(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

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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

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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

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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

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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