## Tuesday, 16 March 2004 09:00–17:00

EUROPEAN BREAST CANCER SCREENING GROUP MEETING

# Breast cancer screening in Europe – current status

1 INVITED

### Detection of an increased breast cancer risk

B. Kuschel. *Klinikum rechts der Isar, Department of obstetrics and gynaecology, München, Germany*

About 15–25% of breast cancer patients report about a positive family history. Highly penetrant germline BRCA1 and BRCA2 mutations account for ~20% of familial breast cancer clustering. The remaining 80% is likely genetic in origin and the result of the combined effects of many genetic and environmental variants, which individually have little effect. By analysing pedigree data of breast and/or ovarian cancer families, individual breast and ovarian cancer risk can be estimated. Genetic testing for genes as BRCA1/2 (in exceptionally rare cases for other genes like PTEN,P53,CHK2) is available. The cumulative lifetime-risk for BRCA1 mutation carriers is 65% for breast-, 40% for ovarian cancer. BRCA2 mutation carriers have got a 45% risk for breast-, 11% for ovarian cancer. Elevated risk estimations and/or genetic testing may lead to intensified surveillance and prevention strategies.

2 INVITED

### Mammography/ultrasound in women with an increased risk for breast cancer

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A familial predisposition is the most important factor that increases the cumulative life time risk (CLTR) of breast cancer. CLTR may vary from 15–30% in women with moderate risk to 60% CLTR at age 75 in carriers of a BRCA1 or BRCA2 germline mutation.

The Nation-wide Breast Cancer Screening Program in The Netherlands provides breast screening by mammography in women 50–75 years old; if the CLTR of a woman under this age is the same or higher, annual examination by mammography and physical examination is recommended. A simple table with Dutch guidelines in primary care is shown in Table 1.

Table 1

| No. of relatives affected | Breast cancer < 50 yrs of age in at least one relative | Breast cancer ⩾ 50 yrs of age in all affected relatives |
|---|---|---|
| 1 first degree | Annual examination | No further research and follow-up |
| 2 first degree | General practitioner should consult a clinical geneticist | Annual examination |
| 3 first degree | Referral clinical geneticist | Referral clinical geneticist |
| 1 second degree | No further research and follow-up | No further research and follow-up |
| 2 second degree | General practitioner should consult a clinical geneticist | Annual examination |
| 3 second degree | General practitioner should consult a clinical geneticist | General practitioner should consult a clinical geneticist |

Source: Dutch College of General Practitioners

Table 2

| Age group | Cancer rate/1000 | | Sensitivity | |
|---|---|---|---|---|
| | No High Risk[a] | High Risk[a] | No High Risk[a] | High Risk[a] |
| 30–39 yrs | 1.6 | 3.2 | 69.5 | 63.2 |
| 40–49 yrs | 2.7 | 4.7 | 77.5 | 70.2 |
| 50–59 yrs | 4.6 | 6.6 | 80.2 | |

[a] Based on Family History.

Several large studies provide screening parameters separately for women with and without a familial predisposition. Cancer detection rates in women with a first degree relative with a history of breast cancer were similar to those in women a decade older without such a history. The sensitivity of screening was influenced primarily by age (Table 2).

3 INVITED

### MRI for screening women with an increased risk of breast cancer

C. Kuhl. *Medizinische Universitätsklinik Bonn, Radiologische Klinik, Bonn, Germany*

While the majority of breast cancer cases is due to sporadic cases, about 5%–10% are associated with or due to a genetic predisposition for the disease. Accordingly, familial (or hereditary) breast cancer accounts for at least 9100 new breast cancer cases in the United States per year (it should be well understood that the term "familial breast cancer" does not necessarily refer to a specific breast cancer type or to an actual breast cancer case, but it describes a *genetic condition* that puts the carrier at high risk to *develop* breast cancer). The breast and ovarian cancer susceptibility genes identified thus far, BRCA1 and BRCA2, account for only about 50% of the genetically induced breast cancer cases; for the remaining cases, other, yet undefined BRCA genes are suspected.

The lifetime risk to eventually develop breast cancer accumulates to 80%–90% and 60%–80% for carriers of the BRCA1- and BRCA2-mutation, respectively. Moreover, if a gene carrier already survived breast cancer, she faces a 65% risk to develop a second primary breast or ovarian cancer. As opposed to patients with sporadic breast cancer, women with familial breast cancer tend to develop the disease at a significantly younger, i.e. at a pre-menopausal age; according to recent data, about 50% already had breast cancer by the age of 50. In addition, breast cancers arising in mutation carriers exhibit adverse histopathologic features and prognostic factors; with respect to sporadic breast cancers, they are more likely to be high grade, receptor-negative, such that an early diagnosis seems even more crucial. Accordingly, the current screening recommendations (that refer to sporadic breast cancer) may not be sufficient (and will most probably not start early enough) for gene carriers.

Due to the high risk to develop breast cancer, and due to the early onset of the disease, a close screening of proven or suspected gene carriers should start at a substantially earlier age than is recommended for the general population, i.e. at the age of 25–30. On the other hand, BRCA-related gene products have been implicated in cell cycle regeneration and DNA repair. Accordingly, a pathogenic mutation in a BRCA gene can be expected to increase a carrier's vulnerability towards mutagenic agents, like e.g. ionizing radiation. The possibly increased radiosensitivity of mutation carriers should mandate the careful use of mammography in these women. To further investigate the effectivness of different breast imaging modalities in this subset of women, several multicenter screening trials are underway in Europe, Canada, and the US. This talk serves to summarize the current status of these trials, including our own results.

4 INVITED

### Breast biopsy techniques and protocols: Core/Vacuum

A.R.M. Wilson. *Nottingham City Hospital, Breast Institute, Nottingham, UK*

**Introduction:** The triple test – the combination of clinical examination, imaging and needle biopsy for cytology or histology – is the gold standard for the diagnosis of breast disease; image-guided breast biopsy is an integral and essential part of this process.

**Rationale for the triple test:** Needle biopsy is highly accurate in determining the nature of most breast lesions and should be preferred to open surgical biopsy. Patients with benign conditions avoid unnecessary surgery; carrying out open surgical biopsy for diagnosis should be regarded as a failure of the diagnostic process. For patients who prove to have breast cancer needle biopsy provides accurate understanding of the type and extent of disease so ensuring that patients, and the doctors treating them, are able to make informed treatment choices. Needle biopsy not only provides accurate information on the nature of malignant disease, such as histological type and grade, but also facilitates the assessment of tumour biology and genetics.

**Which biopsy technique?** The current methods available for breast tissue diagnosis are:

- Fine needle aspiration for cytology (FNAC)
- Needle core biopsy for histology (NCB)
- Vacuum assisted mammotomy (VAM)
- Open surgical biopsy FNAC verses Needle Core Biopsy

There has been much debate about the comparative benefits of fine needle aspiration of cytology and core biopsy. In general terms 14 gauge 20mm throw automated core biopsy provides significantly better sensitivity, specificity and positive predictive values. Results with core biopsy are particularly better than FNA for stereotactic biopsy of microcalcifications