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A Hybrid Radiomics–Deep Learning Feature-Fusion Framework with Explainable Artificial Intelligence for Accurate Liver Cancer Prediction from Computed Tomography Images

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ABSTRACT

Hepatocellular Carcinoma (HCC) is one of the common cancer-related mortality causes across the world. The black-box nature (semantic opacity) of current deep learning models used in computer-aided detection hinders clinical management of HCC, particularly the lack of early and interpretable diagnosis. In this work, a hybrid fusion framework at the feature level is developed to enhance the accuracy and interpretability of predicting liver cancer using computed tomography (CT) images. CT volumes dataset from the multi-center Liver Tumor Segmentation (LiTS) benchmark were pre-processed using Hounsfield-Unit windowing, isotropic resampling and automated, spatial-pyramid-pooling-based segmentation. A 3-D deep feature was extracted using a 3-dimensional ResNet-10 backbone and a 562-dimensional hybrid vector was created by concatenation PyRadiomics descriptors selected by Lasso, balanced with Synthetic Minority Over-sampling Technique (SMOTE), an eXtreme Gradient Boosting (XGBoost) model optimized by GridSearchCV was then used for classification. To obtain both spatial and feature-level explainability, Gradient-weighted Class Activation Mapping (Grad-CAM) and SHapley Additive exPlanations (SHAP) are applied. The AUC-ROC of the optimized hybrid classifier was 0.921 and an overall accuracy of 85% and sensitivity of 0.95 for low tumor-burden cases were obtained. Predictions were shown to be based on biologically relevant regions of the tumor, and not on anatomical noise by using Grad-CAM heatmaps. The results suggest that a radiomics–deep learning fusion model with explainability and transparency has high diagnostic accuracy and clinical interpretability, and can be used as a reliable model for decision support in the field of hepatic oncology.

Keywords: *Hepatocellular carcinoma; Radiomics;* Deep learning; Feature-level fusion; Explainable artificial intelligence; XGBoost

INTRODUCTION

Liver cancer is one of the deadliest forms of cancer, among the top three causes of cancer death and is one of the most difficult to treat, especially in the context of healthcare systems around the world (Grover & Gupta, 2024; Ma et al., 2024). The major liver cancers are predominantly Hepatocellular Carcinoma (HCC) which is rising due to the increasing prevalence of chronic hepatitis B and C, cirrhosis, intake of aflatoxin and metabolic liver diseases (Shiwlani et al., 2024; Pande et al., 2025). Chronic HBV infection remains a leading cause of cirrhosis and hepatocellular carcinoma worldwide, with a particularly high burden in Nigeria (Bala Doma et al., 2025). In addition to this, epidemiological projections suggest that liver cancer incidence rates could approach almost 1.4 million per year by 2040 (Grover & Gupta, 2024) and the diagnosis of liver cancers is often at a late stage when they are unresectable or not suitable for transplantation (Lal et al., 2025; Saeed et al., 2025).

Currently, the diagnosis of HCC is done through computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography and biopsy (Pande et al., 2025). These approaches are labor-intensive, demand a significant amount of manual analysis of 3D scan volumes and have inter-observer variability, while biopsy poses risks of bleeding and infection (Grover & Gupta, 2024; Huang et al., 2025a). Bo et al. (2024) in a recent review of the field of artificial-intelligence (AI) radiomics in Computers in Biology and Medicine, pointed to the fact that radiomic pipelines are currently in the forefront of diagnosis and individual treatment plan and prognosis of HCC, but the translation of radiomics to routine clinical practice is still hindered by the heterogeneity of acquisition protocols and limited external validation.

Traditional machine learning (TML) algorithms (e.g., Support Vector Machines, Random Forest and eXtreme Gradient Boosting) have been traditionally based on hand-crafted radiomic or clinical features. Ensemble TML approaches are not yet out of the competition: El Atifi et al. (2025) optimized the performance of the classifiers (Random Forest, AdaBoost and Gradient Boosting) by training them on tabular liver-patient records and found that the optimized Random Forest reached an accuracy of 85.17%, which indicated the power and weakness of "all-engineered" pipelines. These models, however, demand handcrafted features for implementation, which are challenging to select from the domain knowledge, and are not able to capture the whole complexity of pathological patterns existing in imaging data (Sethia et al., 2025; Hariharan et al., 2025).

Since that time, the deep learning (DL) architectures which are able to learn hierarchical representations directly from raw imaging data have revolutionized medical image analysis. In liver-cancer detection, the performance of convolutional networks such as ResNet, U-Net and DeepLab V3+ spans from 94-99% (Grover & Gupta, 2024; Li & Zhao, 2025; Mondol et al., 2025) and deep representation learning isn't limited to diagnosis, but is expanding to precision

oncology. In the case of liver cancer, the researchers have created a model named PathSynergy, using Graph Neural Network (GNN) and deep learning to generate synergistic drug pairings to target HCC treatment, which will take place within the HCC care continuum, as published in Briefings in Bioinformatics by Zhang et al., (2025). Despite these successes, several factors make it difficult to apply DL in clinical practice, including the black-box aspects of deep networks, the large amount of annotated data required and the high computational cost (Hu et al., 2026; Yang & Niu, 2026). The trade-off between prediction and transparency has been shown to be a potential solution with radiomics–deep learning fusion. Huang et al. (2025a) fused the two types of features, clinicoradiologic features and ResNet-18-derived radiomic features, using logistic-regression, obtaining the AUC of 0.808 for predicting MVI in HCC, suggesting that fusing the two types of features could be superior to the single type prediction. Huang et al. (2025b) (Academic Radiology) enhanced this pipeline by adding a DeepLab V3+ segmenter for the tumour, before multiregional feature fusion, obtaining a training AUC of 0.968 for prediction of microvascular invasion and early recurrence, but still noted the absence of external multicentric validation. It is worth noting, however, that the combination of deep learning and radiomics also achieved a higher AUC than the radiomics model alone (0.917 vs 0.839) and that Zhao et al. (2024) noted some limitations of manual segmentation and the limited number of patients from a single center for generalizability.

Overall, the current literature shows three significant gaps: (1) still, most hybrid fusion pipelines rely on complex fusion and deep architectures with higher predictive performance, but they are black-box models, whereas interpretable models exhibit lower predictive performance; (2) most hybrid pipelines are trained on a single-institution dataset, which limits their generalisability (Huang et al., 2025b; Zhao et al., 2024); and (3) most of the segmentation and feature extraction are still manual, and very few studies combine feature-level fusion with dual explainable artificial intelligence (XAI) to explain both spatial and feature-level decisions of the model. This research will answer these unknowns by developing and testing a fully automated hybrid feature level fusion framework that integrates radiomic descriptors, ResNet-10-derived deep representations and fuse the vector with a SMOTE balanced, GridSearchCV optimized XGBoost model, and auditing model predictions using dual Grad-CAM and SHAP explainability in a multi-center, heterogeneous CT cohort. Specifically, it aims to: (i) propose a fusion framework at the feature level to optimize the classification of liver malignancies, (ii) alleviate the problem of algorithmic opacity by using two mechanisms – Grad-CAM mechanism and SHAP mechanism, (iii) test the framework with both heterogeneous and multi-center cohorts to avoid overfitting the model, and (iv) compare the result of the framework with that of standalone baselines in diagnosis based on sensitivity, specificity, F1-score and the Area Under the Receiver Operating Characteristic Curve.

MATERIALS AND METHODS

The detail of the methods and techniques used to facilitate replication of the study is provided in this section. This study was carried out in accordance with the Design Science Research (DSR) paradigm that was operationalized as a quantitative machine-learning experiment consisting of five steps: data acquisition, data pre-processing and data segmentation, two types of feature extraction, hybrid fusion of features at the level of classifiers, and explainable performance evaluation.

Framework Design

The framework design allows for generalizability across sites, and reduces the risk of overfitting resulting from single-institution studies. Model training and testing was performed on the multi-center Liver Tumor Segmentation (LiTS) benchmark dataset of 131 three-dimensional computed tomography (CT) volumes acquired in different clinical centers and with a variety of scanner-noise profiles and acquisition protocols. We ingested raw volumes, as spatial metadata in 3-dimensional tensors (height × width × depth), in NIfTI format to ensure the anatomical information is retained. After finishing the data pre-processing, dual feature extraction layer was designed to extract the radiomics features from the data using Lasso-based feature extraction and to extract the deep features from the data using ResNet-10 deep feature representation. Adopted an optimized XGBoost for classification followed by Explainability layer and performance evaluation. Figure 1 below shows the model that has been designed.

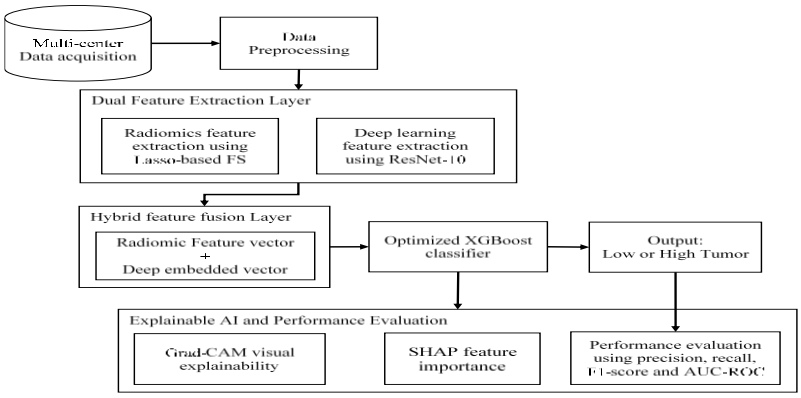

Figure 1: Proposed Hybrid Radiomics–Deep Learning Feature-Fusion Architecture with Dual Explainable AI Integration

Image Pre-processing and Automated Segmentation

Hounsfield Unit (HU) window was set from −100 to 400 to provide a good contrast between the liver parenchyma and artefacts from non-hepatic soft-tissues and bone. The voxel intensities were z score normalized, and voxel variation across scanners was reduced by isotropic resampling to 1.0 × 1.0 × 1.0 mm³ with B-spline interpolation:

$$z_i = \frac{x_i - \mu}{\sigma} \quad (1)$$

Where xi is the original voxel intensity, μ is the population mean and σ is the population standard deviation. Then, to segment irregular boundaries of hepatic lesions, an automated segmentation network, defined as an encoder–decoder convolutional network with multi-scale contextual feature capture using atrous spatial pyramid pooling (ASPP), was used to get a binary volumetric mask of the same spatial dimension as the subsequent feature-extraction streams.

Parallel Feature Representation Streams

Radiomic feature extraction (Stream A). The features extracted from the region of interest segmented using PyRadiomics were first order intensity statistics, three-dimensional shape descriptors, and textural matrices (Gray Level Co-occurrence Matrix and Gray Level Size Zone Matrix). To alleviate the curse of dimensionality and to choose the most discriminative and non-invasive biomarkers, the Least Absolute Shrinkage and Selection Operator (LASSO) was employed which minimizes:

$$\min_{\beta} \left[\frac{1}{2n}\sum_{i=1}^{n}\left(y_i - X_i^T\beta\right)^2 + \lambda \sum_{j=1}^{p}\left|\beta_j\right|\right] \quad (2)$$

Here, X is the radiomic feature matrix, y is the diagnostic label, β are the radiomic feature coefficient matrix and λ is the L1 regularization penalty which was optimized using cross validation. This gives rise to a small representation of the image with a 50-dimensional radiomic vector, Vrad.

Deep representation learning (Stream B). In order to avoid overfitting for ultra-deep networks, a constrained 3-D ResNet-10 backbone has been used, in which, the residual learning blocks are defined a:

$$y = F(x,\{W_i\}) + x \quad (3)$$

Here, x is the input, y is the output of the residual block and F(x,{Wi}) is a residual mapping to be learned. A terminal Global Average Pooling layer was used to obtain a 512 dimension dense embedding, Vdeep, after convolution.

Hybrid Feature-Level Fusion and Classification

Vrad and Vdeep were batch-normalised to comparable magnitude and then concatenated with each other to form a hybrid vector of 562 dimensions:

$$F_{hybrid} = \left[V_{rad} \oplus V_{deep}\right] \quad (4)$$

Fhybrid was classified using an eXtreme Gradient Boosting (XGBoost) model, which builds an ensemble of decision trees by sequentially minimizing a regularized objective function:

$$Obj(\Theta) = \sum_i L(y_i,\hat{y}_i) + \sum_k \Omega(f_k) \quad (5)$$

For a differentiable loss function, L, and a penalty on model complexity, Ω, to prevent over fitting. But, the training set was extremely imbalanced (79 low burden cases versus 25 high burden cases) and so the Synthetic Minority Over-sampling Technique (SMOTE) was employed prior to classification, and hyperparameters were tuned using GridSearchCV.

Explainable Artificial Intelligence Integration

We used the Gradient-weighted Class Activation Mapping (Grad-CAM) to obtain the spatial saliency heatmap from the terminal convolutional layer of the ResNet-10 backbone. For class c the importance of each feature map k was calculated as:

$$\alpha_k^c = \frac{1}{Z}\sum_i\sum_j \frac{\partial Y^c}{\partial A_{ij}^k} \quad (6)$$

And combined with the forward activation maps through a ReLU non-linearity to retain only features that positively influence the predicted class:

$$L_{Grad-CAM}^c = ReLU\left(\sum_k \alpha_k^c A^k\right) \quad (7)$$

To quantify the contribution of each radiomic feature and deep feature to the fusion classifier, SHapley Additive exPlanations (SHAP) method was used, which is based on cooperative game theory:

$$\varphi_i = \sum_{S\subseteq N\setminus\{i\}} \left[\frac{|S|!(|N|-|S|-1)!}{|N|!}\right] \left[f(S\cup\{i\}) - f(S)\right] \quad (8)$$

Performance Evaluation and Implementation Tools

The following standard diagnostic metrics were used to compare the models' performance with the performance of standalone deep-learning and traditional-machine-learning models on the independent, held-out test cohort:

$$Sensitivity = \frac{TP}{TP+FN} \quad (9)$$

$$Specificity = \frac{TN}{TN+FP} \quad (10)$$

$$F1-score = 2 \times \frac{Precision \times Sensitivity}{Precision + Sensitivity} \quad (11)$$

Additionally, the Area under the Receiver Operating Characteristic Curve (AUC-ROC) was determined to evaluate the discriminative performance at any probability cut-off point. The framework was coded in python and CUDA was used to speed up the calculations using GPU. NIfTI images were input/outputted, windowed in HU and resampled & normalized with MONAI, radiomic extracted and selected with LASSO with PyRadiomics and Scikit-learn, deep-representation extracted with PyTorch, fused and classified with the XGBoost library and post-hoc interpretation performed with the Grad-CAM and SHAP libraries. Each stratified partitioning, cross validation and benchmarking was done with Scikit-learn library.

RESULTS AND DISCUSSION

Feature-Level Fusion and Class-Imbalance Handling

This hybrid pipeline led to the creation of a 562-dimensional feature space of 50 PyRadiomics descriptors and 512 deep features from ResNet-10. The training pool was quite imbalanced; 79 low burden scans and 25 high burden scans. Combining SMOTE with hyperparameter tuning using GridSearchCV ensured that XGBoost classifier model would not be biased towards the majority class, and retain sensitivity to the clinically important minority (high burden) class.

Explainable Artificial Intelligence Outcomes

SHAP analysis (Figure 2) revealed that selected deep embedding dimensions from ResNet-10 together with textural and shape radiomic features ranked among the most important predictors. Higher values of these features were consistently associated with high tumor burden. This shows the hybrid vector works not just on interpretable radiomic descriptors, but also works on abstract deep features.

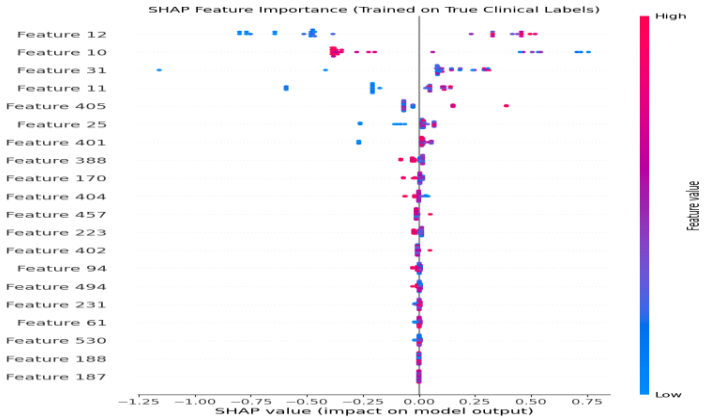

Figure 2: SHAP Feature-Importance Plot for the Hybrid Fusion Classifier

The heatmaps (Grad-CAM) generated by the last convolutional layer of ResNet-10 backbone (figure 3) when plotted on CT slices from the source showed the top located regions in the map, which were mostly located inside the segmented tumors, indicating that the deep-representation stream was learning meaningful semantic features from the tumor context rather than the anatomical information surrounding the background.

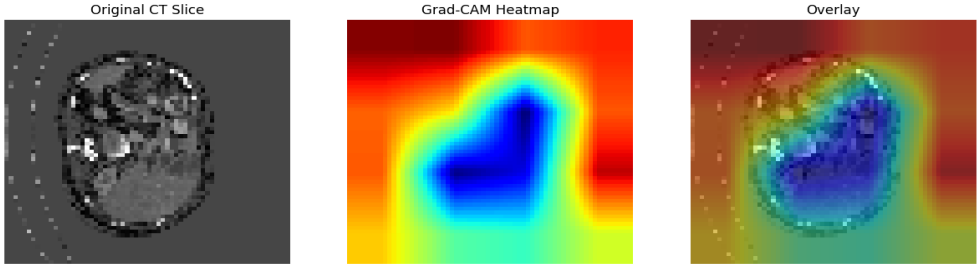

Figure 3: Grad-CAM Heatmap Validation on a Representative CT Slice

Diagnostic Performance Benchmarking

The Area under the Receiver Operating Characteristic Curve (AUC-ROC), and overall diagnostic accuracy of the optimized hybrid XGBoost classifier were 0.921 and 85% respectively on an external multi-center test set of 27 3-D computed tomography (CT) scans held out of the training-process (Figure 4). The performance obtained (Table 1) was a recall of 0.95 and precision of 0.86 for low tumor burden class and precision of 0.83 and recall of 0.62 for high tumor burden class on a class-wise basis.

Table 1: Class-Specific Diagnostic Performance Metrics

Metric	Low Tumor Burden (Class 0)	High Tumor Burden (Class 1)
Precision	0.86	0.83
Recall (Sensitivity)	0.95	0.62

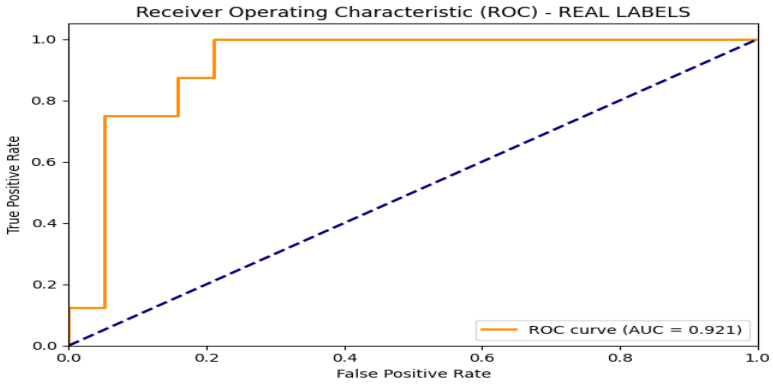

Figure 4: Receiver Operating Characteristic (ROC) Curve of the Hybrid Classifier

The confusion matrix that was obtained is shown in Table 2 and Fig. 5, which includes 18 TNs, 5 TPs, 3 FNs and 1 FP. This distribution is indicative of high specificity – few benign cases were over-treated – and has direct clinical relevance for prioritising radiology workflow, with the majority of cases with very severe tumour burden being correctly identified.

Table 2: Confusion Matrix Summary

Classification Outcome	Count
True Negatives	18
True Positives	5
False Negatives	3
False Positives	1

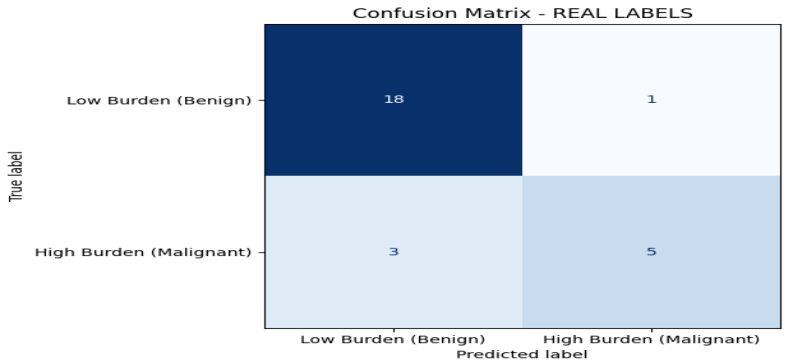

Figure 5: Confusion Matrix of the Hybrid Classifier on the Independent Test Cohort

Discussion

The primary objective of designing a feature-level fusion architecture to optimize the classification of hepatic malignancies was successfully realized, yielding an AUC-ROC of 0.921. Huang et al. (2025a) and Zhao et al. (2024) found similar results, as they demonstrated that models using both traditional radiomics features and deep learning features outperformed single-modality-based models. In a similar way, Zhao et al., (2024) achieved an AUC of 0.917 with a combination of 50 PyRadiomics features and 512 deep semantic features from a ResNet-10 backbone, and their performance was comparable to that of the current study, which proved the validity of the hybrid paradigm to keep the semantic reliability of radiomics and take advantage of the computational power of CNNs.

Both SHAP and Grad-CAM aim to directly solve the problem of opacity of algorithms that has been emphasized in recent studies in the context of explainable artificial intelligence. As pointed out by Pande et al. (2025) and Chowdhury et al. (2025) one major obstacle for clinical trust and deployment of advanced deep-learning models is their black-box characteristics. The validation of the Grad-CAM in the present study shows great spatial correlation between the heatmaps and the actual tumor region, highlighting the network's focus on semantically relevant features for tumor diagnosis, not background noise from the surrounding anatomy as mentioned by Hu et al., 2026. The SHAP analysis also gives a feature level post-hoc explanation which is required by clinicians when using it in their daily practice.

Hybrid frameworks are evaluated based on data from one institution, which may lead to overfitting due to the use of local imaging methods (Huang et al., 2025b; Zhao et al., 2024), while our proposed framework is tested on data from multi-center and diverse cohorts. Both training and testing of this framework were performed using stratified 5-fold cross validation and oversampling minority classes using SMOTE (Synthetic Minority Over-sampling Technique), which directly addresses the literature's need of multi-center and large-scale validation, and therefore ensures that the diagnostic accuracy of the present framework will be stable if it is used outside a localized training distribution.

The model was validated for its diagnostic performance by inter-comparing its performance with well-established benchmarks and demonstrated to be clinically useful. The overall accuracy of the test was 85% and the test sensitivity was 0.95 for low burden cases, which decreases the risk of overtreatment of the benign cases. This aligns with the broader literature where for instance El Atifi et al. (2025) obtained a comparable accuracy of 85.17% with traditional ensemble classifiers on high dimensional tabular clinical data, while in the current investigation, classifiers were applied to complex, high dimensional imaging tensors, which is a much harder learning task. The use of the shallower ResNet-10 backbone is also in line with the advice given by Zhao et al. (2024) and Ma et al. (2024) to not use very complex models with a comparatively small dataset in medical imaging. The overall performance of accuracy and interpretability is consistent with the results of Zhang et al. (2025), which demonstrated that deep representation learning techniques have the potential to be applied throughout the entire journey of HCC care, from diagnosis to treatment planning, but still need to mature on the path towards multimodality and explainability. The overall methodology is a balance of both computational efficiency and the use of cutting-edge diagnostic measures, providing a realistic pathway towards fully implementing high-performance, automated deep-learning workflows in clinical practice, including in resource-limited settings, and addressing operational challenges identified by Pande et al. (2025).

CONCLUSION

In this study, we introduced and tested a hybrid fusion framework at the feature level to combine structured radiomic features and deep semantic features for improved classification of hepatic malignancy based on CT imaging; and we tackled the black box problem of deep learning by leveraging the two explainability methods, namely, Grad-CAM and SHAP. The optimized eXtreme Gradient Boosting classifier was found to have an AUC-ROC of 0.921, and an overall accuracy of 85% on an independent, multi-center test cohort, which showed that high diagnostic accuracy does not need to be sacrificed for clinical transparency. The backbone was chosen strategically to not be as deep as the current SOTA, ResNet-10, in case of overfitting, and in order to maximize generalizability given data that was known to have heterogeneity across imaging sites, hyperparameter optimization and class balancing (SMOTE) were used. The framework is a true gamechanger for medical image analysis,

by enabling the creation of a unified pipeline that is mostly automated and better combines the semantic reliability of radiomics with the predictive power of deep learning and by providing a blueprint of how to audit complex fusion classifiers with complementary spatial and feature-level explanation. Therefore, it is recommended that such feature-fusion can be used as a second-reader diagnostic tool in oncological institutions to be used in conjunction with the biopsy and/or surgical planning during a multidisciplinary tumor-board discussion. Limitations of this study are the use of only CT images and the small size of the independent test cohort; a future effort should consider extending the framework to include other modalities (e.g., contrast enhanced MRI), tabular biomarkers and genomic profile data, and should be validated for its impact on real world clinical diagnosis and patient survival in large scale, prospective, multi-site clinical trials.

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