has been produced. This study compares the survival of screen detected cancers with symptomatic cancers treated in a single centre.

Methods: 219 women aged 50–64 were diagnosed with breast cancer from the prevalent round of the NHBSP in Oxfordshire between Sept. 1990–Aug. 1993. 279 control patients aged 50–64 were diagnosed with invasive breast cancer in the symptomatic breast clinic between Jan. 1987–Aug. 1993. All data were collected prospectively onto a computerised database.

Results: 5 yr overall survival (OS) in patients with screen detected cancer was significantly better than the control (89.6% v. 74.3%; p = 0.0049 logrank; 59.6% reduction in mortality). In patients with screen detected invasive cancer, this difference was still present (88.5% v 74.3%; p = 0.0048 logrank; 55.3% reduction in mortality). After correction for 1 year lead time bias, these differences were still significant. After 2 years correction, there was a trend to improved survival with screening, which was not statistically significant. OS in interval cancers & non-attenders did not differ from the control group (p = 0.79 & p = 0.27 logrank respectively).

Conclusions: These data refute some of the concerns about the NHBSP & confirm that mammographic screening programmes can lead to the significant improvements in survival as suggested by previous randomised & population based studies.

427 POSTER

Results of mammographic screening 1994–1997

V. Baldi, A. Cicalese, G. Coppola, M. Scarano, E. Gatto. *Department of Radiology, Hospital of Cava de'Tirreni (Salerno), ASL SA1 Campania Region, Italy*

Purpose: Mammographic screening has a determinative importance because reduces mortality-rate for breast cancer in women between 50 and 69 years. Authors report their results about a biennial (94–97) mammographic screening programme.

Methods: Women who accepted have been subjected to mammographic examination with axial and oblique projection. Diagnostic assessment has been performed with ultrasonography a/o eco-guidance FNAB. Results are compared with standards provided by the National Breast Screening Programme in the United Kingdom (UK) and also by Italian Group for Mammographic Screening (GISMa).

Results: 13768 women were invited form 1/11/94 to 31/12/97. 9073 have been tested. Attendance rate was 65.8%. Recall rate to diagnostic assessment was 5.8%. According to results of diagnostic assessment 61 surgical biopsies were performed. 56 carcinomas were detected in 56 women. Cancer detection rate was 0.61%. Detected cancer were non palpable in 60% of cases. Pathologic staging was pT1a in 1 case, pT1b in 8, pT1c in 19, pT2 in 13, pT3 in 1. 16 of 43 cancers involved axillary nodes. 13 of remaining cases were operated in other hospitals and we have no information about results of histologic examination.

Conclusion: Results are acceptable or excellent in comparison with UK and GISMa standards. So that authors suggest an extension of the screening programme to a wider geographic area.

428 POSTER

The experience of breast cancer screening

V. Levshin, T. Fedichkina, V. Droggachih. *Cancer Research Center, Moscow, Russia*

Special interview of 1500 breast cancer (BC) patients show that 81% of them first notice BC symptoms themselves, 10.5% of all cases were revealed by check up nurses, 5.5%-by physician, 3%-by mammography. A prospective sudy has been conducted in Moscow to study the implementation posibilities and efficiency of two BC screening methods: breast self-examination (BSE), yearly clinical breast examination (CBE). Three cohorts two screening and one control, with about 3000 women ages 40–69 in each were formed. The follow up and control the adherence rate showed that regular BSE performed in the corresponding cohort only 31% of women, 24%-performed it unregular and 45%-not at all. 67% of women from other cohort invited for CBE have visited the corresponding screening unit. The analysis of reasons which keep women from screening examinations showed that most of them have not enough knowledge and beliefs concerning BC screening.

429 POSTER

Mass-screening for breast cancer in Japan

N. Fujishima[1], S. Itoh[2], T. Yamakawa[3], K. Izumi[4], T. Sugimoto[5], M. Yoshida[6]. *Department of Surgery; [1]Kochi Red Coss Hospital; [2]Itoh Breast Surgery Clinic; [3]Kochi Municipal Hospital; [4]Nakamura City Hospital; [5]Kochi Medical College; [6]Tonan Hospital, Japan*

In Kochi Prefecture in Japan, where the population of women over 30 is 292,000, we have carried out mass-screening for breast cancer since 1975. We examined women over 30 annually by physical examination, inspection and palpation. At that time we recommended them to perform self-examination every month.

Results: We examined 686,509 women since 1975. 19,602 women were introduced to the hospitals for further examination, and 475 breast cancers were detected. Detection rate gradually decreased from 0.1% to 0.07%, and repeaters increased to 90.2%. It was 0.12% in women who were examined first time, and 0.06% in the others. That did not changed from the beginning. But the rate of early stage breast cancer, 2 cm or less, increased up to 68% in 1996 compared with 40% at the beginning. Also during this period the corrected death rate has been under 8 per 100,000 in Kochi Prefecture, whereas it gradually increased to 12.4 in Japan in 1997. Standard mortality ratio (SMR) declined from 95 to around 80 (the average in Japan is 100). By survey, 69.2% of examiners who have experienced mass-screening performed self-examination.

Conclusion: Mass-screening by physical examination, promoting self-examination, contributed to increase the rate of early stage breast cancer and depress the death rate and SMR.

430 POSTER

Results of screening in a positive family history clinic

M. Lamont[1], A. Sheridan[2], Z. Rayter[1]. *[1]Department of Surgery; [2]Department of Genetics, Bristol Breast Unit, Bristol Royal Infirmary, Bristol, England, UK*

Purpose: It has been estimated that 1 in 200 women will develop breast cancer as a result of genetic predisposition, many of whom will have a positive family history. The aim of this study was to evaluate the utility of a family history clinic in the first year.

Methods: Clinics were held twice a month and guidelines for referral were established. Referral patterns with respect to age and family history were noted. Numbers of referrals to a clinical geneticist and the increased use of mammography were recorded.

Results: A total of 126 new patients were referred in the first year, of whom 89/126 (71%) had a significant family history and 95/126 (75%) were under the age of 50 years. One patient (0.8%) with asymptomatic breast cancer was diagnosed on mammography. It was estimated that the clinic would generate a demand for 783 screening mammograms over the first five years. Eighteen patients (14%) were referred to the clinical geneticist, all of whom were under 40 years of age.

Conclusions: Referral to the clinics was appropriate in most cases and high risk cases were referred for genetic counselling. The family history clinic detected breast cancer in 0.8% of the study population compared to 0.7% in the National Breast Screening Programme and is a worthwhile addition to the breast service.

431 POSTER

Can the mortality of breast cancer be reduced?

D.B. Kingsmore[1], D. Hole[2], C.R. Gillis[2], W.D. George[1]. *[1]Dept. of Surgery, Western Infirmary; [2]West of Scotland Cancer Surveillance Unit, UK*

Introduction: The mortality of breast cancer remains relatively unchanged by the therapeutic advances of the past twenty years. The aim of this study was to investigate the mortality curves of breast cancer and compare these with colorectal cancer.

Methods: All cases of breast cancer from 1980–96 were identified and the pathological stage derived. Cause of death was determined from the Registrar General. The yearly proportional mortality (YPMR) due to breast cancer was determined by tumour size and nodal status. From an existing database of long-term follow-up of colorectal cancer with accurate stage, similar survival curves were drawn.

Results: The YPMR remained almost constant over a ten year period of follow up for tumours that were node negative, or less than 30 mm. This reflects a constant mortality rate which does not decrease with time. For larger tumours and node positive tumours there was a rise in the YPMR for

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

P. Osin, J. Shipley, Y.J. Lui, T. Crook, B.A. Gusterson. *Institute of Cancer Research, Sutton, Surrey SM2 5NG, UK*

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

N. Kroman[1,2], M. Jensen[2], J. Wohlfahrt[1], H.T. Mouridsen[2], P.K. Andersen[1,3], M. Melbye[1]. *[1]Department of Epidemiology Research, Danish Epidemiology Science Centre, Statens Serum Institut; [2]Danish Breast Cancer Cooperative Group, Rigshospitalet; [3]Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark*

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

P.H.M. Elkhuizen[1], A.C. Voogd[4], L.C.J.M. van den Broek[2], T.C. Tan[1], H.C. van Houwelingen[3], J.W.H. Leer[1], M.J. van de Vijver[2]. *Depts. of [1]Clinical Oncology; [2]Pathology; [3]Medical Statistics, Leiden University Medical Center; [4]CCCS, Eindhoven, The Netherlands*

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

M. Douek[1], T. Davidson[1], M.A. Hall-Craggs[2], S.R. Lakhani[3], I. Taylor[1]. *Departments of [1]Surgery; [2]Radiology; [3]Histopathology, University College London Medical School, London W1P 7LD, UK*

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.