ber estimation contribute to the controversies around ERBB-2 amplification incidence and prognostic role.

888 POSTER

### Factors predisposing to chronic pain after breast cancer treatment

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**Purpose:** The study was designed to assess the factors that predispose to chronic post-treatment pain in the breast area and in the ipsilateral arm in patients treated surgically for breast cancer.

Methods: A total of 93 patients with non-metastasised breast cancer who were treated during 1993–1994 answered the questionnaire about pain in the operated breast and in the ipsilateral arm one year after surgery. They were also asked to rate the severity of the acute postoperative pain of their breast surgery on a 5-point verbal rating scale. The Bayesian multivariate model was used. The factors which were included in the analysis were: age, type of operation, size of the tumour, number of lymph nodes removed, involvement of lymph nodes, number of lymph nodes involved, complications of surgery, inensity of the acute postoperative pain remembered by the patient, number of doses of analgesics, number of months from surgery, adjuvant radiotherapy, chemotherapy and endocrine treatment, state and trait anxiety and depression.

Results: The intensity of the acute postoperative pain remembered by the patient, trait anxiety and depression were the most important factors predisposing to chronic pain in the ipsilateral arm. State anxiety, trait anxiety and depression and breast radiotherapy were the factors included in the model of chronic pain in the breast area.

Conclusion: Patients who are anxious and depressed and who experience more acute pain after breast surgery (surgical damage?) and who have radiotherapy are at risk of developing chronic pain.

889 POSTER

## Alteration in NK cell activity during the progression of breast cancer and its modulation by cytokines

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Purpose: In malignant processes alterations in immunological parameters are commonly present. As their impairment is associated with disease progression, the aim of this work was to investigate the activity of natural killer (NK) cells and the possibility of their stimulation with different cytokines in breast cancer patients.

**Methods:** Native NK cell activity and the one after in vitro treatment of PBL  $(4.0 \times 10^8/\text{ml} \text{ of RPMI } 1640)$  with rh IL-2, IL-7, IL-12 and TNF a (100 and 200 U/ml) was determined by the 51-chromium release method for breast cancer patients in clinical stages I–IV.

Results: The activity of NK cells is decreased in all breast cancer patients and it deteriorates with the advance of the malignancy. Treatment with IL-2 significantly enhanced (p < 0.01) NK cell activity of all patients. Contrary to this, IL-7, IL-12 and TNF a did not have this effect, however, when combined with IL-2 they gave similar activation as IL-2 alone.

Conclusion: The activity of NK cells, which are important antitumor effector cells, is depressed in breast cancer patients but it can be significantly augmented by in vitro treatment with IL-2. These results should encourage the application of IL-2 in these patients as adjuvant therapy, especially in advanced stages of breast cancer, where other therapy does not give sufficient results.

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# Analysis of the ability of cytotoxic granules and B7-1 molecule to inhibit nodal metastases of cancer cells in patients with breast and lung cancers

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Purpose: we analyzed for the ability of granzyme B and perforine contained in cytotoxic granules and B7-1, a cell-surface molecule to inhibit nodal metastases of cancer cells in cancer patients.

Methods: Tumor specimens obtained from 23 breast cancer patients and 13 lung cancer patients were studied for granzyme B and perforine

productions and B7-1 expressions, using an immunohistochemical technique. Percentages of positive cells for their expressions and the nodal involvement in each case were compared.

Results: 61%, 22% and 61% in breast cancer patients and 100%, 69% and 38% in lung cancer patients were positive for granzyme B, perforine and B7-1 expressions, respectively. Interestingly, granzyme B and perforine released by NK cells or cytotoxic T lymphocytes were shown to be located in the cytoplasm of cancer cells at different stages. B7-1 molecule was shown to be expressed on cancer cells rather than on tumor infiltrating mononuclear cells. In breast cancer patients, percentages of cancer cells containing either granzyme B or perforine inversely correlated with the nodal metastases. In lung cancer patients, only perforine production was related to the suppression of nodal metastases.

Conclusions: Granzyme and perforine contained in cytotoxic granules were suspected to enter cancer cells following released by effector cells in tumors. This event occurred in the early stages of cancer progression. These cytotoxic factors were thought to play crucial roles in the suppression of cancer cells metastasizing regional nodes in breast and lung cancer patients.

891 POSTER

#### Changes in radiation exposed women's mammary glands

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The research was carried out in accordance with the complex program "Poligon" in 1990–92. The goal of the research was to study 281 women that had lived on the area affected by the nuclear explosion in 1949 and to see the condition of their mammary glands and hormones status. That time they had been 5 to 36 years old. Minimum dose was 400, maximum 2430 mZB. At the examing time (after 41–43 years) they were ages from 48 to 77. Also 187 women from the unaffected area got included into control group. Mammography, ultrasound diagnostic of the mammary glands, immunity tests were given to all of the 468 women.

The analysis of the results showed that radiation exposed women have changes such as adenosis, diffuse or local fibrosis occurrence 3 time higher than the changes in the compared group. 129 women (46%) had corpus luteum insufficiency, hyperestrogenemia laboratory proved. In 34 cases (12%) was found hyperprolactinemia. 19% had hypothyreosis on the diffusus thyreoid hypertrophy background. Immunologic research in the exposed group revealed the symptoms of the secondary immunodeficiency.

Summerizing it up, we can say that radiation-exposed women present a high risk group of developing mammary gland cancer. They need chemioand diet prevention, observation for a timely malignancy diagnostic.

892 POSTER

## HLA genotype can be predictive for the breast cancer susceptibility and outcome

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Purpose: Does HLA-DR genotype contribute into breast cancer risk and aggressiveness?

Methods: DRB-HLA alleles distribution was analyzed by Southern-blot analysis in 44 breast cancer (BC) patients and 120 healthy donors (HD).

Results: The frequency of DRB homozygotes was significantly higher in BC group than in control (31.8% vs. 7.5%). In addition DRB-11 allele was overrepresented in the turnour cohort (25.0% vs. 11.7%; p = 0.007). Moreover, DRB allele distribution correlated with clinical parameters of the disease. DRB homozygosity and the presence of DRB-4 allele were associated with unfavourable prognosticators. In particular, DRB homozygous genotypes occurred more often in women with large turnour size (>5 cm), than in those with moderate turnour size (<5 cm) (75% vs. 18.2%; p = 0.0001). The tendency to correlation between DRB homozygosity and lymph node positiveness was also observed (38.1% vs. 20.0%; p = 0.07). The presence of DRB-4 allele was more typical for large (25.0% vs. 7.6%; p = 0.07) and advanced (23.1% vs. 6.7%; p = 0.05) carcinomas. On the contrary, DRB-3-1 and DRB-7-2 alleles were associated with rather small turnours.

Conclusions: The data might imply possible benefits of HLA-DRB genotyping for the determination of breast cancer risk and outcome.