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

N.B. Teo, B.S. Shoker, M.C. Jarvis, C. Holcome, L. Martin, J.P. Sloane. *Royal Liverpool University Hospital, UK*

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

B. Linderholm, N.-H. Neilsen, J. Bergh, G. Landberg. *Karolinska Hospital, Stockholm, Umeå University Hospital & University Hospital, Malmö, Sweden*

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?

W. Appel, J. Davies, B. Magee, A.L. Stewart, R. Swindell. *Christie Hospital, Manchester, UK*

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

patients (7%). There seemed to be no correlation between central lung depth and irradiation of the cardiac apex in our series.

Long-term follow-up of older series suggests no risk of premature cardiovascular incidents if less than 4% of the cardiac volume is irradiated. 93% of left-sided breast cancer patients can be treated without significant cardiac irradiation, however a minority of patients may need more sophisticated treatment planning to completely eliminate unnecessary cardiac toxicity.

O-106. INTRAOPERATIVE RADIOTHERAPY AFTER BREAST CONSERVING THERAPY – AN ALTERNATIVE TO CONVENTIONAL POSTOPERATIVE BOOST?

R. Reitsamer, F. Peintinger, F. Sedlmayer, M. Kopp, C. Menzel, W. Cimpoca, G. Glück. *Landesklinik für Spezielle Gynäkologie Salzburg; Abteilung für Gynäkologie Landeskrankenhaus Leoben; Landesklinik für Radiotherapie Salzburg, Austria*

Introduction: Local recurrency (LR) rate after breast conserving therapy (BCT) varies between 5% and 8%. One of the reasons for LR could be a "geographic miss" during boost irradiation of the tumor bed. Therefore high quality boost techniques are demanded.

Methods: From 10–98 until 12–00 160 patients with stage I and stage II breast cancer were operated in a dedicated IORT facility. After tumorectomy the tissue surrounding the excision cavity was temporarily approximated by sutures to bring the tissue in the radiation planning target volume. A single fractional dose of 9 Gy was applied to the 90% reference isodose with energies ranging from 4–15 MeV, using round tubes 5 to 6 cm in diameter. After wound healing patients received additional 51 to 56 Gy EBRT to the whole breast.

Results: There were no early complications associated with the use of IORT. In five patients a secondary mastectomy had to be performed because of tumormulticentricity in the final pathological report. Two patients developed rib necrosis. In five patients wound healing problems occurred. To date there has been no local recurrence, cosmesis of the breast has been excellent.

Conclusion: Interim results suggest that IORT after breast conserving therapy could be a reliable alternative to conventional postoperative fractionated boost by accurate dose delivery and avoiding of geographic miss, by enabling of smaller treatment volumes and complete skin sparing and by reducing the postoperative radiation time for 7 to 10 days.

O-107. TARGETED INTRA-OPERATIVE RADIOTHERAPY (TARGIT) FOR BREAST CANCER – A RANDOMISED TRIAL

J.S. Vaidya, M. Baum, J.S. Tobias, J. Houghton, M. Keshtgar, R. Sainsbury, I. Taylor, D. D'Souza, S. Morgan, M. Metaxas, K. Harte, A. Sliski, E. Thomson. *University College London, UK & Photoelectron Corporation, USA*

The need for 6-wks of post-operative radiotherapy after breast conserving therapy is both inconvenient and costly. It may cause many women from geographically remote areas to choose mastectomy. A rationale for avoiding whole breast radiotherapy by delivering intra-operative radiotherapy is emerging.

Whole-organ analysis of mastectomy specimens[1] revealed that 80% of occult cancer foci are situated remote from the index quadrant. In contrast, over 90% of local recurrences after breast conserving therapy occur near the original tumour – even when radiotherapy is not given and irrespective of margin status. Therefore, these occult cancer foci may be clinically irrelevant and targeted radiotherapy to the peri-tumoural area alone might provide local control.

'Intrabeam' (*PeC*) is a portable electron-beam driven device that can deliver therapeutic radiation (soft x-rays) in 20–30 minutes within a standard operating theatre environment. The pliable breast tissue – the target – is wrapped around a spherical applicator – the source – providing truly conformal radiotherapy. The prescribed dose is 5–20 Gy at 1 cm and 0.2 cm respectively, from the tumour bed. The biologically effective dose is 7–53 Gy for $\alpha/\beta = 1$ and 20–120 Gy for $\alpha/\beta = 1.5$.

In our pilot study of 25 patients (age 30–80 years, T = 0.42–4.0 cm), we replaced the routine post-operative tumour bed boost with targeted intra-operative radiotherapy. There have been no major complications and no patient has developed local recurrence, although the median follow-up time is short at 21 months.

Having established the safety and feasibility in the pilot study, we started a randomised trial in March 2000. This compares TARGIT with conventional post-operative radiotherapy for infiltrating duct carcinomas with local recurrence and cosmesis as the main outcome measures. If proven effective, TARGIT could eliminate the need for post-operative radiotherapy potentially saving time, money and breasts.

References

[1] Vaidya JS et al. Multicentricity of breast cancer: whole organ analysis and clinical implications. Br J Cancer 1996 Sep; 74 (5): 820–4

O-108. PERCUTANEOUS MINIMALLY INVASIVE STEREOTACTIC PRIMARY RADIOTHERAPY: A NOVEL APPROACH FOR BREAST CANCER IN ELDERLY WOMEN

J.S. Vaidya, M. Hall-Craggs, M. Baum, J.S. Tobias, M. Keshtgar, R. Sainsbury, I. Taylor, D.P. D'Souza, S.V. Naidu, S. Morgan, K.J. Harte, A.P. Sliski, E. Thomson. *University College London, UK & Photoelectron Corporation, USA*

As the population ages, many elderly women are affected by breast cancer. Local treatment is advisable, in addition to tamoxifen, but many of these women may not be fit enough to stand an operation.

We describe a novel approach of dealing with this growing problem with minimal intervention using three converging technologies:

(a) the Fisher Mammotest table for digital real-time tumour localisation