

Results: The frequency of involved ALN increased from 7.2% (8/111) in pts. with <10 mm, to 26.7% (40/150) in pts. with 11–15 mm and to 36.8% (46/125) in pts with 16–20 mm large tumors ($p = 0.0001$). No ALN involvement was detected in 17 pts. with 3–5 mm large tumors. In summary, increasing TS ($p < 0.002$), higher Grading ($p = 0.03$), detection of tumor cells in bone marrow aspirates ($p = 0.01$), lymph/blood vessel invasion ($p < 0.0001$) and aneuploid tumors with increased S-Phase ($p = 0.03$) were associated with positive ALN. Lymph/blood invasion offered a significant ($p < 0.05$) correlation with ALN status throughout all subgroups of TS, whereas other factors revealed significance only in TS subgroups. Multivariate analysis confirmed an increased risk of ALN involvement in patients with TS 16–20 mm by 6.3 ($p = 0.0001$) and in TS 11–15 mm by 4.5 ($p = 0.0003$) as compared to TS < 10 mm. An additional risk of positive ALN was related to lymph vessel invasion (1.8 fold, $p = 0.03$) and blood vessel invasion (2.6 fold, $p = 0.009$).

Conclusion: The risk of axillary lymph node involvement increased with tumor size and lymph/blood vessel invasion. An axillary lymph node dissection in pts. with breast cancer <5 mm seems no longer justified. In pts. with tumor size < 10 mm and no lymph or blood vessel invasion the risk of positive axillary lymph nodes is very low, so that an axillary lymph node dissection in these pts. seems unnecessary.

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POSTER

Clinico-pathological characteristics of breast cancer associated with thyroid disease

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Purpose: Breast cancer (BC) is a hormone-dependent neoplasm. There is conflicting evidence of clinical correlation between thyroid disease (TD) and BC. TD is common among women and is often associated with autoimmune disorders. The thyroid insufficiency hypothesis sought to relate BC to TD, in particular hypothyroidism. We performed a retrospective analysis of newly diagnosed BC to determine the prevalence of TD.

Methods: Data of 1,287 primary breast cancer patients (pts) treated at MDACC between 6/93 and 9/98, were analyzed. TD was defined as clinical evidence of impairment of thyroid gland function.

Results: TD was found in 128 pts (9.9%); 120 pts were hypothyroid (9.4%) and 8, were hyperthyroid (0.5%). Median age was 51 yrs (range 22–90) and 56.5 yrs (range 25–90) for the entire group and TD pts, respectively. Clinicopathological features of pts according to thyroid status: euthyroid: ER+ and/or PR+ 741 (64%), ER-/PR-: 242 (21%), stage 0-II 990 (86%), stage III 156 (14%); TD: ER+ and/or PR+ 82 (64%), ER-/PR-: 22 (17%), stage 0-II 120 (94%), stage III 8 (6%).

Conclusions: The prevalence of TD in this sample of BC pts is higher than in the general female population. The distribution of receptor status was similar among euthyroid and TD while a predominance of early BC (stage I-II) was noted in the latter group. The biological significance of this clinical association deserves further investigation. Molecular analysis of other members of the steroid receptor superfamily may provide patho-biological correlates.

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POSTER

Bcl-2 expression, cell differentiation and survival in primary breast cancer

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Introduction: The prognostic significance of Bcl-2 expression was examined.

Methods: In 100 patients with infiltrating ductal breast carcinomas Bcl-2 expression was examined, using immunohistochemistry on formalin-fixed, paraffin embedded representative tumor samples. Between Bcl-2 positive and Bcl-2 negative tumors, hormonal receptor state, tumor grade, tumor size and survival were compared. The Nottingham modification of the Bloom-Richardson system graded all tumors. A non parametric Mann-Whitney U test was used to compare both groups.

Results: Bcl-2 was expressed in normal adjacent tissue, in the carcinoma in situ component and in 74% of the tumors. Between the Bcl-2 positive and negative groups, there was a significant difference for estrogen and progesterone receptor positivity, cell differentiation, disease free survival and survival. There was no significant difference for tumor size,

menopausal state or age. Univariate analysis retained tumorgrade, Bcl-2 expression, age, progesterone receptor state and tumor size as prognostic factors. Tumor grade was shown to be an independent prognostic factor by Cox regression multivariate analysis. Bcl-2 expression was of marginal prognostic significance.

Conclusion: These results suggest that Bcl-2 expression in breast tissue is related with cell differentiation. Loss of differentiation is compatible with a loss of Bcl-2 expression. Bcl-2 expression is a highly significant prognostic factor by univariate analysis.

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POSTER

Fine needle aspiration is associated with hematogenous dissemination of breast cancer cells as determined by RT-PCR

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Purpose: The influence of fine needle aspiration on breast cancer cell shedding into the peripheral blood was investigated using reverse transcriptase-polymerase chain reaction (RT-PCR) targeted against β -subunit of human chorionic gonadotropin (β -hCG), cytokeratin 19 (CK19) and cytokeratin 20 (CK20) mRNAs.

Methods: This analysis was performed before and after fine needle aspiration in 20 cases with breast cancer and 24 cases with benign breast tumor. 5 ml of peripheral blood was drawn before and within 30 minutes after puncture. Total RNA was extracted from peripheral blood mononuclear (PBMN) cells. β -actin was used to assess the quality of cDNA. 367 bp RT-PCR products for β -hCG were digested with Styl endonuclease to produce 2 fragments (96 bp and 271 bp).

Results: For the benign cases, the pre-FNA samples were all negative for β -hCG and CK20 and 12.5% (3/24) positive for CK19. After aspiration, β -hCG and CK20 remained negative, whereas 3 cases became positive for CK19 in 21 evaluable cases. For the malignant cases, one pre-FNA sample was positive for all three markers and two other samples were positive for CK19. Of the 19 evaluable cases for β -hCG and CK20, 3 cases were converted to a positive result for β -hCG but none was positive for CK20. For CK19, there was positive signal conversion in only one of 17 evaluable cases.

Conclusion: Fine needle aspiration to breast tumor may cause hematogenous dissemination of breast cancer cells. Although CK19 is more sensitive to detect both benign and malignant epithelial cells in the circulation, β -hCG is more specific for breast cancer cells. CK20 is the least sensitive marker for circulating cells.

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POSTER

Local Recurrence (LR) after Breast Conserving Therapy (BCT); risk factors predicting for subsequent distant metastasis

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Purpose: To study risk factors for subsequent distant metastasis (DM) after LR for patients treated with BCT.

Patients and Methods: From a cohort of 1481 breast carcinomas treated with BCT in the period 1980–1994, we studied 68 pT1-3N0-1 breast tumors which relapsed as first event. Patients who developed LR after or concomitant with DM (defined as diagnosis within 4 months of LR diagnosis) were omitted from analysis. The primary as well as the recurrent tumor was studied. In addition to clinical factors (age at BCT and LR, interval, mode of detection, location and treatment of LR) the histology slides of the primary and the recurrent tumor were reviewed. Immunohistochemical staining was performed for the following proteins: bcl-2, cyclin D1, E-cadherin, EGF receptor, ER, PR, Ki-67, c-erbB-2/neu and p53. Statistical analyses were performed using conditional logistic regression.

Results: In univariate analysis none of the factors of the primary tumor was found to be statistically significantly associated with DM risk after LR. Of the recurrent tumor the following factors were found to be risk factors for high DM risk after LR: interval < 2 years (RR 2.38 (1.22–4.76); $p = 0.008$) and high mitotic count (RR 2.51 (1.03–6.15); $p = 0.04$). All patients with non-invasive recurrent tumor were alive at time of analysis. Patients with a LR detected after 2 years with high mitotic count were found to have the same poor prognosis as patients with LR detected after a short interval.