

**Supplementary Table 1 Multivariate Logistic Regression Analysis of Clinical Predictors for Lymph Node Metastasis (LNM)**

Characteristic		OR [95% CI]	P
CRC_location	Colon	1 (reference)	n/a
	Rectum	1.84 [0.87-3.95]	0.114
CEA (ng/mL)	<5	1 (reference)	n/a
	>5	1.11 [0.46-2.64]	0.815
Age	<60	1 (reference)	n/a
	60-69	0.59 [0.20-1.68]	0.332
	70-79	0.24 [0.09-0.63]	0.004
	>80	0.35 [0.09-1.20]	0.100
T_Stage	T3	1 (reference)	n/a
	T4	1.38 [0.59-3.28]	0.462

Odds Ratios (OR) and 95% Confidence Intervals (CI) reflect the association between each characteristic and LNM status, relative to the reference category. P-values assess the statistical significance of the ORs. Abbreviations: CRC, colorectal cancer; OR, odds ratio; CI, confidence interval; CEA, carcinoembryonic antigen.

**Supplementary Table 2 Detailed Performance Metrics (Mean  $\pm$  SD) for Lymph Node Metastasis Prediction Across 5-Fold Cross-Validation**

Category	Accuracy	Specificity	Sensitivity	NPV	PPV
CONCH	0.639 $\pm$ 0.076	0.415 $\pm$ 0.092	0.900 $\pm$ 0.069	0.823 $\pm$ 0.125	0.571 $\pm$ 0.053
CONCH ROI	0.621 $\pm$ 0.062	0.397 $\pm$ 0.082	0.884 $\pm$ 0.094	0.812 $\pm$ 0.146	0.559 $\pm$ 0.044
CONCH ROI-c	0.701 $\pm$ 0.080	0.676 $\pm$ 0.108	0.733 $\pm$ 0.093	0.746 $\pm$ 0.075	0.670 $\pm$ 0.078
CONCH c	0.768 $\pm$ 0.047	0.799 $\pm$ 0.110	0.737 $\pm$ 0.070	0.781 $\pm$ 0.037	0.770 $\pm$ 0.089
UNI2	0.607 $\pm$ 0.079	0.483 $\pm$ 0.094	0.751 $\pm$ 0.100	0.692 $\pm$ 0.101	0.557 $\pm$ 0.064
UNI2 ROI	0.629 $\pm$ 0.071	0.544 $\pm$ 0.084	0.736 $\pm$ 0.107	0.709 $\pm$ 0.093	0.581 $\pm$ 0.059
UNI2 ROI-c	0.729 $\pm$ 0.071	0.800 $\pm$ 0.129	0.651 $\pm$ 0.070	0.728 $\pm$ 0.049	0.754 $\pm$ 0.132
UNI2 c	0.669 $\pm$ 0.141	0.671 $\pm$ 0.201	0.666 $\pm$ 0.236	0.722 $\pm$ 0.157	0.646 $\pm$ 0.156

Models evaluated include: CONCH (CONCH v1.5 trained on slide-level labels), CONCH-c (CONCH v1.5 trained on case-level labels), CONCH-ROI (CONCH v1.5 trained on slide-level labels with tumor area annotations), CONCH-ROI-c (CONCH v1.5 trained on case-level labels with tumor area annotations), UNI2 (UNI2-h trained on slide-level labels), UNI2-c (UNI2-h trained on case-level labels), UNI2-ROI (UNI2-h trained on slide-level labels with tumor area annotations), and UNI2-ROI-c (UNI2-h trained on case-level labels with tumor area annotations).

**Supplementary Table 3 Per-Epoch Training Duration Across 5-Fold Cross-Validation and Normality Test Results.**

Category	Fold 1	Fold 2	Fold 3	Fold 4	Fold 5	P-value
CONCH	4.80	4.87	4.88	4.87	4.88	<b>0.0126</b>
CONCH c	4.19	4.23	4.10	3.96	3.99	0.435
CONCH ROI	2.85	2.87	2.93	2.97	2.91	0.7628
CONCH ROI-c	1.92	1.87	1.82	1.85	1.86	0.689
UNI2	28.60	28.79	28.66	28.48	28.76	0.7373
UNI2 c	27.21	26.76	26.90	26.33	27.03	0.766
UNI2 ROI	11.95	11.94	12.15	12.44	12.37	0.3188
UNI2 ROI-c	11.58	11.25	11.48	11.38	11.40	0.9809

This table provides a detailed breakdown of the per-epoch training duration (in seconds) for each of the eight model configurations across the five cross-validation folds. The final column displays the p-value from the Shapiro-Wilk test, which was performed to assess the normality of the five data points for each configuration. A p-value less than 0.05 (indicated in bold) suggests a significant deviation from a normal distribution, guiding the selection of a non-parametric statistical test (Mann-Whitney U test) for that comparison. For all other configurations ( $p \geq 0.05$ ), a parametric test (t-test) was deemed appropriate. Model abbreviations are defined as follows: CONCH, CONCH v1.5 slide-level; CONCH-c, CONCH v1.5 case-level; CONCH-ROI, CONCH v1.5 slide-level with ROI; CONCH-ROI-c, CONCH v1.5 case-level with ROI; UNI2, UNI2-h slide-level; UNI2-c, UNI2-h case-level; UNI2-ROI, UNI2-h slide-level with ROI; UNI2-ROI-c, UNI2-h case-level with ROI.

**Supplementary Table 4 Performance Comparison of Machine Learning Models for Lymph Node Metastasis Prediction (Mean  $\pm$  SD)**

model_name	Cohort	Accuracy	Sensitivity	Specificity	PPV	NPV	Precision	Recall	F1
AdaBoost	Cli.	0.585 $\pm$ 0.069	0.767 $\pm$ 0.091	0.428 $\pm$ 0.189	0.546 $\pm$ 0.072	0.676 $\pm$ 0.054	0.546 $\pm$ 0.072	0.767 $\pm$ 0.091	0.631 $\pm$ 0.031
AdaBoost	Cli.+Pat	0.754 $\pm$ 0.135	0.550 $\pm$ 0.331	0.929 $\pm$ 0.087	0.707 $\pm$ 0.407	0.730 $\pm$ 0.126	0.707 $\pm$ 0.407	0.550 $\pm$ 0.331	0.763 $\pm$ 0.097
ExtraTrees	Cli.	0.530 $\pm$ 0.017	0.300 $\pm$ 0.315	0.728 $\pm$ 0.279	0.291 $\pm$ 0.266	0.558 $\pm$ 0.038	0.291 $\pm$ 0.266	0.300 $\pm$ 0.315	0.478 $\pm$ 0.107
ExtraTrees	Cli.+Pat	0.785 $\pm$ 0.058	0.750 $\pm$ 0.132	0.814 $\pm$ 0.064	0.777 $\pm$ 0.057	0.801 $\pm$ 0.087	0.777 $\pm$ 0.057	0.750 $\pm$ 0.132	0.759 $\pm$ 0.080
GradientBoosting	Cli.	0.531 $\pm$ 0.032	0.583 $\pm$ 0.243	0.486 $\pm$ 0.217	0.498 $\pm$ 0.046	0.605 $\pm$ 0.089	0.498 $\pm$ 0.046	0.583 $\pm$ 0.243	0.517 $\pm$ 0.101
GradientBoosting	Cli.+Pat	0.731 $\pm$ 0.116	0.567 $\pm$ 0.351	0.872 $\pm$ 0.155	0.663 $\pm$ 0.392	0.737 $\pm$ 0.135	0.663 $\pm$ 0.392	0.567 $\pm$ 0.351	0.742 $\pm$ 0.072
KNN	Cli.	0.507 $\pm$ 0.050	0.500 $\pm$ 0.295	0.514 $\pm$ 0.309	0.379 $\pm$ 0.214	0.538 $\pm$ 0.063	0.379 $\pm$ 0.214	0.500 $\pm$ 0.295	0.534 $\pm$ 0.035
KNN	Cli.+Pat	0.608 $\pm$ 0.084	0.333 $\pm$ 0.204	0.843 $\pm$ 0.178	0.756 $\pm$ 0.250	0.599 $\pm$ 0.064	0.756 $\pm$ 0.250	0.333 $\pm$ 0.204	0.411 $\pm$ 0.191
LR	Cli.	0.577 $\pm$ 0.061	0.483 $\pm$ 0.379	0.657 $\pm$ 0.340	0.709 $\pm$ 0.270	0.641 $\pm$ 0.114	0.709 $\pm$ 0.270	0.483 $\pm$ 0.379	0.442 $\pm$ 0.230
LR	Cli.+Pat	0.823 $\pm$ 0.034	0.817 $\pm$ 0.091	0.828 $\pm$ 0.064	0.807 $\pm$ 0.043	0.846 $\pm$ 0.064	0.807 $\pm$ 0.043	0.817 $\pm$ 0.091	0.809 $\pm$ 0.042
LightGBM	Cli.	0.523 $\pm$ 0.051	0.583 $\pm$ 0.132	0.471 $\pm$ 0.119	0.486 $\pm$ 0.048	0.571 $\pm$ 0.056	0.486 $\pm$ 0.048	0.583 $\pm$ 0.132	0.526 $\pm$ 0.073
LightGBM	Cli.+Pat	0.731 $\pm$ 0.116	0.483 $\pm$ 0.279	0.943 $\pm$ 0.078	0.716 $\pm$ 0.414	0.694 $\pm$ 0.093	0.716 $\pm$ 0.414	0.483 $\pm$ 0.279	0.715 $\pm$ 0.063
MLP	Cli.	0.638 $\pm$ 0.124	0.450 $\pm$ 0.336	0.800 $\pm$ 0.138	0.607 $\pm$ 0.202	0.658 $\pm$ 0.134	0.607 $\pm$ 0.202	0.450 $\pm$ 0.336	0.481 $\pm$ 0.281
MLP	Cli.+Pat	0.762 $\pm$ 0.074	0.683 $\pm$ 0.091	0.829 $\pm$ 0.082	0.776 $\pm$ 0.097	0.754 $\pm$ 0.064	0.776 $\pm$ 0.097	0.683 $\pm$ 0.091	0.725 $\pm$ 0.086
NaiveBayes	Cli.	0.523 $\pm$ 0.080	0.700 $\pm$ 0.173	0.372 $\pm$ 0.283	0.509 $\pm$ 0.090	0.558 $\pm$ 0.064	0.509 $\pm$ 0.090	0.700 $\pm$ 0.173	0.572 $\pm$ 0.034
NaiveBayes	Cli.+Pat	0.746 $\pm$ 0.121	0.633 $\pm$ 0.366	0.843 $\pm$ 0.093	0.621 $\pm$ 0.348	0.767 $\pm$ 0.143	0.621 $\pm$ 0.348	0.633 $\pm$ 0.366	0.781 $\pm$ 0.053
RandomForest	Cli.	0.554 $\pm$ 0.044	0.467 $\pm$ 0.336	0.629 $\pm$ 0.283	0.425 $\pm$ 0.243	0.600 $\pm$ 0.086	0.425 $\pm$ 0.243	0.467 $\pm$ 0.336	0.528 $\pm$ 0.130
RandomForest	Cli.+Pat	0.777 $\pm$ 0.042	0.667 $\pm$ 0.212	0.871 $\pm$ 0.146	0.864 $\pm$ 0.135	0.775 $\pm$ 0.100	0.864 $\pm$ 0.135	0.667 $\pm$ 0.212	0.720 $\pm$ 0.097
SVM	Cli.	0.608 $\pm$ 0.042	0.517 $\pm$ 0.285	0.686 $\pm$ 0.251	0.679 $\pm$ 0.195	0.643 $\pm$ 0.062	0.679 $\pm$ 0.195	0.517 $\pm$ 0.285	0.505 $\pm$ 0.203
SVM	Cli.+Pat	0.823 $\pm$ 0.044	0.833 $\pm$ 0.084	0.814 $\pm$ 0.120	0.810 $\pm$ 0.114	0.857 $\pm$ 0.053	0.810 $\pm$ 0.114	0.833 $\pm$ 0.084	0.814 $\pm$ 0.038
XGBoost	Cli.	0.561 $\pm$ 0.044	0.500 $\pm$ 0.312	0.614 $\pm$ 0.345	0.580 $\pm$ 0.107	0.607 $\pm$ 0.040	0.580 $\pm$ 0.107	0.500 $\pm$ 0.312	0.476 $\pm$ 0.130
XGBoost	Cli.+Pat	0.746 $\pm$ 0.127	0.567 $\pm$ 0.346	0.900 $\pm$ 0.120	0.685 $\pm$ 0.398	0.738 $\pm$ 0.130	0.685 $\pm$ 0.398	0.567 $\pm$ 0.346	0.758 $\pm$ 0.085

SVM, Support Vector Machines; LightGBM, Light Gradient Boosting Machine; MLP, Multilayer Perceptron. Cli., Models trained using only clinical features. Cli.+Pat., Models trained using combined clinical and pathology features.