Breast cancer seeding associated with core needle biopsies: a systematic review
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CRD summary
This review assessed the prognostic significance of epithelial cell displacement after core needle biopsy in breast cancer patients and concluded that, despite limited data, no increased morbidity was associated with iatrogenic seeding after core needle biopsy. Given a lack of details on study quality and other methodological concerns it is difficult to judge the reliability of these conclusions.

Authors' objectives
To assess the prognostic significance of epithelial cell displacement after a core needle biopsy in breast cancer patients.

Searching
MEDLINE via PubMed, CANCERLIT and Cochrane Controlled Trials Register were searched from inception to 2008 for studies in English and French. Internet pages were searched using the Google search engine. Search terms were reported. Reference lists of relevant publications were screened. Breast cancer conference proceedings were searched.

Study selection
Studies that evaluated tumour cell seeding and/or epithelial cell displacement after a preoperative core needle biopsy in patients with breast cancer were eligible for inclusion. Studies that reported the types of diagnostic needle procedures, assessment of epithelial displacement or the outcome of a comparison between patients with or without preoperative core needle biopsy were eligible for inclusion. Eligible types of core needle biopsy included automated gun core needle biopsy and vacuum assisted core biopsy, regardless of the image guidance. Studies that assessed epithelial cell displacement using fine needle aspiration cytology only were excluded, as were studies of animal models. The review outcomes were rate of malignant tumor cell displacement, local recurrence, relapse-free survival, overall survival and sentinel node metastases.

Most included studies assessed epithelial cells displacement associated with core needle biopsy. The size and type of core needle biopsies varied in the included studies. The median number of needle passes varied from one to 24. The tumour histological type included benign and malignant lesions, invasive ductal carcinoma, invasive lobular carcinoma, ductal carcinoma in situ and lobular carcinoma in situ. The type of surgery included mastectomies and lumpectomies. Most included patients underwent image-guided (ultrasound-guided or stereotactic) 14-gauge core needle biopsy; a minority of patients underwent large-gauge vacuum assisted core needle biopsy. The time between core needle biopsy and surgical treatment in half of included studies ranged from 0 to 112 days. Most included studies were conducted in the USA.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted on the number of patients who experienced an event. Where possible, odds ratios (ORs) with 95% confidence intervals (CIs) were extracted.

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

Methods of synthesis
The studies were combined in a narrative synthesis, supported by accompanying data tables.

Results of the review
Fifteen studies (n=5,369) were included in the review: three prospective studies and 12 retrospective studies. Median follow-up for four studies that reported the outcome of local recurrence rates ranged from 29.7 to 78 months.

**Cells seeding/displacement (nine studies, n=927):** Nine studies reported that malignant tumor cell displacement on surgical excision specimens was found in 22% of patients (range 2% to 63%).

**Other outcome endpoints (six studies, n=4,442):** Four studies reported that there was no significant difference in the local recurrence rate between patients who underwent a preoperative diagnostic needle biopsy and those who underwent an excisional biopsy. Local recurrence rates ranged from 1.1% to 3.7% for core needle biopsy group and from 2.1% to 10.3% for the excisional biopsy group. One study reported that the incidence of sentinel lymph node metastases was significantly higher in patients whose cancer was diagnosed by large-gauge needle core biopsy than those diagnosed using an excisional biopsy (OR 1.48, 95% CI 1.02 to 2.16). Another study reported that patients who underwent preoperative breast biopsy had a 1.37 times (95% CI 1.13 to 1.66) increased risk of sentinel node metastases. One study showed that there was a significant difference in the mortality rate between patients who underwent a preoperative biopsy and those who did not (0% versus 4.7%, p=0.002).

Risk factors associated with cell displacement were reported.

**Authors' conclusions**
No increased morbidity was associated with iatrogenic seeding after a core needle biopsy, although data were limited.

**CRD commentary**
The review addressed a clear research question. Inclusion criteria were broad for the study design. A number of relevant databases were searched for published and unpublished studies, which reduced the potential of publication bias. The restriction to English- and French-language studies meant that language bias could not be ruled out. It was unclear whether sufficient attempts were taken to minimise bias and error in the review process. A formal validity assessment was not carried out. A narrative synthesis was appropriate given the diversity of included studies. The authors' conclusions reflected the evidence presented, but without further details on study quality and given the other methodological concerns, it was difficult to judge the reliability of the authors' conclusions.

**Implications of the review for practice and research**
**Practice:** The authors stated that, according to the relatively high frequency of epithelial cell displacement associated with core needle biopsy, a risk of local recurrence and metastatic spread could not be excluded. This risk should be kept in mind in the surveillance of breast cancer patients diagnosed by core needle biopsy, particularly for those who did not receive adjuvant radiation therapy.

**Research:** The authors stated that larger prospective studies with proper stratification were required to investigate the impact of core needle biopsy on patient survival. Future studies should take into account confounding factors. Studies of new breast core biopsy devices should include cell displacement as an endpoint.

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