FDG-PET and other imaging modalities for the evaluation of breast cancer recurrence and metastases: a meta-analysis

CRD summary
The authors concluded that magnetic resonance imaging appeared to be a more useful supplement to surveillance techniques to assess patients with suspected recurrent and/or metastatic breast cancer. These conclusions should be interpreted with some caution due to the possibility of missed studies, lack of analysis based on direct comparisons and small size and methodological limitations of the included studies.

Authors' objectives
To determine the accuracy of ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), scintimammography (SMM) and positron emission tomography (PET) in diagnosis of breast recurrence and/or metastases.

Searching
MEDLINE, EMBASE, CBM, The Cochrane Library, CancerLit and CNKI were searched from 1995 to August 2008. Search terms were reported and included a diagnostic filter. The review was restricted to studies published in full in English or Chinese.

Study selection
Prospective or retrospective studies that evaluated the accuracy of ultrasound, CT, MRI, scintimammography or PET alone or in combination (but not in sequence) for the evaluation of at least 10 patients with breast cancer recurrence or metastatic breast carcinoma were eligible for inclusion. Studies had to use a reference standard of histopathologic analysis and/or close clinical and imaging follow-up for at least six months and report sufficient data to allow construction of 2x2 tables of test performance. CT studies had to use contrast agent.

Studies that assessed each of the eligible interventions (ultrasound, CT, MRI, PET and/or scintimammography) were included. Mean age ranged from 46 to 60 years where reported. Imaging was conducted to evaluate locoregional recurrence, for suspicion of recurrence, follow-up of breast cancer, restaging of breast cancer, with surgically resected breast cancer, routine screening for recurrence and end of treatment. Imaging techniques varied across studies (details provided in the paper).

Inclusion assessment was carried out independently by a least two reviewers. Disagreements were resolved through consensus between a group of four reviewers.

Assessment of study quality
Study quality was assessed according to QUADAS criteria.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted as 2x2 tables of test performance independently by four reviewers. Data were extracted for detection of recurrent and/or metastatic breast cancer. Data were extracted on a per-lesion or per-patient basis. Disagreements were resolved through consensus.

Methods of synthesis
Summary sensitivity and specificity together with 95% confidence intervals (CIs) were estimated using a random-effects model separately for each imaging modality. A summary receiver operating characteristic (SROC) analysis was conducted using the Moses-Littenberg method. Z-tests were used to compare summary estimates of sensitivity,
specificity, diagnostic odds ratio (DOR) and area under the SROC curve (AUC) for each imaging modality. Threshold effects between studies were assessed using the Spearman correlation coefficient. Heterogeneity was assessed using the \( X^2 \) test and \( I^2 \) statistic. Publication bias was assessed with funnel plots.

**Results of the review**

Forty-three studies were included in the review (n=5,421, range 10 to 1,968). Fifteen studies were prospective and 16 were retrospective; the design was unclear in the other studies. Eighteen studies enrolled consecutive patients; this was unclear in the other studies. Eleven studies avoided verification bias, there was some potential for verification bias in 10 studies and considerable verification bias in 22 studies.

Summary estimates of sensitivity and specificity of ultrasound for detection of recurrence were 86% (95% CI 80% to 90%) for sensitivity and 96% (95% CI 95% to 97%) for specificity (10 studies).

Summary estimates of sensitivity and specificity of CT for detection of recurrence were 85% (95% CI 81% to 88%) for sensitivity and 75% (95% CI 69% to 81%) for specificity (eight studies).

Summary estimates of sensitivity and specificity of MRI for detection of recurrence were 95% (95% CI 92% to 97%) for sensitivity and 93% (95% CI 90% to 95%) for specificity (11 studies).

Summary estimates of sensitivity and specificity of scintimammography for the detection of recurrence were 90% (95% CI 85% to 94%) for sensitivity and 80% (95% CI 72% to 87%) for specificity (seven studies).

Summary estimates of sensitivity and specificity of PET for detection of recurrence were 95% (95% CI 94% to 97%) for sensitivity and 86% (95% CI 82% to 90%) for specificity (21 studies).

There was substantial heterogeneity for all imaging modalities except PET and scintimammography. PET and MRI had significantly higher sensitivity than scintimammography, CT and ultrasound; there was no significant difference between PET and MRI. Ultrasound and MRI had significantly higher specificity than CT, scintimammography and PET; there was no significant difference between ultrasound and MRI. MRI and PET were the most accurate imaging modalities overall with significantly higher diagnostic odds ratios and area under the SROC curves compared to the other imaging modalities.

**Authors' conclusions**

MRI appeared to be a more useful supplement to surveillance techniques to assess patients with suspected recurrent and/or metastatic breast cancer. If MRI showed an indeterminate or benign lesion or MRI was not applicable, PET could be performed in addition.

**CRD commentary**

The review addressed a clear question and inclusion criteria were defined. The literature search was adequate for published studies, but use of a diagnostic filter and restriction of the review to published studies in English or Chinese meant that relevant studies may have been missed and there was a possibility of language and publication biases. This was assessed in the review, but methods used were not appropriate for diagnostic accuracy data. Appropriate steps were taken to minimise bias and errors in the review process. Study quality was assessed using appropriate criteria, but only limited details of the assessment were reported and study quality was not considered in the synthesis of results. Relevant study details were summarised in tables and individual study results were clearly portrayed in tables and figures.

Methods of analysis appeared appropriate, but comparisons between imaging modalities were based on indirect data. Additional analysis focused on the direct comparisons reported in the included studies would have strengthened the authors' conclusions regarding the comparative accuracy of the different techniques.

The authors conclusions were supported by the results, but should be interpreted with some caution due to the possibility of missed studies, lack of analysis based on direct comparisons and small size and methodological limitations of the included studies.

**Implications of the review for practice and research**
Practice: The authors stated that MRI appeared to be a more useful supplement to surveillance techniques to assess patients with suspected recurrent and/or metastatic breast cancer. If MRI showed an indeterminate or benign lesion or MRI was not applicable, FDG-PET could be performed in addition.

Research: The authors stated that there was a need for high-quality prospective studies and multicentre trials to evaluate the accuracy of imaging for breast cancer recurrence. They also stated that there was a need for cost-effectiveness analysis on this topic.

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