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-