(CDI) may have a role in the detection of neovascularity in axillary lymph node metastases in breast cancer patients. 'Power' doppler is a further technical development of CDI that enables flow in smaller vessels to be detected. This technique has been applied in 50 patients with breast cancer and the results compared with the histological findings from surgical clearance of the axilla. The 'power' doppler analysis was based on a subjective assessment nodal vascularity. Nodal size and spectral blood flow patterns were also recorded using conventional grey-scale ultrasound and pulsed-wave doppler.

Results: Ultrasound detected only 8 out of 16 patients with histological involvement of axillary nodes (sensitivity 50%). In only 1 case did the 'power' doppler provide additional information that led to a positive diagnosis. One false-positive and eight false-negative studies were observed (specificity 97%; positive predictive value 89%; negative predictive value 80%).

Conclusion: The low sensitivity of ultra sound (including 'power' doppler) suggests that this modality has a limited role in the detection of axillary node metastases in patients with breast cancer.

PP-4-35 Breast Screening for Women Aged < 50 — Results from a Family History Clinic

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The Nottingham City Hospital breast family history clinic commenced in 1988 due to an increasing demand for screening women at risk. Between 1988 and 1995, 1366 asymptomatic women aged < 50 years presented with a strong family history of breast cancer. The median lifetime relative risk was 2.3 X. They were accepted for screening which consisted of regular clinical assessment and mammography.

Twenty-eight cancers were detected during a median follow-up of 15 months (range 0–96 months). The histological prognostic features of cancers detected in the family history clinic (FHC) were compared with cancers from 65 women aged < 50 with similar family histories but were referred with symptomatic cancers during the same time period. 6/28 (21%) of cancers detected in the FHC were DCIS compared with 3/65 (3%) symptomatic cancers. The numbers of invasive cancers in good, moderate and poor prognosis categories according to the Nottingham Prognostic Index for FHC detected and symptomatic cancers were 6/22 (27%) versus 14/63 (22%), 13/22 (59%) versus 33/63 (52%) and 3/22 (14%) versus 16/63 (25%) respectively.

Patients aged < 50 who attend a family history clinic have a higher proportion of cancers detected as DCIS and fewer poor prognosis cancers than similar patients referred with symptomatic cancers.

PP-4-36 The Position of the Internal Mammary Lymphnode Chain by Scintigraphy and Sonography: A Comparative Study

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The position of the internal mammary lymphnode chain (IMC) of patients with breast carcinomas was determined both, by lymphoscintigraphy (LSG) and sonography (SG). In the case of radiotherapy, it is necessary to make an accurate assessment of the position of the IMC. SG is a non invasive technique, the position of the IMC is determined in an indirect way. LSG is an invasive technique, determining the position of the IMC in a direct way. We entered 120 patients into a comparative study. In the first 4 intercostal spaces (ICS), the distance to the skin (depth in mm) and the distance to the midline (lateralisation in mm) were measured. SG was performed with a 7.5 mHz transducer. The lateralisation of the centre of the internal mammary artery (IMA) was measured by putting the transducer in a transversal position just parasternal in the ICS. This position was marked on the overlying skin. The depth of the centre of the IMA was measured by putting the transducer in a longitudinal way, above this marker. In the case of LSG, 20 MBq Tc-99m nanocolloïd was injected close to the posterior fascia of the rectus abdominis muscle, 4 cm below the xyphoïd process and 3 cm in lateral direction. To represent the midline, cobalt markers were placed onto both, the jugular notch and the xyphoïd process. The first 4 ICS were marked. A radioactive marker (M) was fixed onto the skin above the hotspot (N). Gammacamera images were made 2–4 hours after injection. Lateralisation was measured from the centre of N. Depth (D) was calculated according to the formula $D = 1.4 \times F \times d$ (F = augmentation factor of the film, d = distance between M and N). We found a mean depth by SG of 22 mm (range 13–43), by LSG of 30 mm (10–80); a mean lateralisation found by SG of 34 mm (12–52), by LSG of 27 mm (10–65). Major differences in the position of the IMC, as determined by SG and LSG, were still present after correction for ICS. All these differences could not be explained by the type of surgery: BCT (35%) or mastectomy (60%). Quality controlstudies could not explain these differences. We will perform further investigations.

PP-4-37 Standards, Options and Recommendations (SOR) Project from the FNCLCC*: Non Metastatic Breast Cancer

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The SOR project is a collective work of the french cancer centers community with collaboration from out-centers experts. The objective is to develop clinical practice guidelines in oncology to improve quality of health care and patient outcome. The SOR methodology has been previously published and developed by the FNCLCC with the advice of ANDEM* and AHCPR*. From a critical analysis of literature by a working committee, SOR (with scientific levels of proof) and decision trees for the management of patients with non metastatic breast cancer have been elaborated. Some SOR for other oncological subjects have already been published and the update process is going on. For non metastatic breast cancer, the working committee included 35 experts in the field of radiation, surgery, medical oncology, biology, statistics, and methocology who worked together during more than 2 years. Once the guideline had been defined, the document has been sent to 137 reviewers for peer review, and to the medical committees of the 20 french cancer centers for review and agreement. A final approvement by the FNCLCC executive committee has been obtained. These guideline and decision trees covered all decision steps from diagnosis and treatment to follow-up. The originality of the FNCLCC project was to create an electronic support (CD-Rom) entirely built up from decision trees which have been created to be very easily linked to scientific argumentation based on literature. These decision trees will be presented.

*ANDEM: Agence Nationale pour le Développement de l'Evaluation Médicale, France

*AHCPR: Agency for Health Care Policy Research, USA

PP-4-38 Screening for *BRCA1* and *BRCA2* Germline Mutations — Analysis of 50 Families with Clustering of Cancer

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Family history of breast/ovarian cancer is one of the most frequently used reasons for visiting a genetic counselor. Studies have shown that app. 5–10% of these cases are associated with an inherited predisposition. Recently, two autosomal dominant susceptibility genes have been identified which confer high risk to breast/ovarian cancer, i.e., *BRCA1* and *BRCA2*. This made it possible to test individuals without performing detailed linkage analysis or, sometimes, involving their families. We have chosen to apply the Protein Truncation Test (PTT) because most germline mutations found in these genes result in premature truncated protein and this test can rapidly be set up and executed. Here, we report on the analysis of 50 families who were offered DNA testing. We have examined the largest exons of both genes after PCR of genomic DNA. Right now we have identified four families with a *BRCA1* and two families with a *BRCA2* mutation. Interestingly, four out of six families contained a member having bilateral breast cancer. This finding might be another strong indication for *BRCA1* or *BRCA2* involvement.

PP-4-39 Body Image after Breast Cancer: Results from a Patient Derived Measure

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It is well recognized that the treatment for breast cancer can have an adverse effect on body image. A measure of body image was developed from interviews with breast cancer patients, spouses and content experts. The impact of the diagnosis of breast cancer on an individual's sense of

control over the body or feelings of vulnerability emerged as major theme, and thus a large number of items in the questionnaire measured this aspect of body image. The questionnaire was distributed to 360 women with breast cancer attending oncology clinics in a consecutive fashion. The questionnaire was returned by 308 subjects (85.6%). The mean age of the group was 57 years. 38% of respondents had a mastectomy, 55% a lumpectomy, 7% breast reconstruction and 13% had metastatic disease.

42% of respondents stated agreed that they felt their body had been invaded, 29% agreed that they felt there was a time bomb inside of them and 20% often felt that something was taking over their body. 20% of respondents stated that they often felt damaged, and 28% often felt their body had let them down. 27% often worry that the cancer is spreading, 26% often worry about minor aches and pains while 35% of respondents felt they often need reassurance about their health. 35% felt in control of their body only infrequently or never.

A significant number of women with breast cancer appear to lack a sense of control over their bodies. Further research is being conducted to compare these findings to a population of women without breast cancer.

PP-4-40 Histologic Findings in Prophylactic Mastectomy Specimens from Women with Hereditary Risk Factors

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A family history is one of the major risk factors of breast cancer. We studied the histologic findings in prophylactically removed breasts. Prophylactic bilateral mastectomy was performed either because of a proven BRCA1 mutation, or because of psychological distress as a consequence of a high risk based on the pedigree. In a number of 22 mastectomy specimens a high frequency of fibrocystic changes and proliferative breast disease was observed such as: florid (46%) and atypical (14%) hyperplasia, sclerosing adenosis (36%), adenosis in general (82%), fibroadenomas (23%), papillomatosis (14%) and microcalcifications (41%). Also one invasive breast cancer (4%) with a diameter of 0.7 cm was found, not detected by physical examination and mammography before surgery. These changes were more frequently found than would be expected from known literature data on benign breast disease in general.

In conclusion: genetic susceptibility may cause fibrocystic and/or proliferative breast disease preceding breast cancer (supported by the Dutch Cancer Society; DDHK 95-953).

PP-4-41 The Age Distribution and Biological Characteristics of Interval Cancers in the North West Region of the NHSBSP

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The NHS breast screening programme screens women aged 50–64 every three years. Eventual mortality reduction will be influenced by the incidence and biological characteristics of interval cancers occurring in the programme. We found that the incidence of interval cancers in the third year was 65% of background incidence indicating that the three year interval is too long.

Of 471 interval cancers 73% were infiltrating ductal carcinomas of which 54% were grade 3 tumours. Over 70% of the invasive carcinomas were greater than 15 mm.

The incidence of interval cancers is significantly higher in women aged 50–59 than in women aged 60–64 but their characteristics do not vary with age. These results suggest that for women aged 50–59 the high incidence of interval cancers will greatly reduce the benefit of screening but for women over the age of 60 screening with a three year interval may still produce a mortality reduction similar to that achieved by the Swedish Two County Trial.

PP-5. Adjuvant Systemic Treatment and Intensive Chemotherapy (September 12)

ORAL PRESENTATIONS

PP-5-1 Preliminary Analysis of a Randomized Phase II Study of High-Dose Chemotherapy in High-Risk Breast Cancer

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To prepare for a large multi-center trial of high-dose chemotherapy in high-risk breast cancer, a randomized single-institution study was performed in the Netherlands Cancer Institute between May 1991 and December 1995. Eligible patients had stage II or III breast cancer with a tumor-positive apical axillary lymph node at infraclavicular biopsy, were < 60 years of age and had a WHO performance status of) or 1. The conservative treatment arm consisted of 3 courses of FEC: fluorouracil (500 mg/m^2), epirubicin (120 mg/m^2) and cyclophosphamide (500 mg/m^2). Patients with at least a minimal (clinical) response subsequently underwent definitive surgery (including an axillary lymph node dissection), a fourth course of FEC, radiation therapy and two years of tamoxifen. Patients in the experimental arm received identical treatment, except that the post-operative FEC course was combined with filgrastim to mobilize peripheral blood progenitor cells (PBPC) and was followed by high-dose chemotherapy with CTC: Cyclophosphamide (6 g/m^2), thiotepa (480 mg/m^2) and carboplatin 1600 mg/m^2).

Ninety-five patients were enrolled in the trial and 79 were randomized after surgery: 38 to undergo conventional treatment only and 41 to receive CTC + PBPC transplantation. 35 of the these 41 patients were actually transplanted, all others were managed conservatively. There were no toxic deaths. With a median follow-up of 31 months (range 4–59) and analyzed on an intention-to-treat basis, overall and progression-free survival (PFS) in both groups are identical (projected 4-years survivals 75% and 80%, respectively). Patients who were not randomized (11 × refusal, 4 × lack of response to FEC, 1 × myelodysplasia) did worse, with a projected 4-year PFS of only 20%. The early analysis of this trial does not (yet?) predict a major survival advantage for high-dose therapy.

PP-5-2 Neo-Adjuvant High-Dose FEC Regimen (H-FEC) with G-CSF (G) for Large Early Breast Cancer

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Background: In order to increase conservative surgery in women with resectable breast cancer (T < 3 cm) after neoadjuvant chemotherapy (53% Spielmann M, ASCO, 1990), we included in a phase II study 46 consecutive patients (pts) with large early non inflammatory breast cancer (tumor size > 30 mm). Treatment consisted of 5-FU 1,000 mg/m^2, Epirubicin 100 mg/m^2 and Cyclophosphamide 1,000 mg/m^2 day 1, with G-CSF 5 μg/kg/d days 5 to 12. Courses were q 21 days for a total of four before surgery and radiotherapy. All pts had an histologic procedure (tru-cut or biopsy) before inclusion and gave an informed consent.

Patients characteristics: Mean age 46 years (range 29–64); Mean tumor size (T) 47 mm (range 35–75). Stage IIA: 13 pts, IIB: 15 pts and IIIA: 18. Hormonal receptors (+) in 25, (−) in 14, unknown for 7 pts. Thirty-six pts presented a ductal carcinoma, 3 a lobular one, and 7 an undifferentiated. *Results:* Median delivered Dose Intensity from planned was 97%.. Forty four pts (95%) completed the programmed schema (4 cy). No pts progressed on treatment. Breast conservative surgery could be performed in 28 pts (61%). We found 6 complete pathologic remission (13%). Hematological toxicity (assessed all 3 days) was mild; 13 pts (28%) presented Gr IV neutropenia with 5 febrile aplasia (4 pts). No Grade IV non-hematological toxicity was seen, with no related toxic death.

Conclusion: H-FEC + G showed a high rate of conservative surgery and of histological CR with no severe side effects. A randomised phase III study (*FEC-60* Vs *H-FEC + G*) for large early breast cancer (T > 3 cm) is actually ongoing.