and the relative risk of death depended only on lymph node status (RR = 1.99), tumour grading (RR = 1.32), and size (RR = 1.17) – $p < 0.005$.

Conclusion: Although sex seems to play a limited role in breast cancer prognosis, the data showed in unilateral analysis had some influence on survival. There is great need for further study of this phenomena.

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Prognosticators in axillary node negative breast cancer

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Introduction: Ultimately 30% of all axillary node negative (ANN) breast cancer patients will relapse and die of their disease. Prognostic factors are, therefore, needed to identify high risk patients.

Methods: 221 ANN (median number of 13 nodes examined), T1–3, breast cancer patients were studied. Initial therapy consisted of mastectomy in 71, and breast-conservation-therapy in 150 patients. None of the patients received adjuvant systemic therapy. Prognostic significance of: age, tumour size, estrogen- (ER) and progesterone-receptor (PR) both immunocytochemically (ICA) and by enzyme immuno assay (EIA), mitotic activity index (MAI), DNA-index (DI), S-phase fraction, cathepsin-D, PS2, urokinase plasminogen activator (uPA), and plasminogen activator inhibitor (PAI-1) was prospectively investigated. Disease free survival (DFS) was determined after a median follow up of 61 (range 40 – 88) months. It should be noted that we analysed both local, regional en distant metastases. Continuous and categorical variables were analysed using Cox regression analysis and logrank test, respectively.

Results: The overall 5 year DFS was 85% (38 patients relapsed). Only the following prognosticators: ER-ICA (negative vs positive, n = 149, p = 0.05), DI (diploid vs aneuploid, n = 193, p = 0.05), MAI (cut-off 5 mitoses/10 HPF, n = 152, p = 0.03), uPA (n = 98, p = 0.02) and PAI-1 (n = 98, p = 0.01) are significant prognostic indicators for DFS ($p < 0.05$). ER-ICA and ER-EIA were significantly correlated (t-test for equality of means p = 0.004), ER-EIA showed no prognostic significance, though.

Conclusion: High risk for relapses is associated with MAI > 5, high PAI-1 and uPA, aneuploidy, and a negative ER-ICA score. Prognostic significance was noted for: ER-ICA, while in contrast ER-EIA showed no significance. MAI was significant only with a cut off point of 5 (instead of 10) mitoses per 10 HPF.

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Functional intravital assay of anticancer drug efflux transporters in breast cancer biopsy specimens

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The main task of the investigation is the functional assay of multidrug resistance-related (MDR) anticancer drug transporters in intact breast cancer specimens for prediction of disease prognosis, tumor sensitivity to the MDR drugs and determination of transporters' type. Doxorubicin (DOX) is used as a model MDR drug. The new methodology developed by us previously was used for intravital determination of intratumor uptake and intracellular DOX accumulation in terms of kinetics of DOX fluorescence decrease in medium of incubation of intact tumor specimen with DOX as well as the changes of the index after modifier action. Two modifiers were studied in this investigation: verapamil (VP)-specific inhibitor of P-glycoprotein and MDR-associated protein transporters, as well as sodium azide (SA)-inhibitor of all energy-dependent (ATP-dependent) transporters. The following types of transporters were shown in 30 breast cancer tumor specimens investigated: 1) VP-sensitive transporters only (the effect of SA is comparable to that seen with VP); 2) VP and non-VP-sensitive transporters (the effect of SA is much greater than that of VP); 3) non-VP-sensitive transporters only (there is a modifying effect of SA and no effect of VP). No VP- and SA-sensitive transporters extruding DOX out of the cells were shown in about 30% of the specimens (there is no modifying effect of VP and SA). We believe that exactly this type of the tumors has to be mostly sensitive to MDR-anticancer drugs and disease prognosis according to this index has to be the best among the patients investigated. Supported by Russian State Committee of Science and Technology.

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Depression as prognostic factor in breast cancer

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Purpose: To test the hypothesis that women with primary invasive breast cancer and previous affective or neruotic disorders have a poorer prognosis compared to other women with breast cancer.

Methods: All 36,422 women registered in The Danish Breast Cancer Cooperation Group during the period 1978–1995 comprised the study population. By cross-linkage to the nation-wide Danish Psychiatric Central Register, 939 women admitted with a previous affective or neurotic disorder in psychiatric departments were identified. We used survival analyses, controlled for all the well-documented prognostic factors and analysed for deaths of natural and unnatural causes of death.

Results: Low risk breast cancer patients with a previous affective or neurotic disorders suffered a marginal increased rate of recurrence and a significant increased mortality rate compared to the other women. This could be explained by an increased mortality rate due to unnatural causes. In high risk breast cancer patients the same trends were seen but the results could not be explained by an increased mortality rate due to unnatural causes.

Conclusion: A previous psychiatric admission with affective or neurotic disorder seems to be only a weak negative prognostic factor in breast cancer.

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Loco-regional recurrence in randomized trial of breast cancer TNM stage II. Prognostic factors

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Material and Methods: Loco-regional recurrence (LR) was studied in a material of 1153 patients with breast cancer TNM stage II and randomized into 6 adjuvant treatment groups including RTR (4 groups) and/or Cyclophophamide or tamoxifen. p53 expression and c-erbB-2 oncoprotein were analysed immunohistochemically. Median observation time was 12 years.

Results: Recurrence occurred in 460 patients, 129 of whom had LR ± distant metastasis. The LRs were identical histologically with the primary tumours. p53 expression was observed in 1/3 of the cases with LR as was c-erbB-2 oncoprotein and in 10% both p53 and c-erbB-2. 19% of the 58 patients without RTR had LR and 6% of these showed p53 compared with 8% and 2% respectively of the 71 patients with LR receiving RTR.

Conclusion: No tumour progression was seen histopathologically between the primary tumour and the LR. Among patients with LR not given RTR three times as many cases showed p53 and c-erbB-2 as the corresponding patients given RTR. The results may indicate that RTR in cases with p53 expression results in fewer LR. Further studies have been initiated on oncogenes in the primary tumours in relation to adjuvant therapy and LR.

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The significance of prostate specific antigen (PSA) in breast cancer

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Purpose: The serine protease PSA has been found in breast and some other non-prostatic cancers. The expression of PSA is regulated by steroid hormones. In the present study we have determined PSA levels by ELISA in 1516 primary breast tumors, and have correlated PSA levels with tumor characteristics and clinical outcome.

Methods: The tumors were derived from 1516 patients with primary breast cancer: median age 56 yr (range 24–89 yr), 59% postmenopausal, median follow-up 85 months (13–202 m), relapse rate 47%, deaths 38%.