# Proferred Papers Sessions

## PP-4. Screening — Epidemiology — Imaging Technics (September 12)

### ORAL PRESENTATIONS

#### PP-4-1  Influence of Mammographic Patterns on Breast Cancer Screening Performance

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Dense breast patterns are said to complicate the detection of tumours by mammography. On the basis of the outcomes of 93,812 screening examinations it was studied whether the performance of the Nijmegen breast cancer screening programme differed for women with dense (> 25% of the breast composed of densities) and women with lucent patterns ($\leq$ 25% densities). In the period 1975–1982, the performance in dense patterns was inferior to that in lucent patterns: the proportions of screen-detected tumours among all tumours were 55% and 73%, respectively. Moreover, the screen-detected tumours in dense patterns were larger at diagnosis and the survival of the patients concerned was worse: the 10-year survival rate was 73%, versus 83% for patients with lucent patterns. Difficulties in reading dense patterns also emerged from a lower predictive value of a positive screening test: 29%, versus 48% in lucent patterns. However, with the improvement of the mammography technique in 1982, these differences disappeared to a large extent; the prognosis of tumours detected in dense patterns was no longer worse than that of tumours detected in lucent patterns.

#### PP-4-2  Radiation Risk of Mammography Related to Benefit in Screening Programs: A Favourable Balance?

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The objective was to estimate the number of breast-cancer deaths induced by low dose radiation, compared to the numbers prevented in breast-cancer screening programs with various age-groups and intervals.

A computer simulation-model on the natural history of breast cancer was used, combined with a model from the National Research Council's committee (BEIR-V) on induced breast-cancer mortality from low levels of radiation. The improvement in prognosis due to screening was based on the results of the Swedish overview of the randomized screening trials for breast cancer and the performance of screening in the Netherlands.

For the national screening program in the Netherlands (age group 50–69, 2-year interval, 2 mGy per view) the balance between the number of deaths induced versus prevented is favourable; 1:242. Expanding screening to the age-group 40–49 with a 1- or 2-year interval the balance would be less favourable: 1:66 and 1:97, respectively. To save 8 extra deaths from breast cancer one is expected to be induced by radiation in these scenarios, compared to the Dutch program. If screening is equally effective in young as in women aged 50–69, the marginal value was 1: ± 30.

For screening under the age of 50 the balance in the number of breast-cancer deaths prevented versus induced might not be that favourable, although confidence intervals are wide.

#### PP-4-3  Reduction of Breast Cancer Mortality Due to Mammographic Screening of Elderly Women

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The effect on breast cancer mortality of mammographic screening in women aged 68–82 years was studied prospectively. In the Nijmegen screening programme, which had started in 1975 with biennial one-view mammography, some 7000 women born in the years 1895–1909 were included from round 2 onwards (1977–78). Up to December 31, 1990, 174 cases of breast cancer had been diagnosed. 40 of these patients had died from the disease. The control population consisted of women from the same birth-cohort from Arnhem, a neighbouring city without population screening. Date of entry in the study was 1-1-1978. In Arnhem, 51 out of 183 patients had died from the disease. In the periods 1978–1981, 1982–1985 and 1986–1990, the ratios of the Nijmegen and Arnhem breast cancer mortality rates (RR) were 1.44 (95% CI = 0.67–3.10), 0.81 (95% CI = 0.37–1.79) and 0.53 (95% CI = 0.27–1.04), respectively. In the years 1975–1990, the incidence of breast cancer was slightly lower in Nijmegen than in Arnhem, but the difference was too small to explain completely the reduced breast cancer mortality. The conclusion is that mammographic screening of women over age 67 may yield a 30–35 per cent reduction of the breast cancer mortality rate after 10 years.

#### PP-4-4  The Yield of an Intensive Follow-Up Program for Women at Increased Risk for Breast Cancer

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Aim. To determine of what method and in what stage breast cancer is diagnosed in women with an increased risk for breast cancer — including family history — who were followed according to an intensive control scheme.

Method. Retrospective analysis of 112 patients with breast cancer diagnosed while on periodical follow-up (semi-annual physical examination and annual mammography). Reasons for follow-up within protocol were: pre-malignant lesion in former biopsy (ADH, lobCIS): 25 patients (22%), family history (2 or more first degree relatives with breast cancer): 43 patients (38%), previous biopsy with proliferative benign lesion: 44 patients (40%). Mean follow-up time to breast cancer diagnosis was 80 months (range 1–14 years; 54 patients over 5 years). At first visit, 32 women were younger than 40 years and 43 over 50 years.

Results. Malignancy was mammographically detected in 38 patients (34%); 38 patients had self noticed an abnormality which turned out to be breast cancer, and in 36 patients (32%) the tumour was detected by clinical palpation at routine physical examination.

The clinical tumour size was $\leq$ 2 cm in 49 patients (45%), $\geq$ 2 cm in 31 patients (27%) and clinically occult in 23 (21%). On histology in situ carcinoma was found in 15 patients, a tumour $\leq$ 2 cm in 58 and $\geq$ 2 cm in 36 patients. Lymph node metastases were found in 41 patients (37%). Stage grouping according to histology was as follows: stage 0 = 13%, stage I = 37%, stage II = 43% and stage III = 6% (unknown 1%). The p-stages did not differ between the respective à priori risk groups: 52% of the patients with previous marker lesions (high risk) were diagnosed in p-stage II/III (36% pN+), while 42% of the patients with family history (intermediate risk) had p-stage II/III (28% N+) and 55% of women with a low risk, previous benign breast condition (45% N+). After a mean follow-up time of 73 months (range 11–148) 10 patients have metastases, and 7 of these patients died.

Conclusion. Intensive follow-up for increased risk for breast cancer does not lead to an early detection in the great majority of patients. In our relative young group only in 50% cancer was diagnosed in a probable curable stage (pTis-I pN0). Patients with family history were not diagnosed with earlier stage breast cancer compared to the other risk groups. Apart from regular mammography, patient awareness (i.e. breast self examination) and regular physical examination appears to play a role in the detection of breast cancer.

#### PP-4-5  Prognosis in Patients with Carcinoma in Situ of the Breast. A Population Based Study in Sweden

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The incidence of Carcinoma in situ (CIS) of the breast is increasing. 1992 it constituted 8.6% of all breast cancers detected in Sweden. The high incidence is to a large extent due to mammography screening. We have studied 3405 patients with a primary CIS of the breast, reported to the Swedish Cancer Registry between 1980–1992. Information of breast cancer

death and/or a subsequent invasive breast cancer was also collected from the registry. Medium follow up time was 4.2 years with more than 14,400 person years observed. We found a good prognosis with more than 95% corrected survival after 10 years. The risk of a subsequent invasive cancer on either side was 5% during the follow up period. During the observed period, prognosis was steadily better in each interval studied (80–82, 83–85, 86–88, 89–92). The risk of dying in breast cancer was highest in the youngest and oldest agegroups, which is parallel to what earlier has been shown in patients with an invasive breast cancer. There was a relation between prognosis and if the women studied were in agegroups eligible for screening and living in a county where mammography screening was offered. The study results implies that the natural history of CIS is changing over time and that screening may have influenced this development.

## PP-4-6 Germline Mutation at *BRCA1* Affects the Histoprognostic Grade in Hereditary Breast Cancer

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Histoprognostic grade is a determinant parameter to select the initial therapeutic strategy in breast cancer (BC). Our aim was to analyse the grade repartition in *BRCA1*-BC and to explore the connections between grade and the *BRCA1* gene function. We compared 27 *BRCA1*-BC from 14 families with 4461 cases from a registry and 242 sporadic cases, matching for grade, and constitutive elements, and then considered their repartition in families. We observed a prevalence of Grade 3 ($p < 0.0001$) in *BRCA1*-BC. This was attributed to nuclear polymorphism ($p < 0.0001$), mitotic activity ($p < 0.0001$) and to tubular differentiation ($p = 0.0004$), implying that *BRCA1*-BC are highly proliferating tumors. Moreover it is suggested that grade segregates as a genetic trait within families ($p = 0.0015$), and this was attributed to the mitotic index only ($p = 0.0005$). Thus grade, through its components, could be interpreted as the morphological translation of the *BRCA1* germ-line mutation. Genotype-phenotype correlation may exist between the type of mutation and the aggressiveness of the disease. Such findings are bound to have important impact in the care management of hereditary breast cancer.

## PP-4-7 Early Diagnosis of Inherited Breast Cancer

P. Møller* [1], L. Mæhle, A. Dørum, K. Heimdal, H. Bjørndal, P. Helgerud, H. Quist, R. Kåresen, A. Nysted, J. Varhaug, H. Fjøsne, R. Guleng, J. Due, P. Bøhler, S. Kvinnsland, C. Tropé. [1] *Unit of Medical Genetics, Dept. of Oncology, The Norwegian Radium Hospital, N-0310 Oslo, Norway*

We have decided on clinical criteria to define families at risk, and we have agreed with all major hospitals in Norway on a follow-up program for those at risk (J Cancer Care 2; 94, 1993). We have defined more than thousand women at risk, counselled them, and hereby report the results of the first rounds of examinations as noted in our files by March 28th 1996.

We have by now examined 1173 women aged 43.0 ± 11.3 years (mean ± SD) once or more. Of these, 603 aged 41.9 ± 10.5 have been followed for mean 1.8 years (range 1–5.6). Among these we have found 28 infiltrating cancers/cancers in situ in 26 women (2.2%). Stratified on age groups, pick-up rates were (given as number affected/number in group):

| Age < 30 | 0/149 | Age 50–59 | 6/198 |
| Age 30–39 | 6/372 | Age ≥ 60 | 5/ 98 |
| Age 40–49 | 9/356 | | |

So far, all but two were N0M0, the two had one affected axillary lymph node each. Mutation analysis in the families are being carried out.

We conclude that we have identified a high risk group where premenopausal breast cancer continues to occur, and that we have a program capable of demonstrating most cancers before spread. The follow-up will show the effect of the early treatment given.

Our program meets all ethical standards suggested.

## PP-4-8 Secular Trends in Mortality in Four Large Kindreds with Hereditary Breast-Ovarian Cancer

E.T.M. Hille.

Abstract not available.

## POSTER PRESENTATIONS

## PP-4-9 Breast Cancer and In Vitro Fertilization

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Because of, the increased risk of breast cancer for infertile nulliparous women, the suspected promoter role of estradiol in mammary carcinogenesis, and the high frequency of ovulation inducer treatments, it was interesting to focus on the risk of breast cancer after such a treatment.

So, we reviewed 32 cases during a retrospective survey in ART (Assisted reproductive Techniques) centers in France. Because of the small sample size and the few cases published so far, no statistical study could be made. However, many observations may have gone unnoticed or were not published. However, two hypotheses can be proposed: (1) the facilitating role of stimulation on potential infra-clinical or undiagnosed cancers; The cases recorded in our study seem to support this hypothesis as the recent literature; (2) the initiation of new cancers.

Consequently, we propose: to establish a register for the follow-up of treated women to monitor the advent of new cancers; to increase the follow-up of patients with other associated risk factors.

## PP-4-10 Ultrasound Guided Fine Needle Aspiration Biopsy (FNAB) for Detection of Axillary Node Metastases: A New Diagnostic Method

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The axillary lymph node status is still the most important prognostic indicator in breast cancer. This study was designed to evaluate a non-invasive method for axillary staging using ultrasonography alone and in combination with fine needle aspiration biopsy (FNAB) in 148 patients without palpable nodes with clinical examination. Node size and echo pattern were used as criterion for malignancy. Results of US and FNAB were compared with the histologic results of axillary dissection. Lymph node metastases were present in 62 axillas (41%). The sensitivity of ultrasonography was the highest (87%) when size (length > 5 mm) was used as criterion for malignancy, but specificity was rather low (56%). When nodes with a malignant pattern (echopoor or inhomogenous) were visualized, specificity was 95%. Ultrasound guided FNAB had a sensitivity of 80% and a specificity of 100% and detected metastases in 63% of node positive patients. It is concluded that FNAB is an easy, reliable and cheap method for identification of patients with positive nodes. In case of negative findings other non-invasive diagnostic procedures important to exclude lymph node metastases, like sentinel node mapping, could be performed.

## PP-4-11 The Relationship between Early Life Experience and Risk for Breast Cancer in Premenopausal Women

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*Objective:* To explore the relationship between early life experience and risk for breast cancer, a case control study was conducted in Chongqing, China.

*Methods:* The cases (N = 153) were histologically diagnosed as having breast cancer in premenopausal women aged 24 to 49. Controls (N = 153) were randomly selected from healthy premenopausal women. A standardized questionnaire was used for face-to-face interview.

*Results:* Multiple logistic regression analysis indicated that: (1) Passive smoking and history of hospitalized diseases in childhood (age < 10) and youth (age 10–16) period were positively associated with high risk of breast cancer in their adulthood [odds ratio (OR) = 1.05; 95% confidence interval (CI) = 1.01–1.08 and OR = 2.46, CI = 1.10–5.52, respectively]. (2) Low body weight in childhood and poor family economic situation in youth were negatively associated with high risk of breast cancer [OR = 0.66, CI = 0.48–0.90; and OR = 0.45, CI = 0.31–0.67, respectively]. (3) In adulthood (age > 16), passive smoking at home was positively and low body weight was negatively associated with high risk of breast cancer [OR = 1.02, CI = 1.01–1.04; and OR = 0.67, CI = 0.47–0.95, respectively]. (4) Other significant risk factors were age at early menarche (OR = 0.85, CI = 0.74–0.99) and life stress at any age (OR = 2.33, CI = 1.14–4.74).