Meta-analysis of quantitative diffusion-weighted MR imaging in the differential diagnosis of breast lesions

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CRD summary
This review concluded that diffusion weighted magnetic resonance imaging was useful for differentiating malignant and benign breast lesions. These conclusions were supported by the data, but should be interpreted with some caution due to the possibility of missing studies and unclear generalisability of the findings.

Authors’ objectives
To determine the diagnostic performance of quantitative diffusion weighted magnetic resonance imaging (MRI) in patients with breast lesions.

Searching
MEDLINE and CNKI were searched to May 2009. Search terms were reported. The Cochrane Library and Elsevier and Springer databases were searched to June 2009. Reference lists were screened. The review was restricted to studies published in English or Chinese.

Study selection
Studies that evaluated diffusion weighted MRI against a reference standard of histopathology (performed at surgery and biopsy) and follow-up by ultrasound, mammography or MRI in women with breast lesions were eligible for inclusion. Studies had to include at least 30 lesions of varying pathology with a minimum at least 10 benign and 10 malignant lesions and report sufficient data to populate 2x2 tables of test performance on a per lesion basis. Data had to be extractable separately for diffusion weighted MRI if different MRI techniques were used.

Most of the included studies were conducted in China. Single studies were conducted in Japan, Belgium, Italy and Germany. Mean age ranged from 42 to 58 years (age range 14 to 80 years). The mean apparent diffusion coefficient values of malignancy ranged from 0.82 to 1.36 x10^{-3} mm^2/s and of benign lesions ranged from 1.00 to 1.82 x10^{-3} mm^2/s. Apparent diffusion coefficient thresholds for differentiating malignant and benign lesions ranged from 0.90 to 1.76 x 10^{-3} mm^2/s. The diffusion gradient factor (b value) ranged from zero to 1,000s/mm^2; some studies used multiple b values.

Two reviewers independently assessed studies for inclusion. Disagreements were resolved through referral to a third reviewer.

Assessment of study quality
Two reviewers independently assessed study quality using the 14-item QUADAS tool. Disagreements were resolved through referral to a third reviewer.

Data extraction
Two reviewers independently extracted data to populate 2x2 tables. These data were used to calculate sensitivity, specificity, accuracy, positive and negative likelihood ratios (LR+ and LR-) and positive and negative predictive values (PPV and NPV). Data were extracted separately for different readers, multiple observations per reader and for multiple b values or techniques. Each set of 2x2 data was treated as a separate data set. Disagreements were resolved through referral to a third reviewer.

Methods of synthesis
Summary estimates of sensitivity and specificity, together with 95% CIs, were estimated and summary receiver operating characteristic (SROC) curves were estimated using the Moses-Littenberg model. The Spearman correlation coefficient was used to test for a threshold effect. Heterogeneity was assessed using X^2 and I^2. Sensitivity analysis was conducted by omitting suspicious studies from the analysis. Publication bias was assessed using funnel plots and the fail
Results of the review
Thirteen studies were included (964 lesions, range 41 to 191). All studies included an appropriate patient spectrum, used an appropriate reference standard, provided an adequate description of the index test. All studies avoided disease progression bias, partial verification bias, incorporation bias and clinical review bias. None of the studies reported on whether the reference standard was interpreted blind to the index test results and only one study stated that the index test was interpreted blind to the reference standard. Reference standard execution and withdrawals were reported in two studies. Uninterpretable/intermediate results were reported in four studies.

Sensitivity ranged from 63% to 100% and specificity ranged from 46% to 97%. There was substantial heterogeneity in both estimates ($I^2$>60%). Heterogeneity was reduced ($I^2$=30% and 33%) when analysis was restricted to studies that used a maximum $b$ of 1,000s/mm$^2$. Summary sensitivity for these 11 studies was 84% (95% CI 80% to 87%) and summary specificity was 84% (95% CI 79% to 88%).

Exclusion of two potential outlying studies did not substantially influence the summary estimates although heterogeneity was reduced.

Authors' conclusions
Apparent diffusion coefficient measurement of diffusion weighted imaging was useful for differentiation of malignant and benign breast lesions.

CRD commentary
The review addressed a clear question. Inclusion criteria were adequately defined. The literature search was adequate for published studies. Restriction of the review to studies published in English and Chinese raised the possibility of language and publication biases. This was assessed in the review, but methods used were not appropriate for diagnostic data. Appropriate steps were taken to minimise bias and errors at all stages of the review process. Study quality was assessed using appropriate criteria and the results were clearly presented. Some study details were summarised in tables, but important information such as participants and reference standard details were lacking and so the generalisability of the review findings was unclear. Methods used to pool data were adequate but were not based on the most statistically robust models.

The authors' conclusions were supported by the data, but should be interpreted with some caution due to the possibility of missing studies and unclear generalisability of the findings.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that large-scale randomised controlled trials were required to assess and confirm the clinical value of diffusion weighted imaging in patients with breast lesions.

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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.