

DCE-MRI Radiomics-Based Tumor Habitat Analysis for Three-Class Prediction of HER2 Expression Status in Breast Cancer

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Abstract

Background

HER2 (human epidermal growth factor receptor 2) is one of the core biomarkers for molecular classification, prognosis evaluation, and therapeutic regimen selection in breast cancer. Intratumoral heterogeneity in breast cancer is related to HER2 expression status. Analyzing the heterogeneity within tumor subregions using habitat analysis may be valuable for predicting HER2 expression status in breast cancer.

MATERIALS AND METHODS

A retrospective study enrolled 502 breast cancer patients, 377 patients from Center I, and 125 patients from Center II. All cases were divided into a training set, a validation set, and a test set at a ratio of 8:1:1. Patients were stratified into HER2-zero-expressing, HER2-low-expressing and HER2-overexpressing groups based on pathological findings. Tumor habitat segmentation was performed on DCE-MRI radiomics using three clustering methods: Gaussian mixture model, K-means clustering, and quantile-based clustering. Multi-dimensional radiomic features, including first-order statistical, morphological, texture, and wavelet features, were extracted from each subregion. These radiomic signatures were further integrated with clinical variables. Multiple machine learning classifiers were constructed and trained for HER2 status prediction. Comprehensive model validation and interpretability analysis were finally conducted via receiver operating characteristic curves, confusion matrices, SHAP summary plots, and decision curve analysis to systematically evaluate model performance, feature importance, and clinical utility.

RESULTS

The enhancement pattern, estrogen, family history, histological grade, Ki-67 levels, long diameter, progesterone and vertical diameter differed significantly among the three-class HER2 expression groups. DCE-MRI Habitat identified distinct intratumoral subregions with heterogeneous radiological phenotypes. Habitat-derived heterogeneous features alone achieved satisfactory discriminative performance. The LightGBM model yielded a test set micro-average AUC of 0.865. Habitat texture difference, boundary complexity index, and Shannon entropy showed consistently high feature importance. Decision curve analysis confirmed the Habitat model's prediction of HER2-low-expressing status can effectively improve the net benefit of clinical decision-making.

Conclusion

Habitat-derived heterogeneous features from DCE-MRI can serve as reliable non-invasive biomarkers for HER2 expression status prediction in breast cancer.

Introduction

Breast cancer remains the most prevalent malignancy among women worldwide, and its molecular subtyping is indispensable for precision therapy[1]. Traditionally, the HER2 oncogene has been regarded as a binary biomarker (positive or negative) that dictates eligibility for anti-HER2 agents such as trastuzumab deruxtecan[2]. The recent DESTINY-Breast04 trial upended this dichotomy by demonstrating significant clinical benefits in patients with tumors expressing only trace amounts of HER2, a newly recognized category termed "HER2-low"[2]. Consequently, the field has shifted from a binary to a ternary classification schema: HER2-positive, HER2-low, and HER2-zero[3]. Accurate stratification of patients into these three categories is now critical. The current gold standard, immunohistochemistry (IHC) and/or in situ hybridization (ISH) on invasive biopsies is still plagued by sampling errors, inter-observer variability, temporal instability during treatment, and an intrinsic inability to capture intratumoral heterogeneity[4].

Against this backdrop, the development of a non-invasive biomarker that simultaneously reflects molecular phenotypes and spatial heterogeneity has become urgent. Conventional radiomics pipelines, however, aggregate voxel-level features across the entire tumor, thereby discarding subtle regional differences that may encode distinct biological programs[5]. Inspired by ecological theory, the concept of intratumoral habitats, spatially coherent subregions with homogeneous imaging characteristics, has recently been introduced into oncology[6–11]. Several single center studies have suggested that habitat-based MRI signatures can distinguish HER2-positive from HER2-negative disease, but the critical HER2-low stratum has not yet been addressed[12, 13].

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) allows non-invasive and comprehensive characterization of microscopic functional features of tumors, including blood perfusion and vascular permeability[14]. Tumor habitat analysis enables precise identification of imaging differences among heterogeneous subregions within tumors[15, 16]. When combined with radiomics, these techniques allow high-throughput extraction of subtle quantitative imaging features, providing a novel strategy for non-invasive and accurate assessment of tumor molecular expression status[17, 18]. To date, most studies have focused on the binary classification of human epidermal growth factor receptor 2 (HER2). Research on non-invasive predictive models for the novel clinical three-category classification of HER2 expression remains scarce.

We therefore hypothesized that breast DCE-MRI data integrated with polynomial-expanded heterogeneity descriptors may provide a robust, non-invasive signature for the emerging ternary classification of HER2 status.

Materials and methods

Study design and study population

This retrospective study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Peking University Third Hospital (M20250363), and the requirement for informed consent was waived. A cohort of 502 breast cancer patients was enrolled from the two hospitals, from June 2023 and June 2025, 377 breast cancer patients from Peking University Third Hospital (Center I) were collected; from march 2018 and march 2023, 125 breast cancer patients from National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (Center II), were collected.

The patient enrollment from the two centers are shown in Fig. 1. The inclusion criteria were as follows: (1) Female patients; (2) No evidence of distant metastasis; (3) Availability of complete baseline MRI images obtained within 2 weeks prior to puncture or surgery, including dynamic contrast-enhanced MRI (DCE-MRI) sequences; (4) Completion of pathological immunohistochemical results (including ER, PR, HER2 and Ki-67 markers, etc.). The exclusion criteria were defined as: (1) Patients who had undergone surgery, biopsy, radiotherapy or chemotherapy prior to baseline MRI scanning; (2) Incomplete MRI datasets or images with suboptimal quality; (3) Incomplete or ambiguous pathological findings regarding HER2 expression status. Ultimately, a total of 502 patients met the study's inclusion criteria and were randomly divided into a training set (n = 401), a validation set (n = 50), and a test set (n = 51) at a 8:1:1 ratio.

MRI examination

MRI was conducted using a 3.0-T uMR780 scanner (Shanghai United Imaging Healthcare Co., Ltd.) with an 8-channel breast coil in Institution I, and 3.0-T MRI scanner (GE SignaHDxt) or 3.0-T MRI scanner (GE Signal Pioneer) or 3.0-T MRI scanner (GE Premier) with an 8-channel breast coil in Institution II.

Dynamic contrast-enhanced MRI (DCE-MRI) using the tra-T1WI-3D sequence: an initial T1WI-FS pre-contrast scan was performed, followed by intravenous injection of a gadolinium contrast agent (Gadopentetate Dimeglumine, Magnevist, 0.2 mmol/kg at 2 mL/s) and a 20 mL saline flush. DCE-MRI included one pre-contrast and seven post-contrast phases with each phase for 40s at Institution I, and one pre-contrast and five post-contrast phases with each phase for 45s at Institution II.

Two radiologists from the Institution I, with 15 and 8 years of experience in breast imaging diagnosis, respectively, measured the radiological characteristics of breast cancer on the peak-enhanced DCE phase using breast post-processing software.

Habitat Analysis

The overall workflow is illustrated in Fig. 2. This study encompassed three core phases: (1) DCE-based habitat clustering, (2) heterogeneity feature extraction, and (3) machine learning modeling for HER2 status prediction.

This workflow outlines a radiomics pipeline for predicting breast cancer HER2 status (HER2-zero-expressing, HER2-low-expressing and HER2-overexpressing) using maximum-phase MRI images, starting with raw images that undergo preprocessing steps including N4 bias field correction, intensity normalization, noise reduction, resampling, and contrast enhancement, followed by tumor segmentation, clustering of tumor regions via three methods (GMM, K-means, and quantile-based clustering), extraction of multi-type radiomic features (first-order statistics, shape, texture, and wavelet features) from these clustered regions, integration of these features with clinical data (such as age, menopausal status, tumor size, lymph node status, and histological grade), training of machine learning classification models (including Random Forest, XGBoost, SVM, and Logistic Regression) for HER2 status prediction, and concluding with comprehensive model evaluation and interpretation using ROC curves, a confusion matrix, a SHAP summary plot, and decision curve analysis to assess performance, feature impact, and clinical utility.

Statistical Analysis

All statistical analyses were implemented via SPSS software (Version 25.0, IBM Corp) and R software (Version 4.1.2). Continuous variables were reported as means± standard deviations, whereas categorical variables were summarized as absolute counts (n) and their respective percentages (%). We evaluated each classifier with a consistent suite of performance metrics that jointly capture discrimination and clinical utility: overall accuracy, macro-averaged F1 score, recall, precision and the area under the receiver operating characteristic curve. Pairwise differences in AUC were formally assessed with DeLong's test, adopting a two-sided significance level of 0.05. To interpret the models, we extracted feature importance scores appropriate to their internal structure.

Results

Patient characteristics

A total of 502 patients met the study's inclusion criteria and were randomly divided into a training set (n = 401), a validation set (n = 50), and a test set (n = 51) at a 8:1:1 ratio. The baseline characteristics of dataset from two centers are presented in Table 1.

Table 1
The baseline characteristics of dataset from two centers

Variable	Test set	Training set	Validation set	p-value
ALN	51 (n)	401 (n)	50 (n)	0.4515
Age	48.90 ± 11.98	49.81 ± 11.37	49.26 ± 11.31	0.8392
DWI	51 (n)	401 (n)	50 (n)	0.2333
EP	51 (n)	401 (n)	50 (n)	0.5333
ER	51 (n)	401 (n)	50 (n)	0.096
FH	51 (n)	401 (n)	50 (n)	0.6307
HG	51 (n)	401 (n)	50 (n)	0.0684
Ki-67	51 (n)	401 (n)	50 (n)	0.4824
LD	2.90 ± 1.64	2.58 ± 1.35	2.53 ± 1.07	0.2578
Lob	51 (n)	401 (n)	50 (n)	0.4269
Loc	51 (n)	401 (n)	50 (n)	0.2357
MS	51 (n)	401 (n)	50 (n)	0.889
PR	51 (n)	401 (n)	50 (n)	0.617
Parity	51 (n)	401 (n)	50 (n)	0.5897
Spi	51 (n)	401 (n)	50 (n)	0.1233
TIC	51 (n)	401 (n)	50 (n)	0.5517
VD	2.25 ± 1.46	1.91 ± 1.00	1.83 ± 1.01	0.0789
Note: *P < 0.05 is significant. Continuous: mean ± SD; tested by ANOVA (fallback: Kruskal-Wallis).Categorical: n (%); tested by Chi-square (fallback: Fisher exact).				
TIC: time intensity curve; PR: progestogen; ER: estrogen; ALN:axillary lymph nodes;EP: enhancement pattern; FH:family history;LD:long diameter; Spi: spiculation;Lob:lobulation;HG:histological grade; VD:vertical diameter; MS: menstrual status				

There were no statistically significant differences in the distribution of all clinical, pathological, and imaging features among the training set, test set, and validation set. The baseline characteristics of patients across the three-class HER2 expression subgroups are shown in Table 2. The enhancement pattern(EP), estrogen(ER), family history, histological grade(HG), Ki-67 levels, long diameter, progestoge(PR)and vertical diameter differed significantly among the three-class HER2 expression groups ($p = 0.0144, < 0.001, 0.0220, 0.0082, 0.0002, 0.0065, < 0.001, \text{ and } 0.0031$).

Table 2
The baseline characteristics of HER2 Subgroups

Variable	HER2 = 0	HER2 = 1	HER2 = 2	p-value
ALN	105 (n)	277 (n)	120 (n)	0.0984
Age	48.20 ± 10.79	50.45 ± 12.02	49.11 ± 10.36	0.1891
DWI	105 (n)	277 (n)	120 (n)	0.5528
EP	105 (n)	277 (n)	120 (n)	0.0144*
ER	105 (n)	277 (n)	120 (n)	0.0000*
FH	105 (n)	277 (n)	120 (n)	0.0220*
HG	105 (n)	277 (n)	120 (n)	0.0082*
Ki-67	105 (n)	277 (n)	120 (n)	0.0002*
LD	2.56 ± 1.38	2.48 ± 1.28	2.95 ± 1.45	0.0065*
Lob	105 (n)	277 (n)	120 (n)	0.6322
Loc	105 (n)	277 (n)	120 (n)	0.9273
MS	105 (n)	277 (n)	120 (n)	0.3354
PR	105 (n)	277 (n)	120 (n)	0.0000*
Parity	105 (n)	277 (n)	120 (n)	0.3227
Spi	105 (n)	277 (n)	120 (n)	0.2230
TIC	105 (n)	277 (n)	120 (n)	0.2252
VD	2.03 ± 1.19	1.80 ± 0.96	2.18 ± 1.13	0.0031*
Note: *P < 0.05 is significant. Continuous: mean ± SD; tested by ANOVA (fallback: Kruskal-Wallis).Categorical: n (%); tested by Chi-square (fallback: Fisher exact).				
TIC: time intensity curve; PR: progesterone; ER: estrogen; ALN:axillary lymph nodes;HG:Histological Grade; EP: enhancement pattern; FH:family history;LD:long diameter; Spi: spiculation;Lob:lobulation;HG:histological grade; VD:vertical diameter; MS: menstrual status				

Habitat identification and Feature selection

DCE-MRI radiomic habitat features associated with HER2-zero-expressing, HER2-low-expressing, and HER2-overexpressing statuses were selected in the entire dataset. Ultimately, the top 15 habitat features for differentiating HER2-expressing breast cancers were identified using Least Absolute Shrinkage and Selection Operator (LASSO) (Table 3). The corresponding coefficients of the habitat features in the LASSO regression model are shown in Fig. 3.

Table 3
The top 15 habitat features for differentiating HER2-expressing breast cancers

ANOVA_F	MutualInfo	Lasso_L1	RF_Importance
EP	Rad_ID	PR	Rad_ID
ER	FH	ER	PR
Ki-67	Ki-67	Ki-67	peritumoral_enh
PR	Lob	EP	habitat2_fragme
VD	PR	FH	habitat3_surrou
habitat1_original_shape_MajorAxisLength	habitat1_fraction	Age	habitat2_surrou
habitat1_original_shape_MinorAxisLength	habitat1_original_shape_LeastAxisLength	habitat2_original_shape_MinorAxisLength	interface_h1_h3.
habitat2_original_shape_MajorAxisLength	habitat3_original_shape_Flatness	Parity	habitat2_n_com
habitat2_original_shape_MinorAxisLength	habitat1_n_components	habitat2_original_shape_MajorAxisLength	centroid_dist_h1
habitat3_original_shape_LeastAxisLength	habitat1_fragmentation	peritumoral_enh_std	habitat3_origina
habitat3_original_shape_MajorAxisLength	habitat3_n_components	interface_h1_h3_area_mm2	habitat1_origina
habitat3_original_shape_MinorAxisLength	interface_h1_h2_area_mm2	Lob	habitat1_origina
peritumoral_original_shape_Flatness	habitat1_enh_mean	peritumoral_original_shape_Flatness	habitat2_origina
peritumoral_original_shape_MajorAxisLength	habitat2_enh_std	habitat1_surround_by_others_ratio	Age
peritumoral_original_shape_MinorAxisLength	peritumoral_enh_std	Spi	habitat2_origina

Predictive Model Performance

The performance of different feature selection models in predicting the three-class HER2 expression subgroups is illustrated in Table 4(Only list models with AUC greater than 0.8), and the confusion matrix plot of model performance is presented in Fig. 4.The confusion matrices revealed that different models varied in recognition accuracy across categories and showed distinct tendencies of category confusion. Direct comparison of these matrices allowed for intuitive identification of each model's strengths and weaknesses, with the LightGBM model outperforming the others.

Table 4
The performance of different machine learning models in predicting the three-class HER2 expression

Features	Classifier	AUC	ACC	Precision	Recall	FScore	Kappa	FPR	FNR
RF_Importance	LightGBM	0.865	0.705	0.649	0.647	0.646	0.506	0.157	0.352
ANOVA_F	LDA	0.847	0.667	0.634	0.642	0.635	0.452	0.180	0.358
Lasso_L1	SVM_Linear	0.833	0.706	0.662	0.684	0.669	0.527	0.145	0.316
ANOVA_F	LogisticRegression	0.832	0.667	0.636	0.658	0.635	0.474	0.162	0.342
ANOVA_F	RidgeClassifier	0.830	0.667	0.652	0.676	0.646	0.484	0.156	0.323
MutualInfo	RidgeClassifier	0.830	0.667	0.634	0.660	0.638	0.474	0.162	0.339
MutualInfo	LogisticRegression	0.828	0.667	0.647	0.679	0.647	0.485	0.156	0.321
MutualInfo	LDA	0.824	0.647	0.623	0.630	0.617	0.437	0.177	0.370
ANOVA_F	SVM_Linear	0.824	0.725	0.698	0.709	0.694	0.553	0.143	0.290
RF_Importance	QDA	0.821	0.647	0.602	0.596	0.599	0.402	0.200	0.404

A one-vs-one strategy was used in this study to generate three-class ROC curves, with model performance assessed through test set. For each HER2 expression category, we calculated its TPR and FPR relative to other categories and derived the corresponding AUC values. Additionally, the micro-average AUC was computed as an indicator of the model's overall discriminative ability. A comprehensive comparison of the ROC curves (Figure5)across all models revealed that the LightGBM model outperformed the rest, reaching an average AUC of 0.865.

Interpretability analysis

SHAP analysis (Fig. 6) demonstrated that the key features importance (Fig. 7) presented distinct contribution patterns when the LightGBM model was used to predict breast cancer HER2 status, providing interpretable evidence for non-invasive clinical evaluation of HER2 expression. Decision curve analysis (DCA) (Fig. 8) showed that the HER2-low-expressing prediction model constructed using a one-vs-rest strategy achieved significantly higher net benefit than both the "treat all" and "treat none" strategies within a threshold probability range of 0–0.7, indicating favorable clinical decision-making value. In contrast, the

HER2-zero-expressing, and HER2-overexpressing prediction models only exhibited a weak advantage at very low threshold probabilities, with limited clinical utility. Overall, the model's prediction of HER2-low-expressing status can effectively improve the net benefit of clinical decision-making.

Discussion

This study constructed and validated a novel LightGBM model grounded in DCE-MRI radiomic habitat features, enabling non-invasive three-category prediction of HER2 expression status in breast cancer patients. A strict 8:1:1 partitioning strategy was adopted to divide enrolled cohorts into training, validation and test sets. Baseline comparisons confirmed no significant differences in clinical, pathological and imaging characteristics among the three datasets, which eliminated potential baseline confounding bias and ensured the robustness and credibility of subsequent model development and validation processes. Subgroup analyses further revealed that key conventional clinicopathological and imaging indices, including tumor enhancement pattern, estrogen receptor/progesterone receptor (ER/PR) status, histological grade and tumor diameter, exhibited significant discrepancies across the three HER2 expression subgroups. These findings solidly demonstrate the intrinsic clinical and imaging heterogeneity of breast cancer with varying HER2 expression levels, and provide empirical support for targeted radiomic feature screening and stratified predictive model construction.

Our proposed end-to-end framework, which couples K-means clustering based tumor microenvironment segmentation with machine learning modeling, demonstrates the transformative value of intratumoral spatial heterogeneity in refining HER2 status prediction. By extracting 15 top habitat-derived heterogeneity indicators and integrating polynomial feature expansion with dual LASSO-random forest feature selection, we successfully built high-performance classifiers that outperformed conventional whole tumor radiomics approaches. The superior performance of our models, with the LightGBM model achieving a test set AUC of 0.865 underscores the efficacy of our analytical pipeline.

Previous studies have conducted extensive exploratory work using Habitat analysis to predict HER2 expression in breast cancer[19–23]. Lin Z[19] et al. reported a radiomic habitat model integrating MRI, ultrasound, and clinical information, which achieved an AUC of 0.835 in the test set. Wang S et al.'s study[20] employing the Habitat model based on the XGBoost algorithm reported AUCs of 0.873, 0.845, and 0.865 in the first external test set and 0.865, 0.844, and 0.878 in the second for HER2-zero, HER2-low, and HER2-positive subtypes, respectively. Pan H et al[21]. reported that compared with the intratumoral radiomics model, the habitat model showed superior predictive performance in all cohorts, with an area under the ROC curve (AUC) of 0.820 in the test cohort. Comparative analysis with multiple machine learning algorithms verified the superior predictive efficacy of the established LightGBM model. In the test cohort, the model achieved a micro-average AUC of 0.865, which outperformed other competing models in the differential diagnosis of the three HER2 subtypes. Subsequent confusion matrix and multi-class ROC curve analyses further corroborated the excellent discriminatory ability of the LightGBM model for all HER2 subgroups. These results indicate that DCE-MRI radiomic habitat features can capture subtle phenotypic variations corresponding to different HER2 expression levels.

Model interpretability is a prerequisite for the clinical translation of machine learning based predictive tools. In this research, SHAP analysis was utilized to quantitatively and visually elucidate the contribution patterns of core habitat features in the three-class HER2 prediction model. Compared with conventional black-box machine learning models, the SHAP-based quantification of feature importance and marginal contribution endows the model's predictive outcomes with biological rationality and clinical interpretability, laying a critical foundation for its reliable clinical application. Notably, decision curve analysis (DCA) validated the promising clinical decision-making value of the proposed model. Specifically, the HER2-low prediction model established via the one-vs-rest analytical strategy yielded stable and favorable net clinical benefits. This finding holds important practical implications for individualized clinical diagnosis and therapeutic decision-making for HER2-low breast cancer. As a newly identified intermediate HER2 subtype, HER2-low breast cancer possesses unique biological behaviors and treatment response characteristics, and its accurate identification is essential for guiding targeted therapy and prognostic assessment[24]. By contrast, the limited net clinical benefits of the HER2-zero and HER2-overexpression prediction models may be attributable to the high accuracy and maturity of traditional clinical detection methods for these two subtypes, resulting in marginal incremental clinical value of the auxiliary machine learning model.

Nevertheless, several limitations of the present study need to be acknowledged. First, the sample sizes of the validation and test cohorts were relatively small. Second, all radiomic habitat features were extracted from single-modal DCE-MRI data; integration of multi-modal imaging data may further improve the predictive performance of the model. Third, the generalizability and stability of the model require further validation in large-sample. Fourth, we did not incorporate pharmacokinetic parameters of DCE-MRI (e.g., Ktrans and Ve), which recent studies have shown can complement radiomics features to further improve HER2 prediction accuracy. Future work should focus on expanding the sample size, integrating multi-omics data (e.g., genomic and transcriptomic profiles) to establish a more comprehensive multi-modal predictive model. Additionally, exploring the association between habitat features and treatment response in HER2-positive patients could provide actionable insights for personalized therapeutic strategies, further bridging the gap between radiomics research and clinical practice.

In conclusion, the DCE-MRI radiomic habitat feature-based LightGBM model realizes accurate, interpretable and non-invasive three-stratification evaluation of HER2 expression in breast cancer, with prominent clinical application prospects, particularly for the identification of HER2-low tumors. This novel model serves as an effective auxiliary tool for preoperative non-invasive HER2 subtyping, which can compensate for the deficiencies of invasive immunohistochemical detection.

Declarations

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Competing interests

The authors declare no competing interests.

Ethical approval and consent to participate

This retrospective study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Peking University Third Hospital (M20250363), and the requirement for informed consent was waived.

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Author Contribution

Conception and design: Shi Tan, Yong Cheng; Administrative support: Shi Tan, Yong Cheng; Provision of study materials or patients: Xiaohua Wang ,Wei Guo, Shunan Che,Yao Yao; Collection and assembly of data: Wei Guo, Shunan Che, Xiaohua Wang,Yao Yao, Qianhua Chen, Huimiao Chen; Data analysis and interpretation: Shi Tan, Yong Cheng; Manuscript writing: Wei Guo , Shunan Che, Xiaohua Wang.Wei Guo, Shunan Che, and Xiaohua Wang contributed equally to this work as first authors. Correspondence: Yong Cheng, and Shi Tan

Data Availability

The data generated or analyzed from Center I and Center II, and during the study are available from the corresponding author by request

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Figures

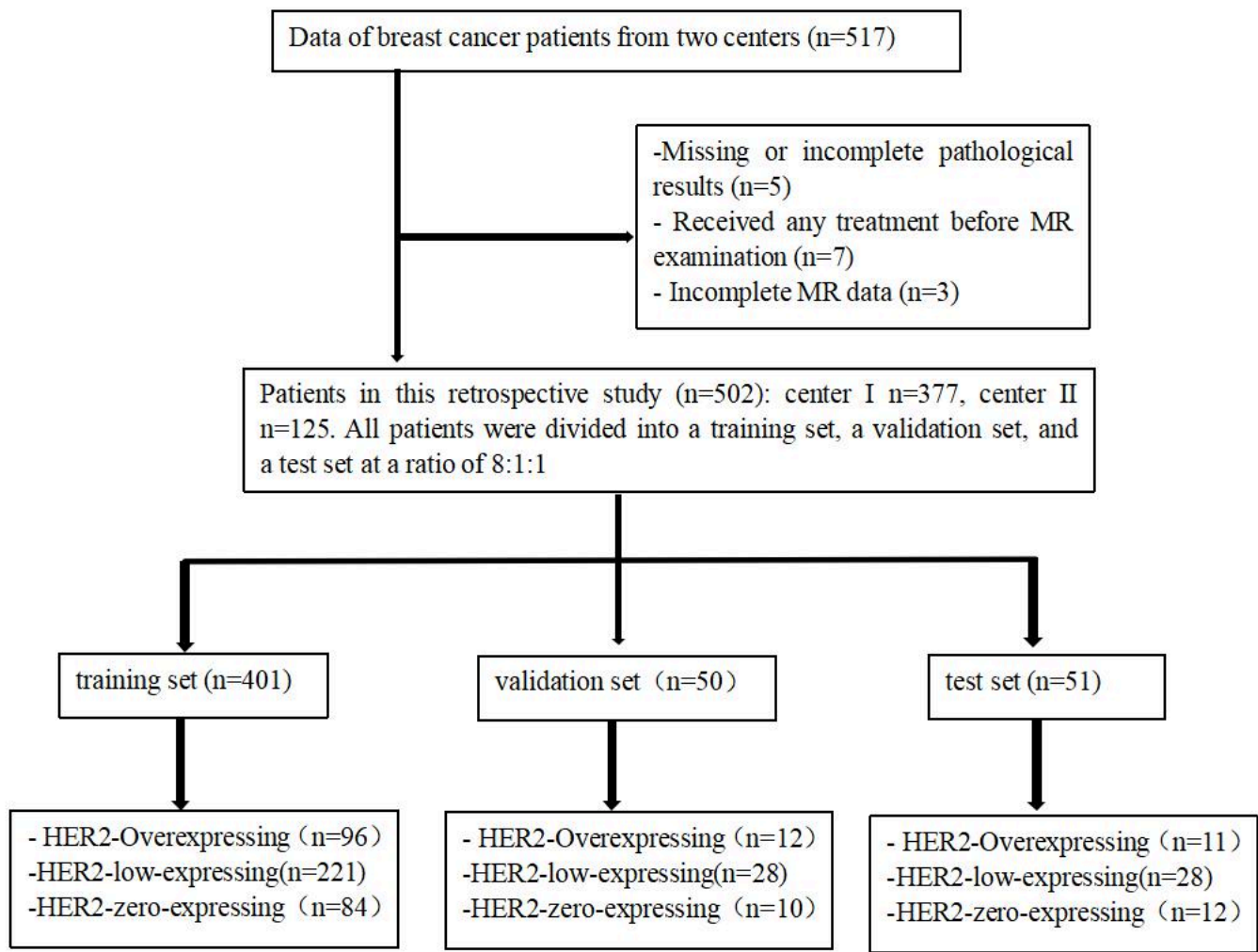


Figure 1

Breast cancer patients enrollment from the Two Center (Peking University Third Hospital) and Center (National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College).

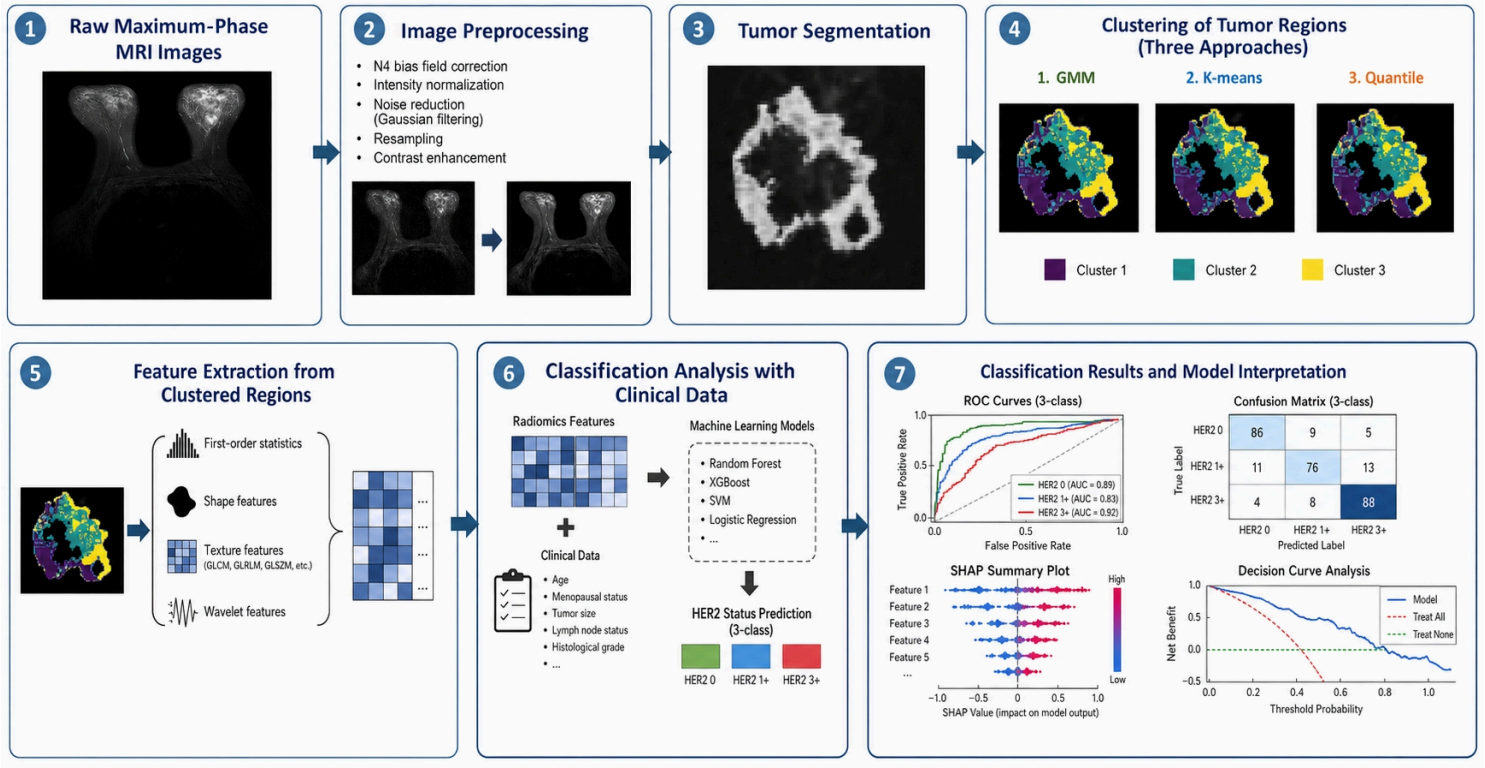


Figure 2

The workflow of DCE- MRI Tumor Habitats Model.

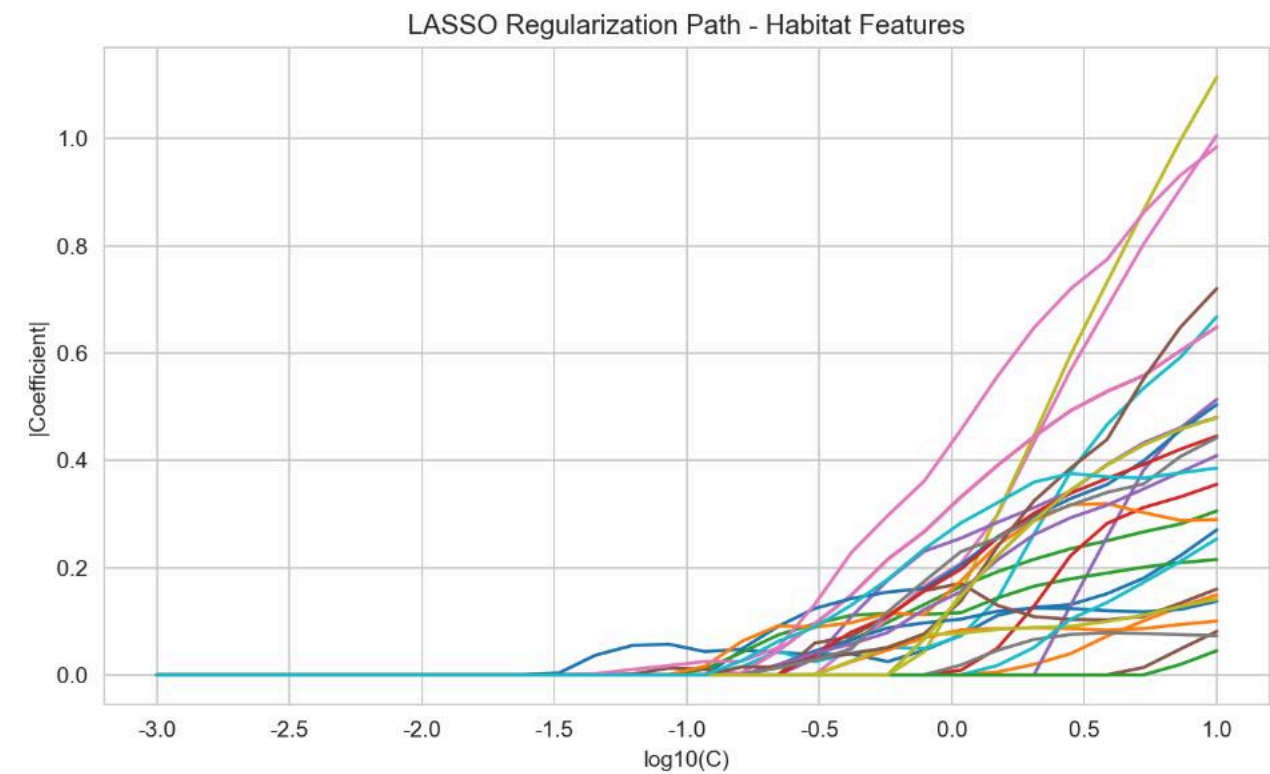


Figure 3

The LASSO Regularization Path of Habitat Features.

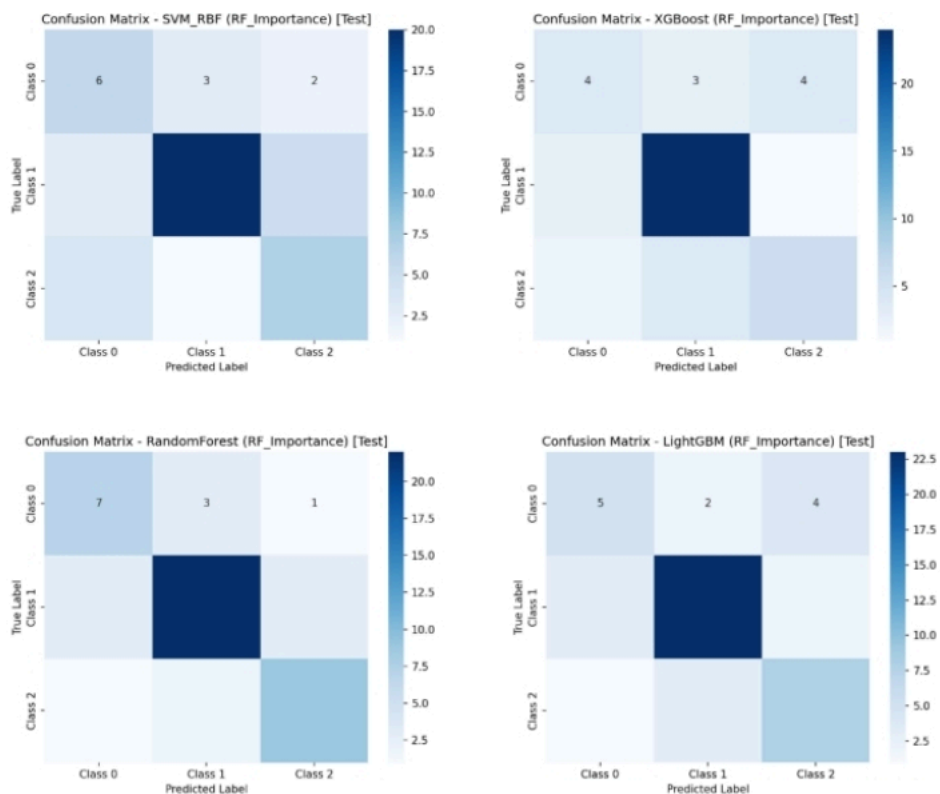


Figure 4

The confusion matrix diagram of test sets for different machine learning models.

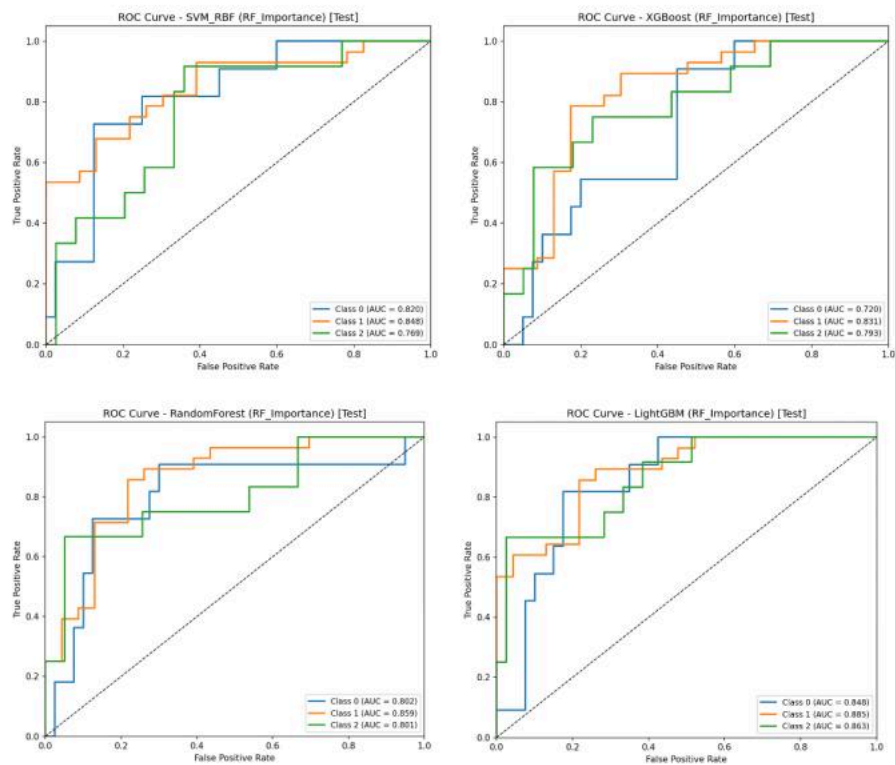


Figure 5

The ROC curve graph of test sets of different machine learning models .

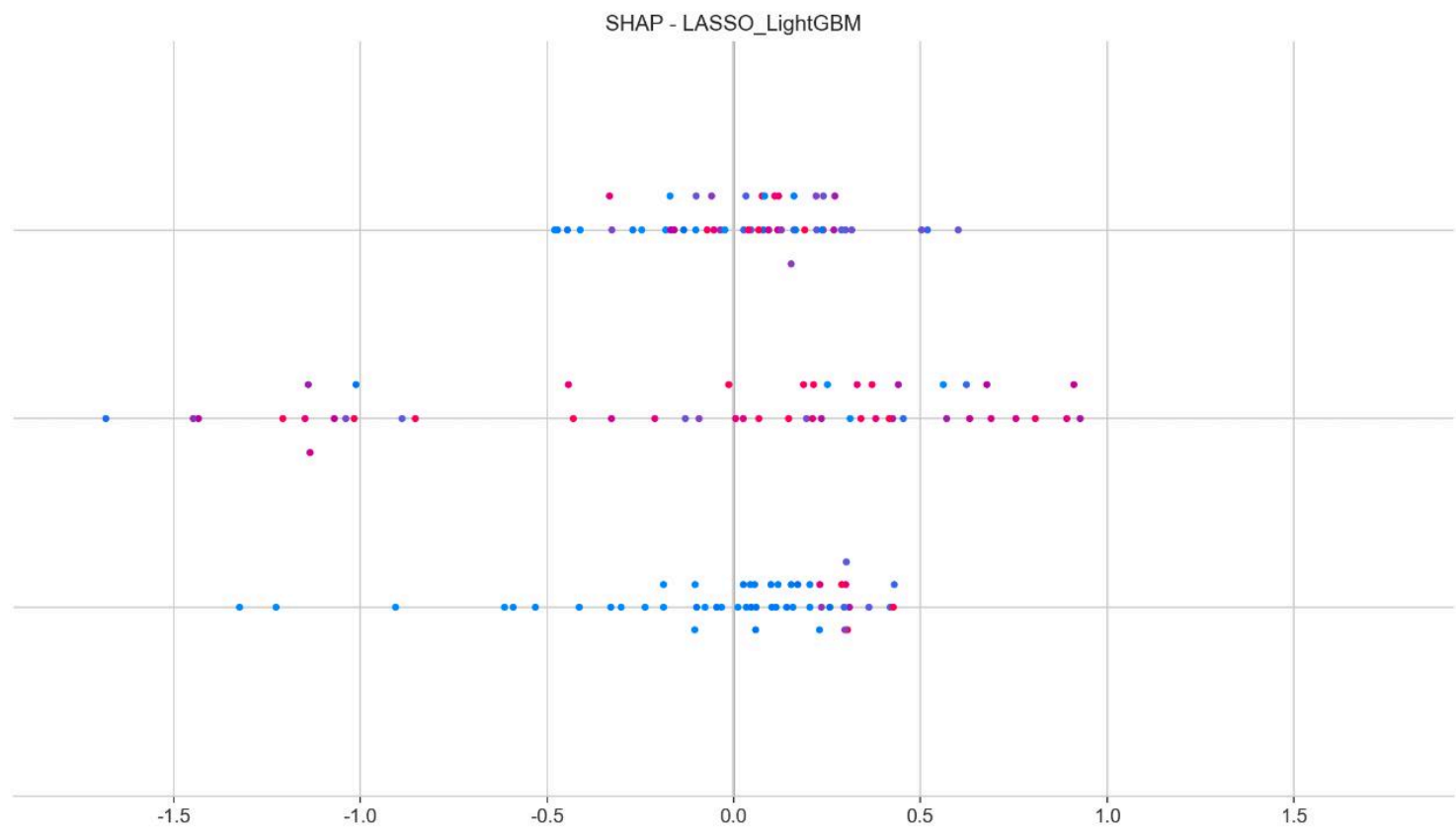


Figure 6
SHAP (SHapley Additive exPlanations) beeswarm plot for the LightGBM model in predicting three-class HER2 expression in breast cancer.

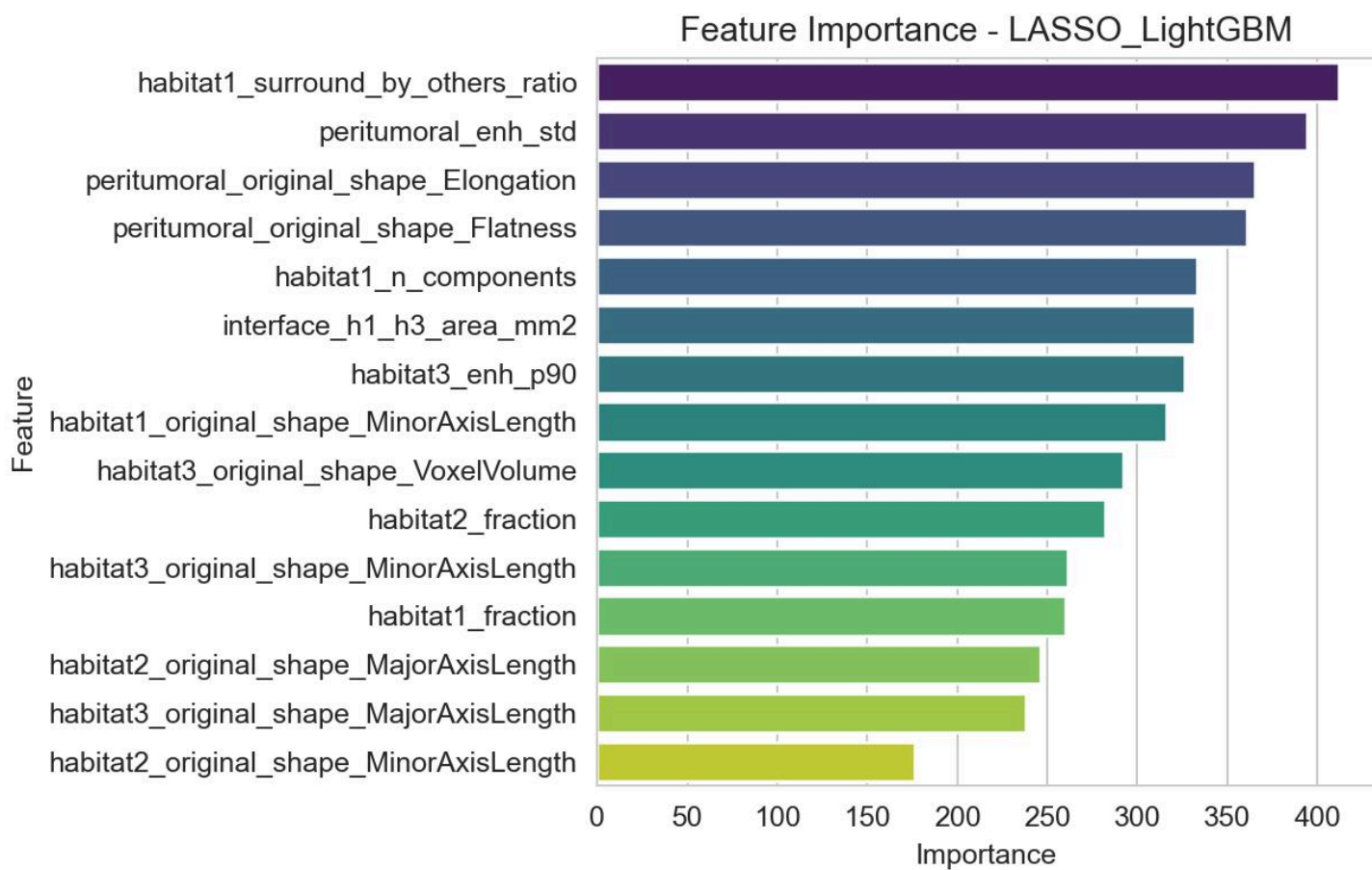


Figure 7

The Key Habitat feature importance of the LightGBM model.

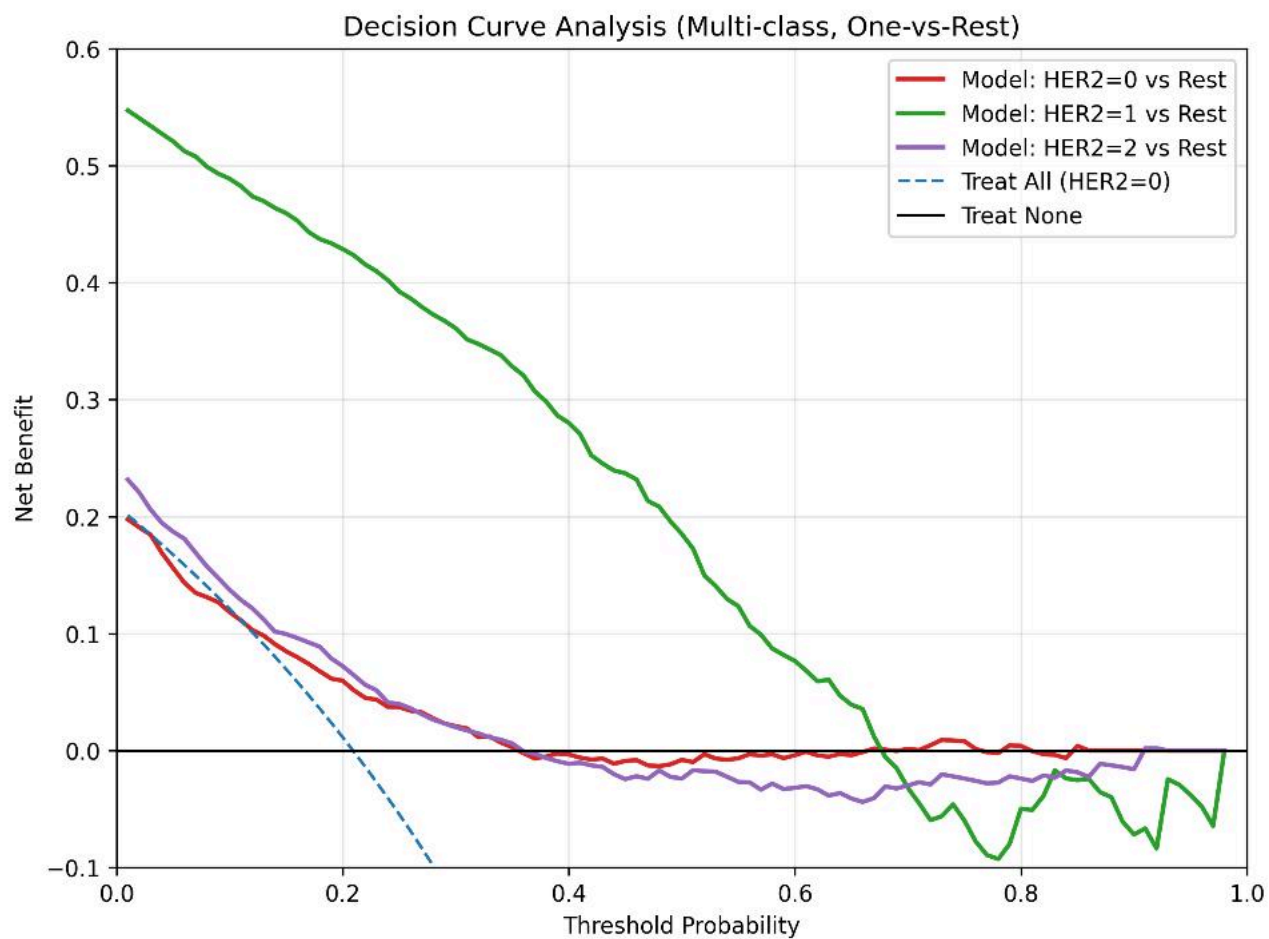


Figure 8

Decision Curve Analysis for Clinical Benefit of Predicting HER3 Three-Tier Expression in Breast Cancer.