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Micrometastases in sentinel node in breast cancer

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Purpose: Axillary lymph node status is one of the most important predictors of outcome in breast cancer patients. Current conventional histology may underestimate stage as a considerable number of node-negative patients develop axillary recurrence. Immunohistochemistry and serial sectioning have been proved to be more sensitive techniques in the detection of micrometastases but these have proved impractical due to the large number of nodes requiring analysis after axillary node sampling or clearance. The advent of sentinel node biopsy has focused examination on one node and facilitates the diagnosis of micrometastases by allowing such additional methods to be more applicable in the routine setting.

Methods: 150 patients with breast carcinoma entered a trial comparing sentinel node to four node biopsy. Using ^{99m}Tc-labelled colloid, it was possible to identify the sentinel node in 91% patients. In 82% of these patients the nodes were negative at routine histological examination. The nodes were cut in multiple sections (3 sections every 100 μm) and stained using cytokeratin 19, broad spectrum cytokeratin, anti-MUC 1 antibodies to detect micrometastases.

Results: There was no difference in the sensitivity between the three antibodies in detecting micrometastases, which were found in 15.8% of the nodes deemed negative at routine histology. In 2 cases there were unicellular foci only and in all the cases micrometastases were localised at the marginal sinus. In one case, one axillary and one intramammary node were hot, and contained micrometastases.

Conclusion: Immunohistochemistry is a sensitive method for detection of micrometastases. The significance of such lesions remains controversial but the advent of sentinel node technique will make their detection easier and should improve understanding of their clinical relevance.

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Mammographic size of ductal carcinoma in situ (DCIS) does not predict the presence of an invasive focus

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Purpose: A proportion of women with DCIS on mammography and/or core biopsy will have an invasive focus on formal histology. This study aims to identify the percentage of such patients who harbour an invasive focus and to ascertain if the features of mammographic and/or core biopsy can predict the presence of an invasive focus.

Methods: 140 patients had a core biopsy diagnosis of DCIS without invasion. All patients had their core biopsy graded and mammography was performed on 128 patients. Mammographic findings were classified by a radiologist blinded to the surgical findings into normal, mass, microcalcifications and the size of calcifications only were measured. Core biopsies were graded into high, intermediate or low v grade DCIS groups. The core biopsy and radiological findings were compared to see if they could predict the presence of invasive disease at surgical excision.

Results: Of the 140 patients, 61 (44%) had an invasive focus. Eight (47%) of the 17 patients with normal mammography had an invasive focus. Four out of 12 patients (33%) with a mammographic mass had evidence of invasion. Of the patients with mammographic calcification, 49 out of 100 had an invasive focus. There was no correlation between calcification, cluster size and risk of an invasive focuss.

Size of microcalcification	N	Invasive	%
<10 mm	21	10	48%
11–25 mm	25	11	40%
26–45 mm	14	6	43%
>45 mm	40	22	55%

In the nine patients with low grade DCIS on core biopsy, two (22%) had an invasive focus. Comparative figures in patients with intermediate and high grade DCIS were five of 16 (31%) and 55 of 109 (50%) respectively ($p > 0.05$).

Conclusion: In contrast to previous studies, this study shows that mammographic size of DCIS does not predict the presence of an invasive focus. Although there is a non-significant trend for the grade of DCIS on core biopsy to correlate with the risk of invasion, we have not identified any subgroup of patients who do not have an appreciable risk of an invasive focus.

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Local recurrence (LR) after breast-conserving therapy (BCT) in node-negative premenopausal patients. Risk factors and influence of Peri-operative Chemotherapy (PeCT); an EORTC Breast Cancer Cooperative Group Study

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Purpose: After BCT patients may develop a LR in the treated breast. Younger age has been found as an independent risk factor for LR. Within a group of relatively young (all premenopausal) node-negative patients we have studied additional risk factors for LR and the effect of PeCT on LR.

Patients and Methods: The EORTC conducted a randomised trial (EORTC 10854) to compare surgery with PeCT (fluorouracil, doxorubicin and cyclophosphamide) versus surgery alone. From patients treated in this trial we selected premenopausal node-negative patients treated with BCT to examine whether histological factors and the expression of various proteins (ER, PR, p53, Ki-67, bcl-2, CD31, c-erbB-2/neu) are risk factors for subsequent LR. Also, the effect of one course of PeCT on the LR risk was studied.

Results: In multivariate analysis age < 43 years (RR: 2.75 (1.46–5.18); p = 0.002) multicentric growth (RR 3.34 (1.27–8.77); p = 0.014) and elevated levels of p53 (RR 2.14 (1.13–4.05); p = 0.02) were associated with higher LR risk. Also, PeCT was found to reduce the risk on LR in all patients (RR 0.47 (0.25–0.86); p = 0.02). Patients < 43 years given one additional course of PeCT achieve similar LR rates as patients >= 43 years treated with BCT alone.

Conclusion: In premenopausal node-negative patients age < 43 years is the most important risk factor for LR after BCT; this risk is greatly reduced by one course of PeCT. The main reason for giving systemic adjuvant treatment is to improve overall survival. The important reduction of LR after BCT is an additional argument for considering systemic treatment in young node-negative breast cancer patients.

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Individualised survival prediction in breast cancer (BC) based on nation-wide follow-up data: The finprog study

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Purpose: Prognostic factors may occur in hundreds of combinations in BC, making decisions on the need of adjuvant therapy problematic especially when both favourable and unfavourable factors occur simultaneously. The study was designed to enable individualised prediction of disease-free (DFS) and overall survival.

Methods: Women diagnosed with BC in defined geographical regions in Finland in 1991–2 were identified from the Finnish Cancer Registry. Information on 50 items from over 2,000 patients were extracted from the hospital records including several prognostic variables (e.g. the number of metastatic and non-metastatic nodes, turnout size, histological type and grade, ER and PgR status, S-phase fraction, p53 and erbB-2), type of treatment and follow-up data. The data were obtained in close to 100% of the patients, and an interactive Internet website was created for survival analysis. Any combination of parameters can be chosen, and a Kaplan-Meier survival curve for the patient group selected is computed online.

Results: Most of the prognostic variables were strongly associated with outcome even when determined nation-wide. Groups with variable outcome could be identified within a single stage. For example, women with screen-detected pT1N0M0 grade 1 cancer (n = 78) had 100% 5-yr DFS, whereas those with pT1N0M0 cancer found outside screening had 96% (n = 96), 82% (n = 132) and 76% (n = 56) 5-yr DFS for histological grade 1, 2 and 3 cancers, respectively.

Conclusion: A survival curve could be created with any factor combination within a few seconds using the interactive web site. We plan to apply artificial neural networks and expand the data set with novel biological prognostic factors.