(range: 13–80 months), 41 patients (24.8%) had recurrent disease and 26 patients (15.7%) died due to recurrent breast cancer. EGFR expression was a significant prognostic factor for the disease free and overall survival of the patients together with lymph node metastasis and Ki67 labeling index in univariate survival analysis but lymph node metastasis was an only significant prognostic factor in multivariate analysis.

Conclusions: EGFR expression was independent of EGFR gene amplification and was intimately associated with HER2 amplification and overexpression. Low frequency of EGFR gene amplification hampers its clinical utility as a tool to identify proper patient population for the specific treatment. In contrast, EGFR protein expression seems to have a role as a useful predictive factor if it is rationally integrated with other biologic predictive factors.

258 Poster

Prevalence of breast cancer-susceptible mutations in women < 36 years with invasive breast cancer and correlation with histopathology features of the primary cancer

A. Chan[1], C. Metcalf[1], P. Watt[1], G. Longman[1], J. Goldblatt[2], I. Walpole[2], E. Edkins[2], C. Saunders[1]. [1]*Royal Perth Hospital, Multidisciplinary Breast Service, Perth, Australia;* [2]*King Edward Memorial Hospital, Genetic Services, Perth, Australia*

The presence of breast cancer-susceptible genetic mutations BRCA1 and 2 is associated with an increased incidence of early-onset breast cancer. Certain histopathological features (higher grade, hormone receptor negativity, medullary or tubulo-lobular type, 'pushing edge' margins and lymphocytic infiltration) are more commonly seen in BRCA-associated cancers. This prospective study assessed whether the presence of these histopathological features was predictive of a BRCA mutation, irrespective of family history of breast or ovarian cancer.

Method: Consecutive patients with breast cancer diagnosed <36y in Perth, Australia were included. Demographic data including validated family history were obtained. Primary breast pathology was reviewed by a single pathologist. Assessment for BRCA mutations were performed by protein truncation test (PTT), denaturing high pressure liquid chromatography (D-HPLC) and multiplex amplifiable probe hybridisation (MAPH). Patients were interviewed by a clinical psychologist before and after receipt of genetic testing results to assess for anxiety and depression.

Results: From November 2002 to August 2004, 47 women aged <36y at breast cancer diagnosis consented to enter the study. Risk factors for breast cancer included Nulliparity 6(12.8%), First full term pregnancy over age 30y 6 (12.8%), 1 relative with breast cancer 20 (42.6%), 2 or more relatives with breast cancer 7 (14.9%). Three patients had bilateral breast cancer. Complete histopathological review is available in 38 patients thus far. Breast cancer pathology was invasive ductal in 35 (92.1%), mixed ductal-lobular 2(5.3%) and medullary 1 (2.6%). The grade was 1, 2 and 3 in 10.8%, 27% and 62.2% respectively. Pushing margins seen in 15 (44.1%). Peritumoral lymphocytic infiltration in 24 (70.6%). ER negative 48.6%, PR negative 50% and Her2 neu 3+ 10.3%. Genetic testing result is currently available for 43 pts. A breast cancer-susceptible genetic mutation was identified in 6 pts (13.7%); 5 (11.4%) BRCA1 and 1 (2.3%) germ-line p53.

Conclusion: The presence of a breast cancer-susceptible genetic mutation in this cohort of early-onset breast cancer was much greater than the anticipated 5% rate in the general population of breast cancer patients. Correlation of the presence of a mutation with the histopathological features of the primary breast cancer for all patients will be presented. Impact of genetic testing on levels of anxiety and depression will be reported.

259 Poster

Comparative study of immunohistochemical phenotype in primary breast cancer tissues and lymph node metastases

G. Burkadze[1], G. Turashvili[2]. [1]*Tbilisi State Medical University, Dept. of Pathological Anatomy, Tbilisi, Georgia;* [2]*Palacky University, Institute of Pathology, Olomouc, Czech Republic*

Background: Nowadays, in breast cancer patients the immunohistochemical profile of primary cancer tissue is important to determine tumor prognosis and particular treatment strategies. However, potential changes in heterogeneity of tumor cells leads us to consider a hypothesis that immunohistochemical expression of these proteins is permanently modifying during cancer development and spread.

Methods: Immunohistochemical examination with monoclonal antibodies against Ki-67, p53, ER and PgR was performed in 98 lymph node-positive invasive breast carcinomas. Both primary tumor tissues and positive lymph nodes were studied.

Results: 14 primary tumors were ER+PgR+, 38 were ER-PgR-, 17 were ER+PgR-, and 29 were ER-PgR+. Lymph node metastases were ER+PgR+ in 9 cases out of 14 ER+PgR+ patients, ER-PgR- in 31 cases out of 38 ER-PgR- patients, ER+PgR- in 11 cases out of 17 ER-PgR- patients, and ER-PgR+ in 22 cases out of 29 ER-PgR- patients. In primary tumor tissues, p53 was positive in 2 ER+PgR+ cases, 35 ER-PgR- cases, 13 ER+PgR- cases, and 27 ER-PgR+ cases. In lymph node metastases, p53 was positive in 1 out of 2 p53+ and ER+PgR+ cases, 28 out of 35 ER-PgR- cases, 9 out of 13 ER+PgR- cases, and 24 out of 27 ER-PgR+ cases. The proliferation index measured by Ki-67 expression in tumor cells was significantly higher in positive lymph nodes than in the primary tumor (32.6% vs 20.5%).

Conclusion: These results suggest the modification of immunohistochemical expression of Ki-67, p53, ER and PgR between primary tumor tissues and lymph node metastases. It seems that metastatic tumor cells show a higher proliferation activity and perhaps aggressiveness in comparison with the primary cancer cells. These differences in proliferation activity might be taken into account when considering the choice of the adjuvant therapy.

260 Poster

Atypical Ductular Hyperplasia (ADH); review of 174 cases diagnosed in a series of 1295 macrobiopsies in a single institution

M.C. Baranzelli, V. Cabaret, M. Chauvet, L. Ceugnart, S. Giard, Y. Belkacemi, J. Bonneterre. *Centre Oscar Lambret, Lille cedex, France*

The diagnosis of ADH on a biopsy is often difficult; the final diagnosis may be different from the one obtained after biopsy. The aim of this study was 1- to compare the diagnosis on the biopsy and after surgery, 2- to evaluate the inter individual reproducibility of the pathological diagnosis.

Patients and Methods: between February 2000 and October 2003, 1295 macrobiopsies have been performed in the centre Oscar Lambret. A diagnosis of ADH according to Page and Tavassoli criteria has been done in 174 patients (13.4%). An evaluable tumorectomy has been performed in 68 cases; the reason for no available surgical specimen in 106 cases was either tumorectomy outside of our center or patient's refusal. A total inclusion of the surgical specimen was performed in 59 cases; in the 9 other cases it was not specified in the pathological reports.

Results: The macrobiopsy scar was found in 55 cases. In 19 patients (26%), the final diagnosis was worse: ductal carcinoma in situ (DCIS) (18), (low grade: 8, intermediate: 7, high grade: 3), and one invasive carcinoma. In 30 patients (44%), preneoplasic lesions were found: ADH (24), lobular neoplasia (LN) (4), flat epithelial atypia (2). In 19 patients (28%), there was only either an usual ductal hyperplasia (UDH) (6), or a fibrocystic dystrophy (13). All the macrobiopsies have been reviewed by two pathologists: 13 out of the 19 cases for whom the final diagnosis was worse have been considered as DCSI (low grade: 6, intermediate: 7); the 6 other cases were considered as initially as ADH. Out of 19 biopsies in which either UDH or fibrocystic dysplasia had been diagnosed on the surgical specimen, after review 6 were considered as UDH. In 4 cases in which the final diagnosis was LN, the retrospective review was ADH. Overall, the diagnosis was truely underevaluated in 7 pts among 72 (10%).

Conclusions: The pathological diagnosis at biopsy is limited by the heterogeneity of the lesions and of the specimens; the interindividual reproducibility has to be further improved; the diagnosis on biopsy specimens should be performed only by trained pathologists.

261 Poster

Prognostic value of Mib1 in a tissue microarray of 855 invasive breast carcinomas

G. MacGrogan[1], M. Desrousseaux[1], I. de Mascarel[1], S. Mathoulin Pélissier[2], M. Debled[3], L. Mauriac[3], M. Durand[3], C. Tunon de Lara[4], H. Laharie Mineur[5], V. Brouste[2]. [1]*Institut Bergonié, Pathology, Bordeaux, France;* [2]*Institut Bergonié, Biostatistics, Bordeaux;* [3]*Institut Bergonié, Oncology, Bordeaux;* [4]*Institut Bergonié, Surgery, Bordeaux;* [5]*Institut Bergonié, Radiotherapy, Bordeaux, France*

Introduction: Grade and mitotic count are important prognostic factors in breast cancer but may be difficult to appreciate in microbiopsy samples. Mib1 may be an alternative to measure proliferation in this setting.

Design: A tissue Microarray (TMA) comprising four 0.6 mm diameter tissue cores of 855 consecutive invasive ductal carcinomas operated on between 01/01/1989 and 12/31/1992 was constructed. Immunohistochemistry for Estrogen Receptor (ER)(1D5), Progesterone Receptor (PR)(PGR636), Her2neu (DA485) and Mib1 was performed. A cut-off of 10% positive tumour cells was chosen for ER and PR. The Herceptest scoring system was used for Her2neu. For Mib1 a cut-off of 20% positive tumour cells corresponding to the 75th percentile in the series was chosen. The prognostic value (probability of metastasis) of these factors as well as patient's age, tumour size, axillary lymph node status (N status), modified Scarff Bloom and Richardson (SBR) grade and peritumoral vascular emboli

were assessed by univariate analysis (Log Rank test) and multivariate analysis (Cox model). Median follow-up was 150(147–152) months.

Results: By univariate analysis, age[(≤40 vs >40 yrs) p = 1.6 10−7], tumour size [(≤20 vs >20 mm) p = 1.1 10−15], modified SBR grade [p = 4.5 10−10], peritumoral vascular emboli [p = 8.9 10−13], N status [p = 4.6 10−13], ER [(<10%vs ≥10%) p = 0.01], PR [(<10% vs ≥10%) p = 0.003], Her2neu [(0+ vs 2+ and 3+) p = 0.0003] and Mib1 [(<20% vs ≥20%) p = 7.5 10−8] were significantly associated with probability of metastasis.

By Cox analysis, the final model showed as independent factors, tumour size [OR = 2.16(1.63–2.86) p < 10−3], vascular emboli [OR = 1.8(1.38–2.42) p < 10−3], N status [OR = 1.8(1.35–2.45) p < 10−3], age [OR = 1.8(1.24–2.67) p = 0.002], Her2neu [OR = 1.58(1.09–2.29) p = 0.015] and grade [OR = 1.7(1.04–2.75) p = 0.03]. Mib1 was selected in this model but was not statistically significant [OR = 1.31(0.96–1.79) p = 0.08].

Conclusion: Mib1 may represent an alternative to grade for prognostication in breast cancer however it did not surpass this factor in this series.

262 Poster

B3 or B4 core breast biopsies: Are they indeterminate?

B. Piramanayagam[1], S. Raman[1], B. Soman[1], F. McGinty[2], J. Donnelly[1], A. Corder[1]. [1]*Hereford County Hospital, General surgery, Hereford, United Kingdom;* [2]*Hereford County Hospital, Pathology, Hereford, United Kingdom*

Introduction: Histological diagnosis is essential in definitive management of breast lesions. However, a small proportion of core biopsies are reported in the uncertain categories (B3 & B4), which can lead to therapeutic dilemmas for the clinician. Our study aims to evaluate the predictive value of these indeterminate biopsies.

Methods: A prospectively maintained BASO database was used to identify patients with B3 or B4 breast core biopsies between Jun-02 and May-05. The retrieved data was analysed using MS Excel®.

Results: Thirty-three patients (21 B3 and 12 B4) were identified during this 3-year study period. The median age was 60 years and in 30 patients, a breast lump was the primary symptom at presentation.

Excision biopsy was performed in 22 patients. Seventeen patients (6 B3 & 11 B4) were identified to have invasive breast cancer or DCIS on subsequent assessment, yielding a positive predictive value of 29% (B3) and 92% (B4).

Patients with age > 70 years seemed to have an increased incidence of invasive cancer. Malignancy was more likely when associated with a high clinical and radiological (P4/5; R4/5) score. It was also evident that FNAC complemented the diagnostic accuracy of core biopsies.

Conclusion: The positive predictive value for diagnosing malignancy is high following a B4 core biopsy and in patients over 70 years. Also, diagnostic accuracy is superior in the presence of a high clinical, radiological and/or cytological score. Further biopsies or advanced imaging may be essential prior to definitive management in these indeterminate lesions.

263 Poster

The histopathological profile of gestational breast cancer

C. Saunders[1], A. Ives[2], J. Harvey[1], G. Sterrett[3], J. Semmens[2]. [1]*University of Western Australia, School of Surgery & Pathology M509, Perth, Australia;* [2]*University of Western Australia, School of Population Health, Perth, Australia;* [3]*PathWest, Perth, Australia*

Few studies have reported on the pathology of gestational breast cancer (GBC) and most have been limited to a basic description. The only reported case-control study was very small (n = 27). It has been reported that GBC is more aggressive, with low expression of hormone receptors.

The aim of this study to establish whether there were any pathological characteristics identified that are unique to gestational breast cancer and which can be related to the disease outcome.

A comparison was made between the pathology from women diagnosed with GBC and women age and date of diagnosis matched diagnosed with non-GBC. GBC cases were identified from the Western Australian Gestational Breast Cancer Project and the non-GBC cases were identified from the PathWest archives. The pathology specimens were retrieved, re-reviewed and where necessary re-staining for hormone receptors was undertaken.

One hundred and twenty (120) GBC cases and 240 non-GBC cases were identified. Tumour size for the GBC cases ranged from 1 to 120 mm (median 20 mm) and lymph node positive status was similar for GBC cases (55%) and non-GBC cases (53%). Proportionally more GBC cases (69%) were histological grade III than non-GBC cases (57%). Analysis of the data continues and will be reported at the conference.

Our preliminary results conclude that women with GBC do have a more aggressive phenotype.

264 Poster

Expression of estrogen receptors alpha and beta (ERa and ERb) and progesterone receptor (PgR) in male breast cancer

M. Litwiniuk[1], M. Teresiak[2], D. Breborowicz[2], V. Filas[1], J. Moczko[1], J. Breborowicz[1]. [1]*Poznan University of Medical Sciences, Poznan, Poland;* [2]*Wielkopolska Cancer Center, Poznan, Poland*

Background: Male breast cancer (MBC) is a rare disease, accounting for only 1% of all breast cancers. Therefore, carcinoma of male breast has not been studied as extensively as carcinoma of the female breast (FBC). Steroid hormone receptors are more frequently positive in MBC than in FBC. The identification of the second human estrogen receptor, ERβ, raised a question of its role in male breast cancer.

The aim of this work was to determine the extent of ERβ expression in male breast cancer and to determine if ERβ expression is correlated with some clinical parameters and biological markers.

Material and Methods: Formalin-fixed, paraffin embedded breast cancer tissues from 28 male patients were used in this study. Immunostaining for ERa, ERβ and PgR (progesterone receptor) was performed using monoclonal antibodies against ERa, PgR (DakoCytomation), and against ERβ (CHEMICON). The EnVision detection system was applied. The study population comprised a control group of 120 women with breast cancer who had been operated in our clinic. The data were analyzed using a nonparametric Fisher-Freeman-Halton test; the statistical significance was considered when $p < 0.05$.

Results: MBC: 67% of tumors were ERa positive, 78.6% were PgR positive and 64.3% were ERβ positive; FBC: 57.5% of tumors were ERa positive, 64% were PgR positive and 55% were ERβ positive. As many as 14% of both MBC and FBC of ERβ positive tumors showed no expression of ERa. In male breast cancer correlations between tumor size, lymph nodes status, grade of malignance, p53, Ki-67 and expression of ERβ were not significant.

Conclusions: The expression of ERβ, like this of ERa, was more frequently positive in MBC than in FBC. In male breast cancer the expression of ERβ was also present in a noticeable proportion of ERa negative tumors. It may eventually result in new strategies in the hormonal treatment of male breast cancer.

265 Poster

Metastatic models in different histologic types of breast lobular carcinoma

R. Balan[1], C. Amalinei[1], F. Pricop[2], F. Dumitrache[2], C. Cotutiu[1]. [1]*University of Medicine and Pharmacy, Pathology, Iasi, Romania;* [2]*Clinical Hospital no. III of Obstetrics and Gynecology, Obstetrics and Gynecology, Iasi, Romania*

There are several histological types of invasive lobular carcinoma (ILC): classical, alveolar, solid, pleomorphic, and tubulo-lobular. To determine whether the metastatic pattern was related to histologic subtype, we retrospectively analyzed a series of 72 cases of metastatic ILC. Tumors were classified in classical or variants forms. Estrogen receptor (ER), progesterone receptor (PR), E-cadherin, and ERB-B2 were assessed in 50 cases. The patterns of metastatic sites were analyzed in the different groups. 68% of cases corresponded to the classical type of ILC. The histologic variants included 23% pleomorphic carcinomas, 4% tubulo-lobular carcinomas, 3% alveolar carcinomas and 2% solid carcinomas. The metastatic sites were axillary lymph nodes (85% of cases), non axillary lymph nodes (8.06% of cases) and ovary (6.99% of cases). No significant corespondence was found between metastatic patterns and histology or E-cadherin expression. No relationship between histologic subtypes and specific patterns of dissemination was observed in this series of metastatic ILC. A high rate of pleomorphic type was found as compared with that observed among ILCs at diagnosis. A high rate of E-cadherin loss was found in metastatic ILCs, which corresponds to complete loss of E-cadherin expression in over 80% of ILCs documented in the literature. The lack of E-cadherin expression found also in metastases emphasized the adverse outcome of the disease.

266 Poster

Intraoperative imprint cytology for evaluation of sentinel lymph node in breast cancer

V. Pérez[1], T. Vela[2], E. Bargallo[2], E. Maafs[2], N. Castañeda[2], T. Ramirez[2], P. Villareal[2], C. Robles. [1]*Instituto Nacional de Cancerologia, Pathology, México, D.F, México;* [2]*Instituto Nacional de Cancerologia, Surgical Oncology, México, D.F, México*

Introduction: Sentinel lymph node (SLN) biopsy in patients with breast cancer has emerged as a conservative and promissing procedure. One of the most important issue is the evaluation intraoperative of the SLN with a high degree of accuracy. Frozen section and/or imprint cytology can be