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## Supplemental information

# Multimodal integration to identify the invasion status of lung adenocarcinoma intraoperatively

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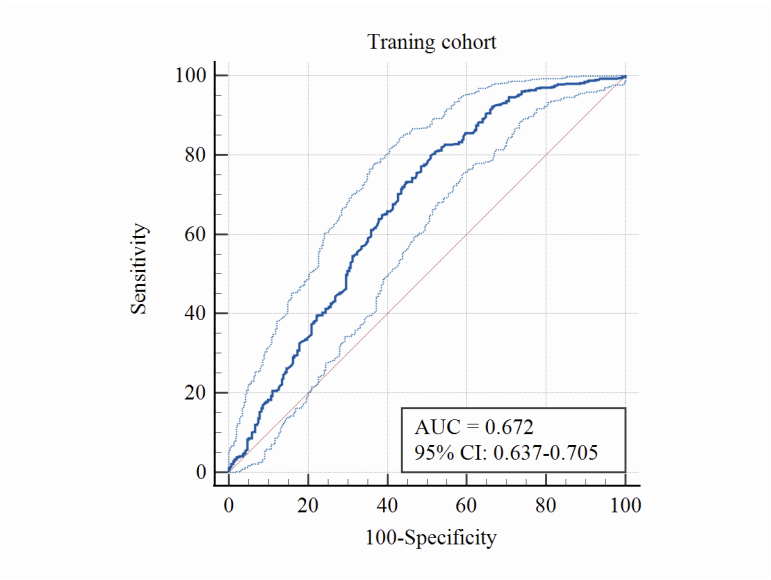



**Figure S1.** Performance of clinical indicators (age and eosinophil count) showed by ROC curve in the multimodal training cohort.

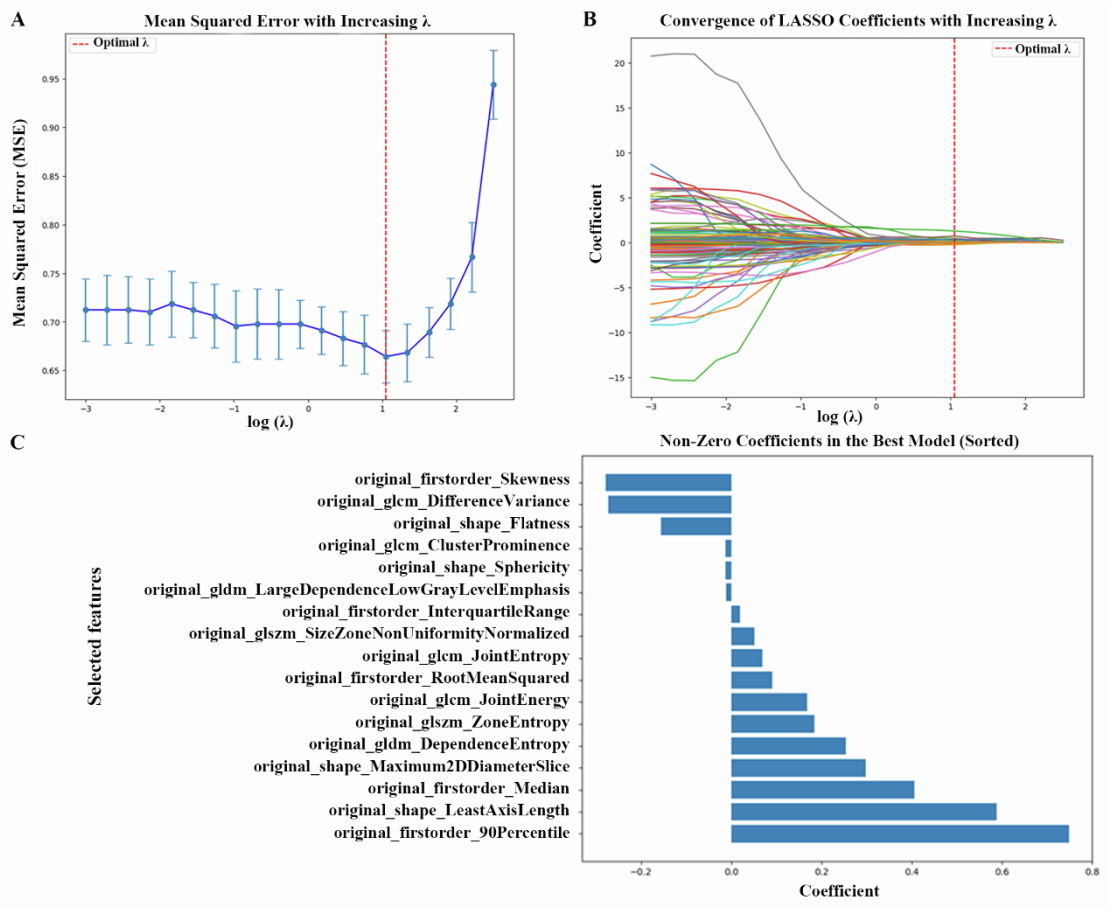
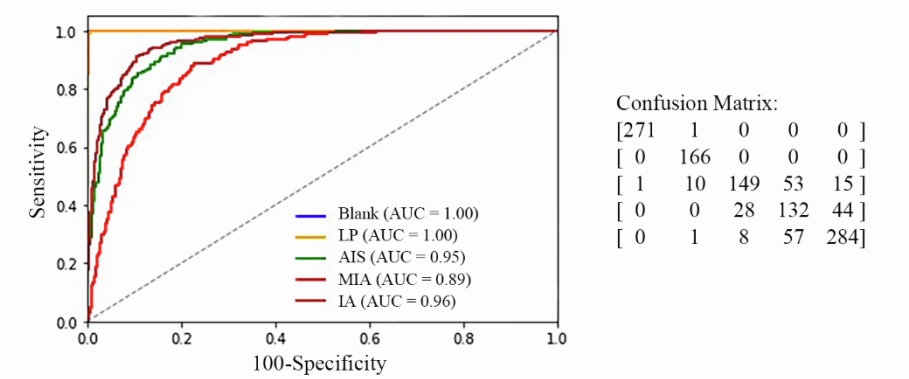



**Figure S2.** Radiomic feature selection using the least absolute shrinkage and the histogram of the Rad-score based on the selected features.




Confusion Matrix:

| | | | | |
|---|---|---|---|---|
| [271 | 1 | 0 | 0 | 0 ] |
| [ 0 | 166 | 0 | 0 | 0 ] |
| [ 1 | 10 | 149 | 53 | 15 ] |
| [ 0 | 0 | 28 | 132 | 44 ] |
| [ 0 | 1 | 8 | 57 | 284] |

Classification Report:

| | precision | recall | f1-score | support |
|---|---|---|---|---|
| 0 | 1.00 | 1.00 | 1.00 | 272 |
| 1 | 0.93 | 1.00 | 0.97 | 166 |
| 2 | 0.81 | 0.65 | 0.72 | 228 |
| 3 | 0.55 | 0.65 | 0.59 | 204 |
| 4 | 0.83 | 0.81 | 0.82 | 350 |
| accuracy | | | 0.82 | 1220 |
| macro avg | 0.82 | 0.82 | 0.82 | 1220 |
| weighted avg | 0.83 | 0.82 | 0.82 | 1220 |

ROC AUC (Macro): 0.96015
ROC AUC (Weighted): 0.96081
Test Loss: 0.47799 Accuracy: 0.82131

**Figure S3.** Predictive performance of EfficientNet B5 model to classify 1220 segmented patches into five pathologic classes, including “Blank”, “LP”, “AIS”, “MIA”, and “IA”.

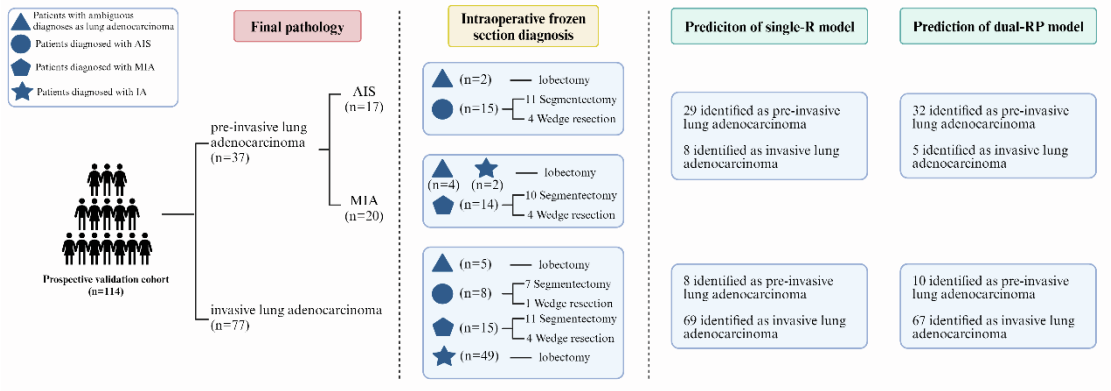



**Figure S4.** Comparison of FP, intraoperative FS diagnosis, and predictions of single-R model and dual-RP model in the prospective validation cohort.

FP, final pathology; FS, frozen section; AIS, adenocarcinoma in situ; MIA, minimally invasive adenocarcinoma; Single-R model, single-modality radiomic model; Dual-RP model, radiomics + pathology dual-modality model.

**Table S1. Radiomic feature groups chosen in this study**

| Feature Names | Feature Names |
|---|---|
| original_shape_Elongation | original_glcm_InverseVariance |
| original_shape_Flatness | original_glcm_MaximumProbability |
| original_shape_LeastAxisLength | original_glcm_SumEntropy |
| original_shape_MajorAxisLength | original_glcm_SumSquares |
| original_shape_Maximum2DDiameterColumn | original_glrlm_GrayLevelNonUniformity |
| original_shape_Maximum2DDiameterRow | original_glrlm_GrayLevelNonUniformityNormalized |
| original_shape_Maximum2DDiameterSlice | original_glrlm_GrayLevelVariance |
| original_shape_Maximum3DDiameter | original_glrlm_HighGrayLevelRunEmphasis |
| original_shape_MeshVolume | original_glrlm_LongRunEmphasis |
| original_shape_MinorAxisLength | original_glrlm_LongRunHighGrayLevelEmphasis |
| original_shape_Sphericity | original_glrlm_LongRunLowGrayLevelEmphasis |
| original_shape_SurfaceArea | original_glrlm_LowGrayLevelRunEmphasis |
| original_shape_SurfaceVolumeRatio | original_glrlm_RunEntropy |
| original_shape_VoxelVolume | original_glrlm_RunLengthNonUniformity |
| original_firstorder_10Percentile | original_glrlm_RunLengthNonUniformityNormalized |
| original_firstorder_90Percentile | original_glrlm_RunPercentage |
| original_firstorder_Energy | original_glrlm_RunVariance |
| original_firstorder_Entropy | original_glrlm_ShortRunEmphasis |
| original_firstorder_InterquartileRange | original_glrlm_ShortRunHighGrayLevelEmphasis |
| original_firstorder_Kurtosis | original_glrlm_ShortRunLowGrayLevelEmphasis |
| original_firstorder_Maximum | original_glszm_GrayLevelNonUniformity |
| original_firstorder_MeanAbsoluteDeviation | original_glszm_GrayLevelNonUniformityNormalized |
| original_firstorder_Mean | original_glszm_GrayLevelVariance |
| original_firstorder_Median | original_glszm_HighGrayLevelZoneEmphasis |
| original_firstorder_Minimum | original_glszm_LargeAreaEmphasis |
| original_firstorder_Range | original_glszm_LargeAreaHighGrayLevelEmphasis |
| original_firstorder_RobustMeanAbsoluteDeviation | original_glszm_LargeAreaLowGrayLevelEmphasis |
| original_firstorder_RootMeanSquared | original_glszm_LowGrayLevelZoneEmphasis |
| original_firstorder_Skewness | original_glszm_SizeZoneNonUniformity |
| original_firstorder_TotalEnergy | original_glszm_SizeZoneNonUniformityNormalized |
| original_firstorder_Uniformity | original_glszm_SmallAreaEmphasis |
| original_firstorder_Variance | original_glszm_SmallAreaHighGrayLevelEmphasis |
| original_glcm_Autocorrelation | original_glszm_SmallAreaLowGrayLevelEmphasis |
| original_glcm_JointAverage | original_glszm_ZoneEntropy |
| original_glcm_ClusterProminence | original_glszm_ZonePercentage |
| original_glcm_ClusterShade | original_glszm_ZoneVariance |
| original_glcm_ClusterTendency | original_gldm_DependenceEntropy |
| original_glcm_Contrast | original_gldm_DependenceNonUniformity |
| original_glcm_Correlation | original_gldm_DependenceNonUniformityNormalized |
| original_glcm_DifferenceAverage | original_gldm_DependenceVariance |
| original_glcm_DifferenceEntropy | original_gldm_GrayLevelNonUniformity |

| | |
|---|---|
| original_glcm_DifferenceVariance | original_gldm_GrayLevelVariance |
| original_glcm_JointEnergy | original_gldm_HighGrayLevelEmphasis |
| original_glcm_JointEntropy | original_gldm_LargeDependenceEmphasis |
| original_glcm_Imc1 | original_gldm_LargeDependenceHighGrayLevelEmphasis |
| original_glcm_Imc2 | original_gldm_LargeDependenceLowGrayLevelEmphasis |
| original_glcm_Idm | original_gldm_LowGrayLevelEmphasis |
| original_glcm_Idmn | original_gldm_SmallDependenceEmphasis |
| original_glcm_Id | original_gldm_SmallDependenceHighGrayLevelEmphasis |
| original_glcm_Idn | original_gldm_SmallDependenceLowGrayLevelEmphasis |

**Table S2. Univariable and multivariable analyses in clinical indicators associated with invasiveness in multimodal training cohort.**

| Characteristics | pre-invasive (254) | invasive (507) | Univariable analysis HR (95%CI) | P value | Multivariable analysis HR (95%CI) | P value |
|---|---|---|---|---|---|---|
| Age, years | 53 (42-62) | 60 (53-66) | 1.06 (1.04-1.07) | <0.001 | 1.10 (1.04-1.17) | 0.001 |
| Sex | | | 0.44 (0.32-0.62) | <0.001 | 0.73 (0.29-1.81) | 0.493 |
| Male | 63 (24.8) | 216 (42.6) | | | | |
| Female | 191 (75.2) | 291 (57.4) | | | | |
| Smoking history | | | 1.26 (0.55-2.91) | 0.583 | | |
| Yes | 43 (16.9) | 98 (19.3) | | | | |
| No | 211 (83.1) | 409 (80.7) | | | | |
| LDH, U/L | 181 (160-201) | 181 (162-201) | 1.00 (0.99-1.01) | 0.850 | | |
| Hematologic indicators, median (IQR) | | | | | | |
| WBCs, $\times10^9$/L | 5.27 (4.39-6.46) | 5.27 (4.48-6.49) | 0.99 (0.90-1.08) | 0.779 | | |
| RBCs, $\times10^9$/L | 4.21 (3.91-4.54) | 4.29 (3.95-4.58) | 1.08 (0.80-1.45) | 0.636 | | |
| Hemoglobin, g/L | 126 (119-138) | 129 (120-140.75) | 1.01 (1.00-1.02) | 0.073 | | |
| HCT, % | 38.40 (36.20-42.30) | 39.10 (36.50-42.40) | 1.02 (0.99-1.06) | 0.216 | | |
| MCV, fl | 92.10 (89.40-94.70) | 92.60 (89.80-95.40) | 1.02 (0.99-1.05) | 0.222 | | |
| MCH, pg | 30.30 (29.40-31.40) | 30.70 (29.60-31.70) | 1.09 (1.01-1.17) | 0.031 | 1.12 (0.94-1.34) | 0.216 |
| MCHC, g/L | 328 (322-336) | 331 (323-338) | 1.02 (1.00-1.03) | 0.020 | 1.00 (0.97-1.03) | 0.927 |
| Platelets, $\times10^9$/L | 213 (177-257) | 206 (172-242) | 1.00 (0.99-1.00) | 0.061 | | |
| Neutrophils, $\times10^9$/L | 2.91 (2.18-3.72) | 2.99 (2.40-3.82) | 1.00 (0.89-1.11) | 0.965 | | |
| Lymphocytes, $\times10^9$/L | 1.73 (1.47-2.16) | 1.69 (1.35-2.10) | 0.85 (0.65-1.11) | 0.222 | | |
| NLR | 1.65 (1.19-2.26) | 1.76 (1.34-2.25) | 1.06 (0.93-1.20) | 0.390 | | |
| Monocytes, $\times10^9$/L | 0.4 (0.3-0.5) | 0.4 (0.3-0.5) | 2.76 (0.97-7.81) | 0.056 | | |
| Eosinophils, $\times10^9$/L | 0.10 (0.06-0.16) | 0.10 (0.07-0.19) | 5.62 (1.29-24.49) | 0.021 | 20.96 (1.18-373.04) | 0.038 |
| Basophils, $\times10^9$/L | 0.03 (0.02-0.04) | 0.03 (0.02-0.04) | 0.35 (0-368.03) | 0.765 | | |
| PDW, fl | 12.70 (11.30-14.35) | 13.20 (11.70-15.70) | 1.09 (1.02-1.16) | 0.016 | 1.02 (0.92-1.12) | 0.753 |
| MPV, fl | 10.50 (9.70-11.20) | 10.30 (9.30-11.20) | 1.01 (0.96-1.06) | 0.760 | | |
| Liver function indicators, median (IQR) | | | | | | |
| AST, U/L | 20 (17-23) | 20 (17-24) | 1.00 (0.98-1.01) | 0.944 | | |
| ALT, U/L | 16 (12-22) | 17 (12-25) | 1.01 (0.99-1.02) | 0.319 | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| ALP, U/L | 66.00 (51.25-77.75) | 69.00 (56.00-82.25) | 1.00 (1.00-1.01) | 0.572 | | |
| γ-GT, U/L | 17.00 (12.00-26.00) | 19.00 (14.00-28.75) | 1.00 (1.00-1.00) | 0.559 | | |
| TBA, μmol/L | 3.64 (2.40-6.44) | 4.00 (2.50-6.18) | 1.00 (0.97-1.02) | 0.779 | | |
| TBIL, μmol/L | 12.23 (9.30-15.57) | 12.10 (9.30-15.40) | 1.00 (0.97-1.03) | 0.875 | | |
| DBIL, μmol/L | 3.80 (2.90-5.00) | 3.90 (2.80-5.10) | 1.02 (0.94-1.11) | 0.560 | | |
| Total protein, g/L | 66.00 (63.00-70.18) | 65.20 (61.90-68.70) | 0.97 (0.94-1.00) | 0.029 | 0.99 (0.94-1.04) | 0.619 |
| Albumin, g/L | 41.40 (39.10-43.70) | 40.65 (38.90-42.90) | 0.94 (0.89-0.98) | 0.006 | 0.94 (0.86-1.04) | 0.216 |
| Globin, g/L | 25.00 (23.20-26.90) | 24.20 (22.20-26.80) | 0.96 (0.91-1.00) | 0.055 | | |
| A/G | 1.66 (1.55-1.80) | 1.70 (1.51-1.86) | 1.34 (0.71-2.53) | 0.374 | | |
| Renal function indicators, median (IQR) | | | | | | |
| BUN, mmol/L | 5.05 (4.33-6.21) | 5.42 (4.49-6.56) | 1.15 (1.03-1.27) | 0.010 | 0.94 (0.79-1.12) | 0.475 |
| Serum creatinine, μmol/L | 59.00 (51.40-68.00) | 64.00 (54.15-74.05) | 1.02 (1.01-1.03) | 0.003 | 1.03 (0.98-1.08) | 0.220 |
| UA, μmol/L | 293.00 (245.00-345.00) | 300.90 (247.00-361.50) | 1.00 (1.00-1.00) | 0.313 | | |
| Creatine kinase, U/L | 76 (58-101) | 72 (55-94) | 1.00 (1.00-1.00) | 0.776 | | |
| eGFR, mL/min per 1.73 $m^2$ | 101.06 (92.67-111.64) | 96.29 (89.39-103.14) | 0.97 (0.95-0.98) | <0.001 | 1.06 (0.99-1.13) | 0.106 |
| Blood glucose and lipids, median (IQR) | | | | | | |
| Glucose, mmol/L | 4.85 (4.50-5.33) | 5.00 (4.60-5.48) | 1.20 (1.02-1.42) | 0.032 | 1.04 (0.82-1.32) | 0.752 |
| TCh, mmol/L | 4.52 (4.00-5.18) | 4.56 (4.00-5.08) | 1.01 (0.83-1.22) | 0.920 | | |
| TG, mmol/L | 1.05 (0.77-1.53) | 1.20 (0.88-1.70) | 1.28 (1.02-1.61) | 0.032 | 1.16 (0.77-1.75) | 0.485 |
| HDLC, mmol/L | 1.27 (1.05-1.53) | 1.16 (0.99-1.44) | 0.44 (0.26-0.72) | 0.001 | 1.18 (0.50-2.81) | 0.710 |
| LDLC, mmol/L | 2.64 (2.19-3.17) | 2.68 (2.24-3.18) | 1.02 (0.81-1.28) | 0.861 | | |
| Coagulation function indicators, median (IQR) | | | | | | |
| TT, seconds | 16.90 (16.20-17.80) | 17.30 (16.40-18.20) | 1.18 (1.05-1.33) | 0.005 | 1.07 (0.84-1.36) | 0.581 |
| FIB, g/l | 2.64 (2.37-3.02) | 2.78 (2.42-3.22) | 1.44 (1.12-1.84) | 0.004 | 1.33 (0.87-2.05) | 0.190 |
| APTT, seconds | 27.90 (25.50-33.50) | 31.30 (26.20-35.60) | 1.05 (1.02-1.08) | 0.002 | 0.98 (0.93-1.03) | 0.437 |
| INR | 0.98 (0.95-1.06) | 1.00 (0.95-1.06) | 2.12 (0.38-12.00) | 0.393 | | |
| PT, seconds | 11.80 (11.10-12.80) | 12.30 (11.40-12.90) | 1.21 (1.06-1.39) | 0.006 | 1.06 (0.83-1.36) | 0.624 |

Data are presented as median (IQR) for continuous variables and n (%) for category variables.
HR, hazard ratio; CI, confidence interval; LDH, lactate dehydrogenase; WBC, white blood cell count; RBC, red blood cell count; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; NLR, neutrophil-to-lymphocyte ratio; PDW, platelet distribution width; MPV, mean platelet volume; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; γ-GT, γ-glutamyl transpeptidase; TBA, total bile acid; TBIL, toal bilirubin; DBIL, direct bilirubin; A/G, albumin/globin; BUN, blood urea nitrogen; UA, urine acid; eGFR, estimated glomerular filtration rate; TCh, total cholesterol; TG, triglyceride; HDLC, high density lipoprotein cholesterol; LDLC, low density lipoprotein cholesterin; TT, thrombin time; FIB, fibrinogen; APTT, activated partial thromboplastin time; INR, international normalized ratio; PT: prothrombin time.

**Table S3. Characteristics of demographic information and clinical indicators of participants in radiology testing, pathology testing, and prospective validation cohorts.**

| Characteristics | Radiology testing cohort (433) | Pathology testing cohort (230) | Prospective validation cohort (114) |
|---|---|---|---|
| Age, years | 56 (48-64) | 57.5 (50-65) | 58 (52-65) |
| Sex | | | |
| Male | 147 (33.9) | 88 (38.3) | 39 (34.2) |
| Female | 286 (66.1) | 142 (61.7) | 75 (65.8) |
| Smoking history | | | |
| Yes | 361 (83.4) | 189 (82.2) | 92 (80.7) |
| No | 72 (16.6) | 41 (17.8) | 22 (19.3) |
| LDH, U/L | 183 (163-205) | 184 (162-203) | 187 (169-204) |
| Hematologic indicators, median (IQR) | | | |
| WBCs, $\times10^9$/L | 5.15 (4.18-6.18) | 5.27 (4.34-6.28) | 5.14 (4.43-6.14) |
| RBCs, $\times10^9$/L | 4.16 (3.87-4.51) | 4.22 (3.98-4.56) | 4.20 (3.97-4.54) |
| Hemoglobin, g/L | 126 (117-137) | 128 (119-136) | 127 (119-138) |
| HCT, % | 37.50 (35.00-40.40) | 0.42 (0.39-34.70) | 38.00 (35.80-41.40) |
| MCV, fl | 90.80 (88.60-93.40) | 92.50 (89.90-95.00) | 90.65 (88.50-94.30) |
| MCH, pg | 30.70 (29.70-31.60) | 30.40 (29.30-31.30) | 30.30 (29.40-31.40) |
| MCHC, g/L | 337 (331-342) | 328 (321-335) | 331.50 (326.00-339.00) |
| Platelets, $\times10^9$/L | 205 (170-243) | 211 (173-250) | 199 (173-239) |
| Neutrophils, $\times10^9$/L | 2.90 (2.20-3.50) | 2.97 (2.24-3.63) | 2.71 (2.20-3.44) |
| Lymphocytes, $\times10^9$/L | 1.68 (1.39-2.02) | 1.70 (1.35-2.03) | 1.71 (1.44-2.10) |
| NLR | 1.71 (1.29-2.13) | 1.75 (1.38-2.16) | 1.48 (1.27-2.00) |
| Monocytes, $\times10^9$/L | 0.40 (0.30-0.50) | 0.42 (0.32-0.51) | 0.41 (0.35-0.50) |
| Eosinophils, $\times10^9$/L | 0.10 (0.07-0.18) | 0.11 (0.07-0.19) | 0.10 (0.08-0.18) |
| Basophils, $\times10^9$/L | 0.02 (0.00-0.03) | 0.02 (0.01-0.04) | 0.02 (0.01-0.04) |
| PDW, fl | 13.00 (12.50-13.50) | 12.90 (11.80-13.90) | 12.75 (12.30-13.40) |
| MPV, fl | 9.90 (8.70-10.80) | 10.55 (9.80-11.50) | 10.30 (9.70-11.00) |
| Liver function indicators, median (IQR) | | | |
| AST, U/L | 21 (18-25) | 19 (16-23) | 21 (19-25) |
| ALT, U/L | 18 (13-27) | 15 (11-22) | 20 (15-26) |
| ALP, U/L | 62.00 (51.00-76.00) | 67.00 (58.00-82.00) | 69.00 (57.00-87.00) |
| γ-GT, U/L | 16.00 (12.00-23.00) | 17.00 (13.00-23.00) | 17.00 (14.00-27.00) |
| TBA, μmol/L | 4.30 (2.70-6.70) | 4.27 (2.31-6.28) | 4.30 (2.60-6.80) |
| TBIL, μmol/L | 12.10 (9.80-15.10) | 12.40 (9.20-15.70) | 11.50 (9.20-16.00) |
| DBIL, μmol/L | 4.50 (3.50-5.60) | 4.00 (2.90-5.30) | 4.20 (3.30-6.30) |
| Total protein, g/L | 64.10 (61.00-67.80) | 64.70 (62.30-69.20) | 64.35 (61.10-68.20) |
| Albumin, g/L | 40.20 (38.40-42.50) | 40.30 (37.80-42.80) | 40.45 (38.30-42.60) |
| Globin, g/L | 23.80 (21.50-26.20) | 25.10 (22.90-27.10) | 24.10 (21.70-26.10) |
| A/G | 1.70 (1.60-1.90) | 1.62 (1.50-1.78) | 1.70 (1.60-1.80) |
| Renal function indicators, median (IQR) | | | |
| BUN, mmol/L | 5.14 (4.30-6.02) | 5.39 (4.39-6.27) | 5.22 (4.45-6.15) |
| Serum creatinine, μmol/L | 60.20 (52.80-72.80) | 62.00 (54.00-74.00) | 60.80 (54.40-71.10) |

| | | | |
|---|---|---|---|
| UA, μmol/L | 305.20 (258.00-359.00) | 296.00 (246.00-352.80) | 285.20 (234.95-352.20) |
| Creatine kinase, U/L | 75 (56-101) | 76 (55-105) | 74 (59-108) |
| eGFR, mL/min per 1.73 $m^2$ | 99.26 (90.16-107.83) | 98.31 (91.00-104.01) | 98.47 (89.88-103.77) |
| Blood glucose and lipids, median (IQR) | | | |
| Glucose, mmol/L | 4.80 (4.50-5.30) | 4.88 (4.54-5.26) | 4.90 (4.60-5.30) |
| TCh, mmol/L | 4.52 (3.95-5.10) | 4.40 (3.72-4.80) | 4.66 (4.05-5.32) |
| TG, mmol/L | 1.10 (0.78-1.60) | 1.17 (0.89-1.73) | 1.19 (0.87-1.81) |
| HDLC, mmol/L | 1.26 (1.05-1.54) | 1.18 (0.94-1.36) | 1.21 (1.06-1.53) |
| LDLC, mmol/L | 2.55 (2.11-3.05) | 2.46 (1.95-2.92) | 2.67 (2.19-3.21) |
| Coagulation function indicators, median (IQR) | | | |
| TT, seconds | 17.80 (17.10-18.50) | 17.30 (16.60-18.15) | 17.90 (17.25-18.55) |
| FIB, g/l | 2.74 (2.46-3.11) | 2.71 (2.31-3.07) | 2.96 (2.58-3.34) |
| APTT, seconds | 35.30 (33.30-37.50) | 28.35 (25.50-34.15) | 34.95 (33.70-37.55) |
| INR | 1.09 (1.05-1.14) | 1.03 (0.97-1.09) | 0.95 (0.91-1.01) |
| PT, seconds | 13.10 (12.70-13.50) | 12.10 (11.30-12.90) | 12.60 (12.25-12.90) |

Data are presented as median (IQR) for continuous variables and n (%) for category variables.
HR, hazard ratio; CI, confidence interval; LDH, lactate dehydrogenase; WBC, white blood cell count; RBC, red blood cell count; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; NLR, neutrophil-to-lymphocyte ratio; PDW, platelet distribution width; MPV, mean platelet volume; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; γ-GT, γ-glutamyl transpeptidase; TBA, total bile acid; TBIL, toal bilirubin; DBIL, direct bilirubin; A/G, albumin/globin; BUN, blood urea nitrogen; UA, urine acid; eGFR, estimated glomerular filtration rate; TCh, total cholesterol; TG, triglyceride; HDLC, high density lipoprotein cholesterol; LDLC, low density lipoprotein cholesterin; TT, thrombin time; FIB, fibrinogen; APTT, activated partial thromboplastin time; INR, international normalized ratio; PT: prothrombin time.

**Table S4. Proportion of invasive classification for pathologic images in three cohorts identified by EfficientNet B5 model**

| Cohort | Invasion status | Classification | | |
|---|---|---|---|---|
| | | AIS, % | MIA, % | IA, % |
| Multimodal training cohort (761) | AIS (84) | 22.53 (15.80-34.70) | 6.02 (3.29-9.00) | 3.27 (1.47-8.04) |
| | MIA (170) | 22.59 (14.64-34.46) | 11.93 (6.38-19.82) | 3.59 (0.81-9.05) |
| | IA (507) | 18.72 (11.88-28.85) | 17.63 (8.93-26.93) | 20.39 (9.95-38.10) |
| Pathology testing cohort (230) | AIS (67) | 23.82 (16.41-34.25) | 4.60 (2.46-8.47) | 2.30 (1.17-7.81) |
| | MIA (63) | 29.28 (18.78-38.90) | 9.30 (5.58-14.34) | 3.52 (1.37-9.55) |
| | IA (100) | 22.81 (12.65-34.74) | 14.84 (9.52-22.98) | 17.51 (6.48-32.92) |
| Prospective validation cohort (114) | AIS (17) | 14.49 (10.16-21.45) | 15.63 (5.16-21.79) | 1.19 (0.20-2.91) |
| | MIA (20) | 28.07 (17.69-33.75) | 18.92 (12.57-33.26) | 1.97 (0.74-5.17) |
| | IA (77) | 14.90 (10.27-24.20) | 21.40 (14.31-33.58) | 19.93 (8.16-30.99) |

Data are presented as median (IQR).
AIS, adenocarcinoma in situ; MIA, minimally invasive adenocarcinoma; IA, invasive adenocarcinoma.

**Table S5. NRI test for prediction improvements of dual-/multi-modality models compared to single-R or single-P models in multimodal training and prospective validation cohorts**

| Initial model | Dual-/Multi-modality model | Multimodal training cohort | | Prospective validation cohort | |
|---|---|---|---|---|---|
| | | NRI (95% CI) | P value | NRI (95% CI) | P value |
| Single-R model | Dual-RC model | 0.0277 (0.0002-0.0555) | 0.0515 | 0.0270 (-0.0364-0.0905) | 0.4038 |
| | Dual-RP model | 0.0652 (0.0258-0.1046) | 0.0012 | 0.0530 (-0.0197-0.1257) | 0.1532 |
| | Multi-RPC model | 0.0296 (-0.0096-0.0689) | 0.1386 | 0.0660 (-0.0108-0.1428) | 0.0921 |
| Single-P model | Dual-PC model | 0.1265 (-0.0237-0.2766) | 0.0988 | -0.5855 (-0.9571- -0.2139) | 0.0020 |
| | Dual-RP model | 0.1403 (0.0892-0.1914) | <0.0001 | 0.1720 (0.0518-0.2922) | 0.0050 |
| | Multi-RPC model | 0.1285 (0.0741-0.1828) | <0.0001 | 0.1580 (0.0281-0.2878) | 0.0171 |

Data were metric value with 95% CI provided in parentheses.

NRI, net reclassification improvement; Single-R model, single-modality radiomic model; Single-P model, single-modality pathologic model; Dual-RC model, radiomics + clinical indicators dual-modality model; Dual-PC model, pathology + clinical indicators dual-modality model; Dual-RP model, radiomics + pathology dual-modality model; Multi-RPC model, radiomics + pathology + clinical indicators multi-modality model.

**Table S6. IDI test for prediction improvements of dual-RC, dual-RP and multi-RPC models compared to single-R model, and dual-PC, dual-RP and multi-RPC models compared to single-P model in multimodal training and prospective validation cohorts**

| Initial model | Dual-/Multi-modality model | Multimodal training cohort | | Prospective validation cohort | |
|---|---|---|---|---|---|
| | | IDI (95% CI) | P value | IDI (95% CI) | P value |
| Single-R model | Dual-RC model | 0.0073 (0.0016-0.0130) | 0.0125 | -0.0167 (-0.0345-0.0011) | 0.0667 |
| | Dual-RP model | 0.0429 (0.0266-0.0593) | <0.0001 | 0.0402 (-0.0037-0.0841) | 0.0724 |
| | Multi-RPC model | 0.0470 (0.0301-0.0639) | <0.0001 | 0.0238 (-0.0252-0.0728) | 0.3415 |
| Single-P model | Dual-PC model | 0.0190 (0.0088-0.0292) | 0.0003 | -0.0194 (-0.0459-0.0070) | 0.1502 |
| | Dual-RP model | 0.1402 (0.113-0.1674) | <0.0001 | 0.1947 (0.1215-0.2679) | <0.0001 |
| | Multi-RPC model | 0.1443 (0.1168-0.1717) | <0.0001 | 0.1782 (0.1070-0.2495) | <0.0001 |

Data were metric value with 95% CI provided in parentheses.

IDI, integrated discrimination improvement; Single-R model, single-modality radiomic model; Single-P model, single-modality pathologic model; Dual-RC model, radiomics + clinical indicators dual-modality model; Dual-PC model, pathology + clinical indicators dual-modality model; Dual-RP model, radiomics + pathology dual-modality model; Multi-RPC model, radiomics + pathology + clinical indicators multi-modality model.

**Table S7. AIC test for prediction improvements of multi-RPC model compared to single-/dual-modality models in the multimodal training cohort**

| Models | AIC value |
|---|---|
| **Single-P model** | 656.47 |
| **Single-R model** | 565.44 |
| **Dual-RC model** | 560.47 |
| **Dual-PC model** | 650.32 |
| **Dual-RP model** | 520.55 |
| **Multi-RPC model** | 517.85 |

Data were metric value with 95% CI provided in parentheses.

AIC, Akaike information criterion; Single-R model, single-modality radiomic model; Single-P model, single-modality pathologic model; Dual-RC model, radiomics + clinical indicators dual-modality model; Dual-PC model, pathology + clinical indicators dual-modality model; Dual-RP model, radiomics + pathology dual-modality model; Multi-RPC model, radiomics + pathology + clinical indicators multi-modality model.

**Table S8. Predictive performance of the models to distinguish AIS and MIA**

| | Multimodal training cohort | Radiology testing cohort | Pathology testing cohort | Prospective validation cohort |
|---|---|---|---|---|
| Single-R model | | | | |
| AUC | 0.660 (0.598-0.718) | 0.724 (0.668-0.775) | - | 0.618 (0.444-0.772) |
| Accuracy | 0.680 (0.618-0.737) | 0.696 (0.639-0.749) | - | 0.622 (0.448-0.775) |
| Sensitivity | 0.544 (0.466-0.621) | 0.567 (0.494-0.638) | - | 0.800 (0.563-0.943) |
| Specificity | 0.738 (0.631-0.828) | 0.837 (0.745-0.906) | - | 0.471 (0.230-0.722) |
| PPV | 0.807 (0.740-0.860) | 0.880 (0.820-0.922) | - | 0.640 (0.519-0.745) |
| NPV | 0.446 (0.395-0.498) | 0.478 (0.433-0.524) | - | 0.667 (0.421-0.846) |
| Single-P model | | | | |
| AUC | 0.658 (0.596-0.716) | - | 0.680 (0.592-0.759) | 0.685 (0.512-0.828) |
| Accuracy | 0.684 (0.623-0.741) | - | 0.600 (0.511-0.685) | 0.622 (0.448-0.775) |
| Sensitivity | 0.568 (0.490-0.644) | - | 0.841 (0.727-0.921) | 1.000 (0.832-1.000) |
| Specificity | 0.750 (0.644-0.838) | - | 0.478 (0.354-0.603) | 0.353 (0.142-0.617) |
| PPV | 0.821 (0.755-0.871) | - | 0.602 (0.540-0.661) | 0.645 (0.561-0.721) |
| NPV | 0.463 (0.411-0.516) | - | 0.762 (0.632-0.856) | 1.000 (1.000-1.000) |
| Dual-RC model | | | | |
| AUC | 0.657 (0.595-0.716) | 0.730 (0.675-0.781) | - | 0.597 (0.423-0.755) |
| Accuracy | 0.676 (0.614-0.733) | 0.699 (0.643-0.752) | - | 0.541 (0.369-0.705) |
| Sensitivity | 0.444 (0.368-0.522) | 0.649 (0.578-0.716) | - | 1.000 (0.832-1.000) |
| Specificity | 0.833 (0.736-0.906) | 0.750 (0.649-0.834) | - | 0.235 (0.068-0.499) |
| PPV | 0.843 (0.763-0.899) | 0.846 (0.791-0.888) | - | 0.606 (0.542-0.667) |
| NPV | 0.427 (0.387-0.468) | 0.504 (0.448-0.560) | - | 1.000 (1.000-1.000) |
| Dual-PC model | | | | |
| AUC | 0.647 (0.585-0.706) | - | 0.679 (0.591-0.758) | 0.641 (0.467-0.792) |
| Accuracy | 0.644 (0.582-0.703) | - | 0.615 (0.526-0.699) | 0.622 (0.448-0.775) |
| Sensitivity | 0.527 (0.449-0.604) | - | 0.778 (0.655-0.873) | 0.750 (0.509-0.913) |

| | | | | |
|---|---|---|---|---|
| Specificity | 0.786 (0.683-0.868) | - | 0.522 (0.397-0.646) | 0.588 (0.329-0.816) |
| PPV | 0.832 (0.762-0.884) | - | 0.605 (0.536-0.670) | 0.682 (0.535-0.800) |
| NPV | 0.452 (0.405-0.500) | - | 0.714 (0.599-0.807) | 0.667 (0.459-0.825) |
| Dual-RP model | | | | |
| AUC | 0.675 (0.613-0.732) | - | - | 0.674 (0.500-0.818) |
| Accuracy | 0.676 (0.614-0.733) | - | - | 0.541 (0.369-0.705) |
| Sensitivity | 0.527 (0.449-0.604) | - | - | 0.600 (0.361-0.809) |
| Specificity | 0.786 (0.683-0.868) | - | - | 0.765 (0.501-0.932) |
| PPV | 0.832 (0.762-0.884) | - | - | 0.750 (0.542-0.884) |
| NPV | 0.452 (0.405-0.500) | - | - | 0.619 (0.472-0.747) |
| Multi-RPC model | | | | |
| AUC | 0.673 (0.612-0.731) | - | - | 0.665 (0.491-0.811) |
| Accuracy | 0.672 (0.610-0.729) | - | - | 0.595 (0.421-0.753) |
| Sensitivity | 0.544 (0.466-0.621) | - | - | 0.600 (0.361-0.809) |
| Specificity | 0.762 (0.657-0.848) | - | - | 0.765 (0.501-0.932) |
| PPV | 0.821 (0.754-0.874) | - | - | 0.750 (0.542-0.884) |
| NPV | 0.454 (0.404-0.505) | - | - | 0.619 (0.472-0.747) |

Data are presented as mean (95% CI).

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; Single-R model, single-modality radiomic model; Single-P model, single-modality pathologic model; Dual-RC model, radiomics + clinical indicators dual-modality model; Dual-PC model, pathology + clinical indicators dual-modality model; Dual-RP model, radiomics + pathology dual-modality model; Multi-RPC model, radiomics + pathology + clinical indicators multi-modality model.