

Development and Validation of an Intratumoral–Peritumoral Radiomics-Clinical Model for Preoperative Prediction of Synchronous Liver Metastasis in Pancreatic Neuroendocrine Tumors

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Abstract

Background

Synchronous liver metastasis is a major determinant of prognosis in patients with pancreatic neuroendocrine tumors (PNETs), yet reliable preoperative identification remains difficult. We evaluated whether a CT-based radiomics model incorporating both intratumoral and peritumoral information could improve the prediction of synchronous liver metastasis.

Methods

This retrospective study included 109 patients with pathologically confirmed PNETs. Patients were randomly assigned to a training cohort ($n = 76$) and a test cohort ($n = 33$). Radiomics features were extracted from intratumoral, 3-mm peritumoral, and combined intratumoral–peritumoral regions. After model comparison, the best-performing radiomics model was combined with the independent clinical predictor identified by logistic regression. Model performance was evaluated using discrimination, calibration, decision curve analysis, and Shapley additive explanations.

Results

Among the radiomics models, the intratumoral–peritumoral model achieved the best performance, with areas under the receiver operating characteristic curve of 0.964 and 0.885 in the training and test cohorts, respectively. Tumor margin was the only independent clinical predictor. Incorporating the radiomics signature with tumor margin further improved model performance, yielding AUCs of 0.967 (95% CI, 0.933–1.000) in the training cohort and 0.907 (95% CI, 0.793–1.000) in the test cohort. The combined model also correctly identified six of eight patients with CT-occult synchronous liver metastasis.

Conclusions

A CT-based radiomics model integrating intratumoral and peritumoral features showed good performance for the preoperative prediction of synchronous liver metastasis in PNETs. Combining radiomics with CT semantic features may assist preoperative risk stratification, including in patients with CT-occult metastases.

1. Introduction

Pancreatic neuroendocrine tumors (PNETs) are rare pancreatic neoplasms characterized by marked biological heterogeneity and diverse clinical behaviors¹. Approximately 40%–50% of patients present

with distant metastases at the initial diagnosis, with the liver being the most common metastatic site²⁻⁴. The liver is the most common site of metastasis in PNETs, and the presence of synchronous liver metastasis indicates advanced disease and is closely associated with treatment selection and long-term prognosis^{5,6}. Therefore, accurate preoperative identification of patients at high risk for synchronous liver metastasis is essential for individualized treatment planning and prognostic assessment.

Contrast-enhanced computed tomography (CT) plays an important role in the diagnosis, staging, and preoperative evaluation of PNETs⁷. In clinical practice, however, the accurate identification of synchronous liver metastasis using CT remains challenging, particularly in patients with small-volume or radiologically occult metastatic lesions^{8,9}. Although routine clinical metrics and CT findings guide daily management, they primarily depict tumor morphology, often failing to reflect the underlying biological mechanisms of metastatic spread. Therefore, reliable noninvasive imaging biomarkers are needed to improve individualized risk stratification beyond conventional clinical and imaging assessment.

Radiomics, which enables the quantitative analysis of medical images by extracting high-dimensional features reflecting tumor heterogeneity¹⁰. Previous studies have demonstrated the potential of radiomics in predicting tumor grade, lymph node involvement, and aggressiveness of PNETs¹¹⁻¹⁴. However, most radiomics studies in PNETs have focused primarily on intratumoral features, whereas the potential value of peritumoral imaging features has received relatively limited attention¹⁵⁻¹⁷. Emerging evidence suggests that the peritumoral region may capture complementary imaging information associated with tumor aggressiveness and metastatic potential, thereby providing incremental value beyond intratumoral features alone¹⁸⁻²⁰. Therefore, integrating intratumoral and peritumoral radiomic features may improve the preoperative prediction of synchronous liver metastasis in patients with PNETs.

Accordingly, this study aimed to develop and validate an intratumoral–peritumoral radiomics–clinical model based on CT for the preoperative prediction of synchronous liver metastasis in patients with PNETs. In addition, SHAP (Shapley Additive Explanations) analysis was applied to visualize and interpret the radiomics model, and the predictive performance of the proposed model was further evaluated in patients with CT-occult synchronous liver metastasis.

2. Methods

2.1 Patients

This retrospective study was approved by the Institutional Review Board of the First Affiliated Hospital of Guangxi Medical University (Approval No. 2026-E0393). Patients with pathologically confirmed PNETs who underwent preoperative contrast-enhanced CT between January 2020 and September 2025 were retrospectively included. Synchronous liver metastasis was confirmed by pathology or characteristic imaging findings at initial diagnosis, whereas its absence was confirmed by surgery and/or at least 6 months of follow-up. After applying the inclusion and exclusion criteria (Fig. 1), 109 patients were

randomly assigned to the training ($n = 76$) and test ($n = 33$) cohorts at a 7:3 ratio. CT-occult synchronous liver metastasis referred to metastases not identified on preoperative CT but confirmed by pathology or additional imaging at initial diagnosis. The overall methodological flow chart of this study is shown in Fig. 2.

2.2 Tumor segmentation

Tumor segmentation was performed on preoperative contrast-enhanced CT images using ITK-SNAP software (version 3.8.0). The primary tumor was manually delineated in three dimensions by a radiologist with 8 years of experience who was blinded to all clinical information. Adjacent normal pancreatic tissue, pancreatic duct, major vessels, and surrounding non-tumorous structures were excluded.

A 3-mm peritumoral ROI was automatically generated by isotropic expansion of the intratumoral ROI using Python and subsequently reviewed and manually corrected. Three ROIs were obtained for each patient: intratumoral, peritumoral (3 mm), and intratumoral–peritumoral.

Segmentation reproducibility was assessed in 40 randomly selected cases independently segmented by a second radiologist with 10 years of experience. Radiomics features with intraclass correlation coefficients (ICCs) > 0.75 were considered reproducible and retained for further analysis.

2.3 Radiomics feature extraction

Radiomics features were extracted from the intratumoral, 3-mm peritumoral, and combined intratumoral–peritumoral ROIs using PyRadiomics (version 3.0.1) following the Imaging Biomarker Standardization Initiative (IBSI) guidelines. Images were resampled to a uniform voxel spacing and normalized before feature extraction.

A total of 1,688 handcrafted features were extracted from each ROI, including shape, first-order, and texture features. Texture features were calculated from the gray-level co-occurrence matrix (GLCM), gray-level run length matrix (GLRLM), gray-level size zone matrix (GLSZM), gray-level dependence matrix (GLDM), and neighboring gray-tone difference matrix (NGTDM). Additional features were extracted from filtered images using wavelet, Laplacian of Gaussian (LoG), and other standard image filters. The extracted features were subsequently used for feature selection and model development.

2.4 Radiomics feature selection and model development

Radiomics feature selection and model development were performed separately for the intratumoral, 3-mm peritumoral, and intratumoral–peritumoral ROIs. Features with zero variance and high inter-feature correlation were sequentially removed to reduce redundancy. Subsequently, the least absolute shrinkage and selection operator (LASSO) regression with 10-fold cross-validation was applied to select the most informative features.

Selected features were standardized using Z-score normalization before model construction. Five machine learning algorithms, including logistic regression (LR), support vector machine (SVM), random forest (RF), k-nearest neighbors (KNN), and Light Gradient Boosting Machine (LightGBM), were used to develop radiomics models for each ROI. Model performance was evaluated using receiver operating characteristic (ROC) curves and the corresponding area under the curve (AUC) in the training and test cohorts. The optimal radiomics model was subsequently selected for integration with the clinical model.

2.5 Development of the clinical model

Clinical variables and CT semantic features were retrospectively collected from the electronic medical records and preoperative contrast-enhanced CT images. Clinical variables included demographic characteristics, inflammatory biomarkers, liver function parameters, and tumor markers. NLR, PLR, and SII were categorized using predefined cutoff values reported in previous studies, whereas the remaining laboratory variables were categorized according to institutional reference ranges^{21–23}.

CT semantic features were independently evaluated by two abdominal radiologists with 8 and 10 years of experience who were blinded to the clinical information. Tumor size was defined as the maximum diameter on arterial-phase CT images. Tumor margin was classified as well-defined or ill-defined according to the presence of an irregular, spiculated, or infiltrative border involving more than 25% of the tumor circumference²⁴. Tumor shape was categorized as regular or irregular. Lesions with predominant hyperenhancement relative to the adjacent pancreatic parenchyma were classified as having strong enhancement, whereas all remaining lesions were classified as having mild/moderate enhancement^{25,26}.

Cystic or necrosis was defined as the presence of non-enhancing low-attenuation areas within the tumor on contrast-enhanced CT images. Calcification was evaluated on unenhanced CT images and recorded as either present or absent²⁶.

Suspicious lymph node metastasis was defined by one or more of the following CT features: a short-axis diameter ≥ 10 mm, round or irregular morphology, heterogeneous enhancement, or central necrosis^{25,27–29}. Main pancreatic duct (MPD) dilatation was defined as an MPD diameter ≥ 3 mm, whereas common bile duct (CBD) dilatation was defined as a CBD diameter ≥ 10 mm^{30,31}.

Univariate logistic regression analysis was performed in the training cohort, and variables with a P value < 0.05 were subsequently entered into a multivariate logistic regression analysis. Independent predictors were used to construct the clinical prediction model.

2.6 Development and evaluation of the radiomics–clinical combined model

The best-performing radiomics model was combined with the independent clinical predictor to develop the radiomics–clinical combined model using logistic regression. Model performance was evaluated in the training and test cohorts using receiver operating characteristic (ROC) curves and the corresponding

area under the curve (AUC). Calibration curves and decision curve analysis (DCA) were used to assess model calibration and clinical utility, respectively. The interpretability of the best-performing radiomics model was evaluated using Shapley additive explanations (SHAP). In addition, the predictive performance of the final radiomics–clinical combined model was further explored in patients with CT-occult synchronous liver metastasis.

2.7 Statistical analyses

Statistical analyses were performed using R software (version 3.4.3). Continuous variables were expressed as mean $\pm$ standard deviation or median (interquartile range), according to their distribution, and compared using the independent-samples t test or Mann–Whitney U test, as appropriate. Categorical variables were presented as frequencies and percentages and compared using the chi-square test or Fisher’s exact test. Univariate and multivariate logistic regression analyses were performed to identify independent clinical predictors of synchronous liver metastasis. All statistical tests were two-sided, and a P value < 0.05 was considered statistically significant.

3. Results

3.1 Baseline characteristics

A total of 109 patients with pathologically confirmed PNETs were retrospectively enrolled and randomly assigned to the training cohort ($n = 76$) and test cohort ($n = 33$) at a ratio of 7:3. The proportions of patients with and without synchronous liver metastasis (SLM) were comparable between the two cohorts ($P = 0.544$). Specifically, 53.95% (41/76) of patients in the training cohort and 45.45% (15/33) in the test cohort had SLM. The baseline clinical characteristics and CT semantic features were well balanced between the two cohorts, with no significant differences observed in any variables (all $P > 0.05$) (Table 1).

Table 1
Baseline characteristics of patients in the training and test cohorts

Characteristics	Total(n = 109)	Test(n = 37)	Train(n = 76)	P value
Age, years	48.83 ± 12.00	50.39 ± 13.00	48.14 ± 11.56	0.371
Platelet, ×10 ⁹	256.13 ± 73.69	249.09 ± 68.31	259.19 ± 76.14	0.628
Neutrophils, ×10 ⁹	4.28 ± 2.14	3.82 ± 1.39	4.47 ± 2.37	0.311
Lymphocyte, ×10 ⁹	1.78 ± 0.69	1.81 ± 0.73	1.77 ± 0.68	0.815
AST/ALT	1.46 ± 1.81	2.07 ± 3.11	1.19 ± 0.57	0.135
Gender				0.169
Female	62(56.88)	15(45.45)	47(61.84)	
Male	47(43.12)	18(54.55)	29(38.16)	
NLR				0.939
≤ 2.4	65(59.63)	19(57.58)	46(60.53)	
> 2.4	44(40.37)	14(42.42)	30(39.47)	
PLR				1.000
≤ 300	104(95.41)	31(93.94)	73(96.05)	
> 300	5(4.59)	2(6.06)	3(3.95)	
SII				0.727
≤ 600	65(59.63)	21(63.64)	44(57.89)	
> 600	44(40.37)	12(36.36)	32(42.11)	
TB				0.594
≤ 17	91(83.49)	29(87.88)	62(81.58)	
> 17	18(16.51)	4(12.12)	14(18.42)	
AST				0.140
≤ 40	87(79.82)	23(69.70)	64(84.21)	
> 40	22(20.18)	10(30.30)	12(15.79)	
ALT				1.000
≤ 50	90(82.57)	27(81.82)	63(82.89)	
> 50	19(17.43)	6(18.18)	13(17.11)	

Characteristics	Total(n = 109)	Test(n = 37)	Train(n = 76)	P value
CEA				0.746
≤ 5	102(93.58)	30(90.91)	72(94.74)	
> 5	7(6.42)	3(9.09)	4(5.26)	
CA125				0.906
≤ 35	98(89.91)	29(87.88)	69(90.79)	
> 35	11(10.09)	4(12.12)	7(9.21)	
CA199				1.000
≤ 37	98(89.91)	30(90.91)	68(89.47)	
> 37	11(10.09)	3(9.09)	8(10.53)	
Size	4.14 ± 2.87	4.57 ± 3.83	3.96 ± 2.34	0.911
Location				0.857
Head	46(42.20)	13(39.39)	33(43.42)	
body and tail	63(57.80)	20(60.61)	43(56.58)	
Tumor margin				0.980
Well-defined	58(53.21)	17(51.52)	41(53.95)	
Ill-defined	51(46.79)	16(48.48)	35(46.05)	
Shape				0.277
Regular	63(57.80)	16(48.48)	47(61.84)	
Irregular	46(42.20)	17(51.52)	29(38.16)	
Enhancement				1.000
Strong	31(28.44)	9(27.27)	22(28.95)	
Mild/Moderate	78(71.56)	24(72.73)	54(71.05)	
Cystic or Necrosis				0.427
No	64(58.72)	17(51.52)	47(61.84)	
Yes	45(41.28)	16(48.48)	29(38.16)	
Calcification				0.432
No	95(87.16)	27(81.82)	68(89.47)	
Yes	14(12.84)	6(18.18)	8(10.53)	

Characteristics	Total(n = 109)	Test(n = 37)	Train(n = 76)	P value
Suspiciouslymphnodemetastasis				1.000
No	81(74.31)	25(75.76)	56(73.68)	
Yes	28(25.69)	8(24.24)	20(26.32)	
MPDdilation				0.101
No	87(79.82)	30(90.91)	57(75.00)	
Yes	22(20.18)	3(9.09)	19(25.00)	
CBDdilation				0.450
No	97(88.99)	31(93.94)	66(86.84)	
Yes	12(11.01)	2(6.06)	10(13.16)	
SLM				
No	53(48.62)	18(54.55)	35(46.05)	0.544
Yes	56(51.38)	15(45.45)	41(53.95)	

3.2 Radiomics feature selection and model development

LASSO regression with 10-fold cross-validation selected 6, 8, and 8 radiomics features from the intratumoral, 3-mm peritumoral, and intratumoral–peritumoral regions, respectively (Fig. 3). Based on these features, five machine learning algorithms were used to construct prediction models. As shown in Fig. 4, the intratumoral–peritumoral SVM model achieved the best performance among all models, with AUCs of 0.964 and 0.885 in the training and test cohorts, respectively, and was selected for subsequent analyses.

3.3 Development of the clinical model

Univariate logistic regression analysis was performed to evaluate the associations between clinical and CT semantic features and synchronous liver metastasis in the training cohort. Variables with statistical significance in the univariate analysis were entered into the multivariate logistic regression model. Tumor margin remained the only independent predictor of synchronous liver metastasis after multivariate analysis (Table 2) and was subsequently incorporated into the clinical model.

Table 2
Univariate and multivariate logistic regression analyses for identifying predictors of synchronous liver metastasis

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Age	1.005(0.997–1.013)	0.277		
Platelet	1(0.999–1.001)	0.971		
Neutrophil	0.992(0.920–1.068)	0.856		
Lymphocyte	0.996(0.816–1.215)	0.973		
AST_ALT	1.006(0.756–1.339)	0.972		
Gender	2.222(1.148–4.301)	0.047	1.016(0.375–2.748)	0.98
NLR	1.5(0.812–2.768)	0.277		
PLR	2(0.267–14.999)	0.571		
SII	1.133(0.633–2.030)	0.724		
TB	2.5(0.945–6.613)	0.121		
AST	5(1.398–17.886)	0.038	0.997(0.190–5.238)	0.998
ALT	3.333(1.129–9.845)	0.067		
CEA	16.351(0-20.661)	1		
CA125	2.5(0.613–9.895)	0.273		
CA199	3.865(0-5.357)	1		
Size	1.172(1.066–1.289)	0.006	0.864(0.696–1.073)	0.267
Location	2.308(1.336–3.983)	0.012	1.348(0.557–3.261)	0.578
Tumor margin	6(2.710-13.277)	< 0.001	6.375(1.745–23.289)	0.019
Shape	3.833(1.804–8.150)	0.003	0.868(0.245–3.080)	0.855

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Enhancement	0.742(0.472–1.166)	0.278		
Cysticnecrosis	2.625(1.326–5.196)	0.02	1.397(0.442–4.419)	0.633
Calcification	3(0.783–11.496)	0.178		
Suspiciouslymphnodemetastasis	9(2.641–30.661)	0.003	4.344(0.951–19.846)	0.112
MPDdilation	1.714(0.784–3.747)	0.257		
CBDdilation	2.333(0.750–7.257)	0.22		

3.4Performance of the radiomics–clinical combined model

The radiomics and clinical models were integrated to construct the combined model. As shown in Fig. 5 and Table 3, the combined model achieved the highest AUC in both the training (0.967, 95% CI: 0.933–1.000) and test cohorts (0.907, 95% CI: 0.793–1.000), outperforming the radiomics model (0.964 and 0.885) and the clinical model (0.794 and 0.789), respectively. Calibration curves showed acceptable agreement between predicted and observed probabilities, and decision curve analysis suggested a potential clinical benefit of the combined model.

Table 3
Performance of the prediction models in the training and test cohorts.

Model	Cohort	AUC(95% CI)	Sensitivity	Specificity	Accuracy	PPV	NPV
Clinic	train	0.794(0.704–0.885)	0.732	0.857	0.789	0.857	0.732
Clinic	test	0.789(0.644–0.932)	0.800	0.778	0.788	0.750	0.824
IntraPeri	train	0.964(0.930–0.997)	0.854	0.971	0.908	0.972	0.850
IntraPeri	test	0.885(0.773–0.996)	0.867	0.778	0.818	0.765	0.875
Combined	train	0.967(0.933–1.000)	0.854	1.000	0.921	1.000	0.854
Combined	test	0.907(0.793–1.000)	1.000	0.778	0.879	0.789	1.000

3.5 Explainability of the intratumoral–peritumoral radiomics model

To improve the interpretability of the selected intratumoral–peritumoral radiomics model, SHAP analysis was performed to quantify the contribution of individual radiomics features to model predictions. The SHAP summary plot demonstrated the relative importance and impact of the selected radiomics features on the prediction of synchronous liver metastasis (Fig. 6A). A representative case of CT-occult synchronous liver metastasis that was correctly identified by the intratumoral–peritumoral radiomics model is presented in Fig. 6B. Although no definite hepatic metastasis was detected on preoperative contrast-enhanced CT, subsequent biopsy confirmed liver metastasis. The corresponding SHAP waterfall plot and force plot further illustrated the contributions of individual radiomics features to the model prediction for this patient (Fig. 6C–D).

3.6 Exploratory analysis in patients with CT-occult synchronous liver metastasis

An exploratory analysis was further performed in eight patients with CT-occult synchronous liver metastasis. Using the predefined probability threshold of 0.5, the final radiomics–clinical combined model correctly classified six of the eight patients (75.00%). The individual predicted probabilities generated by the combined model are presented in Fig. 7. These findings suggest that the proposed model may assist in identifying patients with occult synchronous liver metastasis that cannot be detected by routine contrast-enhanced CT.

Overall, these findings further support the potential clinical applicability of the proposed radiomics–clinical combined model in preoperative risk stratification for synchronous liver metastasis in patients with PNETs.

4. Discussion

In this study, we developed and validated a CT-based intratumoral–peritumoral radiomics–clinical model for the preoperative prediction of synchronous liver metastasis in patients with PNETs. The combined model demonstrated better predictive performance than either the radiomics or clinical model alone. Furthermore, SHAP analysis improved the interpretability of the radiomics model, and the combined model showed potential value in identifying CT-occult synchronous liver metastases.

A major finding of this study is that the intratumoral–peritumoral radiomics model outperformed the intratumoral radiomics model in predicting synchronous liver metastasis in patients with PNETs. This finding suggests that the peritumoral region provides complementary imaging information beyond that captured by the tumor itself. Tumor metastasis is a dynamic process shaped not only by the intrinsic properties of cancer cells but also by their continuous cross-talk with the surrounding microenvironment^{32,33}. Most radiomics studies in PNETs have focused on intratumoral imaging features,

whereas the potential contribution of the peritumoral region has received relatively little attention. However, tumor progression and metastatic dissemination are not confined to the tumor itself but result from continuous interactions between tumor cells and the surrounding microenvironment. This concept has been increasingly supported by radiomics studies across various solid tumors, including lung cancer, breast cancer, hepatocellular carcinoma, and endometrial cancer^{34–39}. For example, Lu et al. showed that a radiomics model integrating intratumoral and peritumoral lung parenchyma features improved the prediction of occult lymph node metastasis in clinical stage T1 lung adenocarcinoma, suggesting that peritumoral imaging information provides complementary value³⁴. Similarly, in breast cancer, researchers found that radiomics signatures incorporating both intratumoral and peritumoral regions consistently outperformed models based on intratumoral or peritumoral features alone for predicting sentinel lymph node status, suggesting that the combination of tumor and surrounding tissue characteristics provides more comprehensive information regarding tumor biology³⁸. Furthermore, a recent study in pituitary adenomas demonstrated that the combination of intratumoral and peritumoral radiomics features improved the prediction of PIT1 expression compared with intratumoral radiomics alone, further supporting the biological relevance of the peritumoral region³⁹. Collectively, these findings suggest that peritumoral radiomics features may provide complementary information to intratumoral features and contribute to a more comprehensive characterization of tumor heterogeneity.

Synchronous liver metastasis reflects aggressive tumor behavior in PNETs and remains a major factor influencing clinical management and prognosis. However, preoperative identification of patients at high risk of liver metastasis remains challenging because conventional CT evaluation mainly relies on morphological characteristics, which may not fully capture the biological heterogeneity associated with metastatic potential. The development of liver metastasis involves multiple biological steps, including local invasion, vascular dissemination, and adaptation to the metastatic microenvironment⁴⁰. Radiomics provides a quantitative approach to extract high-dimensional imaging features that capture subtle variations in tumor intensity, texture, and spatial heterogeneity beyond visual assessment. These imaging signatures may provide indirect information related to tumor progression and metastatic potential. In this study, the intratumoral–peritumoral radiomics model showed better predictive performance than the intratumoral radiomics model alone, suggesting that radiomic features derived from both the tumor and peritumoral regions provide complementary information associated with synchronous liver metastasis. The additional improvement achieved by the combined radiomics–clinical model further suggests that quantitative imaging features and conventional clinical characteristics capture different aspects of tumor behavior. By integrating tumor heterogeneity with routinely available clinical information, the proposed model may provide a more comprehensive assessment of synchronous liver metastasis risk than either approach alone. These findings suggest that radiomics-based approaches may serve as a useful noninvasive strategy for improving preoperative risk stratification and supporting individualized clinical decision-making in patients with PNETs.

An important clinical implication of this study is the potential application of the proposed model in patients with CT-occult synchronous liver metastasis. Although contrast-enhanced CT is routinely used

for staging and preoperative assessment of PNETs, the detection of small or atypical metastatic lesions remains challenging, particularly when lesions lack typical morphological or enhancement characteristics⁴¹. Consequently, some patients may have an underestimated metastatic burden before surgery, which may affect subsequent clinical decision-making. Previous studies in pancreatic and other solid malignancies have demonstrated that radiomic features can improve the detection of occult metastatic disease or predict metastatic potential in patients without obvious radiological evidence of dissemination^{42–45}. For example, CT-based radiomics models have been shown to improve the preoperative prediction of occult lymph node metastasis in early-stage lung adenocarcinoma compared with conventional imaging assessment⁴². Similarly, Zhao et al. have demonstrated that CT-based radiomics features can accurately predict occult liver metastasis and stratify prognostic risk in pancreatic ductal adenocarcinoma, supporting the potential of radiomics to noninvasively characterize tumor aggressiveness and metastatic propensity⁴⁴. Moreover, a multimodal digital biopsy model integrating CT radiomics and clinicopathological variables has been developed for the noninvasive prediction of occult peritoneal metastasis in locally advanced gastric cancer, further supporting the potential of radiomics to characterize metastatic propensity before treatment⁴⁵. Likewise, in this study, the proposed model showed potential value in identifying patients with CT-occult synchronous liver metastasis, suggesting that quantitative imaging features from both the tumor and peritumoral regions may capture early imaging alterations associated with metastatic behavior.

Although the combined radiomics–clinical model achieved the highest predictive performance in our study, its primary value lies in integrating complementary information from different levels rather than substantially improving discrimination alone. Radiomics features quantitatively characterize intratumoral and peritumoral heterogeneity that is not appreciable by visual assessment, whereas CT semantic features remain an integral part of routine clinical interpretation and often reflect macroscopic manifestations of tumor aggressiveness. In the present study, tumor margin was the only independent clinical predictor retained in the final model. An ill-defined tumor margin has previously been associated with infiltrative tumor growth, disruption of the tumor–pancreatic interface, and a more aggressive biological phenotype, all of which may contribute to metastatic dissemination^{46–48}. These findings suggest that radiomics and CT semantic features provide complementary information for characterizing tumor behavior. While radiomics quantitatively captures imaging heterogeneity beyond visual assessment, CT semantic features reflect macroscopic tumor characteristics that remain clinically relevant. Although the combined model provided only a modest improvement over the radiomics model alone, integrating these complementary features may improve individualized preoperative risk assessment.

This study has several limitations. First, its retrospective single-center design and relatively small sample size may limit the generalizability of the findings. Second, although the model showed favorable performance in the internal test cohort, external validation in larger multicenter populations is warranted. Third, only contrast-enhanced CT images were analyzed, and the integration of multimodal imaging may further improve predictive performance. Finally, the biological basis of the radiomics features was not

explored. Future studies incorporating radiogenomic or histopathological analyses may further improve the interpretability and clinical applicability of radiomics models.

5. Conclusion

In conclusion, a CT-based intratumoral–peritumoral radiomics–clinical model was developed for the preoperative prediction of synchronous liver metastasis in PNETs. The model demonstrated favorable performance in both the training and test cohorts and showed potential for identifying CT-occult liver metastasis. This approach may provide a useful noninvasive tool for individualized preoperative risk assessment and treatment planning.

Declarations

Conflicts of Interest: Nothing to Disclose

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Author contributions: Jia-Bei Liu conceived the study, collected and analyzed the data, performed radiomics analysis, and drafted the manuscript. Ying Liu participated in image interpretation, data validation, and manuscript revision. Cheng Tang, Yi-Xun Li, Qian Guo, and Zi-Ning Lyu contributed to data collection and data verification. Peng Peng designed and supervised the study, critically revised the manuscript for important intellectual content, and approved the final version. All authors reviewed and approved the final manuscript.

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Approval No. 2026-E0393). The requirement for informed consent was waived due to the retrospective nature of this study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Figures

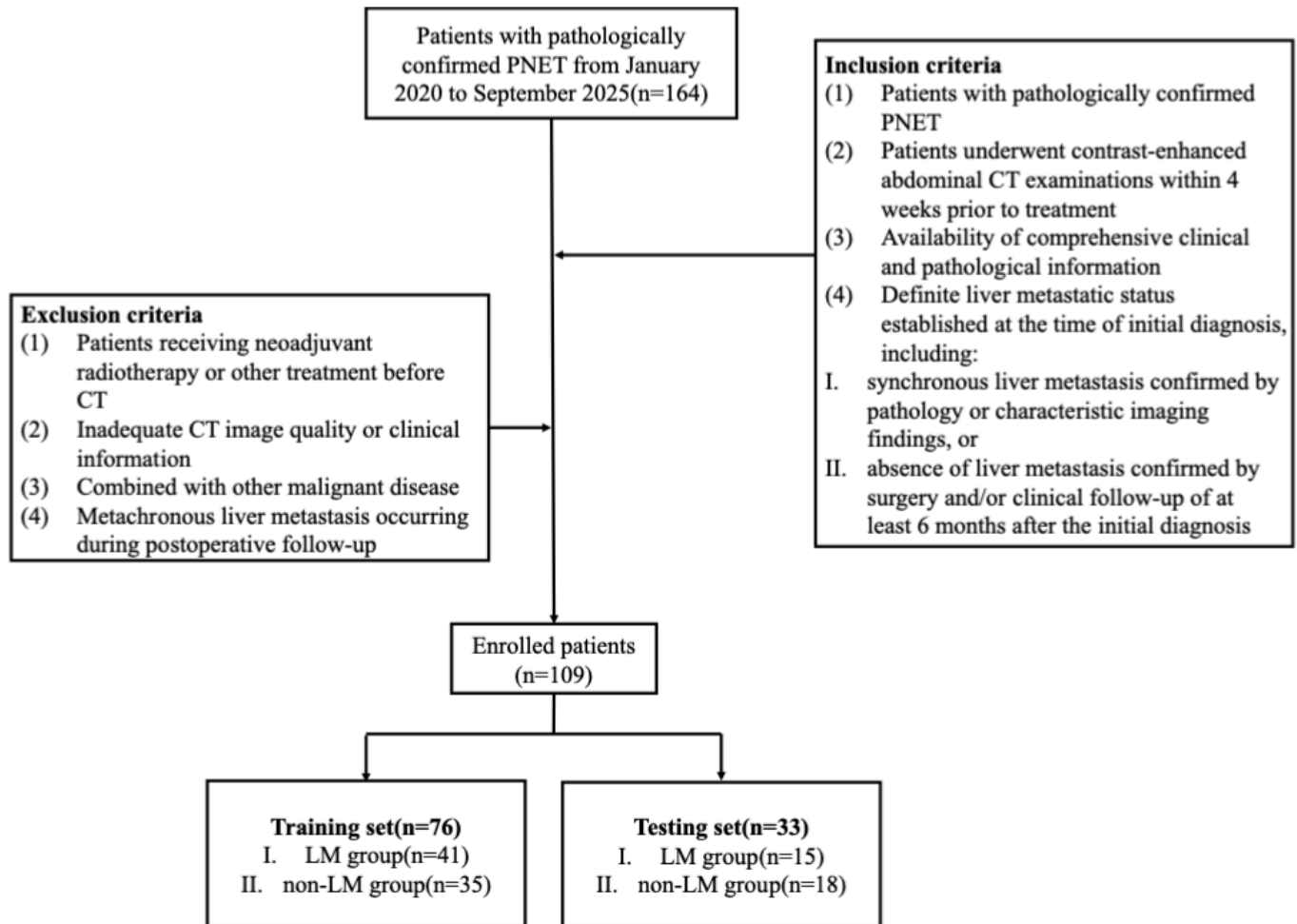


Figure 1

Flow chart of patients' recruitment pathway.

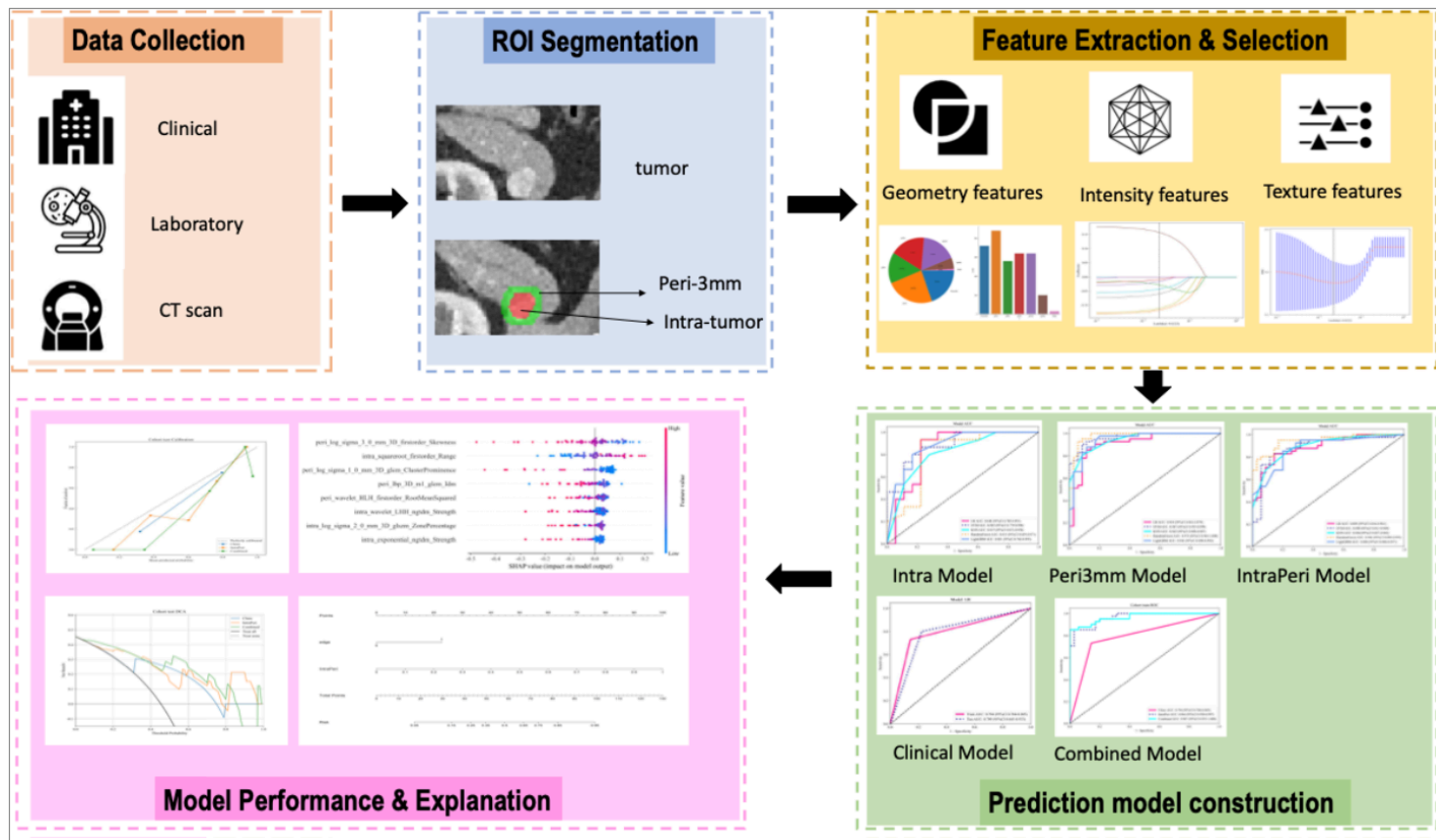


Figure 2

Overall workflow of this study.

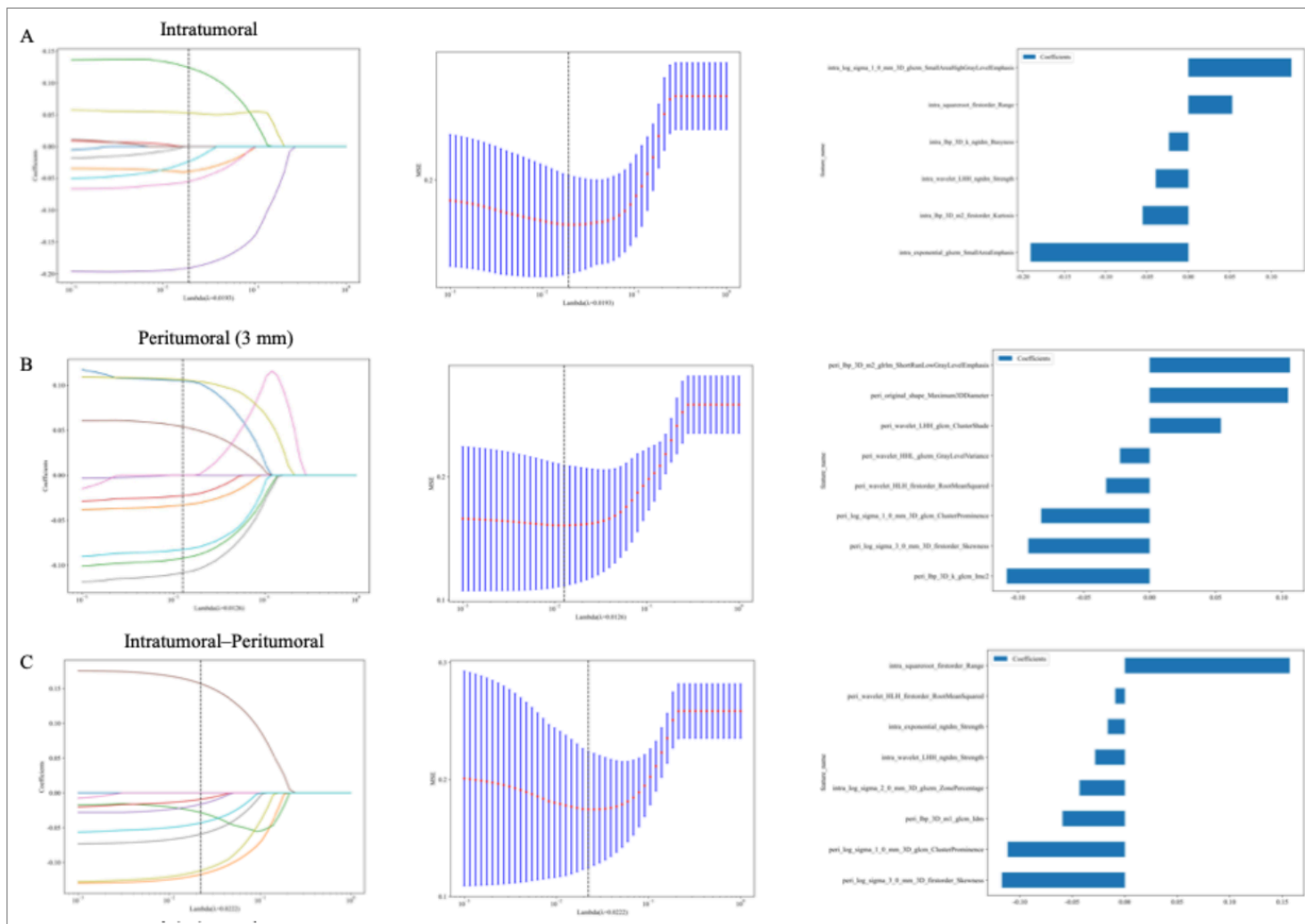


Figure 3

Radiomics feature selection by LASSO regression. Optimal radiomics features were selected using 10-fold cross-validation. A total of 6, 8, and 8 features were retained for the intratumoral region (A), 3-mm peritumoral region (B), and combined intratumoral–peritumoral region (C), respectively.

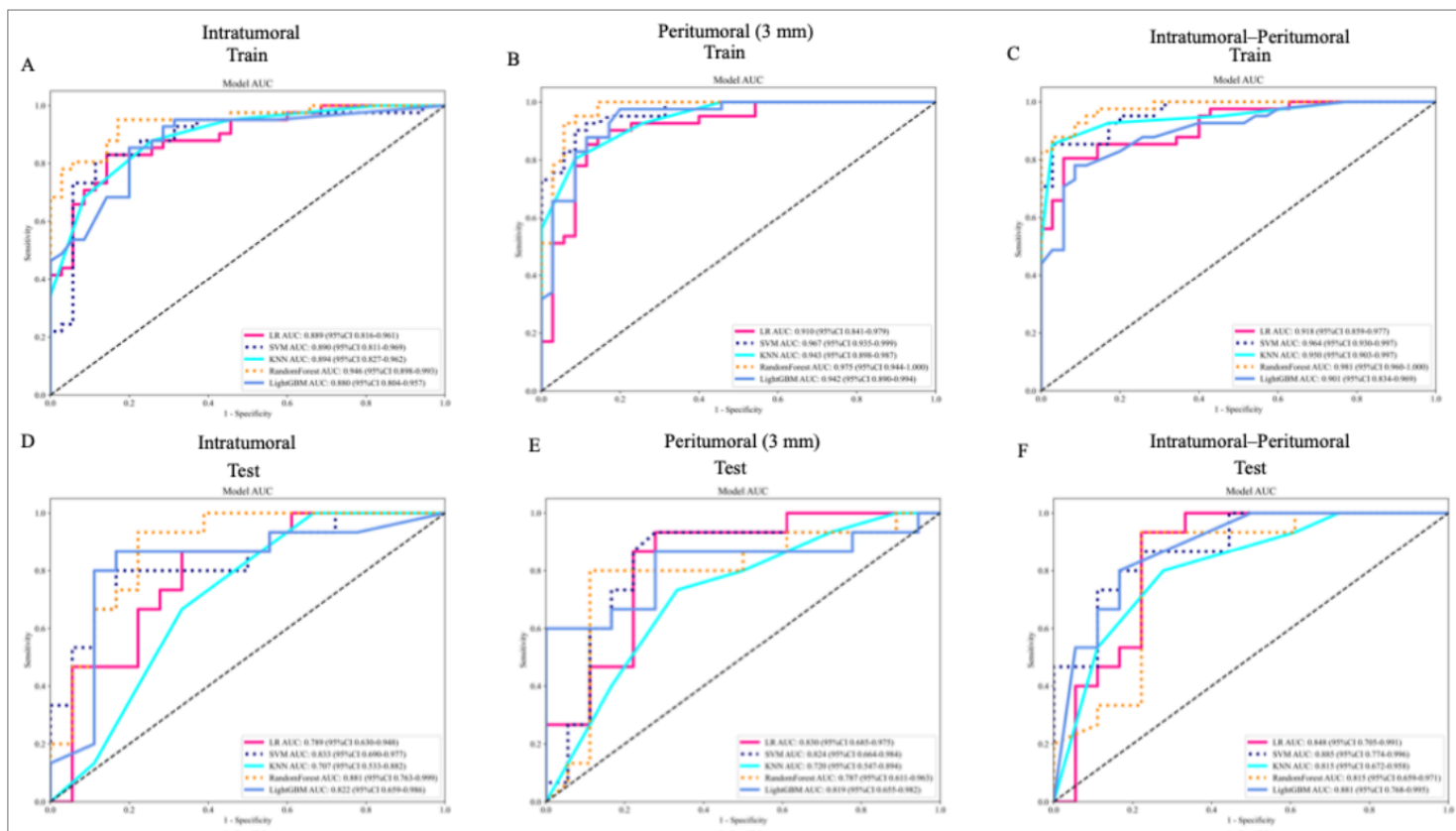


Figure 4

Comparison of receiver operating characteristic (ROC) curves for five machine learning algorithms in predicting synchronous liver metastasis using intratumoral, 3-mm peritumoral, and intratumoral–peritumoral radiomics features. (A–C) Training cohort; (D–F) Test cohort. LR, logistic regression; SVM, support vector machine; RF, random forest; KNN, k-nearest neighbor; LightGBM, Light Gradient Boosting Machine.

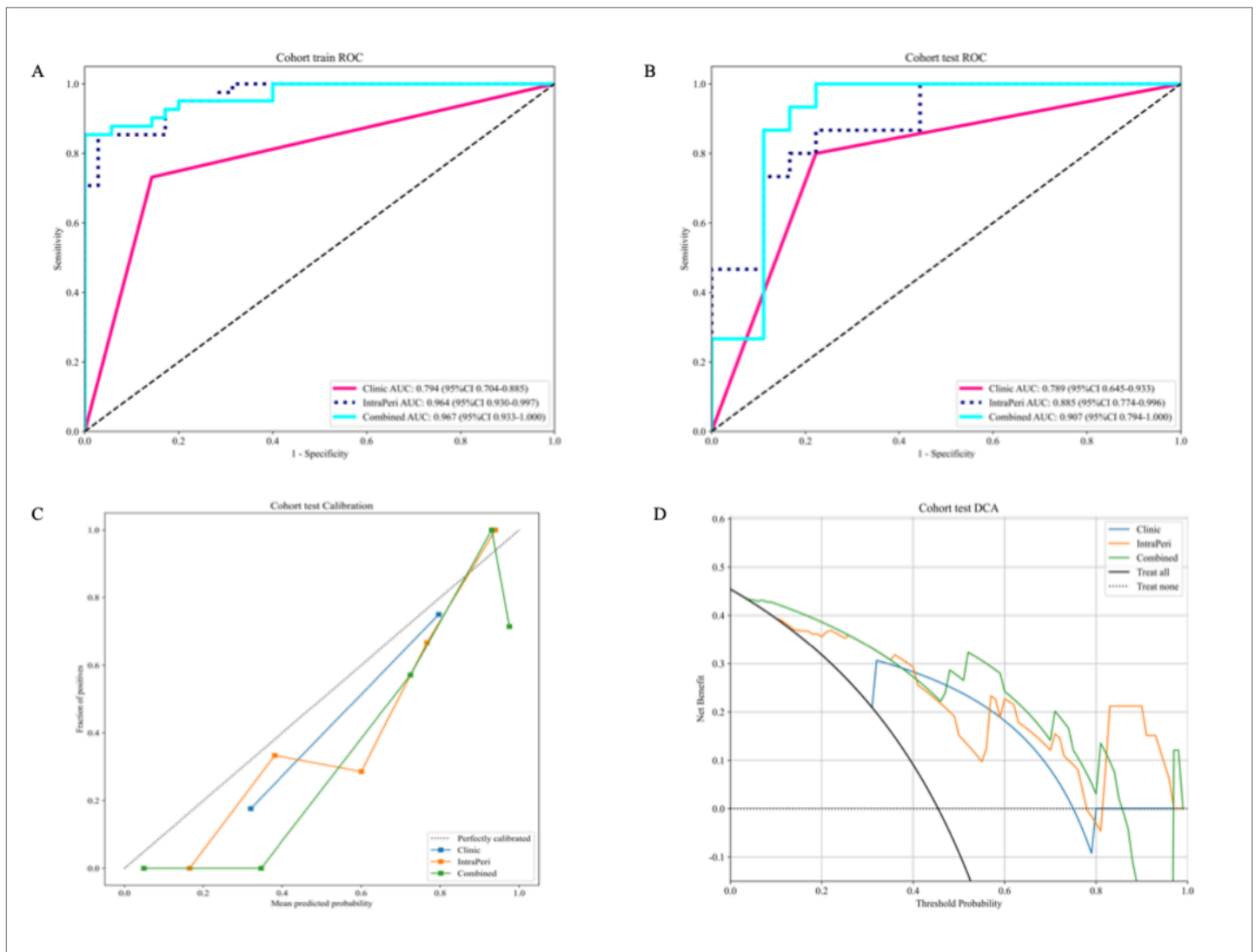


Figure 5

Performance of the clinical model, intratumoral–peritumoral radiomics model, and radiomics-clinical combined model for predicting synchronous liver metastasis in pancreatic neuroendocrine tumors. (A) ROC curves of the three models in the training cohort. (B) ROC curves of the three models in the test cohort. (C) Calibration curves of the three models in the training and test cohorts. (D) Decision curve analysis (DCA) of the three models in the test cohort, demonstrating the clinical utility of the combined model.

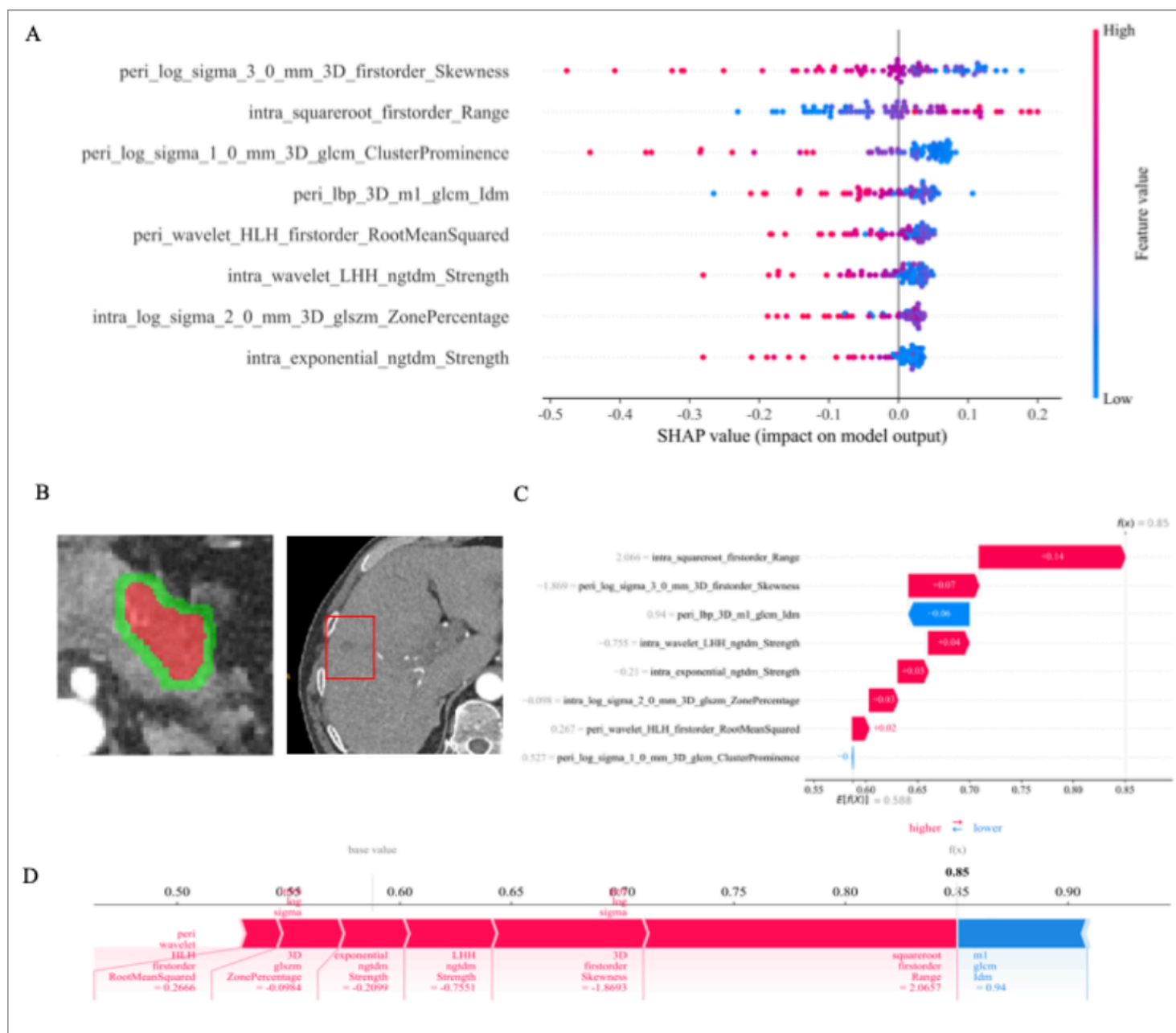


Figure 6

Explainability of the intratumoral-peritumoral radiomics model using SHAP analysis and representative case demonstration. (A) SHAP summary plot showing the contribution and direction of selected radiomics features in the SVM-based intratumoral-peritumoral radiomics model. (B) Representative case of CT-occult synchronous liver metastasis correctly predicted by the model. Although no definite hepatic metastasis was identified on preoperative contrast-enhanced CT, subsequent biopsy confirmed liver metastasis. The primary tumor segmentation, intratumoral region, and 3-mm peritumoral region are displayed. (C) SHAP waterfall plot demonstrating the contribution of selected radiomics features to the individual prediction. (D) SHAP force plot illustrating the feature contributions driving the model prediction toward a high-risk classification.

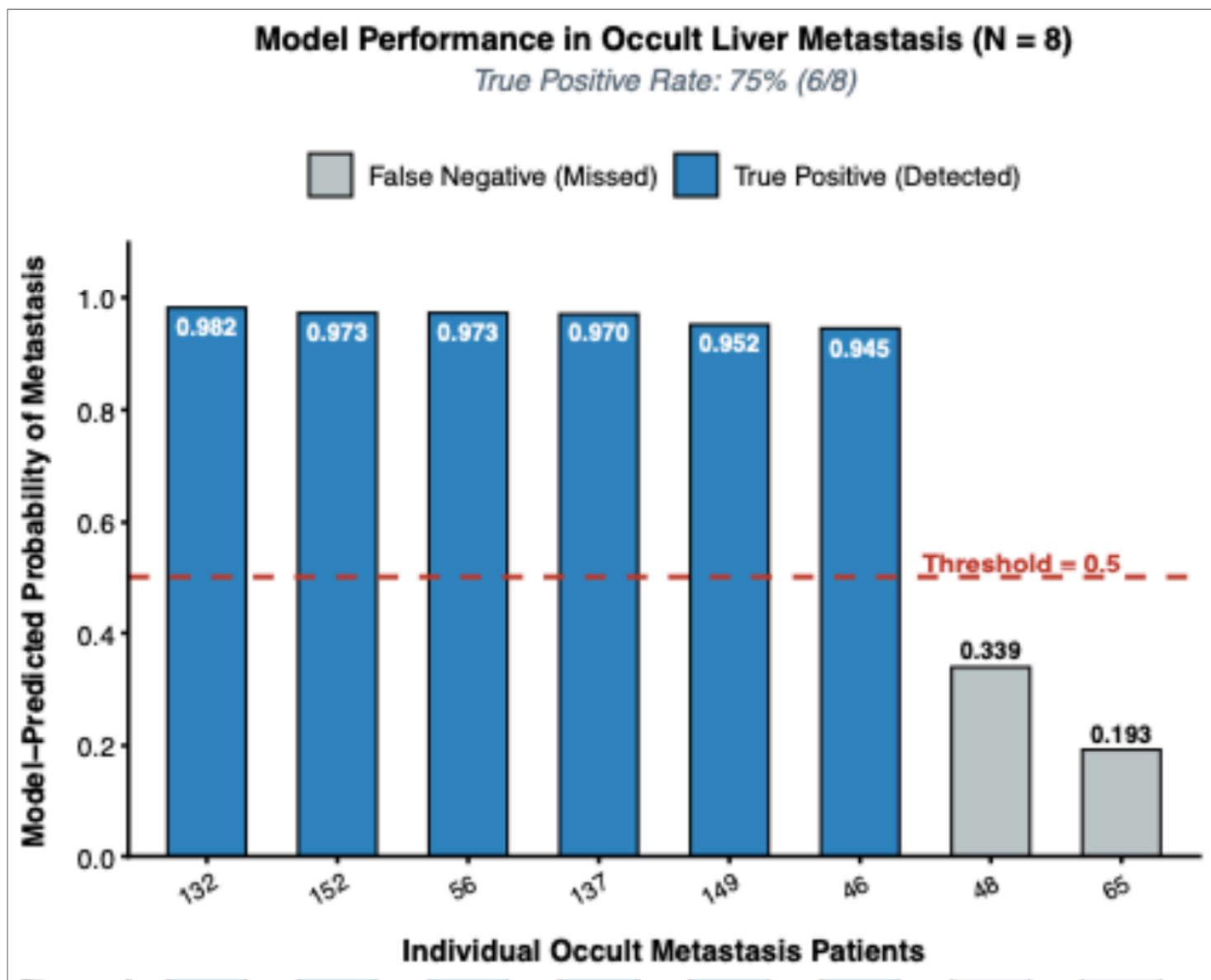


Figure 7

Performance of the radiomics-clinical combined model in identifying CT-occult synchronous liver metastasis. The bar plot illustrates the predicted probability of liver metastasis for each of the eight patients with occult synchronous liver metastasis that were not identified on preoperative contrast-enhanced CT but were subsequently confirmed by biopsy.