PP-9-10 The Prognostic Significance of Protein Tyrosin Kinase, ER, PR, and the Mitotic Activity Index in 86 Primary Breast Cancer Patients

J. Bayrak, M.A. Blankenstein, A. Hennipman, G. Rijksen, Ch. Gimbrère, H. Struikmans*. *University Hospital, Dept. of Radiotherapy, Utrecht (NL)*

In 86 primary breast cancer patients, we evaluated the prognostic significance of PTK (n = 81), ER (n = 83), PR (n = 83), and the mitotic activity index (n = 60). We compared the prognostic significance of these variables with classical prognosticators like; menopausal status, T-stage, N-stage, and histological grading according to Bloom and Richardson.

Protein tyrosin kinases (PTK) are enzymes which phosforylate proteins on tyrosine. These enzymes form an important part of signal tranduction pathways leading to cell proliferation. PTK activities were assayed in cytosolic extracts according to a non-radioactive dot blot method. Estrogen (ER) and Progesterone receptor (PR) levels were measured by enzyme immuno assay in cytosolic fractions. The mitotic activity index (MAI) was defined as the number of mitotic figures per 10 high power fields (HPF). The median follow up period was 30 months (range: 4–50).

After univariate analysis, disease free survival (DFS) was found to be correlated significantly ($p < 0.05$) to: T-stage, N-stage, histological grading, and ER (cut off point: 100 fmol/mg). After multivariate analysis, T-stage, N-stage, and ER (cut off point: 100 fmol/mg) appeared to be independent prognostic factors ($p < 0.05$). According to these preliminary results we demonstrated that PTK, PR and MAI, in contrast to ER, have no additional prognostic significance, with regard to DFS. We will continue this study with a longer follow up and a greater (approximately 500) number of patients.

PP-9-11 Oncogene Evaluation (c-int2, c-erb B2, c-myc) in 265 Breast Carcinoma pT1–T2, pN0–N1, M0

M. Bolla [1], M. Chedin* [1], V. Cunin [1], P. Winckel [2], F. Merlin [1], H. Roth [1], E. Chambaz [1]. [1] *Unite de concertation et laboratoire de biochimie, CHU Grenoble;* [2] *Clinique du mail Grenoble*

Current prognostic factors in breast cancer concern tumoral size (pT), axillary node status (pN), Scarff-Bloom grading and hormonal receptor status. This study was undertaken to evaluate metastatic power of oncogenic parameters as c-int2, c-erbB2, c-myc which are often amplificated in breast cancer.

For the assay, DNA extraction was followed by slot-blot (erbB2, int2) or southern-blot (myc) hybridization method. Semi quantitative evaluation was made by densitometry. Results differ from 0 (no amplification) to amplification level 2–3 (+), 4–5 (++), > 6 (+++).

From 1987 to 1989, 265 invasif breast carcinomas were included in this study: 61.9% of patients were menopaused, 50.2% were axillary nodes noted as pN0, 78.1% were RE+, 34% of patients were Scarff-Bloom grade I, 38.1% grade II and 23.8% grade III. With a median follow-up of 57 months (0–89), 59 relapses were registered. In this study, patients with worse pronostic (pN1b, Scarff-Bloom III, RE-) received medical adjuvant treatment.

Amplification rate to int-2, erbB2, myc was respectively 9.4%, 14.3%, 21%. In univariate survival analysis, erbB2 and myc showed significant association ($p = 0.0009$ and $p = 0.0055$ respectively) when we consider amplification results as four classes (0/+/++/+++).

In contrast the Cox regression model with conventionnal disease parameters do not show significant association whatever the oncogene. Only pN, RE, pT have significative value.

PP-9-12 Breast Cancer Oestrogen-Receptor Negative Tumors, PS_2 Expression and DFI

S. Filipović*, B. Filipović, R. Ilić, R. Djordjević, S. Vrbić, I. Pejčić, S. Veselinović, D. Stojanović. *Clinic of Oncology-University Clinical Center-Niš*

PS_2 protein expression has been reported to have prognostic significance in human breast carcinomas and to correlate with estrogen receptor positivity.

We have examined PS_2 expression in 183 primary NØER+ breast cancer and in 119 NØER− breast cancer and related PS_2 expression to disease behaviour-Cut off point for PS_2 to discriminate between positive and negative was 12 ng/mg protein. Follow up — 5 years.

In group NØER+ 112/183 (66.6%) were PS_2+ ($PS_2 > 12$ ng/mg protein). In group NØER − 18/119 (15.1%) were PS_2+ PS_2+ was associated with good prognosis in the group NØER+ were only 13/112 (11.6%) had recurrence of their disease. In group NØER − 11/18 (61.1%) (NØER − $PS_2 > 12$ ng/mg protein) had recurrence compared with 36/101 (45.6%) (NØER − $PS_2 < 12$ ng/mg protein).

In patient with oestrogen-receptor negative tumors, PS_2 expression predicted a shorter DFI.

PP-9-13 High Positive Rate of PS2 Expression in Forefront Intraductal Cancerous Area in Breast Cancer

T. Yamakawa* [1,2], T. Morimoto [3], M. Sasa [1], S. Numoto [4], Y. Monden [1]. [1] *The Second Department of Surgery, School of Medicine, Tokushima, Japan;* [3] *School of Medical Science, The University of Tokushima, Tokushima, Japan;* [2] *The Department of Surgery Kochi Municipal Hospital, Kochi, Japan;* [4] *The Department of Pathology, Kochi Municipal Hospital, Kochi, Japan*

Multiple sections of 40 consecutive cases with invasive ductal carcinoma of the breast, all of which had wide intraductal cancerous extension, were examined by immunohistochemical analysis for evaluation of hormone dependency in several areas of breast cancer tissues. In this study, we examined the expression of pS2 protein in the central invasive area (CIV), central intraductal cancerous area (CDC) and forefront intraductal cancerous area (FDC). pS2 staining was positive in 52.5% (21/40) of CIV and a significant correlation was found between pS2 expression in CIV and the estrogen receptor status (ER). pS2 staining was positive in 77.5% of CDC and 85.0% of FDC, respectively. A majority (68.4%) of the cases that were negative pS2 in CIV were positive for pS2 in FDC. Moreover, the cases with noncomedo intraductal carcinoma in premenopausal status showed a higher positivity of pS2 expression in FDC than the cases with comedo-carcinoma, though the number of cases of comedo-carcinoma was limited. These findings suggest that endocrine therapy may be useful after breast conserving treatment regardless of the ER status of the primary tumor.

PP-9-14 Clinical Significance of Pyrimidine Nucleoside Phosphorylase Staining in Breast Cancer

S. Tanaka*, T. Kimura [1], R. Miyakawa [1], T. Kamio [1], T. Kato [1], K. Yamamoto [1], S. Kameoka [1], K. Hamano [1], S. Murase, H. Kuramitsu. *Dept. of Surgery, Ushiku Aiwa General Hospital, Ibaraki Pref., 300-12 Japan;* [1] *Dept. of Surgery II, Tokyo Women's Medical College, Tokyo, 162 Japan*

Pyrimidine Nucleoside Phosphorylase (PyNPase) is a synthetic enzyme of converted nuclear acid. Some clinicians found that high PyNPase activity in malignant tumors led to metastasis and cachexia. In a previous study we measured the PyNPase activity of breast cancer tissues and investigated its correlation with other prognostic factors. We found that the lymph-node metastases cases and the lymphatic vessel invasion positive cases were higher than the negative cases ($P = 0.00766$, $P = 0.00095$). So, it is clear that PyNPase activity has a clinical significance as a promising prognostic factor in breast cancer. This enzyme is heterogeneous and present in tumorous tissues.

Therefore, it is important to investigate PyNPase activity correlation with PyNPase staining. We found that the group with higher PyNPase activities had shown more highly stained tissues. From these results, we feel that PyNPase staining is a more useful, simple, and speedy method than measuring of PyNPase activity.

PP-9-15 Analysis of Angiogenesis, PCNA, c-*er b* B-2, and p53 Associated with Long-Term Survival in Japanese Women with Breast Cancer

T. Kato*, T. Kimura, R. Miyakawa, S. Tanaka, H. Muraki, T. Kamio, A. Fujii, K. Yamamoto, S. Kameoka, K. Hamano, M. Kawakami. *Dept. of Surgery II, Tokyo Women's Medical College, Tokyo, Japan*

To evaluate the clinicopathological significance of angiogenesis, we immunohistochemically stained one representative section of the breast tumor with factor VIII-related antigen staining. There were 109 patients with breast cancer from 1971 to 1979. We examined the relationship between microvessel count (MVC) and PCNA, c-*er b* B-2, p53, and other conventional factors. There was no relationship between MVC and PCNA, c-*er b* B.2, p53, age, menopause, clinical tumor size (T), histological classification, nuclear grade, node metastasis, histological grade, mitosis index, necrosis, and lymphatic invasion. However, there was a relationship between MVC and blood vessel invasion ($p < 0.02$). MVC, PCNA, c-*er b* B-2, and p53 were compared with the overall survival rate at 20 years by logrank analysis. A 20-year cumulative survival rate in the two groups of MVC, PCNA, and p53 were statistically significant, while the rate of c-*er b* B-2 was not significant. Cox's multivariate analysis was also performed. T ($p = 0.0187$),

MVC (p = 0.0365), and node metastasis (p = 0.0418) were independent prognostic indicators. However, we cannot confirm PCNA, p53 as significant independent prognostic factors.

PP-9-16 Low and High Molecular Weight Cytokeratins Express the Differentiation of Invasive Breast Carcinoma

H. Takei*[1], Y. Iino[1], T. Yokoe[2], J. Horiguchi[1], M. Maemura[1], Y. Morishita[1]. [1] *2nd Dept. of Surgery, Gunma University School of Medicine, Maebashi, Gunma, Japan;* [2] *Emergency and Critical Care Medicine, Gunma University School of Medicine, Maebashi, Gunma, Japan*

Low molecular weight cytokeratin (LCK) and high molecular weight cytokeratin (HCK) were determined by immunohistochemistry in 90 operable invasive breast carcinomas (IBCs). Fifty nine (65.6%) of 90 tumors were LCK-positive, and 19 (21.1%) HCK-positive. The incidence of LCK positivity was inversely correlated with nuclear grade. Whereas, the incidence of HCK positivity was positively correlated with nuclear grade. The positive correlation between the incidence of LCK positivity and that of estrogen receptor (ER) positivity was found. Whereas the inverse correlation was found between the incidence of HCK positivity and that of ER positivity. The mean level of ER contents (101.9 fmol/mg protein) in LCK-positive tumors was significantly higher than that (20.8 fmol/mg protein) in LCK-negative tumors. However, the mean level of ER contents (10.1 fmol/mg protein) in HCK-positive tumors was significantly lower than that (91.2 fmol/mg protein) in HCK-negative tumors. From the results of this study, the inverse correlation is observed between the immunoreactivity of LCK and that of HCK as the differentiation markers of IBC.

PP-9-17 PCNA Labeling Index and Expression of pS2 and c-*erbB*-2 Protein in Primary Breast Cancer

Jun Horiguchi*, Yuichi Iino, Hiroyuki Takei, Michio Maemura, Takayuki Kano, Yoshio Horii, Masahiro Nagasawa, Hiroshi Matsumoto, Takao Yokoe, Yasuo Morishita. *Second Department of Surgery, Gunma University School of Medicine, Japan*

Proliferating cell nuclear antigen (PCNA) labeling index and expression of pS2 estrogen inducible protein and c-*erbB*-2 protein were examined by immunohistochemistry in 99 primary breast carcinomas. PCNA labeling index ranged from 2 to 76 (mean 25.9). Immunohistochemical positivity with pS2 and c-*erbB*-2 was 57.6% and 17.2%, respectively. There was no relationship between PCNA labeling index and age, tumor size, or lymph node involvement. PCNA labeling index was elevated in high ER level (more than 100 fmol/mg cytosol protein) tumors, compared with low ER level ones. PCNA labeling index was not associated with pS2 immunostaining, however, PCNA labeling index was higher in c-*erbB*-2 positive tumors than negative ones. Patients were divided into two groups according to PCNA labeling index: Low (PCNA < 25%) and high proliferating group (PCNA ≥ 25%). The high proliferating group had a significantly worse overall and disease-free survival rate than the low group.

PP-9-18 French Association of Cytometry Quality Control Report on FCM-DNA Content and S-phase Fraction

J.-L. D'Hautcourt[1], F. Spyratos*[2], P. Vago[3], A. Chassevent[4], On behalf of the Association Française de Cytométrie (AFC). [1] *Clinique St-Joseph, Mons, Belgique, France;* [2] *Centre R. Huguenin, St-Cloud, France;* [3] *INSERM U 254, Montpellier, France;* [4] *Centre P. Papin, Angers, France*

The objective of the first AFC quality control trial was to assess the role of computer software in interpreting FCM-DNA data. Two diskettes, containing 10 files acquired in list mode (LM) and 10 histogram files (H) derived from analyses of various unfixed tumour specimens, were sent to 32 French, Belgian and Swiss laboratories with varying degrees of expertise. 610 responses were obtained from three different computer softwares: Cellfit (44%), Multicycle (44%), and Modfit (12%). 31% of responses were excluded from the final analysis due to inadequate training in how to use the software, or failure to grasp the biological significance of the results. Responses obtained from laboratories that complied with consensus recommendations were remarkably homogeneous, thus demonstrating the feasibility of standardization. A second quality control trial has been carried out in February 1996, and a second set of diskettes, together with a standardized procedure of treatment, has been sent to 58 laboratories willing to participate. The results of both trials will be reported and discussed.

PP-10. Miscellaneous Posters

PP-10-1 Communicating the Results of Breast Biopsies Over the Telephone and in Person. Is there a Difference?

L. Campbell*, R.M. Watkins, C. Teasdale. *Directorate of Surgery, Derriford Hospital, Plymouth PL6 8DH*

Current BASO guidelines suggest that the results of breast biopsy should be given to patients in person. This retrospective study investigates the opinions of patients given their result over the telephone shortly after their biopsy or told in person at a later date. 202 women who had biopsies of impalpable lesions between September 1993 and September 1994 were sent questionnaires. 171 (84%) were returned. 52 (30%) of these patients lived more than 20 miles from the hospital. 76 patients were telephoned with their results. 70 (92%) felt they preferred this. Only three patients with malignant disease said that they would have preferred to wait and hear in person. (Three patients did not know.) 95 patients were told their result in person. 59 (62%) found this satisfactory, but 18 (19%) would rather have heard earlier over the telephone, including 11 patients with malignant disease. (18 did not know.) Overall 91% of patients telephoned with benign results were happy with this. 88% of patients telephoned with malignant results were also satisfied. 19% of patients told personally would have preferred to hear results earlier by telephone, including eleven patients with malignant disease. Telephoning patients may be acceptable in selected cases. A larger prospective trial is required to assess these findings in detail.

PP-10-2 Evaluation of Quality of Life After Conservative Treatment for Intraductal Carcinoma of the Breast

O. Caffo*[1], M. Amichetti[1], M. Arcicasa[2], M. Roncadin[2], A. Rigon[3], O. Lora[3], G. Zini[4], F. Coghetto[5], P.L. Zorat[5]. [1] *Dept. of Radiation Oncology of Trento,* [2] *Dept. of Radiation Oncology of Aviano,* [3] *Dept. of Radiation Oncology of Padova,* [4] *Dept. of Radiation Oncology of Reggio Emilia,* [5] *Dept. of Radiation Oncology of Treviso, Italy*

Purpose: To retrospectively evaluate quality of life (QoL) in patients with ductal carcinoma in situ of the breast (DCIS) treated with conservative surgery plus radiotherapy.

Patients and method: We used a self-compilative validated questionnaire listing a series of 34 items, exploring physical and psychological well-being, sexual adjustment, body image changes, relational life, general life adjustment and level of information about treatment. 82 questionnaires were mailed to DCIS patients treated from 1981 to 1990. To state, 51 questionnaires (62%) has been returned.

Results: The physical well-being was good for most of the patients: only 10% felt ill. In the field of psychological well-being more than 50% of the patients declared to be well, excepting for anxiety found in 55% of the sample. Ten percent of the sexually active women experienced some sexual change. Only 20% of the sample felt a change in body image, but 65% thought that their treated breast was not similar to the untreated one. Very few women experienced a limitation in relational life. About 70% of the sample declared to have a good information about therapies.

Conclusion: In our experience, QoL after CT for DCIS was generally good. This finding can be of value in patient counselling the appropriate treatment.

PP-10-3 Psychologic Impact of Breast Cancer Diagnosis: Coping Strategies

F. Cousson*[1], J.M. Dilhuydy[2], M. Bruchon-Schweitzer[1]. [1] *Université de Bordeaux II, 33076 Bordeaux, France;* [2] *Institut Bergonié, Regional Cancer Center, 33076 Bordeaux, France*

The aim of this prospective research is to investigate and clarify the structure of coping strategies set up by patients just after the announcement of breast cancer diagnosis and to know if the preexisting psychosocial and medical patient characteristics have an effect on the development of their coping strategies. From March 1993 to June 1995, 80 breast cancer patients (T2 > 30 mm, T3 and T4) (age: 30–70 y) treated with neoadjuvant chemotherapy and adjusted locoregional treatment have been included. The data relative to sociobiographical and personality trait factors (anxiety, body