

# Tumor enhancement and shrinkage pattern in dynamic contrast-enhanced magnetic resonance imaging for predicting pathologic complete response after human epidermal growth factor receptor 2 (HER2)-targeted therapy in breast cancer

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> **Background:** Targeted therapy with neoadjuvant chemotherapy for patients with human epidermal growth factor receptor 2 (HER2)-positive breast cancer has increased the rates of pathological complete response (pCR) and breast preservation surgery and improved the overall disease-free survival rate. This study aimed to determine whether tumor enhancement and shrinkage patterns in dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) can predict the efficacy of targeted therapy in patients with HER2-positive breast cancer and differentiate pCR from non-pCR.

> Methods: The data of 64 patients with HER2-positive breast cancer who received targeted therapy prior to surgery were retrospectively collected. All patients had complete postoperative pathological data. The pretreatment evaluation of the tumor enhancement pattern and the shrinkage pattern after two treatment cycles were assessed. The difference in the enhancement and shrinkage patterns between the pCR and non-pCR groups was evaluated via the  $\chi^2$  test. Logistic regression analysis was used to assess the value of enhancement and shrinkage patterns for predicting pCR in patients with HER2-positive breast cancer.

> Results: There were statistically significant differences in tumor size, estrogen receptor (ER) status, lymph node metastasis, enhancement pattern, and shrinkage pattern between the pCR and non-pCR cases. Patients with a tumor size ≤20 mm were likely to achieve pCR. ER status, lymph node metastasis, and enhancement and shrinkage patterns each had good precision for predicting pCR, and the combination of enhancement and shrinkage patterns had the highest prediction accuracy. Multivariate logistic regression analysis indicated that only enhancement pattern had a significant predictive value.

> Conclusions: Among patients with HER2-positive breast cancer, those with tumor size ≤20 mm, ERnegative status, no lymph node metastases, and mass enhancement and concentric shrinkage patterns are more likely to achieve pCR. Mass enhancement combined with concentric shrinkage had the highest accuracy in predicting pCR, indicating that preoperative imaging may be useful for guiding clinical decisions regarding targeted treatments.

> Keywords: Breast cancer; human epidermal growth factor receptor 2 (HER2); targeted therapy; dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI); shrinkage pattern

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# Introduction

In patients with breast cancer, the targeted treatment of anti-human epidermal growth factor receptor 2 (HER2) antibodies is associated with an increase in the diseasefree survival rate (1). The National Comprehensive Cancer Network guidelines include HER2-targeted treatment in the standard treatment scheme for HER2-positive breast cancer (2). The pathological complete response (pCR) rate for patients with HER2-positive after neoadjuvant chemotherapy (NAC) and targeted treatment can reach 40–60% (3-5). In 2014 a large-sample, multicenter study found that patients with HER2-positive breast cancer had the highest rates of breast preservation surgery and pCR after NAC (6). In 2018, Richter *et al.* (7) raised questions about whether patients who achieved pCR needed further surgery. Because there is no accurate predictor of pCR, an inaccurate diagnosis or inappropriate treatment plan could result in local recurrence or overtreatment. Ishitobi *et al.* (8) analyzed 375 patients with breast cancer who had undergone breast preservation surgery and found that ER status and multifocality of residual tumor after NAC were independent predictors of tumor recurrence. Despite these findings, there remain questions regarding the treatment of breast cancer: What kind of patients can achieve pCR after HER2-targeted treatment? How can we predict and identify pCR early? Do medical images have a specific predictive value? To address these issues, we conducted a study to determine whether there was a correlation between residual tumor and dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) enhancement and shrinkage patterns after targeted treatment of patients with HER2-positive breast cancer. We also examined whether the enhancement and shrinkage patterns could predict the efficacy of targeted therapy and identify pCR and non-pCR cases. The findings of this study may help guide clinical management. We present this article in accordance with the STROBE reporting checklist (available at [https://qims.](https://qims.amegroups.com/article/view/10.21037/qims-24-447/rc) [amegroups.com/article/view/10.21037/qims-24-447/rc\)](https://qims.amegroups.com/article/view/10.21037/qims-24-447/rc).

# **Methods**

# *Participants*

We conducted a retrospective analysis of patients with breast cancer treated with NAC in Shenzhen people's hospital between January 2010 and August 2020. The inclusion criteria were as follows: (I) HER2 positivity as confirmed by pathological immunohistochemistry prior to chemotherapy; (II) complete DCE-MRI images obtained before biopsy and after two cycles of NAC; (III) HER2 targeted therapy consisting of trastuzumab, pertuzumab, or their combination; and (IV) availability of complete surgical and pathological data before August 2020. Meanwhile, the exclusion criterion was previous surgery before targeted therapy.

This study was conducted in accordance with the provisions of the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of Shenzhen People's Hospital (No. LL-KY-2022285). The requirement for individual consent was waived due to the retrospective nature of the analysis.

A total of 64 women aged  $27-71$  (47.25 $\pm$ 10.54) years were enrolled in this study. Four types of NAC regimens with HER2-targeted therapy were administered to the patients:

- $\div$  Epirubicin and cyclophosphamide  $\times$  4 $\rightarrow$ taxotere and trastuzumab  $\times$  4 (27 cases): four cycles of epirubicin (100 mg/m; iv; day 1) and cyclophosphamide  $(600 \text{ mg/m}^2 \text{ iv}; \text{day 1})$ , followed by four cycles of taxotere  $(100 \text{ mg/m}^2; \text{iv}; \text{day } 1)$ and trastuzumab (a first dose of 4 mg/kg followed by 2 mg/kg on days 1, 8, and 15) administered every three weeks.
- Epirubicin and cyclophosphamide × 4→paclitaxel and trastuzumab  $\times$  4 (16 cases): four cycles of epirubicin  $(100 \text{ mg/m}^2 \text{ iv}; \text{day 1})$  and cyclophosphamide  $(600 \text{ mg/m}^2 \text{ iv}; \text{day 1})$  every two weeks, followed by four cycles of paclitaxel  $(175 \text{ mg/m}^2 \text{ iv}$  for 3 h; day 1) every two weeks and simultaneous trastuzumab (a

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first dose of 4 mg/kg and then 2 mg/kg on day 1) every week.

- $\div$  Taxotere, carboplatin, and trastuzumab (TCbH)  $\times$  6 (18 cases): six cycles of taxotere (75 mg/m<sup>2</sup> iv; day 1), carboplatin (area under the plasma concentrationtime curve =6 iv; day 1), and trastuzumab (first dose of 8 and 6 mg/kg on day 1) every three weeks.
- Taxotere, carboplatin, trastuzumab, pertuzumab × 6 (3 cases, which were all switched from TCbH  $\times$  6 after two cycles due to unsatisfactory response): six cycles of taxotere  $(75 \text{ mg/m}^2 \text{ iv}; \text{day 1})$ , carboplatin (area under the plasma concentration-time curve =6; iv; day 1), trastuzumab (first dose of 8 mg/kg then 6 mg/kg on day 1), and pertuzumab (first dose of 850 mg and then 420 mg on day 1) every three weeks.

# *Preoperative status of lymph node metastasis and immunohistochemical evaluation*

Preoperative lymph node metastasis status was determined according to pathological biopsy. As per the recommended guidelines for breast cancer immunohistochemistry published by the American Society of Clinical Oncology (9) in 2018, if more than 1% of tumor cells are positive for estrogen receptor (ER) and progesterone receptor (PR) in immunohistochemical staining, this suggests positive ER and PR status. HER2 was detected via HercepTest immunohistochemical staining (Genentech, San Francisco, CA, USA), and the results were scored as 0 (negative), 1+ (negative),  $2+$  (equivocal), or  $3+$  (positive). For scores of  $2+$ or 3+, HER2 status was confirmed through fluorescence in situ hybridization.

# *Postoperative pathological reactivity assessment*

There is no clear consensus regarding the definition of pCR after NAC. In this study, similarly to the studies of Krystel-Whittemore *et al.* and Bitencourt *et al.* (10,11), pCR was defined as nonresidual invasive cancer in the breast or axillary lymph nodes at the time of surgical resection, which could be accompanied by residual intraductal cancer components.

## *Magnetic resonance imaging (MRI)*

All patients underwent DCE-MRI of both breasts using a four-channel surface breast coil on a 3.0-T MRI device (MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany). First, T1- and T2-weighted imaging, T2weighted fat suppression imaging, and diffusion-weighted imaging (with b-values of 50, 400, 800 s/mm<sup>2</sup>) were performed in the transverse position. In the examination, the plain film was first scanned. Subsequently, gadolinium diethylenetriamine penta-acetic acid was injected after 30 seconds of suspension, and five successive scans were performed, each lasting 1 minute. The dynamic-enhanced scanning parameters were as follows: echo time =1.7 ms, repetition time =4.7 ms, scanning field =360 mm, spacing =0 mm, layer thickness =1.6 mm, number of layers =72, and acquisition matrix =448×372. The examination equipment and parameters were the same both before and after treatment.

# *Image evaluation*

The size of the lesion, lymph node metastasis status, and clinical stage were evaluated according to the American Joint Committee on Cancer standards. Two radiologists with 3 and 5 years of experience in breast imaging diagnosis, respectively, read the films separately and recorded the results. If the evaluation results were inconsistent, a consensus was reached before recording. The enhancement pattern before treatment and the shrinkage pattern after two cycles of targeted therapy were observed. According to the 2013 American College of Radiology breast imaging reporting and data system (12), the enhancement mode was classified as mass enhancement or non-mass enhancement. Mass enhancement refers to the occupation of a threedimensional space with a convex edge, while non-mass enhancement refers to the presence of normal glands or adipose tissue between punctate or flaky enhancement. Shrinkage patterns were classified in accordance with the Fukada classification method (13), which defines centripetal contraction as the simple centripetal reduction of a lesion with decreased volume and no fragmentation. All other types of contraction were considered to be noncentripetal contractions (*Figure 1*).

## *Statistical analysis*

SPSS version 22 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis, and the Kolmogorov-Smirnov test was used to determine normal distributions of patient age and lesion size. The pCR and non-pCR groups were compared using an independent samples *t*-test or the Wilcoxon rank-sum test. The  $\chi^2$  test was used to compare the difference between the enhancement and shrinkage



**Figure 1** Schematic diagrams of the (A) mass enhancement and (B) non-mass enhancement shrinkage patterns.

patterns prior to chemotherapy. The interaction between enhancement and shrinkage patterns was described by the patient subgrouping determined by the four possible pattern combinations. A similar approach was adopted for the interaction between enhancement pattern and ER status. Unconditional logistic regression analysis was used to analyze the relevant factors for achieving pCR in HER2 positive patients after targeted treatment. P value, odds ratio (OR), and 95% confidence interval (CI) were calculated, with P<0.05 indicating statistical significance.

# **Results**

# *Comparison of clinical indicators prior to HER2-targeted treatment*

Among the 64 patients with HER2-positive breast cancer, there were 26 cases of pCR and 38 cases of non-pCR. The age of non-pCR group (48.42±11.19 years) was slightly higher than that of the pCR group (45.54±9.46 years), but this difference was not statistically significant. There was, however, a significant difference between the groups in terms of lesion size (P=0.010), with lesions  $\leq$ 20 mm being associated with pCR (6/7, 86%) and lesions >20 mm being associated with non-pCR (37/57, 65%). There was a significant difference between groups in terms of ER status (P=0.025) but not PR status (P=0.265). After targeted treatment, a greater portion of ER-positive patients experienced non-pCR (24/33, 73%) as compared to ERnegative patients. After targeted treatment, the rate of pCR in those without lymph node metastasis was 61.1% (22/36) and was only 14.3% (4/28) in those with lymph node metastasis. No statistically significant difference in NAC regimen was found between the pCR and non-pCR groups (P=0.496) (*Table 1*).

# *Comparison of DCE-MRI enhancement and shrinkage patterns between the pCR and non-pCR groups*

Among the 64 patients with HER2-positive breast cancer, 60.9% (39/64) showed non-mass enhancement. The enhancement patterns showed significant differences in terms of shrinkage pattern, ER status, and lymph node metastasis, as summarized in *Table 2*. Notably, ER-positive lesions were significantly more likely to demonstrate nonmass enhancements (24/39, 61.5%) as compared to ERnegative lesions  $(15/39, 38.5\%)$  (P=0.046), and patients with non-mass enhancement lesions had a higher rate of lymph node metastasis (23/39, 59.0%). After chemotherapy, mass-enhanced lesions were more likely to show centripetal shrinking (18/25, 72.0%) than were non-mass-enhanced lesions (14/39, 35.9%).

There was a statistically significant difference in the enhancement and shrinkage patterns between the pCR and non-pCR groups (P<0.050). Among the 26 patients who achieved pCR, 19 (73.1%) had mass enhancement and 7 (26.9%) had non-mass enhancement; 19 (73.1%) also showed centripetal shrinking. There were 18 cases of mass enhancement with centripetal shrinking, of whom 16 (88.9%) reached pCR; 14 cases of non-mass enhancement with centripetal shrinking, of whom 3 (21.4%) reached pCR; 7 cases of mass enhancement with noncentripetal shrinking, of whom 3 (42.9%) reached pCR; and 25 cases of non-mass enhancement with noncentripetal shrinking, of





Data are presented as n (%). pCR, pathological complete response; ER, estrogen receptor; PR, progesterone receptor; NAC, neoadjuvant chemotherapy; E, epirubicin; C, cyclophosphamide; T, taxotere; H, trastuzumab; P', paclitaxel; Cb, carboplatin; P, pertuzumab.





Data are presented as n (%). ER, estrogen receptor; NME, non-mass enhancement.

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**Table 3** Comparison of the therapeutic effects of targeted therapy in relation to enhancement pattern, shrinkage pattern, the combination of enhancement and shrinkage patterns, and the combination of enhancement patterns and ER status

Group	$pCR$ (n=26)	Non-pCR (n=38)	$\chi^2$	P
Enhancement pattern			21.284	< 0.001
Mass	19(73.1)	6(15.8)		
<b>NME</b>	7(26.9)	32 (84.2)		
Shrinkage pattern			9.328	0.002
Centripetal	19 (73.1)	13 (34.2)		
Noncentripetal	7(26.9)	25(65.8)		
Enhancement + shrinkage			25.821	< 0.001
Mass + centripetal	16 (61.5)	2(5.3)		
Mass + noncentripetal	3(11.5)	4(10.5)		
$NME + centripetal$	3(11.5)	11 (28.9)		
NME + noncentripetal	4(15.4)	21(55.3)		
Enhancement + ER			22.56	< 0.001
$Mass + ER$ negative	13(50.0)	3(7.9)		
Mass + ER positive	6(23.1)	3(7.9)		
$NME + ER$ negative	4(15.4)	11(28.9)		
$NME + ER$ positive	3(11.5)	21(55.3)		

Data are presented as n (%). ER, estrogen receptor; pCR, pathological complete response; NME, non-mass enhancement.

whom 4 (16.0%) reached pCR (*Table 3*). The combination of ER status and enhancement pattern showed a significant correlation with pCR (P<0.001). Specifically, patients with ER-negative and mass-enhanced lesions were more likely to achieve pCR (13/26, 50.0%) than were those who were ER-positive with non-mass enhanced lesions (3/26, 11.5%) (*Table 3*). Typical cases are presented in *Figure 2*.

#### *Predictive value of various indicators for pCR*

Among the above-mentioned indicators with significant differences across groups, the accuracy of pCR prediction was significant for lymph node metastasis, enhancement pattern, shrinkage pattern, enhancement + shrinkage patterns, and enhancement pattern + ER, with receiver operating characteristic (ROC) curves of 0.739, 0.786, 0.694, 0.825, and 0.823 respectively (*Table 4, Figure 3*). Multivariate logistic regression analysis showed that only enhancement pattern was significant among multiple parameters (OR =0.051; 95% CI: 0.005–0.551; P=0.014) (*Table 5*).

#### **Discussion**

The HER2 protein is a membrane protein that shares significant homology with epidermal growth factor receptor. It is classified as an epidermal growth factor and is expressed at low levels in normal tissues (14). HER2 gene amplification and protein overexpression are related to the growth of malignant tumors in terms of tumor cell division, invasion, and angiogenesis (15). The application of anti-HER2 antibodies (trastuzumab, pertuzumab) can significantly improve the prognosis of patients with HER2 positive breast cancer. In addition to tumor size, lymph node metastasis, tissue grading, and hormone receptor status, HER2 gene expression status has been used as an independent prognostic indicator in patients with breast cancer. The guidelines of the American Society of Clinical Oncology and the National Comprehensive Cancer Network both recommend HER2 as an immunohistochemical indicator that can guide clinical treatment for breast cancer. HER2-positive breast cancer accounts for 25% of all breast cancers, and its pCR rate after targeted treatment ranges from 40% to 60% (3-5). The pCR rate for the 64 HER2-



**Figure 2** Dynamic contrast-enhanced magnetic resonance imaging and hematoxylin and eosin staining (10×) from representative cases. Case 1 showed (A) mass enhancement before chemotherapy and (B, arrow) a noncentripetal shrinkage pattern appearing at the edge of the lesion after two cycles of chemotherapy. (C) Pathological results after chemotherapy showed multiple residual invasive nonspecial-type cancers. Case 2 showed (D) mass enhancement before chemotherapy and (E) centripetal shrinkage after chemotherapy. (F) Postoperative pathology showed no residual cancer tissue fibrosis. Case 3 showed (G) non-mass enhancement before chemotherapy and (H) noncentripetal shrinking after chemotherapy, with (I) postoperative pathology demonstrating a small amount of cancer tissue infiltration.

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**Table 4** Performance of clinical and radiological indicators in predicting pCR

pCR, pathological complete response; AUC, area under the curve; CI, confidence interval; ER, estrogen receptor.



**Figure 3** The ROC curves of each parameter in predicting pCR. ER, estrogen receptor; ROC, receiver operating characteristic; pCR, pathological complete response.

positive cases of breast cancer described in our study was 40.6%, which is consistent with that reported in the literature. Patients with HER2-positive breast cancer have a higher rate of pCR and therefore a higher rate of breastconserving surgery. Predicting and evaluating the pCR in patients with breast cancer thus hold considerable clinical significance.

Age is a critical factor in the prognosis of breast cancer; for instance, those patients younger than 35 years have a higher mortality rate than do those older than 50 years (16). Our study found there to be no significant difference in age between the pCR and non-pCR groups of patients with HER2-positive breast cancer. However, there were group

differences in terms of lesion size, lymph node metastasis, and ER status. The patients most likely to gain immediate benefit from targeted therapy were those with small tumors, low ER expression, and no lymph node metastasis. These results are consistent with those of Meisel *et al.* (17). Smaller tumors are typically found early and involve a lower degree of local invasion and a lower possibility of lymph node and distant metastases; therefore, they are associated with a good prognosis. After controlling for receptor status, a study of 38,864 patients found tumor size to be independently associated with pCR, although the association with receptor status was stronger (18). Among hormone receptor indicators, PR is less valuable than is ER for predicting response to hormone therapy. In our study, a smaller proportion of ER-positive patients reached pCR after targeted therapy compared to their ER-negative counterparts. This may be due to the higher activity of the G protein-coupled ER in ER-positive cells, which stimulates the rapid differentiation of cancer cells and has a poor response to HER2-targeted therapy (17,19). It has been reported that a high expression of HER2 is associated with a higher rate of lymph node metastasis and that a high expression of HER2 and lymph node metastasis can be used as independent predictors of prognosis (20). In our study, only 4 of 28 (14.3%) patients with lymph node metastases achieved pCR after targeted treatment.

Breast tumors are heterogeneous and complex. Needle biopsies cannot sufficiently capture the heterogeneity of a whole tumor prior to the administration of NAC (21). A lesion's patterns of enhancement and shrinkage on MRI may reflect its morphological and functional characteristics. Mass enhancement and centripetal shrinkage can indicate consistency between tumor cytology and molecular

$\overline{\phantom{a}}$	$\overline{\phantom{0}}$	$\overline{\phantom{0}}$	$\omega$ i			
Variable	Regression coefficient	Standard error	Wald	OR (95% CI)	P	
Lesion size	$-1.151$	1.460	0.621	$0.316(0.018 - 5.534)$	0.431	
ER	$-0.496$	0.938	0.280	$0.609(0.097 - 3.826)$	0.597	
Lymph node metastasis	$-1.414$	0.811	3.044	$0.243(0.050 - 1.191)$	0.081	
Enhancement pattern	$-2.972$	1.212	6.011	$0.051(0.005 - 0.551)$	0.014	
Shrinkage pattern	0.107	0.937	0.013	1.113 (0.177-6.987)	0.909	
Enhancement + shrinkage	$-1.801$	1.465	1.512	$0.165(0.009 - 2.915)$	0.219	
Enhancement + ER	$-0.263$	1.488	0.031	$0.769(0.042 - 14.200)$	0.860	

**Table 5** Multivariate logistic regression analysis of clinical and radiological indicators in predicting pCR

pCR, pathological complete response; OR, odds ratio; CI, confidence interval; ER, estrogen receptor.

behavior, which suggest a high likelihood of pCR after targeted treatment, meanwhile, noncentripetal shrinkage is related to cell heterogeneity (13,22). Koh *et al.* (23) analyzed the enhancement patterns of 484 cases of breast cancer and found that patients with mass enhancement had a lower histopathological grade and a lower degree of vascular and neural invasion, which may be related to blood supply and the tumor's pattern of growth. Moreover, they found that non-mass enhancement is common in HER2 positive breast cancer. In our study, 60.9% of cases showed non-mass enhancement, among whom only 17.9% achieved pCR; in contrast, 73.1% of cases with mass enhancement achieved pCR. Patients with mass enhancement were also more likely to show a centripetal shrinkage pattern, and the predictive accuracy of mass enhancement combined with centripetal shrinkage was higher than that of any other combination of factors. Among the 18 patients with mass enhancement and centripetal shrinkage, 16 (88.9%) achieved pCR. The two patients who did not achieve pCR had lymph node metastasis. Previous studies have demonstrated that prechemotherapy enhancement patterns and postchemotherapy shrinkage patterns are related to pCR in low-grade luminal breast cancer and that shrinkage pattern can be used as an independent predictor of pCR (24). The results of our study are consistent with those of Heacock *et al.* (22) who reported that the shrinkage pattern of HER2-positive breast cancer could predict efficacy after targeted treatment and that centripetal shrinkage is more predictive of pCR. However, Heacock *et al.* did not conduct a comparative study on enhancement and shrinkage patterns and only used preoperative MRI to evaluate the shrinkage pattern. In our study, MRI was used to evaluate the shrinkage pattern after two treatment cycles. Some patients achieved pCR after treatment, and lesions could

not be detected via MRI. Therefore, the comparative study after two treatment cycles may be more accurate because it can predict patients' pCR earlier and guide clinical management.

# Conclusions

In summary, lesion size, ER status, lymph node metastasis, and MRI patterns of enhancement and shrinkage can be used to predict pCR in patients with HER2-positive breast cancer after targeted treatment, with enhancement pattern being an independent predictor of pCR. Targeting patients with mass enhancement and centripetal shrinkage is the most efficacious approach to achieving pCR, which may help clinicians in identifying patients and tailoring treatment strategies. However, enhancement patterns should be evaluated thoroughly alongside lesion size, ER status, and lymph node metastasis.

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# Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at [https://qims.](https://qims.amegroups.com/article/view/10.21037/qims-24-447/rc) [amegroups.com/article/view/10.21037/qims-24-447/rc](https://qims.amegroups.com/article/view/10.21037/qims-24-447/rc)

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The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the provisions of the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of Shenzhen People's Hospital (No. LL-KY-2022285). The requirement for individual consent was waived due to the retrospective nature of the analysis.

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## **References**

- 1. Curigliano G, Viale G, Bagnardi V, Fumagalli L, Locatelli M, Rotmensz N, Ghisini R, Colleoni M, Munzone E, Veronesi P, Zurrida S, Nolè F, Goldhirsch A. Clinical relevance of HER2 overexpression/amplification in patients with small tumor size and node-negative breast cancer. J Clin Oncol 2009;27:5693-9.
- 2. Hou Y, Nitta H, Wei L, Banks PM, Parwani AV, Li Z. Evaluation of Immune Reaction and PD-L1 Expression Using Multiplex Immunohistochemistry in HER2- Positive Breast Cancer: The Association With Response to Anti-HER2 Neoadjuvant Therapy. Clin Breast Cancer 2018;18:e237-44.
- 3. Di Cosimo S, Appierto V, Pizzamiglio S, Tiberio P, Iorio MV, Hilbers F, de Azambuja E, de la Peña L, Izquierdo M, Huober J, Baselga J, Piccart M, de Braud FG, Apolone G, Verderio P, Daidone MG. Plasma miRNA Levels for Predicting Therapeutic Response to Neoadjuvant Treatment in HER2-positive Breast Cancer: Results from the NeoALTTO Trial. Clin Cancer Res 2019;25:3887-95.
- 4. Duan Y, Song X, Guan L, Wang W, Song B, Kang Y, Jia Y, Zhu Y, Nie F. Comparative study of pathological response evaluation systems after neoadjuvant chemotherapy for breast cancer: developing predictive models of multimodal

ultrasound features including shear wave elastography combined with puncture pathology. Quant Imaging Med Surg 2023;13:3013-28.

- 5. He M, Su J, Ruan H, Song Y, Ma M, Xue F. Nomogram based on quantitative dynamic contrast-enhanced magnetic resonance imaging, apparent diffusion coefficient, and clinicopathological features for early prediction of pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy. Quant Imaging Med Surg 2023;13:4089-102.
- 6. Boughey JC, McCall LM, Ballman KV, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, Leitch AM, Flippo-Morton T, Hunt KK. Tumor biology correlates with rates of breast-conserving surgery and pathologic complete response after neoadjuvant chemotherapy for breast cancer: findings from the ACOSOG Z1071 (Alliance) Prospective Multicenter Clinical Trial. Ann Surg 2014;260:608-14; discussion 614-6.
- 7. Richter H, Hennigs A, Schaefgen B, Hahn M, Blohmer JU, Kümmel S, Kühn T, Thill M, Friedrichs K, Sohn C, Golatta M, Heil J. Is Breast Surgery Necessary for Breast Carcinoma in Complete Remission Following Neoadjuvant Chemotherapy? Geburtshilfe Frauenheilkd 2018;78:48-53.
- 8. Ishitobi M, Ohsumi S, Inaji H, Ohno S, Shigematsu H, Akiyama F, Iwase T, Akashi-Tanaka S, Sato N, Takahashi K, Oura S. Ipsilateral breast tumor recurrence (IBTR) in patients with operable breast cancer who undergo breast-conserving treatment after receiving neoadjuvant chemotherapy: risk factors of IBTR and validation of the MD Anderson Prognostic Index. Cancer 2012;118:4385-93.
- 9. Wolff AC, Hammond MEH, Allison KH, Harvey BE, Mangu PB, Bartlett JMS, Bilous M, Ellis IO, Fitzgibbons P, Hanna W, Jenkins RB, Press MF, Spears PA, Vance GH, Viale G, McShane LM, Dowsett M. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol 2018;36:2105-22.
- 10. Bitencourt AGV, Gibbs P, Rossi Saccarelli C, Daimiel I, Lo Gullo R, Fox MJ, Thakur S, Pinker K, Morris EA, Morrow M, Jochelson MS. MRI-based machine learning radiomics can predict HER2 expression level and pathologic response after neoadjuvant therapy in HER2 overexpressing breast cancer. EBioMedicine 2020;61:103042.
- 11. Krystel-Whittemore M, Xu J, Brogi E, Ventura K, Patil S, Ross DS, Dang C, Robson M, Norton L, Morrow M,

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Wen HY. Pathologic complete response rate according to HER2 detection methods in HER2-positive breast cancer treated with neoadjuvant systemic therapy. Breast Cancer Res Treat 2019;177:61-6.

- 12. Sickles EA, Do CJ, Bassett LW, editors. ACR BI-RADS® Atlas Breast Imaging Reporting and Data System. American College of Radiology, 2013. Available online: https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Bi-Rads
- 13. Fukada I, Araki K, Kobayashi K, Shibayama T, Takahashi S, Gomi N, Kokubu Y, Oikado K, Horii R, Akiyama F, Iwase T, Ohno S, Hatake K, Sata N, Ito Y. Pattern of Tumor Shrinkage during Neoadjuvant Chemotherapy Is Associated with Prognosis in Low-Grade Luminal Early Breast Cancer. Radiology 2018;286:49-57.
- 14. Press MF, Cordon-Cardo C, Slamon DJ. Expression of the HER-2/neu proto-oncogene in normal human adult and fetal tissues. Oncogene 1990;5:953-62.
- 15. Arboleda MJ, Lyons JF, Kabbinavar FF, Bray MR, Snow BE, Ayala R, Danino M, Karlan BY, Slamon DJ. Overexpression of AKT2/protein kinase Bbeta leads to up-regulation of beta1 integrins, increased invasion, and metastasis of human breast and ovarian cancer cells. Cancer Res 2003;63:196-206.
- 16. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, Karaca G, Troester MA, Tse CK, Edmiston S, Deming SL, Geradts J, Cheang MC, Nielsen TO, Moorman PG, Earp HS, Millikan RC. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA 2006;295:2492-502.
- 17. Meisel JL, Zhao J, Suo A, Zhang C, Wei Z, Taylor C, Aneja R, Krishnamurti U, Li Z, Nahta R, O'Regan R, Li X. Clinicopathologic Factors Associated With Response to Neoadjuvant Anti-HER2-Directed Chemotherapy in HER2-Positive Breast Cancer. Clin Breast Cancer 2020;20:19-24.
- 18. Livingston-Rosanoff D, Schumacher J, Vande Walle

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K, Stankowski-Drengler T, Greenberg CC, Neuman H, Wilke LG. Does Tumor Size Predict Response to Neoadjuvant Chemotherapy in the Modern Era of Biologically Driven Treatment? A Nationwide Study of US Breast Cancer Patients. Clin Breast Cancer 2019;19:e741-7.

- 19. Gianni L, Pienkowski T, Im YH, Tseng LM, Liu MC, Lluch A, Starosławska E, de la Haba-Rodriguez J, Im SA, Pedrini JL, Poirier B, Morandi P, Semiglazov V, Srimuninnimit V, Bianchi GV, Magazzù D, McNally V, Douthwaite H, Ross G, Valagussa P. 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. Lancet Oncol 2016;17:791-800.
- 20. Tong ZJ, Shi NY, Zhang ZJ, Yuan XD, Hong XM. Expression and prognostic value of HER-2/neu in primary breast cancer with sentinel lymph node metastasis. Biosci Rep 2017;37:BSR20170121.
- 21. Longo DL. Tumor heterogeneity and personalized medicine. N Engl J Med 2012;366:956-7.
- 22. Heacock L, Lewin A, Ayoola A, Moccaldi M, Babb JS, Kim SG, Moy L. Dynamic Contrast-Enhanced MRI Evaluation of Pathologic Complete Response in Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast Cancer After HER2-Targeted Therapy. Acad Radiol 2020;27:e87-93.
- 23. Koh J, Park AY, Ko KH, Jung HK. Can enhancement types on preoperative MRI reflect prognostic factors and surgical outcomes in invasive breast cancer? Eur Radiol 2019;29:7000-8.
- 24. Shin SU, Cho N, Lee HB, Kim SY, Yi A, Kim SY, Lee SH, Chang JM, Moon WK. Neoadjuvant Chemotherapy and Surgery for Breast Cancer: Preoperative MRI Features Associated with Local Recurrence. Radiology 2018;289:30-8.