factors predicting loco-regional recurrence, whereas a trend was found for MIB-1. Increased Bcl-2 as well as p53 expression were associated with a decreased risk, whereas the presence of MIB-1 was associated with on increased risk.

Conclusion: Results indicate that molecular markers of apoptosis as well as proliferation provide additional information for the risk of loco-regional recurrence after modified radical mastectomy. If confirmed, these markers may play a role in the selection of appropriate loco-regional adjuvant treatment after primary surgery.

455 POSTER

Can assessment of angiogenesis, proliferation and apoptosis predict the need for adjuvant therapy in breast cancer?

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Purpose: Currently decision making on the need for adjuvant chemotherapy in patients with breast cancer is mainly based on the axillary lymph node status. In the present study markers of proliferative actity (PCNA, mitotic activity index), apoptosis (bcl-2, bax, p53) and angiogenesis (factor VIII) were studied in an attempt to predict the risk for recurrence.

Methods: Representative tissue specimens of 131 patients with invasive ductal carcinoma (median follow-up 83 months, range 2–165) were immunohistochemically stained. The evaluation of oncoprotein or PCNA immunoreactivity and vessel density was made on a magnification of 400 in at least ten fields.

Results: No relationship could be observed between bcl-2, bax, p53 status or factor VIII expression and tumour grade, pTNM staging or menopausal status. Kaplan-Meier overall survival analysis combining the bcl-2 status and vessel density showed they have a strong prognostic value ($p < 0.001$). Cox proportional hazards analysis demonstrated that bcl-2 status ($p < 0.001$), vessel density ($p < 0.001$) and tumour grade ($p < 0.02$) were as accurate to predict overall survival as a model containing lymph node status, tumour size and tumour differentiation.

Conclusions: If these data are independently confirmed one should consider to design prospective randomised trials to assess the concept of omitting the axillary lymphadenectomy in breast cancer patients with no palpatory abnormalities in the axilla.

456 POSTER

CA-15.3: Prognostic factor in breast cancer

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Purpose: CA15.3 is the most usefull tumor marker in breast cancer. The low sensitivity of CA15.3 explain that this tumor marker is never used for detection of breast cancer. However, The CA15.3 level at time diagnosis may be a pronostic factor.

Methods: During 7 years from 1986 to 1993, 673 women were treated in our institution for not metastatic breast carcinoma. CA15.3 analysis was performed by radioimmunologic assay (CIS-Bio®) at primary clinical diagnosis time, after initial treatment and during the follow-up. The level of CA15.3 was considered normal if ≤30 kU/l. Survival time was calculated from the time of primary treatment to the time of death or was censored to the last follow-up date if a patient had not died. The follow-up was updated in December 1997. Survival probabilities were estimated according to the Kaplan-Meier product limit method. The prognostic role of CA15.3 was evaluated by a Cox regression model.

Results: In these population of 673 consecutive not metastatic breast cancer patients, 507 (75%) had normal CA15.3 level (group A) and 166 (25%) had pathological initial level of CA15.3 (group B). The median survival time was 71 months in group A patients and 54 months in group B patients ($p < 0.00001$). The disease free median time survival (without metastasis) was 65 months in group A patients and 40 months in group B patients ($p < 0.00001$). After initial treatment 110 patients in group B normalized the level of CA15.3, the median survival time of these patients was higher than those who did not normalized the CA15.3 level after treatment ($p < 0.001$). However, in metastatic patients there is no statistically difference in median survival time between patients with normal or high levels of CA15.3 at time of metastatic disease diagnosis.

Conclusion: These results suggest that initial level of CA15.3 at initial diagnosis time is an important pronostic factor for reccurency and overall survival in not metastatic breast cancer patient. This inexpensive laboratory test may be an important parameter in initial treatment decision and particularly if the level didn't normalize after initial local and regional treatment.

457 POSTER

Prognostic significance of keratins in breast cancer

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Purpose: The normal breast gland contains luminal and basal cells that stains with different keratins. Keratin 8 stains the luminal cells and keratin 14 and 17 mainly stain the basal cells. The prognostic value of keratin 8, 14, and 17 is evaluated in 836 breast cancer patients.

Methods: Sections are cut at 5 μm. Antigen retrieval is performed using microwave oven boiling at 600W for 25 min in TEG buffer. Sections are stained in a TechMate 1000 immunostainer using the DAKO ChemMate Kit BPR/DAB.

Patients admitted for surgery during the period from 1 January 1980 to 31 December 1990 with primary, operable unilateral breast cancer are included. All patients are followed for at least 5 years.

Results: In 662 cases all cells are stained with keratin 8. Total or clonal staining with cytokeratin 14 and 17 occurs in 90 and 115 cases, respectively. The combined staining pattern reveals negative or clonal keratin 8 staining or total or clonal keratin 14 or keratin 17 staining in 274 cases.

In a multivariate Cox regression analysis including tumour size, lymph node status, and histological malignancy grading, the combined staining pattern of cytokeratin 8, 14, and 17 is significant with a worse outcome related to the basal cell markers.

Conclusion: The combined staining pattern of keratin 8, 14 and 17 is a prognostic factor in breast cancer.

458 POSTER

Neural networks improve the prediction of survival in breast cancer

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Traditional prognostic indices are only able to predict outcome for patients with early or advanced breast cancer but are unreliable for the majority of patients who have a moderate prognosis. Neural networks are able to learn the relationships in non-linear complex data sets and thus may provide a more accurate prediction of behaviour in this group. We evaluated the ability of neural networks to prognosticate for breast cancer patients.

Data from 473 patients from the standard local BASO database was utilised. Neural networks were designed with input parameters corresponding to standard NPI parameters, 0–7 perceptrons and a yes/no output neurone. These networks were then trained to predict survival at 36, 48 and 60 months and validated on data not previously seen by the networks. The NPI was also calculated for all patients. Data were censored where appropriate.

Eighty eight percent of patients were in the moderate/good group according to the traditional NPI analysis (0.2 × size + 1 × grade + 1 × no. nodes (0 = 1, 1–3 = 2, > 3 = 3)). Results for the neural network prediction of overall survival are summarised below:

Time Period Accuracy (95% C.I.) PPV NPV 36 months 0.84 (0.7–0.99) 0.84 1.0 48 months 0.82 (0.64–0.97) 0.81 0.86 60 months 0.86 (0.7–0.98) 0.88 0.87 In order to detect patients in the moderate group with a poor prognosis the artificial neural network significantly altered the weights used for the NPI parameters with size being considered far less significant (−0.01–0.016). In addition, the relative importance of the parameters changed for each time interval predicted.

Neural networks provide a more powerful, robust and flexible tool for the prediction of outcome in breast cancer. The greater accuracy provided by neural network analysis will facilitate the planning of adjuvant treatment and follow up for patients with breast cancer.

NPI = Nottingham Prognostic Index. N/PPV = Negative/Positive Predictive Value, C.I. = Confidence Interval