

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 statistical 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 indicate 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