500–600 mg/m$^2$, Methotrexate 40–50 mg/m$^2$, 5 Fluorouracil 500–600 mg/m$^2$ (CMF) × 3–6 cycles. (4) Cyclophosphamide 500–600 mg/m$^2$, Adriamycin/Epirubicin 40–50 mg/m$^2$, 5 Fluorcuracil 500–600 mg/m$^2$ (CAF/CEF) × 3–6 cycles. The breast and glandular areas were irradiated with 40–50 Gy in 15–25 fractions ± 5–10 Gy boost in 2–5 fractions. The overall 2, 5 and 10 year actuarial survival rates are 54%, 28% and 11% respectively. Overall response rates to chemotherapy were 61% (14% CR). Response rates were highest [92% (50% CR)] with CAF/CEF based regimens. The addition of radiotherapy increased the response rate to 93% overall, and with CAF/CEF there was a 75% CR rate. The median time to maximum clinical response was 5 months and 9 months on radiological criteria. Sixty-one patients have relapsed, 54% due to metastases, 15% synchronous local and metastatic disease, 31% local failure only. Thirty-one percent of patients had mastectomy, with only 10% of patients having uncontrolled inoperable local disease after therapy.

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## INCIDENCE AND CAUSES OF LEUCOCYTOPENIA IN POST-OPERATIVELY IRRADIATED BREAST CANCER PATIENTS

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*Purpose:* Leucocytopenia (LCP) (<4000/μl) in breast cancer patients treated by adjuvant chemotherapy (CT) is an excepted side effect. In contrast radiation (RT) induced LCP in postoperatively irradiated breast carcinoma is unusual. We analysed the incidence of RT induced LCP and possible reasons of its occurrence.

*Patients:* From 1989–93 185 patients with primary breast carcinoma (T1–4N0–2 M0) were treated by surgery alone (n = 87), by additional CT with CMF (n = 10), by postoperative RT only (chest wall/breast and/or regional lymph nodes) (n = 54) or by all three modalities (n = 36). All groups were comparable with regard to age. Blood examinations were performed once weekly.

*Results:* LCP was observed in women treated by surgery alone in 4.6%, by surgery and CT in 60%, by postoperative RT in 31.5% and by combined procedure in 88.9%. In all irradiated women (n = 90) leucocytes counts were lower than in those without RT ($P = 0.001$). In contrast to chest wall/breast irradiation alone, all patients treated by CT and RT of the chest wall/breast including regional lymph nodes revealed decreasing leucocytes counts (<4000 n = 14, <2000 n = 5). LCP depended on doses given to the supraclavicular and parasternal region ($P = 0.003$).

*Conclusions:* Our data suggest that the size of irradiated volume can significantly enhance the risk of LCP in primary breast cancer patients treated by CT. Our results enable to define criteria necessary for selection of patients with recommended frequent blood examinations.

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## CORRELATION BETWEEN DOSE INTENSITY, HEMATOLOGICAL TOXICITY AND OUTCOME OF ADJUVANT CHEMOTHERAPY IN BREAST CANCER

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The purpose of the study was to determine significance of total dose (TD), dose intensity of all given cycles (TDI), dose intensity of the two first cycles (DI2) and hematological toxicity on efficacy of doxorubicin (adriamycin) containing adjuvant chemotherapy for stage II and III breast cancer.

*Patients and Methods:* 211 patients with stage II and III breast cancer were treated with 8 cycles of adjuvant chemotherapy (cyclophosphamide, adriamycin and oral ftorafur). TDI, DI2, TD and the impact of hematological toxicity were compared with values for distant disease-free (DDFS) and overall survival (OS).

*Results:* A preliminary analysis indicated that adriamycin DI2 correlated to DDFS. Patients with a lower leukocyte nadir during the chemotherapy had significantly better DDFS. The same trend was established for OS.

*Conclusion:* The initial dose intensity is important to assure the optimal effect from adjuvant chemotherapy. The correlation between lower leukocyte nadir and improved treatment outcome indicates that the better results associated with patients who received the higher dose intensity resulted neither from selection for better tolerance to chemotherapy nor for better performance status.

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## THE EFFECTS OF TAMOXIFEN AND TOREMIFENE ON PLASMA LIPID LEVELS IN POSTMENOPAUSAL EARLY BREAST CANCER PATIENTS

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Tamoxifen as adjuvant therapy for women with breast cancer decreases serum lipids and lipoproteins by its estrogenic agonist effects. We evaluated whether a novel antiestrogen, toremifene, has similar effects.

*Patients and Methods:* 49 postmenopausal early breast cancer patients were randomized to adjuvant tamoxifen or toremifene treatment groups. Total, LDL and HDL cholesterol, apolipoprotein A-I, A-II and B and Lp(a) were measured before treatment and after 12 months.

*Results:* Both antiestrogens reduced significantly serum total and LDL cholesterol and apo B levels. The response of HDL cholesterol to treatment was clearly different between the groups. Toremifene increased the HDL-level 14% whereas tamoxifen decreased it 5% ($P = 0.001$). Both Chol/HDL and LDL/HDL ratios fell more in the toremifene than tamoxifen group ($P = 0.008$; $P = 0.03$, respectively). Toremifene also increased apo A-I level ($P = 0.00007$) and apo A-I/A-II ratio ($P = 0.018$). In both tamoxifen and toremifene treatment groups Lp(a) concentration fell significantly (change: 34% vs 41%).

*Conclusion:* These results provide positive evidence that toremifene has highly antiatherogenic properties with an exceptional potency to improve all lipoproteins which are associated with increased coronary heart disease risk.

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## ADJUVANT ANTIESTROGENS (TAM) VS ESTROGENS (EST) IN POSTMENOPAUSAL NODE POSITIVE (N+) BREAST CANCER PATIENTS

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In 1985–1989 in phase III randomized trial for evaluation of efficacy of adjuvant TAM (20 mg/day for 12 months) and EST (synoestroli 20 mg/day, i.m. for 6 months) were enrolled 172 (87 and 85 respectively) postmenopausal N+ breast cancer patients (pT1–3N1–2M0). The 5-year overall survival were 65.5% in TAM group and 71.7% in EST group ($P > 0.05$).

Toxicity of EST (30.5%) were much higher than TAM (3.4%) ($P < 0.05$). The main side effects of therapy with EST were methrorrhagia and arterial hypertension (grade III). In 19 cases (22.3%) they were the main reasons of early treatment termination. In TAM group the study treatment were well tolerated.

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## SURGICAL THERAPY OF CYSTOSARCOMA PHYLLOIDES (CSP)

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CSP is a rare fibroepithelial tumour. The incidence comes to 1% of all breast neoplasms. Morphological differentiation between benign and malign lesions can be difficult. We examined 21 female patients who underwent surgical treatment on our department from 1/80 to 12/94. The age range was 24 to 82 (mean 54) years.

Median tumour diameter in first treatment was 1.5–10 cm (mean 4 cm). Modified radical mastectomy was performed in 5, simple mastectomy in 3 cases. Thirteen patients were treated by tumourectomy with tumour free resection margins of 2 cm. Median follow up was 6.7 years (8 m–15 y). Six patients (28.5%) showed at least once local recurrence following first treatment (mean 26 month). In one case we saw 5 relapses. From 5 malignant CSP (23.8%) 4 patients died during follow up.

In our examination we observed no correlation between tumour size and recurrence rate. A sufficient wide histologically verified tumour free resection margin seems to be unalterable. According to literature and to our experience axillary dissection is useless even in cases of malignancy.