HRT use	Current (n = 172)	Never (n = 417)	Total (n = 589)
Recurrence present	N = 22 (3%)	N = 41 (6%)	P = 0.3816
Survival (10 years)	91%	88%	P = 0.8495

Conclusion: Overall screen detected breast cancers have good prognosis. Prior HRT use does not adversely affect survival after diagnosis of breast cancer.

O-100. IS HORMONE REPLACEMENT (HRT) – RELATED BREAST CANCER MORE FAVOURABLE? A CASE-CONTROL STUDY

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Prolonged use of HRT increases the risk of developing breast cancer but it has been suggested that HRT-related breast cancer may carry a better prognosis since there is no increase in breast cancer deaths. The prognostic risk factors and outcome in patients who had ever taken HRT have been compared with those who had not, in a case-control study.

All women with primary breast cancer 1980–1999 (n = 1887) prospectively completed a detailed questionnaire on the duration and timing of hormonal therapy.

Patients who had ever used HRT (n = 388) were compared with the same number of never-users who were matched for age and age at diagnosis. The tumour size & grade, the number of positive nodes, the presence of vascular invasion and the oestrogen receptor status were compared between cases and controls. The Nottingham Prognostic Index (NPI) was estimated for both groups and absolute survival was compared by life table analysis (Kaplan Meier).

The mean duration of HRT in the ever-users was 3.7 years. The mean length of follow-up was 68 months. The mean age at diagnosis was 56 in the HRT users and 55 in controls. There was no difference between the 5 prognostic factors & there were similar numbers of cases and controls in each of the NPI prognostic groups: e.g. score < 3.4:43% v. 43%. There was a non-significant trend to a survival advantage in the control patients who had never received HRT. Log rank test (p = 0.57)

There was no evidence that HRT-related breast cancer has a more favourable outcome.

O-101. THE EFFECT OF FAMILY HISTORY ON PROGNOSIS IN BREAST CANCER

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Introduction: Patients with strong family history of breast cancer are more likely to develop a second cancer in the other breast and it is possible that they may have a worse prognosis. The aim of this study was to investigate the effect of family history (FH) on the pathological features of the breast cancer, bilaterality, recurrence-free interval and overall survival.

Method: All (122) patients under the age of 60 years with operable breast cancer and had an FH of one or more first-degree relatives were compared with (244) patients without an FH, matched for age and date of presentation. Tumour size, histological grading, vascular invasion, lymph node status and Nottingham Prognostic Index (NPI) were compared between the two groups. The incidence of synchronous and metachronous tumours in the other breast, disease-free interval and overall survival in each group were compared by life-table analysis.

Results: The pathological features in the two groups were very similar and both groups received similar surgical and adjuvant treatment. The mean follow up for patients with and without FH was 8.9 years and 8.7 years respectively. Patients with an FH had a non-significant trend to develop a metachronous cancer (9.8 v. 5.7%, p = 0.19). There was also a trend towards an overall survival advantage for patients with an FH but this was not statistically significant (p = 0.11).

Conclusion: Patients with a family history of breast cancer may have an increased incidence of a metachronous tumour in the contralateral breast but there is no evidence of worse prognosis.

O-102. C-erbB-2 IN LYMPH NODE NEGATIVE BREAST CANCER: PROGNOSTIC SIGNIFICANCE IN UNIVARIATE AND MULTIVARIATE ANALYSES

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Although the prognostic value of C-erbB-2 in invasive breast cancer patients who are node-positive is established, the data in node-negative patients is inconclusive. We have evaluated the prognostic significance of C-erbB-2 overexpression in a cohort of node-negative patients, none of whom received systemic adjuvant therapy.

Paraffin-embedded node negative primary breast cancers from 678 patients, treated at Nottingham City Hospital were studied immunohistochemically. C-erbB-2 staining was scored as 0, 1, 2, 3; scores of 2 and 3 were classified as positive. Univariate analysis was performed with chi-squared tests to compare immunoreactivity with known pathological and patient variables. Cox regression analysis was performed to evaluate C-erbB-2 over-expression as an independent prognostic factor.

40% (n = 254) of specimens showed overexpression of C-erbB-2. These patients had a worse disease-free interval (p = 0.008) and overall survival (p = 0.044). A significant relationship was also observed with high grade (p < 0.001), ER negativity (p < 0.001), young age (p = 0.028) and Nottingham Prognostic Index (NPI) (p < 0.001). No association was seen with menopausal status, vascular invasion or tumour size. In multivariate analysis for survival, when included with tumour size

and histological grade, C-erbB-2 showed independent prognostic significance ($p < 0.001$).

These data suggest that C-erbB-2 is an independent adverse prognostic factor irrespective of nodal status. Examination of C-erbB-2 expression may thus provide an additional means to identify node negative patients with a poorer than expected outcome.

O-103. ANGIOGENESIS IN DUCTAL CARCINOMA IN SITU (DCIS) OF THE BREAST

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To date no pathological or molecular features have been found to predict for the development of invasive disease in ductal carcinoma in situ (DCIS). The characteristics of vascularisation may be important in determining transformation from in situ to invasive disease.

Periductal and stromal vascular density was determined in DCIS using morphometry and a panel of anti-endothelial antibodies (von Willebrand factor [vWF], CD31, CD141 and CD34). Normal lobules at least 2 mm away were used as controls. Thymidine phosphorylase (TP) expression by DCIS was semi-quantitatively assessed using the H-score method.

Pure DCIS in comparison to normal lobules exhibited a greater density of CD34+ vessels ($P = 0.004$) but a decrease in those stained with vWF ($P = 0.001$). DCIS associated with invasive carcinoma showed a profile similar to that of pure DCIS but with significantly greater numbers of CD34+ ($P = 0.003$) vessels and fewer staining for vWF ($P = 0.030$). When cases of DCIS that subsequently recurred were compared with those that did not, the former had a higher CD34 microvessel density (MVD) ($P < 0.001$). Periductal but not stromal CD34 MVD correlated with recurrence, particularly with an invasive recurrence. For TP expression by DCIS, although relationships were seen between the H-score and MVD, a relationship with recurrence was not identified.

Blood vessels surrounding DCIS appear to have a different phenotype from those around normal breast lobules. Periductal MVD appears to be more important than stromal MVD in predicting for recurrence in DCIS. Recurrent disease does not appear to be related to TP expression.

O-104. HIGHER EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) CORRELATES WITH MUTANT p53, OESTROGEN RECEPTOR (ER) NEGATIVITY, AND SHORTER SURVIVAL TIMES IN PRIMARY BREAST CANCER

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Background: The regulation of the angiogenic factor VEGF is only partly understood. We have earlier shown a high associated between high VEGF expression and mutant p53 by cDNA-based sequencing, while the correlation to accumulated p53 protein determined by immunohistochemistry (IHC) was lower.

Purpose: To determine the possible associations between VEGF and p53 status, routine prognostic factors as ER, grade by Elston-Ellis, and survival.

Patients and Methods: Tumour specimens were obtained from 114 consecutive patients with primary breast cancer between 1988 and 1991. VEGF content was measured by an enzyme linked immunosorbent assay (ELISA). p53 mutations was determined by single stranded chain polymorphism (SSCP), p53 protein by IHC.

Results: Higher VEGF expression was significantly associated with ER-negativity ($p = 0.020$), but independent of nodal status and stage. A trend not reaching statistically significance was found between VEGF and nuclear grade ($p = 0.064$). Higher VEGF content was statistically significantly correlated to mutant p53 determined by SSCP ($p = 0.037$), while no correlation was found with p53 status determined by IHC (0.300). Statistically significant shorter survival times were found for patients with higher VEGF content ($p = 0.035$).

Conclusions: VEGF expression is associated to ER negativity, poor nuclear grade and mutant p53, but not to accumulated p53 protein determined by IHC. The findings indicates that mutant p53 may up-regulate angiogenesis through VEGF. Higher VEGF content was significantly associated to shorter survival times.

O-105. ADJUVANT RADIOTHERAPY FOR BREAST CANCER - DO WE NEED NEW TECHNIQUES?

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Radiotherapy is of proven value in several situations following initial surgery for breast cancer. To assess the risk of serious side effects, two separate audits were conducted at our centre.

First we looked at 348 mastectomy patients who received adjuvant radiotherapy to the chest wall in 1992–93. An electron beam of 8–10 MeV was used to encompass the target volume in a single anterior field, giving 40 Gy in 15 fractions over 3 weeks. CT measurements of the chest wall revealed a mean thickness of 18 mm (range 5–58 mm). Wax bolus was used to give extra or uniform thickness. With a median follow-up of 6.3 years, local disease control was achieved in 93%. There were no clinical parasternal recurrences. Radiation pneumonitis occurred in one patient. CT assessment of cardiac doses suggests that the long-term risk of adverse cardiac effects is very low.

In our second audit, portal images of 110 consecutive patients with left-sided breast cancer receiving radiotherapy following breast conserving surgery in 1999-2000 were reviewed to assess the amount of significant cardiac irradiation with an isocentric megavoltage tangent pair of fields. All patients had been planned on a CT simulator. Central lung depth varied from 1 to 24 mm (mean 14 mm). A portion of the cardiac apex was included in 8