Clinical tumour response:

Preoperative treatment	Complete response	Partial response	Stabilization	Progression
Paclitaxel + Doxorubicin (PD)	34.4%	51.7%	13.7%	0
FAC	10.7%	60.7%	28.5%	0

served in 8 pts (27.5%), received PD, and only 2 pts (7.1%), received FAC (P = 0.003). Conservative surgery was realized in 10 pts (34.4%) in PD group and 8 pts (28.5%) in FAC group (P > 0.05).

Conclusion: Primary treatment of locally advanced breast cancer with Paclitaxel + Doxorubicin more effective than FAC regimen in rate of clinical and pathological complete response. Study is ongoing.

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607 POSTER

Sentinel nodes outside level I- II of the axilla and staging in breast cancer

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Purpose: In many centres preoperative lymphatic mapping and sentinel node biopsy has become a routine method for axillary staging in breast cancer. Previous studies have reported sentinel nodes outside level I-II of the axilla (ExAx) in approximately 20% of breast cancer patients. The role of ExAx sentinel node biopsy in staging of breast cancer is still obscure. The aim of the study was to evaluate the incidence of ExAx sentinel nodes in breast cancer patients. The other purpose was to evaluate the success rate and the complications of ExAx sentinel node biopsy. The third aim was to investigate the incidence of metastases in the ExAx and other hand in the axillary sentinel nodes.

Patients and methods: Between June 2000 and April 2001, 172 clinically node-negative T1-T2 breast cancer patients were submitted to lymphatic mapping and sentinel node biopsy. Lymphoscintigraphy was performed the day before surgery, four hours after intratumoral injection of 80-100 MBq 99m nanocolloid.

Results: Lymphoscintigraphy showed altogether 55 sentinel nodes outside level I-II of the axilla in 30 (18%) patients. Two (1%) patients had only ExAx sentinel nodes in the lymphoscintigraphy. The 55 ExAx nodes included 36 parasternal, 9 subclavicular, 7 intramammary and 1 interpectoral nodes. Altogether 39 (71%) extra-axillar nodes were harvested in 26 (87%) patients. Two (7%) of the 30 patients had metastases in ExAx sentinel nodes only, 3 (10%) in both ExAx and axillary nodes and 9 (30%) in axillary nodes only while 16 (53%) patients had metastases in neither axillary nor in ExAx sentinel nodes. Minimal perforation of parietal pleura occurred in three (10%) patients. They recovered uneventfully without pleural drainage.

Conclusions: Harvesting of the ExAx sentinel nodes is technically more demanding compared to the axillary ones, but does not seem to carry considerable risks for the patients. The ExAx sentinel node biopsy is a potential tool for more accurate staging in breast cancer, because it provides more information compared to axillary staging alone.

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608 POSTER

A phase III trial of taxotere and doxorubicin (AT) versus 5-fluorouracil, doxorubicin and cyclophosphamide (FAC) in patients with unresectable locally advanced breast cancer: an interim analysis

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Aim: This study evaluated the efficacy and safety of AT versus FAC, as neo-adjuvant therapy in patients (pts) with stage IIIA T3 or IIIB unresectable locally advanced breast cancer.

Methods: Between February 1999 and September 2000, 407 chemonaive patients were randomly assigned to either doxorubicin 50mg/m2/

15min followed by taxotere 75mg/m2/1h or 5-fluorouracil 500 mg/m2/bolus, doxorubicin 50 mg/m2/15min and cyclophosphamide 500 mg/m2/bolus, given every 3 weeks for 4 cycles. Clinical and pathological responses, and safety were assessed.

Results: To date, interim data are available for 362 patients treated with AT (n=198) or FAC (N=164). Pts in both arms were well balanced for known prognostic factors; median age was 48 years [range: 23 - 75] and median WHO PS was 0 [range: 0 - 1]. A total of 1380 cycles were administered; median number of cycles was 4 [range: 1 - 4] in both arms, and median Relative Dose Intensity was = or > 98,9% for all drugs. In the 362 patients analysed, the overall response rate was 72% for AT [95% CI: 65 - 78] and 64% for FAC [95% CI: 56 - 71]; 11% CR with AT versus 9% with FAC; 61% PR with AT versus 55% with FAC (p=0,11). Information available for 170 patients (AT: 100 pts, FAC: 70 pts) indicate that 92% of AT pts and 89% of FAC underwent surgery. Analyses on pathological response rates are ongoing. Median progression free survival, at the time of this analysis, was 8.3 months for AT [95% CI: 6.2 - 9.1], and 6.9 months for FAC [95% CI: 4.3 - 12.9]. Main treatment-related toxicities seen respectively in AT/FAC arms (% of pts): Grade 3/4 neutropenia (71/25); febrile neutropenia (10/0); Grade 3/4 nausea (6/5); Grade 3/4 vomiting (6/8); Grade 3/4 diarrhea (7/1); Grade 3 stomatitis (2/0); Grade 3/4 infection (3/0); Grade 3 asthenia (3/1).

Conclusion: The safety profile is favourable in both arms. Neutropenia was the most common adverse event but was predictable and manageable. Interim efficacy data are encouraging, suggesting that taxotere and doxorubicin is a potentially valuable combination in neo-adjuvant therapy of breast cancer.

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609 POSTER

Phylloide tumours of the breast 36 year revision based on clinical experience

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The authors realized a 36 year retrospective study of phylloide breast tumours treated at the Portuguese Oncological Institute - Coimbra, based on clinical diagnosis, histopathological and therapeutical aspects.

The study took place during 2 distinctive periods, the first during 1995 - 2001, where 113 clinical cases were analysed. The second during 1965 -1995, where after careful revision and update of the new histopathological criteria of tumours of 113 patients, only 82 were selected; totalising a final number of 195 patients. The histopathological criteria used to classify and select the tumours were those proposed by Page et al.

Results: Of the 195 patients selected, 68,4% had benign tumours, 25,4% borderline tumours and 6,2% malignant tumours. The study showed that the age of primary occurrence was greatest at the following age groups [16-25 yrs] 30% and [30-50 yrs] 43%. The onset period of time was 14,31 months (SD ± 22,15). On average the tumours measured [2-3 cm] 27% and [4-6 cm] 17%. The tumour lateralization was not statistically significant. In 93% of the cases there were associated fibroadenomas. FNAB was positive for phyllodes tumors in 20,9% of the cases.

Of the different surgical approaches studied, wide local excision was by far the most preferred (96,5%), followed by Modified Radical Mastectomy (1,8%), Simple Mastectomy (0,9%) and finally Quadrantectomy (0,9%). The reiterative operations were performed, 3 operations (2,6%), 2 operations (6,1%) and single operation (91,2%). The recurrence rate studied was 13,4% and the free period of disease was 39,19 months (SD ± 19,94). As far as the parity we verified that 42% were nullipare and 58% primipare and multipare.

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610 POSTER

Testosterone, an hormonal marker for breast cancer in postmenopausal women(PM); preliminary results of a case-control study in Montreal

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Purpose: Breast cancer is a major health problem associated with a high morbidity in many of the more developed countries of the world. It seems that environmental risk factors and lifestyle play important role in the etiology of this disease. We have yet to find a marker that will have an impact in the prediction of breast cancer occurrence. **Methods:** In a case-control study in Montreal, a total of 70 newly diagnosed PM with breast cancer and

70 population-based controls, matched for age, selected by random digit dialing telephone directory method were studied. To test our hypothesis that hyperinsulinaemia (insulin resistance) initiates a cascade of events that may lead to increase androgen production and oestrogen levels and modulate insulin growth factor (IGF) binding protein(BP), we measured fasting insulin levels(IN), free testosterone(FT), SHBG, estradiol as well as IGF-1 and IGFBP-3 from both cases and control. Results: The Odds Ratio (OR) for comparison of the second tertile with first tertile of FT levels was 7.4 with 95% CI of 1.9-28.1. The OR for the third tertile compared to the first was 14.5; 95% CI (3.1-67.9). This indicates a range of 7-14 fold risk increase of breast cancer, associated with plasma FT levels. For IN, the OR of the second and first tertile comparaison was 1.13 (p=0.81) and for the third tertile compared to the first 3.36 (1.15-9.85; p=0.03). No correlation was observed for IGF-1. Conclusion: The preliminary results of this study show that FT levels could be used as an interesting marker to predict the development of breast cancer among PM. Further studies are needed to correlate the possible association between insulin resistance syndrome and increased risk of breast cancer. Supported by the Jean H. Picard foundation

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611   POSTER

The diagnostic value of ultrasonography as adjunct to mammography and clinical examination in breast cancer detection

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Purpose: To determine the diagnostic value of additional breast ultrasonography (US) next to mammography (MAM) and clinical examination (CE) in patients referred for mammography and to define subgroups of patients who benefit most from additional US examination.

Methods and Patients: Between October 1999 and August 2000 a prospective study was performed in which all consecutive patients referred for MAM underwent additional ultrasonographic examination. Results for CE, MAM and US were scored according to the BIRADS-lexicon and linked to pathology results after a minimum follow up period of 6 months.

The diagnostic value of additional US was determined by construction of ROC-curves and comparing the areas under the curves for US+MAM+CE with MAM+CE. Subgroups were defined according to reason of referral and ROC curves were studied.

Results: In total 3835 breasts were examined in 2020 patients. 131 Malignancies were detected in 128 patients leading to a prevalence of 6.3%.

The sensitivity and specificity of US+MAM+CE was 95% and 95% respectively.

Additional ultrasonography significantly improved the diagnostic value in this population (AUC: US+MAM+CE 0.977 versus MAM+CE 0.950, p=0.01).

Patients referred for palpable breast lumps and <50 years as well as patients referred from the National Breast Screening Program did benefit most from additional breast US (p=0.01 and p=0.05 respectively). Breast US had no additional diagnostic value in patients referred for follow up of a former breast malignancy (p=0.30) or benign pathology (p=n.a.). Finally no additional diagnostic value was found for US performance in patients referred for screening and in examination of the contralateral breast (p=0.78).

Conclusions: Systematic breast US in patients referred for MAM significantly improved the diagnostic value. Breast US has additional diagnostic value in patients with palpable breast lumps or an abnormal screening mammogram. There was no additional value for US performance in screening.

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Statistical design in published non-comparative prospective studies of chemotherapy in breast cancer

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Purpose: Several statistical designs for phase II studies have been proposed but their application is still jeopardized. The aim of this survey is to describe the rate of studies with identifiable statistical design in a series of phase II or prospective non-comparative studies of treatment against breast cancer.

Methods: Papers were selected by hand-searching from seven distinguished (impact factor constantly over 2) specialty journals, published between 1995 and 1999. Univariate contingency tables evaluated by the chi-square test and multivariate logistic regression were applied to determine factors predictive of statistical design presence.

Results: 145 studies were selected. A statistical study design was not identifiable in 94 (64.8%) studies. Referral to a previous phase I study, more recent year of trial start, private sponsorship, and multicenter study organization were predictive of the presence of a statistical design at univariate analysis. Multicenter organization was the only independent predictive factor (OR 3.22; 95% CI: 1.48-7.00) with 48.6% of the studies with statistical design as compared to 21.1% among single-center studies. The presence of the statistical design was correlated with higher impact factor and shorter time between study start and publication. Among the 51 studies with statistical design there was a notable heterogeneity in the type of design applied.

Conclusion: Only a minority of the phase II studies in breast cancer published between 1995 and 1999 in high quality journals had a proper statistical design. A wider application of statistical methodology in planning phase II trials is required.

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613   POSTER

Primary male breast carcinoma: actually a worse prognosis compared to female?

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Purpose: Because of the rarity of breast cancer (BC) in males, current management is generally extrapolated from the treatment of female patients (pts). To investigate the relationship between treatment and disease outcome, an analysis of a series of male BC treated at our Institution over a 10-year period was performed.

Patients and methods: The records of 58 consecutive male BC pts were retrospectively reviewed and analyzed with respect to clinical presentation, treatment choice, significant prognostic factors and survival.

Results: The median age at presentation of 64 years (range 28-72); tumor diagnosis was most often by a self-detected lump (67%) or the appearance of nipple discharge (22%); only 7 cases (11%) were investigated with mammography. The most common site were central subareolar region (48%) and the upper outer quadrant (27%). Infiltrating ductal carcinoma was present in 72% of cases, lobular carcinoma in 14%; tumors were usually moderately differentiated (59% of 55 cases with grading information); node metastases were found in 57% of cases; receptor status was available in 52 cases, 34 of which (65%) were ER+ and 32 (59%) were PgR+. Primary treatment consisted of modified radical (84%) or simple (12%); only 2 pts were treated with lumpectomy alone. Forty pts received adjuvant post-operative treatment, including radiation, hormone therapy and chemotherapy, given alone or in combination. Median follow-up of 5.8 years, ranging from 18 to 152 months. The median 5-year disease-free and overall survival was 46% and 54%, respectively. Multiple regression analysis of prognostic factors showed that negative node status (p<0.001) and adjuvant treatment (p<0.003) had a positive impact on DFS; grading (p=0.001), node status (p<0.03) and adjuvant therapy (p<0.003) resulted the strongest parameters influencing survival. No significant difference in survival was found between radical and simple mastectomy, nor among the different adjuvant treatments.

Conclusions: With the limitations of a retrospective study on a small series, our experience showed that prognosis in male pts with BC did not significantly differ from that known in female, also suggesting a benefit from adjuvant treatment. Multiinstitutional prospective trials are needed in this area, specifically focused to identify molecular properties of male BC, particularly in relation to BRCA1 and BRCA2, to optimize treatment strategies in both the adjuvant setting and metastatic disease.