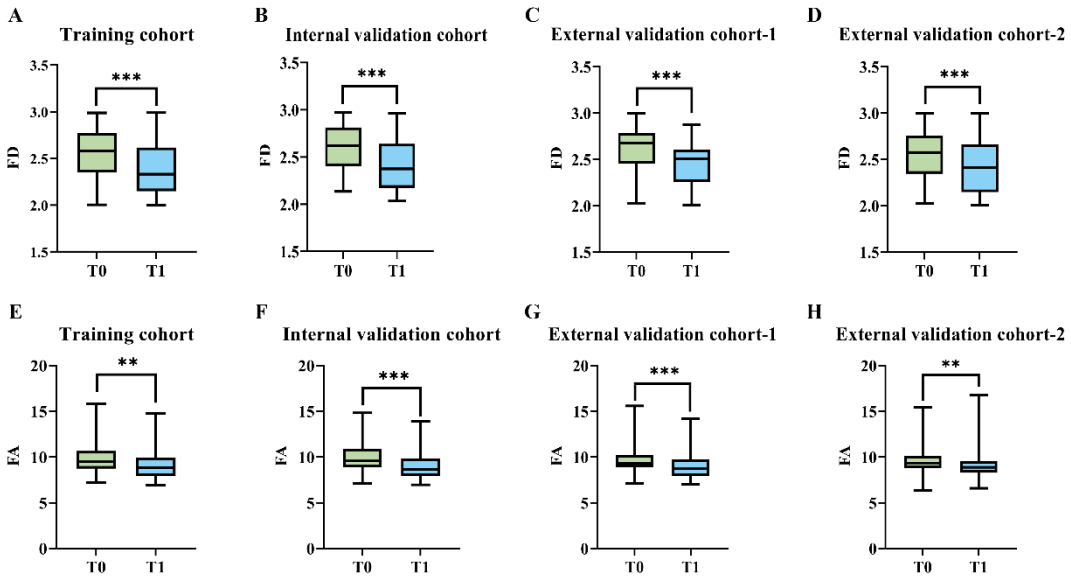
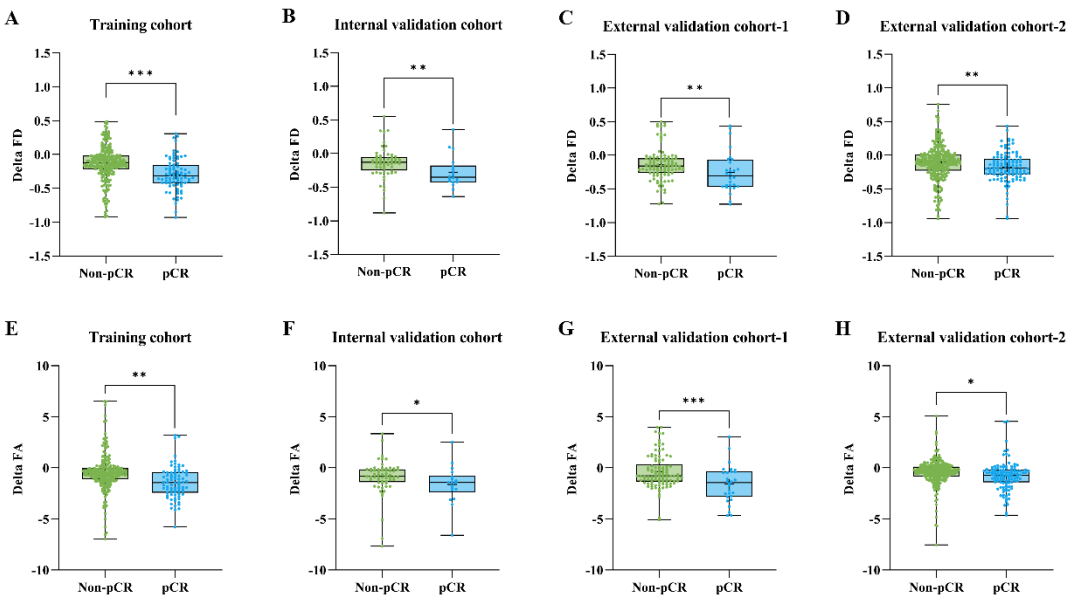
Supplementary Materials

I. Supplementary Figures

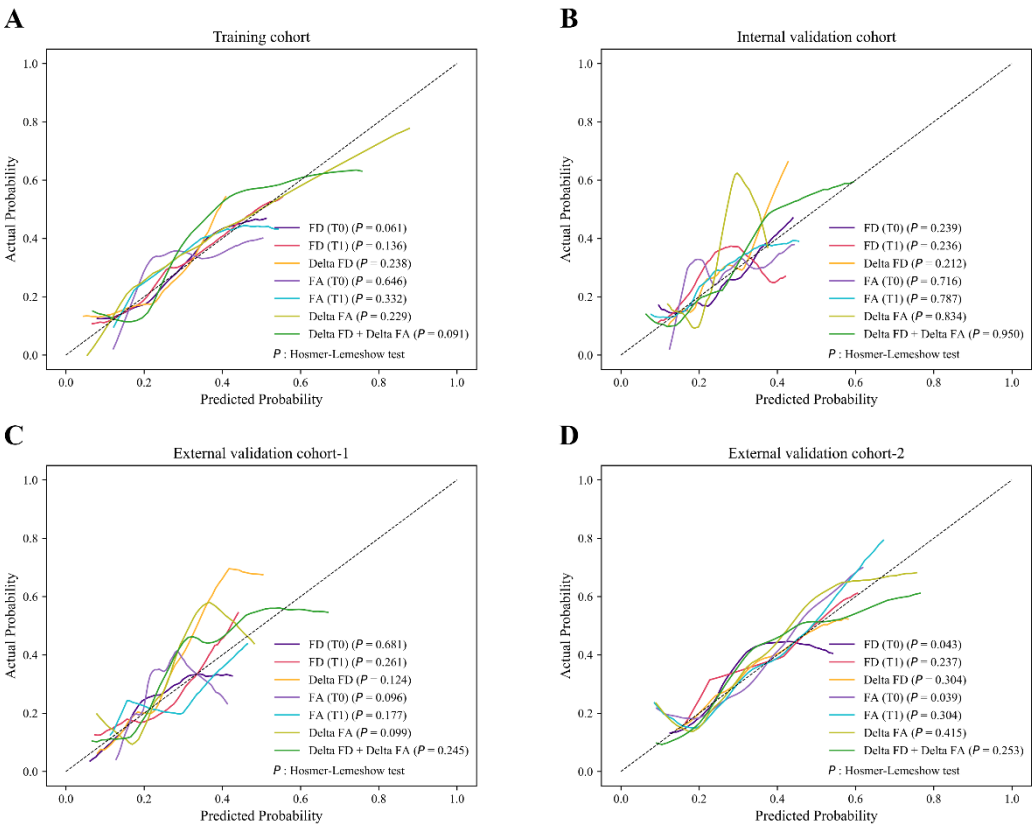
II. Supplementary Tables



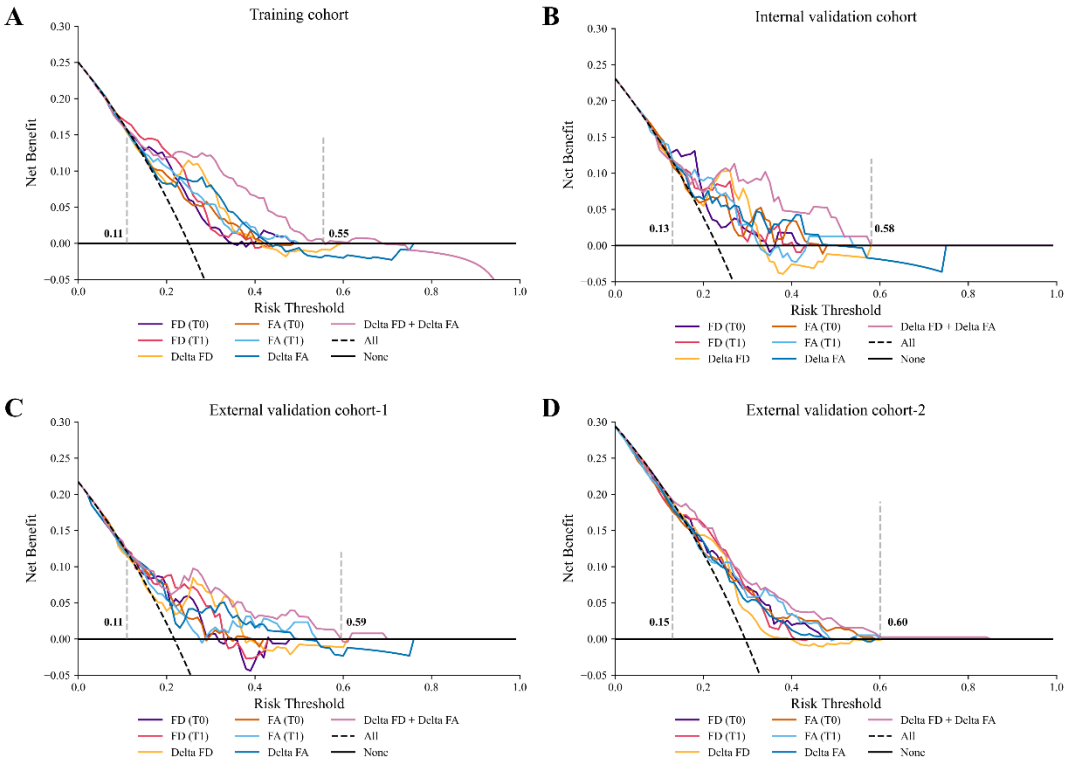
Supplementary Figure 1. Box plots of FD and FA at pre-NAC (T0) and early-NAC (T1) across different cohorts. (A–D) Fractal dimension (FD) values at T0 and T1 in the training cohort, internal validation cohort, external validation cohort 1, and external validation cohort 2, respectively. (E–H) Fractal abundance (FA) values at T0 and T1 in the training cohort, internal validation cohort, external validation cohort 1, and external validation cohort 2, respectively.



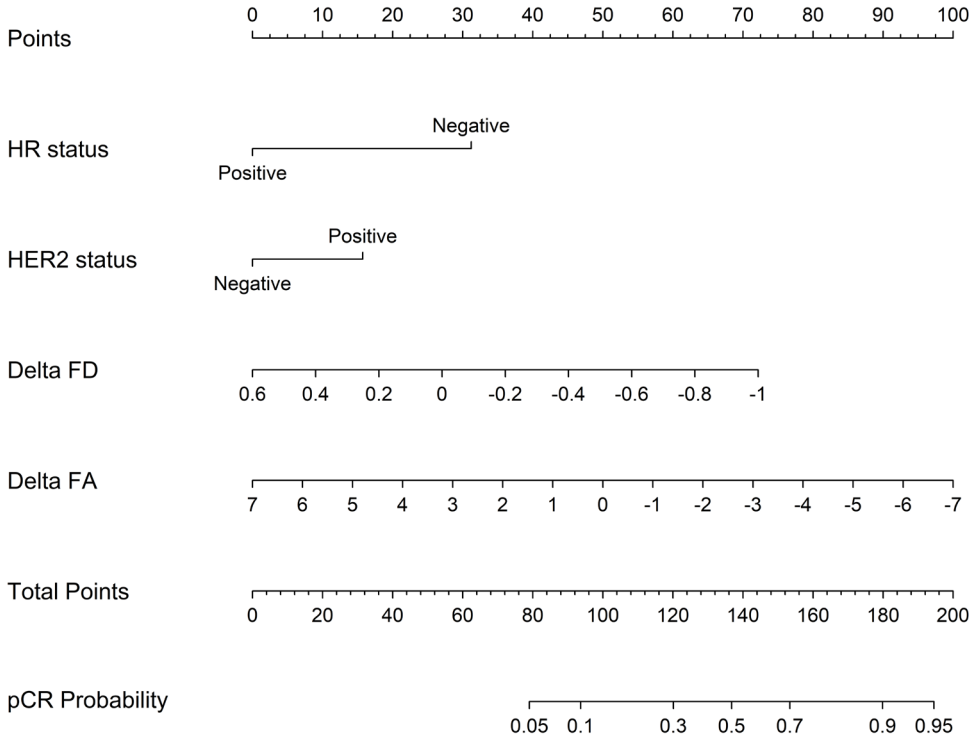
Supplementary Figure 2. Box plots of Delta FD and Delta FA between pCR and non-pCR groups across different cohorts. (A–D) Differences in delta FD (T1–T0) between pCR and non-pCR groups in the training cohort, internal validation cohort, external validation cohort 1, and external validation cohort 2, respectively. (E–H) Differences in Delta FA (T1–T0) between pCR and non-pCR groups in the training cohort, internal validation cohort, external validation cohort 1, and external validation cohort 2, respectively. Significant differences in both delta FD and delta FA were observed between pCR and non-pCR groups across all cohorts (all $P < 0.05$). *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.



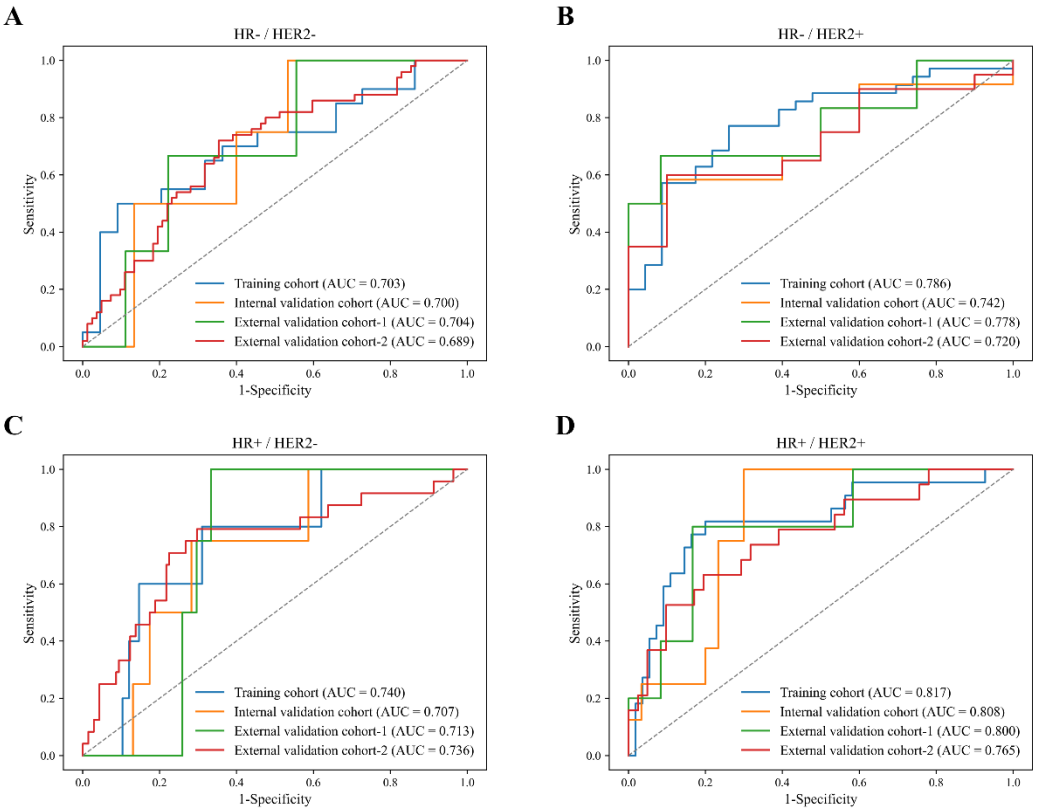
Supplementary Figure 3. Calibration curves of the model across different cohorts. (A–D) Calibration curves for the training cohort, internal validation cohort, external validation cohort 1, and external validation cohort 2, respectively, showing the agreement between predicted probabilities and actual outcomes.



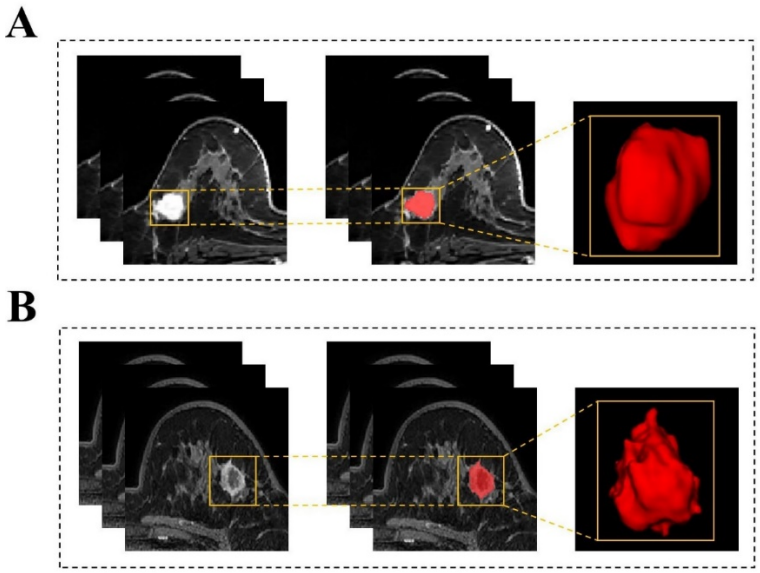
Supplementary Figure 4. Decision curves of the model across different cohorts. (A–D) Decision curves for the training cohort, internal validation cohort, external validation cohort 1, and external validation cohort 2, respectively, illustrating the net clinical benefit of the model across a range of threshold probabilities.



Supplementary Figure 5. A nomogram constructed using clinical features along with delta FD and delta FA. The nomogram incorporates HR status, HER2 status, delta FD, and delta FA. The nomogram formula is as follows: logit(*P*) = -1.328 + 1.449×HR status + 0.698×HER2 status -1.702×delta FD - 0.360× delta FA.



Supplementary Figure 6. Performance of the combined delta model in different molecular subtypes. Receiver operating characteristic (ROC) curves demonstrating the performance of the combined delta model in the following molecular subtypes: (A) HR−/HER2−, (B) HR−/HER2+, (C) HR+/HER2−, and (D) HR+/HER2+.



Supplementary Figure 7. Tumor region segmentation on DCE-MRI images. The entire tumor region was manually delineated for fractal analysis, including all visible components such as enhancing solid tissue, necrosis, calcification, hemorrhage, and other internal structures. (A) shows a solid enhancing tumor type, while (B) shows a mixed tumor type with both enhancing and necrotic components. The rightmost images represent corresponding 3D tumor reconstructions.

Supplementary Table 1. Variance-components analysis of Fractal Analysis for Reader 1 at the First and Second Study

Fractal features	Variance components		COV between readings (%)	COV between patients (%)
	Between readings	Between patients		
FD	0.002	0.056	3.523	278.145
FA	0.011	0.165	5.076	185.222

Note.—CI = confidence interval, COV = coefficient of variation, FA = fractal abundance, FD = fractal dimension.

Supplementary Table 2. Interobserver Agreement for Fractal Analysis for Readers 1 and 2

Fractal analysis	Reader 1 (first study)	Reader 2 (first study)	ICC (95% CI)
FD	2.55 ± 0.25	2.51 ± 0.23	0.869 (0.778, 0.915)
FA	10.63 ± 1.73	10.58 ± 2.05	0.857 (0.719, 0.935)

Note.—FA = fractal abundance, FD = fractal dimension, CI = confidence interval, ICC = intraclass correlation coefficient.

Supplementary Table 3. Linear Mixed Effects Model Analysis of Fractal Dimension

Dependent Variable	Independent Variable	Coefficient β	*P* Value
FD	**Intercept**	10.464	**< 0.001**
	Age	-0.004	0.730
	Menopausal status		
	Premenopausal	Reference	
	Postmenopausal	-0.208	0.268
	HR status		
	Negative	Reference	
	Positive	-0.222	0.192
	HER2 status		
	Negative	Reference	
	Positive	-0.025	0.876
	Ki-67 status		
	Low	Reference	
	High	-0.064	0.716
	Clinical T stage		
	T1-T2	Reference	
	T3-T4	0.142	0.372
	Clinical N stage		
	N0-N1	Reference	
	N2-N3	0.285	0.077
	Time	-0.657	**< 0.001**
	Treatment response		
	Non-pCR	Reference	
	pCR	-0.973	**< 0.001**
	Time×Treatment response	-0.017	0.933

Note.—FA = fractal abundance, FD = fractal dimension, CI = confidence interval, HER2 = human epidermal growth factor receptor2, HR = hormone receptor, OR = odds ratio, pCR = pathologic complete response.

Supplementary Table 4. Linear Mixed Effects Model Analysis of Fractal Abundance

Dependent Variable	Independent Variable	Coefficient β	*P* Value
FA	**Intercept**	2.589	< 0.001
	Age	0.001	0.550
	Menopausal status		
	Premenopausal	Reference	
	Postmenopausal	-0.027	0.328
	HR status		
	Negative	Reference	
	Positive	-0.015	0.565
	HER2 status		
	Negative	Reference	
	Positive	-0.021	0.417
	Ki-67 status		
	Low	Reference	
	High	-0.018	0.483
	Clinical T stage		
	T1-T2	Reference	
	T3-T4	-0.003	0.895
	Clinical N stage		
	N0-N1	Reference	
	N2-N3	0.005	0.830
	Time	-0.153	< 0.001
	Treatment response		
	Non-pCR	Reference	
	pCR	-0.170	< 0.001
	Time×Treatment response	-0.031	0.428

Note.—FA = fractal abundance, FD = fractal dimension, CI = confidence interval, HER2 = human epidermal growth factor receptor2, HR = hormone receptor, OR = odds ratio, pCR = pathologic complete response.

Supplementary Table 5. Sensitivity analyses Stratified by Molecular Subtypes

	Characteristic	Multivariable logistic regression analysis		
		Coefficient	OR (95% CI)	*P* Value
HR-/HER2-	**Age**	-0.001	0.999 (0.966, 1.032)	0.948
	Menopausal status			
	Premenopausal		Reference	
	Postmenopausal	0.153	1.166 (0.812, 1.673)	0.405
	Delta FD	-2.334	0.097 (0.023, 0.406)	**0.001**
	Delta FA	-0.447	0.640 (0.486, 0.842)	**0.001**
HR-/HER2	**Age**	-0.043	0.958 (0.912, 1.006)	0.084
	Menopausal status			
	Premenopausal		Reference	
	Postmenopausal	0.347	1.415 (0.743, 2.692)	0.290
	Delta FD	-1.673	0.187 (0.044, 0.798)	**0.023**
	Delta FA	-0.381	0.683 (0.526, 0.887)	**0.004**
HR+/HER2-	**Age**	-0.007	0.993 (0.950, 1.038)	0.756
	Menopausal status			
	Premenopausal		Reference	
	Postmenopausal	0.059	1.061 (0.681, 1.653)	0.793
	Delta FD	-2.416	0.089 (0.021, 0.371)	**0.001**
	Delta FA	-0.399	0.671 (0.524, 0.859)	**0.002**
HR+/HER2+	**Age**	-0.020	0.980 (0.940, 1.022)	0.356
	Menopausal status			
	Premenopausal		Reference	
	Postmenopausal	0.183	1.200 (0.762, 1.890)	0.430
	Delta FD	-2.719	0.066 (0.016, 0.266)	**< 0.001**
	Delta FA	-0.380	0.684 (0.537, 0.872)	**0.002**

Note.—Data in parentheses are 95% CI. Sensitivity analyses were performed within the overall population (*n* = 911), including the training cohort, internal validation cohort, and two external validation cohorts, stratified by molecular subtypes. FA = fractal abundance, FD = fractal dimension, CI = confidence interval, HER2 = human epidermal growth factor receptor2, HR = hormone receptor, OR = odds ratio.

Supplementary Table 6. Characteristics of Patients in the Genomic Cohort

Characteristic	Genomics cohort (*n* = 383)
Age (years)*	49.0 (41.0-56.0)
Menopausal status	
Premenopausal	190 (49.6)
Postmenopausal	114 (29.8)
Perimenopausal	18 (4.7)
Unknown	61 (15.9)
HR status	
Negative	162 (42.3)
Positive	221 (57.7)
HER2 status	
Negative	293 (76.5)
Positive	90 (23.5)
Molecular subtypes	
HR-/HER2-	132 (34.5)
HR-/HER2+	30 (7.8)
HR+/HER2-	161 (42.0)
HR+/HER2+	60 (15.7)
Treatment response	
Non-pCR	270 (70.5)
pCR	113 (29.5)

Note.—Unless otherwise indicated, numbers represent the count of patients, with percentages in parentheses. *P* values indicate the comparison of variables across all cohorts. HER2 = human epidermal growth factor receptor2, HR = hormone receptor, pCR = pathologic complete response.

Supplementary Table 7. Details of Neoadjuvant Chemotherapy Regimens in the Training and Three Validation Cohorts

Neoadjuvant Chemotherapy regimen	Training cohort (*n* = 320)	Internal validation cohort (*n* = 78)	External validation cohort-1 (*n* = 129)	External validation cohort-2 (*n* = 384)
Adriamycin + Cyclophosphamide	32 (10.0)	2 (2.6)	1 (0.8)	0 (0)
Adriamycin + Cyclophosphamide + Taxane	142 (44.5)	32 (41.0)	39 (30.2)	0 (0)
Adriamycin + Cyclophosphamide + Taxane + Trastuzumab	1 (0.3)	0 (0)	0 (0)	0 (0)
Adriamycin + Cyclophosphamide + Taxane + Pertuzumab	1 (0.3)	0 (0)	0 (0)	0 (0)
Adriamycin + Taxane	2 (0.6)	0 (0)	0 (0)	0 (0)
Cyclophosphamide + Epirubicin + 5-Fluorouracil + Taxane	1 (0.3)	0 (0)	0 (0)	0 (0)
Taxane + Carboplatin + Dose-dense Adriamycin + Cyclophosphamide	1 (0.3)	0 (0)	0 (0)	0 (0)
Epirubicin + Cyclophosphamide	3 (0.9)	0 (0)	0 (0)	0 (0)
Epirubicin + Cyclophosphamide + Taxane	5 (1.6)	4 (5.1)	4 (3.1)	0 (0)
Epirubicin + Cyclophosphamide + Taxane + Trastuzumab	0 (0)	1 (1.3)	5 (3.9)	0 (0)
Nab-Paclitaxel + Capecitabine	2 (0.6)	0 (0.0)	0 (0.0)	0 (0)
Docetaxel + Doxorubicin + Cyclophosphamide	33 (10.3)	16 (20.5)	3 (2.3)	0 (0)
Docetaxel + Adriamycin + Trastuzumab	1 (0.3)	0 (0)	0 (0)	0 (0)
Docetaxel + Cyclophosphamide	7 (2.2)	1 (1.3)	9 (7.0)	0 (0)
Docetaxel + Carboplatin	5 (1.6)	1 (1.3)	2 (1.6)	0 (0)
Docetaxel + Carboplatin + Trastuzumab	11 (3.4)	3 (3.8)	4 (3.1)	0 (0)
Docetaxel + Carboplatin + Trastuzumab + Pertuzumab	40 (12.5)	11 (14.1)	8 (6.2)	0 (0)
Docetaxel + Carboplatin + Trastuzumab + Pertuzumab + Pembrolizumab	1 (0.3)	0 (0)	0 (0)	0 (0)
Docetaxel + Cyclophosphamide + Trastuzumab	2 (0.6)	0 (0)	0 (0)	0 (0)
Docetaxel + Epirubicin + Cyclophosphamide	2 (0.6)	0 (0)	40 (30.9)	0 (0)
Docetaxel + Epirubicin	0 (0)	0 (0)	4 (3.1)	0 (0)
Taxane + Trastuzumab + Pertuzumab	16 (5.0)	7 (9.0)	0 (0)	0 (0)
Docetaxel + Cisplatin	12 (3.8)	0 (0)	0 (0)	0 (0)
Taxane + Lapatinib	0 (0)	0 (0)	5 (3.9)	0 (0)
Taxane + Lapatinib + Trastuzumab	0 (0)	0 (0)	3 (2.3)	0 (0)
Taxane + Lapatinib + Trastuzumab + Pertuzumab	0 (0)	0 (0)	2 (1.6)	0 (0)
Paclitaxel	0 (0)	0 (0)	0 (0)	65 (17.0)
Paclitaxel + ABT 888 + Carboplatin	0 (0)	0 (0)	0 (0)	25 (6.5)
Paclitaxel + AMG 386	0 (0)	0 (0)	0 (0)	49 (12.8)
Paclitaxel + AMG 386 + Trastuzumab	0 (0)	0 (0)	0 (0)	9 (2.3)
Paclitaxel + Ganetespib	0 (0)	0 (0)	0 (0)	41 (10.7)
Paclitaxel + Ganitumab	0 (0)	0 (0)	0 (0)	45 (11.7)
Paclitaxel + MK-2206	0 (0)	0 (0)	0 (0)	25 (6.5)
Paclitaxel + MK-2206 + Trastuzumab	0 (0)	0 (0)	0 (0)	9 (2.3)
Paclitaxel + Neratinib	0 (0)	0 (0)	0 (0)	40 (10.4)
Paclitaxel + Pembrolizumab	0 (0)	0 (0)	0 (0)	27 (7.0)
Paclitaxel + Pertuzumab + Trastuzumab	0 (0)	0 (0)	0 (0)	16 (4.2)
Paclitaxel + Trastuzumab	0 (0)	0 (0)	0 (0)	16 (4.2)

T-DM1 + Pertuzumab	0 (0)	0 (0)	0 (0)	17 (4.4)

Note.—Unless otherwise indicated, numbers represent the count of patients, with percentages in parentheses.

Supplementary Table 8. MRI Acquisition Parameters

	Insitution 1	Insitution 2	Insitution 3
Scanner	Siemens 3.0 T (Prisma)	Siemens 3.0 T (Spectra)	1.5 or 3.0 T
Sequence	CS-VIBE	VIBE	Gradient echo
TR/TE (ms)	4.5/1.6	4.23/1.57	4-10/Minimum
FOV (mm)	360×292	360×360	260×360
Matrix	384×384	300×300	384×512
Slice Thickness (mm)	2.5	1.2	≤ 2.5
Slice orientation	Axial	Axial	Axial
Temporal resolution (s)	4.46	5.4	NA

Note.—Institutions 1 and 2 are from two independent medical centers, while Institution 3 is sourced from the I-SPY2 dataset in The Cancer Imaging Archive (TCIA). For more detailed information, please visit *https://www.cancerimagingarchive.net/*. FOV = field of view, TR = repetition time, TE = echo time, No. = number, ms = millisecond, mm = millimeter.