Can diffusion-weighted MR imaging and contrast-enhanced MR imaging precisely evaluate and predict pathological response to neoadjuvant chemotherapy in patients with breast cancer?

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CRD summary
This review concluded that diffusion-weighted magnetic resonance imaging (MRI) was highly sensitive and contrast-enhanced MRI was highly specific for predicting the pathological response to neoadjuvant chemotherapy in patients with breast cancer. Studies might have been missed, and the specificity of diffusion weighting was not substantially lower than that of contrast enhancement. The conclusions should be considered tentative.

Authors' objectives
To compare the performance of diffusion-weighted magnetic resonance imaging (MRI) and contrast-enhanced MRI to predict the pathological response for patients with breast cancer who were receiving neoadjuvant chemotherapy.

Searching
MEDLINE and EMBASE were searched for articles from January 2000 to January 2012. Search terms were reported and included methodological terms for test accuracy studies. Other databases, such as Science Direct, SpringerLink, Scopus, and Cochrane Database of Systematic Reviews, were checked for relevant articles, and reference lists were cross-checked. Only studies in English were included.

Study selection
Studies that assessed diffusion-weighted MRI or contrast-enhanced MRI for the prediction of pathological response, in at least 10 patients with breast cancer, who were receiving neoadjuvant chemotherapy, were eligible for inclusion. Studies were required to use histopathological analysis as the reference standard, to confirm response, and to report sufficient data for the calculation of 2x2 contingency tables (the numbers of true-positive, false-positive, false-negative, and true-negative results). Studies had to meet at least 10 of the 14 Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria.

In the included studies, where reported, the mean age of participants ranged from 40.5 to 56 years. The initial clinical stage, histopathological diagnosis, tumour receptor status and preoperative chemotherapy regimens varied widely across studies and the details were reported. All but three of the included studies reported using 1.5 Tesla MRI. Where reported, the period between MRI and surgery ranged from one to 45 days.

Two reviewers independently assessed studies for inclusion.

Assessment of study quality
Two reviewers independently assessed study quality using the QUADAS tool. Any disagreements were resolved by a third reviewer.

Data extraction
Data were extracted on the number of true-positive, false-positive, false-negative and true-negative results, for each study and each MRI technique. The study authors were contacted for additional information if necessary. Two reviewers independently extracted the data and any disagreements were resolved by a third reviewer.

Methods of synthesis
A hierarchical regression model was used to estimate the summary receiver operating characteristic curves for contrast-enhanced MRI and diffusion-weighted MRI, and to calculate summary estimates of sensitivity and specificity and the diagnostic odds ratio, with 95% confidence intervals. Summary estimates of the positive and negative likelihood ratios, with 95% confidence intervals, were calculated from the pooled sensitivity and specificity values.

Subgroup analyses were performed for the type of study (prospective versus retrospective), participant selection...
(consecutive versus nonconsecutive or not reported), and blinding (yes versus no or not reported).

**Results of the review**

Thirty-four studies, with 1,932 participants (range 14 to 195), were included in the review. Common areas of methodological weakness were whether the pathology was interpreted without knowing the results of the MRI, and the time that elapsed between the MRI and pathological confirmation.

**Diffusion-weighted MRI:** In six studies, the pooled estimate of sensitivity was 93% (95% CI 82 to 97) and of specificity was 82% (95% CI 70 to 90). The pooled positive likelihood ratio was 5.09 (95% CI 3.09 to 8.38), negative likelihood ratio was 0.09 (95% CI 0.04 to 0.22), and diagnostic odds ratio was 55.59 (95% CI 21.80 to 141.80). There were too few studies for subgroup analysis.

**Contrast-enhanced MRI:** In 30 studies, the pooled estimate of sensitivity was 68% (95% CI 57 to 77) and specificity was 91% (95% CI 87 to 94). The pooled positive likelihood ratio was 7.48 (95% CI 5.29 to 10.57), negative likelihood ratio was 0.36 (95% CI 0.27 to 0.48), and diagnostic odds ratio was 20.98 (95% CI 13.24 to 33.24). Subgroup analyses indicated that studies with consecutive enrolment of participants gave the highest pooled sensitivity estimate, whilst studies with less than 50 participants gave the highest specificity estimate. Blinded interpretation of the MRI and study design (prospective versus retrospective) did not significantly affect the test performance.

**Authors' conclusions**

Diffusion-weighted MRI was highly sensitive and contrast-enhanced MRI was highly specific for predicting the pathological response to neoadjuvant chemotherapy in patients with breast cancer.

**CRD commentary**

The review addressed a clearly stated objective and defined appropriate inclusion criteria. At least two databases were searched for relevant articles, but the restriction to studies in English and the use of terms for test accuracy studies (which reduce the search sensitivity), may have resulted in the omission of relevant studies. Measures to minimise error and bias were applied throughout the review process. The methodological quality of the included studies was assessed and the results were reported in full and incorporated in the authors' interpretation of the findings. Appropriate meta-analytic methods were used to combine the study data and some possible sources of heterogeneity were investigated, but an investigation of clinical heterogeneity, such as initial tumour stage, would have been useful.

The authors' conclusions broadly reflected the data presented, but the reported specificity estimate for diffusion-weighted MRI was not substantially lower than that for contrast-enhanced MRI, and this estimate had a wide confidence interval due to the small data set. It may be that further studies of diffusion-weighted MRI could show adequate performance for this test alone, and the findings should therefore be considered tentative.

**Implications of the review for practice and research**

**Practice:** The authors stated that diffusion-weighted MRI and contrast-enhanced MRI together could improve diagnostic performance in the monitoring of patients with breast cancer, receiving neoadjuvant chemotherapy.

**Research:** The authors stated that further, large prospective studies were needed to assess the value of contrast-enhanced MRI and diffusion-weighted MRI together in preoperative screening for breast cancer treatment.

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**Bibliographic details**


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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.