

Machine Learning-Based Prediction of Overall Survival After Lung SBRT Using Clinical, Dosimetric, and Radiomics Features: a multicenter study

Camille Invernizzi

caminvernizzi@gmail.com

Institut Godinot

Pierre-Louis Benveniste

Polytechnique Montreal

Radouane El Ayachy

Centre Charlebourg

Thomas Leroy

Clinique des Dentellières

Nicolas Blanchard

Clinique des Dentellières

Benjamin Schipman

Institut de Cancérologie de Bourgogne

Christophe Debelleix

Clinique Tivoli-Ducos

Jérôme Chamois

Institut de cancérologie de Rennes-St Grégoire

Yoann Pointreau

Institut inter-Régional de Cancérologie (ICL), Clinique Victor Hugo

Jean-Emmanuel Bibault

INSERM UMR1138, Centre de Recherche des Cordeliers

Article

Keywords: Lung, SBRT, Radiomics, Machine learning

Posted Date: March 8th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-8743399/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Radiomics combined with clinical and dosimetric data may improve outcome prediction after lung stereotactic body radiotherapy (SBRT). This study aimed to develop machine learning models to predict overall survival (OS) after lung SBRT for primary and metastatic lung tumors using planning CT-derived features. Clinical and dosimetric data were retrospectively collected from six centers. Radiomics features were extracted from planning CT scans using double tumor segmentation and selected using statistical filtering. Models were trained using 180 features composed of 124 radiomics, 45 clinical and 11 dosimetric features. A total of 163 patients treated between 2016 and 2018 were included. Patients were divided into primary (n=105) and metastatic (n=58) cohorts. Two XGBoost models were trained to predict OS for either primary or metastatic cohorts, using nested stratified cross-validation and Bayesian hyperparameter optimization. The 20 most influential features identified by SHAP analysis were retained. Death occurred in 26.7% of patients in the primary cohort and 48.3% in the metastatic cohort. The models achieved high predictive performance, with ROC-AUC values of 0.89 and 0.87, respectively. These models provide accurate and well-calibrated OS predictions after lung SBRT, supporting individualized clinical decision-making.

INTRODUCTION

In lung tumors, Stereotactic Body Radiation Therapy (SBRT) is indicated for inoperable early-stage Non-Small Cell Lung Cancer (NSCLC) (1), and is increasingly being used in oligometastatic disease. Randomized phase II studies have shown that SBRT used as local ablative treatment of metastases could improve Overall Survival (OS) or Progression Free Survival (PFS) (2–7).

Tumor response after SBRT for primary lung cancer depends primarily on clinical and dosimetric features. Predictive clinical parameters of patients treated by SBRT for an early-stage NSCLC have been investigated in the study of Luo et al., showing that clinical stage, immobilization device, smoking status, and hemoglobin rate were associated with the prediction of long-term outcomes such as OS, Locoregional Recurrence Free Survival (LRFS), PFS, and Distant Disease Free Survival (DDFS) (8). Dosimetric parameters such as a higher Gross Tumor Volume (GTV) D_{max} Biologically Effective dose with an α/β ratio of 10 (BED_{10}) and a larger percent of the GTV receiving $\geq 110\%$ of the prescribed dose were correlated with a better local control in early-stage NSCLC in a recent study (9).

Lambin et al. defined “Radiomics” as the high-throughput extraction of features of imaging data (10). These quantitative data are automatically extracted and can be used to train machine learning algorithms to predict patient outcomes (11).

A meta-analysis described some of the medical applications of radiomics in the management of lung tumors, especially in detection, diagnosis and prediction (12). Concerning prediction, some studies suggest that radiomics extracted from planning Computed Tomography (CT) could be predictive factors for tumor response after SBRT in lung tumors. Fodor et al. found four radiomic features associated with local progression after SBRT of lung oligometastases from colorectal cancer of 38 patients (13). Regarding survival outcomes, an exploratory analysis of Huynh et al. on planning CT of 113 patients treated with SBRT for NSCLC reports that four radiomics features were predictive of OS and one of Distant Metastasis (DM) (14). However, this study is based on a single-center, which limits the generalizability of the results. Sawayanagi S et al. found one radiomic predictive factor for OS and one predicting model of OS in patients treated by SBRT for NSCLC, but the study also had a mono-centric design (15).

Combining clinical and dosimetric data and the potential predictive role of radiomics, could lead to a more personalized treatment and, therefore, to better outcomes. The aim of the present study was to develop two predictive models of overall OS for patients treated with SBRT for lung tumors.

METHODS

Study design and population

A retrospective multicentric study was performed in six XXXX medical radiation centers (XXXX ; XXXX ; XXXX ; XXXX ; XXXX ; XXXX). Eligible patients were patients treated by lung SBRT for a primary or secondary lung tumor between January 2016 and December 2018. Patients who received immediate or concomitant systemic adjuvant therapy, or who had a history of prior thoracic irradiation in the same area were excluded. If the treated tumor was a metastasis, patients had to be in an oligometastatic situation (defined in the present study as less than five lesions), progressing only in their lung lesion(s), and extra-thoracic disease had to be controlled. Patients who had pulmonary tumors involving the trachea, stem bronchi or large vessels were excluded. Decision of lung SBRT was validated in a multidisciplinary consultation meeting.

Primary and secondary endpoints

The primary clinical endpoint was OS, calculated from the day of the Radiation Therapy (RT) end to death, or to last follow up visit. Secondary endpoints were local relapse (i.e. recurrence in the Planning Target Volume (PTV) after a prior response to treatment), local progression (i.e. progression in the PTV without response to treatment), nodal recurrence (i.e. hilar or mediastinal lymph node metastasis), contralateral or homolateral lung recurrence or distant metastasis (i.e. outside the lung), based on complementary examinations (imaging and/or anatomopathology) and/or medical records.

Data extraction

The initial dataset totalled 180 features:124 radiomics, 45 clinical and 11 dosimetric features (See Supplementary Tables S1 and S2 online). Clinical features were collected directly from the patient's medical records. Treatment planning and delivery, DICOM and RT-STRUCT of planning CT scans were extracted from the ARIA® and MOSAIQ® systems.

DICOM and RT-STRUCT were imported in LIFEX® software (16) in order to extract radiomics. A double extraction was performed from double manual segmentations for each tumor at a lung window level. To limit the variability, dual segmentation was performed by the same physician. The Intraclass-Correlation Coefficient (ICC) was calculated for radiomics features to retain the most robust features from the two segmentations. Features were removed when ICC was lower than 80%, which is a threshold used in previous studies (17,18,19). For patients with multiple lesions, clinical data were the same between the different lesions, radiomic and dosimetric data were calculated by averaging between the different lesions.

The dataset was divided into two cohorts: patients with primary lung tumors (n = 105) and those with metastatic lung lesions (n = 58). In the latter, we included patients with at least one metastatic lesion (also if a patient had both a primary and a metastatic lesion, it was included in the metastatic cohort). Among patients with primary

tumors, 26.7% (n = 28) deaths were recorded, whereas 48.3% (n = 28) deaths occurred in the metastatic group. Distribution of survival times, defined as the interval between the start of treatment and death, were detailed in Supplementary Fig. S3 online.

Ethical considerations

Informed consent

was obtained from all subjects. Data handling was carried out in strict accordance with French and European regulations on data protection, including the General Data Protection Regulation (GDPR 2016/679), in effect since May 25, 2018, and the French Data Protection Act of January 6, 1978, as amended in 2018. The study adhered to the French regulatory framework MR-004. All experimental protocols were approved by the ethics board of the COLib. All patient data were anonymized before any statistical analysis was performed.

Model training and evaluation

Two independent models were trained to predict OS for either the primary or the metastatic cohorts.

Both models trainings and evaluations were performed within a nested cross-validation framework to ensure robust performance estimation.

The training was performed within a nested cross-validation framework: a 5-fold StratifiedKFold outer loop was used to provide an independent test set for unbiased performance estimation, while an inner 3-fold StratifiedKFold loop, executing 50 search iterations, was used within each training partition for hyperparameter optimization.

Hyperparameter tuning was performed via Bayesian optimization using the BayesSearchCV strategy, allowing efficient exploration of the hyperparameter space while minimizing computational overhead. During hyperparameter optimization, model performance was evaluated using the Area Under the Receiver Operating Characteristic Curve (ROC-AUC). Supplementary Table S4 online gives more information on the hyperparameter optimized.

Both models consisted of XGBoost classifiers with a binary:logistic objective function. The LogLoss metric was selected as the optimization objective to ensure well-calibrated probabilistic outputs (20).

For each outer fold, the following metrics were computed to assess predictive and probabilistic performance: ROC-AUC, Brier score, Precision, Recall, and F1-score, Accuracy and Area under the Precision–Recall curve (AUC-PR). Furthermore, to evaluate the reliability of predicted probabilities, calibration curves were generated for each outer fold using ten probability bins (Fig. 1). The mean calibration curve was obtained through interpolation and averaging across folds, providing an overall assessment of the model's probabilistic calibration and its alignment with observed outcome frequencies.

Feature selection

Features were selected using SHapley Additive exPlanations (SHAP) values of the best performing model across outer folds (21). The 20 most influential features identified by SHAP analysis were retained to construct a simplified predictive model, aimed at reducing dimensionality and improving model interpretability. Subsequently, a

second identical nested cross-validation experiment was conducted using exclusively the 20 top-ranked features to estimate model performance on the dataset.

RESULTS

Data and primary and secondary endpoints

From January 2016 to December 2018, 163 patients were treated with lung SBRT for a total of 181 lung tumors. A total of 63 (n=114) of tumors were primary tumors and 37 (n=67) were secondary ones. Table 1a and 1b detail the clinical and average dosimetric characteristics of the two cohorts. Clinical tumor stages of patients with primary tumors were cT1 (n=89; 84.8%) and cT2 (n=16; 13.2%) and their clinical nodal stages were exclusively cN0 (n=105; 100.0%). Three patients were oligometastatic (n=3; 2.9%). Primary and secondary endpoints are detailed in Table 2.

Features used

A total of 5 features were removed from the radiomics feature before training using the ICC.

Table 3 describes the features used by each OS prediction model. Both models leverage all three types of features. In total, the primary tumor model incorporates 2 clinical, 4 dosimetric, and 16 radiomic features, while the secondary tumor model relies on 5 clinical, 5 dosimetric, and 10 radiomic features.

Figure 2 and Figure 3 illustrate the SHAP values for each model trained on the full dataset, highlighting the most influential features contributing to the prediction of OS. The distance from the centerline reflects the magnitude of each feature's impact on the model's decision. Positive SHAP values indicate a contribution toward predicting death, whereas negative values correspond to a contribution toward OS. While for the primary tumor OS model, mean_PTV (i.e mean dose of PTV volume), score_charlson (i.e Charlson's comorbidity score) and GLSZM_SmallZoneHighGreyLevelEmphasis were the top 3 features, for the secondary tumor model, INTENSITY-BASED_IntensitySkewness, tabac (i.e history of smoking) and GLRLM_RunLengthNonUniformity ranked top 3.

Performance of models

The models demonstrated strong discriminative ability, with mean ROC-AUC values of 0.89 ± 0.05 for the primary tumor cohort and 0.87 ± 0.10 for the secondary tumor cohort, indicating high predictive accuracy across cross-validation folds. Calibration quality, assessed by the Brier score, was satisfactory for both models (0.14 ± 0.07 and 0.19 ± 0.12 , respectively), suggesting well-calibrated probability outputs. The primary tumor OS model achieved an F1-score of 0.52 ± 0.06 , while the secondary tumor OS model reached an F1-score of 0.78 ± 0.15 . More details on the predictive performance of both OS models can be found in Supplementary Table S5 online.

Figure 1 presents the average calibration curves obtained from the outer folds of the nested cross-validation for the primary (Figure 1a) and secondary tumor cohorts (Figure 1b). Each mean calibration curve compares to the perfect calibration (dashed orange line). Deviations from the diagonal indicate over- or underestimation of death probabilities.

DISCUSSION

This study introduces two independent models for prediction of OS after SBRT in patients with primary and secondary lung tumors, using a combination of clinical, dosimetric, and radiomic features extracted from planning CT scans. Models were trained within a nested cross-validation framework across six medical centers to ensure generalizability. The 20 top features were selected based on SHAP values. The resulting models achieved strong discriminative performance, demonstrating the potential of integrating clinical, dosimetric and radiomics data for individualized prognosis estimation in lung SBRT.

Compared to prospective studies, our study leveraged a retrospective data collection. This approach inherently biases the data collected. On the bright side, our study included a cohort of 163 patients, compared to a median of 87 patients in similar studies as reported by Cheung et al. (22). Contrary to most studies on the predictive role of radiomics, lung tumors in the present study had numerous different histologies, partly due to their primary or secondary nature (22). Moreover, 73% of patients received SBRT without histological evidence, partly due to the number of secondary tumors (37%) in the study. Finally, we observed that across sites the data collected was heterogeneous, particularly with regard to dosimetric data such as total doses and BED₁₀ where large ranges were measured (total dose: [30.0–60.0] for primary tumors and [33.0–60.0] for secondary tumors; BED₁₀: [45.0–180.0] for primary tumors and [51.15–180.0] for secondary tumors). Moreover, some features extracted from CT planning images were not reported and therefore uncontrolled, in particular the thickness of the slices or the use of the contrast enhancement. However, the heterogeneity induced by the multicentre aspect of the study, closer to real-life treatments, allowed us to increase the robustness of the models trained.

Several methodological choices explain the robustness of the obtained results. First, by dually segmenting the tumors, we were able to remove uncertain radiomic features ($n = 5$) which would have hindered model performance. Second, in preliminary experiments we compared different feature aggregation strategies, demonstrating that averaging dosimetric features across lesions per patient improved stability and predictive performance, compared to summing. Third, evaluation was conducted using a nested cross-validation framework across six independent medical centers. This strategy provided an unbiased estimate of generalization performance while accounting for inter-site variability in data acquisitions. Preliminary experiments using a site as an external test set, revealed highly variable results depending on model initialization, highlighting the instability and limited generalization potential of such site-based external validation. The nested framework therefore offered a more robust and reliable assessment of model performance across heterogeneous data sources.

Bayesian optimization was employed for hyperparameter tuning, offering efficient exploration of the search space and improved convergence compared to other common strategies such as grid search. XGBoost classifiers were selected due to their state-of-the-art performance on tabular data and their ability to deal with missing values in the dataset which are common in medical datasets.

Interestingly, attempts to train a unified model for both primary and secondary tumor cases, even while providing the model with the tumor origin (primitive or metastatic) as an explicit input feature, did not yield satisfactory results. Despite including this categorical variable, the model failed to achieve comparable discriminative performance to the cohort-specific models. This observation suggests that the underlying prognostic determinants governing OS differ between primary and metastatic disease. Consequently, separate modeling for primary and secondary tumors appears to be a more appropriate strategy for capturing the heterogeneity of survival dynamics in lung SBRT patients.

To confirm these prospective results, future studies should be conducted, ensuring more complete and homogeneous clinical and dosimetric data, thereby enhancing the models performances.

Both predictive models, developed respectively for primary and secondary lung tumors, successfully integrated clinical, dosimetric, and radiomic features to estimate OS in patients treated with SBRT. This multimodal integration enabled accurate predictions using only pre-treatment data, achieving strong discriminative performance and satisfactory calibration. Compared to previous studies that relied on radiomics and clinical and/or dosimetric features (23–26), radiomics features only (13,27–33) or combinations of radiomics and conventional imaging features (14,34), the present work demonstrates that combining heterogeneous features within a multicentric framework yields robust and interpretable prognostic models.

Calibration of the primary tumor model (Fig. 1a) exhibits underconfidence in the lower probability range (0.2–0.4) and overconfidence for higher predicted probabilities (0.5–0.9), indicating a tendency to underestimate survival in lower-risk cases and overestimate it in higher-risk ones. In contrast, the secondary tumor model (Fig. 1b) appears slightly overconfident overall, suggesting that predicted death probabilities are generally higher than the observed frequencies. Despite these deviations, both models demonstrate globally consistent calibration, with minor discrepancies likely attributable to inter-site variability and the limited number of cases per center across the six participating sites.

It is worth noting that both models consider a combination of the three categories of features : clinical, dosimetric, and radiomic. This is consistent with the results of our preliminary analyses comparing the performances of a model based solely on clinical features, a model based solely on dosimetric features and a model based solely on radiomics features. The performances of the three separate models were inferior to that of a combined model. Furthermore, the features used by each model differed: a similar proportion of dosimetric features, a larger proportion of clinical features in the secondary lung tumor model and a smaller proportion of radiomic features in the secondary tumor model. Interestingly, the features between the two models are different except for the data on doses received at the PTV (max_PTV, mean_PTV, min_PTV) and the volumetric clinical tumor data (vol_ITV for the primary tumors model ; vol_PTV and vol_GTV for the secondary tumors model). A previous study from Dupic et al. (35) confirmed our conclusions, as PTV volume was also predictive of OS in their multivariate analysis (HR = 1.01, $p = 0.004$). Even more, in their study, Li et al. found that their volumetric feature (short axis x longest diameter) was a predictor for OS (HR1.98, 95% CI 1.44–2.72, $p < 0.001$) (25). Even though the dose received at the PTV had a significant impact on the model, the BED₁₀ did not appear significant, unlike in the study of Avanzo et al. (36) which found that BED₁₀ was a predictive feature of partial or complete response after SBRT.

Both models were also influenced by intensity-based radiomic features. Several studies have similarly reported radiomics signatures predictive of OS on pre-treatment CT scans in patients treated with lung SBRT for NSCLC (14,24,25,29,32). In terms of texture descriptors, the primary tumor model was predominantly driven by NGTDM (Neighbouring Gray Tone Difference Matrix) features, which quantify gray-level differences between a voxel and its neighborhood, whereas the secondary tumor model was mainly influenced by GLRLM (Gray Level Run Length Matrix) features, reflecting the length of consecutive pixels with identical gray levels. For our secondary tumor model, increased heterogeneity (GLRLM_GreyLevelNonUniformity and GLRLM_RunLengthNonUniformity) was associated with worse OS and increased homogeneity favored OS (Fig. 2). Similarly, Aerts et al. identified a prognostic radiomic signature related to intratumoral heterogeneity, associated with poorer OS, whereas more compact or spherical tumors were linked to improved OS (37). Likewise, Yu et al. showed that kurtosis and GLCM (Grey Level Co-occurrence Matrix) homogeneities were significant predictors of OS (29). Huynh et al. also reported

texture heterogeneity as a prognostic factor. In Huynh et al. (14), the predictive factors of OS were tumor diameter, volume, and image intensity. Similarly, in our study tumor diameter (MORPHOLOGICAL_Maximum3DDiameter for both models) and volume (vol_PTV and vol_GTV for the secondary tumors model ; vol_ITV and MORPHOLOGICAL_Volume for the primary tumors model) were retained in both models. As for intensity, the mean intensity (INTENSITY-BASED_MeanIntensity and INTENSITY-BASED_25thIntensityPercentile) was among the most influential features in the secondary tumor model.

SBRT is known to provide high local control (38), and the local recurrence rates observed in this study (10.5% for primary tumors, 17.5% for secondary tumors, and 14.7% overall) are consistent with the literature (39–41). Given these rates, we were expecting to find highly predictive features of local relapse. Surprisingly, our preliminary experiments found that models trained under the same parameters were less predictive of local relapse than they were of OS. Although several studies (23,27,29,30) have reported radiomic predictors of local recurrence, including kurtosis, GLCM homogeneity, and long-run high gray-level emphasis, our findings are consistent with others that either did not assess local control (15, 24,25,34) or reported non-significant results (32). Moreover, several studies have demonstrated improved predictive performance of recurrence using radiomics features extracted from FDG-PET/CT (fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT) rather than CT alone (10,42,43). In particular, Nemoto et al. reported superior performance for recurrence prediction using FDG-PET/CT–derived radiomics, suggesting that PET-based features may be more appropriate for future models aimed at predicting local relapse (43).

Abbreviations

SBRT

Stereotactic Body Radiation Therapy

NSCLC

Non-Small Cell Lung Cancer

OS

Overall Survival

PFS

Progression Free Survival

LRFS

Locoregional Recurrence Free Survival

DDFS

Distant Disease Free Survival

GTV

Gross Tumor Volume

BED10

Biologically Effective dose with an α/β ratio of 10

CT

Computed Tomography

DM

Distant Metastasis

RT

Radiation Therapy

PTV
Planning Target Volume
ICC
Intraclass-Correlation Coefficient
ROC-AUC
Receiver Operating Characteristic - Area Under the Curve
AUC-PR
Area under the Precision–Recall curve
SHAP
SHapley Additive exPlanations
NGTDM
Neighbouring Gray Tone Difference Matrix
GLRLM
Gray Level Run Length Matrix
GLCM
Grey Level Co-occurrence Matrix
FDG-TEP/CT
18-fluoro-2-deoxyglucose (FDG)-positron emission (PET)/Computed Tomography (CT).

Declarations

ACKNOWLEDGMENTS

Not applicable.

AUTHOR CONTRIBUTIONS

CI collected the data. PLB performed statistical analysis and trained the models. CI and PLB wrote the manuscript. JEB contributed to study design and to mentoring on the development of the models. YP and TL provided clinical expertise and mentoring on the research project. REA collected part of the data. NB, BS, CD and JC participated in the overall design of the study and planned the data collection. All authors reviewed the manuscript.

DATA AVAILABILITY STATEMENT

Research data on the predictive model are available at <https://github.com/plbenveniste/lung-treatment-response/releases/tag/r20251222>. Clinical and dosimetry research data are stored in an institutional repository and will be shared upon request to the corresponding author.

FUNDING SOURCE

The authors received no financial support for the research, authorship, or publication of this article.

ADDITIONAL INFORMATION

Competing interest statement

Camille Invernizzi, Pierre-Louis Benveniste, Radouane El Ayachy, Yoann Pointreau, Nicolas Blanchard, Benjamin Schipman, Christophe Debelleix, Jérôme Chamois : the author(s) declare no competing interests.

Thomas Leroy : Merck, Aquilab, Janssen, President of AFCOR and member of the board of SFRO and Colib.

Jean-Emmanuel Bibault : Bayer, Abbvie, Janssen, Jaide, Alphabet, Meta, Apple, Nvidia, Amazon, Microsoft, Tesla.

References

1. Videtic, G. M. M. *et al.* Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline. *Pract. Radiat. Oncol.* **7**, 295–301 (2017).
2. Gomez, D. R. *et al.* Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study. *Lancet Oncol.* **17**, 1672–1682 (2016).
3. Gomez, D. R. *et al.* Local Consolidative Therapy Vs. Maintenance Therapy or Observation for Patients With Oligometastatic Non-Small-Cell Lung Cancer: Long-Term Results of a Multi-Institutional, Phase II, Randomized Study. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* **37**, 1558–1565 (2019).
4. Iyengar, P. *et al.* Consolidative Radiotherapy for Limited Metastatic Non-Small-Cell Lung Cancer: A Phase 2 Randomized Clinical Trial. *JAMA Oncol.* **4**, e173501 (2018).
5. Palma, D. A. *et al.* Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet Lond. Engl.* **393**, 2051–2058 (2019).
6. Phillips, R. *et al.* Outcomes of Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer: The ORIOLE Phase 2 Randomized Clinical Trial. *JAMA Oncol.* **6**, 650–659 (2020).
7. Ost, P. *et al.* Surveillance or Metastasis-Directed Therapy for Oligometastatic Prostate Cancer Recurrence: A Prospective, Randomized, Multicenter Phase II Trial. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* **36**, 446–453 (2018).
8. Luo, L.-M., Wang, Y., Lin, P.-X., Su, C.-H. & Huang, B.-T. The Clinical Outcomes, Prognostic Factors and Nomogram Models for Primary Lung Cancer Patients Treated With Stereotactic Body Radiation Therapy. *Front. Oncol.* **12**, 863502 (2022).
9. Lucia, F. *et al.* Predictive clinical and dosimetric parameters for risk of relapse in early-stage non-small cell lung cancer treated by SBRT: A large single institution experience. *Clin. Transl. Radiat. Oncol.* **45**, 100720 (2024).
10. Lambin, P. *et al.* Radiomics: extracting more information from medical images using advanced feature analysis. *Eur. J. Cancer Oxf. Engl.* **1990** **48**, 441–446 (2012).
11. Rowe, M. An Introduction to Machine Learning for Clinicians. *Acad. Med. J. Assoc. Am. Med. Coll.* **94**, 1433–1436 (2019).
12. El Ayachy, R. *et al.* The Role of Radiomics in Lung Cancer: From Screening to Treatment and Follow-Up. *Front. Oncol.* **11**, (2021).
13. Fodor, A. *et al.* CT radiomic predictors of local relapse after SBRT for lung oligometastases from colorectal cancer: a single institute pilot study. *Strahlenther. Onkol. Organ Dtsch. Rontgengesellschaft AI* **199**, 477–484 (2023).

14. Huynh, E. *et al.* CT-based radiomic analysis of stereotactic body radiation therapy patients with lung cancer. *Radiother. Oncol. J. Eur. Soc. Ther. Radiol. Oncol.* **120**, 258–266 (2016).
15. Sawayanagi, S. *et al.* Establishment of a Prediction Model for Overall Survival after Stereotactic Body Radiation Therapy for Primary Non-Small Cell Lung Cancer Using Radiomics Analysis. *Cancers* **14**, 3859 (2022).
16. Nioche, C. *et al.* LIFEx: A Freeware for Radiomic Feature Calculation in Multimodality Imaging to Accelerate Advances in the Characterization of Tumor Heterogeneity. *Cancer Res.* **78**, 4786–4789 (2018).
17. Grove, O. *et al.* Quantitative computed tomographic descriptors associate tumor shape complexity and intratumor heterogeneity with prognosis in lung adenocarcinoma. *PloS One* **10**, e0118261 (2015).
18. Koo, T. K. & Li, M. Y. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J. Chiropr. Med.* **15**, 155–163 (2016).
19. Parmar, C. *et al.* Robust Radiomics feature quantification using semiautomatic volumetric segmentation. *PloS One* **9**, e102107 (2014).
20. Chen, T. & Guestrin, C. XGBoost: A Scalable Tree Boosting System. in *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining* 785–794 (Association for Computing Machinery, New York, NY, USA, 2016). doi:10.1145/2939672.2939785.
21. Lundberg, S. M. & Lee, S.-I. A unified approach to interpreting model predictions. in *Proceedings of the 31st International Conference on Neural Information Processing Systems* 4768–4777 (Curran Associates Inc., Red Hook, NY, USA, 2017).
22. Cheung, B. M. F. Radiomics in stereotactic body radiotherapy for non-small cell lung cancer: a systematic review and radiomic quality score study. *Radiat. Oncol. J.* **42**, 4–16 (2024).
23. Li, Q. *et al.* Imaging features from pretreatment CT scans are associated with clinical outcomes in nonsmall-cell lung cancer patients treated with stereotactic body radiotherapy. *Med. Phys.* **44**, 4341–4349 (2017).
24. Li, Q. *et al.* CT imaging features associated with recurrence in non-small cell lung cancer patients after stereotactic body radiotherapy. *Radiat. Oncol. Lond. Engl.* **12**, 158 (2017).
25. Kakino, R. *et al.* Application and limitation of radiomics approach to prognostic prediction for lung stereotactic body radiotherapy using breath-hold CT images with random survival forest: A multi-institutional study. *Med. Phys.* **47**, 4634–4643 (2020).
26. Huang, B.-T., Wang, Y. & Lin, P.-X. Developing a clinical-radiomic prediction model for 3-year cancer-specific survival in lung cancer patients treated with stereotactic body radiation therapy. *J. Cancer Res. Clin. Oncol.* **150**, 34 (2024).
27. Mattonen, S. A., Ward, A. D. & Palma, D. A. Pulmonary imaging after stereotactic radiotherapy—does RECIST still apply? *Br. J. Radiol.* **89**, 20160113.
28. Mattonen, S. A., Palma, D. A., Haasbeek, C. J. A., Senan, S. & Ward, A. D. Early prediction of tumor recurrence based on CT texture changes after stereotactic ablative radiotherapy (SABR) for lung cancer. *Med. Phys.* **41**, 033502 (2014).
29. Yu, W. *et al.* Development and Validation of a Predictive Radiomics Model for Clinical Outcomes in Stage I Non-small Cell Lung Cancer. *Int. J. Radiat. Oncol. Biol. Phys.* **102**, 1090–1097 (2018).
30. Lafata, K. J. *et al.* Association of pre-treatment radiomic features with lung cancer recurrence following stereotactic body radiation therapy. *Phys. Med. Biol.* **64**, 025007 (2019).

31. Franceschini, D. *et al.* A radiomic approach to predicting nodal relapse and disease-specific survival in patients treated with stereotactic body radiation therapy for early-stage non-small cell lung cancer. *Strahlenther. Onkol. Organ Dtsch. Rontgengesellschaft A* **196**, 922–931 (2020).
32. Starkov, P. *et al.* The use of texture-based radiomics CT analysis to predict outcomes in early-stage non-small cell lung cancer treated with stereotactic ablative radiotherapy. *Br. J. Radiol.* **92**, 20180228 (2019).
33. Somasundaram, E. *et al.* Clinical Nomogram Using Novel Computed Tomography-Based Radiomics Predicts Survival in Patients With Non-Small-Cell Lung Cancer Treated With Stereotactic Body Radiation Therapy. *JCO Clin. Cancer Inform.* **7**, e2200173 (2023).
34. Huynh, E. *et al.* Associations of Radiomic Data Extracted from Static and Respiratory-Gated CT Scans with Disease Recurrence in Lung Cancer Patients Treated with SBRT. *PloS One* **12**, e0169172 (2017).
35. Dupic, G. *et al.* Significant Correlation Between Overall Survival and Mean Lung Dose in Lung Stereotactic Body Radiation Therapy (SBRT). *Front. Oncol.* **10**, 1577 (2020).
36. Avanzo, M. *et al.* Combining computed tomography and biologically effective dose in radiomics and deep learning improves prediction of tumor response to robotic lung stereotactic body radiation therapy. *Med. Phys.* **48**, 6257–6269 (2021).
37. Aerts, H. J. W. L. *et al.* Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. *Nat. Commun.* **5**, 4006 (2014).
38. Timmerman, R. *et al.* Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* **24**, 4833–4839 (2006).
39. Baumann, P. *et al.* Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic body radiotherapy. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* **27**, 3290–3296 (2009).
40. Onishi, H. *et al.* Stereotactic hypofractionated high-dose irradiation for stage I nonsmall cell lung carcinoma: clinical outcomes in 245 subjects in a Japanese multiinstitutional study. *Cancer* **101**, 1623–1631 (2004).
41. Fakiris, A. J. *et al.* Stereotactic body radiation therapy for early-stage non-small-cell lung carcinoma: four-year results of a prospective phase II study. *Int. J. Radiat. Oncol. Biol. Phys.* **75**, 677–682 (2009).
42. Li, H., Galperin-Aizenberg, M., Pryma, D., Simone, C. B. & Fan, Y. Unsupervised machine learning of radiomic features for predicting treatment response and overall survival of early stage non-small cell lung cancer patients treated with stereotactic body radiation therapy. *Radiother. Oncol. J. Eur. Soc. Ther. Radiol. Oncol.* **129**, 218–226 (2018).
43. Nemoto, H. *et al.* Evaluation of the performance of both machine learning models using PET and CT radiomics for predicting recurrence following lung stereotactic body radiation therapy: A single-institutional study. *J. Appl. Clin. Med. Phys.* **25**, e14322 (2024).

Tables

Table 1a. Clinical and dosimetric data of patients and tumors in the two cohorts.

Data are numbers (%). SD = Standard Deviation. CKD = Chronic Kidney Disease. CVA = Cerebrovascular Accident. TIA = Transient Ischemic Attack. SAS = Sleep Apnea Syndrome. BMI = Body Mass Index.*7 patients were treated for both a secondary tumor and another localized tumor.

Patients	Primary tumors (N=105)	Secondary tumors (N=58)
Age, median [range], years	72.0 [46.0-90.0]	70.0 [48.0-93.0]
Sexe		
Men	65 (61.9)	35 (60.3)
Women	40 (38.1)	23 (39.7)
Performans Status	<i>1 (1.0)</i>	<i>7 (12.1)</i>
<i>N/A</i>	20 (19.0)	18 (31.0)
0	74 (70.5)	32 (55.2)
1	10 (9.5)	1 (1.7)
2	0 (0.0)	0 (0.0)
3	0 (0.0)	0 (0.0)
4		
Smoking status	<i>3 (2.9)</i>	<i>10 (17.2)</i>
<i>N/A</i>	10 (9.5)	17 (29.3)
Never smokers	92 (87.6)	31 (53.4)
Former or active smokers	<i>17 (16.2)</i>	<i>2 (6.5)</i>
<i>N/A</i>	63 (60.0)	17 (54.8)
Ceased smokers	25 (23.8)	12 (38.7)
Current smokers	6.1±1.8	9.2±2.0
Charlson Comorbidity Index, means±SD	0 (0.0)	0 (0.0)
Leukemia	0 (0.0)	0 (0.0)
Lymphoma	21 (20.0)	8 (13.8)
Myocardial Infarction	100 (95.2)	7 (12.1)*
Localised solid tumor	5 (4.8)	58 (100.0)
Metastatic solid tumor	4 (3.8)	1 (1.7)
Moderate-Severe CKD	13 (12.4)	13 (22.4)
Uncomplicated Diabetes	0 (0.0)	0 (0.0)
End-organ damage Diabetes	1 (1.0)	1 (1.7)

Mild liver disease	2 (1.9)	0 (0.0)
Moderate-severe liver disease	2 (1.9)	0 (0.0)
Peptic ulcer disease	12 (11.4)	8 (13.8)
Peripheral vascular disease	4 (3.8)	2 (3.4)
Connective tissue disease	58 (55.2)	17 (29.3)
Chronic pulmonary disease	3 (2.9)	1 (1.7)
Congestive heart failure	1 (1.0)	0 (0.0)
Dementia	2 (1.9)	2 (3.4)
CVA or TIA	0 (0.0)	0 (0.0)
Aids	0 (0.0)	0 (0.0)
Hemiplegia		
	52 (49.5)	26 (44.8)
Hypertension	<i>17 (16.2)</i>	<i>2 (3.4)</i>
<i>N/A</i>		
	14 (13.3)	3 (5.2)
Sleep Apnea Syndrome		
	23.5 [15.6-41.9]	24.5 [16.4-40.6]
BMI, median [range], kg/m²	<i>82 (78.0)</i>	<i>26 (44.8)</i>
<i>N/A</i>		
	71.5 [42-114]	70.0 [37.0-119.0]
Weight, median [range], kg	<i>75 (71.4)</i>	<i>19 (32.8)</i>
<i>N/A</i>		

Table 1b. Clinical and dosimetric data of patients and tumors in the two cohorts.

Data are numbers (%). SD = Standard Deviation. mMR= modified Medical Research Council.

¹ According to Timmerman (38). ² Other includes clear cell renal cell carcinoma (n=3), invasive ductal carcinoma (n=2), large cell neuroendocrine carcinoma of the lung (n=1).

Patients	Primary tumors (N=105)	Secondary tumors (N=58)
Height , median [range], m	1.7 [1.6-1.8]	1.7 [1.5-1.8]
<i>N/A</i>	<i>82 (78.0)</i>	<i>25 (43.1)</i>
Dyspnea Scale according to mMRC	<i>18 (17.1)</i>	<i>14 (24.1)</i>
<i>N/A</i>	38 (36.2)	32 (55.2)
0	14 (13.3)	6 (10.3)
1	16 (15.2)	2 (3.4)
2	12 (11.4)	3 (5.2)
3	7 (6.7)	1 (1.7)
4		
	114	67
Number of lung tumors per patient	99 (86.8)	47 (70.1)
1	6 (5.3)	10 (14.9)
2	1 (0.9)	0 (0.0)
3		
Tumor location	76 (72.4)	11 (19.0)
Central ¹	29 (27.6)	47 (81.0)
Peripheral		
Tumor histology	19 (18.1)	7 (12.1)
Adenocarcinoma	11 (10.5)	1 (1.7)
Squamous cell	75 (71.4)	44 (75.9)
Unknown	-	6 (10.3)
Other ²		
		9.8±5.6
RADIATION THERAPY		54.0 [33.0-60.0]
Overall duration of radiotherapy , means±SD, days	12.0±6.8	11.0 [5.5-20.0]
Total dose , median [range], Gy	60.0 [30.0-60.0]	
Fractionation schedule , median [range], Gy by fraction	12.0 [5.0-20.0]	

Volumes , median [range],cc		16.6 [3.9-81.0]
PTV	18.6 [1.8-97.2]	16
N/A	4	5.8 [0.6-44.7]
ITV	10.7 [2.2-47.3]	3.1 [0.1-24.6]
GTV	4.3 [0.2-51.2]	4
N/A	4	
PTV doses , means±SD, Gy		47.8±10.4
Dmin PTV	52.8±9.4	10
N/A	4	58.6±9.5
Dmean PTV	64.6±6.2	24
N/A	10	64.9±10.2
Dmax PTV	71.9±6.6	10
N/A	4	
		115.5 [51.2-180.0]
BED (for $\alpha/\beta=10$) , median [range], Gy		132.0 [45.0-180.0]
PTV Coverage , means±SD, %		96.3±4.3
	96.1±5.2	

Table 2. Primary and secondary endpoints in the two cohorts

Patients	Primary tumors (N=105)	Secondary tumors (N=58)
Follow up time , median [range], years	2.0 [0.1-5.3]	3.3 [0.2-5.5]
Deaths	28 (20.2)	28 (48.3)
<i>N/A</i>	<i>1</i> (1.0)	
Local relapse	12 (10.5)	12 (17.9)
Local progression	2 (1.8)	1 (1.5)
Nodal relapse	13 (11.4)	7 (10.4)
Homolateral lung relapse	16 (14.0)	10 (14.9)
Contralateral lung relapse	14 (12.3)	11 (16.4)
Distant metastasis	20 (17.5)	16 (23.9)

Table 3. Features used by both models

	PRIMARY TUMORS	SECONDARY TUMORS
Clinical features	score_charlson	tabac
	BMI	age
		tabac_PA
		poids
		ATCD_loc_1
Dosimetric features	max_PTV	max_PTV
	mean_PTV	mean_PTV
	min_PTV	etalement
	vol_ITV	vol_PTV
		vol_GTV
Radiomic features	INTENSITY-HISTOGRAM_MinimumHistogramGradientGreyLevel	GLRLM_GreyLevelNonUniformity
	NGTDM_Complexity	INTENSITY-BASED_MeanIntensity
	LOCAL_INTENSITY_BASED_GlobalIntensityPeak	INTENSITY-BASED_IntensitySkewness
	MORPHOLOGICAL_Maximum3DDiameter	INTENSITY-BASED_IntensityRange
	INTENSITY-BASED_AreaUnderCurveCIVH	MORPHOLOGICAL_Maximum3DDiameter
	GLSZM_SmallZoneHighGreyLevelEmphasis	INTENSITY-BASED_25thIntensityPercentile
	MORPHOLOGICAL_Volume	GLCM_JointMaximum
	INTENSITY-HISTOGRAM_RootMeanSquare	INTENSITY-BASED_IntensityBasedEnergy
	INTENSITY-HISTOGRAM_IntensityHistogramEntropyLog10	GLRLM_RunLengthNonUniformity
	NGTDM_Coarseness	GLRLM_ShortRunsEmphasis
	INTENSITY-HISTOGRAM_MaximumHistogramGradient	
	INTENSITY-BASED_TotalLesionGlycolysis	
	GLCM_JointEntropyLog2	
	INTENSITY-BASED_IntensityRange	

Figures

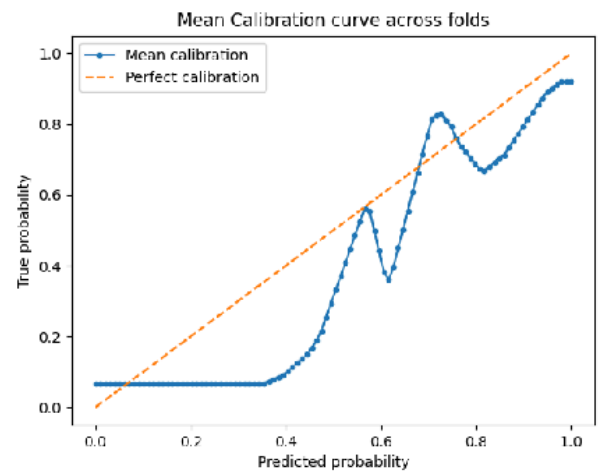
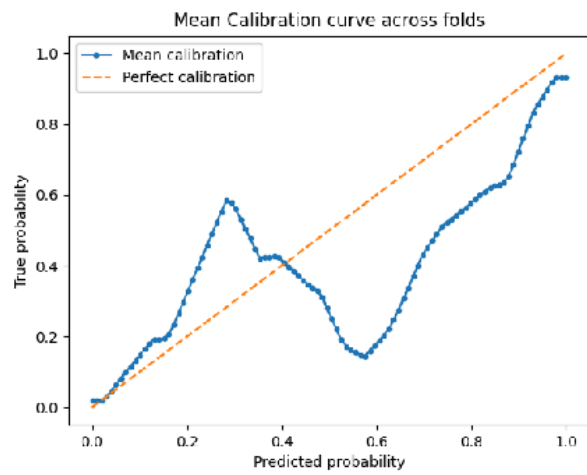


Figure 1a. (left) and 1b. (right)

Figure 1

Average calibration curve across outer folds of the nested cross-validation for the primary (Figure 1a) and secondary (Figure 1b) tumor OS model. The curve compares the mean predicted probabilities of death with observed event frequencies, where the dashed diagonal represents perfect calibration. Deviations from the diagonal indicate over- or underestimation of risk by the model.

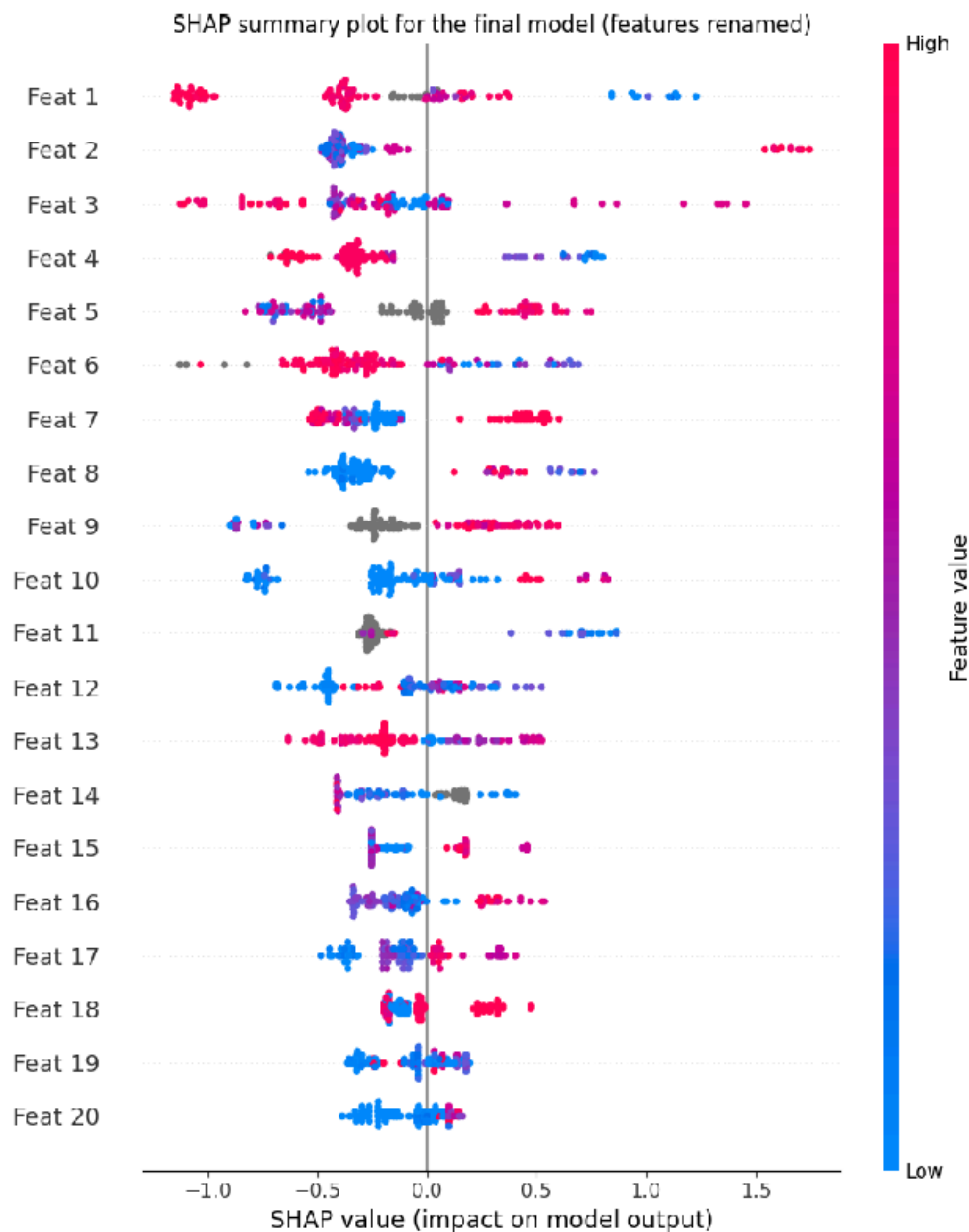


Figure 2.

Figure 2

SHAP values for the OS predictive model in patients with primary lung tumors, showing the 20 most influential features. Feature ranking reflects their impact on model predictions. Positive SHAP values indicate a contribution toward predicting death, while negative values indicate a contribution toward survival. Point colors represent feature values, with lower values shown in blue and higher values in pink. Feat 1 = mean_PTV; Feat 2 = Charlson comorbidity score; Feat 3 = GLSZM_SmallZoneHighGreyLevelEmphasis; Feat 4 = max_PTV; Feat 5 = GLCM_JointEntropyLog2; Feat 6 = min_PTV; Feat 7 = INTENSITY-

HISTOGRAM_MinimumHistogramGradientGreyLevel; Feat 8 = vol_ITV; Feat 9 = LOCAL_INTENSITY_BASED_GlobalIntensityPeak; Feat 10 = INTENSITY-BASED_AreaUnderCurveCIVH; Feat 11 = BMI; Feat 12 = MORPHOLOGICAL_Volume; Feat 13 = INTENSITY-BASED_TotalLesionGlycolysis; Feat 14 = NGTDM_Coarseness; Feat 15 = NGTDM_Complexity; Feat 16 = INTENSITY-BASED_IntensityRange; Feat 17 = MORPHOLOGICAL_Maximum3DDiameter; Feat 18 = INTENSITY-HISTOGRAM_IntensityHistogramEntropyLog10; Feat 19 = INTENSITY-HISTOGRAM_RootMeanSquare; and Feat 20 = INTENSITY-HISTOGRAM_MaximumHistogramGradient.

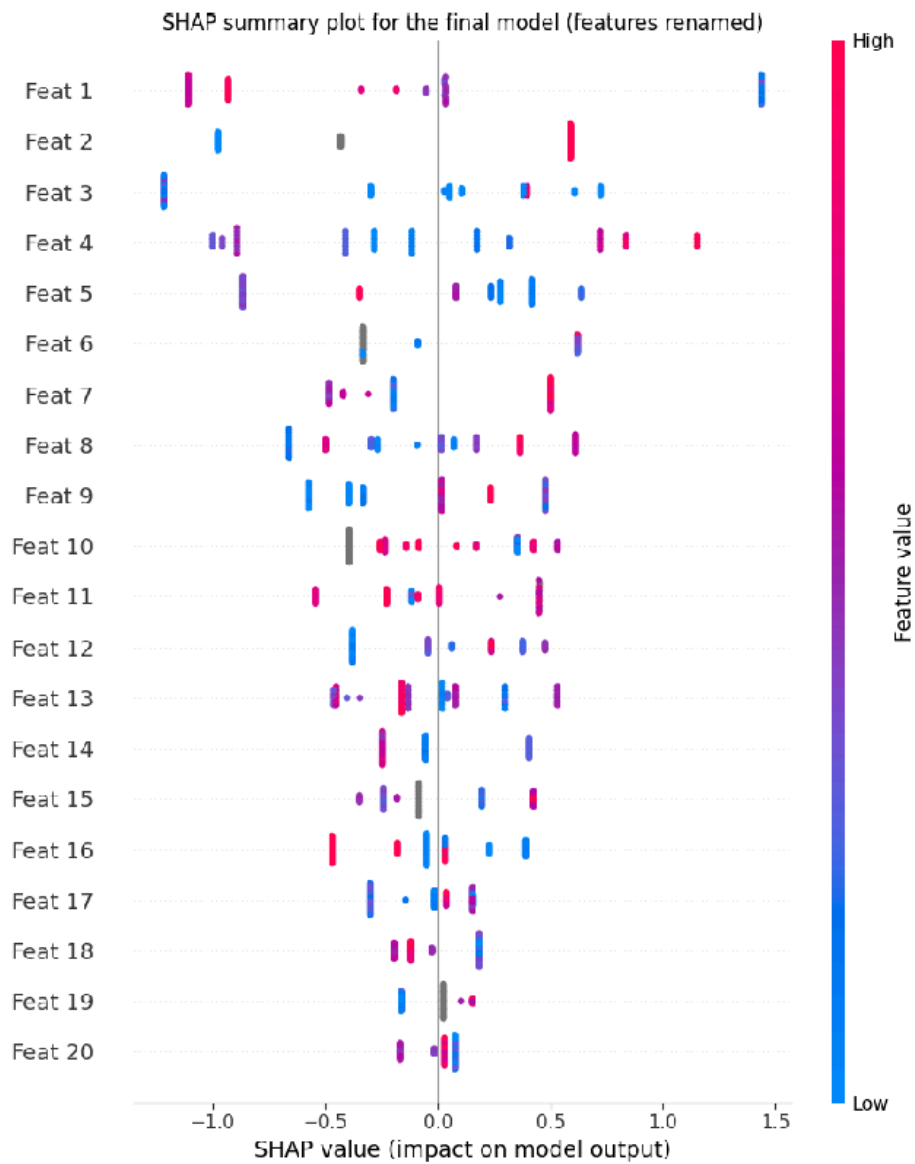


Figure 3.

Figure 3

SHAP values for the OS predictive model in patients with secondary lung tumors, showing the 20 most influential features. Feature ranking reflects their impact on model predictions. Positive SHAP values indicate a contribution toward predicting death, while negative values indicate a contribution toward survival. Point colors represent feature values, with lower values shown in blue and higher values in pink. Feat 1 = INTENSITY-BASED_IntensitySkewness; Feat 2 = tabac; Feat 3 = GLRLM_RunLengthNonUniformity; Feat 4 = etalement; Feat 5 = INTENSITY-BASED_IntensityBasedEnergy; Feat 6 = tabac_PA; Feat 7 = INTENSITY-BASED_MeanIntensity; Feat 8 = MORPHOLOGICAL_Maximum3DDiameter; Feat 9 = GLRLM_GreyLevelNonUniformity; Feat 10 = mean_PTV; Feat 11 = max_PTV; Feat 12 = vol_PTV; Feat 13 = INTENSITY-BASED_IntensityRange; Feat 14 = ATCD_loc_1; Feat 15 = poids; Feat 16 = GLRLM_ShortRunsEmphasis; Feat 17 = vol_GTV; Feat 18 = age; Feat 19 = GLCM_JointMaximum; and Feat 20 = INTENSITY-BASED_25thIntensityPercentile.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementaryinformation.docx](#)