

## **Supplementary Material**

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**Table S1. RTOG/EORTC radiotherapy-induced acute rectal toxicitie morbidity scoring criteria.**

| <b>Grade 0</b> | <b>Grade 1</b>                                                                                                                                                                                                              | <b>Grade 2</b>                                                                                                                                                                  | <b>Grade 3</b>                                                                                                                                                                                                                             | <b>Grade 4</b>                                                                                                                                                                             |
|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| No change      | Increased frequency or change in quality of bowel habits not requiring medication/rectal discomfort not requiring analgesics (Mild diarrhea, mild cramps, 3-5 bowel movements per day,)/slight rectal discharge or bleeding | Diarrhea requiring parasympatholytic drugs (more than 5 bowel movements per day)/mucous discharge not necessitating sanitary pads/rectal or abdominal pain requiring analgesics | Diarrhea requiring parenteral support/severe mucous or blood discharge necessitating sanitary pads/abdominal distention (flat plate radiograph demonstrates distended bowel loops)/obstruction or bleeding requiring surgical intervention | Acute or subacute obstruction, fistula, perforation, ecrosis or sinus tract; GI bleeding requiring transfusion; abdominal pain or tenesmus requiring tube decompression or bowel diversion |

**Table S2. Extracted candidate features and selected features.**

| Type of features              | Candidate features<br>(n=1,449)                                                                                                                                                                                                                                                  | Selected model features                                   |                                            |                   |                               |
|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|--------------------------------------------|-------------------|-------------------------------|
|                               |                                                                                                                                                                                                                                                                                  | Dosimomics<br>(n=9)                                       | Radiomics<br>(n=9)                         | Clinical<br>(n=6) | Combined<br>(n=12)            |
| Dosimomics features (n=1,288) |                                                                                                                                                                                                                                                                                  |                                                           |                                            |                   |                               |
| Dosimomics features           | FOS, GLCM, GLRLM, GLSZM, NGTDM, and GLDM                                                                                                                                                                                                                                         | FOS (n=1), GLSZM (n=1), and GLDM (n=3)                    |                                            |                   | GLDM (n=3) and GLCM (n=1)     |
| Dosimetric features           | Whole Rectum V5, V10, V15, V20, V25, V30, V35, V40, V45, V50, V55, maximum dose, minimum dose, and average dose; Whole Rectum D0.1cc, D1cc, D2cc, D5cc, and D10cc, maximum dose, minimum dose, and average dose                                                                  | D0.1cc <sub>max</sub> , V50, V45, and D1cc <sub>max</sub> |                                            |                   | D0.1cc <sub>max</sub> and V45 |
| Radiomics features (n=135)    |                                                                                                                                                                                                                                                                                  |                                                           |                                            |                   |                               |
| Shape features                | Compactness1, compactness2, convex, convex hull volume, convex hull volume 3D, mass, max 3D diameter, mean breadth, number of objects, number of voxel, orientation, roundness, spherical disproportion, sphericity, surface area, surface area density, volume, voxel size, and |                                                           | Max 3D diameter (n=1) and sphericity (n=1) |                   | Sphericity (n=1)              |

|                          |                                                                                                                                                                                                                                                                                            |                                                                                         |                                         |
|--------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|-----------------------------------------|
| Intensity features       | minor axis length                                                                                                                                                                                                                                                                          |                                                                                         |                                         |
|                          | Intensity direct, Intensity histogram, and neighbor intensity difference                                                                                                                                                                                                                   |                                                                                         |                                         |
| Texture features         |                                                                                                                                                                                                                                                                                            | FOS (n=3), GLRLM (n=1), GLDM (n=2), and GLCM (n=1)                                      | FOS (n=1), GLRLM (n=1), and GLDM (n=2), |
|                          | FOS, GLCM, GLRLM, GLSZM, NGTDM, and GLDM                                                                                                                                                                                                                                                   |                                                                                         |                                         |
| Clinical features (n=25) | Age, weight, height, BMI, FIGO 2018 stage, histology, chemotherapy time, degree of differentiation, concurrent cycles, concurrent strategy, combined surgery, GTV volume, CTV volume, hypertension, diabetes, coronary heart disease, haematological toxicity, late rectal toxicities, ect | BMI, GTV volume, FIGO 2018 stage, Age, Neutrophil toxicities, and adjuvant chemotherapy | Age                                     |
|                          |                                                                                                                                                                                                                                                                                            |                                                                                         |                                         |

Abbreviations: FOS, First order statistics; GLCM, Grey-level co-occurrence matrix; GLRLM, Grey-level run length matrix; NGTDM, Neighbouring gray tone difference matrix; GLSZM, Gray-level size zone matrix; GLDM, Gray-level dependence matrix.

**Table S3. Predictive performance of XGBoost models across different feature subsets.**

| Features | AUC (95% CI)     | <i>p</i> -value |
|----------|------------------|-----------------|
| 8        | 0.76 (0.64-0.87) | 0.174           |
| 12       | 0.80 (0.68-0.90) | -               |
| 15       | 0.76 (0.63-0.87) | 0.104           |
| 17       | 0.78 (0.67-0.89) | 0.537           |
| 22       | 0.77 (0.66-0.88) | 0.365           |

Abbreviations: AUC, Area under curve.

The “Features” column denotes the final feature cap (the number of selected features) determined through LassoCV-based selection process. Results are reported as the Area Under the Curve (AUC) with 95% confidence intervals (CI). P-values are calculated using the DeLong test, with the 12-feature model serving as the reference.

AUCs using the DeLong test; the results show that increasing the feature count beyond 12 yields no statistically significant improvement in performance (*p*-value > 0.05).

**Table S4. The performance of models for the validation and testing cohorts of grade 2 or higher RI-ART.**

| Model/Classifier | Validation Cohort |          |           |           |             |          | Testing Cohort   |          |           |           |             |          |
|------------------|-------------------|----------|-----------|-----------|-------------|----------|------------------|----------|-----------|-----------|-------------|----------|
|                  | AUC (95% CI)      | Accuracy | Precision | Sensitive | Specificity | F1-score | AUC (95% CI)     | Accuracy | Precision | Sensitive | Specificity | F1-score |
| <b>Dosiomics</b> |                   |          |           |           |             |          |                  |          |           |           |             |          |
| SVM              | 0.73 (0.67-0.79)  | 0.70     | 0.76      | 0.73      | 0.67        | 0.74     | 0.76 (0.62-0.86) | 0.77     | 0.83      | 0.78      | 0.76        | 0.81     |
| LR               | 0.73 (0.66-0.79)  | 0.69     | 0.75      | 0.71      | 0.65        | 0.73     | 0.77 (0.62-0.86) | 0.76     | 0.83      | 0.76      | 0.76        | 0.79     |
| RF               | 0.74 (0.68-0.79)  | 0.73     | 0.73      | 0.83      | 0.57        | 0.78     | 0.73 (0.61-0.84) | 0.73     | 0.78      | 0.78      | 0.66        | 0.78     |
| NB               | 0.71 (0.65-0.77)  | 0.68     | 0.72      | 0.74      | 0.59        | 0.73     | 0.68 (0.55-0.81) | 0.64     | 0.71      | 0.69      | 0.55        | 0.70     |
| MLP              | 0.74 (0.67-0.79)  | 0.73     | 0.74      | 0.83      | 0.58        | 0.78     | 0.74 (0.62-0.86) | 0.76     | 0.81      | 0.78      | 0.72        | 0.80     |
| XGB              | 0.74 (0.67-0.80)  | 0.70     | 0.74      | 0.75      | 0.63        | 0.75     | 0.75 (0.62-0.86) | 0.74     | 0.78      | 0.80      | 0.66        | 0.79     |
| <b>Radiomics</b> |                   |          |           |           |             |          |                  |          |           |           |             |          |
| SVM              | 0.68 (0.68-0.80)  | 0.67     | 0.74      | 0.69      | 0.65        | 0.71     | 0.71 (0.59-0.84) | 0.68     | 0.78      | 0.64      | 0.72        | 0.71     |
| LR               | 0.68 (0.66-0.78)  | 0.64     | 0.71      | 0.65      | 0.62        | 0.68     | 0.71 (0.61-0.84) | 0.68     | 0.76      | 0.69      | 0.66        | 0.72     |
| RF               | 0.65 (0.68-0.80)  | 0.66     | 0.67      | 0.80      | 0.45        | 0.73     | 0.68 (0.58-0.82) | 0.65     | 0.69      | 0.78      | 0.45        | 0.73     |
| NB               | 0.65 (0.66-0.78)  | 0.66     | 0.68      | 0.81      | 0.45        | 0.74     | 0.68 (0.56-0.81) | 0.65     | 0.69      | 0.76      | 0.48        | 0.72     |
| MLP              | 0.66 (0.68-0.80)  | 0.67     | 0.68      | 0.84      | 0.43        | 0.75     | 0.70 (0.53-0.79) | 0.66     | 0.69      | 0.82      | 0.41        | 0.75     |
| XGB              | 0.68 (0.67-0.79)  | 0.68     | 0.73      | 0.72      | 0.61        | 0.72     | 0.71 (0.56-0.81) | 0.68     | 0.73      | 0.73      | 0.59        | 0.73     |
| <b>Clinical</b>  |                   |          |           |           |             |          |                  |          |           |           |             |          |
| SVM              | 0.68 (0.61-0.74)  | 0.66     | 0.71      | 0.71      | 0.58        | 0.71     | 0.72 (0.57-0.82) | 0.68     | 0.74      | 0.71      | 0.62        | 0.71     |
| LR               | 0.68 (0.61-0.75)  | 0.67     | 0.72      | 0.70      | 0.61        | 0.71     | 0.71 (0.59-0.84) | 0.68     | 0.76      | 0.69      | 0.66        | 0.71     |
| RF               | 0.70 (0.63-0.75)  | 0.63     | 0.68      | 0.71      | 0.52        | 0.69     | 0.66 (0.50-0.76) | 0.62     | 0.65      | 0.82      | 0.31        | 0.69     |
| NB               | 0.71 (0.64-0.77)  | 0.66     | 0.75      | 0.62      | 0.713       | 0.68     | 0.75 (0.59-0.83) | 0.74     | 0.81      | 0.76      | 0.72        | 0.68     |
| MLP              | 0.70 (0.64-0.76)  | 0.67     | 0.71      | 0.75      | 0.557       | 0.73     | 0.74 (0.59-0.83) | 0.70     | 0.72      | 0.84      | 0.48        | 0.73     |



**Figure S1. Patient inclusion and exclusion criteria.**

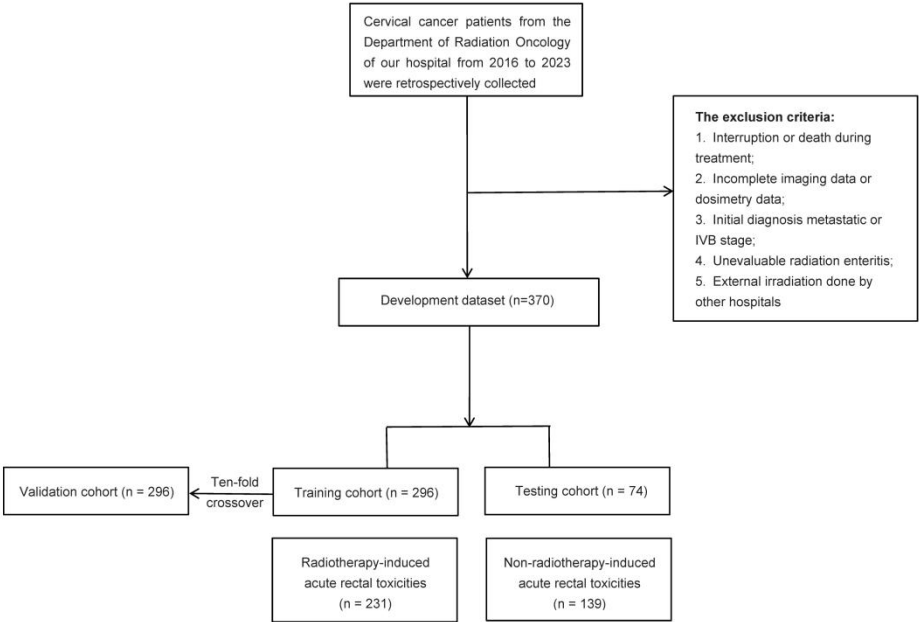
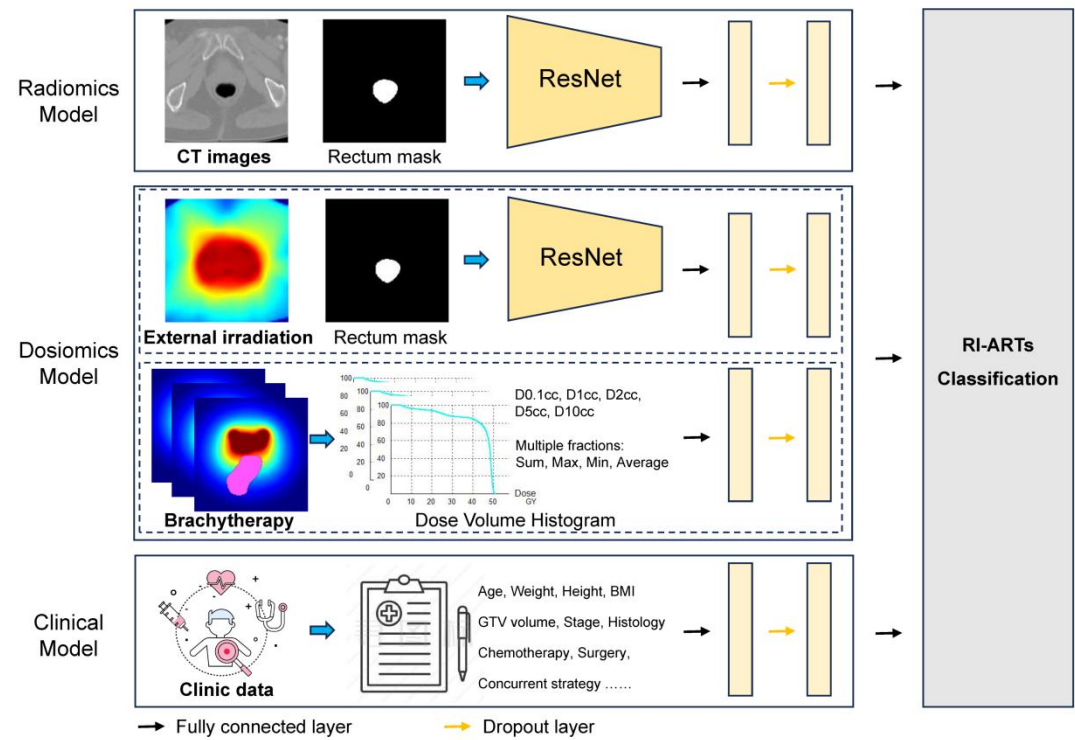


Figure S2. The framework of deep learning model.



Abbreviations: RI-ARTs, Radiotherapy-induced acute rectal toxicities.

Figure S3. Model feature selection process.

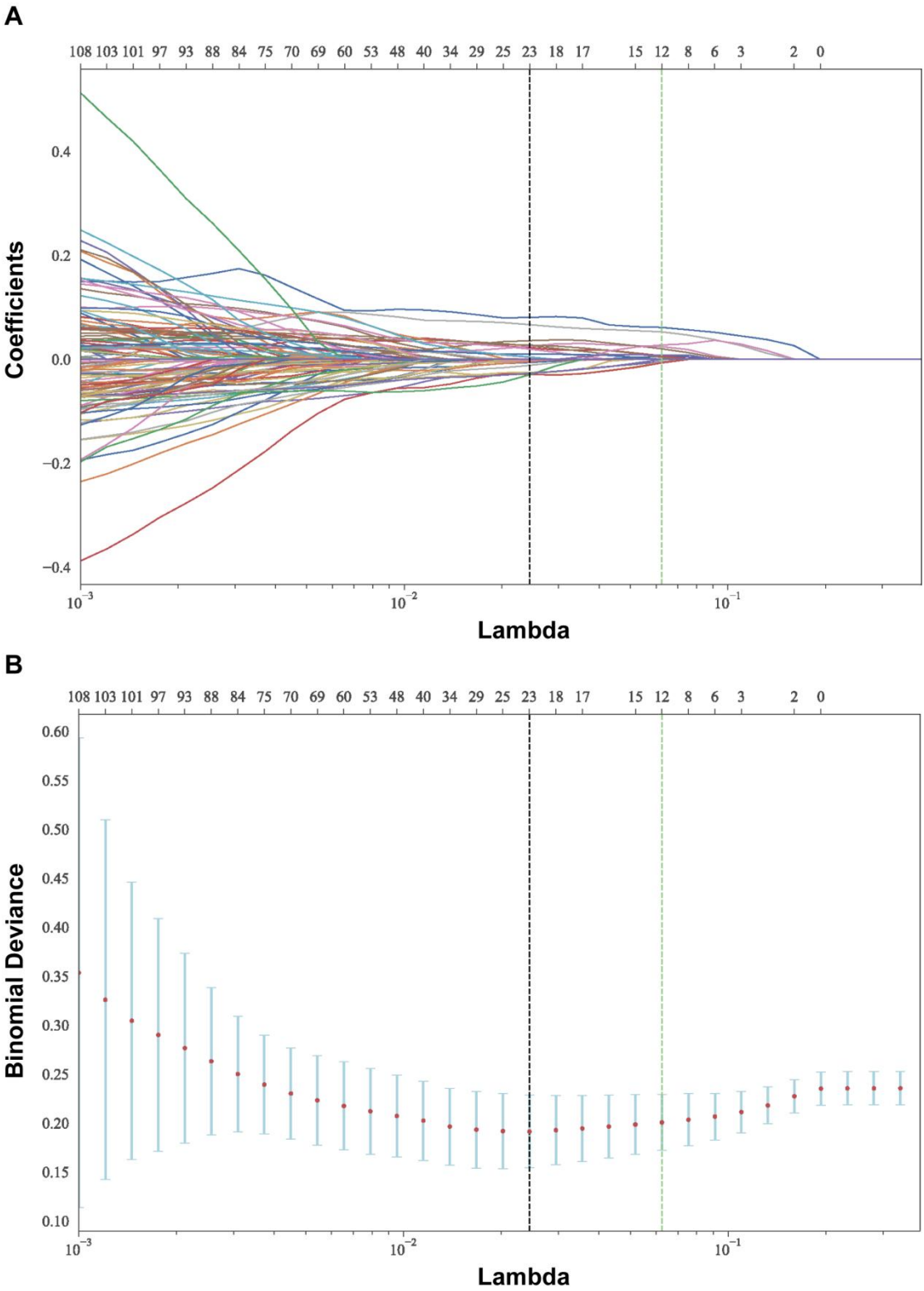
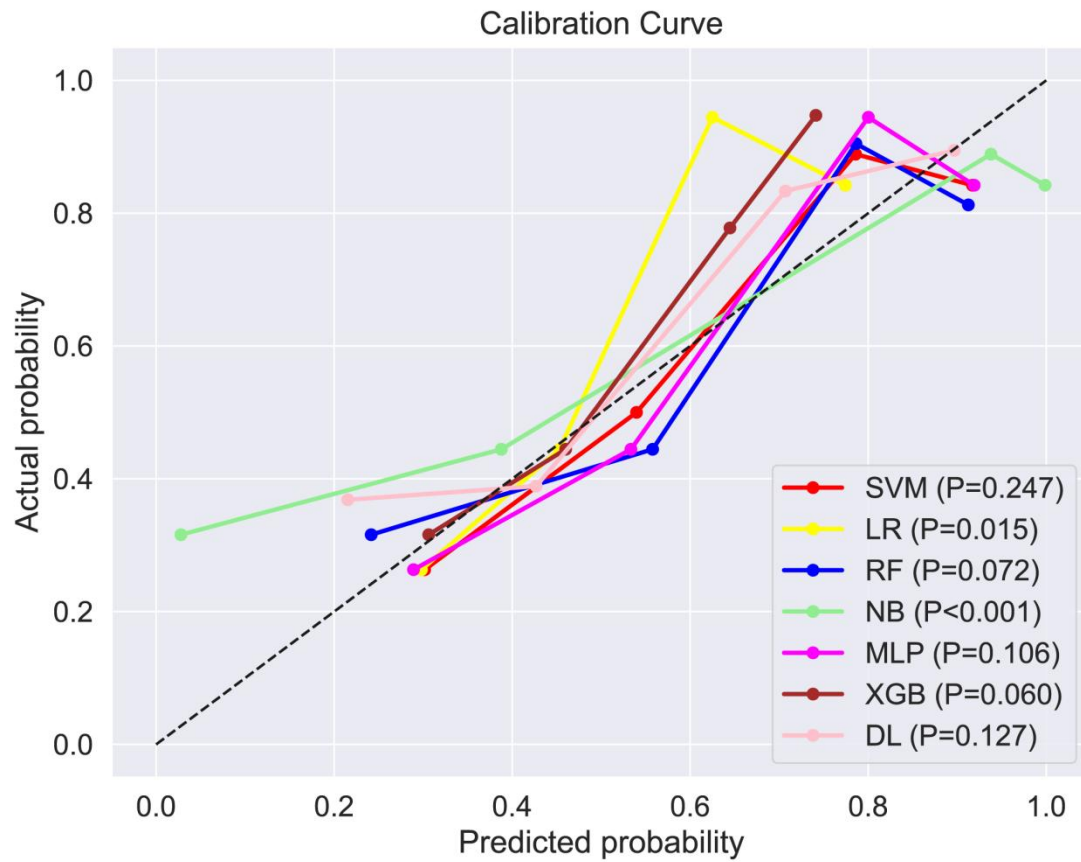
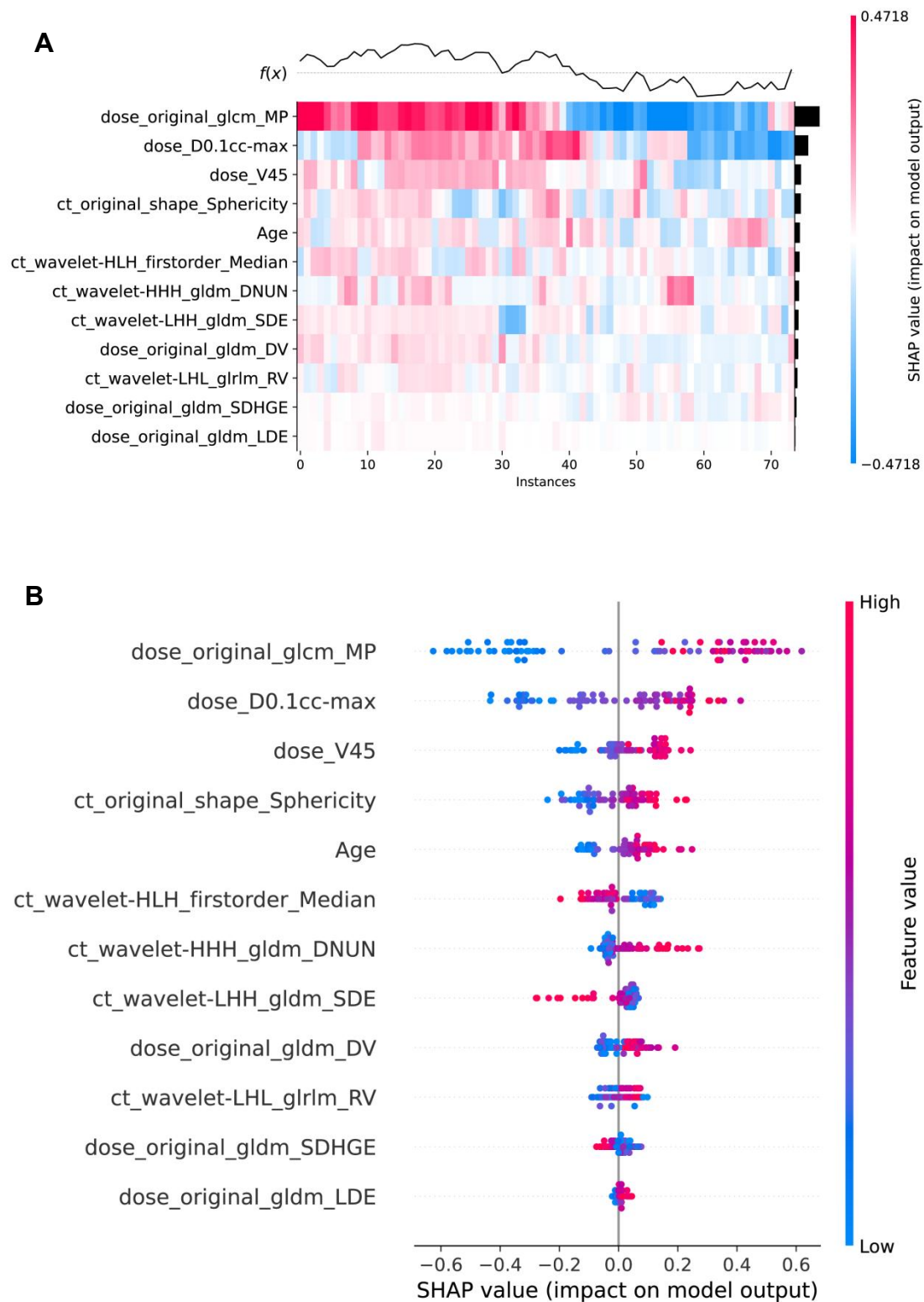


Figure S4. Calibration curves of the predictive model.



Abbreviation: SVM, Support vector machine; LR, Logistic regression; RF, Random Forests; NB, Naive bayes; MLP, Multilayer perceptron; XGB, extreme gradient boosting.

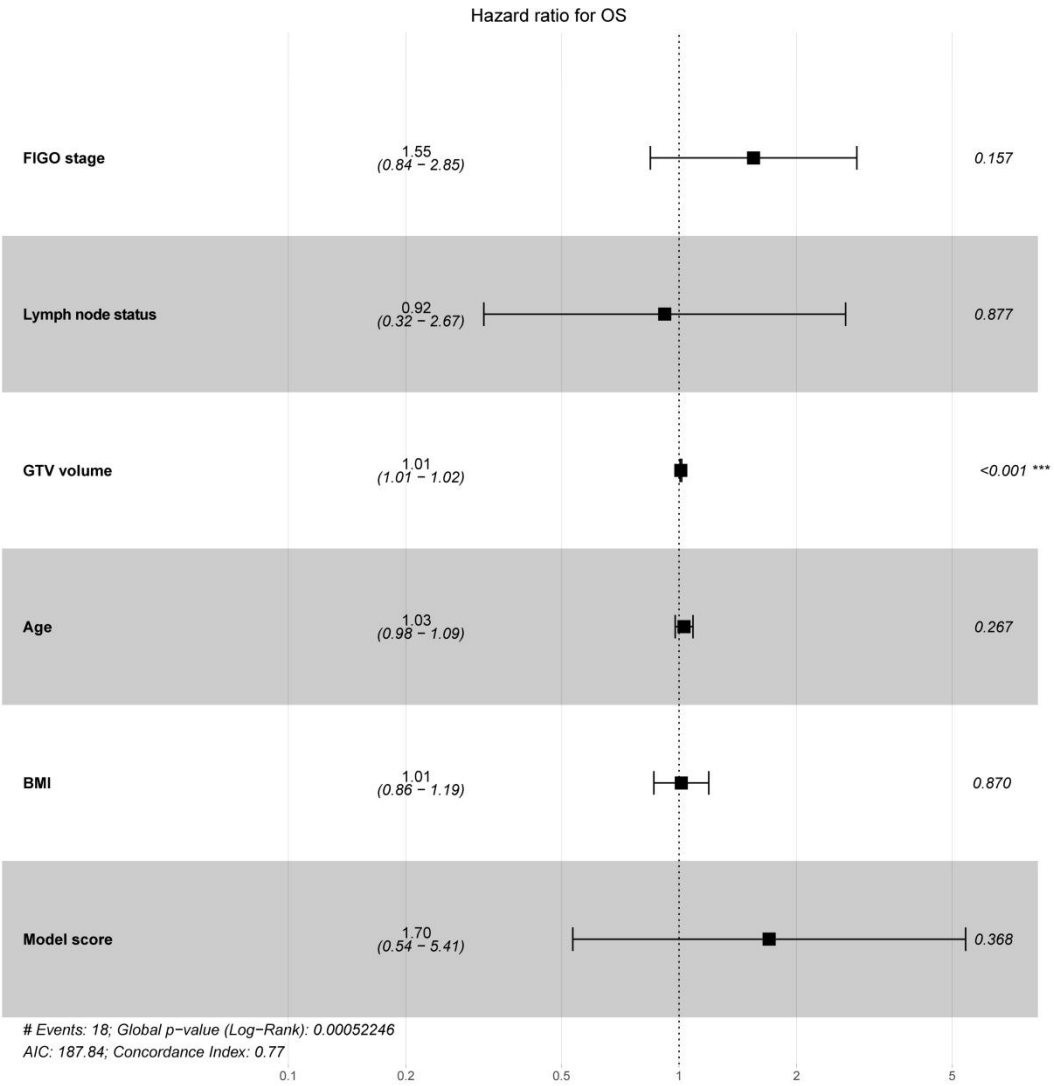
**Figure S5. Select heat maps (A) and tornado plot (B) of key features from the multiomics models.**



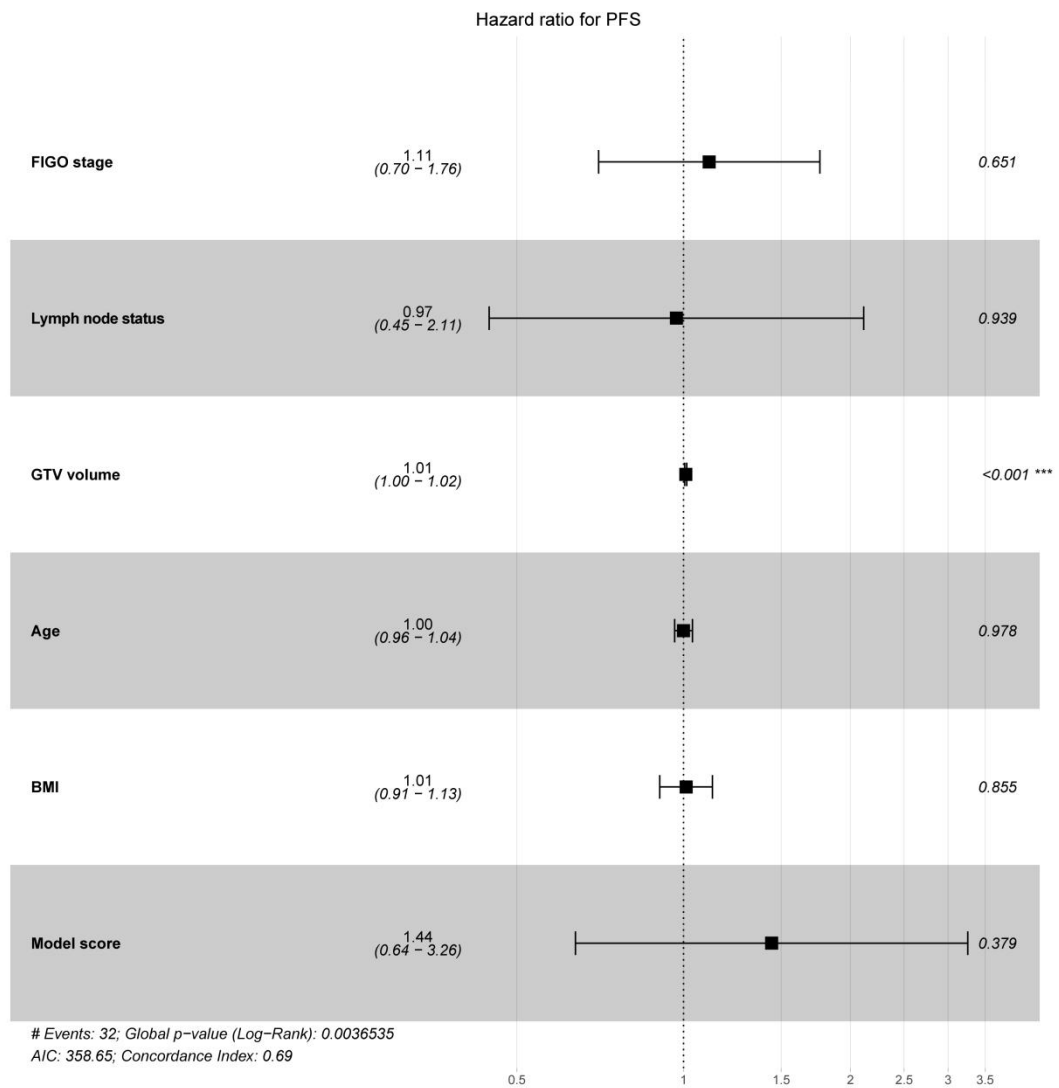
A red dot on the right half of the tornado diagram indicates that the parameter is positively correlated with the RI-ART risk, while a blue dot indicates that the parameter is inversely correlated with the RI-ART risk.

Figure S6. Results of multivariate cox regression analyses.

A



**B**



Abbreviation: OS, overall survival; PFS, progression free survival; BMI, body mass index; GTV, gross tumor volume.