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REVIEW ARTICLE

# Seeding of tumour cells following breast biopsy: a literature review

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**ABSTRACT.** Needle biopsy of the breast is widely practised. Image guidance ensures a high degree of accuracy. However, sporadic cases of disease recurrence suggest that in some cases the procedure itself may contribute to this complication. This article reviews evidence relating to needle biopsy of the breast and the potential for tumour cell migration into adjacent tissues following the procedure. A literature search was undertaken using Medline, Embase and the Cochrane Library. Results are grouped under three categories: histological evidence of spread, clinical evidence of recurrent disease and the likelihood of seeding dependent upon tumour type. There is histological evidence of seeding of tumour cells from the primary neoplastic site into adjacent breast tissue following biopsy. However, as the interval between biopsy and surgery lengthens then the incidence of seeding declines, which suggests that displaced tumour cells are not viable. Clinical recurrence at the site of a needle biopsy is uncommon and the relationship between biopsy and later recurrence is difficult to confirm. There is some evidence to suggest that cell seeding may be reduced when vacuum biopsy devices are deployed.

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Image-guided percutaneous needle biopsy of the breast is widely practised in breast units. In a significant proportion of cases the biopsy is undertaken to confirm a putative diagnosis of malignancy. A variety of needle devices are used. The simplest and least traumatic is fine needle aspiration (FNA), in which a thin fine-gauge needle, commonly 22-G, is inserted into the tumour. Vigorous aspiration is undertaken and the cellular aspirate is either smeared to slide or preserved in transport medium. Larger needles, commonly as large as 11- or 14-G, are frequently deployed, often with the aid of a spring loading device, *e.g.* a biopsy gun (Bard Medical Systems, Tempe, AZ) [1]. More recently vacuum aspiration devices have been deployed to further enhance specimen retrieval.

Inevitably, as the needle transgresses the tumour field and is withdrawn there is the potential for cells located in the tumour to migrate into the adjacent soft tissue and skin as a consequence of the violation of the tissue by the biopsy needle. The possibility of tumour spread following needle biopsy is well recognised but appears, in the majority of cases, to be an infrequent occurrence with little direct impact on patient outcome. Nevertheless, anecdotal reports of probable extension of the tumour down the needle track leading to a local recurrence do exist. In the light of this a comprehensive literature review to determine the potential for this occurrence was performed. This paper describes our search methodology and findings.

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## Method and materials

We searched Medline, Embase and the Cochrane Library by combining keywords and subject headings for needle/percutaneous biopsy and those for neoplasm seeding, metastasis or local recurrence. Further keywords were included to retrieve potentially relevant articles on other percutaneous procedures, such as drainage and ablation. Relevant papers were identified by inspection of titles and abstracts from the initial search and then reviewed.

All analysed papers cited and evaluated in this review are listed in Table 1. Those papers that contributed to patient numbers, yet which were not referenced in the text of the review, are included in the Appendix following the quoted references. Table 1 includes a column on impact factors; this relates to an annual score of the number of times papers have been cited within that journal per year. This shows that all the articles included in this review originate from journals with a credible impact factor rating.

## Results

### *Breast biopsy and histological evidence of spread*

10 papers addressing this subject were reviewed with an overall patient number of 3643.

Although recurrence at the site of a needle biopsy is uncommon, there is nevertheless evidence of seeding of tumour cells from the primary neoplastic site into adjacent breast tissue. Hoorntje et al [2] found needle

**Table 1.** Reviewed papers

| First author [reference] date | Title of paper | Number of patients | Study type | Journal impact factor |
|---|---|---|---|---|
| *Section 1: Histological evidence of spread* | | | | |
| Hoorntje LE [2] 2004 | Tumour cell displacement after 14G breast biopsy | 77 | Evaluation | 2.564 |
| Diaz LK [3] 1999 | Are malignant cells displaced by large gauge needle core biopsy of the breast? | 352 | Comparative | 2.47 |
| Michaelopoulos NV [4] 2008 | Needle track seeding after vacuum-assisted breast biopsy | 31 | Evaluation | 0.97 |
| Hansen NM [5] 2004 | Manipulation of the primary breast tumour and the incidence of sentinel node metastases from invasive breast cancer | 663 | Prospective | 4.32 |
| Peters-Engl C [6] 2004 | The impact of preoperative breast biopsy on the risk of sentinel lymph node metastases | 1890 | Multicentre database project | 4.346 |
| Hu XC [7] 2000 | Fine needle aspiration may shed breast cells into peripheral blood as determined by RT-PCT | 44 | Clinical trial | 1.545 |
| Grabau DA [not referenced] 2003 | Needle biopsy of breast cancer. Appearance of tumour cells along the needle track | 47 | Research support | 2.564 |
| Janssens P [not referenced] 2006 | Caution with microbiopsies of the breast: displaced cancer cells and ballistics | Not stated | Editorial | 2.205 |
| Newman EL [not referenced] 2006 | Does the method of biopsy affect the incidence of sentinel lymph node metastases? | 537 | Review | 1.61 |
| Douglas-Jones AG [not referenced] 2002 | Diagnostic difficulty arising from displaced epithelium after core biopsy in intracystic papillary lesions of the breast | 2 | Case reports | 2.324 |
| *Section 2: Clinical evidence of recurrent disease* | | | | |
| Chao C [8] 2001 | Local recurrence of breast cancer in the stereotactic core needle biopsy site | 3 | Case reports and literature review | 1.61 |
| Stolier A [9] 2000 | A prospective study of seeding of the skin after core biopsy of the breast | 89 | Prospective | 2.363 |
| Harter LP [10] 1992 | Malignant seeding of the needle track during stereotaxic core needle breast biopsy | 1 | Case report | 6.341 |
| Thurfjell MG [11] 2000 | Local breast cancer recurrence caused by mammographically guided punctures | 303 | Case reviews | 0.97 |
| Knight R [12] 2002 | Risk of needle-track seeding after diagnostic image-guided core needle biopsy in breast cancer | 398 | Comparative | 0.58 |
| Fitzal F [not referenced] 2006 | Preoperative core needle biopsy does not increase local recurrence rate in breast cancer patients | 719 | Comparative | 4.696 |
| Kwo S [not referenced] 2006 | Does stereotactic core needle biopsy increase the risk of local recurrence of invasive breast cancer? | Not stated | Editorial | 1.61 |
| Hoopmann M [not referenced] 2003 | Recurrence of breast cancer in the donor site after latissimus dorsi flap | 1 | Case report | 2.743 |
| Uriburu JL [not referenced] 2006 | Local recurrence of breast cancer after skin-sparing mastectomy following core needle biopsy | 61 | Case reports and literature review | 1.61 |
| *Section 3: Tumour type and likelihood of seeding* | | | | |
| Uematsu T [13] 2008 | Risk of needle track seeding of breast cancer: cytological results derived from core wash material | 207 | Pre-clinical | 4.696 |
| Phelan S [14] 2007 | Epithelial displacement during breast needle core biopsy causes diagnostic difficulties in subsequent surgical excision specimens | 7 | Case reports | 2.324 |

**Table 1.** Continued

| First author [reference] date | Title of paper | Number of patients | Study type | Journal impact factor |
|---|---|---|---|---|
| *Section 4: Discussion* | | | | |
| Mann GB [16] 2005 | Reliance on hormone receptor assays of surgical specimens may compromise outcome in patients with breast cancer | 100 | Comparative | 17.793* |
| Clough KB [19] 2010 | Improving breast cancer surgery: a classification and quadrant by quadrant atlas for oncoplastic surgery | >150 | Guideline | 4.130 |
| Liebens F [20] 2009 | Breast cancer seeding associated with core needle biopsies: a systematic review | 5369 | Systematic review | 2.093 |
| Koss LG [not referenced] 1988 | Aspiration biopsy – a tool in surgical pathology | Not stated | Historical review | 4.18 |
| Preece PE [not referenced] 1989 | Cytodiagnosis and other methods of biopsy in the modern management of breast cancer | Not stated | Review | 0.618 |

Number in square brackets corresponds to paper in the Reference list. Papers marked as ''not referenced'' appear in the Appendix.
*This figure is a reflection of the high frequency of publications issued each year.

tracks in 22 out of 64 excised specimens of patients who underwent 14-G needle biopsy and surgery on the same day. Tumour-cell displacement along the needle track was seen in 11 (50%) of these. Thereafter, they attempted to excise the entire 14-G needle track in 13 consecutive cases. Needle tracks were visualised in 11 of these and displaced cells were seen in 7. The time interval between core biopsy and surgical excision was 21 days (range, 7–35). They did not consider excision of the needle track to be feasible as a routine measure but advised radiotherapy for *in situ* and invasive carcinomas after conservative surgery.

Diaz et al [3] examined the post-excision specimens of 352 patients who had already undergone large core needle biopsy. Of these, 76 cases showed tumour displacement of 1 or 2 clusters of cells and 38 showed multiple displaced tumour fragments. Tumour displacement was seen in 37% of biopsies taken with an automated gun and 23% of specimens obtained with a vacuum-assisted needle. Tumour displacement was seen less frequently as the interval between biopsy and surgical excision lengthened. For example, tumour cell seeding was seen in 42% of patients when the interval between biopsy and excision was less than 15 days, but this was only seen in 15% of tumours excised more than 28 days after biopsy. This reduced the incidence of seeding down the needle track with time and was significant ($p<0.005$). This suggests that seeded cells do not survive displacement. Overall, tumour cell displacement occurred in approximately one-third of patients who had undergone a large core needle biopsy. Although numbers are limited, vacuum-assisted biopsy devices appear to be less frequently associated with cell displacement than conventional automated biopsy devices. This is further demonstrated by Michaelopoulos et al [4], who assessed cell seeding following 11-G vacuum-assisted breast biopsy (VABB) in 21 patients with ductal carcinoma *in situ* (DCIS) and 10 patients with invasive ductal carcinoma. No cases of dissemination of cancer cells in the needle track were observed following VABB.

There is conflicting evidence around the suggestion that metastasis to the sentinel lymph node may occur more frequently following needle biopsy. Hansen et al [5] examined 663 patients treated for breast cancer who had had sentinel lymph node biopsy (SLNB). They correlated the SLNB findings with the type of pre-surgical diagnostic technique employed (FNA, core biopsy or excision). They noted that the incidence of lymph node metastasis was statistically significantly greater in the FNA or large core needle biopsy group than in the excision diagnostic group ($p=0.04$). These findings were independent of age, tumour size and grade. However, Peters-Engl et al [6], who examined 1890 patients with primary breast cancer, were unable to confirm this finding and suggested that pre-operative breast biopsy did not cause artificial tumour spread to the SLN.

### *Can tumour cells become displaced into the blood stream at the time of biopsy?*

To evaluate the impact of FNA on breast cell shedding into peripheral blood, Hu and Chow [7] employed a diagnostic test applying reverse transcriptase polymerase chain reaction assay targeted against cytokeratin 19, cytokeratin 20 and the beta-subunit of human chorionic gonadotrophin mRNAs. Blood samples from 24 cases with benign breast diseases and 20 cases with malignancy were withdrawn before and within 10 min of the FNA. In 3 of the 19 patients with proven breast cancer (type not specified), the blood stream negative cases, pre-biopsy, became positive following the FNA procedure. They concluded that undertaking FNA in breast tumours may cause haematogenous dissemination of breast cells.

### *Breast biopsy and clinical evidence of recurrent disease*

9 papers addressing this subject were reviewed; the overall number of patients was 1575.

Despite the pathological demonstration of the potential for breast tumour dissemination and seeding down the needle track it is infrequently reported clinically. However, Chao et al [8] reported two cases of subcutaneous

breast cancer at the site of stereotactic biopsy following mastectomy for the primary breast tumour. The site of skin puncture for the biopsy had not been excised at the time of their surgical treatment. Biopsies had been performed using a 14-G needle and multiple passes were made in both cases. Both patients had had a modified radical mastectomy, but neither had radiotherapy. As a consequence the authors recommended excision of the tumour and biopsy site at the time of the surgery. Stolier et al [9] reported a study of 89 patients in whom biopsy had been performed; 58 of these were ultrasound guided, 31 were via stereotaxis. 8 had multiple biopsy punctures; of these 1 developed skin recurrence at the biopsy site 34 months later. They recommended particular care if the biopsy site was outside the index quadrant and in an area in which no radiation therapy was anticipated. Harter et al [10] reported a single case of tumour seeding following a 14-G needle biopsy of a mucinous carcinoma of the breast.

Thurfjell et al [11] examined the incidence of locally recurrent breast tumours and correlated this with pre-surgical biopsy procedures. They reviewed recurrences from a consecutive series of 303 clinically non-palpable breast cancers treated by breast-conserving surgery after pre-operative localisation. Pre-operative percutaneous biopsies had been done in 71% (214/303) of the cases. The suspicion of seeding or implantation was based on the location of the recurrent lesion by reviewing the needle path in two pre-surgical mammographic projections. The median mammographic follow-up was 5.4 years. Local recurrence occurred in 11% (33/303) of the cases. This is higher than one may expect — local recurrence rates of <3% are now targeted — and may be explained by the absence of post-surgical radiotherapy in a cohort of these patients who were participating in other research trials. For example, the recurrence rate for invasive carcinomas was 3% when supplementary radiotherapy was applied, but was 34% where it was omitted. In three cases it was suspected that recurrence was a consequence of the needle biopsy. In these individuals no radiotherapy had been prescribed. Radiotherapy demonstrated a protective effect from relapse among invasive cancers, but not for DCIS. Interestingly, they also suggested that when pre-operative wire localisation is required the wire tip is positioned posterior to the tumour rather than within it to avoid hitting the primary tumour and predisposing further potential spread of the neoplasm beyond the primary site. However, their methodology referred to mammographic guidewire procedures only and did not consider ultrasound-guided procedures.

Knight et al [12] compared core needle biopsy with needle localisation surgical excision breast biopsy. All patients underwent wide local excision and were followed up for an average of 29.7 months. 297 patients underwent diagnosis by wide core needle biopsy (WCNB) and 101 by needle localisation breast biopsy (NLBB). 15 (3.77%) patients had a local recurrence: 11 (3.70%) in the WCNB group and 4 (3.96%) in the NLBB group. These recurrence rates were not statistically different. They concluded that WCNB was to remain the procedure of choice for diagnosing mammographically detected suspicious breast lesions and there was no evidence of an increased rate of recurrence owing to needle track seeding.

### *Tumour type and likelihood of seeding*

2 papers addressing this subject were reviewed and the overall number of patients was 214.

### *Are different tumour types more or less likely to seed down a needle track?*

Uematsu and Kasami [13] assessed cytology following a wash of the core biopsy needle. The study included biopsies of 207 breast cancers. The core needle without exposed sample notch was washed in saline solution immediately after removal. The incidence of positive cases of cytology derived from core wash material was 65% (134/207), but the 25% frequency of positive cases of invasive lobular carcinoma was significantly lower than the frequencies of DCIS (74%) and invasive ductal carcinoma (69%) ($p=0.001$ and $p<0.01$). Furthermore, the same study suggested that multiple passes were associated with a slightly higher likelihood of seeding (75%) than single passes (66%), but this was not statistically significant ($p=0.3$).

Core biopsies have been reported to complicate post-excision pathological analysis of the resected specimen. Phelan et al [14] reported seven cases where breast tissue trauma, as a consequence of needle core biopsy, resulted in displacement of breast epithelium and led to diagnostic difficulty. Of the seven cases, four were DCIS, two were invasive ductal carcinoma and one proved to be benign. Cell seeding, as a result of the needle biopsy, complicated measurement of tumour size, assessment of surgical margins and the interpretation of possible invasive carcinoma and lymphovascular invasion.

There is insufficient evidence to demonstrate that any one tumour type is more likely to seed than another.

## Discussion

5 papers relating to the content of this Discussion were reviewed and the overall number of patients was 5619.

Breast cancer is common. Patients frequently present with a palpable lump, but a significant proportion is now detected via breast screening programmes. In the UK National Health Service Breast Screening Programme (NHSBSP) women are currently invited from their 50th year of age. The quality assurance programme of the NHSBSP indicates that pre-operative diagnostic rates should be achieved in 80% of cases, with a target of 90% [15]. Diagnoses may be achieved either via FNA or WCNB. The ability of WCNB to identify not only the tumour but frequently its type and stage has encouraged its widespread use. There is also evidence that other prognostic factors, *e.g.* hormone receptor status, are more reliably determined from analysis of cores obtained at needle biopsy than they are by analysis of the formalin fixed gross specimen. This is probably the result of better fixation of the core specimen [16]. We were unable to identify any papers that suggested that spread of a tumour was more likely with WCNB than with FNA, or *vice versa*.

Interestingly, seeding of tumour appears less likely to occur with a biopsy undertaken with a vacuum-assisted device. A variety of products are available, including the Mammatone (Ethicon Endo-Surgery, Inc., Cincinnati,

OH) [17]. These devices allow multiple specimens to be collected without having to remove and reinsert the needle and the vacuum enables multiple tissue samples to be obtained on one needle pass, which then move through a hollow chamber of the probe into a collection chamber. Other vacuum devices, *e.g.* the Vacora (Bard Medical Systems, Tempe, AZ) [18], may use more than one needle insertion, but adopt a coaxial technique with insertion of the biopsy needle through a cannula.

### *Why is there a reduced local recurrence rate?*

Firstly, it is likely that the negative pressure exerted by the vacuum restricts tumour cell migration into adjacent tissues beyond the primary neoplasm. Secondly, when a coaxial technique is employed an externally mounted cannula remains *in situ* on the biopsy needle throughout the biopsy procedure and although many passes may be made the cannula will minimise contact between the biopsy needle and adjacent breast tissue.

To restrict the clinical significance of tumour seeding it has been recommended that consideration should be given to surgical resection of the biopsy track at the time of definitive surgery, especially if this is to be outside the field of any subsequently administered radiotherapy [8]. However, the site of skin puncture and subsequent needle passage may be quite remote from the primary lesion itself and to excise the tumour and the needle track may be problematic. This is particularly the case when a stereotactic approach for diagnosis has been adopted and when a significant amount of breast tissue has been transgressed by the biopsy needle before the primary lesion is sampled; for example, if the patient's breast is positioned in a standard mammogram machine and positioned upright and the needle is directed from the superior aspect of the breast into a neoplasm in the lower half. Violation of the breast tissue may be minimised at biopsy by adoption of a specialised prone biopsy table; however, such equipment is frequently not available. Furthermore, modern oncoplastic surgical techniques sometimes adopt a peri-areola skin incision for removal of tumours by wide local excision to achieve a superior cosmetic effect [19]. This more sophisticated surgical approach may also complicate this recommendation.

In a comprehensive review, Liebens et al [20] noted the many biases in the published literature. For example, there are no randomised control trials comparing the frequency of recurrent disease in patients who had a biopsy with those where it was omitted. Moreover, in most papers the numbers of patients reviewed were small. The circumstances whereby patient selection was undertaken varied. Finally, because clinical recurrence is infrequent the reviewed papers are invariably underpowered to identify any conclusive factors in tumour seeding.

Overall, based on the findings of this review, the likelihood of tumour recurrence as a consequence of a biopsy procedure appears very low. Nevertheless, vigilance from both surgeons and radiologists for this potential complication is still advised. However, this knowledge should not interfere with surgical techniques that may benefit the patient by limiting procedural morbidity and improved cosmesis. Anxious patients, who may inquire about this potential complication, can be reassured that, although it does occur at a microscopic level, the clinical effect appears negligible and biopsy as a cause of disease recurrence appears very rare.

## Acknowledgments

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## Appendix

### *Section 1: Histological evidence of spread*

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