tected groups were compared regarding intraoperative sentinel node detection rates, accuracy, predictive value of a negative sentinel node, and false negative rates.

Results: Intraoperative sentinel node identification was significantly better for symptomatic breast tumours where 112/123 (91%) cases were successfully biopsied compared with 89/113 (79%) screen detected cases ($p < 0.05$). The overall accuracy and predictive value of the negative sentinel node was greater for screen detected lesions although this failed to reach statistical significance (98.9% versus 95.8%, 98.6% versus 91.5% respectively). There was one false negative case in the screen detected group compared with five in the symptomatic group, although due to the low prevalence of axillary lymph node involvement in screen detected population, there was no difference in false negative rates (5.9% screening, 7.8% symptomatic).

Conclusion: Although the accuracy of sentinel node biopsy is maintained for small screen detected breast cancers, failure to identify the mode in approximately 20% of cases may limit the clinical usefulness of the technique in this important patient subgroup.

O-58. PATIENTS WHO ARE NODE NEGATIVE ON AXILLARY NODE SAMPLING: DO THEY RECUR BECAUSE OF OCCULT LYMPH NODE METASTASES MISSED BY THE PATHOLOGIST?

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We examined axillary lymph nodes from 26 node negative breast cancer patients managed by axillary node sampling and no further axillary treatment who subsequently developed axillary recurrence (mean follow up of 7 years) and from 26 matched controls who were node negative on axillary node sample but have not developed axillary recurrence. Lymph nodes were sectioned at 2 additional levels, 100 microns apart. 3 sections at each level were stained with H&E and antibodies to PanCK and MUC1 protein. The original H&E sections from each node were also reviewed.

	No. of cases	No. of nodes	Mets overlooked	No. of Micromets	Total No. of Mets
Axillary Recur Gp	26	133	2 (8%)	2 (8%)	4 (16%)
Control Gp	26	133	0	3 (12%)	3 (12%)

Two patients had metastases overlooked at the time of sampling. 2 patients from the recurrence group and 3 from the control group had axillary nodes which contained nodal micrometastases. Immunohistochemistry was important in identifying all these. Although a small series, this study suggests that axillary recurrence after sampling is not due to missed axillary node metastases but that either the wrong nodes are sampled or axillary recurrence develops subsequently.

O-59. SENTINEL NODE (SN) BIOPSY CAN SAFELY REPLACE AXILLARY NODE SAMPLING FOR STAGING EARLY BREAST CANCER

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Our standard method of assessing axillary node status is sampling of a minimum of four axillary lymph nodes identified by the surgeon. In this study, we assessed the role of SN biopsy in predicting axillary node status and the intraoperative assessment of SN with frozen section (FS) and imprint cytology.

All patients with primary breast cancer up to 2.5 cm in diameter underwent SN identification between April 1998 and March 2001. SN(s) were identified by using both radioisotope and/or blue dye techniques. The SN was assessed intraoperatively using FS only or FS and imprint cytology depending on the availability of cytological expertise. All patients had a sample of a minimum of 4 axillary lymph nodes removed or full axillary clearance if FS of SN was positive.

The SN was identified intraoperatively in 142 of 150 cases (94.66%). An average of 1.3 SN was identified per patient. According to final histology the SN was positive in 51 of 142 patients. Forty-four of these positive SN were identified intraoperatively and 7 were reported falsely negative on FS. Axillary node status was in concordance with the final SN status in all patients. The sensitivity of SN was 100% though the sensitivity of intraoperative assessment was 86.3% (44/51) with a specificity of 100%.

In our unit, axillary sampling does not provide any additional benefit in assessing the axillary nodal status in those patients that have a SN successfully identified. Intraoperative assessment using FS with or without imprint cytology can spare re-operation in up to 86% of node positive patients if axillary clearance is considered to be the best treatment for involved axillae

O-60. SERVICE IMPLICATIONS OF INTRODUCING SENTINEL NODE BIOPSY: EXTRAPOLATIONS FROM THE FIRST 100 PATIENTS RANDOMISED TO THE ALMANAC TRIAL

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Introduction: Randomisation to the ALMANAC Trial sentinel node mapping (SNM) v axillary clearance (AC) started in Guildford in December 1999. In one calendar year surgery was performed on 284 new breast cancers, 33 of which had pure DCIS and the remainder where potentially suitable for the trial.

Methods: 5 groups of patients were identified. 66 had absolute exclusion criteria. 61% of these had positive nodes (N+). 56 had relative exclusion criteria and 14% were N+. 22 refused randomisation and 23% were N+. In 6 patients SNM alone was specifically recommended and all were N−. 100 women accepted randomisation and 26% of these were N+.

Results: 10/49 patients (20%) allocated to AC were N+ whereas 16/51 patients (32%) randomised to SNM alone were N+. These 16 were then converted to complete axillary dissection at a second operation and 12 (75%) had no further positive nodes. Patients randomised to AC had a mean hospital stay of 6.8 days (range 4–10). Those with SNM stayed for 3.6 days (2–7) and those having two operations because of SNM+ a stay of 9.5 days (6–13).

Conclusions: 82% of patients suitable for the Trial were happy to be randomised. This percentage may dwindle once public perception of the value SNM becomes more wide spread. 184 of 250 patients with invasive disease were potentially eligible for SNM outside the context of a Trial (75%). An estimated 317 bed days will be saved by the introduction of the technique into this Unit in one calendar year. Applied across the country this would have a significant implication in the cost of delivering breast cancer surgery.

O-61. CHANGES IN PROLIFERATION IN BREAST CANCER WITH TAMOXIFEN AND CORRELATION WITH TUMOUR RESPONSE

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Before using MIB-1 which has been used as a cell cycle marker as a parameter of response to neoadjuvant therapy, it was thought important to assess the effect of variables such as the nature of the tumour specimen being examined and the variability of results which might be found in specimens taken at the same or different points of time without any intervening treatment.

A study was then carried out to assess the effect of neoadjuvant tamoxifen on proliferation of breast cancer and correlated changes on sequential biopsies and tumour response. Immunohistochemistry for MIB-1 was carried out using avidin-biotin technique and assessed quantitatively using a computerised image analyzer. The variability of MIB-1 measurements in breast cancer was assessed in histological sections from core excision biopsies taken simultaneously in 13 cases and sequentially (with an intervening period of 2-3 weeks) in 17 cases. 50 postmenopausal women with large ER breast cancers were treated with 20 mg/day of tamoxifen for 3 months. Tumours were monitored clinically and radiologically. Response was defined as 25% reduction in tumour volume. Quantitative immunohistochemistry using MIB-1 antibody was performed on biopsies obtained at diagnosis, 10–14 days and 3 months on treatment using image analysis.

Results show no significant differences in values between cores and sections whether taken simultaneously or sequentially. Individual pairs of cores and sections occasionally demonstrated substantial differences. Mean ratio of MIB-1 scores between cores and sections was 0.97 (95% confidence intervals [CI] = 0.68–1.38). However 95% confidence intervals for ratios within individuals were 0.14-6.68. 38 of 50 patients (76%) responded to tamoxifen. MIB-1 staining was significantly reduced at 10–14 days ($p = 0.0015$) and 3 months ($p = 0.0003$) in responding tumours but not in non-responders. At 10–14 days 28/38 (74%) of responding tumours compared with 3/12 (25%) on non-responding tumours showed a decrease in staining, a significant difference between groups, $p = 0.005$.

Changes in proliferation can clearly be detected in biopsy samples at both time points following tamoxifen treatment. These changes differ significantly in responding and non-responding tumours and predate clinical assessment of response; a minority of tumours however show paradoxical changes. Tumour heterogeneity limits the utility of these changes in proliferation in precisely predicting response to treatment in individual cases.

O-62. MORPHOLOGICAL ASSESSMENT OF HEAT SHOCK PROTEIN 27 AND OESTROGEN RECEPTOR ALPHA, POTENTIAL MARKERS OF BREAST CANCER RISK

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The search is continuing for new markers to predict breast cancer risk. Early dysregulation of oestrogen receptor (ERα) and oestrogen regulated heat shock protein 27 (hsp27) may represent an early event in mammary carcinogenesis. Having assembled a cohort of benign lesions with a known outcome, we investigated their morphological and biological markers of risk and survival probability. A case-control study was conducted on benign breast biopsies from 502 patients received at the Royal Liverpool University Hospitals from 1979 to 1999. Morphological classification and the uni- and multivariate analyses were done and the relative risk was assessed for all benign categories including blunt duct adenosis and hyperplasia of usual type (HUT). Foci of HUT ($n = 16$) and surrounding normal lobules ($n = 91$) from cases ($n = 21$) and controls ($n = 28$) were then stained using monoclonal antibodies for hsp27 and ERα and % of positively stained cells was quantified using morphometric image analysis. The expression of hsp27 and ERα was significantly higher in HUT foci from cases compared with controls ($P < 0.001$ and 0.015 respectively). The mean ERα+ cells in HUT was 57% in cases and 30.27% in controls. Among cases, a significant overexpression of hsp27 was found in HUT foci compared with normal lobes ($P < 0.001$). Our data highlight a novel role mediated by hsp27 during mammary carcinogenesis and suggest that overexpression of both hsp27 and ERα may define a subset of hyperplastic phenotypically benign lesions likely to progress to breast cancer. This subset might benefit from selective anti-oestrogen approach.

O-63. COEXPRESSION OF EGFR, HER2, HER3 AND HER4 IN PRIMARY HUMAN BREAST CARCINOMA

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Overexpression of the Human Epidermal Growth Factor Receptor family members HER1 (EGFr) and HER2 (c-erbB-2) are asso-