Contemporary diagnostic imaging modalities for the staging and surveillance of melanoma patients: a meta-analysis

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CRD summary
This review concluded that, in primary staging and surveillance of melanoma, ultrasonography performed best for detecting lymph node metastases and combined positron emission tomography/computed tomography was best for distant metastases. Limitations in the review methods/reporting mean that these conclusions should be viewed cautiously. In addition, no imaging modality showed adequate sensitivity to rule out lymph node metastases at primary staging.

Authors’ objectives
To assess the utility of ultrasonography, computed tomography (CT), positron emission tomography (PET) and PET-CT for the staging and surveillance of malignant melanoma.

Searching
MEDLINE, EMBASE, CANCERLIT and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from January 1990 to June 2009; search terms were reported. No language restrictions were applied. Bibliographies of included studies were screened for additional articles.

Study selection
Studies that assessed the performance of one or more imaging modalities (ultrasonography, CT, PET, or PET-CT) for staging or surveillance of melanoma were eligible for inclusion. Studies had to include more than 10 patients with melanoma. Primary staging studies were required to use sentinel lymph node or distant metastases biopsy with pathological confirmation as the reference standard. Surveillance studies were required to use a minimum follow-up of six months.

The median age of patients in included studies was 55 years (range 14 to 93 years); the median proportion of men was 55% (range 37% to 79%).

The authors did not state how many reviewers selected studies for inclusion.

Assessment of study quality
Two reviewers independently assessed methodological quality using the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) tool to calculate an overall quality score (maximum 14 points). Any disagreements between the reviewers were resolved by consensus or discussion with a third reviewer.

Data extraction
Data to populate 2x2 contingency tables (numbers of true positive, false negative, false positive, and false negative test results) were extracted. These were used to calculate sensitivity, specificity and accuracy values, with 95% confidence intervals (CIs), for each study, imaging modality and clinical application (staging including detection of lymph node or distant metastases; or surveillance).

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Bayesian bivariate models were used to generate overall estimates of sensitivity and specificity, with 95% credible intervals (CrIs), for each imaging modality. Separate analyses were conducted for the detection of lymph node and distant metastases; ultrasound was not included in the distant metastases model. Both models included the imaging modalities as co-variates, as well as the following other co-variates that may account for between study heterogeneity:
study design (prospective/retrospective); reason for imaging (primary staging/re-staging/both); and unit of assessment (patient/lesion).

Funnel plots and the Egger test were used to assess publication bias.

Results of the review
Seventy-four studies were included in the review (primary staging only 30 studies and surveillance only 34 studies). Twenty-two studies reported data for ultrasonography (n=7,085 patients, range 22 to 2008), 13 for CT (n=1,320 patients, range 18 to 250), 45 for positron emission tomography (PET, n=2,853 patients, range 10 to 250) and 13 for PET-CT (n=1,030 patients, range 18 to 250). The mean QUADAS score was 5.8 (standard deviation 2.5); approximately 90% of studies had a quality score of <9.0.

Lymph node metastases - primary staging: For ultrasound, the pooled estimate of sensitivity was 60% (95% CrI 33 to 83) and specificity was 97% (95% CrI 88 to 99). For CT, the pooled estimate of sensitivity was 9% (95% CrI 1 to 52) and specificity was 92% (95% CrI 50 to 99). For PET, the pooled estimate of sensitivity was 30% (95% CrI 12 to 55) and specificity was 96% (95% CrI 87 to 99). For PET-CT, the pooled estimate of sensitivity was 11% (95% CrI 1 to 50) and specificity was 97% (95% CrI 78 to 100).

Lymph node metastases - surveillance: For ultrasound, the pooled estimate of sensitivity was 96% (95% CrI 85 to 99) and specificity was 99% (95% CrI 95 to 100). For CT, the pooled estimate of sensitivity was 61% (95% CrI 15 to 93) and specificity was 97% (95% CrI 70 to 100). For PET, the pooled estimate of sensitivity was 87% (95% CrI 67 to 96) and specificity was 98% (95% CrI 93 to 100). For PET-CT, the pooled estimate of sensitivity was 65% (95% CrI 20 to 93) and specificity was 99% (95% CrI 92 to 100).

Distant metastases - primary staging: For CT, the pooled estimate of sensitivity was 51% (95% CrI 24 to 76) and specificity was 69% (95% CrI 30 to 92). For PET, the pooled estimate of sensitivity was 74% (95% CrI 51 to 88) and specificity was 75% (95% CrI 45 to 91). For PET-CT, the pooled estimate of sensitivity was 80% (95% CrI 53 to 93) and specificity was 87% (95% CrI 54 to 97).

Distant metastases - surveillance: For CT, the pooled estimate of sensitivity was 63% (95% CrI 46 to 77) and specificity was 78% (95% CrI 58 to 90). For PET, the pooled estimate of sensitivity was 82% (95% CrI 72 to 88) and specificity was 83% (95% CrI 70 to 91). For PET-CT, the pooled estimate of sensitivity was 86% (95% CrI 76 to 93) and specificity was 91% (95% CrI 79 to 97).

Funnel plots showed no evidence of publication bias.

Authors' conclusions
Ultrasonography had the best diagnostic performance for detecting lymph node metastases, and PET-CT had the best performance for detecting distant metastases, in both the primary staging and surveillance of melanoma patients.

CRD commentary
The review stated a clear objective; appropriate inclusion criteria were defined. A number of sources were searched for relevant studies and no language restrictions were applied, which minimised the potential for missed studies. It was unclear whether measures to minimise error and/or bias in the review process were applied to study selection and data extraction.

The methodological quality of included studies was assessed (measures were taken to minimise error and/or bias in this assessment). However, the results of quality assessment were only reported as the distribution of summary quality score (not recommended for the QUADAS tool). Appropriate meta-analytic methods were used. Although no evidence of publication bias was identified, given the unreliability of the assessment of publication bias in test accuracy studies, publication bias could not be ruled out.

The authors' conclusions reflect the data presented, but should be viewed with caution given the limitations outlined. It is also worth noting that none of the imaging modalities assessed showed adequate sensitivity to rule out lymph node metastases.
Implications of the review for practice and research

Practice: The authors stated that, in patients with low risk of metastases, PET-CT should not be used without additional clinical indications.

Research: The authors stated that decision analytic modelling studies were needed to assess the effectiveness and cost-effectiveness of alternative surveillance strategies (different imaging modalities and frequencies) with respect to stage-specific patient outcomes.

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