degree is influenced by the type of chemotherapy, the menopausal status and pretreatment obesity.

P18 Plasma lipids and lipoproteins in breast cancer women in relation to body mass index (BMI) and fat distribution (WHR)

A. Dziewulska-Bokiniec, J. Wojtacki, M. Wróblewska, J. Skokowski. *Department of Radiotherapy Maritime Hospital, 81-519 Gdynia, Poland*

Cholesterol or products of its biosynthesis are assumed to play important role in carcinogenesis via influence on DNA synthesis and cell proliferation. Obesity and central body fat distribution are positively related to postmenopausal breast cancer risk. Aim of this study was to assess the lipid/lipoprotein profile of breast cancer women in comparison with healthy controls. Serum levels of total, HDL, LDL cholesterol and triglycerides were evaluated in 150 untreated breast cancer women (mean age 51.0 yrs) and 150 healthy controls (mean age 50.3 yrs), matched by sex, age, BMI and fat distribution (WHR: waist to hip ratio). The mean value of total cholesterol was significantly higher in breast cancer group than in controls (231.6 vs 221.4 mg/dl; $p < 0.03$), as well as LDL cholesterol (155.3 vs 145.4; $p < 0.05$) and triglycerides (132.3 vs 116.4; $p < 0.02$). Obese patients (BMI ≥ 30 kg/m^2) had increased levels of LDL cholesterol in comparison with BMI-matched controls (165.8 vs 138.1 mg/dl; $p < 0.02$). We have not noticed any differences in lipids and lipoproteins plasma concentrations between breast cancer women and controls with central body fat distribution (WHR ≥ 0.8). Association between cholesterol – precursor of sex hormones and lipids disorders observed in breast cancer patients, pronounced in obesity, may constitute "deadly trio" in mammary carcinogenesis.

P19 Value of seric cholesterol in the prognosis and treatment of breast cancer

R. Lazo, S. López. *Unidad Oncológica P. del Río, Cuba*

Knowing that cholesterol is used in the formation of sterоid hormones including estrogens and that estrogenic receptors are an important prognostic factor, we started a study in 1982 with stage II patients of breast cancer. After operation seric cholesterol was indicated to 123 patients (in 99 of them a complete lipid study was performed). Patients did not receive adjuvant chemotherapy. Afterwards relapse was evaluated.

We found that patients with seric cholesterol lower than 6.46 mmol/l had major percent of relapse before 5 years $p < 0.01$. When we studied total cholesterol/HDLC index (i) we found that patients with i lower than 2 had 100% of relapse before 5 years, from 2–4.9 40.9% of relapse before 10 years, from 5–5.9 14% of relapse before 10 years and higher than 60% of relapse before 10 years ($p < 0.001$). It means that relative increase of HDL cholesterol increased the risk of metastases.

When the patients that relapsed were analyzed, we found that group of total cholesterol lower than 5.17 mmol/l had worse response to chemotherapy (CMF and CAF) $p < 0.05$.

If Hoyer's work is analyzed (Women with higher levels of HDL cholesterol had a significative risk of breast cancer), Cuzick and Reiner (Tamoxifen reduces LDL cholesterol), Potischman (Chemotherapy increases seric cholesterol); we would ask three questions. 1) Would seric cholesterol be a monitor for adjuvant chemotherapy and hormonotherapy?. 2) If we keep in 6 the index would we prevent relapse?. 3) Would cholesterol be controlled by a genetic mechanism?

Thursday, February 26, 1998 9.00–18.00

Diagnostics / Markers

P20 Extensive screening of women with high risk node positive breast cancer: An update

M. Crump, R. Abraham, P. Goss, K. Arts. *The Toronto Hospital, University of Toronto, Toronto, Canada*

We have previously reported (J. Clin. Oncol 14: 66, 1966) that extensive staging evaluation detected occult metastases in 23% of women with ≥ 10 positive axillary lymph nodes considered for high dose chemotherapy and autologous marrow support (ABMT). Here we report our expanded experience with this patient population. From 2/93 to 10/97, 129 women with ≥ 10 positive lymph nodes and no evidence of metastases on chest x-ray, bone scan and liver ultrasound were referred to our centre for possible enrollment in a prospective trial of ABMT (CALGB-9082, NCIC-CTG MA13). Forty-two did not undergo protocol staging (CT scan of head, chest, abdomen and pelvis, bilateral bone marrow biopsy): 23 declined participation, 11 had clinical evidence of metastatic disease at referral, 8 were ineligible. Four additional patients were ineligible because of inadequate organ function (low EF, DLCO or bone marrow cellularity). Occult metastatic disease was found by protocol staging evaluation in 14/82 women (17%): Bone marrow 4, liver 2, internal mammary or mediastinal node 4, lung 3, bone 1. This expanded cohort confirms our previous experience with the evaluation of women with high risk breast cancer and emphasizes caution in interpretation of current phase II results of ABMT compared to historical controls, where such extensive evaluation was not performed. Large randomized prospective comparisons of this promising therapy to standard treatment in North America are nearing completion. The final results will not be available for several more years.

P21 High-risk breast cancer patients (>9 involved nodes) M0 at conventional staging procedures: Additional findings suggesting M1-status

S. Mohrmann[1], U. Nitz[1], B. Kuschel[1], A. Adomeit[1], P. Dall[1], A. Dobrovolskaja[1], H.G. Bender[1], M. Frick[2]. [1]*Department of Gynecology and Obstetrics, University of Düsseldorf, Germany;* [2]*Bone Marrow Donor Center, University of Düsseldorf, Germany*

Introduction: Since 6/95 high-risk breast cancer patients younger than 60 years are randomized to dose dense conventional therapy or to tandem high-dose chemotherapy with stem cell support. Beside age and performance status inclusion criteria were R0 resection, N >9, and M0-status as documented by normal clinical examination, negative scintigram, negative chest x-ray and negative abdominal ultrasound. There is growing evidence that tumor load in this subgroup is systematically underestimated (JCO 6/97).

In some patients additional examinations like histological evaluation of resected subscapular lymph nodes, bone-marrow biopsy, supraclavicular ultrasound and bronchoalveolar lavage were performed. Data from these examinations suggesting M0 or M1 status are reported.

Materials and Methods: From 6/95 until 10/97 150 patients were randomized. Operative and histological reports from the first 94 patients were evaluated. Supraclavicular ultrasound and bone-marrow biopsy were performed in 23 and 26 patients respectively.

Results: 70.2% (n = 66) of the patients had modified radical mastectomy. Axillary operative procedure as documented in the operative report consisted in 8.5% of the resection of the lymph nodes of level I–II, in 42.6% of resection of lymph nodes of level I–III. In 46.8% the operative procedure was described as resection of "axillary lymph nodes" without separate histological examination of level I or 2. In 2 cases subscapular lymph node resection and separate histological examination were documented.

None of the bone marrow biopsies (26 histological examinations) revealed bone marrow carcinosis. Supraclavicular ultrasound showed suspicious lymph nodes in 11 of 23 patients despite normal clinical findings in this area.

Conclusion: Our previous data show that about one third of patients with more than 9 involved axillary lymph nodes in breast cancer will have positive subscapular lymph nodes. Therefore the abovementioned operative procedure in the axilla will systematically underestimate the proportion of M1 patients. The same is probably true for supraclavicular ultrasound as documented by the high rate of suspicious findings (11/23) in clinically normal patients. Bone marrow biopsies on the other hand did not reveal histological involvement.

Additional data about CT and immunocytochemical examination of bone marrow will be presented.

P22 Role of single photon emission tomography with ^{99m}Tc-MIBI in diagnosis of metastatic widespread in breast cancer

Ju.E. Riannel, E.M. Slonimskaya, E.V. Barysheva, L.I. Musabaeva, S.A. Velichko, W.Yu. Ussov. *Cancer Research Institute, Tomsk, Russia*

Mammascintigraphy (MS) with the ^{99m}Tc-MIBI has been widely used for detection of primary node of breast cancer. In this study we have evaluated the MS advanced with ^{99m}Tc-MIBI single photon emission computed tomography (SPECT) as a tool for diagnosis of the metastatic widespread in breast cancer.

Planar and SPECT MS were performed in 46 ladies with proven breast carcinoma before treatment. SPECT was carried out in 1 h after injection of 740 MBq of ^{99m}Tc-MIBI. In SPECT study axial, frontal and sagittal slices were reconstructed and reported by non-informed radiologist.

The results of mammascintigraphy were correlated with data of pathologic study of the surgically excised specimen. External axillar, sub- and supraclavicular lymph nodes were analysed separately. The results were as following:

The overall sensitivity was 79.6%. No false-positive cases were observed. In 9 ladies also an increased uptake of ^{99m}Tc-MIBI was observed in parasternal regiones. Like axillar lymph nodes, this has been reported as suspective for the parasternal metastatic involvement, although here without morphologic justification. These results were used in all the cases for design of gamma-radiation

therapy. MS SPECT follow-up in the course of combined chemo- and radiation therapy revealed decrease of ^{99m}Tc-MIBI accumulation by 25–45%, supporting usage of the technique for control of non-surgical treatment.

Groups of lymph nodes	Axillar	Subclavicular	Supraclavicular
Detected by ^{99m}Tc-MIBI mammascintigraphy	28	9	5
Verified pathologically	31	12	7
Sensitivity of ^{99m}Tc-MIBI	90.3%	75%	71.3%

Hencefore we conclude the SPECT mammascintigraphy with ^{99m}Tc-MIBI provides correct data on the extent of metastatic spread in breast cancer and can be used for both design of therapy and also for dynamic follow-up.

P23 Monitoring the efficacy of primary chemotherapy for breast cancer using breast scintigraphy and immunocytochemical bone marrow screening

H. Sommer, R. Tiling, S. Braun, B. Proehl-Steimer, C. Kandziora. *I. Frauenklinik and Dept. Nuclear Medicine Univ. of Munich, D-80337 Munich, Germany*

Primary chemotherapy is indicated for inflammatory breast cancer, primary metastatic breast cancer, and to decrease tumor size to allow lumpectomy instead of mastectomy. To date, conventional monitoring of chemotherapy success includes mammography, ultrasound, and sometimes tumor marker level. These methods are unsuitable to monitor inflammatory breast cancer.

In this pilot-study, breast scintigraphy with Tc-99m-Sestamibi, an established method for tumor differentiation, was used as an alternative method of therapy monitoring in inflammatory breast cancer. Additionally, bone marrow aspirates were obtained from each patient to screen for breast cancer micrometastases before and after chemotherapy, using the pancytokeratin monoclonal antibody A45-B/B3 for tumor cell detection. Up to now ten patients were examined with breast scintigraphy and bone marrow aspiration before and after primary chemotherapy for inflammatory breast cancer. In six patients a clinical regression of disease could be observed.- Parallel a dimished tumor perfusion could be detected by scintigraphy and previously positive micrometastasis in bone marrow aspiration changed to a negative result. Four patients did not respond to chemotherapy and did not show changes in diagnostic results as well.

We conclude that breast scintigraphy and bone marrow screening might be a promising approach to monitor therapeutic efficacy in cases where conventional monitoring fails to predict the clinical outcome

P24 Scintimammography & MR mammography in assessing palpable breast masses and recurrent tumour

H.M. Fenlon, N.C. Phelan, P. O'Sullivan, S. Tierney, T.F. Gorey, J.T. Ennis. *Depts. of Radiology & Surgery, Mater Hospital/University College Dublin, Ireland*

The early detection of recurrent tumour during adjuvant therapy is important in planning management including second-line therapy. We compared prospectively TC-99m tetrofosmin scintimammography (TSM) with MR mammography (MRM) in 47 patients of mean age 51 (26–79) with palpable breast lumps. A remote history of carcinoma in the affected breast was present in 11 patients. All patients had TSM, contrast-enhanced MRM and plain-film mammography (PFM) (age >35) performed on the same day. Al lesions had biopsy or aspiration cytology within two weeks of imaging and the pathology and imaging results were correlated. Claustrophobia in three patients lead to discontinuation of MRM – of the 44 remaining patients the pathology was malignant in 21 and benign in 23. The overall sensitivity of PRM was 81%, with a specificity of 82.4%, a positive predictive value (PPV) of 85% and a negative predictive value (NPV) of 77.8%. The sensitivity of TSM was 95.24%, specificity 91.3%, PPV 90.9% and NPV 95.45%. The sensitivity of MRM was 90.5%, specificity 91.3%, PPV 90.5%, and NPV 91.3%.

Four of the 11 patients with a history of breast cancer had recurrent tumour. In 2 of these 4 patients, PFM failed to detect recurrent carcinoma while suggesting tumour recurrence in 2 of 7 patients with postoperative fibrosis alone. TSM was positive in all 4 patients with recurrent disease and negative in all 7 cases of benign scar tissue. MRM correctly characterised 7 of the 9 lesions with one false positive and one false negative result.

In conclusion, TSM and MRM are both accurate in differentiating benign from malignant breast lesions but TSM is more accurate in evaluating the post-operative and post radiotherapy breast. Because of lower cost, wider availability and high patient acceptance, TSM is superior for the non-invasive characterisation of breast masses, including tumour recurrence and may also have a role in monitoring adjuvant therapy.

P25 Tc-99m-sestamibi scintimammography for the evaluation of breast malignancies

I. Pappo, T. Horne, Y. Horn, R. Orda. *Departments of Surgery "A", Nuclear Medicine and Oncology; Assaf Harofeh Medical Center, Sackler Faculty of Medicine, Tel-Aviv-University, Zerifin, Israel*

We evaluated the efficacy of Tc-99-sestamibi (MIBI) scintimammography for the detection of breast cancer in 351 patients. In two-hundred and twenty five patients with breast abnormalities, the scans were confirmed by histological or cytological results. The other patients who did not have pathological results, were examined because they belonged to high-risk groups, had dense fibroglandular breast or were scanned before starting radiotherapy after having breast lumpectomy.

The mean age of the patients was: 49.8 years (range was: 17–84 years).

The results demonstrated among patients with pathological results, positive scan in 125 women: 86 scans were true positive, while 39 examinations were false positive. In 101 patients scintimammography was negative: 94 examinations were true negative, while in 7 cases the result was false, and the patients suffered of malignant tumor of the breast. Six out of seven false negative results were obtained in patients with non-palpable tumor. Among those patients with pathological results, the obtained sensitivity, specificity, positive and negative predictive values were 92.3%, 70.7%, 68.8% and 93.1% respectively. Total accuracy was: 80%.

Our conclusion from the present study is that MIBI scintimammography is a sensitive and accurate method for the detection of breast malignancies and may be part of the available armamentarium for this purpose.

P26 Evaluation of breast cancer utilizing proton magnetic resonance spectroscopy (MRS)

P.K. Julka, N.R. Jagannathan, M. Singh, P. Raghunathan, O. Coshic, G.K. Rath. *All India Institute of Medical Sciences, New Delhi, India*

This prospective study is to evaluate the response to chemo irradiation in breast cancer utilizing the noninvasive proton MRS. Fortyone patients of infiltrating duct carcinoma of breast were investigated using bilateral breast surface coil. MR image guided in vivo localized NMR spectra were obtained from the tumours and non-tumours portion of the breast of the patients using STEAM RF pulse sequence. The spectra were obtained in pre and post chemo-therapy and radiotherapy settings. Localized proton MR spectra of the unaffected contralateral breast of these patients are dominated by resonances arising from fat and are similar to the breast tissue from normal (control) volunteers, while in the malignant breast tissues the water resonance dominates. Elevated water/fat ratios are measured in malignant tissues, compared with the contralateral unaffected breast tissue of the patients. Statistical analysis of the MRS data demonstrates a decrease in the water/fat ratio in patients receiving full course of chemotherapy compared to the pre-therapy ratio ($p < 0.04$). The observed trend in W/F ratio suggests an attractive marker for diagnosis, prognosis and therapeutic follow-up of breast carcinoma. Further, the water suppressed proton MR spectra of malignant breast tissue reveal several metabolite resonances of low concentration including the choline peak around 3.2 ppm and other minor resonances in the region of 8.5 ppm due to protons of purine and pyrimidine nucleotides, thus providing additional useful markers.

P27 The determination of tissue polypeptide antigen (TPA) in follow-up of breast cancer

R. Findeisen[1], K. Deutschmann[2], B. Richter[2], S. Albrecht[2], W. Distler[2]. *[1]Institute of Clinical Chemistry and Laboratory Diagnostics, Dresden-Friedrichstadt-Hospital, Friedrichstr, 41, D-01067 Dresden, Germany; [2]Department of Gynecology and Obstetrics, Technical University Dresden, Fetscherstr, 74, D-01307 Dresden, Germany*

Breast cancer is one of the most serious diseases in women both in its incidence and death rate. Tumormarker are playing an important role in the follow-up of breast cancer. Giron et al described, that the concentration of TPA in tumor cell cytosol is a good indicator of prognosis (1). Cancer antigen 15-3 (CA 15-3), Carcinoembryonic antigen (CEA) and Tissue polypeptide antigen (TPA) were measured in 464 sera of breast cancer patients and in 71 sera of women without breast cancer. The tumormarkers were determined using immunoluminometric assays (ILMA) manufactured by Buick-Sangtec Diagnostica, Dietzenbach. The assays are characterised by an Interassay-Variance and Intraassay-Variance <4%. The breast cancer patients were staged according to the TNM classification stage 0–IV (by UICC). Median and range of each stage were investigated (2). The cut-off values (95. percentile of tumor-free control group) of CA 15-3, CEA and TPA were determined: specificity, sensitivity, positive, negative predictive value (PV) and efficiency were investigated for these cut-offs and the receiver-operating-characteristic (ROC)-curves were calculated.

Results: The CA 15-3 and TPA median values are measured higher by about 30 percent in patients with stage 0 + 1 than in patients of the tumor-free control