

Supplementary Table 1: Clinicopathological characteristics of BCBM patients.

Characteristics	SEER Cohort (n=173)	Training Cohort (n=161)	Validation cohort (n=149)	Total* (n=310)	t/χ^2	P-value
					(training vs. validation cohorts) [†]	(training vs. validation cohorts)
Age					0.347	0.841
<35 years	6 (3.5)	24 (14.9)	19 (12.8)	43 (13.9)		
35–56 years	70 (40.5)	106 (65.8)	102 (68.5)	208 (67.1)		
>56 years	97 (56.1)	31 (19.3)	28 (18.8)	59 (19.0)		
Tumor location					0.017	0.895
Left	86 (49.7)	68 (42.2)	65 (43.6)	133 (42.9)		
Right	87 (50.3)	93 (57.8)	84 (56.4)	177 (57.1)		
Tumor size					5.802	0.122
T1	30 (17.3)	24 (14.9)	36 (24.2)	60 (19.4)		
T2	51 (29.5)	86 (53.4)	73 (49.0)	159 (51.3)		
T3	29 (16.8)	32 (19.9)	20 (13.4)	52 (16.8)		
T4	63 (36.4)	19 (11.8)	20 (13.4)	39 (12.6)		
Lymph node metastasis					1.168	0.761
N0	37 (21.4)	26 (16.1)	25 (16.8)	51 (16.5)		
N1	72 (41.6)	50 (31.1)	52 (34.9)	102 (32.9)		
N2	22 (12.7)	39 (24.2)	29 (19.5)	68 (21.9)		
N3	42 (24.3)	46 (28.6)	43 (28.9)	89 (28.7)		
Surgery method					0.057	0.972
Improved radical cure	–	131 (81.4)	121 (81.2)	252 (81.3)		
Breast conservation	–	13 (8.1)	13 (8.7)	26 (8.4)		
Unilateral mastectomy	–	17 (10.6)	15 (10.1)	32 (10.3)		
Molecular subtype					0.737	0.864
Luminal A	77 (44.5)	44 (27.3)	37 (24.8)	81 (26.1)		
Luminal B	29 (16.8)	38 (23.6)	32 (21.5)	70 (22.6)		
Triple negative	47 (27.2)	27 (16.8)	29 (19.5)	56 (18.1)		
HER2 enriched	20 (11.6)	52 (32.3)	51 (34.2)	103 (33.2)		
ER					0.028	0.868
Negative	71 (41.0)	89 (55.3)	80 (53.7)	169 (54.5)		
Positive	102 (59.0)	72 (44.7)	69 (46.3)	141 (45.5)		
PR					0.015	0.902
Negative	94 (54.3)	108 (67.1)	98 (65.8)	206 (66.5)		
Positive	79 (45.7)	53 (32.9)	51 (34.2)	104 (33.5)		
HER2					0.061	0.804
Negative	124 (71.7)	108 (67.1)	97 (65.1)	205 (66.1)		
Positive	49 (28.3)	53 (32.9)	52 (34.9)	105 (33.9)		
Ki67					0.042	0.979
<14%	–	14 (8.7)	12 (8.1)	26 (8.4)		
14–30%	–	15 (9.3)	14 (9.4)	29 (9.4)		

>30%	–	132 (82.0)	123 (82.6)	255 (82.3)		
Chemotherapy					3.174	0.075
No	52 (30.1)	50 (31.1)	32 (21.5)	82 (26.5)		
Yes	121 (69.9)	111 (68.9)	117 (78.5)	228 (73.5)		
Targeted therapy					0.385	0.535
No	–	133 (82.6)	118 (79.2)	251 (81.0)		
Yes	–	28 (17.4)	31 (20.8)	59 (19.0)		
Endocrine therapy					0.003	0.960
No	–	99 (61.5)	93 (62.4)	192 (61.9)		
Yes	–	62 (38.5)	56 (37.6)	118 (38.1)		
Radiation therapy					0.016	0.899
No	44 (25.4)	54 (33.5)	48 (32.2)	102 (32.9)		
Yes	129 (74.6)	107 (66.5)	101 (67.8)	208 (67.1)		
Liver metastasis					0.207	0.649
No	144 (83.2)	83 (51.6)	72 (48.3)	155 (50.0)		
Yes	29 (16.8)	78 (48.4)	77 (51.7)	155 (50.0)		
Lung metastasis					<0.001	1.000
No	110 (63.6)	63 (39.1)	58 (38.9)	121 (39.0)		
Yes	63 (36.4)	98 (60.9)	91 (61.1)	189 (61.0)		
Bone metastasis					0.360	0.549
No	87 (50.3)	80 (49.7)	68 (45.6)	148 (47.7)		
Yes	86 (49.7)	81 (50.3)	81 (54.4)	162 (52.3)		
Vascular invasion					1.262	0.261
No	–	96 (59.6)	99 (66.4)	195 (62.9)		
Yes	–	65 (40.4)	50 (33.6)	115 (37.1)		
Nerve invasion					0.762	0.383
No	–	153 (95.0)	137 (91.9)	290 (93.5)		
Yes	–	8 (5.0)	12 (8.1)	20 (6.5)		
Vital status					<0.001	1.000
Dead	131 (75.7)	116 (72.0)	107 (71.8)	223 (71.9)		
Alive	42 (24.3)	45 (28.0)	42 (28.2)	87 (28.1)		
Survival (months)	23.0±20.9	39.0±26.3	36.9±22.8	38.0±24.7	–0.730	0.466

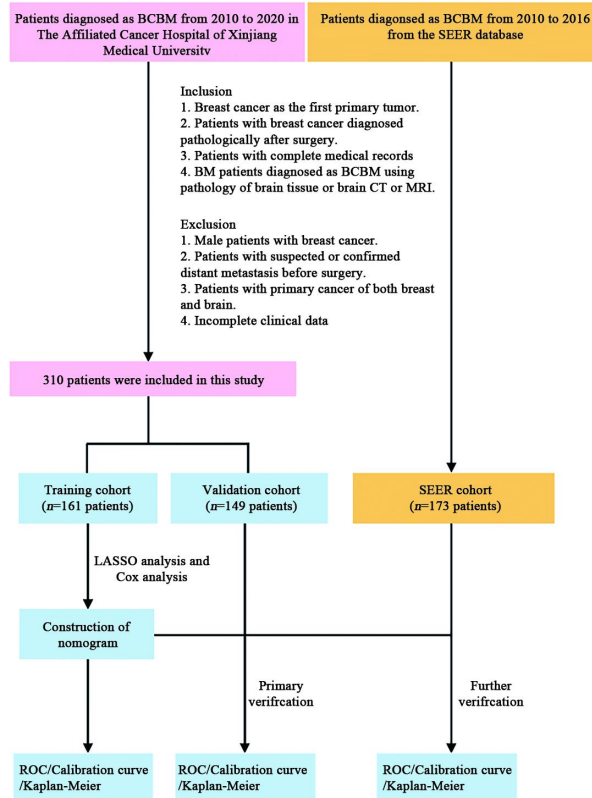
*The total of validation and verification cohorts. Data are expressed as *n* (%) or mean±standard deviation. †In addition to survival (which was tested by *t* test), all factors were tested by chi-squared test. BCBM: Breast cancer brain metastasis; ER: Estrogen receptor; HER2: Human epidermal growth factor receptor-2; PR: Progesterone receptor; SEER: Surveillance, Epidemiology, and End Results Program.

Supplementary Table 2: Univariate Cox regression analysis on patients with brain metastasis of breast cancer.

Characteristics	Hazard ratio	<i>P</i> -value	Characteristics	Hazard ratio	<i>P</i> -value
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	(95% CI)			(95% CI)	
Age			Ki67		
<35	Reference		<14%	Reference	
35–56	0.72 (0.44–1.18)	0.190	14–30%	1.30 (0.50–3.33)	0.591
>56	0.79 (0.43–1.45)	0.448	>30%	2.09 (1.00–4.38)	0.050
Primary site			Chemotherapy		
Left	Reference		No	Reference	
Right	0.62 (0.43–0.89)	0.011	Yes	0.49 (0.33–0.72)	<0.001
ER			Targeted therapy		
Negative	Reference		No	Reference	
Positive	0.78 (0.54–1.14)	0.201	Yes	1.35 (0.83–2.20)	0.221
PR			Endocrine therapy		
Negative	Reference		No	Reference	
Positive	1.17 (0.81–1.71)	0.402	Yes	0.72 (0.49–1.06)	0.094
HER2			Radiotherapy		
Negative	Reference		No	Reference	
Positive	1.67 (1.13–2.47)	0.010	Yes	0.68 (0.46–0.99)	0.045
Tumor size			Lymph node metastasis		
T1	Reference		N0	Reference	
T2	0.75 (0.50–1.12)	0.162	N1	0.50 (0.27–0.90)	0.021
T3	0.81 (0.45–1.45)	0.478	N2	0.86 (0.48–1.53)	0.608
T4	0.75 (0.50–1.12)	0.162	N3	1.71 (1.01–2.91)	0.047
Surgery method			Liver metastasis		
Modified radical mastectomy	Reference		No	Reference	
Protective and radical operation of mastocarcinoma	0.30 (0.12–0.75)	0.010	Yes	1.29 (0.89–1.86)	0.179
Single incision for breast cancer	1.52 (0.88–2.63)	0.134	Lung metastasis		
Molecular subtype			No	Reference	
Luminal A	Reference		Yes	0.56 (0.39–0.81)	0.002
Luminal B	1.75 (1.05–2.91)	0.031	Bone metastasis		
Triple negative	1.33 (0.71–2.51)	0.373	No	Reference	
HER2 enriched	2.16 (1.32–3.51)	0.002	Yes	1.18 (0.81–1.71)	0.381
Nerve invasion			Vascular invasion		
No	Reference		No	Reference	
Yes	2.41 (1.17–4.97)	0.017	Yes	1.56 (1.07–2.28)	0.021

CI: Confidence interval; ER: Estrogen receptor; HER2: Human epidermal growth factor receptor-2; PR: Progesterone receptor.



Supplementary Figure 1: Data collection and analysis processes of this study. BCBM: Breast cancer brain metastasis; LASSO: Least absolute shrinkage and selection operator; ROC: Receiver operating characteristic; SEER: Surveillance, Epidemiology, and End Results Program.