# Role of Magnetic Resonance Imaging in Detection of Pathologic Complete Remission in Breast Cancer Patients Treated With Neoadjuvant Chemotherapy: A Meta-analysis

Yan-Lin Gu, Si-Meng Pan, Jie Ren, Zhi-Xue Yang, Guo-Qin Jiang

## Abstract

Pathologic complete remission after neoadjuvant chemotherapy has a role in guiding the management of breast cancer. The present meta-analysis examined the accuracy of contrast-enhanced magnetic resonance imaging (CE-MRI) and diffusion-weighted magnetic resonance imaging (DW-MRI) in detecting the response to neoadjuvant chemotherapy and compared CE-MRI with ultrasonography, mammography, and positron emission tomography/computed tomography (PET/CT). Medical subject heading terms and related keywords were searched to generate a compilation of eligible studies. The pooled sensitivity, specificity, diagnostic odds ratio, area under summary receiver operating characteristic curve (AUC), and Youden index (Q* index) were used to estimate the diagnostic efficacy of CE-MRI, DW-MRI, ultrasonography, mammography, and PET/CT. A total of 54 studies of CE-MRI and 8 studies of DW-MRI were included. The overall AUC and the Q* index values for CE-MRI and DW-MRI were 0.88 and 0.94 and 0.80 and 0.85, respectively. According to the summary receiver operating characteristic curves, CE-MRI resulted in a higher AUC value and Q* index compared with ultrasonography and mammography but had values similar to those of DW-MRI and PET/CT. CE-MRI accurately assessed pathologic complete remission in specificity, and PET/CT and DW-MRI accurately assessed pathologic complete remission in sensitivity. The present meta-analysis indicates that CE-MRI has high specificity and DW-MRI has high sensitivity in predicting pathologic complete remission after neoadjuvant chemotherapy. CE-MRI is more accurate than ultrasonography or mammography. Additionally, PET/CT is valuable for predicting pathologic complete remission. CE-MRI, combined with PET/CT or DW-MRI, might allow for a more precise assessment of pathologic complete remission.

*Clinical Breast Cancer,* Vol. 17, No. 4, 245-55 

**Keywords:** Breast cancer, Meta-analysis, MRI, NAC, pCR

## Introduction

Neoadjuvant chemotherapy (NAC), also called termed or primary chemotherapy, was first described in patients with locally advanced breast cancer in 1978.[1] It plays a well-established role in the management of breast cancer.[2] One of the advantages of NAC is to downstage the primary tumor and increase the likelihood of successful breast-conserving surgery, avoiding mastectomy.[3] Published clinical trials have shown that breast cancer patients with pathologic complete remission (pCR) after NAC have a significantly better prognosis than those without pCR.[4-9] The accurate assessment of the response to NAC before surgery is crucial in breast cancer management. If pCR cases could be distinguished perfectly from non-pCR cases, additional surgical management would be avoided.

Ultrasonography, mammography, and contrast-enhanced magnetic resonance imaging (CE-MRI) have been widely applied to evaluate and predict the pathologic response in patients with breast cancer who received NAC. However, positron emission tomography/computed tomography (PET/CT) has not been widely used.[10-12] CE-MRI has been proposed to be valuable in predicting

Y.-L.G. and S.-M.P. contributed equally to this report.

Department of General Surgery, The Second Affiliated Hospital of Soochow University, Suzhou, People's Republic of China

Submitted: Sep 15, 2016; Accepted: Dec 26, 2016; Epub: Jan 11, 2017

Address for correspondence: Guo-Qin Jiang, MD, PhD, Department of General Surgery, The Second Affiliated Hospital of Soochow University, 1055 San Xiang Road, Suzhou 215004, People's Republic of China
E-mail contact: jiang_guoqin@163.com


http://dx.doi.org/10.1016/j.clbc.2016.12.010

the responsiveness of breast cancer after NAC.[13] Also, diffusion-weighted MRI (DW-MRI) has been considered a potential tool to predict the response to chemotherapy.[14,15] Therefore, we focused on the performance of MRI (including CE-MRI and DW-MRI) in predicting for pCR after NAC. Despite the value of CE-MRI in detecting the response to NAC, the routine use of CE-MRI remains controversial because of the cost, lengthy imaging time, use of contrast injection, and relatively low sensitivity in detecting pCR.[16] Skaane et al[17] reported that ultrasonography and mammography were the primary tools for evaluating the response to NAC; however, the accuracy was limited.

Most published studies have evaluated MRI and other imaging techniques in isolation, not in the same cohort. In the present study, we examined the evidence of the accuracy of CE-MRI compared with mammography, ultrasonography, and PET/CT in identifying the response to NAC. Londero et al[18] and Rosen et al[19] showed that

**Figure 1** Flowchart of Published Data Search

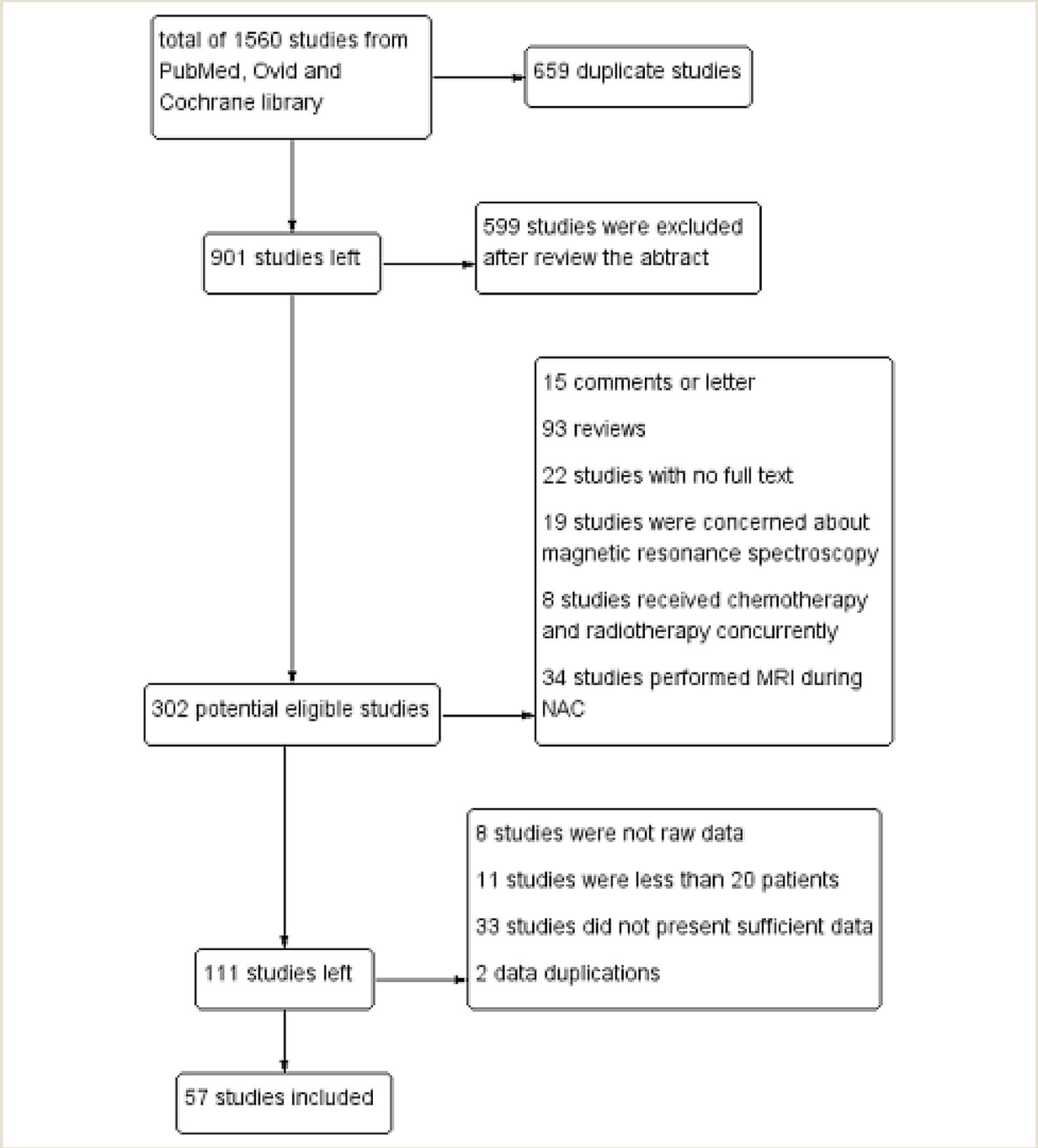


**Table 1 Summary of Main Characteristics of All Eligible Studies**

| Study | Patients (n) | Age (y) | Initial Tumor Size | Histologic Subtype | Magnet Strength (T) | Patient Enrollment Period (y.mo) | pCR Rate (%) | pCR Definition | Blind | Contrast Material (Dose) | CE or DWI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Belli et al[28] | 45 | 53.7 (30-76) | T2-T4 | IDC, ILC | 1.5 | 2000.03-2003.06 | 8.89 | NRD | | 0.2 mL/kg | CE |
| De Los Santos et al[29] | 746 | 49 (20-86) | T1-T4 | IDC, ILC | 3/1.5 | 2002.01-2011.02 | 23.99 | NRD | | NR | CE |
| Abraham et al[30] | 31 | 50 (31-73) | T2-T4 | IDL, ILC | 1.5 | 1990-1994 | 6.45 | NRD | | 0.1 mmol/kg | CE |
| Trecate et al[31] | 30 | NR | T4/LABC | NR | 1.5 | 1995.11-1998.04 | 13.33 | NRD | | 0.1 mmol/kg | CE |
| Balu-Maestro et al[32] | 60 | NR | NR | IDC, ILC | NR | NR | 8.33 | NR | | NR | CE |
| Partridge et al[33] | 52 | 47.3 (29-72) | NR | NR | 1.5 | NR | 15.38 | NRD | | NR | CE |
| Rieber et al[34] | 59 | 51.44 (27-72) | T2-T4 | NR | 1.5 | NR | 8.82 | NRD | | 0.15 mmol/kg | CE |
| Cheung et al[35] | 33 | 44.9 (26-63) | LABC | NR | 1.5 | 1999.12-2001.11 | 12.12 | NRD | | 0.1 mmol/kg | CE |
| Rosen et al[19] | 21 | NR | T2-T4 | IDC | 1.5 | 2000.05-2002.12 | 9.52 | NID | | 0.1 mmol/kg | CE |
| Wasser et al[36] | 31 | NR | T2-T4 | IDC, ILC | 1.5 | 2000.12 | 6.45 | NRD | | 0.1 mmol/kg | CE |
| Bodini et al[37] | 73 | 56 (26-71) | T2-T4 | IDC, ILC | 0.5 | 1998.01-2001.08 | 4.11 | NID | | 0.1 mmol/kg | CE |
| Martincich et al[38] | 31 | 49 (36-65) | T2-T4 | IDC, ILC | 1.5 | NR | 22.58 | NID | Blind | 0.1 mmol/kg | CE |
| Montemurro et al[39] | 21 | 49 (37-64) | LABC | NR | 1.5 | NR | 14.29 | NID | Blind | 0.1 mmol/kg | CE |
| Schott et al[40] | 35 | 48 (26-66) | T2-T3 | IDC, ILC | 1.5 | 2000.11-2002.12 | 11.43 | NRD | Blind | 0.15 mmol/kg | CE |
| Garimella et al[41] | 76 | 52.6 (26-72) | LABC | NR | 1.5 | 1996-2005.04 | 15.79 | NRD | | NR | CE |
| Hsiang et al[42] | 35 | 50 (30-70) | LABC | NR | 1.5 | 2004.10-2006.02 | 51.43 | NR | | 0.1 ml/kg | CE |
| Nakamura et al[43] | 115 | NR | NR | NR | NR | NR | 8.70 | NRD | | NR | CE |
| Bhattacharyya et al[44] | 32 | 42.7 (24-60) | T2-T3 | NR | 1.5 | NR | 15.63 | NID | Blind | 16 mmol/kg | CE |
| Chen et al[45] | 51 | 49.5 (31-77) | T2-T4 | NR | 1.5 | NR | 54.90 | NID | Blind | 0.1 mL/kg | CE |
| Nicoletto et al[46] | 26 | 47 (30-57) | T2-T4 | IDC, ILC | NR | 2001.03-2003.06 | 23.08 | NRD | | NR | CE |
| Bahri et al[47] | 37 | 47.4 (31-69) | T2-T4 | IDC, ILC | 3/1.5 | 2004-2007 | 35.14 | NRD | Blind | 0.1 mmol/kg | CE |
| Moon et al[48] | 195 | 45.5 (22-69) | T1-T4 | NR | 1.5 | 2006.01-2008.02 | 14.87 | NRD | | 0.1 mmol/kg | CE |
| Choi et al[21] | 29 | 45.1 (24-63) | T2-T4 | IDC, ILC | NR | 2004.12-2008.03 | 24.17 | NRD | | NR | CE |
| Dose-Schwarz et al[49] | 46 | 50 (30-66) | T2-T4 | NR | NR | NR | 10.87 | Near pCR | | NR | CE |
| Straver et al[50] | 208 | 46 (23-76) | T1-T4 | IDC, ILC | 3/1.5 | 2000-2008 | 20.19 | NID | | 0.1 mmol/kg | CE |
| Woodhams et al[51] | 70 | NR | NR | IDC, ILC | 1.5 | 2005.01-2008.11 | 12.85 | NID | Blind | 0.1 mmol/kg | CE/DW |
| Wright et al[52] | 50 | 47 (30-72) | T1-T4 | IDC, ILC | 1.5 | 2004.09-2007.05 | 12.00 | NID | | 0.1 mmol/kg | CE |
| Fangberget et al[53] | 22 | 50.7 (37-72) | T2-T4 | IDC, ILC | 1.5 | 2007.04-2008.10 | 36.36 | NID | | 0.1 mmol/kg | CE/DW |
| Park et al[54] | 32 | 45 (28-67) | NR | IDC | 1.5 | 2006.08-2008.05 | 25.00 | NID | | 0.1 mmol/kg | CE |

**Table 1 Continued**

| Study | Patients (n) | Age (y) | Initial Tumor Size | Histologic Subtype | Magnet Strength (T) | Patient Enrollment Period (y.mo) | pCR Rate (%) | pCR Definition | Blind | Contrast Material (Dose) | CE or DWI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Shin et al[55] | 40 | 42.7 (25-62) | NR | IDC | 1.5 | 2005.05-2009.03 | 30.00 | Near pCR | | 0.2 ml/kg | CE |
| Dongfeng et al[56] | 60 | 55 (39-76) | T1-T4 | IDC | 3 | 2008.04-2009.07 | 16.67 | NID | | 0.1 mmol/kg | CE |
| Nessim et al[57] | 129 | 51 | NR | IDC, ILC | NR | NR | 16.28 | NID | | NR | CE |
| Kuzucan et al[58] | 54 | 51 (31-82) | NR | IDC, ILC | 3/1.5 | 2002.05-2010.02 | 31.48 | NID | Blind | NR | CE |
| Abedi et al[59] | 20 | 44.7 (21-68) | LABC | IDC, ILC | NR | 2010.08-2012.04 | 30.00 | NRD | Blind | 0.1 mmol/kg | CE |
| Fujisawa et al[60] | 57 | NR | NR | IDC, ILC | 1.5 | 2007.10-2009.11 | 15.79 | NID | | 0.1 mL/kg | CE |
| Hayashi et al[61] | 569 | 50 (26-76) | NR | NR | NR | 2004-2008 | 15.11 | NID | | NR | CE |
| Hayashi et al[62] | 264 | 51 (23-71) | T1-T4 | IDC | 1.5 | 2003.02-2008.06 | 37.12 | NID | | NR | CE |
| Ko et al[11] | 66 | 44 (23-72) | T2-T4 | IDC, ILC | 3 | 2007.04-2010.12 | 24.09 | NID | Blind | 0.1 mmol/kg | CE |
| Williams et al[12] | 87 | 50 (25-83) | T2-T4 | IDC, ILC | 1.5 | 2004.01-2009.11 | 25.29 | NRD | | 0.1 mmol/kg | CE |
| Bufi et al[63] | 225 | 47 (26-67) | NR | IDC, ILC | 1.5 | 2007-2012 | 17.33 | NRD | Blind | 0.1 mmol/kg | CE/DW |
| Hahn et al[64] | 78 | 43.3 (24-59) | NR | IDC, ILC | 3/1.5 | 2008.07-2009.12 | 24.36 | NID | Blind | 0.1 mmol/kg | CE/DW |
| Lee et al[65] | 122 | 45.9 (29-71) | T1-T4 | IDC | NR | 2011.03-2012.12 | 14.75 | NRD | Blind | NR | CE |
| Tomida et al[66] | 27 | 48.4 (29-66) | NR | IDC | 3/1.5 | NR | 14.81 | NRD | | 0.1 mmol/kg | CE |
| Choi et al[67] | 98 | 50 (29-81) | NR | IDC, ILC | 3/1.5 | 2006-2011 | 17.35 | NID | Blind | 0.2 mmol/kg | CE |
| Diguisto et al[68] | 102 | 48.5 | NR | IDC, ILC | 1.5 | 2008.01-2011.12 | 29.41 | NRD | | NR | CE |
| Lee et al[69] | 39 | 46.9 (24-64) | T1-T4 | NR | NR | 2008-2012 | 28.21 | NID | | NR | CE |
| Lee et al[70] | 71 | 45 (25-67) | NR | NR | 1.5 | 2012.01-2013.02 | 14.08 | NRD | Blind | 0.1 mmol/kg | CE |
| Li et al[71] | 43 | 45 (25-63) | NR | IDC, ILC | 1.5 | 2007.12-2009.06 | 48.83 | NID | Blind | 0.2 mmol/kg | CE |
| Bouzon et al[72] | 92 | 47.2 (31-75) | T1-T4 | IDC, ILC | 1.5 | 2006.10-2013.06 | 30.43 | NID | | 0.1 mmol/kg | CE |
| Schaefgen et al[73] | 150 | 47 | T1-T4 | NR | 1.5 | 2006.01-2011.12 | 30.67 | NRD | | NR | CE |
| Vriens et al[20] | 149 | NR | NR | NR | >1.5 | 2006.02-2009.04 | 16.78 | NID | | NR | CE |
| Zhou et al[74] | 37 | NR | NR | NR | 1.5 | 2010.02-2011.12 | 21.62 | NID | | 0.1 mmol/kg | CE |
| Fukuda et al[75] | 265 | 49.9 (25-78) | T2-T4 | NR | 1.5 | 2005.01-2007.12 | 7.17 | NID | | 0.2 mmol/kg | CE |
| Murata et al[76] | 36 | 54 (26-69) | T2-T4 | NR | 1.5 | 2007.04-2008.09 | 5.56 | NR | | 0.1 mmol/kg | CE/DW |
| Park et al[10] | 34 | 44 (27-60) | T2-T4 | NR | NR | 2001.04-2008.05 | 20.59 | NID | Blind | | DW |
| Shin et al[77] | 41 | 46 (24-68) | T2-T4 | NR | NR | 2009.01-2011.05 | 36.59 | NID | | | DW |
| Weis et al[78] | 33 | 45 (33-67) | T2-T4 | NR | NR | NR | 36.36 | NRD | | | DW |

Data for age presented as mean (range).
Abbreviations: IDL = invasive ductal carcinoma; ILC = invasive lobular carcinoma; LABC = locally advanced breast cancer; NID = no invasive disease; NR = not reported; NRD = no residual disease; pCR = pathologic complete response.

CE-MRI could evaluate the responses to NAC better than mammography or ultrasonography. Vriens et al[20] suggested that ultrasonography is at least as good as CE-MRI in providing information on the residual tumor size after NAC. Additionally, the merits of CE-MRI versus PET/CT have been controversial. Choi et al[21] reported that CE-MRI is better than PET/CT in monitoring the effects of NAC. Chen et al[22] indicated that PET/CT is superior to CE-MRI. We conducted our analysis to provide further evidence for these discussions.

## Materials and Methods

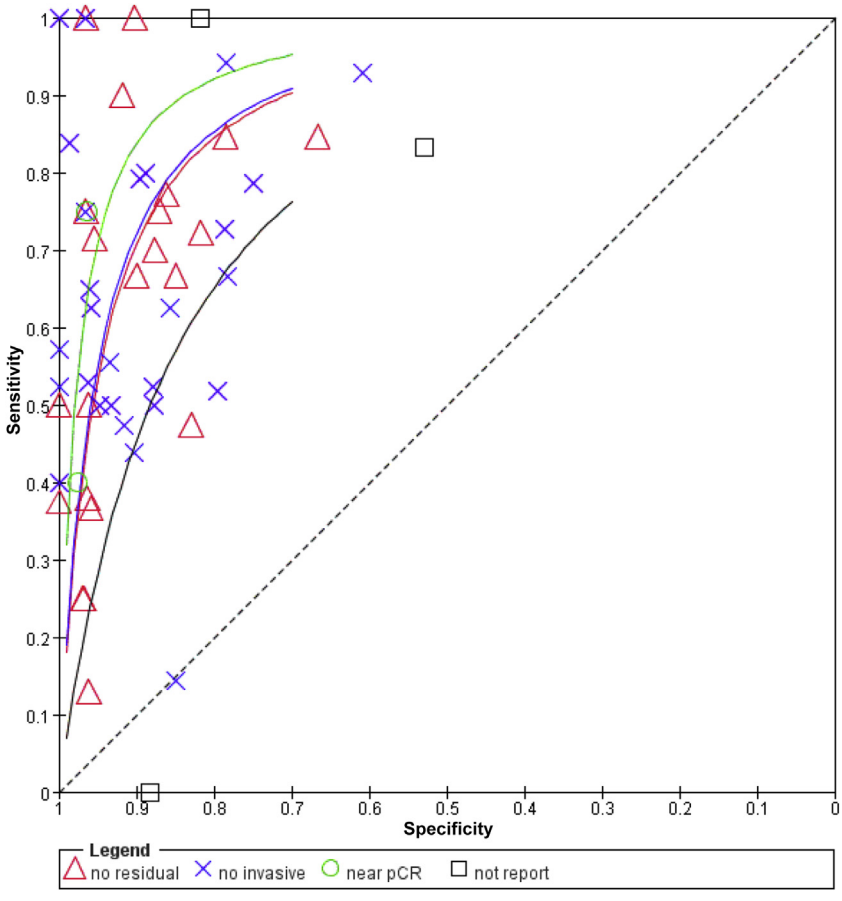
### *Published Data Search and Review*

We systematically searched the published data in PubMed, Ovid, Cochrane Library (from the beginning of 1992 to April 1, 2016). The search terms were selected to link MRI with breast cancer and the response to NAC, using "response," "magnetic resonance imaging OR MR," and "neoadjuvant OR preoperative OR pre-surgery OR primary chemotherapy" AND "breast cancer OR breast tumor OR breast neoplasm OR mammary cancer" as subject heading terms and keywords. All abstracts were screened for eligibility by 1 reviewer, and a 10% sample was assessed independently by a second reviewer to ensure consistent application of the eligibility criteria.

### *Eligibility Criteria*

The inclusion criteria were as follows: (1) patients with newly diagnosed breast cancer who had undergone MRI examination after complete NAC; (2) studies of $\geq$ 20 patients; and (3) studies providing sufficient data, either directly or indirectly through a 2 $\times$ 2 table (the numbers of true-positive, true-negative, false-positive, and false-negative findings) to enable calculation of point estimates and 95% confidence intervals (CIs) for the operating characteristics of MRI compared with the reference standard (pathologic response determined by surgical excision). Studies in which patients were treated with concurrent chemotherapy and radiotherapy were excluded. Also, studies not reported in the

**Figure 2** Summary Receiver Operating Characteristic Curve for Contrast-enhanced Magnetic Resonance Imaging Classified by Pathologic Complete Remission (pCR) Definition. Red Triangles and Red Curve Represent Studies That Defined pCR as the Absence of Both Invasive Cancer and Ductal Carcinoma In Situ (DCIS). Blue Crosses and Blue Curve Represent Studies That Defined pCR as the Absence of Invasive Cancer (DCIS Allowed). Green Circles and Green Curve Represent Studies That Defined pCR as Minimal Residual Disease (Pathologic Minimal Residual Disease or Near pCR). The Black Squares and Black Curve Represent Studies That Did Not Define pCR



English language were excluded. In addition, studies in which MRI was undertaken only during NAC were ineligible. Finally, studies of different diagnostic methods that were presented in combination and could not be separated were excluded.

### *Data Extraction*

For each eligible study, we extracted the following information: first author, number of patients, mean age, clinical characteristics, therapeutic interventions, reference standard, and number of responses and nonresponses. True-positive, false-positive, false-negative, and true-negative values were obtained from the MRI scans and other assessment methods (ultrasonography, mammography, and PET/CT) after a comparison with the pathologic results.

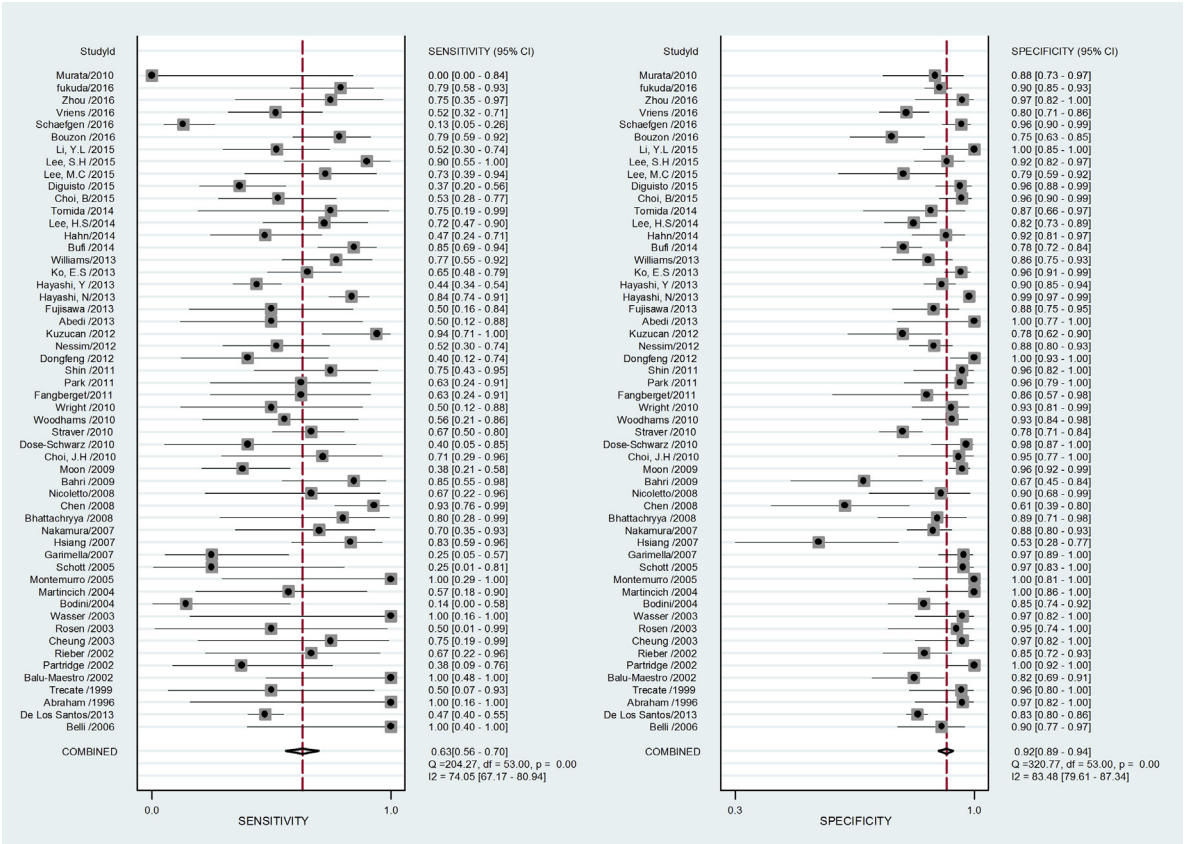
### *Data Synthesis and Statistical Analysis*

For each study, we constructed a 2 × 2 contingency table in which all participants were classified as having positive or negative imaging results and pCR or not after NAC. All analyses were performed using Stata, version 13.0 (StataCorp LP) and MetaDiSc.[23] The heterogeneity among the different studies was analyzed using a $\chi^2$ test and assessed by forest plot, with $Q$ and $I^2$ statistics presented. If heterogeneity was present, defined as $I^2 > 50\%$, the random effects model was selected. Otherwise, the fixed effects model was selected. The threshold effect was an important source of heterogeneity. To judge whether the threshold effect was present, Spearman correlation coefficients (between the logit of sensitivity and logit of specificity) were calculated. A $P$ value for Spearman correlation coefficients of $< .05$ indicated that threshold effects were present among the studies.

To further assess for possible explanations for the heterogeneity of a nonthreshold effect, we applied single-factor meta-regression analysis by the pCR definition, pCR rate (2 studies[24,25] reported that the mean pCR rate was approximately 17%; thus, we chose 17% as the cutoff value), study population era (midpoint of study population enrollment, 2005), dosage of gadolinium-based materials, and whether to accept blind subjects.

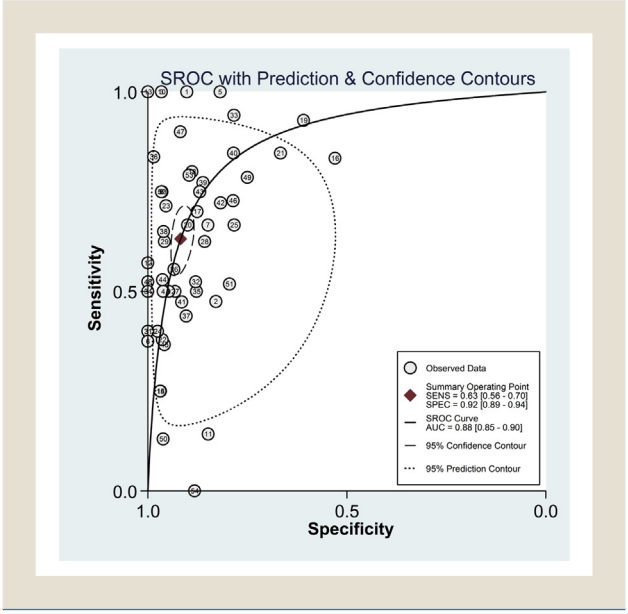
The pooled diagnostic odds ratio was calculated, which expresses how much greater the odds of having a pCR is for those with a positive test result compared with a negative test result. The area under the summary receiver operating characteristic curve (AUC) is an index to evaluate a diagnostic test and summarizes the diagnostic performance as a single number. A perfect test will have an AUC

**Figure 3** Forest Plot of Contrast-enhanced Magnetic Resonance Imaging Sensitivity and Specificity to Predict Pathologic Complete Remission. Black Square and Horizontal Lines Represent the Estimate and 95% Confidence Interval (CI) for Each Study




Abbreviation: StudyID = study identification.

**Figure 4** Summary Receiver Operating Characteristic Curve (SROC) to Predict Pathologic Complete Remission in Primary Breast Cancer Using Contrast-enhanced Magnetic Resonance Imaging




Abbreviations: AUC = area under summary receiver operating characteristic curve; SENS = sensitivity; SPEC = specificity.

close to 1 and a poor test will have an AUC close to 0.5. The Youden index ($Q^*$ index) is another useful statistic and is defined by the point at which sensitivity and specificity are equal, closest to the ideal top-left corner of the receiver operating characteristic space.

Deek's funnel plot was used to evaluate for publication bias. An asymmetric Deek's funnel plot would suggest that a publication bias is present.

## Results

### *Study Selection*

A systematic search yielded a total of 1560 studies from the PubMed, Ovid, and Cochrane Library databases; 659 duplicate studies were excluded. After reviewing the titles and abstracts, 302 studies were considered as potential candidates for inclusion. After an in-depth reading, 191 studies were excluded, because they did not meet our eligibility criteria. Of the remaining 111 eligible studies, 8 studies lacked raw data, 33 studies had not presented sufficient data to construct or calculate the TP, FP, FN, and TN values, and 11 studies had included < 20 patients. Two studies[26,27] were excluded because of repetitive data (investigators with additional studies[28,29]). Thus, 57 studies,[10-12,19-21,28-78] with 5811 cases with MRI data available were included in our present meta-analysis. A flowchart of the published data search is presented in Figure 1.

### *Study Description and Patient Characteristics*

A total of 54 studies with 5272 CE-MRI data cases[11,12,19-21,28-76] and 8 studies with 539 DW-MRI data cases,[10,51,53,63,64,76-78] were eligible for inclusion in the present meta-analysis. The studies that analyzed the accuracy of MRI had enrolled patients from 1990 to 2013 and had included a median of 95 patients (range, 21-746). Most treatment regimens were taxane-based. Trastuzumab was used in 18 studies. Most studies used a 1.5-T magnet strength (73.7%), with a 0.1-mmol/kg dose of contrast material (52.6%). In 17 studies, the radiologists were unaware of the pathologic data. The characteristics of the included studies are listed in Table 1.

The definition of pCR after NAC used in the included studies was not identical. pCR was defined as the complete disappearance of invasive carcinoma and ductal carcinoma in situ (DCIS) in 23 studies.[12,21,28-31,33-35,40,41,43,46-48,59,63,65,66,68,70,73,78] In 3 studies,[32,42,76] the definition of pCR was not reported. In 29 studies,[10,11,19,20,36-39,44,45,50-54,56-58,60-62,64,67,69,71,72,74,75,77] pCR was defined as the absence of invasive cancer, although DCIS might have been present. Two studies[49,55] included few, small scattered foci of microscopic residual invasive tumor, defined as minimal residual disease (or near pCR). The diagnostic indexes of the different definitions are shown in Figure 2.

### *Accuracy of MRI*

The pooled sensitivity of CE-MRI across the studies was 0.64 (95% confidence interval [CI], 0.56-0.70), and the pooled specificity was 0.92 (95% CI, 0.89-0.94). The AUC for CE-MRI across all 54 studies was 0.88 (95% CI, 0.85-0.91). The $Q^*$ index was 0.81 (Figures 3 and 4). The subgroup analysis of different definitions of pCR is shown in Figure 2. Differences in the pooled sensitivity, specificity, and AUC of the different subgroups were not statistically significant.

The pooled sensitivity of DW-MRI across the studies was 0.93 (95% CI, 0.53-0.99), and the pooled specificity was 0.85 (95% CI, 0.68-0.94). The AUC for DW-MRI across all 8 studies was 0.94 (95% CI, 0.91-0.95). The $Q^*$ index was 0.85 (Figures 5 and 6).

### *Comparisons of Accuracy of MRI and Other Tests*

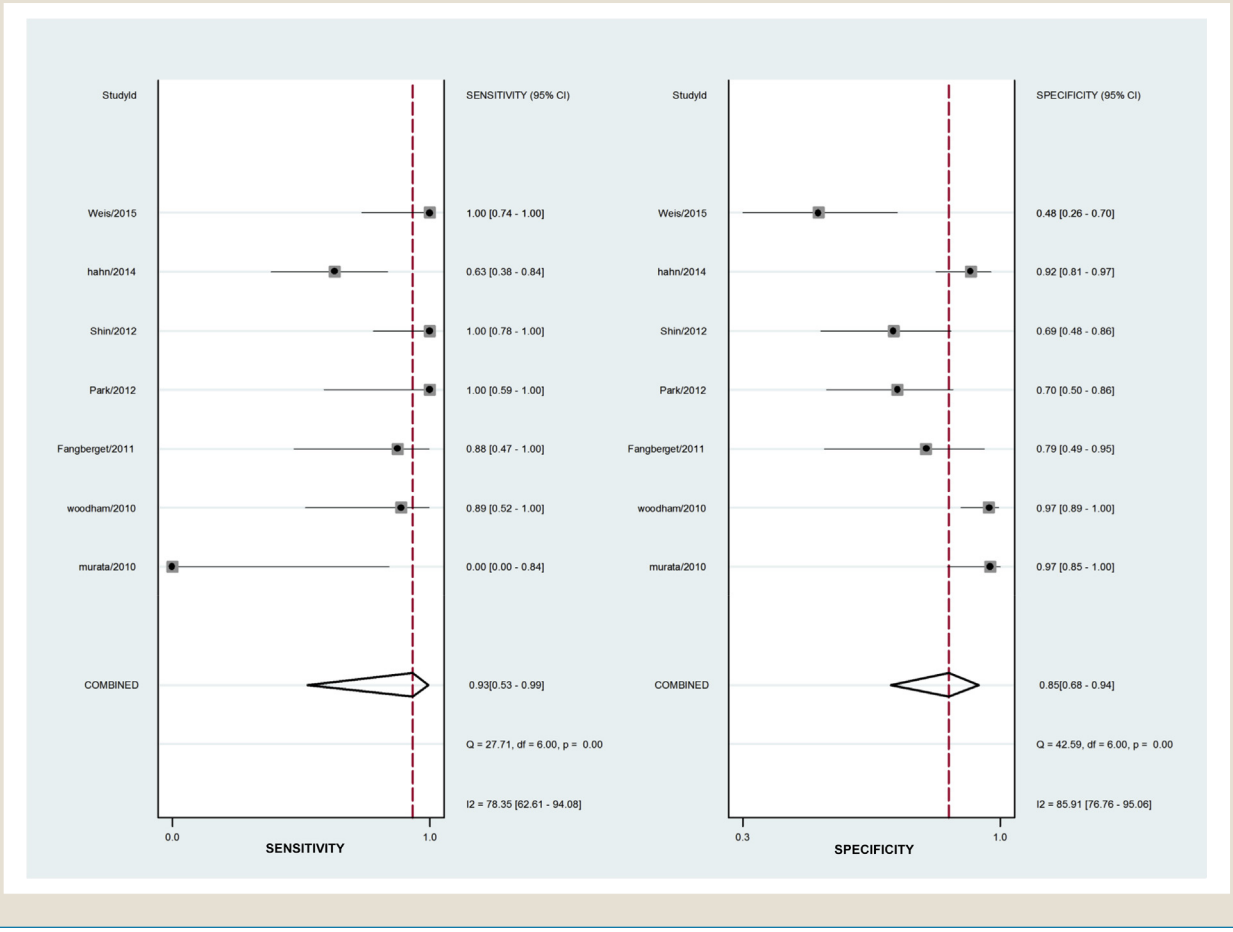
The results of the comparisons between CE-MRI and ultrasonography based on the subgroups from 10 studies[21,39,40,44,49,55,60,69,70,73] in the same cohort of patients are listed in Table 2. CE-MRI and mammography were compared in 4 studies.[40,49,55,73] CE-MRI and PET/CT were compared in 3 studies.[21,49,54] CE-MRI and DW-MRI were compared in 5 studies.[51,53,63,64,76]

Evidence showed that CE-MRI had greater accuracy than ultrasonography and mammography (the AUC 95% CIs did not overlap). Differences between CE-MRI and PET/CT or DW-MRI were not observed. However, the results indicated that PET/CT or DW-MRI had a high sensitivity and CE-MRI, a high specificity. Details are listed in Table 3.

### *Heterogeneity Test*

The present study confirmed that heterogeneity existed in both CE-MRI ($I^2 > 50\%$; $P < .1$) and DW-MRI ($I^2 > 50\%$; $P < .1$) groups. The Spearman correlation coefficients for CE-MRI and DW-MRI were 0.426 ($P = .002$ and $P < .05$) and 0.750 ($P = .052$ and $P > .05$), respectively. These results reflect a threshold effect in

**Figure 5** Forest Plot of Diffusion-weighted Magnetic Resonance Imaging Sensitivity and Specificity to Predict Pathologic Complete Remission. Black Square and Horizontal Lines Represent the Estimate and 95% Confidence Interval (CI) for Each Study




Abbreviation: StudyID = study identification.

the CE-MRI group but no threshold effect in the DW-MRI group.

In the CE-MRI group, a single-factor meta-regression analysis was conducted to evaluate the nonthreshold effect; the coefficients and *P* values are listed in Table 2. The meta-regression analysis showed that no statistically significant differences were present among the subgroups. In the DW-MRI group, meta-regression analysis was not performed, because the sample size was too small (only 8 studies were included). A sensitivity analysis was conducted, and the heterogeneity did not decrease significantly.

The publication bias for both CE-MRI ($P = .14$) and DW-MRI ($P = .65$) was insignificant. The Deek funnel plot for both was symmetrical. These results indicate that the publication bias was not statistically significant.

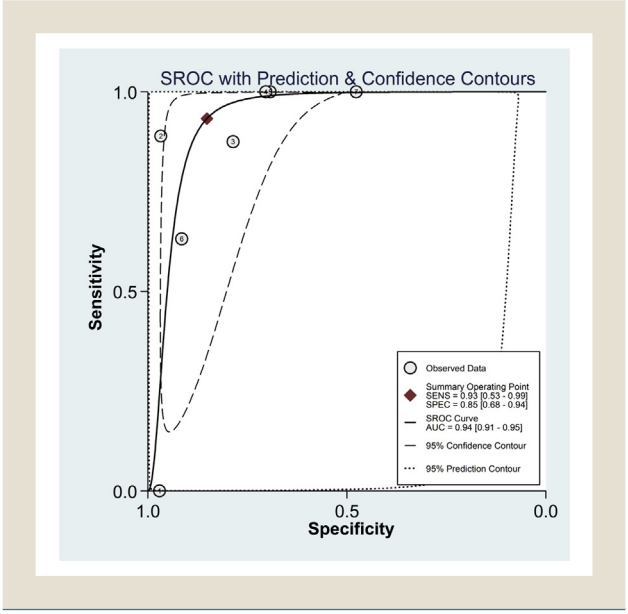
## Discussion

In the present systematic review, we aimed to estimate the accuracy of CE-MRI and DW-MRI to predict pCR after NAC in patients with breast cancer using available data. The studies compared the accuracy of CE-MRI and DW-MRI against that of pathologic results as the reference standard. We found that CE-MRI had a high specificity (correct detection of residual tumor) and relatively low sensitivity in detecting pCR. The low sensitivity might have resulted from the following reasons: reactive inflammation caused by tumor response and healing, surrounding sclerosis and necrosis, perilesional edema, multiple scattered lesions, and the presence of accompanying DCIS.[28,79,80] The sensitivity (0.93) showed that DW-MRI is also an excellent tool for detecting pCR. However, the sample size was small, with only 8 studies available. This result suggests that DW-MRI is a potentially valuable tool with a wide use for detecting pCR.

Because the pCR was not defined uniformly across the studies, the CE-MRI accuracy was independently assessed within groups with similar pCR definitions. In the subgroup that defined pCR as the complete disappearance of invasive carcinoma and DCIS, the $Q^*$ index was 0.81 and the AUC was 0.88 (95% CI, 0.85-0.91). In the subgroup that defined pCR as the absence of invasive cancer, the $Q^*$ index was 0.80 and the AUC was 0.87 (95% CI, 0.83-0.89). No statistically significant differences were found between the subgroups that defined pCR differently.

Several studies have compared CE-MRI with other imaging tools in assessing the response of breast cancer to NAC among different cohorts of patients in 2 separate modalities. In the present analysis,

**Figure 6** Summary Receiver Operating Characteristic Curve (SROC) to Predict Pathologic Complete Remission in Primary Breast Cancer Using Diffusion-weighted Magnetic Resonance Imaging




Abbreviations: AUC = area under summary receiver operating characteristic curve; SENS = sensitivity; SPEC = specificity.

we systematically compared the sensitivity, specificity, $Q^*$ index, and AUC for different imaging techniques in the same cohort of patients who had received NAC. CE-MRI had a greater overall AUC and $Q^*$ index compared with ultrasonography or mammography. This result suggests that PET/CT and DW-MRI might have AUC and $Q^*$ index values similar to those of CE-MRI. In our comparison, we found that DW-MRI and PET/CT had high sensitivity and CE-MRI had high specificity in predicting pCR to NAC in breast cancer patients. This indicates that PET/CT, DW-MRI, and CE-MRI could play different roles in monitoring the responses to NAC and might play complementary predictive roles in the treatment assessment. Park et al[10] suggested that DW-MRI and PET/CT have similar diagnostic accuracy for predicting pCR, and PET/CT had slightly greater diagnostic accuracy than DW-MRI. Additional clinical trials are required to further compare DW-MRI and PET/CT.

Compared with an earlier meta-analysis by Marinovich et al,[81] the present analysis not only added additional studies, but also examined the accuracy of DW-MRI and PET/CT compared with CE-MRI. We also excluded studies that had examined concurrent chemotherapy and radiotherapy, which were included in the analysis by Marinovich et al.[81]

Marinovich et al[81] found no difference in accuracy between CE-MRI and ultrasonography. However, CE-MRI was superior to ultrasonography in our analysis. The pooled sensitivity and specificity was 64% and 92%, respectively, similar to the findings from Yuan et al.[82] Another meta-analysis study compared the accuracy of MRI and PET/CT in predicting pCR[83]; however, MRI and PET/CT were performed during, not after, NAC. In our analysis, all eligible studies must have performed MRI after NAC completion.

The present analysis had some limitations. The major limitation of our analysis was that the studies we examined were not prospectively designed to evaluate MRI accuracy. Therefore, not all patients in the study data had been treated with the same standard, which accounted for the heterogeneity among the studies. The threshold effects were the significant factors resulting in heterogeneity among these studies. The criteria used to access the complete response to NAC by MRI were not standardized. Second, the studies that compared PET/CT and DW-MRI with CE-MRI in same cohort of patients were limited. Third, the breast cancer subtype and treatment regimens can influence CE-MRI accuracy.[84] Investigating the accuracy of responses in different molecular subtypes would allow us to draw more powerful conclusions. Most studies included various disease subtypes and the data were combined, making it difficult to tease apart the contributions from the particular subtypes. Therefore, we were limited in discussing the NAC response accuracy in different molecular subtypes in detail, which could be addressed in the future. Among the studies included in our analysis, we did not find a significant statistical publication bias. However, it is important to note that this finding might have been influenced by studies that were excluded from our analysis.

## Conclusion

We cannot accurately predict whether pCR is achieved until the final breast surgery has been performed, and this will always influence whether chemotherapy and surgery are deficient or excessive beforehand. In the present analysis, we found that CE-MRI had a high specificity and DW-MRI a high sensitivity in assessing the pCR. CE-MRI is more accurate than ultrasonography or mammography. Additionally, PET/CT is valuable for predicting pCR. PET/CT and DW-MRI monitoring reduced the incidence of overestimation using CE-MRI of the treatment response. Thus, PET/CT, DW-MRI, and CE-MRI could play different roles in

**Table 2** Results of Regression Meta-analysis

| Variable | Coefficient | SE | *P* Value |
|---|---|---|---|
| Definition of pCR | 0.177 | 0.1652 | .2889 |
| pCR rate | −0.408 | 0.3367 | .2316 |
| Patient enrollment period | 0.078 | 0.3483 | .9823 |
| Dosage of gadolinium-based materials | 0.087 | 0.0929 | .3529 |
| Blinded study | 0.502 | 0.3722 | .1834 |

Abbreviations: pCR = pathologic complete response; SE = standard error.

**Table 3** Comparisons Among Ultrasonography, Mammography, PET/CT, DW-MRI, and CE-MRI in the Same Cohort of Patients

| Comparison of CE-MRI to Other Modalities | Sensitivity (%) | Specificity (%) | DOR | $Q^*$ Index | Area Under Curve |
|---|---|---|---|---|---|
| CE-MRI | 0.61 (0.39-0.79) | 0.93 (0.89-0.96) | 18.35 (7.93-42.49) | 0.86 | 0.93 (0.90-0.95) |
| Ultrasonography | 0.43 (0.31-0.56) | 0.93 (0.84-0.97) | 6.78 (3.25-14.15) | 0.66 | 0.66 (0.62-0.70) |
| CE-MRI | 0.27 (0.17-0.39) | 0.97 (0.93-0.99) | 13.62 (2.96-62.60) | 0.97 | 0.99 |
| Mammography | 0.38 (0.26-0.50) | 0.91 (0.86-0.95) | 8.76 (2.49-30.75) | 0.52 | 0.53 |
| CE-MRI | 0.60 (0.36-0.81) | 0.97 (0.90-0.99) | 38.00 (8.62-167.58) | 0.91 | 0.96 |
| PET/CT | 0.90 (0.74-0.98) | 0.40 (0.31-0.49) | 4.86 (1.50-15.73) | 0.95 | 0.99 |
| CE-MRI | 0.68 (0.66-0.78) | 0.84 (0.80-0.88) | 13.82 (7.28-26.23) | 0.81 | 0.88 |
| DW-MRI | 0.79 (0.68-0.88) | 0.75 (0.70-0.80) | 18.68 (6.88-50.73) | 0.80 | 0.87 |

Data presented as mean (95% confidence interval).
Abbreviations: CE-MRI = contrast-enhanced magnetic resonance imaging; DW-MRI = diffusion-weighted magnetic resonance imaging; PET/CT = positron emission tomography/computed tomography.

monitoring the response to NAC. Therefore, the combined use of CE-MRI with PET/CT or DW-MRI might yield greater precision in assessing pCR. Additional well-designed clinical trials are required to further investigate this conclusion.

## Acknowledgments

The present study was supported by the Science, Education and Health Foundation of Soochow City (grant KJXW2014011) and the Soochow Science and Technology Project (grant SYS201631). Our project was subject to The Second Affiliated Hospital of Soochow University preponderant clinic discipline group project funding (grant XKQ2015008).

## Disclosure

The authors have stated that they have no conflicts of interest.

## References

1. De Lena M, Zucali R, Viganotti G, et al. Combined chemotherapy-radiotherapy approach in locally advanced (T3b-T4) breast cancer. *Cancer Chemother Pharmacol* 1978; 1:53-9.
2. Makhoul I, Kiwan E. Neoadjuvant systemic treatment of breast cancer. *J Surg Oncol* 2011; 103:348-57.
3. Beasley GM, Olson JA. What's new in neoadjuvant therapy for breast cancer? *Adv Surg* 2010; 44:199-228.
4. Wolmark N, Wang JP, Mamounas E, et al. Preoperative chemotherapy in patients with operable breast cancer: nine-year results from National Surgical Adjuvant Breast and Bowel Project B-18. *Natl Cancer Inst Monogr* 2001; 30:96-102.
5. van der Hage JA, Julien JP, Tubiana-Hulin M, et al. Preoperative chemotherapy in primary operable breast cancer: results from the European Organization for Research and Treatment of Cancer trial 10902. *J Clin Oncol* 2001; 19:4224-37.
6. Bear HD, Anderson S, Smith RE, et al. Sequential preoperative or postoperative docetaxel added to preoperative doxorubicin plus cyclophosphamide for operable breast cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-27. *J Clin Oncol* 2006; 24:2019-27.
7. Mersin H, Yildirim E, Berberoglu U, et al. The prognostic importance of triple negative breast carcinoma. *Breast* 2008; 17:341-6.
8. Symmans WF, Peintinger F, Hatzis C, et al. Measurement of residual breast cancer burden to predict survival after neoadjuvant chemotherapy. *J Clin Oncol* 2007; 25: 4414-22.
9. Chaudry M, Lei X, Gonzalez-Angulo AM, et al. Recurrence and survival among breast cancer patients achieving a pathological complete response to neoadjuvant chemotherapy. *Breast Cancer Res Treat* 2015; 153:417-23.
10. Park SH, Moon WK, Cho N, et al. Comparison of diffusion-weighted MR imaging and FDG PET/CT to predict pathological complete response to neoadjuvant chemotherapy in patients with breast cancer. *Eur Radiol* 2012; 22:18-25.
11. Ko ES, Han BK, Kim RB, et al. Analysis of factors that influence the accuracy of magnetic resonance imaging for predicting response after neoadjuvant chemotherapy in locally advanced breast cancer. *Ann Surg Oncol* 2013; 20:2562-8.
12. Williams M, Eatrides J, Kim J, et al. Comparison of breast magnetic resonance imaging clinical tumor size with pathologic tumor size in patients status post-neoadjuvant chemotherapy. *Am J Surg* 2013; 206:567-73.
13. Hylton N. MR imaging for assessment of breast cancer response to neoadjuvant chemotherapy. *Magn Reson Imaging Clin N Am* 2006; 14:383-9, vii.
14. Belli P, Costantini M, Ierardi C, et al. Diffusion-weighted imaging in evaluating the response to neoadjuvant breast cancer treatment. *Breast J* 2011; 17:610-9.
15. Leong KM, Lau P, Ramadan S. Utilisation of MR spectroscopy and diffusion weighted imaging in predicting and monitoring of breast cancer response to chemotherapy. *J Med Imaging Radiat Oncol* 2015; 59:268-77.
16. Morrow M. Magnetic resonance imaging in the breast cancer patient: curb your enthusiasm. *J Clin Oncol* 2008; 26:352-3.
17. Skaane P, Young K, Skjennald A. Population-based mammography screening: comparison of screen-film and full-field digital mammography with soft-copy reading—Oslo I study. *Radiology* 2003; 229:877-84.
18. Londero V, Bazzocchi M, Del Frate C, et al. Locally advanced breast cancer: comparison of mammography, sonography and MR imaging in evaluation of residual disease in women receiving neoadjuvant chemotherapy. *Eur Radiol* 2004; 14:1371-9.
19. Rosen EL, Blackwell KL, Baker JA, et al. Accuracy of MRI in the detection of residual breast cancer after neoadjuvant chemotherapy. *AJR Am J Roentgenol* 2003; 181:1275-82.
20. Vriens BE, de Vries B, Lobbes MB, et al. Ultrasound is at least as good as magnetic resonance imaging in predicting tumour size post-neoadjuvant chemotherapy in breast cancer. *Eur J Cancer* 2016; 52:67-76.
21. Choi JH, Lim HI, Lee SK, et al. The role of PET CT to evaluate the response to neoadjuvant chemotherapy in advanced breast cancer: comparison with ultrasonography and magnetic resonance imaging. *J Surg Oncol* 2010; 102:392-7.
22. Chen X, Moore MO, Lehman CD, et al. Combined use of MRI and PET to monitor response and assess residual disease for locally advanced breast cancer treated with neoadjuvant chemotherapy. *Acad Radiol* 2004; 11:1115-24.
23. Zamora J, Abraira V, Muriel A, et al. Meta-DiSc: a software for meta-analysis of test accuracy data. *BMC Med Res Methodol* 2006; 6:31.
24. Kong X, Moran MS, Zhang N, et al. Meta-analysis confirms achieving pathological complete response after neoadjuvant chemotherapy predicts favourable prognosis for breast cancer patients. *Eur J Cancer* 2011; 47:2084-90.
25. Bear HD, Anderson S, Brown A, et al. The effect on tumor response of adding sequential preoperative docetaxel to preoperative doxorubicin and cyclophosphamide: preliminary results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27. *J Clin Oncol* 2003; 21:4165-74.
26. Belli P, Romani M, Costantini M, et al. Role of magnetic resonance imaging in the pre and postchemotherapy evaluation in locally advanced breast carcinoma. *Rays* 2002; 27:279-90.
27. De Los Santos J, Bernreuter W, Keene K, et al. Accuracy of breast magnetic resonance imaging in predicting pathologic response in patients treated with neoadjuvant chemotherapy. *Clin Breast Cancer* 2011; 11:312-9.
28. Belli P, Costantini M, Malaspina C, et al. MRI accuracy in residual disease evaluation in breast cancer patients treated with neoadjuvant chemotherapy. *Clin Radiol* 2006; 61:946-53.
29. De Los Santos JF, Cantor A, Amos KD, et al. Magnetic resonance imaging as a predictor of pathologic response in patients treated with neoadjuvant systemic treatment for operable breast cancer. Translational Breast Cancer Research Consortium trial 017. *Cancer* 2013; 119:1776-83.
30. Abraham DC, Jones RC, Jones SE, et al. Evaluation of neoadjuvant chemotherapeutic response of locally advanced breast cancer by magnetic resonance imaging. *Cancer* 1996; 78:91-100.
31. Trecate G, Ceglia E, Stabile F, et al. Locally advanced breast cancer treated with primary chemotherapy: comparison between magnetic resonance imaging and pathologic evaluation of residual disease. *Tumori* 1999; 85:220-8.
32. Balu-Maestro C, Chapellier C, Bleuse A, et al. Imaging in evaluation of response to neoadjuvant breast cancer treatment benefits of MRI. *Breast Cancer Res Treat* 2002; 72:145-52.
33. Partridge SC, Gibbs JE, Lu Y, et al. Accuracy of MR imaging for revealing residual breast cancer in patients who have undergone neoadjuvant chemotherapy. *AJR Am J Roentgenol* 2002; 179:1193-9.

34. Rieber A, Brambs HJ, Gabelmann A, et al. Breast MRI for monitoring response of primary breast cancer to neo-adjuvant chemotherapy. *Eur Radiol* 2002; 12:1711-9.
35. Cheung YC, Chen SC, Su MY, et al. Monitoring the size and response of locally advanced breast cancers to neoadjuvant chemotherapy (weekly paclitaxel and epirubicin) with serial enhanced MRI. *Breast Cancer Res Treat* 2003; 78:51-8.
36. Wasser K, Sinn HP, Fink C, et al. Accuracy of tumor size measurement in breast cancer using MRI is influenced by histological regression induced by neoadjuvant chemotherapy. *Eur Radiol* 2003; 13:1213-23.
37. Bodini M, Berruti A, Bottini A, et al. Magnetic resonance imaging in comparison to clinical palpation in assessing the response of breast cancer to epirubicin primary chemotherapy. *Breast Cancer Res Treat* 2004; 85:211-8.
38. Martincich L, Montemurro F, De Rosa G, et al. Monitoring response to primary chemotherapy in breast cancer using dynamic contrast-enhanced magnetic resonance imaging. *Breast Cancer Res Treat* 2004; 83:67-76.
39. Montemurro F, Martincich L, De Rosa G, et al. Dynamic contrast-enhanced MRI and sonography in patients receiving primary chemotherapy for breast cancer. *Eur Radiol* 2005; 15:1224-33.
40. Schott AF, Roubidoux MA, Helvie MA, et al. Clinical and radiologic assessments to predict breast cancer pathologic complete response to neoadjuvant chemotherapy. *Breast Cancer Res Treat* 2005; 92:231-8.
41. Garimella V, Qutob O, Fox JN, et al. Recurrence rates after DCE-MRI image guided planning for breast-conserving surgery following neoadjuvant chemotherapy for locally advanced breast cancer patients. *Eur J Surg Oncol* 2007; 33: 157-61.
42. Hsiang DJ, Yamamoto M, Mehta RS, et al. Predicting nodal status using dynamic contrast-enhanced magnetic resonance imaging in patients with locally advanced breast cancer undergoing neoadjuvant chemotherapy with and without sequential trastuzumab. *Arch Surg* 2007; 142:855-61.
43. Nakamura S, Ishiyama M, Tsunoda-Shimizu H. Magnetic resonance mammography has limited ability to estimate pathological complete remission after primary chemotherapy or radiofrequency ablation therapy. *Breast Cancer* 2007; 14:123-30.
44. Bhattacharyya M, Ryan D, Carpenter R, et al. Using MRI to plan breast-conserving surgery following neoadjuvant chemotherapy for early breast cancer. *Br J Cancer* 2008; 98:289-93.
45. Chen JH, Feig B, Agrawal G, et al. MRI evaluation of pathologically complete response and residual tumors in breast cancer after neoadjuvant chemotherapy. *Cancer* 2008; 112:17-26.
46. Nicoletto MO, Nitti D, Pescarini L, et al. Correlation between magnetic resonance imaging and histopathological tumor response after neoadjuvant chemotherapy in breast cancer. *Tumori* 2008; 94:481-8.
47. Bahri S, Chen JH, Mehta RS, et al. Residual breast cancer diagnosed by MRI in patients receiving neoadjuvant chemotherapy with and without bevacizumab. *Ann Surg Oncol* 2009; 16:1619-28.
48. Moon HG, Han W, Lee JW, et al. Age and HER2 expression status affect MRI accuracy in predicting residual tumor extent after neo-adjuvant systemic treatment. *Ann Oncol* 2009; 20:636-41.
49. Dose-Schwarz J, Tiling R, Avril-Sassen S, et al. Assessment of residual tumour by FDG-PET: conventional imaging and clinical examination following primary chemotherapy of large and locally advanced breast cancer. *Br J Cancer* 2010; 102: 35-41.
50. Straver ME, Loo CE, Rutgers EJ, et al. MRI-model to guide the surgical treatment in breast cancer patients after neoadjuvant chemotherapy. *Ann Surg* 2010; 251: 701-7.
51. Woodhams R, Kakita S, Hata H, et al. Identification of residual breast carcinoma following neoadjuvant chemotherapy: diffusion-weighted imaging—comparison with contrast-enhanced MR imaging and pathologic findings. *Radiology* 2010; 254: 357-66.
52. Wright FC, Zubovits J, Gardner S, et al. Optimal assessment of residual disease after neo-adjuvant therapy for locally advanced and inflammatory breast cancer—clinical examination, mammography, or magnetic resonance imaging? *J Surg Oncol* 2010; 101:604-10.
53. Fangberget A, Nilsen LB, Hole KH, et al. Neoadjuvant chemotherapy in breast cancer-response evaluation and prediction of response to treatment using dynamic contrast-enhanced and diffusion-weighted MR imaging. *Eur Radiol* 2011; 21: 1188-99.
54. Park JS, Moon WK, Lyou CY, et al. The assessment of breast cancer response to neoadjuvant chemotherapy: comparison of magnetic resonance imaging and 18F-fluorodeoxyglucose positron emission tomography. *Acta Radiol* 2011; 52: 21-8.
55. Shin HJ, Kim HH, Ahn JH, et al. Comparison of mammography, sonography, MRI and clinical examination in patients with locally advanced or inflammatory breast cancer who underwent neoadjuvant chemotherapy. *Br J Radiol* 2011; 84: 612-20.
56. Dongfeng H, Daqing M, Erhu J. Dynamic breast magnetic resonance imaging: pretreatment prediction of tumor response to neoadjuvant chemotherapy. *Clin Breast Cancer* 2012; 12:94-101.
57. C. Nessim, I. Trop, A. Robidoux, et al., Can MRI accurately identify which patients with operable breast cancer will have a pathologic complete response after neoadjuvant therapy? BS12, *ANZ J Surg* **9**, 2013.
58. Kuzucan A, Chen JH, Bahri S, et al. Diagnostic performance of magnetic resonance imaging for assessing tumor response in patients with HER2-negative breast cancer receiving neoadjuvant chemotherapy is associated with molecular biomarker profile. *Clin Breast Cancer* 2012; 12:110-8.
59. Abedi M, Farrokh D, Joulaee A, et al. The validity of MRI in evaluation of tumor response to neoadjuvant chemotherapy in locally advanced breast cancer. *Iran J Cancer Prev* 2013; 6:28-35.
60. Fujisawa T, Hirakata T, Yanagita Y, et al. The detection of pCR after PST by contrast-enhanced ultrasonography for breast cancer. *Breast Cancer* 2013; 20:75-82.
61. N. Hayash, H. Tsunoda, N. Matsuda, et al., Abstract P2-02-11: Accuracy of MRI and ultrasonography in predicting pathologic complete response in breast cancer patients treated with neoadjuvant chemotherapy, *Cancer Res* 2013, 2-02.
62. Hayashi Y, Takei H, Nozu S, et al. Analysis of complete response by MRI following neoadjuvant chemotherapy predicts pathological tumor responses differently for molecular subtypes of breast cancer. *Oncol Lett* 2013; 5:83-9.
63. Bufi E, Belli P, Di-Matteo M, et al. Effect of breast cancer phenotype on diagnostic performance of MRI in the prediction to response to neoadjuvant treatment. *Eur J Radiol* 2014; 83:1631-8.
64. Hahn SY, Ko EY, Han BK, et al. Role of diffusion-weighted imaging as an adjunct to contrast-enhanced breast MRI in evaluating residual breast cancer following neoadjuvant chemotherapy. *Eur J Radiol* 2014; 83:283-8.
65. Lee HS, Ko BS, Ahn SH, et al. Diagnostic performance of breast-specific gamma imaging in the assessment of residual tumor after neoadjuvant chemotherapy in breast cancer patients. *Breast Cancer Res Treat* 2014; 145:91-100.
66. Tomida K, Ishida M, Umeda T, et al. Magnetic resonance imaging shrinkage patterns following neoadjuvant chemotherapy for breast carcinomas with an emphasis on the radiopathological correlations. *Mol Clin Oncol* 2014; 2:783-8.
67. Choi BB, Kim SH. Effective factors to raise diagnostic performance of breast MRI for diagnosing pathologic complete response in breast cancer patients after neoadjuvant chemotherapy. *Acta Radiol* 2015; 56:790-7.
68. Diguisto C, Ouldamer L, Arbion F, et al. MRI evaluation of residual breast cancer after neoadjuvant chemotherapy: influence of patient, tumor and chemotherapy characteristics on the correlation with pathological response. *Anticancer Res* 2015; 35:581-5.
69. Lee MC, Gonzalez SJ, Lin H, et al. Prospective trial of breast MRI versus 2D and 3D ultrasound for evaluation of response to neoadjuvant chemotherapy. *Ann Surg Oncol* 2015; 22:2888-94.
70. Lee SH, Chang JM, Han W, et al. Shear-wave elastography for the detection of residual breast cancer after neoadjuvant chemotherapy. *Ann Surg Oncol* 2015; 22(suppl 3):S376-84.
71. Li YL, Zhang XP, Li J, et al. MRI in diagnosis of pathological complete response in breast cancer patients after neoadjuvant chemotherapy. *Eur J Radiol* 2015; 84:242-9.
72. Bouzon A, Acea B, Soler R, et al. Diagnostic accuracy of MRI to evaluate tumour response and residual tumour size after neoadjuvant chemotherapy in breast cancer patients. *Radiol Oncol* 2016; 50:73-9.
73. Schaefgen B, Mati M, Sinn HP, et al. Can routine imaging after neoadjuvant chemotherapy in breast cancer predict pathologic complete response? *Ann Surg Oncol* 2016; 23:789-95.
74. Zhou J, Li G, Sheng F, et al. Magnetic resonance imaging evaluation of residual tumors in breast cancer after neoadjuvant chemotherapy: surgical implications. *Acta Radiol* 2016; 57:529-37.
75. Fukuda T, Horii R, Gomi N, et al. Accuracy of magnetic resonance imaging for predicting pathological complete response of breast cancer after neoadjuvant chemotherapy: association with breast cancer subtype. *Springerplus* 2016; 5:152.
76. Murata Y, Kubota K, Hamada N, et al. Diffusion-weighted magnetic resonance imaging for assessment after neoadjuvant chemotherapy in breast cancer, based on morphological concepts. *Oncol Lett* 2010; 1:293-8.
77. Shin HJ, Baek HM, Ahn JH, et al. Prediction of pathologic response to neoadjuvant chemotherapy in patients with breast cancer using diffusion-weighted imaging and MRS. *NMR Biomed* 2012; 25:1349-59.
78. Weis JA, Miga MI, Arlinghaus LR, et al. Predicting the response of breast cancer to neoadjuvant therapy using a mechanically coupled reaction-diffusion model. *Cancer Res* 2015; 75:4697-707.
79. Kim HJ, Im YH, Han BK, et al. Accuracy of MRI for estimating residual tumor size after neoadjuvant chemotherapy in locally advanced breast cancer: relation to response patterns on MRI. *Acta Oncol* 2007; 46:996-1003.
80. Yeh E, Slanetz P, Kopans DB, et al. Prospective comparison of mammography, sonography, and MRI in patients undergoing neoadjuvant chemotherapy for palpable breast cancer. *AJR Am J Roentgenol* 2005; 184:868-77.
81. Marinovich ML, Houssami N, Macaskill P, et al. Meta-analysis of magnetic resonance imaging in detecting residual breast cancer after neoadjuvant therapy. *J Natl Cancer Inst* 2013; 105:321-33.
82. Yuan Y, Chen XS, Liu SY, et al. Accuracy of MRI in prediction of pathologic complete remission in breast cancer after preoperative therapy: a meta-analysis. *AJR Am J Roentgenol* 2010; 195:260-8.
83. Liu Q, Wang C, Li P, et al. The role of (18)F-FDG PET/CT and MRI in assessing pathological complete response to neoadjuvant chemotherapy in patients with breast cancer: a systematic review and meta-analysis. *Biomed Res Int* 2016; 2016:3746232.
84. Lobbes MB, Prevos R, Smidt M, et al. The role of magnetic resonance imaging in assessing residual disease and pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy: a systematic review. *Insights Imaging* 2013; 4:163-75.