The complete results and possible explanation of these differences will be presented.

PP-6-4 | **Prognostic Significance of Obvious Peritumoral Emboli in 2692 Primary Operable Breast Carcinoma**

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The prognostic significance of obvious peritumoral emboli (OPE) was evaluated in 2692 consecutive operable infiltrating ductal carcinoma of the breast operated and monitored at our institution between 1975 and 1992 (50.2% N– and 49.8% N+). OPE were assessed in routine practice and defined by the presence of neoplastic emboli within unequivocal vascular lumina including both lymphatic spaces and blood capillaries lined by recognizable endothelial cells adjacent to but outside the margins of the carcinoma. The frequency of OPE was 33.8% (19.6% in N–, 49% in N+). In univariate analysis OPE were related to tumour size ($p < 0.0001$), lymph node stage ($p < 0.0001$) and histologic grade ($p < 0.0001$); they were statistically significant with respect to survival (OS): $p < 10^{-29}$, disease-free survival (DFS): $p < 1.7 \times 10^{-13}$ and metastasis-free survival (MFS): $p < 10^{-29}$. In multivariate analysis in the N– group, OPE were the most predictive factor for MFS ($p = 7.1 \times 10^{-7}$) before size and grade, and for survival ($p = 1.9 \times 10^{-3}$) after tumor size. In the N+ group OPE were the first predictive factor for local recurrence ($p = 4.1 \times 10^{-7}$).

In conclusion this study confirm with a very simple routine approach the prognostic significance of emboli in breast carcinoma. This is particularly interesting in the N– group to select a subset of patients at high risk, for a possible adjuvant therapy.

PP-6-5 | **Does Semi-Quantitative Evaluation Improve the Prognostic Value of Histological Grade in Breast Carcinoma: Comparison of Scarff-Bloom-Richardson (SBR) and Elston-Ellis (EE) Grading Systems in a Series of 825 Cases with a Follow-Up of 10 Years**

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The respective prognostic value of two grading schemes was compared in a retrospective series of 825 patients treated between 1981 and 1988 for a small invasive carcinoma with conservative surgery and radiation therapy. Histological grade was assessed using the criteria developed by SBR and those recently proposed by EE. In addition, the exact number of mitotic figures per 10 high power field was recorded. Our results showed a strong unbalanced distribution of cases with a majority of Grade I cases (61% according to SBR, 50% according to EE) and a low number of Grade III cases (16% according to SBR, 4% according to EE). However, univariate and multivariate analysis showed that both histological grades were strongly correlated to overall and metastasis free survival. Despite the improvement of EE grading scheme in defining more precisely the morphological features, its prognostic value, in this series, was not better than SBR grading's. The number of mitotic figures was unexpectedly low, which could explain these results. We suggest that the mitotic score threshold are too high considering the small tumor sizes or, that due to the retrospective nature of the study, the technical conditions were less than optimal to properly assess the number of mitotic figures.

PP-6-6 | **The Prognostic Importance of Tumour Grade in Lymph Node Positive Breast Cancer**

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Lymph node status is an important prognostic factor in primary breast cancer. However, considerable prognostic heterogeneity exists such that offering adjuvant systemic therapy to all lymph node positive patients may overtreat a low risk subgroup.

We reviewed the results of 636 patients aged < 70 years treated between 1973 and 1988 with histologically proven lymph node positive breast cancer. No patients received adjuvant systemic therapy.

On univariate analysis histological tumour grade and number of lymph nodes involved were found to be significant prognostic variables ($p < 0.01$). Patient age, menopausal status, oestrogen receptor and tumour size were

not significant. In a second representative subgroup of 158 tumours MIB 1, S-phase fraction and erbB-2 were analysed. MIB-1 and S-phase fraction were significant prognostic variables on univariate analysis. On multivariate analysis for survival, tumour grade was the most important factor predicting for survival in the entire group and for the second subgroup.

The 15 year survival and average annual probability of death from breast cancer for lymph node positive grade I patients (n = 87) was 59% and 3.9%/year respectively. This shows that histological grade identifies a group of women who, although lymph node positive, have a 60% chance of surviving 15 years. This is similar to survival in breast cancer patients who are lymph node negative.

PP-6-7 | **Automated Grading in a Prognostic Index**

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The Nottingham prognostic index (NPI) for primary operable breast cancer (NPI = (0.2 × tumour size) + lymph-node stage + histological grade), validated with 15 year survival analysis, remains a powerful clinical tool which defines three subsets of patients with different chances of dying from breast cancer (good, moderate, and poor prognostic groups partitioned by NPI score: < 3.4, 3.4–5.4, > 5.4 respectively). Grade contributes significantly toward NPI scoring but is a semi-objective variable. Quantitative measurement of histological tumour grade derived from automated analysis offers less subjective assessment and potential substitution of conventional techniques. Putative substitutes for grade: MIB1 labelling, cell morphometry (CAS™ image analysis), and proliferative index (PI = % SPF + % G2M) (flow cytometry) were measured on tumour tissue from 102 patients with primary operable breast cancer (median follow-up, 144 months) who received no adjuvant therapy. Multivariate analysis generated a simple (3 level) grade substitute, $G^n = 0.02$ (MIB1 + standard deviation of nuclear size + PI), weighted by NPI score frequency. A new prognostic index, $NPI^n = (0.4 \times$ tumour size) + (0.6 × lymph-node stage) + G^n, defined three subgroups whose survival curves superimposed the corresponding curves generated by the standard NPI. An automated score, G^n, can substitute for histological grade in an established prognostic index.

PP-6-8 | **Prediction of Tumor Response to Neoadjuvant Chemotherapy in Operable Breast Cancer**

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The value of parameters obtained by fine-needle cytopunctures for the prediction of chemosensitivity was evaluated in 105 large operable primary breast carcinoma ((T2 ≥ 30 mm-T3, N0-N1-N2, PEV0-PEV1) treated with AVCMF (3 cycles) or FEC (4 cycles) before surgery. Cytopunctures were studied: before treatment for cytologic nuclear grading (in 2 groups) and S-phase fraction (SPF: 2 groups) by image cytometry; and after one cycle of chemotherapy for cytomorphologic and cell-kinetic changes. 13 patients showed pathologic complete regression (pCR), 26 were scored partial regression (with concordant clinical ≥ 50%, mammographic and histologic findings) and 59 showed no regression. Objective tumor regression and overall pCR were significantly related to high grade, high SPF, and to cytomorphologic and dramatic cell kinetic changes. Univariate analysis showed that high grade and high-SPF remained bad prognostic factors for metastasis free survival (MFS: $p = 0.005$ and $p = 0.003$, respectively; median follow up = 38.5 months). However, the subgroup of patients with pCR experienced a better clinical course (MFS, $p = 0.04$). The Cox model selected 3 variables: node positive, high S-phase and initial tumor size for MFS. At present the subgroup of pCR did not emerge from the Cox model possibly due to its small number of patients.

POSTER PRESENTATIONS

PP-6-9 | **Prognostic Significance of Epidermal Growth Factor Receptor and Estrogen Receptor in Advanced Breast Cancer**

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The Epidermal Growth Factor Receptor EGFR is a specific glycoprotein transmembrane receptor that is believed to be a functional entity constituting