Results: Sentinel nodes were detected in this first period in 51 of the 60 patients (85%). A mean number of 1.47 and a median number of 1 with a range from 1 to 5 sentinel nodes per patient was found. Within the first two levels for routine histology 14 out of 60 cases (23.3%) were positive. In addition 7 cases (11.7%) got positive through serial sections and another 4 cases (6.7%) through immunohistochemistry. Finally in 25 pts. (41.7%) negative SLND predict negative axillary status, in 7 pts (11.7%) positive SLND predict positive axillary status, in 18 pts (30%) the only positive node was the sentinel node. Only in one case of identified negative sentinel nodes, the remaining axillary nodes were positive (1.17%).

Conclusion: In the large majority of patients with breast cancer, areolar intradermal blue-dye injection technique alone can be succesfully used to locate the sentinel node, and thereby provide important and correct information about the axillary status. Our results are comparable with combined blue dye and radioguided peritumoral guided surgery, whereas the method is more simple, less expensive and practicable for all trained surgeons and not related to major centers.

660 POSTER

Clinicopathological study of p73 gene expression in breast carcinomas: an immunohistochemical study with special reference to apoptosis and cell proliferation

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Purpose: To analyze the functional role of the p73 gene in breast carcinomas, it is necessary to examine the fine expression of the p73 gene in carcinoma cells in order to prevent contamination by other cells expressing p73 gene. In this study, we analyzed the immunohistochemical expression of p73 protein in breast carcinomas and its relationship with cell proliferation, apoptosis and clinical features of the carcinoma.

Materials and Methods: Development of the anti-p73 polyclonal antibody; A rabbit was immunized with GST-p73 (amino acids from TQVVKRCPNH to YEPPQVGTEF) for the production of the anti-p73 antibody. Tissue specimens were obtained from 76 patients with breast carcinoma undergoing mastectomy. For the immunohistochemistry of p73, the TSA indirect system (NEN Life Science Products, Inc.) was used. Immunohistochemical expression of the p73 protein was categorized as p73 positive [p73 (+)] (p73 positive carcinoma cell>0.5%) or p73 negative [p73 (-)].

The number of cells displaying mitotic morphology was expressed as the percentage of the total number counted (Mitotic Index, MI). The apoptotic index (AI) was defined as the ratio of TUNEL-positive tumor cells to all counted tumor cells. For statistic analysis, the Mann-Whitney U-test was used. P-values less than 0.05 were considered to be statistically significant.

Results: Sixteen out of 76 (21.1%) cases were p73 (+). The AI (mean ±SD) of p73 (+) cases (1.89 ± 0.90%) was significantly higher than those of p73 (-) cases (0.75 ± 0.73%) ($p < 0.01$). The MI of p73 (+) cases (2.25 ± 1.65%) was also significantly higher than those of p73 (-) cases (0.82 ± 0.96%) ($p < 0.01$).

In 30 cases with high MI (MI > 1%), AI of p73 (+) cases (n: 13, 2.16 ± 0.76) was significantly higher than those of p73 (-) cases (n: 17, 1.52 ± 0.60)($p < 0.05$). In low MI cases (MI<1%), however, there was no significant difference in AI between p73 (+) and p73 (-) cases.

In 8 cases (p73 (+) 2, p73 (-) 6*) of 30 high MI cases, AI was less than 1.2%, and in 22 cases (p73 (+) 11, p73 (-) 11) was higher than 1.2%. All 4 cases with distant metastases in this series were included in this P73 (-) and low-AI (<1.2%) group*.

Conclusion: In breast carcinomas with high proliferative activity; 1. The p73 gene may play a role in the induction of apoptosis. 2. Loss of p73 gene expression and apoptotic regulation of carcinoma may be associated with advanced carcinogenesis and metastatic potential in breast carcinomas.

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Comparison of clinical, radiological and pathological assessment of response to neoadjuvant chemotherapy for primary breast cancer

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Clinical and radiological (mammography and/or ultrasound) assessment based on UICC criteria is commonly used to evaluate response to neoadjuvant chemotherapy in primary breast cancer. More recently, pathological assessment of the post-treatment resected specimen has been advocated. This study compares clinical, radiological and pathological assessments of response to neoadjuvant chemotherapy.

72 patients received 6 cycles of neoadjuvant treatment using FEC (54), AC (10), MMM (5) or CMF (3) chemotherapy. All patients were reassessed both clinically and radiologically (by ultrasound (35), mammography (14) or both modalities (23)) and categorised into complete (CR), partial (PR) or non-responders (NR). Pathological response in the surgical specimen was defined as follows: CR - no residual tumour; PR - histological tumour response; NR - no tumour response.

Response (percent) categorised by various methods of assessment:

	Clinical	Mammography	Ultrasound	Pathological
CR	23 (32)	5 (14)	3 (5)	6 (8)
PR	35 (49)	20 (54)	41 (71)	25 (35)
NR	14 (19)	12 (32)	14 (24)	41 (57)
n	72	37	58	72

Mammographic and ultrasound categorisation of response was identical in 22 of the 23 patients assessed by both modalities. All 23 clinical complete responders achieved a radiological response (CR or PR) with the exception of one patient with stable disease both mammographically and pathologically. However, pathological response varied widely amongst clinical complete responders: 5 CR, 10 PR and 8 NR. Of the 41 patients (57%) with pathological NR, the majority were judged to have responded by other methods: clinical examination 10 NR, 23 PR, 8 CR; radiological assessment 16 NR, 22 PR, 3 CR.

Conclusion: This study highlights the inadequacies of clinical assessment of response to neoadjuvant chemotherapy. A substantial proportion of patients with complete response, either clinically or radiologically, had stable disease by pathological examination. The clinical significance of these results may be revealed by correlation with long-term survival data.

662 POSTER

Preoperative hemoglobin levels do not influence the dissemination of isolated tumor cells in the bone marrow of breast cancer patients

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Background: Perioperative anemia is thought to increase the risk for relapse in patients with breast cancer. It has been speculated that anemia might enhance the hematogenous dissemination of isolated tumor cells (ITC) by inadequate cytokine production. This study evaluates the influence of hemoglobin (Hb) levels on the immunocytochemical detection of ITC in the bone marrow (BM) of breast cancer patients at the time of presentation

Methods: We analyzed bone marrow aspirates from 396 patients at the time of primary diagnosis of primary breast cancer, in which preoperative Hb-level was available. Carcinoma cells were detected using monoclonal antibody A45-B/B3 directed against a common epitope of the cytokeratin (CK) polypeptides, including the heterodimers CK8/18 and CK8/19 and the APAAP technique.

Results: At the time of primary diagnosis, 108 of 396 patients (27%) presented with ITC in the BM. The median Hb-level was 13.8 g/dl. Among those patients with Hb-levels £ 13.8 g/dl, 50 patients (25%) had a positive bone marrow finding, while 58 patients (29%) with Hb-levels > 13.8 g/dl presented with ITC in the bone marrow ($P = 0.63$). In CART analysis, no predictive Hb cutoff levels in terms of tumor cells dissemination could be found.

Conclusion: In a considerable number of patients with primary breast cancer, minimal residual disease can be detected. There is no direct proof that low Hb-levels at the time of presentation increases the risk for hematogenous tumor cells dissemination.