Breast Cancer
Breast Cancer – Diagnostic and Prognostic Features

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MALE BREAST CANCER (M.B.C.) : CLINICO-PATHOLOGICAL CHARACTERISTICS AND PROGNOSTIC FACTORS IN 397 CASES

B. CUTULI, M. VELTEN, M. LACROZE, J.M. DILHUYDY, C. ALLAVENA, B. DE LAPONTAN, M. RESBEUT, F. CAMPANA, Y. GRAIC, J. TORTOCHAUX, V. MONCHO-BERNIER, J.C. HORIOT, M. REME-SAUMON, F. LESAUNIER, T. LESIMPLE, J.C. CUILLERE, E. GAMELIN, T.D. N'GUYEN, M. HERY, G.M. JUNG
Centre Paul Strauss 67085 Strasbourg Cedex France and other French Cancer Centers

From 1960 to 1986, 397 non metastatic M.B.C. were treated in 14 French Cancer Centers. TNM showed 7 T0, 79 T1, 162 T2, 31 T3, 74 T4 and 44 Tx. 72 patients had gynecomastia, 22 family history of B.C. and 14 previous cancer. The first symptoms were the tumor (79 %), nipple retraction (10 %), nipple discharge (5.5 %), Paget's disease (2.7 %). 372 patients underwent surgery (49 lumpectomies and 323 mastectomies), with axillary dissection in 320 cases. 271 patients received locoregional irradiation. 71 and 68 underwent chemotherapy or hormonal therapy.
The histology showed 382 infiltrating carcinomas (I.C.) and 15 D.C.I.S.. Lymph node involvement (pN+) was found in 174 I.C. (56 %), with 84 cases of pN > 3. ER and PgR were positive in 79 % and 77 % of cases. Skin, nipple or muscle involvement were present in 100 cases (25 %). 43 patients developed local recurrence (L.R.) ; 31 patients had regional recurrence (R.R.). 29 and 25 patients respectively developed metastases simultaneously or subsequently to L.R. and R.R. 106 other patients developed metastases. 8 patients had contralateral B.C. and 43 (10.6 %) developed a second metachronous cancer
The overall survival rates (O.S.) are 65 % and 38 % at 5 and 10 years. The corrected S.R. are 74 % and 51 % respectively. The O.S. and C.S. rates at 5 years for T0T1, T2 and T3T4 groups are respectively 85 %, 63 %, 51 % and 88 %, 73 %, 65 %. For the pN- and pN+ groups, the O.S. and C.S. at 5 years are respectively 83 % - 93 % and 63 % - 67 %. Histological axillary involvement remains the best prognostic factor. 187 patients died : 113 by cancer (60.5 %), 43 by intercurrent disease (23 %), 19 by second cancer (10 %), 12 by complications or unknown causes (6.5 %). With exclusion of death by intercurrent disease and second cancer, the prognosis of M.B.C. is similar to women. Axillary involvement and positive hormone receptors are very frequent. At the moment, a prospective study is on hand, especially focused on the epidemiologic and therapeutic aspects.
Key words : Breast Cancer - Male - Prognosis

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IMPROVING THE YIELD OF NEEDLE LOCALIZATION BIOPSIES FOR NONPALPABLE BREAST CARCINOMA IN WOMEN.

Sibirsky O.[1], Criciun I.[2], Cohen P.[3], Ron N.[3], Berg D.[4], Manny I.[1], Durst A.[1]
Dep. of Surgery [1], Radiology [2], Pathology [3], Computer Unit [4], Hadassah Med. Organization, Jerusalem, ISRAEL.

Early Ca. in localized stage has favorable prognosis with appropriate surgical management. Its increased frequency of diagnosis in recent years is a tribute to the success of efforts at early detection, especially, mammographically detection of nonpalpable breast lesions. In order to increase the yield and to reduce unnecessary needle localization biopsies (NLB_x) for False-Positive mammograms (M.), we evaluated retrospectively, the personal, familial, and clinical data of 306 women who underwent NLB_x. An experienced radiologist specializing in M. who was blind to the final diagnosis, revised each M., retrospectively. A separte blind review of all operative pathology was done in parallel, and M. characteristics were then compared to pathologic findings, first by Univariate Analysis (X^2,t-TEST) and then, by Multivariate Regression Analysis (MANOVA) that gave the strongest independent varivables that indicated malignent Ca. THE M. VARIABLES: Localizing sign: Mass (Side, Size, Border, Density) Microcalcifications (Size, Shape, Number, Volume, Segmentality, association-with Density) Asymmetric Density, Neodensity, Architectural Distortion, Enlarged Ducts.
Nonfocalizing sign: Abnormal Veins, Skin changes, Nipple and Areolar abnormalisies, Axillary Lymph Nodes (Size, Number, Calcification) Previous breast Bx, Specimen radiography (Margin), and Previous M. (KV, Number), Late mammograms. ; THE LAB. VARIABLES: CA 15-3 levels.
THE PATHOLOGIC VARIABLES: Malignent-Invasive (ductal, lobular, mucinous, papilary, tubular) Non invasive (DCIS, LCIS) Non malignent (Fibrocystic change, Fibroadenoma) Atypia (Hyperplasia -lobular, ductal, florid; Papillomatosis) and Bx.-Size, ER/PR, Mastectomy variables (if done). Malignent CA. was diagnosed in 114 pts. (37.25%). Their pathological specimens colected and a section from one paraffin block per tumor was stained for factor VIII (immunoperoxidase) that stained endothelial cells and angiogenesis was assessed as ve compared microvessel density and number in Invasive CA. Vs. Non-invasive CA. Vs. in Benign findings.
The radiographic features for malignent CA. obtain by our detailed analysis for Nonpalpable Ca. of the breast can enhance the True-Positive rates, and can hint angiogenesis status.

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PROGNOSTIC SIGNIFICANCE BY LEVEL AND NUMBER OF INVOLVED NODES IN 777 CASES OF BREAST CANCER.

GALIMBERTI V, ZURRIDA S, GRECO M and VERONESI U.
Istituto Nazionale Tumori, Milan - ITALY

Axillary lymph node status is still the main parameter for evaluating prognosis of patients affected with breast carcinoma. From January 1983 to December 1986, 777 consecutive cases with positive axillary nodes were treated. In all cases total axillary dissection was performed and the 3 classic axillary levels were identified. We followed the series of patients for a mean period of 60 months to allow us to evaluate the prognostic weight of both the total number of involved nodes and their distribution by level in the axilla. Mean age 52 years (range 23-84). In 223 cases quadrantectomy, and in 552 cases Halsted or Patey mastectomy, were performed. The average number of lymph nodes removed and examined per patient was similar in both treatments (20.6). Of the 777 patients, the 1st level was the site of metastases in 420 cases (54%), the 1st and 2nd levels were involved in 175 cases (22%) and in 183 cases (23%), all 3 levels were affected. Skip metastases were observed in 9 cases (1.0%). The overall survival for patients with metastases to 1-3 nodes was 80%, with 4-10 nodes was 62% and with > 10 nodes was 35%. Considering overall survival by level it was 82% when the 1st level only was involved, 52% when levels I and II were involved and 38% when all 3 levels were involved. The results of this study show that both the total number of involved axillary nodes and th extent of axillary invasion by level separately have clear and strong prognostic significance. Not surprisingly prognostic analysis reveals considerable correspondence between the two ways of evaluating the prognosis.

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IMPROVEMENT IN THE PROGNOSTIC VALUE OF NUCLEAR COMPONENTS OF CYTOLOGICAL-HISTOLOGICAL MSBR GRADING AND ITS DEPENDENT RELATIONSHIP TO PLOIDY AND S-PHASE STATUS IN PRIMARY OPERABLE BREAST CARCINOMA.

Le Doussal V, Spyratos F, Andrieu C, Briffod M. Centre René Huguenin, St-Cloud, France.

Cytoprognostic grading based on nuclear characteristics (pleomorphism and mitosis count) was correlated with MSBR histological grading in 78 cases of operable breast cancer patients. The cytologic material was obtained by fine-needle cytopunctures and the tumors were histologically controled.
Between the two grading systems, the concordance rate was 76%. In addition, the nuclear DNA content was determined by Flowcytometry and Samba Cell Image Analysis in 68 cytologic samples. The S-Phase fraction could be evaluated in only 48/68 cases (70%). We observed a strongly significant relationship between DNA ploidy status and cytological ($P=0.01$) and histological ($p=0.0016$) gradings and similarly between the two gradings and the S-phase fraction ($p=0.009$ and $p=0.0001$ respectively).
These excellent correlations could be specially important for appreciating the prognosis in non operable breast cancer patients by the simple mean of fine-needle cytopuncture.

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S-PHASE FRACTION AND PLOIDY AS INDEPENDENT PROGNOSTIC CRITERIA IN PRIMARY BREAST CANCER AND THEIR CORRELATION TO TUMOR-CELL ASSOCIATED PROTEASES.

Harbeck N., Yamamoto N., Pache L., Schmitt M., *Dettmar P., Jänicke F., *Höfler H., Graeff H. Frauenklinik und *Pathologisches Institut, Technische Universität, Munich, Germany.

We evaluated 153 primary breast tumors for ploidy and S-phase fraction (SPF) by flow cytometry. For extraction of pure nuclei from the paraffin-embedded sections we used our own "improved Hedley's method". Thirty-nine tumors (25%) were diploid, 114 (75%) aneuploid. S-phase fraction was only determined in diploid tumors. It was possible in 35 tumors: 24 (69%) had a low and 11 (31%) had a high SPF using an optimal cutoff of 7 % (CART method). There was no correlation between ploidy status or SPF and established prognostic factors. Ploidy had no significant impact on relapse-free or overall survival. However, S-phase fraction (SPF) in diploid tumors was a significant prognostic factor for relapse-free survival ($p = 0.02$): low SPF was correlated with a significantly longer relapse-free survival. Tumor-cell associated proteases like urokinase-type plasminogen activator (uPA) and its inhibitor PAI-1 are new markers for invasion. In primary breast cancer they have a significant prognostic impact on relapse-free as well as overall survival. There is no correlation between uPA and established prognostic factors. However, we found a significant positive correlation between PAI-1 and S-phase fraction ($p < 0.05$). Thus, PAI-1 might be a marker for metastasis as well as for proliferation.

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C-erbB2 GENE AMPLIFICATION, AN INDEPENDENT PROGNOSTIC INDICATOR IN NODE-POSITIVE AND NODE-NEGATIVE BREAST CANCERS.

S Prost, M G Lê, S Douc-Rasy, M Gabillot, M Guérin & G Riou. Institut Gustave Roussy, 94800 Villejuif (France).

The aim of our study was to evaluate the prognostic value of the c-erbB2 gene amplification in breast cancer. Gene amplification was analysed by Southern blot hybridization in tumours from 178 patients treated at the Institut Gustave Roussy (mean follow up, 60 months). The relative risks of death and overall relapse were evaluated using the regression model of Cox taking into account the main confounders (age, grading, lymph node status, hormonal receptor status, tumour size and geographical origin of patients). C-erbB2 gene amplification was found to be an independent indicator of poor prognosis for survival but not for overall relapse: however, the patients with c-erbB2 gene amplification had a 5-fold higher risk ($p<0.001$; 95% confidence interval 1.7-16.0) to develop synchroneously multiple distant metastases than other patients. Conclusion: c-erbB2 gene status is a powerful prognostic indicator that might be applied in routine.