption of Explainable AI (XAI) techniques such as SHAP and LIME, which provide feature attribution insights, thereby enhancing model transparency and facilitating clinical trust [20].

Further advancements in interpretable ML models have introduced architectures such as TabNet, which offers both local and global interpretability through feature importance scores at the sample and aggregate levels. By leveraging sparsemax activation (or entmax in certain adaptations), TabNet promotes sparsity in feature selection, ensuring that only the most relevant clinical features are prioritized during prediction [21]. This capability makes TabNet a promising approach for clinical applications where explainability is paramount.

Building upon these developments, this study proposes an XAI-driven framework that integrates ML models with interpretability techniques to predict complications using limited clinical data. By ensuring both predictive accuracy and transparency, the proposed framework aims to enhance clinical decision-making, improve patient safety, and contribute to more efficient healthcare management.

D. Recurrence prediction with PFI and new tumour event type.

Several previous studies have tried both multi-modal as well as multi-omic based approaches to predict the recurrence of lung cancer. A few of which are tabular and graph machine learning for objective and reproduceable early-stage NSCLC recurrence and stratification. It was able to achieve 76% accuracy for the random forest model at predicting relapse evaluated with a 10-fold cross-validation [22]. Another study was able to obtain immune gene prognostic models for LUAD and LUSC based on the TCGA database. Using the GEO and Kaplan–Meier plotter databases, was able to evaluate the validity of the prognostic models. [23] In a different study, three algorithms—support vector machine, multi-layer perceptron, and random forest—were used to generate models with five-fold CV. The models with the blind dataset were also subjected to external validation. The models performed well in external validation as well as CV. [24]

III. METHODOLOGY

The primary objective of this study is to develop and evaluate a multi-omics framework for improving decision support in the management of Non-Small Cell Lung Cancer (NSCLC). This framework integrates various forms of data, including medical imaging, clinical information, and genomic data, to enhance tumor localization, prognostic modeling, and predict complications. The methodological approach includes four primary components: automated tumor localization and TNM staging from PET/CT imaging, an interpretable multi-omics prognostic model, an explainable AI approach for predicting complications, and recurrence prediction for NSCLC patients. Below is a detailed breakdown of the methodologies employed in this research.

A. Machine Learning-Based Tumor Localization and TNM Classification from PET/CT Imaging

An automated tumor localization and TNM staging system was developed using PET/CT DICOM images from the TCIA NSCLC [25] Radio genomic Dataset. The dataset comprises 211 NSCLC patient cases, including CT and PET/CT scans, tumor annotations, segmentation maps, and clinical data such as survival outcomes and genomic markers. To improve classification accuracy and better capture spatial interactions within tumor structures, the 2D image slices were reconstructed into 3D DICOM volumes. This transformation was necessary because, in 2D imaging, labeling errors can cause misclassification, particularly in cases where tumors in the upper lung influence predictions for lower-lung regions. By converting to 3D volumetric data, the model gained improved robustness, enabling more accurate localization and classification of tumors based on comprehensive spatial features. This approach ensures that tumor staging decisions are made using the entire volumetric structure rather than isolated 2D slices. The methodology follows multiple stages, including preprocessing, tumor localization, TNM classification, and evaluation, leveraging custom 3D CNN architectures for accurate feature extraction and classification.

Preprocessing: Image preprocessing was performed to enhance the quality and consistency of DICOM PET/CT scans before feature extraction. The preprocessing pipeline included contrast enhancement, noise reduction, and spatial normalization to ensure uniformity across scans. DICOM images were loaded and converted into a 3D volume, with pixel intensity values adjusted based on Rescale Intercept and Rescale Slope to correct variations in acquisition parameters. To standardize spatial dimensions, the extracted 3D volumes were resized to a fixed shape of (64, 128, 128), preserving anatomical structures across different scans. Noise reduction was implicitly handled through voxel rescaling, and further enhancement techniques, such as Non-Local Means Denoising, were applied to improve image clarity.

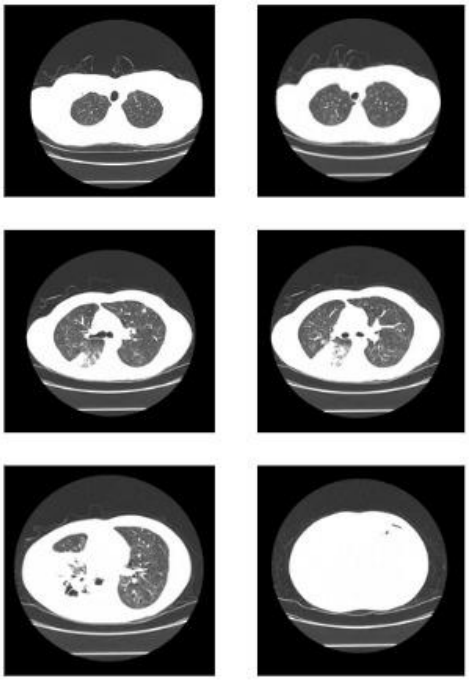

Figure 1 Random 2d Dicom slices of a person

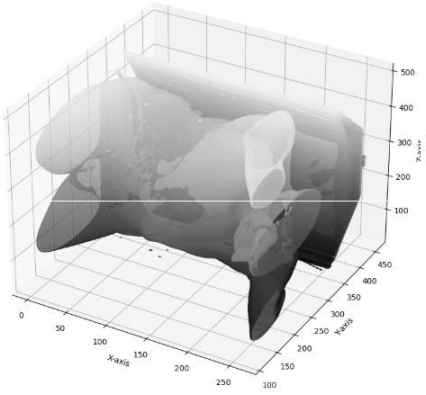

Figure 2 After transform 2d images into 3d image

Feature Extraction: Radiomics-based features, including texture, shape, and intensity, were extracted along with deep learning-derived embeddings from a 3D Convolutional Neural Network (CNN).

Classification: Four classification models were developed using custom 3D CNN architectures: one for tumor localization and three for T-pathology, N-pathology, and M-pathology classification. These models analyzed volumetric medical imaging data to accurately identify tumor regions and classify TNM stages.

Validation: Cross-validation was conducted using an independent dataset, and model performance was assessed using metrics such as accuracy, sensitivity, specificity, and AUC ROC scores.

B. Development of an Interpretable Multi-Omics Prognostic Model for NSCLC

This study utilizes the LUAD subset of the TCGA Pan-Cancer Atlas [26] from the CBIO portal[27], which includes over 470 patients and provides comprehensive multi-omics data, including clinical features, RNA expression levels, somatic mutations, and copy number variations (CNVs). The integration of these diverse data types ensures a robust and holistic survival analysis, improving the interpretability and clinical relevance of prognostic predictions.

Given the high-dimensional nature of the dataset, feature selection was conducted in multiple stages to improve model efficiency and maintain interpretability. Initially, over 2800 features were reduced by incorporating prognostic markers identified from the Human Protein Atlas [28], ensuring the inclusion of biologically meaningful genes while eliminating low-variance and redundant features. This step addressed potential multicollinearity issues that could violate Cox model assumptions. To further refine the feature set, LASSO (Least Absolute Shrinkage and Selection Operator) regression was applied, effectively penalizing less informative variables and reducing the feature count to fewer than 350 while preserving predictive power. Given the heterogeneity of the data—including continuous RNA expression levels, binary mutation status, and segmented CNV data—a robust scaler was employed to normalize features, ensuring that differences in scale did not disproportionately influence the model.

The Cox Proportional Hazards model was selected due to its well-established role in survival analysis, providing both interpretability and effective risk stratification. The model was fit using the refined set of features, allowing for the estimation of hazard ratios and survival probabilities. To balance model complexity and generalizability, hyperparameter tuning was performed using grid search and cross-validation techniques, optimizing the penalization function within the Cox model to prevent overfitting while maintaining predictive accuracy. Patients were then categorized into distinct risk groups based on their predicted hazard ratios, with Kaplan-Meier survival curves and log-rank tests validating the effective separation between high-risk and low-risk cohorts.

The model's discriminative ability was assessed using the concordance index (C-index), which quantifies how well the predicted risk scores correlate with actual survival times, with higher values indicating better prognostic performance. To evaluate predictive accuracy over different time intervals, time-dependent receiver operating characteristic (ROC) curves were generated, providing insight into how well the model-maintained performance across varying survival durations. To ensure robustness, the trained model was externally validated on an independent dataset, if available, to assess its generalizability across different patient cohorts.

To enhance explainability and clinical utility, feature importance analysis was conducted, leveraging the interpretability of the Cox model to identify the most influential prognostic factors, offering insights into potential biomarkers for clinical decision-making. SHAP (SHapley Additive Explanations) values were used to quantify the contribution of each feature to individual risk predictions, improving the transparency of the model's decision-making process. Looking ahead, future work may involve deploying the model as an interactive web-based tool, allowing clinicians to input patient data and receive real-time prognostic assessments, bridging the gap between computational research and clinical application.

C. An Explainable AI Approach for Predicting Complications from Lung Cancer Diagnostic Workups Using Limited Clinical Data

Data for this study was derived from the PLCO Cancer Trial[29]. The original dataset includes records from lung screenings, diagnostic procedures, complications, treatments, and x-ray linkages. After merging and preprocessing, the dataset was reduced to approximately 30,000 records with 34 features. Standard techniques such as imputation, encoding, and normalization were applied to ensure data quality.

The dataset contained demographic details such as age, gender, and smoking status, along with clinical measurements like BMI and blood pressure. It also included diagnostic procedure information and outcome variables such as complication occurrence and severity. Preprocessing was a critical step, where missing values were handled by imputing numerical data with the median and categorical data with the mode. Duplicate records were removed, and outliers were addressed using boxplot analysis and Z-score filtering. Categorical features were encoded using either one-hot or ordinal encoding, while numerical attributes were normalized using Min-Max scaling.

To address class imbalance, the SMOTE-ENN technique was applied, which synthesized minority class samples and refined the majority class distribution. The dataset was then split into an 80/20 training-testing split. Feature engineering played a crucial role in improving predictive performance, including transforming BMI into ordinal categories, categorizing treatment complexity into curative and non-curative, and integrating tumor staging variables into a severity index.

For modeling, we implemented Logistic Regression, Random Forest, and XGBoost as baseline models, with Logistic Regression achieving an AUC-ROC of 0.78 and identifying age and smoking history as significant predictors. Random Forest achieved 82% accuracy, highlighting tumor size and hypertension as key features, while XGBoost improved performance further. The standout model was TabNet, a deep learning model designed for

tabular data, which uses a sequential attention mechanism to dynamically select and process critical features.

D. Recurrence prediction with PFI and new tumour event type.

The gene expression data of 1264 patients was obtained from the porpoise data compiled by Mahmoud et al [26] The phenotype data of 1264 patients was obtained from the xenabrowser TCGA hub, [27] that hosts both gene expression and curated phenotype data for overall survival time, disease free survival time and progression free survival time. 252 of 1264 patients underwent recurrence of lung adenocarcinoma and squamous cell carcinoma.

Although the phenotype dataset did not suffer from the curse of dimensionality, the gene expression data was a combination of more than 2900 columns of gene rna sequences, copy number variations and mutations, whereas phenotype data only consisted of Disease Free, Progression Free, Overall Survival, age at diagnosis, pathological tumor stage, new tumour site and such columns numbering 34 columns. Due to the high dimensionality of the gene data column, the human protein atlas[28] was utilized to reduce the number of columns that would be needed to be fed into the ML model. Through selecting the columns related to the adverse prognosis and nonadverse prognosis, it was able to filter the columns down to just 215. Therefore, only the previously identified and clinically proven genes as well as their related genes were used in the development of the ML model.

After categorical encoding of non-numeric columns and cleaning the dataset of duplicate records as well as various scaling techniques for scaling the numeric data. The preprocessed filtered gene dataset was merged with the phenotype dataset to combine them both. The dataset was then fed into a Cox Proportional hazards model to determine the Progression free interval of LUAD and LUSC for the given patients. An 80-20% train test split was used with the sklearn train test splitter. For the prediction of a Progression Free Interval (PFI) a Random Forest Classifier was used with GridSearch for the best hyper parameters. During the train-test split we maintained positive cases at 40% for both train and test data. Fitting 5 folds for each of 108 candidates, totalling 540 fits. Best parameters: 'max depth': 10, 'min samples leaf': 2, 'min samples split': 2, 'n estimators': 300. Train and test accuracy and precision were 0.9, 0.8242, 0.87 and 0.92 respectively. For the prediction of new tumor event type a Random Forest Classifier was used. Since some of the classes had only one occurrence is was not possible to do k-folds validation. And the test set achieved an accuracy of 0.7105.

IV. FINDINGS

A. AMachine Learning-Based Tumor Localization and TNM Classification from PET/CT Imaging

The developed automated tumor localization and TNM staging system using custom 3D CNN models demonstrated moderate performance in lung cancer assessment. The TNM pathology classification models performed better than the tumor localization model, highlighting the challenges of precise tumor boundary detection in PET/CT imaging. While the models successfully classified tumor progression and staging, their overall accuracy remained within a mid-range level, indicating room for improvement. The results suggest that 3D volumetric analysis improves feature extraction over traditional 2D approaches but still faces challenges in capturing complex tumor structures.

While deep learning-based models offer strong feature extraction capabilities, generalization and interpretability remain key concerns. This study emphasizes the integration of structured tumor annotations and segmentation maps to enhance model reliability. However, inconsistencies in classification across TNM stages indicate the need for further refinement in feature representation and spatial learning.

Given these findings, the system has the potential to support automated TNM staging and tumor localization in clinical workflows, but further improvements are needed for higher accuracy and robustness. Future work will focus on multi-center validation, advanced data augmentation, and explainability techniques such as Grad-CAM to provide deeper insights into feature importance. Additionally, developing an interactive clinical interface for real-time TNM staging predictions will help integrate the system into oncology decision-making processes.

B. An Interpretable Multi-Omics Prognostic Model for NSCLC

The developed prognostic model demonstrates state-of-the-art performance, achieving a C-index of 0.8, surpassing previous works such as Na Sun et al. [15] where a C-index of 0.733 was achieved and Hugo Gomez-Rueda et al. [30] achieved 0.72. This significant improvement underscores the effectiveness of integrating multi-omics data for prognostic analysis, enhancing predictive accuracy and clinical utility. Unlike single-modality models that rely solely on gene expression or histopathology, often facing limitations in predictive power—this study incorporates RNA expression, somatic mutations, and copy number variations to achieve superior survival stratification. The findings reinforce the hypothesis that multi-omics integration is essential for robust prognostic modeling. While deep learning-based approaches have demonstrated potential in prognosis prediction, they often suffer from interpretability challenges. In contrast, the proposed model, grounded in statistical survival analysis, not only delivers high accuracy but also provides clear insights into the impact of individual features. The incorporation of prognostic markers from the Human Protein Atlas ensures that selected features are biologically meaningful, further strengthening the model's reliability.

Given its strong performance, this model has the potential to serve as a decision-support tool for oncologists, aiding in risk assessment and personalized treatment planning. Future work will focus on validating the model on independent cohorts to assess generalizability, enhancing explainability through SHAP analysis to provide deeper insights into biomarker contributions, and developing a user-friendly clinical interface for real-time survival predictions to facilitate seamless integration into clinical workflows.

Feature (Bad Prognosis)	Risk Coefficient
ST6GAL2_mut	0.0564
LAMA3_mut	0.0526
CDK19_rnaseq	0.0443
DAPK1_rnaseq	0.0438
VRK2_rnaseq	0.0425

Table 1 : Major Features related with Bad Prognosis Based on Coefficients from the Cox Model.

Feature (Good Prognosis)	Risk Coefficient
BMP6_rnaseq	-0.0697
CCL14_rnaseq	-0.0659
IL1R2_rnaseq	-0.0587
CTTNBP2_mut	-0.0574
LAMB1_mut	-0.0534

Table 2 : Major Features related with Good Prognosis Based on Coefficients from the Cox Model.

C. An Explainable AI Approach for Predicting Complications from Lung Cancer Diagnostic Workups Using Limited Clinical Data

Out of the Models used, TabNet outperformed all baseline models, achieving an AUC-ROC of 0.92, and its interpretability was enhanced through SHAP and LIME analyses. SHAP values revealed that Age, Pack Years (Cigarette Smoking Exposure), Hypertension, Body Mass Index (BMI), Lung Cancer Stage were the most influential predictors globally, while LIME provided insights into individual predictions, making the model's decisions transparent and actionable for clinicians. This approach not only improved predictive performance but also ensured that the model's outputs were interpretable, making it a valuable tool for clinical decision-making in lung cancer diagnostics.

Feature Importance	Feature Importance
age	0.083902
pack_years	0.081757
hyperten_f	0.078918
bmi_curc	0.070327
lung_stage	0.067948
lung_stage_n	0.065715
sex	0.062295
lung_clinstage	0.05569
trt_days	0.053086
lung_cancer_type	0.048027
trt_numl	0.018493
emphys_f	0.01507

Table 3 : Top 10 Feature Importance for complication prediction In **TabNet Model**

D. Recurrence prediction with PFI and new tumour event type.

Through the Cox PH model, Random Forest Classifiers it was able to identify that the most important features as listed below. For the given C-index for the training and testing cohort and train-test accuracy and prediction.

Feature Importance	Feature Importance
PTPRC rnaseq	2.825889
IKZF1 rnaseq	1.365888
ITGB4 rnaseq	1.120881
IL16 rnaseq	1.015831
SH3GL1 rnaseq	0.996923
SIGLEC7 rnaseq	0.984090
EPHB2 rnaseq	0.931213
SLAMF1 rnaseq	0.909106
IL1RN rnaseq	0.870420
MRC1 rnaseq	0.857908

Table 4: Top 10 features for progression free interval time

Feature Importance	Feature Importance
new tumor event type encoded	0.1538
TBK1 rnaseq	0.0097
NACA rnaseq	0.0076
RPS6KL1 rnaseq 0.0075	0.0075
SLC44A1 rnaseq 0.0074	0.0074
treatment outcome first course encoded	0.0073
MIF rnaseq	0.0072
FIP1L1 rnaseq	0.0069
TWF1 rnaseq	0.0063

Table 5: Top 10 features for progression free interval

Feature Importance	Feature Importance
CBLC rnaseq	0.0189
CBFA2T3 rnaseq	0.0133
PIK3R1 rnaseq	0.0130
MCAM rnaseq	0.0121
STK3 rnaseq	0.0107
TNFRSF10C rnaseq	0.0102
RPS6KB1 rnaseq	0.0100
HLF rnaseq	0.0098
CCR2 rnaseq	0.0096

Table 6 : Top 10 features for new event type

V. Future Works

Future work will focus on enhancing the generalizability and accuracy of the models through multi-cohort testing and validation. By evaluating the AI models across diverse patient populations with varying demographics, cancer stages, and treatment histories, we aim to assess their real-world performance and ensure they are robust and effective in a wide range of clinical scenarios. Collaborating with multiple hospitals and research institutions to gather data from different cohorts will be critical in identifying potential biases and limitations, ensuring the models are clinically applicable and reliable across diverse settings.

Additionally, this multi-cohort validation process will enable continuous refinement of the models as new data emerges, allowing for ongoing improvements in accuracy

and reliability. Retraining the models with fresh datasets will help them remain adaptable to evolving healthcare trends and ensure they continue to provide meaningful, precise predictions. By integrating this approach into the development pipeline, NSCLC360 will maintain clinical relevance and stay effective in supporting decision-making for cancer management, fostering greater trust and adoption among clinicians and healthcare providers.

VI. ConClusions

This study presents an innovative, interpretable-driven decision support system for the prognosis, diagnostics, staging, and recurrence prediction of NSCLC using multi-omics data. By integrating survival analysis models with explainability techniques and machine learning, the system enhances both predictive accuracy and interpretability, thereby improving its clinical utility. The findings highlight the potential of AI-driven, interpretable decision support systems in precision oncology, offering a promising pathway toward more personalized, data-driven treatment strategies.

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