the first 3 years which then tailed off. This curve resembles the curves of mortality from colorectal cancer, which show an exponential decay for each Dukes' stage.

Conclusions: The mortality for most cases of breast cancer is a continual constant ebb and any novel treatment will not show an improvement in mortality for many years. In addition, the optimal method of reducing the mortality will involve a stage migration to a better prognostic grouping, such as expected with mammography.

Friday, 2 October 1998 16:00-18:00

PARALLEL SESSION

Prognostic factors

438 INVITED

Experimental pathology and breast cancer genetics: Looking at malignant and premalignant tissues using new technologies

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The goal is to understand the critical events in carcinogenesis and to apply this to new approaches to diagnosis, prevention and treatment. It is clear that breast cancer is an heterogeneous disease at the molecular level, thus raising the possibility of a future functional classification based on mechanisms rather than morphology. These molecular phenotypes will also confer value on the potential of the tumour to invade, metastasise, and respond or be resistant to new therapeutic strategies which are targeted to the molecular abnormalities. The difficulty is how to identify which of the 30,000 genes expressed by a typical cancer cell are the ones involved in these processes. Many tumours have such a multitude of molecular changes in an individual tumor that it is difficult to identify those changes that are critical to tumour progression from epiphenomena of an unstable genome. The identification of the earliest events in carcinogenesis must be the best hope as we will then be able to target the events that predispose to the other secondary changes before they can occur.

One way forward is in the application of molecular (genomics) and protein profiling (proteomics) to obtain a profile of individual tumours. The applications of technology to facilitate, these analyses, including, comparative genomic hybridisation, laser guided microdissection of *in situ* breast cancer, microarray technology to study expressed cDNAs and 2D gels with mass spectroscopy of complex protein samples will be discussed. The analysis of these data will require a large investment in bioinformatics. Thus computing and modelling of cancer will become increasingly important in the next decade to identify relevant molecules as therapeutic targets and as diagnostics.

439 ORAL

Survival patterns according to age and treatment among breast cancer patients

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Purpose: It has become a dogma that the prognosis of breast cancer declines with increasing age, with the exception that very young women do worse than middle-aged women. However, it is unknown to what extent treatment and stage of disease at diagnosis and the adjustment of expected mortality may influence this association.

Methods: Since 1977 Danish Breast Cancer Cooperative Group has collected detailed information regarding clinical and histopathological presentation, postoperative therapy and follow-up status on Danish women with breast cancer. The risk of dying from breast cancer according to age at diagnosis was adjusted for effect of known prognostic factors and expected mortality.

Results: Overall, 30,623 patients with primary breast cancer were included in the study. Young patients below 50 years of age who did not receive cytotoxic adjuvant treatment (low risk disease) had a significantly increasing risk of dying with decreasing age at diagnosis (adjusted relative risk: 45–49 years: 1 (reference); 40–44 years: 1.08 (0.87–1.35); 35–39 years: 1.36 (1.07–1.72); <35 years: 2.10 (1.59–2.77). A similar trend was not seen in young patients receiving adjuvant treatment (high risk disease). The effect of age was significantly different between the two groups ($p = 0.02$). The effect of age among older women (50+ years) did not differ according to treatment ($p = 0.31$).

Conclusions: The negative prognostic effect of young age is almost restricted to women with low risk disease not receiving adjuvant treatment whereas young women with high risk disease seem to respond to adjuvant treatment in line with middle-aged women. We suggest that young women with breast cancer, on the basis of age alone, should be regarded as high risk patients and be offered cytotoxic adjuvant treatment.

440 ORAL

Risk factors for local recurrence after breast-conserving therapy for invasive carcinomas: A case-control study of histological factors and alterations in oncogene expression

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Purpose: To study risk factors for local recurrence (LR) after breast-conserving therapy (BCT). The association of histologic risk factors and variations in various proteins with LR was studied using a case-control approach.

Methods: Out of a cohort of 1481 tumors treated with BCT, 99 LR were randomly matched, each with 2 controls for age group (≤ and >50 years), pN stage, and follow-up period. Histology slides were reviewed. Immunohistochemical staining was performed for the following proteins: bcl-2, CD31, cyclin D1, E-cadherin, EGF receptor, ER, PR, Ki-67, c-*erb*B2/*neu*, and p53.

Results: 66 cases and 139 controls remained for analysis. The following variables were significant risk factors for LR: young age, high nuclear grade, high mitotic count, extensive DCIS around the tumor but not within the tumor, poorly differentiated type of DCIS, >20% ki-67 positive cells and PR negativity. These risk factors were only found in the patients >50 years. No risk factors were found in patients <50 years.

Conclusion: Age is an important risk factor for LR independent of other risk factors, including alterations in oncogene expression.

441 ORAL

A classification of breast cancer based on contrast enhanced MRI

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Study Objectives: Contrast-enhanced magnetic resonance imaging (MRI) relies on tumour vascularity for breast cancer detection and tumour angiogenesis is known to correlate with poor prognosis. We propose a classification of MRI enhancement patterns and correlate it with known histopathologic prognostic indicators.

Methods: Twenty-one patients with breast cancer underwent pre-operative high resolution breast MRI (transverse T1-weighted 3D FLASH sequence at 1.0 T). Pre- and post-contrast 3D data sets were matched by a rotational and translational registration algorithm to correct for inter-scan motion, using in-house computer software, and subtracted.

Results: 4 distict types of enhancement patterns were recognised: type I (rim); type II (homogeneous); type III (heterogeneous) and type IV (diffuse patchy). Tumours which were well demarcated were called rim (predominantly peripheral enhancement) or homogeneous (enhancement of whole lesion). Tumours which were not well demarcated were called heterogeneous (uneven enhancement of lesion with associated foci of enhancement) or diffuse patchy (main lesion with fine punctate peripheral enhancement). The frequency of enhancement patterns was: rim (n = 3), homogeneous (n = 5), heterogeneous (n = 9) and diffuse patchy enhancement (n = 4). Bloom & Richardson grade I tumours were predominantly homogeneous, grade III tumours were mostly heterogeneous/diffuse patchy and grade II tumours were somewhere in between. Vascular invasion was identified in 9/21 cases with predominantly heterogeneous or diffuse patchy enhancement. High grade DCIS was seen in association with 10 tumours and of these 8 showed heterogeneous or diffuse patchy enhancement.

Conclusion: MRI enhancement patterns may be classified into 4 groups (Types I–IV) which correlate with histopathologic prognostic indicators. MRI may prove useful in providing clinicians with prognostic as well as diagnostic information.