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POSTER

**LOCO-REGIONAL RECURRENCES IN A RANDOMIZED TRIAL OF BREAST CANCER TNM STAGE II—PROGNOSTIC FACTORS**

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Loco-regional recurrence (LR) was studied in 1153 patients with breast cancer all operated with modified mastectomy and randomized into 6 adjuvant treatment groups thus: Premenopausal patients RT and/or Cyclophosphamide; post-menopausal patients RT and/or Tamoxifen. Median observation time 12 years. Recurrence occurred in a total of 460 patients, 128 of whom had LR  $\pm$  distant metastases. The distribution between T1/T2 tumours did not differ in patients with LR compared with the total material. However, premenopausal patients without postoperative RT, with LR had more T2 tumours (83% vs 61%). Patients with LR had significantly more N+ tumours initially compared with the patients in the total study. However, premenopausal patients without postoperative RT did not differ from the patients in the whole study regarding the distribution between N0 and N+.

Premenopausal patients in the total study had significantly more tumours of ductal carcinoma of comedo type compared with the postmenopausal patients (48% vs 35%). Premenopausal patients without postoperative RT with LR had more often tumours of comedo type than those with postoperative RT (61% vs 41%). Postmenopausal patients with or without postoperative RT with LR had significantly more tumours of comedo type than those in the total study (57% vs 35%). Patients with first local recurrence and without progressive disease had a high proportion of lobular tumours (33%), compared with the total study (9%) and all LR (7%).

Unfavourable prognostic factors for developing LR were found in this study to be positive lymph nodes and in postmenopausal patients tumours of comedo type.

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POSTER

**DIAGNOSTIC VALUE OF IMPROVED AGNOR STAINING IN BREAST TUMOR CYTOLOGY**

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The AgNOR technique was applied to cytologic preparations obtained from surgical specimens and fine needle aspiration (FNA) biopsies to evaluate its usefulness in diagnosis of breast lesions. To increase the resolution of AgNORs, some methodological improvements (including hypotonic treatment) were introduced in the processing of surgical and FNA specimens from 60 patients with benign and malignant breast tumors. The nucleoli number, size and shape, and AgNOR pattern (AgNOR number per cell, shape and distribution of AgNOR clusters) were examined. The method appeared to be helpful in distinguishing both between benign and malignant disease, and low and high grade malignancy; its advantage is practical applicability in diagnostic FNA breast cytology.

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PUBLICATION

**IS POSTOPERATIVE MAMMOGRAPHY PRIOR TO DEFINITIVE BREAST IRRADIATION THERAPY USEFUL?**

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Following breast conserving surgery, the presence of abnormalities in postoperative mammography may influence the choice of subsequent treatment. We evaluated 120 pre- and post-operative mammograms of patients who underwent conservative surgery for breast cancer. The median interval between the pre and post-surgical mammograms was 98 days (range, 18–412 days). Clinical records of all patients were reviewed retrospectively. The site of surgery, postoperative complications, histologic characteristics, the dimensions of the resected tissues and the findings on physical examination of the breast before and after surgery were recorded. The pre- and postoperative mammographic findings are analysed and the results compared with the literature.

The purpose of this study was to evaluate the usefulness of postoperative mammography in determining the presence of residual tumor or other abnormalities before starting radiation therapy.

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PUBLICATION

**DIAGNOSIS OF LOCAL RECURRENCE AFTER CONSERVATIVE TREATMENT OF BREAST CANCER**

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Changes in the breast structure after conservative treatment of breast cancer make difficult the follow-up of these patients. The main problem is to differentiate morphological complications (postoperative scar, nodular sclerosis, breast edema) from local recurrence.

64 patients with early breast cancer treated by limited surgery and radiotherapy were followed-up for a medium time of 36 months by: clinical examination, mammography, echography, evaluation of CA 15-3 level and when needed fine needle aspiration and surgical biopsy. The analysis of these diagnostic tools showed that clinical examination proved to be useful especially repeated at short intervals. Mammography alone had a low sensibility and a low positive predictive value, association of echography and fine needle aspiration improved the results and CA 15-3 evaluation had a great sensitivity and specificity. In 9.3% cases diagnosis was possible only by surgical biopsy. 4 patients (6.2%) developed local recurrence in the treated breast within 3 years of initial treatment.

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PUBLICATION

**BCL2 EXPRESSION IN NODE-NEGATIVE BREAST CARCINOMA: A STUDY ON A SERIES OF 190 CASES WITH LONG-TERM FOLLOW-UP**

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**Background:** Bcl2 expression has been demonstrated in breast carcinomas and it has been suggested that Bcl2 expression may be prognostically relevant both in node-negative and node positive tumours. **Aim:** Evaluate the prognostic role of Bcl2 in a series of node negative breast carcinomas (NNBC) and compare it with other prognostic markers [tumor size, grading, estrogen receptor (ER), p53 expression]. **Material & Methods:** The study included a consecutive series of 190 NNBC patients underwent surgery with complete axillary dissection. Eighty cases were treated according to the Milan QUART protocol; 110 were treated with mastectomy. Adjuvant chemotherapy was given to 23 patients, hormoneotherapy to 24. Median follow-up (range) was 60 mos (9–130). Paraffin sections of all tumors were available for immunostaining for Bcl2, ER, and p53. All cases with 20% or more of Bcl2 reactive cells were considered positive. **Results:** 126 cases were Bcl2 positive. Bcl2 expression was associated with ER expression, lack of p53 expression and low grade ( $P < 0.00001, 0.00001, 0.00001$  respectively). No association was seen between Bcl2 expression and relapse free and overall survival (RFS, OS). **Discussion:** The present results are at variance with similar studies on NNBC showing a significant albeit weak association between Bcl2 and RFS and OS.

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PUBLICATION

**OESTROGEN RECEPTOR AND KI67 STATUS IN BREAST CARCINOMAS FOLLOWING PRIMARY CHEMOENDOCRINE THERAPY**

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There has been a paucity of data looking at the effect of chemotherapy on proliferation indices in human breast cancer. We have assessed proliferation index in 155 patients randomised to receive either primary MM (Mitoxantrone, Methotrexate) + Tamoxifen (Tam) prior to surgery (PMT; n = 73, med age 56 yrs) or surgery followed by adjuvant MM + Tam (ADJ; n = 82, med age 55 yrs). Paraffin embedded sections from the surgical excision specimens of both groups were stained immunohistochemically with the MIB-1 monoclonal antibody to Ki67 and a percentage score of positively staining malignant cells obtained. Oestrogen receptor (ER) status was determined by enzyme immunoassay (EIA). ER was not assessable in 9 pts in the PMT arm. Proliferation was significantly lower in the PMT arm (med MIB-1 score 1.7%, range 0–84.5%) compared with the ADJ arm (med MIB-1 score 9.9%, range 0–80%) ( $P = 0.003$ ). In ER positive tumours MIB-1 was significantly

lower in the PMT arm (1.2%) than the ADJ arm (9.45%) ( $P < 0.0001$ ). In ER negative tumours there was no significant difference between the PMT (12.3%) and ADJ (16.1%) arms ( $P = 0.25$ ). These differences indicate that proliferation is reduced following chemo-hormonal therapy but that the effect is largely confined to ER positive tumours. Although the cross sectional nature of the study precludes firm conclusions these data suggest the possibility that in ER negative tumours chemotherapy induced response may be mediated by other processes such as apoptosis. We are currently testing this hypothesis in a prospective longitudinal study.

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PUBLICATION

#### FNA CYTOLOGY IN RELATIONSHIP TO CLINICAL EXAMINATION IN THE DIAGNOSIS OF BREAST CANCER

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In our study we have examined the accuracy of FNA cytodiagnosis in conjunction with clinical diagnosis, in order to attempt to identify patients with primary breast cancer who may be suitable for neoadjuvant therapy without surgical biopsy. A total of 358 patients presented with a palpable breast lump are included in the study. A preliminary diagnosis of clinically benign, suspicious or malignant was made. FNA was performed in 342 patients and the specimens were classified as: benign, suspicious, malignant and inadequate (9%). The accuracy of each assessment was calculated. A positive test in a patient with benign disease was considered a false positive result. FNA cytodiagnosis of definite carcinoma was obtained in 86% of women with breast cancer. Clinical examination by an experienced breast physician together with FNAC detected 99% of the cancers with a 10.4% false positive rate. These results indicate that surgical biopsy rate for diagnosis of breast cancer would be halved if only those patients with suspicious clinical examination or suspicious cytology underwent surgery.

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PUBLICATION

#### SUPER HIGH FREQUENCY (SHF) RADIOTHERMOMETRY FOR EARLY DIAGNOSIS OF BREAST CANCER

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SHF radiothermometry permits to measure temperature distributions in tissues, penetration depth to 20 cm. 1026 pts were involved in the study. Temperature asymmetry (TA)—an absolute examination criterion of pathology—was detected in 12.5%. All the pts have undergone mammography and needle biopsy. A 1.5 – 0.5°C increase and 0.1–0.3°C decrease in temperature was observed in pts with malignant and benign tumors respectively. When there was no TA, histopathological examination showed fibroid tissue without cell proliferation. When TA was present, high proliferation activity was detected. SHF radiothermometry permits to diagnose a benign tumor and to evaluate the grade of proliferation in case of dishormonal hyperplasia in 98.5% and 96.4% cases respectively. So SHF radiothermometry is a simple and secure method for early diagnosis of breast cancer.

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PUBLICATION

#### PROGNOSTIC SIGNIFICANCE OF ESTROGEN RECEPTORS IN 405 PRIMARY BREAST CANCERS (B.C.): A COMPARISON OF IMMUNOHISTOCHEMICAL (ICA) AND BIOCHEMICAL (DCC) METHODS

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ER were determined on 405 primary b.c. by both biochemical and immunoistochemical methods. The aim of this study was to evaluate if one of the two methods is more predictive of prognosis. We considered ERDCC+ if  $\geq 10$  f mol/mg and ERICA+ if  $\geq 45\%$  of cells were stained. Product-limit method and Cox's proportional hazard model were used for the statistical analysis. The median follow-up was 40 months (range 4–95); 98 pts relapsed and 48 died. There is a close association between ERICA and ERDCC (concordance: 81.5%). ERICA status was significantly associated with both DFS and OS (higher in ERICA+); ERDCC status was significantly associated only with OS (higher in ERDCC+). Similar results were obtained when adjustments for the effect of other

prognostic variables (pT, pN, age) were considered. A comparison of DFS and OS when ERICA and ERDCC status were jointly evaluated showed that these methods gave quite similar information on prognosis, so that it is possible to use only one technique.

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PUBLICATION

#### AN EVALUATION OF DNA POLYMERASE $\alpha$ AS A PROGNOSTIC PREDICTOR IN EARLY BREAST CANCER WITH TUMORS SMALLER THAN 2 CM

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We examined the relationship between proliferative activity determined by DNA polymerase  $\alpha$  and clinicopathologic variables in breast cancer patients, and evaluated the usefulness of DNA polymerase  $\alpha$  as a prognostic predictor in 337 early breast cancers with tumors smaller than 2 cm, which had favorable prognoses. About 60% of tumors had lower proliferative activity. A significant correlation was found between DNA polymerase  $\alpha$  and ER, PgR, histological type, or the degree of infiltration into lymphatic vessels which reflect the prognosis. Cancers with higher DNA polymerase  $\alpha$  activity were associated with shorter disease-free and overall survival times. In a multivariate analysis the DNA polymerase  $\alpha$  was found to be an independent and significant factor in early breast cancer.

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PUBLICATION

#### RELATIONSHIP BETWEEN DNA PLOIDY AND DISEASE-FREE SURVIVAL IN NODE-NEGATIVE BREAST CANCER PATIENTS

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Aim of the study is to evaluate prognostic value of DNA ploidy in the group of 106 pts with intraductal invasive adenocarcinoma in stage pT1–2 NO MO and with the Bloom grade II. All pts have been treated by surgery alone. Follow-up was at least 10 years (10–24). Clinical material was subdivided into 2 groups: A—without, B—with dissemination. DNA content was measured by image cytometry. There were 4 types of ploidy: diploidy and low, medium and high grade of aneuploidy. There were significantly higher rate of diploid tumours in the group A (83% vs 17%) and aneuploid tumours in the group B (67% vs 33%). The risk of dissemination was 17% for diploid and 54%, 74%, 100% respectively for aneuploid ones. Among patients with diploidy 83% had 10-years DFS, while nobody from the group of high grade of aneuploidy survive 10 years.

The results suggest that high grade aneuploidy is a significant risk factor for dissemination in node-negative breast cancer patients.

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PUBLICATION

#### CORRELATION BETWEEN PCNA AND FIRST GENERATION MARKERS IN BREAST CANCER PROGNOSIS

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In order to estimate the prognosis of the breast cancer patients, the histologic differentiation, nuclear grade and immunohistochemical assay for proliferating cell nuclear antigen (PCNA) were determined.

The study was randomly done on breast cancer patients in all clinical stages and estimates the correlation between classical histological data with the proliferation activity of the same tumor. The scale of anti-PCNA was between 0–3. In addition, all these parameters were compared, in a multivariate analysis with clinical stage, tumoral volume and axillary lymph node status.

Our results demonstrates that such evaluations might be useful in predicting the risk of progression especially in axillary node-negative (ANN) patients.